

Exploration of the Reactivity and Applications of Diazo Arylidene Succinimides (DAS) under Visible Light and Metal Catalysis

विद्या वाचस्पति की
उपाधि की अपेक्षाओं की आंशिक पूर्ति में प्रस्तुत शोध प्रबंध

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requirements of the degree of Doctor of Philosophy

द्वारा / By
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2025

*“This thesis is dedicated to...
my Family-with gratitude and
love”*



भारतीय विज्ञान

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CERTIFICATE

This is to certify that the research work incorporated in this thesis entitled “*Exploration of the Reactivity and Applications of Diazo Arylidene Succinimides (DAS) under Visible Light and Metal Catalysis*” submitted by **Kajal B. Meher** and the research was carried out by the candidate at Indian Institute of Science Education and Research (IISER), Pune, under my supervision. The work presented here or any part of it has not been included in any other thesis submitted previously for the award of any degree or diploma from any other University or institution.

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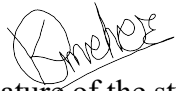
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List of Abbreviations:

°C	degrees Celsius
*	Excited state
μ	micro
Å	angstrom
Ac	Acetyl
ACN	Acetonitrile
AcOH	Acetic acid
AIE	aggregation induced emission
aq	aqueous
Ar	Aryl
atm	atmosphere
ATRA	Atom transfer radical addition
Bn	benzyl (C ₆ H ₅ CH ₂)
BnCl	benzyl chloride
Boc	<i>tert</i> -butoxycarbonyl
bs	broad singlet
Bu	Butyl
calcd.	calculated
CAN	Cerium(IV)-ammonium nitrate
Cat.	catalytic
Cbz	benzyloxycarbonyl
CDCl ₃	Deuterated chloroform
CFL	Compact Fluorescent Lamp
cm ⁻¹	wavenumber(s)
conc.	concentrated
CT	Charge Transfer
d	doublet (NMR)

DAS	diazo arylidene succinimide
dba	Dibenzylideneacetone
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DCE	Dichloroethane
DCM	dichloromethane
dd	doublet of doublet
DDQ	2,3-Dichloro-5,6 dicyanobezoquinone
DEPT	Distortionless Enhancement by Polarization Transfer
DIPEA	<i>N,N</i> -diisopropyl methyl amine
DMAP	<i>N,N'</i> -dimethylamino pyridine
DME	Dimethoxyethane
DMEDA	<i>N,N'</i> -dimethylethylenediamine
DMF	<i>N,N'</i> -dimethyl formamide
DMP	Dess Martin periodinane
DMSO	Dimethylsulfoxide
DMSO- d_6	Duterated dimethyl sulfoxide
dppf	1,1'-Bis(diphenylphosphino)ferrocene
d.r.	Diastereomeric ratio
DTBP	Di-tert-butyl peroxide
DTBQ	3,5-di-tert-butylquinone
DXDMH	1,3-dihalo-5,5-dimethylhydantoin
EDC	1-Ethyl-3-(3-dimethylaminopropyl)carbodiimide
ee	Enantiomeric excess
EnT	Energy transfer
equiv.	equivalents
EPR	Electron paramagnetic resonance
ESI TOF	Electrospray ionisation time-of-flight
ESMS	electrospray mass spectrometry
ET	electron transfer

Et	Ethyl (CH ₃ CH ₂)
EtOAc	ethyl acetate
EtOH	Ethanol
eV	Electron volt
EDG	Electron-donating group
EWG	Electron-withdrawing group
EY	Eosin Y
FTIR	Fourier-transform infrared spectroscopy
g	gram(s)
GC Gas	Chromatography
h	hour(s)
hν	light frequency
HAT	Hydrogen atom transfer
HCl	Hydrochloric acid
HFIP	Hexafluoroisopropanol
HRMS	High Resolution Mass Spectroscopy
HTIB	Hydroxy(tosyloxy)iodobenzene
Hz	Hertz
i-,	iso- Isomeric (branched alkyl chain)
<i>i</i> Bu	isobutyl
ISC	Inter system crossing
<i>i</i> Pr	isopropyl
Imd	Imidazole
<i>J</i>	Spin coupling constant (in NMR spectroscopy)
K	Kelvin
kcal	kilocalories
KOAc	Potassium acetate
L	Ligand
LED	Light emitting diode

LA	Lewis acid
lit.	literature
<i>m</i>	meta
M	molar (mol L ⁻¹)
m	multiplet (in NMR)
M	Metal
m/z	mass to charge ratio
mol%	mole percent
<i>m</i> -CPBA	<i>m</i> -chloroperbenzoic acid
Me	Methyl (CH ₃)
MeCN	Acetonitrile
MeOH	Methanol
mg	milligram
min	minute(s)
mL	millilitres
mmol	millimoles
mol mole(s)	molecular (as in mol. weight)
mp	melting point
MS	Molecular Sieves
NBS	<i>N</i> -bromosuccinimide
NCS	<i>N</i> -chlorosuccinimide
NIS	<i>N</i> -iodosuccinimide
NHPI	<i>N</i> -hydroxyphthalimide
nm	nanometer
NMF	<i>N</i> -methyl formamide
NMP	<i>N</i> -Methyl-2-pyrrolidone
NMR	Nuclear Magnetic Resonance
Nu	Nucleophile
<i>n</i> BuLi	<i>n</i> -butyllithium

NXPI	<i>N</i> -halophthalamide
<i>o</i> -	<i>ortho</i>
ORTEP	Oak Ridge Thermal-Ellipsoid Plot Program
OAc	Acetate
OTf	Trifluoromethanesulfonate
<i>p</i> -	<i>para</i>
PBN	phenyl- <i>N</i> -tert-butyl nitron
PC	Photocatalyst
PC*	Excited state photocatalyst
Ph	Phenyl (C ₆ H ₅)
PPh ₃	Triphenyl phosphine
PPT	Photoinduced proton transfer
PivOH	Pivalic acid
PMDI	pyromellitic diimide
PPAR	peroxisome proliferator-activated receptor
ppm	parts per million
Pr	Propyl
PT	proton transfer
Py	pyridine
q	quartet (NMR)
quin.	quintet
r.t.	room temperature
RB	Round bottom flask
R _f	retention factor (in chromatography)
Rh6G	Rhodamine 6G
s	singlet (NMR)
SET	Single electron transfer
t	triplet (NMR)
<i>t</i> -, <i>tert</i> -	Tertiary (branched alkyl chain)

TBAB	tetrabutyl ammonium bromide
TBAX	Tetrabutyl ammonium halide
TBDMS	<i>tert</i> -Butyldimethylsilyl
TBHP	<i>tert</i> -Butyl hydroperoxide
TBS	<i>tert</i> -Butyldimethylsilyl
<i>t</i> Bu	<i>tert</i> -butyl
td	triplet of doublet
TEMPO	2,2,6,6-Tetramethylpiperidin-1-yl)oxyl
Tf	trifluoromethanesulphonyl (triflyl)
TfO ⁻	triflate
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TMS	Trimethylsilyl
TMEDA	<i>N,N,N',N'</i> -tetramethylaminoethylenediamine
TOF	Turn-over frequency
TS	transition state
Ts	tosyl
UV	ultraviolet
vis	visible
V	Volt
W	Watt
X	Heteroatom
XRD	X-ray diffraction
δ	chemical shift in ppm downfield from trimethylsilane
λ	Wavelength
μM	Micro molar

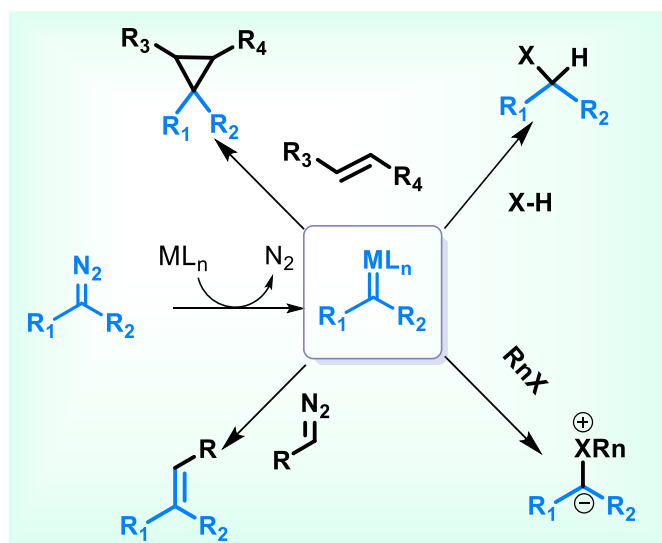
SYNOPSIS

The thesis entitled "*Exploration of the Reactivity and Applications of Diazo Arylidene Succinimides (DAS) under Visible Light and Metal Catalysis*" comprises five chapters.

Chapter 1: Diazo Reactivity Under Metal and Visible-Light Catalysis: A Journey Through Carbenes and Radicals

This chapter gives a brief overview of the journey of diazo compounds and their versatile, multifaceted reactivity. The reactivity of diazo compounds, under transition-metal catalysis and visible-light-mediated photoredox catalysis, for various useful transformations has been highlighted. Diazo compounds serve as valuable precursors to reactive intermediates such as carbenes and radicals, and further utilize them for constructing complex molecular frameworks with precision and selectivity. This chapter presents the structural diversity, preparation techniques, and functional significance of diazo compounds and their utility in modern organic synthesis.

The chapter has presented the development of metal-catalyzed diazo transformations, particularly those involving metal-carbenoid species, which enable controlled and selective carbene transfer reactions. Advances in transition-metal catalysis have allowed the exploration of diazo compounds in a wide array of transformations, including cyclopropanation, C–H insertions, and X–H functionalizations, and sigmatropic rearrangement of oxonium ylide with increasing levels of chemo-, regio-, and stereoselectivity (Scheme 1.1).

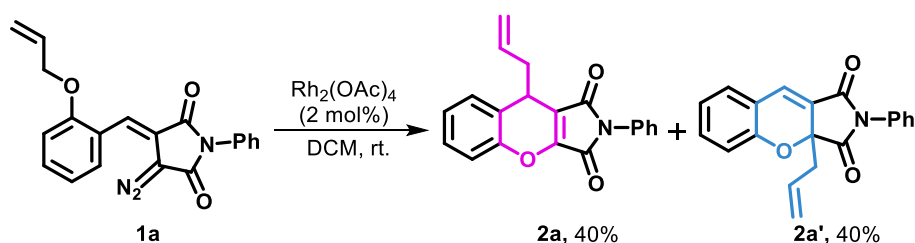


Scheme 1.1: Reactivity of diazo compounds with metal catalysts

Further, the chapter also highlighted the visible-light-mediated activation strategies, wherein diazo compounds engage in radical-based pathways. These include photoinduced electron transfer (PET), proton-coupled electron transfer (PCET), and radical–radical coupling mechanisms. Visible-light catalysis has been growing as a sustainable alternative to traditional methods and has given a new platform to achieve novel transformations that were previously inaccessible through thermal or purely metal-mediated pathways. Additionally, the chapter discussed some of the insights into state-of-the-art synthetic strategies and unique reactivity patterns of vinyl diazo compounds under photochemical conditions as well. Also, the chapter highlighted the challenges associated with the aim of the thesis work at the end of the chapter.

Chapter 2: Oxonium/Sulfonium Ylide Rearrangements to Access Chromenes and Thiochromenes: Concerted or Stepwise Pathway?

This chapter outlines the development of an efficient method for achieving the [1,2]/[1,4]-Shift of diazo arylidene succinimides (DAS) under mild conditions, at room temperature, using a dirhodium(II) catalyst. The transformation is believed to proceed through oxonium or sulfur ylide intermediates, which further undergo a radical-radical recombination process, furnishing useful chromene and thiochromene scaffolds. Chromenes, thiochromenes, and their analogs are well-recognized for their pharmacological activities, including anticancer, anti-HIV, anti-inflammatory, antioxidant, antitubercular, antiviral, antitumor, antibacterial, antimicrobial, antidiabetic, anticoagulant, diuretic, and fungicidal properties. Given the therapeutic potential of these compounds, we proposed that allyloxy- and thioallyl-substituted DAS derivatives could undergo intramolecular rearrangement to generate chromene and thiochromene frameworks.

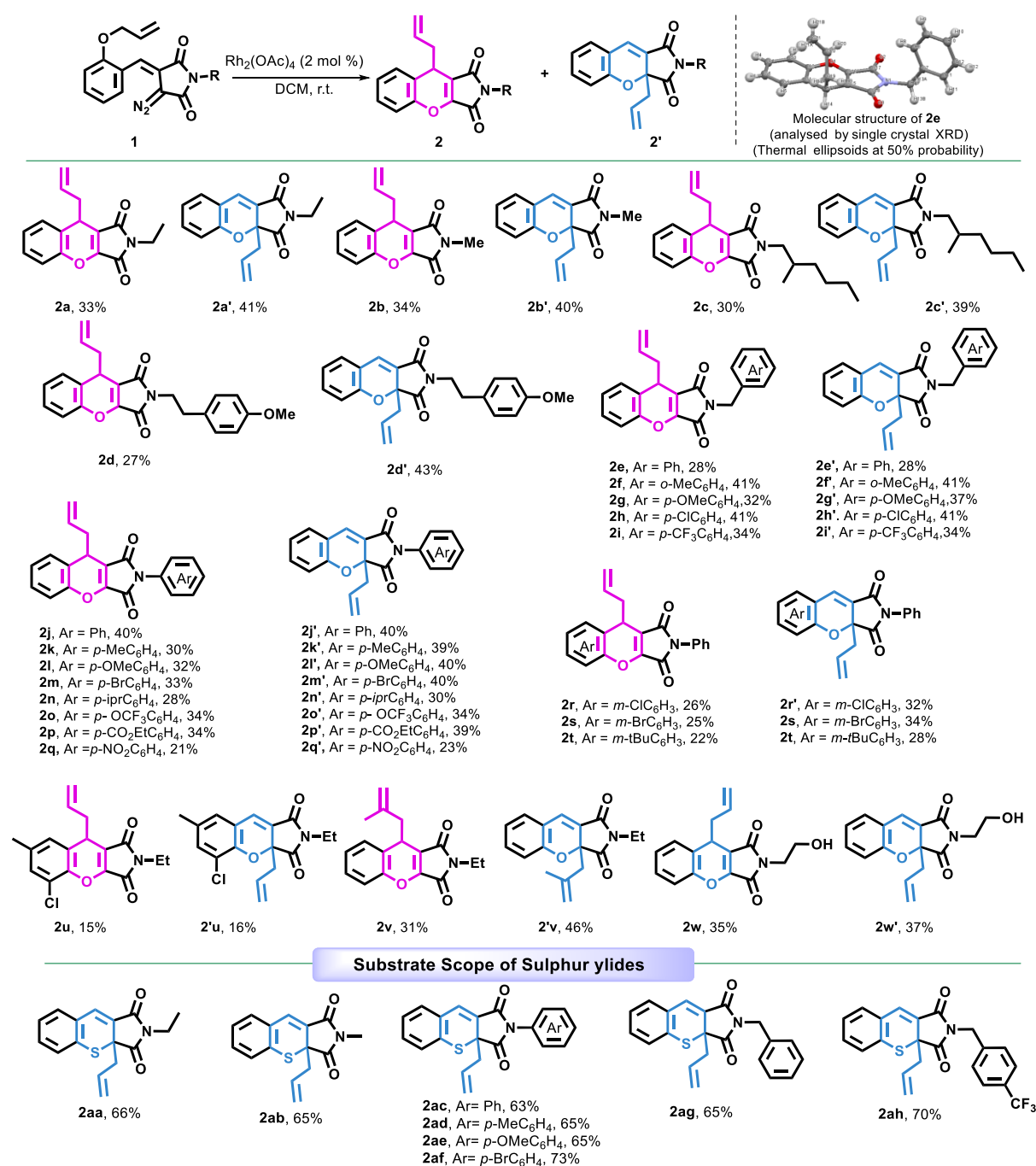


Scheme 2.1: Intramolecular rearrangement of DASs

In order to evaluate this hypothesis, we designed and synthesized suitable DAS derivatives having allyloxy/thioallyl moieties to explore their chemical reactivity. However, the formation of further tapping the reactivity of oxonium ylides remains particularly quite challenging due to their intrinsic instability compared to more conventional Nitrogen- or Sulfur-stabilized

ylides. To validate our hypothesis, we systematically optimized the reaction conditions and identified that DAS **1a** (1 equiv.) with Rh₂(OAc)₄ (2 mol%) in dichloromethane (DCM) at room temperature under a nitrogen atmosphere is an efficient condition to obtain the desired products **2a**, **2a'** (Scheme 2.1).

Having optimized reaction conditions, we investigated the substrate scope by testing various *N*-alkyl/aryl-substituted DAS derivatives (**1a–1q**). The corresponding rearranged products (**2a–2q**, **2a'–2q'**) were obtained successfully (see Scheme 2.2).



Scheme 2.2: Substrate scope of diazo arylidene succinimides

Notably, *N*-benzyl-substituted DAS with electron-donating or electron-neutral groups afforded the corresponding products in higher yields (**2e–2h**, **2e'–2h'**) compared to those with electron-withdrawing groups (**2i**, **2i'**). Various DAS derivatives with different arylidene moieties (**1r–1u**) also underwent smooth rearrangement by furnishing the products (**2r–2u**, **2r'–2u'**) in slightly lower yields, likely due to electronic effects. Methylallyloxy-substituted DAS **1v** successfully gave the corresponding products **2v** and **2v'**. Additionally, *N*-(2-hydroxyethyl)-substituted DAS **1w** furnished the expected rearranged products (**2w**, **2w'**). We then explored the rhodium-catalyzed formation of sulfur ylides using various *N*-substituted DASs bearing electron-donating and electron-withdrawing groups. Remarkably, all substrates afforded the corresponding rearrangement products (**2aa–2ah**) in moderate to good yields (Scheme 2.2).

To demonstrate the practical application of this method, products **2a** and **2a'** were subjected to epoxidation using *m*-chloroperbenzoic acid and hydrogenation with H₂ over Pd/C, respectively. The corresponding epoxidized product and double bond-reduced products were successfully obtained.

Later, control experiments were carried out to investigate the plausible mechanism of this rearrangement reaction. 2-OBn-substituted DAS **1ay** under standard conditions furnished the expected products only in trace amounts. This indicates that the reaction predominantly follows both [1,4]- and [1,2]-shift of oxonium ylide. Radical trapping studies further validated the involvement of a radical pathway in the reaction.

In conclusion, we have successfully developed a dirhodium(II)-catalyzed method for [1,2]- and [1,4]-shift of DAS derivatives at room temperature. We have successfully generated and utilized oxonium and sulfur ylide intermediates to construct chromene and thiochromene frameworks with high selectivity. To the best of our knowledge, this is the first study to explore the reactivity of DAS to achieve the intramolecular rearrangements.

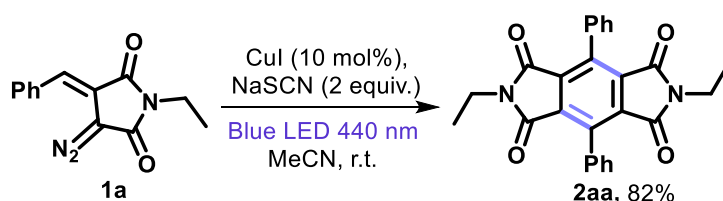
Chapter 3: Visible-Light-Induced Copper-Catalyzed Radical Reaction of Diazo Arylidene Succinimides to Access the Pyromellitic Diimide (PMDI) Core

This chapter presents a copper-catalyzed novel method for directly synthesizing disubstituted pyromellitic diimides (PMDIs) from diazo arylidene succinimides (DAS) under the irradiation of visible light. Diphenyl-substituted PMDIs possess a *p*-terphenyl core in bioactive molecules, and PMDIs are widely used in electronics and sensing applications. Disubstituted PMDIs are also known for aggregation-induced emission,

mechanofluorochromism, and polymeric properties. Despite their importance and versatility across research domains, their potential remains underexplored due to the limited availability of synthetic protocols. Existing methods often require multiple steps, harsh conditions, expensive metal catalysts, and challenges in removing metal residues. Recognizing the significance of the PMDI core and the limitations of conventional methods, there is a strong need for an efficient strategy to synthesize disubstituted PMDI molecules. Leveraging our ongoing research into DAS reactivity, we proposed that photoredox catalysis could facilitate the formation of a carbon radical intermediate from DAS, providing a pathway for the direct synthesis of PMDI. The method developed relies on a novel innovative approach that bypasses the conventional carbene intermediate by generating carbon radicals directly via proton-coupled electron transfer (PCET).

The use of CuI and NaSCN has been proved to be pivotal and it has been proved that it forms copper isothiocyanate (CuNCS) complex in situ, enabling efficient chemoselective radical cyclization. We successfully synthesized a PMDI molecule with known prominent aggregation-induced emission (AIE) properties. Along with the synthesis of symmetric PMDIs, the protocol was also explored to synthesize the challenging synthesis of unsymmetrical PMDIs using two distinct diazo arylidene succinimides, of a carbon radical intermediate from DAS, providing a pathway for PMDI synthesis.

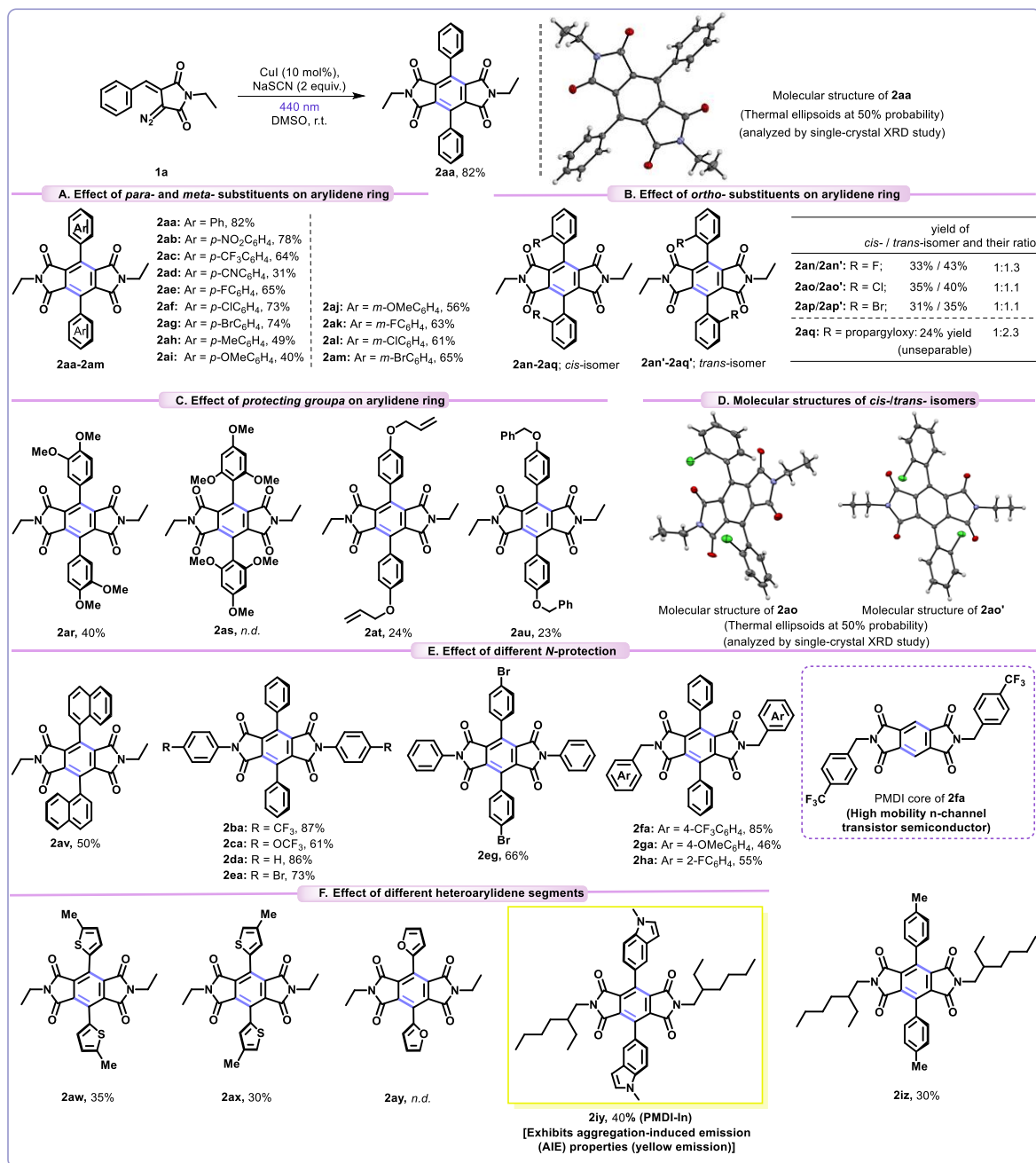
After extensive screening of solvents, light sources, bases, and catalysts, DAS **1a** (1 equiv.), NaSCN (2 equiv.), and CuI (10 mol%) in DMSO, using a degassed reaction mixture under nitrogen and visible light irradiation (Blue LED, 440 nm) proved to be optimum reaction condition to construct the PMDI product **2aa** in excellent yield of 82% in one step from DAS **1a** (Scheme 3.1).



Scheme 3.1: Visible light-mediated reaction of DAS to access PMDI

With the optimized reaction conditions, we have demonstrated the broad substrate scope of diazo arylidene succinimides (DAS) to access the PMDI cores (see scheme 3.2). The *p*-Substituted DAS derivatives bearing electron-withdrawing or electron-deactivating groups on the phenyl ring furnished the corresponding PMDI products (**2aa–2ag**) in moderate to good

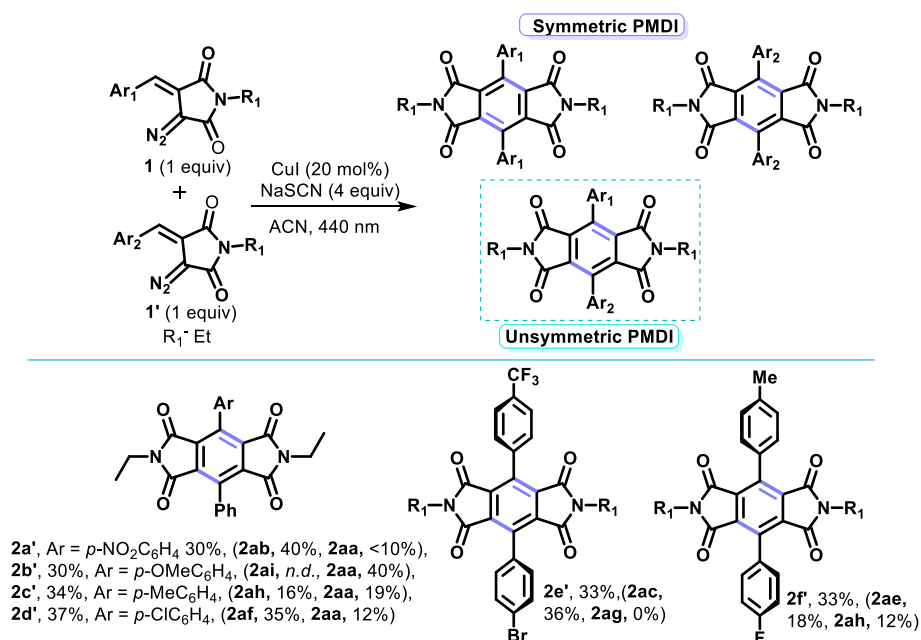
yields (up to 82%, Scheme 3.2), while *p*-cyano DAS afforded **2ad** in moderate yield (31%) possibly due to -CN binding with copper [Cu] in situ. Electron-donating groups gave corresponding products (**2ah**, **2ai**) lower yields up to 49%, while *m*-substituted derivatives afforded the products **2aj–2am** in moderate yields (up to 65% yield). The *o*-Substituted DAS derivatives formed *cis*-/*trans* isomeric products (**2an–2ap**) in the ratio of (1:1.3) up to 76% yield. Molecular structures of isomeric products (*cis*-**2ao**, *trans*-**2ao'**) were confirmed via single-crystal X-ray diffraction (Scheme 3.2).



Scheme 3.2: Substrate scope of DASs for symmetrical PMDIs.

We further demonstrated the versatility of isomeric protocol using various *N*-substituted DASs, including electron-rich and electron-deficient aromatic and aliphatic groups to obtain the corresponding products (**2ba–2iz**) in good to excellent yields, (up to 87%, Scheme 3.2). Additionally, heteroarylidene diazo succinimides afforded the desired products in modest yield (up to 40%, **2aw**, **2iy**). It is important to note that compound **2iy** is recognized for its significant aggregation-induced emission (AIE) properties (Scheme 3.2).

To the best of our knowledge, the synthesis of an unsymmetrical PMDI core was not known in the literature till we explored it. Looking into the importance and challenges, we performed the cross-coupling of two distinct DASs under the reaction conditions. We successfully obtained the unsymmetrical PMDIs (**2a'–2f'**) alongside the anticipated self-coupled products (see Scheme 3.3).



Scheme 3.3: Substrate scope for cross-coupling of DASs for unsymmetrical PMDIs.

We conducted a series of control experiments to gain mechanistic insights into the reaction pathway. The radical nature of the reaction was confirmed by employing BHT, TEMPO, and even the reagent such as CHANT to trap the short-lived radicals under the optimized conditions. Additionally, using electron paramagnetic resonance (EPR) spectroscopy, we further validated the presence of radicals, with a *g*-value of the crossover point of 1.9988. UV-Vis spectra of individual reagents and their mixtures were recorded systematically, and the results clearly indicated the formation of certain photoactive species in situ. A plausible reaction mechanism has been proposed based on the EPR results, control experiments, and single-crystal X-ray diffraction analysis. Based on the evidences it has been

of the CuNCS complex formed in situ to drive the reaction. In conclusion, we have demonstrated sustainable, visible light-promoted synthesis of useful PMDI core directly from DAS via copper catalysis in one pot. This method overcomes traditional challenges by leveraging the radical reactivity of DAS under visible light conditions. The synergistic role of NaSCN and CuI enabled the photoinduced transformation, allowing access to both symmetric and unsymmetric PMDIs efficiently.

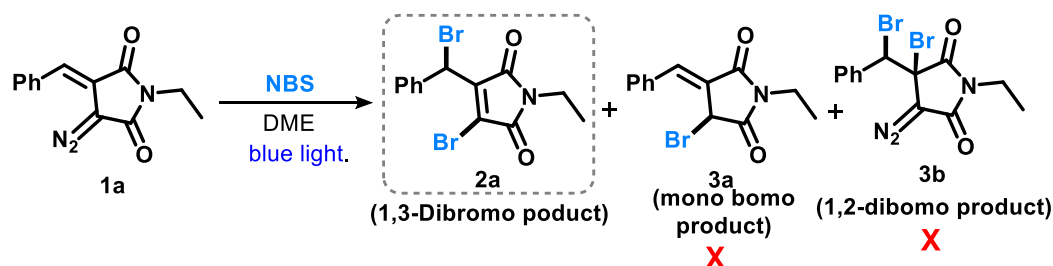
Chapter 4: 1,3-Dibromination of Diazo Arylidene Succinimides (DAS): A Sustainable Approach using Visible Light

This chapter describes a visible-light-driven, carbene-free approach for the direct 1,3-dibromination of diazo arylidene succinimides (DAS) using *N*-bromosuccinimide (NBS). This interesting bromination reaction is initiated through the direct photochemical activation, without the need for any photocatalysts or additives. This protocol proved to be efficient by affording the 1,3-dibromination products under Green LEDs as well as the direct exposure of sunlight.

Organic halides are essential precursors and intermediates in organic chemistry. Vinyl and aryl bromides are known to facilitate significant cross-coupling reactions like Suzuki, Heck, Negishi, and Sonogashira coupling. Bromo compounds have extensive applications in diverse areas and they are found in flame retardants, biocides, gasoline additives, polymers, pharmaceuticals, natural products, and agrochemicals. Halogenation reactions are well known in the literature. Monohalogenation is well-established, and the polyhalogenation, especially dihalogenation, has been predominantly reported for alkenes and alkynes and remains comparatively less explored for the other reactive substrates. In contrast, the bromination of diazo compounds emerged as a fascinating and valuable strategy, given the highly reactive and versatile nature of diazo compounds and their utility in organic synthesis. Despite their potential, only a few studies have been conducted for the bromination of α -diazo compounds, traditionally utilizing bromine or hydrogen bromide as a reagent. However, these conventional methods often require harsh conditions and involve hazardous, toxic reagents, thus significantly limiting their broader applicability in organic synthesis. To date, no studies have been reported on the dihalogenation of cyclic diazo compounds to the best of our knowledge. This highlights that functionalization of DAS with bromo groups would be quite interesting, useful, and also unexplored. Recognizing the importance of bromination, after screening various brominating agents, NBS proved to be an efficient reagent to achieve bromination

without needing acids or any catalysts. Over the years, we have been working on arylidene diazo succinimides (DAS) and explored their reactivity under metal as well as visible light. With our continued interest, we planned to examine the behaviour of DAS for the halogenation. Based on these features, we hypothesize that DAS could undergo 1,3-dibromination when treated with a brominating agent under visible light irradiation.

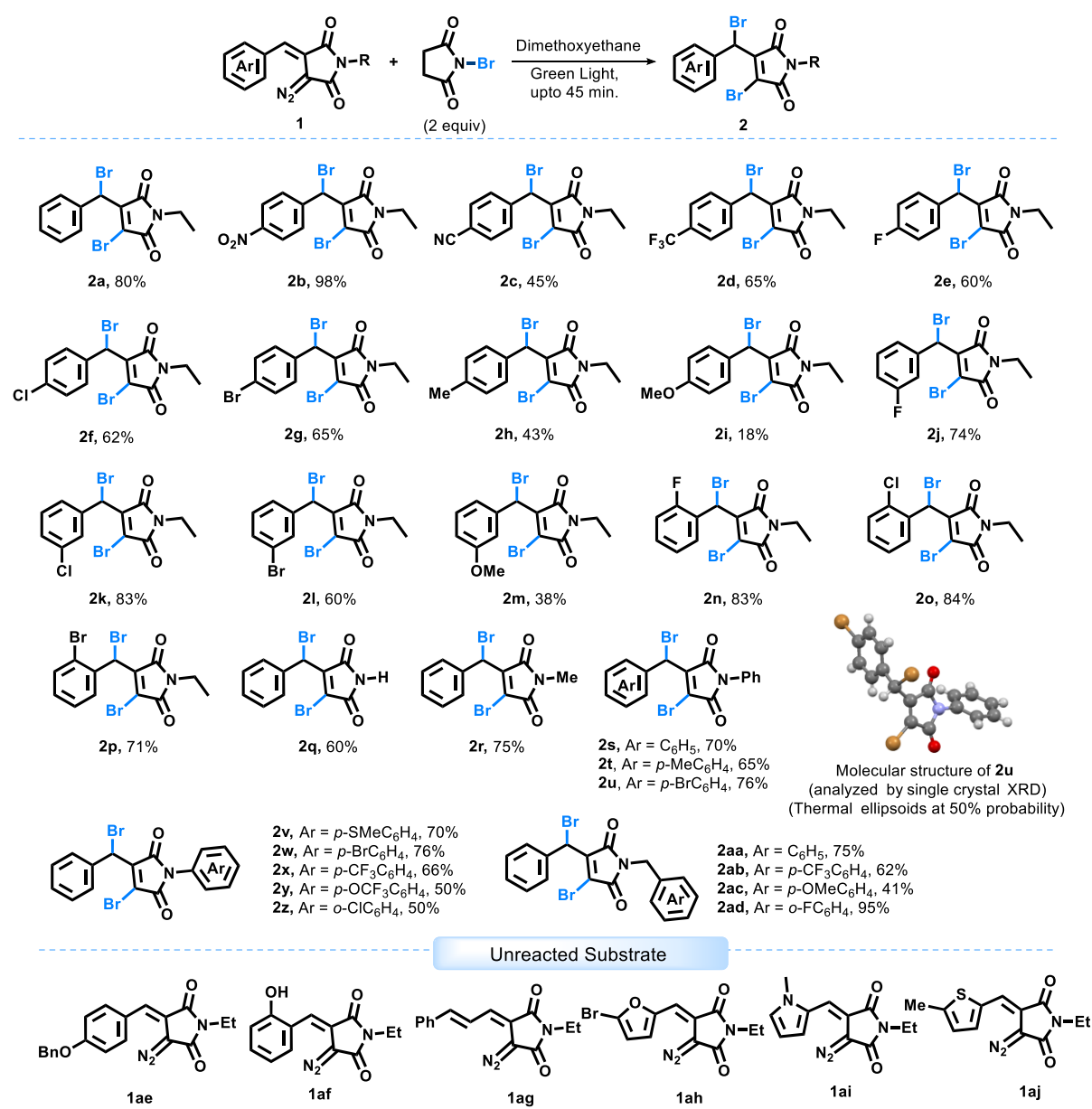
To validate our hypothesis, a systematic screening of brominating reagents and other conditions was conducted. Based on the detailed screening, the DAS **1a** (1 equiv.), NBS (2 equiv.), in DME as solvent under the irradiation of green light (525 nm) in an inert atmosphere at room temperature, proved to be the optimum reaction conditions to afford the selective 1,3-dibromination product **2a** efficiently. Notably, neither the monobromination product **3a** nor the 1,2-dibromination product **3b** were found under the conditions (See scheme 4.1).



Scheme 4.1: Visible light-mediated reaction of DAS to access 1,3-dibromination of DAS

With the optimized reaction conditions in hand, we explored the substrate scope of various DAS derivatives for the 1,3-dibromination (Scheme 4.2). DAS with *p*-substituted electron-withdrawing or electron-deactivating groups on the phenyl ring of the arylidene moiety reacted efficiently, providing the corresponding 1,3-dibrominated products (**2a–2g**) in modest to excellent yields (up to 98%, Scheme 4.2). In contrast, DAS derivatives with electron-donating groups at the *para* position of the phenyl ring furnished the desired products (**2h, 2i**) in relatively lower yields. DAS with *m*-electron-donating substituents yielded the gave the product **2m** in moderate yield (38%, Scheme 4.2). In contrast, DAS having *o*-substituted deactivating groups on the phenyl ring exhibited excellent tolerance by affording the 1,3-dibrominated products (**2n–2p**) with good yields (up to 84%, Scheme 4.2). Furthermore, diverse *N*-substituted DAS reacted efficiently under the conditions to furnish the desired products (**2q–2ad**) in moderate to good yields (Scheme 4.2). Later, we carried out the reaction of **1a** under direct exposure to natural sunlight, and gratifyingly, we obtained the desired product **2a** in good yield (70%, in 5 h).

To elucidate the reaction pathway, we conducted control experiments systematically. To begin with, DAS **1a** was treated with benzaldehyde and styrene separately to observe the product emanating from a classical carbene intermediate (metallo-carbene), if any. However, carbene-trapped products such as epoxide and cyclopropanation were detected. Subsequently, EPR analysis of the reaction mixture revealed the generation of radicals in situ, thus confirming the radical pathway.



Scheme 4.2: Substrate scope of the 1,3-dibromination reaction of DASs

In summary, we have developed a sustainable and efficient protocol for the 1,3-dibromination of DAS by employing NBS as a safer brominating agent under visible light conditions at room temperature. This method works smoothly without needing any photocatalysts or additives, operates under mild conditions to afford the 1,3-dibromination products, in good to excellent

yields. Unlike harsh brominating agents, NBS proved to be practical, user-friendly, and cost-effective for brominating agents, which was used for the diazo arylidene succinimides (DAS) for the first time at the olefinic as well as carbene carbon. The method also works effectively under direct exposure to sunlight, thus enhancing its practical utility.

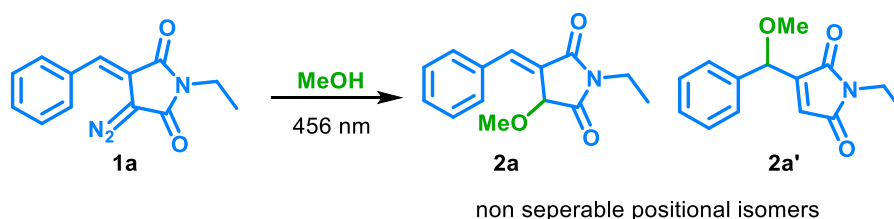
Chapter 5: Photochemical O-H Functionalization of Diazo Arylidene Succinimides via Proton Transfer Promoted by Methanol

This chapter explores a novel photochemical O-H functionalization of diazo arylidene succinimides (DAS), utilizing methanol as a crucial protic solvent under optimized conditions. This method relied on methanol and its role in facilitating the transformation via photoinduced proton transfer (PPT) processes under visible light.

Organic transformations via photoexcited states enhance synthetic efficiency by unlocking inaccessible pathways. The reactions involving photoinduced electron or proton transfer have gained interest over the years. Usually, the diazoalkanes react with O-H groups to form C-O bonds, often relying on metal catalysis to generate metal-carbene intermediates. Though photoinduced electron-transfer reactions are well-studied, the photoexcited proton transfer (PPT) pathway is relatively less explored and primarily relies on UV-excited Brønsted acidic catalysts. Recently, Koenigs and colleagues elegantly explored the PPT pathway to demonstrate novel diazoalkane reactivity under visible light. However, studies on α -diazo carbonyl compounds and other diazoalkanes remain limited in the literature.

Diazo arylidene succinimides (DAS) are key compounds known for their metal-catalyzed carbene transfer reactions. Based on prior studies and our interest in photochemical reactivity, we hypothesized that under visible light conditions, DAS may act as a photobase in an excited state, enabling PPT reactions with mild acids such as methanol to form O-H functionalized products.

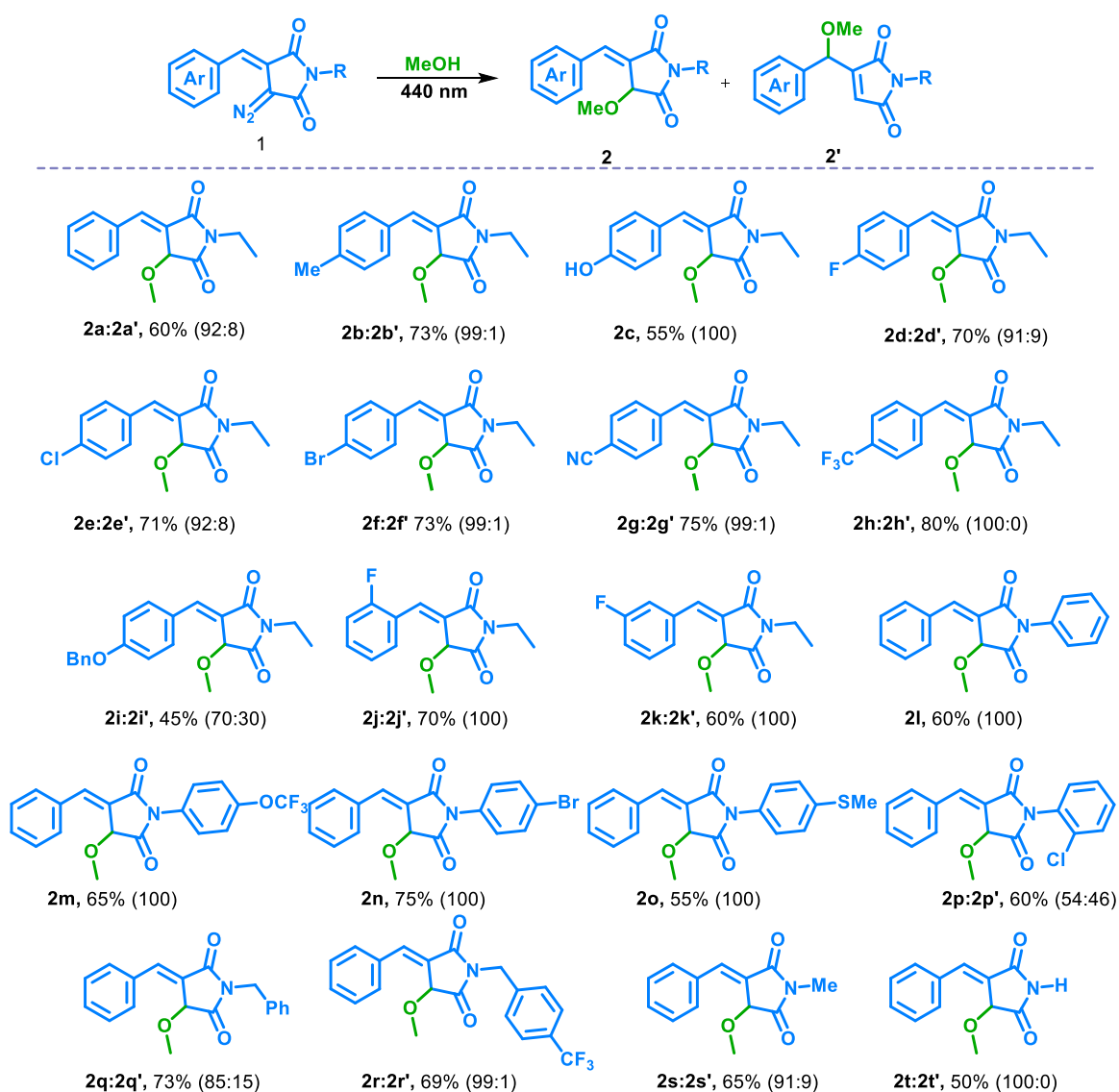
In order to validate the hypothesis, we systematically carried out optimization of the reaction conditions.



Scheme 5.1: Photoinduced proton transfer reaction of DASs

Gratifyingly, diazo arylidene succinimide (DAS) **1a** (1 equiv.) under blue LED illumination (440 nm) in methanol, under degassed nitrogen conditions, afforded the desired functionalized product **2a**, accompanied by an inseparable minor amount of **2a'** in a ratio of 98:2 (Scheme 5.1).

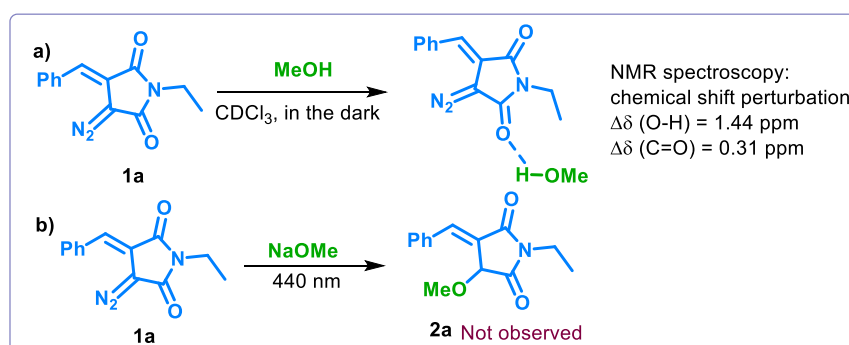
Having the optimized reaction conditions in place, we further examined the reactions of various substituted DAS derivatives (**1a-1t**) with methanol. The substituted DASs demonstrated excellent tolerance under the established conditions to afford the corresponding O-H functionalization products (**2a-2t**) in moderate to good yields (Scheme 5.2).



Scheme 5.2: Substrate scope of the diazo arylidene succinimides for the functionalization with MeOH

To investigate the mechanism, we examined the interaction between methanol and DAS using

^1H and ^{13}C NMR spectroscopy at varying temperatures. A reaction mixture [**1a** (1 equivalent) and MeOH (2 equivalents)] in CDCl_3 displayed notable chemical shift changes in the methanol O-H proton in the ^1H NMR spectrum (1.44 ppm, see Scheme 5.3-a) and the carbonyl carbon of **1a** (0.31 ppm, see Scheme 5.3-a). These findings indicate that possibility of in situ formation of a hydrogen-bonding complex between DAS **1a** and methanol under dark conditions. Additionally, we performed the reaction of DAS **1a** with sodium methoxide under blue light irradiation (440 nm) for 12 h. However, the starting material **1a** decomposed, and we did not observe the formation of the expected product **2a** (Scheme 5.3-b).



Scheme 5.3: Formation of H-bonding complex

These results suggest that the formation of the desired product **2a** likely depends on the hydrogen-bonding interaction between DAS **1a** and methanol, where methanol plays a key role in the hydrogen bonding and in the proton transfer later to drive the reaction. Further studies would shed more insights into this reaction.

In summary, we demonstrated the photochemical O-H functionalization of diazo arylidene succinimides under exposure to visible light. This novel visible light-mediated protocol for the photochemical transformation utilizes methanol, a less reactive protic solvent, as a key component. The key role of methanol in driving the reaction highlights the significance of this optimized method, offering valuable insights into the photoinduced proton transfer (PPT) process. This protocol worked exclusively with methanol, thus highlighting the reactivity profiles of both DAS and methanol under light. The limited reactivity of DAS exclusively with methanol needs to be examined in detail, further looking into various parameters.

(Numbers of substrates and products in the synopsis are different from those in the thesis chapters. Please note that compound numbers have been assigned in the synopsis and subsequent chapters for the flow and convenience of the readers.)

List of Publications

Included in the thesis

1. **Kajal B. Meher**, Debasish Laha, Pankaj D. Dharpure and Ramakrishna G. Bhat* “Visible-Light-Induced Copper-Catalyzed Radical Reactions of Diazo Arylidene Succinimides to Access the Pyromellitic Diimide (PMDI) Core.” *Org. Lett.* **2024**, *26*, 10241–10247.
2. **Kajal B. Meher**, Onkar S. Bankar, Hrishik Mukherjee and Ramakrishna G. Bhat* “Oxonium/Sulfonium Ylide Rearrangements to Access Chromenes and Thiochromenes: Concerted or Stepwise Pathway?” DOI: 10.26434/chemrxiv-2025-pmkz9 (Manuscript accepted in *Chem Asian J.*).
3. **Kajal B. Meher**, Hrishik Mukherjee and Ramakrishna G. Bhat* "1,3-Dibromination of Diazo Arylidene Succinimides (DAS): A Sustainable Approach using Green Light or Sunlight." *Manuscript is ready to be communicated.*
4. **Kajal B. Meher**, Ganesh H. Kondhare and Ramakrishna G. Bhat* “Photochemical O-H Functionalization of Diazo Arylidene Succinimides via Proton Transfer Promoted by Methanol.” *Manuscript under preparation.*

Not included in the thesis

5. Debasish Laha, **Kajal B. Meher**, Onkar S. Bankar, and Ramakrishna G. Bhat* SilverCatalyzed One-Pot Access to Diastereoselective Benzo[5,6]oxepino[2,3-*c*]pyrroles via Formal (5+2)-Annulation of Donor-/Acceptor-Type Aryl Vinyl Diazosuccinimide with Ketones. *Asian J. Org. Chem.* **2022**, *11*, e202200062.
6. Onkar S. Bankar, Debasish Laha, **Kajal B. Meher** and Ramakrishna G. Bhat* “Umpolung Reactivity of Diazo Arylidene Succinimides: Distal C–H Functionalization of α -Thiocarbonyls from the Reactive Carbenoid Center.” *Chem Asian J.* **2023**, *18*, e202300774

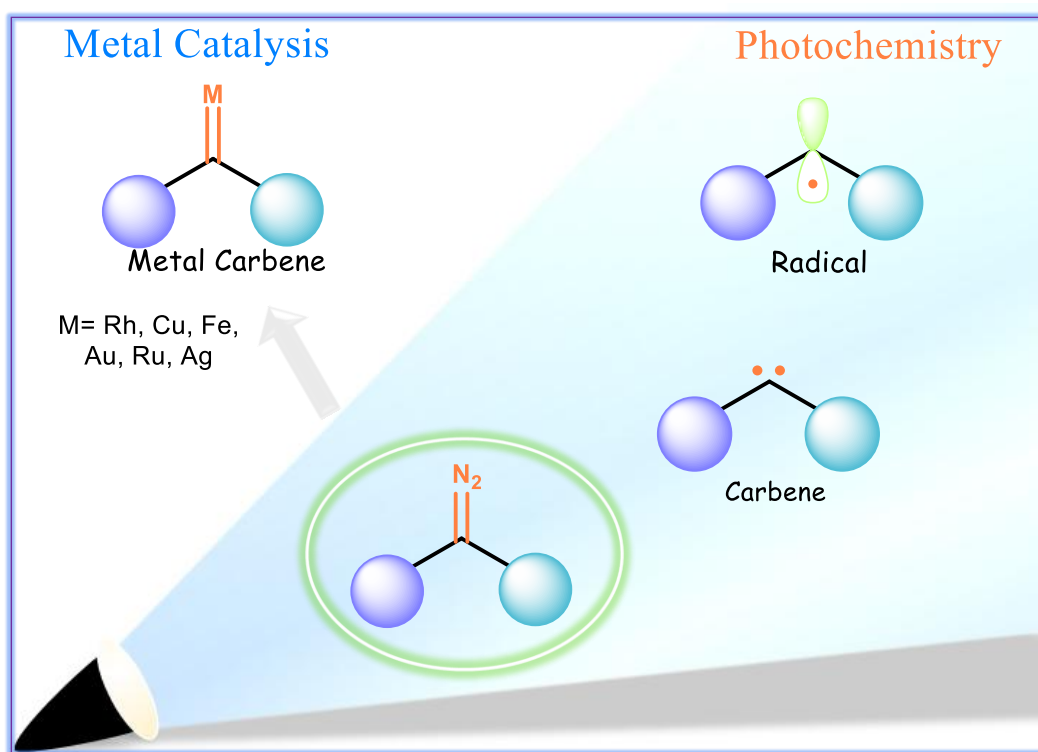
Abstract

Diazo compounds are highly versatile as well as valuable reagents whose reactivity can be fine-tuned through metal catalysis, photochemical activation, and radical pathway to enable divergent and selective synthetic transformations. This thesis has investigated the novel reactivity of diazo arylidene succinimides (DAS) under different reaction conditions design and develop innovative synthetic methodologies with mechanistic insights in great detail. Dirhodium(II)-catalyzed regio-divergent rearrangement of allyloxy/thioallyl containing DAS derivatives enabled the [1,4]/[1,2]-shifts to construct chromene and thiochromene scaffolds. Different DAS derivatives have been employed for a copper-catalyzed radical cyclization via a photoinduced proton-coupled electron transfer (PCET) mechanism to access the disubstituted pyromellitic diimides (PMDIs). This transformation was driven via a carbene-free pathway, and novel radical reactivity of DAS was explored in the presence of copper and visible light. Further expanding the photochemical reactivity of DAS, 1,3-dibromination has been accomplished using N-bromosuccinimide (NBS) via radical pathway to access bromo-functionalized DAS derivatives under the exposure of visible light. The method did not rely on a photocatalysts or any additives and also worked under the direct exposure of natural sunlight. Additionally, a photochemical O–H functionalization has been accomplished and, in this method, methanol has been utilized as a key component in this photoinduced proton transfer (PPT) processes. The reactivity of DAS specific to the methanol under visible light conditions has been demonstrated. This diversifying the O-H functionalization landscape of DAS.

*These studies highlight the use of **metal catalysis as well as photocatalysis to explore novel reactivity of diazo compounds**. The radical reactivity of DAS has been explored under visible light conditions to access useful compounds. The developed methods provide **efficient and scalable** strategies for building **complex molecules**, with promising applications in **modern organic chemistry**.*

Chapter 1

Advances in Metal Catalysis and Photochemical Transformations of Diazo Compounds



Advances in Metal Catalysis and Photochemical Transformations of Diazo Compounds

1

This chapter provides a concise overview of the advancements of diazo compounds and their significant role in organic synthesis. Diazo compounds have proven to be highly versatile reagents, with their reactivity fine-tuned by both metal catalysis and visible light activation. Traditionally, metal catalysts drive key carbene transfer reactions such as cyclopropanation, C–H insertion, and ylide formation via carbenes intermediates. Conversely, photochemical excitation through visible light presents a metal-free alternative, enabling distinct reaction pathways through either direct excitation or photosensitizer-mediated processes. These photoinduced transformations not only replicate conventional reactions but also introduce new radical-driven strategies, expanding the toolkit for bond formation. Furthermore, electronic and steric modulation of diazo precursors dictates the generation of singlet vs. triplet carbenes and radical species, offering precise control over selectivity and efficiency. The integration of metal catalysis, photochemical activation, and radical reactivity establishes a powerful framework in modern organic synthesis, significantly enhancing the applicability of diazo compounds.

1.1 Introduction

Diazo compounds hold a significant and indispensable place in the field of organic chemistry due to their diverse applications and unique reactivity. They have a rich and significant history in organic chemistry, serving as essential tools to explore the modern synthetic methodologies. The journey began in 1883 when Curtius successfully synthesized the first diazo compound, ethyl diazoacetate, using natural glycine.¹ This groundbreaking achievement was followed by von Pechmann's discovery of diazomethane in 1894,² marking yet another milestone in the field. Since these early advances, diazo compounds have remained central to organic chemistry, playing a pivotal role in developing innovative synthetic strategies.³ Diazo compounds, particularly, are notable for acting as carbene equivalents. These compounds decompose under heat, light or metal catalysts, releasing nitrogen gas and forming reactive intermediates such as singlet or triplet state carbenes or metal carbenoids.⁴ These intermediates serve as powerful tools for facilitating diverse chemical transformations, enabling the synthesis of complex molecules in an efficient and innovative manner. While early approaches utilized thermal

activation to promote these transformations, stringent conditions and low selectivity often hinder their effectiveness.⁵ Transition metal catalysis has proven to be a highly effective

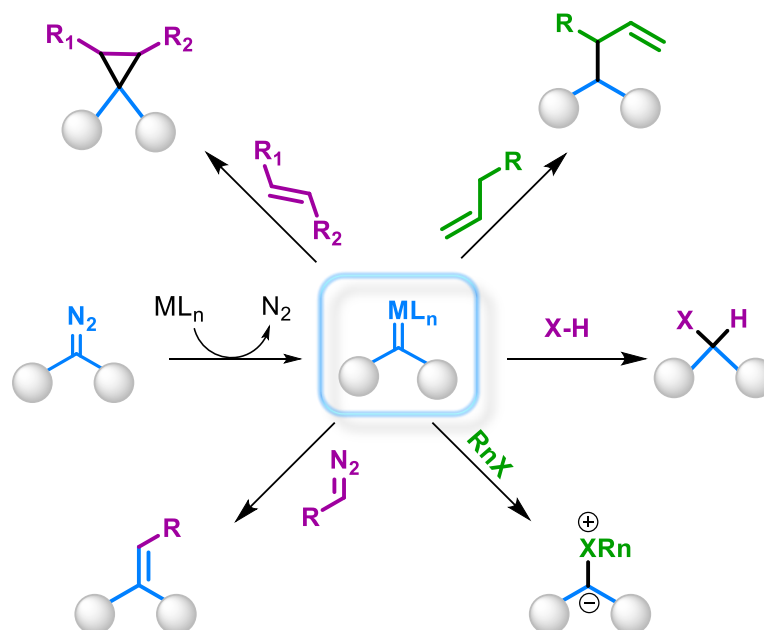
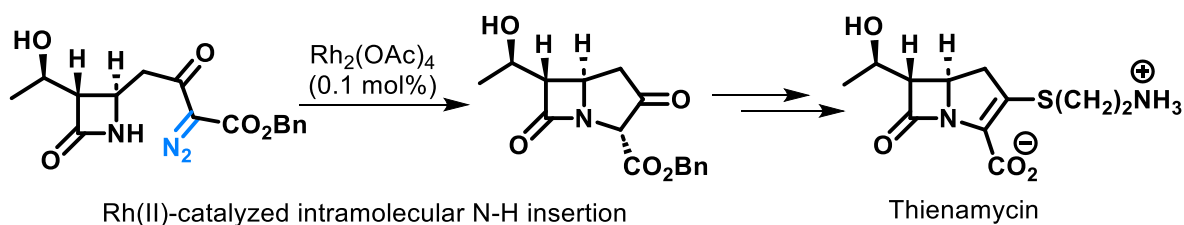


Figure 1.1: Established Reactivity of Diazo Compounds

approach, enabling the generation of tunable metal carbenes with adjustable electronic properties and stability. These reactions often proceed under mild conditions, such as room temperature, while carefully designed catalysts and ligands ensure exceptional control over reactivity and selectivity, including asymmetric transformations. These reactive species enable a variety of powerful synthetic transformations, such as cyclopropanation, X–H insertion, cross-coupling, and ylide formation (Figure 1.1). The field of transition metal-catalyzed reactions involving diazo compounds has been comprehensively explored over the years. Some of the classical diazo compounds, their use as carbene surrogates, classifications, and their utility in synthetic transformations have been discussed briefly.

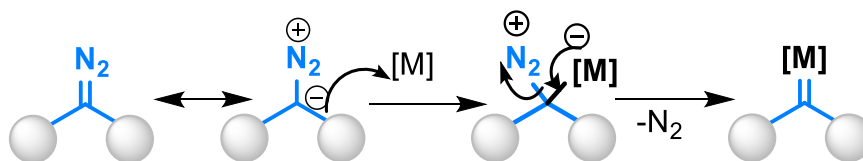
1.2 Diazo Compounds and Their Importance



Scheme 1.1. Application of diazo compound in the production of thienamycin by Merck.

Diazo compounds have also found applications in the pharmaceutical industry for synthesizing drug molecules. A prominent example is using Rh(II)-catalyzed intramolecular N–H insertion in producing β -lactam antibiotics, including thienamycin (Scheme 1.1).⁷

The diazo group features a unique structure and is rich in chemical reactivity. Compounds containing this group are especially useful as metal carbene (metal carbenoid) precursors in transition metal-catalyzed reactions. As depicted in Scheme 1.2, the carbon atom within the diazo compound, possessing a negative charge, can bind to the central metal. This process prompts the extrusion of N_2 , supported by the transfer of the central metal's d-electrons, leading to the formation of a metal carbene.



Scheme 1.2. The formation of metal carbene from the diazo compound.

1.3 Synthesis of Diazo Compounds

Owing to the significance of diazo compounds, numerous methods have been established for their efficient synthesis. These methods provide reliable and controlled access to diazo compounds for various applications.

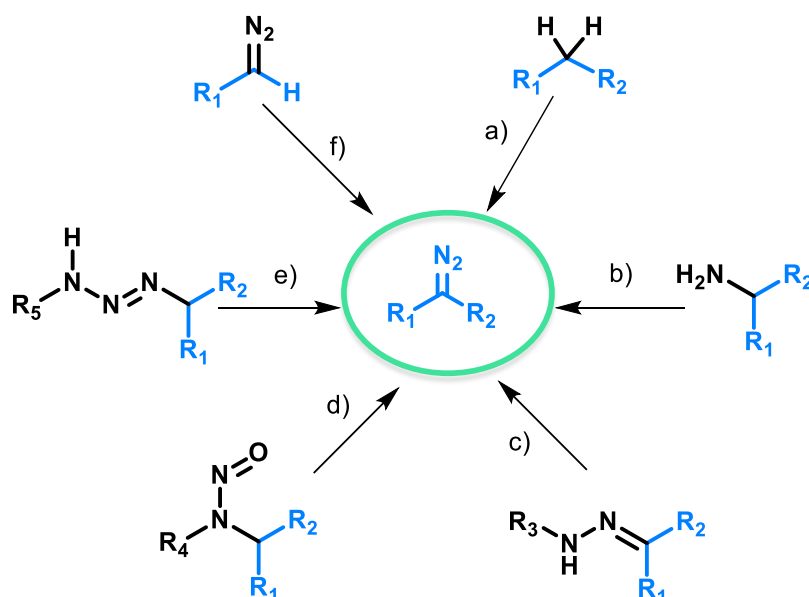


Figure 1.2: Typical methods for preparing diazo compounds: (a) diazo transfer; (b) diazotization; (c) decomposition or oxidation of hydrazones; (d) rearrangement of *N*-alkyl-*N*-nitroso compounds; (e) fragmentation of 1,3-disubstituted alkyl aryl triazenes; and (f) elaboration of more readily available diazo compounds.

Some of the prominent approaches include: (a) diazo transfer, (b) diazotization, (c) decomposition or oxidation of hydrazones, (d) rearrangement of N-alkyl N-nitroso compounds, (e) fragmentation of 1,3-disubstituted acyl (or aryl) triazines, and (f) modification of existing diazo compounds (Figure 1.2).⁸ Among these, the diazo transfer process stands out as the most efficient and reliable synthetic method. The low pK_a of the acceptor carbon's proton makes it suitable to use mild base, which in turn is also beneficial in chemical biology applications. α -Methylene carbonyl compounds upon treatment with diazo transfer reagents such as *p*-acetamido benzene sulfonyl azide or tosyl azide in the presence of a base like 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU) afford the corresponding diazo compounds.

1.4 Classification of Diazo Compounds

Aliphatic diazo compounds are known for their high reactivity and potential explosiveness. Unlike aromatic diazonium ions, they lack stabilization through π back-donation,^{9a} making unstabilized diazo compounds like diazoalkanes generally unsuitable for synthetic applications. However, exceptions include diazomethane (CH₂N₂) and aryl diazomethanes (ArCHN₂), which are commonly generated in situ for the useful transformations.⁹

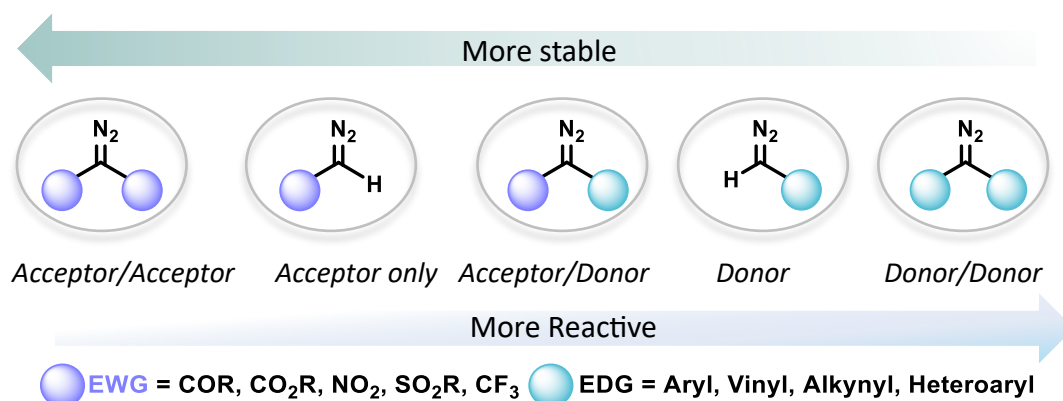


Figure 1.3: Substituent dependence of reactivity-stability of diazo compounds.

The substituents attached to diazo groups play a crucial role in determining the stability and reactivity of the corresponding diazo compounds. Resonance structures reveal that electron-withdrawing (EWG) substituents enhance the stability, while electron-donating (EDG) ones reduce it. Interestingly, research by Davies and co-workers highlights that the diazo compound featuring both electron-donating and electron-withdrawing substituents, such as aryl diazoacetates, exhibit exceptional reactivity and selectivity in transition-metal-catalyzed carbene transfer reactions.¹⁰ The general trend in reactivity and stability for various substituted diazo compounds has been depicted in Figure 1.3.

Looking into their balanced stability, reactivity, accessibility, and practical applications, diazo esters are the most commonly explored. Recent advancements have explored diazo compounds with various functional group substitutions.

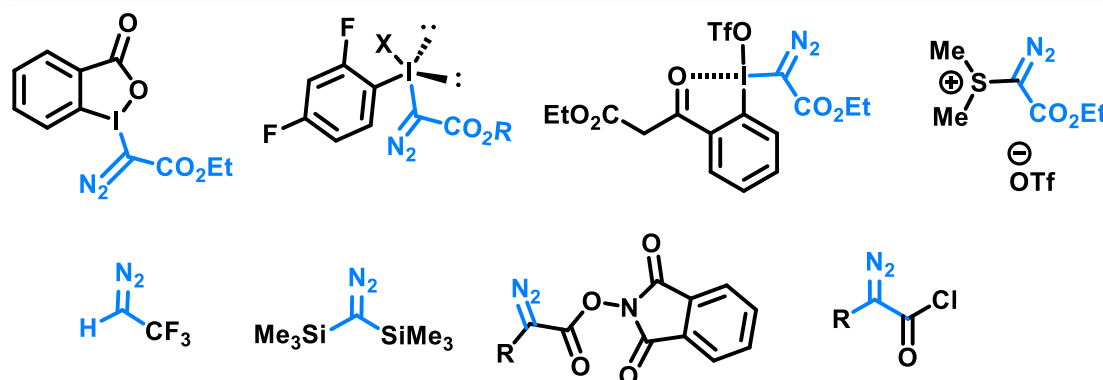


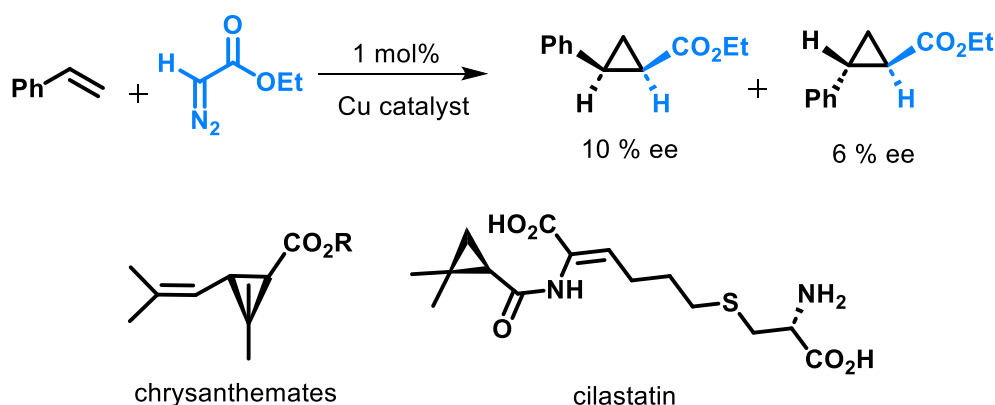
Figure 1.4: Diazo compounds with various functional groups.

As illustrated in Figure 1.4, the diazo group can be modified with substituents like hypervalent iodo,¹¹ sulfonium,¹² trifluoromethyl¹³ trimethylsilyl,¹⁴ photo-reactive ester,¹⁵ chloro,¹⁶ and others. Many of these diazo compounds are stable under standard laboratory conditions and have found specialized applications in organic synthesis as well as in fields like chemical biology.

1.5 Metal-Catalyzed Reactivity of Diazo Compounds

1.5.1 Industrial Applications of Diazo compounds

Over the years, significant progress has been made in classic transition-metal-catalyzed carbene transfer reactions. In the past two decades, research has primarily shifted towards



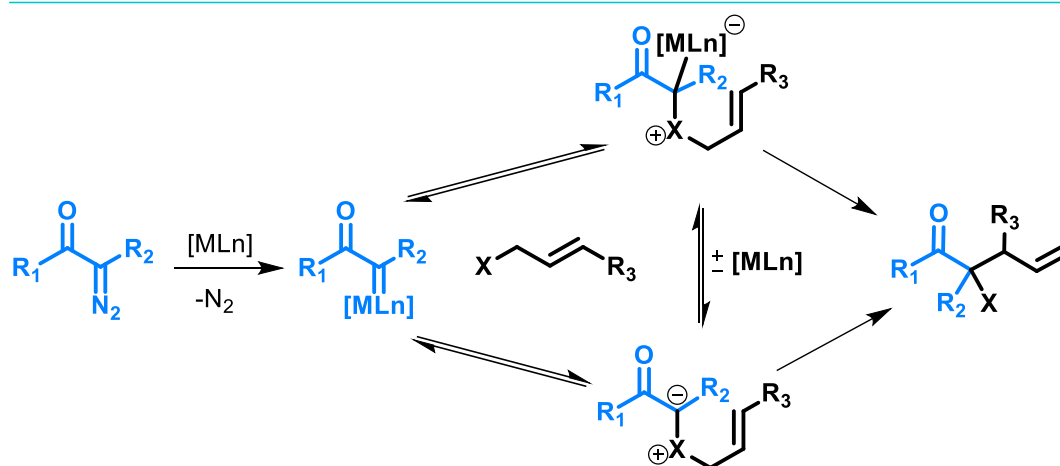
Scheme 1.5: The first asymmetric catalytic cyclopropanation and industrial application

asymmetric catalysis in this field. Notably, Noyori's pioneering work on the cyclopropanation of styrene with ethyl diazoacetate, catalyzed by copper and a chiral Schiff base, marked the

first example of asymmetric catalysis involving a structurally well-defined chiral transition-metal complex, despite achieving low enantioselectivity (Scheme 1.5).¹⁷ Subsequent optimization of this reaction paved the way for its industrial application, including the asymmetric cyclopropanation process used in the production of chrysanthemates (insecticides) and cilastatin (a stabilizer for carbapenem antibiotics).

1.5.2 Metal-Catalyzed Onium Ylide Formation and [2,3]-Rearrangements via Metal-carbenoids

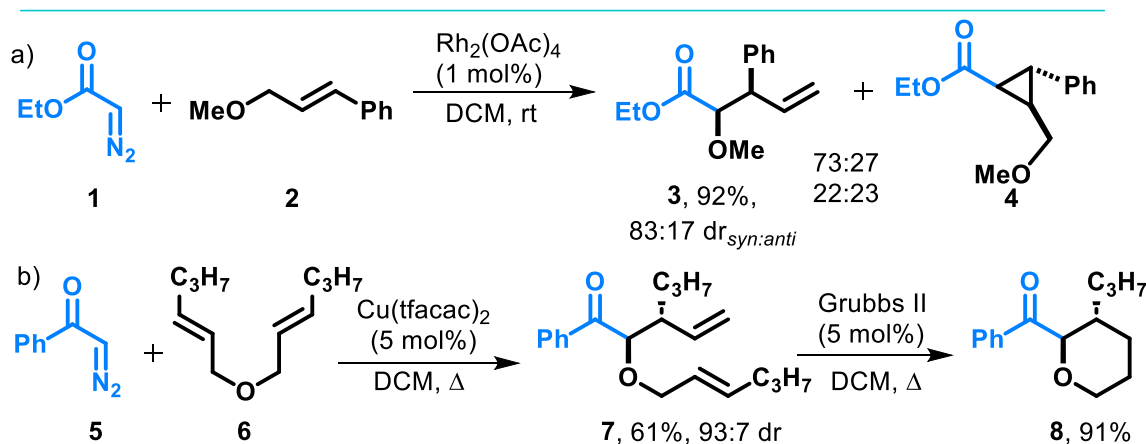
The ability of carbenes and carbenoids to form ylides with Lewis bases (B:), including ethers, sulfides, amines, and carbonyls, has played a pivotal role in advancing the use of diazocarbonyl compounds as synthetic precursors.¹⁸ Beyond straightforward heteroatom-H insertions, the ylides produced during carbene-transfer reactions can participate in [2,3]-sigmatropic rearrangements, [1,2]-shifts¹⁹ (Stevens rearrangement), and other related transformations. Achieving selective formation of the desired [2,3]-sigmatropic rearranged product is crucial, as it represents a significant synthetic advancement by enabling the creation of C–C or C–heteroatom bonds in a single step (Scheme 1.6). However, generating an oxonium ylide is particularly challenging due to its inherent instability, making it more difficult than the stabilization typically seen in *N* or *S*-substituted ylides.²⁰ Catalysts based on rhodium and copper are the most commonly utilized, though iron, cobalt, ruthenium, silver, platinum, and gold complexes have also been employed. Metal carbenoid species can react directly with allylic ethers, to form the corresponding allylic onium ylides, which can subsequently undergo the desired [2,3]-rearrangement (Scheme 1.6).



Scheme 1.6. Onium Ylides Generated from Metal Carbenoids and Subsequent [2,3]-Rearrangement

1.5.2.A Intermolecular Oxonium Ylide Formation and [2,3]-Rearrangement

Doyle and coworkers were the first to report the diastereoselective [2,3]-rearrangement of oxonium ylides resulting from the reaction between catalytically generated rhodium carbenoids and allylic ethers.²¹ For instance, the dropwise addition of ethyl diazoacetate **1** to a solution of $\text{Rh}_2(\text{OAc})_4$ (1 mol %) and allylic ether **2** selectively afforded the [2,3]-rearrangement product **3** in excellent yields with good diastereoselectivity (92% yield; 83:17 diastereomeric ratio - *syn:anti*). However, the competitive cyclopropanation leading to the formation of compound **4** was also observed (Scheme 1.7a). This reaction was effective for both diazoacetates and diazoacetophenones, as well as a limited variety of substituted allylic ethers, with the consistent preference for [2,3]-rearrangement over cyclopropanation in all instances.



Scheme 1.7. Diastereoselective intermolecular oxonium ylide formation and [2,3]-rearrangement of diazo compounds.

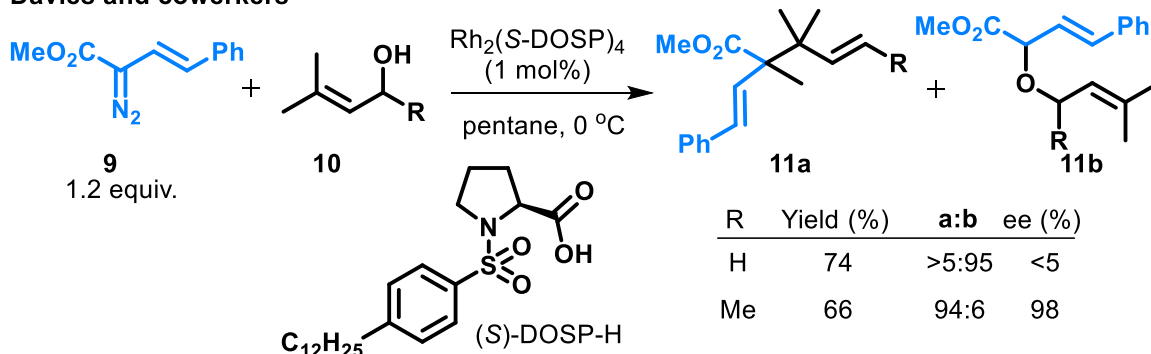
Njardarson and co-workers demonstrated that copper carbenoids, formed via diazo acetophenone **5** decompositions, further undergo oxonium ylide formation followed by [2,3]-rearrangement with various substituted allylic ethers.²² For instance, the reaction with symmetrical allylic ether **6** furnished the compound **7** in moderate yield with very high diastereoselectivity (Scheme 1.7b). Further transformation of compound **7** through ring-closing metathesis, utilizing the Grubbs II catalyst, efficiently afforded the pyran derivative **8** (Scheme 1.7b).

In 2009, Davies and co-workers disclosed a highly enantioselective process for oxonium ylide generation followed by [2,3]-rearrangement of racemic allylic alcohols using acyclic vinyl (donor–acceptor) diazo compounds in the presence of chiral rhodium catalyst (Scheme 1.8a).²³ The substitution pattern of the allylic alcohol plays a crucial role in determining the chemoselectivity of the reaction. For instance, when diazo compound **9** was reacted with primary allylic alcohol **10**, the O–H insertion product **11a** was formed exclusively. In contrast,

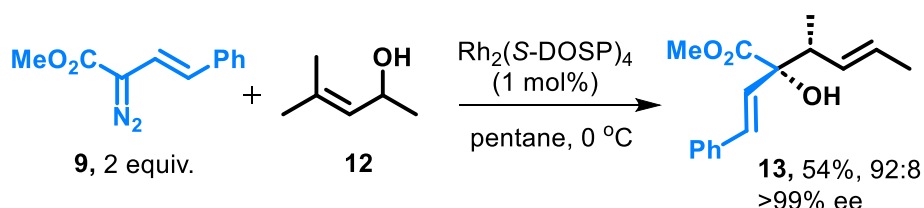
the reaction with secondary allylic alcohol **10** predominantly afforded the [2,3]-rearrangement product **11b**, with good yield and excellent enantioselectivity (Scheme 1.8a). This trend was consistent across various substrates, where substituted secondary and tertiary allylic alcohols produced [2,3]-rearrangement products with high chemo- and enantio-selectivity.

a) Enantioselective [2,3]-Rearrangement Reactions Using Racemic Allylic Alcohol

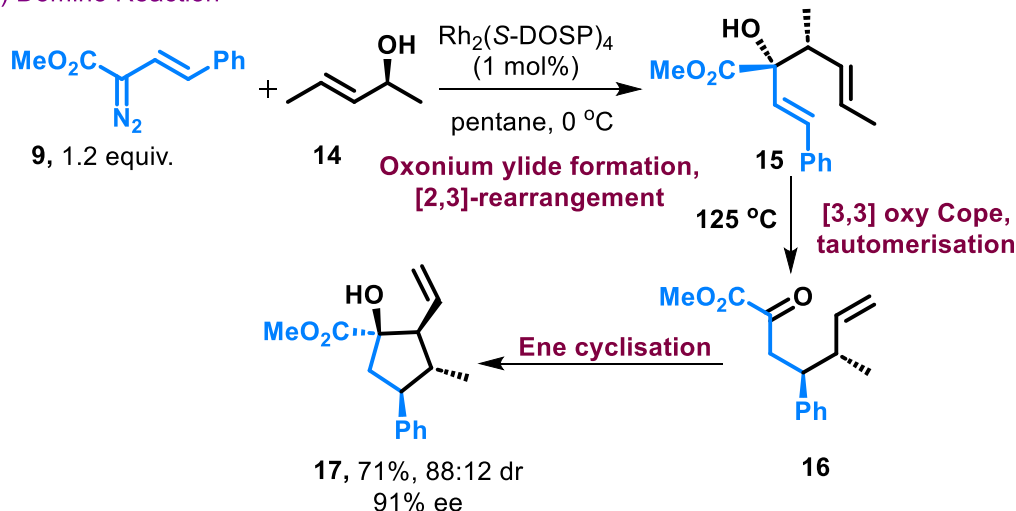
Davies and coworkers



b) Stereospecific [2,3]-Rearrangement of Allylic Alcohols



c) Domino Reaction



Scheme 1.8. Enantioselective and stereospecific [2,3]-sigmatropic rearrangement of diazo compounds

This method was expanded to enable the enantioselective synthesis of products with two vicinal stereocenters²⁴ The reaction is stereospecific, depending on the geometry of the allylic alcohol. The compound (*E*)-**12** reacted with diazo compound **9** to furnish the product **13** (Scheme 1.8b). Further, Davies and co-workers developed a methodology to synthesize highly functionalized

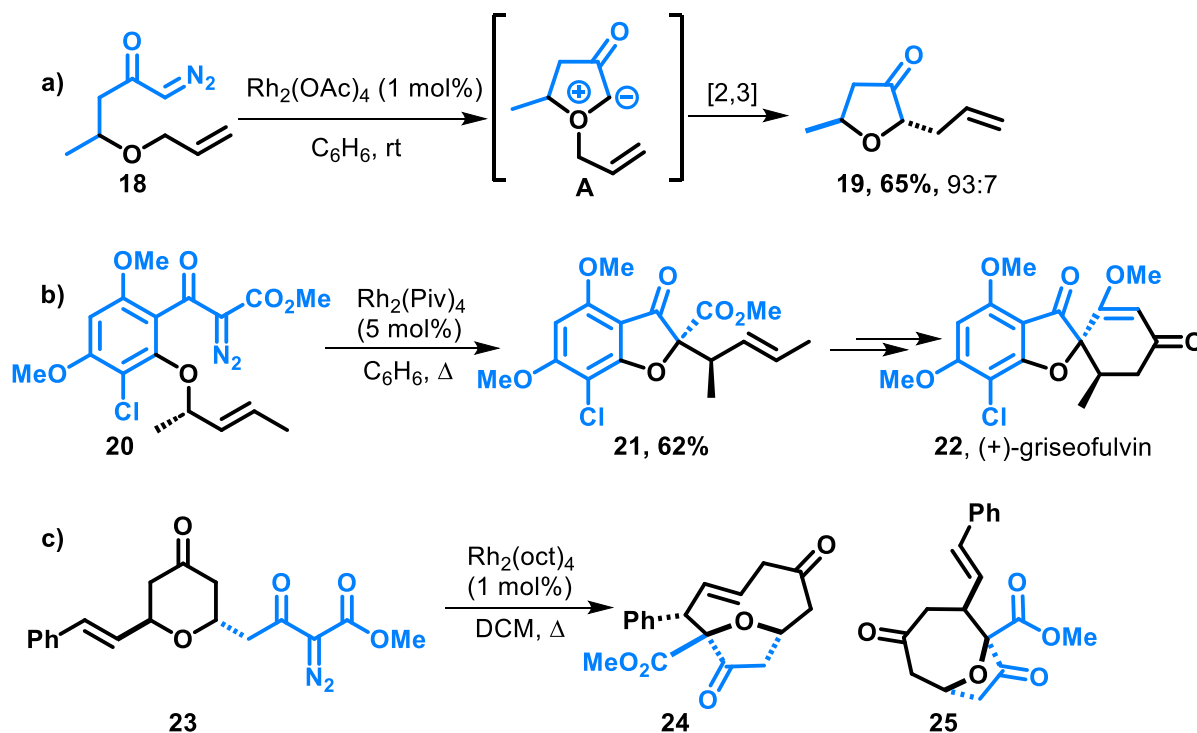
cyclopentane through a domino reaction sequence (Scheme 1.8c).²⁵ Starting with α -alkenyl diazo compounds **9** and allylic alcohols **14** in the presence of a chiral rhodium catalyst,^{25a} the reaction proceeded via oxonium ylide to achieve enantioselective [2,3]-rearrangement product **15**. Subsequent heating triggered an oxy-Cope rearrangement to form **16**, tautomerization, and intramolecular ene cyclization, giving cyclopentanes **17** with four contiguous stereocenters and excellent diastereo- and enantio-selectivity. Utilizing enantiomerically pure allylic alcohols further enhanced enantioselectivity, and the process proved to be effective across various substituted allylic alcohols.

1.5.2.B Intramolecular Oxonium Ylide Formation and [2,3]-Rearrangement

The intramolecular formation and subsequent [2,3]-rearrangement of oxonium ylides derived from diazo compounds provides an effective and potentially stereoselective method for producing a range of highly functionalized oxocyclic compounds. The versatility of these [2,3]-rearrangement products has been extensively showcased by synthesizing various intricate natural products. In 1986, Johnson²⁶ and Pirrung²⁷ independently presented the first instances of diastereoselective catalytic formation and [2,3]-rearrangement of oxonium ylides (Scheme 1.9). Allyloxy-substituted diazo ketone **18** was treated with Rh₂(OAc)₄ (1 mol%), generating the oxonium ylide **A** in situ, which subsequently underwent an intramolecular [2,3]-rearrangement to afford furanone **19** in moderate yield with an impressive diastereomeric ratio (65%, 93:7*anti:syn*), Scheme 1.9a. Notably, these allyloxy diazo ketones displayed excellent chemoselectivity for [2,3]-rearrangement over the alternative [1,2]-rearrangement under the given reaction conditions. Pirrung and his team explored the rhodium catalysis to generate the oxonium ylide-driven [2,3]-rearrangement to achieve the first enantioselective total synthesis of antifungal (+)-griseofulvin **22** (Scheme 1.9b).²⁸ A key step involved the diastereoselective [2,3]-rearrangement of oxonium ylide from enantiomerically pure diazo ketone **20**, using Rh₂(Piv)₄ (5 mol%) to generate the compound **21** as a single stereoisomer (62% Scheme 1.9b). Doyle and his team observed that diazoacetate-substituted tetrahydropyran-4-one **23** exhibited competing [1,2]- and [2,3]-rearrangements via intramolecular oxonium ylide and subsequent rearrangement under rhodium catalysis (Scheme 1.9c).²⁹ The lack of selectivity for the rearrangement products **24** and **25**, irrespective of catalyst structure, pointed to a metal-free ylide pathway. The moderate diastereoselectivity observed was also attributed to the axial-equatorial conformational isomer distribution of the diazoacetate reactant.

Currently, transition-metal-catalyzed reactions involving diazo compounds are of significant interest due to their excellent selectivity. Transition metals are generally expensive and

environmentally hazardous, and their removal is often challenging, presenting a significant concern for the pharmaceutical industry. At the same time, recent advancements in synthetic organic photochemistry have reignited interest in exploring the photochemical properties of diazo compounds. Some of the selected photochemical reactivity of diazo compounds has been presented in the next section.



Scheme 1.9. Intramolecular [2,3]-sigmatropic rearrangement of diazo compounds

1.6. Photochemical Reactivity of Diazo Compounds

Over the years, thermal processes have been extensively studied, whereas the photochemistry of diazo compounds, explored primarily several decades ago, has received comparatively little attention due to its limited selectivity.³⁰ Until recently, contemporary applications were relatively limited. Within physical organic chemistry, photolysis is an essential method for studying denitrogenation reactions of diazo compounds. Consequently, photolysis has significantly contributed to the development of modern carbene chemistry. Platz and co-workers³¹ conducted extensive research on the ultrafast photolysis of diazo compounds to generate the carbenes and their subsequent reactions such as cyclopropanation.^{31d} They discovered that a singlet carbene is directly formed from the excited state of a diazo precursor. They also investigated the solvation dynamics of singlet carbene, observing that its initial absorbance depends on the solvent and is red-shifted in coordinating solvents like alcohols, suggesting hydrogen bond formation. However, generating carbenes from diazo compounds

required high-energy UV irradiation, often using xenon or mercury lamps with filters or monochromators. Since most organic molecules absorb UV light, this caused competitive excitation of various compounds, including solvents, leading to undesired side reactions thus limiting their wider synthetic applications.

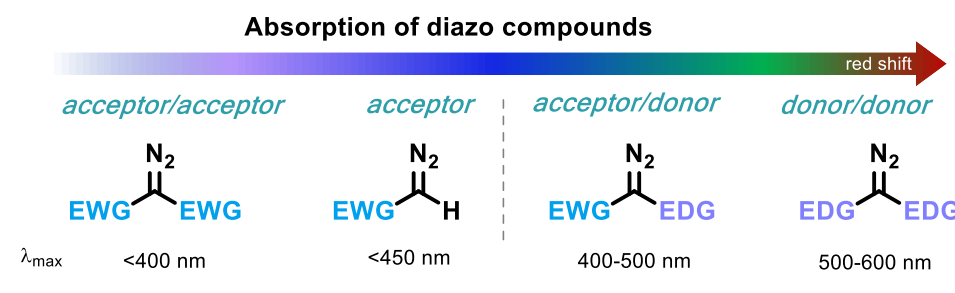


Figure 1.4: Absorption of different diazo compounds

Recently, visible light has gained immense popularity in organic synthesis, emerging as a powerful alternative tool for facilitating diverse chemical transformations. Due to their structural diversity, diazoalkanes can undergo direct photolysis or be activated through photocatalytic processes using visible light. Diazo compounds are frequently coloured molecules, with their absorption properties significantly influenced by the substituents on the carbon carrying the diazo functional group. Interestingly, donor groups, such as aryl rings, often cause a bathochromic shift in the absorption band. As a result, donor-acceptor diazo compounds, like aryl diazoacetates, display strong absorption in the visible light spectrum (Figure 1.4).

The spin state of carbenes plays a crucial role in their reactivity. Typically, diazo compounds undergo photoexcitation under light irradiation, leading to singlet or triplet carbenes (Figure 1.5).³² In one pathway, photolysis of the excited diazo compound generates a singlet carbene, where two nonbonding electrons with antiparallel spins occupy a single hybridized orbital, leaving an empty *p*-orbital. Singlet carbenes exhibit dual reactivity, functioning as electrophiles or nucleophiles depending on the properties of adjacent groups. This reactivity enables diverse transformations such as C-H and X-H insertion reactions and stereospecific additions to alkenes. Triplet carbenes are typically generated via energy transfer from a photosensitizer. Unlike singlet carbenes, they possess nonbonding electrons with parallel spins in separate orbitals, making them effectively diradicals. As a result, they commonly participate in hydrogen atom abstraction or non-stereospecific alkene addition.

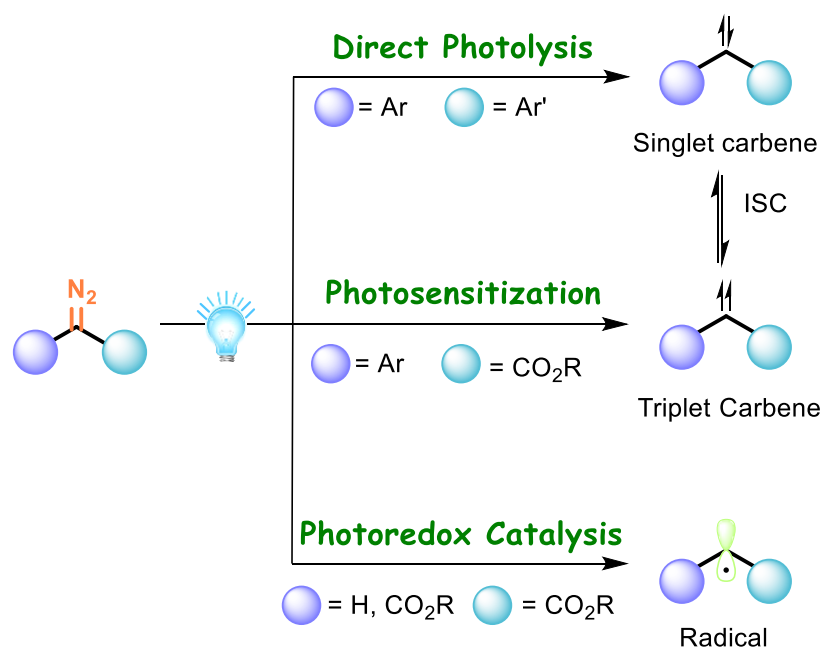
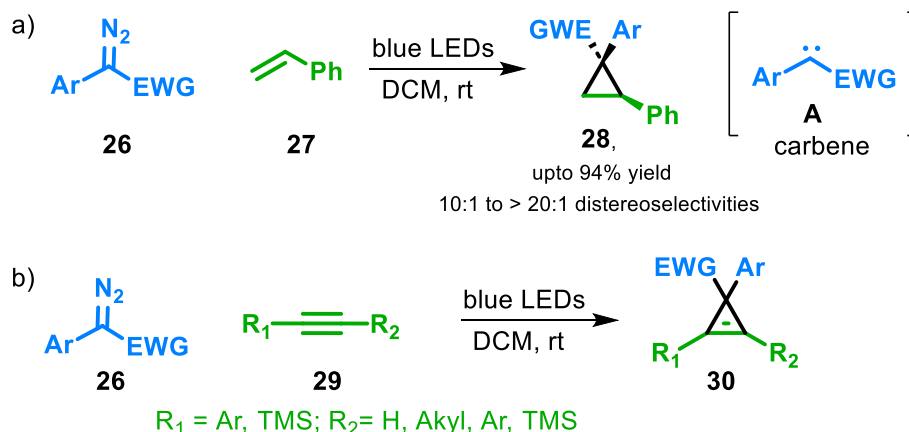


Figure 1.5: Possible Reaction Pathways of Diazo Compounds under Light Irradiation

Diazo compounds that absorb only in the UV region can still undergo transformation under visible light with an appropriate photocatalyst. Photoredox catalysis expands their reactivity, enabling diverse radical transformations. Notably, Gryko and coworkers³³ and Meggers and co-workers³⁴ separately demonstrated using diazo compounds as radical precursors rather than carbene sources. These catalytic methods offer key advantages of photochemical reactions, including using an environmentally friendly, clean energy source under exceptionally mild reaction conditions. Using organic dyes as photocatalysts addresses the major issues associated with expensive and toxic transition metals. These innovations have greatly enhanced the scope for visible-light-driven reactions involving diazo compounds.³⁵

1.6.1 Non-catalyzed photoreactions of diazo compounds

Cyclopropanation is one of the most significant reactions involving diazo compounds. Davies and Jurberg's pioneering work on visible light-induced carbene generation from aryl diazoacetates highlights the easy access of cyclopropane derivatives (Scheme 1.10a).³⁶ Notably, the reaction proceeds efficiently at room temperature, in air, and without an anhydrous condition. Unsubstituted styrene **27** afforded the cyclopropanes **28** efficiently in excellent diastereoselectivity (Scheme 1.10a).

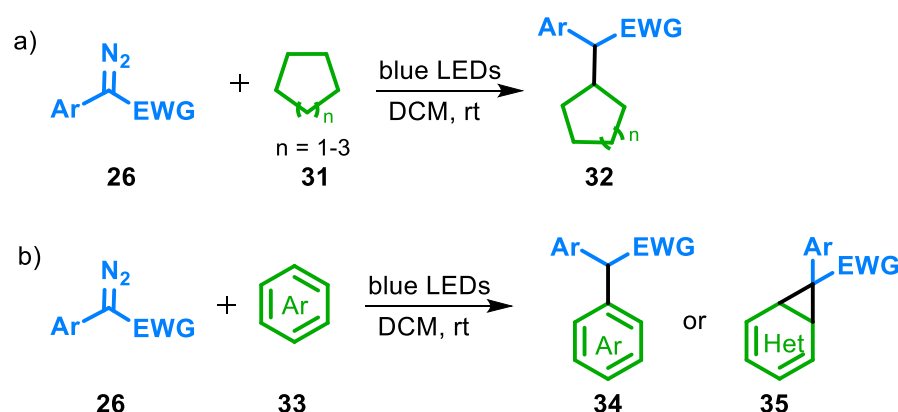


Scheme 1.10: Visible light-mediated [2+1]- cycloaddition reaction of diazo compounds

The photolytic method has been successfully employed for the efficient synthesis of cyclopropanes **30** from alkynes **29** (Scheme 1.10b).³⁷ The use of aryl diazoacetates **26** effectively minimized the side reactions. Additionally, a common challenge with the scaling of photochemical reactions was resolved by conducting the process in a continuous flow setup.

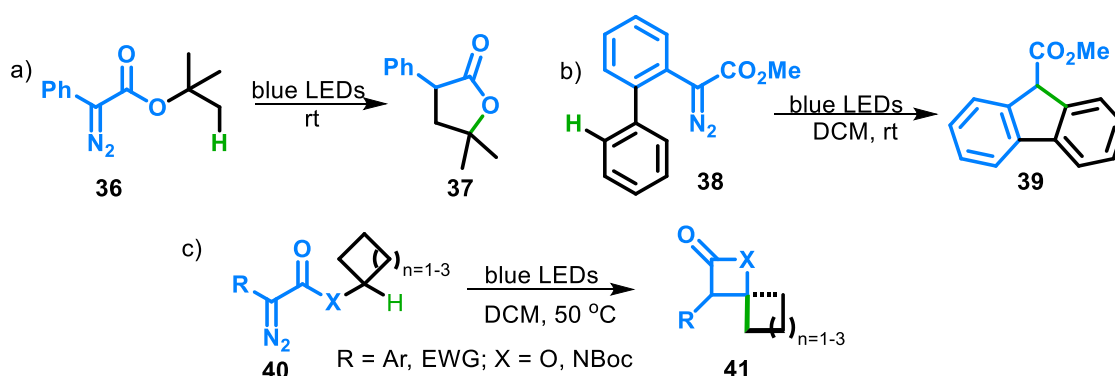
C–H Insertion Reactions

C–H carbene insertion reactions exemplify an innovative approach to chemistry, offering an efficient way to construct new C–C and C–heteroatom bonds with outstanding atom economy. Over the years, research on light-induced reactions of diazo compounds has led to numerous C–H insertion reactions (Scheme 1.11).^{36,38} Formal C–H insertion has emerged as one of the significant strategies for the C–C bond-forming reactions. However, photochemical processes extend beyond merely generating carbenes from diazo compounds, unlocking a diverse range of transformative applications.



Scheme 1.11: Visible light-mediated intermolecular C-H insertion reaction of diazo compounds

Reactions involving cycloalkanes are typically carried out under neat conditions or with a significant excess of the substrate to compensate for their low reactivity. The same study revealed that the C-H insertion reaction of diazo **36** proceeded intramolecularly with C(sp³)-H bond to afford the corresponding 5-membered lactone **37** (Scheme 1.12a). Subsequently, Sun and co-workers expanded this intramolecular approach of the diazo **38** to C(sp²)-H bonds, facilitating the synthesis of fluorene derivatives **39** (Scheme 1.12b).³⁹ Hari and coworkers recently disclosed an effective synthesis of diverse spiro-β-lactones and lactams **41** through this photochemical method (Scheme 1.12c).⁴⁰



Scheme 1.12: Visible light-mediated intramolecular C-H insertion reaction of diazo compounds

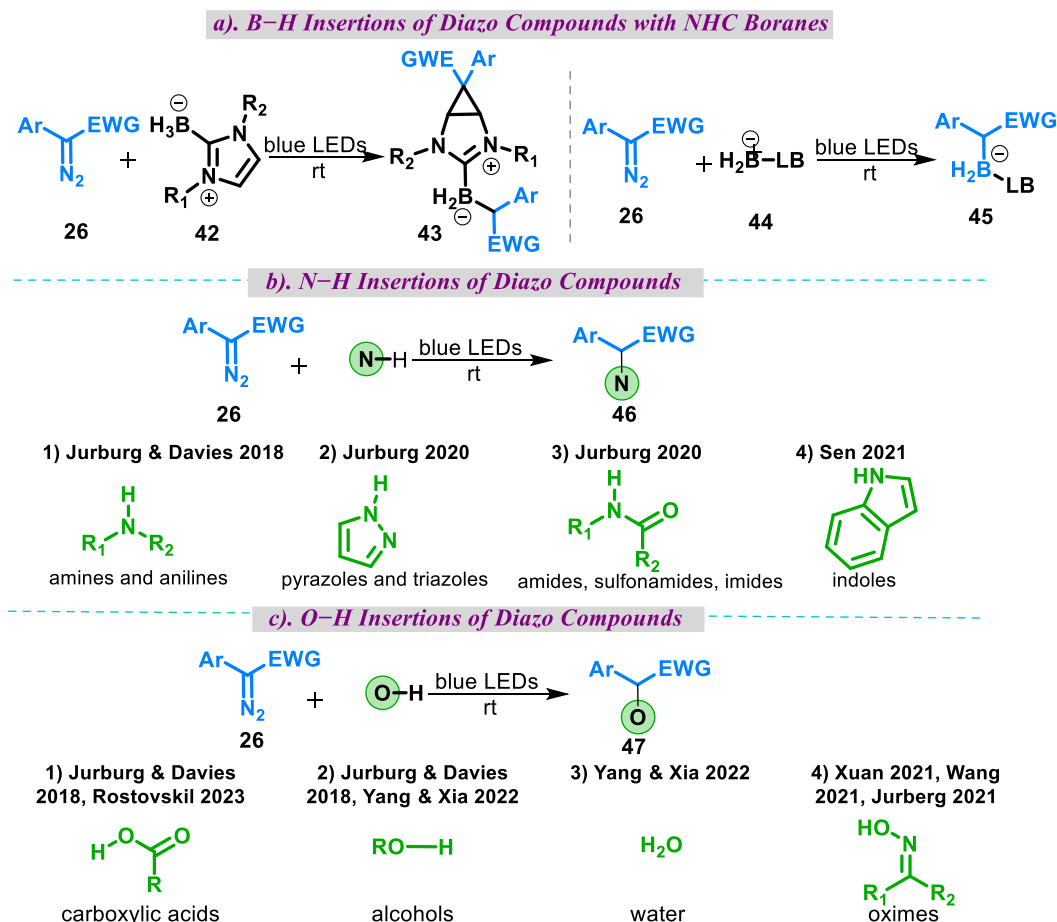
X-H Insertion

Carbene-mediated X-H (X = B, N, O, Si, S) insertion is a powerful approach for forming a wide variety of C-X (heteroatom) bonds. Under photolytic conditions, free carbenes formed from diazo compounds can either engage in nucleophilic interactions with various heteroatoms, followed by protonation, or participate in a concerted reaction pathway.

In the study by Koenigs and Xuan⁴¹ on the cyclopropanation of NHC-boranes using aryl diazoacetates **26**, it was observed that substitutions prevented cyclopropanation at the imidazole site and resulted in B-H insertion products **43** (Scheme 1.13a). Notably, cyclopropanation and B-H insertion can occur simultaneously when both reaction sites on NHC-boranes are available. Other Lewis base-borane complexes **44** also showed efficient reactivity with diazoacetate **26** in this reaction.

In the study conducted by Jurberg and Davies,³⁶ N-H insertion of amines and anilines into aryl diazoacetates **26** was successfully achieved under blue light irradiation (Scheme 1.13b). This approach furnished various N-alkylated products **46** with remarkable efficiency. Looking into

these research findings, several research groups have further developed and refined this photochemical method for synthesizing C–N bonds.^{42–44}



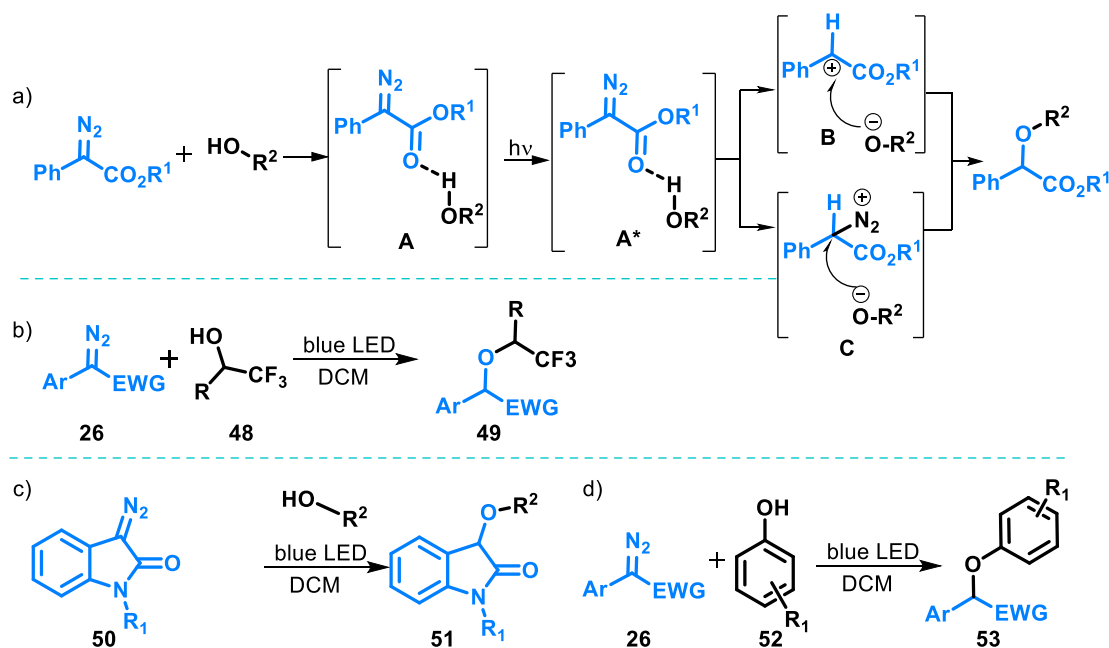
Scheme 1.13: Visible light-mediated C–X insertion reaction of diazo compounds

In 2018, Jurberg and Davies³⁶ demonstrated the efficient O–H insertion of carboxylic acids and alcohols with aryl diazoacetates **26** under blue light irradiation (Scheme 1.13c-1). This method also provided a practical approach for synthesizing trisubstituted hydroxylamines. Furthermore, Yang, Zhou, Huo, and their co-workers disclosed that 2-hydroxypyridines generated in situ from 2-pyridones could participate in O–H insertion reactions. Experiments revealed that reactions with relatively stronger carboxylic acids could proceed in the absence of light, likely involving protonation of the diazo compounds followed by the extrusion of dinitrogen (N_2). Later, Rostovskii and co-workers utilized carboxylic acids containing an azirine group to synthesize corresponding esters. They observed that the photochemically generated free carbenes selectively reacted with the carboxyl group rather than the azirine ring⁴⁵ (Scheme 1.13c-1).

In 2022, Yang and Xia⁴⁶ expanded the scope of alcohols used in these reactions. The same study employed water for O–H insertions to synthesize α -hydroxy esters (Scheme 1.13c-2,3). Independently, Xuan,⁴⁷ Wang,⁴⁸ and Jurberg's⁴⁹ research groups developed the use of oximes in photochemical O–H insertion reactions involving aryl diazoacetates (Scheme 1.13c-4).

Formal O–H Insertions

As previously discussed, light irradiation enables diverse mechanistic pathways to create products unachievable through other traditional transformations. One notable example is the photoexcited proton transfer (PPT) reaction, a ground-breaking strategy developed in recent years. Koenigs and co-workers applied this approach to achieve O–H functionalization of diazo compounds with unreactive and weakly acidic alcohols⁵⁰ (Scheme 1.14). The reaction was proposed to begin with the photoexcitation of complex **A**, which is formed through hydrogen bonding between the diazo compound and alcohol (Scheme 1.14a). Upon photoexcitation, a proton from the O–H group is transferred into the carbon of the diazo group, resulting in ion pair **C** that eventually reacts with a nucleophile to afford the desired products.



Scheme 1.14: Photoexcited Proton Transfer Reactions for O–H Formal Insertions into Diazo Compounds

The pioneering research in this field by Koenigs and colleagues focused on the reaction between Acceptor-Donor type diazo compounds **26** and fluorinated alcohols **48**, which also demonstrated effectiveness with chlorinated and brominated alcohols (Scheme 1.14b).⁵⁰ Additionally, the method was successfully applied to cyclic diazo amides **50** (Scheme 1.14c).⁵¹ This transformation enabled the synthesis of various halogenated ethers, predominantly

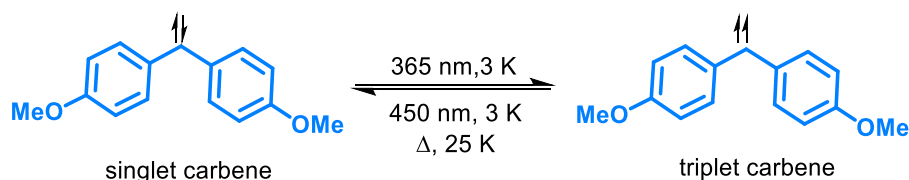
fluorinated ones, with high to excellent yields. Notably, attempts to replicate the reaction in the dark (absence of light) using Cu and Rh catalysts (for generating metal carbene species) did not afford the desired products.

Phenols **52** and a wide range of acceptor-donor type diazo **26** compounds reacted smoothly under photochemical conditions to afford the corresponding selective OH-inserted products **53** (Scheme 1.14d).⁵² The phenols bearing electron-withdrawing groups at the *meta* position gave higher yields, thus highlighting the importance of two key factors: the acidity of phenol and the strength of hydrogen bonding between substrates.

1.6.2 Photocatalyzed reactions of the diazo compound

1.6.2.A: Diazo Compounds as Triplet Carbene Precursors

Compared to the well-studied transformations via singlet carbenes, reactions involving triplet carbenes remain relatively underexplored.⁵³ Direct photolysis of diazo compounds can generate triplet carbenes, but singlet carbenes are more common since nitrogen extrusion usually happens faster than intersystem crossing (ISC). The spin state and energy gap between singlet and triplet carbenes depend on their substituents. The spin state can be controlled by adjusting these groups, such as using donor–donor diazo compounds with tunable aryl rings.

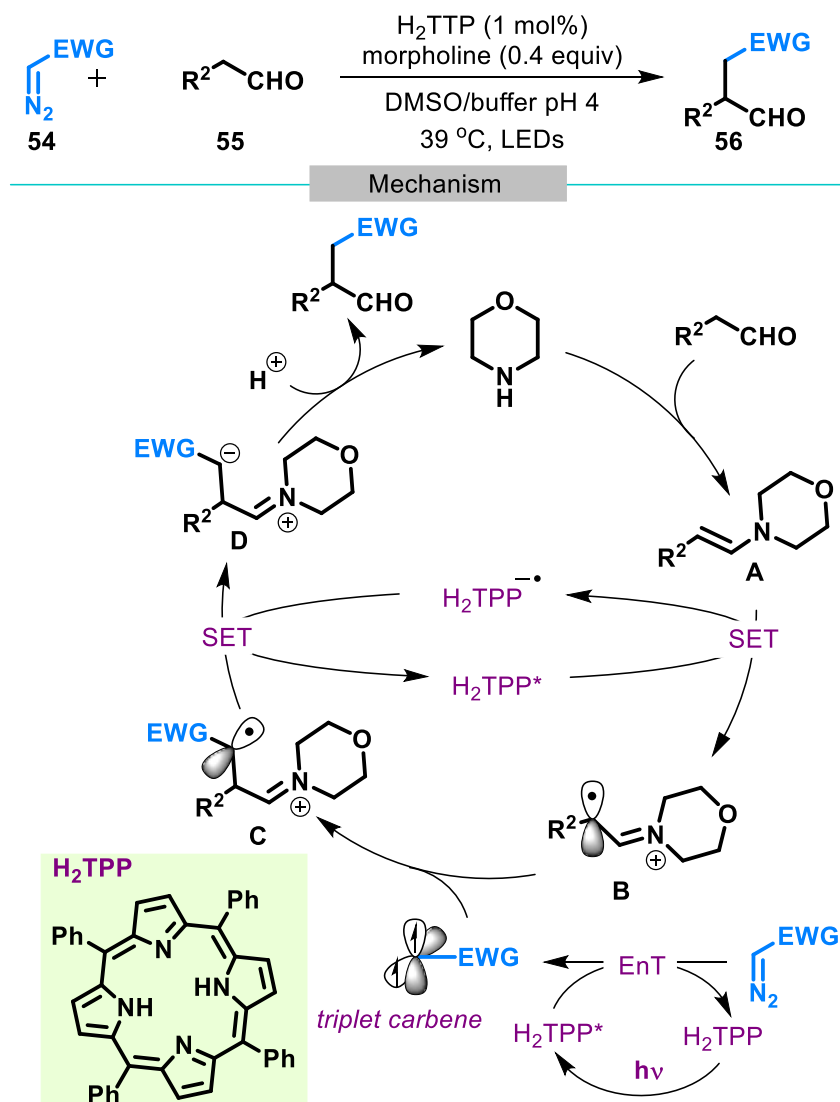


Scheme 1.15: Spin State of Bis(4-methoxyphenyl)carbene

Diphenyl carbene favors the triplet state over the singlet state by 4 kcal/mol.⁵⁴ In contrast, the energy difference between the singlet and triplet states of the electron-rich bis(4-methoxyphenyl)carbene is minimal, with the singlet state being only 0.3 kcal/mol more stable, as reported by Sander and co-workers.⁵⁵ They demonstrated that the spin state of bis(4-methoxyphenyl)carbene can be reversibly toggled between singlet and triplet states by employing different wavelengths (Scheme 1.15).

Another effective method has been reported to generate triplet carbenes through the denitrogenative decomposition of diazo compounds facilitated by energy transfer using a photosensitizer. A photosensitizer allows for the mild and efficient activation of diazo compounds that do not sufficiently absorb visible light. In 2016, Zawada, Kadish, and Gryko's research groups introduced a photosensitized method for directly α -alkylation of aldehydes **56**

using diazo compounds **54** (Scheme 1.16).⁵⁶ This transformation involved acceptor-type diazo compounds undergoing energy transfer reaction with a free base tetraphenyl porphyrin (H_2TPP) catalyst to generate triplet carbenes.



