Unveiling the Reactivity of Cyclic Dithioacetals Under Visible Light Photoredox Catalysis via C–S Bond Cleavage

A thesis submitted in partial fulfilment of the requirements of the degree of

Doctor of Philosophy

by

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Research Supervisor

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Dedicated to my mother

Venu

भारतीय विज्ञान शिक्षा एवं अनुसंधान संस्थान पुणे
INDIAN INSTITUTE OF SCIENCE EDUCATION AND RESEARCH PUNE
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CERTIFICATE

This is to certify that the research work incorporated in this thesis entitled **"*Unveiling the Reactivity of Cyclic Dithioacetals Under Visible Light Photoredox Catalysis via C-S Bond Cleavage*"** submitted by **Pankaj D. Dharpure** 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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DECLARATION

I hereby declare that the thesis entitled "***Unveiling the Reactivity of Cyclic Dithioacetals Under Visible Light Photoredox Catalysis via C–S Bond Cleavage***" submitted for Doctor of Philosophy in Chemistry at Indian Institute of Science Education & Research-Pune (IISER-Pune), has not been submitted by me to any other University or Institution. This work presented here was carried out at the, Indian Institute of Science Education & Research, Pune, India under the supervision of Prof. Ramakrishna G. Bhat.

Date: 28 June 2022
Place: Pune

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Pankaj Dharpure

Contents

ABBREVIATIONS:

°C	degrees Celsius
µ	micro
Å	angstrom
Ac	Acetyl
ACN	Acetonitrile
AcOH	Acetic acid
aq	aqueous
Ar	Aryl
atm	atmosphere
Boc	*tert*-butoxycarbonyl
Bn	benzyl ($C_6H_5CH_2$)
BnCl	benzyl chloride
BQ	benzoquinone
bs	broad singlet
calcd.	calculated
CAN	Cerium(IV)-ammonium nitrate
Cbz	benzyloxycarbonyl
$CDCl_3$	Deuterated chloroform
CFL	Compact Fluorescent Lamp
cm^{-1}	wavenumber(s)
conc.	concentrated
CT	Charge Transfer
d	doublet (NMR)
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

DMAP	*N*,*N*'-dimethylamino pyridine
DMF	*N*,*N*'-dimethyl formamide
DMSO	Dimethylsulfoxide
DMSO-d_6	Duterated dimethyl sulfoxide
DTBP	Di-tert-butyl peroxide
equiv.	equivalents
ER	Electron relay
ESI TOF	Electrospray ionisation time-of-flight
ESMS	electrospray mass spectrometry
Et	Ethyl (CH_3CH_2)
EtOAc	ethyl acetate
eV	Electron volt
EY	Eosin Y
FTIR	Fourier-transform infrared spectroscopy
g	gram (s)
h	hour (s)
HAT	Hydrogen atom transfer
hν	light frequency
HRMS	High Resolution Mass Spectroscopy
Hz	Hertz
IBX	2-Iodoxybenzoic acid
Imd	Imidazole
J	Spin coupling constant (in NMR spectroscopy)
KOAc	Potassium acetate
L	Ligand
LED	Light emitting diode
m	meta
M	molar (mol L^{-1})
m	multiplet (in NMR)
m/z	mass to charge ratio

m-CPBA	*m*-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	*N*-bromosuccinimide
NHPI	*N*-hydroxyphthalimide
nm	nanometer
NMR	Nuclear Magnetic Resonance
Nu	Nucleophile
*n*BuLi	*n*-butyllithium
o	*ortho*
p	*para*
PC	Photocatalyst
PC*	Excited state photocatalyst
Ph	Phenyl (C_6H_5)
ppm	parts per million
PT	proton transfer
Py	pyridine
q	quartet (NMR)
quin.	quintet
r.t.	room temperature
Rf	retention factor (in chromatography)
Rh6G	Rhodamine 6G

s	singlet (NMR)
SET	Single electron transfer
t	triplet (NMR)
t-, *tert-*	Tertiary (branched alkyl chain)
TBAB	tetrabutyl ammonium bromide
TBHP	*tert*-Butyl hydroperoxide
*t*Bu	*tert*-butyl
td	triplet of doublet
TEMPO	2,2,6,6-Tetramethylpiperidin-1-yl)oxyl
Tf	trifluoromethanesulphonyl (triflyl)
Tf	triflate
TFA	Trifluoroacetic acid
THF	Tetrahydrofuran
TLC	Thin Layer Chromatography
TMS	Trimethylsilyl
TMEDA	*N*,*N*,*N'*,*N'*-tetrametylaminoethylenediamine
TOF	Turn-over frequency
TS	transition state
Ts	tosyl
UV	ultraviolet
vis	visible
V	Volt
W	Watt
X	Heteroatom
δ	chemical shift in ppm downfield from trimethylsilane
λ	Wavelength
*	Excited state

SYNOPSIS

The thesis entitled "***Unveiling the Reactivity of Cyclic Dithioacetals Under Visible Light Photoredox Catalysis via C–S Bond Cleavage***" comprises of four chapters.

Aim and background:

Dithianes and dithiolanes are well known for their robust stability and they are used extensively in organic synthesis. Dithianes and dithiolanes are commonly used as carbonyl protecting groups. They have been also employed for their umpolung reactivity as the carbanion generated is relatively stable. It was long thought that usually negative charge (electrons) easily overlaps with the empty *d*-orbital of sulfur atoms. However, computational studies reveal that due to more likely the negative charge delocalizes into σ* orbital of the C–S bond for the higher stability. Innumerable examples have been demonstrated for the synthesis complex organic molecules by forging the C–C bonds through umpolung reactivity of thioacetals. The deprotection of dithioacetals usually require metal reagents such as mercury salts or oxidizing agents. Also, for generating the carbanion from cyclic thioacetals usually strong bases such as *n*BuLi is required.

Ove the years photoredox catalysis has gained a great importance and the same has been explored for many transformations. Different organosulfur compounds have been employed for different transformations using photoredox catalysis. Interestingly, dithioacetals in general and dithianes and dithiolanes in particular have never been explored for synthetic transformations via the selective cleavage of C–S bond under visible light photoredox catalysis. Herein, this thesis presents the systematic exploration of unusual reactivities of cyclic dithioacetals by the selective and controlled cleavage of C–S bond of cyclic dithioacetal via visible light photoredox catalytic conditions under oxygen atmosphere to access useful and interesting molecular scaffolds. All these strategies did not rely on transition metal reagents, external oxidizing agents and strong bases.

Chapter 1:

C–S Bond Formation and Cleavage via Photoredox Catalysis

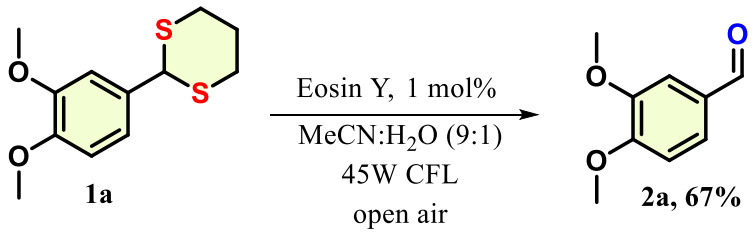
This chapter describes the basics of the photoredox catalysis, the difference between energy transfer mode as electron transfer mode of photocatalysis and subsequent photoredox

catalysis via one electron oxidation or one electron reduction. This chapter also highlights the commonly used photoredox catalysts, catalytic pathways. Also, the basic requirements for the mechanistic investigation have been delineated. Along with the fundamentals of photoredox catalysis, the applications of photoredox catalysis have been presented with examples. The chapter has given an account on the C–S bond formation and cleavage using the different photocatalysts (metal based photocatalyst and the organophotocatalyst) with examples. Finally, the chapter presents few novel reactions of dithianes and dithiolanes.

Chapter 2: ***Visible-light Mediated Dithiane Deprotection Under Metal-Free Conditions via Photoredox Catalysis***

This chapter presents the development of a convenient and easy metal-free deprotection of dithianes via visible-light photoredox catalysis. The chapter illustrates the importance of dithianes as convenient stable protecting groups for carbonyl compounds and few important methods available for their deprotection using metal (mercury) reagents, stoichiometric amount of oxidizing reagents or harsh reaction conditions. Further, the chapter presents a detailed account on the development of methodology for the smooth deprotection of dithianes using visible light as an energy source under metal-free and mild reaction conditions without using the any external oxidizing reagent. We optimized the reaction condition for the deprotection of dithiane **1a** using eosin Y (1 mol%), acetonitrile:water (9:1) as solvent system with irradiation of visible light (45W, CFL) at room temperature under open air condition (Scheme 2.1).

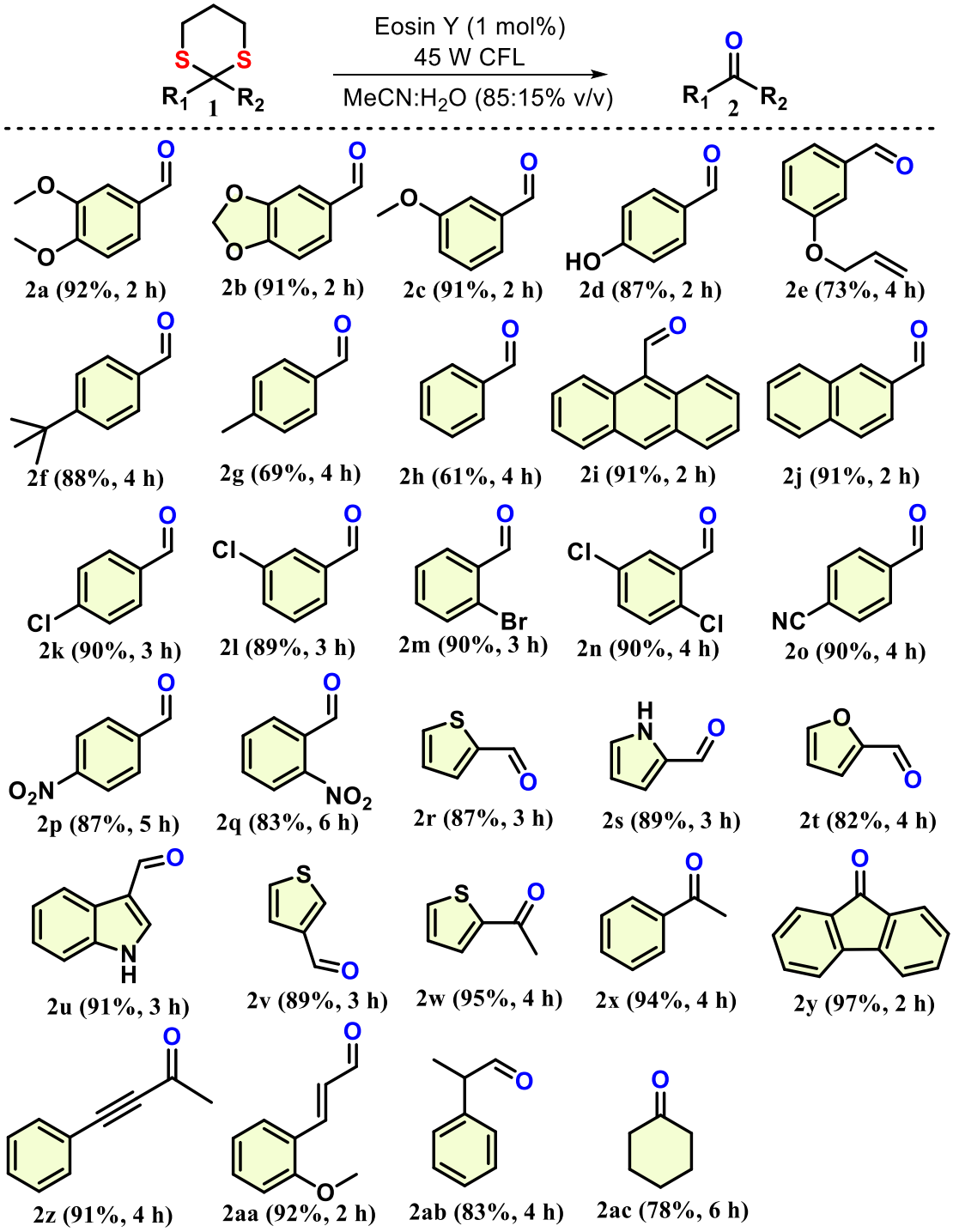
Scheme 2.1 Deprotection of dithiane using Eosin Y as a photocatalyst



In order to demonstrate the generality of this protocol and for the wider applicability, different substrates have been explored under the optimized reaction conditions. Various dithianes (**1a-1v**) under optimum reaction condition of photoredox catalysis underwent smooth deprotection to afford the corresponding aldehydes (**2a-2v,** Table 2.1) in very good yields (up to 97%). Dithianes derived from aldehydes substituted with the electron donating, electron withdrawing substituents and dithianes derived from heteroaromatic aldehydes

underwent smooth deprotection to the corresponding aldehydes under mild condition. Also, different dithianes **1x-1ac** under the photoredox conditions furnished the corresponding ketones **2x-2ac** in very good yields (Table 2.1).

Table 2.1 Substrate scope



Reaction conditions: 1 (0.2 mmol), EY (1 mol%), acetonitrile:water (85:15) 2 mL in open air at room temperature under 45 W CFL.

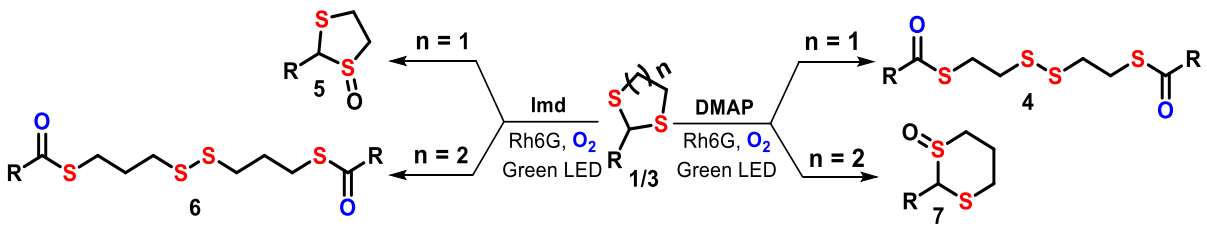
In order to have mechanistic insights in to the reaction pathway, we have carried out few control experiments. The involvement the radical intermediate has been confirmed by the use of TEMPO as a radical quencher in the reaction. Later, other experimental observations unequivocally indicated that light, photocatalyst are essential for the deprotection. We also confirmed the *in situ* generation of superoxide radical anion by carrying out the reaction in presence of benzoquinone and proved that superoxide radical anion is playing an important role during course of reaction.

In conclusion, we have established a visible light mediated facile dithiane deprotection under photoredox catalysis at room temperature. The protocol proved to be highly practical for the deprotection of different cyclic thioacetals under mild and transition-metal free reaction conditions. The method relied on clean energy source such as visible light and did not depend on external oxidizing agents. We believe that this methodology will be useful for the deprotection of cyclic thioacetals.

Chapter 3: *Rearrangement and Sulfoxidation of 1,3-dithioacetals under Basic Photoredox Conditions*

This chapter discloses an interesting reactivity of dithianes **1** and dithiolanes **3** for novel rearrangement reactions or for the direct sulfoxidation by simply switching the bases. The base controlled non-traditional selective oxidative rearrangement of dithianes to afford the corresponding rearranged products disulfide-linked-dithioester **4**/**6** or sulfoxides **5**/**7** by photoredox catalysis has been described. Based on our earlier experience with deprotection of dithianes via photoredox catalysis and looking into the mechanistic pathway, we hypothesized that in presence of appropriate base (alkaline condition) and under oxidizing photoredox catalytic condition dithianes may form thioesters via the abstraction of an acidic proton of an intermediate.

Scheme 3.1 Base promoted exchange of product formation

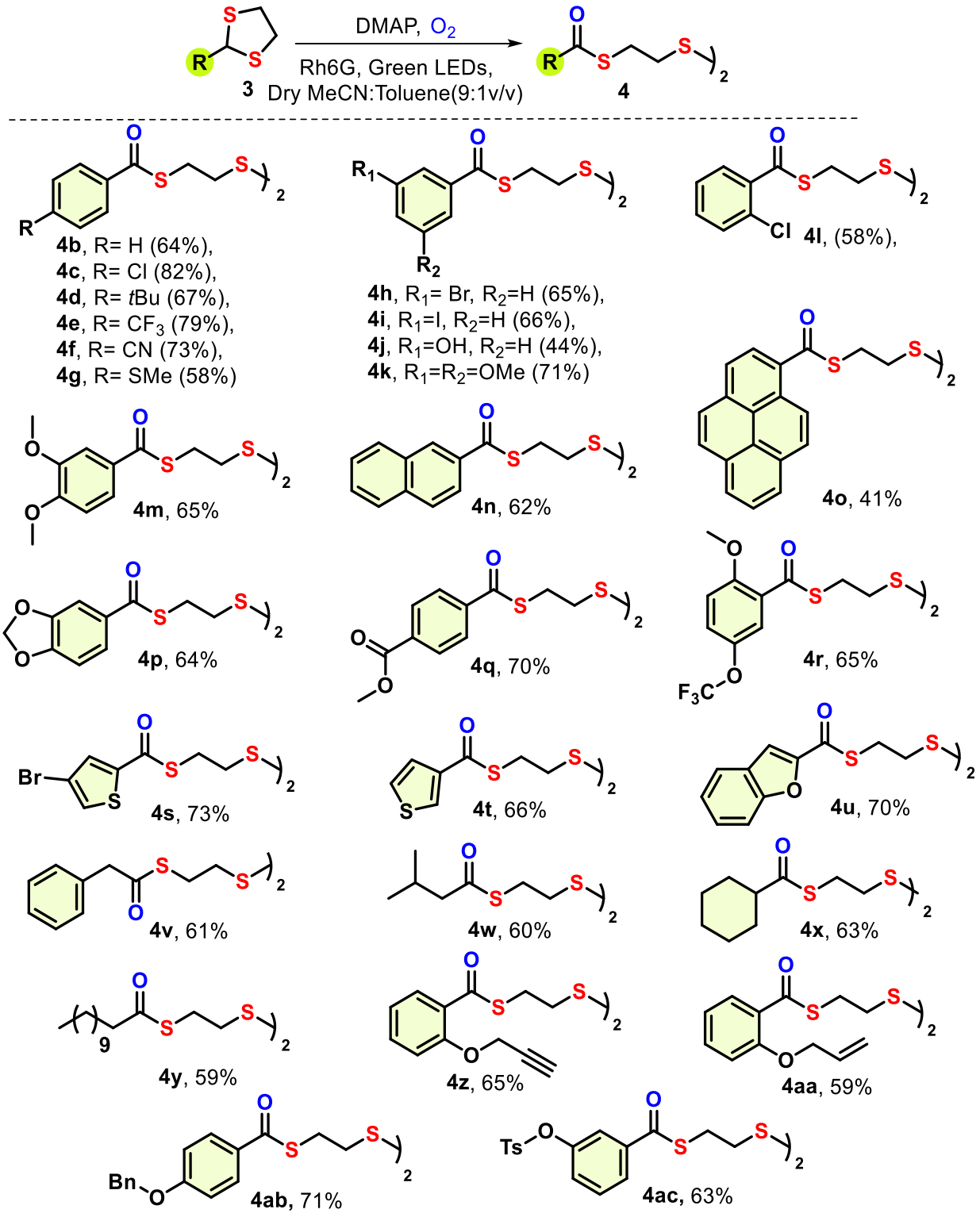


Based on the systematic and exhaustive screening, we optimized the desired reaction of dithiolane **3**, Rh6G (2 mol%) as PC, DMAP as base (2 equiv.) in dry solvent (MeCN: toluene; 9:1, v/v) under oxygen atmosphere by irradiation of light (green LEDs 15 W) to obtain disulfide-linked-dithioester **4** as the rearrangement product. Likewise, we also observed that the switching the base from DMAP to Imidazole led to the formation of corresponding sulfoxide **5** from dithiolanes. Surprisingly, we noticed that dithianes **1** behaved exactly opposite in reactivity when these bases were used to afford the corresponding products **6** and **7** (Scheme 3.1).

This unique and contrast reactivity of dithianes **1** and dithiolanes **3** has been highly surprising unusual and unprecedent in the literature. Based on the earlier theoretical understanding, we surmised that the it could be due to the higher stability of the single electron oxidized species of dithiane in comparison to that of oxidized dithiolane species. The oxidized species of dithiane may be relative more stable due to the σ-σ*3e-2-center bond interaction thus stabilizing the charge due to resonance delocalization. Also, better flexibility of 6-membered ring in dithiane due to relatively higher C–S bond length and larger C–S–C bond angle in comparison to cyclohexane. Encouraged by this unprecedent and unusual results, we optimized the reaction conditions for both dithiane and dithiolanes to access very useful disulfide linked dithioesters and sulfoxides.

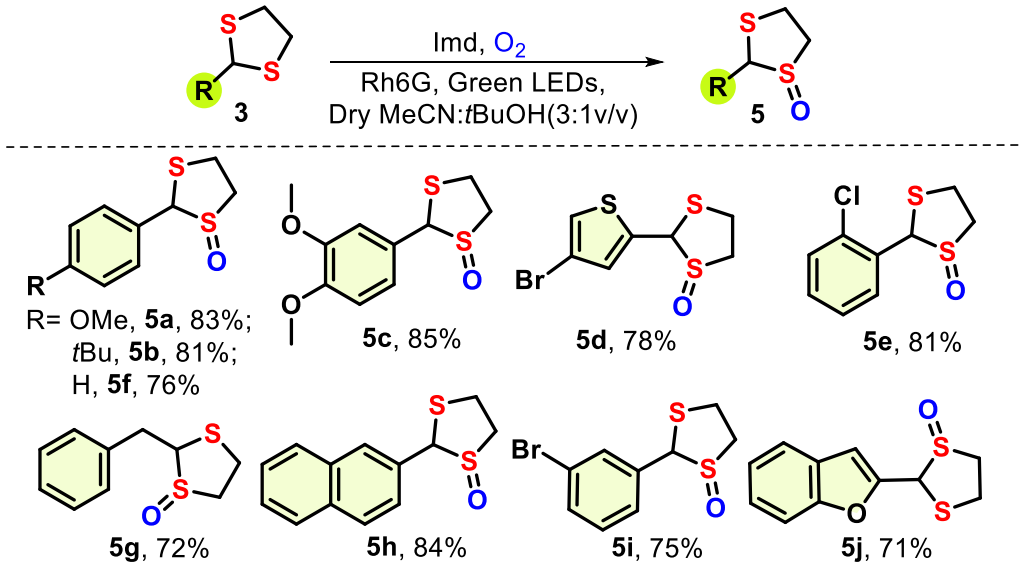
Having optimized the reaction conditions, we synthesized various disulfide linked dithioesters (rearrangement products) **4** starting from corresponding dithiolanes **3** (Table 3.1). The dithiolanes derived from aromatic aldehydes having electron donating, electron withdrawing as well as halo functional groups furnished the corresponding disulfide linked dithioesters **4a**-**4r** in very good yields (up to 82%). Also, the dithiolanes derived from heteroaromatic aldehydes as well as from aliphatic aldehydes offered the desired products (**4s**-**4y**) in good yields (59%-73%, Table 3.1). Also, dithiolanes with phenyl group having different protecting groups delivered the desired products (**4z**-**4ac**) in good yields and the protecting groups remained intact under the established photoredox conditions. We also explored different dithiolanes **3** to access the corresponding sulfoxides **5** in presence of imidazole as a base (Table 3.2). All dithiolanes derived from aldehydes having electron donating as well as electron deactivating functional groups and dithiolanes derived from heteroaromatic aldehydes furnished the sulfoxide products (**5a**-**5j**) in very good yields (71%-85%, Table 3.2).

Table 3.1 Substrate Scope for Dithiolanes Rearrangement



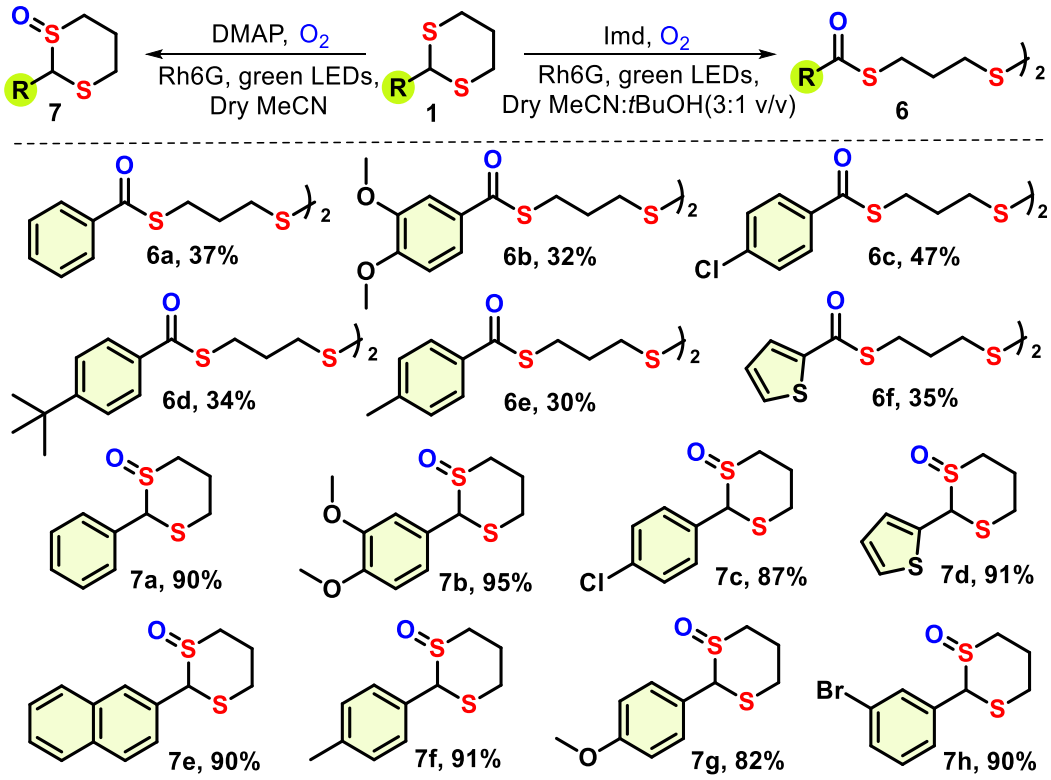
Reaction conditions: 3 (0.2 mmol), Rh6G (2 mol%), DMAP (0.4 mmol), MeCN (1.8 mL), Toluene (0.2 mL), green LEDs (15 W), O_2 balloon.

Table 3.2 Substrate Scope for Dithiolanes Sulfoxidation



Reaction conditions: **3** (0.2 mmol), Imd (1 mmol), Rh6G (2 mol%), MeCN (1.5 mL), *t*BuOH (0.5 mL), green LEDs (15 W), O_2 balloon, 12 h.

Table 3.3 Substrate Scope for Dithianes Rearrangement and Sulfoxidation

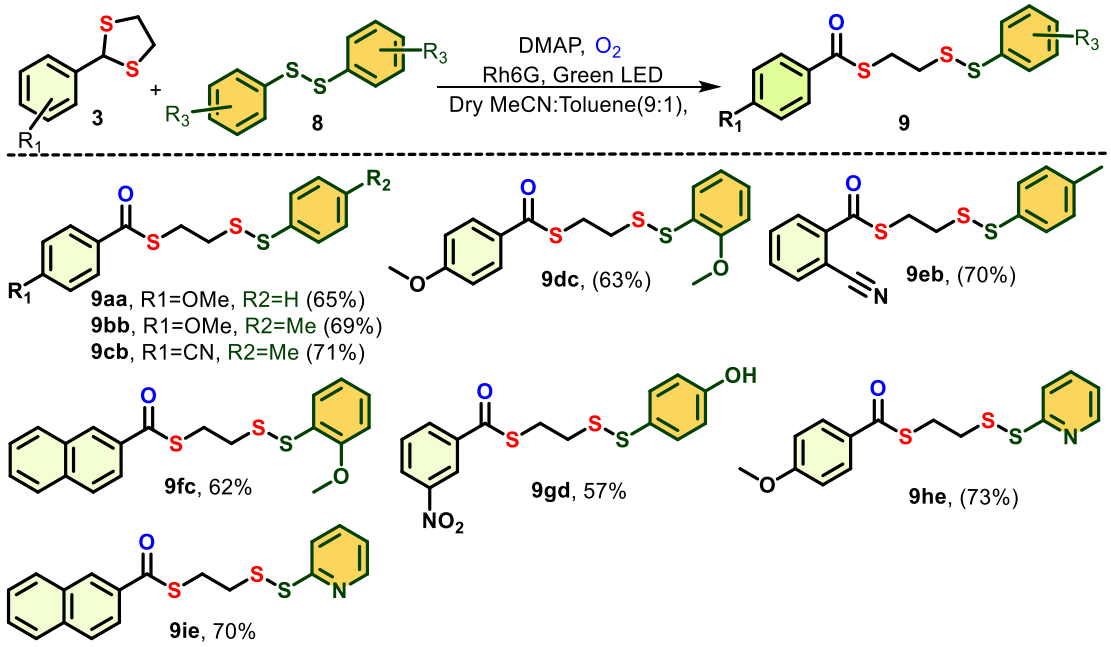


Reaction conditions: **1** (0.2 mmol), Rh 6G (2 mol%), Imidazole (1 mmol), DMAP (0.4 mmol), Dry Solvents (2 mL), green LEDs (15 W), under O_2, 24 h.

Later, dithiane **1**, in presence of Rh6G (2 mol%), imidazole as a base (5 equiv.), anhydrous MeCN and *t*-BuOH (3:1, v/v) afforded the corresponding disulfide-linked-dithioester **6** and dithiane **1** while maintaining all other optimum reaction conditions (except for imidazole) while using DMAP as a base (2 equiv.) afforded the corresponding sulfoxidation products **7** in good yields (Table 3.3). We have successfully synthesized the disulfide-linked-dithioesters (rearrangement products) **6a-6f** in moderate yields (up to 47%). While the dithianes under the optimum reaction conditions afforded the corresponding sulfoxides **7a-7h** in very good yields (Table 3.3).

In order to have the mechanistic insights of the reaction, we carried out a series of control experiments. The radical nature of reaction was confirmed using TEMPO in the reaction of dithiolane under optimum reaction conditions. Later, generation of superoxide radical anion was confirmed by carrying out the reaction in presence of superoxide radical quencher such as benzoquinone. Later, based on the Stern-Volmer experiments and cyclic voltametric studies we unambiguously confirmed the single electron transfer (SET) process during the reaction mechanism. The plausible reaction mechanism of photocatalytic transformation was proposed.

Table 3.4 Substrate Scope



Reaction conditions: 3 (0.2 mmol), **8** (0.6 mmol), DMAP (0.4 mmol), MeCN (1.8 mL), Toluene (0.2 mL), Rh6G (2 mol%), green LEDs (15 W), O_2 balloon.

Considering the predicted reaction mechanism pathway, we hypothesized that thiyl radical intermediate can be utilized by the reaction with diaryl disulfides to access hetero-disulfide compounds. We also hypothesized this transformation would confirm the *in situ* generation of thiyl radical intermediate during the reaction pathway and also it would give a novel strategy to access hetero-disulfides. In order substantiate the reaction mechanism further and also to utilize the protocol for wider application, we treated different dithiolanes **3** and aromatic disulfides **8** under the established optimum reaction conditions to access hetero-disulfides **9** (Table 3.4).

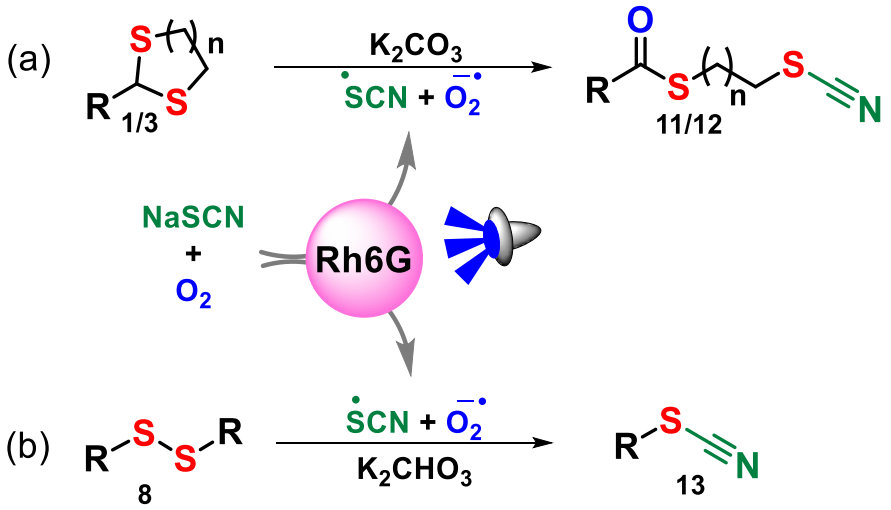
In conclusion, we have developed a photoredox catalyzed base tuneable rearrangement reaction of dithiolanes **3** and dithianes **1** to access a variety of rearrangement products **4**/**6** and sulfoxides **5**/**7** under visible light conditions. For further application, we employed this protocol for the synthesis of hetero-disulfides by utilizing the thiyl radical intermediate with diaryl disulfides. We successfully explored the unusual reactivity of dithiolanes **3** and dithianes **1** under photooxidative reaction conditions by simply swapping the bases. This method did not depend on transition metal or external oxidizing reagents. Also, the protocol afforded very useful disulfide-linked-dithioesters under the irradiation of visible light at room temperature.