Scheme 1.16: Generation of Triplet Carbene via Energy Transfer

The reaction is believed to start with the photoexcitation of H_2TPP from its singlet ground state to an excited state. Energy transfer from the catalyst to diazoacetates generate triplet carbenes, accompanied by the elimination of dinitrogen. In the organocatalytic cycle, enamine intermediate (**A**) formed from aldehyde in the presence of an amine catalyst further interacts with the photoexcited H_2TPP . This leads to the oxidization of enamine **A** and forms the porphyrin radical anion along with an active cation radical (**B**). This cation radical **B** further reacts with the triplet carbene to form a radical intermediate **C**. A subsequent single electron transfer (SET) from the porphyrin radical anion ($H_2TPP^{\cdot-}$) and protonation furnishes the

alkylated product **56**. Importantly, the porphyrin acts as both a photoredox catalyst and a photosensitizer in this process, though chain propagation mechanisms may also play a role.⁵⁷

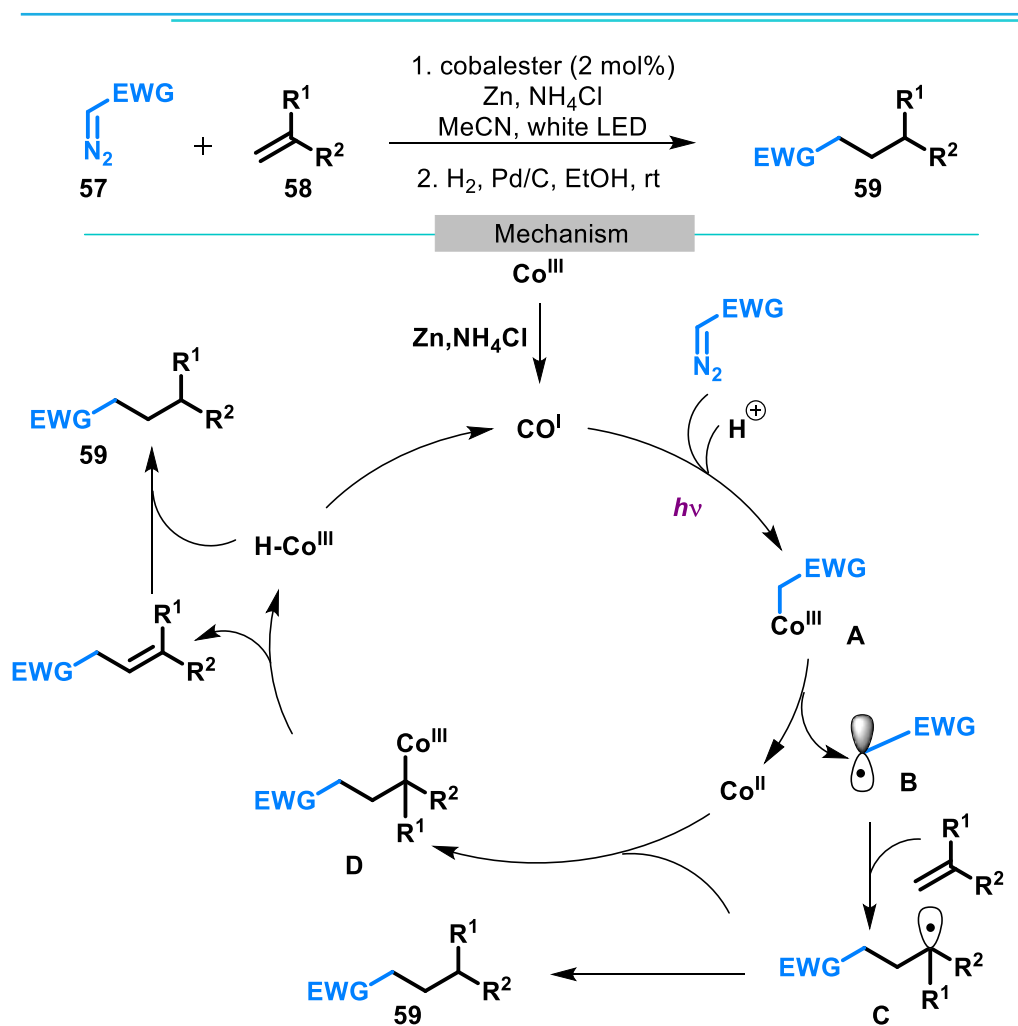
1.6.2.B: Diazo compounds as alkyl or vinyl radical precursors

Diazo compounds are traditional carbene precursors, but radical reactions with them have been less studied. Recent advances in photocatalysis,⁵⁸⁻⁶⁰ transition metal catalysis,^{61,62} and visible-light activation have revealed novel radical reactivities of diazo compounds. These methods enabled the single electron transfer, followed by nitrogen extrusion and protonation, forming radical intermediates. Acceptor-type diazo compounds, such as α -diazo esters, are frequently utilized in these processes, likely due to their restricted absorption in the visible light spectrum, which reduces their susceptibility to decompose or undergo side reactions. The generated radicals can undergo diverse transformations, including additions to alkenes or heteroarenes and recombination with other radical species. These advancements have greatly broadened the synthetic applications of diazo compounds, unlocking newer possibilities in organic synthesis.

Radical Addition to Alkenes

In 2016, Gryko and co-workers developed a cobalt-ester-catalyzed method under white LEDs for generating alkyl radicals from diazoacetates **57**, enabling the alkylation of alkenes **59** (Scheme 1.17).⁶³ The alkyl radicals underwent an intermolecular Heck-type reaction, resulting in a mixture of Heck-type (oxidative) and Giese-type (reductive) products.

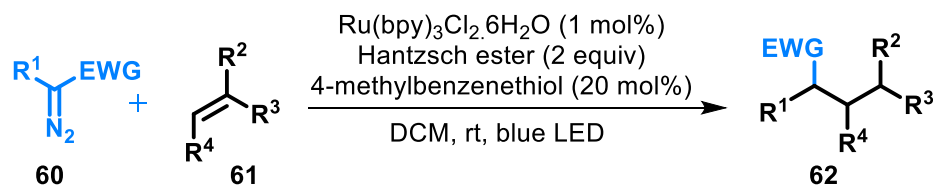
The proposed mechanism starts with reducing cobalt ester, generating the catalytically active Co(I) species. Alkyl-Co(III) intermediate **A** is formed when it reacts with diazo compounds. Subsequent homolytic cleavage of the Co–C bonds produces electrophilic radical **B**, which forms radical **C** upon addition to the electron-rich alkene. This radical can either recombine with Co(II) species or it can undergo proton abstraction, resulting in reduced products **59**. Dehydrocobaltation of intermediate **D** leads to the Heck-type product, while Giese-type products are formed through the reduction by hydridocobalt ester. In all the instances, the usual cobalt-catalyzed cyclopropanation was not observed, underscoring the essential role of visible light.



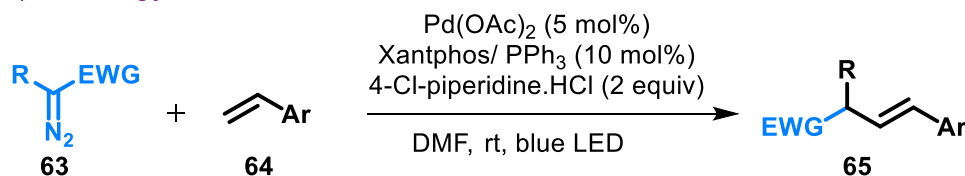
Scheme 1.17: Generation of Alkyl Radicals from Diazo Compounds via Cobalt Catalysis

In 2020, Qiu and Doyle's groups utilized diazo compounds **60** to generate primary and secondary alkyl radicals through the reductive proton-coupled electron transfer (PCET) facilitated by a Ru photocatalyst.⁶⁴ These C-centered radicals effectively reacted with aliphatic alkenes and styrene derivatives, enabling the synthesis of various anti-Markovnikov hydroalkylated products **62** (Scheme 1.18a). Later in 2022, Gevorgyan and co-workers demonstrated a photoinduced alkyl Heck reaction of diazo compounds involving hybrid alkyl-Pd radical species.⁶⁵ A wide variety of acceptor and donor-acceptor diazo compounds **63** effectively reacted with styrene derivatives **64**, resulting in the selective formation of allylic compounds **65** (Scheme 1.18b).

a). Qui & Doyle 2020



b). Gevorgyan 2022



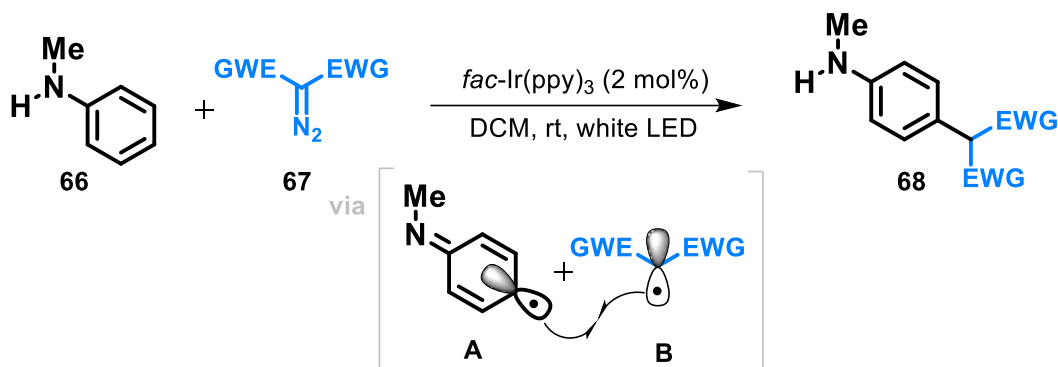
Scheme 1.18: Generation of Alkyl Radicals from Diazo Compounds

Radical–Radical Coupling

In addition to their involvement in radical additions to alkenes and heteroarenes, as previously mentioned, alkyl radicals derived from diazo compounds can also participate in radical–radical couplings. In 2022, Cho and co-workers developed a photocatalytic method for alkylating anilines using acceptor–acceptor type diazo compounds **67** (Scheme 1.19a).⁶⁶ This protocol did not significantly influence electronic effects, with both electron-deficient and electron-rich anilines reacting equally well to afford the products. The proposed mechanism involves radical recombination between persistent radical **A** and transient radical **B**, followed by rearomatization, resulting in *para*-C–C coupled aniline derivatives **68**. In the same year, Hu and Qiu developed a photocatalytic three-component reaction of secondary amines **69**, aldehydes **70**, and diazo compounds **57**, affording various γ -amino acid derivatives **71** in good yields (Scheme 1.19b).⁶⁷ This reaction forms an enamine in situ through the condensation of aldehyde and secondary amine, which are then oxidized by an excited photocatalyst to produce radical intermediate **C**. Radical recombination between intermediate **C** and a transient α -ester radical **D**, followed by reduction with a Hantzsch ester, affords the desired γ -amino acid derivatives **71**. Most recently, Hou and Li presented a photocatalytic strategy for synthesizing indole-fused tricyclic compounds **73** using diazo compounds **57** and *N*-phenylpiperidines **72** (Scheme 1.19c).⁶⁸ The mechanism involves recombining nucleophilic radical **E** and electrophilic radical **D**.

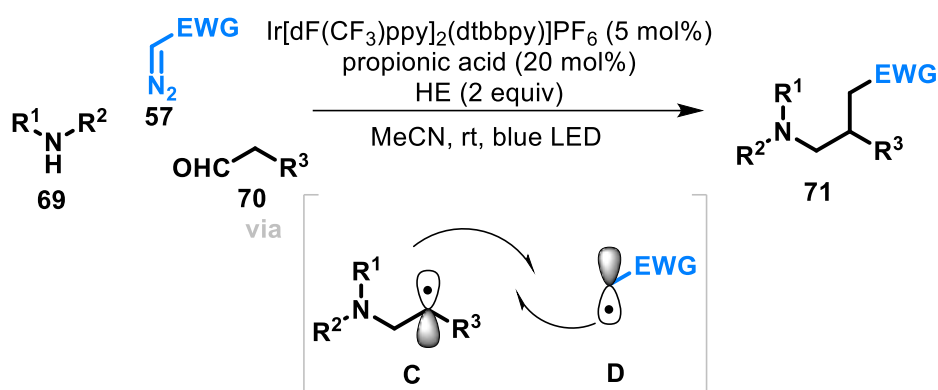
Cho 2022

a). Photocatalytic synthesis of γ -amino acid derivative



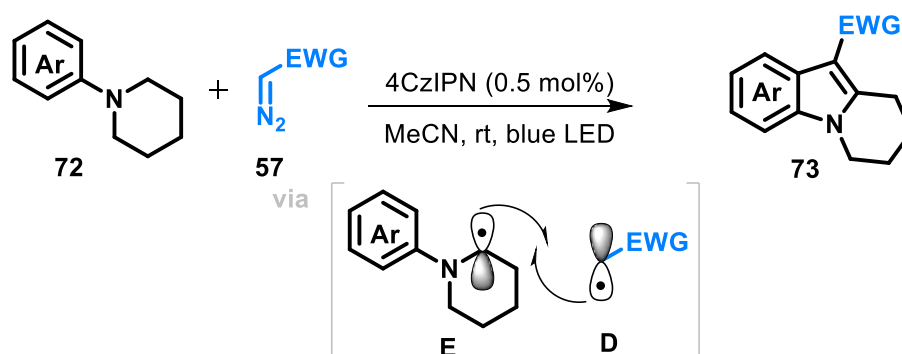
Hu & Qiu 2022

b). Photocatalytic alkylation of anilines



Hu & Li 2023

c). Photocatalytic synthesis of tricyclic compounds

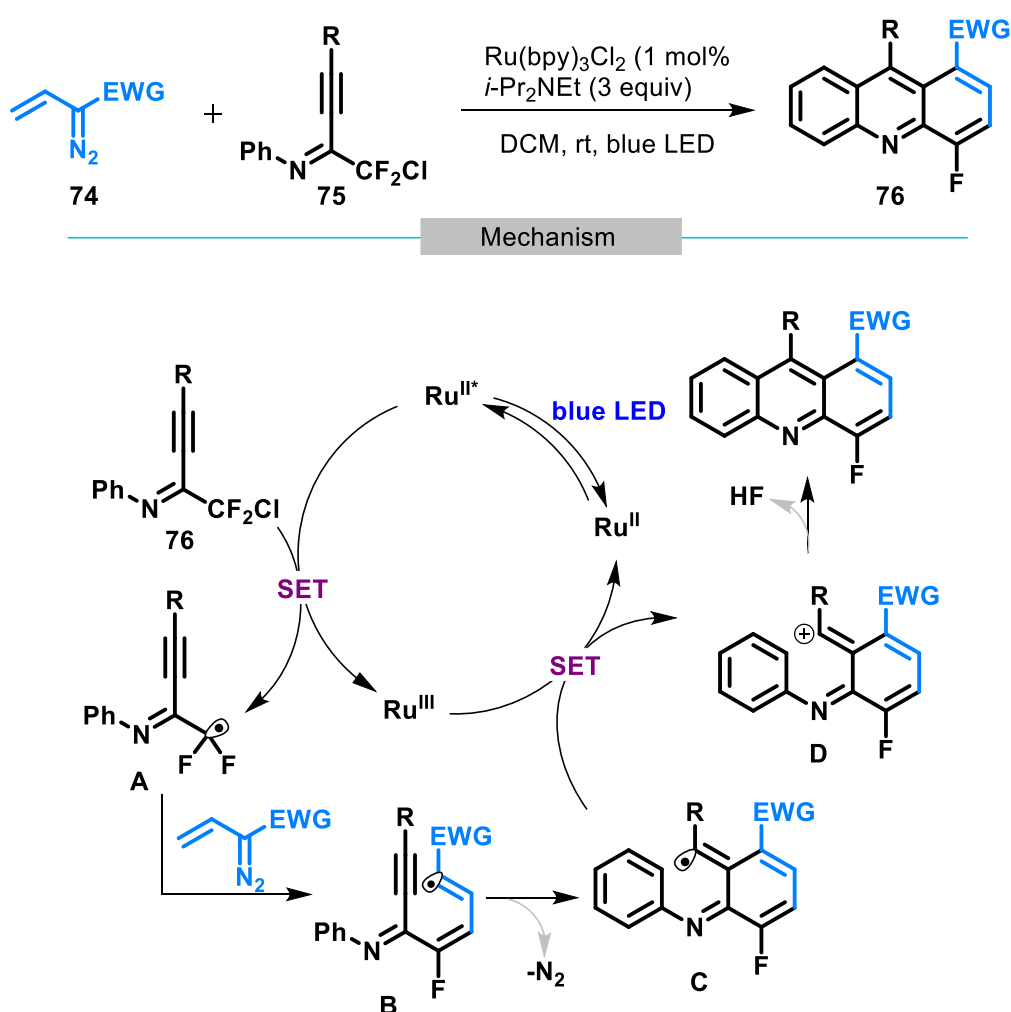


Scheme 1.19: Photocatalytic Transformations Involving Radical–Radical

Diazo compounds as radical acceptors

Diazo compounds can serve as radical acceptors, releasing dinitrogen to generate an additional free radical, which enables cascade transformations. In 2021, Zhou and co-workers employed vinyl diazo compounds **74** act as radical acceptors to synthesize the fluorinated acridines **76** through a cascade radical cyclization reaction (Scheme 1.20).⁶⁹ In this process,

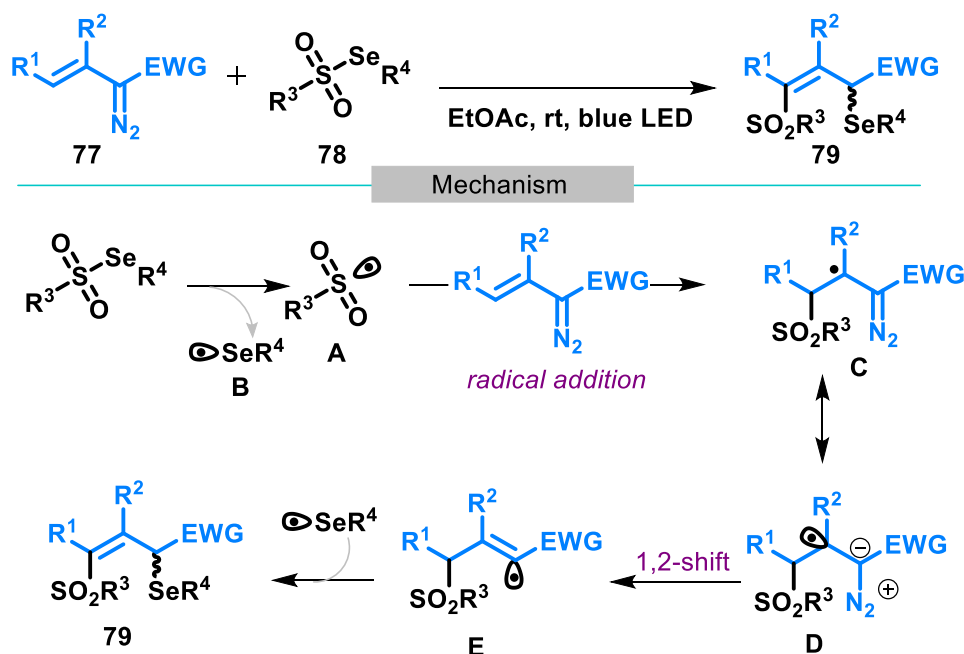
chlorodifluoromethyl alkynyl ketoimine **75** acts as a radical precursor. Upon single-electron reduction by a photoexcited Ru-complex, a difluoromethyl radical **A** is formed. The vinyl diazo compounds then trap this radical to generate vinyl radical **B**, which further undergoes intramolecular addition to the C–C triple bond of the ketoimine to generate the vinyl radical **C**. Intramolecular homolytic aromatic substitution (HAS) and subsequent oxidation produce vinyl cation **D**, which eliminates HF to form the desired final product: 4-fluoroacridine **76**. Ke and Zhou further reported an atom transfer radical addition (ATRA) reaction targeting fluorinated vinyl iodides and notably, this does not require any external photocatalysts or additives.⁷⁰



Scheme 1.20: Synthesis of 4-Fluoroacridines via Cascade Radical Cyclization

In subsequent studies, the same research group developed a photochemical 1,3-selenosulfonylation reaction utilizing vinyl diazo compounds **77** (Scheme 1.21).⁷¹ In this transformation, selenosulfonates **78** acted as radical precursors, facilitating the efficient synthesis of various γ -seleno allylic sulfones **79**. The proposed mechanism is believed to

proceed via the visible light-induced homolysis of the Se–S bond to generate sulfonyl radical intermediate **A** and selenyl radicals **B**. The electrophilic tosyl radical **A** then adds on to the C–C double bond of vinyl diazo compounds to form radical **C** (resonating structure **D**). A subsequent 1,2-radical shift and dinitrogen extrusion lead to the formation of vinyl radical **E**, which reacts with selenosulfonates **B** to produce the 1,3-selenosulfonylation product **79**.



Scheme 1.21: 1,3-Functionalization of Vinyl and Alkynyl Diazo Compounds

1.7. Conclusions

Metal catalysts and visible light irradiation profoundly influence the reactivity of diazo compounds, each enabling distinct reaction pathways. While metal catalysts traditionally drive carbene transfer reactions such as cyclopropanation and C–H insertion, the photochemical activation offers an alternative approach that expands the reaction landscape. Visible light excitation can bypass the conventional metal-catalysed reactions, emphasizing the unique mechanistic role of photoinduced transformations.

Beyond carbene chemistry, diazo compounds also exhibit radical reactivity under photochemical conditions. Photoexcitation or interaction with photosensitizers can generate radical species, facilitating unconventional bond formations and expanding their synthetic potential. The tunability of these processes through substituent effects allows controlled access to singlet or triplet carbenes and radical intermediates, offering new strategies for selective and efficient transformations. The synergy between metal catalysis, photochemistry, and radical

reactivity significantly broadens the utility of diazo compounds in modern synthetic organic chemistry.

1.8. Aim of the work:

My research has primarily focused on exploring the reactivity of diazo compounds and designing and developing metal-catalyzed and visible-light-mediated reactions of diazo compounds for constructing useful compounds. By exploring alternative and novel synthetic transformations under mild reaction conditions, practical alternatives to conventional methods have been developed. Some of the strategies depend on UV light, hazardous reagents, or stoichiometric amounts of toxic substances under elevated temperatures; the thesis has aimed to avoid these and use alternative, sustainable routes to access interesting scaffolds in an efficient manner.

Over the years, diazocarbonyl compounds have long been recognized as versatile synthetic precursors in various transition-metal-catalyzed transformations, including insertion reactions, cyclopropanation, and ylide formation, owing to their diverse electronic properties. However, expensive catalysts, harsh reaction conditions, and a limited substrate scope often hinder these approaches. Additionally, vinyl diazo compounds have emerged as crucial three-carbon synthons in cycloaddition reactions. Yet, their utility is often complicated by *Z/E*-configurational isomerism and the reactivity of substituents on the double bond, making stereospecific transformations particularly challenging.

To address some of these limitations, my research has focused on cyclic vinyl diazo compounds, specifically diazo aryldiene succinimide (DAS). Our research group has been working extensively on the chemistry of diazo compounds. We have recently reported metal-catalyzed transformations of DAS, including epoxidation, cycloaddition, and sigmatropic rearrangement with sulfur ylides. The structural advantages of DAS, particularly its cyclic framework, contribute to enhanced stability, controlled reactivity, stereoselectivity, and broad applicability in cycloaddition reactions. Furthermore, DAS exhibits unique and unprecedented activation modes due to the interplay between its diazo carbon and vinylogous terminus, making the reactivity of its metallo-vinyl carbene intermediates particularly challenging to control.

The distinct appeal of DAS lies in this delicate balance between stability and reactivity, which I have explored under both metal catalysis and visible-light activation.

In photochemical reactions, multiple reactive intermediates including singlet, triplet carbenes and radicals play a crucial role, making mechanistic predictions particularly complex. Despite these challenges, I have systematically investigated these transformations, analyzing the role of the photocatalyst at different reaction stages, identifying key intermediates, and rationalizing their reactivity. The ultimate goal of my doctoral research has been to design and *develop novel synthetic methodologies, expand the reaction scope, and establish efficient strategies for organic synthesis*. Importantly, many disclosed transformations are highly challenging and, in most cases, impossible to achieve through conventional non-photochemical methods. The development of novel synthetic strategies has addressed some challenges and limitations, which have been discussed in the subsequent chapters in detail.

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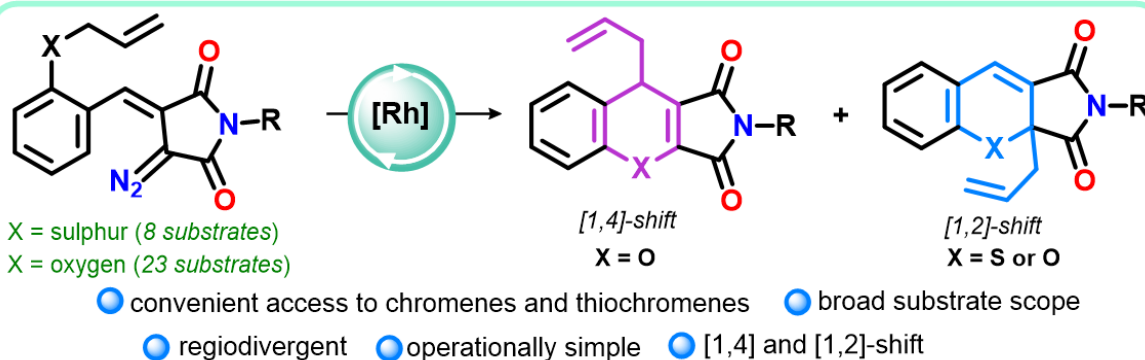
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Chapter 2

Intramolecular Sigmatropic Rearrangement of Diazoarylidene succinimides (DAS) via Rhodium Catalysis: An Access to Chromenes and Thiochromenes



Intramolecular Sigmatropic Rearrangement of DAS: Access to Chromenes & Thiochromenes

2

A dirhodium(II)-catalyzed regio-divergent rearrangement of oxonium and sulfonium ylides, derived from diazo arylidene succinimides (DAS), has been achieved under mild conditions. Strategically designed allyloxy and thioallyl-substituted DAS derivatives were synthesized to study their reactivity. The reaction is proposed to proceed through oxonium or sulfur ylide intermediates, undergoing [1,2]- or [1,4]-sigmatropic shifts to form chromene and thiochromene frameworks respectively. The protocol for the first time successfully explored the sigmatropic rearrangement for constructive bioactive chromene and thiochromene scaffolds at room temperature.

2.1 Introduction:

Chromenes, thiochromenes, and their analogs are highly versatile heterocyclic scaffolds widely present in many natural and synthetic bioactive compounds.¹ These frameworks exhibit diverse pharmacological properties, including anticancer, anti-HIV, anti-inflammatory, antioxidant, antitubercular, antiviral, antitumor, antibacterial, antimicrobial, antidiabetic, anticoagulant, diuretic, and fungicidal activities.² Several FDA-approved drugs, such as Tazarotene, Flupentixol, and Meticrane, feature these core structures, highlighting their clinical significance. Beyond these, chromenes and thiochromenes also play a crucial role in materials science. They serve as key components in laser dyes, organic light-emitting devices (OLEDs), optical brighteners, organic scintillators, triplet sensitizers, and fluorescence probes.³

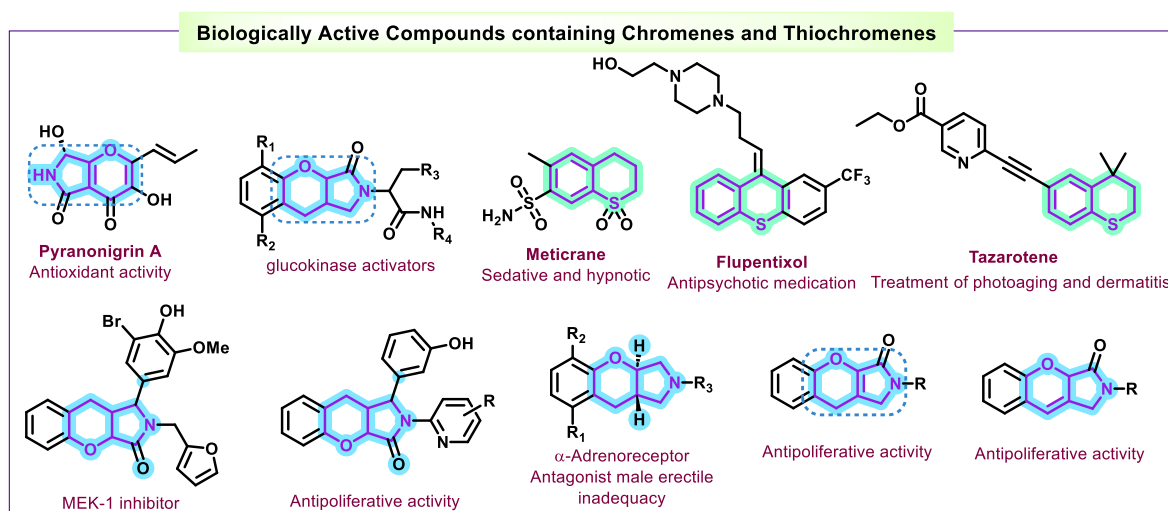
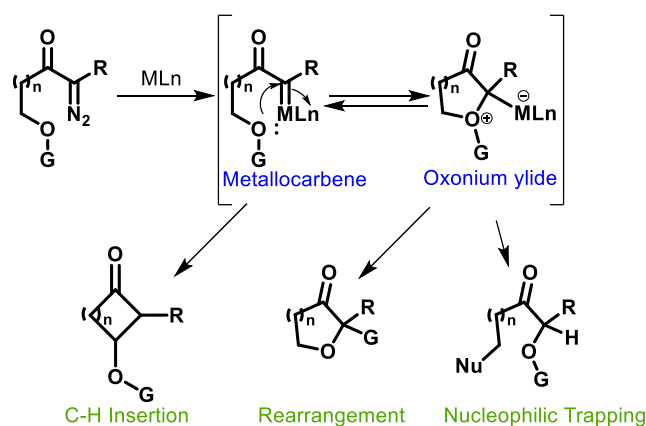


Figure 2.1: Selected examples of pharmaceutically active and photochromatic compounds having chromene and thiochromene scaffolds.

Additionally, certain derivatives exhibit remarkable photochromic properties, making them valuable in advanced optoelectronic and photonic applications³ (Figure 2.1). The broad functional diversity of these heterocycles underscores their importance across multiple scientific disciplines.

Diazo compounds serve as crucial precursors for metal carbenoid generation in transition metal-catalyzed reactions. Their high reactivity with metal catalysts makes them invaluable for constructing diverse molecular frameworks in organic synthesis.⁴ The sigmatropic rearrangement of oxygen and sulfur ylides is a versatile reaction in organic chemistry, as it efficiently furnishes C–C, C–O, and C–S bonds.⁵ Classical [2,3]- and [1,2]-sigmatropic rearrangements, such as the Doyle–Kirmse, Stevens, and thia–Sommelet–Hauser rearrangements, mainly involve acyclic diazo compounds and sulfur ylides derived from allyl sulfides, alkyl sulfides, or α -thioesters.^{6–8} Moreover, the intramolecular addition of metal carbenoids to heteroatom lone pairs, leading to the direct formation of ylides, has recently garnered widespread attention as an efficient approach for the synthesis of cyclic ylides.⁹

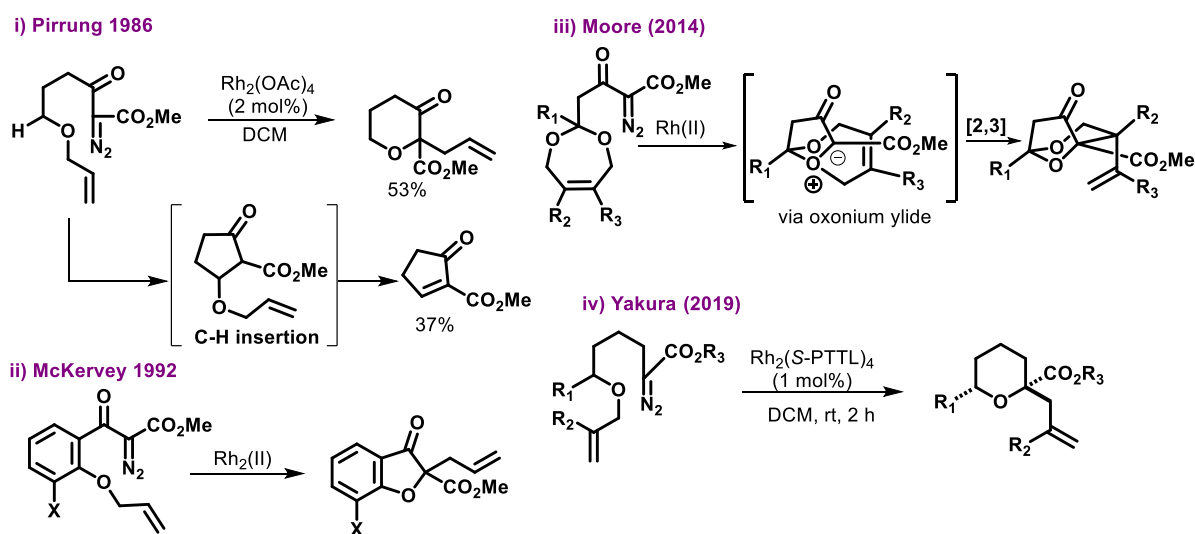
However, due to their inherent instability, oxonium ylides present greater challenges in both formation and reactivity control compared to conventional nitrogen- or sulfur-stabilized ylides. Additionally, oxonium ylides can undergo competing reaction pathways, including: (i) rearrangement either via a [2,3]-sigmatropic shift or a [1,2]-Stevens shift,¹⁰ and (ii) cyclopropanation or C–H insertion at positions alpha to the ethereal oxygen.¹¹ The dirhodium(II)-catalyzed synthesis of cyclic oxonium ylides has been extensively studied, frequently leading to a concerted [2,3]-sigmatropic rearrangement involving the allylic group in diazoketoesters.¹² In contrast, reports of [1,2]-shifts in oxonium ylides are typically limited to their cyclic ylides.¹³



Scheme 2.1: Possible reactive pathways upon formation of an oxonium ylide

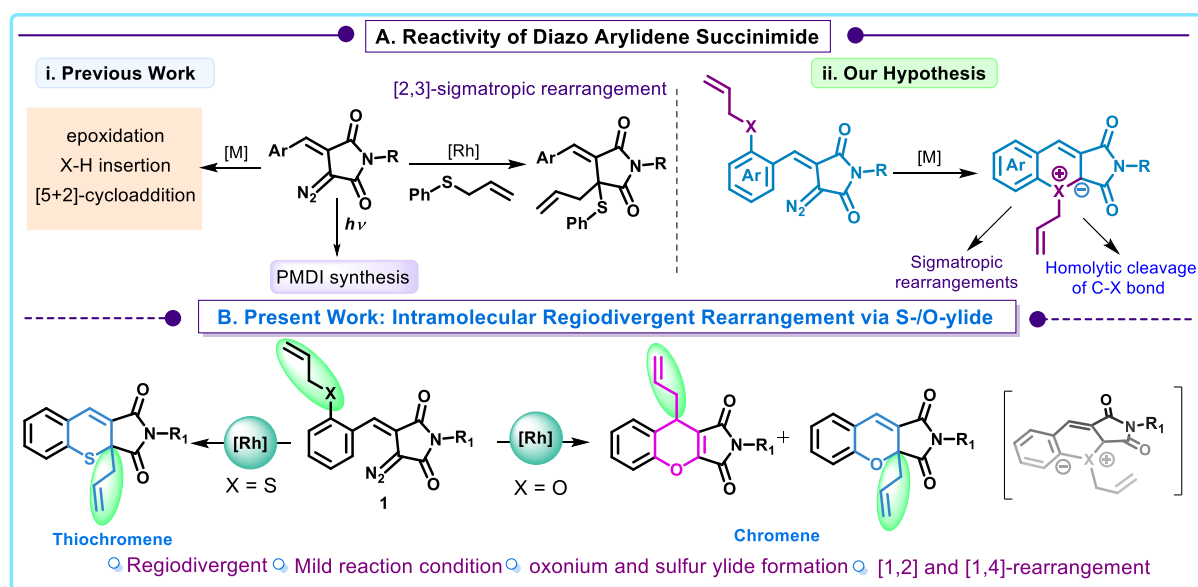
Among the significant transformations of diazo compounds, the Doyle–Kirmse reaction effectively promotes [2,3]-sigmatropic rearrangements in the presence of allyl sulfides. The

dirhodium(II)-catalyzed intramolecular oxonium ylide formation from α -diazocarbonyl compounds and subsequent [2,3]-sigmatropic rearrangement represents one of the most direct and powerful methods for the construction of substituted cyclic ethers. Although the dirhodium(II)-catalyzed generation of five-membered oxonium ylides and their subsequent [2,3]-sigmatropic rearrangement in 5-allyloxy-2-diazo-3-ketoesters is well-documented^{4a,b} similar processes with six-membered oxonium ylides are still uncommon^{4c,d} (Scheme 2.2). In 1986, the Pirrung group^{4g} demonstrated that treating 6-allyloxy-2-diazo-3-ketoesters with dirhodium(II) tetraacetate in dichloromethane led to the formation of 2-allyl-2-methoxycarbonyl-3-oxotetrahydropyran in 53% yield. This transformation proceeds through oxonium ylide generation followed by a [2,3]-sigmatropic rearrangement (Scheme 2.2-i). Additionally, 2-cyclopentene-1-one was isolated in 37% yield, resulting from methylene C–H insertion and subsequent allyl alcohol elimination. Subsequently, in 1992, McKervery^{4h} and co-workers introduced the first catalytic enantioselective variant of this transformation, employing a chiral Rh(II) catalyst, $[\text{Rh}_2(\text{S-binaaphtholphosphate})_2(\text{O}_2\text{C}^-\text{OH})_2]$. They achieved enantioselectivities of up to 30% ee via [2,3]-sigmatropic rearrangement of oxonium ylides derived from diazo compounds (Scheme 2.2-ii). Later, in 2014, Moore^{12d} and colleagues described a Rh(II)-catalyzed oxonium ylide formation followed by a [2,3]-sigmatropic rearrangement involving α -diazo- β -ketoesters bearing γ -cyclic unsaturated acetal substituents (Scheme 2.2-iii). More recently, in 2019, Yakura^{12e} and co-workers reported that 6-allyloxy-2-diazo-3-oxocarboxylates, substituted at the 6-position with alkyl or aryl groups, underwent smooth $\text{Rh}_2(\text{S-PTTL})_4$ -catalyzed rearrangements. These reactions delivered 6-substituted 2-allyl-3-oxotetrahydropyran-2-carboxylates with high diastereoselectivity and good yields in a chemoselective and stereoselective manner (Scheme 2.2-iv).



Scheme 2.2: Selected examples of intramolecular sigmatropic rearrangement of oxygen ylide

Diazo arylidene succinimides (DASs) stand out among diazo compounds due to their unique reactivity, attributed to the coexistence of alkene and diazo functional groups. Their distinct structural features drive diverse chemical transformations, including cycloaddition under metal and light, X–H insertion, and sigmatropic rearrangements (Scheme 2.3A-i).¹⁴ Our research group recently developed a Rh(II)-catalyzed intermolecular [2,3]-sigmatropic rearrangement utilizing DAS and allyl sulfides and interesting reactions of DAS (Scheme 2.3Ai).^{14c} Despite extensive studies, achieving selective [1,2]- or [1,4]-shifts via oxonium ylides while avoiding the dominant [2,3]-rearrangement pathway remains a significant challenge in the literature.¹⁵ A regioselective protocol enabling such rearrangements would be highly advantageous for the synthesis of structurally complex heterocycles, including chromenes and thiochromenes. In this context, we postulated that 2-allyloxy- or 2-thioallyl-substituted diazoacetates (DAS), under appropriate transition metal catalysis, could generate transient cyclic oxonium or sulfonium ylide intermediates. These species may undergo intramolecular sigmatropic rearrangement or homolytic cleavage of ylides (Scheme 2.3A-ii).



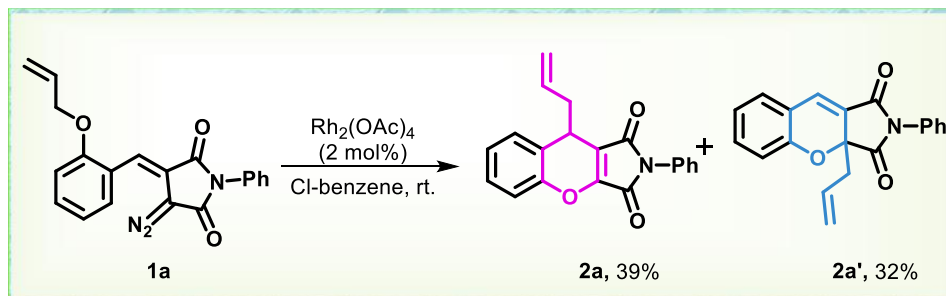
Scheme 2.3: Previous reports of DASs and present work

In this work, we describe a rhodium-catalyzed intramolecular regio-divergent [1,2]- and [1,4]-rearrangement of oxonium enabling the room-temperature synthesis of chromene and thiochromenes derivatives (Scheme 2.3-B).

2.2 Results and Discussion

To test our hypothesis, we initiated our study with 2-allyloxy-substituted DAS **1a** as a model substrate, employing Rh₂(OAc)₄ in chlorobenzene. This reaction yielded a mixture of **2a** and **2a'** rearrangement products at room temperature (Table 2.1, Entry 1). Encouraged by this initial

result, we further systematically optimized the reaction conditions. Several catalysts were evaluated, including silver, copper, cobalt, and rhodium complexes. Among them, rhodium acetate emerged as the most efficient catalyst for this transformation (Table 2.1, Entries 1-8).



Entry	Catalyst	Sovent	Yield of 2a/2a'
1	$\text{Rh}_2(\text{OAc})_4$	Cl-benzene	39/32
2	CuI	Cl-benzene	n.d.
3	$\text{Cu}(\text{OAc})_2 \cdot \text{H}_2\text{O}$	Cl-benzene	n.d.
4	$\text{Cu}(\text{OTf})_2$	Cl-benzene	n.d.
5	$\text{C}_{30}\text{H}_{24}\text{CoF}_{12}\text{N}_6\text{P}_2$	Cl-benzene	n.d.
6	AgNTf_2	Cl-benzene	n.d.
7	$[(\text{C}_6\text{H}_5)_3\text{P}]_3\text{RhCl}$	Cl-benzene	n.d.
8	$[(\text{C}_6\text{H}_5)_3\text{P}]_3\text{RhCl}_2$	Cl-benzene	n.d.
9	$\text{Rh}_2(\text{OAc})_4$	EtOAc	20/40
10	$\text{Rh}_2(\text{OAc})_4$	DCM	40/40
11	$\text{Rh}_2(\text{OAc})_4$	DMF	NR
12	$\text{Rh}_2(\text{OAc})_4$	Dioxane	NR
13	$\text{Rh}_2(\text{OAc})_4$	MeCN	10/10
14	$\text{Rh}_2(\text{OAc})_4$	DMSO	trace
15	$\text{Rh}_2(\text{OAc})_4$	F-benzene	27/33
16	No catalyst	DCM	NR

Table 2.1: Optimization of Reaction Conditions; ^a**General reaction conditions:** **1a** (0.2 mmol), $\text{Rh}_2(\text{OAc})_4$ (2 mol%), Cl-benzene A.R. grade (0.055 M), room temp., 30 min., under degasified condition with N_2 . ^bIsolated yields. ^cDCM was used as a solvent, (n.d.= not detected, and NR = no reaction).

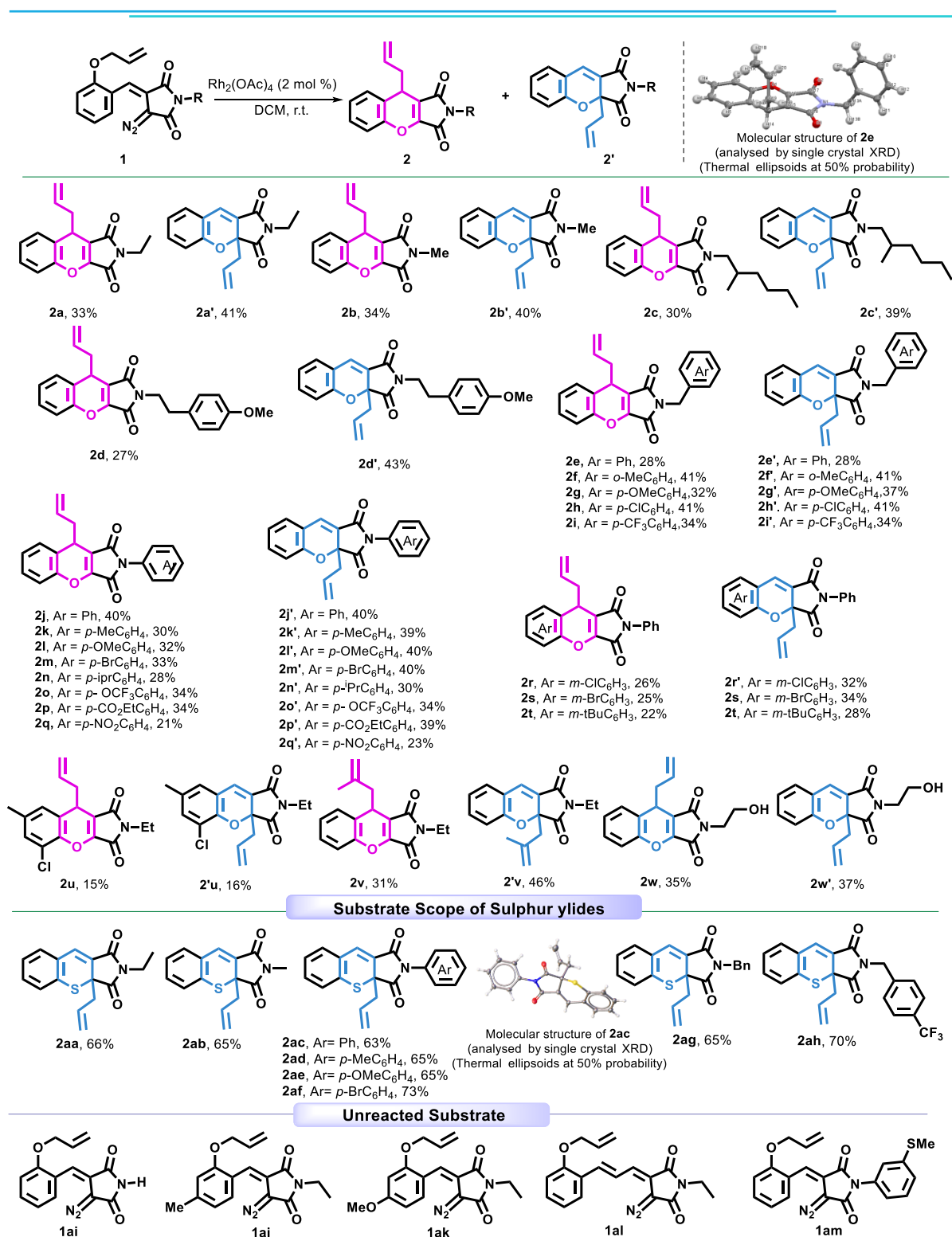
Later, various solvents were screened, and among all, dichloromethane was found to be the most effective for forming rearrangement products **2a/2a'** (Table 2.1, Entries 9-15). A control experiment without $\text{Rh}_2(\text{OAc})_4$ failed to furnish any detectable product, confirming the

catalyst's crucial role in the transformation (Table 2.1, Entry 16). Based on these findings, DAS **1a** (1 equiv.) with Rh₂(OAc)₄ (2 mol%) in DCM at room temperature under a nitrogen atmosphere proved to be the optimum reaction conditions for the rearrangement.

2.3 Substrate Scope

Having obtained the optimum reaction conditions, we further examined the substrate scope by screening a variety of *N*-alkyl and *N*-aryl substituted diazo arylidene succinimides (**1a-1q**). Under the reaction conditions, all the substrates successfully produced the expected rearrangement products (**2a-2q**, **2a'-2q'**) (see Scheme 2.4). We observed that *N*-benzyl-substituted diazo compounds containing electron-donating and electron-deactivating groups gave higher yields (**2e-2h**, **2e'-2h'**) compared to those with electron-withdrawing groups (**2i**, **2i'**) (Scheme 2.4). We also investigated the functional group compatibility of *N*-aryl-substituted DAS derivatives. We found that electron-donating and electron-withdrawing substituents on the phenyl ring were well tolerated under the reaction conditions to afford the desired products in moderate to good yield (**2i-2q**, **2i'-2q'**, Scheme 2.4). Additionally, various DAS derivatives featuring different aryl groups in the arylidene moiety, though reacted smoothly, afforded the desired products albeit in relatively low yields (**2r-2u**, **2r'-2u'**), likely due to electronic effects. The methylallyloxy-substituted DAS **1v** successfully underwent the reaction, furnishing the corresponding rearranged products (**2v**, **2v'**, Scheme 2.4). Notably, the *N*-(2-hydroxyethyl)-substituted DAS **1w** also participated in the transformation, yielding the expected products **2w** and **2w'**.

Next, we focused on investigating the rhodium-catalyzed formation of sulfur ylides to expand the scope of this methodology further. In this regard, various *N*-substituted DASs (**1aa-1ah**) were tested under the optimized reaction conditions, including alkyl and aryl groups with electron-withdrawing and electron-donating substituents (Scheme 2.4). The reaction exclusively obtained the corresponding rearrangement products (**2aa-2ah**) in good yields. *N*-alkyl-substituted DASs reacted efficiently, providing products (**2aa-2ab**) in good yields. Similarly, *N*-phenyl DASs with electron-donating and deactivating groups underwent selective rearrangement, affording products (**2ac-2af**) with excellent regioselectivity in good yield. Additionally, *N*-benzyl-substituted DASs reacted smoothly to obtain the expected products (**2ag-2ah**) in good yields (Scheme 2.4). In contrast to thioallyl-derived substrates, allyloxy-derived DASs gave a mixture of rearrangement products, likely due to the inherent instability of the oxonium ylide intermediate.

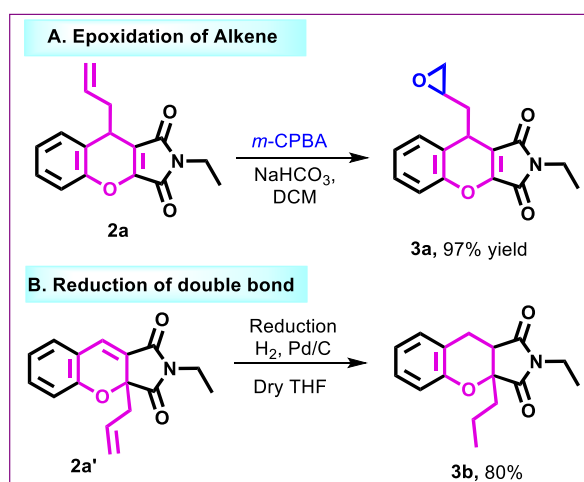


Scheme 2.4: Substrate scope. ^aGeneral reaction conditions: diazo compound **1** (1.0 equiv., 0.2 mmol), $\text{Rh}_2(\text{OAc})_4$ (2 mol%) in DCM (0.055 M) under nitrogen (degassed) at room temperature (28 °C) for 30 min- 60 min.

Allyloxy-substituted DAS derivatives (**1ai–1am**) exhibited poor reactivity, likely due to electron-donating substituents or extended π -conjugation. Notably, cinnamyl-substituted (**1ai**) and heteroaromatic-conjugated DAS showed diminished activity. Unlike thioallyl analogues,

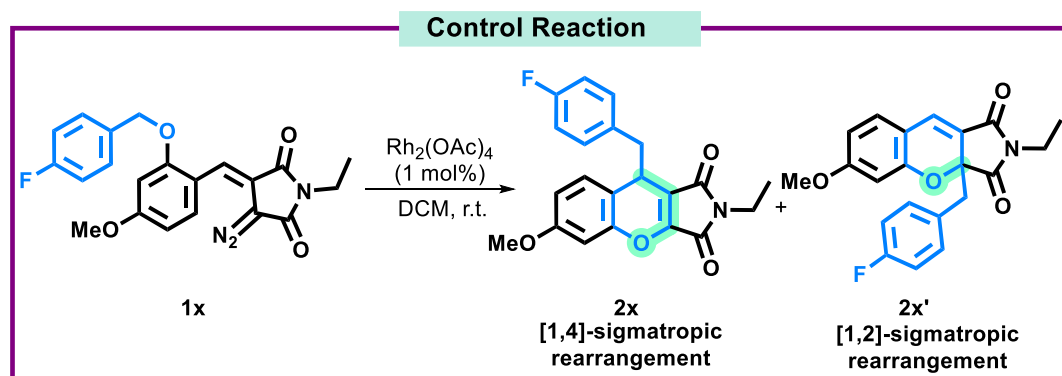
allyloxy DASs produced mixed rearrangement products, presumably due to the instability of the oxonium ylide intermediates

Later, we utilized the isolated products (**2a** and **2a'**) for the known transformations to highlight the synthetic applicability of the [1,2]- and [1,4]-rearrangement products. Epoxidation of **2a** with *m*-chloroperbenzoic acid in DCM furnished the epoxide **3a** with an excellent yield of 97% (Scheme 2.5-A). Additionally, the compound **2a'** under hydrogenation conditions (H_2 and Pd/C, rt) gave the corresponding reduction product **3b** in 80% yield (Scheme 2.5-B), where both internal and terminal double bonds were reduced.



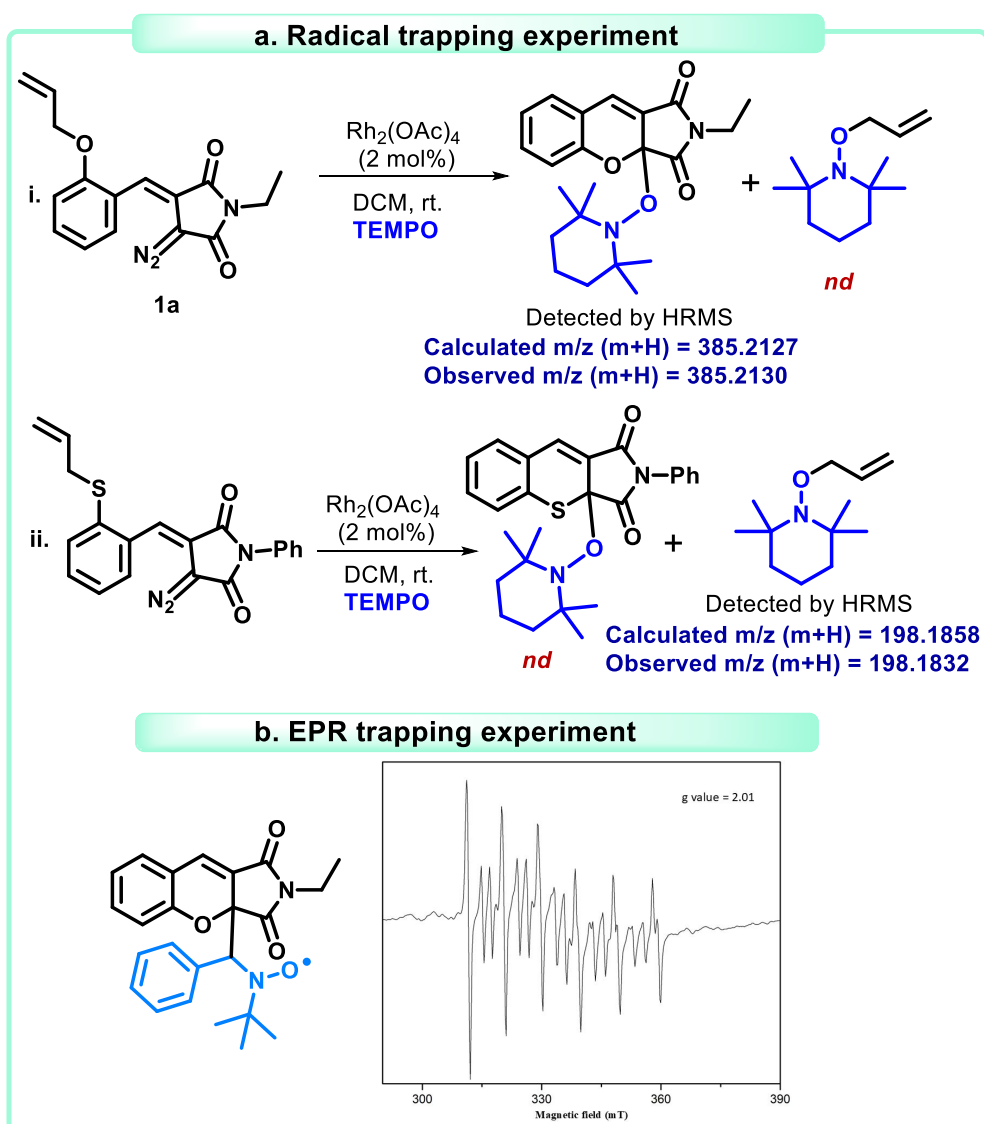
Scheme 2.5: Synthetic utility of products **2a** and **2a'**

We conducted control experiments to gain insight into the mechanistic pathway and the specific rearrangement involved during the course of the reaction. In this regard, we investigated the reactivity of 2-OBn-substituted DAS **1x** under standard conditions to understand the reaction mechanism. We obtained the products **2x** and **2x'**, which strongly indicate that the reaction follows a [1,4]- and [1,2]-shift of the oxonium ylide (see Scheme 2.6).



Scheme 2.6: Control Reaction

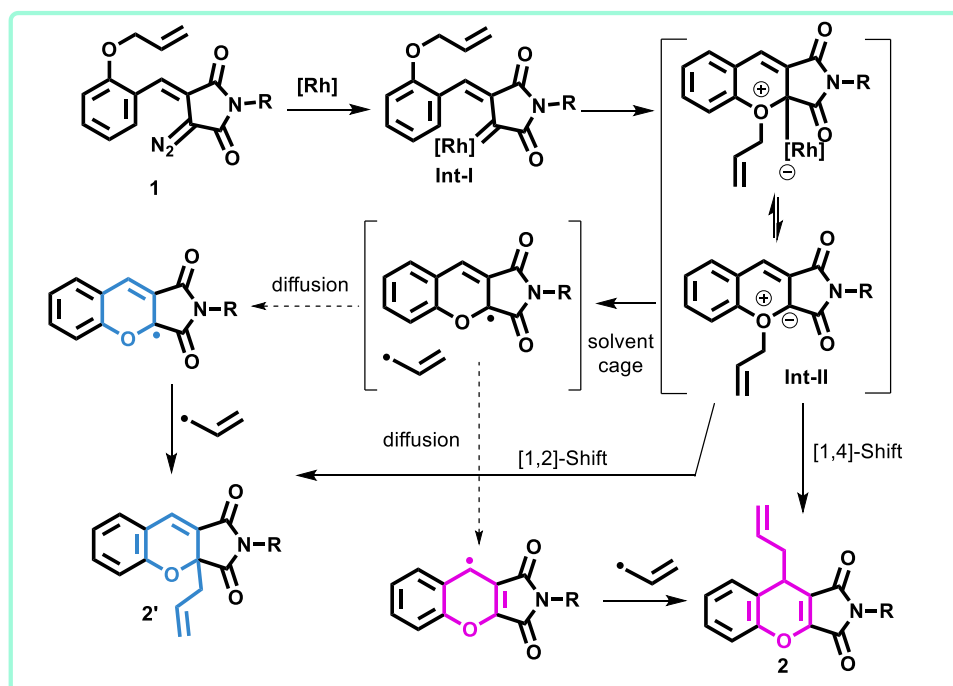
To probe the reaction mechanism, we conducted a radical trapping experiment using TEMPO under standard conditions. After 10 minutes of stirring, the formation of a TEMPO-adduct was confirmed by high-resolution mass spectrometry (HRMS) (Scheme 2.7a). Furthermore, electron paramagnetic resonance (EPR) analysis was performed on the incomplete reaction mixture containing DAS **1a**, Rh₂(OAc)₄, and the spin-trapping agent PBN (N-tert-butyl- α -phenylnitrone), which is commonly used to capture transient carbon-centered radicals. A distinct EPR signal was detected, with a g-value of 2.01 at the crossover point, consistent with the formation of a nitroxide radical.¹⁶ This observation confirms the generation of a carbon-centered radical intermediate in the reaction pathway (Scheme 2.7b).



Scheme 2.7: Radical Trapping Experiments

Based on control experiments, EPR spectroscopic data, and literature precedents¹⁷, a plausible reaction mechanism is proposed (Scheme 2.8). The diazo compound **1** react with the rhodium

catalyst to form a rhodium-carbene intermediate (**Int-I**), which then facilitates the generation of an oxonium ion intermediate (**Int-II**). This species undergoes homolytic cleavage of the C–O bond, producing radical intermediates that subsequently recombine to yield the final products **2** and **2'** (see Scheme 2.8).



Scheme 2.8: Plausible Mechanism

2.4 Conclusions:

In conclusion, we have successfully investigated the reactivity of 2-allyloxydiazo arylidene succinimides (DAS) under rhodium catalysis, leading to the formation of both [1,2]- and [1,4]-shift products via an oxonium ylide intermediate. Remarkably, even the relatively unstable and inherently reactive oxonium ylide was capable of delivering regio-divergent products, underscoring its synthetic potential and scope for further optimization. The reaction conditions also proved effective for the generation of sulfur ylides, which underwent highly selective rearrangement to yield structurally defined products. A diverse array of DAS derivatives responded well to the catalytic system, enabling the efficient synthesis of chromene and thiochromene frameworks under mild, room-temperature conditions. Overall, the intramolecular rearrangement behavior of DAS compounds has been thoroughly explored, supported by mechanistic insights obtained through control experiments, radical trapping studies, EPR spectroscopy, and single-crystal X-ray diffraction analysis.

2.5 Experimental Section:

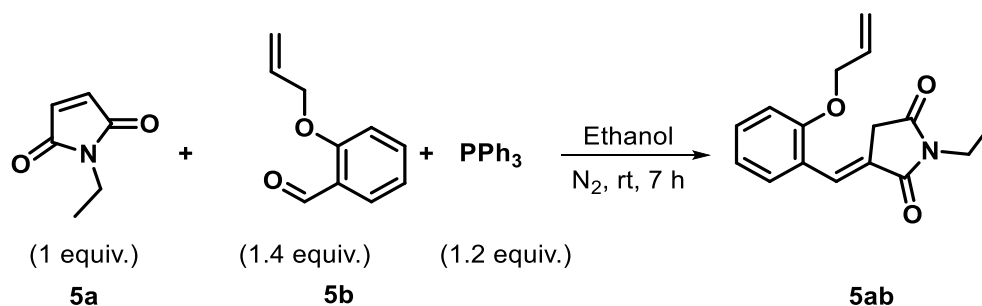
2.5.1. General Information:

Reagent Information: All reactions were carried out with distilled and anhydrous solvents using oven-dried glassware under a dry Argon atmosphere unless otherwise stated. All the reagents were purchased from commercial sources and used as received unless otherwise indicated. Thin-layer chromatography (TLC) was performed using silica gel 60 GF₂₅₄ pre-coated aluminum backed plates (2.5 mm) with detection by UV light. Column chromatographic purification of products was carried out using silica gel (100-200 mesh). The mixture of petroleum ether and ethyl acetate was used as gradient elution for column chromatography.

Analytical Information: All isolated compounds were characterized by ¹H NMR and ¹³C{¹H} NMR spectra were recorded on Bruker Avance III HD Ascend 400 MHz spectrometers. Nuclear Magnetic Resonance spectra were recorded in CDCl₃. The NMR spectra were recorded using tetramethylsilane (TMS) as the internal standard. ¹H NMR spectra were recorded at 400 MHz, and ¹³C{¹H} NMR spectra were recorded at 100/150 MHz (Bruker), unless otherwise noted. Chemical shifts (δ) are reported in ppm downfield from CDCl₃ (δ = 7.26 ppm) and from DCM-*d*₂ (δ = 5.32 ppm) for ¹H NMR and relative to the central CDCl₃ resonance (δ = 77.16 ppm) for ¹³C{¹H} NMR spectroscopy. For ¹H NMR, data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = double doublet, t = triplet, q = quartet, m = multiplet), coupling constants (*J*) are given in Hz and integration. ¹³C{¹H} NMR spectra were recorded with complete proton decoupling. ¹⁹F NMR spectra were recorded at 377 MHz. Mass samples were analyzed by high-resolution mass spectrometry (HRMS) using ESI TOF. Single-crystal diffraction analysis data were collected at 100 K with a Bruker Kappa Apex III CCD Duo diffractometer (operated at 1500 W power: 50 kV, 30 mA) using graphite monochromatic Mo Kα radiation.

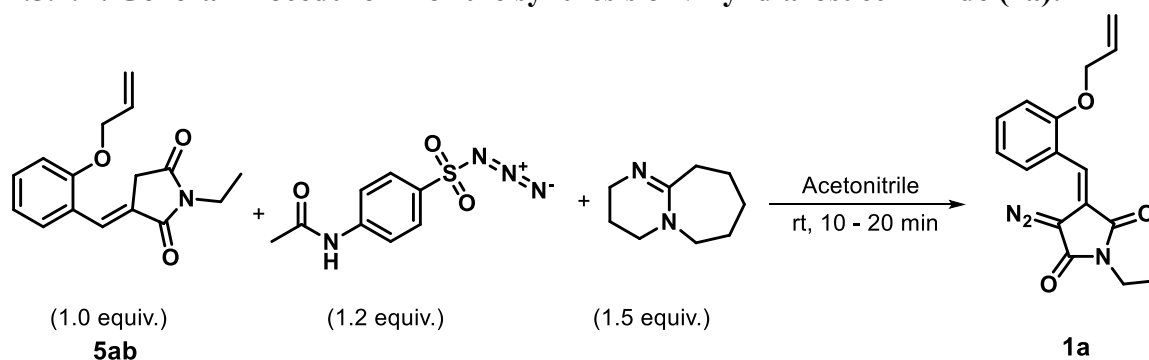
2.5.2. Preparation of Starting Materials:

2.5.2.A. General procedure-A for the synthesis of vinyl succinimides (5ab):



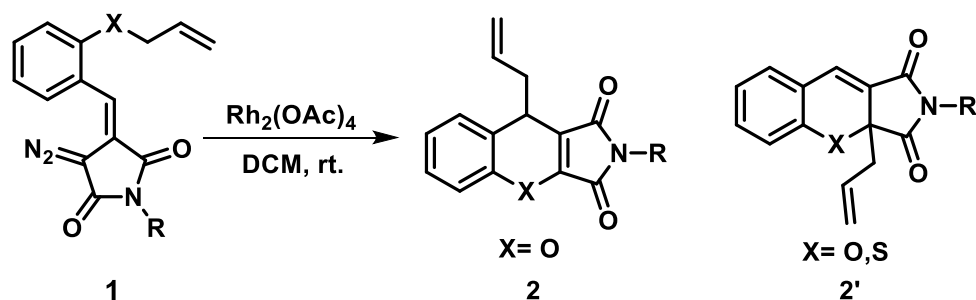
To the stirred solution of *N*-ethyl maleimide **5a** (0.5 g, 1.0 equiv., 4.0 mmol) in ethanol (20 mL) was added triphenylphosphine (1.26 g, 1.2 equiv., 4.8 mmol) portion-wise at room temperature under N₂ atmosphere. The initial pink-coloured reaction mixture slowly turned to white suspension over a period of 10-15 minutes of initial stirring. After the continuous stirring over 30 min, 2-(allyloxy)benzaldehyde **5b** (824 μ L, 1.4 equiv., 5.6 mmol) was added in one portion into the reaction mixture at room temperature. During this addition, the white suspension slowly turned into a clear solution. The reaction mixture was allowed to stir for 6 h. Upon completion of the reaction (monitored by TLC), the white solid formed during the course of the reaction was filtered through a sintered glass funnel and was washed with ethanol (6 mL x 2). The crude product **6a** was obtained as a white solid (890 mg, 82% yield) and used for the next step without further purification.^[1]

2.5.2.B. General Procedure-B for the synthesis of vinyl diazosuccinimide (**1a**):



To the stirred solution of (*E*)-3-(2-(allyloxy)benzylidene)-1-ethylpyrrolidine-2,5-dione **5ab** (2.17 g, 1.0 equiv., 8 mmol) in 30 mL acetonitrile were added 4-acetamido benzene sulfonyl azide (2.31 g, 1.2 equiv., 9.6 mmol) and DBU (1.79 mL, 1.5 equiv., 12 mmol) at 0 °C temperature under inert atmosphere. The reaction mixture was stirred for 10 minutes while maintaining the reaction temperature (0 °C). The reaction mixture was then quenched with saturated solution of NH₄Cl and the product was extracted with diethyl ether (30 mL x 3). The combined organic layer was washed with brine solution and dried over anhydrous Na₂SO₄. The extract was filtered and evaporated under reduced pressure. The crude product was purified using column chromatography over silica gel to afford (*E*)-3-(2-(allyloxy)benzylidene)-4-diazo-1-ethylpyrrolidine-2,5-dione **1a** as an orange solid (2.20 g, 92% yield).^[2]

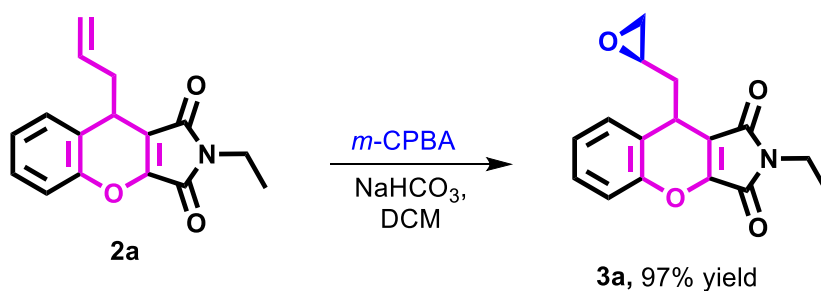
2.5.2.C. General procedure-C for the intramolecular rearrangement of diazo arylidene succinimide to synthesis of chromenes and thiochromenes.



To a reaction tube equipped with a magnetic stir bar were added diazo compound **1a** (1.0 equiv., 0.2 mmol), and $\text{Rh}_2(\text{OAc})_4$ (1 mol%) in DCM (0.055 M). The tube was capped with a rubber septum, and the mixture was degassed with nitrogen gas. The resulting solution was stirred upto 30 minutes at room temperature until the diazo compound **1a** was completely consumed (as monitored by TLC analysis). The reaction mixture was evaporated under reduced pressure. The crude mixture was purified by column chromatography on silica gel with hexanes/ethyl acetate mixture as an eluent to give the corresponding product **2a/2a'** white solids.

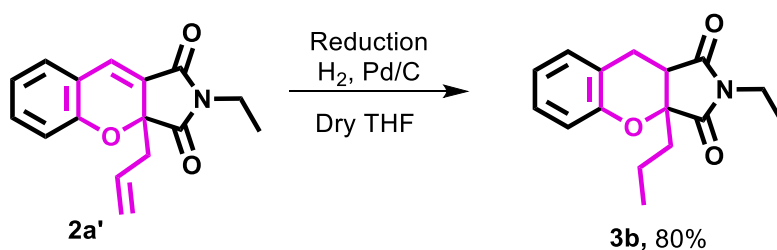
2.5.3 General procedure-C for the Epoxidation of 2a

To a round bottom flask equipped with a magnetic stir bar were added compound **2a** (1.0 equiv., 30 mg), *m*-CPBA (3 equiv.), NaHCO_3 (5 equiv.) in DCM (2mL). The mixture was then stirred at room temperature (28 °C) for up to 15 hours, with periodic TLC analysis. The reaction mixture was extracted with ethyl acetate (10 mL x 3). The combined organic layer was washed with brine solution and dried over anhydrous Na_2SO_4 . The extract was filtered and evaporated under reduced pressure. The compound **3a** was obtained as liquid (97% 31 mg) after purification using column chromatography over silica gel.



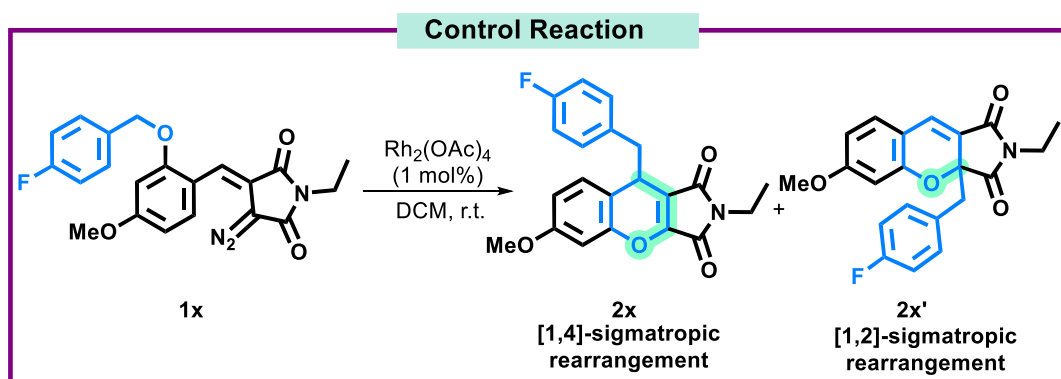
2.5.4 General procedure for hydrogenation of 2a'

To a solution of the chromene **2a'** (0.12 mmol, 30 mg) in dry THF (2 mL), Pd/C (10 % w/w, 1 mol%) was added and the mixture was stirred under H₂ atmosphere for overnight. After completion of the reaction (monitored by TLC), the catalyst was removed through celite filtration, the solvent was evaporated under reduced pressure. The compound **3b** was obtained as liquid (80% 24.5 mg) after purification using column chromatography over silica gel.

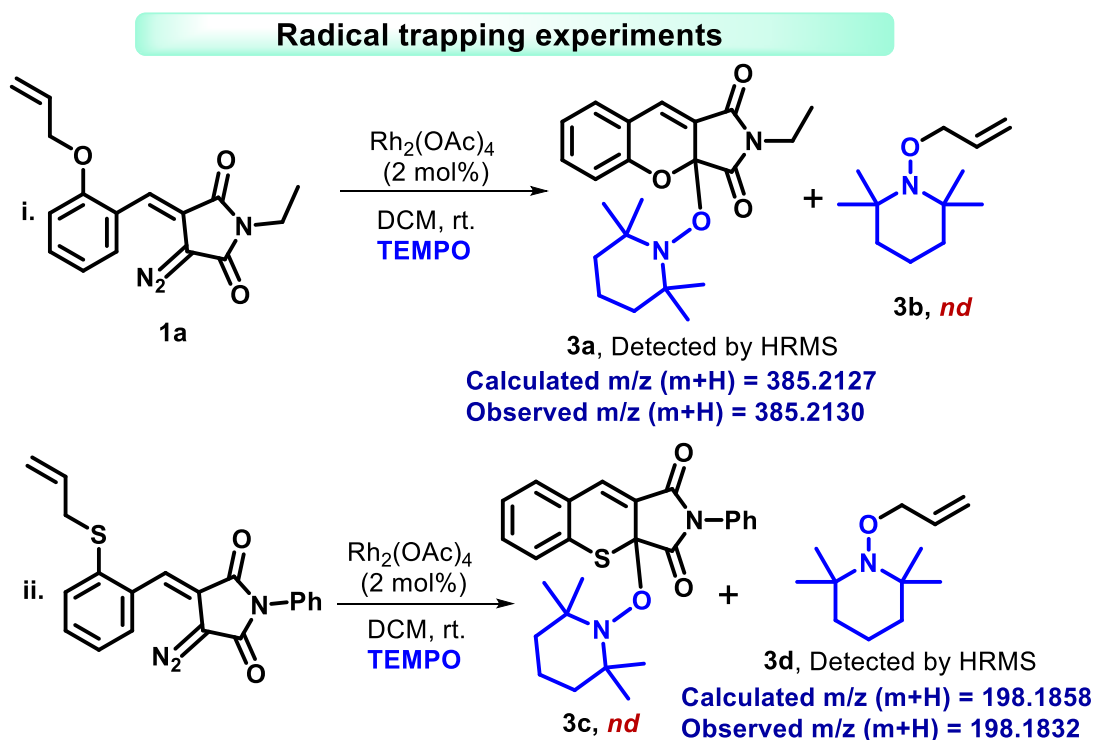


2.5.5. General procedure-C for the control experiment

To a reaction tube equipped with a magnetic stir bar were added 2-homoallyloxy substituted diazo compound **1ad** (1.0 equiv., 30 mg), and Rh₂(OAc)₄ (1 mol%) in DCM (2mL). The tube was capped with a rubber septum, and the mixture was degassed with nitrogen gas. The mixture was then stirred at room temperature (28 °C) for up to 1 hour, with periodic TLC analysis. We observe the product **2y** and **2y'** even in the trace. This result strongly suggests that the reaction proceeds via a [1,4]- and [1,2]- shift.



2.5.6. Radical Trapping Experiments



Procedure: i) To a reaction tube equipped with a magnetic stir bar were added 2-homoallyloxy substituted diazo compound 1a (1.0 equiv., 30 mg), and $\text{Rh}_2(\text{OAc})_4$ (1 mol%) in DCM (2mL). The tube was capped with a rubber septum, and the mixture was degassed with nitrogen gas. The mixture was then stirred at room temperature (28 °C) for up to 30 min. After that, the crude reaction mixture was analyzed by HRMS spectroscopy, and the TEMPO-trapped adduct 3a was detected by HRMS.

ii) To a reaction tube equipped with a magnetic stir bar were added 2-homoallyloxy substituted diazo compound 1ac (1.0 equiv., 30 mg), and $\text{Rh}_2(\text{OAc})_4$ (1 mol%) in DCM (2mL). The tube was capped with a rubber septum, and the mixture was degassed with nitrogen gas. The mixture was then stirred at room temperature (28 °C) for up to 30 min. After that, the crude reaction mixture was analyzed by HRMS spectroscopy, and the TEMPO-trapped adduct 3d was detected by HRMS.

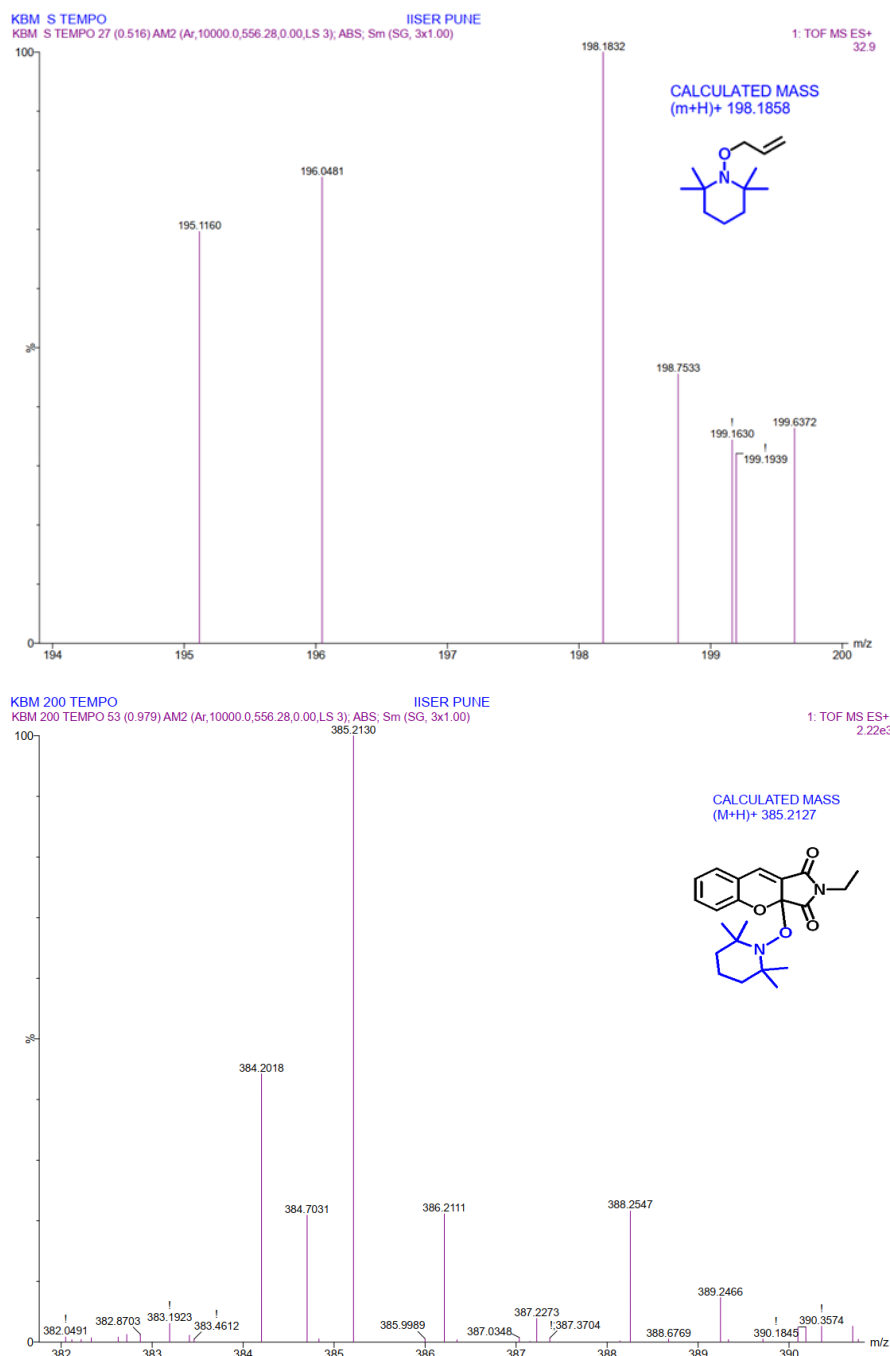


Figure 2.2: HRMS Spectrum

2.5.7. Procedure for EPR Analysis:

X-Band EPR measurements for the detection of radical study were carried out using a JON Bruker BioSpin connected to a Bruker EMX plus spectrometer with a radio wave source (9.4035 GHz) at room temperature.

Procedure: To a reaction tube equipped with a magnetic stir bar, diazo compound 1a (1.0 equiv., 10 mg), Rh₂(OAc)₄ (2 mol%), and N-tert-butyl- α -phenylnitrone (PBN, 1.2 equiv.) in DCM were added. The tube was capped with a rubber septum and the mixture was degassed with nitrogen gas. After that, the solution was stirred for 10 minutes at room temperature and the reaction mixture was transferred to an EPR tube, which was then subjected to the EPR measurement.

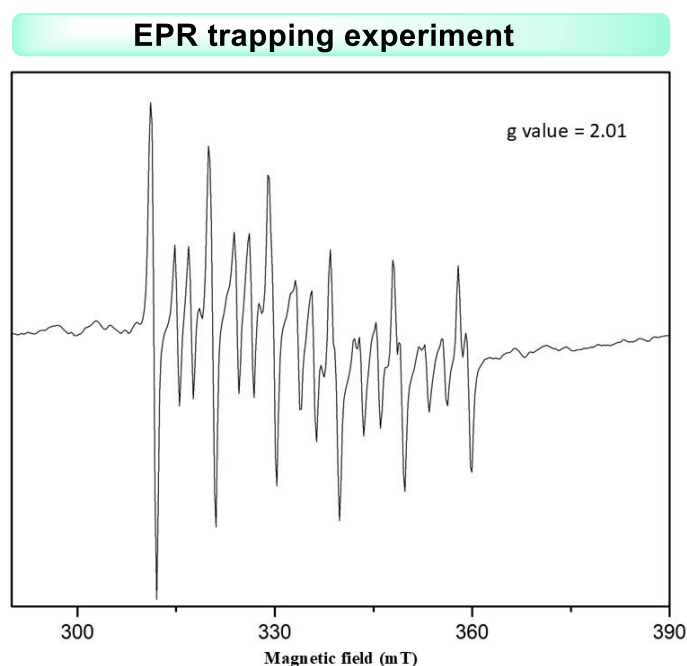
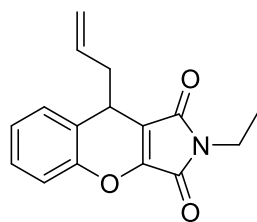


Figure 2.3. X-band EPR spectrum of reaction mixture

2.6 Characterization of synthesized compounds:

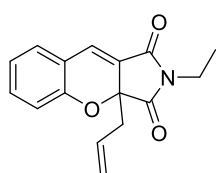
9-allyl-2-ethylchromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2a): Compound **2a** was synthesized following the general procedure-C. The product was obtained as white solid, 13 mg (34% yield); R_f =0.5 (petroleum ether/EtOAc 90:10);



¹H NMR (400 MHz, CDCl₃): δ 7.26 (ddt, J = 10.2, 7.6, 1.8 Hz, 2H), 7.21 – 7.15 (m, 2H), 5.52 (dddd, J = 16.8, 10.2, 8.4, 6.3 Hz, 1H), 5.01 – 4.88 (m, 2H), 4.11 (t, J = 4.7 Hz, 1H), 3.59 (q, J = 7.2 Hz, 2H), 2.81 – 2.54 (m, 2H), 1.20 (t, J = 7.2 Hz, 3H).

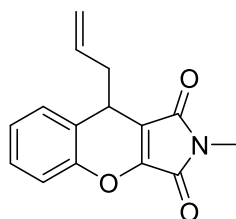
¹³C{¹H} NMR (100 MHz, CDCl₃): δ 169.07, 164.02, 151.79, 150.95, 133.5, 129.5, 128.8, 126.0, 122.5, 119.0, 118.0, 113.0, 40.2, 32.7, 32.1, 14.2.; HRMS (ESI TOF) m/z : calcd for C₁₆H₁₆NO₃ (M + H)⁺: 270.1130, Found: 270.1131

3a-allyl-2-ethylchromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2a'): Compound **2a'** was synthesized following the general procedure-C. The product was obtained as white solid, 13 mg (34% yield); $R_f=0.5$ (petroleum ether/EtOAc 90:10);



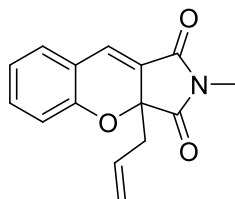
^1H NMR (400 MHz, CDCl_3): δ 7.36 (s, 1H), 7.35 – 7.30 (m, 2H), 7.09 (dd, $J = 8.7, 0.9$ Hz, 1H), 7.04 (td, $J = 7.4, 1.1$ Hz, 1H), 5.69 – 5.49 (m, 1H), 5.13 – 4.99 (m, 2H), 3.65 (qd, $J = 7.1, 4.5$ Hz, 2H), 2.77 – 2.56 (m, 2H), 1.21 (t, $J = 7.2$ Hz, 3H). **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3):** δ 172.8, 165.5, 153.2, 132.8, 130.0, 128.6, 127.2, 124.1, 123.1, 121.6, 120.8, 118.1, 77.5, 39.1, 33.5, 13.2. HRMS (ESI TOF) m/z : calcd for $\text{C}_{16}\text{H}_{16}\text{NO}_3$ ($\text{M} + \text{H}$) $^+$: 270.1130, Found: 270.1129

9-allyl-2-methylchromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2b): Compound **2b** was synthesized following the general procedure-C. The product was obtained as white solid, 13 mg (34% yield); $R_f=0.5$ (petroleum ether/EtOAc 90:10);



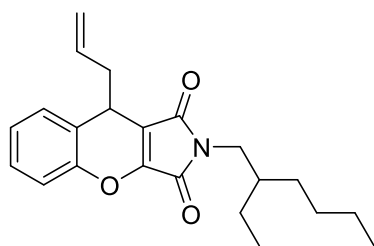
^1H NMR (400 MHz, CDCl_3): δ 7.31 – 7.22 (m, 2H), 7.23 – 7.14 (m, 2H), 5.53 (dddd, $J = 16.7, 10.2, 8.3, 6.3$ Hz, 1H), 5.03 – 4.87 (m, 2H), 4.11 (t, $J = 4.7$ Hz, 1H), 3.03 (s, 3H), 2.75 (dddt, $J = 14.1, 8.3, 4.7, 1.0$ Hz, 1H), 2.62 (dddt, $J = 14.0, 6.2, 4.8, 1.4$ Hz, 1H). **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3):** δ 169.24, 164.22, 151.91, 150.92, 133.42, 129.55, 128.78, 126.09, 122.51, 119.13, 118.06, 113.12, 40.19, 32.08, 23.58. HRMS (ESI TOF) m/z : calcd for $\text{C}_{15}\text{H}_{14}\text{NO}_3$ ($\text{M} + \text{H}$) $^+$: 256.0974, Found: 256.0975.

3a-allyl-2-methylchromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2b'): Compound **2b'** was synthesized following the general procedure-C. The product was obtained as white solid, 15.5



mg (40% yield); $R_f=0.47$ (petroleum ether/EtOAc 90:10); **^1H NMR (400 MHz, CDCl_3):** δ 7.37 (s, 1H), 7.33 (dd, $J = 7.5, 1.6$ Hz, 2H), 7.09 (dt, $J = 8.7, 0.9$ Hz, 1H), 7.05 (td, $J = 7.5, 1.1$ Hz, 1H), 5.61 (ddt, $J = 16.7, 10.3, 7.5$ Hz, 1H), 5.16 – 4.97 (m, 2H), 3.08 (s, 3H), 2.72 – 2.62 (m, 2H). **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3):** 173.2, 165.7, 153.2, 132.9, 130.1, 128.6, 127.3, 124.0, 123.1, 121.5, 120.8, 118.1, 77.7, 39.1, 24.4. HRMS (ESI TOF) m/z : calcd for $\text{C}_{15}\text{H}_{14}\text{NO}_3$ ($\text{M} + \text{H}$) $^+$: 256.0974, Found: 256.0970.

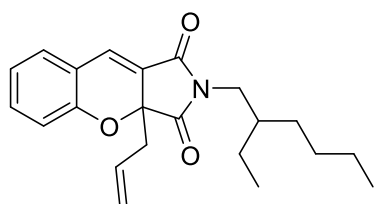
9-allyl-2-(2-ethylhexyl)chromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2c): Compound **2c** was



synthesized following the general procedure-C. The product was obtained as white solid, 16 mg (30% yield); R_f =0.5 (petroleum ether/EtOAc 90:10);

^1H NMR (400 MHz, CDCl_3): δ 7.30 – 7.23 (m, 2H), 7.21 – 7.15 (m, 2H), 5.51 (dddd, J = 16.6, 10.2, 8.5, 6.1 Hz, 1H), 5.03 – 4.76 (m, 2H), 4.12 (t, J = 4.6 Hz, 1H), 3.42 (d, J = 7.3 Hz, 2H), 2.77 (ddd, J = 13.5, 8.6, 4.6 Hz, 1H), 2.62 (dddt, J = 13.8, 6.1, 4.8, 1.4 Hz, 1H), 1.73 (p, J = 6.9 Hz, 1H), 1.35 – 1.16 (m, 10H), 0.95 – 0.84 (m, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 169.5, 164.4, 151.6, 151.0, 133.5, 129.5, 128.8, 126.1, 122.6, 119.0, 118.1, 112.9, 41.6, 40.2, 38.5, 32.1, 30.6, 28.7, 23.9, 23.2, 14.2, 10.6. HRMS (ESI TOF) m/z : calcd for $\text{C}_{22}\text{H}_{28}\text{NO}_3$ ($\text{M} + \text{H}$) $^+$: 354.2069, Found: 354.2076.

3a-allyl-2-(2-ethylhexyl)chromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2c'):Compound **2c'**

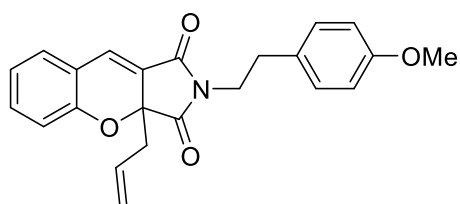


was synthesized following the general procedure-C. The product was obtained as white solid, 21 mg (39% yield); R_f =0.47 (petroleum ether/EtOAc 90:10);

^1H NMR (400 MHz, CDCl_3): 7.36 (s, 1H), 7.37 – 7.29 (m, 2H), 7.09 (d, J = 8.5 Hz, 1H), 7.04 (td, J = 7.5, 1.1 Hz, 1H), 5.85 – 5.40 (m, 1H), 5.21 – 4.83 (m, 2H), 3.75 – 3.21 (m, 2H), 2.92 – 2.33 (m, 2H), 1.83 – 1.68 (m, 1H), 1.39 – 1.17 (m, 10H), 0.89 (td, J = 7.2, 4.3 Hz, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 173.3, 166.1, 153.3, 132.8, 130.0, 128.8, 127.1, 124.1, 123.1, 121.4, 120.9, 118.1, 77.4, 42.4, 39.1, 38.0, 30.6, 28.5, 24.0, 23.1, 14.2, 10.5. HRMS (ESI TOF) m/z : calcd for $\text{C}_{22}\text{H}_{28}\text{NO}_3$ ($\text{M} + \text{H}$) $^+$: 354.2069, Found: 354.2070

3a-allyl-2-(4-methoxyphenethyl)chromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2d):

Compound **2d** was synthesized following the general procedure-C. The product was obtained as white solid, 15 mg (27% yield); R_f =0.45 (petroleum ether/EtOAc 90:10);

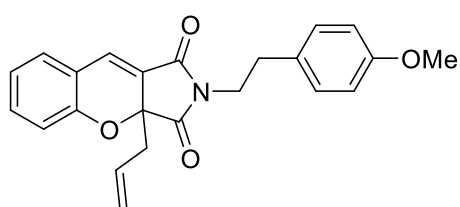


^1H NMR (400 MHz, CDCl_3): δ 7.35 (s, 1H), 7.34 – 7.27 (m, 2H), 7.21 (t, J = 7.8 Hz, 1H), 7.12 – 7.07 (m, 1H), 7.04 (td, J = 7.5, 1.2 Hz, 1H), 6.84 (dt, J = 7.8, 1.1 Hz, 1H), 6.81 – 6.72 (m, 2H), 5.53 (dddd, J = 17.1, 10.2, 7.8, 7.1 Hz, 1H), 5.12 – 4.92 (m, 2H), 3.97 – 3.79 (m, 2H), 3.78 (s, 3H), 2.93 (dd, J = 8.5, 7.0 Hz, 2.68 – 2.41 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 172.8, 165.5, 159.9, 153.2, 139.2, 132.9, 130.0, 128.7, 127.3, 124.0, 123.1, 121.4, 120.8, 118.1, 114.4, 112.6, 77.4, 55.3, 39.4,

39.1, 33.7. **HRMS (ESI TOF) m/z :** calcd for $C_{23}H_{22}NO_4$ ($M + H$)⁺: 376.1549, Found: 376.1548.

9-allyl-2-(4-methoxyphenethyl)chromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2d'):

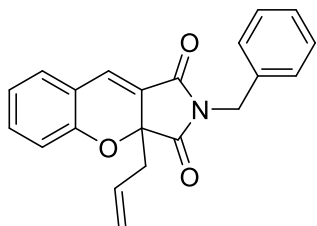
Compound **2d'** was synthesized following the general procedure-C. The product was obtained as white solid, 24 mg (43% yield); R_f =0.43 (petroleum ether/EtOAc 90:10);



1H NMR (400 MHz, $CDCl_3$): 1H NMR (400 MHz, Chloroform-*d*) δ 7.30 – 7.21 (m, 2H), 7.24 – 7.12 (m, 3H), 6.84 – 6.72 (m, 3H), 5.48 (dddd, J = 16.7, 10.2, 8.3, 6.4 Hz, 1H), 4.96 (ddd, J = 10.2, 1.9, 0.9 Hz, 1H), 4.88

(dq, J = 17.0, 1.4 Hz, 1H), 4.08 (t, J = 4.6 Hz, 1H), 3.87 – 3.61 (m, 5H), 2.90 (t, J = 7.5 Hz, 2H), 2.78 – 2.50 (m, 2H). **$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$):** δ 168.9, 163.9, 159.9, 151.7, 150.9, 139.5, 133.4, 129.5, 128.8, 126.1, 122.5, 121.3, 119.1, 118.0, 114.5, 112.3, 55.3, 40.1, 38.8, 34.8, 32.1. **HRMS (ESI TOF) m/z :** calcd for $C_{23}H_{22}NO_4$ ($M + H$)⁺: 376.1549, Found: 376.1551.

3a-allyl-2-benzylchromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2e): Compound **2e** was synthesized following the general procedure-C. The product was obtained as white solid, 14

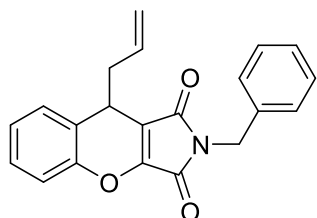


mg (28% yield); R_f =0.5 (petroleum ether/EtOAc 90:10);

1H NMR (400 MHz, $CDCl_3$): δ 7.45 – 7.38 (m, 2H), 7.37 (s, 1H), 7.37 – 7.25 (m, 5H), 7.08 (dt, J = 8.6, 1.1 Hz, 1H), 7.04 (td, J = 7.5, 1.1 Hz, 1H), 5.41 (ddt, J = 17.5, 10.1, 7.5 Hz, 1H), 4.95 (dq, J = 17.0,

1.4 Hz, 1H), 4.88 (dt, J = 10.1, 1.2 Hz, 1H), 4.79 – 4.67 (m, 2H), 2.63 (dt, J = 7.5, 1.1 Hz, 2H). **$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$):** δ 172.7, 165.3, 153.2, 135.5, 132.9, 130.1, 129.2, 128.8, 128.3, 128.2, 127.6, 123.9, 123.1, 121.5, 120.7, 118.1, 77.5, 42.2, 39.2. **HRMS (ESI TOF) m/z :** calcd for $C_{21}H_{18}NO_3$ ($M + H$)⁺: 332.1287, Found: 332.1285.

9-allyl-2-benzylchromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2e'): Compound **2e'** was

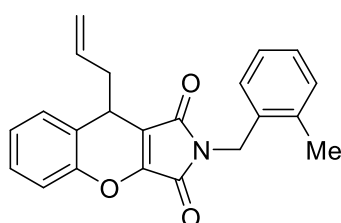


synthesized following the general procedure-C. The product was obtained as white solid, 14 mg (28% yield); R_f =0.48 (petroleum ether/EtOAc 90:10);

1H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.28 (m, 3H), 7.32 – 7.21 (m, 4H), 7.23 – 7.13 (m, 2H), 5.51 (dddd, J = 16.6, 10.2, 8.4, 6.2 Hz, 1H), 4.96 (ddt, J = 10.1, 1.9, 0.9 Hz, 1H), 4.94 – 4.85 (m, 1H), 4.70 (d, J = 2.3 Hz, 2H), 4.11 (t, J = 4.7 Hz, 1H), 2.86 – 2.68 (m, 1H), 2.62 (dddt, J = 13.9, 6.2, 4.8, 1.4 Hz, 1H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 168.9, 163.8, 151.9, 151.0, 136.5, 133.5, 129.5, 128.8, 128.3, 127.9, 126.1, 122.5, 119.1, 118.1, 113.2, 41.3, 40.2, 32.2, 29.8. HRMS (ESI TOF) *m/z*: calcd for C₂₁H₁₈NO₃ (M + H)⁺: 332.1287, Found: 332.1288.

9-allyl-2-(2-methylbenzyl)chromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2f): Compound **2f** was synthesized following the general procedure-C. The product was obtained as white solid,

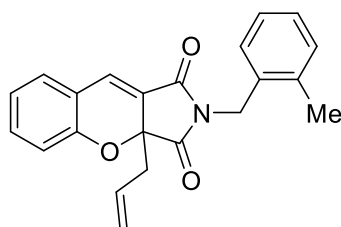


21.5 mg (41% yield); *R_f*=0.57 (petroleum ether/EtOAc 90:10);

¹H NMR (400 MHz, CDCl₃): δ 7.32 – 7.22 (m, 2H), 7.24 – 7.11 (m, 6H), 5.53 (dddd, *J* = 16.6, 10.2, 8.5, 6.1 Hz, 1H), 5.05 – 4.87 (m, 2H), 4.71 (d, *J* = 3.2 Hz, 2H), 4.13 (t, *J* = 4.6 Hz, 1H), 2.82 – 2.72 (m, 1H), 2.63 (dddt, *J* = 13.9, 6.1, 4.6, 1.4 Hz, 1H), 2.42 (s,

3H). ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 168.9, 163.9, 151.8, 150.9, 135.9, 134.3, 133.5, 130.6, 129.5, 128.8, 127.9, 127.8, 126.3, 126.1, 122.5, 119.6, 118.1, 113.2, 40.2, 38.9, 32.1, 19.4. HRMS (ESI TOF) *m/z*: calcd for C₂₂H₂₀NO₃ (M + H)⁺: 346.1443, Found: 346.1440.

3a-allyl-2-(2-methylbenzyl)chromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2f'): Compound **2f'** was synthesized following the general procedure-C. The product was obtained as white solid, 21.5 mg (41% yield); *R_f*=0.55 (petroleum ether/EtOAc 90:10);



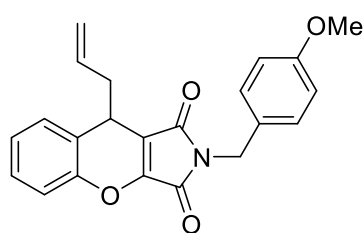
¹H NMR (400 MHz, CDCl₃): δ 7.39 (s, 1H), 7.34 (td, *J* = 7.1, 1.8 Hz, 2H), 7.31 – 7.24 (m, 1H), 7.22 – 7.10 (m, 3H), 7.09 (dt, *J* = 8.8, 1.0 Hz, 1H), 7.05 (td, *J* = 7.5, 1.1 Hz, 1H), 5.51 (ddt, *J* = 16.8, 10.2, 7.5 Hz, 1H), 5.04 – 4.93 (m, 2H), 4.77 (d, *J* = 1.7 Hz, 2H), 2.66 (dt, *J* = 7.5, 1.1 Hz, 2H), 2.47 (s, 3H). ¹³C{¹H} NMR (100

MHz, CDCl₃): δ 172.9, 165.5, 153.3, 136.5, 133.3, 132.9, 130.6, 130.1, 129.0, 128.5, 128.1, 127.6, 126.2, 123.9, 123.1, 121.6, 120.8, 118.1, 77.51, 39.6, 39.2, 19.6. HRMS (ESI TOF) *m/z*: calcd for C₂₂H₂₀NO₃ (M + H)⁺: 346.1443, Found: 346.1449.

9-allyl-2-(4-methoxybenzyl)chromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2g):

Compound **2g** was synthesized following the general procedure-C. The product was obtained as white solid, 17.5 mg (32 % yield); *R_f*=0.4 (petroleum ether/EtOAc 90:10);

¹H NMR (400 MHz, CDCl₃): δ 7.32 – 7.21 (m, 4H), 7.17 (ddd, *J* = 13.9, 7.7, 1.4 Hz, 2H), 6.86 – 6.77 (m, 2H), 5.50 (dddd, *J* = 16.6, 10.2, 8.4, 6.3 Hz, 1H), 5.01 – 4.92 (m, 1H), 4.89



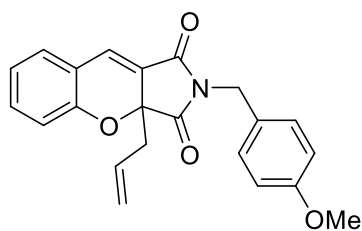
(dt, $J = 17.0, 1.6$ Hz, 1H), 4.63 (d, $J = 3.1$ Hz, 2H), 4.09 (dd, $J = 5.7, 3.6$ Hz, 1H), 3.78 (s, 3H), 2.84 – 2.49 (m, 2H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 168.9, 163.8, 159.3, 151.8, 150.9, 133.5, 129.9, 129.9, 129.5, 128.8, 126.1, 122.5,

119.1, 118.0, 114.1, 113.2, 55.4, 40.7, 40.2, 32.1. HRMS (ESI TOF) m/z : calcd for $\text{C}_{22}\text{H}_{20}\text{NO}_4$ ($\text{M} + \text{H}^+$): 362.1392, Found: 362.1394.

3a-allyl-2-(4-methoxybenzyl)chromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2g')

(2g'):

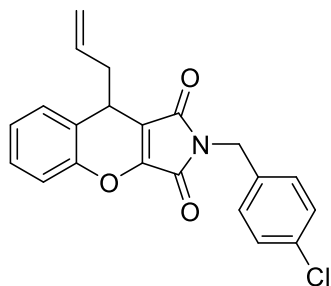


Compound **2g'** was synthesized following the general procedure-C. The product was obtained as white solid, 20 mg (37 % yield); R_f =0.9 (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): 7.39 – 7.31 (m, 3H), 7.31 (d, $J = 7.4$ Hz, 2H), 7.07 (dt, $J = 8.7, 1.0$ Hz, 1H), 7.03 (td, $J = 7.5, 1.1$ Hz, 1H),

6.87 – 6.79 (m, 2H), 5.41 (ddt, $J = 17.5, 10.1, 7.5$ Hz, 1H), 5.01 – 4.83 (m, 2H), 4.67 (d, $J = 3.4$ Hz, 2H), 3.77 (s, 3H), 2.62 (dt, $J = 7.6, 1.0$ Hz, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 172.7, 165.4, 159.5, 153.2, 132.8, 130.7, 130.0, 128.3, 127.8, 127.4, 124.0, 123.1, 121.5, 120.7, 118.0, 114.0, 77.5, 55.4, 41.6, 39.1. HRMS (ESI TOF) m/z : calcd for $\text{C}_{22}\text{H}_{20}\text{NO}_3$ ($\text{M} + \text{H}^+$): 346.1443, Found: 346.1441.

9-allyl-2-(4-chlorobenzyl)chromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2h):

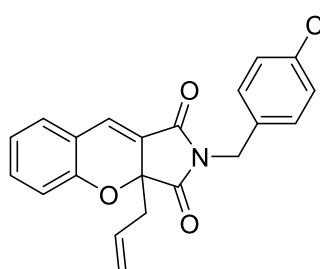
Compound **2h** was synthesized following the general procedure-C. The product was obtained as white solid, 22.5 mg (41% yield); R_f =0.55 (petroleum ether/EtOAc 80:20)



^1H NMR (400 MHz, CDCl_3): δ 7.36 – 7.30 (m, 3H), 7.30 – 7.22 (m, 3H), 7.18 (ddd, $J = 13.8, 7.7, 1.4$ Hz, 2H), 5.51 (dddd, $J = 16.7, 10.2, 8.5, 6.2$ Hz, 1H), 4.96 (dd, $J = 10.3, 1.9$ Hz, 1H), 4.90 (dq, $J = 17.0, 1.5$ Hz, 1H), 4.70 (d, $J = 2.2$ Hz, 2H), 4.11 (t, $J = 4.6$ Hz, 1H), 2.83 – 2.52 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 168.9, 163.8, 151.9, 150.9, 136.5, 133.5, 129.5, 128.8, 128.8,

128.3, 127.9, 126.1, 122.5, 119.1, 118.1, 113.2, 41.3, 40.2, 32.2. HRMS (ESI TOF) m/z : calcd for $\text{C}_{21}\text{H}_{17}\text{ClNO}_3$ ($\text{M} + \text{H}^+$): 366.0897, Found: 366.0890.

3a-allyl-2-(4-chlorobenzyl)chromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2h'): Compound **2h'** was synthesized following the general procedure-C. The product was obtained as white solid, 22.5 mg (41% yield); $R_f=0.5$ (petroleum ether/EtOAc 90:10)

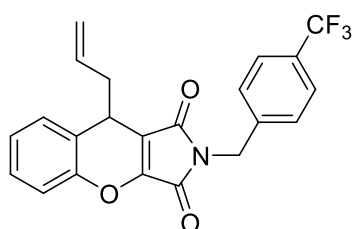


^1H NMR (400 MHz, CDCl_3): δ 7.46 – 7.39 (m, 2H), 7.37 (s, 1H), 7.31 (qd, J = 8.4, 7.9, 6.2 Hz, 4H), 7.08 (d, J = 8.1 Hz, 1H), 7.04 (td, J = 7.4, 1.1 Hz, 1H), 5.41 (ddt, J = 17.4, 10.1, 7.5 Hz, 1H), 4.95 (dq, J = 16.9, 1.4 Hz, 1H), 4.88 (dd, J = 10.1, 1.6 Hz, 1H), 4.80 – 4.58 (m, 2H), 2.63 (d, J = 7.5 Hz, 2H). **$^{13}\text{C}\{^1\text{H}\}$ NMR (100**

MHz, CDCl_3): δ 172.7, 165.3, 153.2, 135.5, 132.9, 130.0, 129.2, 128.7, 128.3, 128.2, 127.5, 123.9, 123.1, 121.5, 120.7, 118.0, 77.5, 42.1, 39.1. **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{21}\text{H}_{17}\text{ClNO}_3$ ($\text{M} + \text{H}$) $^+$: 366.0897, Found: 366.0898.

9-allyl-2-(4-(trifluoromethyl)benzyl)chromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2i):

Compound **2i** was synthesized following the general procedure-C. The product was obtained as white solid, 20.5 mg (34% yield); $R_f=0.45$ (petroleum ether/EtOAc 90:10);

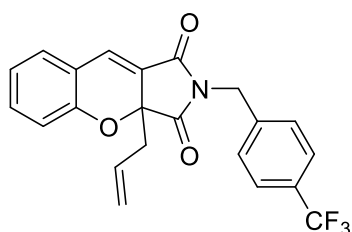


^1H NMR (400 MHz, CDCl_3): δ 7.58 (d, J = 8.1 Hz, 2H), 7.44 (d, J = 8.1 Hz, 2H), 7.30 – 7.23 (m, 2H), 7.23 – 7.14 (m, 2H), 5.51 (dddd, J = 16.6, 10.2, 8.5, 6.2 Hz, 1H), 4.97 (ddd, J = 10.1, 1.9, 1.0 Hz, 1H), 4.91 (dq, J = 16.9, 1.5 Hz, 1H), 4.74 (d, J = 1.4 Hz, 2H), 4.12 (t, J = 4.6 Hz, 1H), 2.87 – 2.54 (m, 2H). **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3):** δ 168.7, 163.6, 151.9, 150.8, 140.4 – 140.1 (m), 135.3 – 120.3 (m),

, 133.4, 130.4, 129.5, 128.9, 128.6, 126.3, 125.8 (q, J = 3.8 Hz), 122.4, 119.1, 118.1, 113.4, 40.7, 40.2, 32.1. **^{19}F NMR (377 MHz, CDCl_3):** δ -62.6. **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{22}\text{H}_{17}\text{F}_3\text{NO}_3$ ($\text{M} + \text{H}$) $^+$: 400.1161, Found: 400.1161

3a-allyl-2-(4-(trifluoromethyl)benzyl)chromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2i'):

Compound **2i'** was synthesized following the general procedure-C. The product was obtained as white solid, 20.5 mg (34 % yield); $R_f=0.40$ (petroleum ether/EtOAc 90:10);

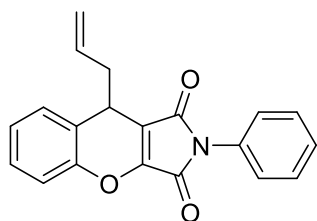


^1H NMR (400 MHz, CDCl_3): δ 7.58 (d, J = 8.4 Hz, 2H), 7.53 (d, J = 8.3 Hz, 2H), 7.40 (s, 1H), 7.34 (t, J = 7.6 Hz, 2H), 7.12 – 7.01 (m, 2H), 5.43 (ddt, J = 17.4, 10.1, 7.5 Hz, 1H), 4.96 (dt, J = 16.9, 1.5 Hz, 1H), 4.89 (dd, J = 10.1, 1.6 Hz, 1H), 4.78 (s, 1H), 2.65

(ddd, $J = 7.7, 3.1, 1.3$ Hz, 2H). **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3):** δ 172.6, 165.2, 153.2, 144.2 – 144.1 (m), 139.2, 133.1, 130.2, 129.5, 128.2, 128.1, 128.1 – 119.9 (m), 125.8 (q, $J = 3.7$ Hz), 123.4, 123.2, 121.6, 120.6, 118.1, 77.6, 41.6, 39.1. **^{19}F NMR (377 MHz, CDCl_3):** δ -62.7. **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{22}\text{H}_{17}\text{F}_3\text{NO}_3$ ($\text{M} + \text{H}$) $^+$: 400.1161, Found: 400.1154.

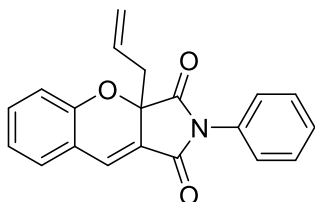
9-allyl-2-phenylchromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2j):

Compound **2i** was synthesized following the general procedure-C. The product was obtained as white solid, 19 mg (40 % yield); $R_f = 0.6$ (petroleum ether/EtOAc 90:10);



^1H NMR (400 MHz, CDCl_3): δ 7.51 – 7.44 (m, 2H), 7.40 – 7.34 (m, 3H), 7.34 – 7.27 (m, 2H), 7.23 (ddd, $J = 8.1, 5.7, 1.5$ Hz, 2H), 5.59 (dddd, $J = 16.7, 10.2, 8.4, 6.2$ Hz, 1H), 5.10 – 4.91 (m, 2H), 4.21 (t, $J = 4.7$ Hz, 1H), 2.83 (dddt, $J = 13.1, 8.4, 4.7, 1.0$ Hz, 1H), 2.68 (dddt, $J = 12.6, 6.2, 4.8, 1.3$ Hz, 1H). **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3):** δ 168.0, 162.9, 151.7, 150.9, 133.5, 131.2, 129.6, 129.3, 128.9, 127.9, 126.3, 126.3, 122.5, 119.3, 118.1, 113.2, 40.2, 32.2. **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{20}\text{H}_{16}\text{NO}_3$ ($\text{M} + \text{H}$) $^+$: 318.1130, Found: 318.1127.

3a-allyl-2-phenylchromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2j'):

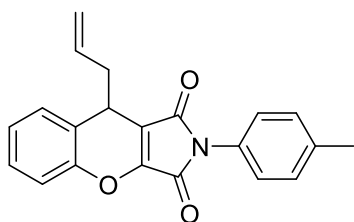


Compound **2i'** was synthesized following the general procedure-C. The product was obtained as white solid, 19 mg (40 % yield);

$R_f = 0.5$ (petroleum ether/EtOAc 90:0); **^1H NMR (400 MHz, CDCl_3):** δ 7.53 – 7.46 (m, 3H), 7.45 – 7.41 (m, 1H), 7.40 – 7.31 (m, 4H), 7.14 (dt, $J = 8.7, 1.0$ Hz, 1H), 7.08 (td, $J = 7.5, 1.1$ Hz, 1H), 5.75 (dddd, $J = 17.1, 10.4, 8.1, 7.0$ Hz, 1H), 5.31 – 5.03 (m, 2H), 2.90 – 2.70 (m, 2H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 172.2, 164.7, 153.3, 133.1, 131.2, 130.2, 129.4, 129.0, 128.6, 126.5, 123.5, 123.2, 122.0, 120.7, 118.1, 77.7, 39.4.; **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{20}\text{H}_{16}\text{NO}_3$ ($\text{M} + \text{H}$) $^+$: 318.1130, Found: 318.1129.

9-allyl-2-(p-tolyl)chromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2k) Compound **2k** was synthesized following the general procedure-C. The product was obtained as white solid, 15 mg (30 % yield); $R_f = 0.5$ (petroleum ether/EtOAc 80:20);



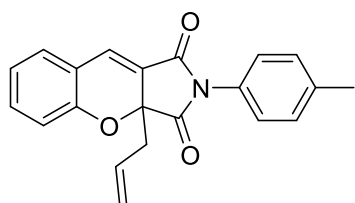
¹H NMR (400 MHz, CDCl₃): δ 7.34 – 7.26 (m, 4H), 7.25 – 7.19 (m, 4H), 5.58 (dddd, *J* = 16.7, 10.2, 8.4, 6.3 Hz, 1H), 5.10 – 4.90 (m, 2H), 4.20 (t, *J* = 4.7 Hz, 1H), 2.90 – 2.74 (m, 1H), 2.67 (dddt, *J* = 13.8, 6.1, 4.8, 1.3 Hz, 1H), 2.39 (s, 3H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 168.1, 163.0, 151.7,

151.0, 138.0, 133.5, 129.9, 129.6, 128.9, 128.5, 126.3, 126.2, 122.51, 119.2, 118.1, 113.2, 40.2, 32.2, 21.3. **HRMS (ESI TOF) *m/z*:** calcd for C₂₁H₁₈NO₃ (M + H)⁺: 332.1287, Found: 332.1286.

3a-allyl-2-(p-tolyl)chromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2k'):

Compound **2k'** was synthesized following the general procedure-C. The product was obtained as white solid, 19.5 mg (39 % yield); *R_f*=0.45 (petroleum ether/EtOAc 80:20);



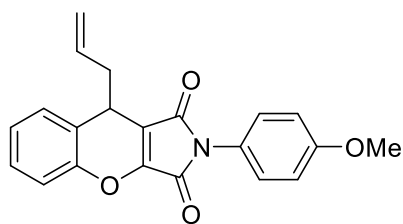
¹H NMR (400 MHz, CDCl₃): δ 7.49 (s, 1H), 7.41 – 7.32 (m, 2H), 7.29 (d, *J* = 8.2 Hz, 2H), 7.25 – 7.17 (m, 2H), 7.14 (dt, *J* = 8.7, 0.9 Hz, 1H), 7.08 (td, *J* = 7.5, 1.1 Hz, 1H), 5.74 (dddd, *J* = 17.1, 10.4, 8.1, 7.0 Hz, 1H), 5.26 – 5.12 (m, 2H), 2.90 – 2.73 (m,

2H), 2.39 (s, 3H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 172.3, 164.9, 153.3, 139.1, 133.1, 130.1, 130.0, 128.6, 128.5, 128.4, 126.3, 123.6, 123.2, 121.9, 120.8, 118.1, 77.7, 39.4, 21.4. .