Chapter 4: ***A Direct Synthesis of Thiocyano-Thioesters from Cyclic Dihioacetals via Photoredox Catalysis***

This Chapter discloses a method for the direct cyanation of cyclic dithioacetals and diaryl disulfides by exploring the synthetic potential of sodium thiocyanate via visible light photoredox catalysis to access thiocyano-thioesters. We have successfully demonstrated the introduction of two different functional groups in single pot to access thioester-thiocynates and alkyl thiocyanates respectively. Cyanation of organic compounds is one of the very important processes to access nitriles directly. However, the conventional cyanation process requires toxic metal cyanide reagents usually under harsher and elevated reaction conditions. Alternatively, over the recent years, the cyanation has been achieved using thiocyanate salt as a “CN source”. However, its utility is limited to a few types of organic compounds. Owing to the importance of the thiocyano-thioesters and looking at the available methods for the cyanation, we explored sodium thiocyanate as NaSCN (**10**) as a “CN source” to directly cyanate dithiolanes **3**/ dithianes **1** and diaryl disulfides **8** under visible light photoredox

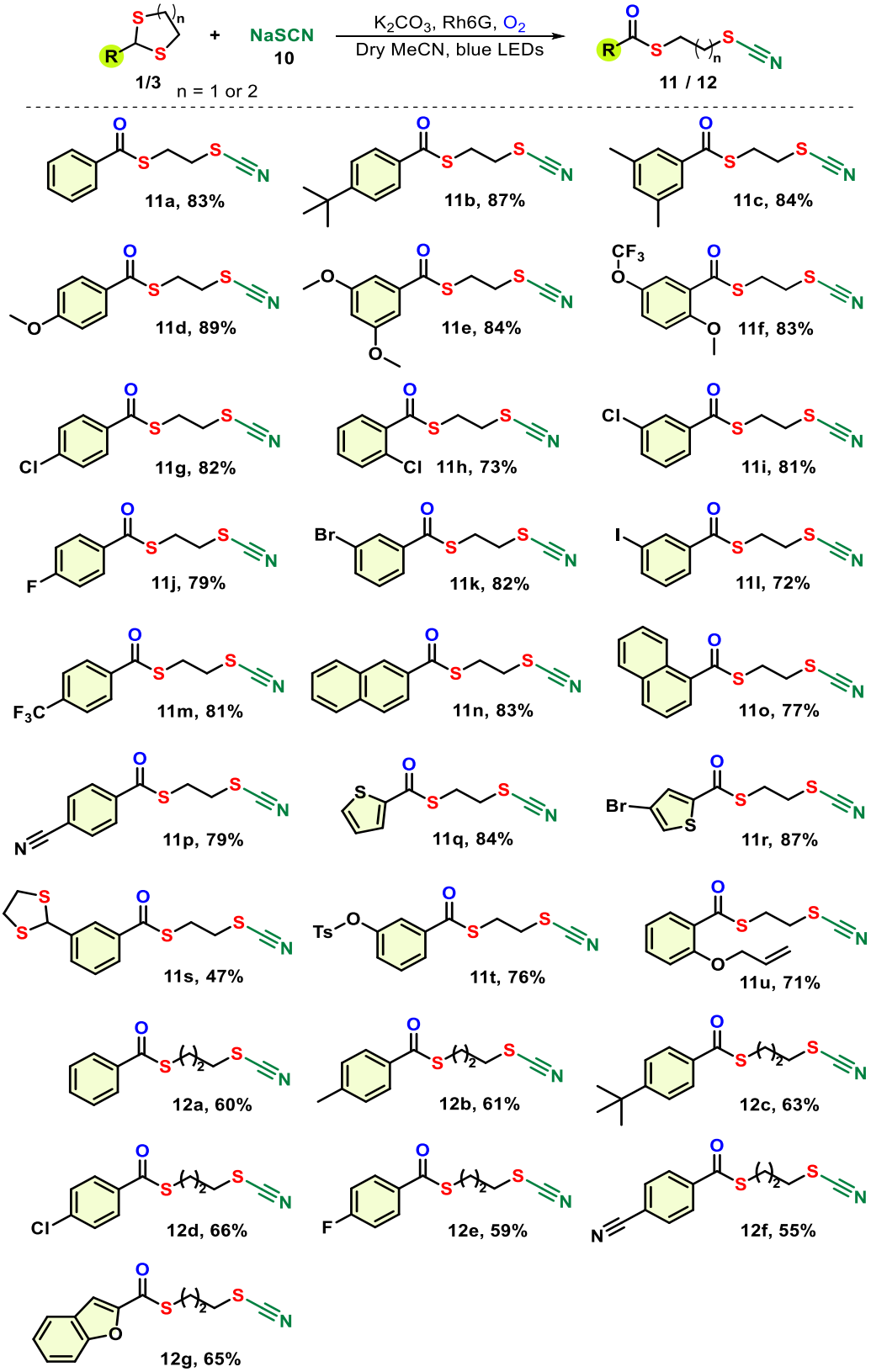
conditions. Based on our exhaustive screening, dithiolanes **3**/ dithianes **1**/ diaryl disulfides **8** in presence of Rh6G as a photocatalyst (2 mol%), NaSCN (5 equiv.), K_2CO_3 (2 equiv.) in dry acetonitrile proved to be the optimum condition to access thiocyano-thioesters **11**/**12** in very good yields.

Scheme 4.1 Cyanation of dithiolanes/dithianes and aryl-disulfides using NaSCN



Having optimized the reaction condition, we explored a broader substrate scope for the cyanation starting from different dithiolanes **3** and dithianes **1** to access novel and useful products **11** or **12** in very good yields (Table 4.1). Dithiolanes derived from aromatic aldehydes having electron donating/rich, electron-deactivating and -withdrawing substituents worked nicely under the reaction conditions to afford the desired thiocyano-thioesters (**11a-11p**) in very good yields (Table 4.1). Dithiolanes derived heteroaromatic aldehydes also reacted efficiently to furnish the expected products (**11q**, **11r**). The substrate having two dithiolanes selectively underwent cyanation at one of the dithiolane units to afford the corresponding **11s** in modest yield. Even different protecting groups on dithiolane tolerated under established optimum reaction conditions to furnish the corresponding thiocyano-thioesters (**11t-11u**). For the wider applicability and for the generality of the methodology, we explored the substrate scope for different dithianes **1.** Dithianes derived from aromatic aldehydes having electron donating/electron withdrawing substituents and dithianes derived from aromatic heteroaromatic aldehydes under the standardized reaction conditions furnished the expected desired products (**12a-12g**) (Table 4.1).

Table 4.1 Substrate scope for cyanation of dithianes and dithiolanes

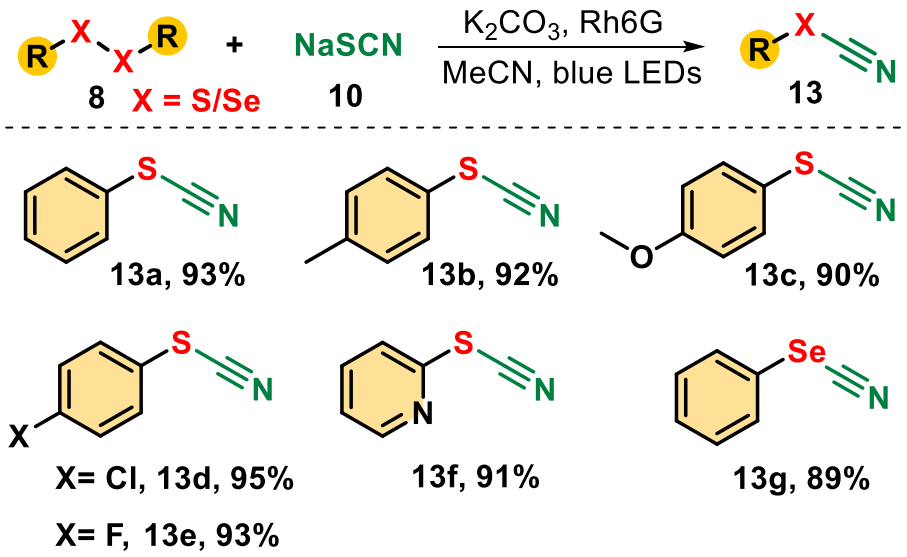


Reaction conditions: 0.1 mmol **3**/**1**, (2 mol%) Rh6G, (0.2 equiv.) K_2CO_3, (0.5 equiv.) NaSCN, 2 mL MeCN, O_2 baloon, 15 W blue LEDs

In order to have understandings of the plausible reaction pathway, we carried out few control experiments. Under the optimized conditions, dithiolane **3a** in presence of TEMPO did not react and thus indicating involvement of a radical intermediate during the course of the reaction. Later control experiments also proved that oxygen and light are essential for the desired transformation. While the reaction of **3a** in presence of DABCO (singlet oxygen quencher) did not interfere with the overall transformation thus revealing that there is no role of singlet oxygen in the reaction mechanism. Also, the treatment of **3a** with (superoxide radical anion quencher) *p*-benzoquinone under optimum reaction conditions did not furnish the expected product **12a** thus clearly indicating that superoxide radical anion is involved during the reaction pathway. In addition to control experiments, Stern-Volmer plot and cyclic voltametric studies supported the proposed mechanism and the involvement of thiocyanate radical radical intermediate.

Next to explore the broader application of transformation and also to validate the oxidized thiocyanate radical intermediate, we carried out the cyanation of diaryl disulfides **8** to access useful aryl thiocyantes **13** under the reaction condition (Table 4.2). Electronically neutral as well as electron rich diaryl disulfides tand heteroaromatic disulfides offered the corresponding desired products (**13a-f)** in excellent yields (up to 95%, Table 4.2).

Table 4.2 Substrate scope for cyanation of disulfide



Reaction conditions: 0.1 mmol **8**, (2 mol%) Rh6G, (0.2 mmol) K_2CO_3, (0.5 mmol) NaSCN, (2 mL) MeCN; 15W blue LEDs; O_2 baloon.

In conclusion, we have successfully developed the cyanation of dithiane **1**, dithiolane **3** and disulfide **8** via visible light photoredox catalysis. The protocol explored the use of non-toxic cyanating reagent such as sodium thiocyanate under blue light irradiation as clean energy source. The protocol did not rely on external oxidizing reagents except for oxygen and did not use any toxic transition metal reagents for the transformation. The transformation provided a direct and easy access to thiocyante-thioesters and aryl thiocyantes from dithiolanes/dithianes and diaryl disulfides respectively.

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LIST OF PUBLICATIONS:

- **Pankaj Dharpure**, Anindita Bhowmick, Praksh Warghude, Ramkrishan G. Bhat, Visible-light mediated facile dithiane deprotection under metal free conditions. *Tetrahedron Letters*, **2020**, *61*, 151407.

- **Pankaj Dharpure**, Mousumi Behera, Archana S. Thube, Ramkrishan G. Bhat. Base dependent 1,3-dithioacetals rearrangement over sulfoxidation under visible-light photocatalysis to access disulfide-linked-dithioesters. (*manuscript communicated*-https://chemrxiv.org/engage/chemrxiv/article-details/61696070cada1f27dfd6f006).

- **Pankaj Dharpure**, Archana Thube, Mousumi Behera, Ramkrishan G. Bhat, Direct synthesis of thiocynate-thioesters from the cyclic thioacetals using visible-light photoredox catalysis. *Org. Lett.* **2022**, *24*, 6919–6924.

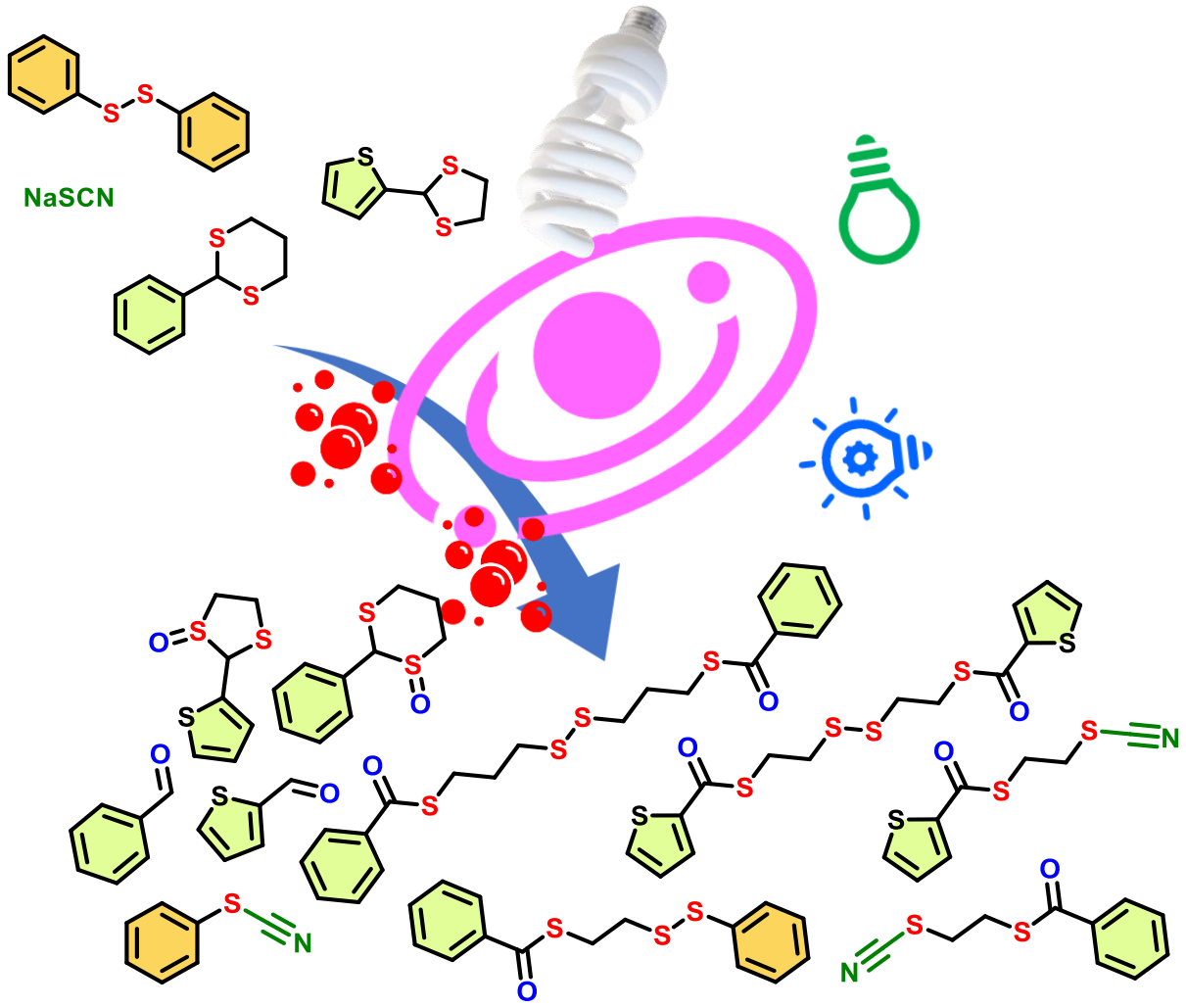
- Prakash Warghude, **Pankaj Dharpure**, Ramkrishan G. Bhat, Cycloaddition of isatin-derived MBH carbonate and 3-methyleneoxindols and cyclopropyl spirooxindoles: Catalyst controlled [3+2] and [2+1] annulations. *Tetrahedron Letters*, **2018**, *59*, 4076.

- Anindita Bhowmick, Praksh Warghude, **Pankaj Dharpure**, Ramkrishan G. Bhat, Direct access to α-acyloxycarbonyl compounds and esters *via* oxidative esterification of aldehydes under visible light. *Org. Chem. Front.***,** **2021**, *8*, 4777.

- Vikas Khade, Archana Thube, **Pankaj Dharpure** and Ramakrishna G. Bhat, Direct synthesis of 1,3-dithiolanes from terminal alkynes via visible light photoredox catalysis. *Org. Biomol. Chem.*, **2022**, *20*, 1315.

- Siddharth Kambale, Parimal Maliekal, **Pankaj Dharpure**, Purav Badani and Anil Karnik. Synthesis of Concave and Vaulted 2H-Pyran-Fused BINOLs and Corresponding [5] and [7]-Oxa-helicenoids: Regioselective Cascade-Concerted Route and DFT Studies *J. Org. Chem.* **2020**, *85*, 7738.

Chapter 1. C–S Bond Formation and Cleavage via Photoredox Catalysis



Chapter 1

C-S Bond Formation and Cleavage via Photoredox Catalysis

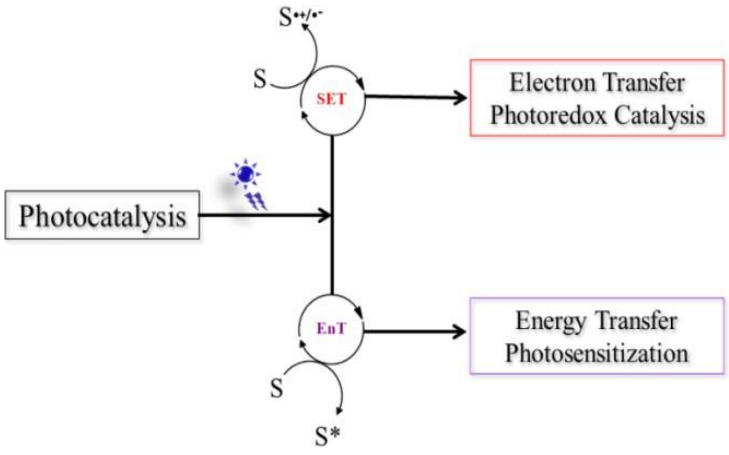
1.1 Abstract:

This chapter describes the fundamentals of photoredox catalysis and their application in the organic synthesis and their mode of operations in brief. An emphasis has been placed on metal-free C–S bond formation as well as the C–S bond cleavage protocols under mild reaction conditions via a controlled single electron transfer mode of photoredox catalysis. Likewise, importance and reactivity of dithioacetals and their recent transformations via photoredox catalysis has been discussed.

1.2 Introduction to photocatalysis

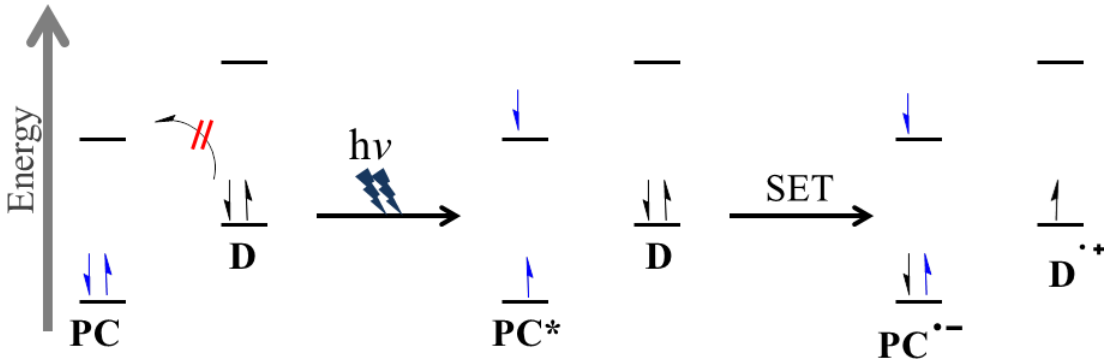
Photocatalysis has greatly emerged as one of the important pillars of catalysis and has been explored widely in the field of organic synthesis, as it can be achieved under sustainable reaction conditions using clean energy source. Photocatalysis harnesses the energy of visible light to excite a photocatalyst to drive the reactions. Also, it is user friendly under mild reaction and the visible light is benign compare to the UV light.[1] Interestingly, most of the organic molecules do not absorb the visible light and

Fig 1.1 Types of photocatalysis



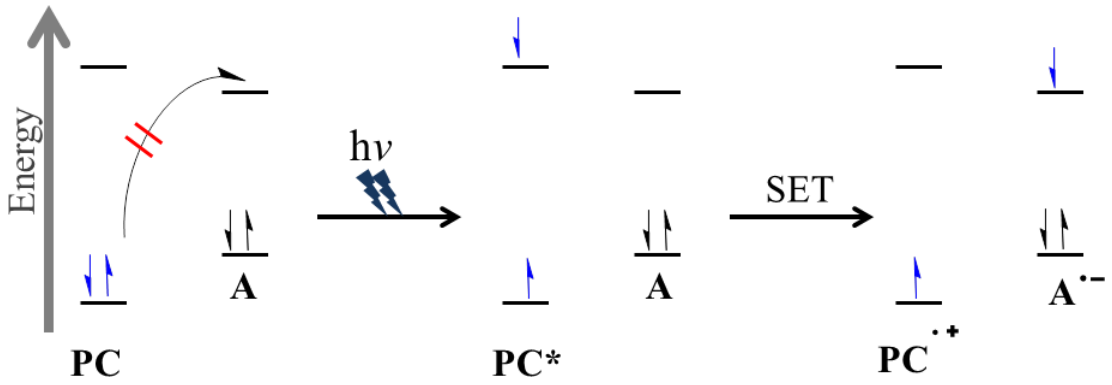
the selective excitation of a suitable photocatalyst using visible light can be achieved in the reaction pot to prevent the side reactions unlike the UV light.[2] In photocatalysis, upon irradiation of light, photocatalyst (**PC**) gets excited **(PC*)** then in turns involves in the energy transfer or electron transfer with the suitable substrate. Electron transfer mode is known as photoredox catalysis while the energy transfer mode is known as energy transfer photosensitization or energy transfer photocatalysis (**Fig 1.1**). If the excited photocatalyst does not participate in either of mode of action then it usually decays to a ground state by means of radiative (emission) or non-radiative pathway. This has been well studied by Jablonski diagram.[3] The photocatalytic processes relying on both modes of action have been widely utilized for the selective organic transformations. However, this thesis work has been constrained only on single electron transfer mode (Photoredox catalysis). In photoredox catalytic cycle, the excited photocatalyst (PC*) either transfers a single electron to a suitable substrate or abstract a single electron from a suitable substrate to generate a radical intermediate of substrate and corresponding oxidized/reduced photocatalyst respectively. Later, one more single electron transfer (**SET**) process from a reduced photocatalyst ($PC^{\cdot-}$) or to an oxidized photocatalyst ($PC^{\cdot+}$) to regenerate the original ground state photocatalyst (PC). The single electron transfer mode of photocatalysis involves a cycle of *oxidation* followed by *reduction* of photocatalyst or vice-versa. Hence, it is a redox neutral process and this mode of photocatalysis is known as photoredox catalysis. Single electron transfer (**SET**) is a thermodynamic process and **SET** happens only when transfer of electron is energetically favourable and this could be possible in two ways as depicted in the Fig 1.2 and 1.3.[3, 4]

Fig. 1.2 Single electron transfer through reductive quenching



After excitation of **PC**, one electron is elevated to a higher energy level **SOMO** of **PC*** and creates a hole at lower energy level **SOMO** of **PC***. The excited state **PC*** has an electron in a higher energy **SOMO** and this is of higher energy with respect to energy of **HOMO** of ground state **PC.** Also, hole at lower energy **SOMO** of **PC*** is relatively in lower energy than that of **LUMO** of ground state **PC**. Hence, the excited photocatalyst (**PC***) acts as a stronger oxidative or reductive quencher than its ground state counterpart (**PC**). The excited **PC** has dual nature and plays dual role as, one electron oxidant or one electron reductant depending on the nature of corresponding substrate/ intermediate. Alternatively, the excited state photocatalyst may deactivated to a ground state if the triplet excited state does not stay for sufficient time in the excited state to carry out the bi-molecular reaction. In reductive quenching, **PC*** act as an oxidant and takes one electron from higher energy **HOMO** of the donor (**Fig 1.2**). While, in an oxidative quenching, **PC*** act as a reductant and gives one electron to an empty **LUMO** of acceptor (lower energy) from its higher energy **SOMO**of **PC*** (**Fig 1.3**).

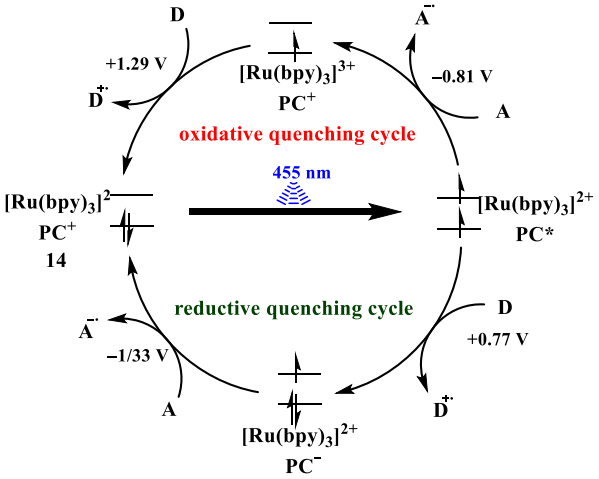
Fig. 1.3 Single electron transfer through oxidative quenching



In general, for single electron transfer process in bi-molecular reactions, two molecules must come close to each other by less than 30 Å. Over the years, advantage of the excited PC has been elegantly utilized for the synthesis of C–C, C–heteroatom bonds to access the useful compounds. Moreover, the photoredox catalysis has been merged with organocatalysis to obtain the enantio-selectivity and merged with metal catalysis to achieve the C–H bond functionalization of organic molecules which were otherwise tedious to realize via traditional routes at higher reaction temperature.

1.2.1 General Principle of Photoredox catalysis

Fig. 1.4 Photoredox cycle of Ru(II) photocatalyst



General mode of action of photoredox catalysis involves an excitation of PC by the irradiation of light at suitable wavelength (at absorption maxima of PC). As discussed earlier, the excited PC* has an elevated electron at higher energy SOMO orbital and a hole at lower energy SOMO orbital thus, it acts as a good oxidizing as well as reducing agent compare to that of ground state PC.[5] In order to understand the complete photoredox catalytic cycle as an example well known photocatalyst $[Ru(bpy)_3]^{2+}$ (PC) has been selected. [Ru(II)] catalyst has absorption maximum at 455 nm, thus upon excitation by the irradiation of blue light, it generates an excited singlet state through metal-to-ligand charge transfer (by promotion of electron from the t_{2g} metal-centered orbital to a π^* ligand-centered orbital). Further, a short-lived singlet excited state (femtosecond range, 10^{-15}) relaxes to a long-lived triplet excited state via intersystem crossing (ISC) (configurational spin flip of electron in the π^* ligand-centered orbital).[6] Excited PC, [Ru(II)]* is overall neutral even after electronic transition. However, it creates oxidized metal center as well as reduced form of ligand within the molecule. The spin forbidden decay of triplet excited state to a ground state makes the triplet excited state long-lived, having a lifetime of μs that would be sufficient to carry out the bi-molecular SET reaction which is operated in the range of *ns-ps* time scale.[6] The excited triplet state of [Ru(II)] catalyst has one electron at higher energy orbital and a hole at lower energy orbital. In view of this, the excited state of [Ru(II)]* can either give an electron from its higher energy orbital (to act as reductant) or it receives an electron to its lower energy orbital to fill in the hole (to act as oxidant). The choice of PC to act as an oxidant or reductant depends on the nature of neighboring substrates as SET is a thermodynamic process as depicted in Fig 1.2 and 1.3. In an oxidative quenching cycle, Ru(II)* transfers an electron to a acceptor molecule (A) results in a generation of the radical anion ($A^{\bullet-}$) and thus gets oxidized to form Ru(III) species. In subsequent electron transfer process, it takes an electron from the donor (D)

and regenerates a the ground state Ru(II) species to complete the redox cycle. On the other hand, in the reductive quenching cycle, at first SET process from donor to excited photocatalyst Ru(II)* takes place to generate radical cation donor ($D^{\bullet+}$) and reduced form of photocatalyst Ru(I). In subsequent SET process, Ru(I) transfers an electron to an acceptor to regenerate the Ru(II). It is very important to note that the two photocatalytic cycles are exactly reverse in nature and sequence of SET steps but overall cycles are electronically neutral. Most of the time, it is necessary to direct the photocatalytic cycle selectively towards either of these modes in order to obtain the desired product in good yields and to accelerate the rate of reaction. Usually, this can be achieved by adding an external additive. Some additives are very selective for the particular cycle listed as below:

1) *Oxidative quencher*: $S_2O_8^{2-}$, $ArNO_2$, Vilogens, Fe^{3+}, Ag^+, etc.,

2) *Reductive quencher*: Et_3N, $^iPr_2NEt$, $(CO_2)_2^{2-}$, Xanthate, Ascorbate, etc.,

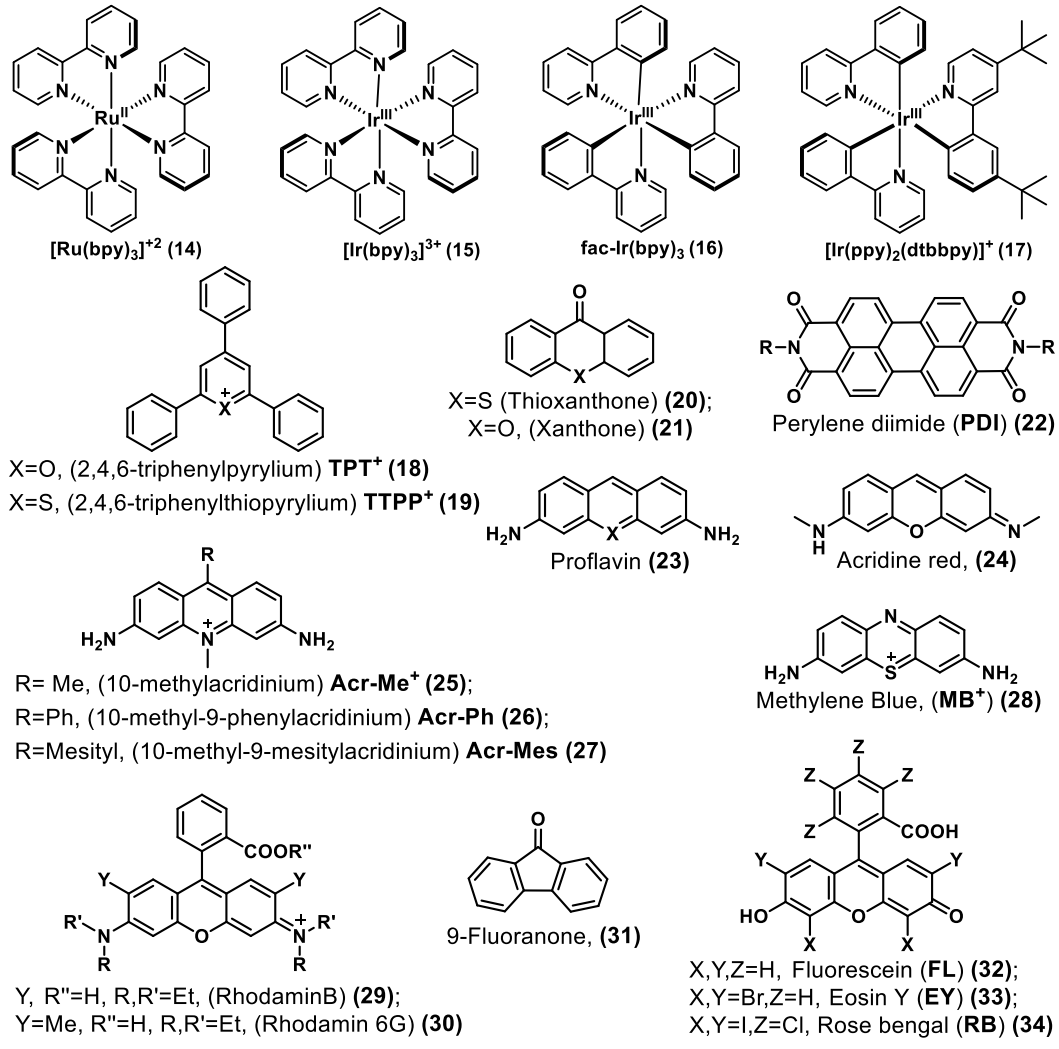
Oxidative quenchers are usually electron deficient or electron withdrawing species and it gains one electron more efficiently from the PC* and restricts the unwanted reaction through oxidative quenching cycle. On the other hand, reductive quenchers are electron rich in nature thus readily donates the electron and reduces the PC* to carry out reductive quenching cycle. If the reaction requires the use of oxidative/reductive quencher to drive the catalytic cycle, then the overall transformation is no longer an atom economical in nature.

1.2.2 Types of visible light photoredox catalysts

Mostly the visible light absorbing PC are more prevalent for executing the photoredox catalysis and they are generally categorized as a transition metal photocatalyst (transition-metal complexes) and organophotocatalysts (organic dyes). Traditionally, transition-metal complexes have been explored in photoredox catalysis as they have good redox properties with long lived excited triplet state. Especially, during the renaissance of photocatalysis, Ru and Ir based transition metal complexes have been well explored for the different organic transformations. Apart from these, there are other transition-metal based photocatalysts such as Fe(III) polypyridyl

compounds and Cu(I) complexes have been also reported for the photoredox reactions. However, these PC have limitations for wider applications as they possess a short-lived excited state lifetime and relatively tedious procedures for their synthesis. In this context, the organic dyes have emerged as very good PC for the organic synthesis with the absorption maximum in the visible-light region. These Visible light absorbing organophotocatalysts have wide rage for the redox potential and proved to be sustainable alternatives to an expensive transition-metal based PC.[7] Among various organophotocatalysts eosin Y (EY, 33) and acridinium (Acr, 25-27) based photocatalyst are relatively most explored PC due to their good redox activity and long-lived excited state in comparison to other organic dyes.[8,9]

Fig. 1.5 Some of the common photocatalysts used in the photoredox catalysis



Over the years, organophotocatalysts are proving to be highly versatile for various transformations in comparison to transition metal based PC for due to their high redox potential, cost effectiveness and the environmentally benign nature. Since, ruthenium and iridium are the rarest elements on the earth making them highly expensive and limit their bulk production. Also, relative toxicity is a matter of concern in some cases even at lower concentration. In order to carry out bimolecular SET reactions, ideal PC must have absorption in the visible region, good quantum yield, sufficient excited state lifetime (μs - *m*s), reversible excited state properties and good solubility in the different reaction solvents. Considering these parameters, organic organophotocatalysts have been emerged as very versatile PCs to explore various organic transformations under clean energy source.