HRMS (ESI TOF) *m/z*: calcd for C₂₁H₁₈NO₃ (M + H)⁺: 332.1287, Found: 332.1268.

9-allyl-2-(4-methoxyphenyl)chromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2l):

Compound **2l** was synthesized following the general procedure-C. The product was obtained as white solid, 16 mg (32% yield); *R_f*=0.35 (petroleum ether/EtOAc 90:10);

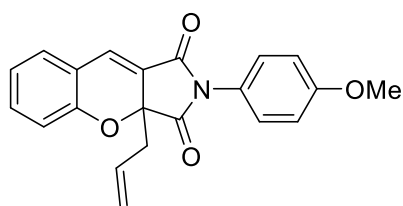


¹H NMR (400 MHz, CDCl₃): δ 7.33 – 7.28 (m, 2H), 7.27 – 7.17 (m, 4H), 7.01 – 6.95 (m, 2H), 5.58 (dddd, *J* = 16.7, 10.2, 8.4, 6.2 Hz, 1H), 5.09 – 4.73 (m, 2H), 4.19 (t, *J* = 4.7 Hz, 1H), 3.83 (s, 3H), 2.81 (ddd, *J* = 13.5, 8.5, 4.7 Hz, 1H), 2.67

(dddd, *J* = 15.5, 7.6, 4.4, 1.4 Hz, 1H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** 168.3, 163.2, 159.2, 151.7, 150.9, 133.5, 129.6, 128.9, 127.9, 126.2, 123.8, 122.5, 119.2, 118.1, 114.6, 113.1, 55.6, 40.2, 32.2. **HRMS (ESI TOF) *m/z*:** calcd for C₂₁H₁₈NO₄ (M + H)⁺: 348.1236, Found: 348.1235.

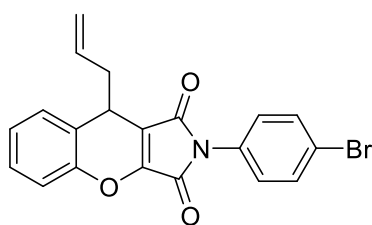
3a-allyl-2-(4-methoxyphenyl)chromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2l'):

Compound **2l'** was synthesized following the general procedure-C. The product was obtained as white solid, 21 mg (40% yield); *R_f*=0.35 (petroleum ether/EtOAc 90:10);



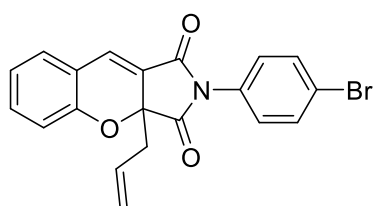
¹H NMR (400 MHz, CDCl₃): δ 7.49 (s, 1H), 7.36 (ddq, *J* = 5.6, 3.9, 1.6 Hz, 2H), 7.28 – 7.22 (m, 2H), 7.13 (dt, *J* = 8.7, 0.9 Hz, 1H), 7.07 (td, *J* = 7.5, 1.1 Hz, 1H), 7.03 – 6.97 (m, 2H), 5.73 (dddd, *J* = 17.2, 10.4, 8.1, 7.0 Hz, 1H), 5.26 – 5.07 (m, 2H), 3.83 (s, 3H), 2.95 – 2.63 (m, 2H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 172.4, 165.0, 159.8, 153.3, 133.0, 130.1, 128.6, 128.3, 127.7, 123.8, 123.6, 123.2, 121.9, 120.8, 118.1, 114.7, 77.7, 55.6, 39.4. **HRMS (ESI TOF) *m/z*:** calcd for C₂₁H₁₈NO₄ (*M* + H)⁺: 348.1236, Found: 348.1240.

9-allyl-2-(4-bromophenyl)chromeno[2,3-*c*]pyrrole-1,3(2H,9H)-dione (2m): Compound **2m**



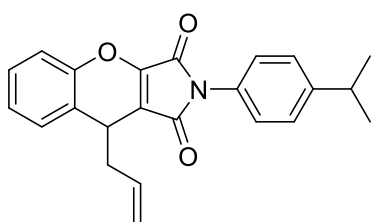
was synthesized following the general procedure-C. The product was obtained as white solid, 20 mg (33% yield); *R_f* = 0.6 (petroleum ether/EtOAc 90:10); **¹H NMR (400 MHz, CDCl₃):** δ 7.61 – 7.54 (m, 2H), 7.28 (tt, *J* = 7.3, 5.1 Hz, 4H), 7.24 – 7.17 (m, 2H), 5.56 (dddd, *J* = 16.6, 10.2, 8.4, 6.2 Hz, 1H), 5.18 – 4.85 (m, 2H), 4.18 (t, *J* = 4.7 Hz, 1H), 2.80 (ddd, *J* = 13.5, 8.5, 4.8 Hz, 1H), 2.74 – 2.55 (m, 1H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 167.6, 162.4, 151.8, 150.8, 133.4, 132.4, 130.3, 129.6, 129.0, 127.5, 126.4, 122.3, 121.5, 119.3, 118.1, 113.4, 40.2, 32.2. **HRMS (ESI TOF) *m/z*:** calcd for C₂₀H₁₅BrNO₃ (*M* + H)⁺: 396.0235, Found: 396.0232.

3a-allyl-2-(4-bromophenyl)chromeno[2,3-*c*]pyrrole-1,3(2H,3aH)-dione (2m'): Compound



2m' was synthesized following the general procedure-C. The product was obtained as white solid, 24 mg (40% yield); *R_f* = 0.5 (petroleum ether/EtOAc 90:10); **¹H NMR (400 MHz, CDCl₃):** δ 7.66 – 7.56 (m, 2H), 7.51 (s, 1H), 7.42 – 7.34 (m, 2H), 7.30 – 7.21 (m, 2H), 7.14 (dt, *J* = 8.7, 0.9 Hz, 1H), 7.08 (td, *J* = 7.5, 1.1 Hz, 1H), 5.71 (dddd, *J* = 17.1, 10.4, 8.1, 6.9 Hz, 1H), 5.27 – 5.05 (m, 2H), 2.95 – 2.68 (m, 2H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 171.7, 164.3, 153.26, 133.3, 132.5, 130.2, 130.2, 129.0, 128.4, 127.9, 123.3, 123.1, 122.9, 122.1, 120.6, 118.1, 77.7, 39.4. **HRMS (ESI TOF) *m/z*:** calcd for C₂₀H₁₅BrNO₃ (*M* + H)⁺: 396.0235, Found: 396.0236.

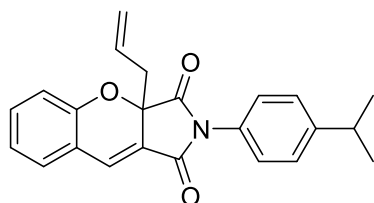
9-allyl-2-(4-isopropylphenyl)chromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2n):Compound



2n was synthesized following the general procedure-C. The product was obtained as white solid, 15 mg (28 % yield); R_f = 0.35 (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): δ 7.31 (dt, J = 7.2, 2.0 Hz, 3H), 7.30 – 7.22 (m, 3H), 7.21 (ddd, J = 8.2, 5.4, 1.6 Hz, 2H), 5.57 (dddd, J = 16.6, 10.2,

8.4, 6.2 Hz, 1H), 5.06 – 4.91 (m, 2H), 4.19 (t, J = 4.7 Hz, 1H), 2.93 (hept, J = 6.9 Hz, 1H), 2.81 (ddd, J = 13.5, 8.5, 4.7 Hz, 1H), 2.66 (dddt, J = 13.9, 6.1, 4.7, 1.4 Hz, 1H), 1.25 (d, J = 7.0 Hz, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 168.2, 163.1, 151.7, 150.9, 148.8, 133.5, 129.6, 128.9, 128.7, 127.4, 126.3, 126.2, 122.5, 119.2, 118.1, 113.2, 40.2, 34.0, 32.2, 24.1. HRMS (ESI TOF) m/z : calcd for $\text{C}_{23}\text{H}_{22}\text{NO}_3$ ($M + \text{H}$) $^+$: 360.1600, Found: 360.1604.

3a-allyl-2-(4-isopropylphenyl)chromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2n'):

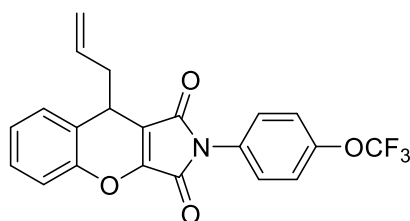


Compound **2n'** was synthesized following the general procedure-C. The product was obtained as white solid, 16.5 mg (30 % yield); R_f = 0.35 (petroleum ether/EtOAc 90:10);

^1H NMR (400 MHz, CDCl_3): δ 7.50 (s, 0H), 7.36 (ddt, J = 14.4, 8.6, 2.1 Hz, 2H), 7.28 – 7.21 (m, 1H), 7.14 (dt, J = 8.7, 0.9 Hz, 0H), 7.08 (td, J = 7.5, 1.1 Hz, 0H), 5.74 (dddd, J = 17.2, 10.5, 8.1, 7.0 Hz, 0H), 5.24 – 5.14 (m, 1H), 2.95 (hept, J = 6.9 Hz, 0H), 2.91 – 2.73 (m, 1H), 1.27 (d, J = 7.0 Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 172.3, 164.9, 153.3, 149.8, 133.1, 130.2, 128.7, 128.6, 128.4, 127.5, 126.3, 123.6, 123.2, 121.9, 120.8, 118.1, 77.7, 39.4, 34.1, 24.0. HRMS (ESI TOF) m/z : calcd for $\text{C}_{23}\text{H}_{22}\text{NO}_3$ ($M + \text{H}$) $^+$: 360.1600, Found: 360.1601.

9-allyl-2-(4-(trifluoromethoxy)phenyl)chromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2o):

Compound **2o** was synthesized following the general procedure-C. The product was obtained as white solid, 20.5 mg (34 % yield); R_f = 0.5 (petroleum ether/EtOAc 90:10);



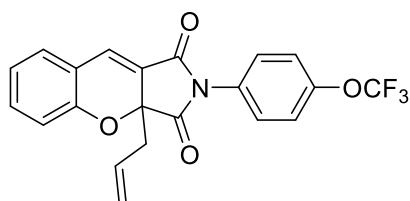
^1H NMR (400 MHz, CDCl_3): δ 7.47 – 7.41 (m, 2H), 7.34 – 7.27 (m, 4H), 7.26 – 7.20 (m, 2H), 5.58 (dddd, J = 16.6, 10.2, 8.4, 6.2 Hz, 1H), 5.08 – 4.92 (m, 2H), 4.21 (t, J = 4.7 Hz, 1H), 2.87–2.63 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 167.6, 162.5, 151.8, 150.8, 148.2 (dd, J = 3.7, 1.7

Hz), 133.4, 129.8, 129.6, 129.0, 127.4, 126.4, 124.4, 122.3, 121.9, 120.4 (d, J = 262.2 Hz),

119.3, 118.1, 116.7, 113.4, 40.2, 32.2. ¹⁹F NMR (377 MHz, CDCl₃) δ -57.9. HRMS (ESI TOF) *m/z*: calcd for C₂₁H₁₅F₃NO₄ (M + H)⁺: 402.0953, Found: 402.0960.

9-allyl-2-(4-(trifluoromethoxy)phenyl)chromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2o')

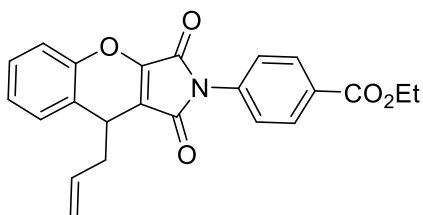
Compound **2o'** was synthesized following the general procedure-C. The product was obtained as white solid, 20.5 mg (34 % yield); *R_f*=0.45 (petroleum ether/EtOAc 90:10); ¹H NMR (400



MHz, CDCl₃): δ 7.47 – 7.42 (m, 2H), 7.34 – 7.27 (m, 4H), 7.26 – 7.20 (m, 2H), 5.58 (dddd, *J* = 16.6, 10.2, 8.4, 6.2 Hz, 1H), 5.07 – 4.93 (m, 2H), 4.21 (t, *J* = 4.7 Hz, 1H), 2.88 – 2.63 (m, 2H). ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 172.0, 164.4, 153.3, 149.11 – 149.01 (m), 133.4, 130.3, 129.6,

129.1, 128.4, 127.9, 123.3, 123.0, 122.1, 120.6, 118.7 (q), 118.2, 77.7, 39.4. ¹⁹F NMR (377 MHz, CDCl₃): δ -57.8. HRMS (ESI TOF) *m/z*: calcd for C₂₁H₁₅F₃NO₄ (M + H)⁺: 402.0953, Found: 402.0956.

ethyl 4-(9-allyl-1,3-dioxo-3,3a-dihydrochromeno[2,3-c]pyrrol-2(1H)-yl)benzoate (2p):

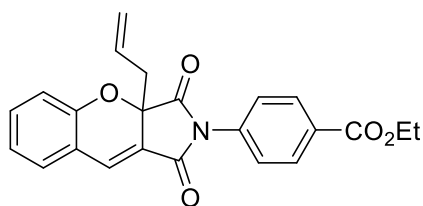


Compound **2p** was synthesized following the general procedure-C. The product was obtained as white solid, 20 mg (5.5 % yield); *R_f*=0.35 (petroleum ether/EtOAc 90:10);

¹H NMR (400 MHz, CDCl₃): δ 8.18 – 8.10 (m, 2H), 7.56 – 7.48 (m, 2H), 7.36 – 7.26 (m, 2H), 7.28 – 7.19 (m, 2H), 5.58 (dddd, *J* = 16.6, 10.2, 8.4, 6.2 Hz, 1H), 5.11 – 4.87 (m, 2H), 4.40 (q, *J* = 7.1 Hz, 2H), 4.21 (t, *J* = 4.7 Hz, 1H), 2.93 – 2.63 (m, 2H), 1.40 (t, *J* = 7.1 Hz, 3H). ¹³C{¹H} NMR (100 MHz, CDCl₃): δ 167.5, 166.0, 162.3, 151.8, 150.8, 135.4, 133.3, 130.5, 129.6, 129.4, 129.0, 126.4, 125.3, 122.3, 119.4, 118.1, 113.5, 61.3, 40.2, 32.2, 14.5. HRMS (ESI TOF) *m/z*: calcd for C₂₃H₂₀NO₅ (M + H)⁺: 390.1341, Found: 390.1338.

ethyl 4-(3a-allyl-1,3-dioxo-3,3a-dihydrochromeno[2,3-c]pyrrol-2(1H)-yl)benzoate (2p')

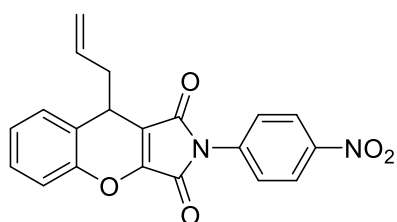
Compound **2p'** was synthesized following the general procedure-C. The product was obtained as white solid, 23 mg (39 % yield); *R_f*=0.5 (petroleum ether/EtOAc 90:10);



¹H NMR (400 MHz, CDCl₃): δ 8.22 – 8.08 (m, 2H), 7.53 (s, 1H), 7.51 – 7.44 (m, 2H), 7.38 (ddt, *J* = 7.6, 2.9, 1.7 Hz, 2H), 7.18 – 7.12 (m, 1H), 7.09 (td, *J* = 7.4, 1.1 Hz, 1H), 5.73 (dddd, *J* = 17.1, 10.4, 8.1, 6.9 Hz, 1H), 5.24 – 5.13 (m, 2H),

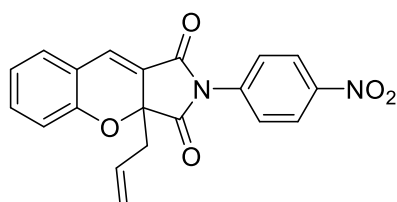
4.40 (q, $J = 7.1$ Hz, 2H), 2.92 – 2.68 (m, 2H), 1.40 (t, $J = 7.1$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 171.8, 165.8, 164.2, 153.3, 135.1, 133.3, 130.7, 130.6, 130.3, 129.1, 128.4, 126.2, 123.3, 123.0, 122.1, 120.6, 118.1, 77.7, 61.4, 39.4, 14.4. HRMS (ESI TOF) m/z : calcd for $\text{C}_{23}\text{H}_{20}\text{NO}_5$ ($\text{M} + \text{H}$) $^+$: 390.1341, Found: 390.1336.

9-allyl-2-(4-nitrophenyl)chromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2q): Compound **2q** was synthesized following the general procedure-C. The product was obtained as white solid, 11.5 mg (21 % yield); R_f =0.4 (petroleum ether/EtOAc 90:10);



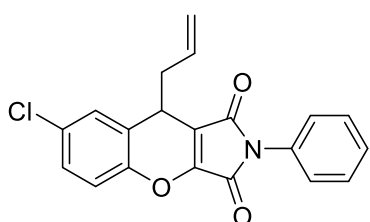
^1H NMR (400 MHz, CDCl_3): δ 8.38 – 8.28 (m, 2H), 7.75 – 7.65 (m, 2H), 7.37 – 7.27 (m, 2H), 7.29 – 7.20 (m, 2H), 5.58 (dddd, $J = 16.6, 10.2, 8.4, 6.2$ Hz, 1H), 5.04 (ddd, $J = 10.2, 1.9, 0.9$ Hz, 1H), 5.00 (dq, $J = 17.0, 1.5$ Hz, 1H), 4.23 (t, $J = 4.7$ Hz, 1H), 2.94 – 2.57 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 167.0, 161.9, 152.0, 150.7, 146.1, 137.3, 133.2, 129.6, 129.1, 126.6, 125.5, 124.6, 122.1, 119.5, 118.2, 113.9, 40.1, 32.2. HRMS (ESI TOF) m/z : calcd for $\text{C}_{20}\text{H}_{15}\text{N}_2\text{O}_5$ ($\text{M} + \text{H}$) $^+$: 363.0981, Found: 363.0982.

3a-allyl-2-(4-nitrophenyl)chromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2q'): Compound **2q'** was synthesized following the general procedure-C. The product was obtained as white solid, 12.5 mg (23 % yield); R_f =0.35 (petroleum ether/EtOAc 90:10);



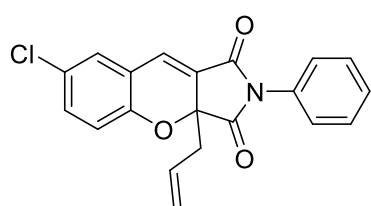
^1H NMR (400 MHz, CDCl_3): δ 8.39 – 8.31 (m, 2H), 7.68 – 7.60 (m, 2H), 7.57 (s, 1H), 7.41 (td, $J = 7.4, 1.5$ Hz, 2H), 7.15 (dt, $J = 8.6, 1.0$ Hz, 1H), 7.11 (td, $J = 7.5, 1.1$ Hz, 1H), 5.72 (dddd, $J = 17.0, 10.4, 8.2, 6.9$ Hz, 1H), 5.25 – 5.12 (m, 2H), 2.93 – 2.71 (m, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 171.5, 163.8, 153.2, 147.2, 136.8, 133.6, 130.4, 129.9, 128.3, 126.9, 124.6, 123.5, 122.4, 122.3, 120.5, 118.2, 77.8, 39.5. HRMS (ESI TOF) m/z : calcd for $\text{C}_{20}\text{H}_{15}\text{N}_2\text{O}_5$ ($\text{M} + \text{H}$) $^+$: 363.0981, Found: 363.0984.

9-allyl-7-chloro-2-phenylchromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2r): Compound **2r** was synthesized following the general procedure-C. The product was obtained as white solid, 14 mg (26 % yield); R_f =0.5 (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): δ 7.50 – 7.43 (m, 2H), 7.40 – 7.33 (m, 3H), 7.32 –



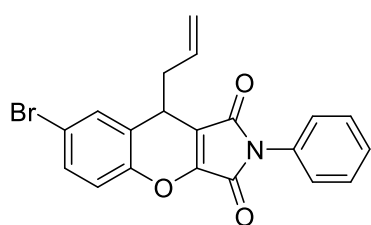
7.29 (m, 1H), 7.28 – 7.24 (m, 1H), 7.17 (d, $J = 8.7$ Hz, 1H), 5.58 (dddd, $J = 16.7, 10.3, 8.4, 6.2$ Hz, 1H), 5.16 – 4.88 (m, 2H), 4.17 (t, $J = 4.6$ Hz, 1H), 2.98 – 2.75 (m, 1H), 2.66 (dddt, $J = 13.9, 6.1, 4.7, 1.4$ Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 167.6, 162.5, 151.5, 149.5, 132.9, 131.4, 131.1, 129.3, 129.3, 129.1, 128.1, 126.3, 124.3, 119.8, 119.5, 112.9, 40.0, 32.4. HRMS (ESI TOF) m/z : calcd for $\text{C}_{20}\text{H}_{15}\text{ClNO}_2$ ($\text{M} + \text{H}$) $^+$: 352.0740, Found: 352.0742.

3a-allyl-7-chloro-2-phenylchromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2r'): Compound **2q'** was synthesized following the general procedure-C. The product was obtained as white solid, 17 mg (32 % yield); $R_f=0.45$ (petroleum ether/EtOAc 90:10);



^1H NMR (400 MHz, CDCl_3): δ 7.50 (dd, $J = 8.3, 6.7$ Hz, 2H), 7.46 – 7.40 (m, 2H), 7.37 – 7.29 (m, 4H), 7.09 (d, $J = 8.7$ Hz, 1H), 5.80 – 5.65 (m, 1H), 5.28 – 5.06 (m, 2H), 2.81 (qd, $J = 13.1, 7.6$ Hz, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 171.7, 164.3, 151.8, 132.8, 131.1, 129.4, 129.1, 128.2, 128.1, 127.3, 126.4, 124.9, 122.3, 121.9, 119.4, 78.0, 39.4. HRMS (ESI TOF) m/z : calcd for $\text{C}_{20}\text{H}_{15}\text{ClNO}_2$ ($\text{M} + \text{H}$) $^+$: 352.0740, Found: 352.0742.

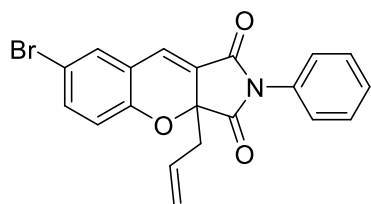
9-allyl-7-bromo-2-phenylchromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2s): Compound **2s**



was synthesized following the general procedure-C. The product was obtained as white solid, 15 mg (25 % yield); $R_f=0.5$ (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): δ 7.50 – 7.43 (m, 3H), 7.43 – 7.33 (m, 4H), 7.11 (d, $J = 8.7$ Hz, 1H), 5.58 (dddd, $J = 16.7, 10.2, 8.4, 6.2$ Hz, 1H), 5.11 – 5.04 (m, 1H), 5.02 (dq, $J = 16.9, 1.5$ Hz, 1H), 4.17 (t, $J = 4.6$ Hz, 1H), 2.89 – 2.60 (m, 2H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 167.6, 162.5, 151.4, 150.0, 132.9, 132.3, 132.0, 131.1, 129.3, 129.3, 128.0, 126.3, 124.7, 119.8, 118.9, 113.0, 40.0, 32.3. HRMS (ESI TOF) m/z : calcd for $\text{C}_{20}\text{H}_{15}\text{BrNO}_2$ ($\text{M} + \text{H}$) $^+$: 396.0235, Found: 396.0242.

3a-allyl-7-bromo-2-phenylchromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2s'): Compound **2s'** was synthesized following the general procedure-C. The product was obtained as white solid, 20 mg (34 % yield); $R_f=0.45$ (petroleum ether/EtOAc 90:10);

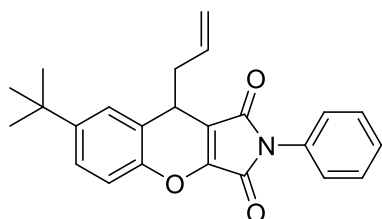


¹H NMR (400 MHz, CDCl₃): δ 7.53 – 7.40 (m, 6H), 7.36 – 7.29 (m, 2H), 7.03 (d, *J* = 8.6 Hz, 1H), 5.72 (dddd, *J* = 17.1, 10.3, 8.0, 7.0 Hz, 1H), 5.29 – 5.03 (m, 2H), 2.94 – 2.52 (m, 2H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 171.7, 164.3, 152.3,

135.7, 132.4, 131.1, 129.4, 129.1, 128.2, 127.2, 126.4, 124.8, 122.5, 122.3, 119.8, 115.3, 77.9, 39.5. **HRMS (ESI TOF) *m/z*:** calcd for C₂₀H₁₅BrNO₂ (*M* + *H*)⁺: 396.0235, Found: 396.0236.

9-allyl-7-(tert-butyl)-2-phenylchromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2t):Compound

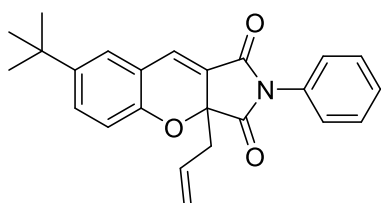


2t was synthesized following the general procedure-C. The product was obtained as white solid, 12.5 mg (22 % yield); *R_f* = 0.5 (petroleum ether/EtOAc 90:10);

¹H NMR (400 MHz, CDCl₃): δ 7.53 – 7.42 (m, 2H), 7.41 – 7.31 (m, 3H), 7.34 – 7.27 (m, 2H), 7.18 – 7.11 (m, 1H), 5.62

(dddd, *J* = 16.6, 10.1, 8.4, 6.2 Hz, 1H), 5.14 – 4.88 (m, 2H), 4.18 (t, *J* = 4.8 Hz, 1H), 2.92 – 2.52 (m, 2H), 1.33 (s, 9H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 168.1, 163.0, 151.9, 149.4, 148.7, 133.9, 131.3, 129.2, 127.9, 126.4, 126.3, 125.9, 121.65, 119.0, 117.5, 113.1, 40.5, 34.7, 32.4, 31.5. **HRMS (ESI TOF) *m/z*:** calcd for C₂₄H₂₄NO₃ (*M* + *H*)⁺: 374.1756, Found: 374.1755.

3a-allyl-7-(tert-butyl)-2-phenylchromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2t'):



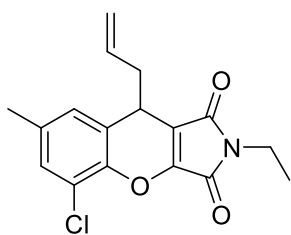
Compound **2t'** was synthesized following the general procedure-C. The product was obtained as white solid, 15.5 mg (28 % yield); *R_f* = 0.45 (petroleum ether/EtOAc 90:10);

¹H NMR (400 MHz, CDCl₃): 7.54 – 7.45 (m, 3H), 7.46 – 7.37

(m, 2H), 7.38 – 7.31 (m, 3H), 7.07 (d, *J* = 8.5 Hz, 1H), 5.86 – 5.48 (m, 1H), 5.28 – 5.05 (m, 2H), 2.98 – 2.67 (m, 2H), 1.33 (s, 9H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 172.3, 164.8, 151.1, 146.2, 131.3, 130.5, 129.3, 129.1, 129.0, 128.7, 126.8, 126.5, 123.2, 121.9, 120.1, 117.6, 77.8, 39.3, 34.4, 31.5. **HRMS (ESI TOF) *m/z*:** calcd for C₂₄H₂₄NO₃ (*M* + *H*)⁺: 374.1756, Found: 374.1760.

9-allyl-5-chloro-2-ethyl-7-methylchromeno[2,3-c]pyrrole-1,3(2H,9H)-dione

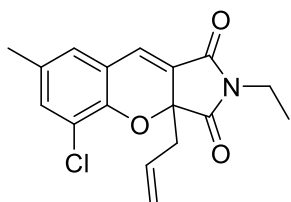
(2u):Compound **2u** was synthesized following the general procedure-C. The product was obtained as white solid, 8 mg (15 % yield); *R_f* = 0.4 (petroleum ether/EtOAc 90:10);



¹H NMR (400 MHz, CDCl₃): δ 6.95 – 6.74 (m, 2H), 5.50 (dddd, *J* = 16.7, 10.3, 8.4, 6.3 Hz, 1H), 5.04 – 4.97 (m, 1H), 4.95 (dq, *J* = 16.9, 1.4 Hz, 1H), 4.05 (t, *J* = 4.6 Hz, 1H), 3.89 (s, 3H), 3.58 (q, *J* = 7.2 Hz, 2H), 2.81 – 2.67 (m, 1H), 2.58 (dddt, *J* = 13.9, 6.0, 4.6, 1.3 Hz, 1H), 1.19 (t, *J* = 7.2 Hz, 3H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** 168.7, 163.4, 151.4, 149.5, 139.5, 133.1, 131.0, 124.7, 120.2, 119.5, 112.7, 111.9, 56.4, 39.8, 32.7, 32.4, 14.2. **HRMS (ESI TOF) *m/z*:** calcd for C₁₇H₁₇ClNO₃ (M + H)⁺: 318.0897, Found: 318.0899.

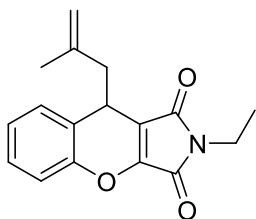
3a-allyl-5-chloro-2-ethyl-7-methylchromeno[2,3-c]pyrrole-1,3(2*H*,3*aH*)-dione (2u'):

Compound **2u'** was synthesized following the general procedure-C. The product was obtained as white solid, 9 mg (16 % yield); *R_f*=0.35 (petroleum ether/EtOAc 90:10);



¹H NMR (400 MHz, CDCl₃): ¹H NMR (400 MHz, Chloroform-*d*) δ 7.27 (s, 1H), 6.96 – 6.89 (m, 2H), 5.58 (ddt, *J* = 18.9, 9.5, 7.5 Hz, 1H), 5.12 (s, 1H), 5.12 – 5.05 (m, 1H), 3.87 (s, 3H), 3.74 – 3.54 (m, 2H), 2.69 (dd, *J* = 7.5, 3.2 Hz, 2H), 1.20 (t, *J* = 7.2 Hz, 3H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 172.1, 165.2, 150.1, 141.3, 128.4, 127.7, 126.0, 125.4, 122.1, 121.8, 120.7, 115.6, 77.7, 56.5, 38.8, 33.6, 13.2. **HRMS (ESI TOF) *m/z*:** calcd for C₁₇H₁₇ClNO₃ (M + H)⁺: 318.0897, Found: 318.0895.

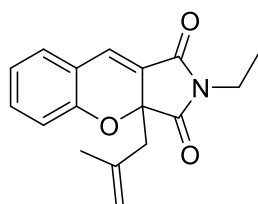
2-ethyl-9-(2-methylallyl)chromeno[2,3-c]pyrrole-1,3(2*H*,9*H*)-dione (2u):Compound **2u**



was synthesized following the general procedure-C. The product was obtained as white solid, 13 mg (31 % yield); *R_f* = 0.6 (petroleum ether/EtOAc 90:10);

¹H NMR (400 MHz, CDCl₃): δ 7.31 – 7.21 (m, 2H), 7.20 – 7.12 (m, 2H), 4.76 (q, *J* = 1.7 Hz, 1H), 4.50 (dd, *J* = 2.3, 1.2 Hz, 1H), 4.13 (t, *J* = 5.5 Hz, 1H), 3.59 (q, *J* = 7.2 Hz, 2H), 2.66 (ddd, *J* = 13.5, 6.0, 0.8 Hz, 1H), 2.54 (ddd, *J* = 13.5, 4.9, 1.1 Hz, 1H), 1.56 (t, *J* = 1.1 Hz, 3H), 1.19 (t, *J* = 7.2 Hz, 3H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 169.1, 164.1, 151.5, 150.7, 141.9, 129.8, 128.7, 125.8, 123.4, 118.1, 115.1, 113.7, 45.3, 32.6, 31.4, 23.0, 14.2. **HRMS (ESI TOF) *m/z*:** calcd for C₁₇H₁₈NO₃ (M + H)⁺: 284.1287, Found: 284.1288.

2-ethyl-3a-(2-methylallyl)chromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2v'):Compound **2v'**

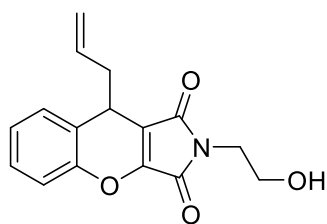


was synthesized following the general procedure-C. The product was obtained as white solid, 19.5 mg (46 % yield); R_f =0.5 (petroleum ether/EtOAc 90:10);

^1H NMR (400 MHz, CDCl_3): δ 7.37 – 7.31 (m, 3H), 7.12 – 7.08 (m, 1H), 7.05 (td, J = 7.5, 1.1 Hz, 1H), 4.89 (t, J = 1.6 Hz, 1H), 4.73 (dd, J = 1.9, 1.0 Hz, 1H), 3.77 – 3.52 (m, 2H), 2.68 (s, 2H), 1.70 (t, J = 1.2 Hz, 3H), 1.21 (t, J = 7.2 Hz, 3H). **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3):** δ 173.1, 165.8, 153.3, 137.5, 132.8, 130.0, 126.6, 124.8, 123.1, 120.8, 118.1, 117.8, 77.9, 41.9, 33.6, 24.1, 13.1. **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{17}\text{H}_{18}\text{NO}_3$ ($\text{M} + \text{H}$) $^+$: 284.1287, Found: 284.1290.

9-allyl-2-(2-hydroxyethyl)chromeno[2,3-c]pyrrole-1,3(2H,9H)-dione (2w): Compound **2w**

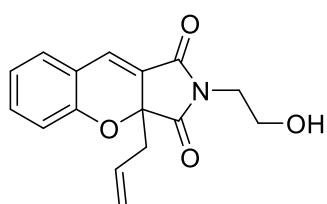
was synthesized following the general procedure-C. The product was obtained as white solid, 15 mg (35 % yield); R_f =0.4 (petroleum ether/EtOAc 80:20);



^1H NMR (400 MHz, CDCl_3): δ 7.30 – 7.23 (m, 2H), 7.18 (ddd, J = 14.2, 7.6, 1.4 Hz, 2H), 5.53 (dddd, J = 16.7, 10.2, 8.3, 6.3 Hz, 1H), 5.03 – 4.84 (m, 2H), 4.32 – 4.16 (m, 2H), 4.11 (t, J = 4.7 Hz, 1H), 3.80 (td, J = 5.1, 2.0 Hz, 2H), 2.75 (ddd, J = 13.4, 8.3, 4.7 Hz, 1H), 2.62 (dtd, J = 15.4, 6.1, 1.5 Hz, 1H). **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3):** δ 168.8, 163.8, 151.8, 150.8, 133.4, 129.5, 128.8, 126.1, 122.4, 119.1, 118.0, 113.2, 61.7, 40.1, 36.7, 20.9. **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{16}\text{H}_{16}\text{NO}_4$ ($\text{M} + \text{H}$) $^+$: 286.1079, Found: 286.1082.

3a-allyl-2-(2-hydroxyethyl)chromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2w'):Compound **2w'**

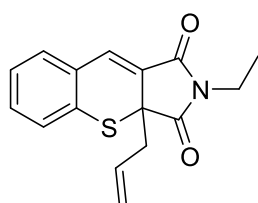
was synthesized following the general procedure-C. The product was obtained as white solid, 16 mg (37 % yield); R_f =0.35 (petroleum ether/EtOAc 80:20);



^1H NMR (400 MHz, CDCl_3): δ 7.38 (s, 1H), 7.33 (d, J = 7.5 Hz, 2H), 7.11 – 7.07 (m, 1H), 7.05 (td, J = 7.5, 1.1 Hz, 1H), 5.65 (ddt, J = 16.8, 10.3, 7.5 Hz, 1H), 5.14 – 5.01 (m, 2H), 4.33 – 4.18 (m, 2H), 3.86 (dt, J = 6.4, 4.5 Hz, 2H), 2.68 (dd, J = 7.5, 1.1 Hz, 2H).

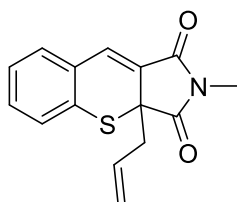
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 170.8, 165.3, 153.2, 133.0, 130.1, 128.6, 127.7, 123.6, 123.1, 121.5, 120.7, 118.1, 61.0, 39.1, 37.5, 20.9. **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{16}\text{H}_{16}\text{NO}_4$ ($\text{M} + \text{H}$) $^+$: 286.1079, Found: 286.1076.

3a-allyl-2-ethylthiochromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2aa): Compound **2aa** was synthesized following the general procedure-C. The product was obtained as white solid, 28.5 mg (66 % yield); R_f =0.5 (petroleum ether/EtOAc 90:10);



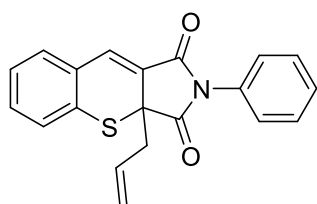
^1H NMR (400 MHz, CDCl_3): δ 7.47 (s, 1H), 7.45 (dd, J = 7.5, 1.7 Hz, 1H), 7.42 (dd, J = 7.7, 1.3 Hz, 1H), 7.30 (td, J = 7.6, 1.7 Hz, 1H), 7.27 – 7.21 (m, 1H), 5.54 (ddt, J = 16.7, 10.4, 7.5 Hz, 1H), 5.09 – 4.96 (m, 2H), 3.78 – 3.47 (m, 2H), 2.66 (dt, J = 7.2, 1.1 Hz, 2H), 1.21 (t, J = 7.2 Hz, 3H). **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3):** δ 174.3, 167.2, 132.4, 131.4, 130.8, 130.3, 129.6, 129.6, 128.7, 126.8, 126.5, 121.2, 48.4, 42.0, 34.0, 13.2. **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{16}\text{H}_{16}\text{NO}_2\text{S}$ ($\text{M} + \text{H}$) $^+$: 286.0902, Found: 286.1082.

3a-allyl-2-methylthiochromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2ab): Compound **2ab** was synthesized following the general procedure-C. The product was obtained as white solid, 26.5 mg (65 % yield); R_f =0.6 (petroleum ether/EtOAc 90:10);



^1H NMR (400 MHz, CDCl_3): δ 7.48 (s, 1H), 7.45 (dd, J = 7.5, 1.7 Hz, 1H), 7.43 – 7.39 (m, 1H), 7.30 (td, J = 7.6, 1.7 Hz, 1H), 7.27 – 7.21 (m, 1H), 5.78 – 5.27 (m, 1H), 5.20 – 4.68 (m, 2H), 3.10 (s, 3H), 2.76 – 2.37 (m, 2H). **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3):** δ 174.5, 167.4, 132.3, 131.4, 130.8, 130.2, 129.8, 129.6, 128.7, 126.8, 126.4, 121.1, 48.7, 41.9, 24.8. **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{15}\text{H}_{14}\text{NO}_2\text{S}$ ($\text{M} + \text{H}$) $^+$: 272.0745, Found: 272.0746

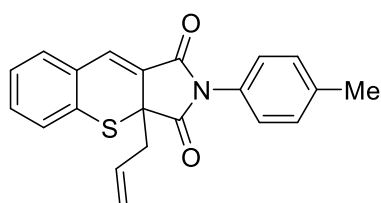
3a-allyl-2-phenylthiochromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2ac): Compound **2ac** was synthesized following the general procedure-C. The product was obtained as white solid, 31.5 mg (63 % yield); R_f =0.5 (petroleum ether/EtOAc 90:10);



^1H NMR (400 MHz, CDCl_3): δ 7.61 (s, 1H), 7.54 – 7.39 (m, 5H), 7.38 – 7.31 (m, 3H), 7.29 (dd, J = 7.5, 1.4 Hz, 1H), 5.86 – 5.45 (m, 1H), 5.24 – 4.90 (m, 2H), 3.17 – 2.04 (m, 2H). **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3):** δ 173.6, 166.4, 132.4, 131.6, 131.5, 131.1, 130.9,

130.2, 129.6, 129.3, 129.0, 128.8, 126.9, 126.5, 125.97, 121.6, 48.8, 42.4. **HRMS (ESI TOF)** m/z : calcd for $C_{20}H_{16}NO_2S$ ($M + H$)⁺: 334.0902, Found: 334.0907.

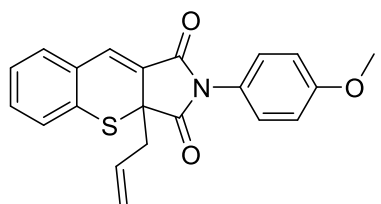
3a-allyl-2-(p-tolyl)thiochromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2ad): Compound **2ad** was synthesized following the general procedure-C. The product was obtained as white solid, 34 mg (65 % yield); R_f =0.4 (petroleum ether/EtOAc 90:10);



¹H NMR (400 MHz, CDCl₃): δ 7.62 (s, 1H), 7.51 (dd, J = 7.5, 1.6 Hz, 1H), 7.48 (dd, J = 7.8, 1.3 Hz, 1H), 7.40 – 7.25 (m, 4H), 7.29 – 7.22 (m, 2H), 5.71 (ddt, J = 17.5, 10.2, 7.5 Hz, 1H), 5.21 – 5.09 (m, 2H), 2.84 – 2.77 (m, 2H), 2.42 (s, 3H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 173.7, 166.5, 139.1, 132.4, 131.5, 131.0, 130.8, 130.2, 130.0,

129.6, 128.8, 128.8, 126.9, 126.3, 126.1, 121.5, 48.8, 42.4, 21.4. **HRMS (ESI TOF)** m/z : calcd for $C_{21}H_{18}NO_2S$ ($M + H$)⁺: 348.1058, Found: 348.1058.

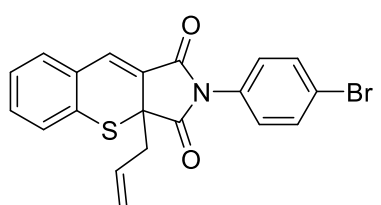
3a-allyl-2-(4-methoxyphenyl)thiochromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2ae): **¹H NMR (400 MHz, CDCl₃):** Compound **2ae** was synthesized following the general procedure-



C. The product was obtained as white solid, 35.5 mg (65 % yield); R_f =0.5 (petroleum ether/EtOAc 90:10);

δ 7.60 (s, 1H), 7.49 (dd, J = 7.5, 1.6 Hz, 1H), 7.48 – 7.45 (m, 1H), 7.34 (td, J = 7.6, 1.6 Hz, 1H), 7.30 – 7.26 (m, 2H), 7.04 – 6.97 (m, 2H), 5.79 – 5.61 (m, 1H), 5.21 – 5.06 (m, 2H), 3.84 (s, 3H), 2.88 – 2.65 (m, 2H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 173.8, 166.7, 159.8, 132.4, 131.5, 131.0, 130.7, 130.2, 129.6, 128.7, 127.7, 126.9, 126.0, 124.1, 121.5, 114.6, 55.6, 48.7, 42.4. **HRMS (ESI TOF)** m/z : calcd for $C_{21}H_{18}NO_3S$ ($M + H$)⁺: 364.1007, Found: 364.1009.

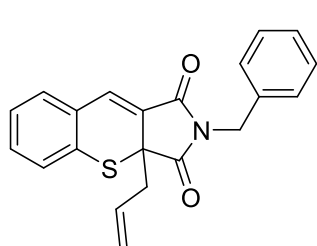
3a-allyl-2-(4-bromophenyl)thiochromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2af): Compound **2ae** was synthesized following the general procedure-C. The product was obtained as white solid, 45 mg (73% yield); R_f =0.5 (petroleum ether/EtOAc 90:10);



¹H NMR (400 MHz, CDCl₃): δ 7.60 (dd, J = 6.7, 1.9 Hz, 3H), 7.48 (dd, J = 7.5, 1.6 Hz, 1H), 7.48 – 7.41 (m, 1H), 7.33 (td, J = 7.6, 1.6 Hz, 1H), 7.31 – 7.21 (m, 3H), 5.65 (dddd, J = 17.1, 10.2, 8.0, 7.0 Hz, 1H), 5.22 – 4.99 (m, 2H), 2.93 – 2.38 (m, 2H).

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 173.3, 166.0, 132.5, 132.4, 131.7, 131.3, 131.2, 130.5, 130.1, 129.5, 128.8, 128.0, 127.0, 125.6, 122.8, 121.7, 48.8, 42.4. **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{20}\text{H}_{15}\text{BrNO}_2\text{S}$ ($\text{M} + \text{H}$) $^+$: 412.0007, Found: 412.0005.

3a-allyl-2-benzylthi chromeno[2,3-c]pyrrole-1,3(2*H*,3*aH*)-dione (2ag): Compound 2ag was synthesized following the general procedure-C. The product was obtained as white solid,

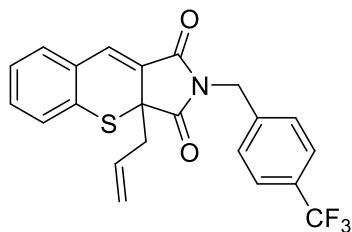


45 mg (73% yield); R_f =0.5 (petroleum ether/EtOAc 90:10); **^1H NMR (400 MHz, CDCl_3):** δ 7.45 – 7.38 (m, 2H), 7.37 (s, 1H), 7.37 – 7.25 (m, 5H), 7.08 (dt, J = 8.6, 1.1 Hz, 1H), 7.04 (td, J = 7.5, 1.1 Hz, 1H), 5.41 (ddt, J = 17.5, 10.1, 7.5 Hz, 1H), 4.95 (dq, J = 17.0, 1.4 Hz, 1H), 4.88 (dt, J = 10.1, 1.2 Hz, 1H), 4.79 – 4.67 (m, 2H),

2.63 (dt, J = 7.5, 1.1 Hz, 2H). **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3):** δ 173.7, 166.6, 149.8, 132.4, 131.5, 131.0, 130.8, 130.2, 129.6, 129.3, 128.7, 127.4, 126.9, 126.3, 126.1, 121.5, 48.8, 42.4, 34.1. **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{21}\text{H}_{18}\text{NO}_2\text{S}$ ($\text{M} + \text{H}$) $^+$: 348.1058, Found: 348.1062.

3a-allyl-2-(4-(trifluoromethyl)benzyl)thi chromeno[2,3-c]pyrrole-1,3(2*H*,3*aH*)-dione

(2ah): Compound 2ah was synthesized following the general procedure-C. The product was obtained as white solid, 44 mg (70 % yield); R_f =0.5 (petroleum ether/EtOAc 90:10);

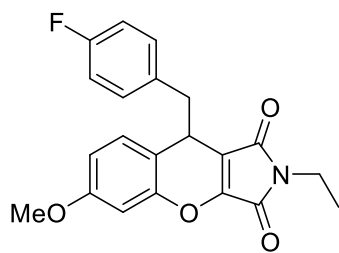


^1H NMR (400 MHz, CDCl_3): δ 7.58 (d, J = 8.2 Hz, 2H), 7.52 (d, J = 9.1 Hz, 3H), 7.46 (dd, J = 7.5, 1.6 Hz, 1H), 7.42 (dd, J = 7.8, 1.4 Hz, 1H), 7.31 (td, J = 7.6, 1.7 Hz, 1H), 7.29 – 7.21 (m, 1H),

5.35 (ddt, J = 17.5, 10.1, 7.5 Hz, 1H), 4.89 (dq, J = 17.0, 1.4 Hz, 1H), 4.81 (d, J = 6.7 Hz, 3H), 2.63 (d, J = 7.6 Hz, 2H). **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3):** δ 174.1, 166.8, 139.5 – 139.1 (m), 136.0 – 120.0 (m), 133.0 – 129.5 (m), 132.3, 131.6, 131.0, 130.5, 130.10, 129.4, 129.2, 128.8, 126.9, 125.9, 125.8 (q, J = 3.7 Hz), 121.3, 120.0, 48.6, 42.0 (d, J = 3.2 Hz), 29.8. **^{19}F NMR (377 MHz, CDCl_3):** δ -62.7. **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{22}\text{H}_{17}\text{F}_3\text{NO}_2\text{S}$ ($\text{M} + \text{H}$) $^+$: 416.0932, Found: 416.0928.

2-ethyl-9-(4-fluorobenzyl)-6-methoxychromeno[2,3-c]pyrrole-1,3(2*H*,9*H*)-dione (2y):

Compound 2y was synthesized following the general procedure-C. The product was obtained as white solid, 3 mg (11% yield); R_f =0.5 (petroleum ether/EtOAc 90:10);

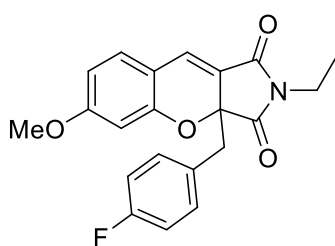


¹H NMR (400 MHz, CDCl₃): δ 7.05 (d, *J* = 8.6 Hz, 1H), 6.85 – 6.78 (m, 2H), 6.76 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.67 (dd, *J* = 8.5, 5.5 Hz, 2H), 6.61 (d, *J* = 2.6 Hz, 1H), 4.23 (t, *J* = 4.7 Hz, 1H), 3.79 (s, 3H), 3.59 (q, *J* = 7.2 Hz, 2H), 3.21 – 3.07 (m, 2H), 1.20 (t, *J* = 7.2 Hz, 3H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 163.7, 161.1, 159.9, 151.7 (d, *J* = 5.1 Hz), 132.9, 131.1, 131.0, 130.3, 115.2, 115.1, 113.9, 113.2, 112.8, 102.8, 55.7, 41.4, 33.3, 32.7, 14.2. **HRMS (ESI TOF) *m/z*:** calcd for C₂₁H₁₉FNO₄ (M + H)⁺: 368.12098, Found: 368.1299.

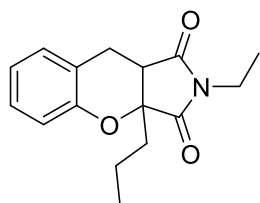
2-ethyl-3a-(4-fluorobenzyl)-6-methoxychromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione (2y'):

Compound **2y** was synthesized following the general procedure-C. The product was obtained as white solid, 8 mg (29% yield); *R_f*=0.45 (petroleum ether/EtOAc 90:10);

¹H NMR (400 MHz, CDCl₃): ¹H NMR (401 MHz, Chloroform-*d*) δ 7.40 (s, 1H), 7.29 (d, *J* = 8.5 Hz, 1H), 7.10 – 7.00 (m, 2H), 6.97 – 6.87 (m, 2H), 6.71 (d, *J* = 2.5 Hz, 1H), 6.64 (dd, *J* = 8.5, 2.5 Hz, 1H), 3.84 (s, 3H), 3.38 – 3.22 (m, 3H), 3.15 (d, *J* = 12.7 Hz, 1H), 0.81 (t, *J* = 7.2 Hz, 3H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 172.7, 165.4, 163.8, 161.3, 155.1, 131.8 (d, *J* = 8.0 Hz), 131.2, 128.3 (d, *J* = 3.2 Hz), 127.5, 120.5, 115.6 (d, *J* = 21.4 Hz), 113.9, 110.0, 103.2, 78.7, 55.8, 39.5, 33.1, 12.7. **HRMS (ESI TOF) *m/z*:** calcd for C₂₁H₁₉FNO₄ (M + H)⁺: 368.12098, Found: 368.1296.

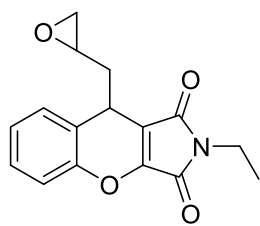


2-ethyl-3a-propyl-9,9a-dihydrochromeno[2,3-c]pyrrole-1,3(2H,3aH)-dione:



¹H NMR (400 MHz, CDCl₃): δ 7.19 – 7.10 (m, 1H), 7.09 (dt, *J* = 7.6, 1.3 Hz, 1H), 6.99 – 6.91 (m, 2H), 3.38 (q, *J* = 7.2 Hz, 2H), 3.20 (dd, *J* = 6.9, 3.0 Hz, 1H), 3.11 (dd, *J* = 14.7, 2.9 Hz, 1H), 2.94 (ddt, *J* = 14.8, 6.9, 1.1 Hz, 1H), 2.13 (ddd, *J* = 13.8, 12.2, 4.5 Hz, 1H), 1.91 (ddd, *J* = 13.8, 12.1, 4.6 Hz, 1H), 1.65 – 1.51 (m, 1H), 1.47 – 1.31 (m, 1H), 1.02 (t, *J* = 7.3 Hz, 3H), 0.83 (t, *J* = 7.2 Hz, 3H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 176.6, 176.0, 154.0, 128.6, 128.3, 124.9, 123.5, 118.4, 82.1, 46.1, 38.1, 33.9, 26.0, 16.7, 14.3, 12.8. **HRMS (ESI TOF) *m/z*:** calcd for C₁₆H₂₀NO₃ (M + H)⁺: 274.1443, Found: 274.1448.

2-ethyl-9-(oxiran-2-ylmethyl)chromeno[2,3-c]pyrrole-1,3(2H,9H)-dione

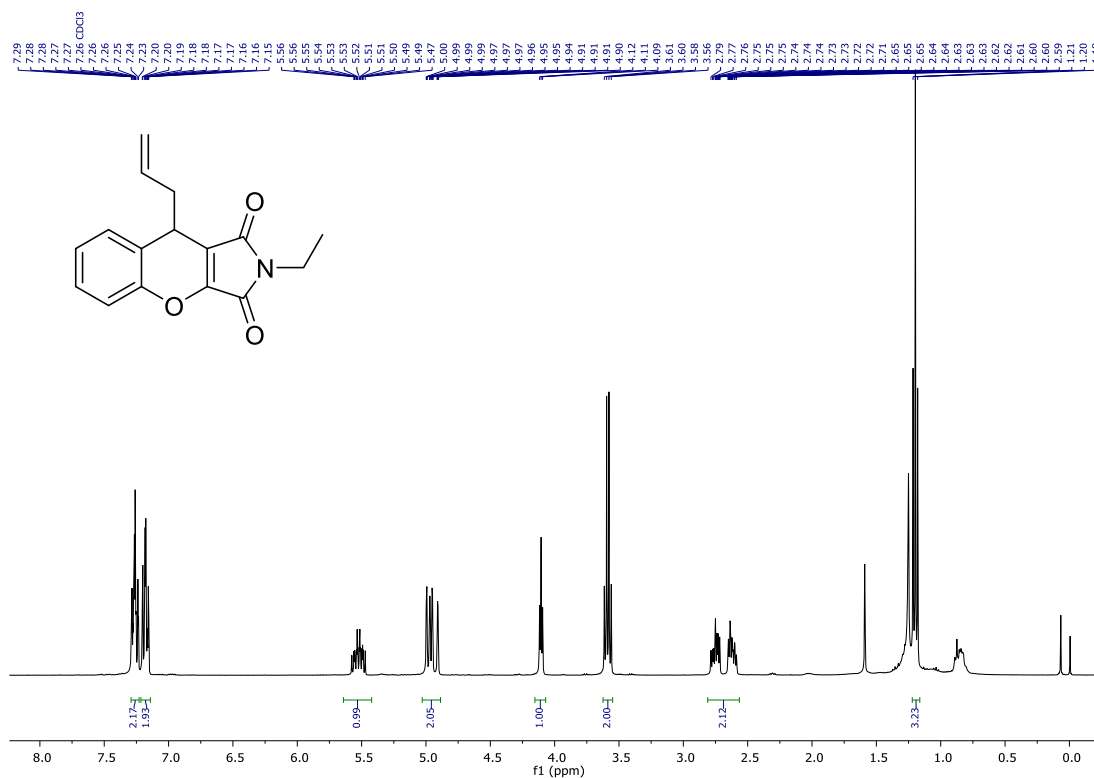


¹H NMR (400 MHz, CDCl₃): δ 7.29 (dt, *J* = 11.5, 3.2 Hz, 2H), 7.25 – 7.17 (m, 2H), 4.18 (dt, *J* = 17.1, 5.2 Hz, 1H), 3.61 (q, *J* = 7.2 Hz, 2H), 2.92 (tt, *J* = 5.9, 3.1 Hz, 0.38H), 2.85 (ddd, *J* = 8.0, 4.0, 2.8 Hz, 0.62H), 2.72 (t, *J* = 4.5 Hz, 0.38H), 2.61 (t, *J* = 4.4 Hz, 0.62H), 2.41 (dd, *J* = 5.1, 2.6 Hz, 0.38H), 2.32 (dd, *J* = 5.0, 2.6 Hz, 0.62H), 2.19 (ddd, *J* = 14.5, 5.4, 3.9 Hz, 0.64H), 2.14 – 2.03 (m, 1.36H), 1.22 (t, *J* = 7.2 Hz, 3H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 169.1, 164.0, 151.4, 150.9, 129.6, 129.1, 126.2, 122.4, 118.3, 113.4, 49.5, 46.5, 39.8, 32.7, 29.8, 14.2.

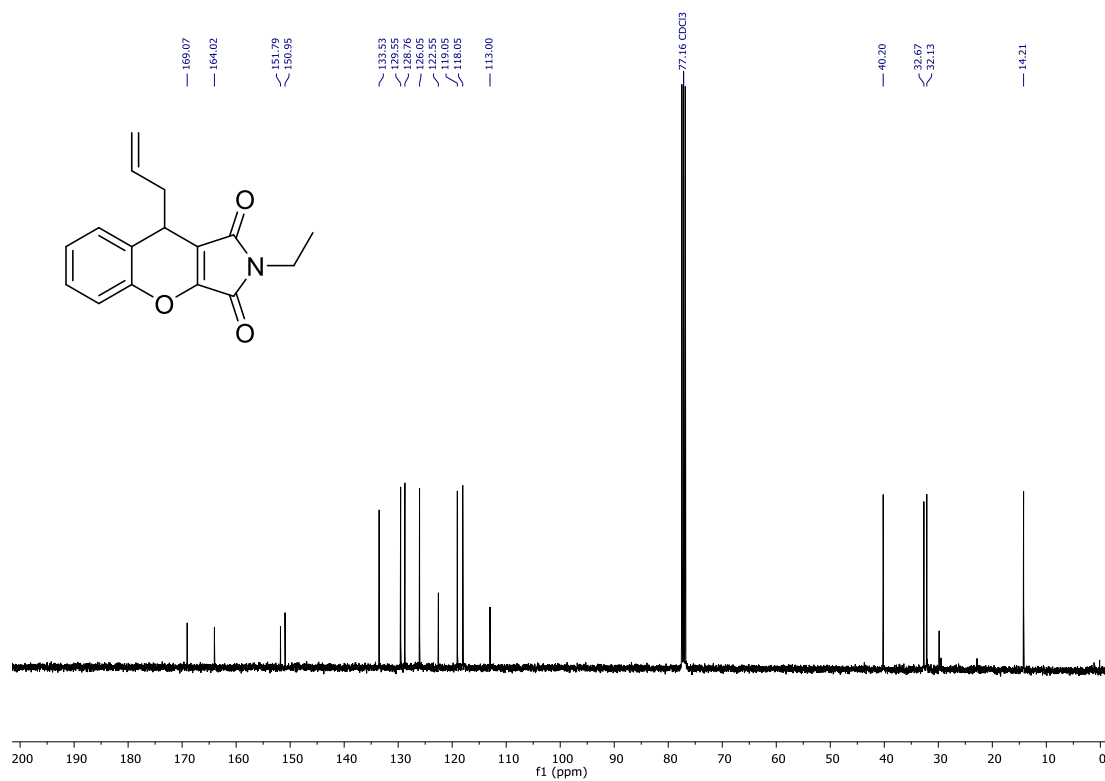
HRMS (ESI TOF) *m/z*: calcd for C₁₆H₁₆NO₄ (M + H)⁺: 286.1079, Found: 286.1082.

2.7 Selected Copies NMR Spectra (^1H , $^{13}\text{C}\{^1\text{H}\}$ and ^{19}F):

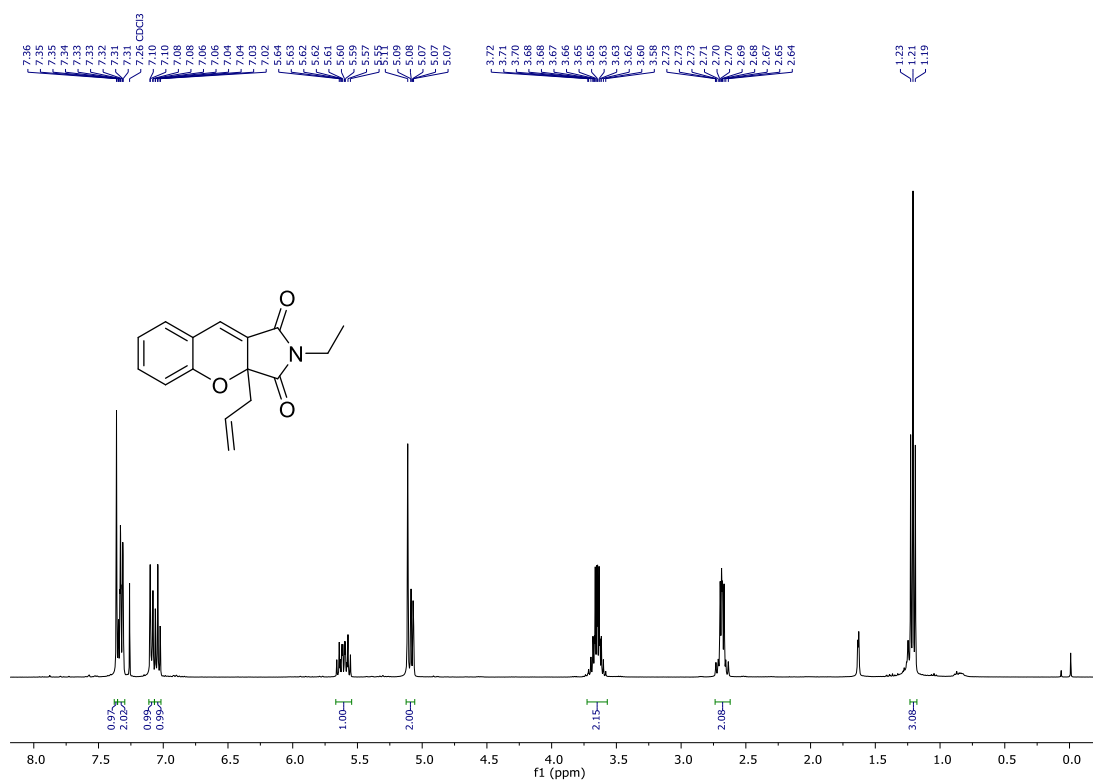
^1H NMR (400 MHz, CDCl_3) Spectrum of **2a**



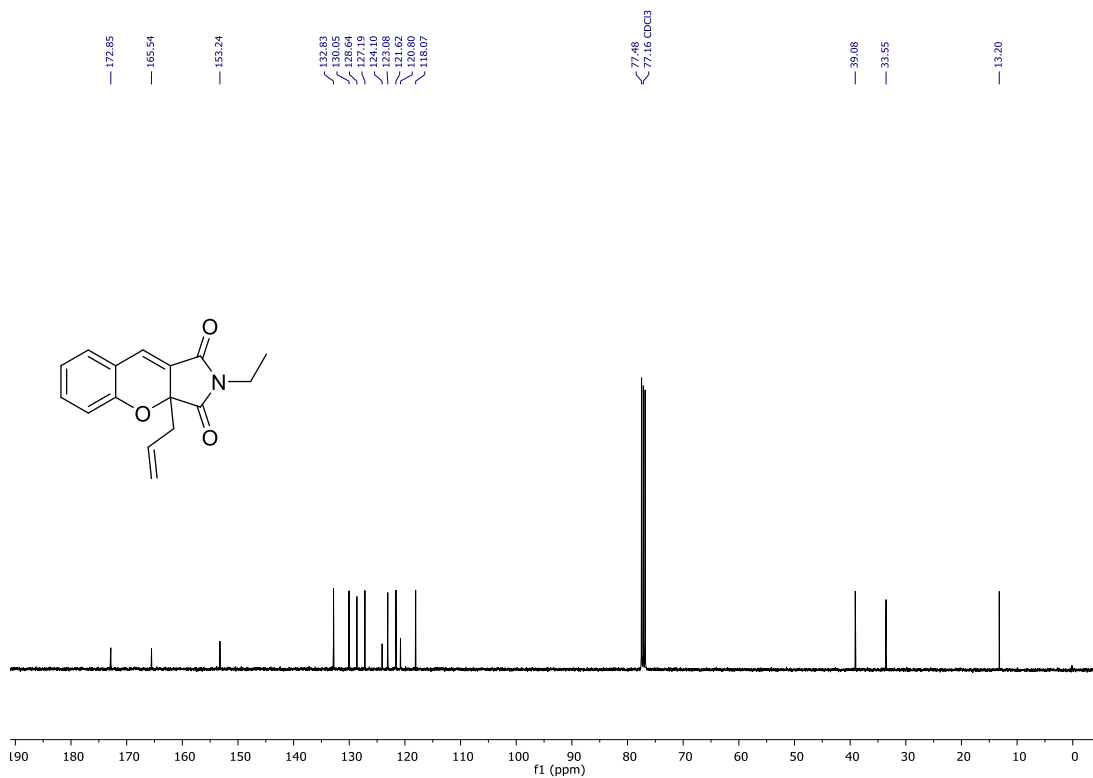
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2a**



^1H NMR (400 MHz, CDCl_3) Spectrum of **2a'**



$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2a'**



Chemical structure: COC1=CC=C(C=C1)CCN2C(=O)c3cc4ccccc4oc3C2C=C

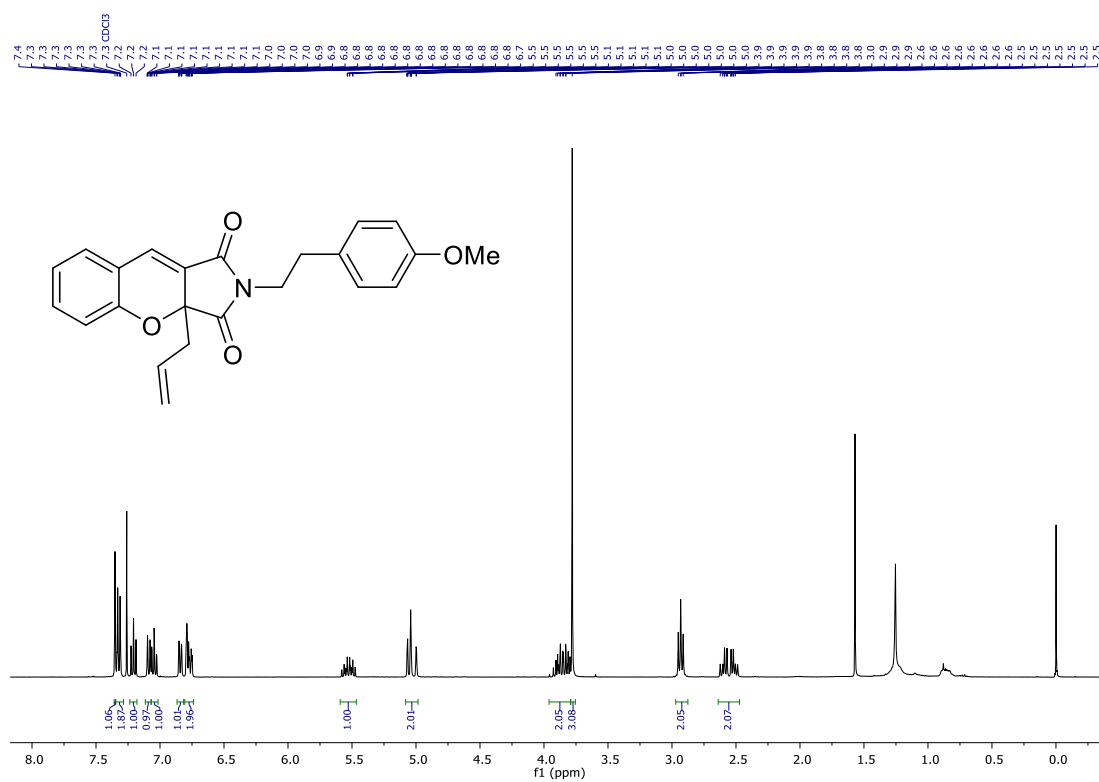
¹H NMR spectrum (CDCl₃) showing peaks from 0.0 to 7.5 ppm. The spectrum includes a methoxy singlet at 3.8 ppm, allyl protons between 4.9-5.5 ppm, aromatic protons between 6.8-7.4 ppm, and a solvent peak at 7.26 ppm. Integration values are provided below the baseline.

Chemical structure of the compound is shown above the spectrum.

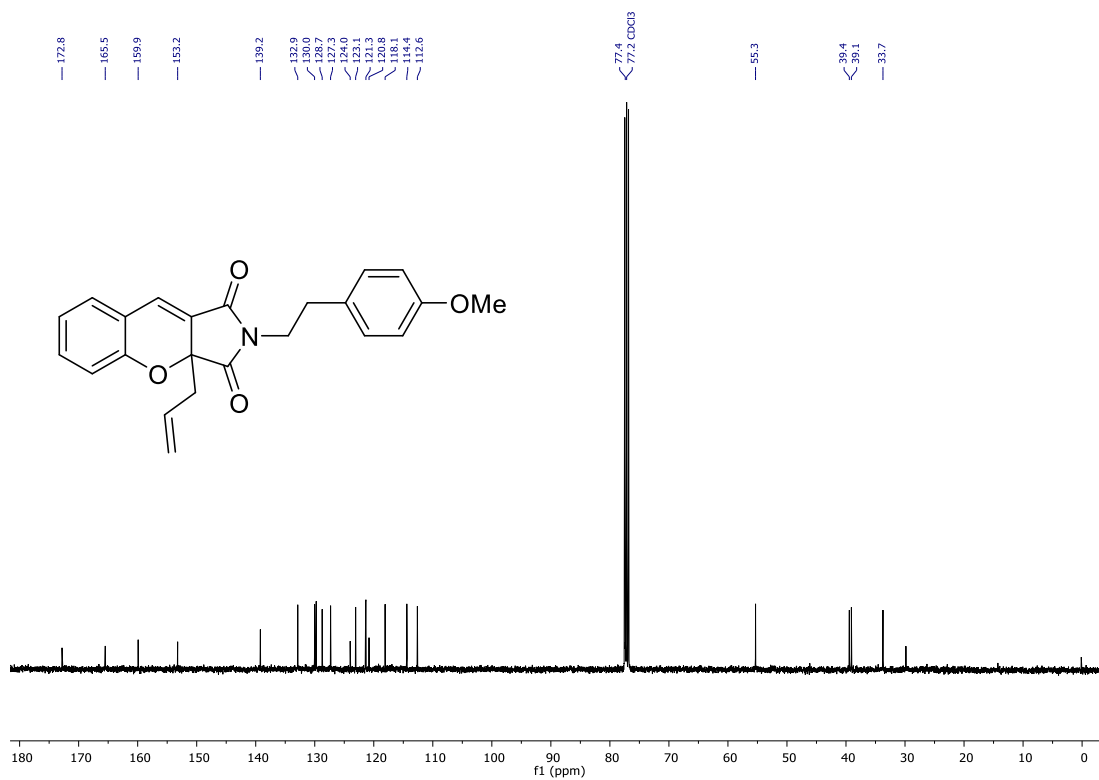
¹³C NMR spectrum (CDCl₃) showing chemical shifts (ppm) for the compound. The spectrum displays peaks corresponding to the structure, including aromatic and carbonyl regions (110-160 ppm), the CDCl₃ solvent peak (77.2 ppm), and aliphatic regions (30-60 ppm).

Chemical Shift (ppm)
168.9
163.9
159.9
151.7
150.9
139.5
133.4
129.5
128.8
126.1
122.5
121.3
119.1
118.0
114.6
112.3
77.2 (CDCl ₃)
55.3
40.1
38.8
34.8
32.1

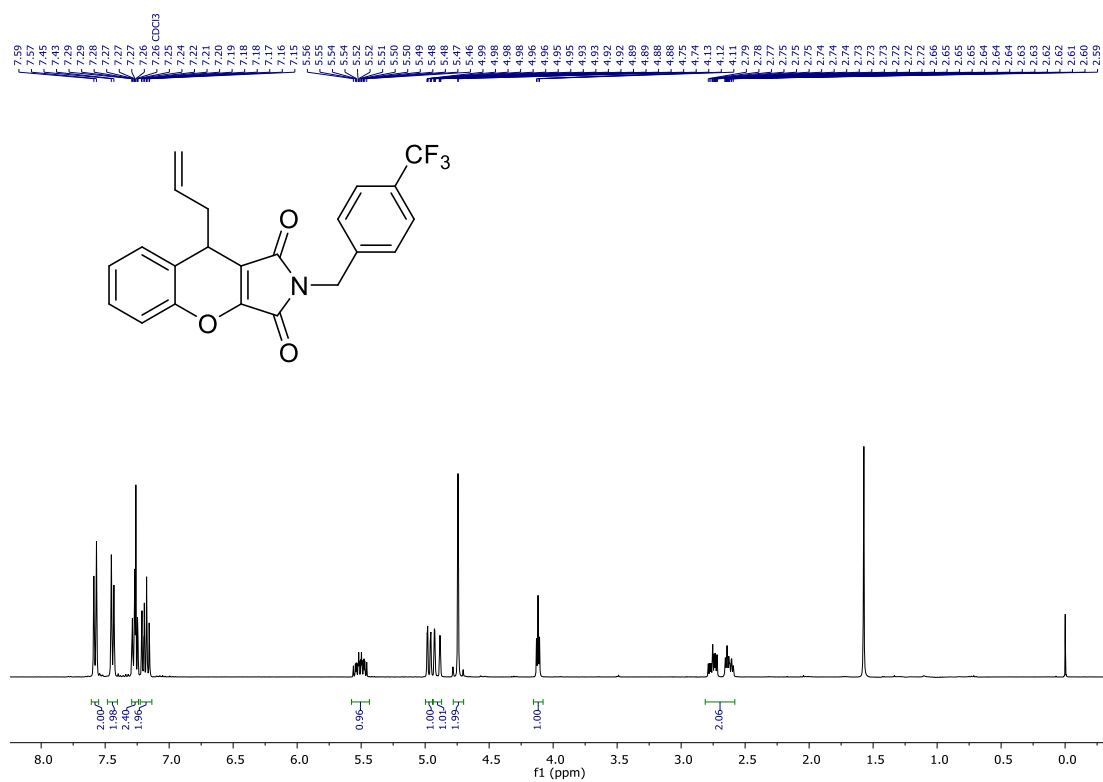
^1H NMR (400 MHz, CDCl_3) Spectrum of **2d'**



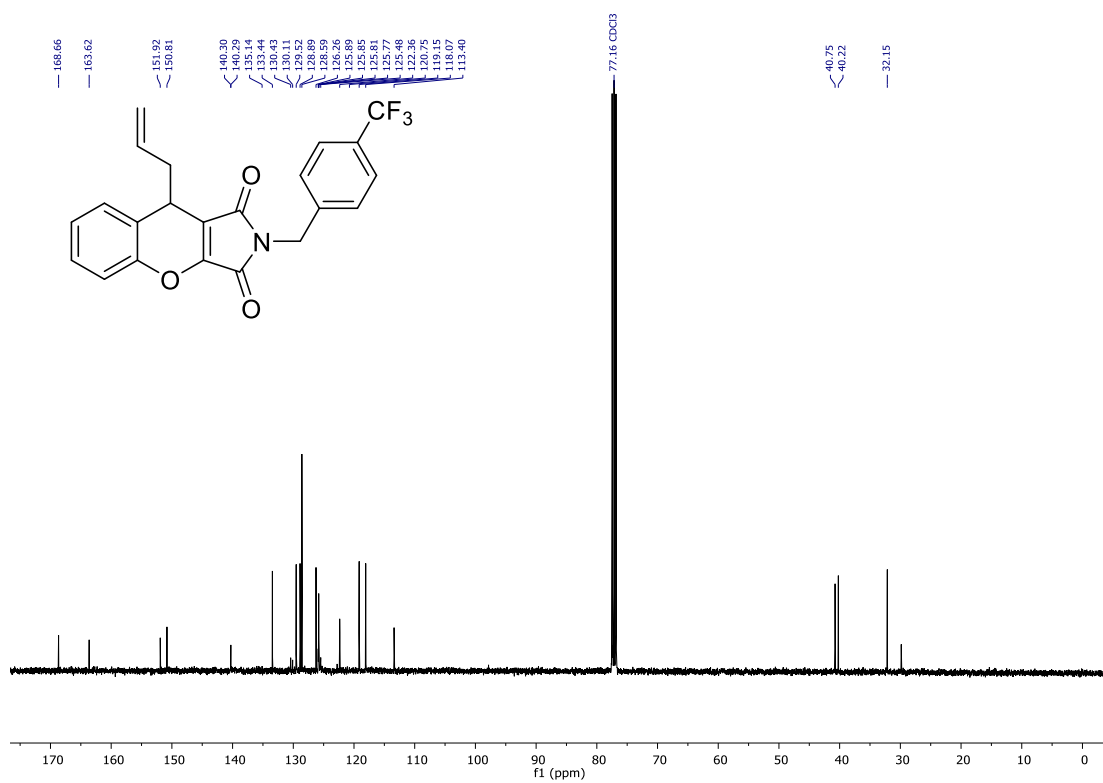
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2d'**



¹H NMR (400 MHz, CDCl₃) Spectrum of **2i**



¹³C{¹H} NMR (100 MHz, CDCl₃) Spectrum of **2i**



Chemical structure: C=CCc1c2ccccc2oc3c1C(=O)N(Cc4ccc(C(F)(F)F)cc4)C3=O

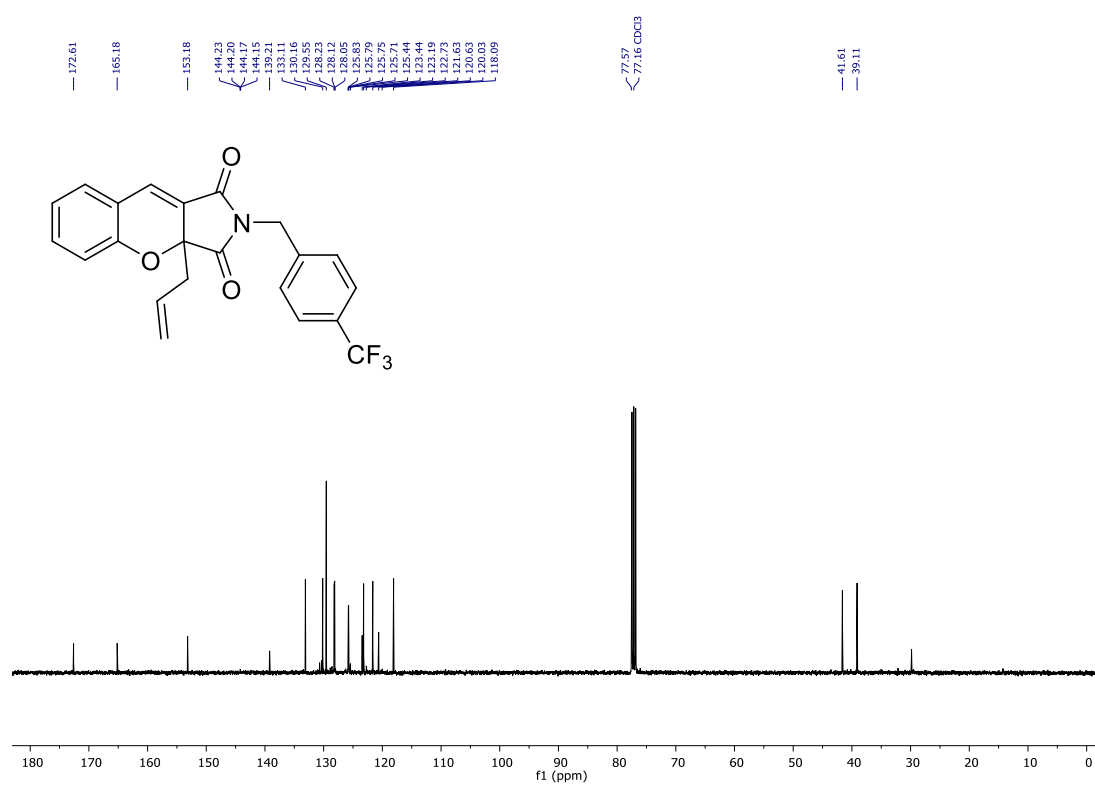
¹³C NMR spectrum (ppm):

Chemical Shift (ppm)
42.64

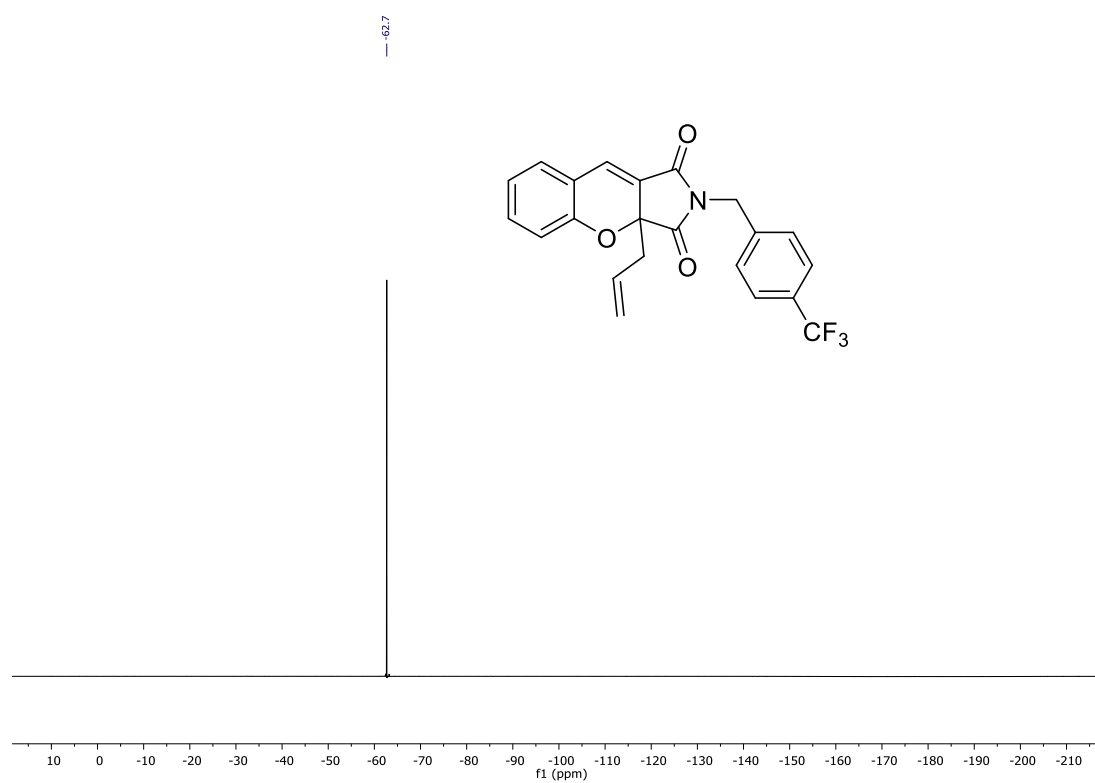
Chemical structure of 2-(2-allyl-2-oxo-2H-chromene-5-yl)-N-(4-(trifluoromethyl)benzyl)maleimide is shown above the ^1H NMR spectrum. The spectrum displays peaks corresponding to the compound, with integration values indicated below the peaks.

Integration values (from left to right): 2.04, 2.01, 2.01, 1.95, 0.99, 1.04, 1.05, 2.10, 2.02.

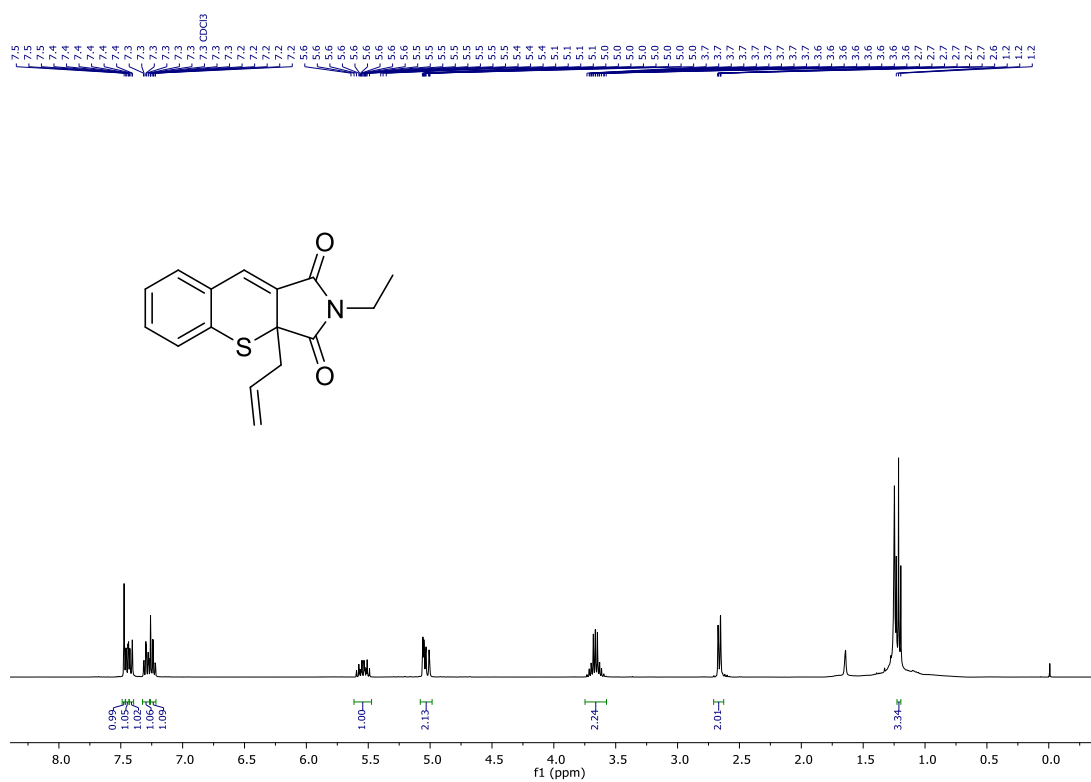
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2i'**



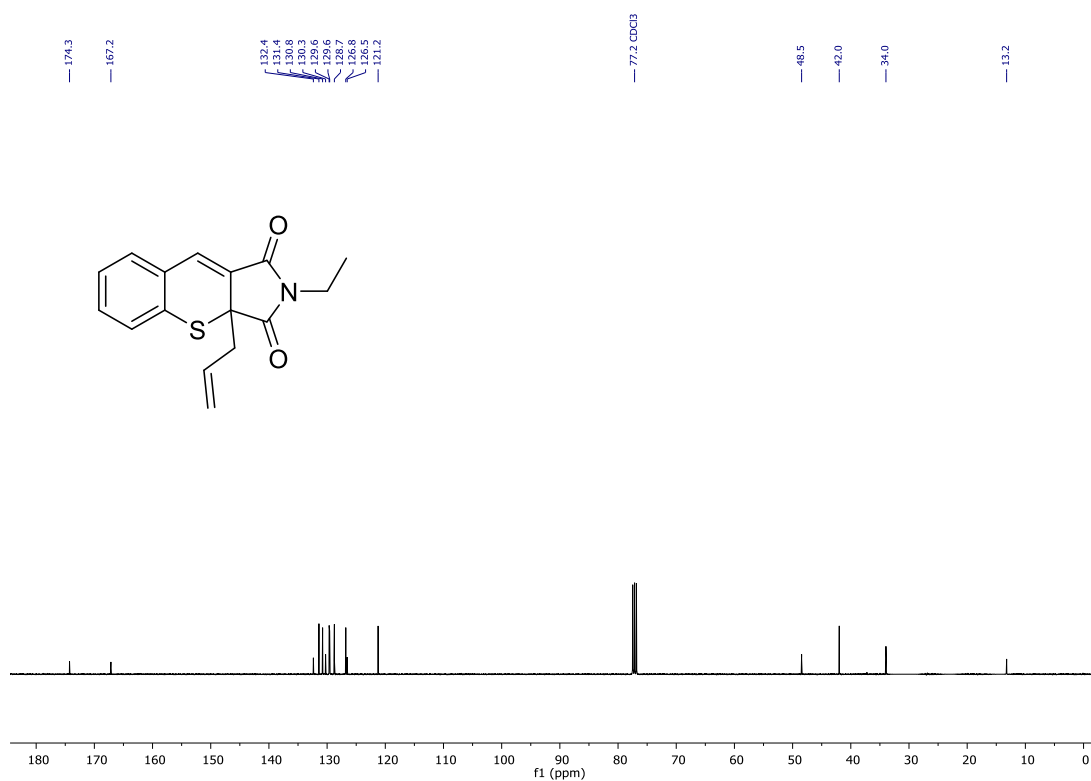
^{19}F NMR (377 MHz, CDCl_3) Spectrum of **2i'**



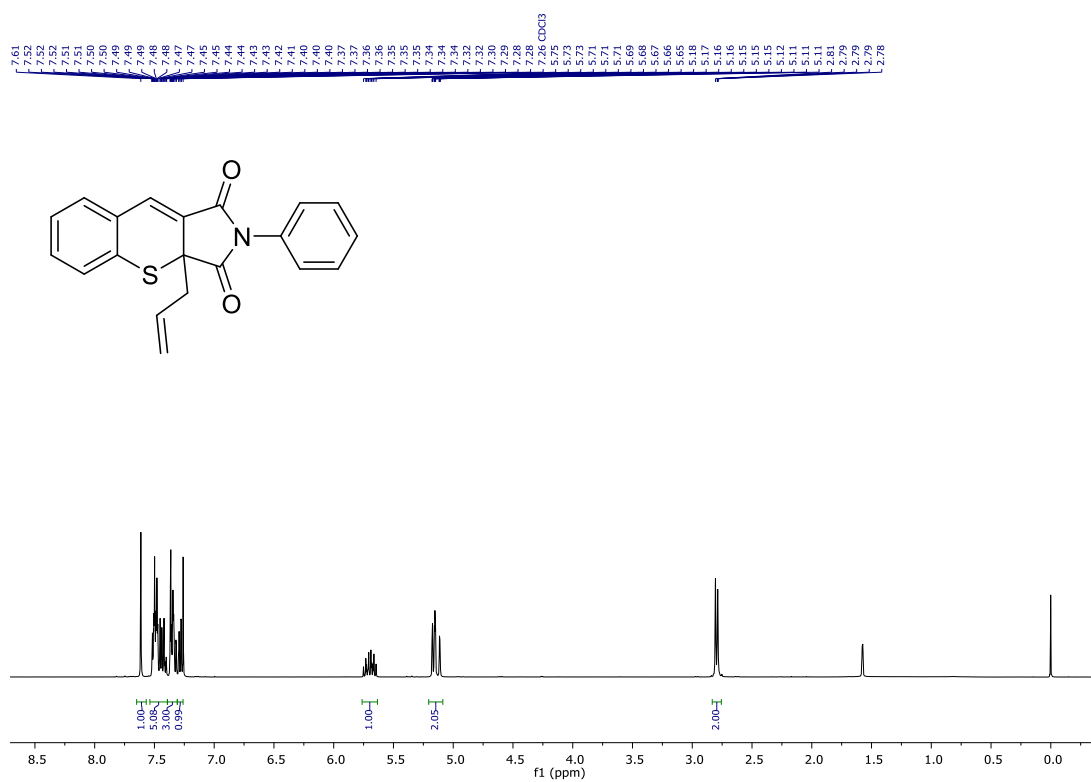
^1H NMR (400 MHz, CDCl_3) Spectrum of **2aa**



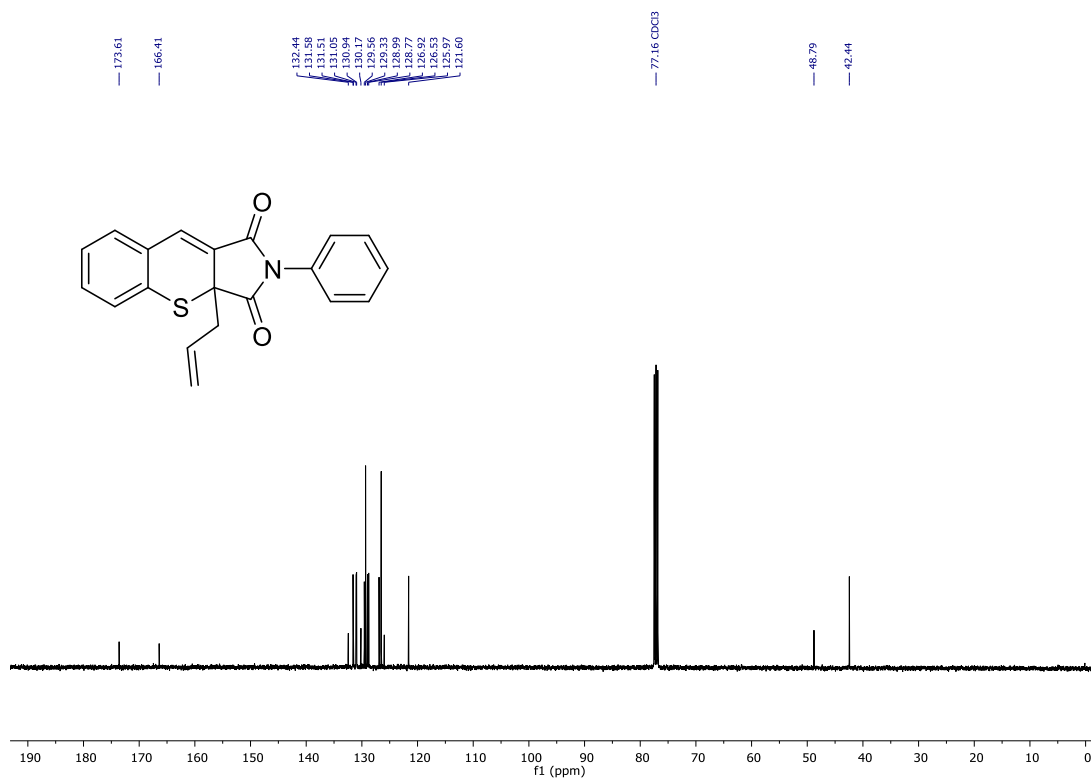
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2aa**



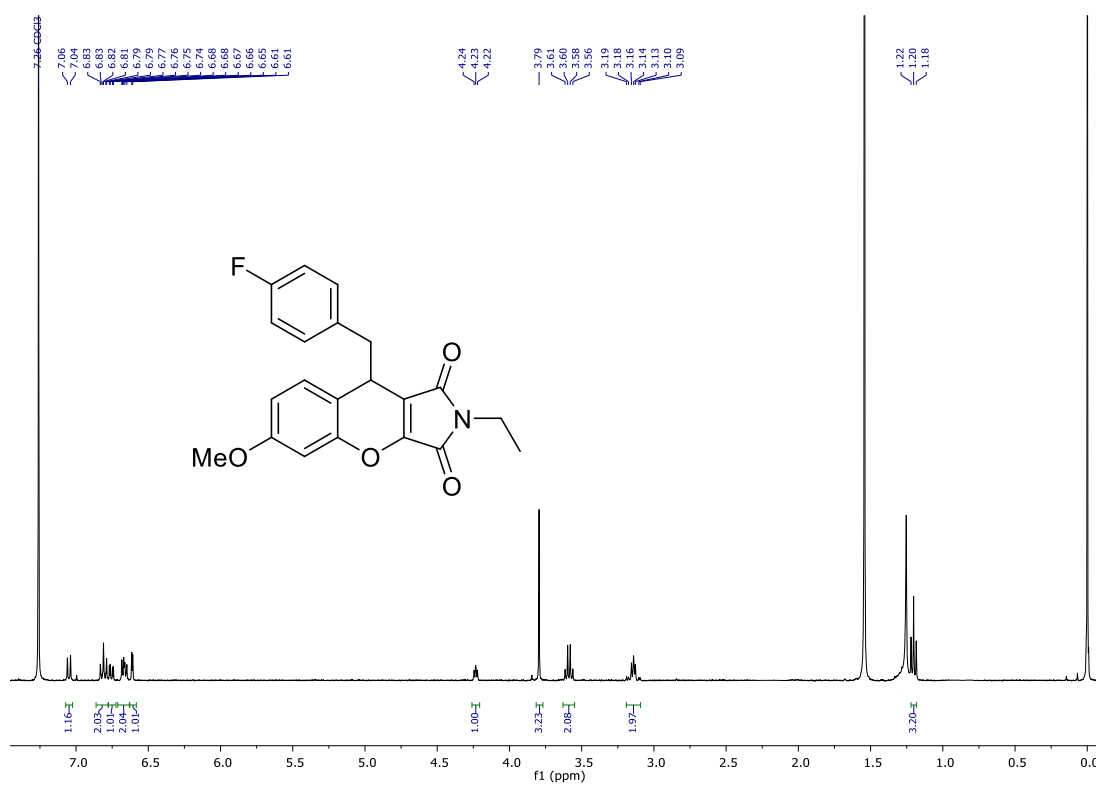
¹H NMR (400 MHz, CDCl₃) Spectrum of **2ac**



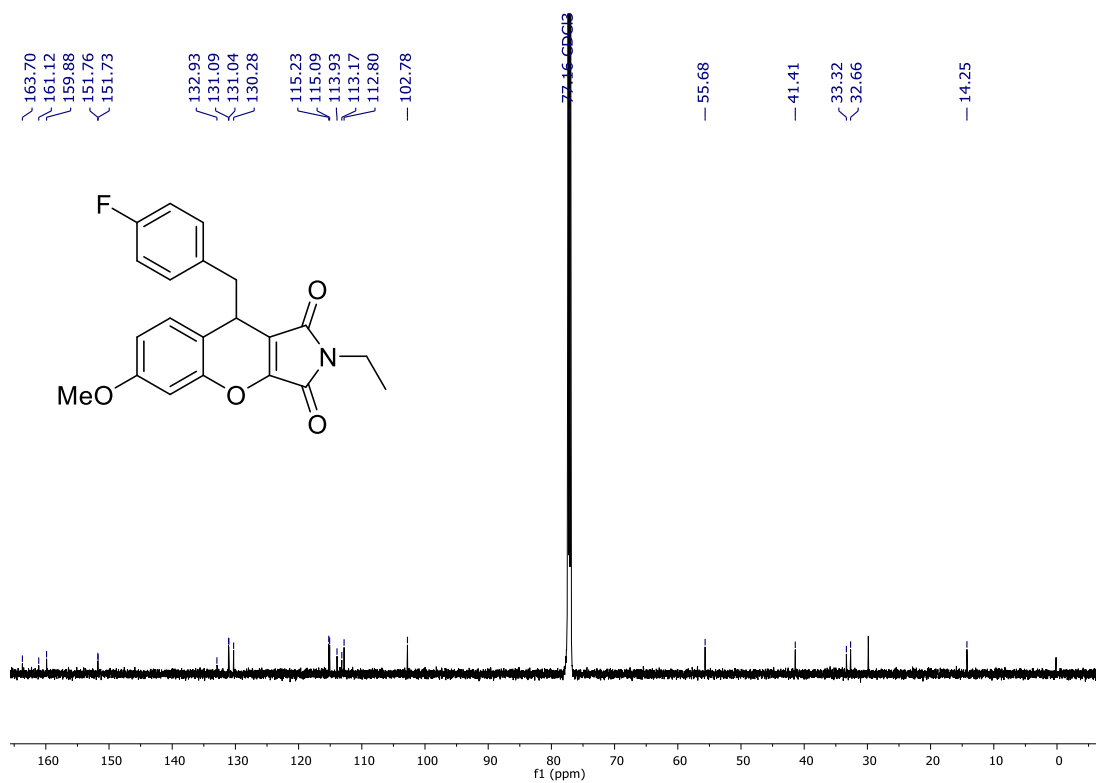
¹³C{¹H} NMR (100 MHz, CDCl₃) Spectrum of **2ac**



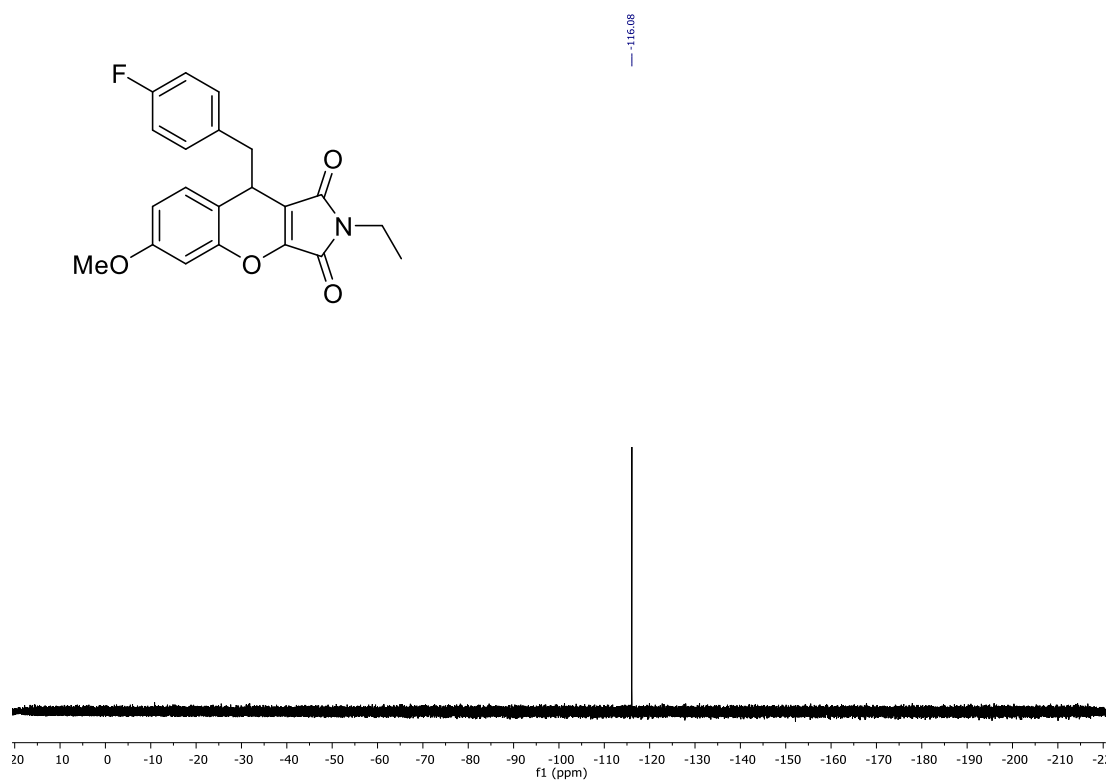
^1H NMR (400 MHz, CDCl_3) Spectrum of **2y**



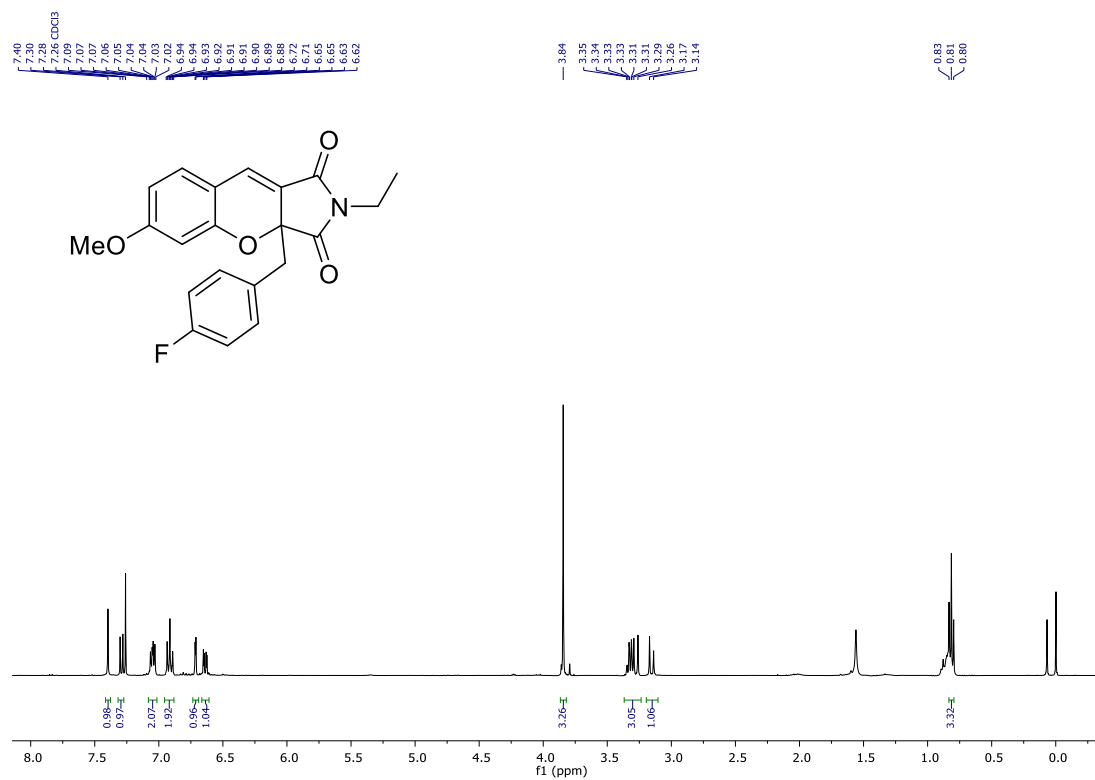
$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) Spectrum of **2y**



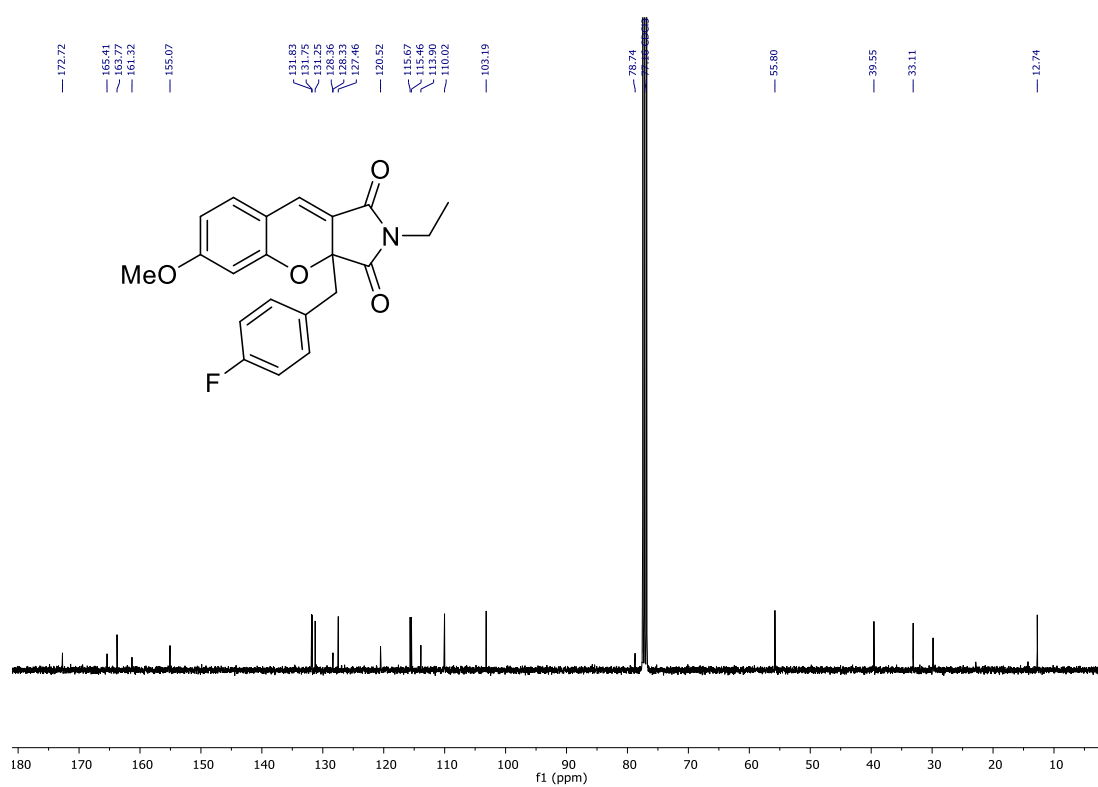
^{19}F NMR (377 MHz, CDCl_3) Spectrum of **2y**



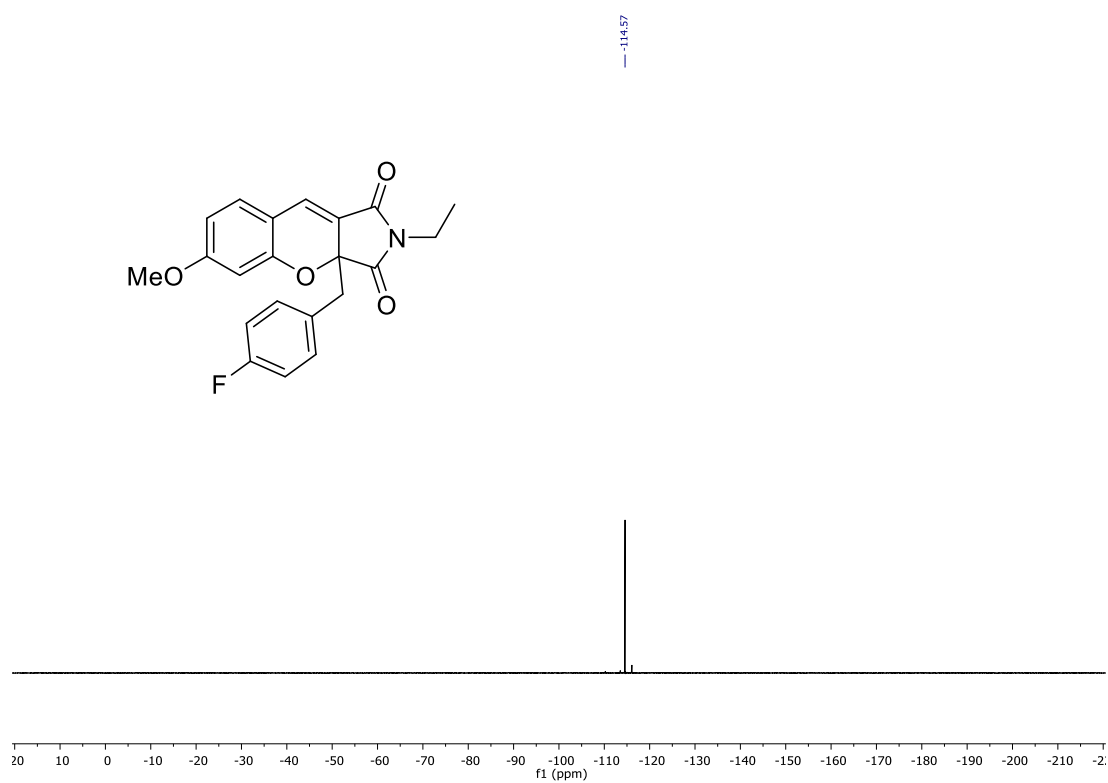
^1H NMR (400 MHz, CDCl_3) Spectrum of **2y'**



$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2y'**



^{19}F NMR (377 MHz, CDCl_3) Spectrum of **2y'**



CCN1C(=O)C2(CCC2Oc3ccccc13)C(=O)N1

¹H NMR spectrum (400 MHz, CDCl₃) of 1-ethyl-2-ethyl-2-phenylisoindolin-1-one. The spectrum shows peaks in the aromatic region (7.0-7.2 ppm), a methine peak (3.3 ppm), a methylene peak (2.1 ppm), and an ethyl group (1.0-1.4 ppm). Integration values are provided below the peaks.

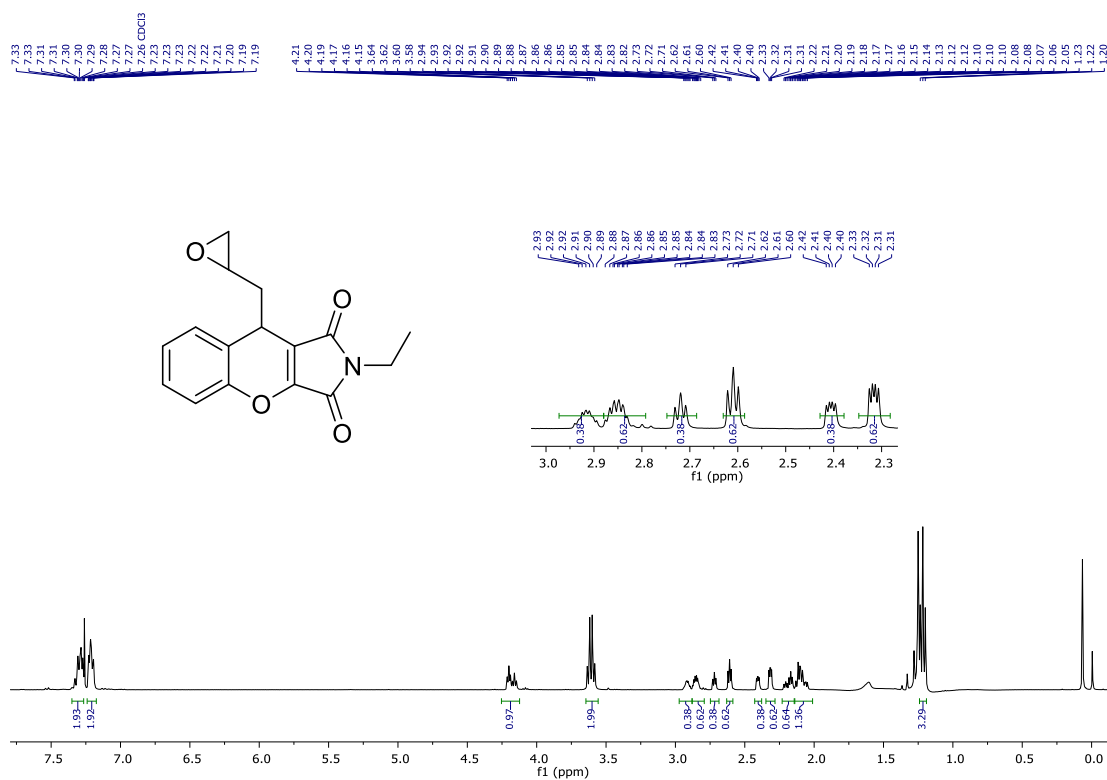
Chemical Shift (ppm)	Integration
7.16, 7.15, 7.14, 7.13, 7.12, 7.11, 7.10, 7.09, 7.08, 7.07, 7.06, 7.05, 7.04, 7.03, 7.02, 7.01, 7.00	0.99, 0.98, 1.94
3.30, 3.29, 3.28, 3.27, 3.26, 3.25, 3.24, 3.23, 3.22, 3.21, 3.20, 3.19, 3.18, 3.17, 3.16, 3.15, 3.14, 3.13, 3.12, 3.11, 3.10, 3.09, 3.08, 3.07, 3.06, 3.05, 3.04, 3.03, 3.02, 3.01, 3.00	2.00, 1.00, 1.00
2.14, 2.13, 2.12, 2.11, 2.10, 2.09, 2.08, 2.07, 2.06, 2.05, 2.04, 2.03, 2.02, 2.01, 2.00	1.01, 1.04
1.60, 1.59, 1.58, 1.57, 1.56, 1.55, 1.54, 1.53, 1.52, 1.51, 1.50, 1.49, 1.48, 1.47, 1.46, 1.45, 1.44, 1.43, 1.42, 1.41, 1.40, 1.39, 1.38, 1.37, 1.36, 1.35, 1.34, 1.33, 1.32, 1.31, 1.30, 1.29, 1.28, 1.27, 1.26, 1.25, 1.24, 1.23, 1.22, 1.21, 1.20, 1.19, 1.18, 1.17, 1.16, 1.15, 1.14, 1.13, 1.12, 1.11, 1.10, 1.09, 1.08, 1.07, 1.06, 1.05, 1.04, 1.03, 1.02, 1.01, 1.00	1.08, 1.12, 3.05, 3.08

Chemical structure of the compound is shown above the spectrum.

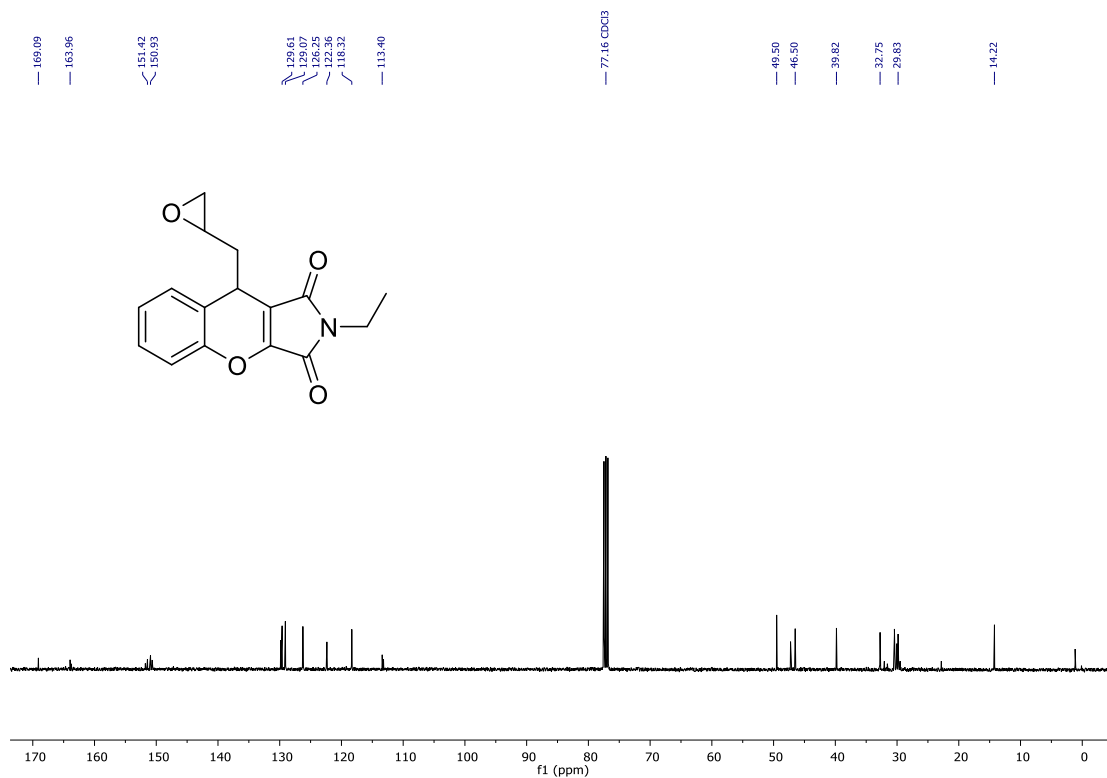
¹³C NMR spectrum (CDCl₃) showing chemical shifts (ppm) on the x-axis (0 to 180 ppm) and intensity on the y-axis. The spectrum displays several peaks corresponding to the compound's structure.

Chemical Shift (ppm)
176.58
176.02
153.98
128.62
128.33
128.07
123.50
118.44
82.13
77.16 (CDCl ₃)
46.15
38.15
33.90
26.03
16.67
12.85
12.81

¹H NMR (400 MHz, CDCl₃) Spectrum of **3a**



¹³C{¹H} NMR (100 MHz, CDCl₃) Spectrum of **3a**



2.8. Crystal Data

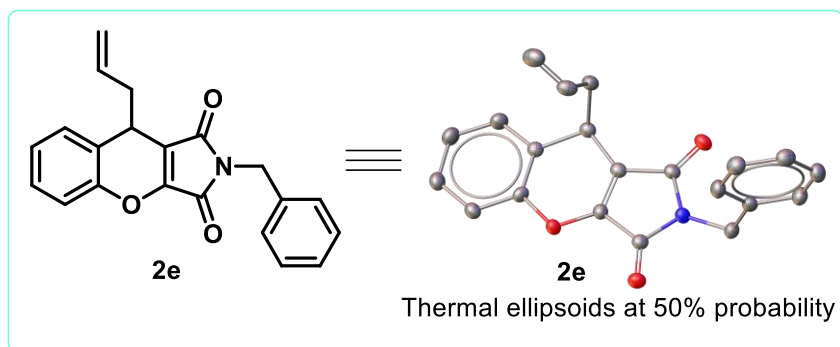
Table 1 Crystal data and structure refinement for 2e

Identification code	2e
Empirical formula	C ₂₁ H ₁₇ NO ₃
Formula weight	331.3710
Temperature/K	273(2)
Crystal system	monoclinic
Space group	P2 ₁ /n
a/Å	10.681(5)
b/Å	5.460(3)
c/Å	27.830(14)
α /°	90
β /°	96.057(15)
γ /°	90
Volume/Å ³	1613.7(14)
Z	32
$\rho_{\text{calc}}/\text{cm}^3$	1.364
μ/mm^{-1}	0.092
F(000)	696.0
Crystal size/mm ³	? × ? × ?
Radiation	MoK α (λ = 0.71073)
2 Θ range for data collection/°	2.944 to 57.448
Index ranges	-14 ≤ h ≤ 14, -5 ≤ k ≤ 7, -37 ≤ l ≤ 37
Reflections collected	22796
Independent reflections	4139 [R_{int} = 0.0828, R_{sigma} = 0.0777]
Data/restraints/parameters	4139/0/228
Goodness-of-fit on F ²	1.043

Final R indexes [$I \geq 2\sigma(I)$] $R_1 = 0.0524$, $wR_2 = 0.1250$

Final R indexes [all data] $R_1 = 0.0987$, $wR_2 = 0.1570$

Largest diff. peak/hole / $e \text{ \AA}^{-3}$ 0.36/-0.44

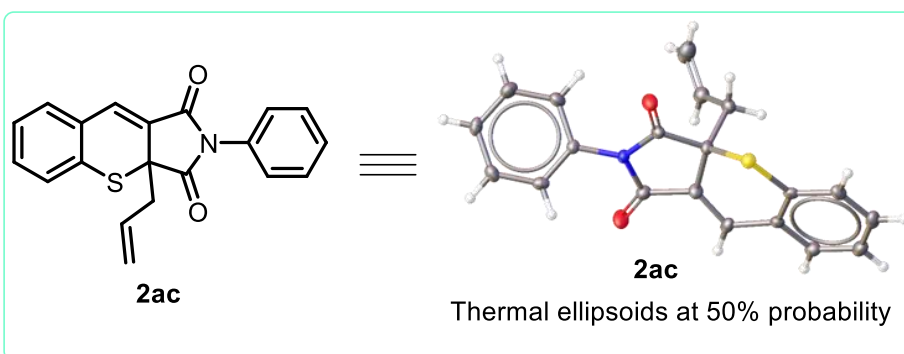


Crystal Structure of 2ac

Table 2: Crystal data and structure refinement for 2ac.

Identification code	2ac
Empirical formula	$C_{20}H_{15}NO_2S$
Formula weight	333.4050
Temperature/K	296.15
Crystal system	orthorhombic
Space group	$Pna2_1$
$a/\text{\AA}$	7.6921(9)
$b/\text{\AA}$	10.8954(15)
$c/\text{\AA}$	18.882(3)
$\alpha/^\circ$	90
$\beta/^\circ$	90
$\gamma/^\circ$	90

Volume/Å ³	1582.4(4)
Z	20
$\rho_{\text{calc}}/\text{cm}^3$	1.399
μ/mm^{-1}	0.216
F(000)	696.0
Crystal size/mm ³	0.328 × 0.219 × 0.169
Radiation	Mo K α (λ = 0.71073)
2 θ range for data collection/°	4.314 to 50.116
Index ranges	-8 ≤ h ≤ 9, -12 ≤ k ≤ 12, -22 ≤ l ≤ 22
Reflections collected	27019
Independent reflections	2796 [R_{int} = 0.0549, R_{sigma} = 0.0266]
Data/restraints/parameters	2796/1/217
Goodness-of-fit on F ²	1.094
Final R indexes [$I \geq 2\sigma(I)$]	R_1 = 0.0323, wR_2 = 0.0786
Final R indexes [all data]	R_1 = 0.0351, wR_2 = 0.0803
Largest diff. peak/hole / e Å ⁻³	0.28/-0.41
Flack parameter	0.02(3)



2.9 References

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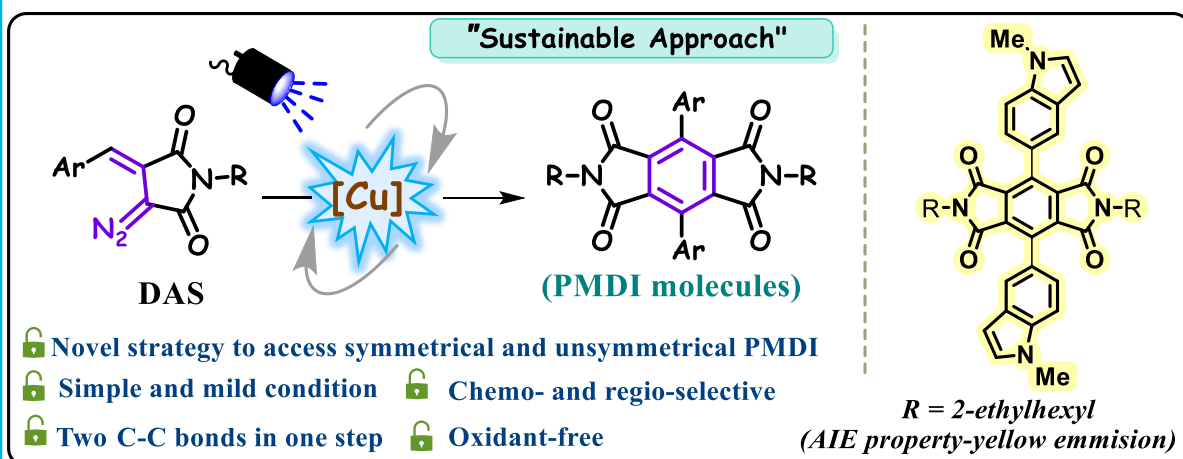
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Chapter 3

Visible-Light-Induced Copper-Catalyzed Radical Reactions of Diazo Arylidene Succinimides to Access the Pyromellitic Diimide (PMDI) Core



Visible-Light-Induced Copper-Catalyzed Radical Reactions of DAS to Access the PMDI Core

3

A facile, mild, and efficient method for the synthesis of disubstituted pyromellitic diimides (PMDIs) from diazo arylidene succinimides has been developed using a copper catalyst under the irradiation of visible light. This novel transformation introduces an unconventional route for generating carbon radicals directly from diazo arylidene succinimides (DAS), bypassing the conventional carbene intermediate. This approach successfully overcame the long-standing paradigm in PMDI synthesis. This unprecedented and efficient copper-catalyzed chemoselective radical cyclization proceeds through the proton-coupled electron transfer (PCET) process. Notably, the choice of NaSCN, along with the copper catalyst, forms a new copper complex, CuNCS in situ which plays a pivotal role in this overall photoinduced transformation. Additionally, we synthesized a known PMDI molecule that is known for its prominent aggregation-induced emission (AIE) properties. The application of this protocol has been further extended for the relatively challenging synthesis of unsymmetrical PMDIs from two different diazo arylidene succinimides. Mechanistic insights have been obtained through a series of controlled experiments, UV-visible spectroscopy, EPR studies, and single-crystal X-ray diffraction analysis.

3.1 Introduction:

Highly substituted aromatic compounds are very important and useful in organic synthesis owing to their varied electronic properties. However, the steric strain of molecules is a big barrier to synthesizing them efficiently under ambient reaction conditions.¹ The construction of highly substituted benzene frameworks efficiently and practically is quite challenging, thus making it an area of interest for synthetic organic chemists to build various valuable molecules.² Highly substituted aromatic compounds and their derivatives are core to many useful natural products,³ pharmaceuticals,⁴ and bioactive compounds.⁵ Disubstituted pyromellitic diimide (PMDI) scaffold is one of the valuable members of the family with hexasubstituted aromatic compounds having two distinct cores: *p*-terphenyls and PMDI. The *p*-terphenyl core is found in numerous natural products and bioactive compounds.⁶ While, the PMDI-based compounds are used in organic electronics and sensing applications. Furthermore, disubstituted PMDI compounds are well known for their aggregation-induced emission, mechanofluorochromic properties, and polymeric properties (see Figure 3.1).⁷ Even though

this scaffold is very important and useful in different research fields, its application and further exploration are highly limited, as there are seldom synthetic protocols in the literature to access the PMDI-based compounds.⁸

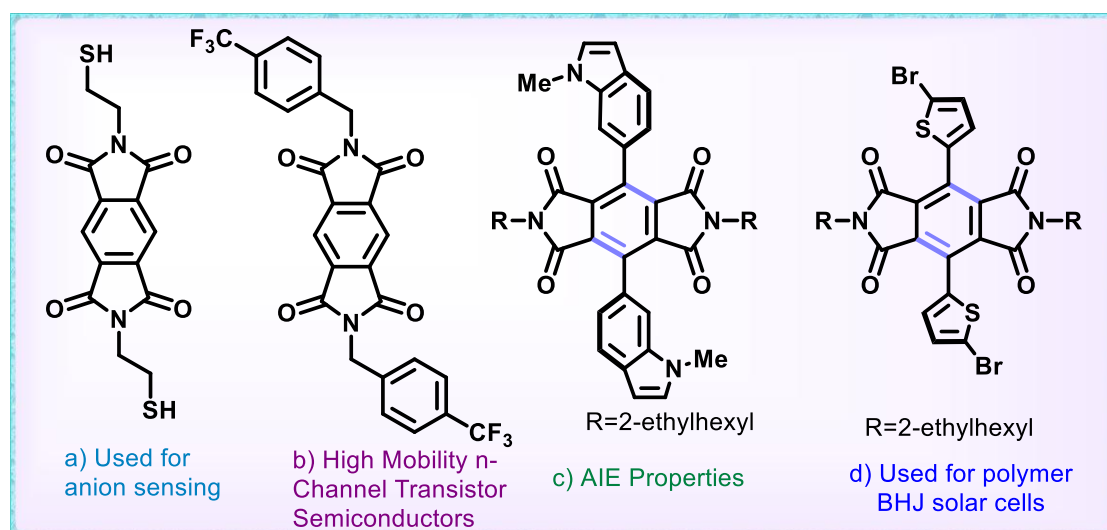
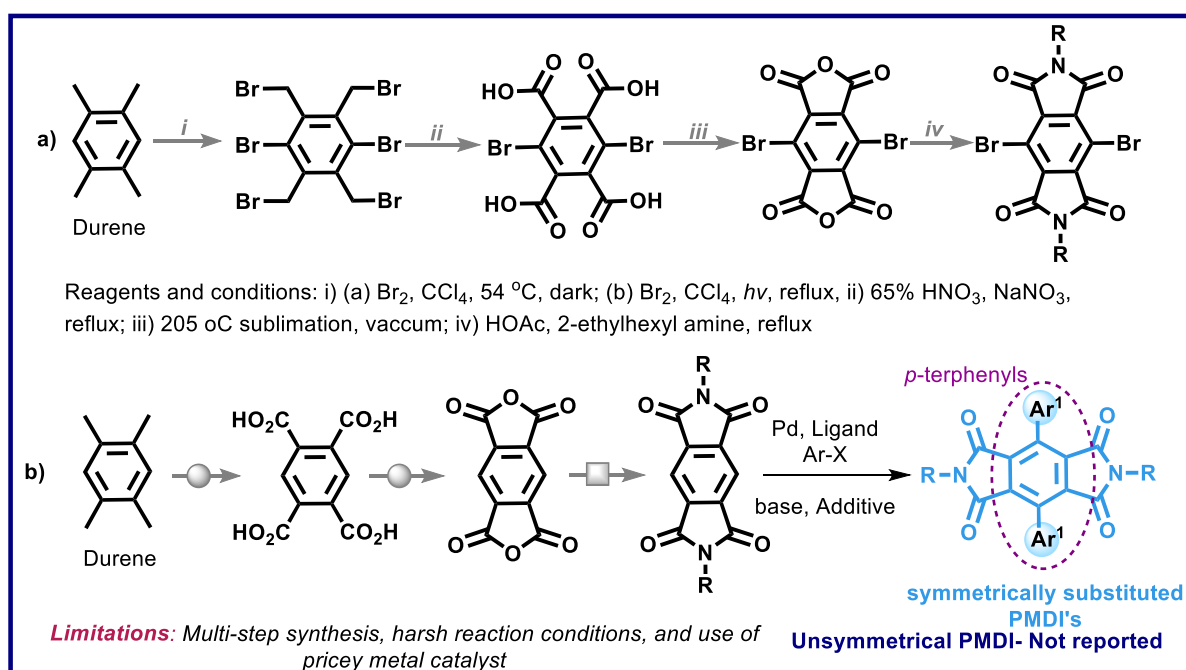


Figure 3.1: Importance of PMDI molecules

In 1961, the synthesis of 3,6-dibromo PMDI was first reported by Hopff^{6b}, with subsequent simplifications introduced by Watson^{6c} in 2011, who streamlined the procedure by reducing steps and eliminating unnecessary purification (Scheme 3.1a).



Scheme 3.1: Traditional Routes for the PMDI Synthesis

Starting from durene, the compound dibromo PMDI was formed. Notably, imidization in glacial acetic acid prevents unwanted nucleophilic aromatic substitution at brominated ring

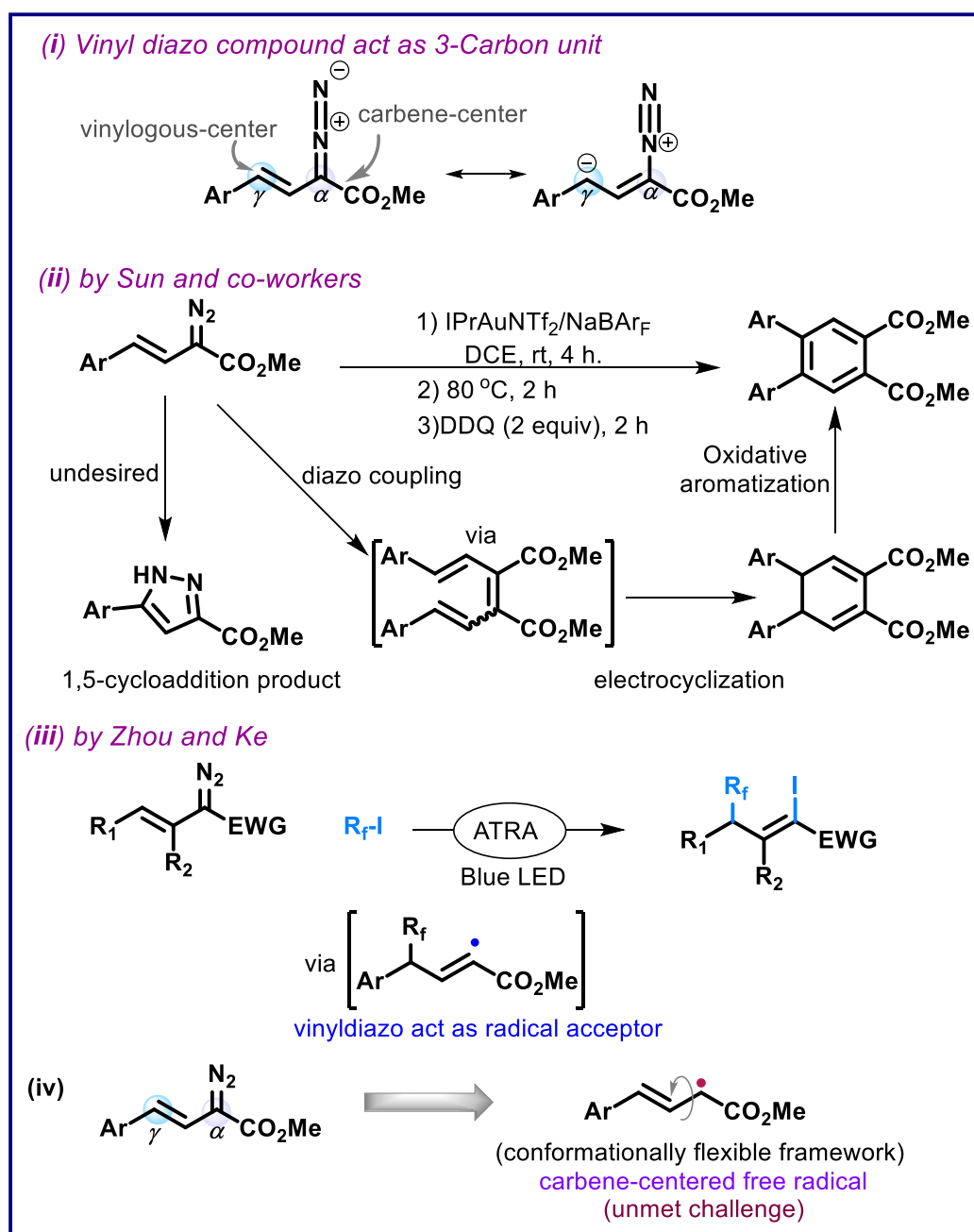
positions, ensuring the efficiency and purity of the final product. PMDI compounds typically require complex multi-step syntheses, often involving challenging bromination steps for prefunctionalization. Eliminating bromination improves atom economy while simplifying the production of PMDI-based materials. This was exemplified in 2017, when Sommer⁷ reported a method for activating PMDI's C–H bonds and enabling its reaction with aromatic halides (Scheme 3.1b).

Existing methods typically require multistep procedures, harsh conditions, and expensive metal catalysts and often pose challenges in removing metal residues.^[6b,7] Some of these drawbacks of the earlier methods seriously limit their wider applications. Thus, a facile method for synthesizing disubstituted PMDI molecules via a sustainable synthetic route in a minimum number of steps is highly desirable. The short synthetic approach, yet convenient, efficient for accessing such valuable but challenging compounds, is highly desirable. Herein, in this chapter, we have disclosed a simple yet elegant synthetic strategy for constructing PMDI at ambient reaction conditions. A systematic and detailed mechanistic study has been carried out to understand the mechanistic pathway, and it is revealed that the radical intermediate is a key intermediate that is generated in situ from vinyl diazo compounds in the presence of copper salt and NaSCN under irradiation of visible light (blue LEDs).

Radical chemistry has witnessed remarkable progress over the years, with numerous state-of-the-art methods emerging through the exploration of its versatile reactivity under photoredox catalysis.^[8] Notably, certain acceptor-type diazo compounds, when subjected to photoredox conditions, undergo cycloaddition and functionalization via carbon-centered radical intermediates instead of the conventional carbene pathway.^[9] On the other hand, vinyl diazo compounds exhibit unique reactivity due to the dual presence of an alkene and a diazo group, offering reactive sites at both the α - and γ -positions (Scheme 3.2-i). This dual functionality has enabled the development of several robust synthetic strategies. In particular, acyclic vinyl diazo compounds have been widely utilized as 3-carbon building blocks for (3 + n)-cyclization reactions.^[10,11]

Sun and co-workers^[11] have demonstrated a gold-catalyzed intermolecular cross-coupling of two molecules of vinyl diazoacetates, forming the corresponding triene, which proceeds through a metal-carbene intermediate, followed by an electrocyclization at an elevated temperature leads to cyclized product, this further oxidized to generate a substituted benzene in the presence of a suitable oxidant (Scheme 3.2-ii). In contrast, under photochemical conditions, acyclic vinyl diazo compounds can act as nucleophiles.^[12] In 2020, Zhou and co-

workers reported the first use of vinyl diazoacetates as radical acceptors in an atom transfer radical addition (ATRA) reaction with RfI, enabling the formation of 1,3-difunctionalized adducts under visible light irradiation (Scheme 3.2-iii).^[12c] Despite progress in the photochemical radical chemistry of diazo compounds,^{9,10} the direct formation of carbene-centered radicals from vinyl diazo compounds through nitrogen extrusion under light remains elusive (Scheme 3.2-iv).

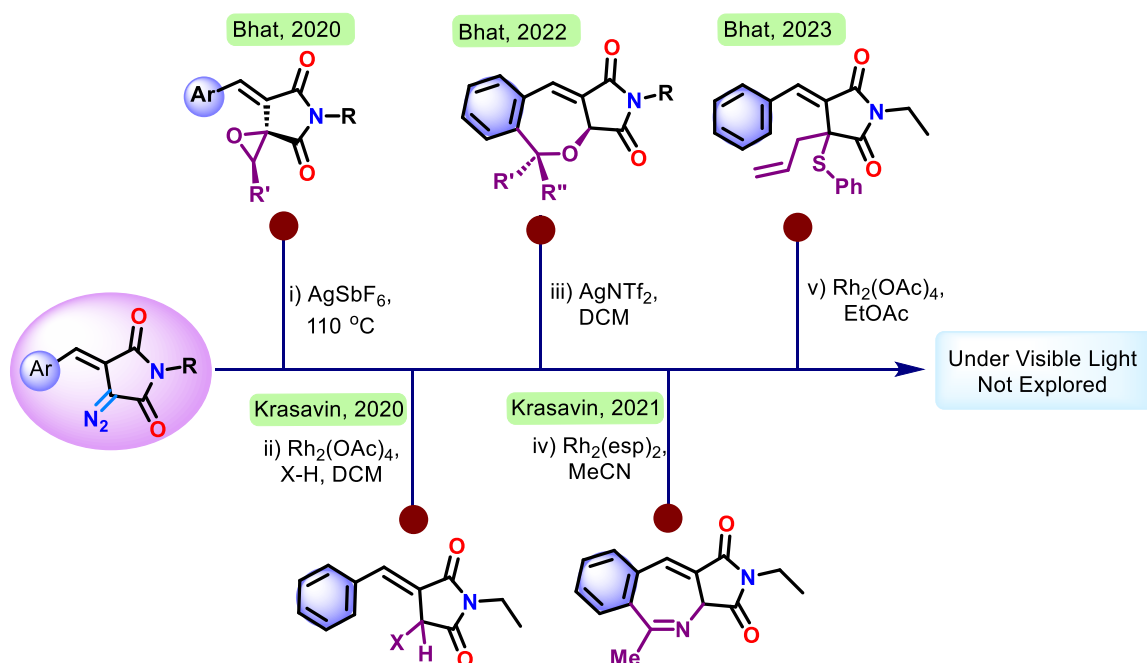


Scheme 3.2: Reactivity of acyclic vinyl diazo compound with metal and light

Cyclic diazo compounds such as diazo arylidene succinimides (DASs) are relatively rarely studied under photochemical reaction conditions, in comparison to acyclic vinyl diazo compounds. Diazo arylidene succinimides serve as valuable carbene precursors, readily

synthesized from benzylidene succinimides through previously established protocols. Catalytically derived from stable vinylic diazosuccinimides, metallo-vinyl carbenesuccinimides or vinyl carbenesuccinimides exhibit electrophilic behavior at the metal carbene carbon and nucleophilic properties at the vinylogous carbon. These metallo-vinyl carbenesuccinimides function as versatile synthons, enabling the formation of metallo-adducts when reacted with appropriate dipolarophiles or nucleophiles.^{14,15}

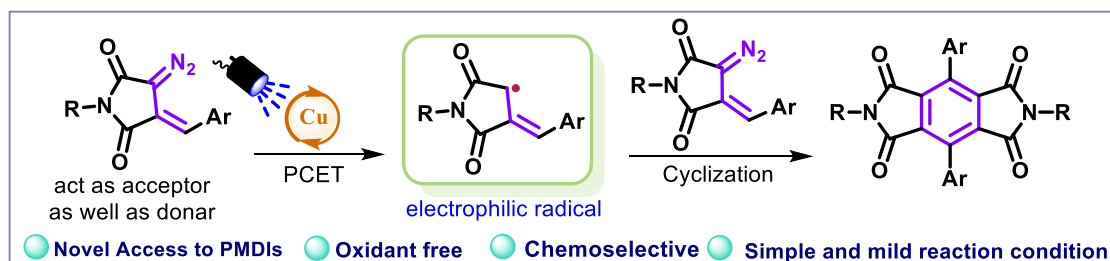
A few examples of metallo-vinyl carbenesuccinimides serving as reactive metallo-1,1- or 1,3-adducts under diverse metal-catalyzed conditions have been depicted in scheme 3.3. However, to the best of our knowledge, the reactivity of DASs under visible light remains unexplored and thus gives an opportunity to explore their reactivity. Their absorption of DAS **1a** primarily in the near-UV region suggests that they may exhibit low or negligible reactivity under visible light irradiation. Therefore, investigating DAS reactivity under visible light and establishing a new protocol represents a significant challenge.



Scheme 3.3: Reactivity of diazo arylidene Succinimide with metal catalyst compound with metal catalysis

Photoredox catalysis has evolved as a sustainable alternative to traditional synthetic methodologies. In contrast to ruthenium and iridium-based photocatalysts,¹⁶ copper salts are relatively abundant, commercially available, cost-effective, and exhibit excellent photoexcited redox properties as well.¹⁷ Notably, Cu(I) salts have a strong affinity for halide and pseudohalide ligands. Interestingly, the in-situ generation of photocatalysts by combining

copper salts with substrates or ligands offers a practical approach for achieving rapid and synthetic transformations, bypassing the need for multi-step synthesis.^{17a,19}



Scheme 3.4: Visible light-promoted PMDI synthesis from diazo compounds

Owing to the significance of the PMDI core and the limitations of traditional methods (Scheme 3.4), an efficient and practical approach to access di-substituted PMDI molecules is highly desirable. Our research group has been exploring the varied reactivity of DAS under different reactions.⁶ With our continuous interest in the reactivity of DAS and further to extend the scope of DAS under visible light, we hypothesized that photoredox catalysis could enable the formation of a carbon radical intermediate from DAS, paving the way for the synthesis of the PMDI core. Herein, in this chapter, we describe a straightforward and efficient protocol for PMDI synthesis via visible light photoactivated copper-catalyzed radical cyclization of DAS under mild reaction conditions (Scheme 3.4).

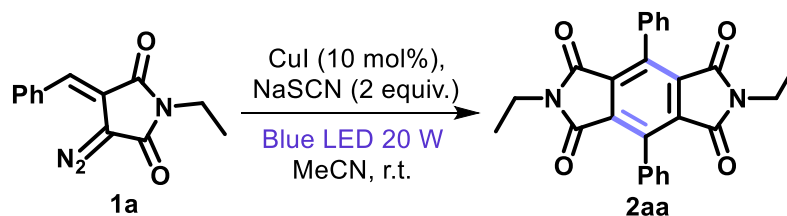
3.2 Results and Discussion

3.2.1 Reaction optimization

In order to validate our hypothesis on the visible light reactivity of DAS in copper salt, we commenced our investigation using DAS **1a** as the model substrate. To begin with, we explored the reaction of **1a**, in the presence of CuI (10 mol%) as the catalyst and NaSCN (2 equiv) as the ligand/base in acetonitrile. The reaction mixture upon irradiation with blue LEDs (20 W) for 24 h at 30 °C furnished the desired PMDI product **2aa**, which was obtained in a moderate yield (60%, Table 3.1, Entry 1). Later, we carried out a series of control reactions, which confirmed that light, NaSCN, and CuI are essential for this transformation (Table 3.1, Entries 2–4). The reaction in anhydrous acetonitrile did not produce the desired product **2aa**, emphasizing the crucial role of moisture in the process (Table 3.1, Entry 5). Subsequently, the reaction was conducted in an oxygen-rich environment; however, the expected product was not obtained (Table 3.1, Entry 6). Later, replacing CuI with Eosin Y (10 mol%) as the photocatalyst in the reaction of **1a**, while keeping all other initial conditions same, led to the formation of the desired product **2aa**, though with a reduced yield (45%) compared to the initial conditions

(Table 3.1, Entry 7). The results showed that the copper catalyst is relatively more efficient than the Eosin Y.

Table 3.1: Control Reactions



Entry	Variation from initial tested condition ^a	Yield of 2aa (%)
1	none	60
2	No CuI	<i>n.d.</i>
3	No NaSCN	<i>n.d.</i>
4	No Light	<i>n.d.</i>
5	Dry MeCN	<i>n.d.</i>
6	O ₂ instead of N ₂	<i>n.d.</i>
7	Eosin Y	45

^[a]**Reaction conditions:** unless otherwise noted, the reactions were carried out with diazo compound **1a** (1.0 equiv., 0.2 mmol), NaSCN (2.0 equiv., 0.4 mmol), CuI (10 mol%) in solvent (0.05 M) under nitrogen (degassed) at room temperature (28 °C) under blue light (20 W-459nm) until **1a** was consumed completely. ^[b]Yields of **2aa** were determined by ¹H NMR spectroscopic analyses of the reaction mixture using 1,3,5-trimethoxybenzene as the internal standard. *n.d.* = not detected.

Encouraged by this preliminary finding, we have done further extensive screening of different copper and other metal catalysts, bases, solvents, and light sources to optimize the reaction conditions further (Table 3.2). However, catalysts other than CuI either furnished the desired product **2aa** in lower yields or failed to furnish the desired product **2aa** (Table 3.2, Entries 115). Maintaining CuI as a constant, we examined the reaction using various salts, and found that NaSCN was the most effective (Table 3.2, Entries 16-20). Following this, we screened various solvents, both polar and non-polar, and among all, DMSO proved to be the most efficient solvent for the desired transformation (Table 3.2, Entries 21-27). Subsequently, we investigated the effects of different light sources (LEDs of different wavelengths) on the outcome of the reaction yield of **2a** (Table 3.2, Entries 28-32). Among all, we observed that blue LED (440

nm) furnished the desired product **2aa** in the highest yield (Table 3.2, Entry 29). While the reaction under the visible light (either below or above 440 nm, Blue LEDs) gave the desired products in relatively lower yields (Table 3.2, Entries 28-32). Notably, the reaction in the absence of light but at an elevated temperature (50 °C) did not afford the desired product **2aa** (Table 3.2, Entry 33). These results clearly indicate that visible light is essential for the reaction, and heat generated if any due to LEDs, is not responsible for the transformation. Subsequently, we examined the catalyst loading and varied the stoichiometry of NaSCN (Table 3.2, Entries 34-44). Based on the systematic and detailed screening, DAS **1a** (1 equiv.), NaSCN (2 equiv.), and CuI (10 mol%) in DMSO, using a degassed reaction mixture (nitrogen) under blue LED illumination (440 nm), prove to be the optimum reaction condition to obtain the desired PMDI product **2aa** in very good yield (Table 3.2, Entry 29).

Entry	Catalyst (10 mol%)	Light	Solvent	Base (2 equiv.)	Time (h)	Yield (%) ^b 2aa
1	CuI	blue LED	MeCN	NaSCN	24	60
2	CuCl	blue LED	MeCN	NaSCN	24	16
3	CuBr	blue LED	MeCN	NaSCN	24	15
4	Cu(OAc) ₂ .H ₂ O	blue LED	MeCN	NaSCN	24	35
5	CuSO ₄ .5H ₂ O	blue LED	MeCN	NaSCN	24	15
6	Rh ₂ (OAc) ₄	blue LED	MeCN	NaSCN	24	<i>n.d.</i>
7	Sc(OTf) ₃	blue LED	MeCN	NaSCN	24	<i>n.d.</i>
8	Cu ₂ O	blue LED	MeCN	NaSCN	24	<i>n.d.</i>
9	CuCN	blue LED	MeCN	NaSCN	24	20
10	CuBr.SMe ₂	blue LED	MeCN	NaSCN	24	25
11	CuBr ₂	blue LED	MeCN	NaSCN	24	21
12	Cu(OAc) ₂	blue LED	MeCN	NaSCN	24	32
13	CuCl ₂ .H ₂ O	blue LED	MeCN	NaSCN	24	<i>n.d.</i>
14	FeCl ₂	blue LED	MeCN	NaSCN	24	<i>n.d.</i>
15	[Ir]	blue LED	MeCN	NaSCN	24	<i>n.d.</i>

16	CuI	blue LED	MeCN	KSCN	24	54
17	CuI	blue LED	MeCN	NH ₄ SCN	24	<i>n.d.</i>
18	CuI	blue LED	MeCN	KI	24	30
19	CuI	blue LED	MeCN	KBr	24	18
20	CuI	blue LED	MeCN	KCl	24	8
21	CuI	blue LED	DMF	NaSCN	24	40
22	CuI	blue LED	THF	NaSCN	24	<i>n.d.</i>
23 ^c	CuI	blue LED	EtOAc	NaSCN	24	30
24	CuI	blue LED	DMSO	NaSCN	24	72
25	CuI	blue LED	DCM	NaSCN	24	<i>n.d.</i>
26	CuI	blue LED	DCE	NaSCN	24	<i>n.d.</i>
27	CuI	blue LED	EtOAc: DMSO	NaSCN	24	65
28	CuI	427 nm	DMSO	NaSCN	5	42
29	CuI	440 nm	DMSO	NaSCN	12	82
30	CuI	456 nm	DMSO	NaSCN	24	75
31	CuI	467 nm	DMSO	NaSCN	24	72
32	CuI	525 nm	DMSO	NaSCN	72	30
33	CuI	Dark, 50 °C	DMSO	NaSCN	24	<i>n.d.</i>
34	CuI (3 mol%)	440 nm	DMSO	NaSCN	12	52
35	CuI (5 mol%)	440 nm	DMSO	NaSCN	12	48
36	CuI (7 mol%)	440 nm	DMSO	NaSCN	12	59
37	CuI (10 mol%)	440 nm	DMSO	NaSCN	12	82
38	CuI (15 mol%)	440 nm	DMSO	NaSCN	12	70
39	CuI	440 nm	DMSO	NaSCN (0.5 equiv)	12	30
40	CuI	440 nm	DMSO	NaSCN	12	40

				(1 equiv)		
41	CuI	440 nm	DMSO	NaSCN (1.5 equiv)	12	50
42	CuI	440 nm	DMSO	NaSCN (2.5 equiv)	12	60
43	CuI	440 nm	DMSO	NaSCN (3 equiv)	12	50
44	CuI	440 nm	DMSO	NaSCN (5 equiv)	12	<i>n.d.</i>

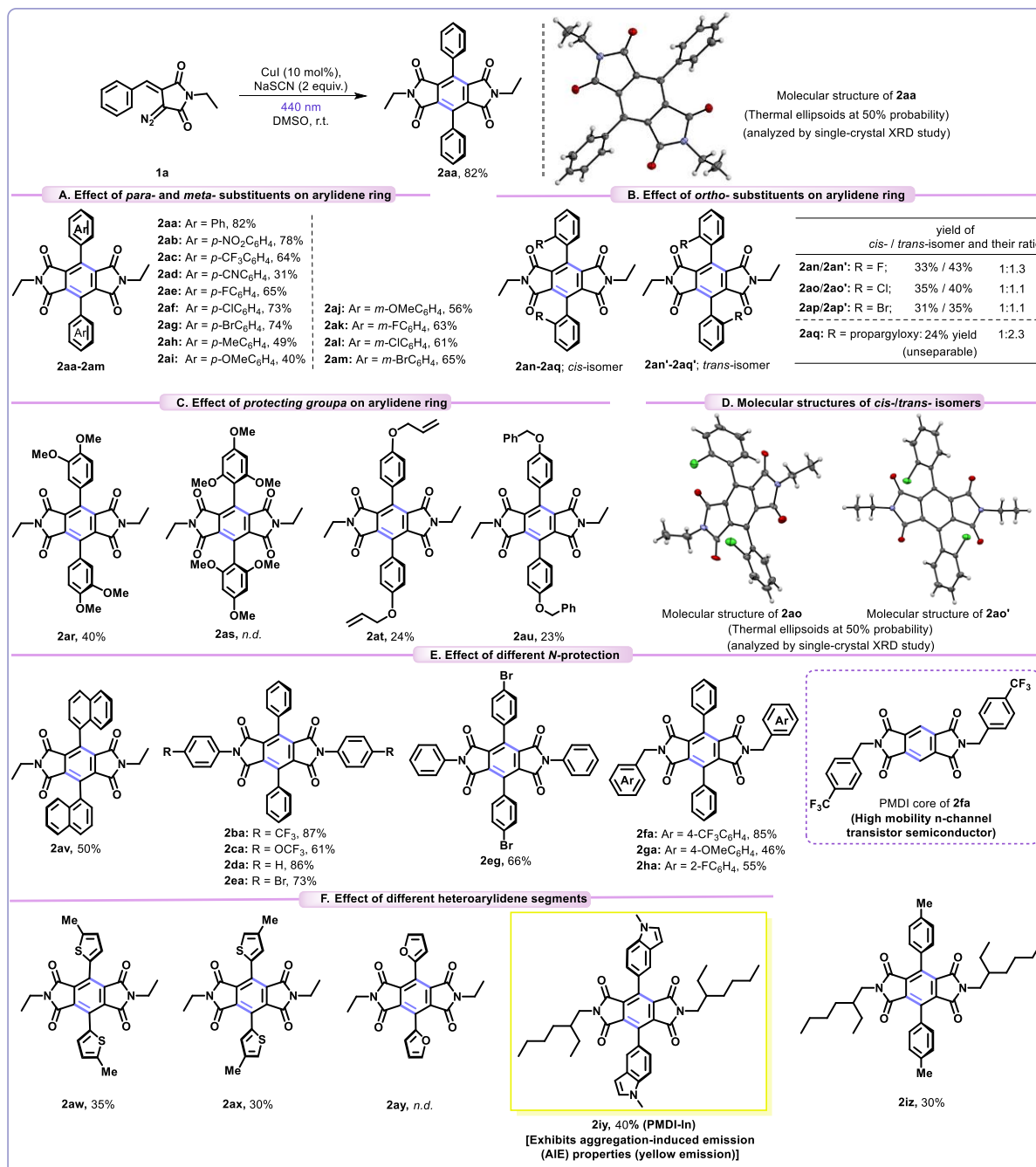
Table 3.2: Optimization of Reaction Conditions^a, ^[a]**Reaction conditions:** unless otherwise noted, the reactions were carried out with diazo compound **1a** (1.0 equiv., 0.2 mmol), NaSCN (2.0 equiv., 0.4 mmol), CuI (10 mol%) in solvent (0.05 M) under nitrogen (degassed) at room temperature (28 °C) under blue LED (20 W-459 nm) until **1a** was consumed completely. ^[b]Yields of **2aa** were determined by ¹H NMR spectroscopic analyses of the reaction mixture using 1,3,5-trimethoxybenzene as the internal standard. *n.d.* = not detected. ^[c]Mixture of ethyl acetate and DMSO taken in the ratio of 9:1. [Ir] = Ir[dF(CF₃)ppy]₂(dtbpy))PF₆

3.3 Substrate Scope of Diazo Compounds

Having obtained the optimized reaction conditions, we further explored the substrate scope of the reaction by varying the substituent on the phenyl ring of the aryl diazo compounds. *p*-Substituted DASs having electron-deactivating as well as electron-withdrawing groups on the phenyl ring of DAS (**1a-1g**) reacted smoothly under the optimized reaction conditions to afford the corresponding desired products (**2aa-2ag**) in moderate to good yields (up to 82%, Scheme 3.5). However, *p*-cyano (CN) substituted DAS derivative (**1ad**) afforded the corresponding desired product **2ad** in modest yield (31%, Scheme 3.5). Lowering in the yield of desired product **2ad** may be possibly due to the binding of the -CN group with [Cu] catalyst, thus diminishing the reactivity.

However, DASs having electron-donating groups at the *p*-position on the phenyl ring (**1h, 1i**) afforded the corresponding desired products (**2ah, 2ai**) relatively in lower yields (up to 49%, Scheme 3.5). Furthermore, DAS derivatives (**1j-1m**) with various substituents at meta position on the phenyl ring reacted smoothly to afford the corresponding products (**2aj-2am**) in moderate to good yields (up to 65%, scheme 3.5). Whereas, DAS with *o*-substituents (**1n-1p**) afforded the corresponding isomeric products (**2an-2ap**) (up to *cis-/trans* isomers-1:1.3) in

moderate to good yield (up to 76%, Scheme 3.5). The molecular structure of these isomers (*cis*-2ao, *trans*-2ao') has been confirmed by single crystal X-ray diffraction analysis.^[21]



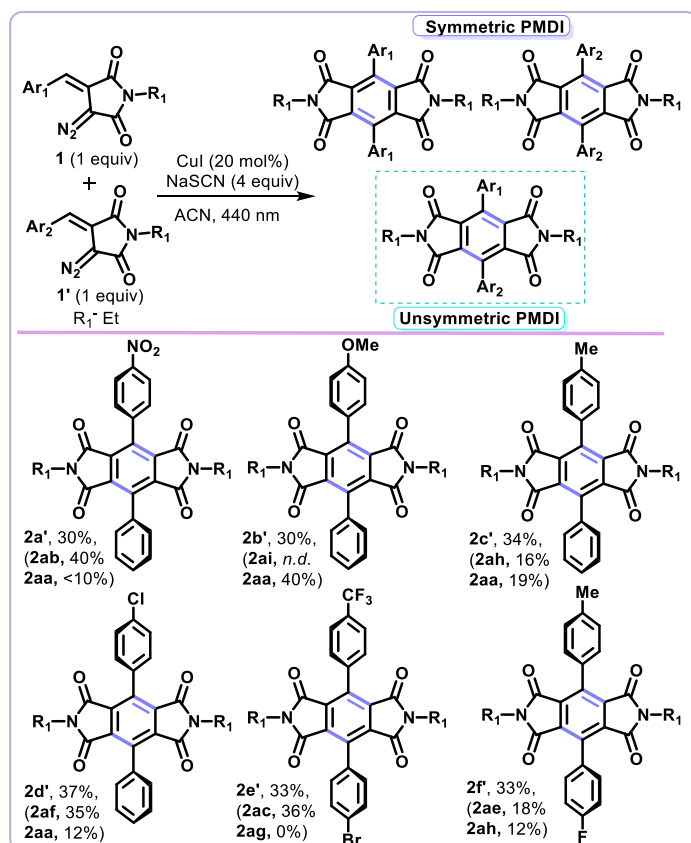
Scheme 3.5: Substrate Scope of Diazo Arylidene Succinimides (DASs). ^aGeneral reaction conditions: diazo compound **1** (1.0 equiv., 0.2 mmol), NaSCN (2.0 equiv., 0.4 mmol), CuI (10 mol%) in DMSO (0.055 M) under nitrogen (degassed) at room temperature (28 °C) under blue light for 12 h.

The *o*-propargyloxy phenyl derivative DAS **2aq** produced the corresponding desired product **2aq** in a relatively low yield (24%, *cis*-/*trans* ratio 1:2.3, Scheme 3.5). Similarly, the disubstituted (3,4-dimethoxy) DAS **1r** showed reduced reactivity, possibly due to electronic

factors, furnishing the desired product **2ar** in a modest (40%, Scheme 3.5). 2,4,6-Trimethoxy DAS (**1s**) did not react under optimized reaction conditions, likely due to steric hindrance. DAS derivatives **1t-1u** with protecting groups tolerated the reaction conditions well, however, furnished the desired products (**2at**, **2au**) in low yields (up to 24%, Scheme 3.5). Notably, the naphthalene-substituted DAS **1v** afforded the desired product **2av** in good yield of (50%, Scheme 3.5).

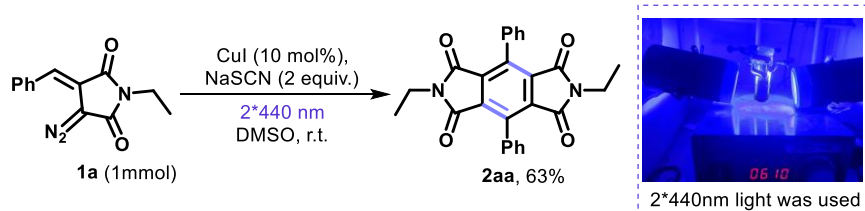
Later, in order to demonstrate the versatility of the protocol, we explored the reaction of various *N*-substituted DASs, including electron-rich and electron-deficient aromatic (**2ba-2eg**) and aliphatic groups (**2fa-2ha**, **2iy**, **2iz**). The substrates (**1a-1z**) reacted successfully to afford the corresponding products (**2ba-2iz**) in good to excellent yields (87%, Scheme 2.5). Heteroarylidene-derived DAS (**1w-1y**) successfully furnished the desired products (**2aw** and **2iy**) in modest yields of (up to 40%, Scheme 3.5). However, under reaction conditions, the furan-substituted derivative **1y** did not afford the corresponding desired product **2ay**, likely due to inherent electronic or steric factors. The PMDI core of compound **2fa** stands out among all the products, as it is a well-known high-mobility *n*-channel transistor semiconductor with significant applications in electronic devices.²¹ The compound **2fa** has been synthesized elegantly using the developed protocol in a very good yield, more importantly, under mild reaction conditions with a lesser number of steps, (85%, Scheme 2.5). Along with other examples, the method proved to be efficient and useful. Additionally, the practicality of this novel method has been demonstrated through the synthesis of **2iy**, a compound renowned for its prominent aggregation-induced emission (AIE) properties, which is known for its applications in optoelectronic materials and bioimaging.²² Also, the successful preparation of **2iy** highlights the ability of the protocol to synthesize structurally and functionally valuable compounds. Encouraged by the success with symmetric PMDIs, we further explored the synthesis of unsymmetric PMDIs, which had not been documented previously in the literature. The crosscoupling of two different DASs presented a significant challenge due to subtle electronic differences between the substrates.

Nonetheless, gratifyingly, under the reaction conditions, different DASs reacted smoothly in the reaction successfully to afford the unsymmetric PMDIs (**2a'-2f'**) alongside the expected self-coupled products (Scheme 3.6). Despite modest yields, this marks the first direct synthesis of unsymmetric PMDI cores, offering a straightforward synthetic approach to these structurally unique useful molecules. The success of this interesting and novel transformation underscores the dual role of the diazo arylidene succinimide (DAS) functioning both as a donor as well as an acceptor in the formation of the desired PMDI product.



Scheme 3.6: Substrate Scope for Unsymmetrical PMDIs. ^aGeneral reaction conditions: **1** and **1'** (0.1 mmol each) NaSCN (2.0 equiv., 0.2 mmol), CuI (20 mol%) in DMSO (0.055M) under nitrogen (degassed) at room temperature (28 °C) under light for 12 h. Self-coupled products are given in parentheses.

Furthermore, the method proved to be practical and scalable (1 mmol scale) to access the desired compound **2aa** in good yield (63%, Scheme 2.7).

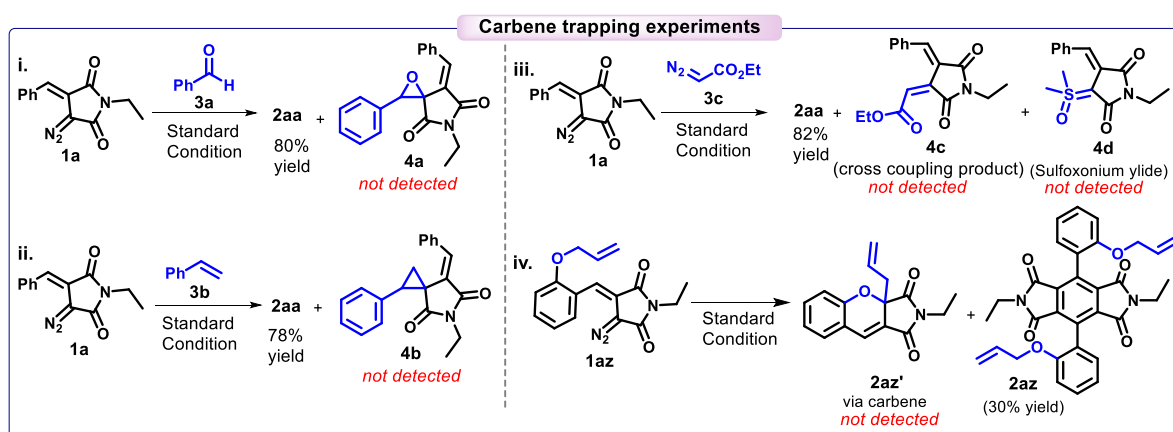


Scheme 3.7. Scale up Reaction: ^aGeneral reaction conditions: diazo compound **1** (1.0 equiv., 1 mmol), NaSCN (4 mmol), CuI (10 mol%) in DMSO (0.1 M) under nitrogen (degassed) at room temperature (28 °C) under blue light for 40 h.

3.4 Mechanistic Investigations: Control Experiments

To better understand the reaction pathway, several control experiments were conducted. To determine whether the reaction proceeds via a classical carbene intermediate (metallo-carbene), we planned to investigate the interaction between diazo arylidene succinimide **1a** and an aldehyde under optimized conditions. Previously, we reported the silver-catalyzed synthesis of

epoxides from DAS derivatives **1** and aldehydes, demonstrating that aldehydes effectively trap the in situ-generated carbene intermediate (metal-carbenoid). However, when DAS **1a** was reacted with benzaldehyde **3a** under optimized conditions, the expected epoxide product **4a** was not observed, even in trace amounts. Instead, PMDI **2aa** was obtained in good yield (75%, Scheme 3.8-i). This result clearly indicates that this reaction may not proceed through a carbene intermediate. To validate this further, we carried out the classic reaction wherein the treatment of **1a** with styrene **3b** under standard reaction conditions did not furnish the cyclopropanation product **4b** (Scheme 3.8-ii). Both of these control experiments indicate that this photoinduced protocol may be proceeding through an intermediate other than the carbene (metallo-carbene) intermediate.

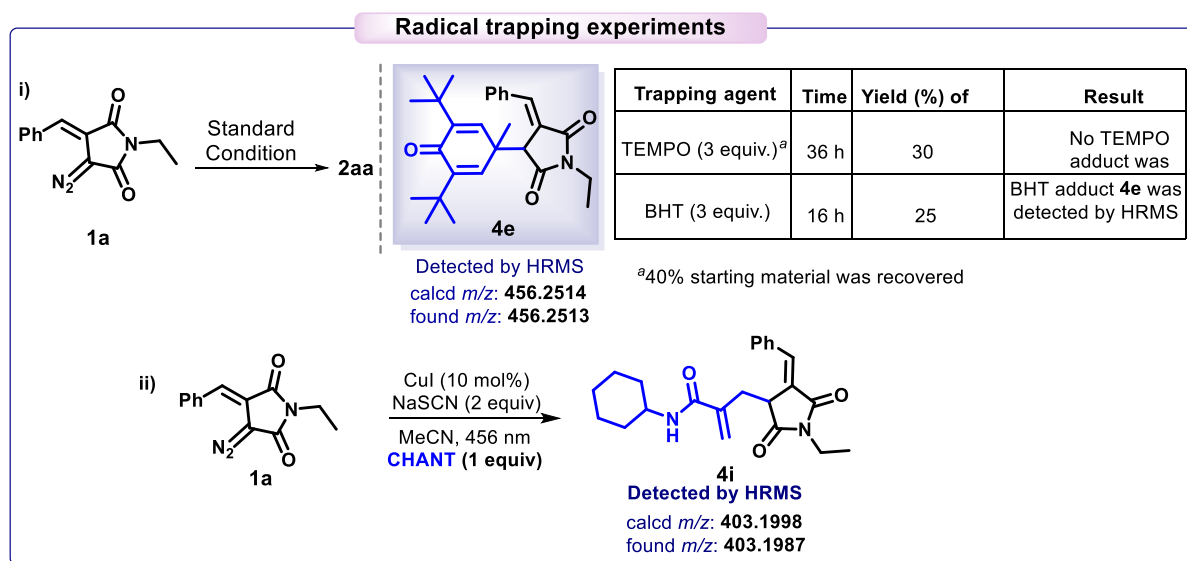


Scheme 3.8: Carbene Trapping Experiments; **Standard condition:** diazo compound **1** (1.0 equiv., 0.2 mmol), NaSCN (2.0 equiv., 0.4 mmol), CuI (10 mol%) in DMSO (0.055 M) under nitrogen (degassed) at room temperature (28 °C) under blue light for 12 h.

Ethyl diazoacetate (EDA) **3c** is renowned for its carbene-trapping ability under photochemical conditions.^[24] Interestingly, the reaction of **1a** with EDA **3c** as a trapping reagent under the standard reaction conditions did not give the cross-coupling product **4c** and sulfoxonium ylide product **4d** (through DMSO solvent); instead, we obtained the cycloaddition product **2aa** (80%, Scheme 3.8-iii). This outcome validates that carbene may not be generated during the course of the reaction. It is also possible that the desired cyclization is outcompeting any intermolecular reactions with other substrates. In order to investigate this, we synthesized a new substrate, **1az**, having an internal olefin. The compound **1az** under standard conditions exclusively afforded the self-dimerized PMDI product **2az**. We did not observe the intramolecular [2,3]-sigmatropic rearrangement product **2az'** even in trace (Scheme 3.8-iv). The preference for the intermolecular self-dimerization product **2az** over the intramolecular

rearrangement product **2az'** clearly implies that the reaction is unlikely to proceed through a carbene intermediate, suggesting the involvement of an alternative reaction pathway.

To determine whether the involvement of a radical intermediate in the reaction, we further performed the radical trapping experiments. In this regard, we carried out the reaction of **1a** in the presence of TEMPO and BHT separately, while maintaining the standard reaction conditions. We observed that the reaction slowed down significantly in the presence of TEMPO to afford the desired products in lower yields. Further, we have also observed the BHT-trapped adduct **4e** (detected by HRMS, Scheme 3.9-i).



Scheme 3.9: Radical Trapping Experiments

Additionally, we have carried out radical trapping experiment with BHT in MeCN-*d*₃, we observe product **2aa** along with BHT trapping adduct **4e**, **4f**, **4g**, and **4h**. This result clearly implies that the generation of radicals during the course of reaction to furnish the desired product **2aa**. The formation of protonated adducts **4e** and deuterated adduct **4f** indicates that the either the solvent or the moisture in the solvent may be the proton source (Scheme 3.9-ii). All these findings strongly support the generation of a radical intermediate during the progression of the reaction. In order to examine further, a novel allyl-TEMPO-based radical trapping agent has been developed to detect the short-lived radical intermediates generated in situ in the reaction. Recognizing the difficulty of trapping radicals in short-lived radical traps, we synthesized a CHANT radical trapping agent based on literature reports²⁴ (allyl-TEMPO), which is known to stabilizes short lived radicals and facilitates the trapping process. The reaction of **1a** in the presence of CHANT reagent while maintaining other standard conditions,

furnished the radical-trapped adduct **4i** (detected by HRMS, Scheme 3.9-iii), providing evidence for the formation of the radical intermediate (Scheme 3.9-iii). This result unambiguously provided further evidence for the formation of radical intermediates. These findings further suggest the involvement of radical intermediate in the reaction.

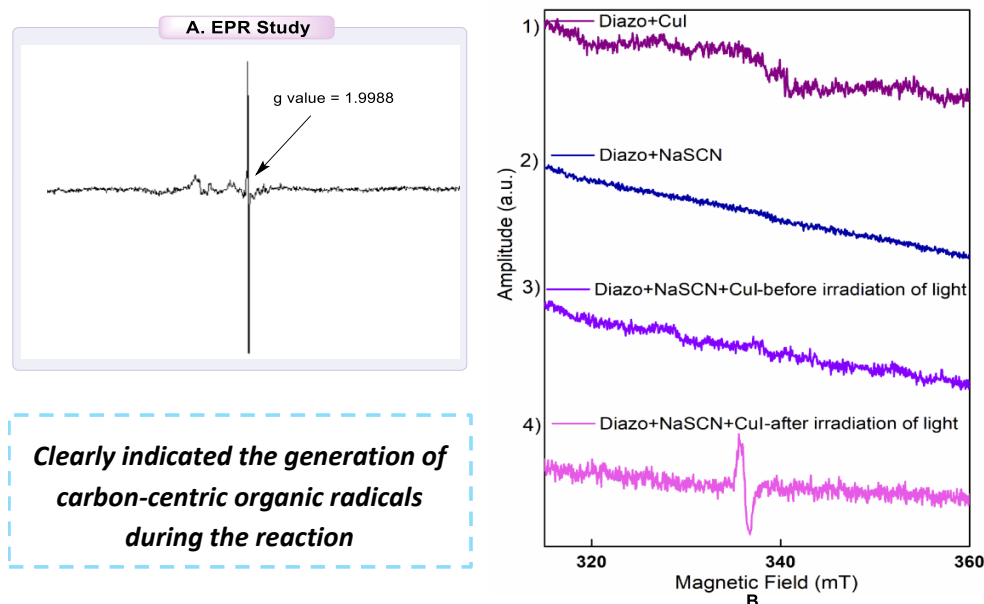


Figure 3.2: X-band EPR spectrum reaction mixture of control experiments.

In order to further affirm the presence of the radical during reaction pathway, we monitored this photoinduced reaction using electron paramagnetic resonance (EPR) spectroscopy. An EPR analysis of an incomplete reaction mixture (CuI, NaSCN, and diazo **1a**) under the standard reaction condition indicated that carbon-centric organic radicals being generated during the reaction. The ‘g’ factor of the crossover point of the peak was found to be 1.9959 (Figure 3.2), which is the peculiar characteristic of the free radical nature of an unpaired electron carried out in a few control experiments under EPR spectroscopy (Figure 3.2).

After that we performed some EPR control experiment of the reaction mixture containing diazo compound **1a**, NaSCN, and CuI was measured before shining the light. Later, the reaction mixture containing diazo compound **1a**, NaSCN in the absence of CuI under the illumination of light was examined under the EPR spectrometer. Finally, the EPR spectrometer was used to analyze the reaction mixture of diazo **1a** and CuI under light irradiation conditions, excluding the NaSCN. However, in all these three experiments we did not observe any detectable EPR signals. These results clearly demonstrate that the generation of radical intermediate is favorable and possible only under the optimized reaction conditions (Figure 3.2A and B).^[25]

Finally, to examine the role of light in the reaction, we have recorded UV/Vis spectra of individual reagents as well as the mixtures of reagents to gain additional insights into the reaction mechanism (Figure 3.3). Interestingly, only the solution containing CuI and NaSCN showed a broad absorption band in the visible range (350–450 nm), whereas the other solutions, including individual reagents and their mixtures, did not absorb above >400 nm.

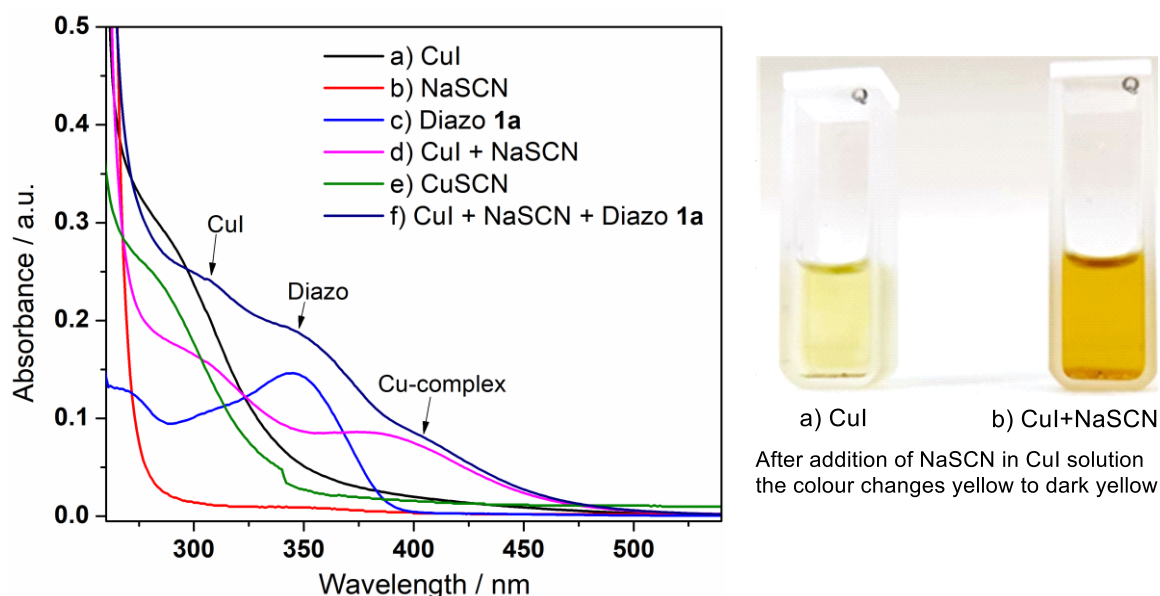


Figure 3.3: UV-Vis absorbance spectra of individual components and their mixture.

These results are quite interesting and indicate that a certain photoactive visible light-absorbing species might have formed in situ. The absorption spectrum for the newly formed copper complex in situ is different from CuSCN. This result clearly indicates that mixture of CuI and NaSCN did not generate the usually anticipated CuSCN complex in situ.

We have also observed the colour of the solution of copper iodide changes after the addition of NaSCN it turns yellow to dark yellow (Figure 3.3).

After that we have also recorded the UV/vis spectrum of other copper salts and their mixture with NaSCN. UV-Visible study shows that λ_{max} of the mixture of CuI + NaSCN is higher than the mix of CuBr + NaSCN and CuCl + NaSCN, which means that CuI forms a complex with NaSCN faster than CuBr and CuCl (Figure 3.4).

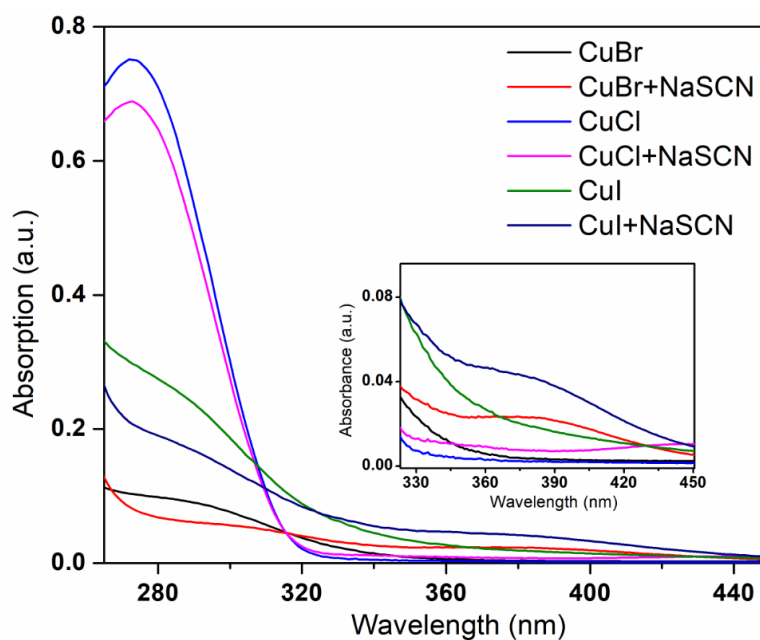
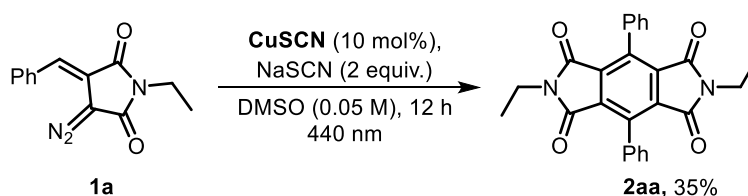


Figure 3.4. UV-Vis absorbance spectra of copper catalyst and their complexes

In order to validate this result experimentally, we carried out the reaction of **1a** using CuSCN (instead of CuI) while maintaining other reaction conditions to obtain the desired product **2aa** in very low yield (35%, Scheme 3.10). This result suggests that CuSCN is not an active complex for the reaction, else the reaction would have afforded the desired product efficiently.



Scheme 3.10 Control reaction with CuSCN instead of CuI

In order to confirm this further, additionally, we have successfully obtained the molecular structure of the mixture of CuI and NaSCN after multiple attempts using single crystal X-ray diffraction analysis (Figure 3.5). The diffraction data clearly indicate that the copper isothiocyanate (CuNCS) complex formation from the mixture of CuI and NaSCN.

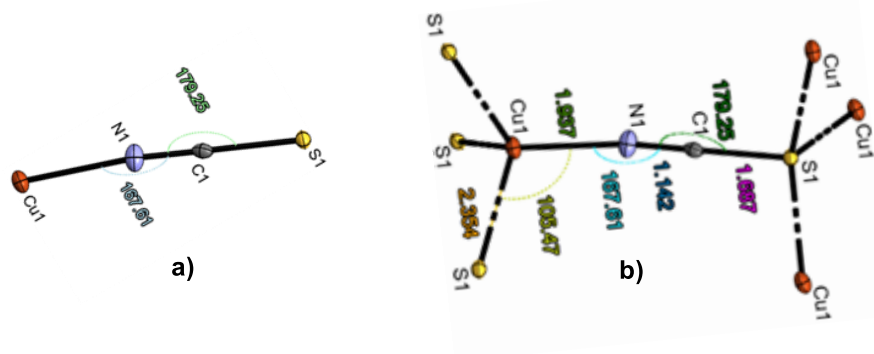
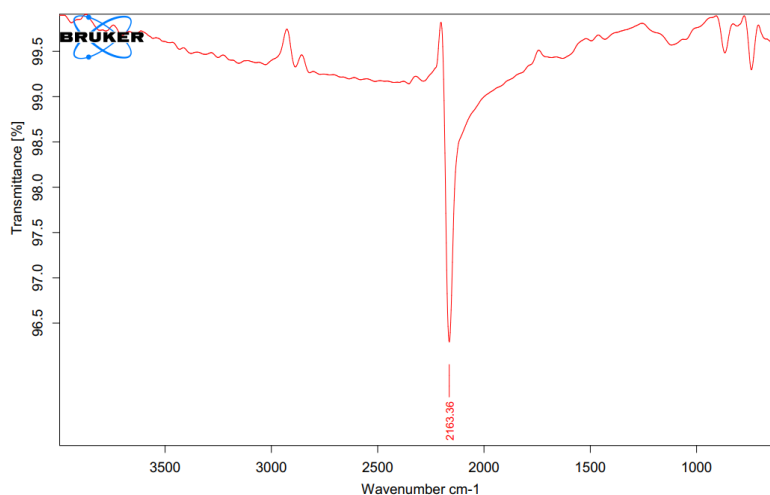
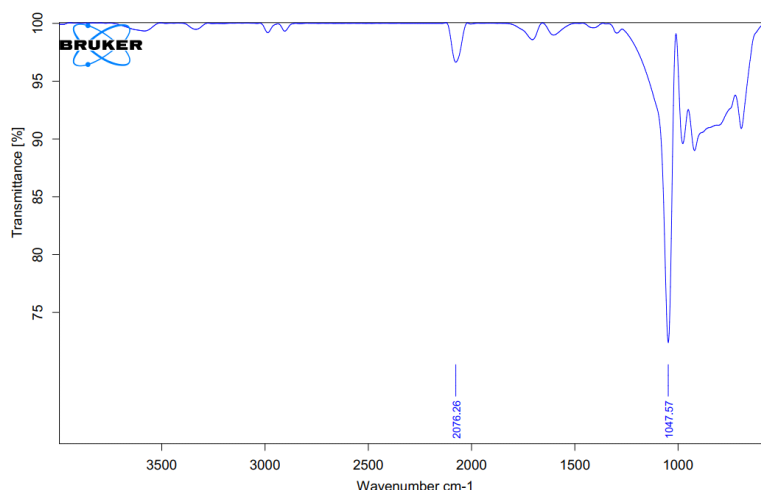


Figure 3.5: Molecular Crystal Structure of NaSCN, a) Asymmetric unit, b) Asymmetric unit with repeating pattern

Later we recorded the FT-IR spectra of CuSCN as well as the mixture of CuI and NaSCN separately (Figure 3.6). The IR stretching of the CuSCN complex and the mixture of CuI and NaSCN were found to be different. As expected, we observed a peak at 2163 cm^{-1} for CuSCN and at 2076 cm^{-1} for CuNCS. These results indicate that CuSCN and the mixture of CuI and NaSCN (CuNCS) are distinct. CuI+NaSCN mixture resulted in the formation of copper isothiocyanate (CuNCS).



A. IR stretching of CuSCN

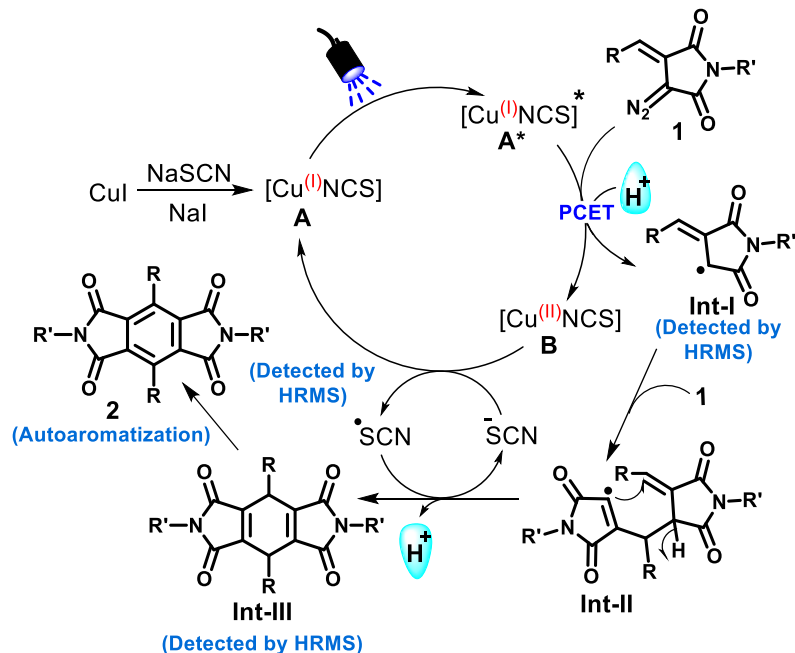


B. IR stretching of mix of CuI+NaSCN

Figure 3.6: FT IR spectra of A) CuSCN and B) CuI+NaSCN complex

Based on the reaction outcome, single crystal X-ray diffraction analysis and FT-IR spectra, it's very clear that copper isothiocyanate (CuNCS) complex generated in situ is the active catalyst that was driving the reaction in presence of light.

Based on the systematic control experiments, UV-visible absorption studies, X-ray diffraction analysis, and FTIR spectra, a plausible mechanism is depicted in Scheme 3.11.



Scheme 3.11: Plausible mechanism

The copper iodide (CuI) reacts with the NaSCN to form the Cu(I)NCS complex A in situ. The copper complex further gets excited to $[\text{Cu(I)NCS}]^* \text{-A}^*$, which eventually undergoes proton-coupled electron transfer (PCET) with DAS **1** to generate the carbon-centric radical

intermediate **Int-I** (detected by HRMS) via the extrusion of nitrogen along with formation of the corresponding oxidized ground state copper (II) complex [Cu(II)NCS] **B**. The **Int-I** then reacts with DAS **1** to form the intermediate **Int-II**. Further, the thiocyanate anion (SCN^-) interacts with copper (II) complex **B** to form the thiocyanate radical ($\cdot\text{SCN}$) by regenerating the [Cu(I)NCS], a complex **A**. The in situ generated thiocyanate radical abstracts an electron from the intermediate **Int-II** leading to the facile intramolecular cyclization to furnish **Int-III** (detected by HRMS). This intermediate eventually cyclizes by losing a hydrogen radical. The hydrogen radical interacts with the thiocyanate radical ($\cdot\text{SCN}$) to generate proton and thus regenerates the SCN^- anion (see scheme 3.11). Finally, **Int-III** undergoes auto-aromatization via radical pathway to form the final desired PMDI product **2aa**.

3.5 Conclusion

In summary, we have successfully demonstrated an efficient visible light-promoted direct synthesis of pyromellitic diimides (PMDI) starting from diazo arylidene succinimides (DAS) via copper catalysis. This synthetic strategy provides a sustainable alternative route by unlocking the radical reactivity of arylidene diazo compounds, diverging from traditional methods, thus overcoming a long-standing paradigm in PMDI synthesis. The protocol opens up a new avenue for the unique photoreactivity of diazo arylidene succinimides, which plays a dual role as a donor as well as an acceptor. Importantly, the synergistic combination of NaSCN and the copper catalyst plays a pivotal role in facilitating this photoinduced transformation. An easy and practical approach has been demonstrated to access symmetrical as well as unsymmetrical PMDIs. Mechanistic insights have been acquired through a series of control experiments, UV-visible, FT-IR, EPR studies, and single-crystal X-ray diffraction analysis.

3.6 Experimental section

3.6.1 General Information:

Reagent Information: All reactions were carried out with distilled and anhydrous solvents using oven-dried glassware under a dry Argon atmosphere unless otherwise stated. All the reagents were purchased from commercial sources and used as received unless otherwise indicated. Thin-layer chromatography (TLC) was performed using silica gel 60 GF254 pre-coated aluminum backed plates (2.5 mm) with detection by UV light. Column chromatographic

purification of products was carried out using silica gel (100-200 mesh). The mixture of petroleum ether and ethyl acetate was used as gradient elution for column chromatography.

Analytical Information: All isolated compounds were characterized by ^1H NMR, and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra were recorded on a 400 MHz Jeol ECS-400 and Bruker Avance III HD Ascend 400 MHz spectrometers. Nuclear Magnetic Resonance spectra were recorded in CDCl_3 and in $\text{DCM-}d_2$. The NMR spectra were recorded using tetramethylsilane (TMS) as the internal standard. ^1H NMR spectra were recorded at 400 MHz, and $^{13}\text{C}\{^1\text{H}\}$ NMR spectra were recorded at 100/150 MHz (Bruker and Jeol), unless otherwise noted. Chemical shifts (δ) are reported in ppm downfield from CDCl_3 ($\delta = 7.26$ ppm) and from $\text{DCM-}d_2$ ($\delta = 5.32$ ppm) for ^1H NMR and relative to the central CDCl_3 resonance ($\delta = 77.16$ ppm) and $\text{DCM-}d_2$ resonance ($\delta = 54.00$ ppm) for $^{13}\text{C}\{^1\text{H}\}$ NMR spectroscopy. For ^1H NMR, data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = double doublet, t = triplet, q = quartet, m = multiplet), coupling constants (J) are given in Hz and integration. $^{13}\text{C}\{^1\text{H}\}$ NMR spectra were recorded with complete proton decoupling. ^{19}F NMR spectra were recorded at 377 MHz. Mass samples were analyzed by high-resolution mass spectrometry (HRMS) using ESI TOF. Single crystal X-ray diffraction data were collected on a Bruker SMART APEX four-circle diffractometer equipped with a CMOS photon 100 detector (Bruker Systems Inc.) with Microfocus ($\text{I}\mu\text{S}$) using Mo $\text{K}\alpha$ radiation (0.71073 Å) and Cu $\text{K}\alpha$ radiation (1.5418 Å). UV-Vis absorption spectra were recorded on the UV-1900 UV-Vis Spectrophotometer.

Photoreactor Setup: Light-mediated reactions studies were carried out in our custom fabricated photoreactor (Figure 3.7).

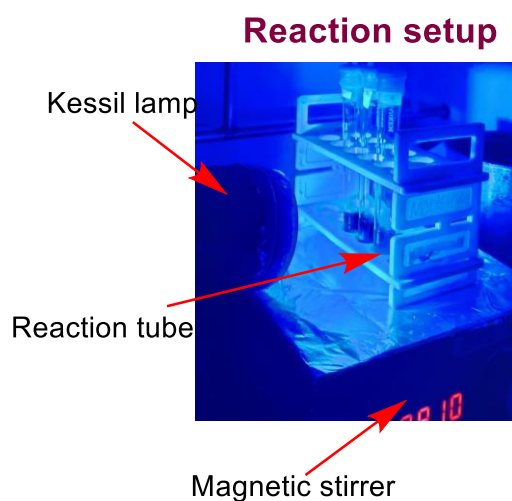


Figure 3.7. Reaction setup.

Blue (emission maximum at 440 nm) light was supplied to each reaction vial with the use of 20 W blue LEDs and Kessil lamp (of overall 40 W with 50% intensity when power applied)

with stirring at a distance of ~5 cm (with cooling using fan) while maintaining the temperature at 28 °C.

Note: For initial optimization, we have used blue LED- 20 W (commercially available, which has a broad wavelength). The exact wavelength of the Blue LEDs has been recorded using Ocean Optics USB4000 Fiber Optic Spectrometer. The wavelength was found to be λ_{max} 459 nm (Figure 3.8).

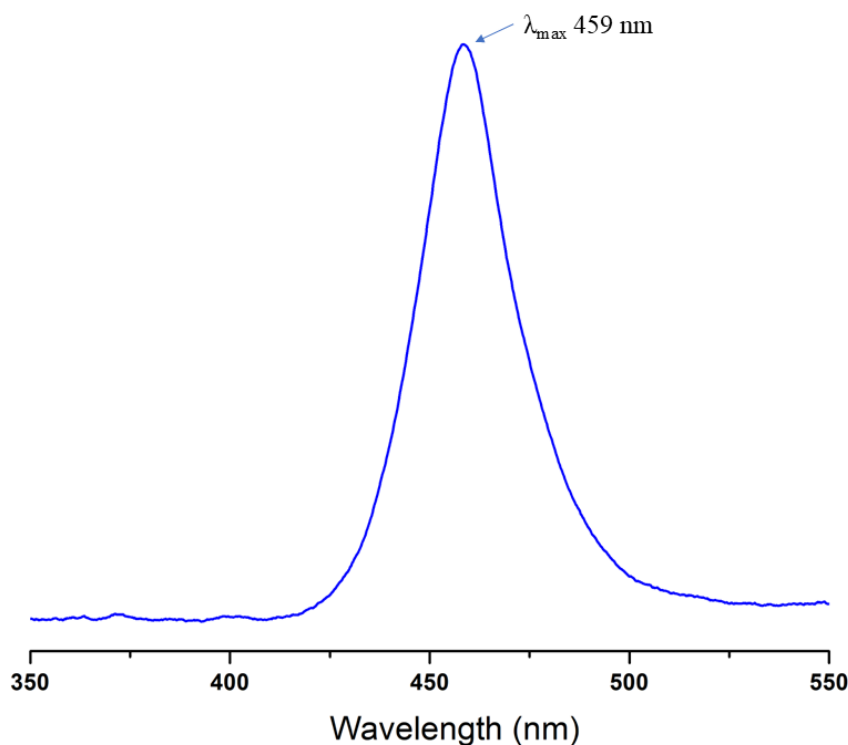
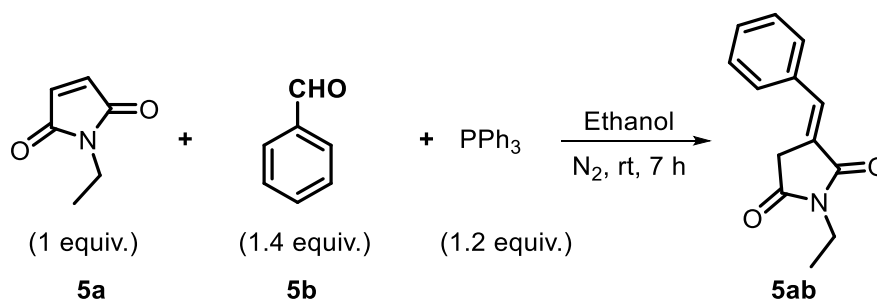


Fig 3.8. Wavelength of Blue LED (used in initial optimization).

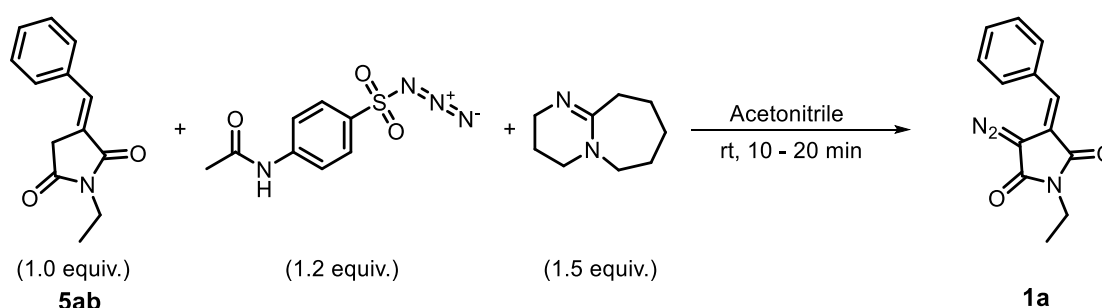
3.6.2 General procedure-A for the synthesis of vinyl succinimides (**5ab**):



To the stirred solution of N-ethyl maleimide **5a** (0.5 g, 1.0 equiv., 4.0 mmol) in ethanol (20 mL) was added triphenylphosphine (1.26 g, 1.2 equiv., 4.8 mmol) portion-wise at room temperature under N_2 atmosphere. The initial pink-coloured reaction mixture slowly turned to

white suspension over a period of 10-15 minutes of initial stirring. After the continuous stirring over 30 min, benzaldehyde **5b** (571 μ L, 1.4 equiv., 6.0 mmol) was added in one portion into the reaction mixture at room temperature. During this addition, the white suspension slowly turned into a clear solution. The reaction mixture was allowed to stir for 7 h. Upon completion of the reaction (monitored by TLC), the white solid formed during the course of the reaction was filtered through a sintered glass funnel and was washed with ethanol (6 mL x 2). The crude product **5ab** was obtained as a white solid (700 mg, 81% yield) and used for the next step without further purification.^[28]

3.6.3 General Procedure-B for the synthesis of vinyl diazosuccinimide(**1a**):

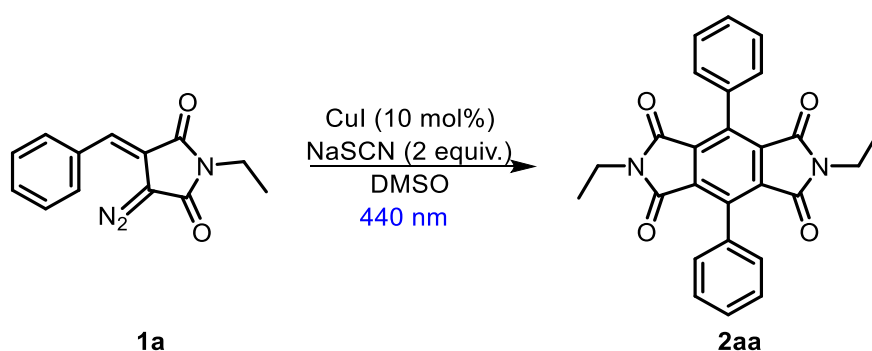


To the stirred solution of (*E*)-3-benzylidene-1-ethylpyrrolidine-2,5-dione **5ab** (2.15 g, 1.0 equiv., 10 mmol) in 30 mL acetonitrile, were added 4-acetamidobenzenesulfonyl azide (2.88 g, 1.2 equiv., 12 mmol) and DBU (2.24 mL, 1.5 equiv., 15 mmol) at 0 °C temperature under inert atmosphere. The reaction mixture was stirred for 10 minutes while maintaining the reaction temperature (0 °C). The reaction mixture was then quenched with saturated solution of NH₄Cl and the product was extracted with diethyl ether (30 mL x 3). The combined organic layer was washed with brine solution and dried over anhydrous Na₂SO₄. The extract was filtered and evaporated under reduced pressure. The crude product was purified using column chromatography over silica gel to afford (*E*)-3-benzylidene-4-diazo-1-ethylpyrrolidine-2,5-dione **1a** as orange solid (2.257 g, 94% yield).^{15a}

3.6.4 General procedure-C for the visible light promoted PMDI synthesis with diazo compound **2aa**.

To a reaction tube equipped with a magnetic stir bar were added diazo compound **1a** (1.0 equiv., 0.2 mmol), NaSCN (2.0 equiv., 0.4 mmol), and CuI (10 mol%) in DMSO (0.055 M). The tube was capped with a rubber septum, and the mixture was degassed with nitrogen gas. The resulting solution was irradiated by a 440 nm blue LED with stirring at a distance of ~5 cm

(with cooling using fan) at 28 °C for about 12 h until the diazo compound **1a** was completely consumed (as monitored by TLC analysis). The reaction mixture was extracted with DCM, and the combined organic layer was dried over anhydrous Na₂SO₄. The extract was filtered and evaporated under reduced pressure. The crude mixture was purified by column chromatography on silica gel with hexanes/ethyl acetate mixture as an eluent to give the corresponding product **2aa** light yellow solid (35 mg, 82% yield).



3.6.5. Procedure for EPR Analysis

X-Band EPR measurements for the detection of radical study were carried out using a JON Bruker BioSpin connected to Bruker EMX plus spectrometer with a radio wave source (9.4035 GHz) at room temperature.

Procedure: To a reaction tube equipped with a magnetic stir bar were added diazo compound **1a** (1.0 equiv., 0.2 mmol), NaSCN (2.0 equiv., 0.4 mmol), and CuI (10 mol%) in ethyl acetate:DMSO (9:1). The tube was capped with a rubber septum and the mixture was degassed with nitrogen gas. After that, the solution was stirred for 1 h at a distance of ~5 cm from a 440 nm blue LED at room temperature (28 °C) and the reaction mixture was transferred to an EPR tube, which was then subjected to the EPR measurement.

Similar procedure was followed to perform for the EPR analysis of controlled reaction mixtures, such as 1) Diazo **1a** + CuI, 2) Diazo **1a** + NaSCN, 3) Diazo **1a** + NaSCN + CuI (EPR measured before shining the light), 4) Diazo **1a** + NaSCN + CuI (after shining light).

3.6.6 Procedure for UV/Vis Spectra

UV-Vis absorbance spectra of individual components and their mixture.

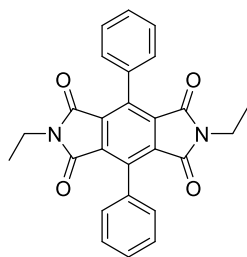
UV-Vis absorbance spectra of each component CuI (600 mM CuI in 2 mL DMSO), NaSCN (8 mM NaSCN in 2 mL DMSO), diazo **1a** (10 mM diazo in 2 mL DMSO), CuSCN (500 mM CuSCN in 2 mL DMSO), and their mixture CuI + NaSCN (600 mM CuI + 8 mM NaSCN in 2 mL DMSO), CuI + NaSCN + diazo **1a** (600 mM CuI, 8 mM NaSCN and 10mM diazo **1a** in 2 mL DMSO).

3.5.7. Crystallization Procedure for CuNCS Complex:

CuI (0.03 mmol) and NaSCN (1:20) were taken in a glass vial and the mixture was dissolved in acetonitrile (200 μ L). After that 0.5 mL of toluene was added into it and wrapped the vial mouth with parafilm. Then the vial was kept at room temperature for a month. The crystal was obtained as colourless cubic shape and analysed by single crystal x-ray analysis. **CCDC:** 2323319.

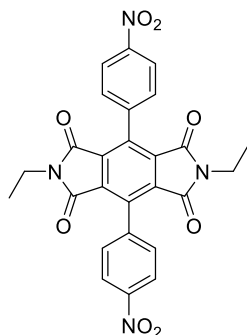
3.7 Characterization data

2,6-diethyl-4,8-diphenylpyrrolo[3,4-*f*]isoindole-1,3,5,7(2*H*,6*H*)-tetraone (2aa): Compound



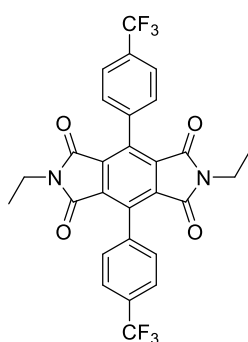
2aa was synthesized following the general procedure-C. The product was obtained as light yellow solid, 35 mg (82% yield); R_f =0.35 (petroleum ether/EtOAc 80:20), mp 320–322 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.58 – 7.51 (m, 6H), 7.50 – 7.41 (m, 4H), 3.62 (q, J = 7.2 Hz, 4H), 1.19 (t, J = 7.2 Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.4, 137.7, 134.5, 131.0, 129.4, 129.4, 127.9, 33.5, 13.7; HRMS (ESI TOF) m/z : calcd for $\text{C}_{26}\text{H}_{21}\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 425.1501, Found: 425.1500.

2,6-diethyl-4,8-bis(4-nitrophenyl)pyrrolo[3,4-*f*]isoindole-1,3,5,7(2*H*,6*H*)-tetraone (2ab):



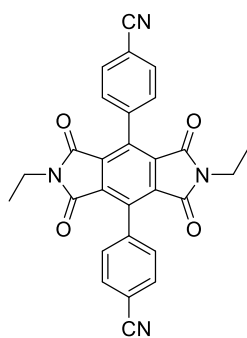
Compound **2ab** was synthesized following the general procedure-C. The product was obtained as orange solid, 40 mg (78% yield); R_f =0.6 (petroleum ether/EtOAc 60:40), mp 315–318 °C. ^1H NMR (400 MHz, CD_2Cl_2): δ 8.40 – 8.35 (m, 4H), 7.69 – 7.64 (m, 4H), 3.62 (q, J = 7.2 Hz, 4H), 1.18 (t, J = 7.2 Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CD_2Cl_2): δ 165.3, 149.0, 138.3, 135.8, 135.0, 131.2, 123.3, 34.1, 13.8; HRMS (ESI TOF) m/z : calcd for $\text{C}_{26}\text{H}_{19}\text{N}_4\text{O}_8$ ($\text{M} + \text{H}$) $^+$: 515.1203, Found: 515.1202.

2,6-diethyl-4,8-bis(4-(trifluoromethyl)phenyl)pyrrolo[3,4-*f*]isoindole-1,3,5,7(2*H*,6*H*)-



tetraone (2ac): Compound **2ac** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 36 mg (64% yield); R_f =0.45 (petroleum ether/EtOAc 80:20), mp 300–305 °C. ^1H NMR (400 MHz, CD_2Cl_2 :TFA): δ 7.80 (d, J = 8.0 Hz, 4H), 7.61 (d, J = 8.0 Hz, 4H), 3.65 (q, J = 7.2 Hz, 4H), 1.19 (t, J = 7.2 Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CD_2Cl_2 :TFA): δ 166.2, 160.3 (q, J = 43.1 Hz), 137.0, 135.1, 135.1 – 135.0 (m), 132.0 (q, J = 32.7 Hz), 130.4, 125.4 (q, J = 3.7 Hz), 124.7 (q, J = 272.2 Hz), 115.0 (q, J = 284.8 Hz), 34.4, 13.7; ^{19}F NMR (377 MHz, CH_2Cl_2 :TFA): δ -63.2; HRMS (ESI TOF) m/z : calcd for $\text{C}_{28}\text{H}_{19}\text{F}_6\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 561.1249, Found: 561.1251.

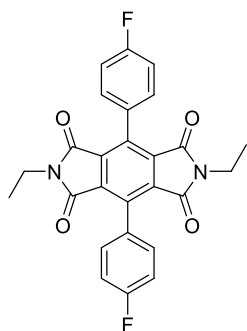
4,4'-(2,6-diethyl-1,3,5,7-tetraoxo-1,2,3,5,6,7-hexahydropyrrolo[3,4-f]isoindole-4,8-



diyl)dibenzonitrile (2ad): Compound **2ad** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 15 mg (31% yield); R_f =0.5 (petroleum ether/EtOAc 60:40), mp 343–345 °C.

^1H NMR (400 MHz, CDCl_3): δ 7.48 – 7.39 (m, 4H), 7.25 – 7.18 (m, 4H), 3.63 (q, J = 7.2 Hz, 4H), 1.20 (t, J = 7.2 Hz, 6H); **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3):** δ 165.3, 164.8, 162.3, 136.8, 134.6, 131.6, 131.5, 126.5, 126.5, 115.2, 115.0, 33.6, 13.7; **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{28}\text{H}_{19}\text{N}_4\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 475.1406, Found: 475.1382.

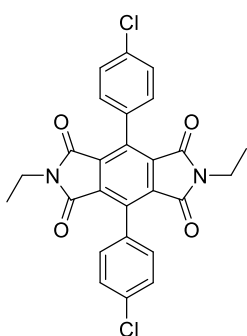
2,6-diethyl-4,8-bis(4-fluorophenyl)pyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2ae):



Compound **2ae** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 30mg (65% yield); R_f =0.4 (petroleum ether/EtOAc 80:20), mp 322–323 °C. **^1H NMR (400 MHz, CDCl_3):** δ 7.49 – 7.40 (m, 4H), 7.25 – 7.19 (m, 4H), 3.64 (q, J = 7.2 Hz, 4H), 1.20 (t, J = 7.2 Hz, 6H); **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3):** δ 165.3, 163.6 (d, J = 249.3 Hz), 136.8, 134.6, 131.5 (d, J = 8.5 Hz), 126.5 (d, J = 3.5 Hz), 115.1 (d, J = 22.0 Hz), 33.6, 13.7; **^{19}F NMR (377 MHz, CDCl_3):**

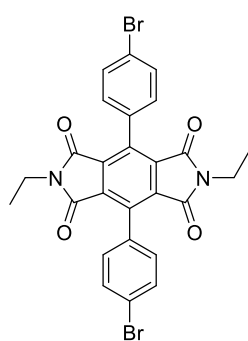
δ -111.6; **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{26}\text{H}_{19}\text{F}_2\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 461.1313, Found: 461.1301.

4,8-bis(4-chlorophenyl)-2,6-diethylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2af):



Compound **2af** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 36 mg (73% yield); R_f =0.45 (petroleum ether/EtOAc 80:20), mp 258–265 °C. **^1H NMR (400 MHz, CDCl_3):** δ 7.53 – 7.48 (m, 4H), 7.42 – 7.36 (m, 4H), 3.63 (q, J = 7.1 Hz, 4H), 1.20 (t, J = 7.2 Hz, 6H); **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3):** δ 165.2, 136.7, 135.9, 134.5, 130.9, 129.1, 128.3, 33.7, 13.7; **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{26}\text{H}_{19}\text{Cl}_2\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 493.0722, Found: 493.0718.

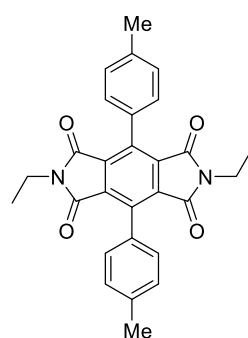
4,8-bis(4-bromophenyl)-2,6-diethylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2ag):



Compound **2ag** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 44 mg (74% yield); $R_f=0.45$ (petroleum ether/EtOAc 80:20), mp 383–389 °C. ^1H NMR (400 MHz, CD_2Cl_2): δ 7.68 – 7.63 (m, 4H), 7.37 – 7.31 (m, 4H), 3.60 (q, $J = 7.2$ Hz, 4H), 1.17 (t, $J = 7.2$ Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CD_2Cl_2): δ 165.6, 136.6, 134.9, 131.8, 131.3, 130.7, 124.0, 33.9, 13.9; HRMS (ESI TOF) m/z : calcd for $\text{C}_{26}\text{H}_{19}^{81}\text{Br}_2\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 582.9691, Found:

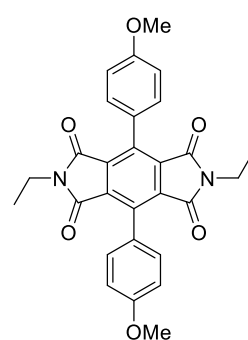
582.9695

2,6-diethyl-4,8-di-p-tolylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2ah): Compound



2ah was synthesized following the general procedure-C. The product was obtained as light yellow solid, 22 mg (49% yield); $R_f=0.45$ (petroleum ether/EtOAc 80:20), mp 303–308 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.34 (d, $J = 0.9$ Hz, 8H), 3.62 (q, $J = 7.2$ Hz, 4H), 2.47 (s, 6H), 1.18 (t, $J = 7.2$ Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.5, 139.4, 137.8, 134.5, 129.4, 128.7, 128.0, 33.5, 21.7, 13.7; HRMS (ESI TOF) m/z : calcd for $\text{C}_{28}\text{H}_{25}\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 453.1814, Found: 453.1813.

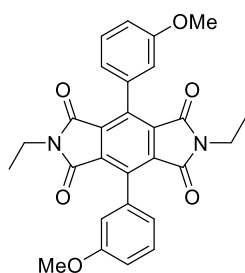
2,6-diethyl-4,8-bis(4-methoxyphenyl)pyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2ai):



Compound **2ai** was synthesized following the general procedure-C. The product was obtained as yellow solid, 19.5 mg (40% yield); $R_f=0.4$ (petroleum ether/EtOAc 80:20), mp 325–327 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.46 – 7.36 (m, 4H), 7.08 – 7.02 (m, 4H), 3.90 (s, 6H), 3.63 (q, $J = 7.2$ Hz, 4H), 1.19 (t, $J = 7.2$ Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.6, 160.6, 137.5, 134.5, 131.2, 122.7, 113.3, 55.4, 33.5, 13.7; HRMS (ESI TOF) m/z : calcd for $\text{C}_{28}\text{H}_{25}\text{N}_2\text{O}_6$ ($\text{M} + \text{H}$) $^+$: 485.1713,

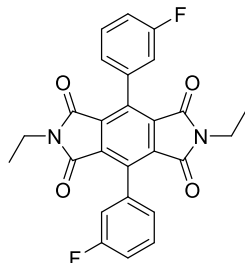
Found: 485.1716.

2,6-diethyl-4,8-bis(3-methoxyphenyl)pyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2aj):



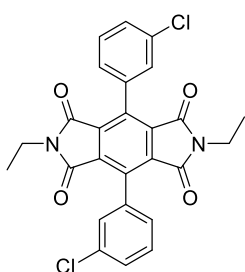
Compound **2aj** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 28 mg (56% yield); R_f =0.2 (petroleum ether/EtOAc 80:20), mp 237–242 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.45 (t, J = 7.9 Hz, 2H), 7.08 (ddd, J = 8.4, 2.6, 1.0 Hz, 2H), 7.04 – 7.00 (m, 2H), 6.98 (dd, J = 2.5, 1.6 Hz, 2H), 3.86 (s, 6H), 3.63 (q, J = 7.2 Hz, 4H), 1.19 (t, J = 7.2 Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.2, 159.0, 137.4, 134.5, 132.3, 129.0, 121.6, 115.5, 114.4, 55.4, 33.5, 13.7; HRMS (ESI TOF) m/z : calcd for $\text{C}_{28}\text{H}_{25}\text{N}_2\text{O}_6$ ($\text{M} + \text{H}$) $^+$: 485.1713, Found: 485.1710.

2,6-diethyl-4,8-bis(3-fluorophenyl)pyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2ak):



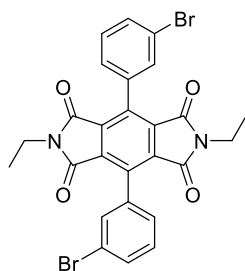
Compound **2ak** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 29 mg (63% yield); R_f =0.4 (petroleum ether/EtOAc 80:20) mp 397–400 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.50 (ddd, J = 8.4, 7.6, 5.7 Hz, 2H), 7.29 – 7.25 (m, 2H), 7.22 (ddd, J = 7.6, 1.7, 1.0 Hz, 2H), 7.16 (ddd, J = 9.2, 2.5, 1.6 Hz, 2H), 3.64 (q, J = 7.2 Hz, 4H), 1.20 (t, J = 7.2 Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.0, 162.2 (d, J = 246.8 Hz), 136.3 (d, J = 2.4 Hz), 134.5, 132.9 (d, J = 8.5 Hz), 129.6 (d, J = 8.2 Hz), 125.1 (d, J = 3.3 Hz), 116.7 (d, J = 23.1 Hz), 116.5 (d, J = 21.0 Hz), 33.6, 13.7; ^{19}F NMR (377 MHz, CDCl_3): δ -113.1; HRMS (ESI TOF) m/z : calcd for $\text{C}_{26}\text{H}_{19}\text{F}_2\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 461.1313, Found: 461.1313.

4,8-bis(3-chlorophenyl)-2,6-diethylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2al):



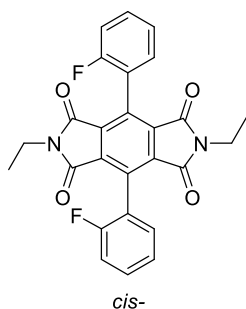
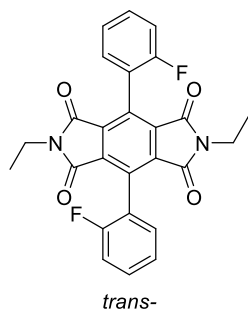
Compound **2al** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 30 mg (61% yield); R_f =0.4 (petroleum ether/EtOAc 80:20), mp 271–277 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.53 (ddd, J = 8.1, 2.1, 1.2 Hz, 2H), 7.50 – 7.41 (m, 4H), 7.34 (dt, J = 7.6, 1.4 Hz, 2H), 3.64 (q, J = 7.2 Hz, 4H), 1.21 (t, J = 7.2 Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.0, 136.2, 134.5, 133.9, 132.5, 129.6, 129.5, 129.2, 127.6, 33.7, 13.7; HRMS (ESI TOF) m/z : calcd for $\text{C}_{26}\text{H}_{19}\text{Cl}_2\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 493.0722, Found: 493.0716.

4,8-bis(3-bromophenyl)-2,6-diethylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2am):



Compound **2am** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 38 mg (65% yield); R_f =0.4 (petroleum ether/EtOAc 80:20) mp 269–273 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.69 (tt, J = 1.9, 0.7 Hz, 1H), 7.67 (tt, J = 2.0, 0.6 Hz, 1H), 7.59 (ddt, J = 2.0, 1.3, 0.6 Hz, 2H), 3.64 (q, J = 7.2 Hz, 5H), 1.21 (t, J = 7.2 Hz, 8H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.0, 136.1, 134.5, 132.7, 132.5, 132.3, 129.4, 128.1, 122.0, 33.7, 13.7; HRMS (ESI TOF) m/z : calcd for $\text{C}_{26}\text{H}_{19}\text{Br}_2\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 580.9712, Found: 580.9716, $\text{C}_{26}\text{H}_{19}^{81}\text{Br}_2\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 582.9691, Found: 582.9692

2,6-diethyl-4,8-bis(2-fluorophenyl)pyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2an and 2an'): Compound **2an'** and **2an** was synthesized following the general procedure-C. Both



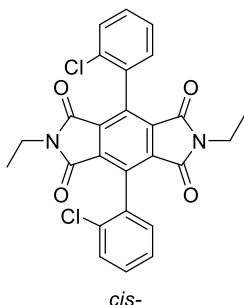
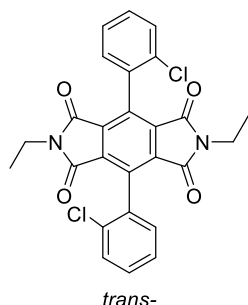
the isomers were isolated and separated using column chromatography.

Trans-isomer (**2an'**): Obtained as light yellow solid, 20 mg (43% yield); R_f = 0.45 (petroleum ether/EtOAc 80:20), mp 259–267 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.56 (dddd, J = 8.3, 7.2, 5.3, 1.8 Hz, 2H), 7.45 (td, J = 7.4, 1.7 Hz, 2H), 7.32 (td, J = 7.6, 1.1 Hz, 2H), 7.25 (ddd, J = 9.6, 8.0, 1.0 Hz, 2H), 3.65 (q, J = 7.2 Hz, 4H), 1.21 (t, J = 7.2 Hz, 6H); ^{13}C NMR (151 MHz, CDCl_3): δ 165.2, 165.1, 160.0 (dd, J = 247.2, 4.5 Hz), 135.1, 131.8 (d, J = 8.2 Hz), 131.4 (dd, J = 7.9, 2.4 Hz), 130.8 (d, J = 6.1 Hz), 123.7 (dd, J = 11.8, 3.5 Hz), 118.8 (d, J = 16.0 Hz), 115.5 (d, J = 21.4 Hz), 115.5 (d, J = 21.5 Hz), 33.6, 13.7; ^{19}F NMR (377 MHz, CDCl_3): δ -113.5. HRMS (ESI TOF) m/z : calcd for $\text{C}_{26}\text{H}_{19}\text{F}_2\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 461.1313, Found: 461.1307.

Cis-isomers (**2an**): Obtained as light yellow solid, 15.4 mg (33% yield); R_f =0.35 (petroleum ether/EtOAc 80:20), mp 266–271 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.56 (dddd, J = 8.3, 7.2, 5.3, 1.8 Hz, 2H), 7.43 (td, J = 7.4, 1.8 Hz, 2H), 7.31 (td, J = 7.5, 1.1 Hz, 2H), 7.29 – 7.22 (m, 2H), 3.65 (q, J = 7.2 Hz, 4H), 1.21 (t, J = 7.2 Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): δ 165.1, 165.1, 160.0 (dd, J = 247.2, 4.6 Hz), 135.1, 131.8 (d, J = 8.3 Hz), 131.4 (d, J = 7.8 Hz), 130.9 (d, J = 6.2 Hz), 123.7 (dd, J = 11.7, 3.4 Hz), 118.8 (d, J = 15.8 Hz), 115.5 (d, J =

21.4 Hz), 115.5 (d, $J = 21.5$ Hz), 33.6, 13.7; ^{19}F NMR (377 MHz, CDCl_3): δ -113.1. HRMS (ESI TOF) m/z : calcd for $\text{C}_{26}\text{H}_{19}\text{F}_2\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 461.1313, Found: 461.1313.

4,8-bis(2-chlorophenyl)-2,6-diethylpyrrolo[3,4-*f*]isoindole-1,3,5,7(2*H*,6*H*)-tetraone (2ao and 2ao'): Compound 2ao' and 2ao was synthesized following the general procedure-C. Both

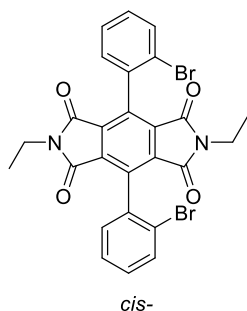
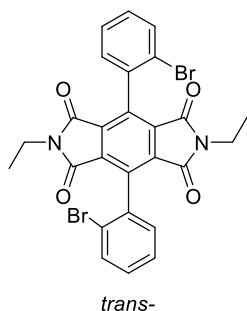


the isomers were isolated and separated using column chromatography.

Trans-isomer (2ao'): Obtained as light yellow solid, 18.5 mg (40% yield); R_f = 0.5 (petroleum ether/EtOAc 80:20), mp 290–298 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.58 (dd, $J = 7.8, 1.3$ Hz, 2H), 7.54 – 7.48 (m, 2H), 7.48 – 7.41 (m, 4H), 3.63 (qd, $J = 7.2, 0.9$ Hz, 4H), 1.21 (t, $J = 7.2$ Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): δ 165.1, 135.0, 134.0, 133.0, 130.8, 130.7, 130.4, 129.5, 126.7, 33.6, 13.7; HRMS (ESI TOF) m/z : calcd for $\text{C}_{26}\text{H}_{19}\text{Cl}_2\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 493.0722, Found: 493.0726.

Cis-isomer (2ao): Obtained as light yellow solid, 16 mg (35% yield); R_f = 0.25 (petroleum ether/EtOAc 80:20), mp 297–301 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.59 (dd, $J = 8.0, 1.3$ Hz, 2H), 7.51 (td, $J = 7.6, 1.8$ Hz, 2H), 7.44 (td, $J = 7.5, 1.3$ Hz, 2H), 7.38 (dd, $J = 7.5, 1.8$ Hz, 2H), 3.63 (q, $J = 7.2$ Hz, 4H), 1.21 (t, $J = 7.2$ Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): δ 165.1, 135.0, 134.1, 133.1, 130.8, 130.7, 130.3, 129.5, 126.6, 33.6, 13.7; HRMS (ESI TOF) m/z : calcd for $\text{C}_{26}\text{H}_{19}\text{Cl}_2\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 493.0722, Found: 493.0730.

4,8-bis(2-bromophenyl)-2,6-diethylpyrrolo[3,4-*f*]isoindole-1,3,5,7(2*H*,6*H*)-tetraone (2ap and 2ap'): Compound 2ap' and 2ap was



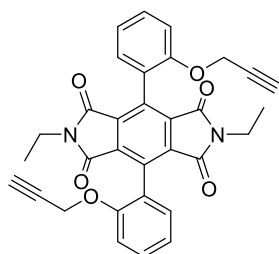
synthesized following the general procedure-C. Both the isomers were isolated and separated using column chromatography.

Trans-isomer (2ap'): Obtained as light-yellow solid, 20.5 mg (35% yield); R_f = 0.5 (petroleum ether/EtOAc 80:20), mp 230–239 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.80 – 7.71 (m, 2H), 7.53 – 7.47 (m, 2H), 7.43 (ddd, $J = 8.0, 6.5, 2.0$ Hz, 4H), 3.63 (qd, $J = 7.0, 1.5$ Hz, 4H), 1.21 (t, $J = 7.2$ Hz, 6H); ^{13}C NMR (150 MHz, CDCl_3): δ 165.1, 135.6, 134.8, 132.8, 132.6, 130.9, 130.2, 127.3, 122.7, 33.6, 13.8; HRMS (ESI TOF) m/z : calcd for $\text{C}_{26}\text{H}_{19}^{81}\text{Br}_2\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 582.9691, Found: 582.9692.

Cis-isomer (**2ap**): Obtained as light-yellow solid, 18 mg (31% yield); R_f =0.2 (petroleum ether/EtOAc 80:20), mp 237–240 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.77 (dd, J = 7.9, 1.2 Hz, 1H), 7.50 (td, J = 7.5, 1.3 Hz, 1H), 7.43 (td, J = 7.7, 1.8 Hz, 2H), 7.39 (dd, J = 7.4, 1.8 Hz, 1H), 3.63 (q, J = 7.2 Hz, 3H), 1.21 (t, J = 7.2 Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.1, 135.6, 134.9, 132.8, 132.6, 130.9, 130.0, 127.3, 122.7, 33.6, 13.7; HRMS (ESI TOF) m/z : calcd for $\text{C}_{26}\text{H}_{19}\text{Br}_2\text{N}_2\text{O}_4$ ($M + \text{H}$) $^+$: 580.9691, Found: 580.9714.

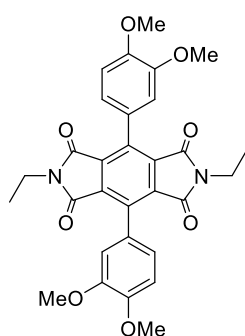
2,6-diethyl-4,8-bis(2-(prop-2-yn-1-yloxy)phenyl)pyrrolo[3,4-*ff*]isoindole-1,3,5,7(2H,6H)-tetraone (2aq):

Compound **2aq** was synthesized following the general procedure-C. The product was obtained as yellow solid, 13 mg (24% yield); R_f =0.25 (petroleum ether/EtOAc 80:20); *cis*:-*trans*- = 1:2.3 mp 235–240 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.52 (ddd, J = 8.3, 7.5, 1.7 Hz, 2H), 7.37 (ddd, J = 22.3, 7.5, 1.7 Hz, 2H), 7.21 – 7.12 (m, 4H), 4.65 (dd, J = 4.5, 2.4 Hz, 4H), 3.67 – 3.57 (m, 4H), 2.45 (t, J = 2.4 Hz, 1H), 2.43 (t, J = 2.4 Hz, 1H), 1.19 (t, J = 7.2 Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.6, 155.7, 135.1, 133.1, 131.1, 131.0, 121.2, 121.0, 112.5, 78.6, 75.6, 56.9, 33.3, 13.8; HRMS (ESI TOF) m/z : calcd for $\text{C}_{32}\text{H}_{25}\text{N}_2\text{O}_6$ ($M + \text{H}$) $^+$: 533.1713, Found: 533.1712.