1.2.3 Redox potential of photocatalyst

The SET is a first step of the photoredox catalytic cycle that is greatly influenced by the redox potential of PC*. While, the second SET step is based on the redox potential of the ground state PC. By considering the redox potentials of both excited as well as ground state of the photocatalyst, suitable substrate is required to carry out the successful photoredox reactions.[2a,10] One of the greatest advantages of organic photocatalyst is the possibility of varying the redox potential of the photocatalyst by changing or manipulating the substituent on the photocatalysts, can be done easily achieved to access the wider redox potential window. The redox potential of the exited state cannot be determined directly whereas the redox potentials of the ground state of the PC can be calculated directly by recording the cyclic voltammogram. This would indirectly help in calculating the redox potential of the exited state by following modified Rehm-Weller equations (See Eq. 1 & 2).

$$E^0(PC^{\bullet+}/PC^*) = E^0(PC^{\bullet+}/PC) - E_{00} \quad \text{Eq. 1}$$

$$E^0(PC^*/PC^{\bullet-}) = E^0(PC/PC^{\bullet-}) + E_{00} \quad \text{Eq. 2}$$

E^{00} is the photoexcitation energy (0-0 transition, energy gap between the zeroth vibrational levels of the ground and excited states) of the photocatalyst.

1.2.4 Mechanistic investigation by Stern-Volmer experiment and cyclic voltammetry

The Stern-Volmer experiment measures the quenching of emission intensity of PC at a fixed concentration and with the increasing concentration of substrate. If the SET takes place between substrate and PC, there would be a decrease in the emission intensity with the increase in the concentration of substrate.[11] However, the experiment does not distinguish whether the quenching is either due to the energy transfer or electron transfer mode of photocatalysis. Both the electron transfer as well as the energy transfer mode shows the similar trend, decrease in emission intensity with increasing concentration of substrate. Stern-Volmer graph is a plot of concentration of substrate against the ratio of measured emission intensities of photocatalyst (I_0/I). I is the emission intensity of PC in presence of substrate and I_0 is the emission intensity of PC in presence of substrate. The slope provides the value of Stern-Volmer constant. It is very important to note that this experiment only gives us the information about whether or not the bimolecular reaction happening between PC and substrate. Further, in order to distinguish between the energy transfer and electron transfer modes, an additional cyclic voltametric study can shed the light on this ambiguity to a certain extent. However, in a complex situation only the time dependent absorption spectroscopic study of PC can provide the clear and unambiguous insight into the mechanistic pathways whether or not the SET is happening between the PC* and the organic molecule (substrate).

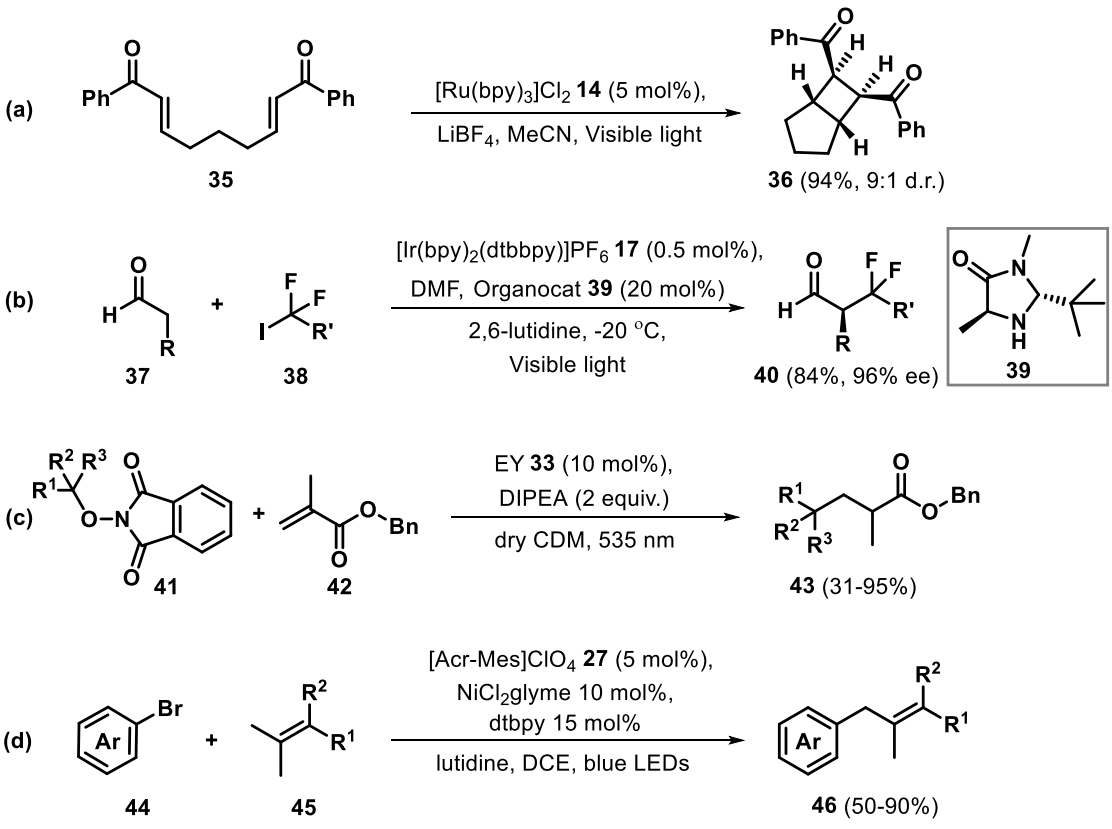
1.3 Application of photoredox catalysis in organic synthesis

Applications of visible light photoredox catalysis for the wide variety of organic transformations to construct various organic scaffolds under milder reaction conditions have been achieved over the recent years and have been growing rapidly every year. Apart from accessing the known transformations under the milder reaction conditions, the photocatalysis has provided the novel way of generating the reactive intermediates and the complex product formation in a straightforward way that were tedious to be achieved via traditional pathways.[2]

1.3.1 Application of photoredox catalysis for the synthesis of C–C bond formation

Yoon and coworkers reported the diastereo-selective intra-molecular [2+2] cyclization of conjugated carbonyl compounds **35** using $Ru(bpy)_3Cl_2$ **14** PC under visible light to offered the corresponding fused cyclic product **36** in a good yield with very good diastereomeric ratio (9:1 *dr,* Scheme 1.1a).[12] MacMillan research group reported many elegant organic transformations using visible light photoredox chemistry and as a representative example enantio-selective *α*-difluoroalkylation of aldehydes **37** has been highlighted (Scheme 1.1b). The protocol relied on merging of visible light photoredox catalysis with organocatalysis starting from aldehyde **37** and difluoroiodo alkane **38** using $[Ir(bpy)_2(dtbbpy)]PF_6$ **17** as a PC and imidazolidinone **39** as an organocatalyst in presence of 2,6-lutidine (lutidine is used to accelerate the reductive cycle) to offer the product **40** in a good yields (~84%, Scheme 1.1b).[13] König and coworker reported the decarboxylative alkylation of wide variety of acrylate **42** by reductive cleavage of *N*-(acyloxy)phthalimide **41** to access **43** through

Scheme 1.1 Photordox catalyzed reactions for the C–C bond formation

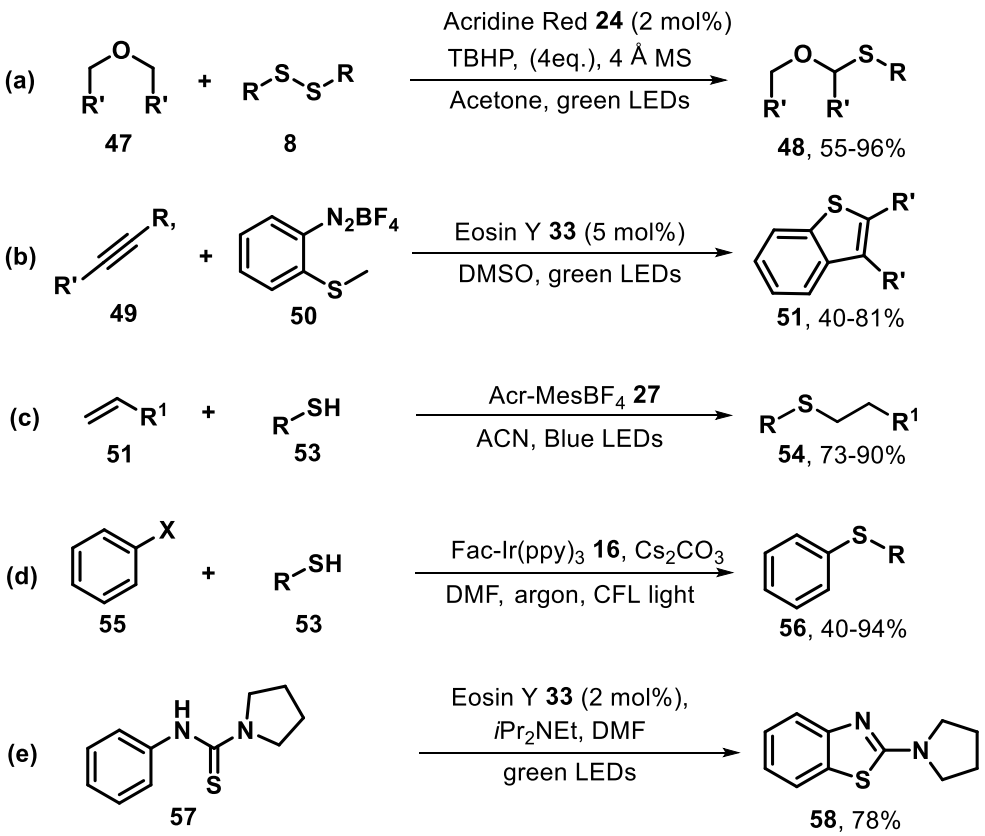


cross coupling reaction using EY **33** catalyzed photoredox condition in a good yields (up to 95%, Scheme 1.1c).[14] Rueping and coworker reported the Acr-Mes **27** and Nickel dual catalyzed direct cross-coupling of aryl bromide **44** with allylic C(Sp^3)-H bonds of tetrasubstituted alkene **45** under blue LEDs irradiation at room temperature to access the **46** in a good yields (up to 90%, Scheme 1.1d).[15]

1.3.2 Application of photoredox catalysis for the synthesis of C-S bond formation

Recently, organo photoredox catalysts have also been explored for the formation of C–S and S–S bonds to access useful different sulfur containing compounds under milder reaction condition using visible light (Scheme 1.2).[16] The reaction of dialkyl ethers **47** with disulfides **8** in presence of acridine red as a PC and TBHP as an oxidant furnishes the corresponding α-sulfur substituted ethers **48** via direct C–S bond formation α to oxygen atom of ethers **47** under the green LEDs in moderate to excellent yields(55%-96%, Scheme 1.2a).[17]

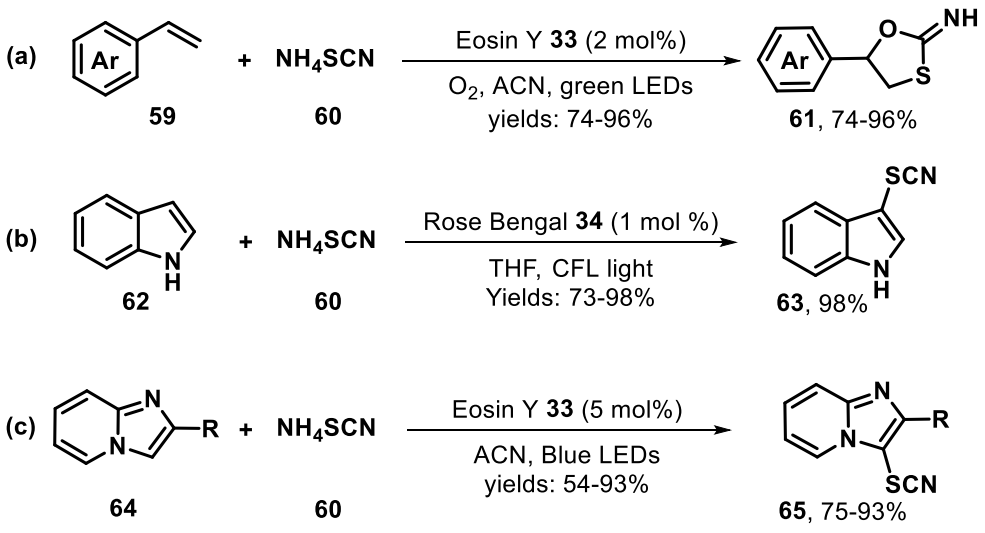
Scheme 1.2 C-S bond formation from thiols, disulfide and thioethers



The reaction of diazonium salt aryl thioether **50** and alkyne **49** in presence of EY **33** as a photocatalyst under green LEDs offered the corresponding substituted benzothiophenes **51** in moderate to good yields (40%-81%, Scheme 1.2b).[16] The reaction of thiols **53** with the alkenes **51** in presence of Acr-Mes **27** PC offered the thioether **54** by addition of thiol to a double bond under visible light condition (Scheme 1.2c).[19] The reaction of thiols **53** and aryl halides **55** in presence of Fac-Ir(ppy)$_3$ as a PC under the mild reaction condition at a room temperature in argon atmosphere offers the corresponding thioethers **56** via the facile formation of C–S bond (Scheme 1.2d).[20] The substituted benzothiozoles **58** has been achieved via photoredox catalysis using EY **33** as PC under green light irradiation starting from the *N*-aryl thiourea **57** (Scheme 1.2e).[21]

Different thiocyanate salts have been also well explored in the organic synthesis for the C–S bond formation using photoredox catalysis (Scheme 1.3). Thiocyanate salt is a good electron donor hence, it is easily oxidized by the PC* through SET process to offer the reactive thiocyanate radical (˙SCN) that can further easily react with suitable organic molecules to form C–S bond to access different organosulfur compounds. The reaction of styrene **59** with ammonium thiocyanate **60** in presence of EY **33** as a photocatalyst under oxygen atmosphere and green LEDs irradiation furnished the corresponding 5-aryl-2-imino-1,3-oxathiolanes **61** in a good to excellent yield (up to 96%, Scheme 1.3a).[22]

Scheme 1.3 C-S bond formation from ammonium thiocyanate

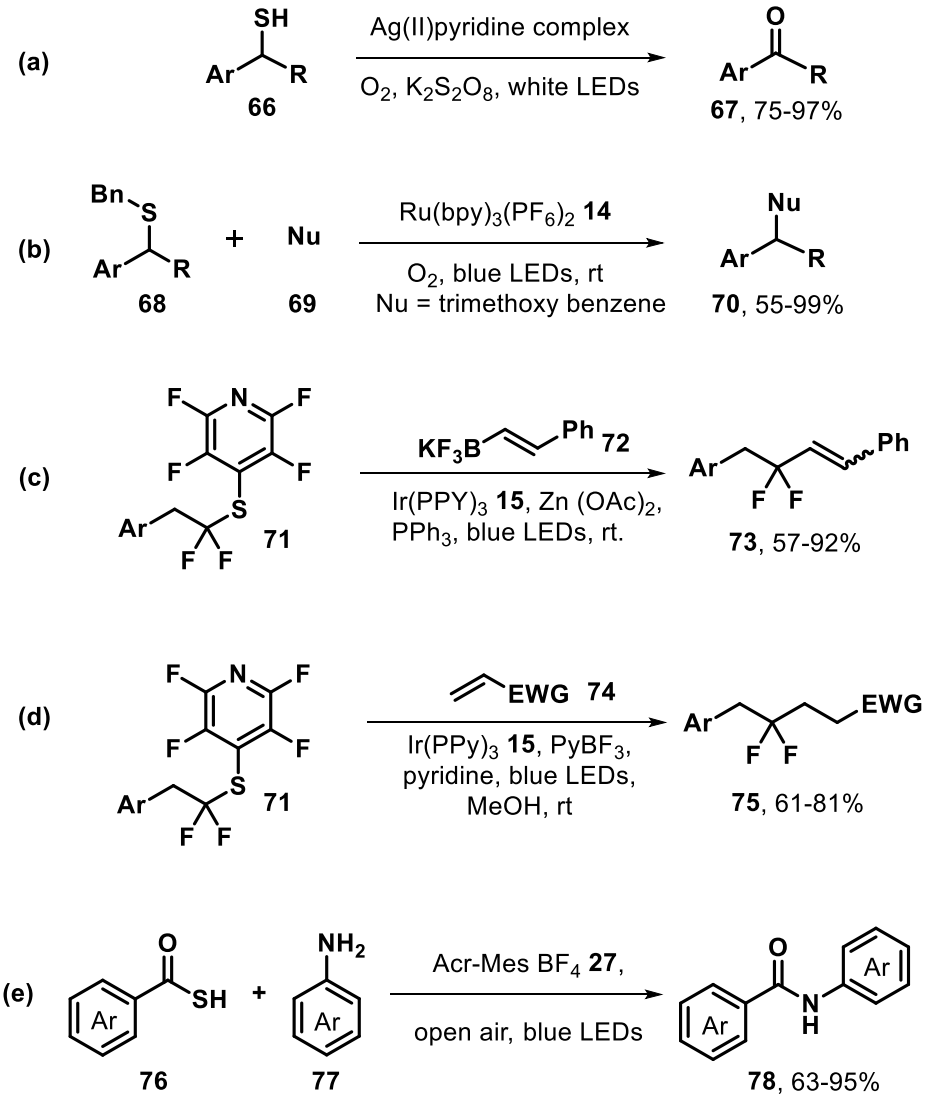


Even the electron rich aromatic compounds such as indoles **62** reacted with ammonium thiocyanate **60** in presence of Rose Bengal **34** as an organophotocatalyst to furnish the corresponding 3-thiocyanano indoles **63** in excellent yields (Scheme 1.3b).[23] Similarly, the direct thiocyanation of other heterocyclic compounds such as imidazo[1,2-a]pyridines **64** has been achieved using easily accessible ammonium thiocyanate **60** and EY **33** (5 mol%) under the blue LEDs irradiation to furnish the corresponding product **65** in good yields (75%-93%, Scheme 1.3c).[24]

1.3.3 Application of photoredox catalysis for the cleavage of C–S bond

It has been well proven that single electron oxidation of a sulfur atom is very easy and efficient under the photoredox catalytic conditions and this in turn facilitates the C–S bond cleavage much more easily and efficiently in comparison to α-C–H bond cleavage. If the sulfur atom is in oxidized form, then the C–S^+ bond cleavage would go through either via the reduction of sulfur atom or via the homolytic cleavage of bond.[25] The oxidation of secondary thiols **66** using Ag(II)pyridine complex and $K_2S_2O_8$ as an oxidant under visible light irradiation and oxygen atmosphere offered the corresponding ketones **67** via the C–S bond cleavage (Scheme 1.4a).[26] Similarly, the *in situ* cleavage of benzylic C–S bond of benzylic thioether **68** followed by the nucleophilic attack (Nu-trimethoxy benzene, **69**) in presence of $Ru(bpy)_3(PF_6)_2$ blue LEDs irradiation to offered the corresponding product **70**. This reaction goes via the C–S bond cleavage followed by C–C bond formation (Scheme 1.4b).[27] Pyridine substituted thioethers **71** upon treatment with the alkynyl trifluoroborane **72** in presence of $Ir(PPy)_3$ **15** as a photocatalyst, zinc acetate and triphenyl phosphine under blue LEDs irradiation to offered the corresponding olefin derivatives **73** in good to excellent yields (Scheme 1.4c).[28] Similarly, the same pyridyl substituted thioether **71** upon treatment with activated olefin (Acrylate **74**) in presence of $Ir(PPy)_3$ **15** and $PyBF_3$ under blue LEDs irradiation furnished the desired product **75** in absence of zinc acetate via C–S bond cleavage followed by C–C bond formation (Scheme 1.4d).[28] The reaction of thiocarboxylic acids **76** with the aromatic amine **77** in presence of the Acr-$MesBF_4$ **27** as a PC under blue light irradiation under open air offered the corresponding amide **78** in a good to excellent yields via the cleavage of C–S bond followed by the C–C bond formation (63%-95%, Scheme 1.4e).[29]

Scheme 1.4 Different transformations of organic compounds through C-S bond cleavage

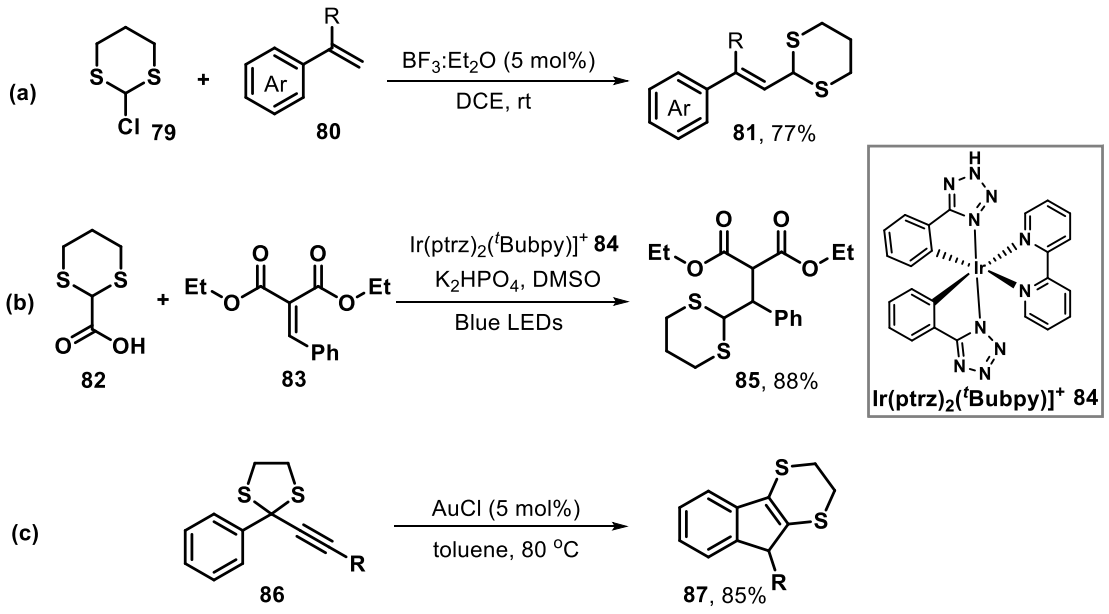


1.4 Novel transformations of cyclic dithioacetals

Dithioacetals are one of the very important class of sulfur compounds and the reactivity of cyclic dithioacetals have been employed as umpolung for various C–C bond construction to access important complex organic compounds. In cyclic dithioacetals two C–S bonds are present on the same carbon atom and they can be synthesized easily starting from aldehyde and alkyl dithiols using conventional acid catalyzed reaction or under neutral conditions or even under blue light irradiation in presence/absence of PC.[30]

This thesis is mainly focused on different transformations of cyclic dithioacetals using photoredox catalysis under visible light irradiation. Apart from the well-known and well explored umpolung reactions, cyclic dithioacetals have been seldom explored based on their different reactivity for synthetic transformations. Some of the very few selected examples have been highlighted based on the novel reactivity of cyclic dithioacetals (Scheme 1.5). Tang and coworkers reported the radical oxidative coupling of 2-chloro-dithiane **79** with substituted olefins **80** reported in presence of BF_3:Et_2O catalyst (5 mol%) to access the **81** in good yields (up to 77%, Scheme 1.5a).[31] Cozzi and coworkers describes the Michael addition of dithiane-2-carboxylic acid **82** with alkylidene diethyl malonate **83** in presence of Ir-complex **84** as a PC under blue LEDs irradiation at room temperature to furnished the corresponding cyclic dithioacetal substituted product **85** in a very good yields (Scheme 1.5b).

Scheme 1.5 Novel reactions of cyclic dithioacetals



[32] Later, Wang and coworkers have reported an elegant gold catalyzed reactions of alkyne substituted cyclic dithioketals **86** derivatives to form the corresponding Indeno-dithiine **87** derivatives via the migration of C–S bond in dithioketal **86** in to alkyne moiety and through pentannulation of aromatic ring at elevated reaction temperature (Scheme 1.5c).[33]

1.5 Aims and rationale of this thesis work

Cyclic dithioacetals such as dithianes and the dithiolanes have been well explored in synthetic transformation tapping the ability of their umpolung reactivity to synthesize different natural products and useful organic compounds. Cyclic thioacetals have been very commonly prepared to protect the carbonyl compounds due to their robust stability under both basic as well as acidic reaction conditions. The stability of cyclic thioacetals under various reaction conditions, make C–S bond cleavage quite difficult as well as challenging to deprotect and also to access different compounds especially by exploring novel transformations of cyclic thioacetals via the C–S bond cleavage. In order to activate cyclic thioacetals to access the carbonyl compounds, usually metal catalysts (mercury)/oxidizing reagents/halogenative reagents/alkylating reagents have been used. It is well known in the literature that the sulfur atom of thioacetal interacts with the deprotecting reagents there by facilitates the C–S bond cleavage. However, most of these metal based deprotecting reagents are usually toxic in nature and moreover they are used in stoichiometric amount as well and this leads to a serious concern of environmental toxicity. The other deprotecting reagents are very reactive, highly oxidizing and used in stoichiometric amounts under harsh reaction conditions and some of these drawbacks limit their applications. To the best of our knowledge, selective cleavage of C–S bond of cyclic dithioacetal under milder reaction condition for accessing useful organic compounds have been seldomly explored. In this regard, the development of novel synthetic protocols for the selective C–S bond cleavage of cyclic dithioacetals under the metal free conditions without using the reactive oxidizing reagent or the alkylating reagent is highly desirable for accessing novel compounds.

In this thesis, efforts have been made to tap the synthetic potential of cyclic dithioacetals under visible light photoredox catalysis to achieve newer synthetic transformations to access novel and interesting compounds. The thesis has been constructed on the different synthetic transformations of cyclic dithioacetals under photoreodox catalysis. The ability of photoredox catalysis has been explored as it provides the milder reaction conditions to carry out the organic transformations in a controlled manner by a selective SET process. It is well known that the under photoredox catalytic conditions the single electron oxidation of sulfur atom takes places

easily leading to reactive intermediate. This would provide a route to access different organic molecules from organosulfur compounds easily under different photoredox catalysis.[26-29] Considering these efficient transformations of organosulfur compounds, we hypothesized that under suitable photoredox catalytic conditions, the selective single electron oxidation of the cyclic dithioacetal can be achieved so as to cleave the C–S bonds easily to access the corresponding carbonyl compounds. Also, we envisaged that under the controlled photocatalytic reaction conditions, selective C–S bond cleavage could be achieved to access useful compounds. In this regard, we planned to evaluate the reactivity of cyclic thioacetals meticulously using different factors to accelerating the C–S bond cleavage in controlled manner by carefully choosing reagents and photocatalysts.

1.6 Conclusions

In conclusion, the photoredox catalysis is based on the controlled SET process and provides very selective synthetic transformations by using visible light as clear energy source under milder reaction conditions at room temperature. More importantly, because of the new mode of reactivity, the photoredox catalysis has emerged as one of the powerful catalytic tools in organic synthesis under ambient reaction conditions. Among many organosulfur compounds, the cyclic dithioacetals have been seldomly explored under photoredox conditions to develop novel synthetic organic transformations to access useful organic compounds. In the forthcoming chapters of this thesis, novel reactivities of cyclic dithioacetals and synthesis of novel as well useful compounds have been disclosed under photoredox catalysis.

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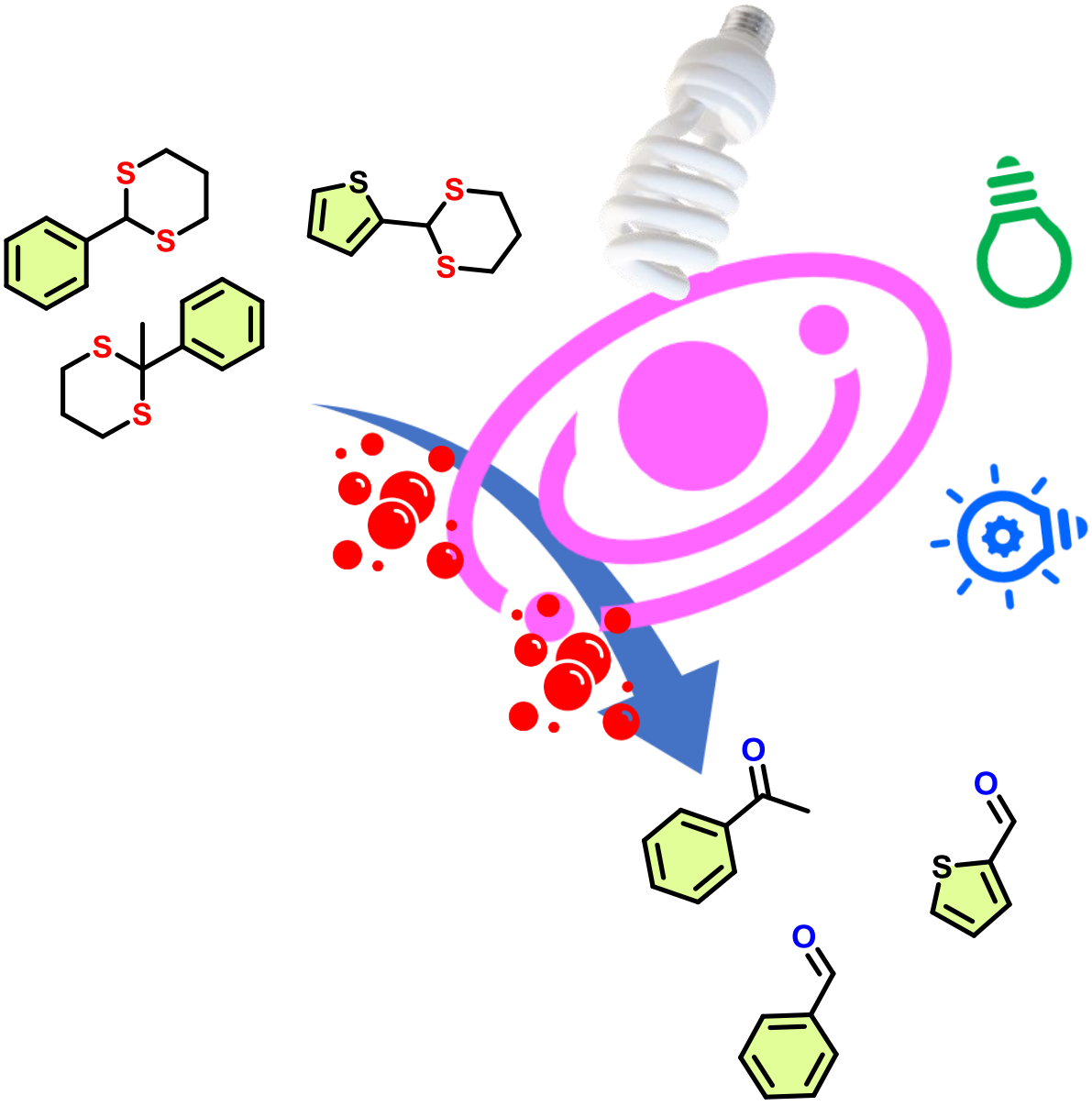
Chapter 2: Visible-light Mediated Dithiane Deprotection Under Metal-Free Conditions via Photoredox Catalysis



Chapter 2

Visible-light Mediated Dithiane Deprotection Under Metal-Free Conditions via Photoredox Catalysis

2.1 Abstract:

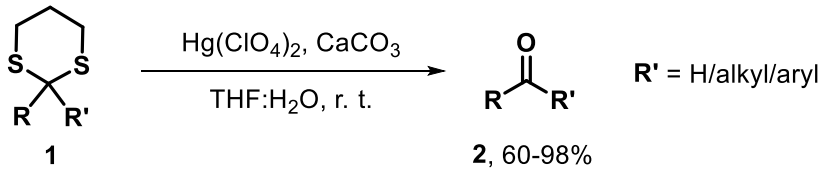
A metal-free strategy for the selective and facile deprotection of dithianes using the visible light photoredox catalysis has been developed. The protocol works under mild reaction conditions in presence of Eosin Y (1 mol%) as an organophotocatalyst, air (oxygen) as an oxidant under visible light as an energy source. Synthetic application has been shown by the selective deprotection of a wide range of cyclic dithioacetals to access corresponding aldehydes and ketones.

2.2 Introduction:

Dithianes are known as stable protecting groups for carbonyl functionalities such as aldehydes and ketones due to their robustness under both acidic as well basic reaction conditions. Hence, usually harsh conditions are required for the deprotection of thioacetals.[1a] Apart from the usual protection strategy, dithianes have been widely employed for tapping the umpolung reactivity to forge the C-C bond forming transformations using different kinds of electrophiles.1[b-d] Different natural products and drugs molecules have been synthesized through the umpolung reactivity of cyclic dithioacetals.[1,2] However, the dithiane deprotection remains to be one of the most crucial steps in the multi-step synthesis of complex molecules as it usually requires harsh reaction conditions.[1a,3] Even after the wide utility and importance of dithianes, the selective dithiane deprotection is challenging and still remains as the area of interest to be pursued. As many deprotection protocols have their own merits and demerits owing to the intrinsic properties of the reagents used for the deprotection of different dithianes.[3] Obviously, more efficient, straightforward, milder, economically viable and environmentally benign protocol for the deprotection of dithianes is highly demanding.[3] Generally, the deprotection of dithiane by the cleavage of C-S bond have been achieved by

using the metal catalysts, halogenative reagents, reactive electrophilic reagents or oxidizing reagents that can coordinate to/react with/oxidize the sulfur atom of dithiane thus leading to the C–S bond cleavage and hydrolysis to access the expected carbonyl functionality under different reaction conditions.[3]

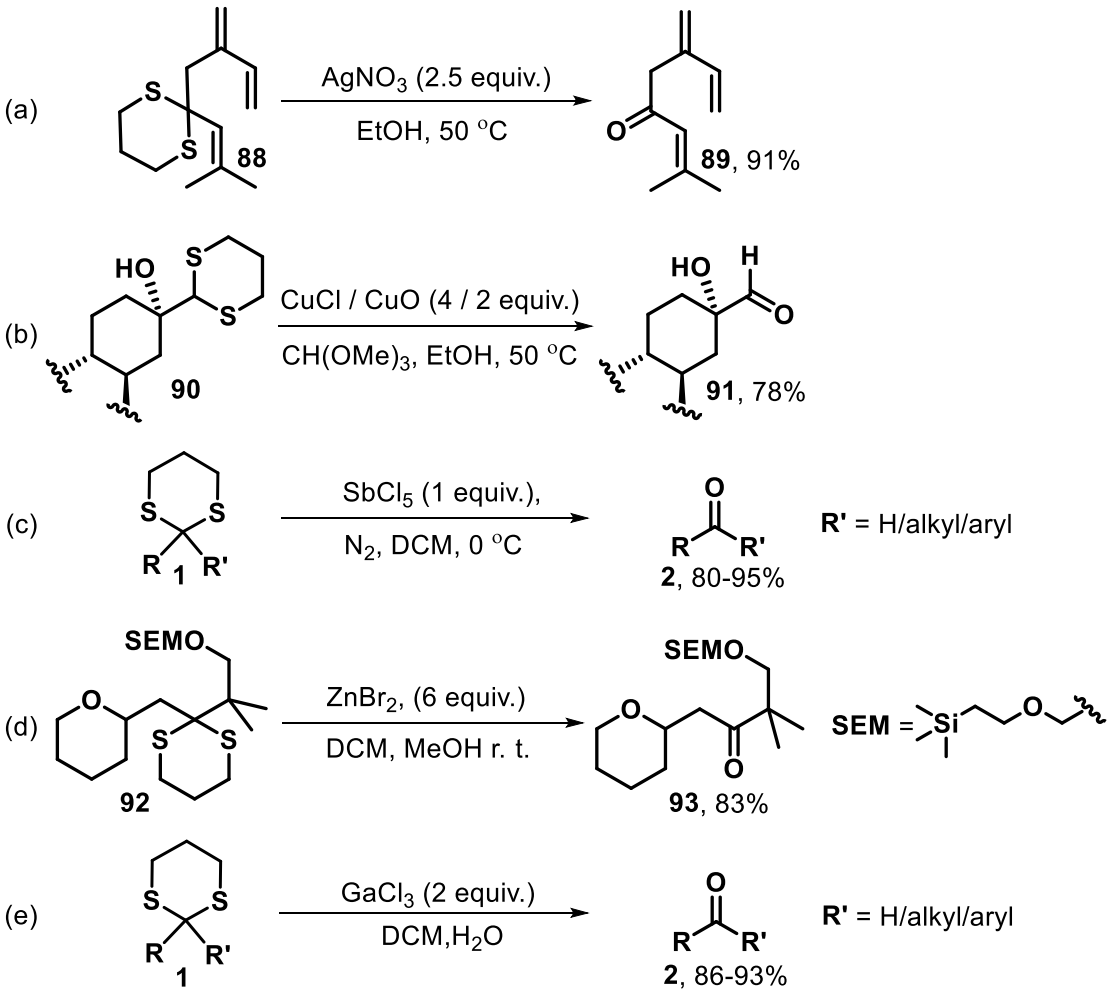
Scheme 2.1 Deprotection of dithiane using mercury salt



Corey and co-workers for the very first time reported the deprotection of dithianes **1** using mercury salt to access corresponding carbonyl compounds **2** (Scheme 2.1). This strategy is still rarely used in some of the transformations even though it is known for high mercury toxicity. The stoichiometric requirement of mercury salt (selective binding of Hg metal to sulfur atom) seriously limits its wider applications due to the cost and higher toxicity and possible health hazard (Scheme 2.1).[4, 5]

Other metal-based approaches have been well optimized for the deprotection of the dithianes. The deprotection of olefin substituted dithianes **88** required an excess amount of silver nitrate (2.5 equiv.) in ethanol at an elevated temperature (50 ^{o}C) to corresponding ketones **89** (Scheme 2.2a). Hydroxy derivative of dithiane **90** upon treatment with copper reagents [CuCl (4 equiv.) and CuO (2 equiv.)] afforded the corresponding deprotection product hydroxy aldehyde derivatives **91** in good yields (78%, Scheme 2.2b). However, the requirement of high stoichiometric amount of metal reagents and elevated reaction temperature limits its wider application. The deprotection of dithianes **1** has also been achieved using $SbCl_5$ (1 equiv.) under the nitrogen atmosphere to access the corresponding deprotected carbonyl products **2** in good to very good yields (80%-95%, Scheme 2.2c). The deprotection of ether derived dithianes **92** has been reported using zinc bromide (6 equiv.) of to furnish the corresponding ketones **93** in good yields (83%, Scheme 2.2d). Even the $GaCl_3$ (2 equiv.) has been employed to carry out the deprotection of dithianes **1** in aqueous DCM to afford the carbonyl compounds **2** in good yields (86%-93%, Scheme 2.2e). It's has been well established that usually the transition metal reagents such as $AgNO_3$, $Tl(NO_3)$, $CuCl_2$, $FeCl_3$, $Fe(acac)_3$, $SbCl_5$, $ZnBr_2$, $GaCl_3$

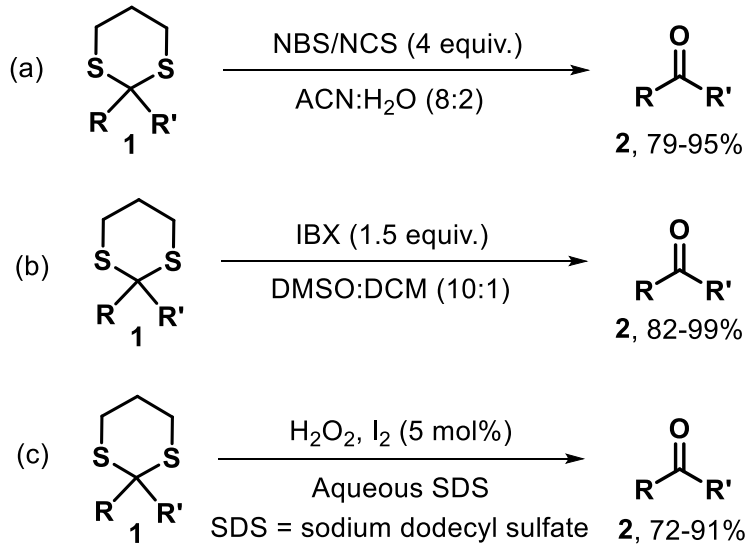
Scheme 2.2 Deprotection of dithiane using metal catalysts



approaches are usually expensive (equimolar amount or more the 2 equiv.) and generates transition metal waste during the process leads to intrinsic environmental toxicity.

In order to avoid transition metal reagents, halogenation reagents such as NBS (*N*-bromosuccinimide)[13,14] or NCS (*N*-chlorosuccinimide)[13,15] or hypervalent iodine[16] have gained importance. These reagents react with sulfur atom to form the sulfur-halogen bond to facilitate the cleavage of C-S bond finally leading to the deprotection. These types of reagents are used in stoichiometric amounts and sometimes even along with oxidizing reagents. The deprotection of dithianes **1** using NBS or NCS (4 equiv.) have been achieved in aqueous acetonitrile under relatively milder reaction conditions (Scheme 2.3a). Hypervalent iodine reagent such as IBX (1.5 equiv.) has been utilized effectively for the deprotection of dithiolanes **1** in DMSO:DCM via the oxidation of sulfur atom (Scheme 2.3b). Also, the use of iodine (5 mol%) along with aqueous H_2O_2 (30%) in presence of aqueous SDS (sodium dodecyl sulfate) has been explored to deprotect the dithianes **1** via the formation of

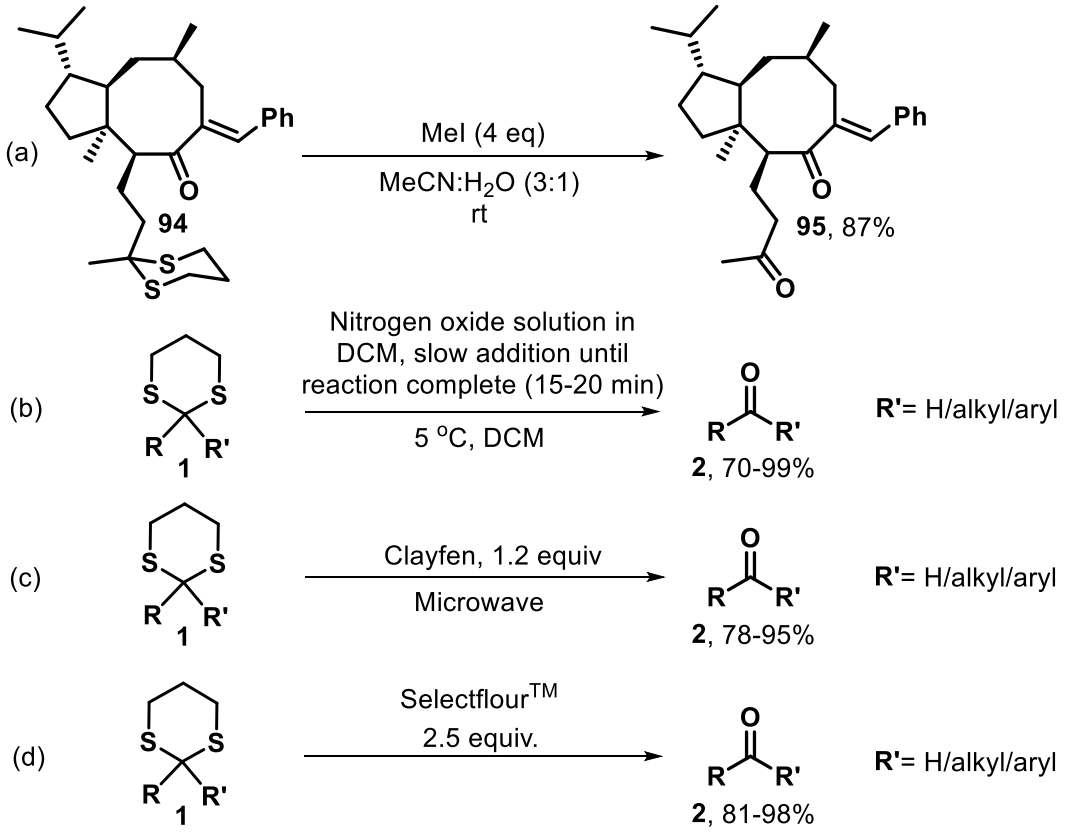
Scheme 2.3 Deprotection of dithiane using the halogenative reagents



micellar environment (Scheme 2.3c). Though some of these methods are quite successful, but due to their intrinsic reactive properties and oxidizing reactivity of halogenation reagents wider application for variety of dithianes is limited.

The reactive electrophilic reagents such as methyl iodide, allyl bromide and tert-butylnitrite have also been utilized for the deprotection of dithianes.[3,17,18,19] The oxidizing reagents such as Oxone[20], Selectfluor[21], and Clayfen[22] have been employed for the deprotection of dithianes **1** successfully. The octanone derived dithianes **94** has been deprotected using excess amount of methyl iodide (4 equiv.) in aqueous acetonitrile in good yields (87%, Scheme 2.4a).[17] Cyclic 1,3 thioacetals **1** have been unmasked using slow addition of solution of 'nitrogen oxide' in DCM at low temperature (5 ^{o}C) to access the corresponding carbonyl compounds **2** in a good yields (up to 99%, Scheme 2.4b).[19] Similarly, clayfen 1.2 equivalent under microwave conditions as well as selectflour 2.5 equivalent have been utilized as oxidative reagents in stoichiometric amounts for the deprotection of dithianes **1** to access the corresponding carbonyl compounds **2** in good yields (see Scheme 2.4c and d).[21, 22] However, the high reactivity of these reagents limits their wider application in the complex molecules with sensitive functional groups. These very reactive reagents are known to alkylate or oxidize different reactive sites in the complex molecules. Although these transition metal reagents, halogenation reagents, electrophilic and strong oxidizing reagents have proven their potential for the selected dithianes; however, utilities are

Scheme 2.4 Deprotection of dithiane using electrophilic and oxidative reagents

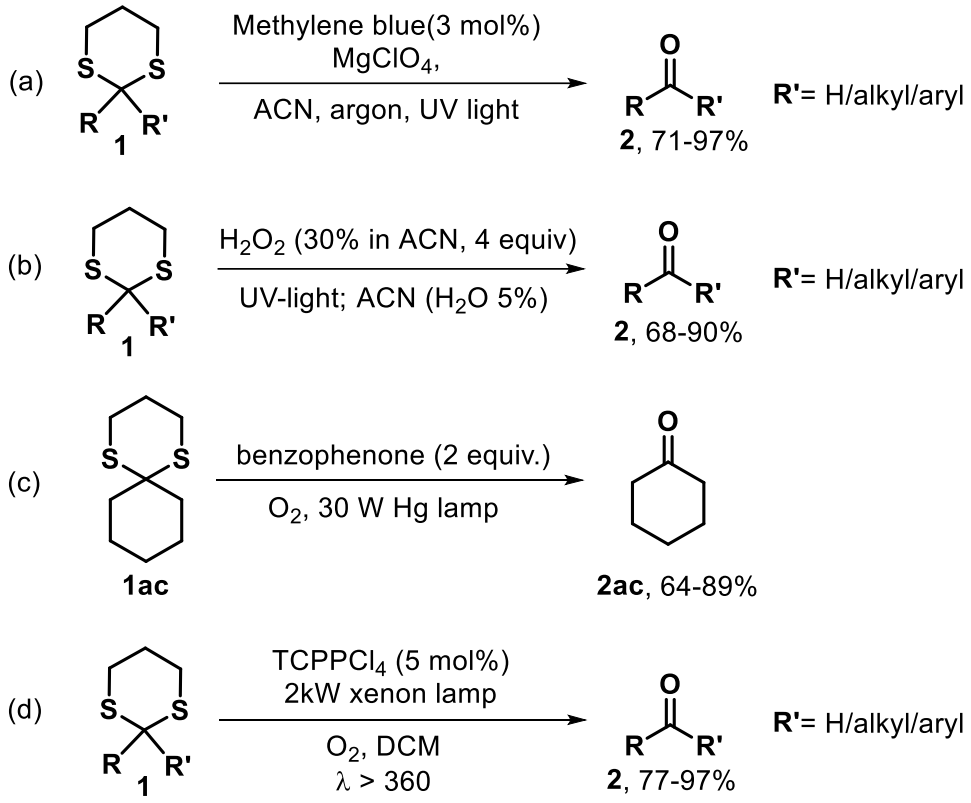


Selectfluor™ (1-chloromethyl-4-fluoro-1,4-diazoniabicyclo [2,2,2] octane bis(tetrafluoroborate)

limited due to toxicity, relying on stoichiometric amounts of reactive reagents, harsh reaction conditions along with side reactions.

In this regard, efforts have been focussed on the UV light mediated deprotection of dithianes **1.** The deprotection of dithianes **1** has been achieved using methylene blue (3 mol%) along with $MgClO_4$ under the irradiation of UV light in a good yield (up to 97%, Scheme 2.5a).[25] Likewise, dithianes **1** have been unmasked using 30% H_2O_2 under UV irradiation in aqueous acetonitrile for 2-4 h (Scheme 2.5b).[26] Benzophenone (2 equiv.) in presence of oxygen atmosphere under irradiation of UV light (Hg lamp, 30 W) deprotected the dithianes **1** in good yields (Scheme 2.5c).[27] As the UV light is of very high energy, it usually triggers the unwanted side reactions of few sensitive compounds along with deprotection. Also, many organic molecules absorb the UV light thus not leading to clean transformations and meticulous monitoring of reaction is required since; long UV irradiation of reaction mixture usually leads to a decrease in the yield of reaction.

Scheme 2.5 Photochemical deprotection of dithiane



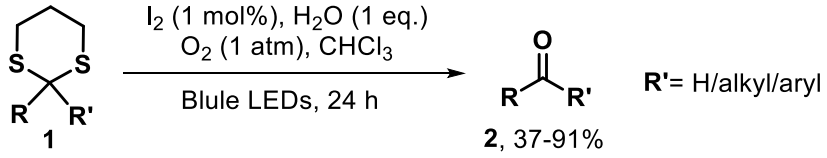
On the other hand, visible light is relatively less energetic and the same has been explored elegantly for the deprotection of dithianes **1** using different sensitizers such as 9,10-dicyanoanthracene, Methylene Green, meso-tetraphenylporphine and 2,4,6-tris (4-chlorophenyl) pyrylium perchlorate ($TCPPCl_4$). In the year 1990, dithianes **1** have been shown to undergo deprotection in presence of $TCPPCl_4$ (5 mol%) in presence of oxygen atmosphere under the irradiation of visible light (2 kW xenon light) (Scheme 2.5d).[28,29,30] However, these interesting protocols required the expensive special experimental set-up as well the method suffered due to inefficiency in the deprotection of electron deficient dithioacetals. These impede the wider applications of these protocols for further utility.

Over the last 15 years, there has been a fast growth of visible light photocatalysis and has been renaissance for accessing many interesting organic compounds using efficient photocatalysts under relatively controlled and milder reaction conditions due to SET process initiated by excited state photocatalyst (PC*) generated under irradiation of visible light.

Very recently, Lei *et al.*[31,] and Zhimin Xing *et al.*[32] have independently reported the blue LEDs mediated protection of aldehydes and ketones (acetalization and dithioacetalization) respectively. However, the selective and controlled deprotection of dithianes **1** remains

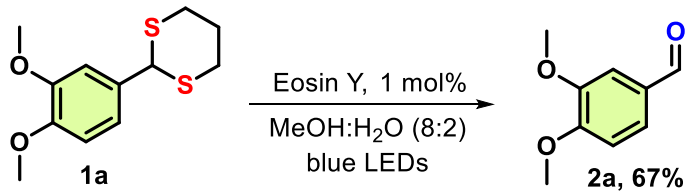
unexplored under visible light. More recently, during the same time we published our "metal-free visible light mediated protocol for the deprotection of dithiane" Opatz and co-workers reported the visible light mediated deprotection of dithiane using the iodine as a visible light photocatalyst in aqueous acetonitrile (Scheme 2.6).[33]

Scheme 2.6 Deprotection of dithiane under visible light



In the year 2018, König and coworker have described the photocatalytic formation of carbon–sulfur bonds. Where in it has been revealed that photocatalyst can easily oxidize the sulfur atom by the SET mechanism and this would facilitate to the cleavage of oxidized C–$S^{\cdot+}$ bond.[34] Inspired by this, we hypothesized that under suitable photoredox catalytic conditions and using appropriate photocatalyst along with the tuning of reaction conditions, the cyclic dithioacetals can be deprotected by the irradiation of visible light. In this regard, we focused on developing novel strategy for the deprotection of cyclic dithioacetals. Herein, in this chapter we present the visible light mediated facile and selective dithiane deprotection under metal-free conditions using Eosin Y (1 mol %) in aqueous acetonitrile at room temperature (Scheme 2.7).

Scheme 2.7 Deprotection of dithiane using eosin Y as a photocatalyst

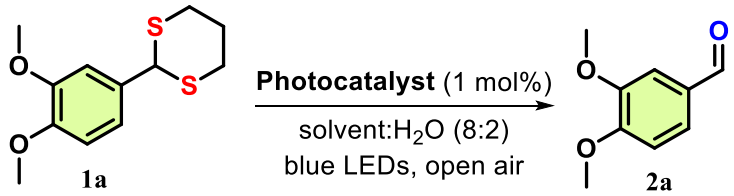


2.3 Result and Discussion

2.3.1 Reaction optimization

Encouraged by this initial result, we further planned to systematically optimize the deprotection of dithianes **1**. Later, the reaction of dithiane **1a** in presence of Eosin Y (1 mol%) in acetonitrile and water as solvent mixture (8:2, 20% water, v/v) in open air under the irradiation of blue led afforded the corresponding aldehyde **2a** smoothly in 78% yield (Table 2.1, entry 2). We further planned to screen different photocatalysts to optimise this

Table 2.1 Screening of photocatalysts



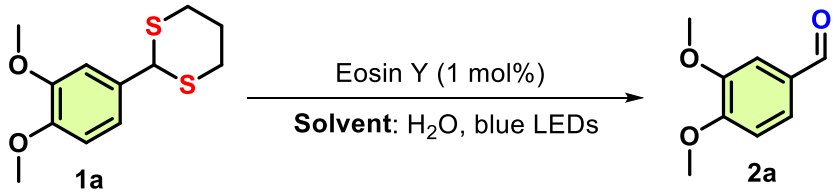
Entry	Catalyst	Solvent	Yield (%)
1	Eosin Y (EY)	MeOH : H_2O	67
2	Eosin Y	MeCN : H_2O	78
3	(-)-Riboflavin	MeCN : H_2O	30
4	Rhodamine	MeCN : H_2O	10
5	TPP-BF_4	MeCN : H_2O	52
6	Acr^+-Mes	MeCN : H_2O	47
7	$Ru(bpy)_3Cl_2$	MeCN : H_2O	50
8	$[Ir(dtbbpy)(ppy)_3](PF_6)$	MeCN : H_2O	45
9[b]	Eosin Y	MeCN : H_2O	0
10[c]	None	MeCN : H_2O	0

1a (0.2 mmol), catalyst 1 mol%, solvent (1.6 mL) and water (0.4 mL), in open air at room temperature under 30 W blue LEDs; [b]Without LED; [c]Without EY.

transformation. The photocatalysts such as Riboflavin and Rhodamine in acetonitrile and water (20% water, v/v) were observed to be not efficient for the deprotection furnishing the corresponding the aldehyde **2a** in poor yields (30 and 10 % yields, Table 2.1, entries 3-5).

While, reaction of **1a** presence of other photocatalysts such as triphenylpyrilium tetrafluoroborate (TPP-BF_4) **18**, Acr^+-Mes **27**, $Ru(bpy)_3Cl_2$ **14**, and $[Ir(dtbbpy)(ppy)_3](PF_6)$ **17** in acetonitrile and water (20% water, v/v) proved to be advantageous by affording the desired aldehyde **2a** in modest yields (Table 2.1, entries 5, 6, 7 and 8). Among all the photocatalysts screened, Eosin Y (EY) **33** proved to be the efficient catalyst for the desired transformation. Further, we observed that the reaction in the absence of either photocatalyst (Eosin Y) or the visible light did not work thus indicating that both are essential for the desired transformation (Table 2.1, entries 9 and 10).

Table 2.2 Screening of solvents



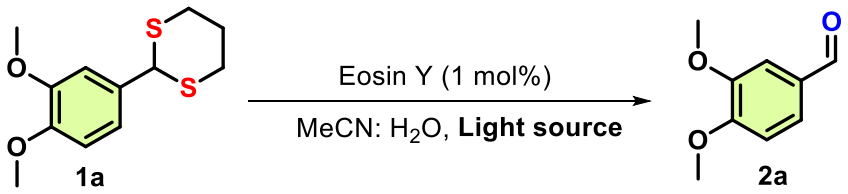
Entry	Solvent	Light source	Time (h)	Yield (%)
1	MeOH	Blue LED	2	67
2	^{t}BuOH	Blue LED	2	60
3	THF	Blue LED	2	53
4	1,4-dioxane	Blue LED	2	40
5	EtOAc	Blue LED	2	75
6	DCM	Blue LED	2	73
7	$CHCl_3$	Blue LED	2	73
8	MeCN	Blue LED	2	79
9	Toluene	Blue LED	2	58
10	DMSO	Blue LED	6	N. R.
11	DMF	Blue LED	2	63

1a (0.2 mmol), EY (1 mol%), solvent (1.6 mL) and water (0.4 mL), in open air at room temperature under 30 W blue LEDs

Subsequently, we screened different solvents with 20% water for optimizing the deprotection of dithiane **1a** while maintaining the initial standard reaction conditions of Eosin Y (1 mol%), in open atmosphere under the irradiation of visible light (blue LEDs, 30W, See Table 2.2

Entries 1-11). Solvents such as MeOH, ^{t}BuOH, THF and 1,4-dioxane along with 20% water did not prove to be efficient for the desired deprotection (Table 2.2 entries 1-4). While the solvents such as EtOAc, DCM, chloroform with 20% water found to be relatively more beneficial for the desired transformation providing the aldehyde **2a** in good yields (Table 2.2, entry 5, 6 and 7). Among all the solvents screened, acetonitrile in water proved to be the optimum solvent for the desired deprotection of cyclic dithiane **1a** to afford **2a** in very good yield (79%, Table 2.2, entry 8). While non polar solvent such as toluene in water offered the deprotection product **2a** in moderate yield (Table 2.2, entry 9)**.** While the desired transformation in DMSO did not work (Table 2.2, entry 10) and the DMF afforded the deprotection product **2a** in moderate yield under the standard conditions (Table 2.2, entry 11). We observed that the polar aprotic as well as polar protic solvents proved to favour the desired transformation. As EY has proved to be suitable photocatalyst for this transformation and based on the absorption spectrum of EY (absorption 450-540 nm),[35] we decided to screen different light sources for the desired reaction. In this regard we screened different light sources such as blue LEDs, green LEDs and CFL for deprotection of **1a** while maintaining the initial standard conditions (see Table 2.3, entries 1-4). We observed that blue LEDs facilitated deprotection but led to the over oxidation of aldehyde **2a** to corresponding carboxylic acid leading to the decrease in yield of **2a** (Table 2.3, entries 1-2)

Table 2.3 Screening of light-source

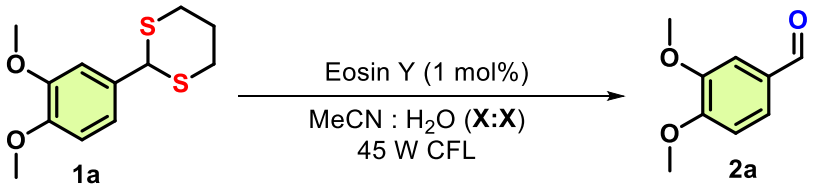


Entry	Light source	Time (h)	Yield (%)
1	15 W Blue LED	2	80
2	30 W Blue LED	2	79
3	50 W Green LED	2	83
4	23 W CFL	4	86
5	45 W CFL	2	85

1a (0.2 mmol), EY (1 mol%), MeCN:H_2O (85:15), in open air at r.t., light source

probably blue LEDs might have generated heat. While reaction of **1a** under the irradiation of the green LEDs and CFL light afforded the deprotection to aldehyde **2a** in relatively good yield and we did not observe any over oxidation of aldehyde **2a** (Table 2.3, entries 3, 4 and 5). In order to ensure the effect of amount of water on over all transformation and the yield of **2a.** The reaction of **1a** were carried out with Eosin Y (1 mol%) in open air using different percentages of water in acetonitrile under CFL irradiation at room temperature (Table 2.4). We observed that with the increase in percentage of water in acetonitrile, the rate of reaction enhanced and starting material **1a** was consumed completely in a short period of time.

Table 2.4: **Screening of different percentage of water**



Entry	Light source	% of water	Time (h)	Yield (%)
1	CFL 45 W	0	18	75
2	CFL 45 W	5	8	92
3	CFL 45 W	10	2	93
4	CFL 45 W	15	2	92
5	CFL 45 W	20	2	85
6	CFL 45 W	25	2	68
7	CFL 45 W	50	2	40
8[a]	CFL 45 W	15	2	91

Reaction conditions: **1a** (0.2 mmol), EY (1 mol%), acetonitrile and water at different percentage in open air at room temperature under 45 W CFL, [a]under oxygen atmosphere

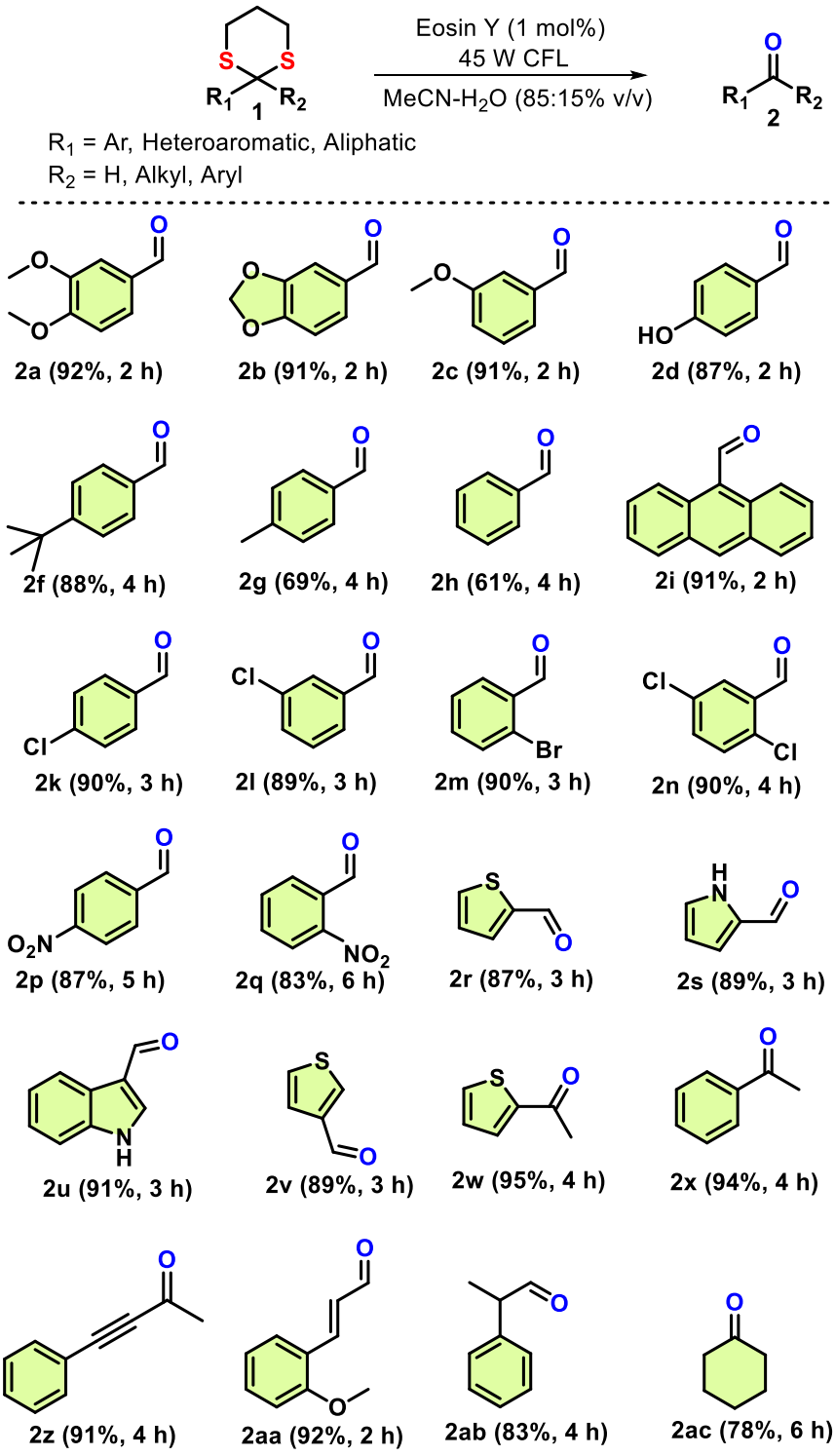
However, the yield of deprotection product **2a** decreased significantly with the increase in the percentage of water in acetonitrile. The experimental results revealed that excess of water in the reaction promoted the over-oxidation of aldehyde **2a** to the corresponding carboxylic acid and hence inversely reduced the yield of desired product **2a** (Table 2.4 entries 4-7). Based on the experimental observation, 10-15% of water in acetonitrile is established to be optimum for the efficient deprotection of **1a** to afford the aldehyde **2a** in excellent yield (Table 2.4,

entry 3 and 4). Based on the thorough screening for the deprotection of dithiane **1a,** EY (1 mol%) in MeCN : H_2O (85:15% v/v), CFL (45 W) in open air is the standardized reaction condition to afford the corresponding aldehyde **2a** in high yield.

2.3.2 Substrate scope for deprotection of dithiane 1

Having optimized the reaction condition for the desired transformation, we selected the different substrate scope to explore the efficiency and practicality of this protocol (Table 2.5). To begin with we explored the deprotection of electron-rich aromatic cyclic thioacetals or dithianes. Under the optimized reaction conditions, cyclic thioacetals derived from electron-rich aromatic aldehydes (**1a-1g**) underwent smooth transformation to afford the deprotected aldehydes (**2a-2g**) in 2 h (up to 92% yield, Table 2.5). Dithianes derived from electronically neutral as polyaromatic aldehydes (**1h-1j**) underwent smooth deprotection under the optimized reaction conditions to afford the expected aromatic aldehydes (up to 91% yield, Table 2.5, **2h-2j**). The Cyclic thiacetals derived from aromatic aldehydes (**1k-1q**) having electron deactivating as well electron withdrawing substituents reacted efficienty to afford the respective aromatic aldehydes (**2k-2q**) in good to excellent yields (Table 2.5). We observed that thioacetal derived from aldehydes containing electron deactivating/electron withdrawing substituents required more reaction time for the complete deprotection. Also, sterically crowded thioacetals did not have any impact on the deprotection as well as on the yield of the desired product. Dithianes derived from heteroaromatic aldehydes (**1r-1v**) furnished the corresponding heteroaromatic aldehydes (**2r-2v**) (82%-91% yield, Table 2.5). Dithianes (dithioketals **1w-y**) derived from ketones also reacted well under the optimized conditions to afford the particular ketones (**2w-2y**) (94%-97% yield, Table 2.5). The thioacetals (**1z-1aa**) derived from a, b-unsaturated ketone/aldehyde also underwent easy deprotection under the standardized reaction conditions to afford the deprotection to a desired products **2z-2aa** (up to 92% yields, Table 2.5). Our efforts to deprotect some of thioacetals derived aliphatic aldehydes such as *n*-butanal, heptanal, valeraldehyde, isovaleraldehyde, isobutyraldehyde and pivaldehyde were not successful. Gratifyingly, thioacetals (**1ab, 1ac**) derived from aliphatic aldehyde/ketone underwent smooth dithiane deprotection under the optimized reaction conditions to furnish corresponding product **2ab** and **2ac** respectively in good yields (Table 2.5).