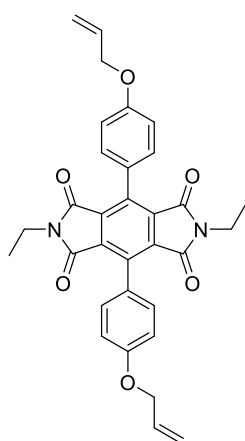


4,8-bis(3,4-dimethoxyphenyl)-2,6-diethylpyrrolo[3,4-*ff*]isoindole-1,3,5,7(2H,6H)-tetraone (2ar):

Compound **2ar** was synthesized following the general procedure-C. The product was obtained as orange solid, 22 mg (40% yield); R_f =0.25 (petroleum ether/EtOAc 60:40) mp 292–296 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.06 – 6.96 (m, 6H), 3.97 (s, 6H), 3.90 (s, 6H), 3.64 (q, J = 7.2 Hz, 4H), 1.20 (t, J = 7.2 Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.4, 150.1, 148.3, 137.4, 134.6, 123.0, 122.6, 113.4, 110.3, 56.1, 55.9, 33.5, 13.7; HRMS (ESI TOF) m/z : calcd for $\text{C}_{30}\text{H}_{29}\text{N}_2\text{O}_8$ ($M + \text{H}$) $^+$: 545.1924, Found: 545.1919.



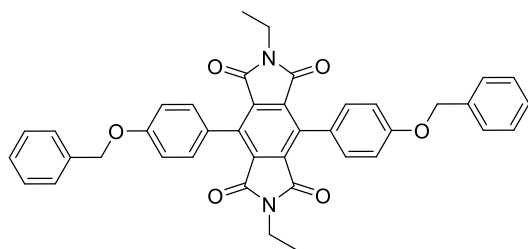
4,8-bis(4-(allyloxy)phenyl)-2,6-diethylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone



(2at): Compound **2at** was synthesized following the general procedure-C. The product was obtained as yellow solid, 13 mg (24% yield); R_f =0.3 (petroleum ether/EtOAc 80:20), mp 221–229 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.46 – 7.33 (m, 4H), 7.10 – 7.02 (m, 4H), 6.11 (ddt, J = 17.2, 10.6, 5.3 Hz, 2H), 5.47 (dq, J = 17.3, 1.5 Hz, 2H), 5.33 (dq, J = 10.5, 1.3 Hz, 2H), 4.63 (dt, J = 5.3, 1.4 Hz, 4H), 3.63 (q, J = 7.2 Hz, 4H), 1.19 (t, J = 7.2 Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.6, 159.7, 137.5, 134.5, 133.3, 131.2, 122.9, 118.0, 114.0, 69.0, 33.5, 13.7; HRMS (ESI TOF) m/z : calcd for $\text{C}_{32}\text{H}_{29}\text{N}_2\text{O}_6$ ($\text{M} + \text{H}$) $^+$: 537.2025, Found:

537.2021.

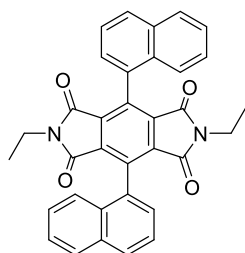
4,8-bis(4-(benzyloxy)phenyl)-2,6-diethylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone



(2au): Compound **2au** was synthesized following the general procedure-C. The product was obtained as yellow solid, 14.5 mg (23% yield); R_f =0.2 (petroleum ether/EtOAc 80:20), mp 268–278 °C.

^1H NMR (400 MHz, CDCl_3): δ 7.51 – 7.46 (m, 4H), 7.43 – 7.40 (m, 6H), 7.39 – 7.33 (m, 4H), 7.16 – 7.11 (m, 4H), 5.14 (s, 4H), 3.64 (q, J = 7.2 Hz, 4H), 1.20 (t, J = 7.2 Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.6, 159.9, 137.5, 136.9, 134.5, 131.2, 128.8, 128.3, 127.9, 123.0, 114.1, 70.2, 33.5, 13.7; HRMS (ESI TOF) m/z : calcd for $\text{C}_{40}\text{H}_{33}\text{N}_2\text{O}_6$ ($\text{M} + \text{H}$) $^+$: 637.2339, Found: 637.2336.

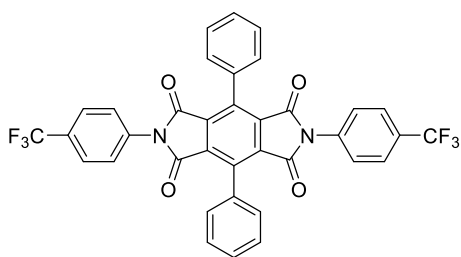
2,6-diethyl-4,8-di(naphthalen-1-yl)pyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2av):



Compound **2av** was synthesized following the general procedure-C. The product was obtained as yellow solid, 26.5 mg (50% yield); R_f =0.35 (petroleum ether/EtOAc 80:20) mp 260–262 °C. ^1H NMR (400 MHz, CDCl_3): δ 8.08 (dt, J = 8.3, 0.9 Hz, 2H), 8.01 (ddd, J = 8.3, 3.8, 1.2 Hz, 2H), 7.67 (ddd, J = 8.3, 7.0, 3.3 Hz, 2H), 7.61 – 7.51 (m, 4H), 7.51 – 7.38 (m, 4H), 3.51 (qd, J = 7.1, 1.8 Hz, 4H), 1.09 (td, J = 7.2, 1.3 Hz, 6H);

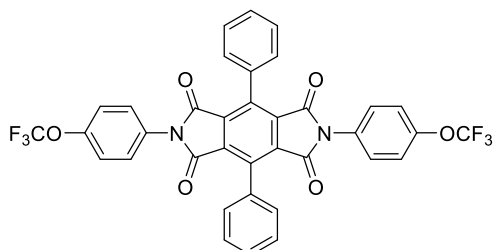
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.1, 135.8, 135.8, 133.4, 133.4, 131.9, 131.8, 129.8, 129.8, 129.5, 129.5, 129.1, 129.0, 126.9, 126.8, 126.8, 126.7, 126.2, 126.2, 125.1, 125.1, 124.5, 124.5, 33.5, 13.6; HRMS (ESI TOF) m/z : calcd for $\text{C}_{34}\text{H}_{25}\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 525.1814, Found: 525.1808.

4,8-diphenyl-2,6-bis(4-(trifluoromethyl)phenyl)pyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-



tetraone (2ba): Compound **2ba** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 57 mg (87% yield); R_f = 0.3 (petroleum ether/EtOAc 80:20), mp 400 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.71 – 7.66 (m, 4H), 7.61 – 7.47 (m, 14H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 163.8, 139.4, 134.3, 134.2, 130.5, 130.4 (d, J = 32.9 Hz), 129.8, 129.2, 128.1, 126.6, 126.2 (q, J = 3.7 Hz), 123.8 (d, J = 272.4 Hz); ^{19}F NMR (377 MHz, CDCl_3): δ -62.7; HRMS (ESI TOF) m/z : calcd for $\text{C}_{36}\text{H}_{19}\text{F}_6\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 657.1249, Found: 657.1246.

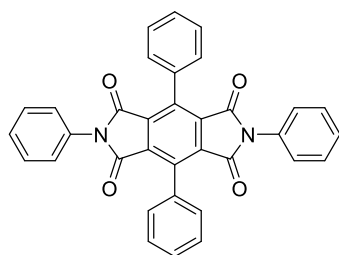
4,8-diphenyl-2,6-bis(4-(trifluoromethoxy)phenyl)pyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-



tetraone (2ca): Compound **2ca** was synthesized following the general procedure-C. The product was obtained as orange solid, 42mg (61% yield); R_f = 0.45 (petroleum ether/EtOAc 80:20), mp 235–240 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.59 – 7.49 (m, 10H), 7.46 – 7.41 (m, 4H), 7.29 – 7.25 (m, 4H); $^{13}\text{C}\{^1\text{H}\}$

NMR (100 MHz, CDCl_3): δ 164.1, 148.7, 139.2, 134.3, 130.5, 129.8, 129.4, 129.3, 128.1, 127.9, 121.6; 120.5 (q, J = 258.1 Hz). ^{19}F NMR (377 MHz, CDCl_3): δ -58.0; HRMS (ESI TOF) m/z : calcd for $\text{C}_{36}\text{H}_{19}\text{F}_6\text{N}_2\text{O}_6$ ($\text{M} + \text{H}$) $^+$: 689.1147, Found: 689.1136.

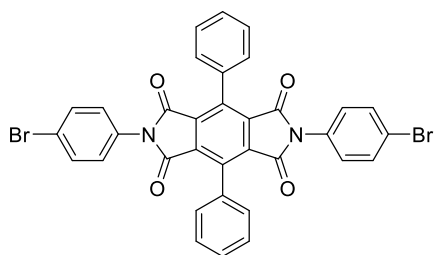
2,4,6,8-tetraphenylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2da): Compound **2da**



was synthesized following the general procedure-C. The product was obtained as light yellow solid, 45 mg (86% yield); R_f = 0.3 (petroleum ether/EtOAc 80:20) mp 350–352 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.52 (d, J = 1.7 Hz, 10H), 7.44 – 7.31 (m, 10H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 164.4, 138.9, 134.3, 131.0,

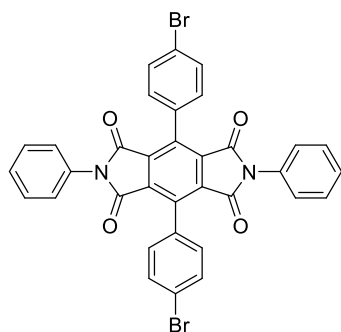
130.8, 129.5, 129.4, 129.1, 128.5, 128.0, 126.6; HRMS (ESI TOF) m/z : calcd for $\text{C}_{34}\text{H}_{21}\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 521.1501, Found: 521.1500.

2,6-bis(4-bromophenyl)-4,8-diphenylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2ea):



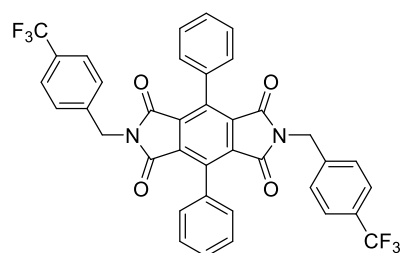
Compound **2ea** was synthesized following the general procedure-C. The product was obtained as orange solid, 22.6 mg (73% yield); R_f =0.25 (petroleum ether/EtOAc 80:20), mp 378–383 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.59 – 7.47 (m, 14H), 7.29 – 7.25 (m, 4H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 164.0, 139.0, 134.3, 132.2, 130.6, 130.0, 129.7, 129.3, 128.1, 127.9, 122.3; HRMS (ESI TOF) m/z : calcd for $\text{C}_{34}\text{H}_{19}^{81}\text{Br}_2\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 678.9691, Found: 678.9703.

4,8-bis(4-bromophenyl)-2,6-diphenylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2eg):



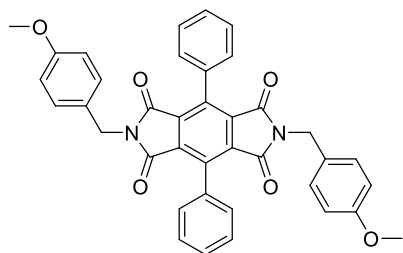
Compound **2eg** was synthesized following the general procedure-C. The product was obtained as yellow solid, 45 mg (66% yield); R_f =0.4 (petroleum ether/EtOAc 80:20) mp 392–400 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.67 – 7.62 (m, 4H), 7.46 – 7.41 (m, 4H), 7.41 – 7.33 (m, 10H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 164.2, 137.8, 134.3, 131.3, 131.1, 130.8, 129.3, 129.2, 128.7, 126.5, 124.3; HRMS (ESI TOF) m/z : calcd for $\text{C}_{34}\text{H}_{19}^{81}\text{Br}_2\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 678.9691, Found: 678.9687.

4,8-diphenyl-2,6-bis(4-(trifluoromethyl)benzyl)pyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2fa):



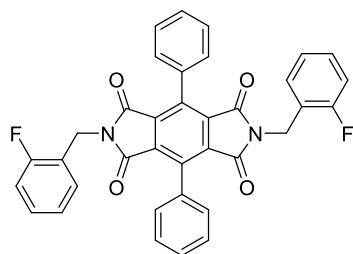
Compound **2fa** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 58 mg (85% yield); R_f =0.4 (petroleum ether/EtOAc 80:20), mp 367–370 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.62 – 7.50 (m, 10H), 7.46 (d, J = 8.2 Hz, 4H), 7.44 – 7.38 (m, 4H), 4.75 (s, 4H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 164.9, 139.5 – 139.3 (m), 138.3, 134.4, 130.6, 130.5 (d, J = 32.5 Hz), 129.7, 129.6, 129.4, 128.0, 125.9 (q, J = 3.7 Hz), 124.0 (q, J = 271.9 Hz), 41.7; ^{19}F NMR (377 MHz, CDCl_3): δ -58.0. HRMS (ESI TOF) m/z : calcd for $\text{C}_{38}\text{H}_{23}\text{F}_6\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 685.1562, Found: 685.1558.

2,6-bis(4-methoxybenzyl)-4,8-diphenylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone



(2ga): Compound **2ga** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 28 mg (46% yield); R_f =0.3 (petroleum ether/EtOAc 80:20), mp 300–305 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.57 – 7.49 (m, 6H), 7.42 – 7.38 (m, 4H), 7.31 – 7.27 (m, 4H), 6.79 – 6.75 (m, 4H), 4.63 (s, 4H), 3.74 (s, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.1, 159.5, 137.9, 134.5, 130.9, 130.8, 129.5, 129.4, 128.1, 127.9, 114.1, 55.4, 41.6; HRMS (ESI TOF) m/z : calcd for $\text{C}_{38}\text{H}_{29}\text{N}_2\text{O}_6$ ($\text{M} + \text{H}$) $^+$: 609.2026, Found: 609.2023.

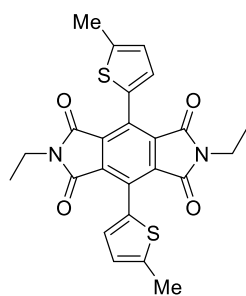
2,6-bis(2-fluorobenzyl)-4,8-diphenylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2ha):



Compound **2ha** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 32 mg (55% yield); R_f =0.4 (petroleum ether/EtOAc 80:20), mp 290–298 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.57 – 7.49 (m, 6H), 7.47 – 7.42 (m, 4H), 7.30 – 7.19 (m, 4H), 7.05 – 6.96 (m, 4H), 4.81 (s, 4H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 164.9, 160.7 (d, J = 248.6 Hz), 138.2, 134.5,

130.7 (d, J = 6.6 Hz), 130.6, 129.9 (d, J = 8.3 Hz), 129.6, 129.4, 127.9, 124.4 (d, J = 3.7 Hz), 122.6 (d, J = 14.5 Hz), 115.8 (d, J = 21.4 Hz), 35.7 (d, J = 4.6 Hz); HRMS (ESI TOF) m/z : calcd for $\text{C}_{36}\text{H}_{23}\text{F}_2\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 585.1626, Found: 585.1617.

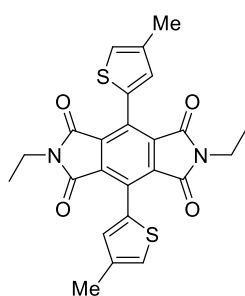
2,6-diethyl-4,8-bis(5-methylthiophen-2-yl)pyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone



(2aw): Compound **2aw** was synthesized following the general procedure-C. The product was obtained as orange solid, 16.5 mg (35% yield); R_f =0.5 (petroleum ether/EtOAc 80:20), mp 253–258 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.05 (d, J = 3.5 Hz, 2H), 6.88 (dt, J = 3.2, 1.1 Hz, 2H), 3.66 (q, J = 7.2 Hz, 4H), 2.60 (d, J = 1.1 Hz, 6H), 1.22 (t, J = 7.2 Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.0, 143.4, 135.4, 131.1, 130.5,

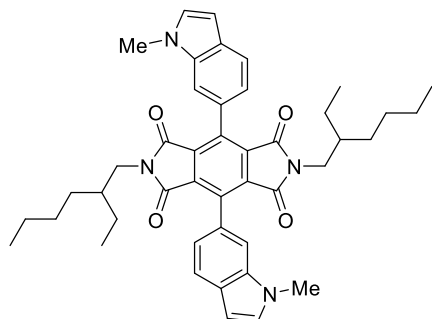
127.3, 125.5, 33.6, 15.6, 13.7; HRMS (ESI TOF) m/z : calcd for $\text{C}_{24}\text{H}_{21}\text{N}_2\text{O}_4\text{S}_2$ ($\text{M} + \text{H}$) $^+$: 465.0943, Found: 465.0937.

2,6-diethyl-4,8-bis(4-methylthiophen-2-yl)pyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2ax):



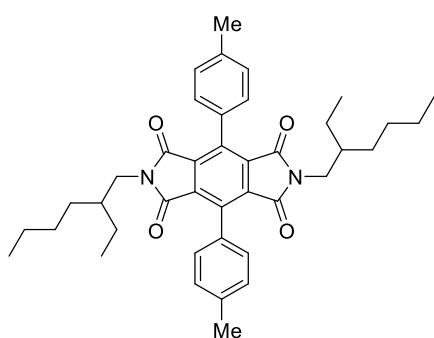
Compound **2ax** was synthesized following the general procedure-C. The product was obtained as orange solid, 14 mg (30% yield); $R_f=0.4$ (petroleum ether/EtOAc 80:20), mp 243–247 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.19 (t, $J = 1.3$ Hz, 2H), 7.05 (d, $J = 1.4$ Hz, 2H), 3.66 (q, $J = 7.2$ Hz, 4H), 2.38 (d, $J = 1.1$ Hz, 6H), 1.22 (t, $J = 7.2$ Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 164.8, 137.6, 135.4, 132.2, 131.2, 129.6, 123.8, 33.6, 15.9, 13.7; HRMS (ESI TOF) m/z : calcd for $\text{C}_{24}\text{H}_{21}\text{N}_2\text{O}_4\text{S}_2$ ($\text{M} + \text{H}$) $^+$: 465.0943, Found: 465.0938.

2,6-bis(2-ethylhexyl)-4,8-bis(1-methyl-1H-indol-6-yl)pyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2iy):



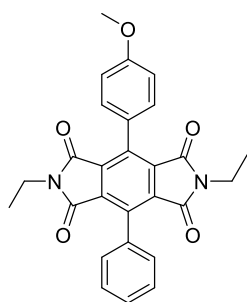
Compound **2iy** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 28 mg (40% yield); $R_f=0.4$ (petroleum ether/EtOAc 80:20); ^1H NMR (400 MHz, CDCl_3): mp 230–235 °C. δ 7.73 (d, $J = 1.6$ Hz, 2H), 7.47 (d, $J = 8.4$ Hz, 2H), 7.32 (dd, $J = 8.4, 1.7$ Hz, 2H), 7.10 (d, $J = 3.1$ Hz, 2H), 6.57 (d, $J = 3.1$ Hz, 2H), 3.85 (s, 6H), 3.44 (d, $J = 7.4$ Hz, 4H), 1.74 (hept, $J = 6.3$ Hz, 2H), 1.21 (tdd, $J = 11.4, 5.9, 3.8$ Hz, 16H), 0.81 (dt, $J = 11.9, 7.1$ Hz, 12H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 166.2, 139.0, 137.1, 134.5, 129.5, 128.0, 123.3, 122.7, 121.8, 108.5, 102.0, 42.5, 38.0, 33.1, 30.6, 28.5, 24.0, 23.1, 14.1, 10.5; HRMS (ESI TOF) m/z : calcd for $\text{C}_{44}\text{H}_{51}\text{N}_4\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 699.3910, Found: 699.3901.

2,6-bis(2-ethylhexyl)-4,8-di-p-tolylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2iz):



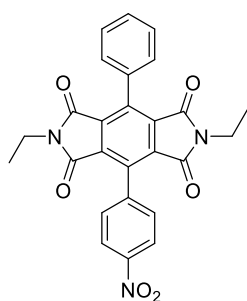
Compound **2iz** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 28 mg (30% yield); $R_f=0.5$ (petroleum ether/EtOAc 80:20);, mp 300–305 °C. ^1H NMR (400 MHz, CDCl_3): δ 7.34 (s, 8H), 3.45 (d, $J = 7.4$ Hz, 4H), 2.47 (s, 6H), 1.75 (hept, $J = 7.5$ Hz, 2H), 1.23 (dd, $J = 14.7, 7.9$ Hz, 16H), 0.88 – 0.79 (m, 12H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.9, 139.3, 137.8, 134.4, 129.5, 128.7, 128.0, 42.7, 38.0, 30.6, 28.5, 24.0, 23.1, 21.8, 14.1, 10.5; HRMS (ESI TOF) m/z : calcd for $\text{C}_{40}\text{H}_{49}\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 621.3692, Found: 621.3690.

2,6-diethyl-4-(4-methoxyphenyl)-8-phenylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-



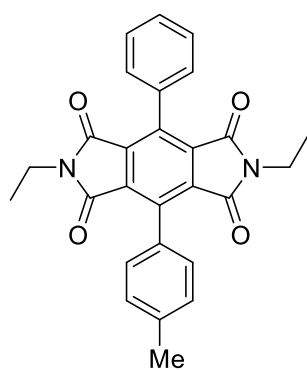
tetraone (2b'): Compound **2b'** was synthesized following the general procedure-C. The product was obtained as yellow solid, 14 mg (31% yield); R_f =0.2 (petroleum ether/EtOAc 80:20), mp 222–228 °C. **^1H NMR (400 MHz, CDCl_3)**: δ 7.57 – 7.50 (m, 3H), 7.48 – 7.38 (m, 4H), 7.09 – 7.02 (m, 2H), 3.90 (s, 3H), 3.62 (q, J = 7.2 Hz, 4H), 1.19 (t, J = 7.2 Hz, 6H); **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3)**: δ 165.6, 165.4, 160.6, 137.9, 137.2, 134.6, 134.4, 131.2, 131.1, 129.4, 129.3, 127.9, 122.6, 113.3, 55.4, 33.5, 13.7; **HRMS (ESI TOF) m/z** : calcd for $\text{C}_{27}\text{H}_{23}\text{N}_2\text{O}_5$ ($\text{M} + \text{H}$) $^+$: 455.1607, Found: 455.1601.

2,6-diethyl-4-(4-nitrophenyl)-8-phenylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone



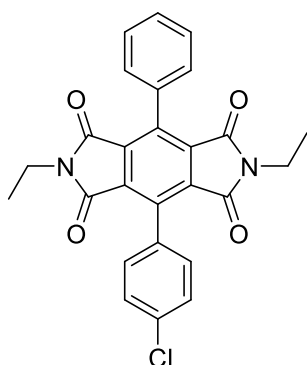
(2a'): Compound **2a'** was synthesized following the general procedure-C. The product was obtained as yellow solid, 14 mg (30% yield); R_f =0.65 (petroleum ether/EtOAc 60:40), mp 385–387 °C. **^1H NMR (400 MHz, CDCl_3)**: δ 8.41 – 8.36 (m, 2H), 7.66 – 7.62 (m, 2H), 7.58 – 7.52 (m, 3H), 7.46 (dt, J = 8.1, 2.2 Hz, 2H), 3.63 (q, J = 7.2 Hz, 4H), 1.19 (t, J = 7.2 Hz, 6H); **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3)**: δ 165.2, 165.0, 148.5, 138.9, 137.9, 134.6, 134.5, 134.4, 130.7, 130.5, 129.7, 129.4, 128.0, 123.2, 33.7, 13.7; **HRMS (ESI TOF) m/z** : calcd for $\text{C}_{27}\text{H}_{23}\text{N}_4\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 470.1352, Found: 470.1348.

2,6-diethyl-4-phenyl-8-(p-tolyl)pyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2c')



Compound **2c'** was synthesized following the general procedure. The product was obtained as yellow solid, 15 mg (34% yield); R_f =0.2 (petroleum ether/EtOAc 80:20), mp 255–260 °C. **^1H NMR (400 MHz, CDCl_3)**: δ 7.57 – 7.50 (m, 3H), 7.48 – 7.42 (m, 2H), 7.38 – 7.32 (m, 4H), 3.62 (q, J = 7.2 Hz, 4H), 2.48 (s, 3H), 1.18 (t, J = 7.2 Hz, 6H); **$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3)**: δ 165.5, 165.4, 139.5, 138.0, 137.5, 134.5, 134.5, 131.1, 129.41, 129.38, 129.35, 128.7, 127.9, 33.5, 21.7, 13.7; **HRMS (ESI TOF) m/z** : calcd for $\text{C}_{27}\text{H}_{23}\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 439.1658, Found: 439.1657.

4-(4-chlorophenyl)-2,6-diethyl-8-phenylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone



(2d'): Compound **2d'** was synthesized following the general procedure-C. The product was obtained as yellow solid, 17 mg (37% yield); R_f =0.4 (petroleum ether/EtOAc 80:20), mp 290–294 °C. ^1H NMR (400 MHz, CH_2Cl_2 - d_2): δ 7.60 – 7.49 (m, 5H), 7.48 – 7.43 (m, 2H), 7.42 – 7.38 (m, 2H), 3.63 (q, J = 7.2 Hz, 4H), 1.19 (t, J = 7.2 Hz, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CH_2Cl_2 - d_2): δ 165.3, 165.2, 165.2, 138.0, 136.3, 135.9, 135.8, 134.6, 134.5, 134.4, 130.8, 129.5, 129.3, 129.3, 128.2, 127.9, 33.6, 13.7.

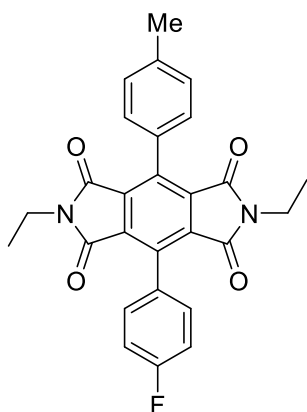
HRMS (ESI TOF) m/z : calcd for $\text{C}_{26}\text{H}_{20}\text{ClN}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 459.1112, Found: 459.1109.

4-(4-bromophenyl)-2,6-diethyl-8-(4-(trifluoromethyl)phenyl)pyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2e')

(2e'): Compound **2e'** was synthesized following the general procedure-C. The product was obtained as yellow solid, 19 mg (33% yield); R_f =0.5 (petroleum ether/EtOAc 75:25), mp 385–388 °C. ^1H NMR (400 MHz, CH_2Cl_2 - d_2): δ 7.79 (dd, J = 8.2, 3.8 Hz, 3H), 7.68 – 7.64 (m, 1H), 7.60 (dd, J = 7.8, 5.4 Hz, 3H), 7.37 – 7.32 (m, 1H), 3.61 (q, J = 7.2 Hz, 4H), 1.17 (t, J = 7.2 Hz, 6H). $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CH_2Cl_2 - d_2): δ 165.51, 165.50, 165.4, 137.0, 136.4, 136.0, 135.8, 135.6, 135.0, 134.9, 131.8, 131.3 (d, J = 4.7 Hz), 130.6, 125.2 – 125.0 (m), 124.8 (q, J = 272.3 Hz), 124.1, 33.98, 33.94, 13.9.

HRMS (ESI TOF) m/z : calcd for $\text{C}_{27}\text{H}_{19}\text{BrF}_3\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 571.0480, Found: 571.0478.

2,6-diethyl-4-(4-fluorophenyl)-8-(p-tolyl)pyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H)-tetraone (2f')



(2f'): Compound **2f'** was synthesized following the general procedure-C. The product was obtained as yellow solid, 15 mg (33% yield); R_f =0.5 (petroleum ether/EtOAc 80:20);, mp 305–309 °C. ^1H NMR (400 MHz, CDCl_3) δ 7.48 – 7.40 (m, 2H), 7.34 (s, 4H), 7.25 – 7.18 (m, 2H), 3.63 (q, J = 7.2 Hz, 4H), 2.48 (s, 3H), 1.19 (t, J = 7.2 Hz, 6H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.4, 165.3, 163.5 (d, J = 248.9 Hz), 139.5, 138.2, 136.4, 134.5, 131.6, 131.5, 129.4, 128.7, 127.8, 126.7 (d, J = 3.4 Hz), 115.2, 115.0, 33.5, 21.7, 13.7; ^{19}F NMR (377 MHz, CDCl_3): δ -111.8. HRMS (ESI TOF) m/z : calcd for $\text{C}_{27}\text{H}_{22}\text{FN}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 457.1564, Found: 457.1562.

4,8-bis(2-(allyloxy)phenyl)-2,6-diethylpyrrolo[3,4-f]isoindole-1,3,5,7(2H,6H) tetraone(2az):

Compound **2az** was synthesized following the general procedure-C. The product was obtained

as yellow solid, 15 mg (30% yield); R_f = 0.25 (petroleum

ether/EtOAc 80:20); *cis*:-*trans*- = 1:2.3, mp 226–230 °C. ^1H

NMR (400 MHz, CDCl_3): δ 7.49 (ddd, J = 8.3, 7.4, 1.7 Hz, 2H),

7.37 (td, J = 7.4, 1.7 Hz, 2H), 7.12 (tt, J = 7.5, 1.2 Hz, 2H), 7.04

(d, J = 8.3 Hz, 2H), 6.02 – 5.68 (m, 2H), 5.26 – 4.98 (m, 4H), 4.52

(dq, J = 5.0, 1.8 Hz, 4H), 3.60 (qd, J = 7.2, 1.4 Hz, 4H), 1.17 (td,

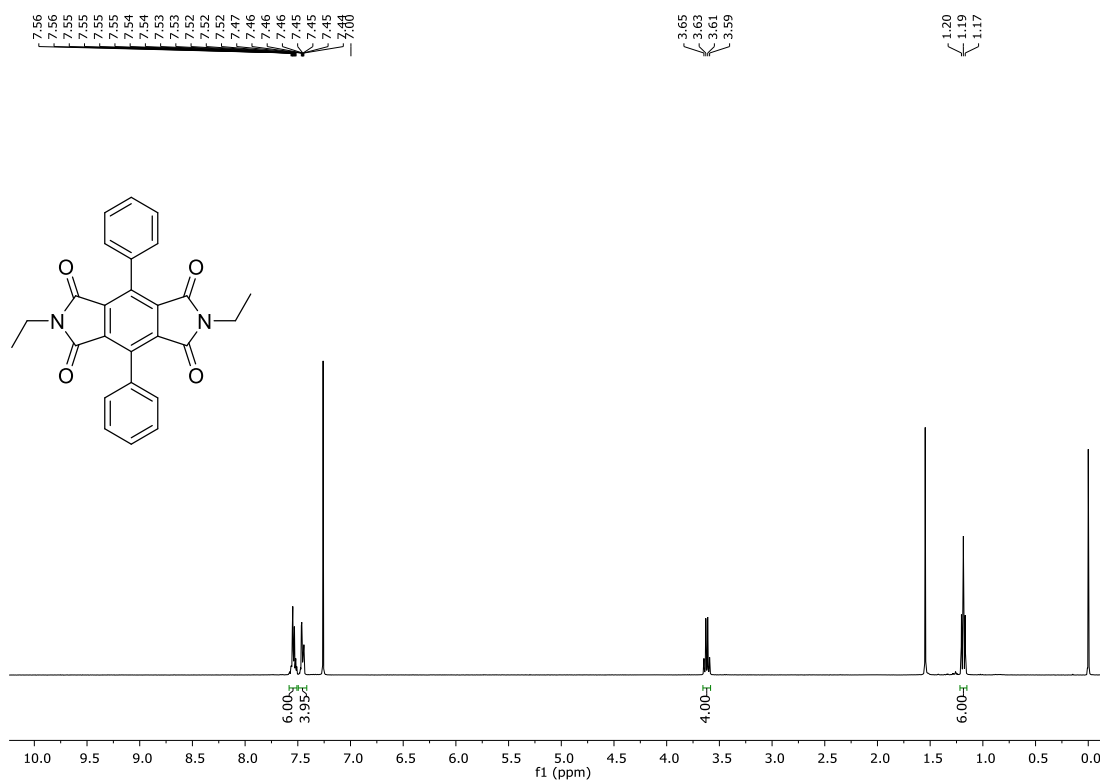
J = 7.2, 1.0 Hz, 6H). $^{13}\text{C}\{^1\text{H}\}$ **NMR (100 MHz, CDCl_3):** δ 169.1,

164.0, 151.8, 150.9, 133.5, 129.5, 128.8, 126.1, 122.6, 119.1, 118.1, 113.0, 40.2, 32.7, 32.1,

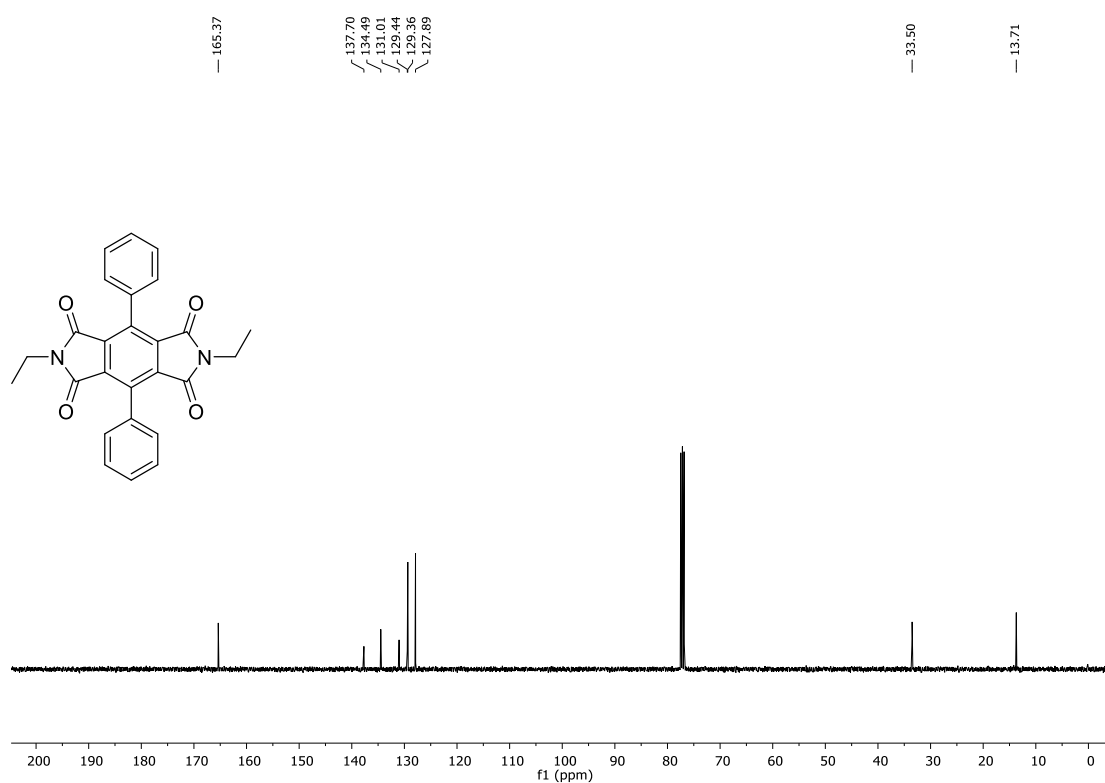
14.2. **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{32}\text{H}_{29}\text{N}_2\text{O}_6$ ($\text{M} + \text{H}$) $^+$: 537.2026, Found: 537.2025.

3.8. Selected Copies NMR Spectra (^1H , $^{13}\text{C}\{^1\text{H}\}$ and ^{19}F):

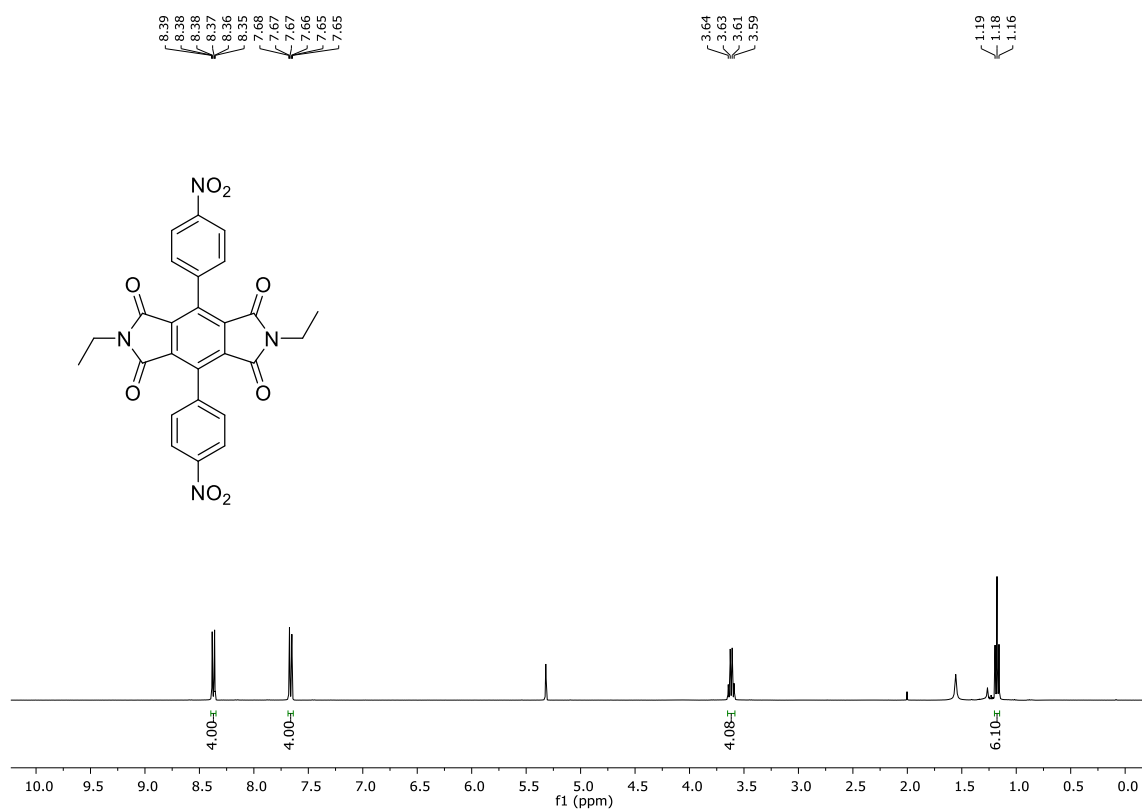
^1H NMR (400 MHz, CDCl_3) Spectrum of **2aa**



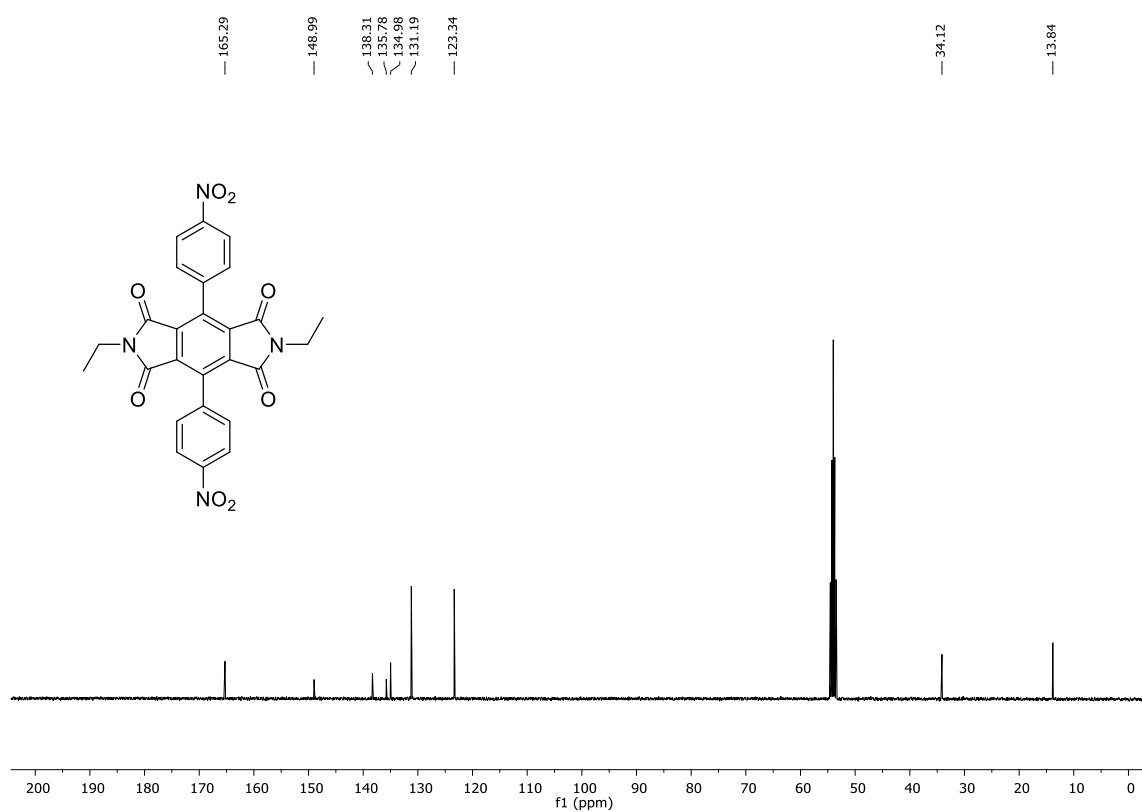
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2aa**



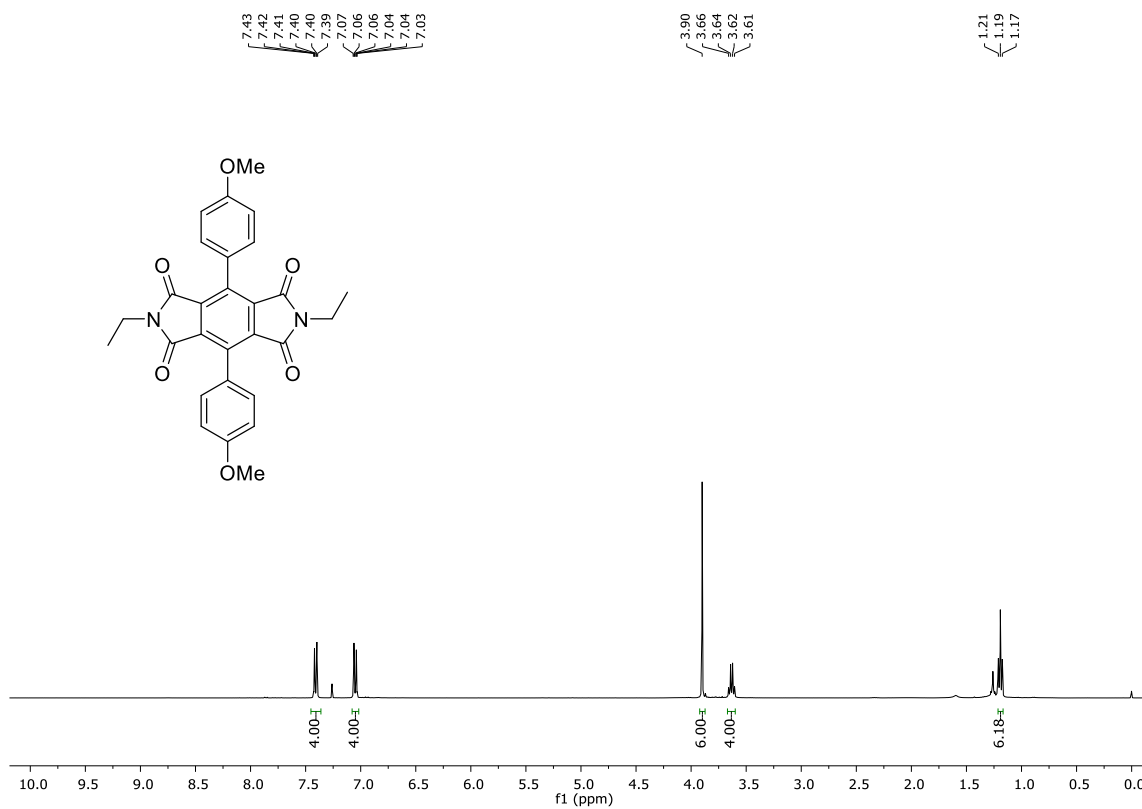
^1H NMR (400 MHz, CD_2Cl_2) Spectrum of **2ab**



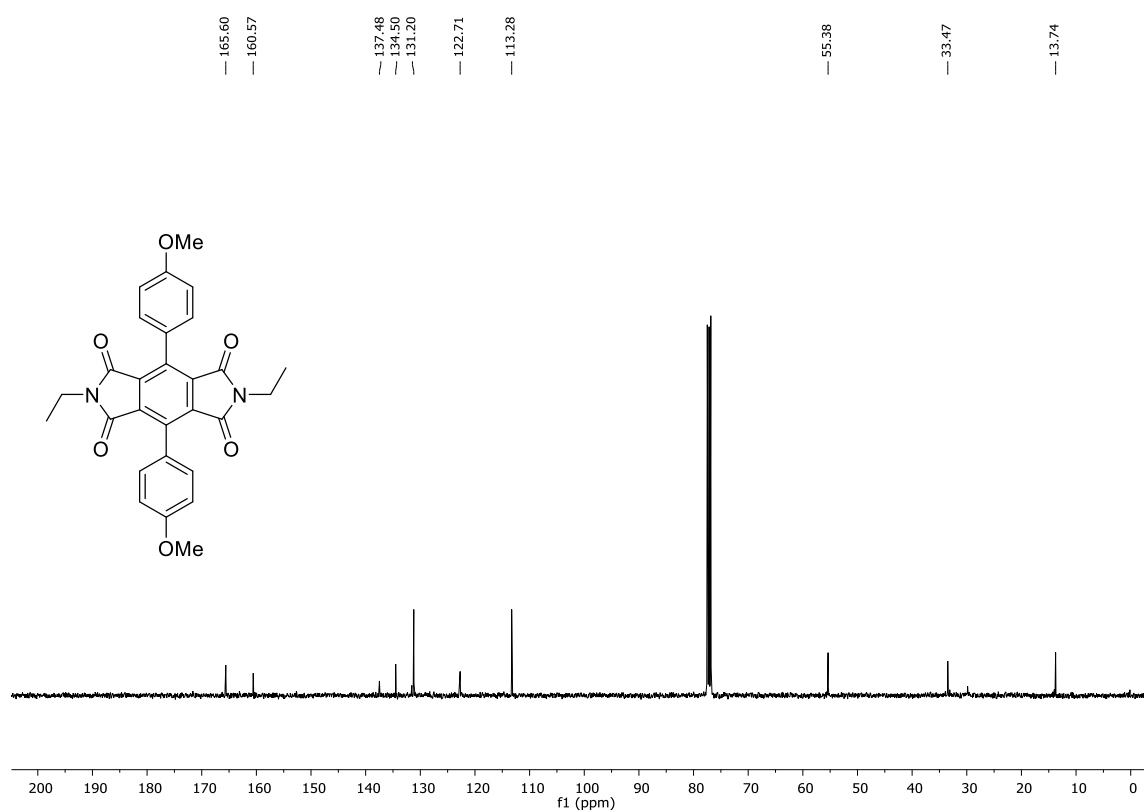
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CD_2Cl_2) Spectrum of **2ab**



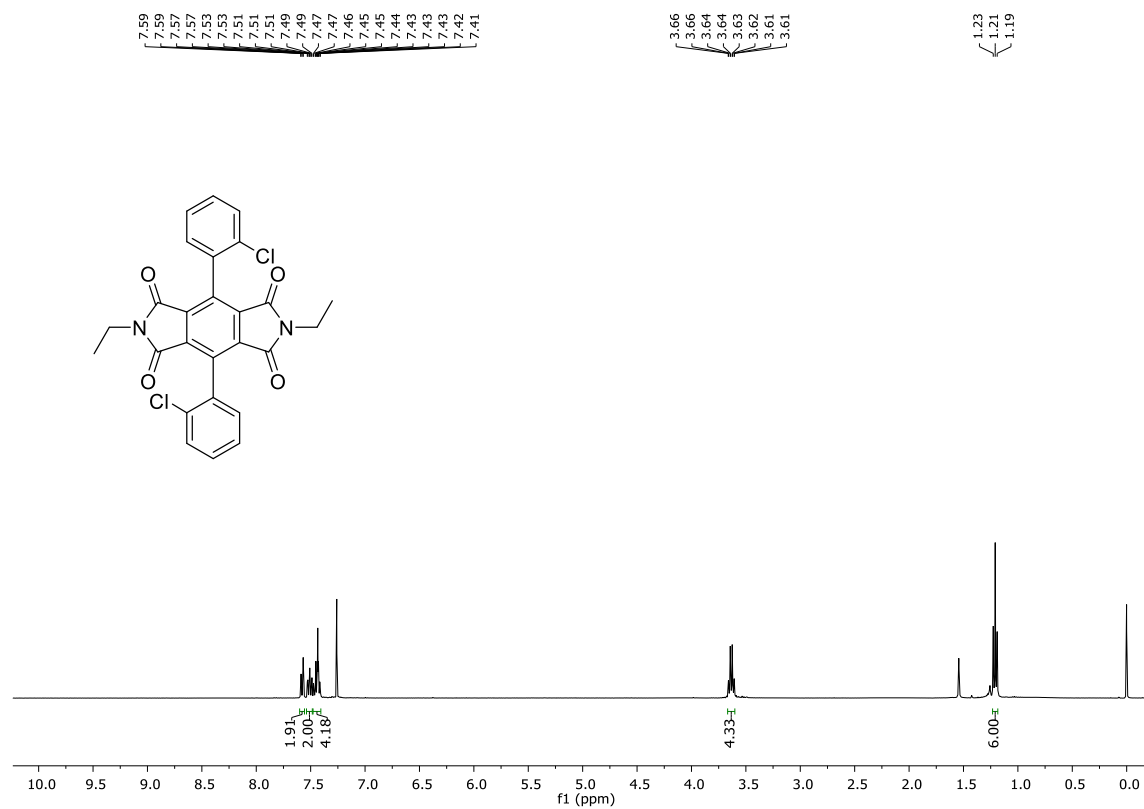
^1H NMR (400 MHz, CDCl_3) Spectrum of **2ai**



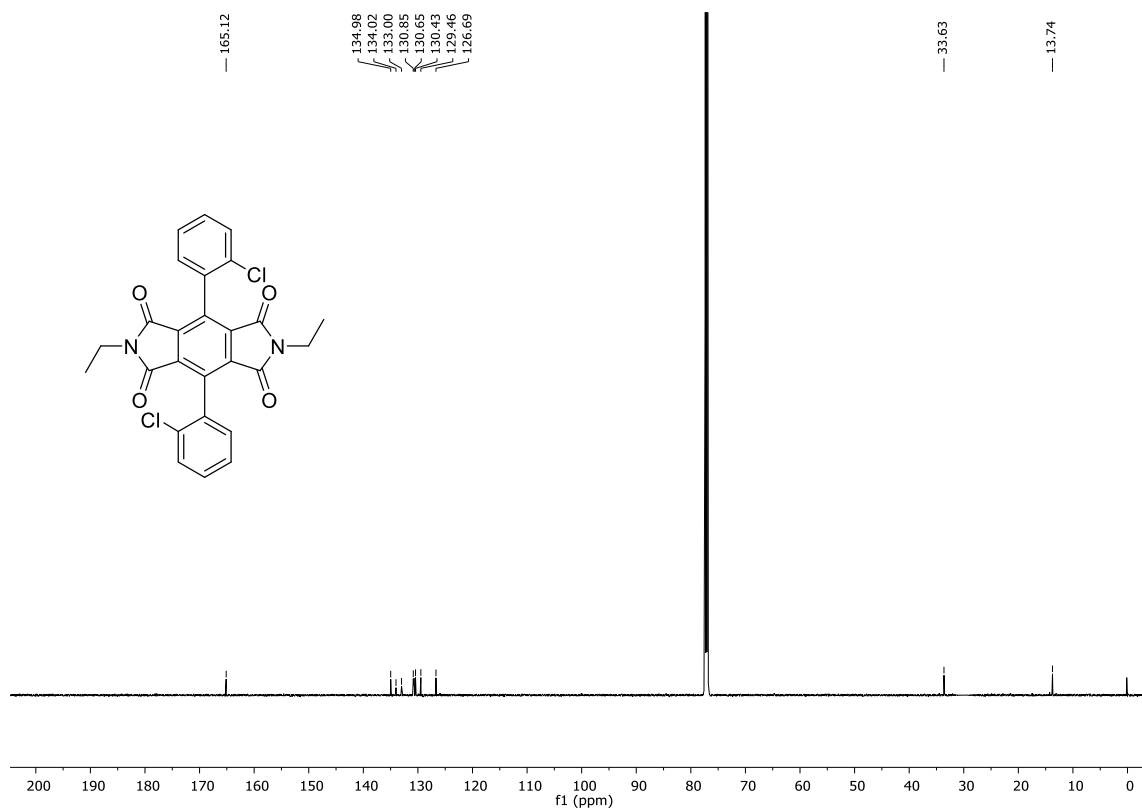
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2ai**



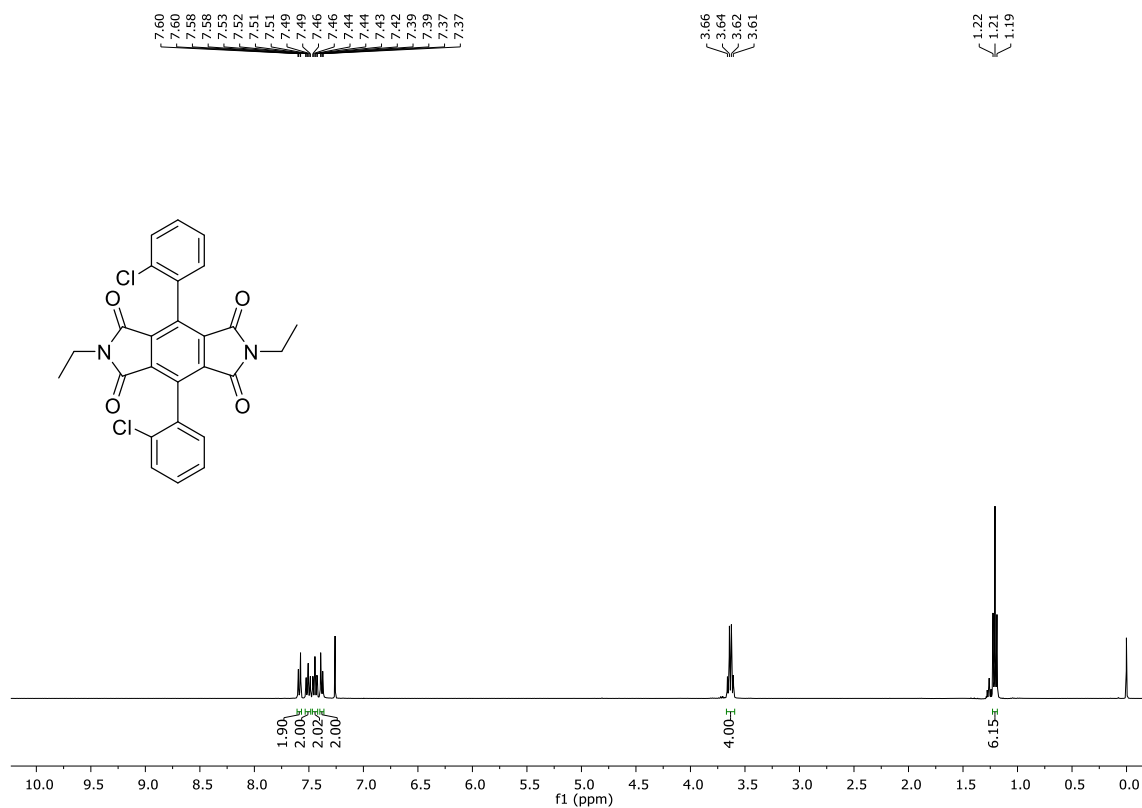
^1H NMR (400 MHz, CDCl_3) Spectrum of **2ao'**



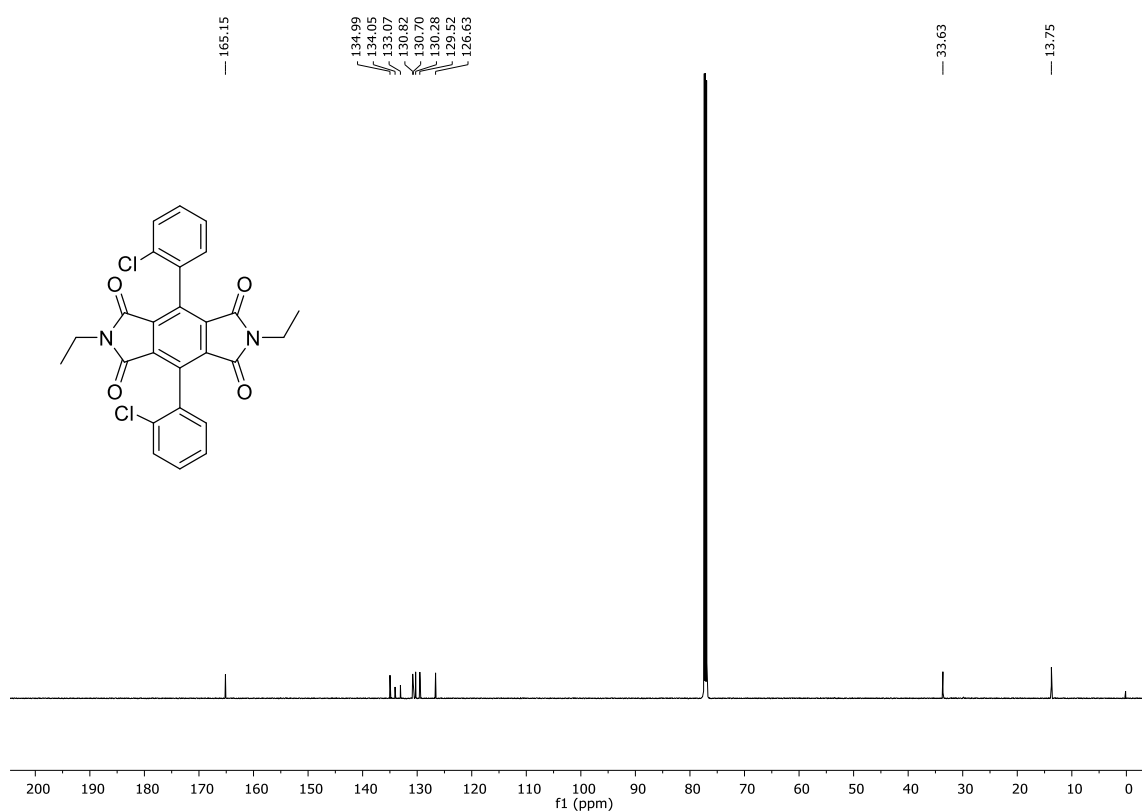
$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) Spectrum of **2ao'**



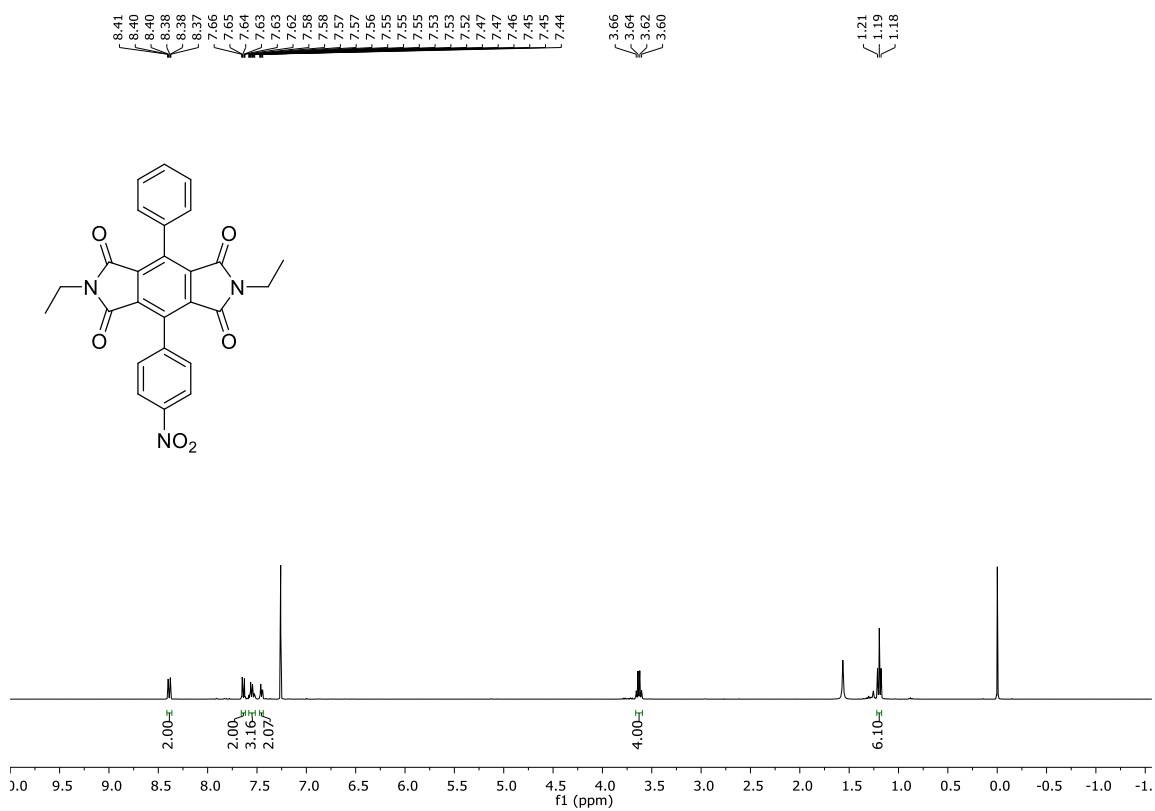
^1H NMR (400 MHz, CDCl_3) Spectrum of **2ao**



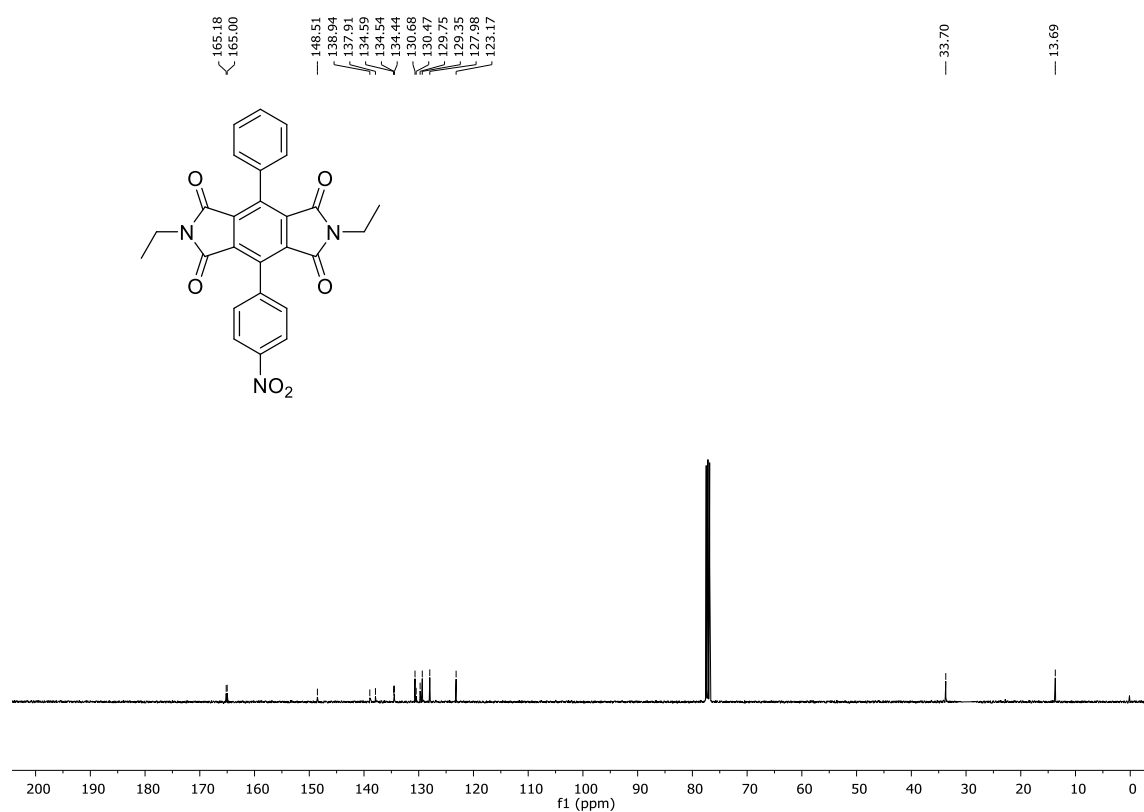
$^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3) Spectrum of **2ao**



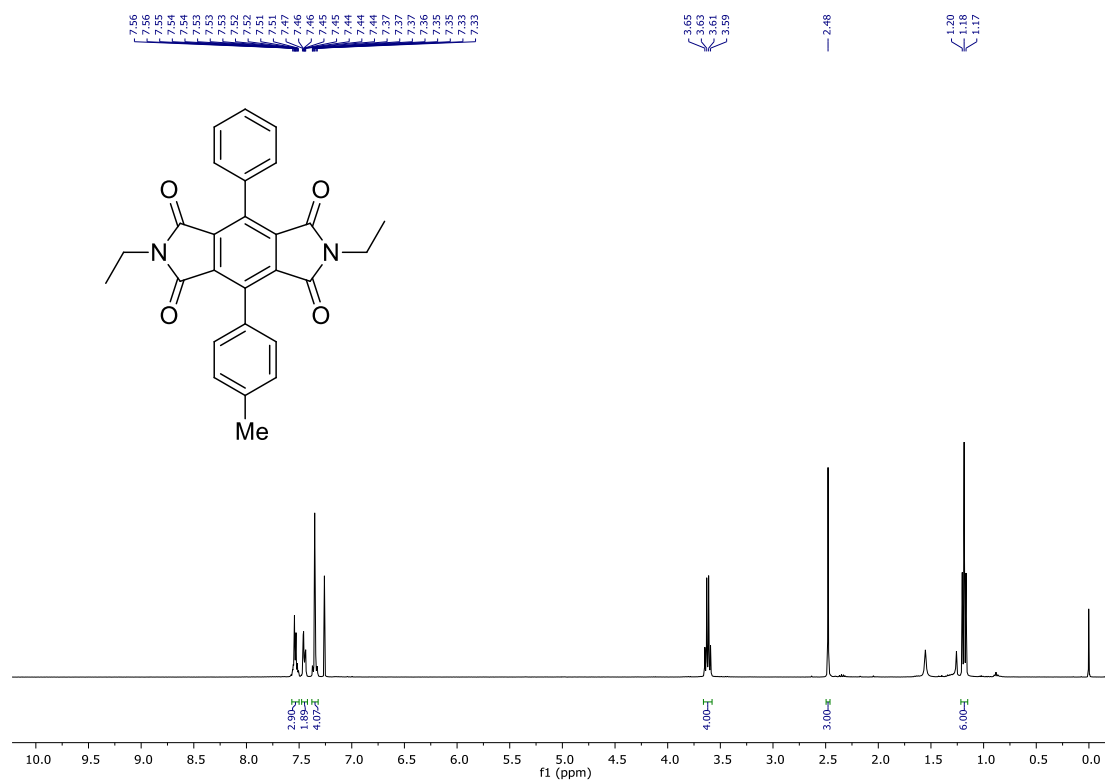
^1H NMR (400 MHz, CDCl_3) Spectrum of **2a'**



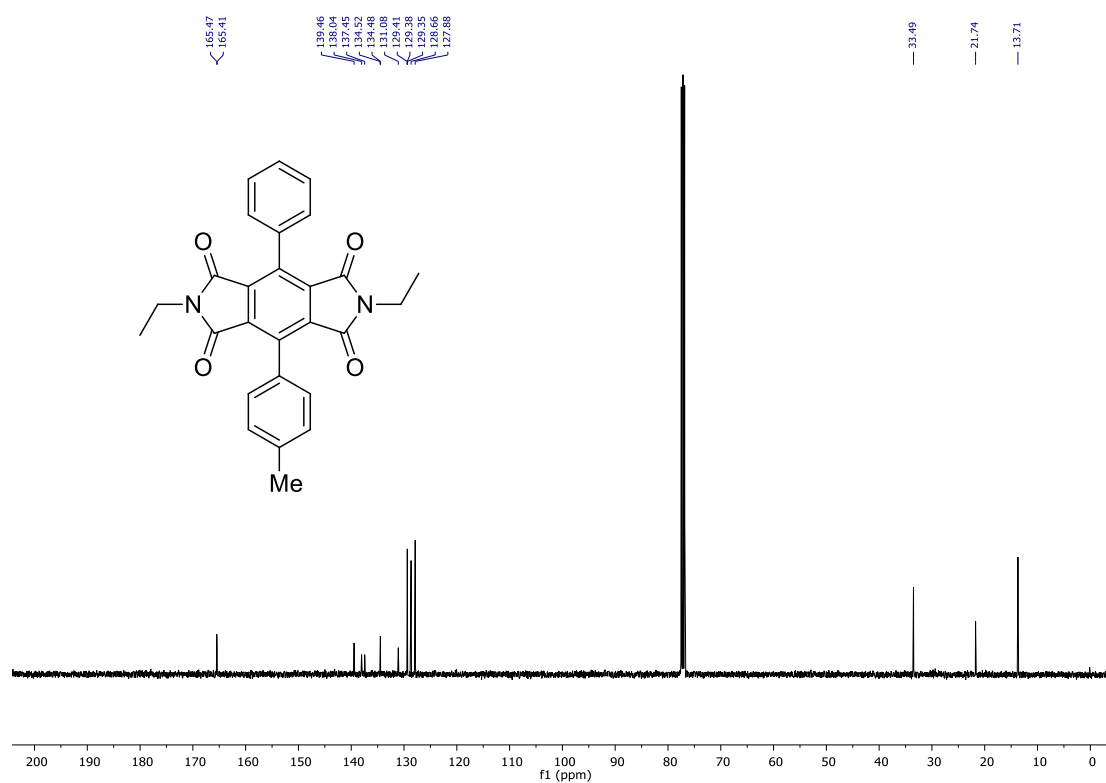
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2a'**



^1H NMR (400 MHz, CDCl_3) Spectrum of **2c'**

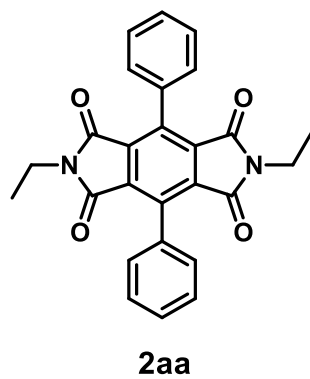


$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2c'**



3.9. Crystal Data

a) For compound **2aa**:



Datablock: TRY_a

Bond precision: C-C = 0.0030 A Wavelength=0.71073

Cell: a=10.877 (2) b=8.3217 (17) c=11.346 (2)
alpha=90 beta=91.952 (7) gamma=90

Temperature: 100 K

	Calculated	Reported
Volume	1026.4 (3)	1026.4 (4)
Space group	P 21/c	P 21/c
Hall group	-P 2ybc	-P 2ybc
Moiety formula	C26 H20 N2 O4	C26 H20 N2 O4
Sum formula	C26 H20 N2 O4	C26 H20 N2 O4
Mr	424.44	424.44
Dx, g cm ⁻³	1.373	1.373
Z	2	2
Mu (mm ⁻¹)	0.094	0.094
F000	444.0	444.0
F000'	444.21	
h, k, lmax	14, 11, 15	14, 11, 15
Nref	2562	2546
Tmin, Tmax		
Tmin'		

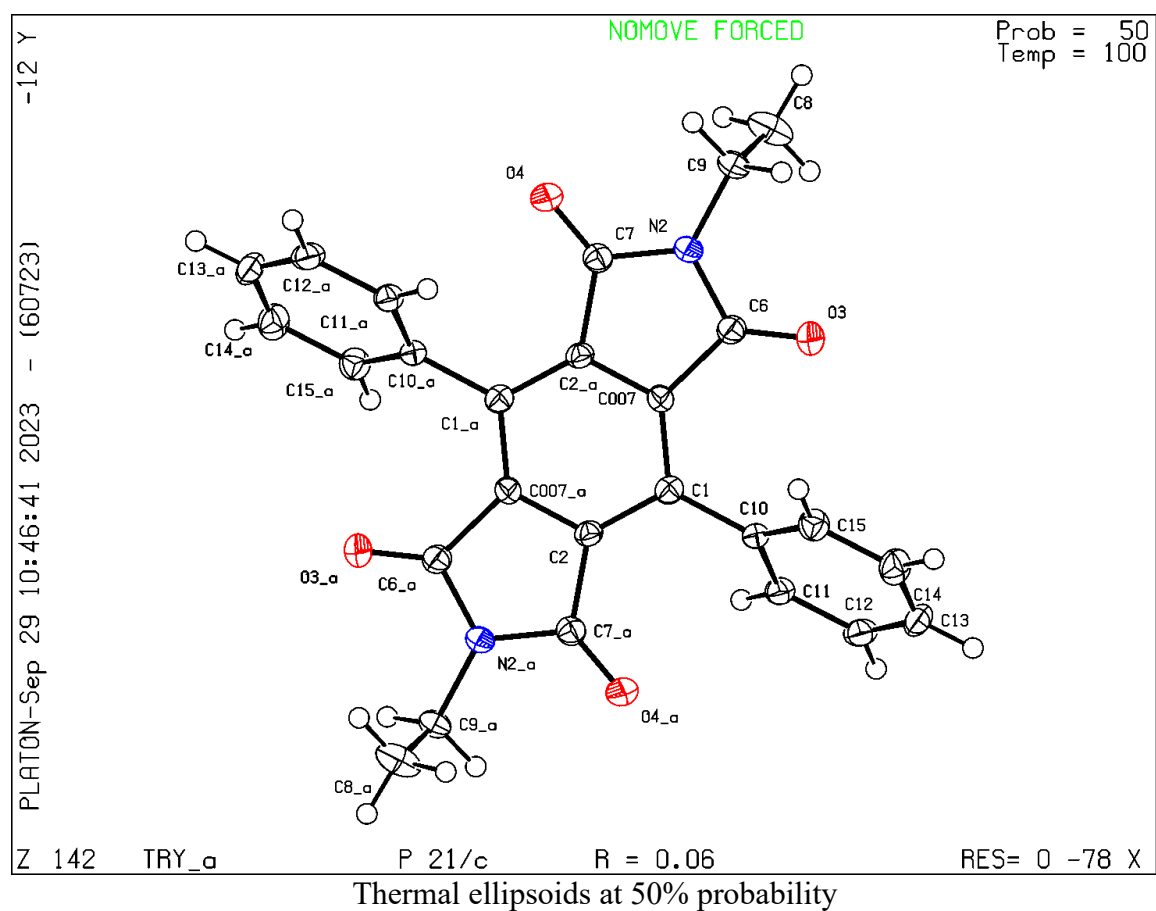
Correction method= Not given

Data completeness= 0.994 Theta (max)= 28.357

R(reflections)= 0.0618 (1583) wR2(reflections)=
0.2012 (2546)

S = 1.072 Npar= 147

Molecular structure of compound 2aa analyzed by single crystal XRD analysis:



Crystallization: sample was dissolved in a 5% Dichloromethane in hexane system and allowed it to crystallize by solvent diffusion method.

Datablock: KBM4 a

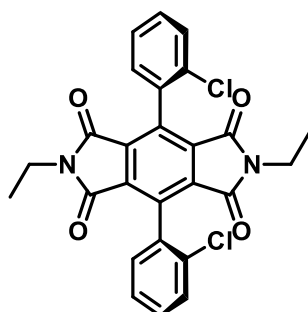
Bond precision:	C-C = 0.0100 A	Wavelength=0.71073		
Cell:	a=9.071 (4)	b=10.908 (4)	c=22.755 (9)	
	alpha=89.228 (8)	beta=90	gamma=90	
Temperature:	100 K			

	Calculated	Reported
Volume	2251.3(16)	2251.3(16)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C26 H18 Cl2 N2 O4	C26 H18 Cl2 N2 O4
Sum formula	C26 H18 Cl2 N2 O4	C26 H18 Cl2 N2 O4
Mr	493.32	493.32
Dx, g cm-3	1.456	1.456
Z	4	4
Mu (mm-1)	0.326	0.326
F000	1016.0	1016.0
F000'	1017.61	
h, k, lmax	10, 12, 25	10, 12, 25
Nref	6593	6459
Tmin, Tmax		
Tmin'		

Correction method= Not given

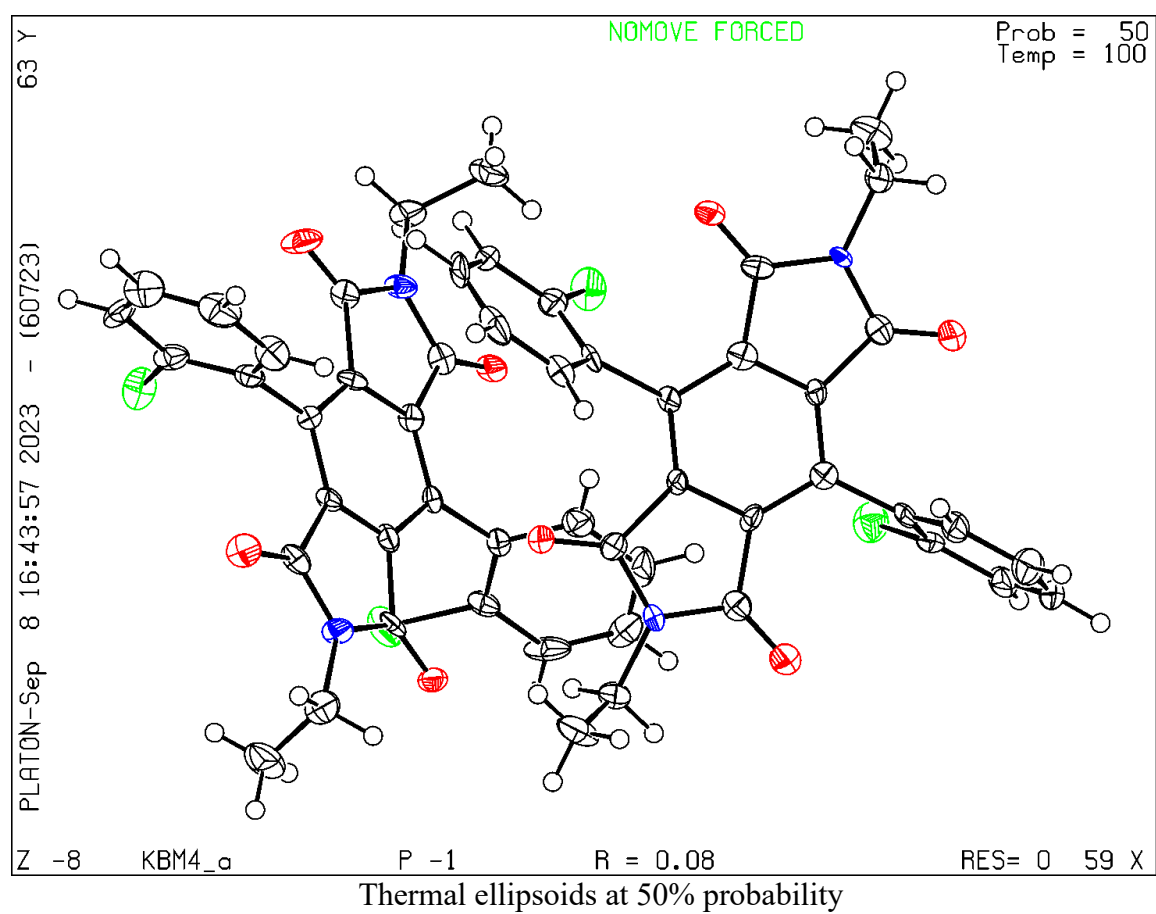
Data completeness= 0.980 Theta (max)= 23.411