Table 2.5 Reaction scope for dithiane deprotection



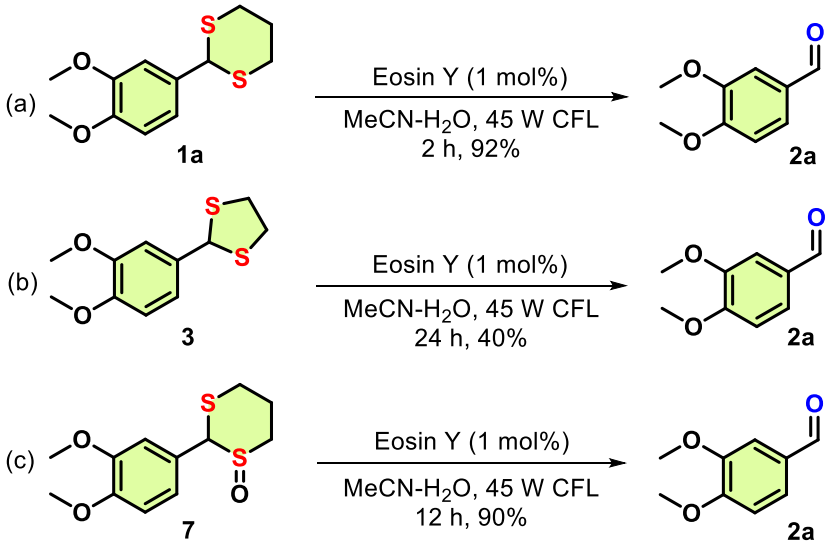
Reaction conditions: **1** (0.2 mmol), EY (1 mol%), acetonitrile:water (85:15) 2 mL in open air at room temperature under 45 W CFL, [a]under oxygen atmosphere.

2.4 Mechanistic study

2.4.1 Control experiments

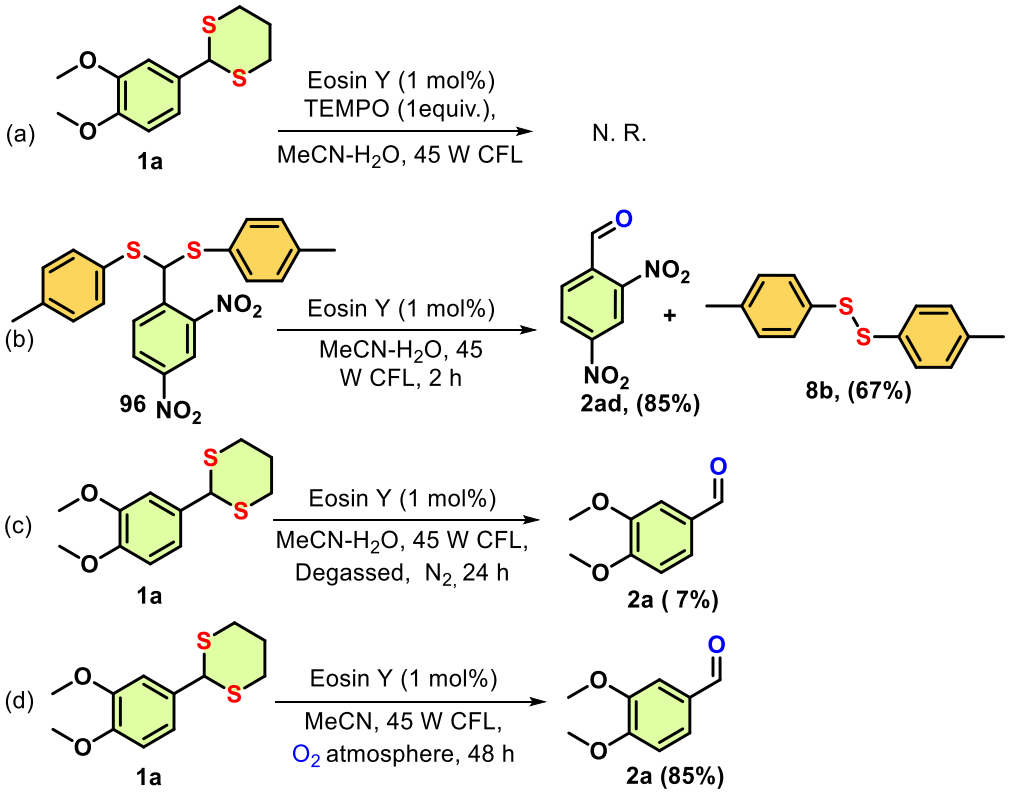
Further, to have understanding about the reactivity patterns and reaction mechanism, we explored the deprotection of 1, 3-dithiane **1a**, 1,2-dithiane **3** and 1,3-sulfoxide **7** under the optimized reaction conditions. Interestingly, we observed that 1,3-dithianes **1a** as well as 1,3-sulfoxide **7** underwent complete deprotection to furnish the corresponding aldehyde **2a** in 2 h and 12 h respectively in excellent yields (Scheme 2.7a and c). However, the under the similar reaction conditions, the deprotection of 1,2-dithiane **3** was quite sluggish to afford the corresponding aldehyde **2a** in modest yield even after the prolonged reaction time (40% yield, Scheme 2b).

Scheme 2.7 Deprotection of dithiane, dithiolane and the sulfoxides.



In order to have further understanding of thioacetal deprotection pathway, we have carried out some control experiments (Scheme 2.8). The reaction of dithiane **1a** in presence of (a radical trapping agent) TEMPO under the optimized reaction condition did not work and the starting material **1a** was recovered (Scheme 2.8a). This result clearly indicated that TEMPO might have trapped the radical intermediate and the possibly the reaction pathway must be radical in nature. Later, we carried out the deprotection of 4-methylphenyl thioacetal derivative **96** derived from 2, 4-dinitrobenzaldehyde under the slandered reaction condition (Scheme 2.8b).

Scheme 2.8 Control experiments



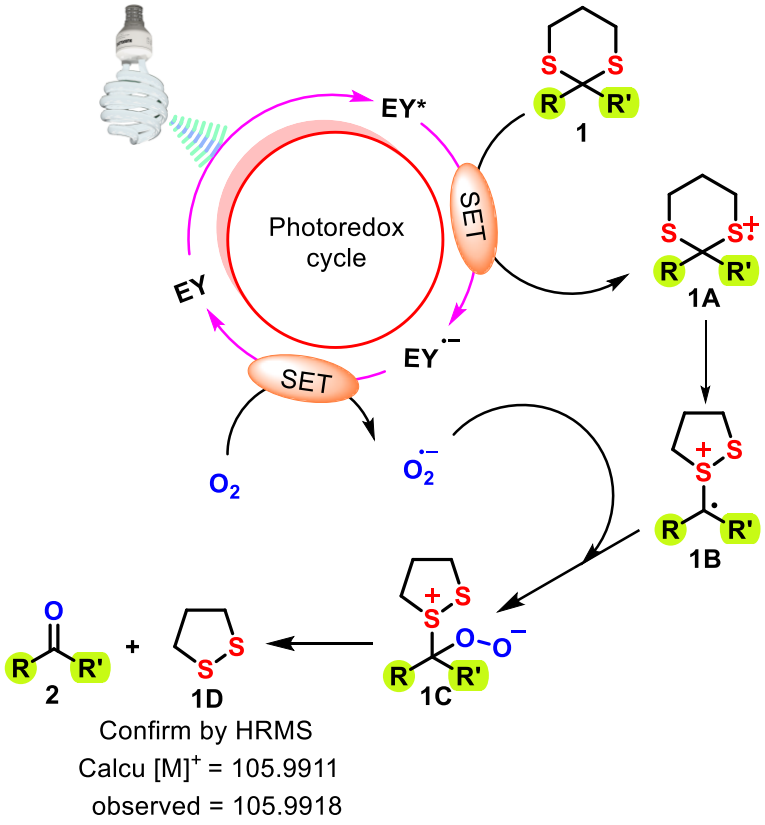
We observed that along with deprotection (formation of aromatic aldehyde **2ad**), a significant amount of side product 4-methylphenyldisulfide **8x** was formed in a 67% (Scheme 2.8b). This result indicates that dithiane deprotection must be undergoing via the formation of disulfide bond during the course of the pathway. Succeeding, to establish the exact role of oxygen as well as water in dithiacetal deprotection process, we carried out controlled experiments. The reaction of **1a** under the optimum reaction condition in MeCN : H_2O (85:15) but in the absence of oxygen (under nitrogen atmosphere) did not work smoothly affording the corresponding aldehyde **2a** in very poor yield (7%, Scheme 2.8c). This result unambiguously established the requirement of oxygen for the desired dithioacetal deprotection. Also, the oxygen is incorporated in the deported aldehyde/ketone from oxygen and not from water. While the reaction of **1a** under the optimum reaction condition but in only acetonitrile (anhydrous ACN) and under oxygen atmosphere (purge for 5 min) offers the corresponding aldehyde **2a**, in 85% yield with very slow reaction rate (after 48 h) along with the over-oxidized product in higher yield (Scheme 2.8d). This result revealed that oxygen is necessary for the deprotection of dithiane and the oxygen atom is coming from the oxygen

not from the water. Further the water molecules are also required to accelerate the deprotection of dithiane.

2.5 Plausible reaction mechanism

Based on our control experimental observations and preceding literature,[36] a plausible mechanism for the dithiane **1** deprotection under visible light has been depicted below (Scheme 2.9). On irradiation with visible light (CFL bulb), the photocatalyst eosin Y (**EY)** gets excited as **EY***. This excited photocatalyst **EY*** further oxidizes the thioacetal **1** to corresponding oxidized species **1A** via single electron transfer (SET) process and gets reduced to $\mathbf{EY}^{\bullet -}$.

Scheme 2.9 Plausible reaction mechanism



Afterwards, the next SET process takes place through the oxidation of $\mathbf{EY}^{\bullet -}$ (loss of electron) by reacting with molecular oxygen to afford the corresponding photocatalyst **EY** and superoxide radical anion thus completing the photocatalytic cycle. The *in situ* generated intermediate **1A** readily rearranges to **1B** by forming S–S bond. This intermediate **1B** upon

reacting with superoxide radical anion forms the intermediate **1C**.[36] This would further breakdown to form the desired product aldehyde **2** along with the by-product cyclic disulfide **1D**. HRMS data further supported the formation of cyclic disulfide **1D** thus supporting the mechanistic pathway (Scheme 2.9). Further to generalize this protocol for the wider practicality, we carried out the dithiane deprotection of **1a** and **1x** on a gram scale under optimum reaction condition to afford the aldehydes and ketones **2a** and **2x** in good to excellent yields 87% and 92% respectively.

2.6 Conclusions

In summary, we have established a transition metal-free visible light mediated facile dithiane deprotection under photoredox catalysis at room temperature. The protocol proved to be highly practical for the deprotection of different cyclic thioacetals under mild reaction conditions using clear energy source. Under the reaction conditions substrates including neutral, strongly electron donating as well electron-deficient thioacetals worked efficiently with the minimum over-oxidation of aldehyde to corresponding carboxylic acid. Even the sterically demanding thioacetals and heterocyclic thioacetals were deprotected smoothly. The method also proved to be scalable on gram quantity. We believe that this methodology will be useful for the deprotection of cyclic thioacetals. We hope that in future the deprotection of thioacetals derived from aliphatic aldehydes will be optimised.

2.7 Experimental section

2.7.1 General Reagent Information:

All reactions were set up in open air, or under oxygen while subject to irradiation from blue LEDs, Green LEDs, CFL (IBRA Pure 30W Blue LED Flood Light, IP Rating: IP66; or Ormit 50W Green LED Flood Light, IP Rating: IP66; Philips Tornado Compact Fluorescent Bulb 45W (CFL) (available from local market and Amazon). Unless otherwise noted, chemicals ordered from commercial venders were used without further purification. Thioacetals/thioketals were synthesized following the literature procedures. Compounds **1** or **3** were prepared according to reported procedure. The TLC was performed using silica gel 60

GF254 pre-coated aluminum backed plates (2.5 mm). Visualization was accomplished by irradiation with UV light at 254 nm / 2,4-DNP staining or vanillin staining agent. Silica gel (100-200 mesh) was used to performed column chromatography and compounds were eluted with hexane and ethyl acetate. NMR spectra were recorded to characterized the isolated molecules ^{1}H NMR at 400 MHz, and $^{13}C\{^{1}H\}$ NMR spectra (proton decoupled) were recorded at 100 MHz (Bruker Avance III HD Ascend 400 MHz and Jeol ECS-400). Chemical shifts values for protons are written in parts per million (ppm) downfield from TMS (tetramethylsilane) and are referenced to residual protium in the NMR solvent ($CDCl_3$: δ 7.26). Chemical shifts for carbon are reported in parts per million (ppm) downfield from TMS and are referenced to the carbon resonances of the solvent ($CDCl_3$: δ 77.16). The NMR coupling constants (*J*) are given in Hz. Multiplicity is denoted as pollowes: (m = multiplate, p = pentate, q = quartet, t = triplet, d = doublet, s = singlet, br = broad). 19F NMR were recorded on Bruker Avance III HD Ascend 400 MHz at 377 MHz. IR spectra were obtained using a FT-IR spectrophotometer as neat and are reported in cm^{-1}. Mass samples were analyzed by High-resolution mass spectrometry using ESI TOF. Mass samples were analyzed by High-Resolution Mass Spectroscopy (HRMS) using ESI-TOF. Buchi B-540 apparatus were used to record the melting point in a capillary tube and are uncorrected. Emission spectra were obtained from HORIBA Jobin-Yvon Fluoromax-4 spectrofluorometer, with xenon light source in a Hellma fluorescence cuvette (3mL, 1.0 cm path length).

2.7.2 General procedure A: Dithiane protection of aldehyde and ketones[2f]

To a round-bottom glass flask charged with magnetic stir bar and aldehyde/ketone (1 equiv, 1.5 mmol) was added the DCM (15 mL). Next, catalytic amount of SiO_2 and PTSA was added and then 1,3-propanedithiane or 1,2-ethanedithiane (1.1 equiv., 1.65 mmol) was added at the end and the reaction mixture was refluxed for 6 to 8 h. upon completion of reaction, the reaction mixture was cooled down to room temperature and excess 1,3-propanedithiane was quenched by adding saturated potassium hydroxide solution (5 mL) and stirred for 20-30 min, and finally extracted with DCM (3 x 20 mL). The organic DCM extracts were combined, dried over sodium sulfate, filtered, and concentrated. The crude was further purified by column chromatography to obtained the pure compound **1/3**.

2.7.3 General Procedure B: Deprotection of dithianes

To a clean screw-top vial (25 mL) equipped with a stir bar was charged with EY (1 mol%), dithioacetal **1/3** (1 equiv., 0.2 mmol), H_2O (0.3 mL), and acetonitrile (1.7 mL). The reaction mixture was stirred continously for 2-8 h under the irradiation of 45 W CFL bulb in open air. The reaction mixture was quenched by the addition of water (15 mL) and further extracted with ethyl acetate (3 x 15 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered, and concentrated under vacuum. The crude residue was further purified by column chromatography over silica gel using ethyl acetate and pet. ether as eluent to obtained the deprotection product **2**.

2.7.4 Characterization data

2-(3-(allyloxy)phenyl)-1,3-dithiane (1e): Compound **1e** was synthesized following the general procedure A. Compound **1e** was obtained as yellow oil (89%, 336 mg); eluent (petroleum ether/ethyl acetate = 8:2); R_f = 0.4; FTIR cm^{-1} (neat): 1225, 1446, 1599, 1679, 2928; ^1H NMR (400 MHz, $CDCl_3$) δ 1.97 – 1.87 (m, 1H), 2.15 (dtd, *J* = 14.1, 4.5, 2.3 Hz, 1H), 2.89 (ddd, *J* = 14.6, 4.3, 3.2 Hz, 2H), 3.08 – 3.00 (m, 2H), 4.53 (dt, *J* = 5.3, 1.5 Hz, 2H), 5.12 (s, 1H), 5.27 (dq, *J* = 10.5, 1.4 Hz, 1H), 5.41 (dq, *J* = 17.3, 1.6 Hz, 1H), 6.04 (ddt, *J* = 17.3, 10.5, 5.3 Hz, 1H), 6.84 (ddd, *J* = 8.3, 2.5, 1.0 Hz, 1H), 7.05 – 7.02 (m, 2H), 7.25 – 7.20 (m, 1H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 25.22, 32.18, 51.60, 68.89, 114.06, 115.16, 117.82, 120.31, 129.81, 133.22, 140.61, 158.91,**;** HRMS (ESI-TOF) m/z calcd for $C_{13}H_{16}OS_2$ $[M]^+$ 252.0643, found 252.0654.

4-(tert-butyl)benzaldehyde (**1f**): Compound **1f** was synthesized following the general procedure A. Compound **1f** was obtained as white solid (99%, 374 mg), mp 85-87 ^oC; eluent (petroleum ether/ethyl acetate = 19:1), R_f = 0.5; FTIR cm^{-1} (neat): 1271, 1415, 1466, 1509, 2898, 2955,; ^1H NMR (400 MHz, $CDCl_3$) δ1.29 (s, 9H), 1.97 – 1.85 (m, 1H), 2.17 – 2.10 (m, 1H), 2.91 – 2.85 (m, 2H), 3.07 – 3.00 (m, 2H), 5.15 (s, 1H), 7.41 – 7.33 (m, 4H), $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 25.19, 31.36, 32.22, 34.67, 51.17, 125.74, 127.41, 136.12, 151.41,; HRMS (ESI TOF) m/z calcd for $C_{11}H_{15}O$ $[M + H]^+$ 163.1123, found 163.1158.

2-(2,5-dichlorophenyl)-1,3-dithiane (**1n**): Compound **1n** was synthesized following the general procedure A. Compound **1n** was obtained as light pink color solid (98%, 389 mg); mp 96-97 ˚C; eluent (petroleum ether/ethyl acetate = 8:2); R_f = 0.5; FTIR cm^{-1} (neat): 1415,

1445, 1529, 2893, 3005,; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.99 – 1.89 (m, 1H); 2.22 – 2.16(m, 1H), 2.96 – 2.90 (m, 2H), 3.15 – 3.08 (m, 2H), 5.57 (s, 1H), 7.20 (dd, *J* = 8.6, 2.5 Hz, 1H), 7.29 (d, *J* = 8.6 Hz, 1H), 7.67 (d, *J* = 2.5 Hz, 1H), ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 25.11, 32.26, 47.23, 129.67, 129.91, 133.5, 138.34, 130.76, 130.85,; HRMS (ESI TOF) m/z calcd for $C_{10}H_{11}Cl_2S_2$ $[M + H]^+$ 264.9679, found 264.9678.

2-(1,3-dithian-2-yl)-1H-pyrrole (**1s**): Compound **1s** was synthesized following the general procedure A. Compound **1s** was obtained as grey color solid (93%, 258 mg); mp 99-103 ^{o}C; eluent (petroleum ether/ethyl acetate = 8:2); R_f =0.4; FTIR cm^{-1} (neat): 3278, 3106, 2908, 1699, 1562, 1422, 1270; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.97 – 1.87 (m, 1H), 2.16 – 2.07 (m, 1H), 2.92 – 2.89 (m, 4H), 5.23 (s, 1H), 6.17 – 6.13 (m, 1H), 6.27 (dq, *J* = 2.7, 0.9 Hz, 1H), 8.48 (s, 1H), ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 25.36, 30.21, 42.54, 107.88, 118.39, 108.78, 128.36,; HRMS (ESI TOF) m/z calcd for $C_8H_{12}NS_2$ $[M + H]^+$ 186.0411, found 186.0405.

2-methyl-2-(thiophen-2-yl)-1,3-dithiane (**1w**): Compound **1w** was synthesized following the general procedure A. Compound **1w** was obtained as white solid (97%, 314 mg); mp 63.5-65.5 ˚C; eluent (petroleum ether/ethyl acetate = 9:1); R_f = 0.47; FTIR cm^{-1} (neat): 3126, 2929, 1687, 1545, 1407, 1265; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.83 (s, 3H), 1.94 – 1.85 (m, 1H), 2.04 – 1.97 (m, 1H), 2.76 – 2.70 (m, 2H), 2.95 – 2.87 (m, 2H), 6.95 – 6.92 (m, 1H), 7.25 – 7.19 (m, 2H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 24.52, 28.56, 34.59, 50.36, 126.24, 126.9, 127.20, 152.17,; HRMS (ESI TOF) m/z calcd for $C_9H_{13}S_3$ $[M + H]^+$ 217.0179, found 217.0178.

2-methyl-2-(phenylethynyl)-1,3-dithiane (**1z**): Compound 1ab was synthesized following the general procedure A. Compound 1ab was obtained as colorless oil (91%, 391 mg);eluent (petroleum ether/ethyl acetate = 19:1); R_f = 0.4; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.45 (s, 3H), 7.40 – 7.36 (m, 2H), 7.48 – 7.43 (m, 1H), 7.59 – 7.55 (m, 2H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 32.9, 88.4, 90.4, 120, 128.7, 120, 130.8, 133.1, 184.7,; HRMS (ESI TOF) m/z calcd for $C_{13}H_{15}S_2$ $[M + H]^+$ 235.0610, found 235.0617.

2-(3,4-dimethoxyphenyl)-1,3-dithiane 1-oxide (**7**):[35] Compound **1a''** was synthesized following the literature. Compound **1a''** was obtained as white solid (83%, 339 mg); mp 138-140 ˚C; eluent (petroleum ether/ethyl acetate = 6:4); R_f = 0.4; FTIR cm^{-1} (neat): 2924, 2850, 1656, 1588, 1511, 1260, 1135; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.38 – 2.26 (m, 1H), 2.51 – 2.44 (m, 1H), 2.73 – 2.61 (m, 2H), 2.89 – 2.79 (m, 1H), 3.56 – 3.49 (m, 1H), 3.84 (s, 3H),

3.86 (s, 3H), 4.47 (s, 1H), 6.84 (d, *J* = 8.3 Hz, 1H), 6.88 (d, *J* = 2.1 Hz, 1H), 6.97 (dd, *J* = 8.3, 2.2 Hz, 1H),; $^{13}C\{^{1}H\}$ NMR ($CDCl_3$, 100 MHz): δ (ppm) 29.6, 31.6, 54.8, 55.9, 55.9, 69.5, 111.3, 111.5, 121.5, 125.6, 149.3, 149.9,; HRMS (ESI TOF) m/z calcd for $C_{12}H_{17}O_3S_2$ $[M + H]^+$ 273.0619, found 273.0617.

2-(3,4-dimethoxyphenyl)-1,3-dithiane (**2a**)*:* Compound **2a** was synthesized following the general procedure B. Compound **2a** was obtained as white solid (92%, 30.6 mg); mp 39-41 ˚C; eluent (petroleum ether/ethyl acetate = 7:3); R_f = 0.39; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.95 (s, 3H), 3.97 (s, 3H), 6.99 (d, *J* = 8.2 Hz, 1H), 7.42 (d, *J* = 1.8 Hz, 1H), 7.47 (dd, *J* = 8.2, 1.9 Hz, 1H), 9.86 (s, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 55.94, 56.22, 108.91, 110.42, 126.90, 130.07, 149.65, 154.52, 190.95,; HRMS (ESI-TOF) m/z calcd for $C_9H_{10}O_3$ $[M]^+$ 166.0630, found 166.0632.

Benzo[d][1,3]dioxole-5-carbaldehyde (**2b**): Compound **2b** was synthesized following the general procedure B. Compound **2b** was obtained as white solid (91%, 27.3 mg); mp 35-38 ˚C; eluent (petroleum ether/ethyl acetate = 7:3); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.08 (s, 2H), 6.93 (d, *J* = 7.9 Hz, 1H), 7.44 – 7.25 (m, 2H), 9.81 (s, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 102.2, 107.0, 108.4, 128.8, 132.0, 148.8, 153.2, 190.4,; HRMS (ESI-TOF) m/z calcd for $C_8H_7O_3$ $[M + H]^+$ 151.0395, found 151.0398.

3-methoxybenzaldehyde (**2c**): Compound **2c** was synthesized following the general procedure B. Compound **2c** was obtained as light yellow oil (91%, 24.8 mg); eluent (petroleum ether/ethyl acetate = 8:2); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.86 (s, 3H), 7.17 (dt, *J* = 6.6, 2.7 Hz, 1H), 7.40 – 7.38 (m, 1H), 7.46 – 7.43 (m, 2H), 9.97 (s, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 55.5, 112.1, 121.6, 123.6, 130.1, 137.8, 160.2, 192.2,; HRMS (ESI-TOF) m/z calcd for $C_8H_8O_2$ $[M]^+$ 136.0524, found 136.0518.

4-hydroxybenzaldehyde (**2d**): Compound **2d** was synthesized following the general procedure B. Compound **2d** was obtained as light brown solid (87%, 21.3 mg); mp 110-113˚C; eluent (petroleum ether/ethyl acetate = 7:3); R_f = 0.4; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.35 (s, 1H), 7.03 – 6.91 (m, 2H), 7.87 – 7.74 (m, 2H), 9.86 (s, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 116.2, 130, 132.7, 161.8, 191.4,; HRMS (ESI TOF) m/z calcd for $C_7H_7O_2$ $[M + H]^+$ 123.0446, found 123.0449.

3-(allyloxy)benzaldehyde (**2e**): Compound **2e** was synthesized following the general procedure B. Compound **2e** was obtained as light yellow oil (73%, 23.7 mg); eluent (petroleum ether/ethyl acetate = 8:2); R_f = 0.4;; ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.59 (dt, *J* =

5.2, 1.4 Hz, 2H), 5.31 (dt, *J* = 10.5, 1.3 Hz, 1H), 5.46 – 5.41 (m, 1H), 6.10 – 6.01 (m, 1H), 7.19 (dt, *J* = 6.9, 2.4 Hz, 1H), 7.46 – 7.39 (m, 3H), 9.96 (s, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 68.9, 113.1, 118.1, 122.1, 123.6, 132.6, 137.8, 159.1, 192,; HRMS (ESI TOF) m/z calcd for $C_{10}H_{11}O_2$ $[M]^+$ 163.0759, found 163.0417.

4-(tert-butyl)benzaldehyde (**2f**): Compound **2f** was synthesized following the general procedure B. Compound **2f** was obtained as colorless oil (88%, 28.5 mg); eluent (petroleum ether/ethyl acetate = 19:1); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (s, 9H), 7.54 (d, *J* = 8.2 Hz, 2H), 7.81 (d, *J* = 8.6 Hz, 2H), 9.97 (s, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 31, 35.3, 126, 129.7, 134.1, 158.4, 192,; HRMS (ESI TOF) m/z calcd for $C_{11}H_{15}O$ $[M + H]^+$ 163.1123, found 163.1123.

4-methylbenzaldehyde (**2g**): Compound **2g** was synthesized following the general procedure B. Compound **2g** was obtained as colorless oil (69%, 16.6 mg); eluent (petroleum ether/ethyl acetate = 19:1); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.95 (s, 1H), 2.43 (s, 3H), 7.32 (d, *J* = 7.9 Hz, 2H), 7.77 (d, *J* = 8.1 Hz, 2H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 130, 22, 129.8, 145.7, 192.1,; HRMS (ESI TOF) m/z calcd for C_8H_9O $[M + H]^+$ 121.0653, found 121.0654.

Benzaldehyde (**2h**): Compound **2h** was synthesized following the general procedure B. Compound **2h** was obtained as colorless oil (61%, 13 mg); eluent (petroleum ether/ethyl acetate = 19:1); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.55 – 7.51 (m, 2H), 7.65 – 7.61 (m, 1H), 7.89 – 7.87 (m, 2H), 10.02 (s, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 129.1, 129.9, 134.6, 136.5, 192.6,; HRMS (ESI TOF) m/z calcd for C_7H_7O $[M + H]^+$ 107.0497, found 107.0501.

Anthracene-9-carbaldehyde (**2i**): Compound **2i** was synthesized following the general procedure B. Compound **2i** was obtained as yellow solid (91%, 37.5 mg); mp 100-103˚C; eluent (petroleum ether/ethyl acetate = 9:1); R_f = 0.45; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.53 – 7.47 (m, 2H), 7.66 – 7.60 (m, 2H), 8.01 – 7.97 (m, 2H), 8.58 (s, 1H), 8.95 – 8.89 (m, 2H), 11.45 (s, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 123.6, 124.7, 125.7, 129.2, 129.4, 131.1, 132.2, 135.3, 193.0,; HRMS (ESI TOF) m/z calcd for $C_{15}H_{11}O$ $[M + H]^+$ 207.0810, found 207.0807.

2-naphthaldehyde (**2j**): Compound **2j** was synthesized following the general procedure B. Compound **2j** was obtained as yellow solid (91%, 28.5 mg); mp 56-59˚C; eluent (petroleum ether/ethyl acetate = 9:1); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.66 – 7.56 (m, 2H), 8.00

– 7.88 (m, 4H), 8.32 (s, 1H), 10.15 (s, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 122.9, 127.2, 128.2, 129.2, 129.2, 129.6, 132.7, 134.2, 134.7, 136.6, 192.4,; HRMS (ESI TOF) m/z calcd for $C_{11}H_9O$ $[M + H]^+$ 157.0653, found 157.0658.

4-chlorobenzaldehyde (**2k**): Compound **2k** was synthesized following the general procedure B. Compound **2k** was obtained as white solid (90%, 25.3 mg); mp 45-47˚C; eluent (petroleum ether/ethyl acetate = 9:1); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, *J* = 8.4 Hz, 2H), 7.83 (d, *J* = 8.5 Hz, 2H), 9.99 (s, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 129.6, 131, 134.8, 141.1, 191,; HRMS (ESI TOF) m/z calcd for C_7H_6ClO $[M + H]^+$ 141.0107, found 141.0112.

3-chlorobenzaldehyde (**2l**): Compound **2l** was synthesized following the general procedure B. Compound **2l** was obtained as colourless oil (89%, 25 mg); eluent (petroleum ether/ethyl acetate = 9:1); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 – 7.46 (m, 1H), 7.58 (ddd, *J* = 8.0, 2.1, 1.1 Hz, 1H), 7.77 – 7.75 (m, 1H), 7.83 (dtd, *J* = 2.1, 1.0, 0.5 Hz, 1H), 9.97 (s, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 128.1, 129.2, 130.5, 134.4, 135.4, 137.8, 190.9,; HRMS (ESI TOF) m/z calcd for C_7H_6ClO $[M + H]^+$ 141.0107, found 141.0102.

2-bromobenzaldehyde (**2m**): Compound **2m** was synthesized following the general procedure B. Compound **2m** was obtained as colourless oil (90%, 33.3 mg); eluent (petroleum ether/ethyl acetate = 9:1); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.45 – 7.42 (m, 2H), 7.64 (dd, *J* = 7.3, 1.4 Hz, 1H), 7.92 – 7.89 (m, 1H), 10.35 (s, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 127.2, 128, 130, 133.6, 134, 135.5, 192,; HRMS (ESI TOF) m/z calcd for C_7H_6BrO $[M + H]^+$ 184.9602, found 184.9604.

2,5-dichlorobenzaldehyde (**2n**): Compound **2n** was synthesized following the general procedure B. Compound **2n** was obtained as white solid (90%, 13.5 mg), mp 52-55˚C; eluent (petroleum ether/ethyl acetate = 8:2); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42 (s, 1H), 7.51 – 7.48 (m, 1H), 7.86 (t, *J* = 2.1 Hz, 1H), 10.4(s, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 129.2, 131.9, 133.4, 133.9, 135.0, 136.0, 188.5,; HRMS (ESI TOF) m/z calcd for $C_7H_4Cl_2O$ $[M + H]^+$ 174.9717, found 174.9729.

4-formylbenzonitrile (**2o**): Compound **2o** was synthesized following the general procedure B. Compound **2o** was obtained as white solid (90%, 23.6 mg); mp 98-101˚C; eluent (petroleum ether/ethyl acetate = 8:2); R_f = 0.5;; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.83 (dd, *J* = 8.0, 0.5 Hz, 2H), 7.98 (dd, *J* = 8.5, 0.6 Hz, 2H), 10.08 (s, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz,

$CDCl_3$): δ 117.6, 117.8, 130, 133, 138.8, 190.8,; HRMS (ESI TOF) m/z calcd for C_8H_6NO $[M+H]^+$ 132.0449, found 132.0449.

4-nitrobenzaldehyde (**2p**): Compound **2p** was synthesized following the general procedure B. Compound **2p** was obtained as Yellow solid (87%, 26.3 mg); mp 101-104˚C; eluent (petroleum ether/ethyl acetate = 7:3); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 8.8 Hz, 2H), 8.40 (d, *J* = 8.7 Hz, 2H), 10.16 (s, 1H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 124.5, 130.6, 140.2, 151.2, 190.5; HRMS (ESI TOF) m/z calcd for $C_7H_6NO_3$ $[M + H]^+$ 152.0348, found 152.0352.

2-nitrobenzaldehyde (**2q**): Compound **2q** was synthesized following the general procedure B. Compound **2q** was obtained as yellow solid (83%, 25.5 mg); mp 41-42˚C; eluent (petroleum ether/ethyl acetate = 7:3); R_f = 0.4; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.82 – 7.73 (m, 2H), 7.96 – 7.92 (m, 1H), 8.13 – 8.08 (m, 1H), 10.41 (s, 1H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 124.61, 129.74, 131.46, 133.83, 134.20, 149.69, 188.26,; HRMS (ESI TOF) m/z calcd for $C_7H_6NO_3$ $[M + H]^+$ 152.0348, found 152.0347.

Thiophene-2-carbaldehyde (**2r**): Compound **2r** was synthesized following the general procedure B. Compound **2r** was obtained as brown oil (87%, 19.5 mg); eluent (petroleum ether/ethyl acetate = 9:1): R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 – 7.19 (m, 1H), 7.78 – 7.75 (m, 2H), **9**.93 (s, 1H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 128.4, 135.2, 136.4, 144.1, 183.1,; HRMS (ESI TOF) m/z calcd for C_5H_5OS $[M + H]^+$ 113.0061, found 113.0070.

1H-pyrrole-2-carbaldehyde (**2s**): Compound **2s** was synthesized following the general procedure B. Compound **2s** was obtained as white solid (89%, 16.9 mg); mp 39-43 ˚C; eluent (petroleum ether/ethyl acetate = 8:2); R_f = 0.4; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.31 (s, 1H), 7(s, 1H), 7.18 (s, 1H), 9.48 (s, 1H), 11.24 (s, 1H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 34.3, 45.4, 50.6, 55.7,102.7,; HRMS (ESI TOF) m/z calcd for C_5H_6NO $[M + H]^+$ 96.0449, found 96.0450.

Furan-2-carbaldehyde (**2t**): Compound **2t** was synthesized following the general procedure B. Compound **2t** was obtained as yellow oil (82%, 15.7 mg); eluent (petroleum ether/ethyl acetate = 19:1); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.62 (dd, *J* = 3.6, 1.7 Hz, 1H), 7.27 (dd, *J* = 3.6, 0.8 Hz, 1H), 7.72 – 7.68 (m, 1H), 9.67 (s, 1H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 112.57, 121.26, 148.09, 152.84, 177.80,; HRMS (ESI TOF) m/z calcd for $C_5H_5O_2$ $[M + H]^+$ 97.0290, found 97.0289.

1H-indole-3-carbaldehyde (**2u**): Compound **2u** was synthesized following the general procedure B. Compound **2u** was obtained as Yellow solid (91%, 26.5 mg); mp 190-195 ˚C; eluent (petroleum ether/ethyl acetate = 7:3); Rf= 0.38; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 – 7.32 (m, 2H), 7.47 – 7.44 (m, 1H), 7.86 (d, *J* = 3.1 Hz, 1H), 8.35 – 8.32 (m, 1H), 8.75 (s, 1H), 10.08 (s, 1H),; ^{13}C{^{1}H} NMR (100 MHz, DMSO-D_6) δ 112.84, 118.49, 121.19, 122.66, 123.98, 124.39, 137.4, 139.01, 185.75,; HRMS (ESI TOF) m/z calcd for C_9H_8NO $[M+H]^+$ 146.0606, found 146.0597.

Thiophene-3-carbaldehyde (**2v**): Compound **2v** was synthesized following the general procedure B. Compound **2v** was obtained as dark brown oil (89%, 20 mg); eluent (petroleum ether/ethyl acetate = 9:1); R_f = 0.4; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38 (dd, *J* = 5.1, 2.9 Hz, 1H), 7.57 – 7.52 (m, 1H), 8.13 (dd, *J* = 2.8, 1.0 Hz, 1H), **9.94** (s, 1H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 125.5, 127.5, 136.8, 143.1, 185.1,; HRMS (ESI TOF) m/z calcd for C_5H_4OS $[M + H]^+$ 113.0061, found 113.0070.

1-(thiophen-2-yl)ethanone (**2w**): Compound **2w** was synthesized following the general procedure B. Compound **2w** was obtained as dark yellow oil (95%, 24 mg); eluent (petroleum ether/ethyl acetate = 9:1); R_f = 0.45; ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.57 (s, 3H), 7.13 (dd, *J* = 5, 3.8 Hz, 1H), 7.64 (dd, *J* = 5.0, 1.2 Hz, 1H), 7.7 (dd, *J* = 3.8, 1.2 Hz, 1H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 26.96, 128.19, 132.57, 133.86, 144.59, 190.81,; HRMS (ESI TOF) m/z calcd for C_6H_7OS $[M + H]^+$ 127.0218, found 127.0217.

Acetophenone (**2x**): Compound **2x** was synthesized following the general procedure B. Compound **2x** was obtained as colourless oil (94%, 23.1 mg); eluent (petroleum ether/ethyl acetate = 19:1); R_f = 0.61; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.59 (s, 3H), 7.46 (t, *J* = 7.6 Hz, 2H), 7.58 – 7.54 (m, 1H), 7.97 – 7.94 (m, 2H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 26.7, 128.4, 128.7, 133.2, 137.2, 198.3,; HRMS (ESI TOF) m/z calcd for C_8H_9O $[M + H]^+$ 121.0653, found 121.0655.

9H-fluoren-9-one (**2y**): Compound **2y** was synthesized following the general procedure B. Compound **2y** was obtained as yellow solid (97%, 35 mg); mp 80-81˚C; eluent (petroleum ether/ethyl acetate = 8:2); R_f = 0.42; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.24 (ddt, *J* = 8.1, 5.5, 2.6 Hz, 2H), 7.47 – 7.38 (m, 4H), 7.64 – 7.56 (m, 2H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 120.4, 124.3, 129.1, 134.1, 134.7, 144.4, 194,; HRMS (ESI TOF) m/z calcd for $C_{13}H_9O$ $[M]^+$ 181.0653, found 181.0658.

4-phenylbut-3-yn-2-one (**2z**): Compound **2z** was synthesized following the general procedure B. Compound **2z** was obtained as colourless oil (91%, 28 mg); eluent (petroleum ether/ethyl acetate = 9:1); R_f = 0.45; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.45 (s, 3H), 7.40 – 7.36 (m, 2H), 7.48 – 7.43 (m, 1H), **7**.59 – 7.55 (m, 2H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 32.9, 88.4, 90.4, 120, 128.7, 130.8, 133.1, 184.7,; HRMS (ESI TOF) m/z calcd for $C_{10}H_9O$ $[M+H]^+$ 145.0653, found 145.0657.

(E)-3-(2-methoxyphenyl)acrylaldehyde (**2aa**): Compound **2aa** was synthesized following the general procedure B. Compound **2aa** was obtained as white solid (92%, 29.8 mg); mp 42-45˚C; eluent (petroleum ether/ethyl acetate = 15:5); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.91 (s, 3H), 6.79 (dd, *J* = 16.1, 7.9 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 7.03 – 6.98 (m, 1H), 7.41 (ddd, *J* = 8.8, 7.5, 1.7 Hz, 1H), 7.55 (dd, *J* = 7.7, 1.7 Hz, 1H), 7.84 (d, *J* = 16.1 Hz, 1H), 9.69 (d, *J* = 7.9 Hz, 1H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 55.5, 111.3, 120.8, 122.9, 128.8, 128.9, 132.7, 148.2, 158.3, 194.5,; HRMS (ESI TOF) m/z calcd for $C_{10}H_{11}O_2$ $[M + H]^+$ 163.0759, found 163.0750.

2-phenylpropanal (**2ab**): Compound **2ab** was synthesized following the general procedure B. Compound **2ab** was obtained as colourless oil (83%, 22.3 mg); eluent (petroleum ether/ethyl acetate = 19:1); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.44 (d, *J* = 7.1 Hz, 3H), 3.66 – 3.60 (m, 1H), 7.22 – 7.20 (m, 2H), 7.32 – 7.28 (m, 1H), 7.40 – 7.36 (m, 2H), 9.68 (d, *J* = 1.4 Hz, 1H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ (ppm) 14.7, 53.1, 127.6, 128.4, 129.2, 137.8, 201.2,; HRMS (ESI TOF) m/z calcd for $C_9H_{11}O$ $[M + H]^+$ 135.0810, found 135.0815.

Cyclohexanone (**2ac**): Compound **2ac** was synthesized following the general procedure B. Compound **2ac** was obtained as colourless oil (91%, 17.9 mg); eluent (petroleum ether/ethyl acetate = 99:1); R_f = 0.6; ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.62 – 1.50 (m, 2H), 1.80 – 1.63 (m, 4H), 2.18 (dd, *J* = 8.4, 4.2 Hz, 4H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 24.8, 26.9, 41.8, 212.1,; HRMS (ESI TOF) m/z calcd for $C_6H_{11}O$ $[M + H]^+$ 99.0810, found 99.0818.

((2,4-dinitrophenyl)methylene)bis(p-tolylsulfane) (**96**): Compound **69** was synthesized following the general procedure A. Compound **96** was obtained as brown colour viscous oil (91%, 554 mg); eluent (petroleum ether/ethyl acetate = 7:3); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.31 (s, 6H), 6.29 (s, 1H), 7.08 – 7.05 (m, 4H), 7.24 – 7.21 (m, 4H), 8.04 (d, *J* = 8.7 Hz, 1H), 8.31 (ddd, *J* = 8.7, 2.4, 0.4 Hz, 1H), 8.60 (d, *J* = 2.3 Hz, 1H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 21.37, 54.63, 120.05, 126.99, 128.52, 130.23, 132.48, 133.91, 139.62,

142.07, 146.72, 147.73,; HRMS (ESI TOF) m/z calcd for $C_{21}H_{18}N_2O_4S_2$ $[M]^+$ 426.0708, found 426.0698.

2,4-dinitrobenzaldehyde (**2ad**): Compound **2ad** was synthesized following the general procedure A. Compound **2ad** was obtained as yellow solid (85%, **33.3** mg); mp 63-68˚C; eluent (petroleum ether/ethyl acetate = 7:3); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.15 (d, *J* = 8.4 Hz, 1H), 8.63 (ddd, *J* = 8.4, 2.2, 0.7 Hz, 1H), 8.97 (d, *J* = 2.1 Hz, 1H), 8.97 (d, *J* = 2.1 Hz, 1H), 10.48 (s, 1H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 120.3, 128.7, 131.6, 135.5, 149.5, 150.1,186.5,; HRMS (ESI TOF) m/z calcd for $C_7H_5N_2O_5$ $[M + H]^+$ 197.0198, found 197.0202.

1,2-di-p-tolyldisulfane (**8b**): Compound **8b** was obtained as yellow colour oil (67%, **33.0** mg); yellow solid; eluent (petroleum ether/ethyl acetate = 18:1); R_f = 0.5; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.49 (s, 6H), 7.41 (d, *J* = 8.0 Hz, 4H), 7.92 (d, *J* = 8.5 Hz, 4H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 21.9, 127.1, 130.4, 141.7, 147.0,; HRMS (ESI TOF) m/z calcd for $C_{14}H_{14}S_2$ $[M]^+$ 246.0537, found 246.0530.

2.8 Appendix II: ^{1}H and ^{13}C spectral data of representative compounds

Compound No.	Figure II.X	Data	Page No.
1a	Fig. II. 1 and II. 2	^{1}H and ^{13}C	49
2a	Fig. II. 3 and II. 4	^{1}H and ^{13}C	50

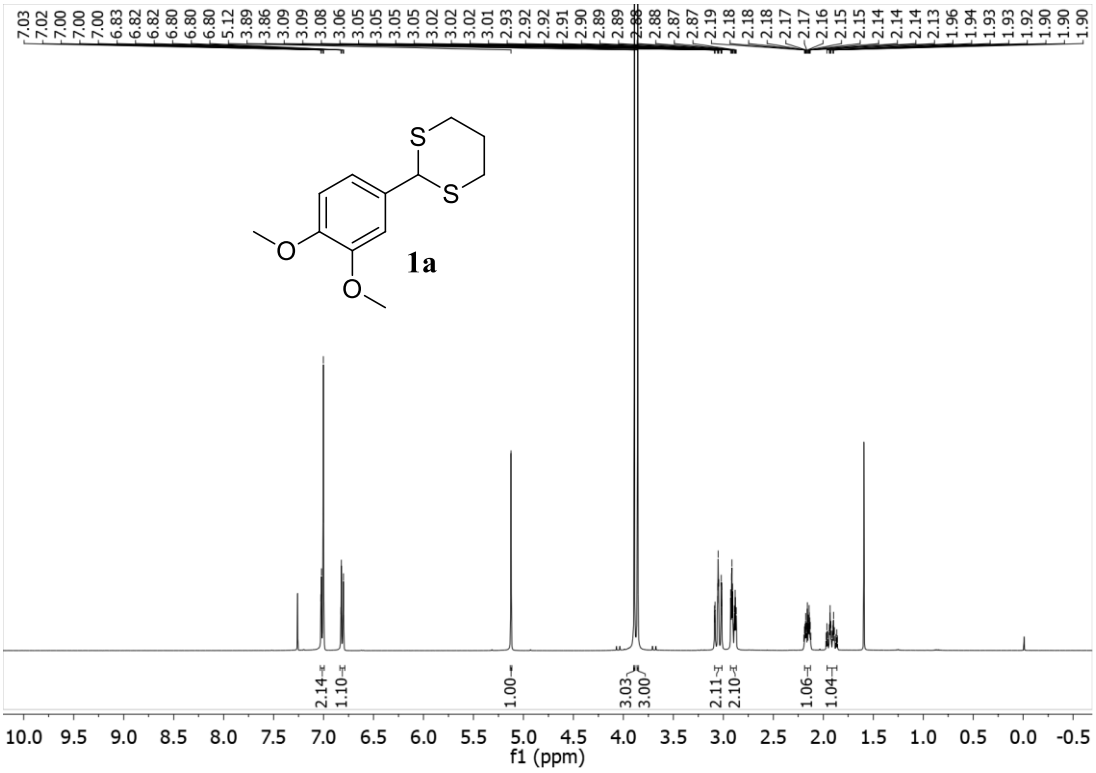


Fig. II. 1: ^{1}H NMR spectrum of **1a**, $CDCl_3$, 400 MHz

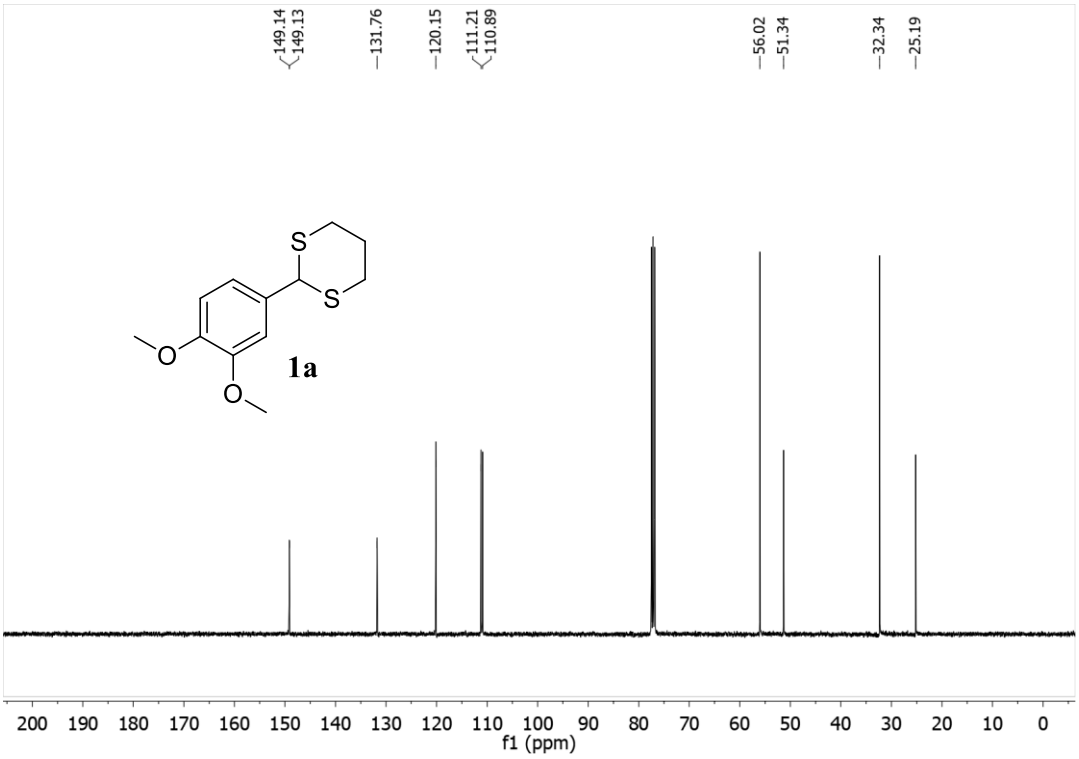


Fig. II. 2: ^{13}C {^{1}H} NMR spectrum of **1a**, $CDCl_3$, 100 MHz

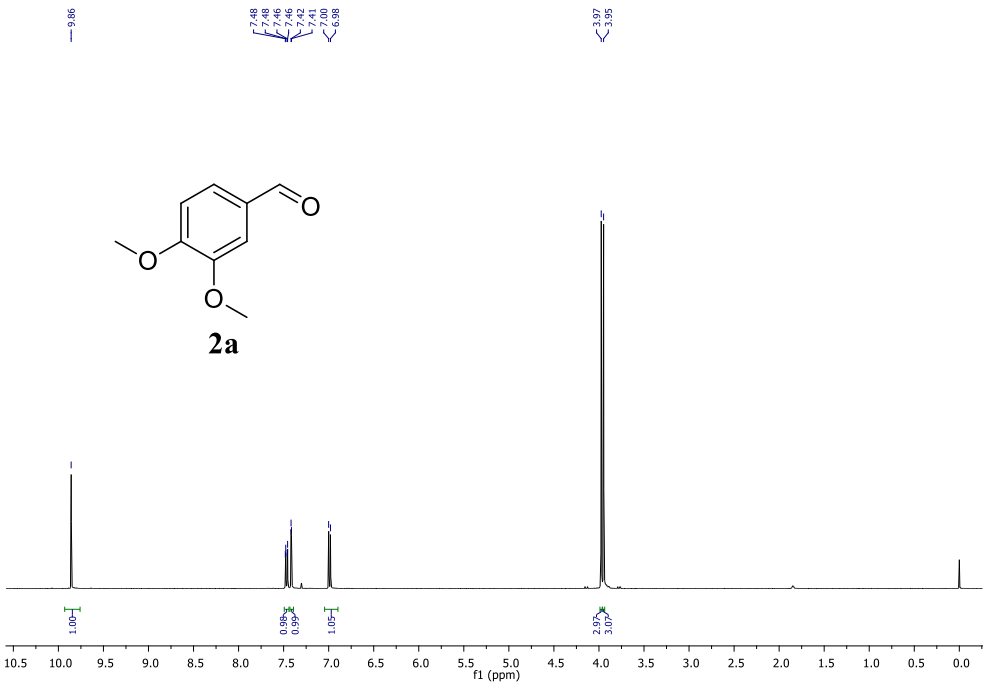


Fig. II. 3: ^{1}H NMR spectrum of 2**a**, $CDCl_3$, 400 MHz

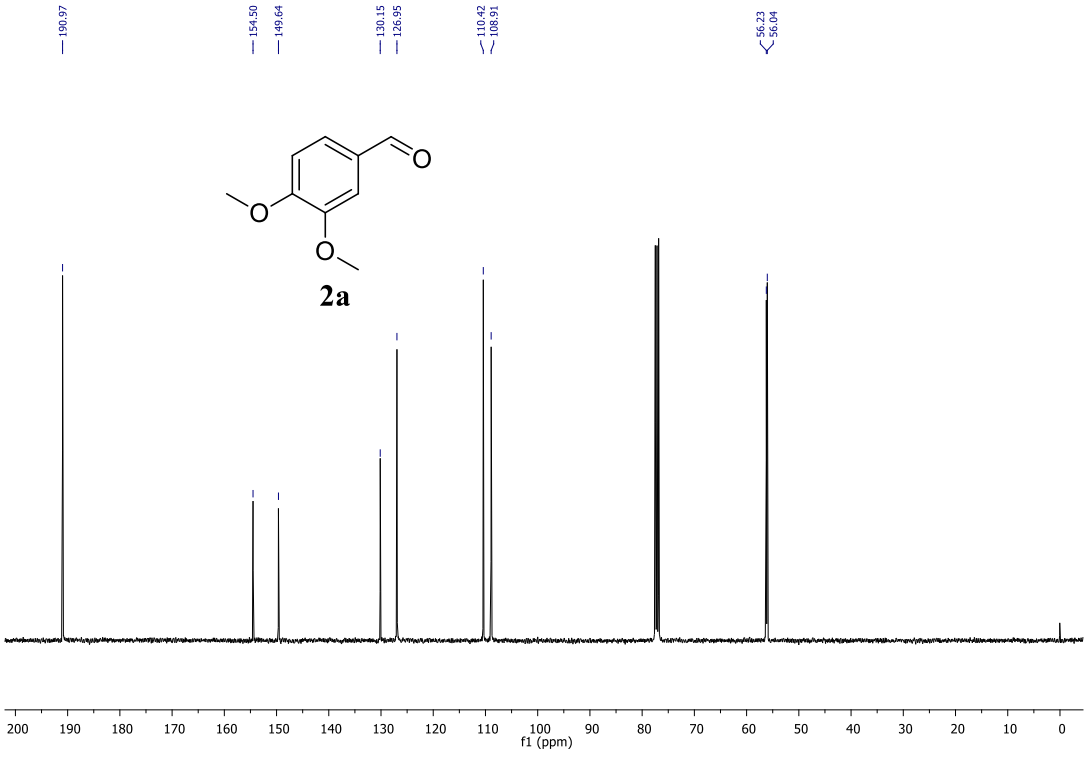


Fig. II. 3: ^{13}C {^{1}H} NMR spectrum of **2a**, $CDCl_3$, 100 MHz

1.9 References and Notes

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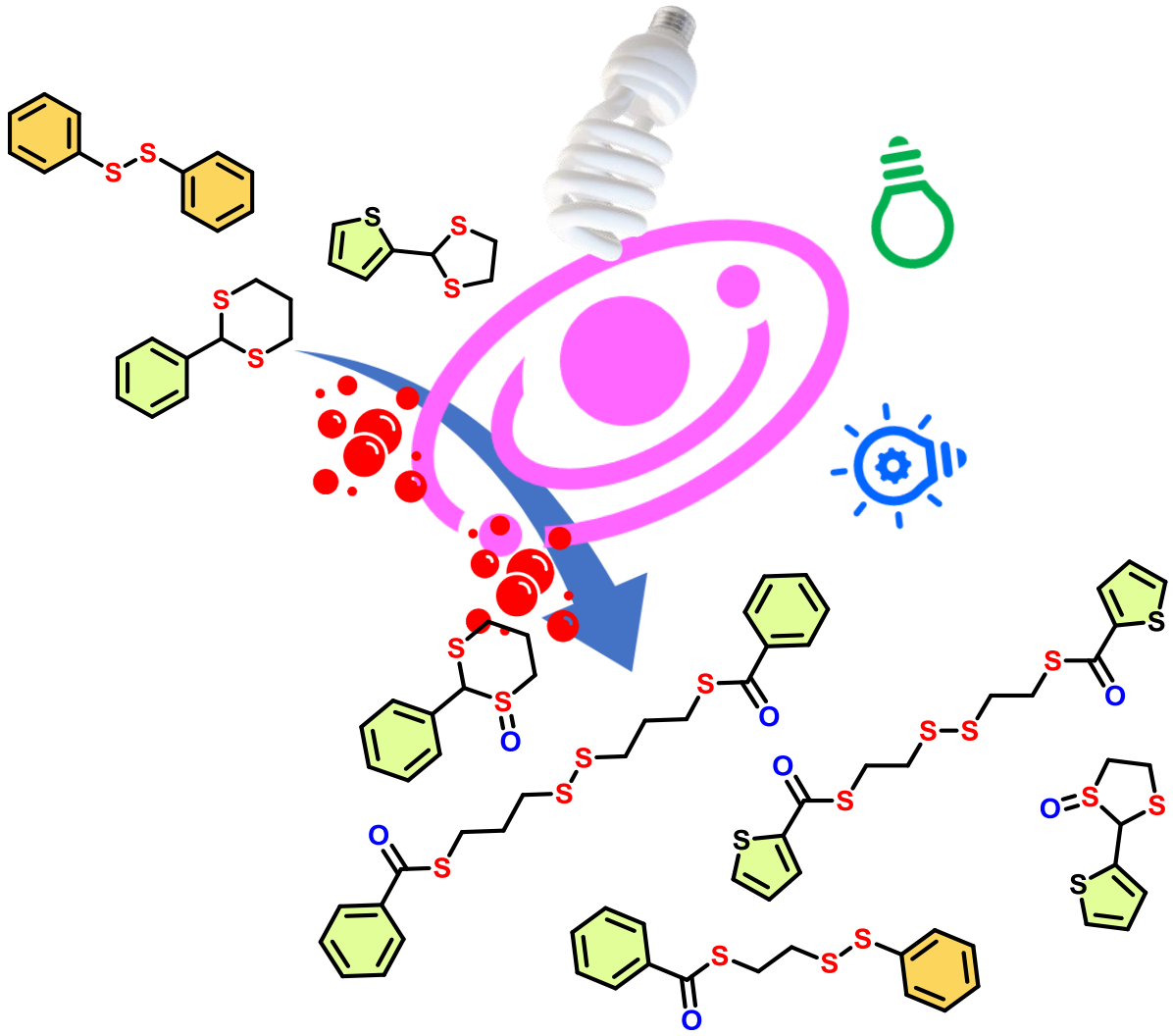
Chapter 3: Rearrangement and Sulfoxidation of 1,3-dithioacetals under Basic Photoredox Conditions



Chapter 3

Rearrangement and Sulfoxidation of 1,3-dithioacetals under Basic Photoredox Conditions

3.1 Abstract:

The oxidation or deprotection of 1,3-dithiolanes into the corresponding sulfoxides or carbonyl compounds are well-established classical processes. In this chapter, base controlled non-traditional selective oxidative rearrangement of 1,3-dithioacetals to furnish disulfide-linked-dithioesters or sulfoxides via photoredox catalysis using visible light has been presented. The unusual reactivity of 5- and 6-membered rings of dithiolanes was observed by swapping the DMAP and Imidazole bases. This observed mode of novel reactivity of dithiolanes is opposite and unique to that of the commonly well recognized reactivity of thioacetals under oxidative reaction conditions. Also, hetero-disulfides have been synthesized by trapping the in situ generated thiyl radical with disulfides as an application of the protocol. A series of control experiments along with cyclic voltammetry as well as Stern-Volmer studies performed to understand the mechanistic insights of the transformation.

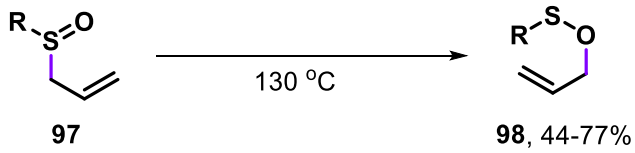
3.2 Introduction

Over the last few years photoredox catalysis has been growing very fast and is an emerging as useful area of organic synthesis. It facilitates a process for the selective transfer of an electron between suitable organic compounds and the excited state photocatalyst under the milder reaction condition to carry out useful organic transformations.[1] Undeniably, with this mode of reactivity, the photoredox catalysis has provides a new opportunity to design and carry out the different transformations and rearrangements in a controlled manner via SET mechanism.[1] The rearrangement reactions plays significant role and have a paramount importance for providing the direct access to a diverse functional groups through formation

and cleavage of multiple bonds in one pot. The rearrangement reactions provide unusual products in cost effective manner and they are also environmentally friendly as number of steps are decreased, reduces the waste material and solvent usage, saves time and manpower too. These features enhance the utility of rearrangement reactions. In this regard, development of novel rearrangement reactions starting from different precursors to access useful compounds are still challenging and requires attention. However, design and development of rearrangement reaction requires suitable substrates with appropriate reaction conditions so as to facilitate the cleavage and formation of multiple bonds in a controlled manner and this is a difficult and challenging task to achieve in one pot. Among many types of rearrangement reactions, rearrangement reactions of sulfur containing compounds are well documented in the literature.[2] Some of the selected representative rearrangements of organosulfur compounds have been discussed.

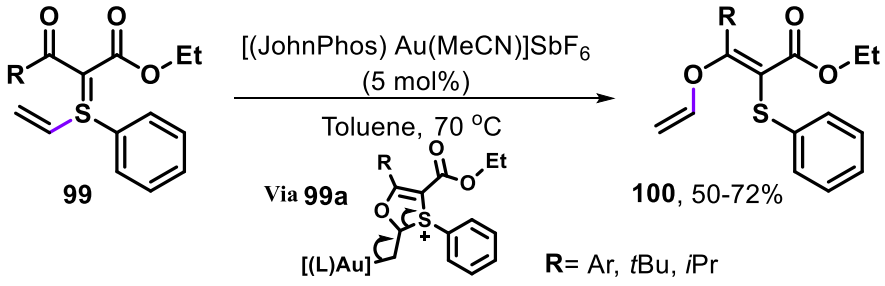
3.2.1. Rearrangements of organosulfur compounds

Scheme 3.1 Mislow-Braverman-Evans Rearrangement



One of the well-known rearrangements of sulfur containing compounds is the [2,3]-sigmatropic rearrangement of allylic sulfoxides **97** to the corresponding allylic sulfenate ester **98** and this is known as Mislow−Braverman−Evans Rearrangement (Scheme 3.1).[3]

Scheme 3.2 Au-Catalyzed [1,4]-Vinyl Migration from Sulfur to Oxygen

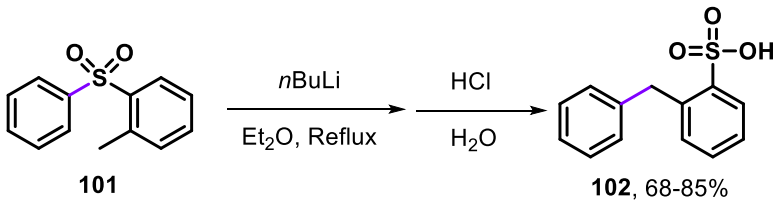


Thermally activated sulfoxonium ylides **99** in presence of π-acidic catalyst undergoes rearrangement reaction via gold catalyzed 1,4–vinyl migration (through an intermediate **99a**) to afford the alkenyl sulfides **100** (Scheme 3.2). This Au–catalyzed [1,4]–vinyl migration (*S*-to-*O* vinyl transfer) takes place at 70 °C in toluene by the cleavage of C–S bond and the formation of C–O bond (Scheme 3.2).[4]

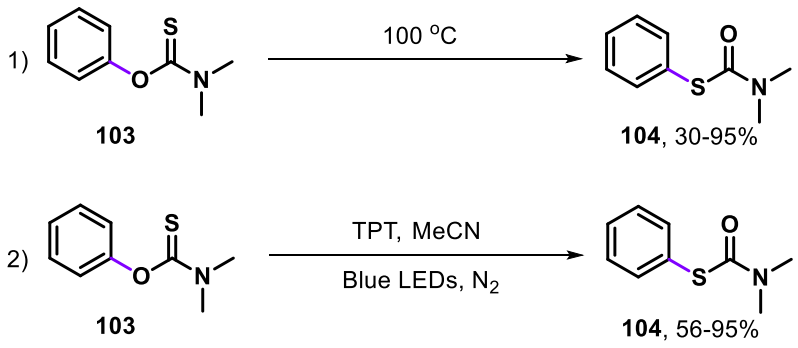
Another class of rearrangement reaction involves the rearrangement by generating the anion at the benzylic position. This rearrangement reaction is known as Truce–Smiles rearrangement reaction that takes place via the *in situ* generation of the benzylic anion by *n*BuLi with the *o*-methyl-diaryl sulfone **101** followed by *ipso*-attack of the anion on other phenyl ring. This would lead to a migration of aryl ring from the sulfur to carbon to form new C–C bond by C–S bond cleavage to access the aryl sulfonic acids **102** (Scheme 3.3a$_1$).[5] The Newman–Kwart rearrangement reaction is the thermal rearrangement of *O*-aryl thiocarbamate **103** to the corresponding *S*-aryl thiocarbamate **104** at an elevated temperature (100 °C) via the *O* to *S* migration of phenyl group. This rearrangement can also be achieved photochemically using the triphenylpyrillium tetrafluoroborate (TPT) as a photocatalyst under blue light irradiation.

Scheme 3.3 Phenyl Migration Rearrangement Reactions

a. **Truce–Smiles Rearrangement Reaction**



b. **Newman–Kwart Rearrangement**



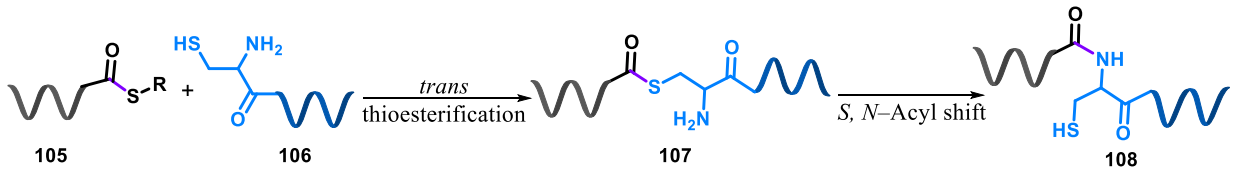
The rearrangement takes place by the generation of sulfur radical followed by the rearrangement of radical leading to the formation of C–S bond via the cleavage of C–O (Scheme 3.3b2).[6]

Dithioacetals are another class of important sulfur compounds and significantly explored so as to masked aldehydes and ketones due to their stability under mild basic as well as acidic conditions.[7] Among them the cyclic dithioacetals have been widely utilized for their umpolung reactivity to access crucial C–C bond forming transformation to synthesized many natural products as well as their important synthetic precursors.[8] It is well known in the literature that most of the times, the C–S bond cleavage under oxidizing reaction conditions furnishes the corresponding carbonyl compounds.[9]

3.2.2. Importance of thioesters

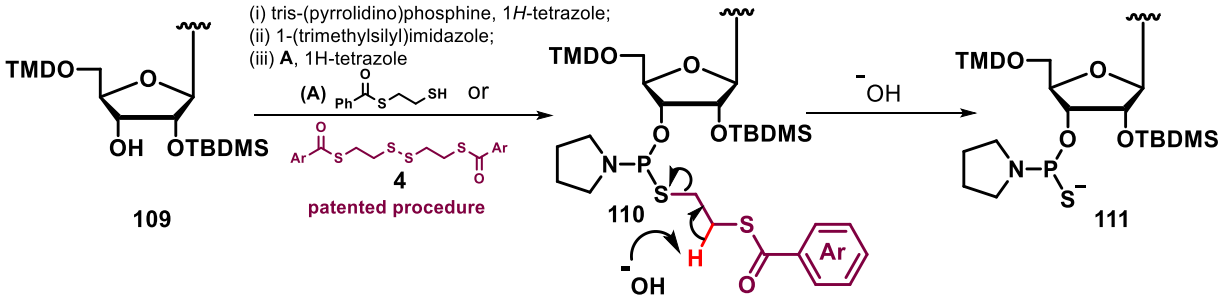
Owing to the importance of thioesters, their synthesis from different stable precursors is very interesting as well as useful. Thioesters are ubiquitously found as an intermediates in many biomimetic as well as biosynthetic pathways such as; fatty acid, esters, polyketide, non-ribosomal peptide syntheses and also in natural products synthesis.[10] Likewise, thioesters **107** (formed through the transesterification of **105** with **106)** have a pivotal role in the NCL (native chemical ligation) via *S,N*-acyl shift with amine group to form an amide derivative **108** (Scheme 3.4). Thioester play an important role in the signal regulation by lipidation of G–coupled protein (receptor) and to probe the enzymatic assembly lines.[11]

Scheme 3.4 Native Chemical Ligation by *S, N* – acyl shift



Notably, disulfide-linked-dithioesters **4** have been regularly used for the phosphorodithioate-modified DNA synthesis for gene silencing activity through solid phase synthesis **111** via the reaction of **109** and disulfide-linked-dithioesters **4** (through intermediate **110)** due to the ease of deprotection of such kind of molecules under the mild basic reaction condition as the rest of the DNA moiety remains untouched (Scheme 3.5).[12]

Scheme 3.5 Utility of disulfide-linked-dithioesters in the Phosphorodithioate-modified DNA Synthesis.