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R(reflections)= 0.0821( 3181)      wR2(reflections)=
S = 1.045                        0.1727( 6459)
Npar= 618
```



cis-isomer
2ao

Molecular structure of compound 2ao analyzed by single crystal XRD analysis:



Crystallization: sample was dissolved in a 5% Chloroform in hexane system and allowed it to crystalize by solvent diffusion method

c) For Compound 2ao':

Datablock: KB4_a

Bond precision: C-C = 0.0052 Å

Wavelength=0.71073

Cell: a=10.824(4) b=10.919(4) c=11.068(4)
alpha=110.357(10) beta=94.452(10) gamma=111.142(9)
Temperature: 100 K

	Calculated	Reported
Volume	1112.6(7)	1112.6(7)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C ₂₆ H ₁₈ Cl ₂ N ₂ O ₄	C ₂₆ H ₁₈ Cl ₂ N ₂ O ₄
Sum formula	C ₂₆ H ₁₈ Cl ₂ N ₂ O ₄	C ₂₆ H ₁₈ Cl ₂ N ₂ O ₄
Mr	493.32	493.32
D _x , g cm ⁻³	1.473	1.473
Z	2	2
Mu (mm ⁻¹)	0.330	0.330
F ₀₀₀	508.0	508.0
F ₀₀₀ '	508.81	
h, k, l _{max}	12, 12, 13	12, 12, 13
N _{ref}	3909	3895
T _{min} , T _{max}		
T _{min} '		

Correction method= Not given

Data completeness= 0.996

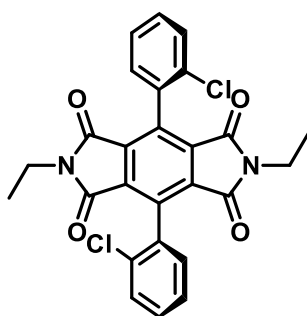
Theta(max)= 24.988

R(reflections)= 0.0526(2465)

wR₂(reflections)=
0.1068(3895)

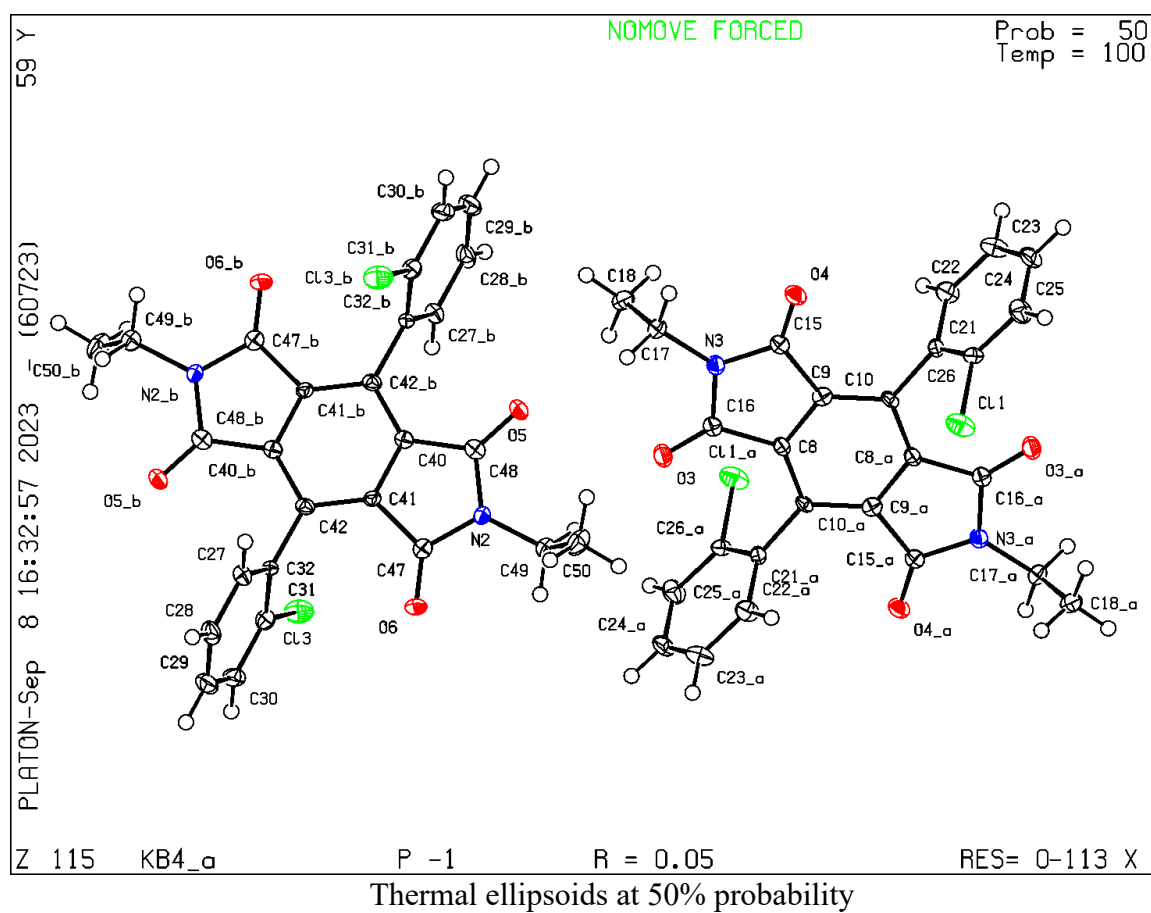
S = 1.049

N_{par}= 310



**Trans-isomer
2ao'**

Molecular structure of compound 2ao' analyzed by single crystal XRD analysis:



Crystallization: sample was dissolved in a 5% Chloroform in hexane system and allowed it to crystallize by solvent diffusion method

d) Crystal data of the CuNCS complex:

Datablock

Bond precision: N- C = 0.0080 Å Wavelength=1.54178

Cell: a=7.2380 (7) b=6.6637 (7) c=11.0454 (11)
alpha=90 beta=90 gamma=90

Temperature: 150 K

	Calculated	Reported
Volume	532.74 (9)	532.74 (9)
Space group	P b c a	P b c a
Hall group	-P 2ac 2ab	-P 2ac 2ab
Moiety formula	C Cu N S	C Cu N S
Sum formula	C Cu N S	C Cu N S
Mr	121.63	121.62
Dx, g cm ⁻³	3.033	3.033
Z	8	8
Mu (mm ⁻¹)	16.072	16.072
F000	464.0	464.0
F000'	451.28	
h, k, lmax	9, 8, 13	9, 8, 13
Nref	551	544
Tmin, Tmax	0.148, 0.200	0.418, 0.754
Tmin'	0.023	

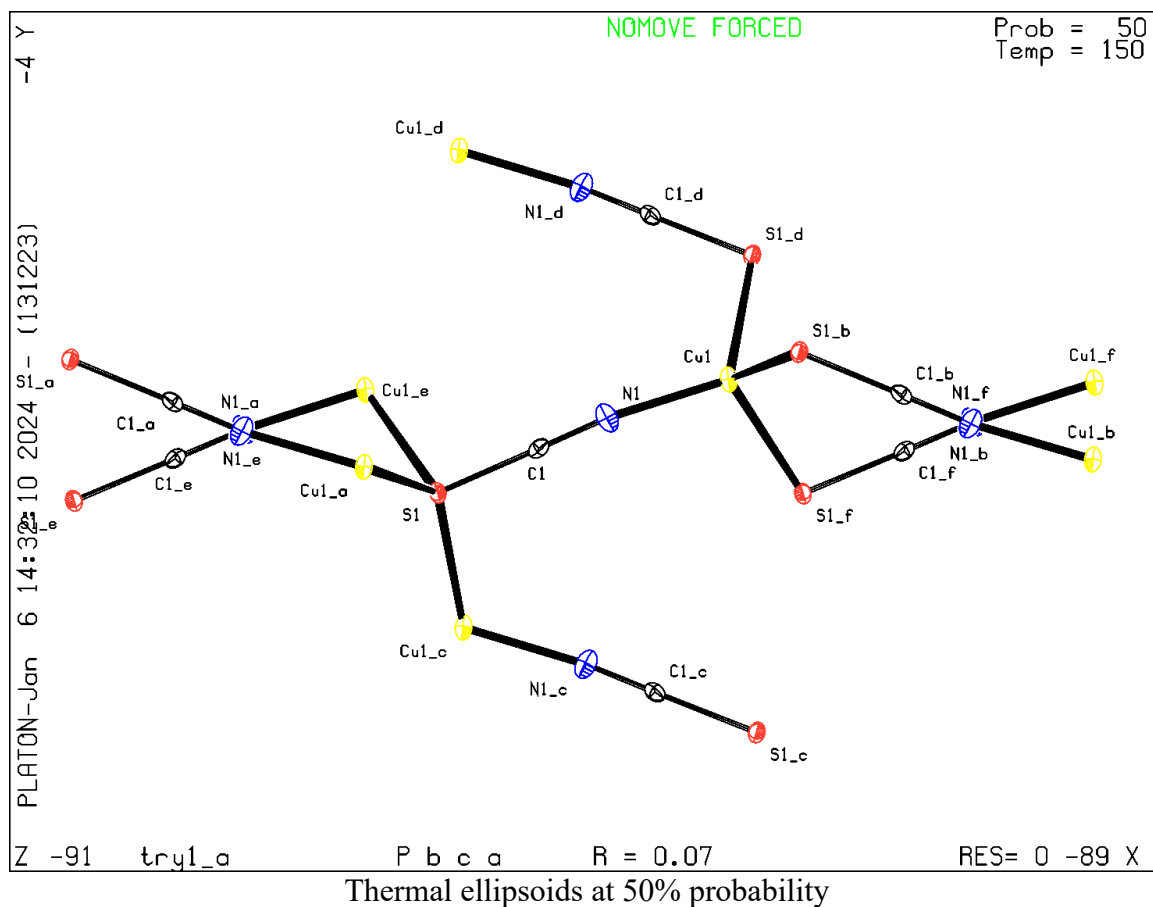
Correction method= # Reported T Limits: Tmin=0.418
Tmax=0.754 AbsCorr = MULTI-SCAN

Data completeness= 0.987 Theta(max)= 75.142

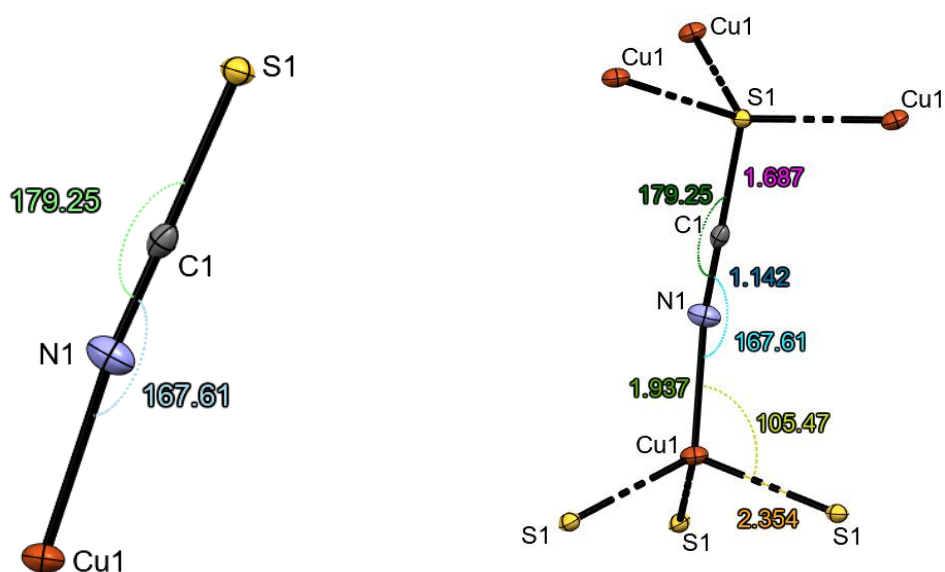
R(reflections)= 0.0724 (531) wR2(reflections)=
0.2128 (544)

S = 1.198 Npar= 37

Molecular structure of CuNCS complex analyzed by single-crystal XRD analysis:



Crystallization: The sample was dissolved in a 60% Toluene: MeCN system and allowed it to crystallize by solvent diffusion method



3.10. References

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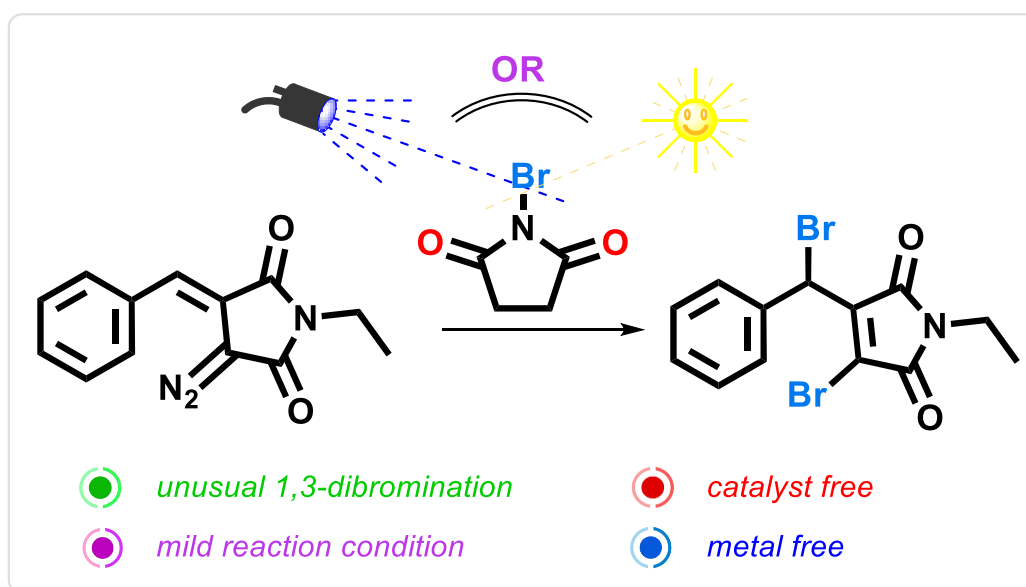
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Chapter 4

1,3-Dibromination of Diazo Arylidene Succinimides (DAS): A Sustainable Approach using Visible Light



1,3-Dibromination of Diazo Arylidene Succinimides (DAS): Sustainable Approach using Visible Light

4

An efficient visible-light driven strategy for 1,3-dibromination of diazo arylidene succinimide (DAS) is achieved with N-bromosuccinimides (NBS) through a carbene-free pathway. The reaction undergoes direct photochemical activation without the requirement of a photocatalyst or an additive to access 1,3-dibromo arylidene succinimides in good yield. This transformation is proposed to proceed through a radical mechanism in which NBS acts as a radical donor and the diazo arylidene succinimide (DAS) acts as a radical acceptor. The protocol proved to be easy and practical to access bromo-functionalized DAS derivatives that can be utilized for further functionalization. The protocol also works under direct exposure to sunlight as well.

4.1 Introduction:

Organic halides are widely used as precursors and intermediates in various organic transformations. Also, from a retrosynthetic standpoint, they can serve as flexible synthetic counterparts for cationic, radical, or anionic carbon-based synthons, thus, distinguishing them from other functional groups in terms of reactivity and strategic utility (Figure 1).¹ Vinyl and aryl bromides play a very useful role in facilitating well-known cross-coupling reactions (Suzuki, Heck, Negishi, Sonogashira etc.). Alkyl or aryl bromides are also used in nucleophilic substitutions (SN^1 , SN^2), Grignard reaction, lithiation and metalation, radical reactions, elimination processes, halogen-metal exchange, and electrophilic bromination. They play an essential synthetic precursor for various useful synthetic transformations.² Many bromides have found extensive applications in flame retardants, biocides, gasoline additives, polymers, pharmaceuticals, natural products, and agrochemical synthesis.³ However, the necessity of advancing halogenation strategies that optimize atom economy, minimize chemical steps, and enhance operational efficiency remains a significant challenge.

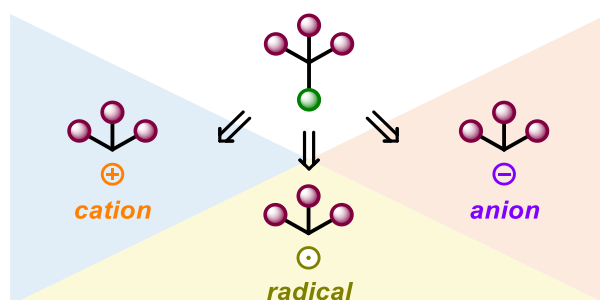


Figure 1. Organohalide disconnections to corresponding synthons

Recently, diazo compounds have been extensively used in organic synthesis, serving as key intermediates in the design of novel methodologies for diverse chemical transformations.⁴ In the presence of transition metal catalysts, diazo compounds undergo nitrogen release through interaction between their polarized carbon center and the vacant orbitals of the metal, making diazo compounds valuable precursors for metal-carbene species.⁵ By choosing suitable reaction conditions and substrates, electrophilic metal-carbene species can facilitate the synthesis of various halogenated products via halogen bond insertion, ylide formation, sigmatropic rearrangements or cycloaddition reactions.

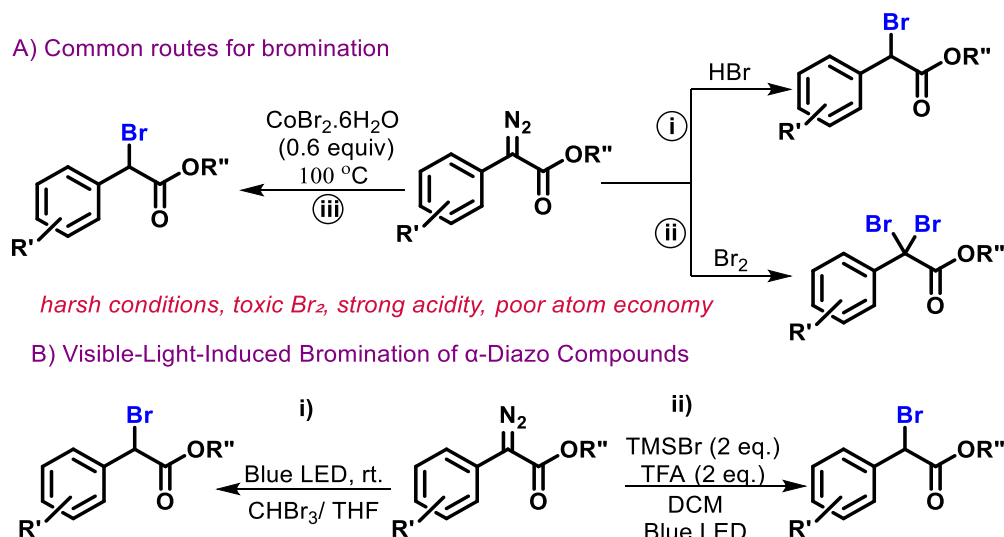
However, bromination of diazo compounds stands out as a particularly interesting and useful strategy, as diazo compounds are usually very reactive and have varied reactivity.⁶ To the best of our knowledge, only a very few studies have focused on the bromination of α -diazo compounds. Traditionally, this transformation has relied on elemental bromine or hydrogen bromide (Scheme 4.1A-i, ii).⁷ However, this approach is not very attractive as it requires harsh conditions and careful handling, as bromine is known for its hazards and toxicity. Whereas HBr is a strong acid and is limited by its acidity and slow reactions. The toxicity and hazardous nature of these reagents make them relatively less attractive for the wide applicability in organic synthetic transformations.

Alternatively, in metal (Ru, Ag, Rh etc.) catalyzed reactions, diazo compounds are commonly used as carbene precursors for halogenation, enabling the introduction of halogen atoms into organic molecules.⁸ Recently, Gu and co-workers reported a cobalt-mediated bromination of α -diazo phenylacetate derivatives.⁹ Though this method is interesting, the method relies on high temperatures (100 °C) and a stoichiometric amount of cobalt(II) bromide. This leads to potential functional group incompatibility, significant waste, and environmental pollution as well (Scheme 4.1A-iii).

Photoinitiation is a mild and efficient sustainable approach for converting diazo groups into carbene intermediates in situ under mild conditions, facilitating interesting transformations. However, only a very few methods are available for the photoinduced halogenation of diazo esters.¹⁰ In 2024, Wu and coworkers have recently reported an interesting protocol on visible-light-induced bromination of α -diazo compounds using bromoform (Scheme 4.1 B-i).^{10a}

Notably, the reaction proceeds exclusively under blue light irradiation, without the need for a photocatalyst or any additive, up to 15 h. After that, very recently in 2025, Liu and coworkers have disclosed the photoinduced halogenation of α -diazo carbonyl compounds under visible light using TMSBr under acidic conditions (TFA).^{10b} This approach utilizes TMSBr as a

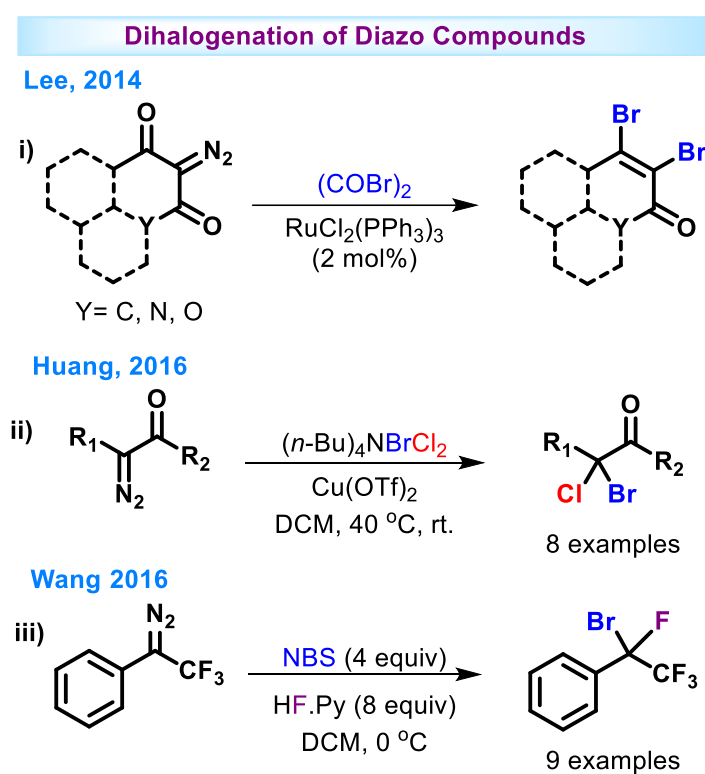
halogenation reagent and operates efficiently at room temperature for up to four hours, without requiring additional metal catalysts (Scheme 4.1 B-ii). While bromination has been documented for acyclic diazo compounds, the bromination of cyclic vinyl diazo compounds remains unexplored.



Scheme 4.1: Previous bromination methods of diazo esters

On the other hand, among the various types of halogenation reactions, monohalogenation, where a single halogen atom is introduced into the substrate, is a well-established process.¹¹ However, polyhalogenation reactions, especially dihalogenation, have been comparatively less explored. For a long time, 1,2-dibromination of alkenes has been a simple and effective approach for synthesizing vicinal brominated compounds,¹² taking advantage of the abundance of alkenes as feedstocks. Traditional methods rely on hazardous halogens or halide salts with strong oxidizers, often leading to low atom economy, side reactions, and limited functional group compatibility.¹³ More recently, diazo compounds have also been employed in dihalogenation reactions.¹⁴ In 2014, Lee and coworkers documented a ruthenium-catalyzed dihalogenation reaction of diazo compounds using oxalyl halides, enabling the one-step synthesis of α,β -dihaloenones with moderate to good yield (Scheme 4.2-i).^{14a} Subsequently, in 2015, the same research group carried out the reaction utilizing AuFeAg nanoparticles as a recyclable catalyst, achieving the products α,β -dihaloenone with excellent yields.^{14b} Later, in 2016, Huang and co-workers reported an efficient copper-catalyzed one-pot gem-bromochlorination of α -diazo carbonyl compounds under mild conditions, employing tetrabutylammonium dichlorobromide (TBADCB) as the halogen source (Scheme 4.2-ii).^{14c} In 2016, Wang et al. reported a general approach to the geminal difunctionalization of α -diazo

arylmethyl phosphonates providing easy access to geminal dihalo-functionalization of α -diazoaryl methylphosphonates (Scheme 4.2-iii). Utilizing a series of easily available halogenating agents, namely HF·Py and NBS, a variety of dihalogenated phosphonates were synthesized from α -diazoarylmethylphosphonates with high efficiency and in high yields under mild reaction conditions.^{14d}



Scheme 4.2: Dihalogenation of diazo compounds

Despite sporadic investigations, reports on the dihalogenation of diazo compounds are scarce in the literature. The existing literature predominantly focuses on 1,2-dihalogenation or geminal dibromohalogenation, often employing metal catalysts or requiring cryogenic conditions. To date, 1,3-dihalogenation of diazo compounds has not been documented. Owing to the importance of brominated compounds, there are no methods currently exist for achieving 1,3-dihalogenation. Developing an efficient and sustainable synthetic approach for constructing dibrominated molecules is highly desirable and inherently challenging.

To overcome limitations in halogenation, electrophilic halogenating reagents like *N*-halosuccinimides (NXS) and 1,3-dihalo-5,5-dimethylhydantoin (DXDMH) offer safer C–X bond formation. Among these, NXS and DXDMH are noteworthy for their bench stability and cost-effectiveness, though they often exhibit limited reactivity and selectivity (Figure 4.2).¹⁵ To enhance their reactivity, various strategies have been developed to generate halogenating

reactive species, mainly through the use of N-, P-, S-, or Se-based Lewis base catalysts, or by applying Brønsted base catalysis.¹⁶⁻¹⁸ Their reactivity also depends on solvents and additives, with halogen radical species ($X^\bullet$) released under various conditions, while bond cleavage occurs via light, heat, or nonpolar solvents.¹⁹

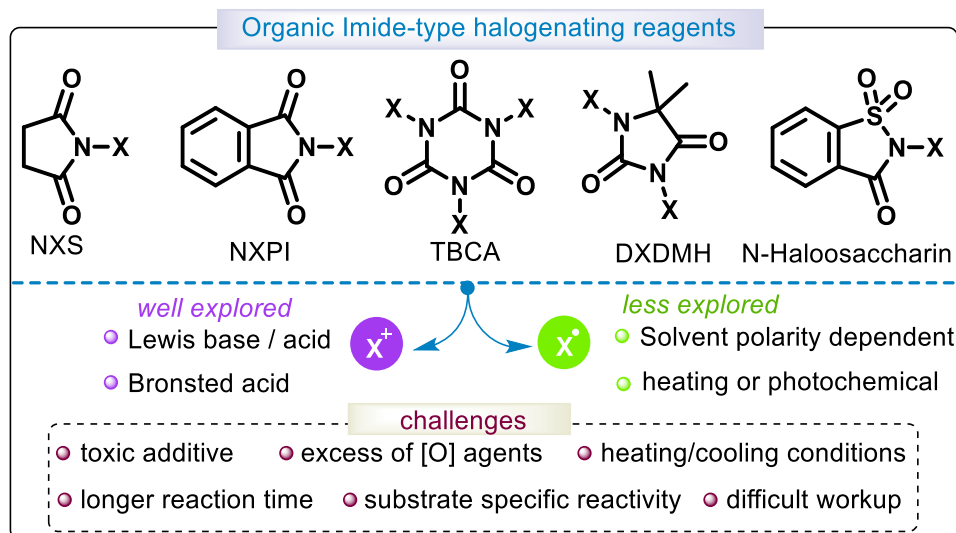


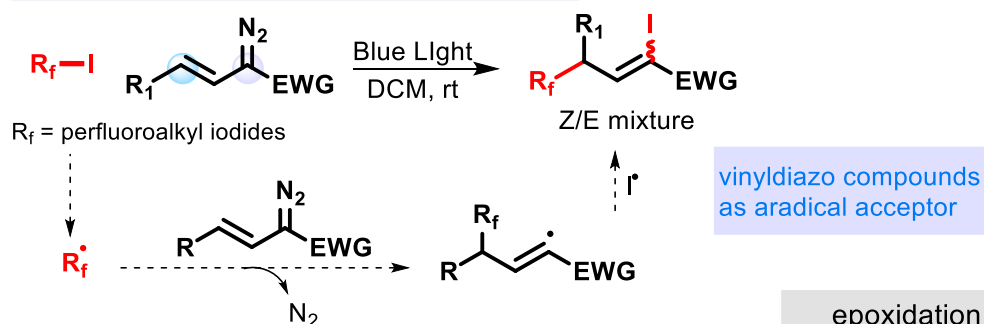
Figure 4.2. Organic imide type halogenating Reagents

Vinyl diazo compounds exhibit unique reactivity due to the presence of vinyl and diazo functionality on geminal carbon, and these groups are stabilized by the resonance effect. Owing to the interesting dual reactivity of vinyl diazo compounds, various powerful synthetic strategies have been developed, especially targeting the α - and γ -positions. Notably, acyclic vinyl diazo compounds are frequently utilized as 3-carbon building blocks.²⁰ Zhou and coworkers have recently reported visible light-promoted 1,3-addition of perfluoroalkyl iodides to vinyl diazoacetates (Figure 4.3-A). This reaction was initiated without the use of external photocatalysts or additives. During this reaction, the initial Rf radical arises from the homolytic dissociation of a radical pair complex, which originates from a triplet free vinylcarbene and perfluoroalkyl iodide.

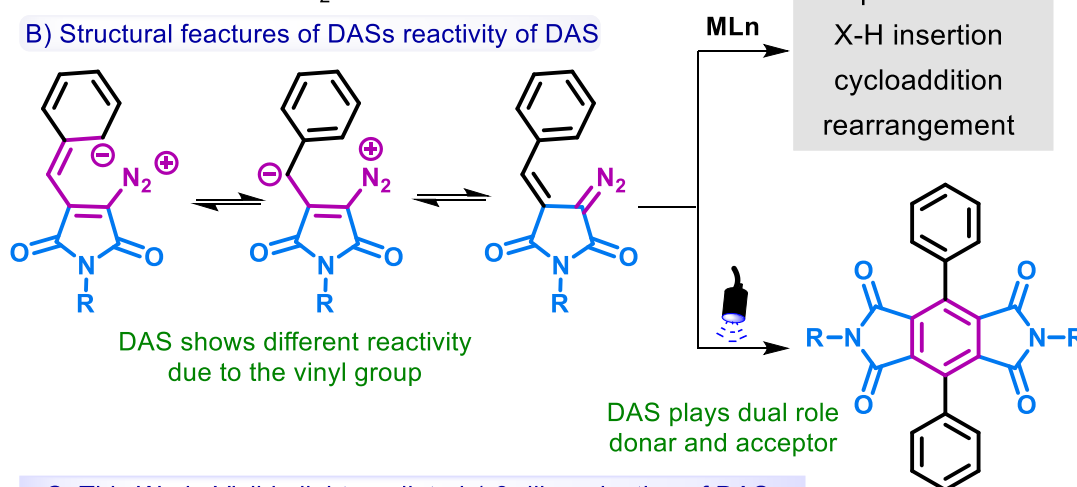
On the other hand, cyclic diazo compounds such as diazo arylidene succinimides (DASs) are structurally unique and are relatively less explored for photochemical reactivity. Our research group has been working on the interesting chemistry of cyclic diazo compounds such as DAS and diazo pyrazolone scaffolds and have been exploring their reactivity under both metal and visible light conditions.²¹ Earlier in Chapter 3, we developed a visible-light-induced, copper-catalyzed radical reaction of DASs by expanding the diazo chemistry, thus enabling an efficient pyromellitic diimide synthesis (Figure 4.3-B).²¹ⁱ We observed that, DASs notably function both

as radical acceptors and donors, underscoring their versatility in radical transformations and photochemical applications.

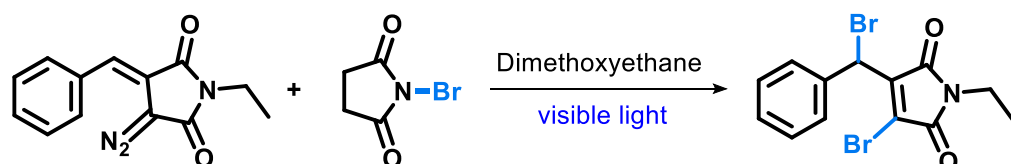
A) 1,3-addition of R_fI to vinyl diazoacetates



B) Structural features of DASs reactivity of DAS



C. This Work: Visible light mediated 1,3-dibromination of DAS



developed 1,3-dibromination catalyst free oxidant free mild reaction condition

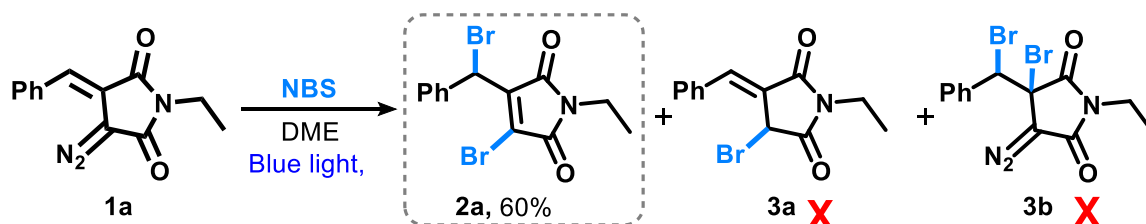
Scheme 4.3: Reactivity of acyclic and cyclic vinyl diazo compounds

N-Bromosuccinimide (NBS) has emerged as a user-friendly alternative to environmentally harmful bromine. Recognizing its potential, we considered NBS a promising reagent for the bromination without requiring any acid or catalyst. Notably, 1,3-dibromination of diazo compounds has not been previously reported, and 1,3-dibromo DAS derivatives would be of synthetic importance. Herein, we disclose a photocatalyst or additive-free visible light-mediated 1,3-dibromination of diazo arylidene succinimides under mild conditions using NBS (Figure 4.3-C).

4.2 Results and discussion:

We commenced with the reaction of diazo arylidene succinimide (**1a**) with NBS in dimethoxy ethane under irradiation of visible light 440 nm, blue LED light. Gratifyingly, to our surprise, the reaction reacted smoothly to afford the desired dibromination product (**2a**) in moderate yield (60%) in very short reaction time, just in 1 hour (Table 4.1, entry 1). Interestingly, neither the monobromination product **3a** nor the 1,2-dibromination product (at the vinyl moiety) **3b** were detected.

Synthesis of 2a: Optimization of Reaction^a



Entry	Solvent/Condition	Light Source	Reagent	Yield of 2a (%) ^b
1	Dimethoxy Ethane (DME)	440 nm	NBS	60
2	DMSO	440 nm	NBS	<i>n.d.</i>
3	DMF	440 nm	NBS	<i>n.d.</i>
4	MeOH	440 nm	NBS	<i>n.d.</i>
5	MeCN	440 nm	NBS	26
6	EtOAc	440 nm	NBS	23
7	TEO	440 nm	NBS	55
8	DCM	440 nm	NBS	16
9	Diethyl ether	440 nm	NBS	13
10 ^c	DME	440 nm	NBS	62
11	DME	427 nm	NBS	45
12	DME	456 nm	NBS	55
13	DME	467 nm	NBS	70
14	DME	525 nm	NBS	81
15	DME	525 nm	NCS	0
16	DME	525 nm	NIS	0

Entry	Solvent/Condition	Light Source	Reagent	Yield of 2a (%) ^b
17	DME	525 nm	TBCA	55
18	DME	525 nm	DBDMH	60
19	DME	No light	NBS	25

Table 4.1: ^aGeneral reaction conditions: **1a** (0.2 mmol), NBS (2 equiv.), Dimethoxy ethane (DME) A.R. grade (0.055 M), room temp. 30 min., degasified condition with N₂, under blue LED 440 nm irradiation. ^bIsolated yields, (n.d.= not detected). ^cEosiy Y photocatalyst added.

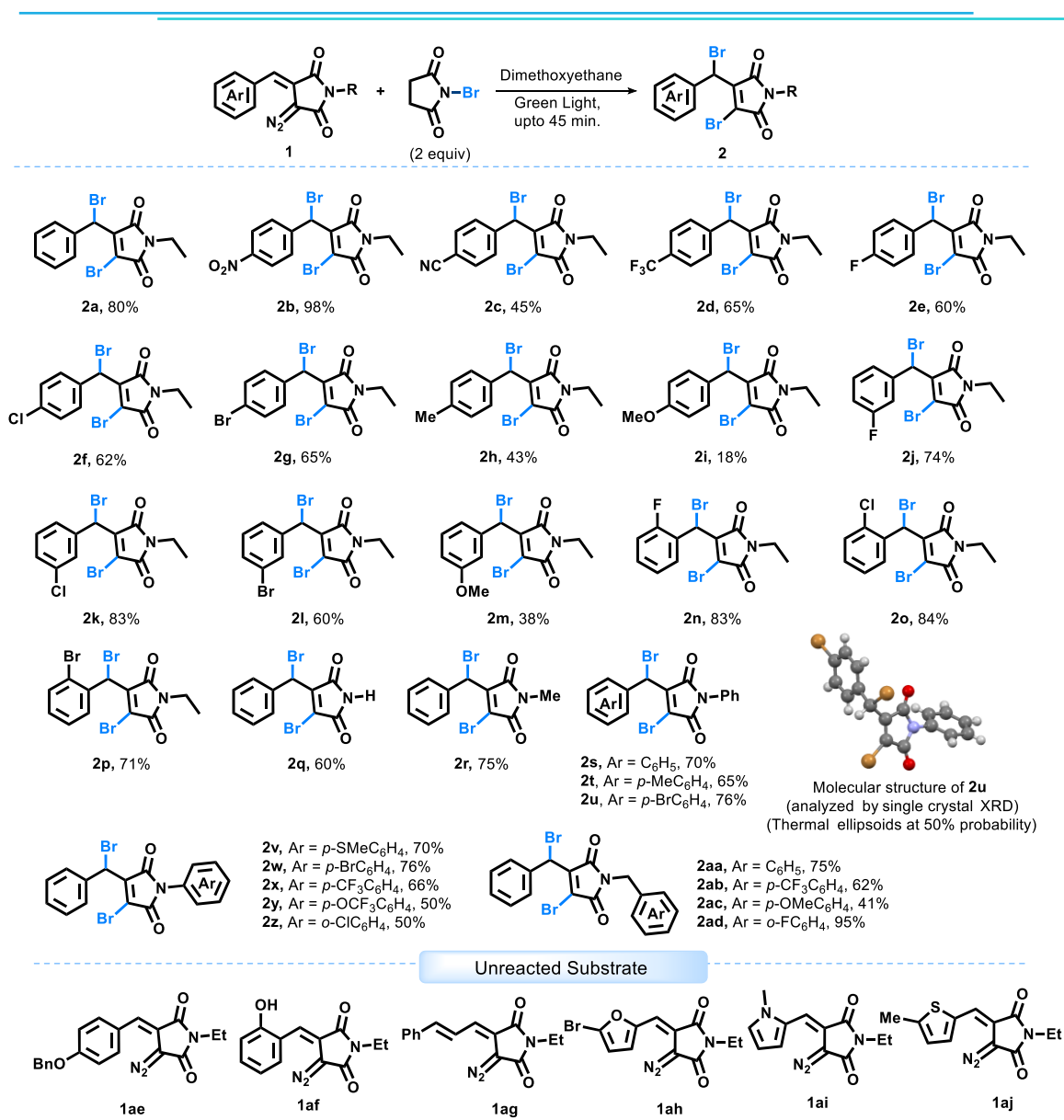
Encouraged by this initial success, in order to optimize the reaction further, we carried out a solvent screening so as to assess the impact of different solvents on overall reaction efficiency. We did not observe any traceable amount of the desired product **2a** in polar solvents such as DMSO, DMF, and methanol (Table 4.1, Entries 2-4). While reaction in other solvents such as acetonitrile, ethyl acetate, dichloromethane, and diethyl ether afforded the desired product **2a** in lower yields, triethyl orthoformate (TEO) furnished the desired product in modest yield (Table 4.1, entries 5–9). Among all the solvents, DME proved to be the best solvent to afford the desired 1,3-dibromination product (**2a**) with a 60% isolated yield (Table 4.1, entry 1). Later, we conducted this reaction in the presence of a photocatalyst to obtain the corresponding product **2a**. However, we did not observe a significant change in the yield, suggesting that a photocatalyst is not necessary for this transformation (Table 4.1, entry 10). Further, we screened a range of light sources with different wavelengths (Table 4.1, entries 11-14). Among all, we observed that green LEDs (525 nm) furnished the desired 1,3-dibromination product **2a** in very good yield (81%, Table 4.1, Entry 13). Later, we screened different halogenating agents to examine the effect on the 1,3-dihalogenation. Halogenating agents such as *N*-chlorosuccinimide (NCS) and *N*-iodosuccinimide (NIS) proved to be ineffective in promoting this reaction, thus highlighting the distinct reactivity of the NBS under the conditions and generation of the bromine radical from NBS under the conditions (Table 4.1, Entries 15, 16). To gain further insights, we evaluated imide-based brominating reagents, including tribromoisocyanuric acid (TBCA), and 1,3-dibromo-5,5-dimethylhydantoin (DBDMH). Although these reagents afforded the desired product **2a**, the yields were notably lower than those achieved with the use of NBS (Table 4.1, Entries 17-18). Later, we carried out the reaction in the absence of light, furnishing the desired product **2a** in lower yield after prolonged reaction time, 36 h (25%, Table 4.1, entry 14). These control experiments highlighted the necessity of light irradiation in facilitating the desired transformation.

A *N*-chlorosuccinimide (NCS) and *N*-iodosuccinimide (NIS) proved ineffective in promoting this reaction, highlighting the distinct reactivity of the bromine radical (Table 4.1, entry 19). This result clearly indicate that light was necessary to facilitate the desired transformation. Based on the detailed screening the diazo benzylidene succinimide **1a** (1 equiv.), NBS (2 equiv.), in dimethoxy ethane (DME) under the irradiation of green LEDs (525 nm) in inert atmosphere at room temperature, proved to be the optimum reaction condition to obtain the desired 1,3-dibromination product **2a** in very good yield.

4.3 Substrate Scope

Having obtained the optimized reaction conditions, we further investigated the substrate scope of different DAS derivatives for the 1,3-dibromination. DAS derivatives containing various *p*-substituted electron-deactivating or electron-withdrawing groups on the phenyl ring of arylidene moiety efficiently reacted under optimized reaction conditions to furnish the corresponding 1,3-dibrominated products (**2a–2g**) in modest to excellent yield (up to 98%, Scheme 4.4). DAS having electron-donating groups at *para* position of the phenyl group (**1h–1i**) afforded the desired products (**2h, 2i**), in lower yield (Scheme 4.4). Possibly, the electron-donating groups reduce the reactivity at the vinylic position in DAS. DAS with the *m*-electron-deactivating substituents on the phenyl ring showed very good reactivity by affording the desired products (**2j–2l**) efficiently (upto 83%, Scheme 4.4). While DAS with *m*-electron-donating substituted afforded the desired product **2m** in modest yield. Furthermore, *o*-substituted DAS with deactivating groups exhibited good tolerance under the reaction conditions by affording the desired 1,3-dibromination products (**2n–2p**) in very good yield (upto 84%).

Later, we evaluated the reactivity of different N-substituted DAS (**1q–1ad**) and observed that all these substrates reacted smoothly under the reaction conditions to afford the desired products (**2q–2ad**) in moderate to good yields. However, certain DAS (**1ae–1aj**) did not undergo the reaction, likely due to specific substituents having electron-donating ability or due to the extended conjugation, thereby reducing the reactivity. For example, cinnamyl-substituted diazo arylidene succinamides (**1ag**) or DAS with heterocyclic systems (**1ah, 1aj**) exhibit electron-donating ability due to the lone pair of heteroatoms, reducing the reactivity, and do not afford the desired products even after prolonged reaction time.

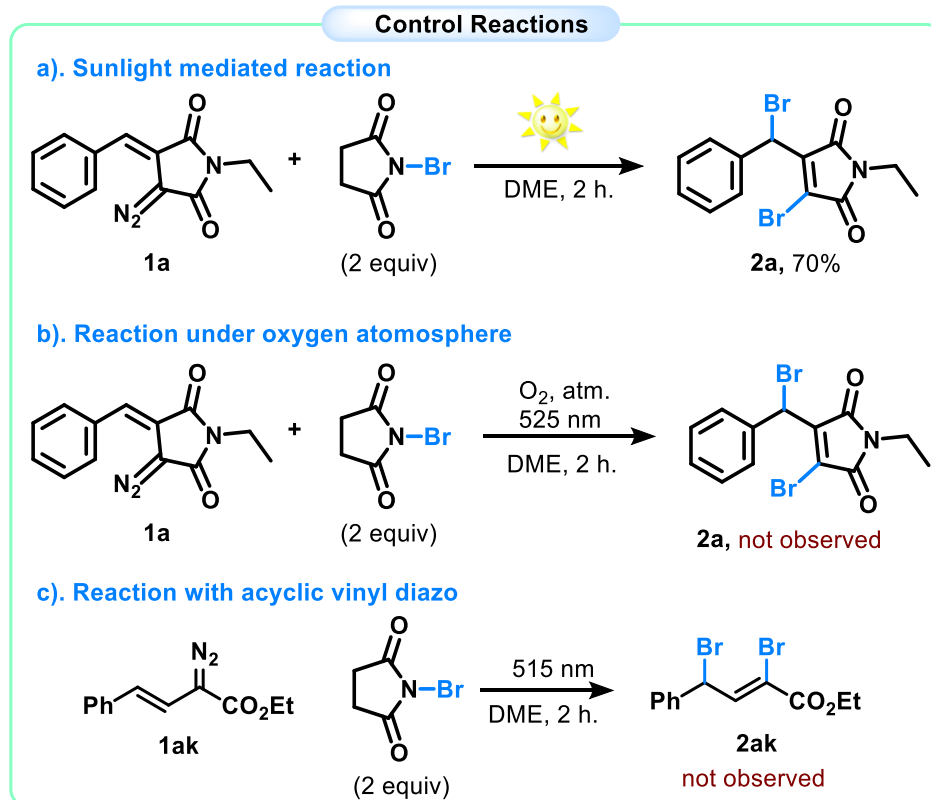


Scheme 4.4: Substrate scope of various DASSs, ^aGeneral reaction conditions: Diazo Arylidene Succinimides **1** (1.0 equiv., 0.2 mmol), NBS (2.0 equiv., 0.4 mmol), in DME (0.055 M) under nitrogen (degassed) at room temperature (28 °C) under green light 525 nm upto 1 h.

4.4 Control Reactions

The reaction of **1a** was subsequently performed under direct exposure of natural sunlight as the light source, and we gratifyingly obtained the desired product **2a**, in good yield (Scheme 4.5-a). The reaction carried out in an oxygen-rich atmosphere did not furnish the desired product **2a**. Indicating that oxygen may interfering in the reaction pathway to inhibit the formation of the desired product (Scheme 4.5-b). Additionally, acyclic vinyl diazo compound **1ak** was subjected to the standard reaction condition so as substrate to evaluate their potential for 1,3-dibromination reaction. Surprisingly, unlike the cyclic diazo compounds like DAS, acyclic vinyl

diazo compound **1ak** did not afford the corresponding 1,3-dibromination product **2ak** and the starting material neither consumed nor decomposed (Scheme 4.5-c). This result highlights the incompatibility of acyclic vinyl diazo compounds for established reaction conditions while emphasizing the notable and specific reactivity of DASs.

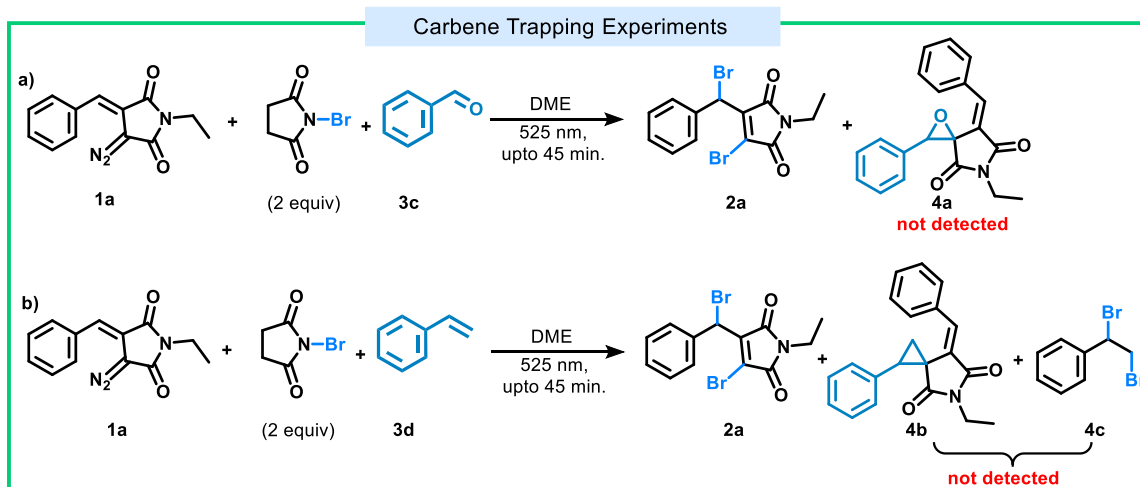


Scheme 4.5. Control Reactions

4.5 Control Experiments and Mechanistic Investigation

To better understand the reaction pathway, we further conducted several control experiments. To begin with, to investigate whether the reaction proceeds via a classical carbene intermediate (metallo-carbene), we treated DAS **1a** with benzaldehyde **3c**^{21d} under the standard reaction conditions. However, we did not observe the corresponding epoxide product **4a**, even in trace, instead we obtain the 1,3-dibromination product **2a** (Scheme 4.6-a). This result clearly indicates that reaction doesn't proceed via carbene intermediate. Later we treated the DAS **1a** with styrene **3d** to trap carbene intermediate if any. However, we did not observe any cyclopropanation product **4b** and also surprisingly we did not observe any dibromination product emanating from the reaction of styrene **4c** (Scheme 4.6b). However, we isolated the 1,3-dibromination product **2a** exclusively (Scheme 4.6b). This result further supported that the reaction does not likely involve a carbene intermediate during the course of the reactions and

suggests an alternative reaction pathway involving the an intermediate other than carbene intermediate.



Scheme 4.6: Carbene Trapping Experiments

In order to investigate whether or not radical is being generated during the course of the reaction, we conducted electron paramagnetic resonance (EPR) spectroscopy analysis on the reaction mixture before and after light irradiation. The EPR analysis of an incomplete reaction mixture comprising DAS **1a** and NBS in DME revealed the presence of a radical during the course of the reaction. The *g*-value at the peak's crossover point is 2.56, which is more characteristic of a bromine radical rather than a carbon radical.²² As a measure of a radical's magnetic properties, the *g*-value tends to be higher for bromine radicals compared to most carbon radicals (Figure 4.2).

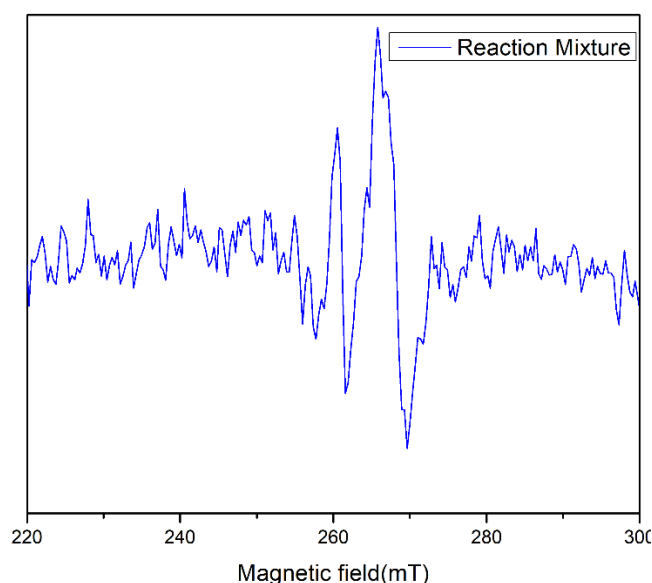


Figure 4.2: EPR spectrum of the reaction mixture

Additionally, we performed electron paramagnetic resonance (EPR) analysis on the incomplete reaction mixture of DAS **1a**, NBS, and PBN (phenyl-N-tert-butyl nitron). Phenyl-N-tert-butyl nitron (PBN) is a spin-trapping agent commonly employed in EPR spectroscopy to detect short-lived radicals, if any, generated in situ. Interestingly, we detect a signal in the EPR spectroscopy, and the g-value at the crossover point was measured at 2.002, indicating that the carbon radical was trapped by the spin trap PBN (N-tert-butyl- α -phenylnitron). The resulting spin adduct typically exhibits a g-value of 2.002, which shows that nitroxide radicals,²³ confirming the nature of the spin adduct formed in this case (Figure 4.3).

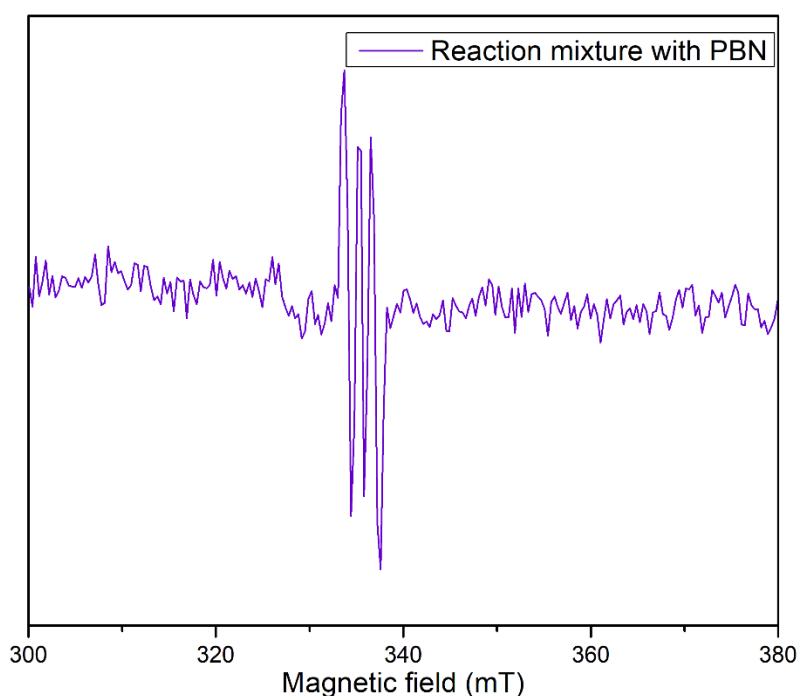


Figure 4.3: EPR spectrum of the spin adduct with PBN

Later, we carried out several controlled experiments to validate the radical formation under different conditions:

- DAS **1a** + NBS before light irradiation.
- DAS **1a** + NBS after 10 minutes of irradiation of green light (525 nm LED).
- DAS **1a** + NBS + phenyl-N-tert-butyl nitron (PBN) before light irradiation.
- DAS **1a** + NBS + phenyl-N-tert-butyl nitron (PBN) after 10 minutes of light irradiation.

Notably, we did not observe any signal specific to radical underscoring. This indicates that light is essential for initiating the reaction through the generation of the radical in situ (Figure 4.4). Later, We utilized the phenyl-*N*-tert-butyl nitron (PBN) is a spin-trapping agent commonly employed in EPR spectroscopy to detect and characterize transient free radicals. Initially, we recorded the EPR spectrum of the reaction mixture containing DAS **1a**, NBS, and PBN (without shining light), and we did not observe any signal in the EPR spectroscopy (Figure 4.4c). Later, the reaction mixture containing DAS **1a**, NBS, and PBN was exposed to green LEDs for 10 minutes, and the EPR spectrum was re-recorded. As expected, we observed the spectrum, which clearly proves that the radical generated in situ was trapped by PBN (Figure 4.4-d). This finding validates the efficiency of PBN to identify short-lived radical species.

Based on the control experimental results, it is very clear that light is crucial to drive the reaction, and the light induces the formation of radical species, which in turn facilitate the 1,3-dibromination product. These control experiments, coupled with the EPR spectroscopy, gave insight into the mechanistic pathway.

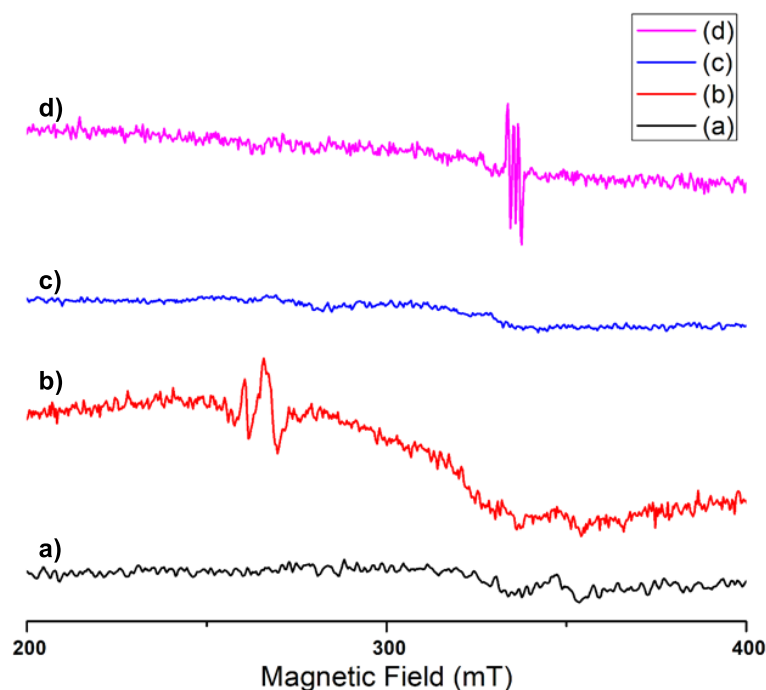
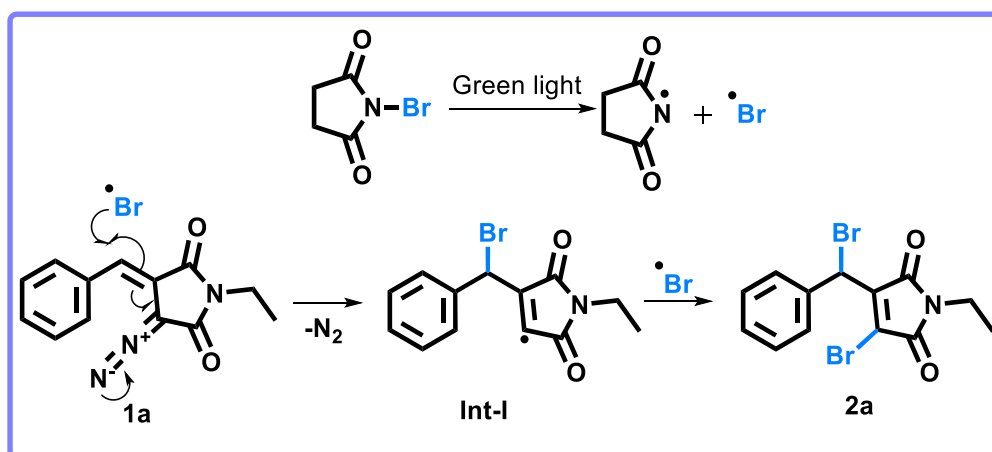


Figure 4.4: EPR spectrum of control experiments

4.6 Proposed Mechanism

Based on the inference observed through the control experimental results and literature precedence,²⁴ most plausible mechanisms have been proposed. NBS (*N*-bromosuccinimide), upon the irradiation of visible light (525 nm, Green LEDs), undergoes homolytic cleavage to form bromine radical and the corresponding succinimide nitrogen radical. This highly reactive bromine radical interacts with DAS **1a**, which acts as a radical acceptor, initiating a key transformation by the extrusion of nitrogen and forming the corresponding bromo-inserted vinylic radical DAS intermediate **Int-I**. This intermediate **Int-I** further reacts with another bromine radical to afford the final desired product **2a**.

This proposed mechanism highlights the importance of bromine radicals and the radical-accepting behaviour of DAS for facilitating the interesting synthetic transformation in the absence of a photocatalyst or an additive.



Scheme 4.7: Proposed mechanism

4.7 Conclusion

In summary, we have developed a simple yet efficient and eco-friendly protocol for the 1,3-dibromination of diazo arylidene succinimides (DASs) using *N*-bromosuccinimides (NBS) as a safer alternative brominating agent under visible light conditions. Notably, this methodology does not rely on the photocatalysts or additional reagents, works smoothly under the clean energy of visible light, thus making it a highly sustainable and efficient transformation. The reaction proceeds under mild conditions to afford 1,3-dibromination products in good to excellent yield. This simple and practical method proved to be practical as it did not use any hazardous brominating agent, explored the use of safer and cost-effective solid reagents such

as NBS to achieve the efficient debromination of DAS selectively. Also, importantly, the protocol worked smoothly and efficiently under direct exposure to sunlight, thus broadening the scope of the protocol.

4.8 Experimental section:

4.8.1 General information:

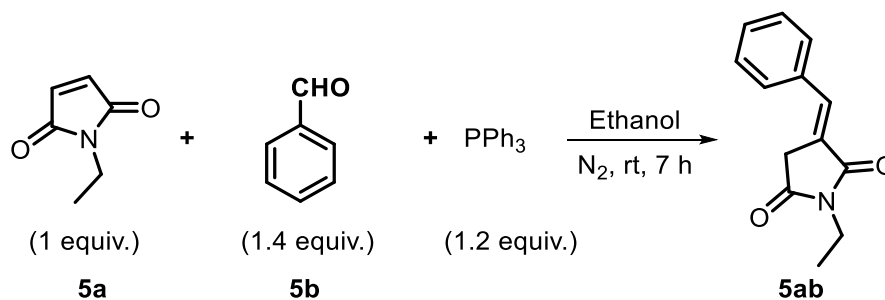
Reagent Information: All reactions were carried out with distilled and A.R. grade solvents using oven-dried glassware under a dry Argon atmosphere unless otherwise stated. All the reagents were purchased from commercial sources and used as received unless otherwise indicated. Thin-layer chromatography (TLC) was performed using silica gel 60 GF₂₅₄ pre-coated aluminum-backed plates (2.5 mm) with detection by UV light. Column chromatographic purification of products was carried out using silica gel (100-200 mesh). The mixture of petroleum ether and ethyl acetate was used as a gradient elution for column chromatography.

Analytical Information: All isolated compounds were characterized by ¹H NMR, and ¹³C{¹H} NMR spectra were recorded on a 400 MHz Jeol ECS-400 and Bruker Avance III HD Ascend 400 MHz spectrometers. Nuclear Magnetic Resonance spectra were recorded in CDCl₃. The NMR spectra were recorded using tetramethyl silane (TMS) as the internal standard. ¹H NMR spectra were recorded at 400 MHz, and ¹³C{¹H} NMR spectra were recorded at 100 MHz (Bruker), unless otherwise noted. Chemical shifts (δ) are reported in ppm downfield from CDCl₃ (δ = 7.26 ppm) and from DCM-*d*₂ (δ = 5.32 ppm) for ¹H NMR and relative to the central CDCl₃ resonance (δ = 77.16 ppm) and DCM-*d*₂ resonance (δ = 54.00 ppm) for ¹³C{¹H} NMR spectroscopy. For ¹H NMR, data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = double doublet, t = triplet, q = quartet, m = multiplet), coupling constants (*J*) are given in Hz and integration. ¹³C{¹H} NMR spectra were recorded with complete proton decoupling. ¹⁹F NMR spectra were recorded at 377 MHz. Mass samples were analysed by high-resolution mass spectrometry (HRMS) using ESI TOF. Single crystal X-ray diffraction data were collected on a Bruker SMART APEX four-circle diffractometer equipped with a CMOS photon 100 detector (Bruker Systems Inc.) with Microfocus (I μ S) using Mo K α radiation (0.71073 Å).

Photoreactor Setup: Light-mediated reactions studies were carried out in a locally fabricated photoreactor designed in our lab. Green (emission maximum at 525 nm) light was supplied to

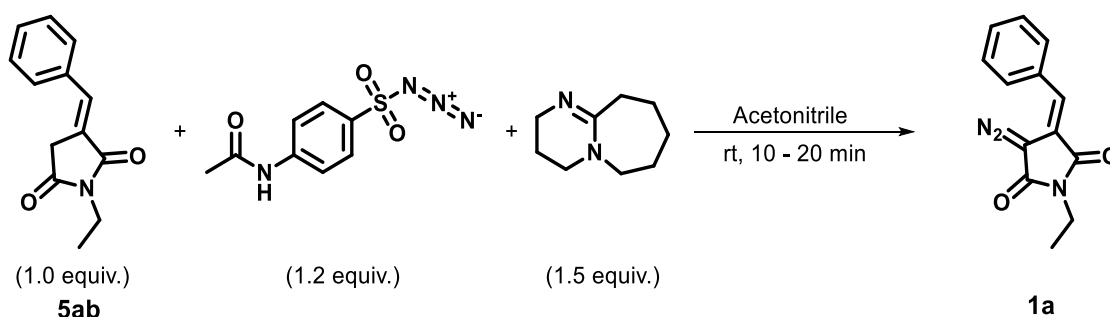
each reaction vial with the use of Kessil lamp (40 W with 50% intensity when power applied) with stirring at a distance of ~5 cm (with cooling using fan) while maintaining the temperature at 28 °C.

4.8.2. General procedure-A for the synthesis of vinyl succinimides (**5ab**):



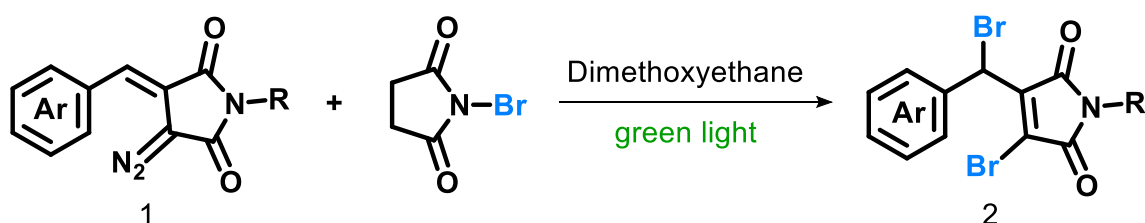
To the stirred solution of *N*-ethyl maleimide **5a** (0.5 g, 1.0 equiv., 4.0 mmol) in ethanol (20 mL) was added triphenylphosphine (1.26 g, 1.2 equiv., 4.8 mmol) portion-wise at room temperature under N_2 atmosphere. The initial pink-coloured reaction mixture slowly turned to white suspension over a period of 10-15 minutes of stirring. After the continuous stirring for over 30 min, benzaldehyde **5b** (571 μL , 1.4 equiv., 6.0 mmol) was added in one portion into the reaction mixture at room temperature. During this addition, the white suspension slowly turned into a clear solution. The reaction mixture was allowed to stir for 6 h. Upon completion of the reaction (monitored by TLC), the white solid formed during the course of the reaction was filtered through a sintered glass funnel and was washed with ethanol (6 mL x 2). The crude product **5ab** was obtained as a white solid (700 mg, 81% yield) and used for the next step without further purification.^[23]

4.8.3. General Procedure-B for the synthesis of vinyl diazosuccinimide(**1a**):



To the stirred solution of (*E*)-3-benzylidene-1-ethylpyrrolidine-2,5-dione **5ab** (2.15 g, 1.0 equiv., 10 mmol) in 30 mL acetonitrile, were added 4-acetamidobenzenesulfonyl azide (2.88 g, 1.2 equiv., 12 mmol) and DBU (2.24 mL, 1.5 equiv., 15 mmol) at 0 °C temperature under inert atmosphere. The reaction mixture was stirred for 10 minutes while maintaining the reaction temperature (0 °C). The reaction mixture was then quenched with saturated solution of NH₄Cl and the product was extracted with diethyl ether (30 mL x 3). The combined organic layer was washed with brine solution and dried over anhydrous Na₂SO₄. The extract was filtered and evaporated under reduced pressure. The crude product was purified using column chromatography over silica gel to afford (*E*)-3-benzylidene-4-diazo-1-ethylpyrrolidine-2,5-dione **1a** as orange solid (2.257 g, 94% yield).^[2]

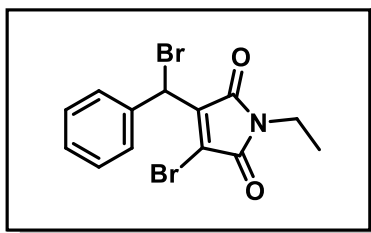
4.8.4. General procedure-C for the visible light promoted 1,3-dibromination of DASs



To a reaction tube equipped with a magnetic stir bar were added diazo compound **1a** (1.0 equiv., 0.1 mmol), NBS (2 equiv.) in DME (0.055 M). The tube was capped with a rubber septum, and the mixture was degassed by purging with nitrogen gas. The resulting solution was irradiated by 525 nm Green LEDs with stirring at a distance of ~5 cm (with cooling using fan) at 28 °C (measured using IR sensor Thermometer) for about 2 h until the diazo compound **1** was completely consumed (as monitored by TLC analysis). The reaction mixture was evaporated under reduced pressure. The crude mixture was purified over column chromatography using silica gel with hexanes/ethyl acetate mixture as an eluent to obtain the corresponding product **2** colourless liquid.

4.8.5 Characterization of synthesized compounds:

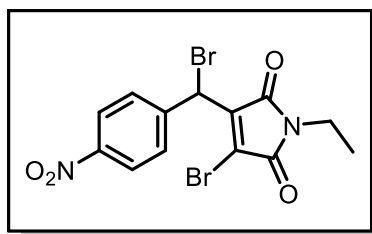
3-bromo-4-(bromo(phenyl)methyl)-1-ethyl-1*H*-pyrrole-2,5-dione (2a): Compound **2a** was



synthesized following the general procedure-C. The product was obtained as colourless liquid, 30 mg (80% yield); $R_f=0.6$ (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): δ 7.66 – 7.56 (m, 2H), 7.42 – 7.28 (m, 3H), 6.11 (s, 1H), 3.62 (q, $J = 7.2$ Hz, 2H), 1.21 (t, $J = 7.2$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$

NMR (100 MHz, CDCl_3): δ 166.9, 164.5, 141.6, 135.6, 129.3, 129.0, 128.6, 126.5, 41.0, 34.3, 14.0. HRMS (ESI TOF) m/z : calcd for $\text{C}_{13}\text{H}_{12}\text{Br}_2\text{NO}_2$ ($\text{M} + \text{H}$) $^+$: 371.9235, Found: 371.9230.

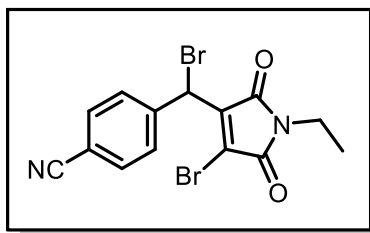
3-bromo-4-(bromo(4-nitrophenyl)methyl)-1-ethyl-1*H*-pyrrole-2,5-dione (2b): Compound



2b was synthesized following the general procedure-C. The product was obtained as colourless liquid, 41 mg (98% yield); $R_f=0.35$ (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): δ 8.27 – 8.15 (m, 2H), 7.87 – 7.75 (m, 2H), 6.15 (s, 1H), 3.63 (q, $J = 7.2$ Hz, 2H), 1.22 (t, $J = 7.2$ Hz,

3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 166.6, 164.0, 148.2, 142.18, 140.6, 129.8, 127.6, 124.1, 39.3, 34.5, 13.9. HRMS (ESI TOF) m/z : calcd for $\text{C}_{13}\text{H}_{11}\text{Br}_2\text{N}_2\text{O}_4$ ($\text{M} + \text{H}$) $^+$: 416.9086, Found: 416.9085.

4-(bromo(4-bromo-1-ethyl-2,5-dioxo-2,5-dihydro-1*H*-pyrrol-3-yl)methyl)benzonitrile

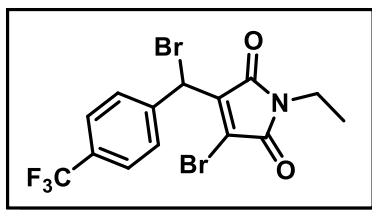


(2c): Compound **2c** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 18 mg (45% yield); $R_f=0.3$ (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): δ 7.78 – 7.71 (m, 2H), 7.71 – 7.62 (m, 2H), 6.10 (s, 1H), 3.62 (q, $J = 7.2$ Hz, 2H), 1.22 (t, $J = 7.2$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 166.6,

164.0, 140.6, 140.4, 132.7, 129.5, 127.5, 118.2, 113.2, 39.7, 34.5, 13.9. HRMS (ESI TOF) m/z : calcd for $\text{C}_{14}\text{H}_{11}\text{Br}_2\text{N}_2\text{O}_2$ ($\text{M} + \text{H}$) $^+$: 396.9187, Found: 396.9187.

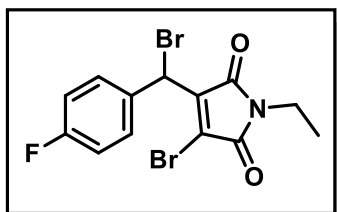
3-bromo-4-(bromo(4-(trifluoromethyl)phenyl)methyl)-1-ethyl-1*H*-pyrrole-2,5-dione

(2d): Compound **2d** was synthesized following the general procedure-C. The product was obtained as white solid, 29 mg (65% yield); $R_f=0.45$ (petroleum ether/EtOAc 90:10)



¹H NMR (400 MHz, CDCl₃): δ 7.75 (d, *J* = 8.2 Hz, 2H), 7.63 (d, *J* = 8.3 Hz, 2H), 6.12 (s, 1H), 3.63 (q, *J* = 7.2 Hz, 2H), 1.22 (t, *J* = 7.2 Hz, 3H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 166.7, 164.2, 141.0, 139.3, 131.4 (q, *J* = 32.8 Hz), 129.1, 127.9, 126.0 (q, *J* = 3.8 Hz), 127.9 – 119.5 (m), 39.8, 34.4, 13.9. **¹⁹F NMR (377 MHz, CDCl₃):** δ -62.8. **HRMS (ESI TOF) *m/z*:** calcd for C₁₄H₁₁Br₂F₃NO₂ (M + H)⁺: 439.9109, Found: 439.9105.

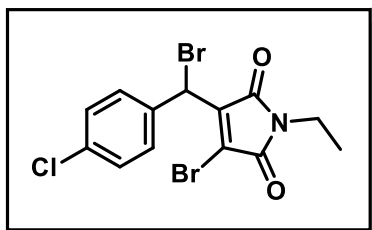
3-bromo-4-(bromo(4-fluorophenyl)methyl)-1-ethyl-1H-pyrrole-2,5-dione (2e): Compound



2e was synthesized following the general procedure-C. The product was obtained as colourless liquid, 23.5 mg (60% yield); *R_f*=0.6 (petroleum ether/EtOAc 90:10); **¹H NMR (400 MHz, CDCl₃):** δ 7.66 – 7.56 (m, 2H), 7.11 – 7.00 (m, 2H), 6.07 (s, 1H), 3.62 (q, *J* = 7.2 Hz, 2H), 1.22 (t, *J* = 7.2 Hz, 3H).; **¹³C{¹H} NMR**

(100 MHz, CDCl₃): δ 166.8, 164.3, 163.0 (d, *J* = 249.7 Hz), 141.4, 131.4 (d, *J* = 3.3 Hz), 130.6 (d, *J* = 8.4 Hz), 126.4, 116.0 (d, *J* = 22.0 Hz), 40.2, 34.4, 13.9. **¹⁹F NMR (377 MHz, CDCl₃):** δ -111.82. **HRMS (ESI TOF) *m/z*:** calcd for C₁₃H₁₁Br₂FNO₂ (M + H)⁺: 389.9141, Found: 389.9150.

3-bromo-4-(bromo(4-chlorophenyl)methyl)-1-ethyl-1H-pyrrole-2,5-dione (2f): Compound

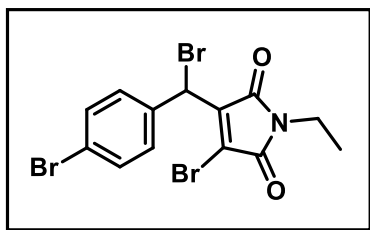


2f was synthesized following the general procedure-C. The product was obtained as colourless liquid, 25.5mg (62% yield); *R_f*=0.6 (petroleum ether/EtOAc 90:10); **¹H NMR (400 MHz, CDCl₃):** δ 7.60 – 7.52 (m, 2H), 7.38 – 7.30 (m, 2H), 6.06 (s, 1H), 3.62 (q, *J* = 7.2 Hz, 2H), 1.21 (t, *J* = 7.2 Hz, 3H).

¹³C{¹H} NMR (100 MHz, CDCl₃): δ 166.8, 164.3, 141.2, 135.3, 134.0, 130.0, 129.2, 126.7, 40.1, 34.4, 13.9. **HRMS (ESI TOF) *m/z*:** calcd for C₁₃H₁₁Br₂ClNO₂ (M + H)⁺: 405.8825, Found: 405.8825.

3-bromo-4-(bromo(4-bromophenyl)methyl)-1-ethyl-1H-pyrrole-2,5-dione (2g):

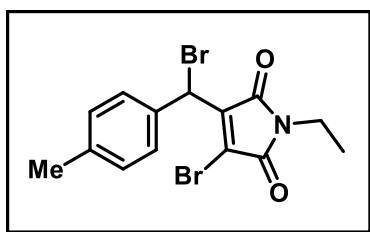
Compound **2g** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 30mg (65% yield); *R_f*=0.55 (petroleum ether/EtOAc 90:10)



¹H NMR (400 MHz, CDCl₃): δ 7.50 (s, 4H), 6.04 (s, 1H), 3.62 (q, *J* = 7.2 Hz, 2H), 1.21 (t, *J* = 7.2 Hz, 3H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 166.8, 164.3, 141.2, 134.6, 132.2, 130.3, 126.7, 123.5, 40.2, 34.4, 13.5. **HRMS (ESI TOF) *m/z*:** calcd for C₁₃H₁₁Br₃NO₂ (*M* + *H*)⁺: 449.8340,

Found: 49.8343.

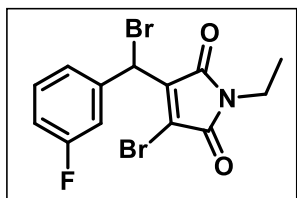
3-bromo-4-(bromo(p-tolyl)methyl)-1-ethyl-1*H*-pyrrole-2,5-dione (2h): Compound **2h** was



synthesized following the general procedure-C. The product was obtained as colourless liquid, 17 mg (43% yield); *R_f*=0.5 (petroleum ether/EtOAc 90:10); **¹H NMR (400 MHz, CDCl₃):** δ 7.53 – 7.47 (m, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 6.08 (s, 1H), 3.62 (q, *J* = 7.2 Hz, 2H), 2.35 (s, 3H), 1.21 (t, *J* = 7.2

Hz, 3H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 166.94, 164.5, 141.7, 139.4, 132.6, 129.7, 128.5, 126.2, 41.1, 34.3, 21.3, 13.9. **HRMS (ESI TOF) *m/z*:** calcd for C₁₄H₁₄Br₂NO₂ (*M* + *H*)⁺: 385.9391, Found: 385.9394.

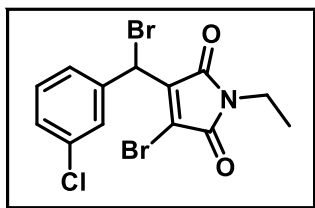
3-bromo-4-(bromo(3-fluorophenyl)methyl)-1-ethyl-1*H*-pyrrole-2,5-dione (2j): Compound



2j was synthesized following the general procedure-C. The product was obtained as colourless liquid, 29 mg (74% yield); *R_f*=0.55 (petroleum ether/EtOAc 90:10); **¹H NMR (400 MHz, CDCl₃):** δ 7.40 (dq, *J* = 9.1, 1.8 Hz, 1H), 7.36 – 7.31 (m, 2H), 7.08 – 6.99 (m,

1H), 6.07 (s, 1H), 3.63 (q, *J* = 7.2 Hz, 2H), 1.22 (t, *J* = 7.2 Hz, 3H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 166.7, 164.3, 162.8 (d, *J* = 247.7 Hz), 141.2, 137.8 (d, *J* = 7.6 Hz), 130.5 (d, *J* = 8.4 Hz), 126.9, 124.1 (d, *J* = 3.1 Hz), 116.3 (d, *J* = 15.2 Hz), 116.1 (d, *J* = 17.6 Hz), 39.9, 39.9, 34.4, 13.9. **¹⁹F NMR (377 MHz, CDCl₃):** δ -111.3. **HRMS (ESI TOF) *m/z*:** calcd for C₁₃H₁₀Br₂FNO₂ (*M* + *H*)⁺: 388.9062, Found: 388.9065.

3-bromo-4-(bromo(3-chlorophenyl)methyl)-1-ethyl-1*H*-pyrrole-2,5-dione (2k):

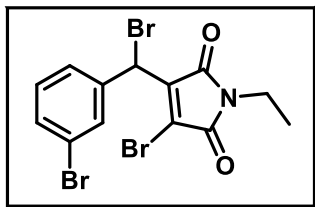


Compound **2k** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 34 mg (83% yield); *R_f*=0.6 (petroleum ether/EtOAc 90:10); **¹H NMR (400 MHz, CDCl₃):** δ 7.61 (d, *J* = 2.0 Hz, 1H), 7.52 – 7.46 (m, 1H), 7.31 (dd, *J* = 4.9, 1.8 Hz, 2H), 6.05 (s, 1H), 3.63 (q, *J* = 7.2 Hz,

2H), 1.22 (t, *J* = 7.2 Hz, 3H). **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 166.8, 164.3, 141.1, 137.4,

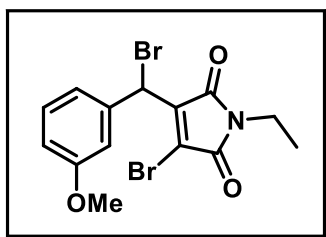
134.9, 130.2, 129.4, 128.8, 127.0, 126.8, 39.8, 34.4, 13.9. **HRMS (ESI TOF) m/z :** calcd for $C_{13}H_{11}Br_2ClNO_2$ ($M + H$)⁺: 405.8845, Found: 405.8840.

3-bromo-4-(bromo(3-bromophenyl)methyl)-1-ethyl-1H-pyrrole-2,5-dione (2l):



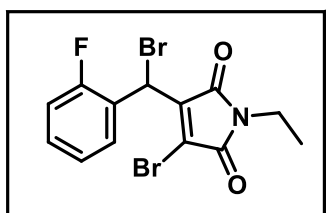
Compound **2l** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 27 mg (60% yield); R_f =0.45 (petroleum ether/EtOAc 90:10); **1H NMR (400 MHz, $CDCl_3$):** δ 7.75 (t, J = 2.0 Hz, 1H), 7.60 – 7.51 (m, 1H), 7.47 (ddd, J = 8.0, 2.0, 1.0 Hz, 1H), 7.24 (t, J = 7.4 Hz, 1H), 6.03 (s, 1H), 3.62 (q, J = 7.2 Hz, 2H), 1.22 (t, J = 7.2 Hz, 3H). **$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$):** δ 166.7, 164.3, 141.1, 137.6, 132.4, 131.6, 130.5, 127.3, 127.0, 122.9, 39.7, 34.4, 13.9. **HRMS (ESI TOF) m/z :** calcd for $C_{13}H_{11}Br_3NO_2$ ($M + H$)⁺: 449.8340, Found: 449.9354.

3-bromo-4-(bromo(3-methoxyphenyl)methylene)-1-ethylpyrrolidine-2,5-dione (2m):



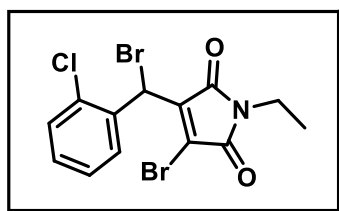
Compound **2m** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 15.5 mg (38% yield); R_f =0.4 (petroleum ether/EtOAc 90:10); **1H NMR (400 MHz, $CDCl_3$):** δ 7.32 – 7.25 (m, 1H), 7.24 (t, J = 2.2 Hz, 1H), 7.19 – 7.11 (m, 1H), 6.88 (dt, J = 8.2, 1.6 Hz, 1H), 6.08 (s, 1H), 3.84 (s, 3H), 3.63 (q, J = 7.2 Hz, 2H), 1.23 (t, J = 7.2 Hz, 3H). **$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$):** δ 166.9, 164.4, 160.0, 141.5, 137.0, 130.0, 126.5, 120.6, 114.8, 114.5, 55.5, 40.9, 34.3, 13.9. **HRMS (ESI TOF) m/z :** calcd for $C_{14}H_{14}Br_2NO_3$ ($M + H$)⁺: 401.9340, Found: 401.9349.

3-bromo-4-(bromo(2-fluorophenyl)methyl)-1-ethyl-1H-pyrrole-2,5-dione (2n):



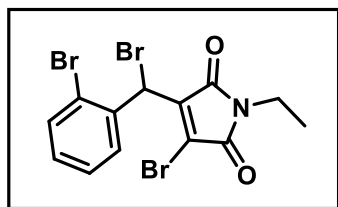
Compound **2n** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 33 mg (84% yield); R_f =0.55 (petroleum ether/EtOAc 90:10); **1H NMR (400 MHz, $CDCl_3$):** δ 7.97 (td, J = 7.8, 1.7 Hz, 1H), 7.35 (dddd, J = 8.2, 7.1, 5.2, 1.8 Hz, 1H), 7.22 (td, J = 7.7, 1.2 Hz, 1H), 7.03 (ddd, J = 10.5, 8.2, 1.2 Hz, 1H), 3.67 – 3.56 (m, 2H), 1.21 (t, J = 7.2 Hz, 3H). **$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$):** δ 166.7, 164.4, 159.3 (d, J = 248.9 Hz), 141.0, 132.3 (d, J = 1.8 Hz), 131.1 (d, J = 8.4 Hz), 126.6, 124.7 (d, J = 3.7 Hz), 122.6 (d, J = 12.4 Hz), 115.5 (d, J = 21.4 Hz), 34.3, 34.2 (d, J = 4.9 Hz), 13.9. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -114.9. **HRMS (ESI TOF) m/z :** calcd for $C_{13}H_{11}Br_2FNO_2$ ($M + H$)⁺: 389.9141, Found: 389.9145.

3-bromo-4-(bromo(2-chlorophenyl)methyl)-1-ethyl-1H-pyrrole-2,5-dione (2o):



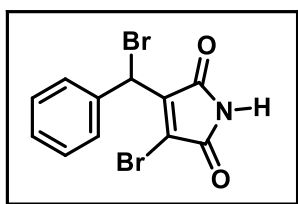
Compound **2o** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 34.5 mg (84% yield); R_f =0.55 (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): δ 8.12 (dd, J = 7.7, 1.7 Hz, 1H), 7.41 – 7.27 (m, 3H), 6.46 (s, 1H), 3.62 (qd, J = 7.2, 1.0 Hz, 2H), 1.21 (t, J = 7.2 Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 166.8, 164.5, 140.8, 133.1, 132.5, 132.5, 130.5, 129.6, 127.4, 126.7, 38.5, 34.3, 13.9. HRMS (ESI TOF) m/z : calcd for $\text{C}_{13}\text{H}_{11}^{81}\text{Br}_2\text{ClNO}_2$ ($\text{M} + \text{H}$) $^+$: 409.8804, Found: 409.8806.

3-bromo-4-(bromo(2-bromophenyl)methyl)-1-ethyl-1H-pyrrole-2,5-dione (2p):



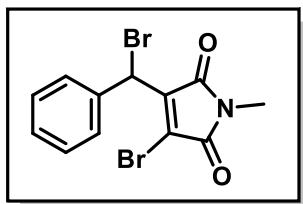
Compound **2p** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 32 mg (71% yield); R_f =0.6 (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): δ 8.14 (dd, J = 8.0, 1.6 Hz, 1H), 7.62 – 7.51 (m, 1H), 7.42 (td, J = 7.7, 1.3 Hz, 1H), 7.22 (td, J = 7.7, 1.6 Hz, 1H), 6.42 (s, 1H), 3.62 (qd, J = 7.2, 1.0 Hz, 2H), 1.22 (t, J = 7.2 Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 166.8, 164.5, 140.8, 134.1, 133.4, 133.0, 130.7, 128.0, 126.7, 122.6, 41.1, 34.3, 14.0. HRMS (ESI TOF) m/z : calcd for $\text{C}_{13}\text{H}_{11}\text{Br}_3\text{NO}_2$ ($\text{M} + \text{H}$) $^+$: 449.8340, Found: 449.8338.

3-bromo-4-(bromo(phenyl)methyl)-1H-pyrrole-2,5-dione (2q):



Compound **2q** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 20 mg (60% yield); R_f =0.4 (petroleum ether/EtOAc 80:20); ^1H NMR (400 MHz, CDCl_3): δ 8.01 (s, 1H), 7.63 – 7.57 (m, 2H), 7.41 – 7.30 (m, 3H), 6.09 (s, 1H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 166.5, 164.0, 142.7, 135.2, 129.3, 129.0, 128.5, 127.0, 40.7. HRMS (ESI TOF) m/z : calcd for $\text{C}_{11}\text{H}_8\text{Br}_2\text{NO}_2$ ($\text{M} + \text{H}$) $^+$: 343.8922, Found: 343.8920.

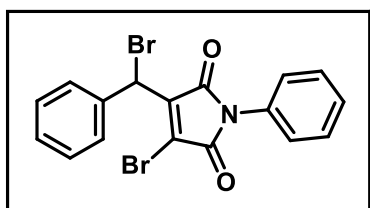
3-bromo-4-(bromo(phenyl)methyl)-1-methyl-1H-pyrrole-2,5-dione (2r):



Compound **2r** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 27 mg (75% yield); R_f =0.55 (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): δ 7.66 – 7.56 (m, 2H), 7.42 – 7.28 (m, 3H), 6.11 (s, 1H), 3.23 (s, 3H),

$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 166.9, 164.5, 141.6, 135.6, 129.3, 129.0, 128.6, 126.5, 41.0, 26.3. HRMS (ESI TOF) m/z : calcd for $\text{C}_{12}\text{H}_{10}\text{Br}_2\text{NO}_2$ ($\text{M} + \text{H}$) $^+$: 357.9078, Found: 357.9080.

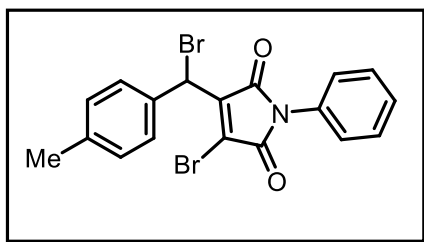
3-bromo-4-(bromo(phenyl)methyl)-1-phenyl-1H-pyrrole-2,5-dione (2s): Compound **2s**



was synthesized following the general procedure-C. The product was obtained as colourless liquid, 30 mg (70% yield); R_f =0.6 (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): δ 7.71 – 7.63 (m, 2H), 7.46 (dd, J = 8.3, 6.8 Hz, 2H), 7.43 – 7.31 (m, 6H), 6.20 (s, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz,

CDCl_3): δ 165.9, 163.5, 141.6, 135.3, 131.0, 129.4, 129.3, 129.1, 128.7, 128.5, 126.9, 126.1, 41.0. HRMS (ESI TOF) m/z : calcd for $\text{C}_{17}\text{H}_{12}\text{Br}_2\text{NO}_2$ ($\text{M} + \text{H}$) $^+$: 419.9235, Found: 419.9230.

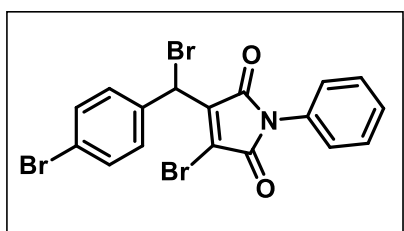
3-bromo-4-(bromo(p-tolyl)methyl)-1-phenyl-1H-pyrrole-2,5-dione (2t): Compound **2t** was



synthesized following the general procedure-C. The product was obtained as colourless liquid, 28.5 mg (65% yield); R_f =0.55 (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): δ 7.62 – 7.51 (m, 2H), 7.51 – 7.42 (m, 2H), 7.42 – 7.31 (m, 3H), 7.22 – 7.15 (m, 2H), 6.17

(s, 1H), 2.36 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) δ 165.9, 163.6, 141.7, 139.5, 132.5, 131.1, 129.8, 129.3, 128.6, 128.5, 126.6, 126.1, 41.0, 21.3. HRMS (ESI TOF) m/z : calcd for $\text{C}_{18}\text{H}_{14}\text{Br}^{81}\text{BrNO}_2$ ($\text{M} + \text{H}$) $^+$: 435.9371, Found: 435.9395.

3-bromo-4-(bromo(4-bromophenyl)methyl)-1-phenyl-1H-pyrrole-2,5-dione (2u):

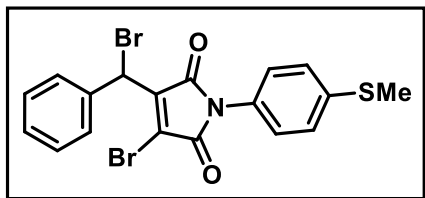


Compound **2u** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 38 mg (76% yield); R_f =0.6 (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): δ 7.58 – 7.50 (m, 4H), 7.47 (dd, J = 8.4, 6.9 Hz, 2H), 7.42 – 7.36 (m, 1H), 7.36 – 7.31

(m, 2H), 6.13 (s, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.8, 163.4, 141.2, 134.4, 132.2,

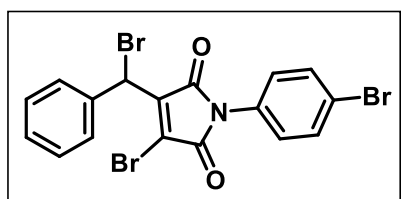
130.9, 130.4, 129.4, 128.6, 127.1, 126.1, 123.6, 40.11. **HRMS (ESI TOF) m/z :** calcd for $C_{17}H_{11}Br_3NO_2$ ($M + H$)⁺: 497.8340, Found: 497.8345.

3-bromo-4-(bromo(phenyl)methyl)-1-(4-(methylthio)phenyl)-1H-pyrrole-2,5-dione (2v):



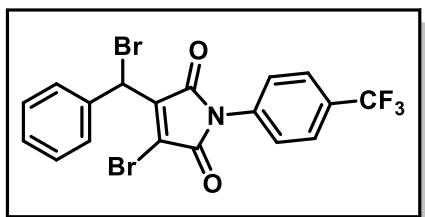
Compound **2v** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 33 mg (70% yield); R_f = 0.55 (petroleum ether/EtOAc 90:10); **1H NMR (400 MHz, $CDCl_3$):** δ 7.68 – 7.62 (m, 2H), 7.43 – 7.32 (m, 3H), 7.34 – 7.26 (m, 2H), 7.29 – 7.22 (m, 2H), 6.18 (s, 1H), 2.48 (s, 3H). **$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$):** δ 165.9, 163.5, 141.7, 139.5, 135.3, 129.4, 129.1, 128.7, 127.8, 126.9, 126.9, 126.4, 40.9, 15.8. **HRMS (ESI TOF) m/z :** calcd for $C_{18}H_{14}Br_2NO_2S$ ($M + H$)⁺: 465.9112, Found: 465.9110.

3-bromo-4-(bromo(phenyl)methyl)-1-(4-bromophenyl)-1H-pyrrole-2,5-dione (2w):



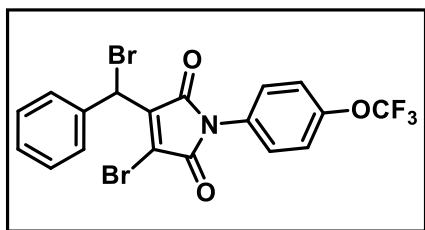
Compound **2w** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 38 mg (76% yield); R_f = 0.6 (petroleum ether/EtOAc 90:10); **1H NMR (400 MHz, $CDCl_3$):** δ 7.71 – 7.60 (m, 2H), 7.60 – 7.52 (m, 2H), 7.44 – 7.29 (m, 3H), 7.29 – 7.20 (m, 2H), 6.17 (s, 1H). **$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$):** δ 165.5, 163.2, 141.8, 135.2, 132.5, 130.1, 129.4, 129.1, 128.7, 127.4, 126.9, 122.2, 40.9. **HRMS (ESI TOF) m/z :** calcd for $C_{17}H_{11}Br_3NO_2$ ($M + H$)⁺: 497.8340, Found: 497.8346.

3-bromo-4-(bromo(phenyl)methyl)-1-(4-(trifluoromethyl)phenyl)-1H-pyrrole-2,5-dione (2x):



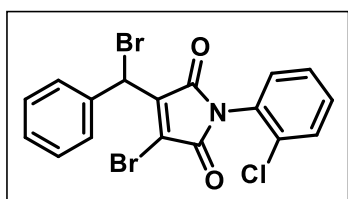
Compound **2x** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 32.5 mg (66% yield); R_f = 0.45 (petroleum ether/EtOAc 90:10); **1H NMR (400 MHz, $CDCl_3$):** δ 7.73 (d, J = 8.5 Hz, 2H), 7.70 – 7.59 (m, 2H), 7.55 (d, J = 8.4 Hz, 2H), 7.46 – 7.33 (m, 3H), 6.20 (s, 1H). **$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$):** δ 165.41, 163.09, 141.95, 135.09, 134.45 – 133.90 (m), 130.26 (d, J = 33.0 Hz), 129.48, 129.13, 128.67, 127.02, 126.46 (q, J = 3.7 Hz), 125.84, 127.94 – 119.86 (m), 40.81. **^{19}F NMR (377 MHz, $CDCl_3$):** δ -62.7. **HRMS (ESI TOF) m/z :** calcd for $C_{18}H_{11}Br_2F_3NO_2$ ($M + H$)⁺: 487.9109, Found: 487.9112.

3-bromo-4-(bromo(phenyl)methyl)-1-(4-(trifluoromethoxy)phenyl)-1H-pyrrole-2,5-



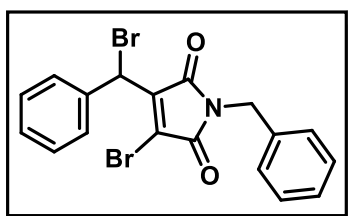
dione (2y): Compound **2y** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 25 mg (50% yield); R_f = 0.45 (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): δ 7.72 – 7.63 (m, 2H), 7.46 – 7.34 (m, 5H), 7.34 – 7.28 (m, 2H), 6.19 (s, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.6, 163.3, 149.2 – 148.0 (m), 141.9, 135.2, 129.5, 129.4, 129.1, 128.7, 127.4, 126.9, 121.8, 120.5 (q, J = 257.5 MHz), 40.9. ^{19}F NMR (377 MHz, CDCl_3): δ -57.9. HRMS (ESI TOF) m/z : calcd for $\text{C}_{18}\text{H}_{11}\text{Br}_2\text{F}_3\text{NO}_2$ ($\text{M} + \text{H}$) $^+$: 503.9058, Found: 503.9054.

3-bromo-4-(bromo(phenyl)methyl)-1-(2-chlorophenyl)-1H-pyrrole-2,5-dione (2z):



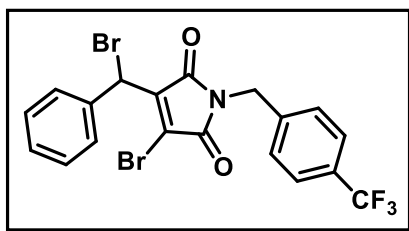
Compound **2z** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 23 mg (50% yield); R_f =0.65 (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): δ 7.66 (ddd, J = 7.6, 3.9, 1.7 Hz, 2H), 7.54 (ddd, J = 7.7, 4.6, 1.7 Hz, 1H), 7.46 – 7.35 (m, 5H), 7.29 (ddd, J = 12.1, 7.7, 2.0 Hz, 1H), 6.21 (d, J = 3.1 Hz, 1H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 165.3, 162.9, 162.9, 142.4, 142.2, 135.4, 135.1, 133.2, 133.2, 131.2, 130.7, 130.7, 130.6, 129.4, 129.3, 129.1, 129.1, 128.8, 128.7, 128.6, 127.9, 126.9, 126.9, 40.9, 40.9. HRMS (ESI TOF) m/z : calcd for $\text{C}_{17}\text{H}_{11}\text{Br}_2\text{ClNO}_2$ ($\text{M} + \text{H}$) $^+$: 453.8845, Found: 453.8840.

1-benzyl-3-bromo-4-(bromo(phenyl)methyl)-1H-pyrrole-2,5-dione (2aa): Compound **2aa**



was synthesized following the general procedure-C. The product was obtained as colourless liquid, 33mg (75% yield); R_f = 0.6 (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): δ 7.65 – 7.57 (m, 2H), 7.42 – 7.28 (m, 8H), 6.10 (s, 1H), 4.70 (s, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 166.7, 164.3, 141.7, 135.5, 135.4, 129.3, 129.0, 129.0, 128.9, 128.6, 128.3, 126.6, 42.8, 41.0. HRMS (ESI TOF) m/z : calcd for $\text{C}_{18}\text{H}_{14}\text{Br}_2\text{NO}_2$ ($\text{M} + \text{H}$) $^+$: 433.9391, Found: 433.9395.

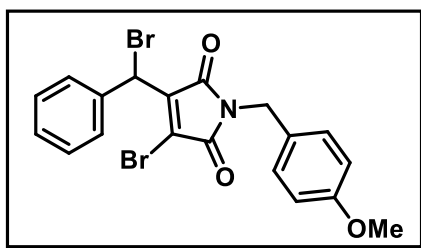
3-bromo-4-(bromo(phenyl)methyl)-1-(4-(trifluoromethyl)benzyl)-1H-pyrrole-2,5-dione (2ab):



(**2ab**): Compound **2ab** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 31 mg (62% yield); $R_f=0.5$ (petroleum ether/EtOAc 90:10); ^1H NMR (400 MHz, CDCl_3): δ 7.70 – 7.55 (m, 4H), 7.47 (d, $J = 8.0$ Hz, 2H), 7.41 – 7.30 (m, 3H), 6.10 (s, 1H), 4.75 (s, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 166.6, 164.2, 142.0, 139.2, 135.3, 131.3 – 129.9 (m), 129.4, 129.2, 129.1, 128.6, 126.0 (q, $J = 3.7$ Hz), 125.4, 124.04 (q, $J = 271$ Hz), 42.3, 40.9. ^{19}F NMR (377 MHz, CDCl_3): δ -62.7. HRMS (ESI TOF) m/z : calcd for $\text{C}_{19}\text{H}_{13}\text{Br}_2\text{F}_3\text{NO}_2$ ($\text{M} + \text{H}$) $^+$: 501.9265, Found: 501.9260.

3-bromo-4-(bromo(phenyl)methyl)-1-(4-methoxybenzyl)-1H-pyrrole-2,5-dione (2ac):

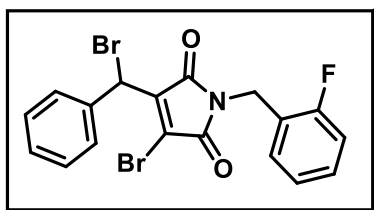
Compound **2ac** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 19 mg (41% yield); $R_f=0.6$ (petroleum ether/EtOAc 60:40)



^1H NMR (400 MHz, CDCl_3): δ 7.65 – 7.50 (m, 2H), 7.44 – 7.28 (m, 5H), 6.91 – 6.76 (m, 2H), 6.09 (s, 1H), 4.64 (s, 2H), 3.78 (s, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 166.8, 164.4, 159.6, 141.7, 135.5, 130.4, 129.3, 129.0, 128.6, 127.8, 126.6, 114.3, 55.4, 42.3, 41.0. HRMS (ESI TOF) m/z : calcd for $\text{C}_{19}\text{H}_{16}\text{Br}_2\text{NO}_3$ ($\text{M} + \text{H}$) $^+$: 463.9497, Found: 463.9495.

3-bromo-4-(bromo(phenyl)methyl)-1-(2-fluorobenzyl)-1H-pyrrole-2,5-dione (2ad):

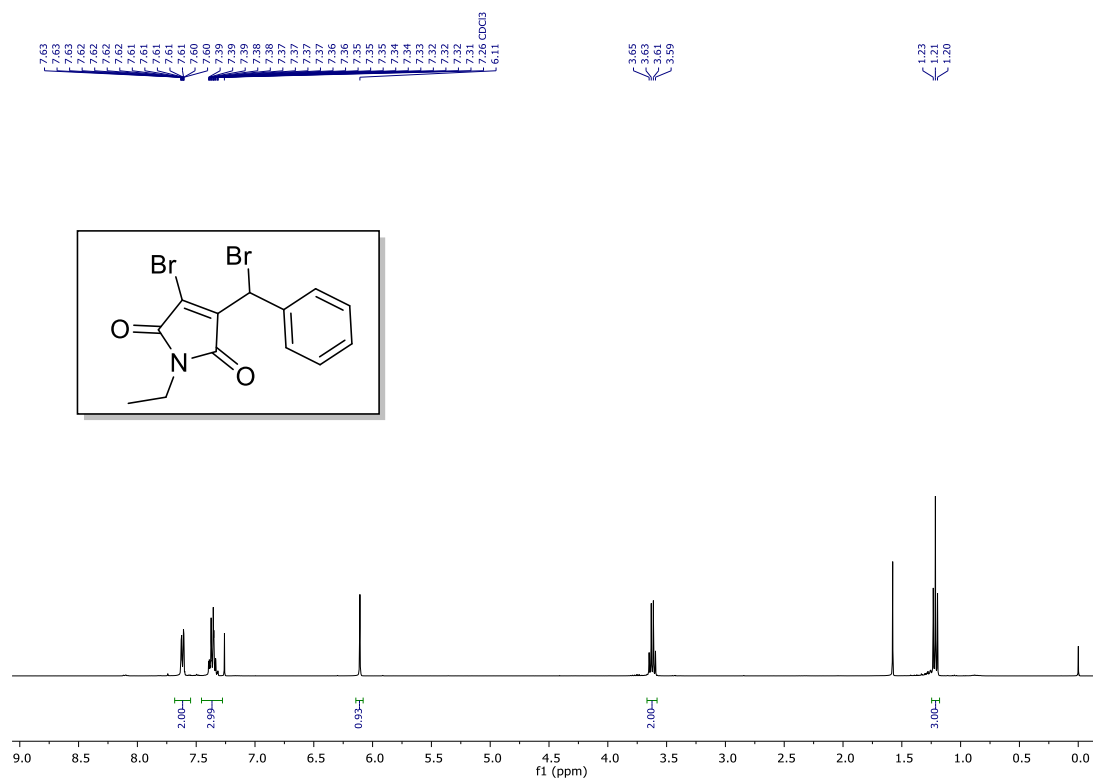
Compound **2ad** was synthesized following the general procedure-C. The product was obtained as colourless liquid, 43 mg (95% yield); $R_f=0.6$ (petroleum ether/EtOAc 90:10)



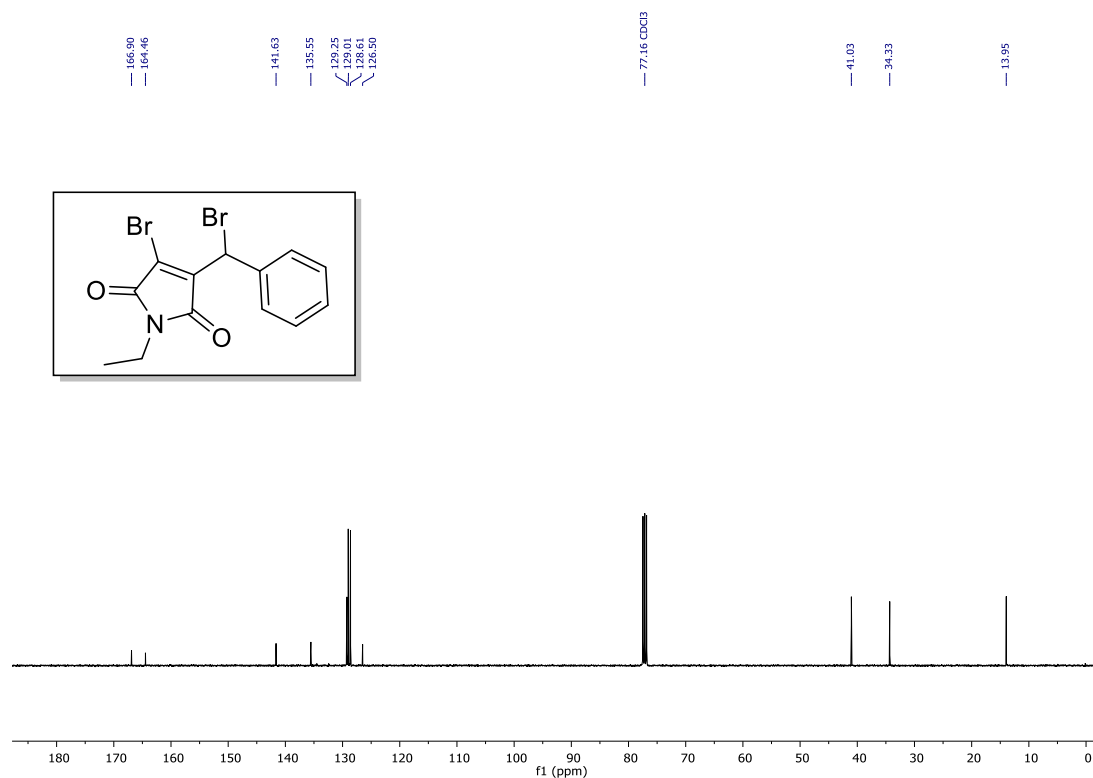
^1H NMR (400 MHz, CDCl_3): δ 7.61 (dd, $J = 7.9, 1.8$ Hz, 2H), 7.40 – 7.27 (m, 5H), 7.10 (td, $J = 7.6, 1.2$ Hz, 1H), 7.05 (ddd, $J = 9.7, 8.1, 1.1$ Hz, 1H), 6.11 (s, 1H), 4.79 (s, 2H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 166.5, 164.1, 160.7 (d, $J = 248.4$ Hz), 141.9, 135.4, 130.6 (d, $J = 3.5$ Hz), 130.2 (d, $J = 8.1$ Hz), 129.3, 129.0, 128.6, 126.6, 124.5 (d, $J = 3.7$ Hz), 122.3 (d, $J = 14.5$ Hz), 115.8 (d, $J = 21.3$ Hz), 40.9, 36.5 (d, $J = 4.6$ Hz). ^{19}F NMR (377 MHz, CDCl_3): δ -117.2. HRMS (ESI TOF) m/z : calcd for $\text{C}_{18}\text{H}_{13}\text{Br}_2\text{FNO}_2$ ($\text{M} + \text{H}$) $^+$: 451.9297, Found: 451.9291.

4.8.6 Selected Copies NMR Spectra (^1H , $^{13}\text{C}\{^1\text{H}\}$ and ^{19}F)

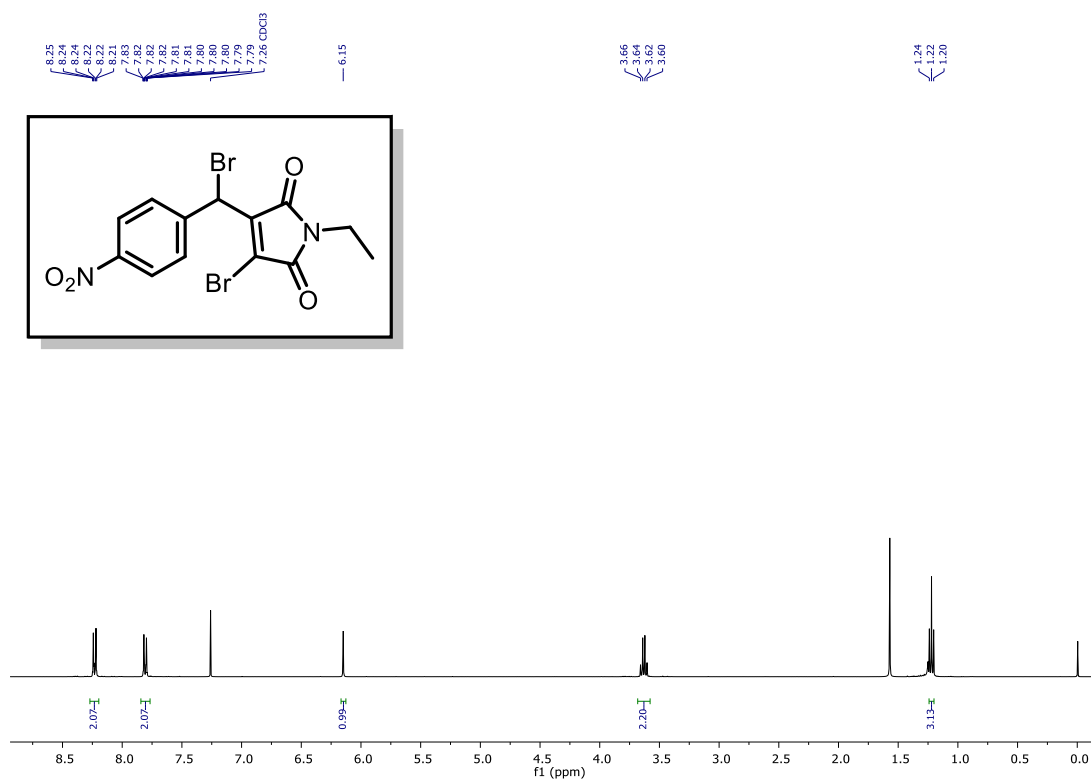
^1H NMR (400 MHz, CDCl_3) Spectrum of **2a**



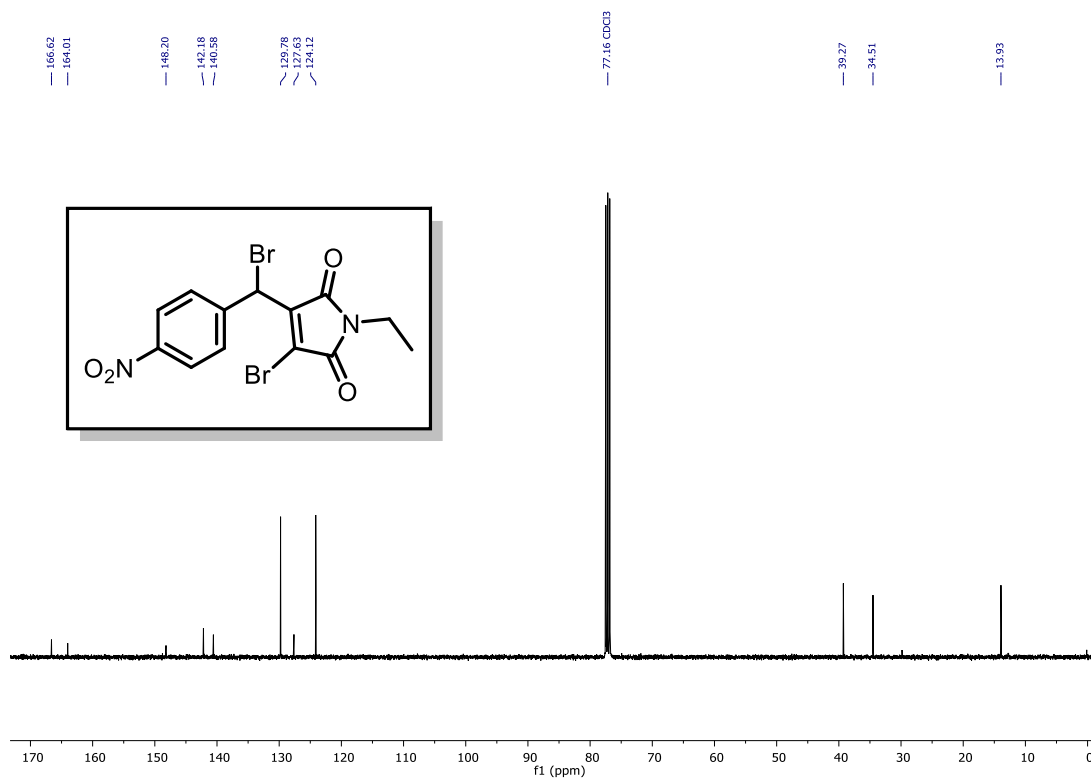
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2a**



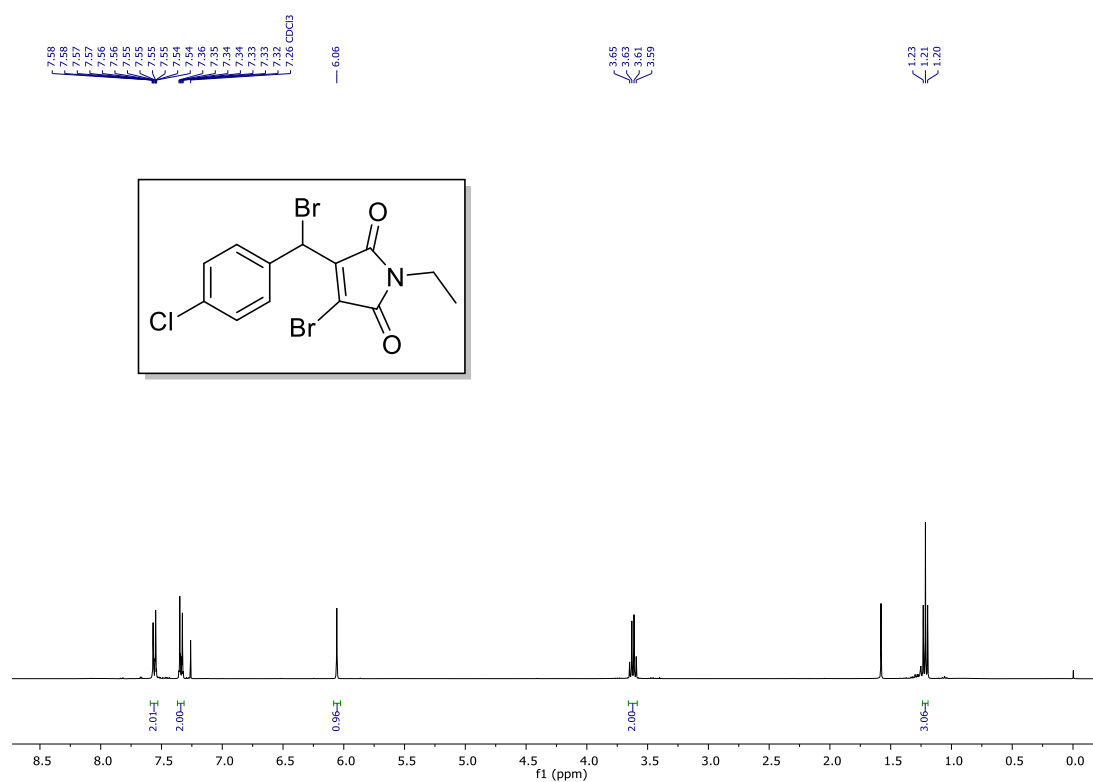
^1H NMR (400 MHz, CDCl_3) Spectrum of **2b**



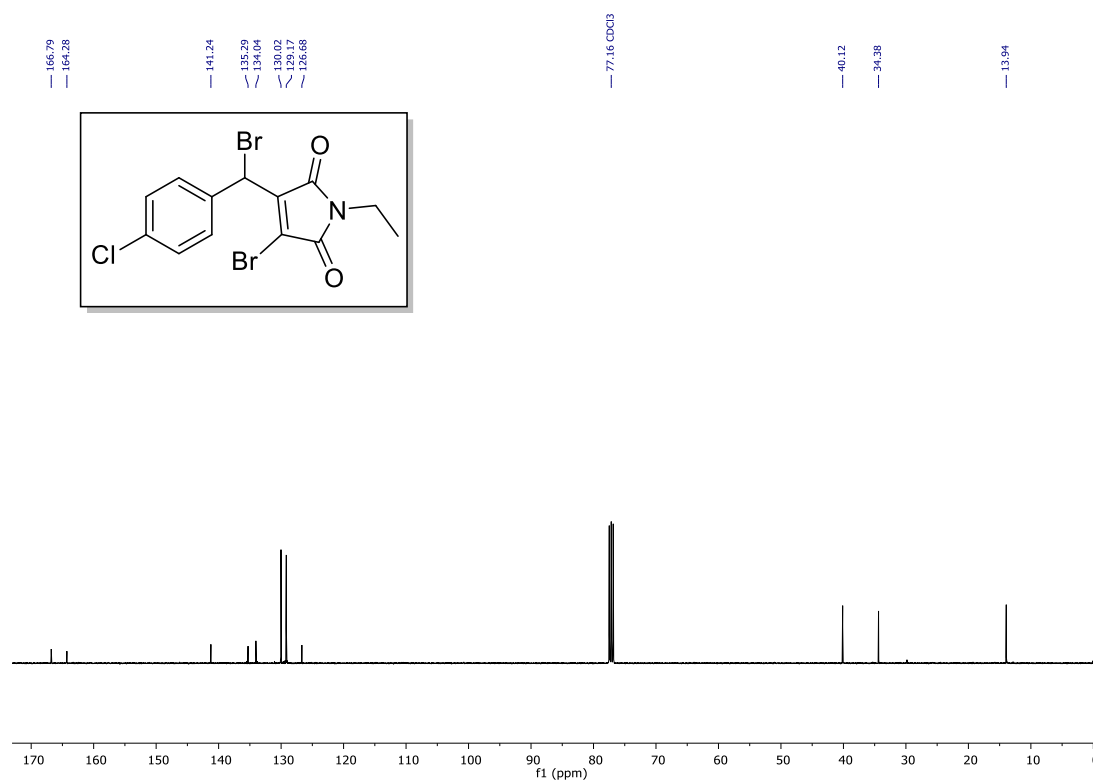
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2b**



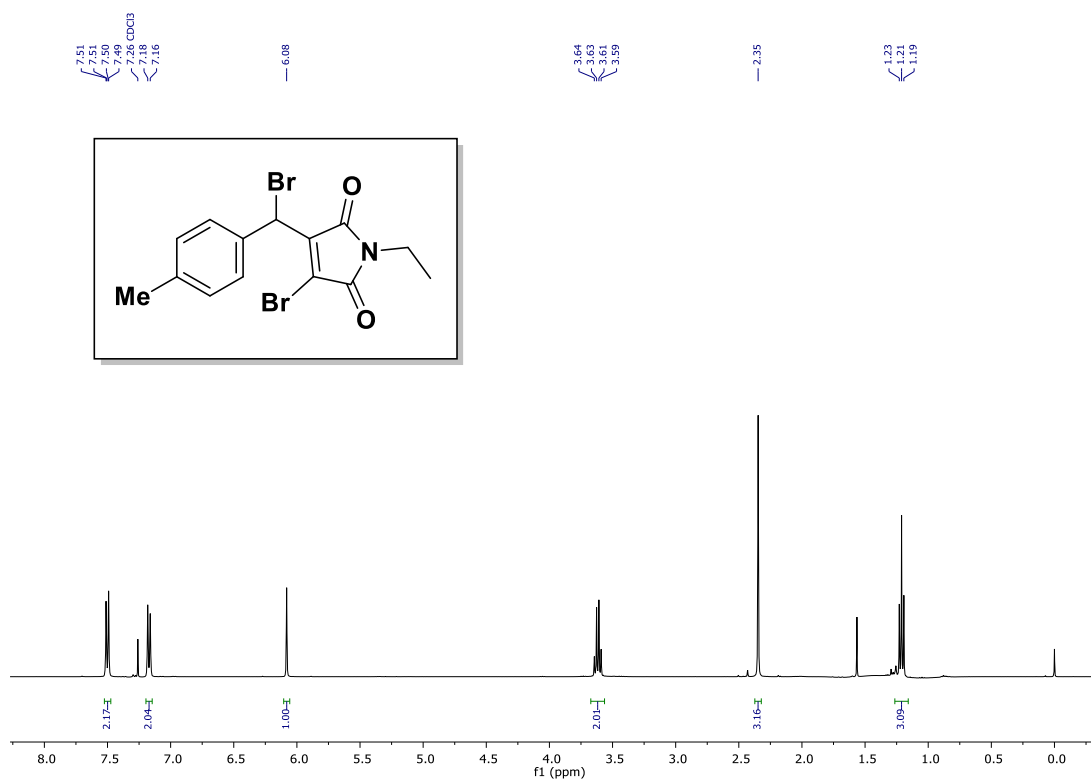
^1H NMR (400 MHz, CDCl_3) Spectrum of **2f**



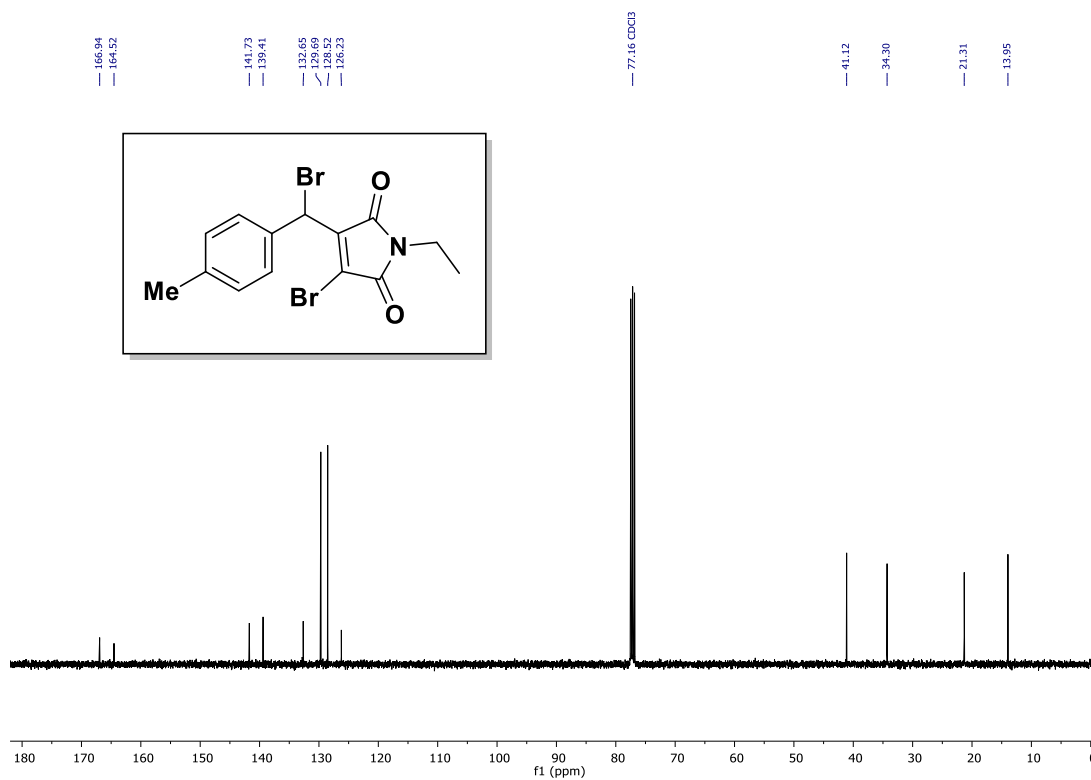
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2f**



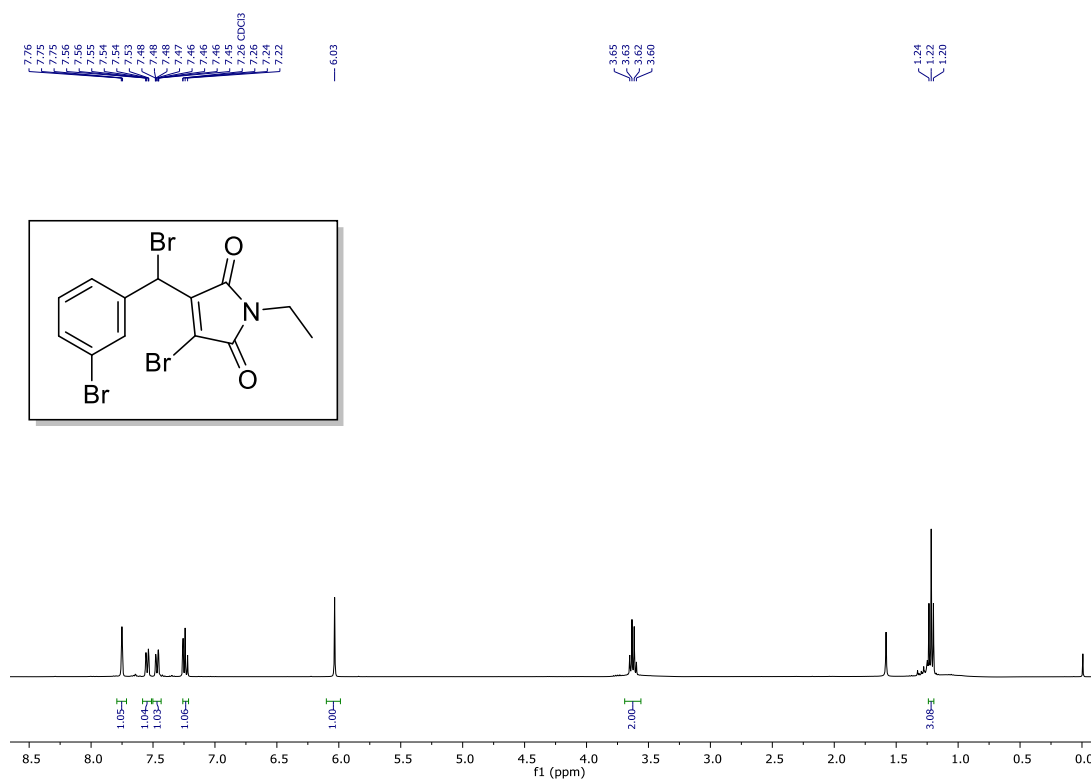
^1H NMR (400 MHz, CDCl_3) Spectrum of **2h**



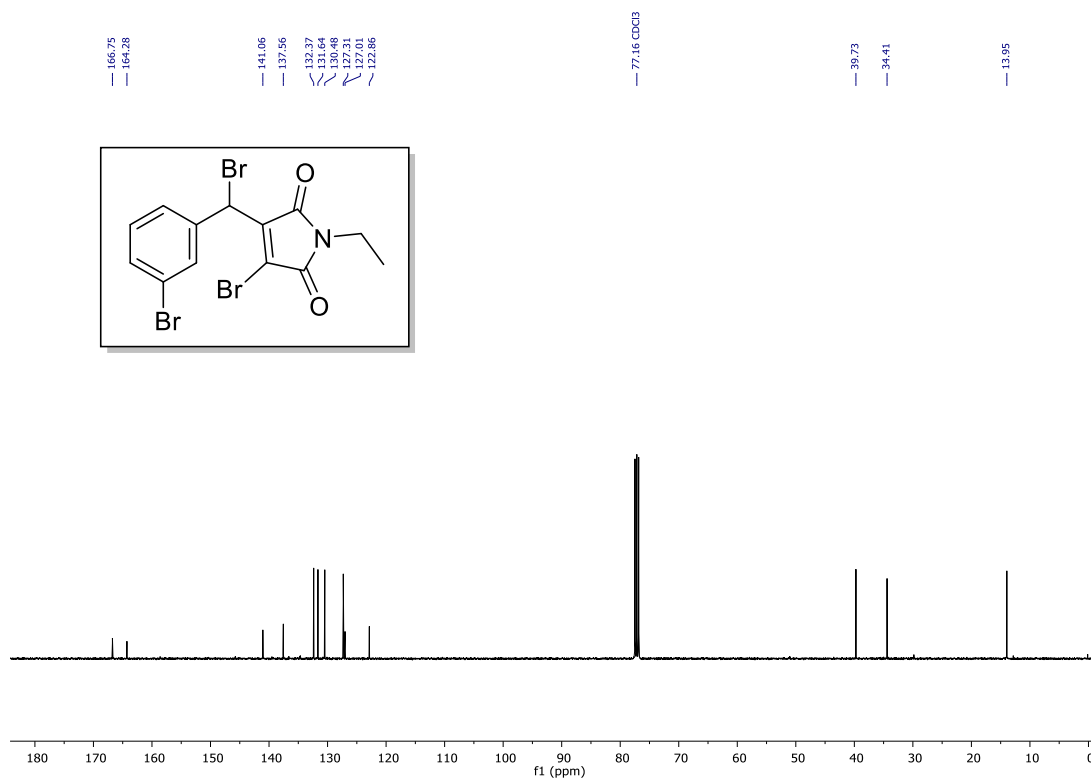
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2h**



¹H NMR (400 MHz, CDCl₃) Spectrum of **21**



¹³C{¹H} NMR (100 MHz, CDCl₃) Spectrum of **21**



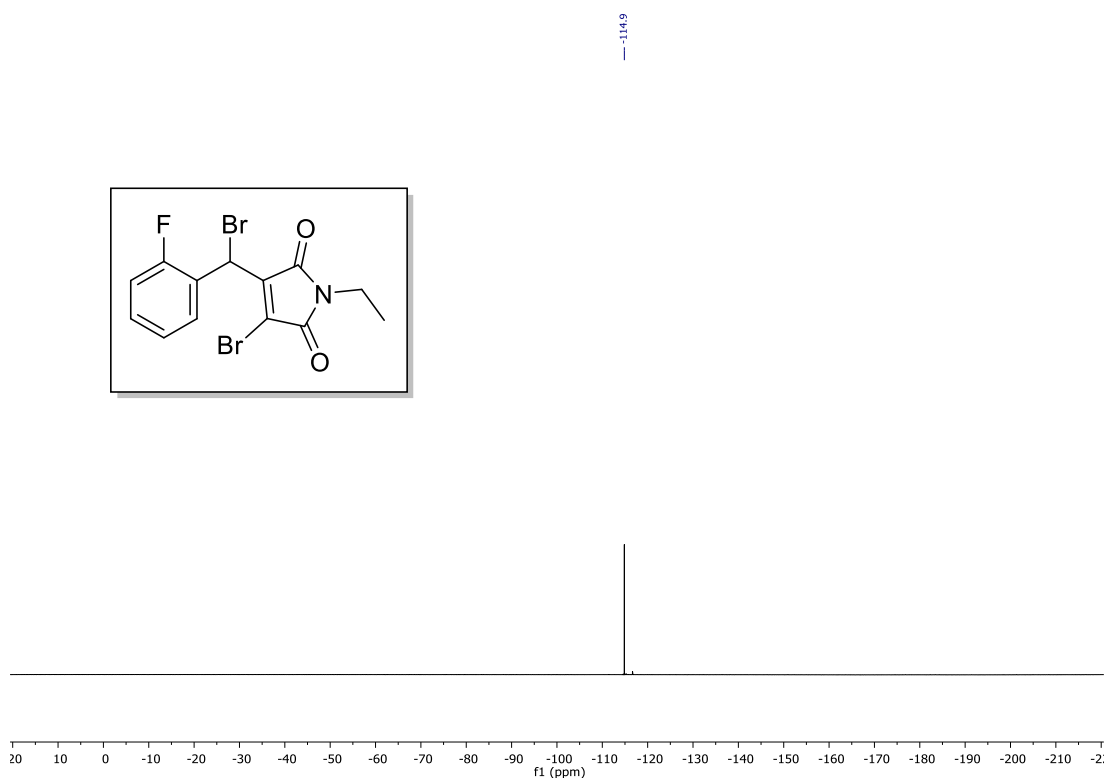
Chemical structure: BrC1(C(F)(Br)C2=CC=CC=C2)OC(=O)N1CC

¹H NMR spectrum (CDCl₃) showing peaks at 8.00 (1H), 7.44 (1H), 7.33 (1H), 7.23 (1H), 7.11 (1H), 6.44 (1H), 3.66 (2H), 3.66 (2H), and 1.22 (3H).

Chemical structure of 2-bromo-3-(2-bromo-2-fluorophenyl)-4-ethylisoxazolin-5-one is shown. The structure features a central isoxazolinone ring substituted with a bromine atom at position 2 and a 2-bromo-2-fluorophenyl group at position 3. The nitrogen atom of the isoxazolinone ring is substituted with an ethyl group.

¹³C NMR spectrum (CDCl₃) showing chemical shifts (ppm) for the compound. The spectrum displays peaks corresponding to the carbonyl carbons (166.7, 164.4, 160.5, 158.1), the isoxazolinone ring carbons (140.9, 132.3, 132.3, 131.2, 131.1, 129.6, 128.7, 122.7, 122.6, 115.6, 115.4), the solvent (77.2), the ethyl group carbons (34.3, 34.2, 34.1), and the methyl carbons (13.9).

¹⁹F NMR (377 MHz, CDCl₃) Spectrum of **2n**



4.9. Crystal Data of compound 2u

Bond precision: C-C = 0.0116 Å Wavelength=0.71073

Cell: a=8.1465(10) b=9.9066(14) c=11.2373(15)

alpha=69.599(4) beta=78.185(4) gamma=83.707(4)

Temperature: 296 K

	Calculated	Reported
Volume	831.28(19)	831.28(19)
Space group	P -1	P -1
Hall group	-P 1	-P 1
Moiety formula	C ₁₇ H ₁₀ Br ₃ N O ₂	?
Sum formula	C ₁₇ H ₁₀ Br ₃ N O ₂	C ₁₇ H ₁₀ Br ₃ N O ₂

Mr	499.96	499.99
Dx,g cm-3	1.997	1.998
Z	2	2
Mu (mm-1)	7.287	7.287
F000	480.0	480.0
F000'	478.57	
h,k,lmax	11,13,15	11,13,15
Nref	4494	4425
Tmin,Tmax		

Tmin'

Correction method= Not given

Data completeness= 0.985

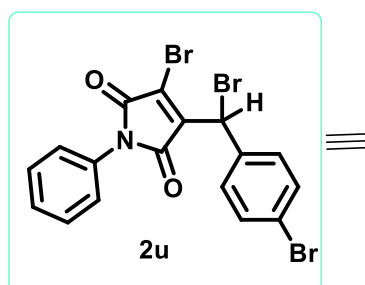
Theta(max)= 29.152

R(reflections)= 0.0843(3398)

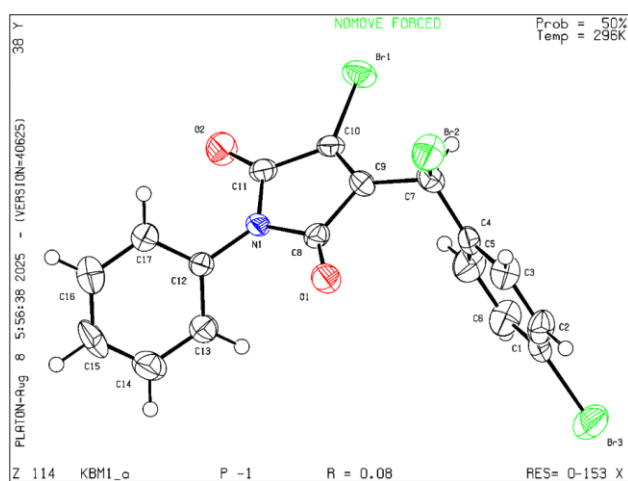
wR2(reflections)= 0.1494(
4425)

S = 1.272

Npar= 208



CCDC- 2479070



Thermal ellipsoids at 50% probability

4.10. References:

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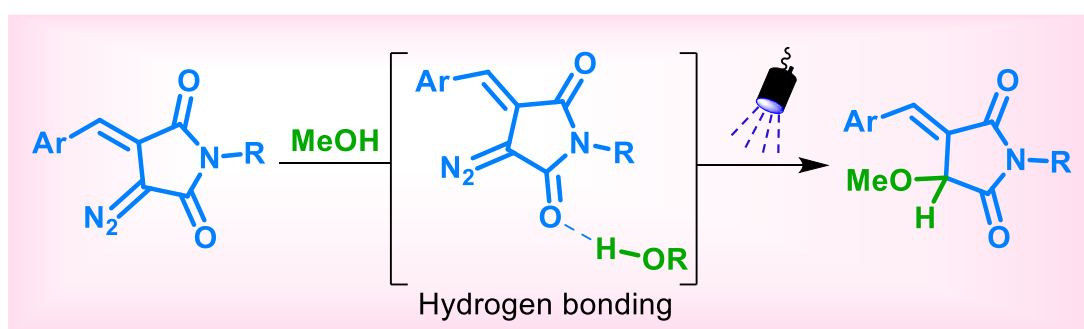
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Chapter 5

Photochemical O-H Functionalization of Diazo Arylidene Succinimides via Proton Transfer Promoted by Methanol



Photochemical O-H Functionalization of DAS via Proton Transfer Promoted by Methanol

5

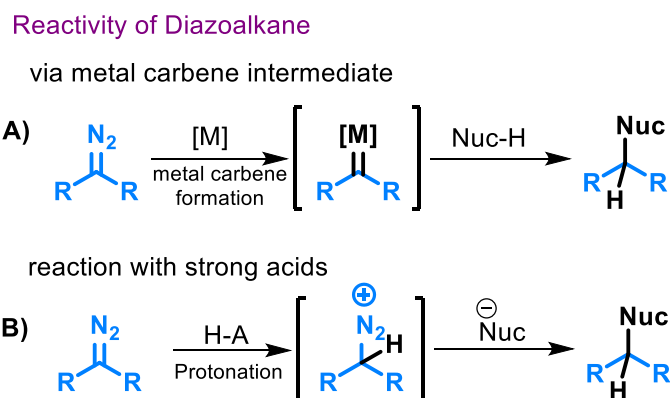
Methanol is a relatively less reactive protic solvent commonly used either as a solvent or employed for protonation in organic synthesis, and also plays a pivotal role in novel photochemical transformations. This chapter presents a mild and efficient reaction of diazo arylidene succinimide (DAS) with methanol, enabling the synthesis of ether derivatives with good yields. The transformation occurs exclusively upon the photoexcitation, which triggers a protonation-substitution mechanism leading to the desired ether product. Investigations into the scope of this reaction reveal that other acidic alcohols fail to undergo the O-H functionalization reactions. These findings underscore the potential of methanol in facilitating a unique photochemical pathway to access the DAS-derived ether derivative. Also, this method explored the novel reactivity of methanol with DAS under photochemical conditions.

5.1 Introduction

Organic transformation leveraging photoexcited states has emerged as a powerful strategy for enhancing synthetic efficiency. The methods relying on visible light photoredox catalysis enable unique and highly effective chemical transformations to access the traditionally inaccessible compounds via standard ground-state conditions.^{1,2} Owing to this strategy, driven by photoinduced electron or proton transfer, has gained significant attention.³ Particularly, in the past decade, the resurgence of photoredox catalysis has strengthened the photoinduced electron-transfer process further, and it has become one of the key strategies in organic synthesis.⁴

The exploration of the reaction between diazo alkanes and hydroxy group (O-H) serves as a significant strategy for constructing C-O bonds.⁵ Generally, this reaction proceeds through two distinct mechanistic pathways: (a) carbene transfer from the diazoalkane to non-acidic alcohol substrates, or (b) proton transfer from Brønsted acidic substrates to the diazoalkane, followed by a nucleophilic substitution reaction. Acidic substrates like carboxylic acids undergo the proton transfer mechanism to afford an ester product.⁶ One of the most widely utilized approaches for O-H functionalization reactions involve metal catalysts. These metal catalysts facilitate the formation of metal-carbene intermediates in situ (upon reaction with diazoalkanes), subsequently interact with alcohols through ylide formation, followed by the

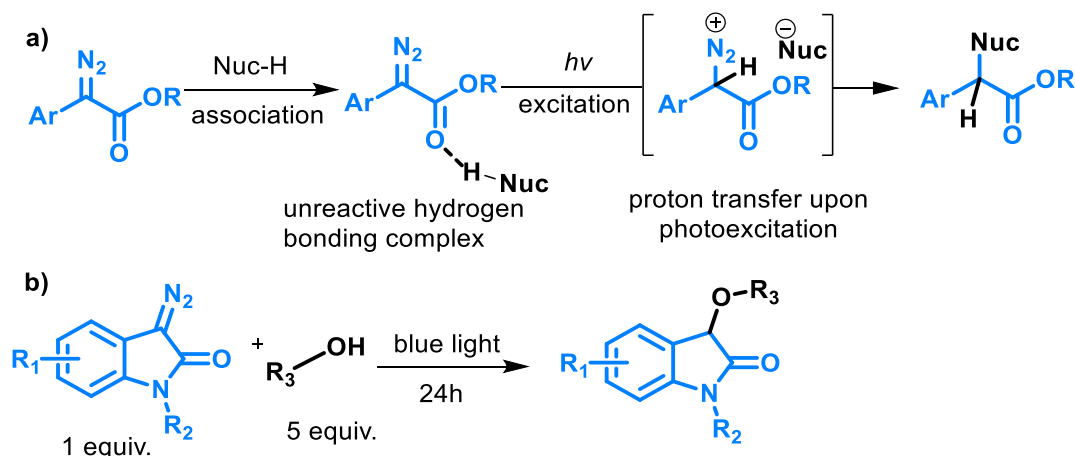
1,2-proton shift,⁷ to afford the O–H functionalization product (Scheme 5.1-A). Due to the highly reactive nature of the carbene intermediate, transition metal complexes have traditionally played a vital role in promoting efficient and selective carbene transfer reactions. Today, a wide array of metal-based catalysts is employed for finely tuning both the reactivity and selectivity of a variety of chemical transformations.⁸ More recently, the incorporation of strong Brønsted acids has enhanced this approach, enabling protonation reactions of diazoalkanes using catalytic quantities of acid (Scheme 5.1-B).⁹



Scheme 5.1: Reactivity of Diazo Alkane

Unlike photoinduced electron-transfer reactions, the use of photoexcited proton transfer (PPT) remains relatively rare in organic synthesis,¹⁰⁻¹⁴ despite the known applications of photoacids^{11,12} and photobases⁸ in areas such as pH control and protein folding.¹⁰ Recent research on PPT-based reactions¹¹ primarily focuses on UV-light-driven excitation of Brønsted acidic catalysts. These catalysts exhibit a lower pK_a upon excitation than in their ground state, facilitating the photocatalytic transformations through proton transfer mechanism. Recently, Koenings and co-workers have broadened the scope of diazoalkane in photochemistry by introducing photoinduced proton transfer reactions under visible light. This breakthrough reveals a new mode of reactivity of diazoalkanes under light-driven conditions, extending their potential beyond conventional photochemical applications (Scheme 5.2-a).^{15a}

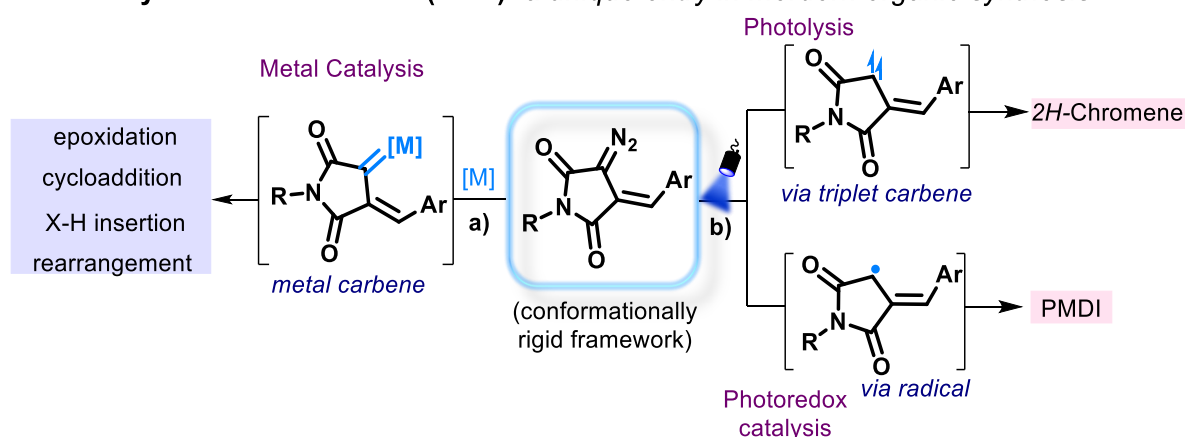
Later, the same research group disclosed a photochemical approach to O–H bond functionalization utilizing acidic alcohols and cyclic diazoamides (Scheme 5.2-b).^{15b} While there have been some reports on this topic, strategies based on photoinduced proton transfer for activating unreactive precursors containing diazoalkanes remain scarce. To the best of our knowledge, only a limited number of studies on photoinduced proton transfer reactions have investigated the reactivity of other types of diazoalkanes.¹⁵



Scheme 5.2: Photoinduced proton transfer reactions of diazo compounds