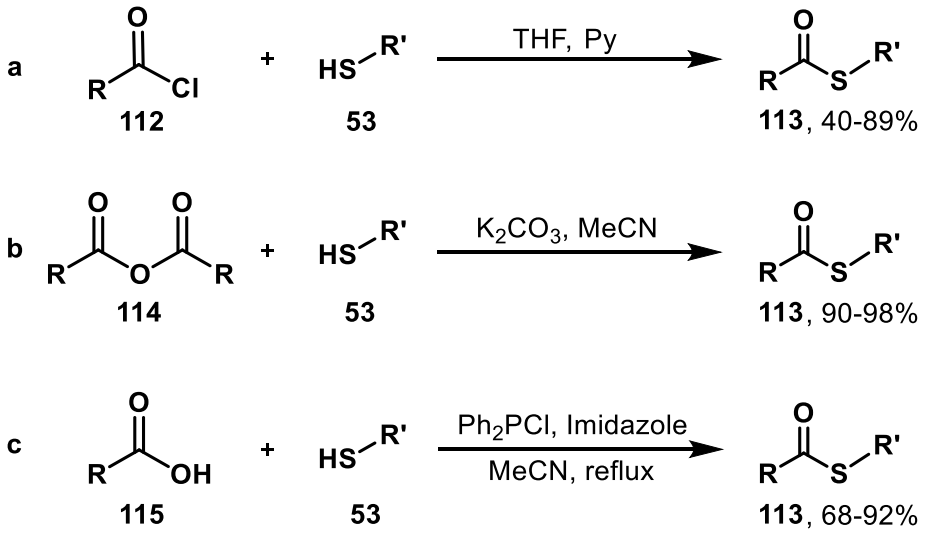


Owing to the importance of thioesters in many biosynthetic pathways as well as in DNA synthesis and also for their use in different transformations to synthesize useful organic functionalities, the synthesis of thioesters is always desirable. Apart from the existing methods that require highly reactive starting materials or the harsh reaction conditions, the synthesis of thioesters starting from easily available and less reactive substrates under mild reaction conditions is required.

3.2.3. Synthesis of thioesters

Traditionally, the synthesis of thioesters has been achieved from carboxylic acids/acid chloride/acid anhydride by reaction with thiols (Scheme 3.6).[13]

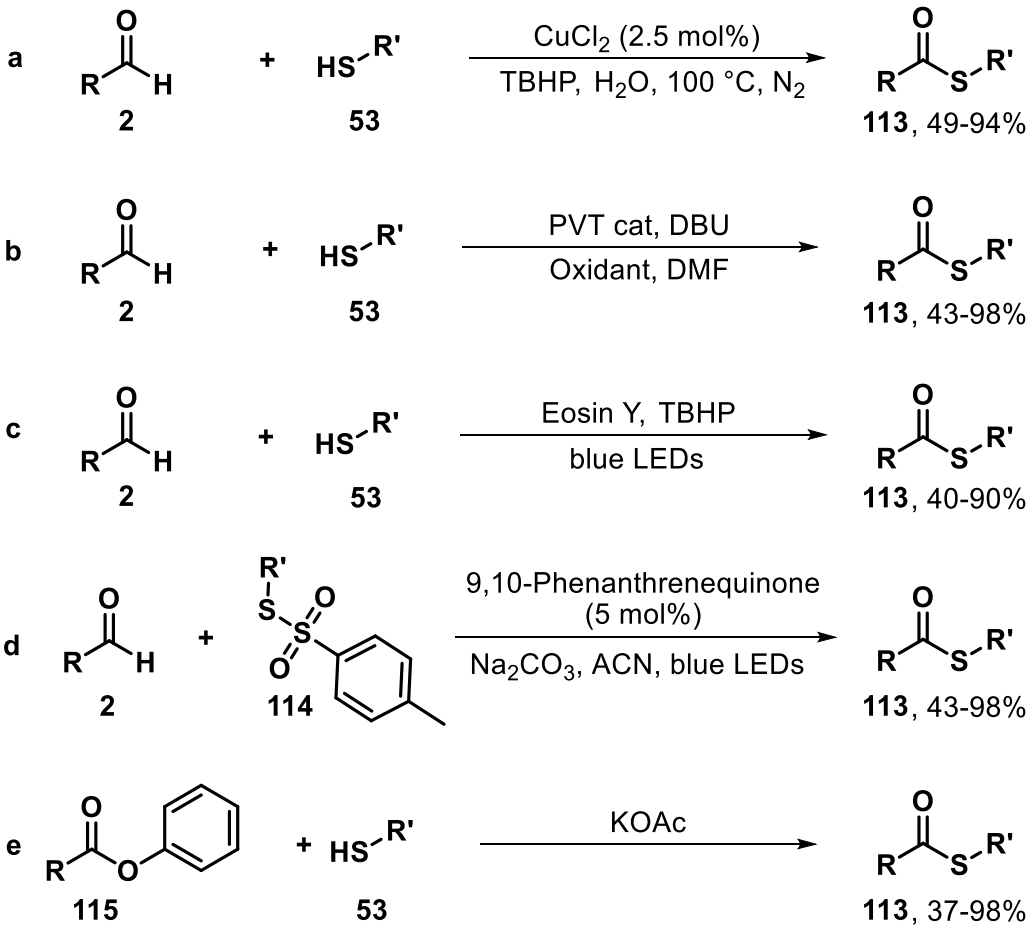
Scheme 3.6 Synthesis of thioesters from acid chloride, acid anhydride and carboxylic acids



Highly reactive acid chlorides **112** reacts with thiols **53** under alkaline conditions to afford the particular thioesters **113** (40%-89% yield, Scheme 3.6a). Likewise, reactive acid anhydrides **114** reacts easily with thiols **53** under alkaline conditions to afford the thioesters **113** (90%-98% yields, Scheme 3.6b). On the other hand, the thioester synthesis starting from the less reactive carboxylic acid **115** is not very straightforward. In this regard, carboxylic acid **115** have been activated *in situ* by treating with phosphorous reagent under alkaline conditions so as to react with thiols **53** to access the corresponding thioesters **113** in a good yield (up to 92%, Scheme 3.6c).[13]

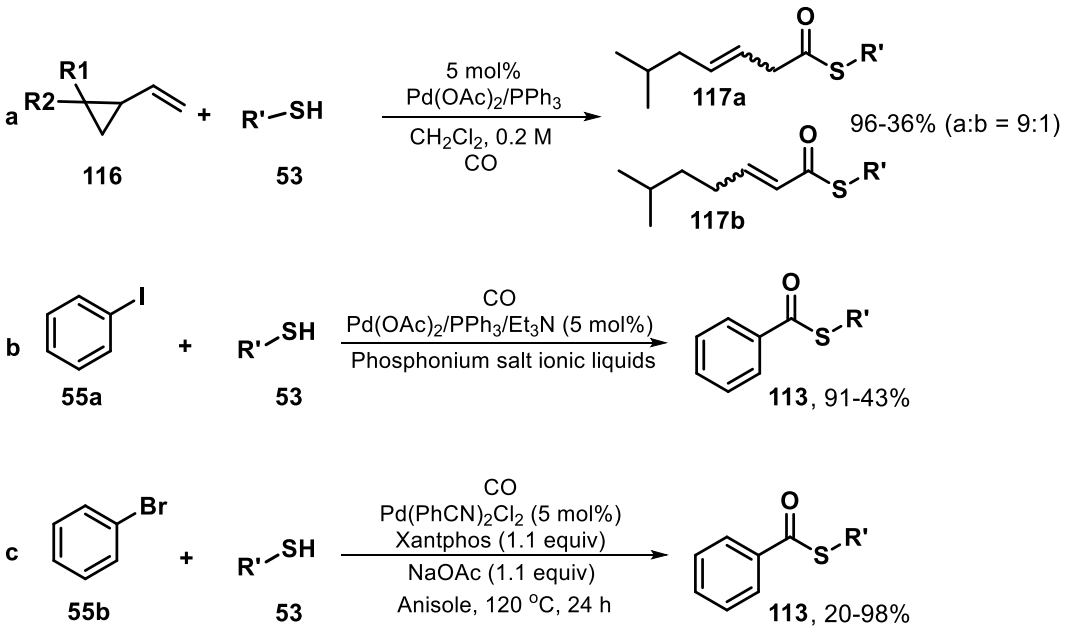
Apart from these conventional methods, many efforts have been made to synthesize the thioesters starting from other compounds. Some of these methods relied on transition metal catalysts as well as activating-promoting/oxidizing reagents to access thioesters (Scheme 3.7). Though some of these methods are useful however, wider applications have been limited due to reaction conditions.

Scheme 3.7 Synthesis of thioesters from the aldehydes and esters



The synthesis of thioesters **113** starting from aldehydes **2** has been reported using copper catalyst ($CuCl_2$) and in presence of oxidizing reagent such as *tert*-butyl hydroperoxide at an elevated temperature (100 ^oC) (Scheme 3.7a).[14] Similarly, the synthesis of thioesters **113** has been disclosed starting from aldehydes **2** and thiols **53** using poly(3,4-dimethyl-5-vinylthiazolium) catalyst (PVT) in presence of DBU as base and stoichiometric amount of phenazine as an oxidant (Scheme 3.7b).[15] Very recently, thioesters **113** have been also synthesized starting from aldehydes **2** and thiols **53** under photoredox catalytic conditions using Eosin Y as a photocatalyst and TBHP as a HAT catalyst (Scheme 3.7c).[16] Thioesters **113** have been synthesized from thiosulfonate *S*-esters **114** and aldehydes **2** in presence of 9,10-phenanthrenequinone as a photo-induced HAT catalyst via the generation of an acyl radical (Scheme 3.7d).[17] Phenyl esters **115** have been successfully employed along with thiols **53** in presence of potassium acetate to access thioesters **103** though with limited substrate scope (Scheme 3.7e).[18]

Scheme 3.8 Synthesis of thioesters through thiocarbonylation using metal catalyst



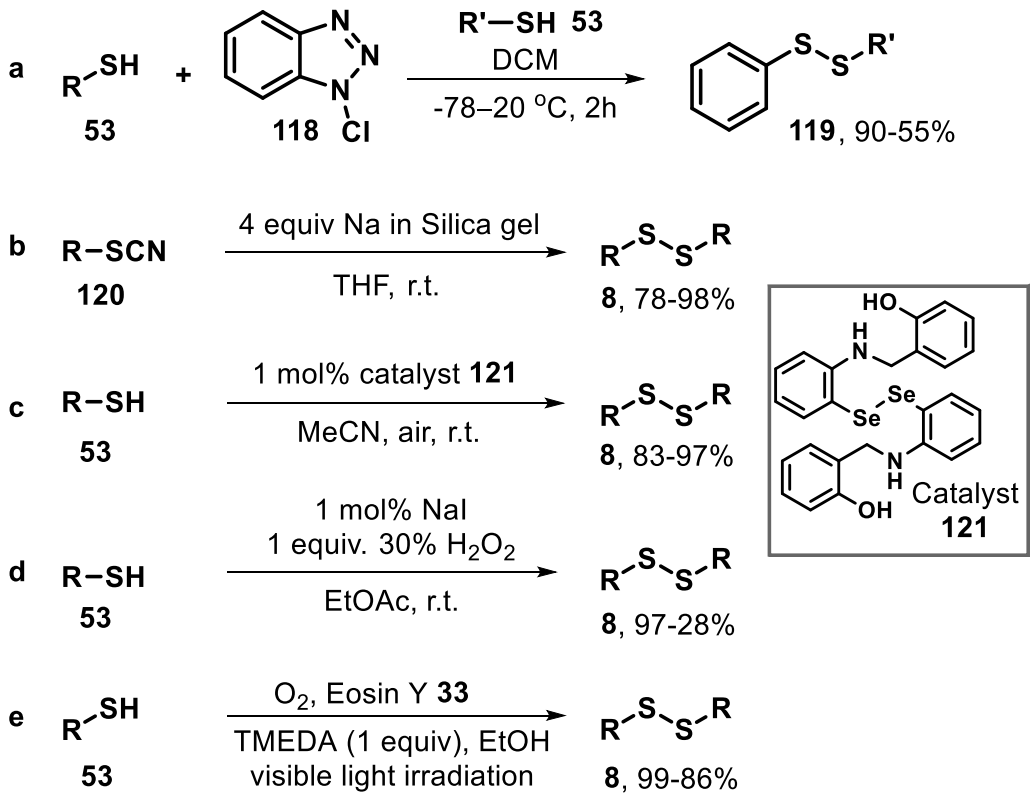
Alternatively, thioesters have been also synthesized via thiocarbonylation of different compounds using transition metal catalyst and carbon monoxide. The palladium catalyzed thiocarbonylation of the vinyl cyclopropanes **116** with thiols **53** and carbon monoxide has been explored to access the thioesters **117a/b** via by cyclopropane ring opening through

organometallic catalytic pathway (Scheme 3.8a).[19] The thiocarbonylations of aryl iodides **55a** and the aryl bromides **55b** have been achieved using thiols **53** and CO in presence of different palladium catalysts under two different reaction conditions to access thioesters (Scheme 3.8b, c).[20, 21] However, these elegant thiocarbonylation protocols requires the use of expensive as well as toxic palladium catalysts and relies on the highly toxic carbon monoxide gas, elevated temperature in some cases.[19-21]

3.2.4. Synthesis of disulfide

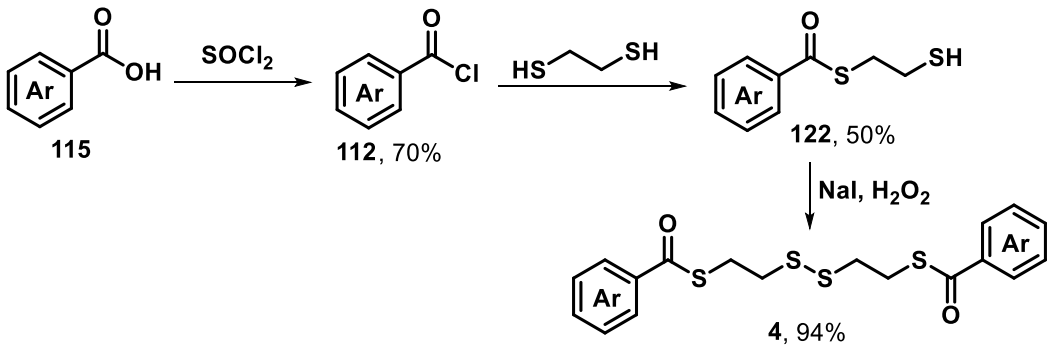
Like thioesters, disulfide-linkages are an important and significant thread in maintaining the structure, function and stability of peptides and proteins. The synthesis of different disulfides under oxidative reactions conditions are known in the literature.[22] Simple disulfides **119** have been synthesized easily from thiols **53** and *N*–chloro benzotriazole **118** at a very low temperature (Scheme 3.9a).[23] Alkyl thiocynates **120** have been utilized to access the corresponding alkyl disulfides **8** using sodium metal (4 equiv.) in silica gel (Scheme 3.9b).[24]

Scheme 3.9 Synthesis of different disulfides



Interestingly, disulfides **8** have been synthesized starting from thiols **53** and using diaryl diselenide as catalyst **121** (1 mol%) relying on the principle of reversible bond formation between the sulfur and selenium atoms (Scheme 3.9c).[25] Disulfides **8** have been also synthesized from thiols **53** using NaI (1 mol%) under oxidizing reaction conditions (H_2O_2) (Scheme 3.9d).[26] Even the photoredox catalysis has been explored for the synthesis of disulfides **8** starting from thiols **53** in presence Eosin Y (1 mol%) and molecular oxygen via SET process (Scheme 3.9e).[27] Undeniably, due to their reversible reactivity and wide utility, thioesters as well as disulfides functionalities have been extensively employed for the labeling of biomolecules (proteins, nucleic acid, carbohydrate, lipids).[28] Moreover, these useful scaffolds have been employed sophisticatedly in the drug delivery and synthesis of biomolecules.[29] Looking at the enormous utility and dynamic reactivity of these thioesters and disulfides, surprisingly there are hardly any straightforward protocols to obtain the compounds encompassing both disulfide and thioester functionalities. Some of the available limited methods requires the multi-steps to synthesize the compounds containing disulfide and thioester moieties (Scheme 3.10).[12] a carboxylic acid such as benzoic acid **115** and 1,2-ethane dithiol have been utilized to synthesize compound **4** under oxidizing reaction conditions. Benzoic acid **115** was treated with $SOCl_2$ to generate the corresponding acyl chloride **112** which upon treatment with 1,2-ethane dithiol afforded the **122**. This on treatment with NaI/H_2O_2 afforded the disulfide-linked-dithioesters **4** in good yields however the overall yield of the reaction is quite less (nearly 33%) starting from the acids **115** (Scheme 3.10). However, the synthesis of disulfide-linked-dithioesters **4** starting from a substrate in straightforward method on lesser number of steps or one pot is quite challenging and demanding.

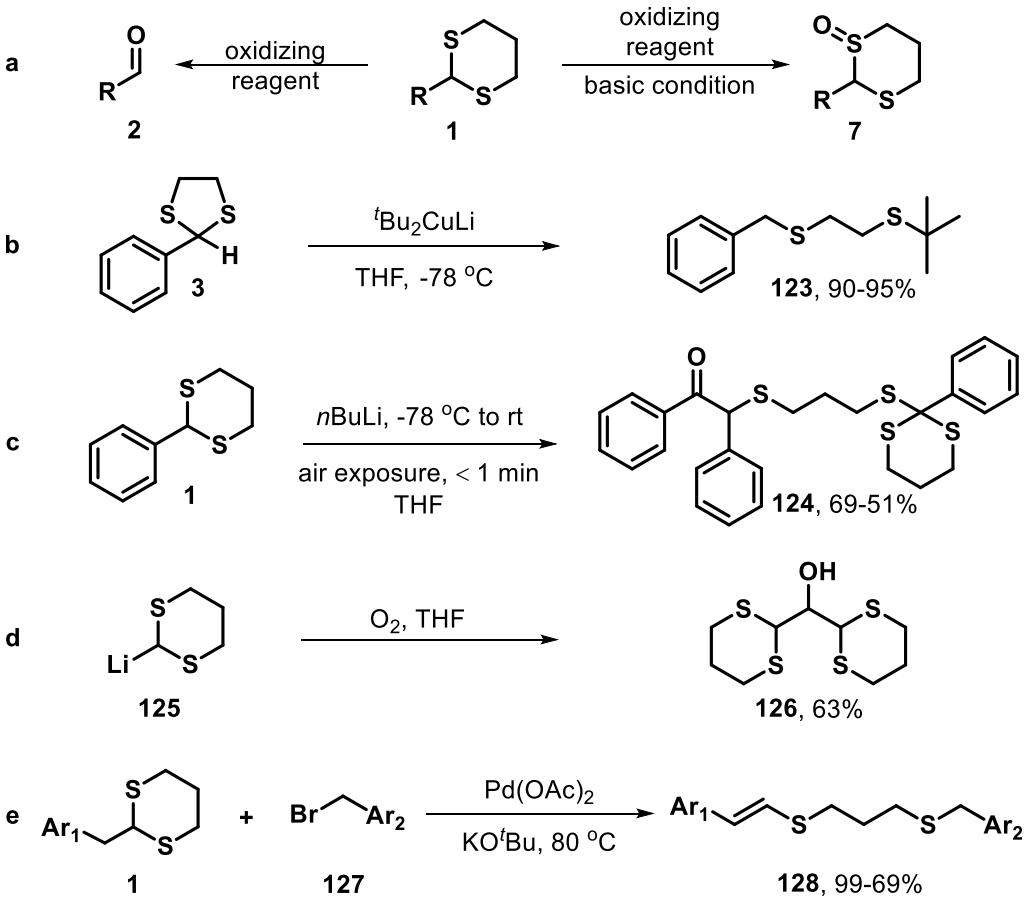
Scheme 3.10 Multi-step synthesis of disulfide-linked-dithioesters



3.2.5. Different transformations of cyclic dithioacetals

Over the past few years, the visible light photoredox catalysis has been explored successfully for many transformations as it relies on clean energy source under milder and sustainable reaction conditions. In general, many useful organic compounds have shown very exciting reactivities under photoredox catalysis and in particular different organosulfur compounds have been explored for their reactivity under photoredox catalysis.[30] The direct C–S bond cleavage under mild reaction conditions has been elegantly explored using the photoredox catalysis and oxidizing reaction conditions.[31] Astonishingly, the selective and controlled cleavage of single C–S bond of dithioacetals under the oxidizing reaction conditions has not been documented using the photocatalysis till date.

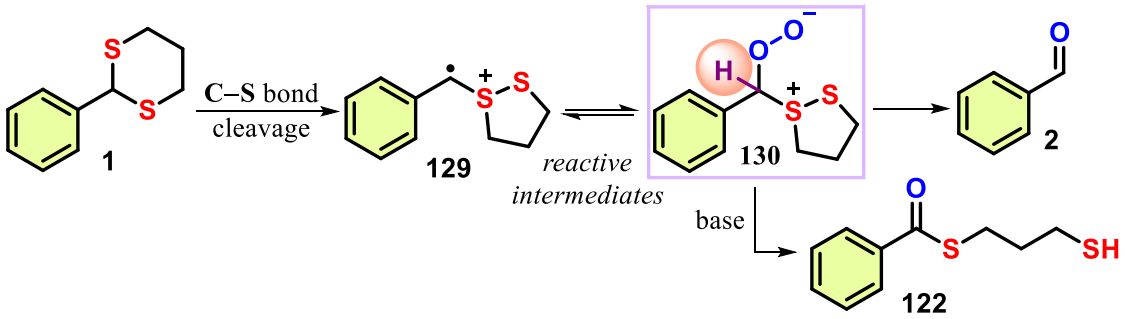
Scheme 3.11 Different transformations of cyclic-dithioacetals by C-S bond cleavage



Owing to the difficulty in cleaving the one C–S bond in a controlled manner and without breaking the second C–S bond under oxidizing reaction conditions as it may oxidize easily and subsequently facilitate the cleavage. Usually, the cleavage of first C–S bond instantaneously assists the cleavage of the next C–S bond to furnish the deprotected aldehydes **2** as observed in case of **1** (Scheme 3.11a). Typically, cyclic thioacetals derived from aldehydes **1** may undergo simple oxidation of sulfur atom to afford the corresponding sulfoxide as final product **7** without the C–S bond cleavage (Scheme 3.11a).[32, 33] On the contrary to the earlier observations, researchers have discovered different rearrangement reactions of cyclic dithioacetals (**1** and **3**) by exploring reactivity of *in situ* generated lithiated dithioacetals intermediates to afford the corresponding products **123** and **124** respectively by cleavage of C–S bonds (Scheme 3.11b, c).[34,35] Even the reaction of lithiated thioacetal **125** in presence of molecular oxygen has been explored to form corresponding alcohol **126** in a good yield **(** 60%, Scheme 3.11d).[35] These rearrangement reactions of thioacetals proceed through the C–S bond cleavage of dithioacetals without much of control. However, the requirement of cryogenic temperature and the use of strong bases such as *n*-butyl lithium limits the wider applicability for different substrate scopes of these rearrangements (Scheme 3.11b-d).[34,35,36] The clean synthesis of thioester from highly reactive *in situ* generated lithiated dithioacetal intermediate under the reaction condition may not be a viable idea as the organolithium reagent is well known to attack the reactive esters/thioesters to form corresponding ketones or *tert*-alcohols. Recently, Schmink and coworkers have demonstrated $Pd(OAc)_2$ mediated synthesis of dithioethers **128** starting from thioacetals **1** and aryl bromides **127** in presence of KO^tBu through the selective C–S bond cleavage of thioacetals in absence of oxidizing reagents at an elevated reaction temperature (Scheme 3.11e).[37] This protocol reported the cleavage of the C–S bond of cyclic dithioacetal to offer novel olefins-thioethers product **128** in one single step. Apart from tapping the umpolung of reactivity, cyclic dithioacetals have been seldom employed for other kind of transformation in the literature to the best of our knowledge. Very few reactions have been explored by the selective cleavage of single C–S bond of cyclic dithioacetals and almost all the reported procedures, furnished interesting and unusual yet unique rearranged products. However, to the best of our knowledge the selective and controlled cleavage of single C–S bond of cyclic dithioacetal to access the thioester under oxidizing reaction conditions has not been well thought by organic chemist. The synthesis of thioesters from cyclic dithioacetals has not been achieved via traditional routes so far possibly because the difficulty in selective C–S cleavage under the oxidizing reaction conditions as it may lead to undesirable products.

Since, we have been pursuing the organic transformation involving sulfur containing compounds via photoredox catalysis, we became curious to explore the development of challenging strategies. Earlier, we had established the visible light mediated facile deprotection of dithianes (Chapter 2). While we were investigating the mechanistic pathway of the deprotection of cyclic dithiane to the corresponding aldehyde via photoredox catalysis (Chapter 2),[32a] we believed conceivably that the deprotection of dithiane is going through a distinct reactive intermediate and by the cleavage of C–S bond. Also, based on our earlier literature reports by Peñéñory *et al* [32b] and Kiyoshi *et al*[38] we hypothesized that cyclic dithioacetals **1** under photoredox catalysis in presence of appropriate base (alkaline condition) under oxidizing condition may lead to the formation of thioesters **122** by abstracting the acidic proton of the intermediate **130** using a mild base (Scheme 3.12). As reported earlier that *in situ* generated intermediate **129 (**from cyclic dithioacetal **1)** react with superoxide radical anion to proceed to the next intermediate **130**. This intermediate in the presence of base (abstraction of a proton) may lead to thioester **122** (Scheme 3.12) if not then **130** usually offers the corresponding aldehyde **2**.[38]

Scheme 3.12 Hypothesis



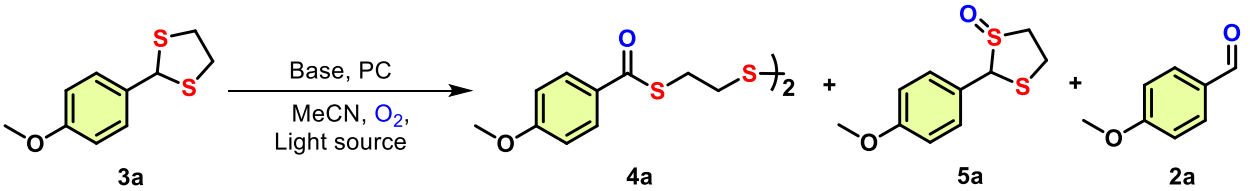
To validate our hypothesis, we planned to explore the proposed strategy in a systematic way. Herein, in this chapter, we describe switchable transformations for the synthesis of disulfide-linked-dithioester and sulfoxides from 1,3-dithiolanes/1,3-dithianes in a controlled manner by simply swapping the bases via visible light photoredox catalysis under oxygen atmosphere. This transformation is driven by the rearrangement of cyclic dithioacetals via single C–S bond cleavage under green light irradiation in alkaline conditions.

3.3 Results and Discussion

3.3.1 Optimization studies for the dithiolane transformations

Initially the separate reaction of **1a** as well as **3a** in presence of EY and K_2CO_3 as a base in open-air under the irradiation of green LEDs was set-up. Gratifyingly, the product disulfide-linked-dithioester **4** was isolated only in case of dithiolane **3a** (5-membered cyclic dithioacetal) however from the dithiane **1a** (6-membered cyclic dithioacetal) it offered the corresponding deprotected aldehyde **2a**.

Table 3.1. Optimization of the reaction



Entry	Photo Cat.	Atmosphere	Base	2a	3a	1a'
1[a]	Eosin Y	Open Air	K_2CO_3	33	trace	50
2[a]	Rh6G	Open Air	K_2CO_3	33	trace	52
3[b]	Rh6G	O_2	K_2CO_3	60	22	0
4[b]	Rh6G	O_2	--	24	43	29
5[b]	Rh6G	Argon	K_2CO_3	0	0	0
6[b]	--	O_2	K_2CO_3	0	0	0
7[b,c]	Rh6G	O_2	K_2CO_3	0	0	0
8[d]	Rh6G	O_2	DMAP	70	16	Trace
9[e]	Rh6G	O_2	Imd	17	70	Trace
10[f]	Rh6G	O_2	Imd	04	83	Trace

Reaction conditions: 1a (0.2 mmol), Imd (1 mmol), DMAP (0.4 mmol), MeCN (2 mL), PC (2mol%), K_2CO_3 (0.4 mmol), green LEDs (15 W), under O_2/Ar balloon 6 h. [b]dry MeCN, [c]60 °C No light source, [d]dry (MeCN 1.8 mL+dry toluene 0.2 mL), [e]dry ACN, [f]dry (MeCN 1.5 mL+*t*-BuOH 0.5 mL), Yields are in percentage.

Based on this result, we commenced our screening with a dithiolane **3a** in presence of a PC, EY (2 mol%) and K_2CO_3 as a base in open-air under the irradiation of green LEDs (15 W) at room temperature. The reaction afforded the product disulfide-linked-dithioester **4** from

starting dithiolane **3** along with the deprotection product aldehyde **2a** (Table 3.1, entry 1). Later the screening of **3a** reactions using Rh6G as PC, K_2CO_3 as a base in open-air under the irradiation of green LEDs (15 W) to furnish the product **4a** as observed in case of EY (Table 3.1, entry 2). Later, we observed that the reaction of **3a** using Rh6G, K_2CO_3 under oxygen atmosphere (oxygen balloon) under the irradiation of light (green LEDs 15 W) in anhydrous acetonitrile furnished the respective rearrangement product **4a** comparatively in a higher yield (60%, Table 3.1, entry 3). This result indicated that the presence of moisture facilitated the deprotection of **3a** to yield corresponding aldehyde **2a**. Encouraged by the initial results and to optimize the reaction further to enhance the yields, different photocatalysts such as; EY, Rh6G, $Ru(bpy)_3Cl_2$, $Ir(bpy)_3$, Acr-perchlorate and TPPT were screened for the rearrangement reaction with the irradiation of green LEDs (Appendix-IIIA, Table 1). Based on the screening, we observed that amongst all the PCs, Rh6G found to be more suitable for the rearrangement reaction. Later, we screened different solvents under the initial standardized conditions to optimize the yield of rearrangement product **4a** (Appendix-IIIA, Table 2). Interestingly, among all the solvents the reaction of **3a** in dry acetonitrile and toluene mixture (9:1 v/v) offered the highest yield of **4a** (62%) in relatively lesser reaction time (Appendix-III, Table 2). Based on our further experiments we concluded that base, oxygen atmosphere, dry reaction condition, Rh6G (2 mol%) and green LEDs are absolutely necessary for this transformation (Table 3.1, entries 4-7). We also observed that the starting material remains as it is, in absence of light even at an elevated temperature (60 ^oC, Table 3.1, entry 7). This indicated that light is essential to initiate the transformation. Further, to optimize the base, different bases screened for rearrangement of **3a** while maintaining other optimized reaction conditions. Among all the bases, we observed that DMAP delivered the rearranged product **4a** in maximum yield and the respective sulfoxide **5a** in trace amount (Table 3. Appendix-IIIA).

During the base screening we observed that the rearrangement reaction of **3a** in presence of imidazole as a base afforded the sulfoxide **5a** in significantly higher yield and the yield of desired **4a** reduced (Table 3.1, entry 9). Alongside, we screened different solvents for the reaction of **3a** in presence of imidazole as a base and among all the solvents, the combination of anhydrous MeCN and *t*-BuOH as solvent (3:1) proved to be optimum and the yield of **5a** was decreased (Table 31, entry 10 and Appendix-IIIA, table 4).