Cyclic diazo compounds such as diazo arylidene succinimides (DAS) represent another significant class of diazo compounds that have been extensively explored in various metal-catalyzed carbene transfer reactions, to access epoxides, cycloaddition adducts, X–H insertion products, and rearrangement products (Scheme 5.3a).¹⁶ Moreover, the photochemical reactivity of this diazo compound has lately been studied, which opened up an exceptionally different reactivity to serve as triplet carbene¹⁶ⁱ as well as carbon-centric radical reactivity under low-energy visible light irradiation (Scheme 5.3b). More importantly, this diazo substrate allowed a paradigm shift in organic synthesis to deliver easy access to PMDI molecules, as demonstrated very recently.^{16j}

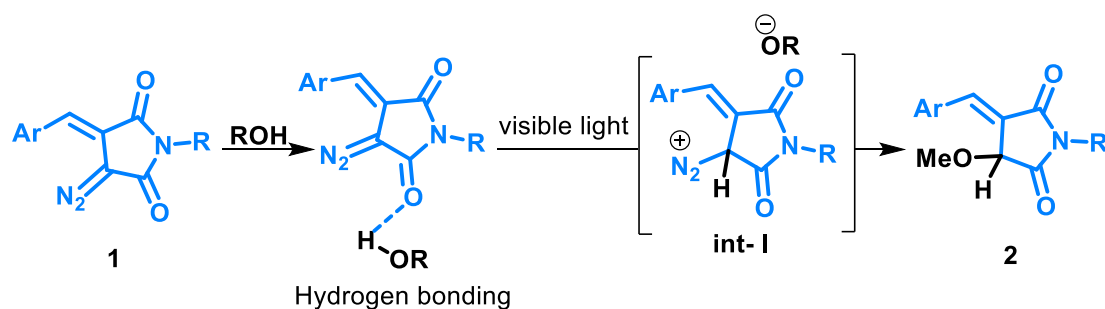
Diazo arylidene succinimide (DAS): a unique entry in modern organic synthesis



Scheme 5.3: Reactivity of diazo arylidene succinimide with metal catalysis and visible light

The photoinduced proton transfer (PPT) strategy offers a conceptually novel pathway in organic synthesis, ideally utilizing mild and low-energy visible light to drive the reaction.

On the basis of previous reports, we thought to explore the reactivity of DAS **1** with mild acids like alcohols under visible light irradiation. We hypothesized that DAS **1** may interact with alcohols, leading to the formation of a diazonium ion (**int-I**) under the irradiation of visible light. Subsequently, nucleophilic substitution takes place to afford the desired functionalized product **2** via PPT reaction (Scheme 5.4). This approach could unveil a new reactivity mode for DAS and expand the scope of known O–H functionalization reactions.



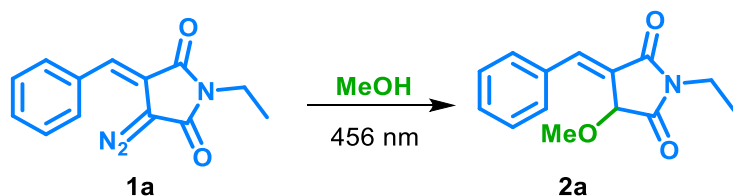
Scheme 5.4: Present work on photoinduced proton transfer reaction of DAS

5.2 Results and discussion

In order to validate the hypothesis, we planned to select methanol as a model substrate. Methanol is characterized by its distinct hydrogen-bonding properties, weak nucleophilicity, and mild acidity and is typically considered relatively inert in terms of functionalization. In this regard, to examine the reactivity of diazo arylidene succinimide (DAS) under photochemical applications, we treated methanol with DAS **1a** at room temperature under the irradiation of visible light under an inert atmosphere (456 nm, blue LED). Gratifyingly, we obtained the corresponding O–H functionalization product **2a** in moderate yield. NMR analysis also indicated the presence of a minor positional isomer, **2a'**, in a 98:2 ratio. However, the two isomers could not be separated (Table 5.1, Entry 1). Encouraged by this initial result, we further screened different LEDs of varied wavelengths (Table 5.1, Entries 1-4), and among all, the 440 nm Blue LED proved to be the most efficient to obtain the desired product **2a** in the highest yield (Table 1, Entry 3). Subsequently, we explored the reaction of **1a** with methanol (10 equiv) as a reagent (instead of solvent) in various other solvents. However, the desired product **2a** did not form even in trace amounts (Table 1, Entries 4-12). Additionally, altering the ratio of methanol to acetonitrile (1:1 to 1:4) as solvent under the irradiation of blue LED (440 nm)

afforded the desired product **2a** in relatively lower yield (Table 1, entries 13-16). Later, we carried out the reaction under an oxygen atmosphere while maintaining other standard conditions; however, the desired product **2a** was not obtained even in trace (Table 5.1, entry 17). This result indicated that the presence of oxygen may be interfering with the reaction pathway. Later, we performed the reaction in the absence of light while maintaining other reaction conditions. However, the reaction did not work even after prolonged reaction time (36 h), and the desired product was not found, even in trace amounts, and the starting material **1a** was not consumed. (Table 5.1, entry 18). Based on the exhaustive screening, diazo arylidene succinimide (DAS) **1a** (1 equiv.), under the illumination of blue LED (440 nm, 20W) in methanol under inert conditions (degassed with nitrogen) proved to be the optimum reaction condition to obtain the desired product **2a** (Table 5.1, entry 3).

Optimization of Reaction Conditions^a



Entry	Solvent	Light	Yield of 2a (%) ^b
1	Methanol	456 nm	55(52)
2	Methanol	427 nm	40
3	Methanol	440 nm	65 (60)
4	Methanol	467 nm	50
5 ^c	MeCN	440 nm	<i>n.d.</i>
6 ^c	THF	440 nm	<i>n.d.</i>
7 ^c	CHCl ₃	440 nm	<i>n.d.</i>
8 ^c	1,4-dioxane	440 nm	<i>n.d.</i>
9 ^c	F-benzene	440 nm	<i>n.d.</i>
10 ^c	Toluene	440 nm	<i>n.d.</i>
11 ^c	DCM	440 nm	<i>n.d.</i>
12 ^c	EtOAc	440 nm	<i>n.d.</i>

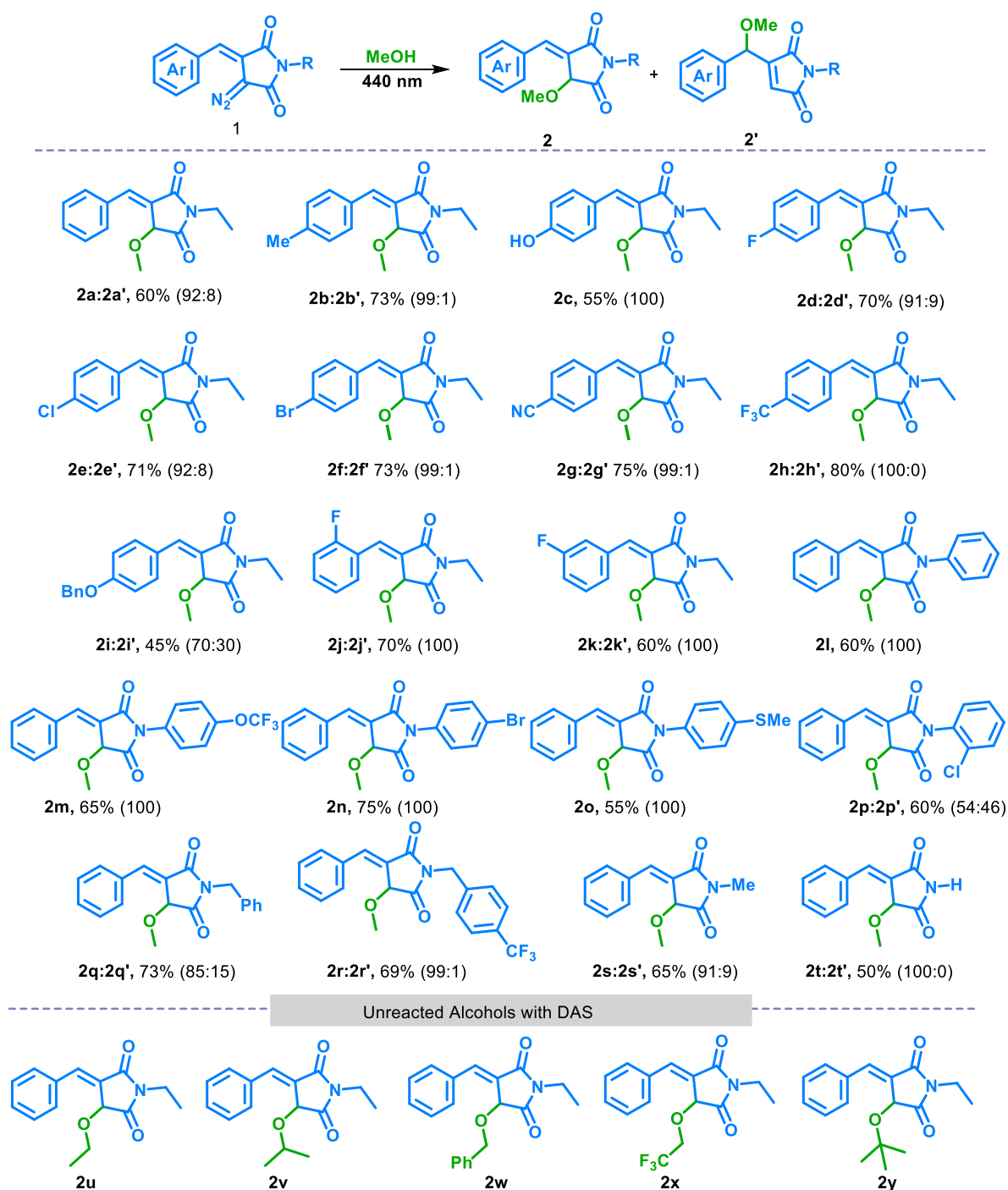
13	MeOH/MeCN (1:1)	440 nm	51
14	MeOH/MeCN (1:2)	440 nm	35
15	MeOH/MeCN (1:3)	440 nm	20
16	MeOH/MeCN (1:4)	440 nm	15
17	Methanol (O ₂ atm.)	440 nm	<i>n.d.</i>
18	Methanol	No light	<i>n.d.</i>

Table 5.1: Reaction conditions^a: Diazo **1a** (1 equiv), blue LEDs (440 nm), 12 h, 30 °C, MeOH (A. R. Grade was used). ^b = yields are calculated by ¹H NMR by using 1,3,5-trimethoxybenzene as an internal standard; ^c = 10 equiv of MeOH was used. *Note: All yields were determined using NMR analysis of the crude reaction mixture. Due to the lower amount of formation of the positional isomer, accurately calculating the ratio proved challenging.*

5.3 Substrate Scope of Diazo Arylidine Succinimides

Having obtained the optimized reaction conditions, we further explored the substrate scope of various substituted DASs with methanol. To our delight, all the substituted DAS derivatives (**1a-1s**) reacted under the optimized reaction conditions to furnish the corresponding O-H functionalization products (**2a-2s**) in moderate to good yields. Initially, we examined various DAS derivatives having electron-donating, electron-deactivating, and electron-withdrawing groups at the *para*-position of the phenyl group. In all the cases, all functional moieties tolerated the optimized reaction conditions well and afforded the corresponding products efficiently with moderate to good yield (**2a-2h**). However, we observed that in all the cases we observed the respective positional isomers (**2a'-2h'**) in very small quantities and all the efforts to separate them were unsuccessful (Scheme 5.5). The major products have been isolated along with a small quantity of inseparable positional isomers, and the ratio of isomers have been calculated using ¹H-NMR. Later, we explored the reaction of the -OBn protected DAS derivative (**1i**) under the optimized reaction condition to furnish the desired product (**2i**) in slightly lower yield compared to other derivatives. We also investigated the reactivity of *ortho*- and *meta*-substituted DAS derivatives (**1j,1k**) under the optimized reaction conditions to obtain the corresponding products (**2j, 2k**) with moderate to good yields (upto 70%). Next, we explored different *N*-substituted DAS derivatives (**1l-1p**) featuring various aryl substituents reacted smoothly under the optimized reaction conditions to furnish the desired products (**2l-2p**) in moderate to good yield (upto 75%, Scheme 5.5). Furthermore, *N*-benzyl/alkyl-

substituted DASs also exhibited excellent tolerance to the optimized reaction conditions and afforded the corresponding products (**2q–2s**) in moderate to good yield (upto 73%, Scheme 5.5). Overall, various DAS derivatives having different electronic and steric properties reacted smoothly with methanol to afford the corresponding O-H functionalized products.

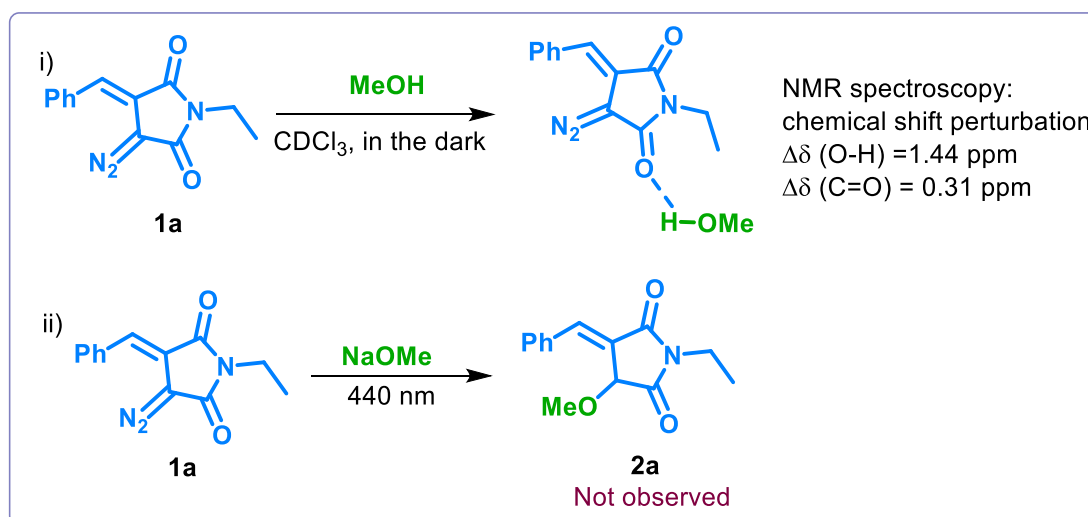


Scheme 5.5: Substrate scope; **Reaction conditions^a:** Diazo **1a** (1 equiv), blue LEDs (440 nm), 12 h, 30 °C, 4 mL MeOH used as a solvent and substrate (A. R. Grade was used), all yields are isolated.

Later, we planned to explore the substrate scope of different alcohols with DAS under the optimized reaction conditions. Initially, like methanol, we screened different alcohols as such as ethanol, isopropanol, trifluoroethanol, benzyl alcohol as solvents with DAS **1a** under the optimized reaction conditions. However, unfortunately reactions did not work efficiently and we observed that the desired products were either obtained only in trace amounts or not formed at all. All other efforts of further optimizing the reaction conditions such as raising temperature, equivalents, combination of solvent effects etc. were unsuccessful. It is quite intriguing to note that though methanol reacted smoothly, yet other alcohols of similar nature, or alcohols having higher or lower acidity, nucleophilicity of alcohols did not react at all. This is quite surprising as well as interesting about the reactivity of methanol and it needs to be studied in depth.

5.4 Study of Hydrogen Bonding

Later, we examined the interaction between methanol and DAS **1a** using ^1H and ^{13}C NMR spectroscopy under varying temperature conditions. Upon examining a solution of a stoichiometric mixture of reaction [**1a** (1 equivalent) and MeOH (2 equivalents)] in CDCl_3 , we observed notable chemical shift perturbations in the ^1H NMR spectrum of the O-H proton of methanol is 1.44 ppm (Figure 5.1A) and the **1a** carbonyl carbon is 0.31 ppm (figure 5.1B). This data suggests a potential hydrogen-bond interaction between DAS **1a** and methanol. This result indicates that a favourable hydrogen bonding complex forms between methanol and **1a** in situ under dark conditions (Scheme 5.6-i).



Scheme 5.6: Formation of H-bonding complex

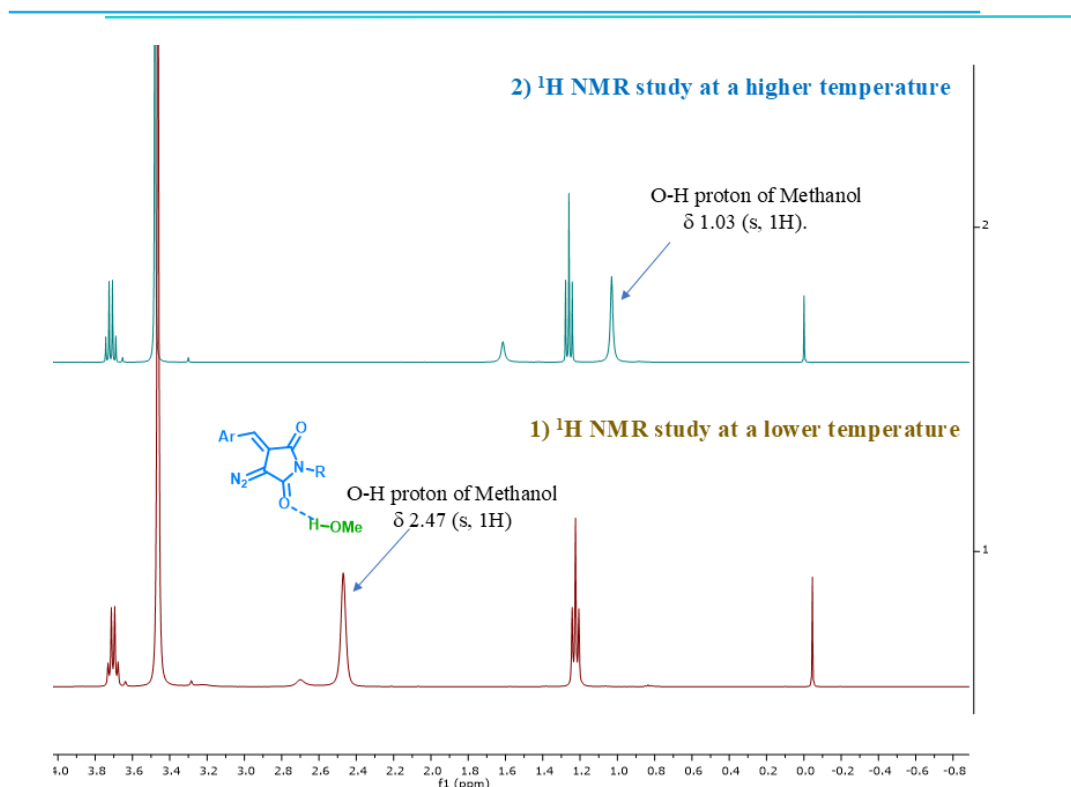


Figure 5.1A: ^1H NMR study of Hydrogen bond interaction between diazo **1a** and methanol.

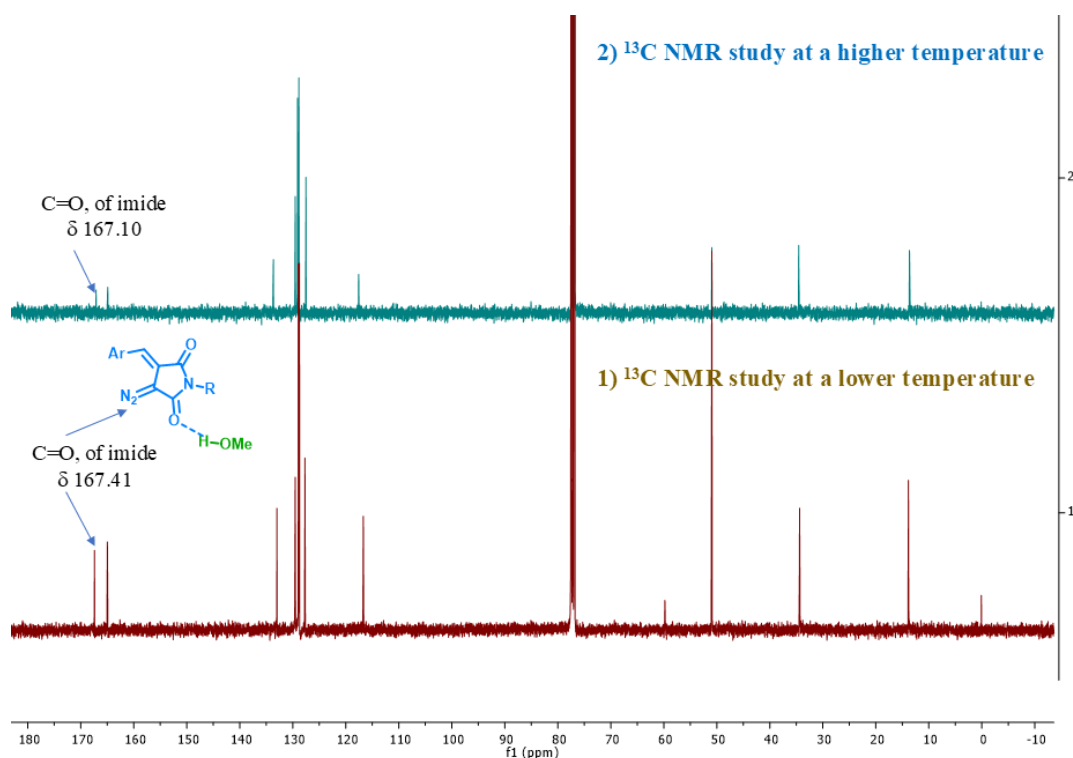


Figure 5.1B: ^{13}C NMR study of Hydrogen bond interaction between diazo **1a** and methanol.

Furthermore, we conducted the reaction of DAS **1a** with sodium methoxide under blue light irradiation (440 nm) for 12 h. However, the reaction leads to the decomposition of the starting

material and we did not observe the desired product **2a** even in trace (Scheme 5.6-ii). We observed that the reaction did not proceed when sodium methoxide was directly used as a reactant instead of methanol. This highlights the importance of hydrogen in methanol.

These findings indicate that the formation of the desired product **2a** is likely reliant on the hydrogen-bonding interaction between DAS **1a** and methanol. Seems like the hydrogen-bonded complex plays a pivotal role in facilitating the proton transfer and the subsequent steps necessary for this transformation. We believe that the absence of this crucial interaction, hydrogen bonding (as seen in the case of sodium methoxide), may not drive the reaction, and the importance of hydrogen bonding, reactivity of alcohols, needs to be studied further in detail.

5.5 Mechanistic experiments on the O-H functionalization

To further investigate the reaction mechanism, we carried out a time-dependent ^1H NMR experiment to check the proton transfer process (PT). The diazo compound **1a**, dissolved in Methanol- d_4 while maintaining the standard reaction conditions, was subjected to ^1H -NMR analysis at various time intervals (0 to 2 h).

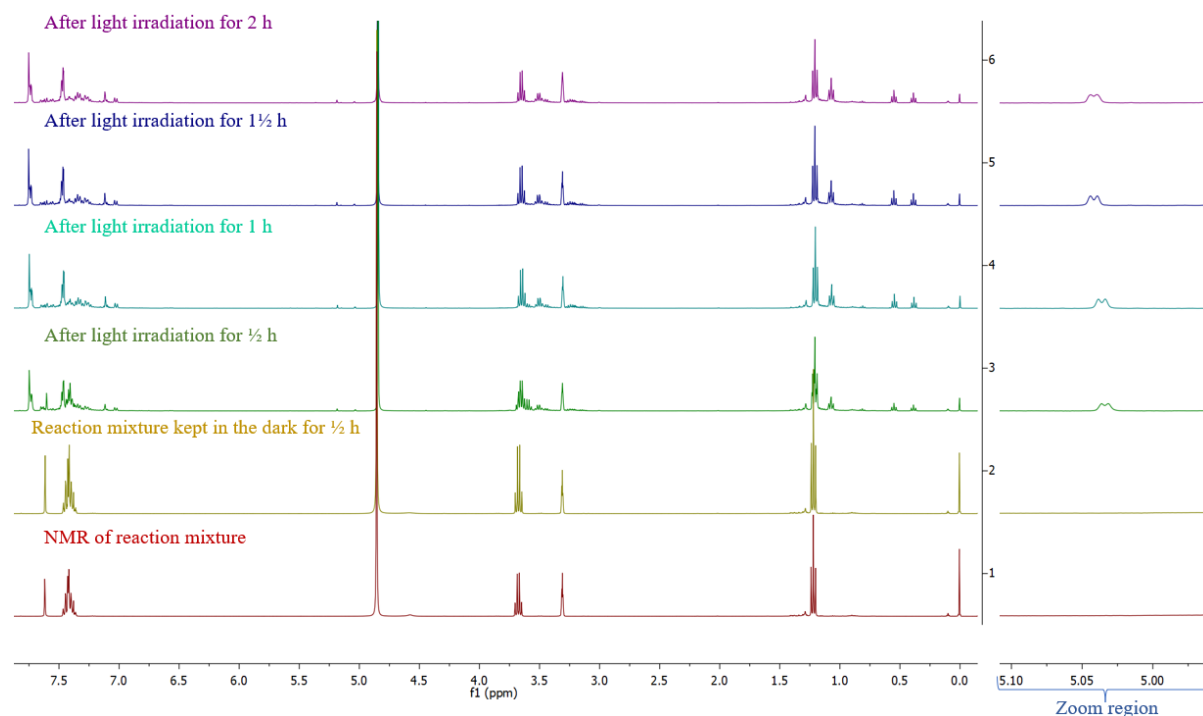
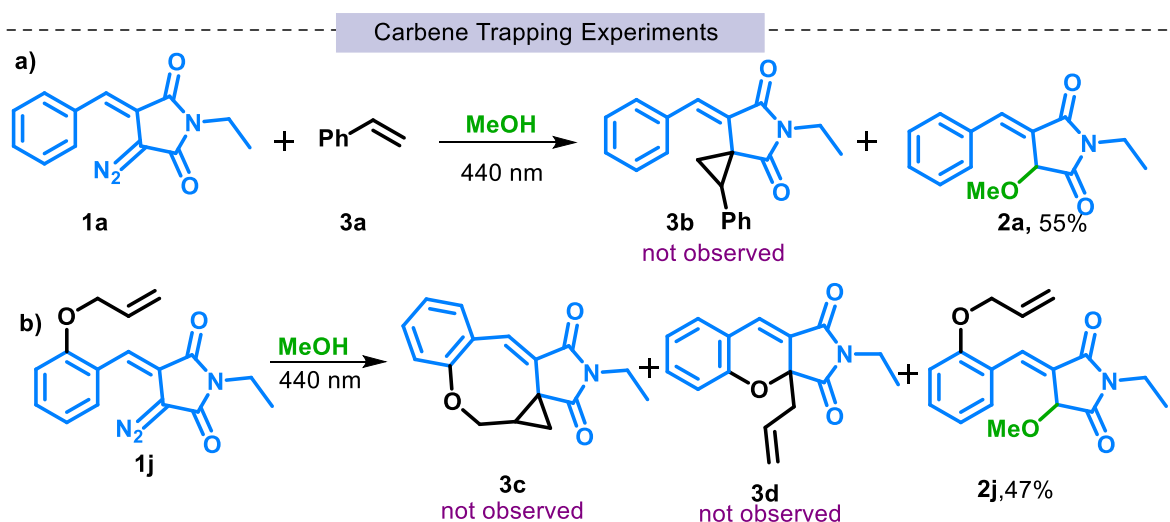


Figure 5.2: Time-dependent ^1H NMR study for proton transfer process.

Initially, we recorded the ^1H NMR spectrum of the reaction mixture. Subsequently, the NMR tube was kept in the dark (no exposure to light) for 30 minutes, after which we recorded the ^1H NMR spectrum again of the solution. However, no changes were observed in the NMR during

this step. Afterward, we recorded the ^1H NMR spectra at various time intervals under exposure to light irradiation. Upon irradiating the reaction mixture with blue LED light (440 nm) for 30 min, a new signal emerged at 5.04 ppm, and no signal was observed in the absence of light. This newly observed signal strongly supports that the proton transfer process occurs exclusively in the presence of light, and may be facilitated by moisture in the solvent as the proton source, since Methanol- d_4 lacks available protons (Figure 5.2). The results clearly demonstrate that proton transfer occurs after light is essential for this transformation. Based on this observation, we strongly believe that the reaction is likely proceeding through a photoinduced proton transfer (PPT) process.

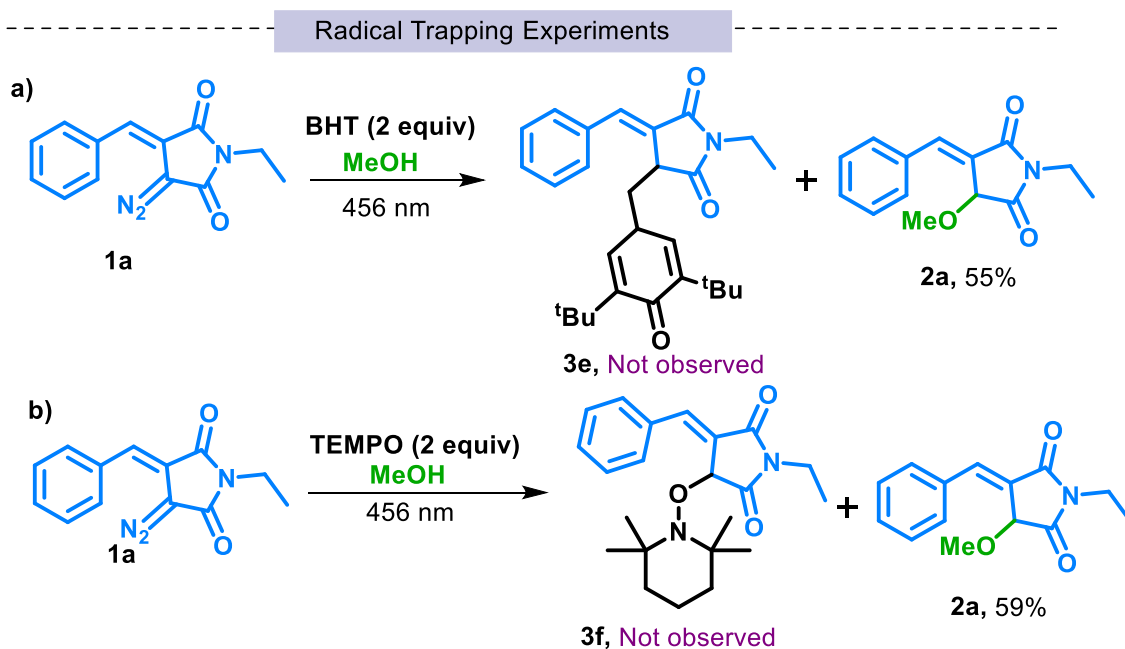
To gain further insights into the reaction pathway, we carried out a few control experiments (Scheme 5.7). To determine whether the reaction proceeds via a classical carbene intermediate, the reaction of **1a** and methanol was carried out in the presence of styrene **3a** while maintaining the other standard conditions. However, we obtained the O-H functionalized product **2a**, and we did not observe any cyclopropanation product **3b** even in trace (Scheme 5.7-a). This result suggests that this reaction does not proceed via a carbene intermediate. Later, we synthesized 2-allyloxy-substituted diazo **1j**. The reaction of **1j** under the optimized reaction conditions, afforded the product **2j** and we did not observe either the cyclopropanation product **3c** or rearranged product **3d** (Scheme 5.7-b). This result clearly suggest that the reaction does not proceed through a carbene pathway.



Scheme 5.7: Carbene trapping experiments

To investigate the involvement of a radical intermediate during the course of the reaction, radical trapping experiments were carried out using compound **1a** with TEMPO as well as BHT

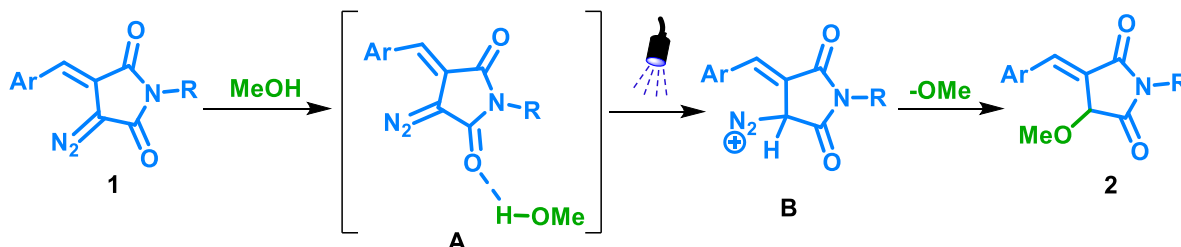
as radical scavengers under the standard reaction conditions. However, we did not observe any radical trapping adducts; instead, only the product **2a** was detected (Scheme 5.8). These findings suggest that the reaction may not proceed via a radical intermediate as well.



Scheme 5.8: Radical trapping experiments

5.6 Proposed Mechanism

Based on the above control experiments and previous studies,¹⁵ a plausible reaction mechanism has been proposed. Initially, DAS **1** interacts with methanol to form a hydrogen-bonded complex, **A**. Upon light irradiation, a proton transfer occurs, leading to the formation of diazonium ion **B**. This intermediate **B** subsequently reacts with methoxide to afford the O-H functionalization product **2**.



Scheme 5.9: Proposed Mechanism

5.7 Conclusion

In summary, we demonstrated the photochemical O-H functionalization of diazo arylidene succinimides under exposure to visible light. Through this investigation, we successfully developed a novel protocol for photochemical transformation utilizing methanol, a less reactive protic solvent, as a key component. The pivotal role of methanol in facilitating the reaction highlights the significance of this optimized method, offering valuable insights into photoinduced proton transfer (PPT) processes and expanding the scope of functionalization techniques. This protocol worked exclusively with methanol, thus highlighting the reactivity profiles of both DAS and methanol under light. However, this limitation also needs to be examined in detail regarding the excited state photoreactions and behaviour of molecules, looking into various parameters.

5.8 Experimental section:

5.8.1 General information:

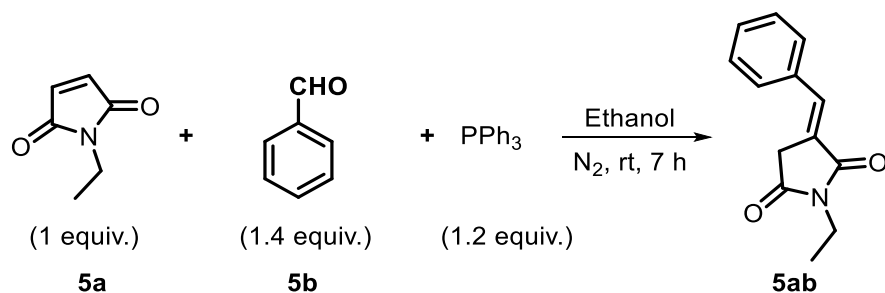
Reagent Information: All reactions were carried out with distilled and A.R. grade solvents using oven-dried glassware under a dry Argon atmosphere unless otherwise stated. All the reagents were purchased from commercial sources and used as received unless otherwise indicated. Thin-layer chromatography (TLC) was performed using silica gel 60 GF₂₅₄ pre-coated aluminum-backed plates (2.5 mm) with detection by UV light. Column chromatographic purification of products was carried out using silica gel (100-200 mesh). The mixture of petroleum ether and ethyl acetate was used as a gradient elution for column chromatography.

Analytical Information: All isolated compounds were characterized by ¹H NMR, and ¹³C{¹H} NMR spectra were recorded on a 400 MHz Jeol ECS-400 and Bruker Avance III HD Ascend 400 MHz spectrometers. Nuclear Magnetic Resonance spectra were recorded in CDCl₃. The NMR spectra were recorded using tetramethyl silane (TMS) as the internal standard. ¹H NMR spectra were recorded at 400 MHz, and ¹³C{¹H} NMR spectra were recorded at 100 MHz (Bruker), unless otherwise noted. Chemical shifts (δ) are reported in ppm downfield from CDCl₃ (δ = 7.26 ppm) and from DCM-*d*₂ (δ = 5.32 ppm) for ¹H NMR and relative to the central CDCl₃ resonance (δ = 77.16 ppm) and DCM-*d*₂ resonance (δ = 54.00 ppm) for ¹³C{¹H} NMR spectroscopy. For ¹H NMR, data are reported as follows: chemical shift, multiplicity (s =

singlet, d = doublet, dd = double doublet, t = triplet, q = quartet, m = multiplet), coupling constants (J) are given in Hz and integration. $^{13}\text{C}\{^1\text{H}\}$ NMR spectra were recorded with complete proton decoupling. ^{19}F NMR spectra were recorded at 377 MHz. Mass samples were analysed by high-resolution mass spectrometry (HRMS) using ESI TOF. Single crystal X-ray diffraction data were collected on a Bruker SMART APEX four-circle diffractometer equipped with a CMOS photon 100 detector (Bruker Systems Inc.) with Microfocus (I μ S) using Mo K α radiation (0.71073 Å).

Photoreactor Setup: Light-mediated reactions studies were carried out in a locally fabricated photoreactor designed in our lab. Blue (emission maximum at 440 nm) light was supplied to each reaction vial with the use of Kessil lamp (40 W with 50% intensity when power applied) with stirring at a distance of ~5 cm (with cooling using a fan) while maintaining the temperature at 28 °C.

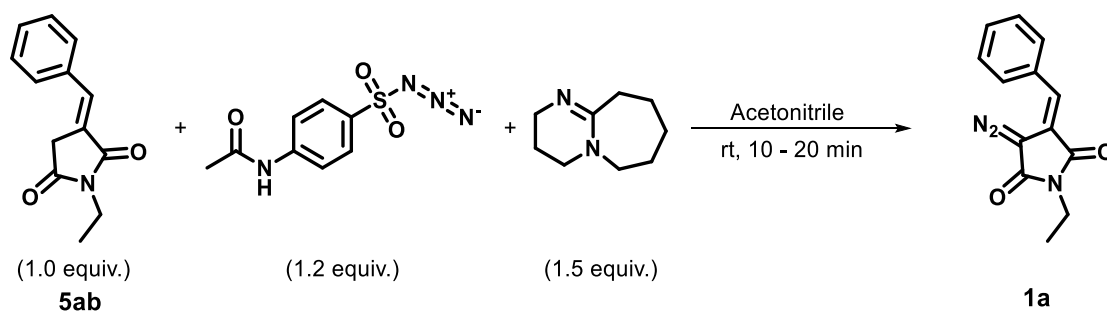
5.8.2. General procedure-A for the synthesis of vinyl succinimides (**5ab**):



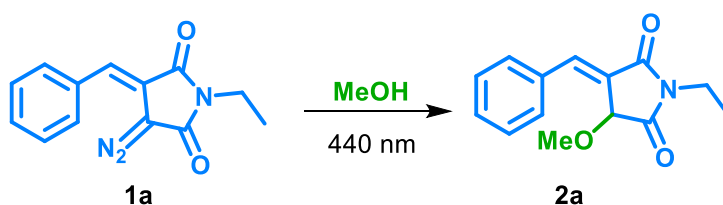
To the stirred solution of *N*-ethyl maleimide **5a** (0.5 g, 1.0 equiv., 4.0 mmol) in ethanol (20 mL) was added triphenylphosphine (1.26 g, 1.2 equiv., 4.8 mmol) portion-wise at room temperature under N_2 atmosphere. The initial pink-coloured reaction mixture slowly turned to white suspension over a period of 10-15 minutes of stirring. After the continuous stirring for over 30 min, benzaldehyde **5b** (571 μL , 1.4 equiv., 6.0 mmol) was added in one portion into the reaction mixture at room temperature. During this addition, the white suspension slowly turned into a clear solution. The reaction mixture was allowed to stir for 6 h. Upon completion of the reaction (monitored by TLC), the white solid formed during the course of the reaction was filtered through a sintered glass funnel and was washed with ethanol (6 mL x 2). The crude product **5ab** was obtained as a white solid (700 mg, 81% yield) and used for the next step without further purification.^[23]

5.8.3. General Procedure-B for the synthesis of vinyl diazosuccinimide(1a):

To the stirred solution of (*E*)-3-benzylidene-1-ethylpyrrolidine-2,5-dione **5ab** (2.15 g, 1.0 equiv., 10 mmol) in 30 mL acetonitrile, were added 4-acetamidobenzenesulfonyl azide (2.88 g, 1.2 equiv., 12 mmol) and DBU (2.24 mL, 1.5 equiv., 15 mmol) at 0 °C temperature under inert atmosphere. The reaction mixture was stirred for 10 minutes while maintaining the reaction temperature (0 °C). The reaction mixture was then quenched with saturated solution of NH₄Cl and the product was extracted with diethyl ether (30 mL x 3). The combined organic layer was washed with brine solution and dried over anhydrous Na₂SO₄. The extract was filtered and evaporated under reduced pressure. The crude product was purified using column chromatography over silica gel to afford (*E*)-3-benzylidene-4-diazo-1-ethylpyrrolidine-2,5-dione **1a** as orange solid (2.257 g, 94% yield).^[2]



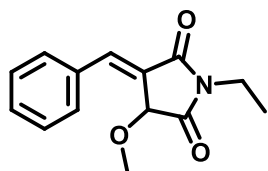
5.8.4. General procedure-C for the visible light promoted 1,3-dibromination of DASs



To a reaction tube equipped with a magnetic stir bar were added diazo compound **1a** (1.0 equiv., 0.2 mmol) in methanol (0.055 M). The tube was capped with a rubber septum, and the mixture was degassed by purging with nitrogen gas. The resulting solution was irradiated by 440 nm blue LEDs with stirring at a distance of ~5 cm (with cooling using fan) at 28 °C (measured using IR sensor Thermometer) for about 24 h until the diazo compound **1** was completely consumed (as monitored by TLC analysis). The reaction mixture was evaporated under reduced pressure. The crude mixture was purified over column chromatography using silica gel with hexanes/ethyl acetate mixture as an eluent to obtain the corresponding product **2** yellowish solid.

5.9. Characterization of synthesized compounds:

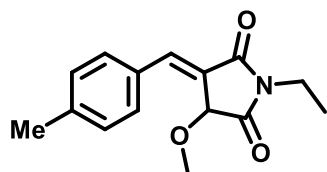
(E)-3-benzylidene-1-ethyl-4-methoxypyrrolidine-2,5-dione (2a): Compound **2a** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 29.5 mg (60% yield); $R_f=0.5$ (petroleum ether/EtOAc 90:10);



^1H NMR (400 MHz, CDCl_3): δ 7.80 (d, $J = 1.9$ Hz, 1H), 7.75 – 7.63 (m, 2H), 7.45 (dd, $J = 5.0, 1.9$ Hz, 3H), 4.87 (d, $J = 2.0$ Hz, 1H), 3.69 (q, $J = 7.2$ Hz, 2H), 3.52 (s, 3H), 1.24 (t, $J = 7.2$ Hz, 3H);

^{13}C { ^1H } NMR (100 MHz, CDCl_3): δ 173.6, 169.3, 140.0, 133.2, 131.4, 131.1, 129.1, 123.9, 73.5, 55.6, 33.9, 13.3. **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{14}\text{H}_{16}\text{NO}_3$ ($\text{M} + \text{H}$) $^+$: 246.1130; Found: 246.1128.

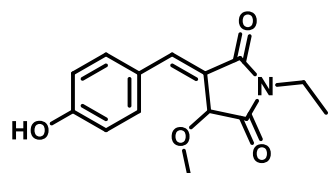
(E)-1-ethyl-3-methoxy-4-(4-methylbenzylidene)pyrrolidine-2,5-dione (2b): Compound **2b** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 38 mg (73% yield); $R_f=0.45$ (petroleum ether/EtOAc 90:10);



^1H NMR (400 MHz, CDCl_3): δ 7.79 (d, $J = 1.9$ Hz, 1H), 7.61 (d, $J = 8.2$ Hz, 2H), 7.27 (d, $J = 8.2$ Hz, 2H), 4.88 (d, $J = 1.9$ Hz, 1H), 3.70 (q, $J = 7.2$ Hz, 2H), 3.51 (s, 3H), 2.41 (s, 3H), 1.25 (t, $J = 7.2$ Hz, 3H). **^{13}C { ^1H } NMR (100 MHz, CDCl_3):** δ 173.8, 169.6,

141.9, 140.1, 131.6, 130.5, 130.0, 122.6, 73.6, 55.5, 33.9, 21.7, 13.3. **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{15}\text{H}_{18}\text{NO}_3$ ($\text{M} + \text{H}$) $^+$: 260.3130; Found: 260.3131.

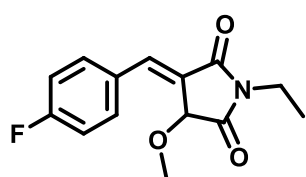
(E)-1-ethyl-3-(4-hydroxybenzylidene)-4-methoxypyrrolidine-2,5-dione (2c): Compound **2c** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 29 mg (55% yield); $R_f=0.35$ (petroleum ether/EtOAc 90:10);



^1H NMR (400 MHz, CDCl_3): δ 7.76 (d, $J = 1.9$ Hz, 1H), 7.67 – 7.61 (m, 2H), 6.95 – 6.90 (m, 2H), 5.72 (s, 1H), 4.90 (d, $J = 1.9$ Hz, 1H), 3.70 (q, $J = 7.2$ Hz, 2H), 3.48 (s, 3H), 1.25 (t, $J = 7.2$ Hz, 3H); **^{13}C { ^1H } NMR (100 MHz, CDCl_3):** δ 173.9, 169.8, 158.6,

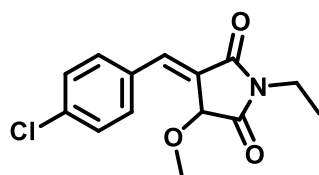
139.9, 133.9, 126.1, 120.6, 116.3, 73.7, 55.1, 33.9, 13.4. **HRMS (ESI TOF) m/z :** calcd for $\text{C}_{14}\text{H}_{16}\text{NO}_4$ ($\text{M} + \text{H}$) $^+$: 262.1079; Found: 262.1075

(E)-1-ethyl-3-(4-fluorobenzylidene)-4-methoxypyrrolidine-2,5-dione (2d): Compound **2d** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 37 mg (70% yield); $R_f=0.5$ (petroleum ether/EtOAc 90:10);



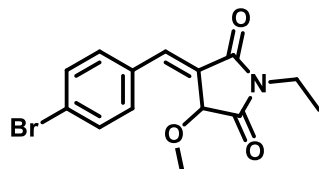
^1H NMR (400 MHz, CDCl_3): δ 7.78 (d, $J = 2.0$ Hz, 1H), 7.75 – 7.69 (m, 2H), 7.19 – 7.12 (m, 2H), 4.86 (d, $J = 2.0$ Hz, 1H), 3.70 (q, $J = 7.2$ Hz, 2H), 3.51 (s, 3H), 1.25 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 173.4, 169.3, 165.6, 163.1, 138.8, 133.7 (d, $J = 8.8$ Hz), 129.5 (d, $J = 3.4$ Hz), 123.3 (d, $J = 2.4$ Hz), 116.5 (d, $J = 21.8$ Hz), 73.5, 55.5, 34.0, 13.3; ^{19}F NMR (377 MHz, CDCl_3) δ -107.5. HRMS (ESI TOF) m/z : calcd for $\text{C}_{14}\text{H}_{15}\text{FNO}_3$ ($\text{M} + \text{H}$) $^+$: 264.1036; Found: 264.1030

(E)-3-(4-chlorobenzylidene)-1-ethyl-4-methoxypyrrolidine-2,5-dione (2e): Compound **2e** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 40 mg (71% yield); $R_f=0.5$ (petroleum ether/EtOAc 90:10);



^1H NMR (400 MHz, CDCl_3): 7.76 (d, $J = 2.0$ Hz, 1H), 7.70 – 7.61 (m, 2H), 7.44 (dd, $J = 8.7, 2.4$ Hz, 2H), 4.87 (d, $J = 2.0$ Hz, 1H), 3.76 – 3.62 (m, 2H), 3.51 (s, 3H), 1.25 (t, $J = 7.2$ Hz, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 173.3, 169.0, 138.5, 137.3, 132.5, 131.6, 131.5, 129.4, 124.2, 73.3, 55.5, 33.9, 13.2. HRMS (ESI TOF) m/z : calcd for $\text{C}_{14}\text{H}_{15}\text{ClNO}_3$ ($\text{M} + \text{H}$) $^+$: 280.0740; Found: 280.0740.

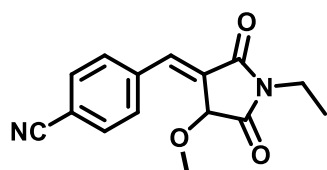
(E)-3-(4-bromobenzylidene)-1-ethyl-4-methoxypyrrolidine-2,5-dione (2f): Compound **2f** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 46 mg (71% yield); $R_f=0.5$ (petroleum ether/EtOAc 90:10);



^1H NMR (400 MHz, CDCl_3): δ 7.74 (d, $J = 2.0$ Hz, 1H), 7.62 – 7.55 (m, 4H), 4.85 (d, $J = 2.0$ Hz, 1H), 3.70 (q, $J = 7.2$ Hz, 2H), 3.51 (s, 3H), 1.25 (t, $J = 7.2$ Hz, 3H). $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 173.2, 169.0, 140.7, 138.5, 132.6, 132.4, 125.8, 124.4, 73.3, 55.5, 33.9, 13.2. HRMS (ESI TOF) m/z : calcd for $\text{C}_{14}\text{H}_{15}\text{BrNO}_3$ ($\text{M} + \text{H}$) $^+$: 324.0235; Found: 324.0236.

(E)-4-((1-ethyl-4-methoxy-2,5-dioxopyrrolidin-3-ylidene)methyl)benzonitrile (2g):

Compound **2g** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 40.5 mg (75% yield); R_f =0.35 (petroleum ether/EtOAc 90:10);

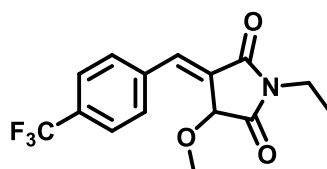


^1H NMR (400 MHz, CDCl_3): δ 7.84 – 7.70 (m, 5H), 4.85 (d, J = 2.0 Hz, 1H), 3.78 – 3.66 (m, 2H), 1.26 (t, J = 7.2 Hz, 3H); ^{13}C { ^1H } NMR (100 MHz, CDCl_3): δ 172.9, 168.6, 137.4, 137.3, 132.8, 131.5, 127.6, 118.3, 114.1, 73.3, 56.1, 34.2, 13.3. HRMS (ESI

TOF) m/z : calcd for $\text{C}_{15}\text{H}_{15}\text{N}_2\text{O}_3$ ($\text{M} + \text{H}$) $^+$: 271.1083; Found: 271.1080.

(E)-1-ethyl-3-methoxy-4-(4-(trifluoromethyl)benzylidene)pyrrolidine-2,5-dione (2h):

Compound **2h** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 50 mg (80% yield); R_f =0.4 (petroleum ether/EtOAc 90:10);

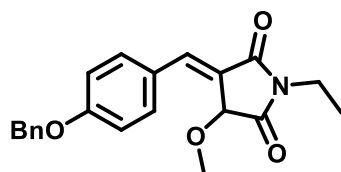


^1H NMR (400 MHz, CDCl_3): δ 7.88 – 7.77 (m, 3H), 7.72 (d, J = 8.2 Hz, 2H), 4.86 (d, J = 2.0 Hz, 1H), 3.72 (q, J = 7.2 Hz, 2H), 3.54 (s, 3H), 1.26 (t, J = 7.2 Hz, 3H); ^{13}C { ^1H } NMR (100 MHz, CDCl_3): δ 173.1, 168.8, 138.1, 136.48, 131.4, 126.6, 126.1 (q, J =

3.7 Hz), 125.2, 128.20 – 119.63 (m), 73.41, 56.00, 34.13, 13.27; ^{19}F NMR (377 MHz, CDCl_3): δ -63.02. HRMS (ESI TOF) m/z : calcd for $\text{C}_{15}\text{H}_{15}\text{F}_3\text{NO}_3$ ($\text{M} + \text{H}$) $^+$: 314.1004; Found: 314.1000.

(E)-3-(4-(benzyloxy)benzylidene)-1-ethyl-4-methoxypyrrolidine-2,5-dione (2i):

Compound **2i** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 32 mg (70% yield); R_f =0.45 (petroleum ether/EtOAc 90:10);

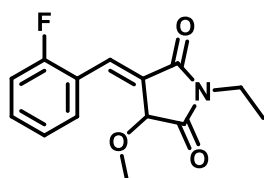


^1H NMR (400 MHz, CDCl_3): 7.76 (d, J = 1.9 Hz, 1H), 7.71 – 7.61 (m, 2H), 7.50 – 7.29 (m, 5H), 7.12 – 6.95 (m, 2H), 5.13 (s, 2H), 4.89 (d, J = 1.9 Hz, 1H), 3.70 (q, J = 7.2 Hz, 2H), 3.48 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H); ^{13}C { ^1H } NMR (100 MHz, CDCl_3):

HRMS (ESI TOF) m/z : calcd for $\text{C}_{21}\text{H}_{22}\text{NO}_4$ ($\text{M} + \text{H}$) $^+$: 352.1549; Found: 352.1542.

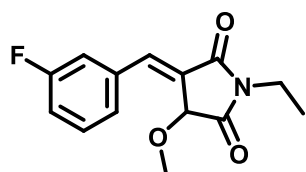
(E)-1-ethyl-3-(2-fluorobenzylidene)-4-methoxypyrrolidine-2,5-dione (2j):

Compound **2j** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 37 mg (70% yield); R_f =0.45 (petroleum ether/EtOAc 90:10);



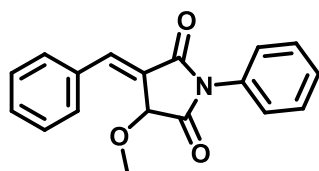
¹H NMR (400 MHz, CDCl₃): δ 8.03 (d, *J* = 2.1 Hz, 1H), 7.78 (td, *J* = 7.7, 1.8 Hz, 1H), 7.49 – 7.37 (m, 1H), 7.23 (td, *J* = 7.6, 1.2 Hz, 1H), 7.14 (ddd, *J* = 10.5, 8.3, 1.2 Hz, 1H), 4.85 (d, *J* = 2.1 Hz, 1H), 3.70 (q, *J* = 7.2 Hz, 2H), 3.50 (s, 3H), 1.24 (t, *J* = 7.2 Hz, 3H); **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 173.52, 168.80, 161.86 (d, *J* = 254.9 Hz), 132.89 (d, *J* = 9.0 Hz), 131.44 (d, *J* = 5.8 Hz), 131.09 (d, *J* = 1.7 Hz), 126.00 (d, *J* = 1.3 Hz), 124.72 (d, *J* = 3.9 Hz), 121.43 (d, *J* = 11.4 Hz), 116.08 (d, *J* = 22.1 Hz), 73.81 (d, *J* = 2.1 Hz), 56.14, 33.96, 13.26. **HRMS (ESI TOF) *m/z*:** calcd for C₁₄H₁₅FNO₃ (M + H)⁺: 264.1036; Found: 264.1032

(E)-1-ethyl-3-(3-fluorobenzylidene)-4-methoxypyrrolidine-2,5-dione (2k): Compound **2k** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 32 mg (60% yield); *R_f*=0.45 (petroleum ether/EtOAc 90:10);



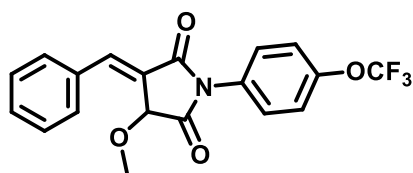
¹H NMR (400 MHz, CDCl₃): δ 7.77 (d, *J* = 1.9 Hz, 1H), 7.50 – 7.37 (m, 3H), 7.21 – 7.12 (m, 1H), 4.83 (d, *J* = 2.0 Hz, 1H), 3.71 (q, *J* = 7.2 Hz, 2H), 3.57 (s, 3H), 1.26 (t, *J* = 7.2 Hz, 3H); **¹³C {¹H} NMR (100 MHz, CDCl₃):** δ 173.3, 169.0, 164.3, 138.6 (d, *J* = 2.6 Hz), 130.7 (d, *J* = 8.1 Hz), 127.5 (d, *J* = 3.0 Hz), 125.44, 117.8 (dd, *J* = 56.0, 21.9 Hz), 73.4, 56.0, 34.0, 13.3; **¹⁹F NMR (377 MHz, CDCl₃):** δ -111.72. **HRMS (ESI TOF) *m/z*:** calcd for C₁₄H₁₅FNO₃ (M + H)⁺: 264.1036; Found: 264.1038

(E)-3-benzylidene-4-methoxy-1-phenylpyrrolidine-2,5-dione (2l): Compound **2l** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 35 mg (60% yield); *R_f*=0.5 (petroleum ether/EtOAc 90:10);



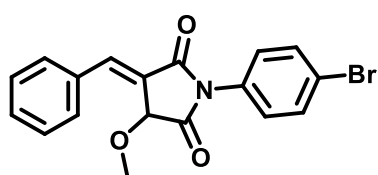
¹H NMR (400 MHz, CDCl₃): δ 7.95 (d, *J* = 2.0 Hz, 1H), 7.78 – 7.73 (m, 2H), 7.53 – 7.47 (m, 5H), 7.45 – 7.38 (m, 3H), 5.02 (d, *J* = 1.9 Hz, 1H), 3.66 (s, 3H); **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 172.8, 168.6, 141.5, 133.2, 131.7, 131.6, 131.4, 129.3, 129.3, 128.9, 126.5, 123.6, 77.5, 76.8, 73.7, 56.2. **HRMS (ESI TOF) *m/z*:** calcd for C₁₈H₁₆NO₃ (M + H)⁺: 294.1130; Found: 294.1133.

(E)-3-benzylidene-4-methoxy-1-(4-(trifluoromethoxy)phenyl)pyrrolidine-2,5-dione (2m): Compound **2m** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 49 mg (65% yield); *R_f*=0.4 (petroleum ether/EtOAc 90:10);



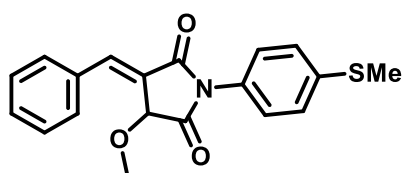
¹H NMR (400 MHz, CDCl₃): δ 7.96 (d, *J* = 1.9 Hz, 1H), 7.77 – 7.71 (m, 2H), 7.52 – 7.46 (m, 5H), 7.38 – 7.32 (m, 2H), 5.00 (d, *J* = 1.9 Hz, 1H), 3.67 (s, 3H); **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 172.4, 168.2, 148.8 (q, *J* = 1.7 Hz), 141.9, 133.0, 131.5, 131.4, 129.9, 129.2, 127.8, 123.1, 121.6, 120.4 (q, *J* = 258.2 Hz), 73.6, 56.3. **HRMS (ESI TOF) *m/z*:** calcd for C₁₉H₁₅F₃NO₃ (*M* + *H*)⁺: 378.0953; Found: 378.0955.

(*E*)-3-benzylidene-1-(4-bromophenyl)-4-methoxypyrrolidine-2,5-dione (2n): Compound **2n** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 50 mg (75% yield); *R_f*=0.5 (petroleum ether/EtOAc 90:10);



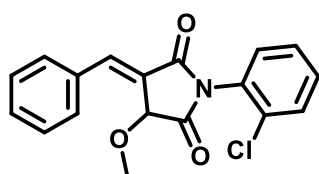
¹H NMR (400 MHz, CDCl₃): δ 7.95 (d, *J* = 2.0 Hz, 1H), 7.77 – 7.71 (m, 2H), 7.66 – 7.61 (m, 2H), 7.50 (pd, *J* = 3.9, 2.1 Hz, 3H), 7.34 – 7.29 (m, 2H), 4.99 (d, *J* = 1.9 Hz, 1H), 3.66 (s, 3H); **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 172.4, 168.3, 142.0, 133.1, 132.5, 131.6, 131.5, 130.7, 129.3, 128.0, 123.3, 122.7, 73.7, 56.4. **HRMS (ESI TOF) *m/z*:** calcd for C₁₈H₁₅BrNO₃ (*M* + *H*)⁺: 372.0235; Found: 372.0230.

(*E*)-3-benzylidene-4-methoxy-1-(4-(methylthio)phenyl)pyrrolidine-2,5-dione (2o): Compound **2o** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 37 mg (55% yield); *R_f*=0.45 (petroleum ether/EtOAc 90:10);



¹H NMR (400 MHz, CDCl₃): δ 7.94 (d, *J* = 1.9 Hz, 1H), 7.77 – 7.72 (m, 2H), 7.52 – 7.47 (m, 3H), 7.38 – 7.31 (m, 4H), 5.00 (d, *J* = 1.9 Hz, 1H), 3.65 (s, 3H); **¹³C{¹H} NMR (100 MHz, CDCl₃):** δ 172.7, 168.6, 141.6, 139.9, 133.2, 131.6, 131.4, 129.3, 128.5, 126.9, 126.7, 123.5, 73.7, 56.3, 15.8. **HRMS (ESI TOF) *m/z*:** calcd for C₁₉H₁₈NO₃S (*M* + *H*)⁺: 340.1007; Found: 340.1005

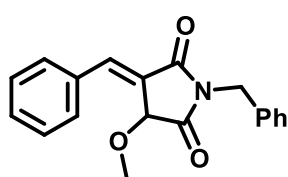
(*E*)-3-benzylidene-1-(2-chlorophenyl)-4-methoxypyrrolidine-2,5-dione (2p): Compound **2p** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 39 mg (60% yield); *R_f*=0.5 (petroleum ether/EtOAc 90:10);



¹H NMR (400 MHz, CDCl₃): δ 7.99 (d, *J* = 2.0 Hz, 1H), 7.96 (d, *J* = 2.0 Hz, 1H), 7.80 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.75 (dd, *J* = 6.7, 3.0 Hz, 2H), 7.57 (ddd, *J* = 9.4, 6.4, 2.3 Hz, 2H), 7.53 – 7.47 (m,

6H), 7.48 – 7.37 (m, 4H), 7.38 – 7.31 (m, 1H), 7.30 – 7.23 (m, 1H), 5.16 (d, $J = 1.9$ Hz, 1H), 5.09 (d, $J = 1.9$ Hz, 1H), 3.68 (s, 3H), 3.57 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 172.2, 172.1, 168.0, 167.9, 142.1, 141.8, 133.1, 133.0, 132.6, 132.3, 132.0, 131.9, 131.7, 131.6, 131.5, 131.5, 131.0, 130.7, 130.6, 130.4, 130.1, 129.8, 129.7, 129.3, 129.2, 128.0, 123.5, 123.1, 73.9, 73.9, 56.5, 55.1. HRMS (ESI TOF) m/z : calcd for $\text{C}_{18}\text{H}_{15}\text{ClNO}_3$ ($\text{M} + \text{H}$) $^+$: 328.0740; Found: 328.0742.

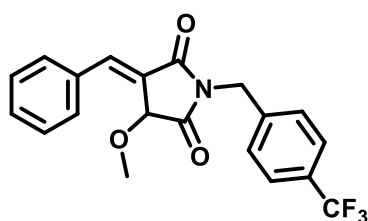
(E)-1-benzyl-3-benzylidene-4-methoxypyrrolidine-2,5-dione (2q): Compound **2q** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 45 mg (73% yield); $R_f=0.5$ (petroleum ether/EtOAc 90:10);



^1H NMR (400 MHz, CDCl_3): δ 7.83 (d, $J = 1.9$ Hz, 1H), 7.69 (dd, $J = 6.7, 2.9$ Hz, 2H), 7.50 – 7.38 (m, 5H), 7.37 – 7.26 (m, 3H), 4.89 (d, $J = 1.9$ Hz, 1H), 4.80 (d, $J = 2.4$ Hz, 2H), 3.49 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 173.5, 169.3, 140.6, 135.7, 133.2,

131.5, 131.2, 129.2, 128.9, 128.9, 128.2, 123.7, 73.2, 55.8, 42.6. HRMS (ESI TOF) m/z : calcd for $\text{C}_{19}\text{H}_{17}\text{NO}_3$ ($\text{M} + \text{H}$) $^+$: 307.1208; Found: 307.1210

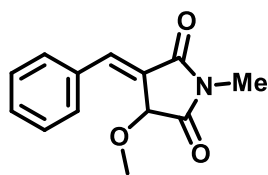
(E)-3-benzylidene-4-methoxy-1-(4-(trifluoromethyl)benzyl)pyrrolidine-2,5-dione (2r): Compound **2r** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 55 mg (73% yield); $R_f=0.45$ (petroleum ether/EtOAc 90:10);



^1H NMR (400 MHz, CDCl_3): δ 7.84 (d, $J = 2.0$ Hz, 1H), 7.73 – 7.66 (m, 2H), 7.59 (d, $J = 8.2$ Hz, 2H), 7.54 (d, $J = 8.1$ Hz, 2H), 7.50 – 7.43 (m, 3H), 4.90 (d, $J = 1.9$ Hz, 1H), 4.84 (s, 2H), 3.52 (s, 3H); $^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3): δ 173.4, 169.1, 141.1, 140.19 – 138.65 (m), 139.5, 139.5, 133.0, 131.5,

131.4, 131.16 – 122.50 (m), 131.66 – 128.35 (m), 129.2, 129.2, 125.89 (q, $J = 3.7$ Hz), 123.5, 73.7, 56.0, 42.0; ^{19}F NMR (377 MHz, CDCl_3) δ -62.7. HRMS (ESI TOF) m/z : calcd for $\text{C}_{20}\text{H}_{17}\text{F}_3\text{NO}_3$ ($\text{M} + \text{H}$) $^+$: 376.1161; Found: 376.1156.

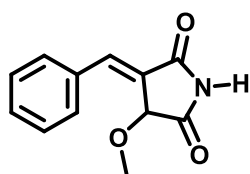
(E)-3-benzylidene-4-methoxy-1-methylpyrrolidine-2,5-dione (2s): Compound **2s** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 30 mg (65% yield); $R_f=0.55$ (petroleum ether/EtOAc 90:10);



¹H NMR (400 MHz, CDCl₃): δ 7.82 (d, *J* = 2.0 Hz, 1H), 7.74 – 7.66 (m, 2H), 7.46 (dd, *J* = 5.0, 1.9 Hz, 3H), 4.88 (d, *J* = 1.9 Hz, 1H), 3.54 (s, 3H), 3.14 (s, 3H); **¹³C {¹H} NMR (100 MHz, CDCl₃):** δ 173.9, 169.7, 140.2, 133.1, 131.5, 131.2, 129.2, 123.8, 73.7, 55.9, 29.8.

HRMS (ESI TOF) *m/z*: calcd for C₁₃H₁₃NO₃ (M + H)⁺: 231.0895; Found: 231.0890.

(*E*)-3-benzylidene-4-methoxypyrrolidine-2,5-dione (2t): Compound **2t** was synthesized following the general procedure-C. The product was obtained as light yellow solid, 22 mg (50% yield); *R_f*=0.3 (petroleum ether/EtOAc 90:10);

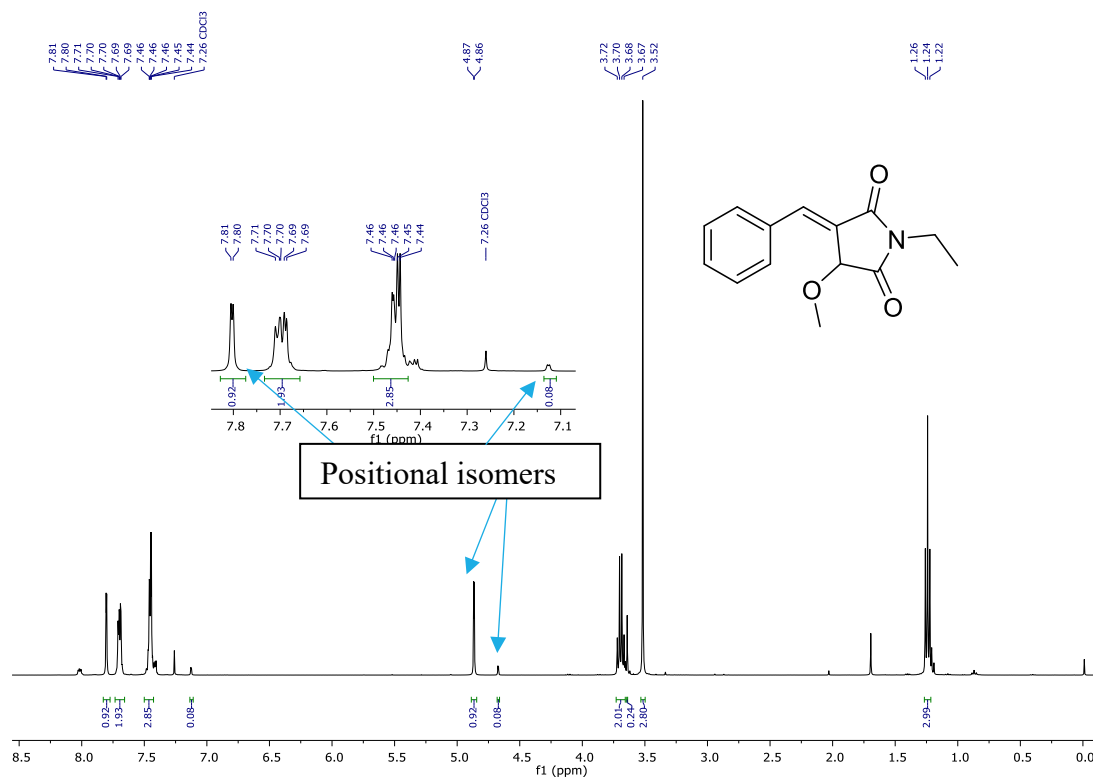


¹H NMR (400 MHz, CDCl₃): δ 8.85 (s, 1H), 7.84 (d, *J* = 2.0 Hz, 1H), 7.77 – 7.65 (m, 2H), 7.54 – 7.36 (m, 3H), 4.94 (d, *J* = 2.0 Hz, 1H), 3.56 (s, 3H); **¹³C {¹H} NMR (100 MHz, CDCl₃):** δ 173.9, 169.5, 141.4, 132.9, 131.6, 131.4, 129.2, 124.3, 74.5, 55.8. **HRMS (ESI TOF) *m/z*:**

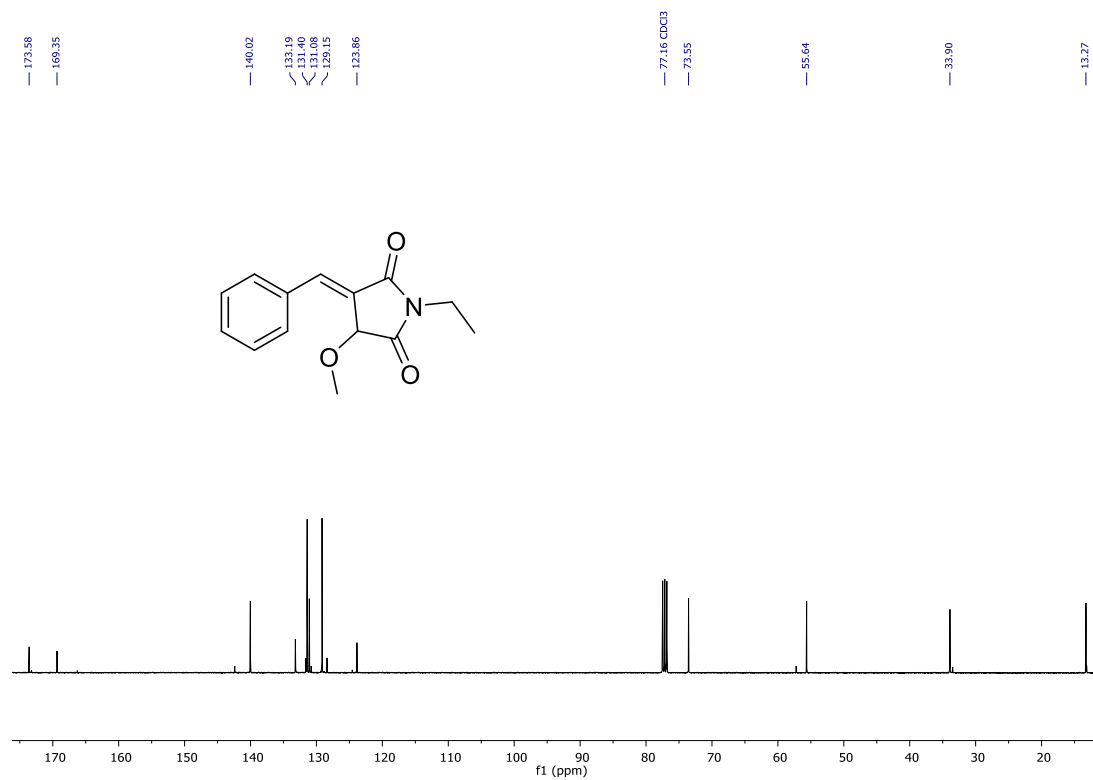
calcd for C₁₂H₁₁NO₃ (M + H)⁺: 217.0739; Found: 217.0741.

5.10. Selected Copies of NMR Spectra (^1H , $^{13}\text{C}\{^1\text{H}\}$ and ^{19}F):

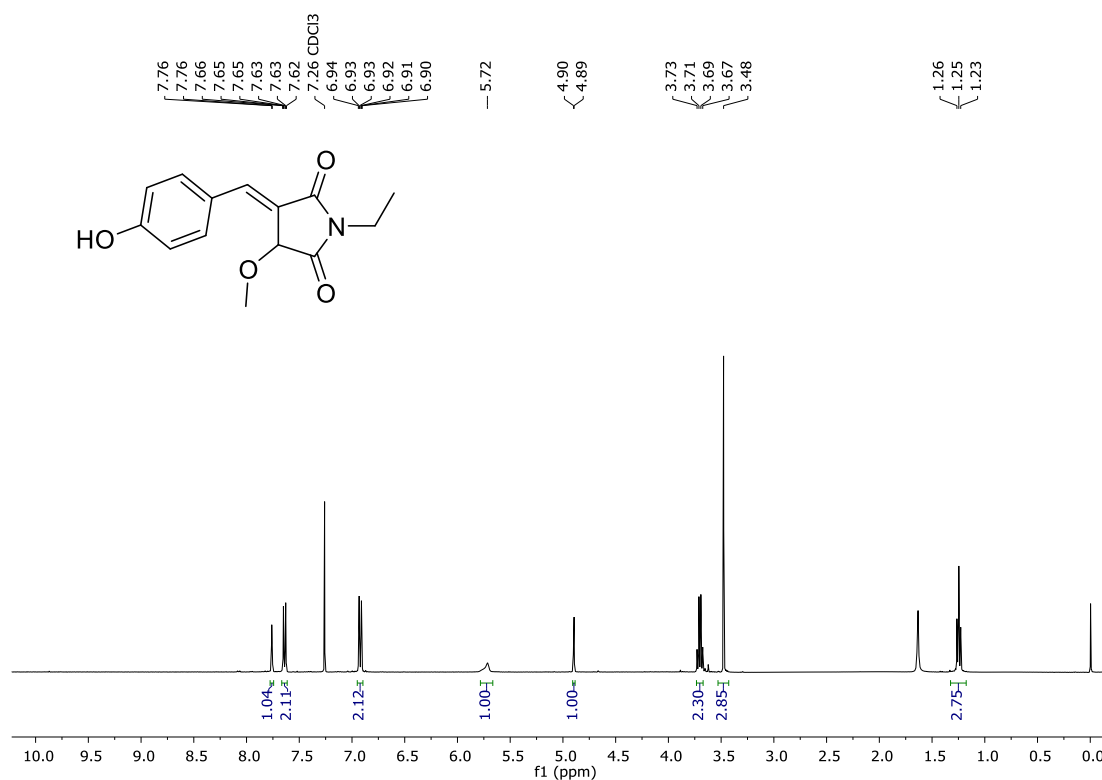
^1H NMR (400 MHz, CDCl_3) Spectrum of **2a**



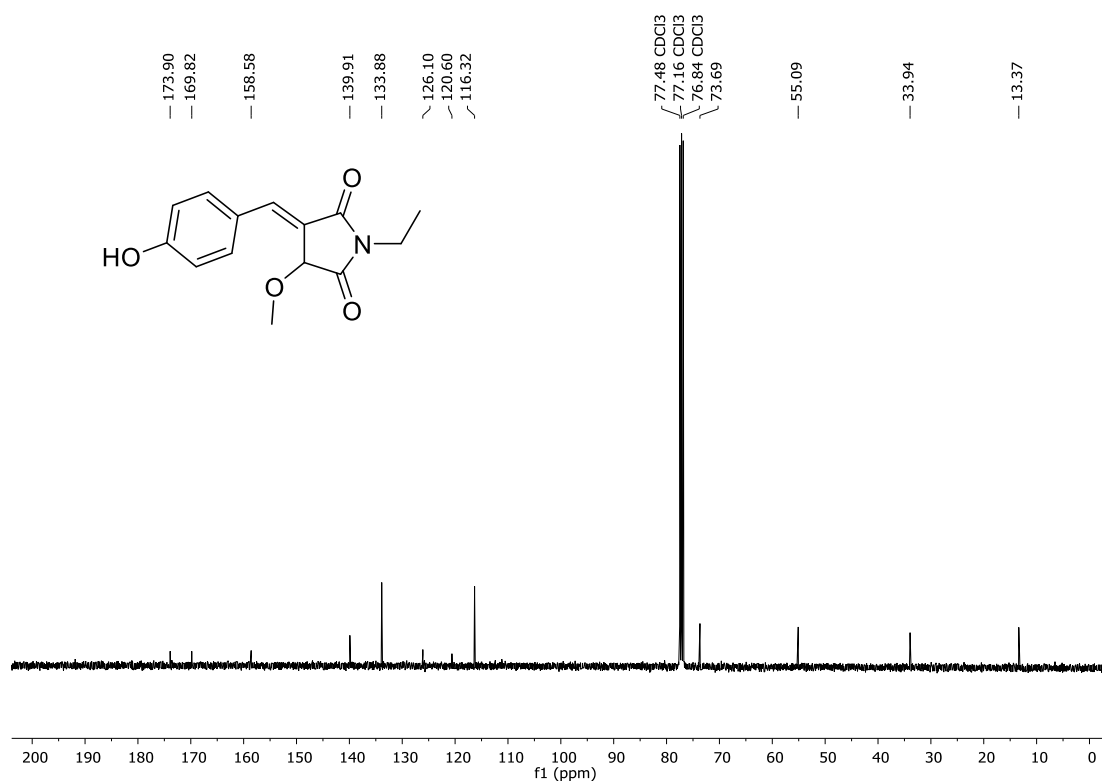
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2a**



^1H NMR (400 MHz, CDCl_3) Spectrum of **2c**



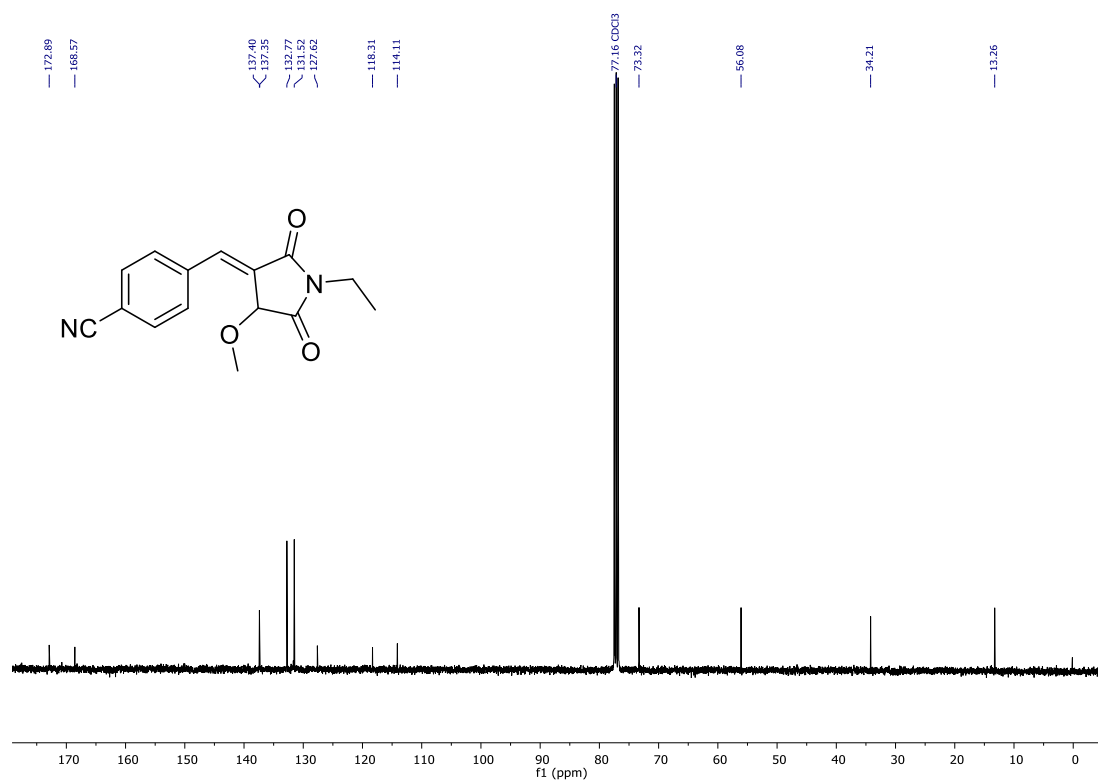
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2c**



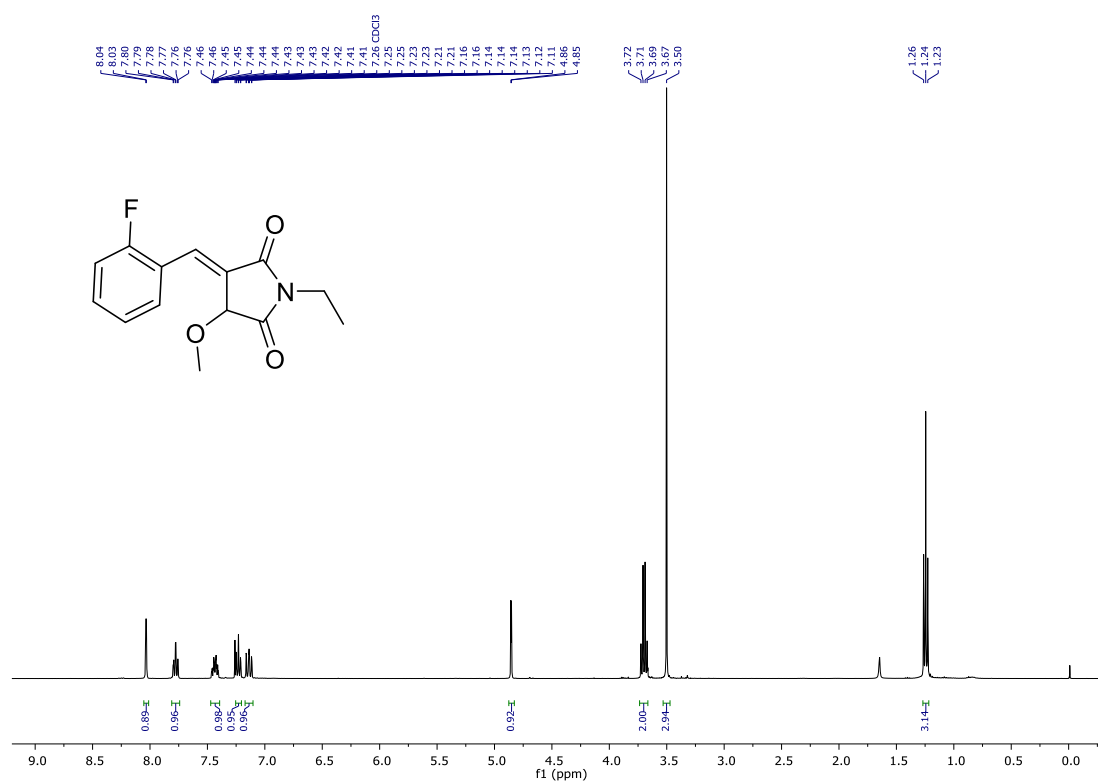
^1H NMR (400 MHz, CDCl_3) Spectrum of **2g**



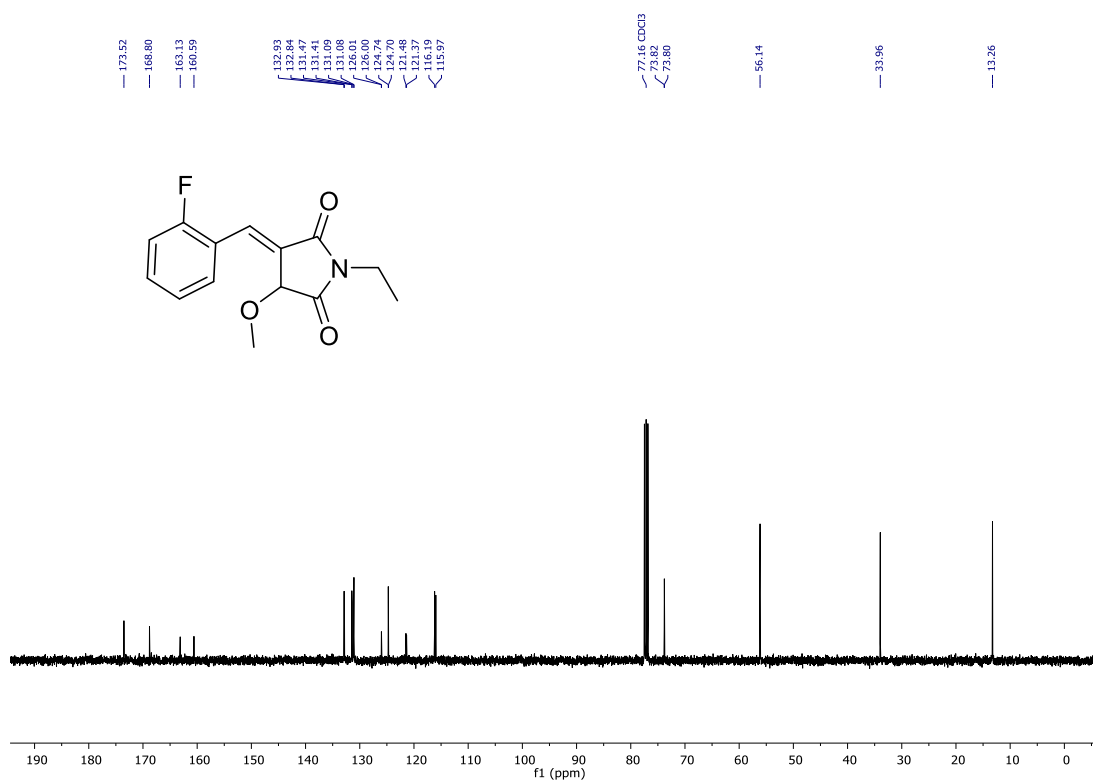
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2g**



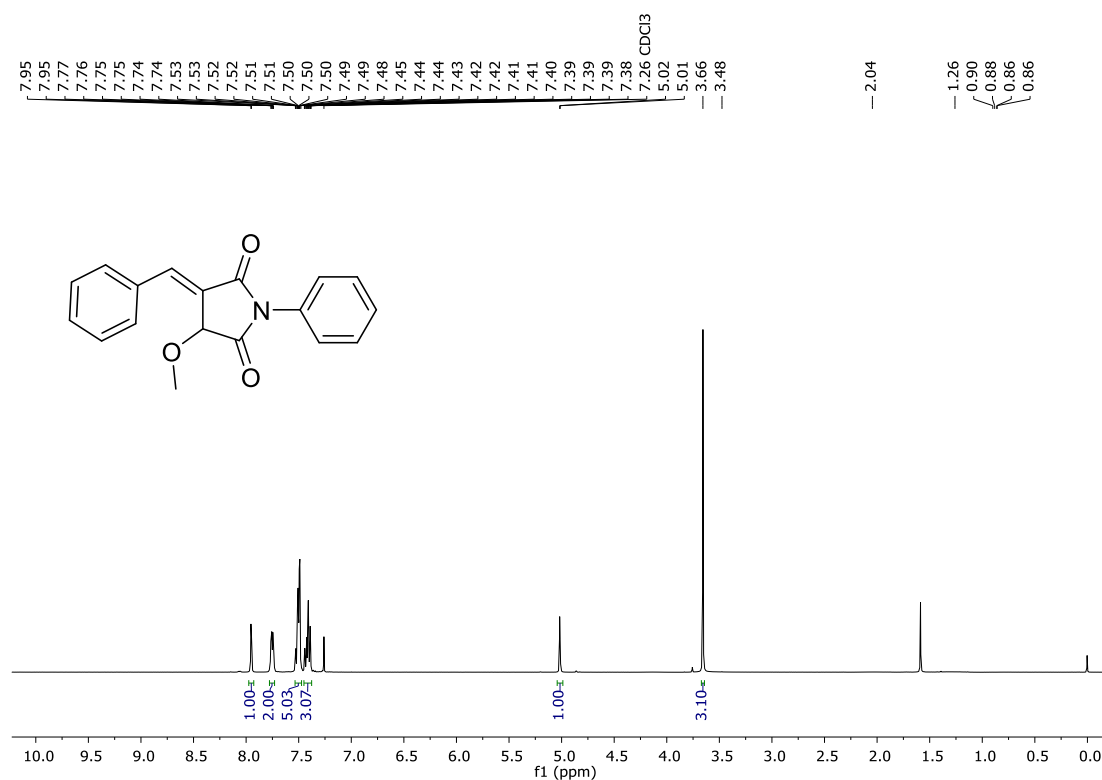
^1H NMR (400 MHz, CDCl_3) Spectrum of **2j**



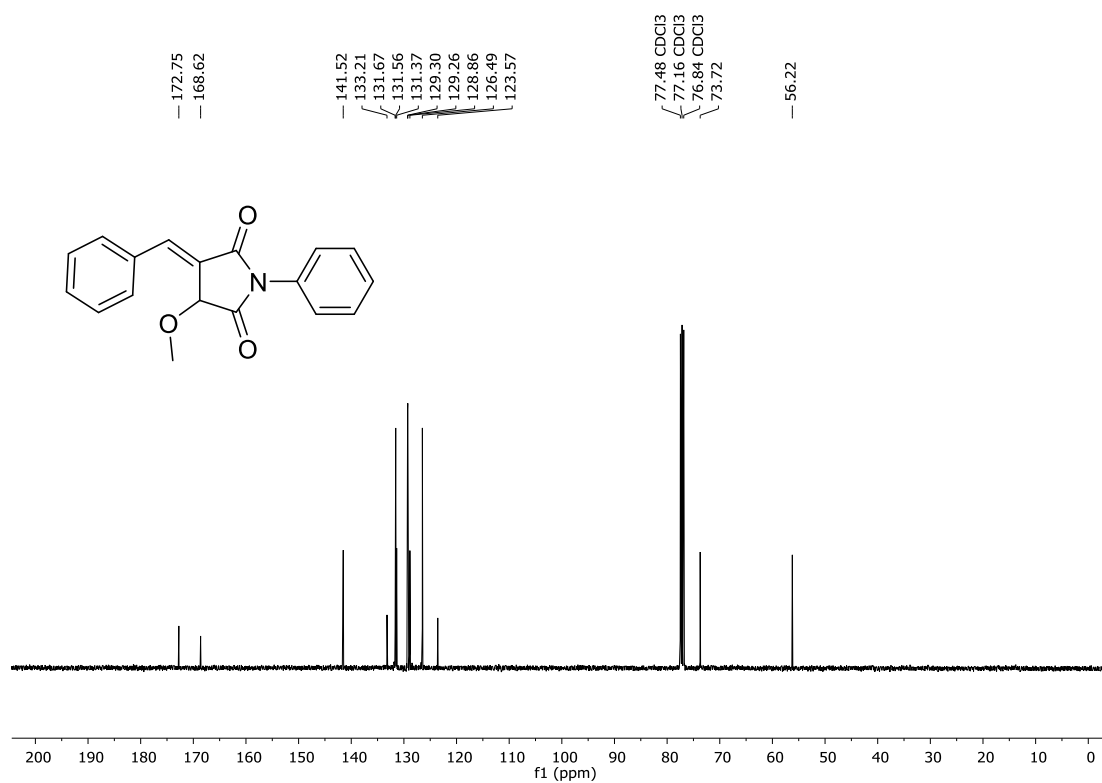
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2j**



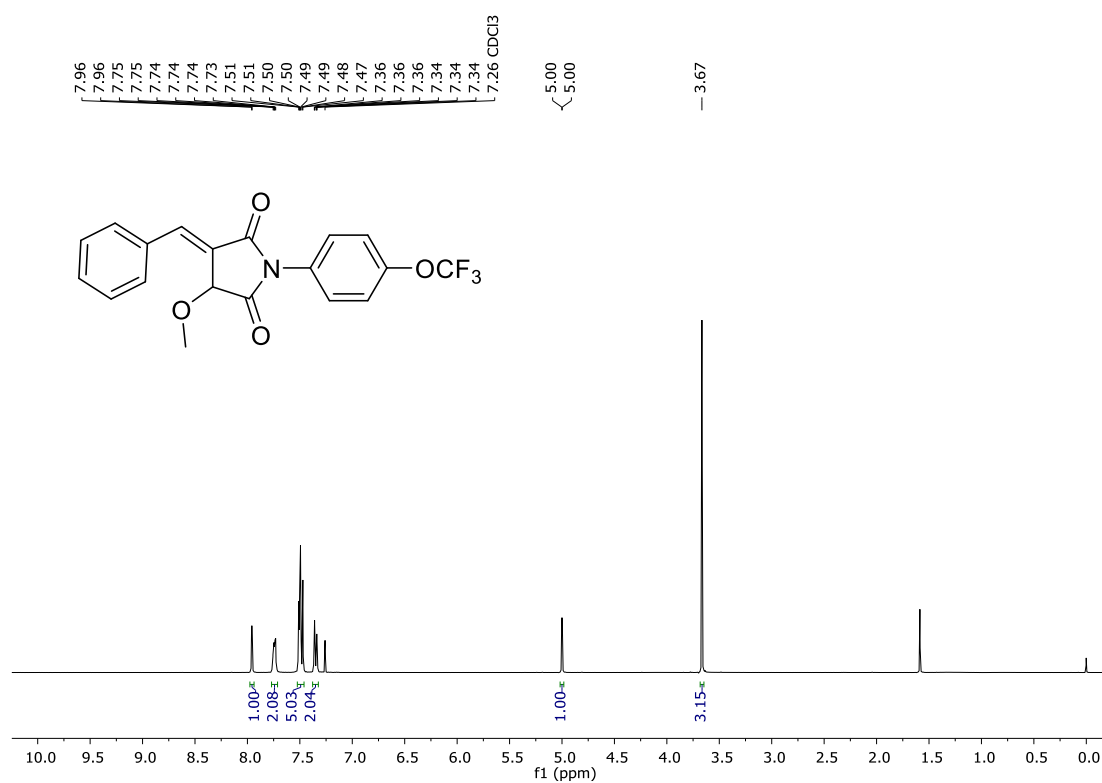
¹H NMR (400 MHz, CDCl₃) Spectrum of **21**



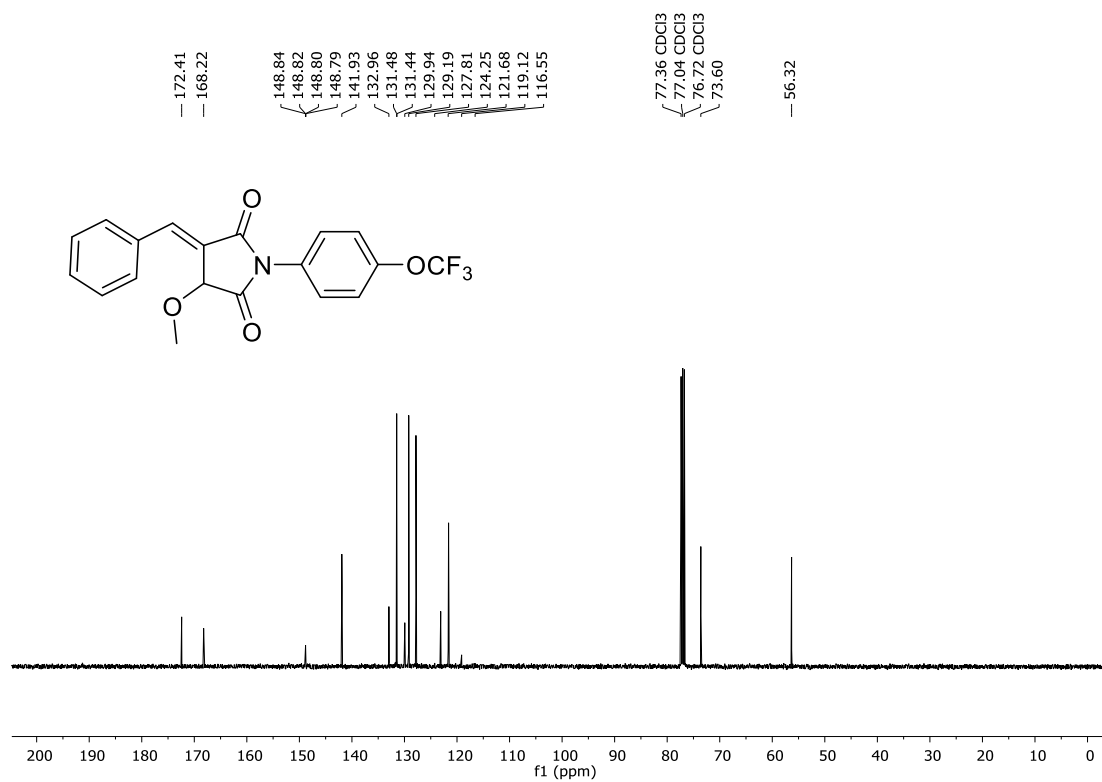
¹³C {¹H} NMR (100 MHz, CDCl₃) Spectrum of **21**



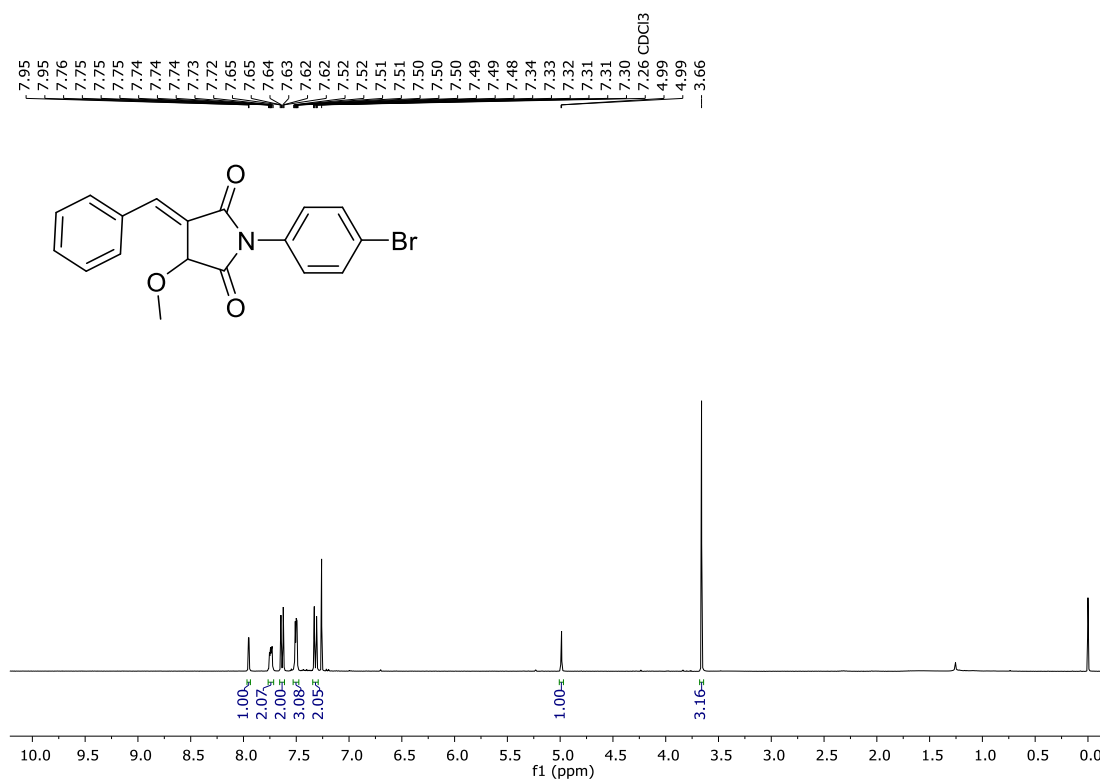
^1H NMR (400 MHz, CDCl_3) Spectrum of **2m**



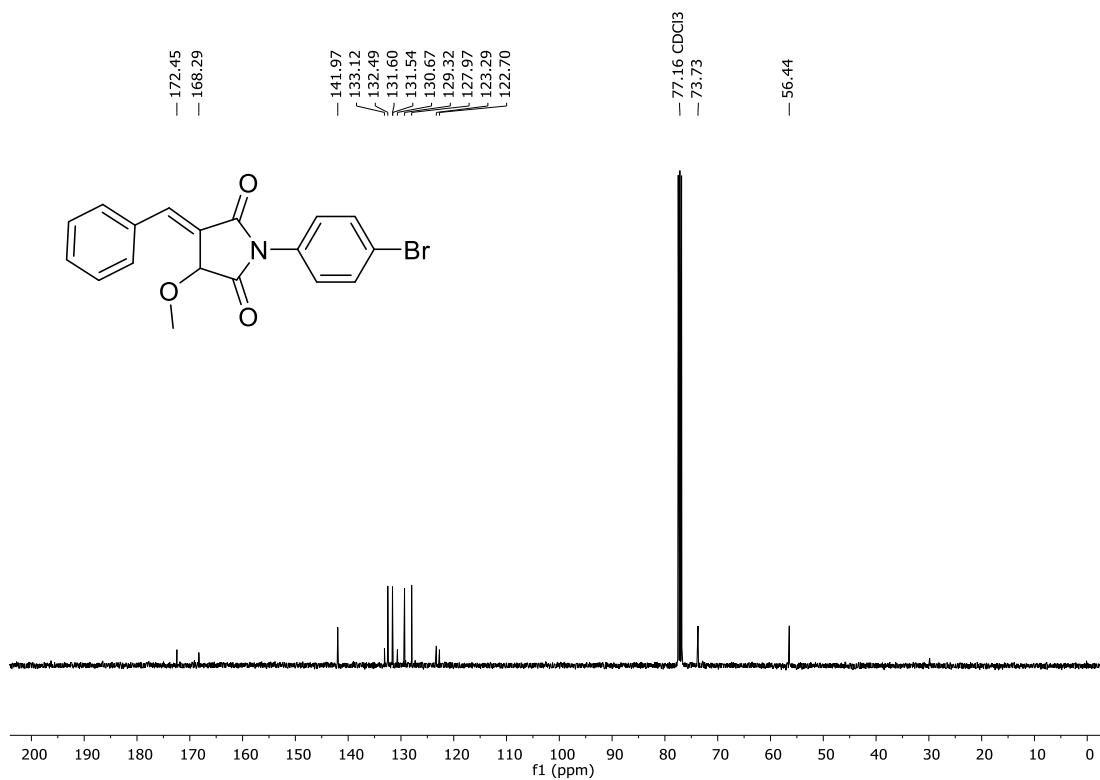
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2m**



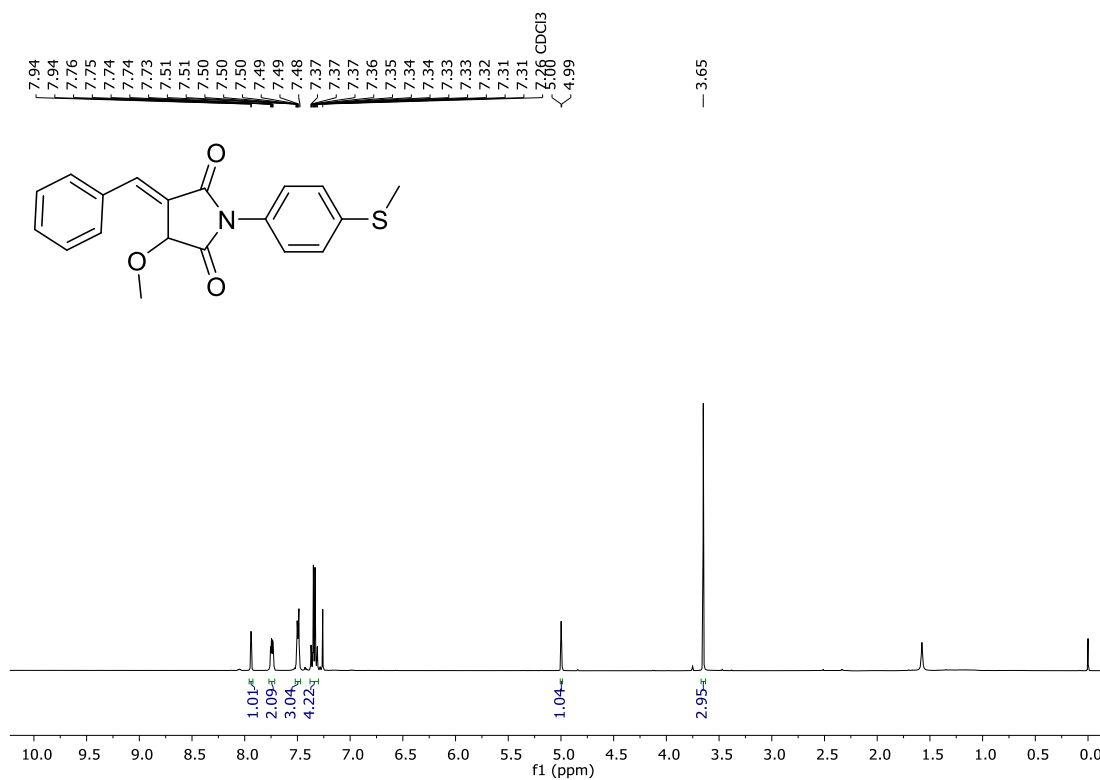
^1H NMR (400 MHz, CDCl_3) Spectrum of **2n**



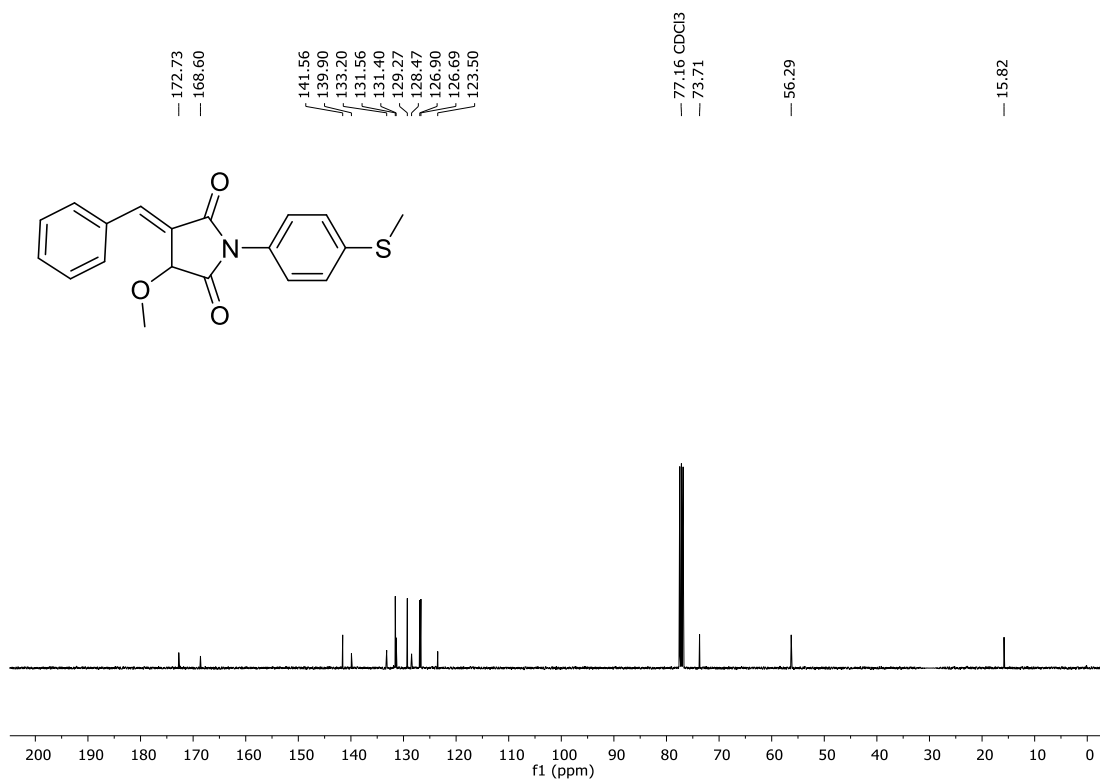
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2n**



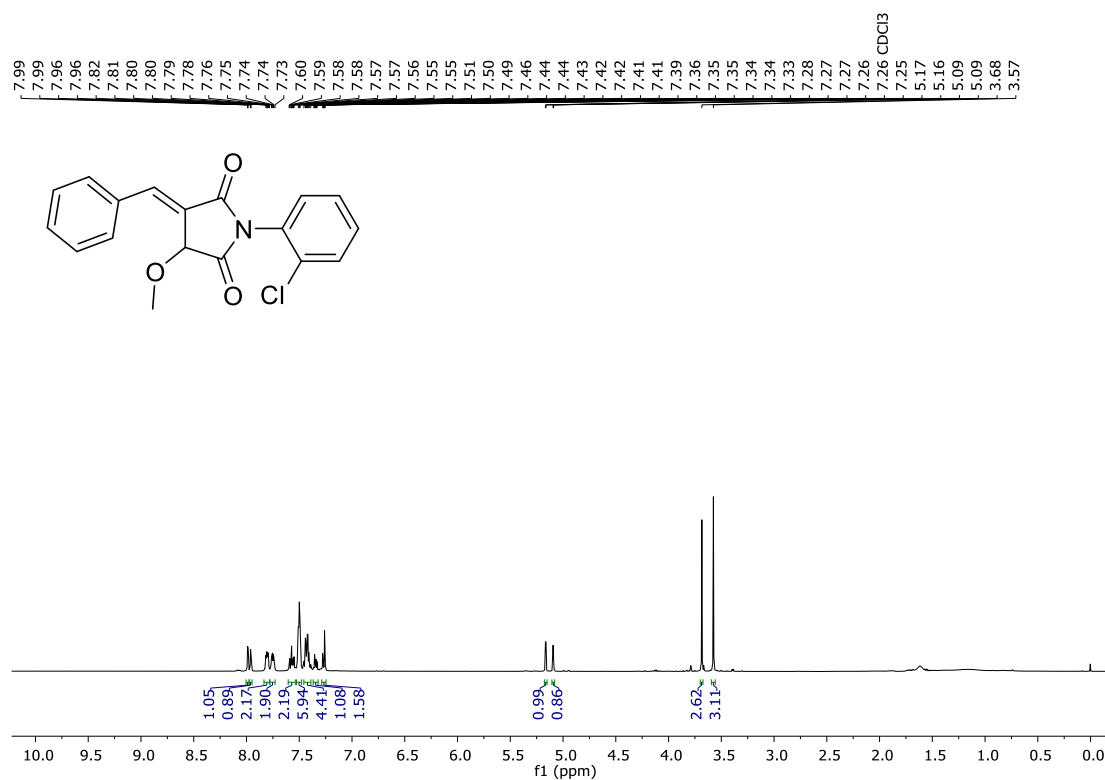
^1H NMR (400 MHz, CDCl_3) Spectrum of **2o**



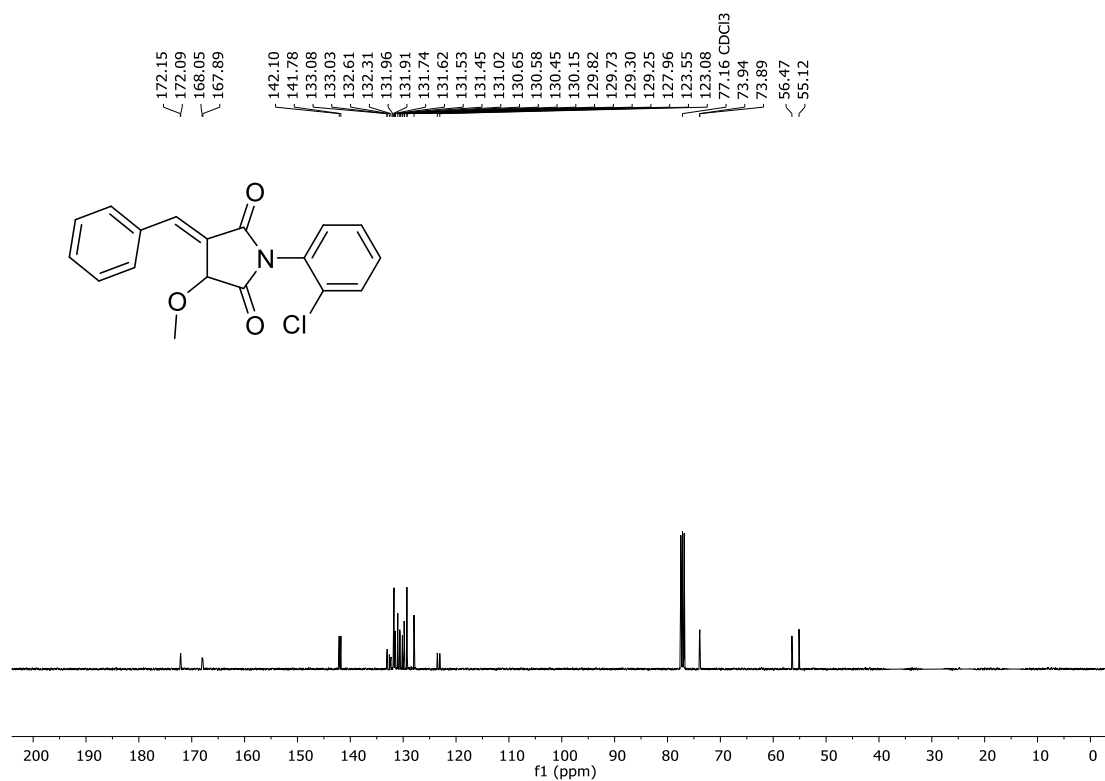
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2o**



^1H NMR (400 MHz, CDCl_3) Spectrum of **2p**



$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) Spectrum of **2p**



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The thesis works greatly focussed at the comprehensive exploration of novel methodologies for the functionalization and transformation of diazo arylidene succinimides (DAS). All the chapters have explored the novel reactivity of DAS under both metal as well as visible light conditions. Efforts have also been emphasized towards achieving the mild, practical, sustainable reaction conditions with a stress on the detailed investigations on insights. A regio-divergent dirhodium(II)-catalyzed rearrangement strategy has been developed, enabling the efficient synthesis of chromene and thiochromene scaffolds through selective [1,2]/[1,4]- shifts (Figure 6.1). Many molecules with these core scaffolds are known to exhibit bioactivity and this method gives an easy platform to design different chromene and thiochromene molecules of potential bioactivity.

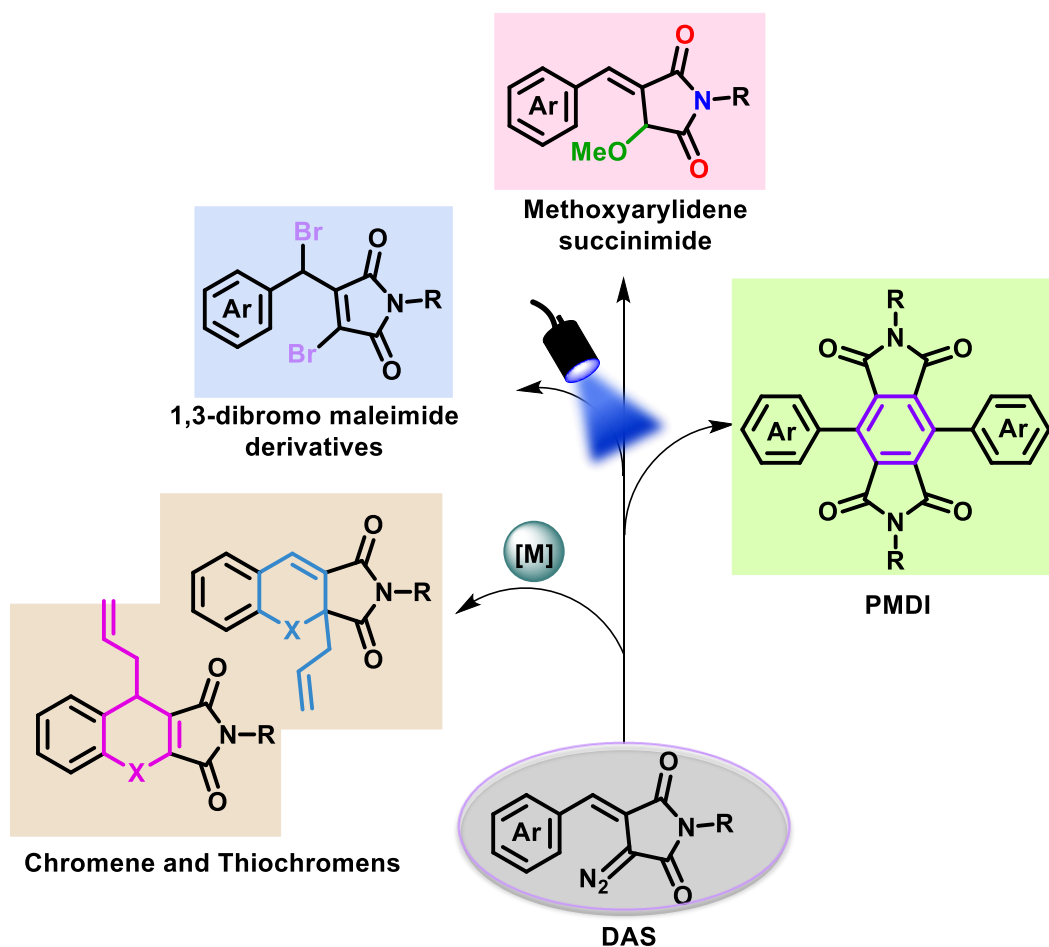


Figure 6.1: Exploring the reactivity of diazo arylidene succinimide under various conditions

Further expanding the chemical versatility of DAS, a copper-catalyzed radical cyclization process has been established, wherein a photoinduced proton-coupled electron transfer (PCET) mechanism drives the selective formation of disubstituted pyromellitic diimides (PMDIs), circumventing traditional carbene intermediates. This protocol introduces a previously unexplored pathway for PMDI synthesis.

Furthermore, a visible-light-induced 1,3-dibromination of DAS using *N*-bromosuccinimide (NBS) has been developed successfully. This operationally simple transformation proceeds via a radical mechanism without the need for external photocatalysts or additives, and remarkably, the protocol also works smoothly under exposure of ambient sunlight. The resulting 1,3-dibromo-functionalized maleimide derivatives could be utilized further as synthetic precursors to synthesize useful compounds and could be explored in different transformations.

Later, a photochemical direct O–H functionalization of DAS has been explored with methanol. Also, the mechanistic investigation of this challenging transformation has been explored and it is consistent with photoinduced proton transfer (PPT) processes. The detailed spectroscopic and crystallographic studies supported the proposed reaction pathway with intermediates.

These developed protocols and systematic studies could further build a strong foundation in chemistry novel **DAS** derivatives. Also, the combining metal catalysis, radical reactions, and photochemistry may open up new opportunities. These methods would surely expand synthetic potential of DASs, further advancing radical-driven and light-induced scalable transformations to construct molecules of optoelectronic materials and biologically relevant compounds.

Future prospectives:

The diverse reactivity of diazo arylidene succinimides (DAS) under visible light and metal catalysis has been successfully demonstrated throughout the thesis. DAS has proven to be a multifaceted scaffold, capable of acting as a carbene precursor as well as a radical source, and functioning both as a radical donor and acceptor. The reactivity of DAS could be further tuned accordingly and this gives a great opportunity to explore the untapped potential of different DAS derivatives. These unique properties open up several promising directions for future research:

- **Reactivity with Nucleophiles and Electrophiles:** Given the photochemical responsiveness of DASs, future studies could be explored by controlling their reactivity with various nucleophiles and electrophiles under visible light irradiation. This may lead to novel bond-forming strategies and further expand the synthetic utility of DASs under mild and sustainable reaction conditions.

-
- **Biological Evaluation of Chromene and Thiochromene Derivatives:** In Chapter 2, the synthesis of chromene and thiochromene frameworks was achieved via regio-divergent rearrangement. As these scaffolds are structurally related to known bioactive molecules. In future these molecules could be evaluated for their biological activity, potentially uncovering new therapeutic candidates. If there is a lead, further modifications could be made.
 - **Functional Applications of PMDI Derivatives:** Chapter 3 disclosed a novel copper-catalyzed radical cyclization strategy for the one-pot synthesis of disubstituted pyromellitic diimides (PMDIs), which exhibit promising features such as semiconductor behavior and aggregation-induced emission (AIE). Further investigation into the optoelectronic properties of the remaining PMDI derivatives could validate their potential in organic electronics and photonic materials.
 - **Sustainable Catalysis Using Organophotocatalysts:** The copper catalysis has been successfully explored for the synthesis of PMDI. In this regard, future efforts could be explored by using organophotocatalysts to achieve similar transformations under more environmentally benign conditions. This would align with the broader goal of sustainable synthetic methodology as well.
 - **Optimization for Unsymmetrical PMDI Synthesis:** Though the unsymmetrical PMDIs have been synthesized, systematic optimization has not been explored for the selective synthesis of unsymmetrical PMDIs. Future research could focus on refining reaction conditions to achieve high-yielding and regioselective access to unsymmetrical PMDI derivatives, thereby broadening the scope and applicability of the methodology.

Synthetic Utility of Vinylic Bromides: In Chapter 4, a visible-light-induced 1,3-dibromination of DAS has been developed. These brominated products offer valuable synthetic handles for further functionalization via cross-coupling or nucleophilic substitution reactions. Exploring such transformations would significantly enhance the impact and applicability of this methodology.

DAS may provide a platform for interdisciplinary applications in medicinal chemistry, materials science, and sustainable synthesis. The continued exploration on the reactivity of DAS reactivity and synthesis of novel DAS derivatives hold a significant promise for both fundamental research and practical innovation.

Visible-Light-Induced Copper-Catalyzed Radical Reactions of Diazo Arylidene Succinimides to Access the Pyromellitic Diimide (PMDI) Core

Kajal B. Meher, Debasish Laha, Pankaj D. Dharpure, and Ramakrishna G. Bhat*



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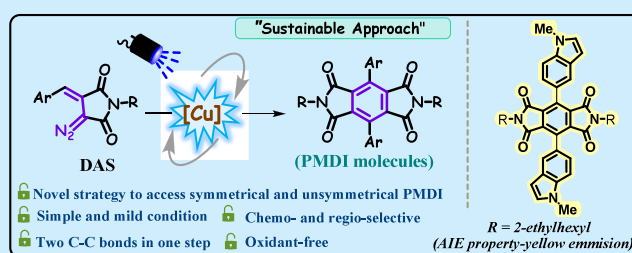
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ABSTRACT: The synthesis of pyromellitic diimides (PMDIs) through visible-light-promoted copper-catalyzed reaction of diazo arylidene succinimides has been accomplished without the use of external oxidants. This transformation involves a carbon radical from diazo arylidene succinimides with a copper catalyst or photocatalyst via the proton-coupled electron transfer (PCET) process. This approach successfully challenges a long-standing paradigm in the synthesis of PMDIs. Notably, copper complex (CuNCS) formed in situ proved to be playing a pivotal role to drive the reaction via photoinitiation. Additionally, we synthesized a PMDI molecule known for its prominent aggregation-induced emission (AIE) property. For the very first time, we have synthesized unsymmetrical PMDIs by employing the developed protocol.



Highly substituted aromatic compounds are useful scaffolds in organic synthesis because of their unique electronic properties, which makes their construction a challenging yet intriguing task for chemists.¹ These compounds and their derivatives play a crucial role in various useful natural products,² pharmaceuticals,³ and bioactive compounds.⁴ The disubstituted pyromellitic diimide (PMDI) scaffold is a valuable member of the hexasubstituted aromatic compound family featuring two distinct cores: *p*-terphenyls and PMDI. The *p*-terphenyl core is found in numerous natural products and bioactive compounds,^{5a} whereas the PMDI-based compounds are used in organic electronics and sensing applications.^{5b,6} Moreover, disubstituted PMDI compounds are renowned for their aggregation-induced emission (AIE), mechanofluorochromic, as well as polymeric, properties.⁶ Even though PMDI-based compounds are valuable for diverse applications, yet efficient synthetic methods for this scaffold are rarely documented.^{6b,7} All of these reported protocols involve multistep synthesis, harsh reaction conditions, use of expensive metal catalysts and metal leaching that limit their wider applicability (Scheme 1A).^{6b,7} Over the years, radical chemistry has made significant advancements, and many state-of-the-art methods have been developed by exploiting its versatile reactivity via photoredox catalysis.⁸ Certain acceptor-type diazo compounds under photoredox catalytic conditions lead to cycloaddition and functionalization via carbon-centered radical intermediates rather than the traditional carbene intermediates.⁹ In contrast, vinyl diazo compounds display distinct reactivity due to the presence of two valuable functional moieties—alkene and diazo groups. Several potent

synthetic approaches have been established featuring reactive sites at the α - and γ -positions. Many of these methods employ acyclic vinyl diazo compounds as a 3-carbon building block for (3 + *n*)-cyclization.^{10,11} In particular, Sun and co-workers¹² have reported gold-catalyzed Z-selective cross-coupling followed by benzannulation reaction of vinyl diazo compounds at an elevated temperature (via carbene intermediate) to access tetrasubstituted benzene ring (Scheme 1B-i). On the contrary, acyclic vinyl diazo compounds under photochemical conditions act as nucleophiles,^{12a,b} while Zhou and Li et al. have observed their role as radical acceptors in the presence of other radical species^{12c} (Scheme 1B-ii). Despite these advancements in the photochemical radical chemistry of diazo compounds,^{9,13} the direct generation of carbene-centered radicals from vinyl diazo compounds (via extrusion of nitrogen) under light illumination has not yet been achieved (Scheme 1B-iii). Unlike acyclic vinyl diazo compounds, diazo arylidene succinimides (DASs) are relatively uncommon and less studied under photochemical conditions. Their distinctive structural features lead to significantly different chemical behavior than acyclic vinyl diazo compounds (Scheme 1C).¹⁴ Recently documented reactions of DASs have involved various transition metal catalysts (Scheme 1C-i),^{14,15} which proceed

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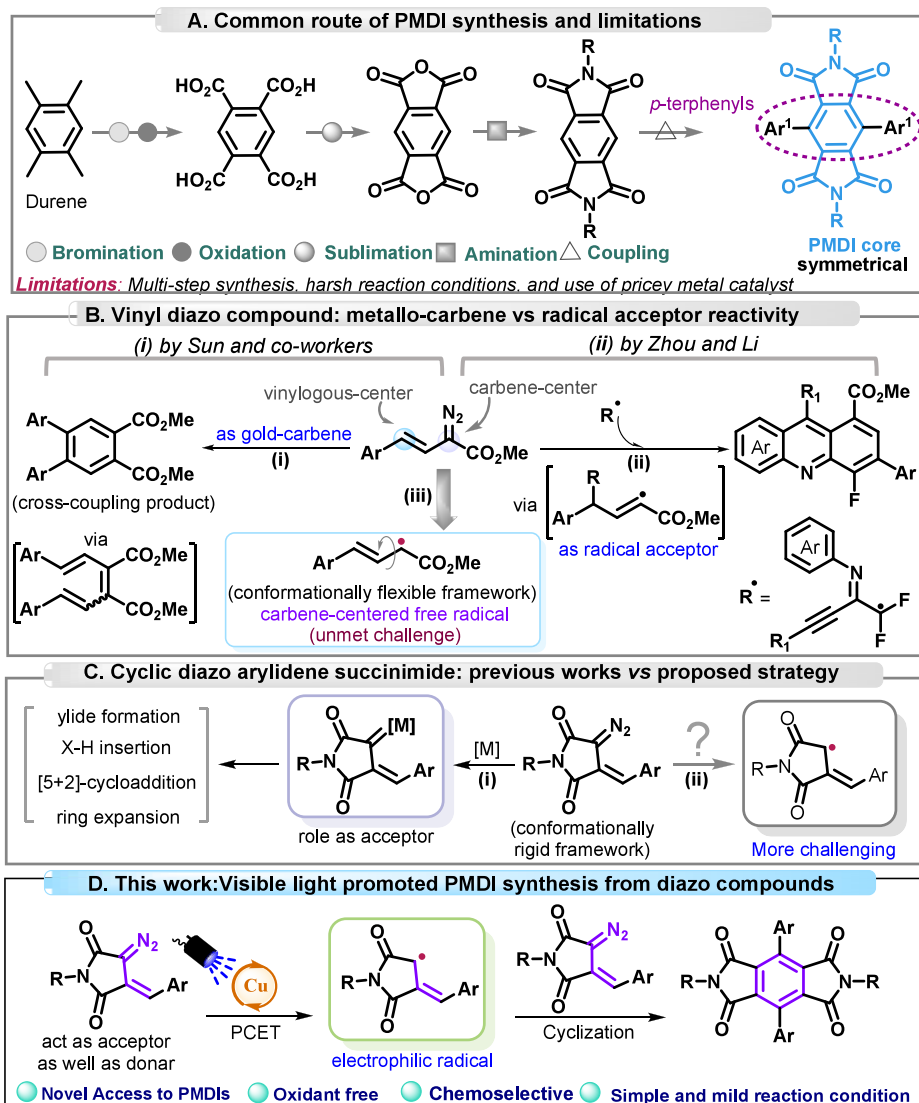
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Scheme 1. Breaking Boundaries—Revealing a Synthetic Strategy to Access PMDI Core



through carbene intermediates. To the best of our knowledge, the reactivity of DASs under visible light has not been explored. DASs may be less reactive or unreactive under visible light irradiation because of their absorption in the near-UV regions. Thus, exploring the reactivity of DASs under visible light and developing a new protocol is challenging.

Over the years, photoredox catalysis has emerged as a sustainable alternative to many traditional methods. Unlike ruthenium and iridium-based photocatalysts,¹⁶ copper salts are abundant and cost-effective, and their complexes show robust photoexcited redox properties.¹⁷ Notably, halide and pseudo-halide ligands have a strong affinity toward Cu(I) salts.¹⁸ Intriguingly, the in situ generation of photocatalysts by combining copper salts with substrates/ligands is a useful strategy to achieve a short synthetic transformation, thus avoiding multistep synthesis.^{17a,19}

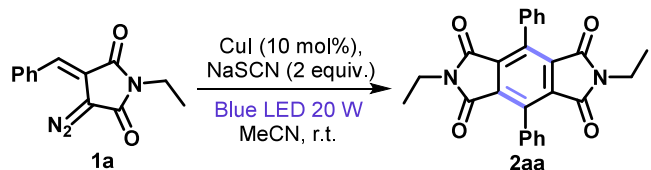
Because of the importance of the PMDI core and looking into traditional methods (Scheme 1A), there is a strong need for a synthetic approach to access disubstituted PMDI molecules easily. Due to our continuous interest in investigating the reactivity of DAS under visible light, we speculated that the formation of a carbon radical intermediate

from DAS could occur through photoredox catalysis, potentially facilitating PMDI core synthesis. Herein, we present a simple yet elegant protocol for the synthesis of PMDI via the photoactivated copper-catalyzed radical cyclization of DAS under mild reaction conditions (Scheme 1D).²⁰

We initiated our study by selecting DAS **1a** as a model substrate with the combination of CuI catalyst and NaSCN as the ligand/base in acetonitrile. After irradiation with blue LEDs (20 W) for 24 h at 30 °C, the desired PMDI product **2aa** was obtained in 60% yield (Table 1, entry 1). The control experiments clearly revealed that light, NaSCN, and CuI are essential for successful transformation (Table 1, entries 2–4).

Further, the reaction in anhydrous acetonitrile failed to furnish the desired product **2aa**, highlighting the essential role of moisture in the reaction (Table 1, entry 5; see details in Supporting Information Table S1). The reaction of **1a** in the presence of an oxygen atmosphere did not furnish the desired product **2aa** (Table 1, entry 6). Additionally, we performed a reaction with photocatalyst eosin Y instead of CuI, and the desired product **2aa** was observed with 45% yield (Table 1 entry 7). Further, an exhaustive screening of different metal

Table 1. Optimization of the Reaction



entry	variation from the initial tested reaction conditions ^a	yield (%) 2aa
1	none	60
2	no light	n.d.
3	no NaSCN	n.d.
4	no CuI	n.d.
5	dry MeCN	n.d.
6	O ₂ balloon	n.d.
7	eosin Y	45
8 ^{c,d}	440 nm	82
9 ^c	no light, 50 °C	n.d.

^aGeneral initial reaction conditions: **1a** (0.2 mmol), CuI (10 mol %), NaSCN (2.0 equiv), MeCN AR grade (0.055 M), blue LEDs (20 W) at 459 nm, 24 h, 30 °C under degassed condition with N₂. ^bIsolated yields. ^cDMSO (0.04 M) was used as solvent (AR grade was used) with Kessil Lamp (440 nm, 40 W, 50% intensity). ^dReaction was completed in 12 h (n.d. = not detected).

catalysts, solvents, bases, and light sources under varied conditions was explored for further optimization to obtain **2aa** efficiently (see the details in [Supporting Information Tables S2–S8](#)). Based on the exhaustive screening, diazo arylidene succinimide (DAS) **1a** (1 equiv), NaSCN (2 equiv), and CuI (10 mol %) under the illumination of blue LED (440 nm) in DMSO (degassed reaction mixture using nitrogen) proved to be the optimal reaction condition ([Table 1](#), entry 8). The reaction in the absence of light, even at an elevated temperature (50 °C), failed to furnish desired product **2aa** ([Table 1](#), entry 9). This clearly indicated that visible light is essential to drive the reaction.

Having the optimized reaction conditions, we explored the substrate scope by varying substitutions at the aryl ring of the diazo compounds. As demonstrated in [Scheme 2](#), *p*-substituted DASs having electron-deactivating and electron-withdrawing groups (**1aa–1ag**) reacted smoothly to afford the corresponding desired products (**2aa–2ag**) in moderate to good yields (up to 82%). However, the *p*-CN derivative afforded the corresponding DAS derivative **2ad** in modest yield (31%, [Scheme 2](#)). This could be attributed to the binding of the –CN group with the [Cu] catalyst, thus leading to diminished reactivity. However, *p*-substituted DASs bearing electron-donating groups (**1ah, 1ai**) afforded the corresponding desired products (**2ah, 2ai**) in relatively lower yields (up to 49%, [Scheme 2](#)). Furthermore, DAS derivatives (**1aj–1am**) with various meta-substituents reacted smoothly to afford the corresponding products (**2aj–2am**) in moderate to good yields (up to 65%).

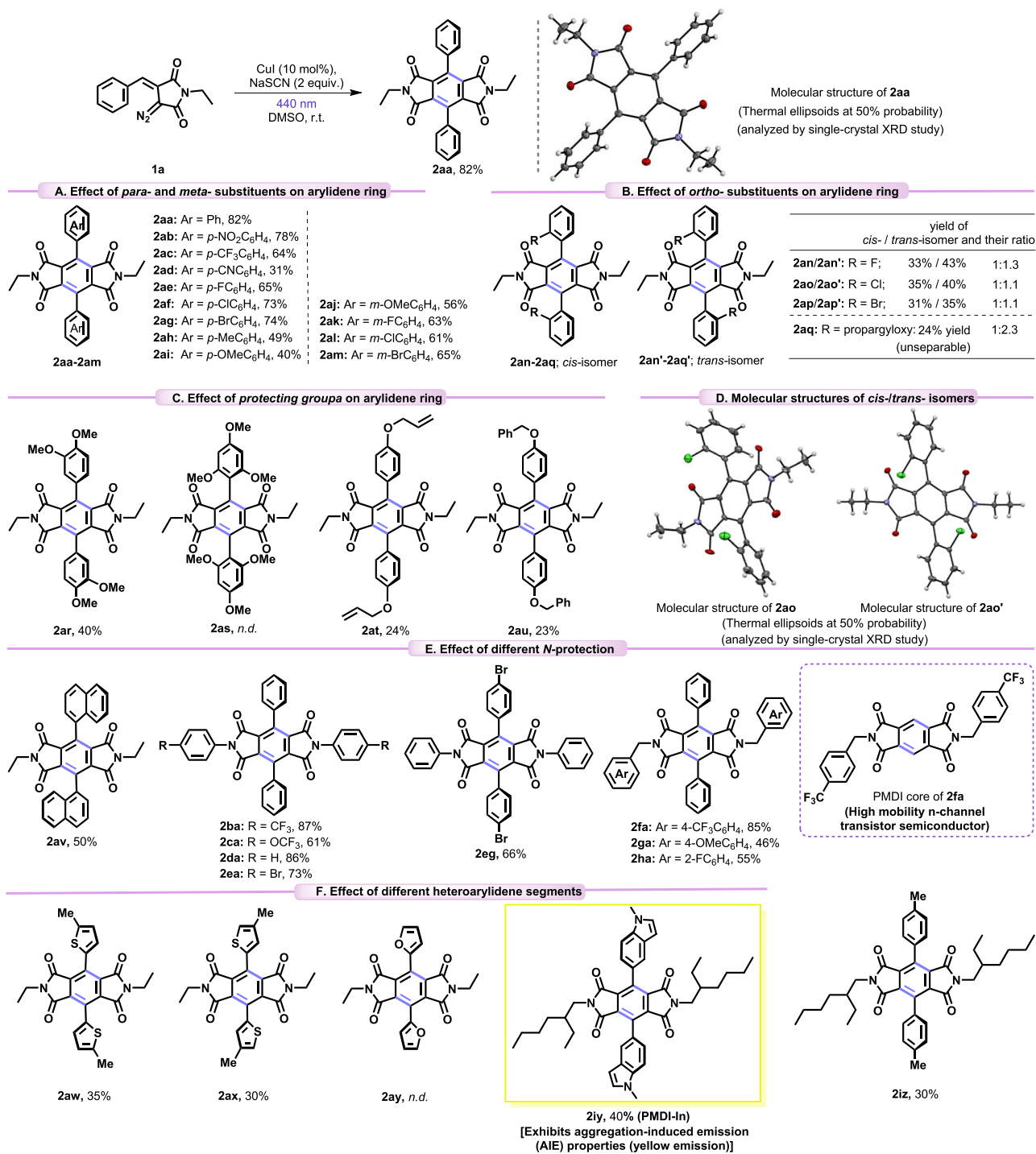
DASs with *o*-substituents (**1an–1ap**) afforded the respective isomeric products (**2an–2ap**) (*cis*–/*trans*–isomers 1:1.3) in moderate to good yields (up to 76%, [Scheme 2](#)). Single-crystal X-ray analysis confirmed the molecular structures of these isomers (*cis*–**2ao**, *trans*–**2ao'**). The *o*-propargyloxy derivative furnished the corresponding product **2aq** in a relatively low yield (24%, *cis*–/*trans* ratio 1:2.3, [Scheme 2](#)). Furthermore, disubstituted (3,4-dimethoxy)–DAS **1ar** was relatively less reactive because of electronic factors and furnished the desired

product **2ar** in a modest yield (40%, [Scheme 2](#)). However, 2,4,6-trimethoxy DAS **1as** did not react under optimum reaction conditions, possibly because of steric hindrance. DAS derivatives having protecting groups tolerated the reaction conditions to afford the desired products (**2at, 2au**) albeit in lower yields (up to 24%). Notably, naphthalene-substituted DAS afforded the desired product **2av** in a good yield of 50% ([Scheme 2](#)).

Next, we expanded the method's versatility using various *N*-substituted DASs, including electron-rich and electron-deficient aromatic (**2ba–2eg**) and aliphatic groups (**2fa–2ha, 2iy, 2iz**). These compounds (**1ba–1iz**) afforded the corresponding products (**2ba–2iz**) in good to excellent yields (up to 87%, [Scheme 2](#)). Even the heteroarylidene diazo succinimides (**1aw–1iy**) afforded the desired products in modest yields (**2aw–2iy**, up to 40% yield), while the furan-substituted derivative **1ay** did not afford product **2ay**. The PMDI core of compound **2fa** is a well-known high-mobility *n*-channel transistor semiconductor.²¹ Recognizing its significance, we successfully synthesized an analogue of this core **2fa** in very good yield (85%, [Scheme 2](#)). Further, the practicability of this protocol has been demonstrated by synthesizing a valuable compound **2iy**, which is known for its prominent aggregation-induced emission (AIE) properties.²²

The successful synthesis of symmetric PMDIs prompted us to explore the synthesis of unsymmetric PMDI. Though the cross-coupling of two different DASs is more complex than homocoupling because of slight electronic differences, we have successfully obtained unsymmetrical PMDIs along with the expected self-coupled products (see [Scheme 3](#)). To the best of our knowledge, the synthesis of an unsymmetrical PMDI core has not been documented until date. Gratifyingly, the protocol gave direct access to unsymmetrically substituted PMDI molecules, though in modest yields. This reaction also proves that the diazo compound plays a dual role, such as a donor and an acceptor, to form the product. We have also successfully scaled up the synthesis of **2a** (1 mmol, 63% yield; see the [Supporting Information S29](#)).

We conducted several control experiments to gain insight into the reaction pathway. To investigate, if the reaction involves a classical carbene intermediate (metallocarbene), we carried out the carbene trapping experiment with benzaldehyde, styrene, and ethyl diazoacetate (EDA). EDA is known for trapping carbenes under photochemical conditions.²³ We observed no products emanating from carbene trapping in all these experiments (see details in [Supporting Information S11 Figure 1.8](#)). It is also possible that the desired cyclization is outcompeting any intermolecular reactions with other substrates. Further, we synthesized a new substrate **1az** having an internal olefin under standard conditions to exclusively afford self-dimerized PMDI product **2az** and we did not observe intramolecular [2,3]-sigmatropic rearrangement product **2az'** (see [Supporting Information S11 Figure 1.8](#)). This preference for the intermolecular self-dimerization product **2az** over intramolecular rearrangement **2az'** suggests that the reaction is unlikely to involve a carbene intermediate, thereby pointing to an alternative reaction pathway (see [Supporting Information Section 4.1](#)). Subsequently, for detecting a radical intermediate, if any, we carried out the reaction in the presence of BHT; the reaction afforded the BHT-trapped adduct **4e** (detected by HRMS; see [Supporting Information Section 4.2](#)). Additionally, we synthesized short-lived radical trapping agent CHANT²⁴ (allyl-TEMPO). This reagent enhances radical

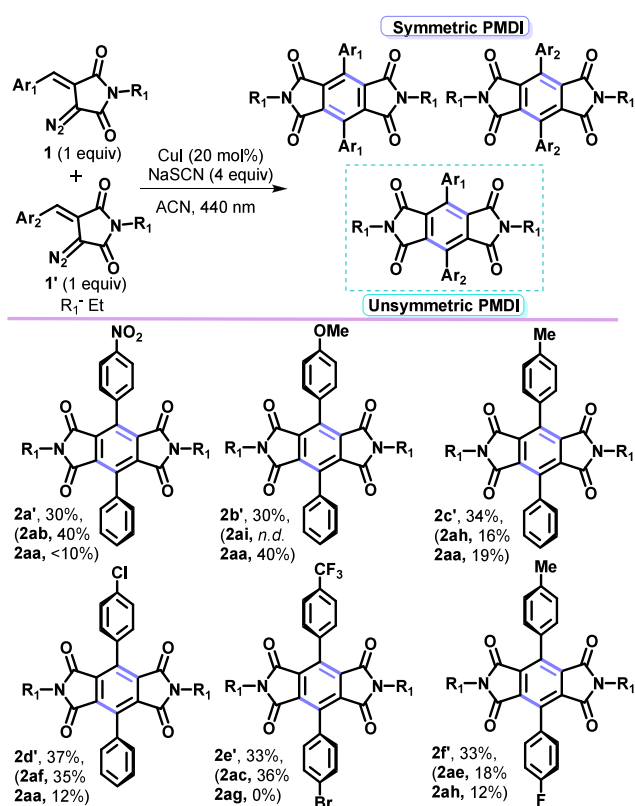
Scheme 2. Substrate Scope for the [3 + 3]-Cycloaddition Reaction of DASs^a

^aGeneral reaction conditions: diazo compound **1** (1.0 equiv, 0.2 mmol), NaSCN (2.0 equiv, 0.4 mmol), CuI (10 mol %) in DMSO (0.055 M) under nitrogen (degassed) at room temperature (28 °C) under blue light for 12 h.

stability, thereby simplifying the trapping process. We performed the reaction with CHANT to afford radical-trapped adduct **4i**, which supported the generation of the radical intermediate (see Supporting Information S11 Figure 1.8). All of these findings strongly indicate the presence of radical intermediates in the reaction.

EPR analysis of an incomplete reaction mixture (CuI, NaSCN, and **1a**) and a few control experiments clearly indicated the generation of carbon-centric organic radicals

during the reaction. The 'g' factor of the crossover point of the peak was found to be 1.9988, which is the peculiar characteristic of the organic free radical nature of an unpaired electron (see Supporting Information S18–S19).²⁵ Finally, UV–vis spectra of individual reagents and their mixtures were recorded to gain additional insights into mechanistic pathway. Interestingly, the mixture of CuI and NaSCN showed a broad absorption band in the visible range (350–450 nm), whereas individual reagents and their mixtures did not absorb above

Scheme 3. Substrate Scope for the Synthesis of Unsymmetric PMDIs^{a,b}

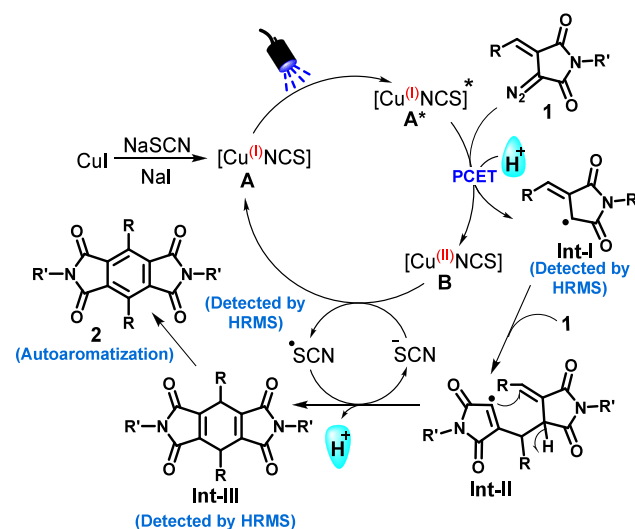
^aGeneral reaction conditions: 1 and 1' (0.1 mmol each), NaSCN (2.0 equiv, 0.2 mmol), CuI (20 mol %) in DMSO (0.055 M) under nitrogen (degassed) at room temperature (28 °C) under light for 12 h. Self-coupled products are given parentheses. ^bRefer to Scheme 2 for the structures of homocoupled products

>400 nm (See Supporting Information Section 4.4).²⁶ These interesting results indicate that certain photoactive species might have formed in situ. The absorption spectra of the copper complex and CuSCN were completely distinct, thus indicating that CuI and NaSCN do not form CuSCN in situ. Using CuSCN in the reaction gave a low yield of 2aa (35%; see Supporting Information Section 4.5). This result suggests that CuSCN is not an active complex in the reaction. Additionally, we successfully obtained the crystal structure of a mixture of CuI and NaSCN after multiple attempts. The FT-IR spectra and single-crystal X-ray analysis also confirmed the in situ formation of the CuNCS complex (see Supporting Information Section 4.6, S23–S24).

Based on the EPR studies, a series of control experiments, and single-crystal X-ray analysis of the CuNCS complex, a proposed mechanism is depicted in Scheme 4. Initially, CuI and NaSCN generated the active ground-state CuNCS complex A in situ. Copper complex A forms excited-state copper(I) complex A* upon visible light irradiation.

The copper complex A* then undergoes proton-coupled electron transfer (PCET) with DAS 1 to generate the carbon-centered radical intermediate Int-I via nitrogen extrusion, along with furnishing the corresponding oxidized ground-state copper(II) complex B. The Int-I reacts with DAS 1 to form the intermediate Int-II. Further, the thiocyanate anion (SCN[−]) interacts with copper(II) complex B to form the thiocyanate radical (·SCN) by regenerating copper(I) complex A. Then,

Scheme 4. Proposed Reaction Mechanism



the thiocyanate radical abstracts an electron from the intermediate Int-II leading to intramolecular cyclization to furnish Int-III and eventually loses a proton to regenerate SCN[−] (see ESI, Figure 1.9). Finally, Int-III undergoes autoaromatization via radical pathway to form desired PMDI product 2.

We have demonstrated an efficient visible-light-promoted direct synthesis of PMDIs from DAS via copper catalysis. This synthetic strategy provides a sustainable route for PMDI synthesis by unlocking the radical reactivity of DAS, thus overcoming a long-standing paradigm in PMDI synthesis. Importantly, the synergistic combination of NaSCN and the copper catalyst plays a pivotal role in facilitating this photoinduced transformation. This easy and convenient protocol has been demonstrated to access symmetric, as well as unsymmetric PMDIs. Mechanistic insights have been achieved through a series of control experiments, UV–visible, FT-IR, and EPR studies and single-crystal X-ray diffraction analysis.

■ ASSOCIATED CONTENT

Data Availability Statement

The data underlying this study are available in the published article and its Supporting Information.

Supporting Information

The Supporting Information is available free of charge at <https://pubs.acs.org/doi/10.1021/acs.orglett.4c03604>.

General information, detailed experimental procedures, characterization data for all new compounds and NMR spectra, as well as EPR data (PDF)

Accession Codes

Deposition Numbers 2298346, 2298355, 2298357, and 2323319 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via the joint Cambridge Crystallographic Data Centre (CCDC) and Fachinformationszentrum Karlsruhe Access Structures service.

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Notes

The authors declare no competing financial interest.

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■ DEDICATION

Dedicated to Prof. Srinivasan Chandrasekaran on the occasion of his 80th birthday.

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(26) Association of NaSCN with different copper salts, such as CuI, CuBr, and CuCl, has been examined over UV-vis absorbance spectra. The results indicated that copper iodide and sodium thiocyanate complex (CuI + NaSCN) is accomplished in situ, thus resulting in a more intense and broad absorbance band.

Oxonium/Sulfonium Ylide Rearrangements to Access Chromenes and Thiochromenes: Concerted or Stepwise Pathway?

Kajal B. Meher,^[a] Onkar S. Bankar,^[a] Hrishik Mukherjee,^[a] and Ramakrishna G. Bhat*^[a]

Dirhodium(II)-catalyzed regio-divergent intramolecular rearrangement of oxonium and sulfonium ylides, generated from diazo arylidene succinimides (DAS), has been achieved at room temperature. Allyloxy-substituted DAS derivatives were strategically designed and synthesized to explore their reactivity under metal catalysis. The transformation is proposed to proceed

via oxonium ylide intermediate, followed by [1,2]- and [1,4]-shifts, leading to the chromene framework. This strategy was further extended to thioallyl-substituted DASs to access thiochromenes under mild reaction conditions. For the first time, intramolecular rearrangement has been explored on DAS derivatives to synthesize bioactive chromene and thiochromene scaffolds.

1. Introduction

Chromenes, thiochromenes, and their analogs are versatile heterocyclic scaffolds commonly found in natural and synthetic bioactive compounds.^[1] Many exhibit a wide range of pharmacological properties, including anticancer, anti-HIV, anti-inflammatory, antioxidant, antitubercular, antiviral, antitumor, antibacterial, antimicrobial, antidiabetic, anticoagulant, diuretic, and fungicidal activities.^[2] Notably, these heterocyclic cores feature FDA-approved drugs such as tazarotene, flupentixol, and meticrane. Beyond medicinal applications, chromenes and thiochromenes play significant roles in materials science, including their use in laser dyes, organic light-emitting devices (OLEDs), optical brighteners, organic scintillators, triplet sensitizers, and fluorescence probes. Additionally, some derivatives exhibit exceptional photochromic properties.^[3]

Diazo compounds are essential building blocks for the generation of metal carbenoids in transition metal-catalyzed synthetic transformations. Their strong reactivity with metal catalysts makes them indispensable in organic synthesis for constructing diverse molecular frameworks.^[4] The sigmatropic rearrangement of oxygen/sulfur ylides is a highly versatile bond reorganization process in organic chemistry. This process provides an efficient platform for constructing C—C and C—O/C—S bonds.^[5] Classical [2,3]- and [1,2]-sigmatropic rearrangements, including the Doyle–Kirmse, Stevens, and thia–Sommelet–Hauser rearrangements, predominantly involve acyclic diazo compounds and sulfur ylides derived from allyl sulfides, alkyl sulfides, or α -thioesters.^[6–8] Moreover, the direct formation of ylides

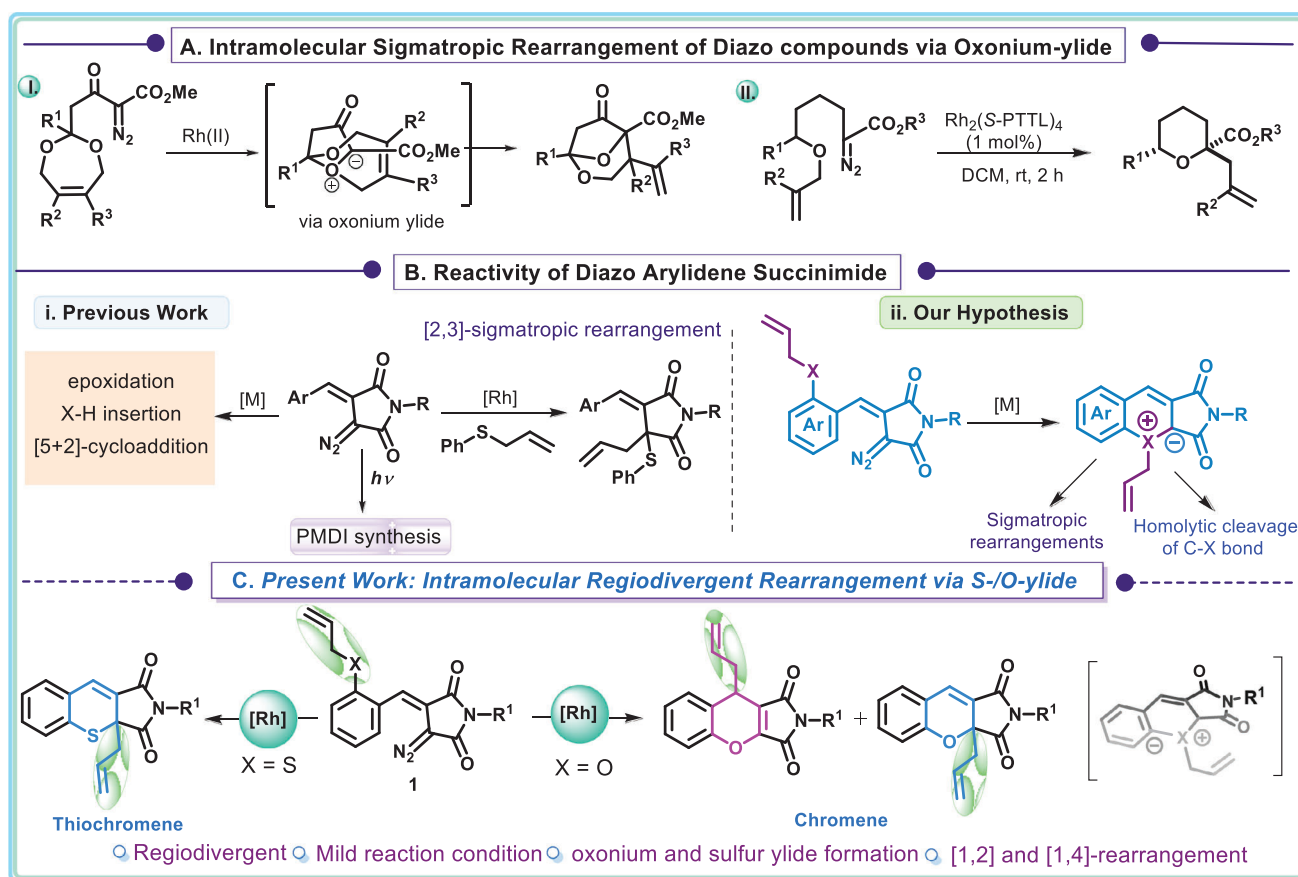
through the intramolecular addition of metal carbenoids to heteroatom lone pairs has recently gained significant attention, emerging as a mild and efficient strategy for synthesizing cyclic ylides.^[9]

However, the formation and subsequent reactivity of oxonium ylides are more challenging than those of traditional nitrogen- or sulfur-stabilized ylides, due to their inherent instability. In addition, oxonium ylides are prone to competing reaction pathways, viz., i) rearrangement (by either [2,3]-sigmatropic shift or [1,2]-Stevens shift),^[10] ii) cyclopropanation, and C–H insertion into bonds α to ethereal oxygen are also favorable.^[11] There have been several reports on the dirhodium(II)-catalyzed formation of cyclic oxonium ylides, typically followed by a concerted [2,3]-sigmatropic rearrangement involving an allylic moiety of diazoketoesters (see Scheme 1A).^[12] However, examples of [1,2]-shift of oxonium ylides in the literature are typically restricted to cyclic ylides.^[12c,13]

Among various diazo compounds, diazo arylidene succinimides (DASs) exhibit unique reactivity due to alkene and diazo functional groups. Their distinct structural characteristics contribute to their diverse chemical behavior, enabling their application in various synthetic transformations such as cycloaddition, X–H insertion, and sigmatropic rearrangements.^[14] However, only a few reported examples wherein, DAS are being utilized to generate the corresponding sulfur ylide. Our group recently reported a Rh(II)-catalyzed intermolecular [2,3]-sigmatropic rearrangement using DAS and allyl sulfides (Scheme 1Bi).^[14c] However, based on the literature, achieving selective [1,2]- or [1,4]-shift over the [2,3]-pathway via oxonium ylides remains challenging.^[15] A selective approach would be highly desirable for accessing complex molecules like chromenes and thiochromenes. Owing to the significance, we hypothesized that 2-allyloxy- or 2-thioallyl-substituted DAS, under suitable metal catalysis, could generate transient cyclic oxonium or sulfonium ylides, enabling intramolecular sigmatropic rearrangements or homolytic cleavage of ylides (Scheme 1Bii).

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Scheme 1. Intramolecular rearrangement of diazo compounds and the reactivity of diazo arylidene succinimide.

In this study, we present a rhodium-catalyzed intramolecular regio-divergent rearrangement of allyloxy/thioallyl substituted DAS, enabling the synthesis of chromene and thiochromene derivatives at room temperature (see Scheme 1C).

2. Results and Discussion

To validate our hypothesis, we began our investigation using 2-allyloxy-substituted DAS **1a** as a model substrate with $\text{Rh}_2(\text{OAc})_4$ in chlorobenzene. Notably, this resulted in a mixture of **2a** and **2a'** rearrangement products at room temperature. Initial results prompted us to optimize the reaction conditions systematically. We first screened various catalysts, including silver, copper, cobalt, ruthenium, and rhodium complexes. Among all, rhodium acetate proved to be the most effective catalyst for this reaction (Table 1, entries 2–5, see Table S1).

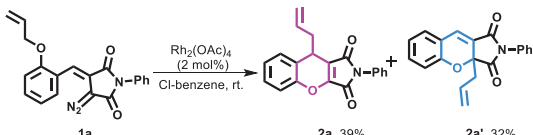
We screened various solvents, and among them, dichloromethane proved to be the most effective for obtaining the rearrangement products **2a/2a'** (Table 1, entry 6 and see Table S2). A control experiment conducted in the absence of $\text{Rh}_2(\text{OAc})_4$ failed to produce the desired products, even in trace amount, confirming the essential role of the catalyst in the transformation (Table 1, entry 7). The reactions were performed at different temperatures to investigate product selectivity between **2a** and **2a'** (see Table S4), however, no significant

changes were observed. Based on these studies, the optimum reaction conditions for the rearrangement products found to be DAS **1a** (1 equiv.) with $\text{Rh}_2(\text{OAc})_4$ (2 mol%) in DCM at room temperature under a nitrogen atmosphere.

Having obtained the optimum reaction conditions, we planned to explore the substrate scope by screening a wide range of *N*-alkyl/aryl substituted diazo arylidene succinimides (**1a–1q**) under optimized reaction conditions.

Gratifyingly, we obtained the corresponding rearrangement products (**2a–2q**, **2a'–2q'**) (See Scheme 2). We observed that *N*-benzyl substituted diazo compounds with electron-donating and electron-deactivating groups furnished the corresponding products (**2e–2h**, **2e'–2h'**) in relatively higher yields in comparison to the *N*-benzyl substituted diazo compounds having electron-withdrawing groups **2i**, **2i'** (Scheme 2). We also assessed the functional group compatibility of *N*-aryl substituted DAS derivatives, and we observed that both electron-donating and electron-withdrawing substituents on the phenyl group were well tolerated by affording the desired products in moderate to good yields (**2j–2q**, **2j'–2q'**, Scheme 2). Even various DAS derivatives having different aryl groups (arylidene moiety) also reacted smoothly to furnish the corresponding desired products (**2r–2u**, **2r'–2u'**) in slightly lower yields, and this may be due to the electronic effect. Even the methylallyloxy substituted DAS **1v** reacted under the reaction conditions to give the corresponding rearranged products (**2v**, **2v'**, Scheme 2). Interestingly, the *N*-(2-

Table 1. Optimization of reaction conditions.^{a)}

		
Entry	Variation from tested Reaction Conditions ^{a)}	Yield of 2a/2a' ^{b)}
1	None	39/32
2	AgNTf ₂	n.d.
3	C ₃₀ H ₂₄ CoF ₁₂ N ₆ P ₂	n.d.
4	[(C ₆ H ₅) ₃ P] ₃ RuCl ₂	n.d.
5	Cu(OAc) ₂ ·H ₂ O/Cu(OTf) ₂	n.d.
6 ^c	Rh ₂ (OAc) ₄	40/40
7	No catalyst	n. d.

^{a)} General reaction conditions: **1a** (0.2 mmol), Rh₂(OAc)₄ (2 mol%), A.R. grade (0.055 M), room temp., 30 min., under degassed conditions with N₂. ^{b)} Isolated yields. ^{c)} DCM was used as a solvent, (n.d. = not detected).

hydroxyethyl) substituted DAS **1w** afforded the corresponding products **2w**, **2w'**.

Later, we switched our attention toward exploring the rhodium-catalyzed formation of sulfur ylide so as to extend the generality of the protocol. In this regard, various *N*-substituted DASs, having alkyl and aryl groups with EWGs and EDGs, were explored under the reaction conditions. Interestingly, we exclusively obtained the corresponding rearrangement products (**2aa–2ah**). *N*-alkyl substituted DASs reacted smoothly under the conditions, affording the corresponding products (**2aa–2ab**) in good yields. *N*-phenyl DASs bearing electron-donating and -deactivating groups underwent selective rearrangement, affording the corresponding products (**2ac–2af**) in good yields with excellent regioselectivity. Finally, we examined the reactivity of *N*-benzyl substituted DAS and obtained the corresponding products (**2ag–2ah**) exclusively in good yields (Scheme 2).

We observed that allyloxy DAS (**1ai–1am**) failed to react under the optimum reaction conditions, likely due to the electron-donating properties of specific substituents or because of the presence of extended conjugation. In particular, cinnamyl-substituted diazo succinimides **1ai** or DAS directly conjugated to heterocyclic systems may display diminished reactivity. Unlike the thioallyl-derived substrates, we observed that allyloxy-derived DASs furnished a mixture of rearrangement products, probably due to the intrinsic instability of the oxonium ylide intermediate.

We conducted several transformations to demonstrate the synthetic utility of the [1,2] and [1,4]-rearrangement products for further applications. The product **2a** was subjected to epoxidation with *m*-chloroperbenzoic acid in DCM to obtain the corresponding epoxide product **3a** (97%, Scheme 3A). The compound **2a'** was later subjected to hydrogenation (H₂, Pd/C) to obtain the corresponding reduction product **3b** (80%, Scheme 3B). Both the internal and terminal double bonds were successfully reduced.

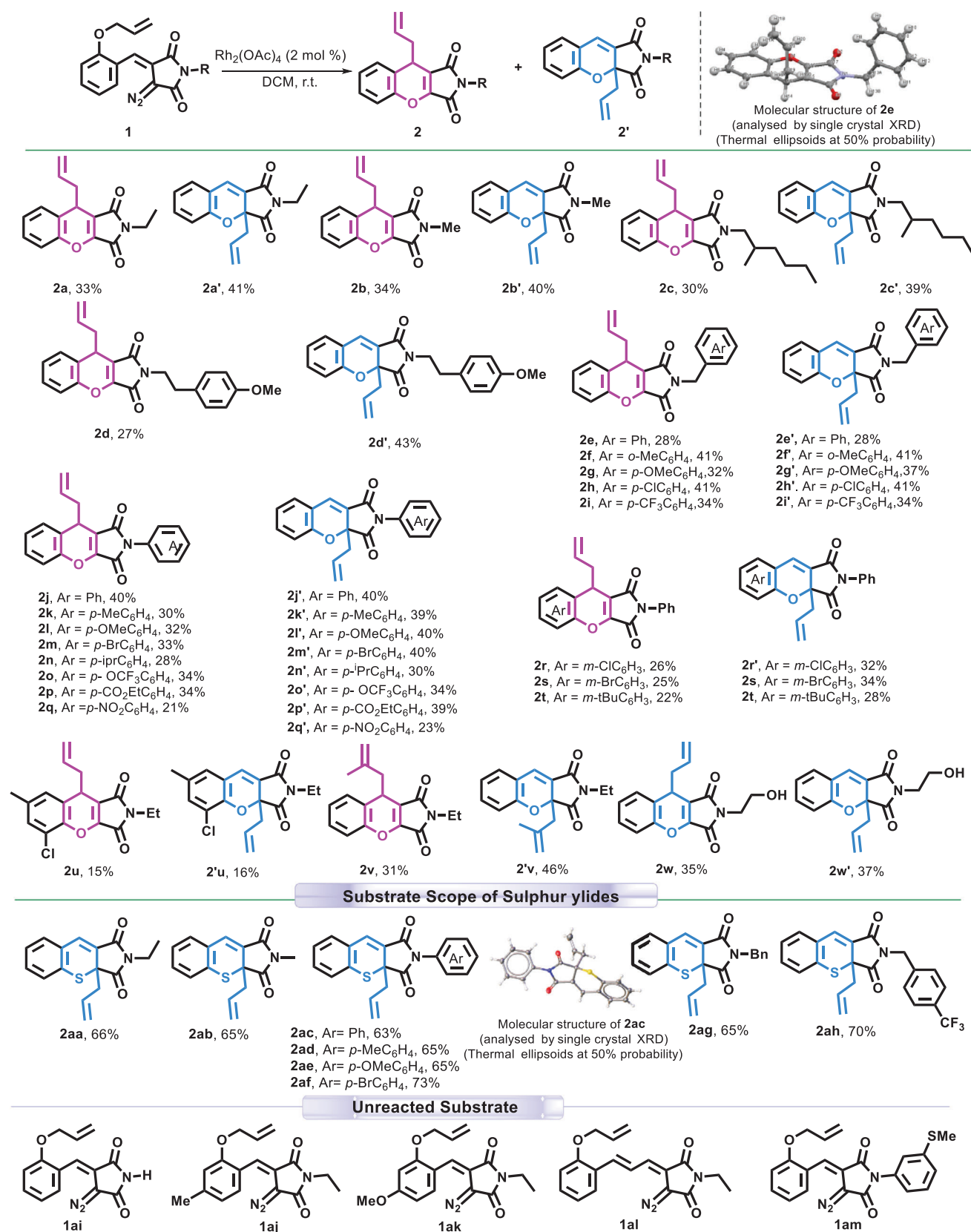
Further, we have done control experiments to analyze the specific rearrangements involved in the reaction and to understand the mechanistic pathway.

To investigate the reaction mechanism, we explored the reaction of *O*-benzylic substituted DAS **1x** instead of the *O*-allyl DAS under standard reaction conditions. The reaction afforded the corresponding products **2x** and **2x'**. This result suggests that the reaction may be proceeding via [1,4]- and [1,2]-shift of the oxonium ylide (see Scheme 4).

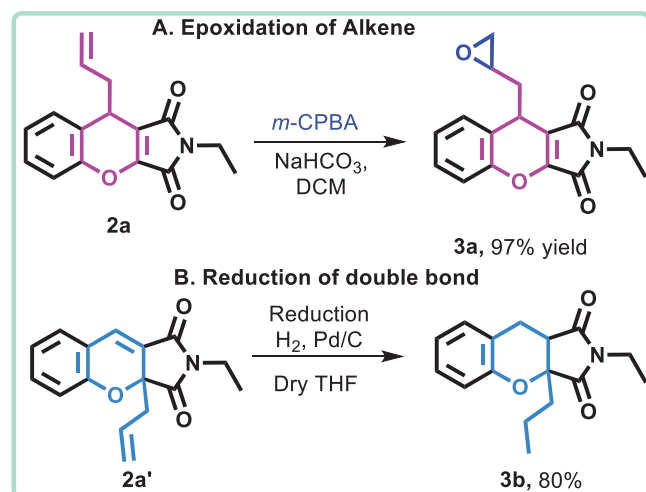
Further, in order to investigate the reaction mechanism, we conducted a radical trapping experiment using a radical scavenger such as TEMPO under the standard optimum reaction conditions. The TEMPO-trapped adduct (after 10 min of stirring) was confirmed by high-resolution mass spectrometry (HRMS) (Scheme 5a).

Additionally, we performed electron paramagnetic resonance (EPR) analysis of the incomplete reaction mixture of DAS **1a**, Rh₂(OAc)₄, and PBN (phenyl-*N*-tert-butyl nitron). PBN is a spin-trapping agent commonly employed in EPR spectroscopy to detect short-lived radicals (PBN is generally used to trap carbon-centered radicals). Gratifyingly, we observed a signal in the EPR spectrum, and the *g*-value at the crossover point was measured at 2.01. This result clearly supports that the spin adduct of carbon-centered radical was trapped by the spin trap agent - PBN (*N*-tert-butyl- α -phenylnitron). The spin adduct exhibited a *g*-value of 2.01, thus indicating that of a nitroxide radical,^[16] confirming the nature of the spin adduct formed (Scheme 5b).

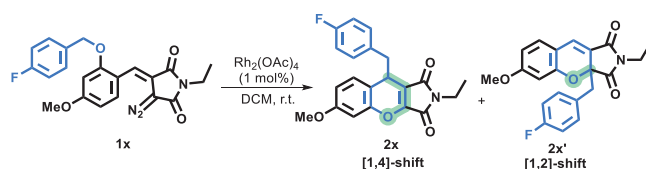
Based on the results observed from control experiments, EPR analysis, and insights from the literature precedence,^[13d,15c,17] the plausible reaction mechanism is depicted (Scheme 6). Diazo compound **1** reacts with the rhodium catalyst to form a rhodium-carbene intermediate (**Int-I**), which subsequently leads to the formation of an oxonium ion intermediate (**Int-II**). This reactive intermediate further undergoes homolytic cleavage of the C–O bond to generate radical species, which eventually



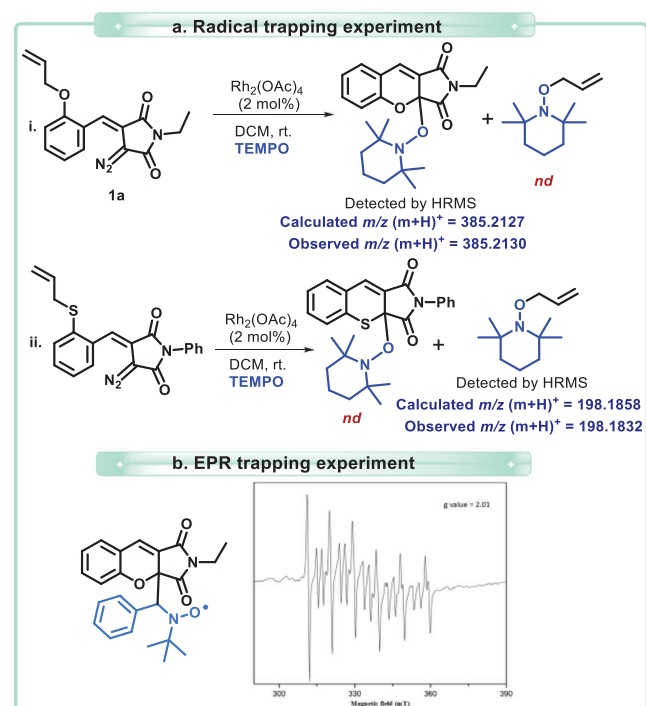
Scheme 2. Substrate scope for the intramolecular rearrangement of DASs. Reaction conditions: diazo compound **1** (1.0 equiv., 0.2 mmol), $\text{Rh}_2(\text{OAc})_4$ (1 mol%) in DCM (0.055 M) under nitrogen (degassed) at room temperature (28 °C) for 30 min - 60 min.



Scheme 3. Synthetic utility.

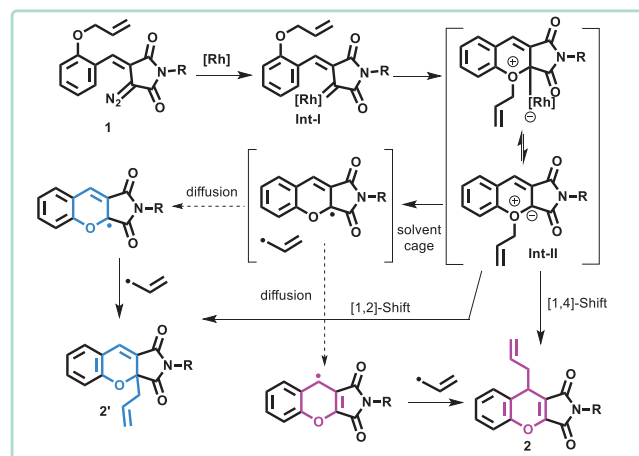


Scheme 4. Control reaction.



Scheme 5. Radical trapping experiments.

undergo radical recombination to furnish the products **2** and **2'**.



Scheme 6. Proposed mechanism.

3. Conclusion

In summary, we have successfully explored the reactivity of 2-allyloxydiaz aryldiene succinimides (DAS) under rhodium catalysis to obtain the [1,2]- and [1,4]-shift products via an oxonium ylide intermediate. Even relatively and intrinsically unstable oxonium ylide led to regio-divergent products, thus demonstrating the potential of this reactive intermediate for further optimization and synthetic utility. The reaction conditions also worked well for forming sulfur ylide and the subsequent highly selective rearrangement. A wide range of DAS derivatives worked well under the reaction conditions to furnish chomene and thiochromene scaffolds at room temperature. The reactivity of diazoaryldiene succinimides (DAS) toward intramolecular rearrangement has been explored. Mechanistic insights have been acquired through control experiments, radical trapping experiments, EPR study, and single crystal X-ray diffraction analysis.

Supporting Information

General information, detailed experimental procedures, characterization data for all new compounds, and NMR spectra are in the ESI. Data for the crystal structure reported in this manuscript have been deposited at the Cambridge Crystallographic Data Centre (CCDC) under the deposition numbers CCDC [2433561](#) (compound **2e**) and CCDC [2472115](#) (compound **2ac**).

Acknowledgments

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Delhi, for the fellowship. Authors also thank Sandeep Kaulage, IISER Pune, for the kind help in obtaining SC-XRD data.

Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the [Supporting Information](#) of this article.

Keywords: [1,2]/[1,4]-shift • Chromenes • Diazo arylidene succinimide • Regiodivergent • Thiochromenes

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Silver-Catalyzed One-Pot Access to Diastereoselective Benzo[5,6]oxepino[2,3-c]pyrroles via Formal (5 + 2)-Annulation of Donor-/Acceptor-Type Aryl Vinyl Diazosuccinimide with Ketones

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Abstract: A silver triflimide catalyzed one-pot protocol for the diastereoselective synthesis of dihydrobenzoxepines has been developed. Silver triflimide was found to be an efficient catalyst for the formal (5 + 2)-cycloaddition to access dihydrobenzoxepines as a single diastereomer using vinyl diazo-succinimides as 5-C-synthons and ketones. An unmet challenge of utilizing the donor-/acceptor-type vinyl diazo-succinimides as 5-C-synthons under silver-catalysis is pre-

sented. This protocol was found to be highly regio-, chemo- and diastereoselective, and works well with aliphatic as well as aromatic methyl ketones bearing electron deactivating as well as donating groups to afford dihydrobenzo[5,6]oxepino[2,3-c]pyrroles. The control experiments and time-dependent NMR studies revealed the plausible mechanism of this transformation. The protocol also proved to be scalable on the gram-scale synthesis.

Introduction

The fused polycyclic architecture containing 6-7-5 or 5-7 fused ring framework such as benzoxepine motif belongs to one of the important classes of oxygenated heterocycles found in pharmaceutical agents^[1a] and numerous natural products^[1b-d] having diverse biological activities (Figure 1). The stereoselective syntheses of these highly substituted oxygenated heterocycles have immensely been pursued by the scientific community.^[2] Directly accessing this scaffold is highly challenging and few approaches have been explored in this regard.^[3] It is well known that the transient carbonyl ylide, generated *in situ* via transition-metal-catalyzed decomposition of diazo compounds can either be paired with suitable trapping agents (or dipolarophiles) or it can be utilized in cyclization (intramolecularly or intermolecularly) to access oxygenated heterocycles.^[4-6] A few methods involving vinyl carbonyl compound have been revealed the preferential formation of dihydrofurans [via (4 + 1)-annulation] or a mixture of dihydrofurans and dihydrobenzoxepines [via (6 + 1)-annulation] from specific ylide starting from ester and ketone moiety respectively (Scheme 1A).^[6e] However, the stereoselective synthesis of either of these scaffolds is quite challenging and it typically needs an elegant ligand-controlled strategy (Scheme 1B).^[7] Very recently, Schneider and co-workers^[8a] reported a protocol for the construction of bicyclic framework: oxa-bridged dibenzoxacines (5-8 fused rings) via formal (4 + 3)-cycloaddition^[8b-e] involving carbonyl ylide as reactive intermediate. Besides, the reaction of vinyl diazo compounds with aldehydes usually known to form a mixture of oxiranes [via (2 + 1)-cycloaddition] and dihydrofurans [via

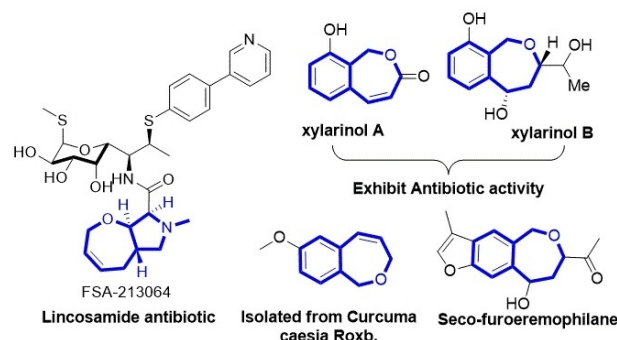
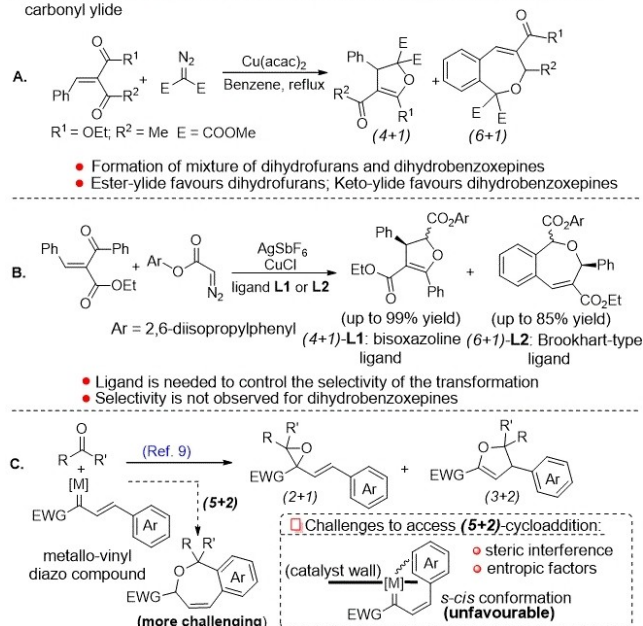


Figure 1. Examples of natural bioactive 1,3-dihydrobenzo[c]oxepines and oxepino[2,3-c]pyrrole.

■ **Previous methods:** Cycloaddition strategies to form oxygenated heterocycles via carbonyl ylide



Scheme 1. Access to oxygenated heterocycles via carbonyl ylides.

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formal (3+2)-cycloaddition] through carbonyl ylide involving metal carbene intermediates (Scheme 1C).^[9] It is important to note that the synthesis of benzoxepine derivatives is quite challenging and moreover cycloannulation *via* alternative formal (5+2)-cycloaddition *via* carbonyl ylide has not been explored till date to the best of our knowledge; wherein vinyl diazo compounds act as 5-C-synthons. The major challenge in this aspect to explore the vinyl carbenoid as 5-C synthon is limited due to the intrinsic steric hindrance emanating from *Z*-configuration around the C=C bond between benzylidene group and the 'catalyst wall' thus making it unfavorable for the desired transformation (See Scheme 1C inset).^[10] Secondly, construction of the seven-membered heterocyclic scaffold such as oxepine *via* the direct cyclization needs high activation energy mainly owing to the combined effect of entropic factors and the non-bonding interactions in the transition state.^[11]

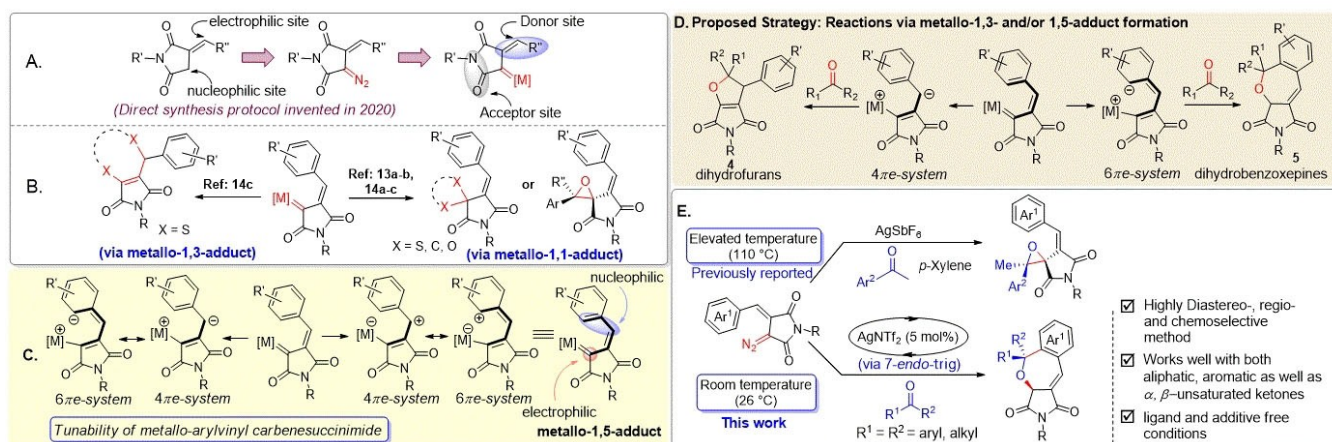
The vinyl diazosuccinimide, a useful carbene precursor for the tandem annulation reaction and this can be directly prepared from benzylidene succinimides^[12] following our earlier reported procedure and other protocols (Scheme 2A).^[13] The metallo-carbenoid of vinyl carbenesuccinimides or vinyl carbenesuccinimides are generated catalytically from stable vinylic diazosuccinimides (*Z*-geometry across C=C bond) that exhibit electrophilic character at metal carbene carbon and nucleophilic character at vinylogous carbon (Scheme 2A). These metallo-vinyl carbenesuccinimides have emerged as useful synthons to access metallo-1,1-^[13a-b,14a-c] or 1,3-^[14c] adducts when paired with suitable dipolarophiles or nucleophiles to construct cyclic ring structures involving π -electrocyclization^[13a,14b-f] (Scheme 2B and 2C). Looking at these important features and owing to the importance of oxaheterocycles, we envisioned that the metallo-aryl vinyl carbenesuccinimide could be employed for the cycloannulation with carbonyl compounds *via* (3+2)- and/or (5+2)-cycloaddition to access dihydrofurans and/or dihydrobenzoxepines respectively under suitably optimized reaction conditions (Scheme 2D).^[14f] Herein, for the first time, we report the silver catalyzed direct diastereoselective synthesis of dihydrobenzoxepine derivatives exclusively by exploring the

potential of aryl vinyl diazosuccinimide with ketones under ligand-free condition.

Results and Discussion

Our previous report had demonstrated the 4 π -electrocyclization strategy *via in situ* generation of transient carbonyl ylide from metallo-aryl vinyl diazosuccinimide under silver catalysis (AgSbF₆) to access oxiranes at elevated temperature (see Scheme 2E).^[13a] The single crystal X-ray analysis^[15] of the phenyl vinyl diazosuccinimide **1a** revealed that the benzylidene group is oriented in *s-cis* conformation with a dihedral angle (θ) ~34° (slightly twisted, see SI, page no. S73–S74). Looking at this observation we surmised that even though it is a great challenge, metallo-aryl vinyl diazosuccinimide could be explored for different type of reactivity under suitable conditions wherein aryl group may participate in the reaction as it would be slightly inclined away from the 'catalyst wall' as shown in Table 1. We envisioned that the *in situ* generated carbonyl ylide (from metallo-aryl vinyl diazosuccinimide) may undergo 6 π -electrocyclization to form dihydrofuran **4** or 8 π -electrocyclization followed by rearomatization to afford the dihydrobenzoxepines **5** (see Scheme 2C and D).

In order to validate our hypothesis, initially we treated (*E*)-3-benzylidene-4-diazo-1-ethylpyrrolidine-2,5-dione **1a** with few ketones, aldehydes, amides and esters. Among all the substrates that were screened for the optimization, compound **1a** reacted with either acetophenone **2a** or acetone **2k** to afford the desired dihydrobenzoxepines **5aa** or **5ak** as single diastereomer in modest yields respectively (up to 50%, see Appendix-I, SI for details). No trace of product **4** was observed in all of these cases. Encouraged by the initial results, we further sought to optimize the reaction conditions to enhance the yield of diastereomer **5aa**. In this regard, we explored the reaction of **1a** and **2a** using rhodium (Table 1, Entry 1), silver (Table 1, Entries 2–5), copper, iron and gold catalysts in DCM at room temperature (See SI, Table-S1 Entries 11–19). Gratifyingly, among all, the reaction of acetophenone **2a** with aryl vinyl



Scheme 2. General characteristics of metallo-aryl vinyl carbenesuccinimide and the current challenges.

Table 1. Selected Optimization Results^[a]

Entry	Catalyst [5 mol%]	Solvent	Time [h]	Yield ^[b] [%] of 3aa/4aa/5aa
1	Rh ₂ (esp) ₂	CH ₂ Cl ₂	2	< 5/0/31
2	AgSbF ₆	CH ₂ Cl ₂	2	19/0/40
3	AgOTf	CH ₂ Cl ₂	2	18/0/38
4	AgBF ₄	CH ₂ Cl ₂	2	< 5/0/20
5	AgNTf ₂	CH ₂ Cl ₂	2	11/0/57
6	–	CH ₂ Cl ₂	24	NR
7 ^[c]	AgNTf ₂	CH ₂ Cl ₂	4	0/0/34
8 ^[d]	AgNTf ₂	CH ₂ Cl ₂	10	0/0/23
9 ^[e]	AgNTf ₂	CH ₂ Cl ₂	2	15/0/35
10 ^[f]	AgNTf ₂	CH ₂ Cl ₂	2 min	25/0/24
11 ^[f]	AgSbF ₆	CH ₂ Cl ₂	2 min	27/0/23
12 ^[g]	AgNTf ₂	CH ₂ Cl ₂	2	5/0/70

[a] Reaction conditions: unless otherwise noted, the reactions were carried out with diazo compound **1a** (1.0 equiv., 0.2 mmol), **2a** (1.0 equiv., 0.2 mmol), AgNTf₂ (5 mol%) and dry CH₂Cl₂ (0.1 M) at room temperature (26 °C) under argon atmosphere. [b] Isolated yields. [c] 0 °C; [d] –20 °C; [e] 60 °C; [f] Diazo compound **1a** was completely consumed in 2 min at 110 °C. [g] dry CH₂Cl₂ (0.033 M) was used. NR- No reaction. In all cases single diastereomer of **5aa** was obtained.

diazosuccinimide **1a** in presence of silver triflimide (AgNTf₂, 5 mol%) in dry CH₂Cl₂ afforded the corresponding dihydrobenzoxepine **5aa** at room temperature (57% yield, Table 1, Entry 5) along with **3aa** as a minor product. The catalytic activity of different silver catalysts was seemed to be dependent on the counter anions. The non-coordinating and low nucleophilic (Tf₂N[–]) counter anion was found to more prominent over others to effect the transformation. We also observed that the reaction did not work in the absence of catalyst for the prolonged reaction time (Table 1, Entry 6). In order to improve the yield of **5aa** and to optimize the reaction conditions further, different solvents, additives, stoichiometric ratio of the substrates, catalyst loading (see SI, Table S2, S4–6) were screened. Later we carefully investigated the other parameters such as temperature (Table 1, Entries 7–11, see SI Table S2 for details) and reactant concentration (Table 1, Entry 10, see SI Table S7). We also observed that in all the cases no trace of compound **4aa** was detected during the course of the reaction. Based on the exhaustive screening, we observed that **1a** (1 equiv.) and **2a** (1 equiv.) in presence of AgNTf₂ (5 mol%) as catalyst in dry CH₂Cl₂ (0.033 M) at 26 °C for 2 h under inert atmosphere proved to be the optimum reaction condition (Table 1, Entry 12).

Having obtained the optimized reaction condition, we planned to extend this protocol for the wider substrate scope. Initially we planned to explore the reactivity of phenyl vinyl diazosuccinimide **1a** with different ketones. Different methyl aryl ketones (**2a–2l**) reacted with **1a** in presence of silver triflimide (5 mol%), in dry DCM at room temperature to afford the corresponding 5-aryl-5-methyl substituted dihydrobenzoxepines (**5aa–5an**) in moderate to good yields (up to 74%, See Table 2). We observed that aryl methyl ketones bearing electron donating groups afforded the corresponding dihydrobenzoxepines (**5aa–5ac**) in relatively higher yields than that of aryl

Table 2. Substrates Scope for the Formal (5 + 2)-cycloaddition reaction^[a]

Ketone scope 	
Diazo scope 	
Application: 	

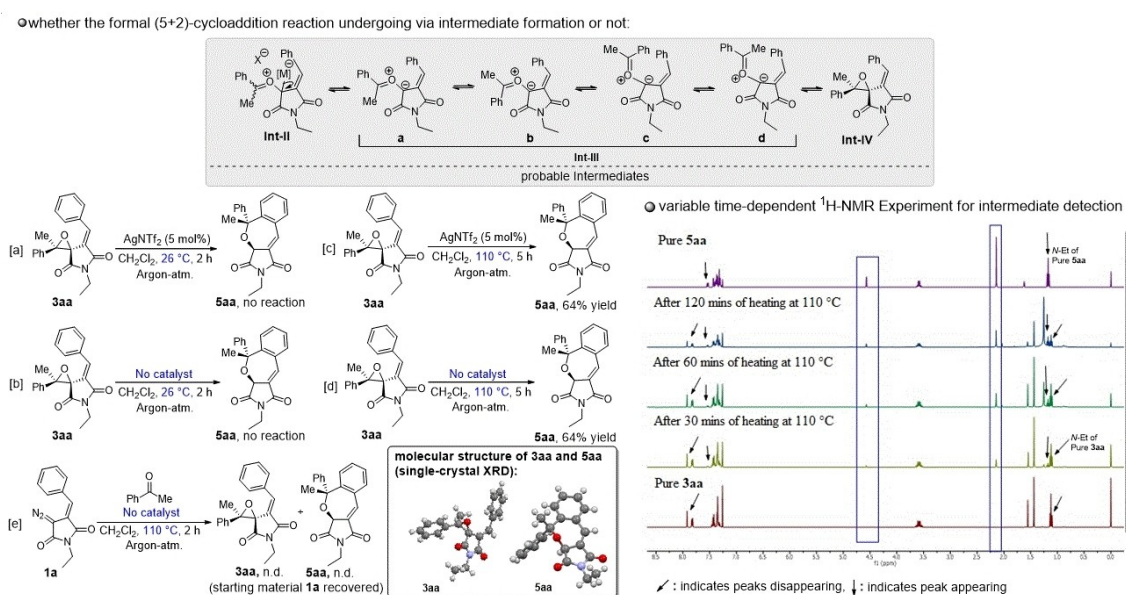
[a] Reaction conditions: unless otherwise noted, the reactions were carried out with diazo compound **1a** (1.0 equiv., 0.2 mmol), **2** (1.0 equiv., 0.2 mmol), AgNTf₂ (5 mol%) and dry CH₂Cl₂ (0.033 M) at room temperature (26 °C) under argon atmosphere over 2 h. In all cases single diastereomer was obtained.

methyl ketones having electron-deactivating substituents at *para*- and *meta*-position of phenyl ring (**5ad–5ah**). Surprisingly, the desired dihydrobenzoxepine **5ai** was not formed as 2,4-dichlorophenyl methyl ketone **2i** did not react with **1a** under the optimized reaction condition. Further, we explored the reaction of **1a** with electron rich aliphatic methyl ketones including cyclic ketone such as cyclohexanone **2j** to afford the corresponding dihydrobenzoxepine derivatives (**5aj–5al**). Even the enone such as methyl styryl ketone reacted with **1a** to give the desired product **5an** in modest yield (50%, Table 2).

Later, we planned to explore formal (5+2)-cycloaddition for a range of aryl-substituted and *N*-substituted aryl vinyl diazo-succinimides with different ketones. In this regard, we treated different *N*-substituted benzylidene diazo compounds (**1b–1e**) with acetophenone **2a** under optimized reaction condition to afford the corresponding desired products (**5ba–5ea**) (see Table 2). We observed that among all the *N*-substituted benzylidene diazo compounds screened, *N*-ethyl substituted benzylidene diazo compound **1a** proved to be optimum substrate by affording the desired product **5aa** in relatively higher yield. In view of this, we planned to explore the reactivity of different *N*-ethyl substituted vinyl diazo compounds (**1f–1n**) bearing different substituents with electron-rich and -deficient/-deactivated groups at different positions of phenyl ring of the vinyl diazo succinimide. The reaction of acetophenone **2a** with *N*-ethyl substituted vinyl diazo compounds (**1f–1k**) under the optimized reaction conditions afforded the target products (**5fa–5ka**) in moderate to good yields at room temperature in a very short time (up to 68%, 2 h). It is interestingly, we obtained the desired product **5aa** in 64% yield after 5 h (Scheme 3c). interesting that the *N*-ethyl substituted vinyl diazo compound derived from α -naphthal (**1k**) reacted smoothly, while β -naphthal derived derivative (**1l**) did not react probably due to electronic and steric reasons. We observed that the vinyl diazo com-

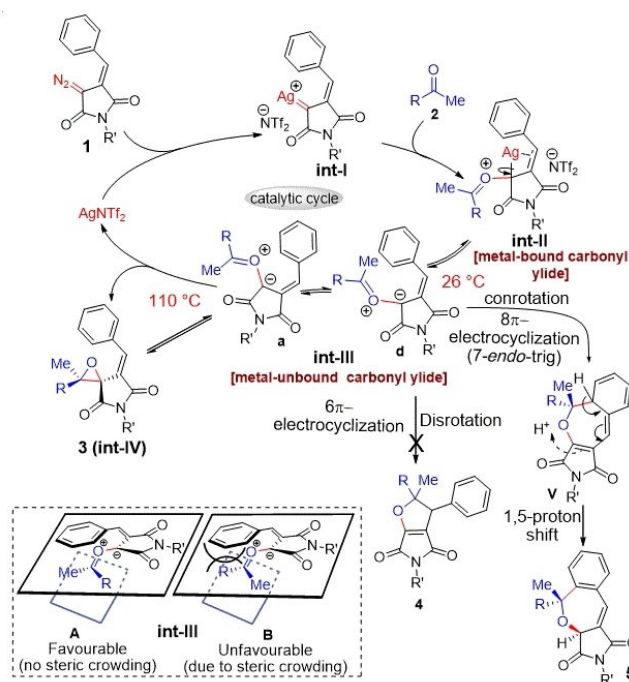
pounds bearing electron deactivating groups (–F, –Cl, –Br) at different positions of phenyl ring, afforded the target products in relatively higher yields than that of electron rich system (**1b–1d**, **1j**). Unfortunately, the *N*-ethyl substituted vinyl diazo compounds having methoxy group (**1m**) at *meta* position found to be not reactive. We reasoned that probably due to the presence of electron donating group (–OMe), the carbenoid carbon would be relatively less electrophilic for desirable reaction. In order to validate this, we replaced the methoxy group with the electron deactivating acetyloxy group at the same position (*meta*, **1n**) and treated with acetophenone **2a** under the optimized reaction condition. Gratifyingly, we obtained the corresponding desired product **5na** in moderate yield (61%, Table 2). It is interesting to note that relatively sensitive benzylidene scaffold containing *p*-methyl group at phenyl ring (**5da**, **5ja**) tolerated the optimized reaction conditions. Later, in order to generalize the practicality of the protocol, we explored the reaction of **1a** and **2a** on gram scale quantity and further as an application, the transformation of **5aa** was carried to obtain the pyrrolidinone derivative **7aa** (see Table 2 or Appendix-II, SI). All the dihydrobenzoxepines were obtained as single diastereomer. We obtained the molecular structure of **5ga** using single crystal X-ray analysis^[15] and the structures of all the other compounds were deduced based on analogy.

In order to have an insight into the reaction mechanism, we performed few control experiments systematically. To verify whether or not the reaction undergoes *via* carbonyl ylide (**int-II** or **III**, Scheme 3) or epoxide (**int-IV**, Scheme 3), we initially prepared the corresponding epoxide^[15] (**int-IV** or **3aa**) using the reported procedure.^[13a] This epoxide **3aa** under the optimized reaction conditions did not afford the desired product **5aa** even in trace and the unreacted epoxide **3aa** was recovered (Scheme 3a). Likewise, we observed that reaction did not afford



Scheme 3. Control Experiments for Intermediate Detection.

the desired product **5 aa** when carried out in absence of catalyst at room temperature (Scheme 3b). These results confirm that epoxide **3 aa** (**int-IV**) is not the intermediate for the desired transformation at room temperature. The **int-II** (four different conformational forms of metal-bound carbonyl ylides in one inset, see Scheme 3) and **int-III** (four different conformational forms of the corresponding metal-unbound carbonyl ylides) might be generating from the reaction of aryl vinyl diazosuccinimide under silver catalysis, presented here. It is reported by Huisgen that the epoxide can undergo electrocyclic ring opening reaction upon heating (absence of any catalyst). This report confirms about the *in situ* formation of carbonyl ylide at the room temperature reaction condition.^[16a–b] In this regard, in order to verify the possible formation of intermediate (**int-II** or **III**), we further treated compound **3 aa** (epoxide) with AgNTf₂ (5 mol%) at an elevated temperature (110 °C, Scheme 3c). Interestingly we obtained the desired product **5 aa** in 64% yield after 5 h (Scheme 3c). To understand the possible role of silver catalyst as well as carbonyl ylide, we performed the reaction in the absence of AgNTf₂ at elevated temperature (110 °C, Scheme 3d). To our surprise we obtained compound **5 aa**^[15] in almost similar yield (Scheme 3d, for more details, see SI). Considering Huisgen's^[16a–b] and Eberbach's reports^[16c] on the electrocyclic ring-opening equilibria of oxirane to carbonyl ylide and different conformational forms of carbonyl ylide, we surmise that at an elevated temperature, epoxide **3 aa** would open up to form metal-unbound carbonyl ylide (see **int-IIIld**, Scheme 3). This result was further supported by the time-dependent ¹H-NMR experiment wherein signals for the epoxide **3 aa** were disappearing over a period of time at an elevated temperature to form **5 aa** (Scheme 3, for more details, see SI page no. S34–35). We also strongly believe that even at room temperature the reaction would undergo via the same intermediate (**int-IIIld**) to afford **5 aa**. Apart from that an attempt to trap the carbonyl ylide intermediate (**int-III**) with different dienophiles^[6d] were unsuccessful. We observed that none of dienophiles reacted with the epoxide (**int-IV**) either at 26 °C or at 110 °C. In order to understand the role of catalyst, we carried out the reaction of **1 a** and acetophenone **2 a** in the absence of catalyst at 110 °C for prolonged reaction time (Scheme 3e). Interestingly, we did not obtain either the desired product **5 aa** or the epoxide **3 aa** even in trace thus supporting the role of catalyst in the desired transformation (Scheme 3e). Earlier also we had observed that the reaction at room temperature did not work in the absence of catalyst and the starting material **1 a** was recovered (26 °C, see Table 1, Entry 6). These two results indicate that probably a reactive silver carbenoid (**int-I**, see Scheme 4) species might be forming *in situ* that eventually may be forming carbonyl ylide (**int-IIIld**) via the corresponding counter anion stabilized metal-bound carbonyl ylide (**int-II**) both at room temperature as well as at elevated temperature. These combined results clearly depicted that the epoxide (**int-IV**) may not be the favourable intermediate and probably the desired product **5 aa** might be forming via carbonyl ylide (**int-IIIld**) at room temperature. These control experiments suggest that among the three plausible intermediates, the carbonyl ylide (**int-IIIld**) is the plausible intermediate for the formation of



Scheme 4. Plausible Mechanism for the (5 + 2)-Annulation.

dihydrobenzoxepine **5 aa** products. Moreover, a metal-unbound (free-ylide) carbonyl ylide intermediate, generating *in situ*, is proposed to be operative here based on the control experimental observations (for details, see SI page no. S33–35). We surmise that relatively better coordinating and more nucleophilic counter anion Tf₂N[−] might be acting as a superior promoter in facilitating the formation of **int-IIIld** faster and easily at room temperature than that of SbF₆[−] anion.^[17] We also noted that the anticipated product **4 aa** (see Table 1) has not been detected during the transformation. This might be the cause of steric hindrance exerted by the benzylidene group (phenyl ring tilted towards the carbonyl moiety) on vinyl succinimide, occurring in the transition state or in the carbonyl intermediate (**int-IIIld**).

Based on the experimental observations and preceding literature,^[16b–c,18] the plausible mechanism has been proposed (See Scheme 4). The vinyl diazosuccinimide **1** under the reaction conditions generates the silver carbenoid (**int-I**) by the extrusion of dinitrogen. This intermediate (**int-I**) further reacts with the ketone **2** (approaches from sterically less hindered site; see Scheme 4, inset) to form metal unbound carbenoid (**int-IIIld**) via the corresponding counter anion stabilized metal bound carbonyl ylide (**int-II**). This intermediate would further undergo 8π-electrocyclization (7-endo-trig) to form species **V** which after the successive (1,5)-proton abstraction affords the corresponding desired oxepine **5**. Also, at higher temperature **int-IV** (**3**) might be in equilibrium with the **int-IIIld** to form the desired product **5** as well (Scheme 4).

Conclusion

In summary, we have demonstrated the formal (5 + 2)-cyclo-addition route to access the dihydrobenzoxepines in one-pot using vinyl diazosuccinimide as 5-C-synthons and ketones very effectively for the first time. The silver triflimide proved to be an efficient catalyst for this transformation and the protocol found to be highly regio-, chemo- and diastereo-selective. The method proved to be general as it worked well with aliphatic and aromatic methyl ketones bearing electron deactivating as well as donating groups to afford the corresponding benzo[5,6]oxepino[2,3-c]pyrroles as single diastereomer with a broad substrates scope. The control experiments and time-dependent NMR studies gave an insight into the plausible reaction mechanism of this transformation. The protocol proved to be scalable on gram quantity as well.

Experimental Section

General procedure for the synthesis of vinyl succinimides (6a–6n): The compounds were prepared according to a previously reported method^[13a]

To the stirred solution of *N*-ethyl maleimide (3 g, 1.0 equiv., 24 mmol) in ethanol (120 mL) was added triphenylphosphine (7.55 g, 1.2 equiv., 29.0 mmol) in portion at room temperature under N₂ atmosphere. The initial pink coloured reaction mixture slowly turned to white suspension over a period of 5–6 min of initial stirring. After which, benzaldehyde (3.5 mL, 1.4 equiv., 34 mmol) was added dropwise into the reaction mixture at room temperature. During this addition, the white suspension slowly turned into clear solution. The reaction mixture was allowed to stir for 6 h. Upon completion of the reaction (monitored by TLC), the white solid formed during the course of the reaction was filtered through sintered glass funnel and was washed with ethanol (10 mL × 2). The crude product 6a was obtained as white solid (3.40 g, 66% yield) and this was used for the next step without further purification.

General Procedure for the synthesis of vinyl diazosuccinimides (1a–1n): The compounds were prepared according to a previously reported method^[13a]

To the stirred solution of (*E*)-3-benzylidene-1-ethylpyrrolidine-2,5-dione **6a** (2.15 g, 1.0 equiv., 10 mmol) in 30 mL acetonitrile, were added 4-acetamidobenzenesulfonyl azide (2.88 g, 1.2 equiv., 12 mmol) and DBU (2.24 mL, 1.5 equiv., 15 mmol) at 0 °C temperature under inert atmosphere. The reaction mixture was stirred for 10 minutes while maintaining the temperature (0 °C). The reaction mixture was then quenched with saturated solution of NH₄Cl and the product was extracted with diethyl ether (30 mL × 3). The combined organic layers were washed with brine solution and dried over anhydrous Na₂SO₄. The extract was filtered and evaporated under reduced pressure. The crude product was purified using column chromatography over silica gel to afford (*E*)-3-benzylidene-4-diazo-1-ethylpyrrolidine-2,5-dione **1a** as orange solid (2.257 g, 94% yield).

General procedure for the synthesis of dihydrobenzo[5,6]oxepino[2,3-c]pyrrole-1,3(2*H*)-dione (5): An oven-dried 25 mL two necked round bottom (RB) flask equipped with a magnetic stirrer bar was charged with AgNTf₂ (3.9 mg, 5 mol%)

under argon-atmosphere and the RB flask was covered up with aluminium foil. Then dry CH₂Cl₂ (5 mL) and acetophenone **2a** (23.6 μL, 1.0 equiv., 0.2 mmol) were added subsequently and the mixture was stirred at room temperature under for a minute. After that, vinyl diazosuccinimide **1a** (48.3 mg, 1.0 equiv., 0.2 mmol) in CH₂Cl₂ (1 mL) was added to the reaction mixture dropwise over 2 h and the stirring was continued for 10 min more for full consumption of diazo compound. The progress of the reaction was monitored by TLC. After completion of the reaction, the solvent was removed under reduced pressure. The crude product obtained was purified by column chromatography (petroleum ether/EtOAc 92:8) over silica gel to furnish the desired product **5a** as white solid (47 mg, 70% yield). The slight excess amount of acetophenone **2a** was recovered during the purification.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: Annulation • Diastereoselective • Dihydrobenzoxepines • Silver catalysis • Vinyl diazosuccinimide

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Umpolung Reactivity of Diazo Arylidene Succinimides: Distal C–H Functionalization of α -Thiocarbonyls from the Reactive Carbenoid Center

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Herein, for the first time we have explored the umpolung reactivity of the vinylogous carbon center of diazo arylidene succinimide (DAS) through rhodium catalysis to achieve [2,3]-Stevens rearrangement of α -thioether esters. The protocol has successfully demonstrated the distal C–H bond functionalization of the α -thioether esters. Alongside, the carbenoid reactivity of DAS has also been achieved with Doyle-Kirmse reaction of allyl/propargyl phenyl sulfides. The protocol proved to be practical to synthesize a wide variety of [2,3]-Stevens

rearrangement products exclusively and the possible side products emanating from Pummerer rearrangement and [1,2]-Stevens rearrangement were not observed. This catalytic protocol works smoothly in environmentally benign solvent under open air to afford the corresponding desired products with excellent diastereo-, regio- and chemo-selectivities in good to excellent yields. The protocol also proved to be scalable on gram quantity.

Introduction

Umpolung or the reversal of the inherent polarity has been pioneered by D. Seebach and E. J. Corey^[1] and the strategies based on umpolung reactivity have been proved to be powerful for introducing different functional groups at the sites that are typically inaccessible by the classical approaches due to electronic mismatch.^[2] Some of the conventional examples of carbonyl umpolung or anion relay are the cyclic dithianes, *N*-heterocyclic carbenes (NHCs).^[3] Recently, König and co-workers have reported the umpolung difunctionalization of carbonyl compounds *via* the visible light initiated radical addition to the *N*-sulfonylhydrazones to form α -functionalized carbanions *in situ*.^[4] Diazo compounds are very useful synthetic intermediates and have been employed for the C–H bond functionalization of various compounds *via* in-situ generation of metal-carbenoid species.^[5] It is also well known that the vinyl metal carbenoid intermediates would undergo a wide variety of transformations with electron rich systems.^[6] However, to enforce the reversal of reactivity in a diazo compound, especially in vinyl diazo compounds is highly challenging owing to their 1,3-dipolar nature that makes them competent and compatible for the electrophilic addition/substitution reactions.^[7] Consequently, inducing the inversion of polarity of

the diazo compounds at the carbenoid center (metallo-carbene center) is generally achieved by the combined effect of metal complex and suitable substrate.^[8] Interestingly, the metallo-arylidene succinimide^[9] prepared from the corresponding Michael acceptor-arylidene succinimide has emerged as a versatile reagent in the last few years. It has a diverse regioselectivity pattern due to the relatively rigid and fixed *Z*-configuration (selective orientation of benzylidene ring towards the cyclic imide, Scheme 1A).^[10] This is a quite unique property unlike the metallo-acyclic vinyl carbene that is relatively more flexible and *E*-selective^[11] in nature. The vinylogous carbon center (or arylidene segment) of diazo arylidene succinimide (DAS) known to exhibit the nucleophilic reactivity at the vinylogous center (Scheme 1A-I). This nucleophilic reactivity of DAS has been explored by the generation of ylide that eventually facilitates the intramolecular cycloaddition reactions *via* metallo-1,1-,^[9,12] 1,3-^[12a] and 1,5-^[10,13] adducts. The rearrangement of ylides has been explored increasingly for the synthesis of various complex building blocks and bioactive molecules.^[14] In particular, sulfur ylides have gained a great importance due to their wider reactivity and greater stability.

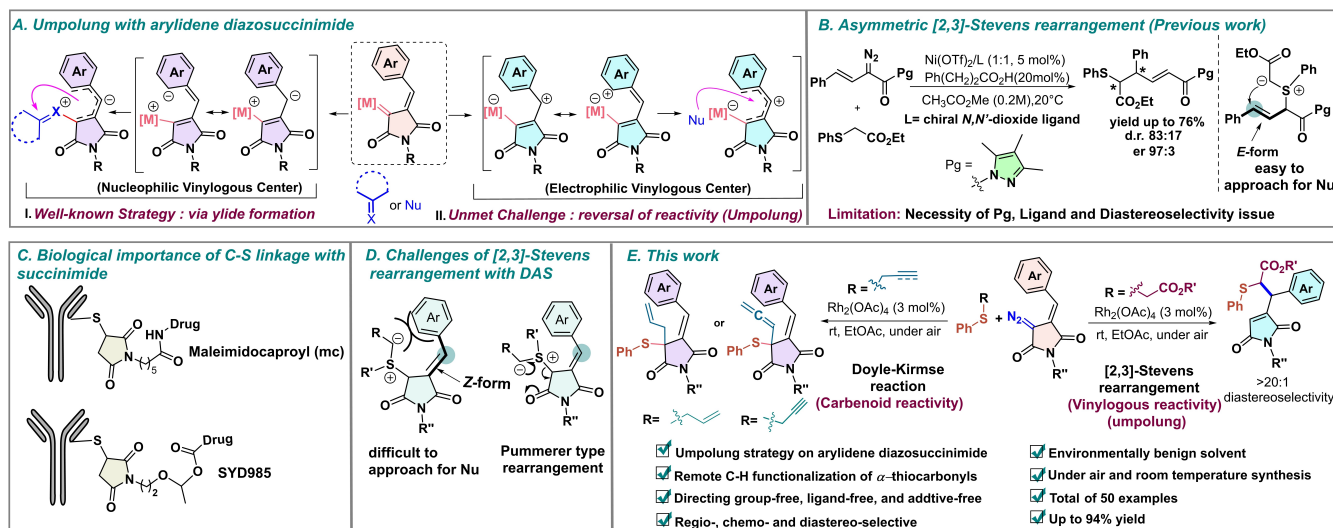
The strength of sulfur ylides have been demonstrated in Doyle-Kirmse^[15] and Stevens^[16] rearrangements *via* [2,3]- and [1,2]-sigmatropic rearrangements respectively under catalyst/ligand-controlled system to achieve the selectivity. However, [2,3]-Stevens rearrangement with diazo compounds has been rarely explored in the literature. Recently, asymmetric [2,3]-Stevens rearrangement of α -thiocarbonyl compound with the acyclic vinyl diazo compounds has been achieved *via* nickel catalysis that greatly relied on the strength of ligand as well as the protecting group (Scheme 1B).^[17] However, high degree of diastereoselectivity could not be achieved for this transformation possibly due to the relatively flexible reaction site (Scheme 1B).^[17]

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Scheme 1. General characteristics of metallo-arylidene carbenesuccinimide and the current challenges.

It is very important to note that the maleimide–sulfur linkage/methylene succinimide–sulfur linkage plays a significant role in chemical biology with many potential applications such as bioconjugation,^[18] in biomedicines and pharmaceuticals (Scheme 1C).^[19] Many with maleimide scaffold and sulfur containing compounds are known for their biological importance as well.^[20] Thus the development of user-friendly, economical and practical method to construct sulfur-maleimide linkage is highly desirable.

Though, metallo-arylidene succinimides have been explored for its nucleophilic reactivity at vinylogous center, interestingly, the inversion of this nucleophilic reactivity at vinylogous carbon center (or arylidene segment of DAS) has not been achieved till date to the best of our knowledge (Scheme 1A-II). It would be a great challenge to enforce the electrophilic reactivity at vinylogous carbon center (or arylidene segment of DAS) of metallo-carbene by the reversal of polarity. Hence, in order to achieve the unexplored umpolung reactivity of DAS is quite challenging due to the posing steric hindrance of the aryl group to that of sulfur ylide intermediate and also the feasibility of the competitive Pummerer type rearrangement^[21] (Scheme 1D).

Herein, we present a distal functionalization of ethyl(arylthiol)acetates by exploring the umpolung reactivity of vinyl diazosuccinimide (DAS) through an in situ formation of sulfonium ylide *via* rhodium-catalysis under ligand-free conditions at room temperature (Scheme 1E).^[22]

Results and Discussion

In order to explore the novel reactivity of DAS, we commenced with a model substrate **1a** (1 equiv., 0.2 mmol) and ethyl α -(phenylthiol)acetate **2a** (1.2 equiv.) in presence of $\text{Rh}_2(\text{OAc})_4$ (3.0 mol%) as a catalyst in ethyl acetate under open atmosphere. To our delight, after 20 min at room temperature, the desired product **3aa** was obtained in excellent yield with

exclusive diastereoselectivity (90% yield, >20:1 dr, Table 1, Entry 1). However, the reaction did not work in the absence of $\text{Rh}_2(\text{OAc})_4$ (Table 1, Entry 2). Further, we explored the reaction of DAS **1a** with **2a** in presence of iron catalyst (FeTPPCL). However, DAS **1a** did not react even under prolonged reaction time (see ESI, Table S1, Entry 1, Page S5). The reaction in presence of CuI led to the decomposition of diazo succinimide **1a**, but surprisingly, the desired [2,3]-Stevens rearranged product β -phenyl- β -(thioester)-*N*-substituted maleimide **3aa** was ob-

Table 1. Optimization of reaction conditions^[a]

Entry	Variation from the standard reaction condition ^[a]	Yield ^[b] (%) of 3aa	dr ^[c]
1	None	94 (90)	> 20:1
2	No $\text{Rh}_2(\text{OAc})_4$	NR	–
3	$\text{Cu}(\text{OTf})_2$	56	13.3:1
4	No air	94	> 20:1
5	10 mol% of $\text{Rh}_2(\text{OAc})_4$	92	> 20:1
6	2a (1.0 equiv.) and 1a (1.2 equiv.)	92	> 20:1

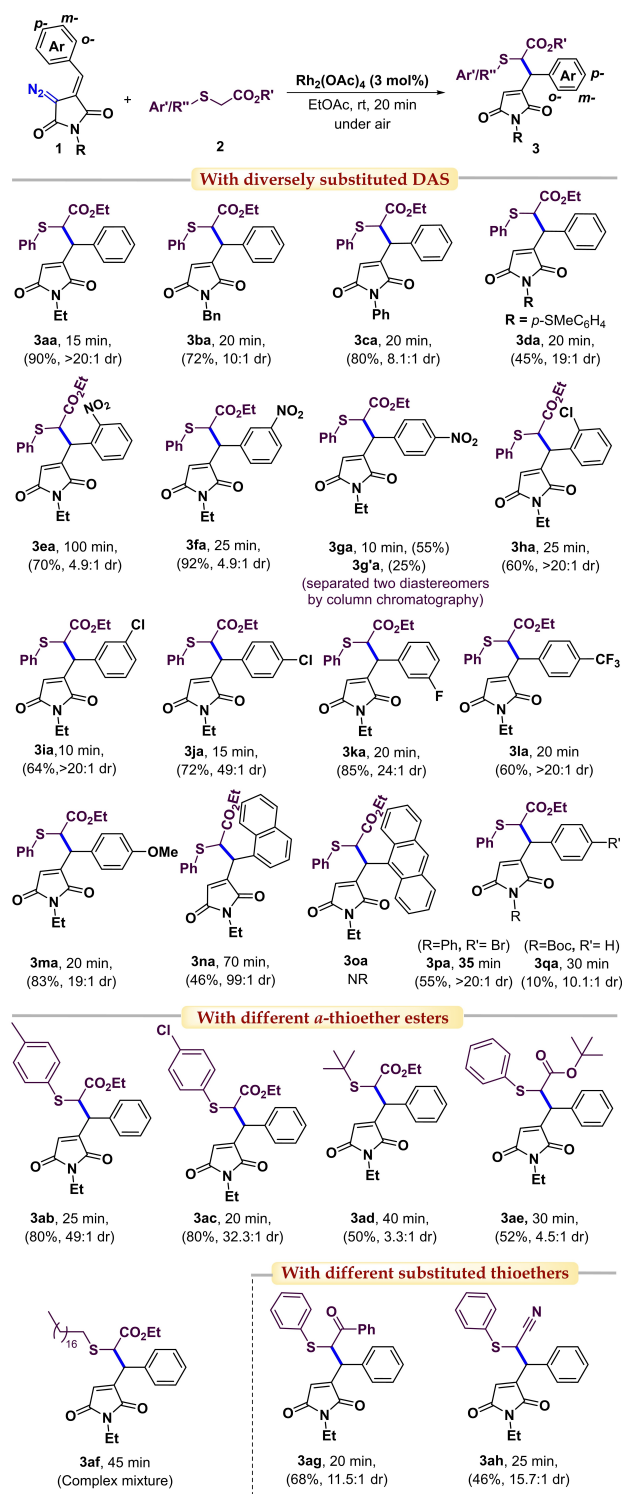
^[a]Standard Reaction conditions: Unless otherwise noted, sulfide **2a/2a'** (0.24 mmol, 1.2 equiv.) and catalyst (3.0 mol%) were dissolved in 1.0 mL ethyl acetate. Then a solution of DAS **1a** (0.2 mmol, 1.0 equiv.) in 1.0 mL of the same solvent was added to the reaction mixture at room temperature under air. ^[b]Yields of **3aa/4aa'** were determined by ¹H NMR spectroscopic analyses of the reaction mixture using 1,3,5-trimethoxybenzene as the internal standard. The isolated yield of the products was given in parentheses. ^[c]dr = Diastereomeric ratio (detected by ¹H NMR spectroscopic analysis). NR = No reaction.

tained, albeit in very poor yield with poor diastereoselectivity (10% yield, 4:1 dr, see ESI, Table S1, Entry 3, Page S5). Next, we screened various copper and silver catalysts (see ESI, Table S1, Entries 4–10, Page S5). Among all, $\text{Cu}(\text{OTf})_2$ and $[\text{Cu}(\text{CH}_3\text{CN})_4]\text{PF}_6$ gave the desired product **3aa** in relatively moderate yield with good diastereoselectivity (up to 65% yield 10:1:1 dr, see ESI, Table S1, Entries 6 and 7, Page S5). However, we observed that the reaction under open air/moisture afforded the desired product **3aa** in relatively lower yield when $\text{Cu}(\text{OTf})_2$ was used as a catalyst (Table 1, Entry 3). We strongly believe that it might be due to the moisture sensitivity of copper catalyst. Based on the initial results, we screened few more rhodium catalysts (see ESI, Table S1, Entries 12 and 13, Page S5). Among all the catalysts screened, gratifyingly $\text{Rh}_2(\text{OAc})_4$ (3 mol%) proved to be the most efficient catalyst to afford the desired product **3aa** in excellent yield with exclusive diastereoselectivity. More importantly, we did not observe the formation of any competitive rearrangement side-products such as **3Aaa** (Pummerer rearrangement) and **3Baa** (1,2-Stevens rearrangement) (see Table 1).

Later, in order to enhance the yield of the desired product **3aa** further, we explored the reaction of DAS **1a** (1 equiv.) and ethyl α -(phenylthiol)acetate **2a** in presence of rhodium acetate in different solvents (see ESI, Table S2, Page S6). Among all, ethyl acetate turned out to be the most advantageous solvent affording the desired diastereoselective distal C–H functionalized product **3aa** in excellent yield (Table 1, Entry 1). Later, we have also looked into the standardization of the optimum reaction temperature (ranging from 0 °C to 60 °C) for the efficient transformation and the reaction worked efficiently at room temperature (see ESI, Table S3, Entry 2, Page S6). Later, the reaction in presence as well as in the absence of air did not affect the outcome of the reaction and overall yield of the product **3aa** (Table 1, Entries 1 and 4). We observed that increasing the catalyst loading (from 3 to 10 mol%) reduced the overall reaction time (12 min), while lowering the catalyst loading enhanced the reaction time (see Table 1, Entry 5, see ESI, Table S4, Page S7). However, we observed that there was no significant impact on the overall yield and diastereoselectivity of the desired product **3aa** in both the cases.

Having obtained the optimum reaction conditions and in order to validate this unusual umpolung type reactivity of DAS at vinylogous center, we further planned to explore the substrate scope by screening different diazo arylidene succinimides (DASs) **1** and α -(alkyl/arylthiol) acetates **2** under the optimum reaction conditions. In this regard, we synthesized a few *N*-substituted DAS derivatives (**1b–1d**) and they were investigated for the distal C–H functionalization with ethyl α -(phenylthiol) acetate **2a** under the optimized reaction conditions. Unlike, the electron inducing and less sterically bulky *N*-ethyl DAS **1a**, *N*-benzyl DAS **1b** furnished the desired product **3ba** in relatively lower yield with moderate diastereoselectivity (72%, 10:1 dr, Scheme 2).

However, electronically withdrawing *N*-phenyl DAS **1c** and *N*-(*p*-SMe)-phenyl DAS **1d** afforded the corresponding desired products **3ca** and **3da** in good to modest yields respectively with poor diastereoselectivity (Scheme 2). Among the different



Scheme 2. Substrates scope for [2,3]-Stevens rearrangement products^[a]. **Reaction Conditions:** Unless otherwise noted, sulfide **2a** (0.24 mmol, 1.2 equiv.) and $\text{Rh}_2(\text{OAc})_4$ (3 mol%) were dissolved in 1.0 mL ethyl acetate. Then a solution of DAS **1a** (0.2 mmol, 1.0 equiv.) in 1.0 mL of the same solvent was added to the reaction mixture at room temperature under air.

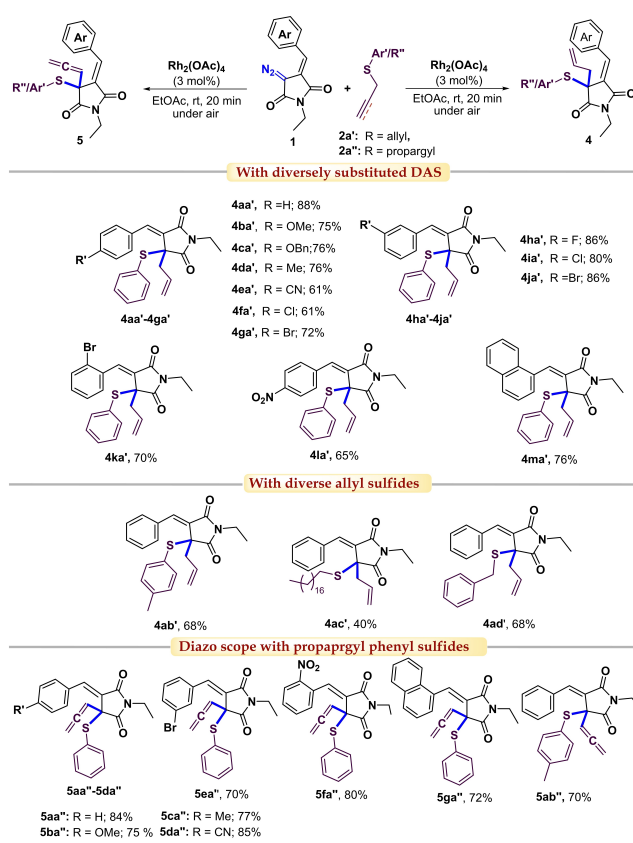
N-substituted DAS, *N*-ethyl substituted DAS **1a** proved to be efficient to furnish the corresponding desired product **3aa** in excellent yield and diastereoselectivity in 15 min (90% yield,

> 20:1 dr, Scheme 2). We further plan to explore the reactivity of different *N*-ethyl DASs (**1e–1o**) bearing different electron-rich, electron-deficient and deactivated groups at different positions of the phenyl ring of the DAS. We observed that the DASs bearing NO_2 group at *o*-, *m*-, and *p*-position of the phenyl ring (**1e–1g**) reacted smoothly with ethyl α -(phenylthiol)acetate **2a** to afford the corresponding desired products (**3ea–3ga**) relatively in higher yields with good diastereoselectivity (up to 85% yield, 4.9:1 dr, Scheme 2). We observed that *o*-phenyl substituted DAS **1e** required more time for the complete transformation due to the steric factor. We have successfully separated the two diastereomers of the desired product **3ga** (**3ga** and **3g'a**). The DAS derivatives (**1h–1l**) containing electron deactivating groups (F, Cl, and CF_3) at different positions of the phenyl ring upon treatment with ethyl α -(phenylthiol)acetate **2a** afforded the corresponding desired products (**3ha–3la**) in moderate to good yields (up to 85% yield, 4.9:1 dr, Scheme 2). The *p*-methoxyphenyl substituted DAS **1m** afforded the desired product **3ma** in very good yield with high diastereoselectivity (up to 83% yield, 19:1 dr, Scheme 2).

The sterically hindered DAS derivative **1n** furnished the desired product **3na** in lower yield and the anthracenyl derived DAS **1o** did not react at all (Scheme 2). Interestingly, *N*-phenyl substituted DAS **1p** under the standard reaction conditions afforded the **3pa** in excellent diastereoselectivity though in moderate yield. Whereas *N*-Boc protected DAS **1q** offered corresponding product **3qa** in very low yield (Scheme 2).

In order to explore the general reactivity pattern and the practicality of the protocol, different α -(alkyl/aryl thiol)acetates (**2b–2f**) were treated with *N*-ethyl DAS **1a** under the optimized reaction conditions. The compounds **2b–2e** furnished the corresponding products **3ab–3ae** in good yields with low diastereoselectivity, while the **2f** led to a complex mixture of **3af** (Scheme 2). These results indicated that the increase in the steric hindrance around sulfonium ylide intermediate leads to decrease in diastereoselectivity.

Later, in order to examine the umpolung reactivity of metallo-carbene of DAS **1a** we planned to explore the reactivity of few different aryl alkyl sulfides such as α -thiophenyl acetophenone **2g**, α -thiophenyl acetonitrile **2h** and allyl phenyl sulfide **2a'** under the standard reaction conditions. Interestingly, we obtained the corresponding desired [2,3]-Stevens rearrangement products **3ah** (68% yield, 11.5:1 dr, Scheme 2) and **3ai** (46% yield, 15.7:1 dr, Scheme 2). However, to our surprise, allyl phenyl sulfide **2a'** furnished the Doyle-Kirmse product **4aa'** exclusively at room temperature (88%, Scheme 3). This result prompted us to glean into the literature further for the Doyle-Kirmse reaction. Very recently, copper catalyzed Doyle-Kirmse reaction has been reported using allyl phenyl sulfides at an elevated temperature (50 °C) under inert and dry condition.^[23] Looking at our initial result, we surmised that sulfides having α -acidic hydrogen are prone for the [2,3]-Stevens rearrangement while the allyl phenyl sulfide with relatively less acidic hydrogen may not undergo 1,3-hydrogen transfer easily to furnish the desired [2,3]-Stevens rearrangement products. The plausible



Scheme 3. Substrates scope for Doyle-Kirmse reaction products^[a] **Reaction Conditions:** Unless otherwise noted, Allyl/Propargyl phenyl sulfide **2a** (0.24 mmol, 1.2 equiv.) and $\text{Rh}_2(\text{OAc})_4$ (3.0 mol%) were dissolved in 1.0 mL ethyl acetate. Then a solution of DAS **1a** (0.2 mmol, 1.0 equiv.) in 1.0 mL of the same solvent was added to the reaction mixture at room temperature under air.

mechanism for the transformation has been depicted (see ESI, Page S31).

Excited by this interesting observation on site-selective reactivity of two different type of sulfonium ylides, we planned to explore the rhodium catalysed Doyle-Kirmse reaction with DAS as it is not known in the literature. In this regard, we carried out the optimization of rhodium catalysed Doyle-Kirmse reaction systematically (see ESI, Table S6 and Table S7, Pages S8–9). Based on the exhaustive screening of many reaction parameters, **1a** (1.0 equiv.) and **2a** (1.2 equiv.) in presence of $\text{Rh}_2(\text{OAc})_4$ (3.0 mol%) as a catalyst in EtOAc (0.1 M) at 27 °C for 20 min under air proved to be optimum reaction condition to furnish the desired product **4aa'** in excellent yield (Scheme 3). Having obtained the optimization condition, we further planned to investigate the reactivity of few different sulfides with a variety of DAS derivatives. A wide range of substituted arylidene diazo-succinimides (**1b–1g**) having EWG as well as EDG substituents at the *para*-position afforded the corresponding Doyle-Kirmse products (**4ba'–4ga'**) in good yields (up to 85%, Scheme 3). The DAS derivatives (**1h–1j**) having electron deactivating substituents (F, Cl, and Br) at *m*-position of the aryl ring afforded the corresponding products (**4ha'–4ja'**) in very good yields (up to 86%, Scheme 3). The DAS derivative with

nitro group afforded the desired product **4la'** in moderate yield (65% yield, Scheme 3). The DAS having the naphthyl moiety **1m** afforded the desired product **4ma'** in good yield (76% yield, Scheme 3). Later, we explored the reaction with different aryl/long chain alkyl sulfides (**2b'–2d'**) to afford the corresponding rearranged thioether products (**4ab'**, **4ac'** and **4ad'**) in moderate to good yields (up to 68% yield, Scheme 3). We further explored the reactivity of propargyl phenyl sulfide **2a''** by treating with different DAS derivatives (**1ba–1ga**) having electron donating and electron withdrawing groups to afford the corresponding desired products (**5ba''–5ga''**) in moderate to good yields (up to 85% yield, Scheme 3).

It is very important to highlight that unlike the copper catalyzed protocol,^[23] this rhodium catalyzed (3 mol%) Doyle-Kirsme reaction worked smoothly at room temperature in very short time (20 min) and is found to be not sensitive to air as well as moisture. Notably, this rhodium catalysed strategy also effectively utilized green solvent such as ethyl acetate for the successful transformation. Also, the protocol is user friendly as it works even in ordinary test tube under open air and did not need any special glass apparatus.

In order to investigate the competitive intramolecular vs. intermolecular reactivity of DAS, we explored the reaction of ethyl α -(phenylthiol)acetate **2a** with a modified DAS **1r** having nucleophilic site (Scheme 4A). Surprisingly, we observed that reaction furnished the corresponding intramolecular cyclized product **3r** in moderate yield (50%) and the corresponding [2,3]-Stevens rearrangement product **3ra** was obtained in lower yield with very high diastereoselectivity (22% yield, 24:1 dr, Scheme 4A). In order to examine the preferred regioselectivity

of thioether substrate, we prepared the ethyl α -(benzylthiol)acetate **2i** with two reactive methylene sites attached to the sulfur. The reaction of **2i** with DAS **1a** afforded the [2,3]-Stevens rearrangement products **6ag** and **3ai** in modest yields with excellent diastereoselectivity (Scheme 4B). This result further indicated that more acidic α -hydrogen leads to a facile [2,3]-Stevens rearrangement. Later, in order to examine the chemoselectivity of this transformation, we synthesized the substrate **2j** (having both α -arylthio- and α -aryloxy ester moieties) that has two potential sites to form either sulfur ylide or oxygen ylide. Interestingly, reaction of **2j** with DAS **1a** under the rhodium catalysis furnished the corresponding **7aj** as a sole product (57% yield, Scheme 4C). This observation clearly indicated that sulfur ylide is more favourable and preferred over oxygen ylide possibly due to the higher electronegativity of the oxygen atom that makes the oxygen ylide less stable. Further in order to demonstrate the practicability of the protocol, we carried out the reaction of **1a** with **2a** on a gram scale to afford the distal C–H functionalized product **3aa** in good yield with high diastereoselectivity (78% yield, >20:1 dr, Scheme 4D). Also, as an application of the strategy, product **3aa** was treated with *m*-CPBA to obtain the corresponding sulfone **8aa** (58%, Scheme 4D).

Conclusions

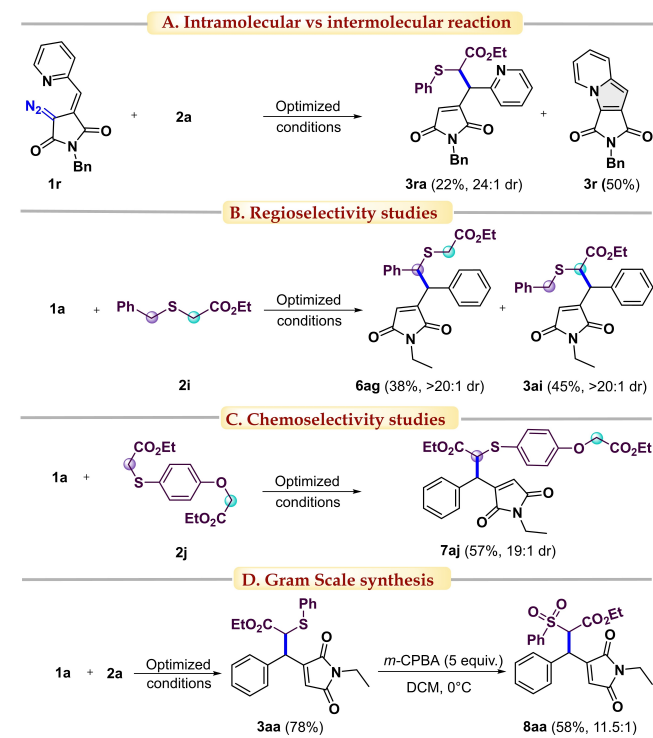
In summary, we have successfully demonstrated the tuneable reactivity of diazo arylidene succinimides (DASs) to selectively achieve both [2,3]-Stevens rearrangement as well as Doyle-Kirsme reaction *via* rhodium catalysis at room temperature under open atmosphere. We have also achieved the unexplored umpolung reactivity of the DAS with alkyl/aryl α -(arylthiol) acetates to access [2,3]-Stevens rearranged products *via* C–C and C–S bond formation for the first time. It has been shown that the substrates play significant role in influencing the reactivity of diazo arylidene succinimides (DASs). This distal C–H functionalization protocol has effectively utilized the environmentally friendly solvent such as ethyl acetate and the protocol proved to be scalable on gram quantity.

Supporting Information

General experimental procedures, the detailed optimization of the reaction conditions, general characterization data, NMR spectra and the proposed mechanism.

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Scheme 4. Chemo-/Regio-selectivity studies and gram scale synthesis.

Conflict of Interests

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available in the supplementary material of this article.

Keywords: Umpolung reactivity • Diazo arylidene succinimide (DAS) • [2,3]-Stevens rearrangement • Doyle-Kirmse reaction • Diastereoselective

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