Finally, we also screened the different additives to further increase the yield of product **4** by screening with different oxidizing reagents and other additives in order to check the suitable

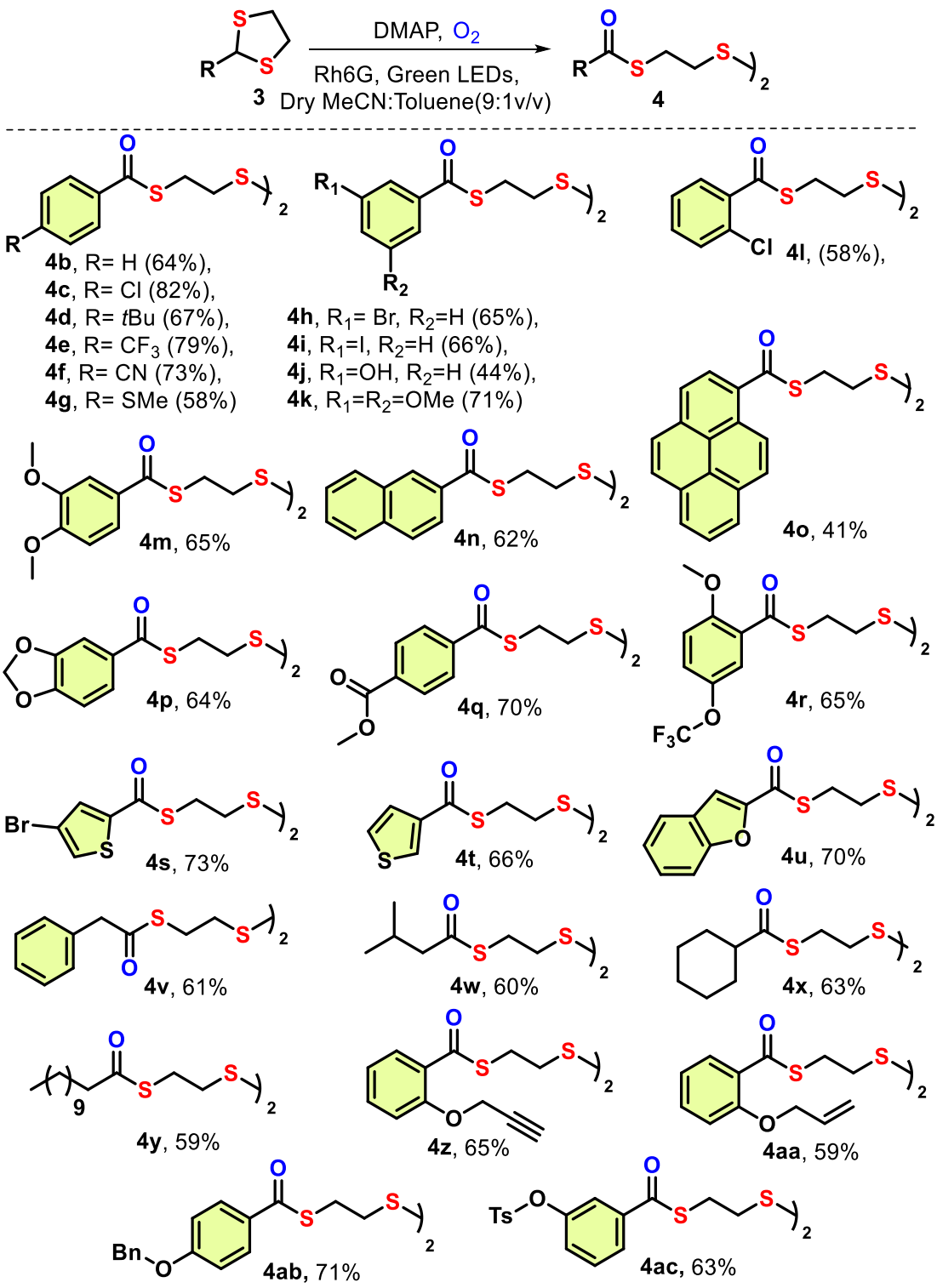
oxidizing reagent and to restrict the other parallel photocatalytic cycle operating during the reaction (Appendix-IIIA, table 5). Experimental results showed that the molecular oxygen is the best oxidizing agent to obtain the product **4a** in good yield. While, the screening of other additives such as: nitrobenzene, 2,4-dinitrobenzaldehyde, dimethyl sulfide, thioanisole, S_8 and Se powder prove to be fruitless in order enhance the yield of **2a** (Appendix-IIIA, table 5).

After the exhaustive screening dithiolane **3a**, Rh6G (2 mol%) as PC, DMAP as base (2 equiv.) in dry solvent (MeCN: toluene; 9:1, v/v), oxygen atmosphere under the irradiation of light (green LEDs, 15 W) established as the optimized reaction conditions to achieved the rearrangement product **4a** in higher yield. Likewise, along with the optimization to access **4a** we also optimized the reaction condition for obtaining sulfoxide **5a** in higher yield. Based on screening, dithiolane **3a**, Rh6G (2 mol%) as a PC, imidazole as base (5 equiv.), oxygen atmosphere in anhydrous solvent (MeCN: *t*BuOH; 3:1, v/v) under the irradiation of green LEDs (15 W) established as an optimum reaction condition to obtain **5a** exclusively.

3.3.2 Substrate scope for the rearrangement (4) and Sulfoxidation (5)

With the optimized reaction conditions in hand to access disulfide-linked-dithioester **4a**, we set out to explore the substrate scope for disulfide-linked-dithioesters starting from different cyclic dithioacetals. In this regard different dithiolanes **3** were synthesized starting from different aldehydes and 1,3-propane dithiol (Experimental section, 3.8.2 general procedure A). Different dithiolanes **3a-3z, 3aa-3ac**) under the standardized reaction conditions reacted smoothly to the respective rearrangement products in good to very good yields (**4a-4z, 4aa-4ac**) (Table 3.2). A wide variety of 1,3-dithiolanes derived from aldehydes containing electron donating/electron withdrawing substituents at *p*-position furnished the rearrangement products (**4a-4g**) respectively **(**up to 82% yields). Even the dithiolanes derived from aldehydes containing *m*-substituents as well as dithiolanes derived from aldehydes containing *o*-substituent reacted efficiently to afford the desired rearrangement products (**4h-**

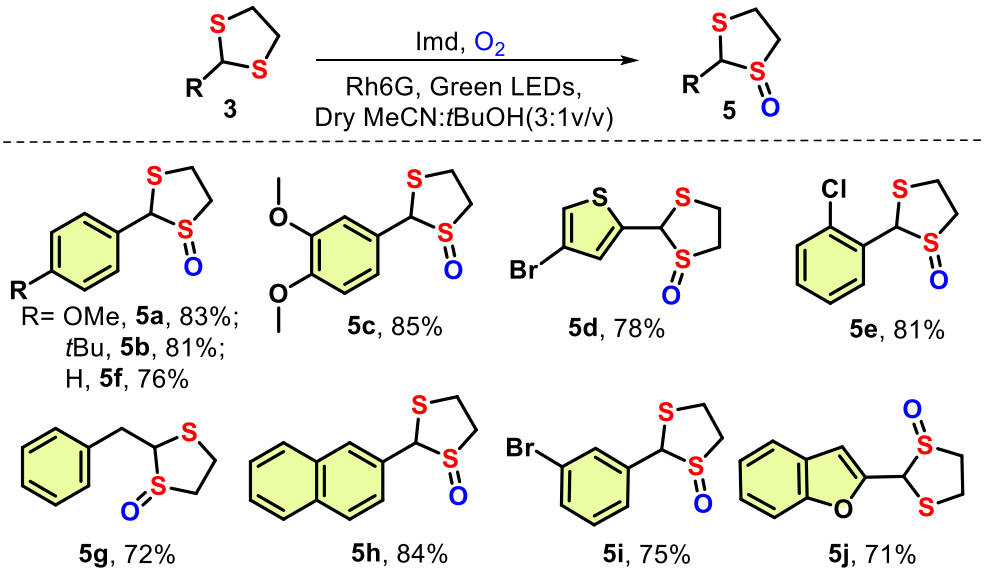
Table 3.2 Substrate scope for rearrangement of dithiolane



Reaction conditions: 3 (0.2 mmol), DMAP (0.4 mmol), MeCN (1.8 mL), Toluene (0.2 mL), Rh6G (2 mol%), Oxygen balloon, green LEDs (15 W).

-4k) (up to 71% yields, Table 3.2) and **4l** in moderate yield (58%) respectively. The dithiolane with *ortho* substituent might have given relatively less yield probably due to the steric crowding. The dithiolane **3n** derived from 2-naphthaldehyde offered the corresponding product in moderate yield under the optimized reaction condition (**4n,** 61%). However, the dithiolane **3o** derived from pyrene aldehyde furnished the particular disulfide-linked-dithioester **4o** in modest yield (41%). Dithiolane derivatives derived from different aldehydes containing dioxolane, ester and trifluoromethyl group reacted smoothly to afford the corresponding rearranged products (**4p, 4q, 4r)** (up to 70% yields, Table 3.2). The dithiolanes derived from different heterocyclic aldehydes also worked nicely to afford the disulfide-linked-dithioesters **4s-4u** respectively (up to 73% yield). Even the aliphatic thioacetals also provided the desired products (**4v-4y**, up to 63% yield) under the standardized reaction conditions. Dithiolanes containing different protecting group substituted aryl rings (OTs, OBn, *O*-allyl, *O*-propargyl) tolerated the reaction conditions well and furnished the corresponding rearrangement product (**4z-4ac**, up to 71% yield, Table 3.2).

Table 3.3 Substrate scope for sulfoxidation of dithiolane



Reaction conditions: 3 (0.2 mmol), Imd (1 mmol), MeCN (1.5 mL), *t*BuOH (0.5 mL), Rh6G (2 mol%), green LEDs (15 W), Oxygen balloon, 12 h.

Next, we have checked the substrate scope for the sulfoxidation product **5** from dithiolanes under the standardized conditions in using of 5 equiv. of imidazole Rh6G (2 mol%), in MeCN:*t*BuOH (3:1) mixture under oxygen atmosphere by green LEDs irradiation (Table

3.3). All the corresponding sulfoxide (**5a, 5b, 5d, 5h, 5l-5n, 5s, 5u, 5v**) were isolated in good to very good yields (up to 85%, Table 3.3). Dithiolane derived from multi-aromatic as well as heteroaromatic aldehydes worked smoothly to provide the corresponding sulfoxides (**5d, 5h** and **5j**) in a good yield (up to 84%, Table 3.3). However, the dithiolane derived from electron withdrawing groups or aliphatic groups did not offered exclusive product formation multiple spots were observed.

3.3.3 Optimization studies for the dithiane transformations

Next, we turned our attention to extend our protocol to other cyclic dithioacetals such as 1,3-dithianes. We commenced a model reaction of phenyl-1,3-dithiane **1a** as a substrate and DMAP as a base under optimized reaction conditions. Surprisingly, we achieved the unexpected sulfoxide product **7a** in excellent yield (90%, Table **3.9**) instead of the predicted rearranged disulfide-linked-disulfide **6a**.

This result has been highly surprising and, in this regard, we gleaned through literature to understand it further. Though, we did not find any precedence on such kind transformation, however, based on the available literature based on the σ-σ*-3e-2-center interaction between the two sulfur atoms, we strongly believe that owing to an extra stability provided in single electron oxidized six membered cyclic 1,3-dithiane species because of the σ-σ*-3e-2-centered interaction might have restrict the ring opening and led to the formation of sulfoxide **7a**. However, this kind of extra stability is not present in the oxidized 1,3-dithiolane (5-membered ring) species reported by the Asmus et al.[39]

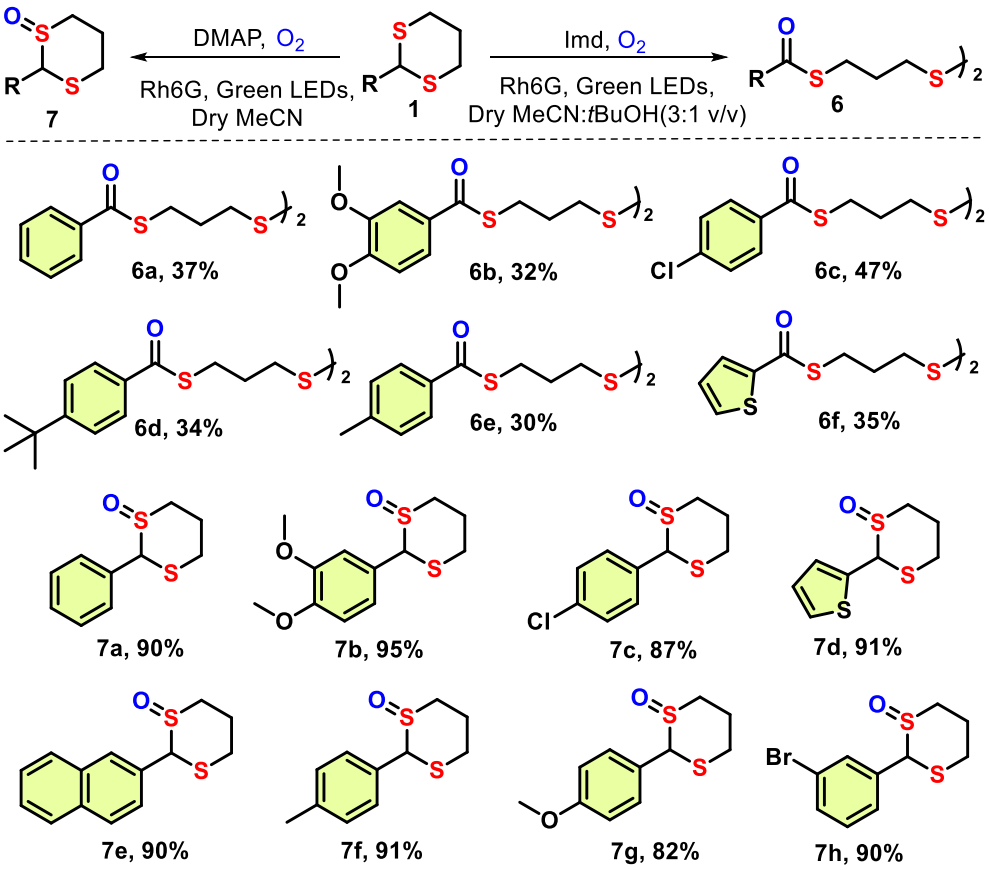
We then directed our attention to achieve the rearrangement product **6a** starting from 1,3-dithiane. In this regard we screened different PC, bases, solvents and other conditions systematically (AppendixIIIA; Table 6-8). After the systematic and detailed screening, dithiane **1a**, Rh6G (2 mol%), imidazole as a base (5 equiv.), anhydrous MeCN and *t*-BuOH (3:1, v/v) turned out to be optimal reaction conditions to afford the corresponding disulfide-linked-dithioester **6a**. Our further attempt to enhance the yield of disulfide-linked-dithioester **6a** by increasing the reaction temperature (50 ^{o}C) while maintaining the other reaction conditions was unproductive as the desired product was formed only in trace amount. Similarly, we also switched our attention to optimize the reaction conditions to synthesize the corresponding sulfoxide **7** exclusively starting from **1**. In this regard, we carried out the exhaustive screening of different solvents and bases systematically (Appendix IIIA; Table 8-9). Based on our detailed and exhaustive screening, phenyl-1,3-dithiane **1a**, Rh6G (2 mol%)

as a photocatalyst, DMAP as a base (2 equiv.), O_2 atmosphere in dry MeCN, green LEDs (15 W) established as an optimized condition to obtain the corresponding **7a**.

3.3.4 Substrate scope for the disulfide-linked-dithioesters (6) and dithiane-sulfoxide (7)

With the optimized reaction conditions in hand for both rearrangement **6** and sulfoxidation **7** of dithiane **1**, we explored the wider substrate scope for this protocol for both sulfoxidation and the rearrangement reaction by using different dithianes. In this regard, we synthesized different dithianes starting from various aldehydes following the reported procedures (See Experimental section). Different substrates **(1a, 1b, 1c, 1d, 1e, 1f)** under the optimized conditions afforded the respective rearranged products disulfide-linked-dithioesters (**6a**, **6b**, **6c**, **6d**, **6e**, **6f**) in moderate yields (up to 47%, Table 3.4).

Table 3.4 substrate scope for dithiane rearrangement and the sulfoxidation



Reaction conditions: 1 (0.2 mmol), Rh 6G (2 mol%), DMAP (0.4 mmol), Imd (1 mmol), Dry Solvents (2 mL), under oxygen, green LEDs (15 W), 24 h.

While, the dithiane substrates (**1a**, **1b**, **1c**, **1e**, **1g**, **1h**, **1i**, **1j**) under the optimized reaction conditions for sulfoxide reacted smoothly to furnish the corresponding sulfoxides (**7a**, **7b**, **7c**, **7e**, **7g**, **7h, 7i**, **7j**) in excellent yields (Table 3.4, up to 95%). These experimental results indicated under the photocatalytic reaction conditions 1,3-dithianes favoured sulfoxide products **7** over rearrangement products **6**.

We surmise that possibly oxidized form of 6-membered cyclic thioacetals is relatively more stable and they may be undergoing slower ring opening. This unusual and anomalous reactivity of six-membered dithiane **1** may be due to the favorable σ-σ* 3e-2-centered bond formation in the single electron oxidized six-membered dithiane.[39] We also hypothesize that imidazole played a significant role not only as a base but also as hydrogen bond donor. Probably, imidazole might be forming hydrogen bonding with the lone pair of sulfur atom and this might have led to the disturbance in the internal stability of oxidized 1,3-dithane and favoured the ring opening to furnish the rearrangement product **6**. While, DMAP as a base furnished the sulfoxide selectively, possibly because DMAP may not disturb the weak σ-σ*-3e-2 centered bond in an oxidized 1,3-dithiane as there is no scope for hydrogen bonding. Hence, the positive charge on sulfur radical cation may be stable and survive for a longer time. Due to this superoxide radical anion may easily react with the oxidized sulfur atom to furnish the exclusive sulfoxide product **7** instead of disulfide-linked-disulfide **6**.

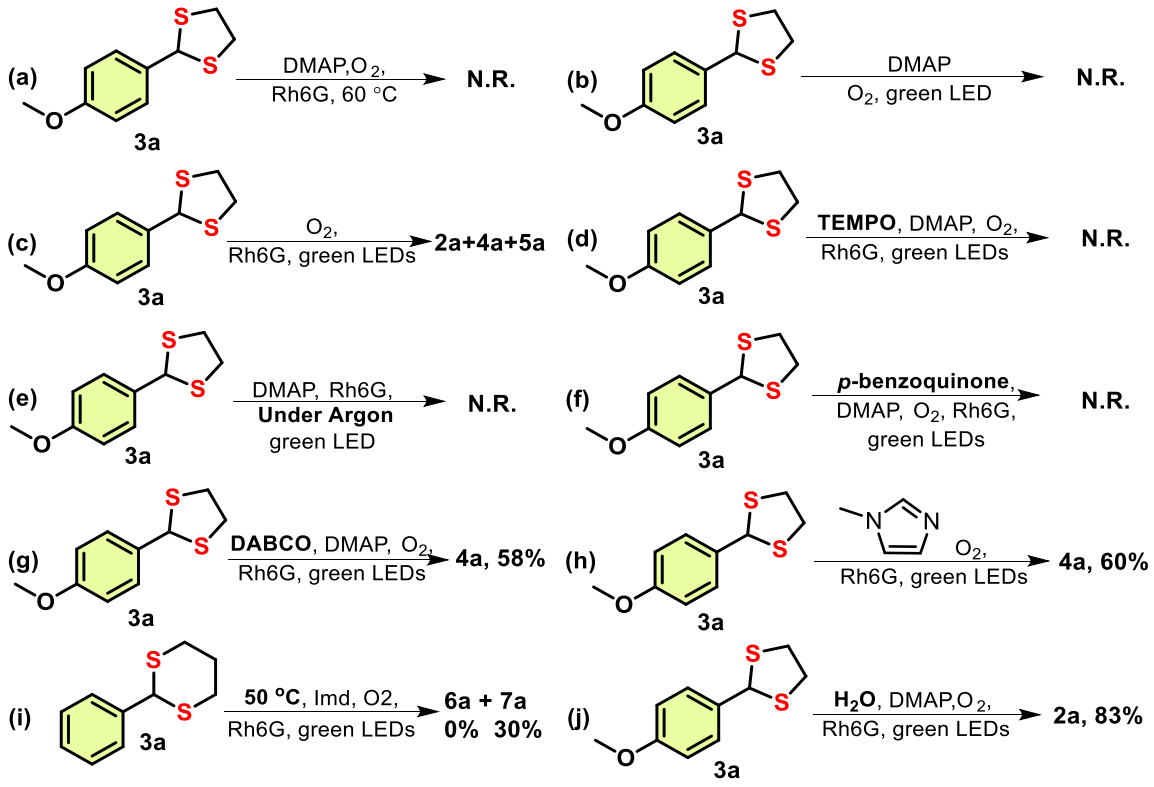
3.4 Mechanistic study

3.4.1 Control Experiments:

Further to understand the most probable reaction pathways, we closely monitored some control experiments to confirm the role of each reagent as well as the necessity of a particular base and molecular oxygen in the reaction pathways. The reaction of **3a** in absence of light at 60 ^{o}C did not work and starting material was recovered as it is, thus suggesting the requirement of light to initiate the transformation (Scheme-3.13a). This also confirmed that the temperature does not play any role in the reaction pathways and the transformation is photocatalytic in nature (Scheme-3.13a). In order to substantiate the photocatalytic pathway of reaction mechanism further, we have carried out the reaction in absence of Rh6G

(photocatalyst) under green LEDs (Scheme-3.13b). The reaction did not proceed without photocatalyst Rh6G suggesting the necessity of photocatalyst (Scheme-3.13b). While reaction in the absence of base furnished three different products this suggesting the key role of base in determining the selectivity of the reaction (Scheme-3.13c).

Scheme 3.13 Control experiments

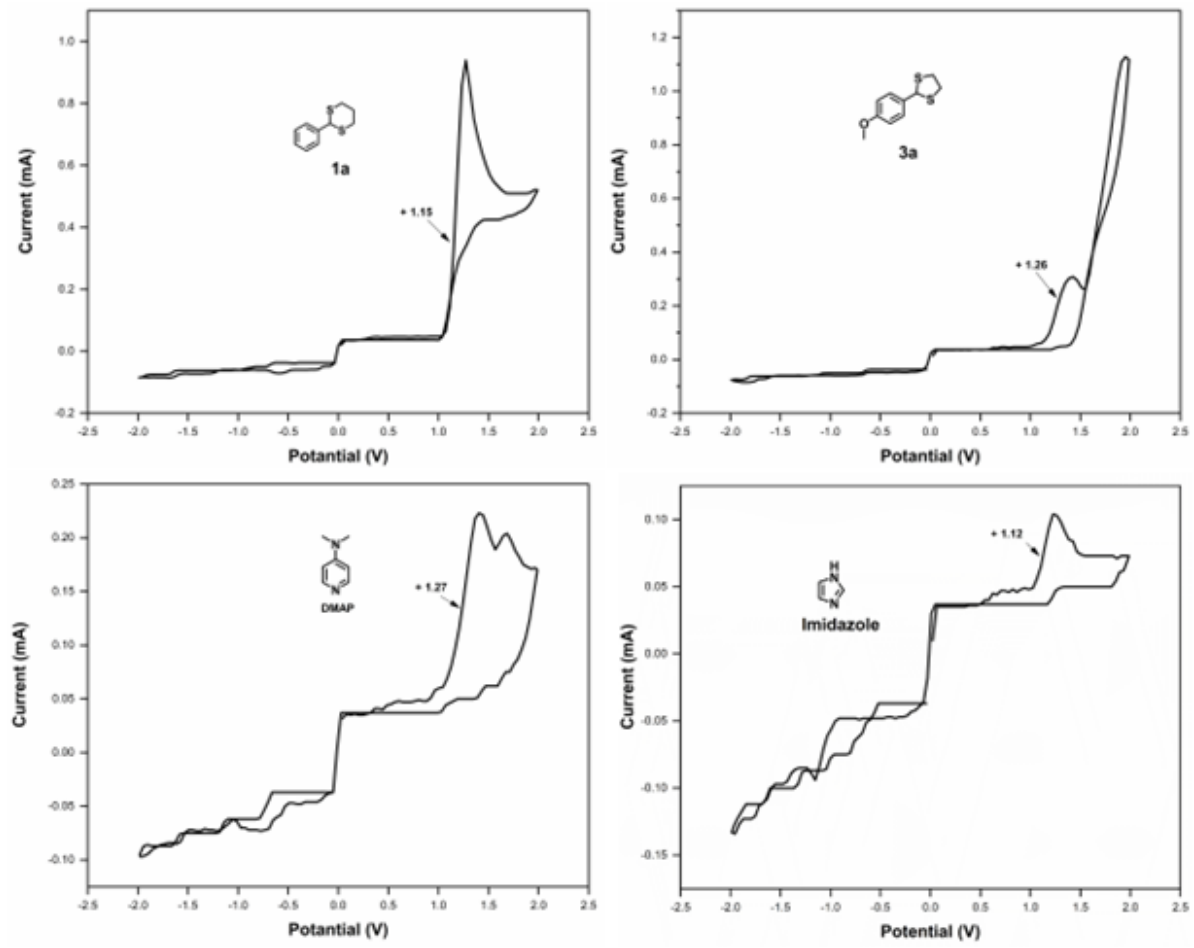


The reaction of **3a** in presence of TEMPO (radical quencher) did not offer the product and this result suggested that reaction pathway is radical in nature (Scheme-3.13d). Moreover, the reaction without oxygen atmosphere (argon atmosphere) did not furnish any product signifying the requirement of oxygen (Scheme-3.13e). In order to confirm the exact species that is generating from the oxygen during the course of the reaction, we carried out the reaction of **3a** in presence of *p*-benzoquinone (as superoxide radical anion quencher) and the in presence of DABCO (singlet oxygen quencher).[40,41] The reaction did not proceed in presence of *p*-benzoquinone thus supported the generation of superoxide radical anion species during the reaction mechanism (Scheme-3.13f).[40] On the other hand, the reaction proceeded smoothly in presence of DABCO thus indicating the no role of singlet oxygen in

the reaction pathway (Scheme-3.13g).[41] Subsequently, to corroborate the role of hydrogen bonding in case of imidazole as a base, we have carried out the two different experiments. Initially, we done the reaction of **3a** using *N*-methyl imidazole (absence of hydrogen). The reaction offered the rearrangement product **4a** instead of sulfoxide **5a** (as observed in case of DMAP) confirming the potential role of hydrogen bonding in reaction pathway. Later, we done the reaction of 1-phenyl-1,3-dithane **1a** in presence of imidazole as a base but at an elevated temperature (50 ℃). Interestingly, the reaction at higher temperature offered the sulfoxide product instead of the rearrangement product albeit in a low yield. We strongly believe that (at 50 ℃) hydrogen bonding might not be effective and also the concentration of the oxygen molecules decreases in the reaction mixture with the increase in the reaction temperature (Scheme 3.13h and i). While the presence of water molecule in the reaction led to the deprotection of **3a** to give aldehyde **2a** as a major product (Scheme 3.13, j).

3.4.2 Cyclic voltammetry studies

Fig. 3.1 Cyclic Voltammogram

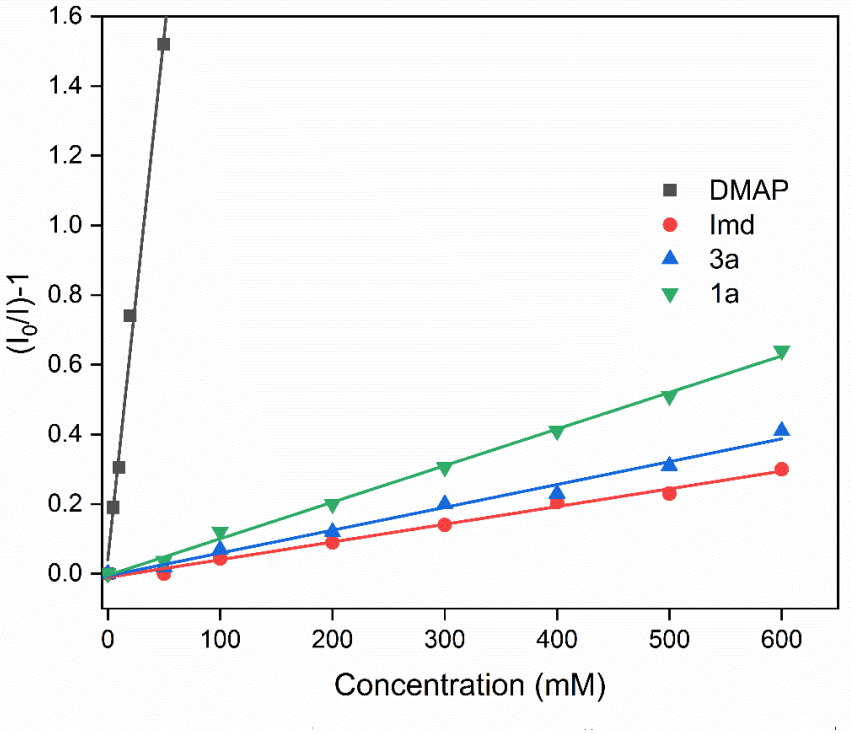


In order to understand the reaction mechanism, we have carried out the cyclic voltammetry studies of **1a**, **3a**, **DMAP** and Imidazole (**Imd**) (Fig. 3.1). We observed the redox potential of **1a**, **3a** and **DMAP** and **Imd** are within the range of Rh6G* and hence electron transfer is possible with all the species (Fig 3.1). CV measurements suggested that (see ESI 4.2 AE) all compounds have redox potential [**1a** dithiane (+1.26 V), **3a** dithiolane (+1.15 V), DMAP (+1.27 V), Imidazole (+1.12 V) vs Ag/AgCl] in the close range of Rh6G* (+1.39 V).[24] The cyclic voltammetry was performed using a IKA ElectraSyn 2.0, a glassy carbon working electrode, a platinum plated counter electrode, and Ag/AgCl reference electrode. Sample were prepared with a substrate concentration of 3 mM and 100 mM tetrabutylammonium perchlorate in MeCN solution. Data was collected with a scan rate of 50 mV/s.

3.4.3 Stern-Volmer study

Further, to confirm the priority of different species for the SET process with Rh6G*, we have carried out the emission quenching experiments with Rh6G with the increase in concentration of DMAP, Imidazole, dithiolane and dithiane separately at a constant concentration of Rh6G (1 µm) (Fig 3.2). Emission spectra were collected on Horiba Jobin-Yvon, Fluoromax-4 spectrophotometer with xenon light source with excitation and emission slit widths of 1/1 nm.

Fig. 3.2 Stern-Volmer graph



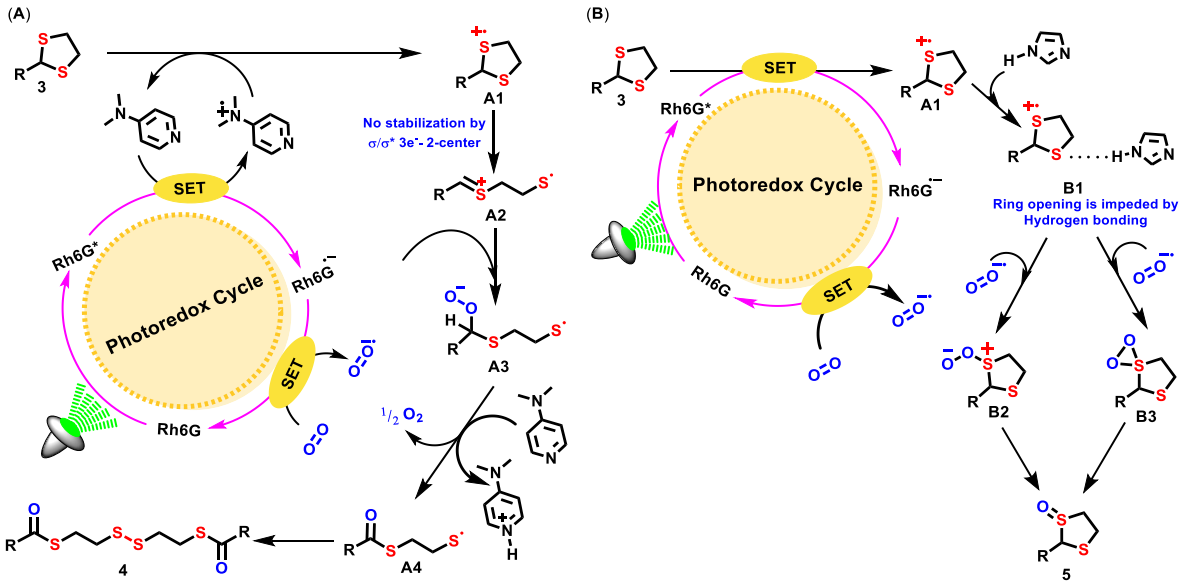
Experiments were carried out using a 1 µM solution of **Rh6G** in acetonitrile and variable concentrations of quencher (**DMAP**/**Imd**/**1a**/**4a**) in a Hellma fluorescence cuvette (3 mL, path length 1.0 cm). Samples were excited at 515 nm and the intensity of emission was monitored at 548 nm.

The result of experiments showed the quenching of emission intensity with the increase in the concentration of DMAP is much more prominent at much lower concentration than the quenching with dithiane **3a** and dithiolane **1a** (Fig 3.2). It is clear that SET process with excited-state PC* is more facile for DMAP in relative to **1a**/**4a** and more favourable for **1a**/**4a** with respect to Imd (imidazole) (see Fig 3.2). Based upon these observations, we predict that the excited Rh6G***** (+1.39 V vs SCE)[42] easily oxidized the DMAP by SET process (+1.27 V, DMAP) to form the corresponding oxidized species $DMAP^{\bullet+}$ (Fig. 3.3A). Then the oxidized $DMAP^{\bullet+}$ would further oxidized the **1a** (+1.26 V) to regenerates DMAP by second SET. Cyclic voltammetry and Stern-Volmer experiments clearly implies that DMAP takes part in the reductive quenching cycle because of its high SET rate with the Rh6G*. On the other hand, reaction in presence of imidazole, dithiolane or the dithiane takes part in the first step of reductive quenching cycle with Rh6G* (instead of imidazole because of its low SET rate with the Rh6G*). Based on the earlier literature, single electron oxidized species of the six membered cyclic dithioacetals are relatively well stabilized by the transannular interaction between the two sulfur atoms through 3e-2center σ-σ* bond.[39] However, such type of interaction is absent in the corresponding five membered cyclic counterpart because of more planar structure of the five membered ring of dithioacetals. Since, the oxidized species **C1** (Fig. 3.4) is well stabilized by transannular interaction, the ring opening in six-membered cyclic-dithioacetal is not favorable. While ring opening is highly facile in case of five membered cyclic-dithioacetals due to the instability of single electron oxidized species **A1** as there is no favorable 3e-2center σ-σ* bond interaction (Fig. 3.3). While, the stabilization of oxidized species in six-membered cyclic-dithioacetals via the weak 3e-2center σ-σ* bond is disturbed possibly due to hydrogen bonding, it may lead to ring opening. Conceivably, based on our control experiments, imidazole is the suitable base that can disturb 3e-2center σ-σ* bond resulting in ring opening to afford the rearrangement product.

3.5 Proposed mechanism

Considering the experimental observations and the preceding literature reports,[32, 39-42] we have described the plausible reaction mechanisms of four different reaction pathways under optimized reaction conditions. First, upon irradiation with the green light Rh6G gets excited (Rh6G*) and this excited state Rh6G* involves in the SET process with DMAP (+1.27 V) to generate the $Rh6G^{\bullet-}$ radical anion and oxidized $DMAP^{\bullet+}$ species because of the higher SET rate of the DMAP with the Rh6G* observed from the Stern-Volmer graph (Fig 3.3a).

Fig. 3.3 Plausible Reaction Mechanism for dithiolane rearrangement and sulfoxidation.

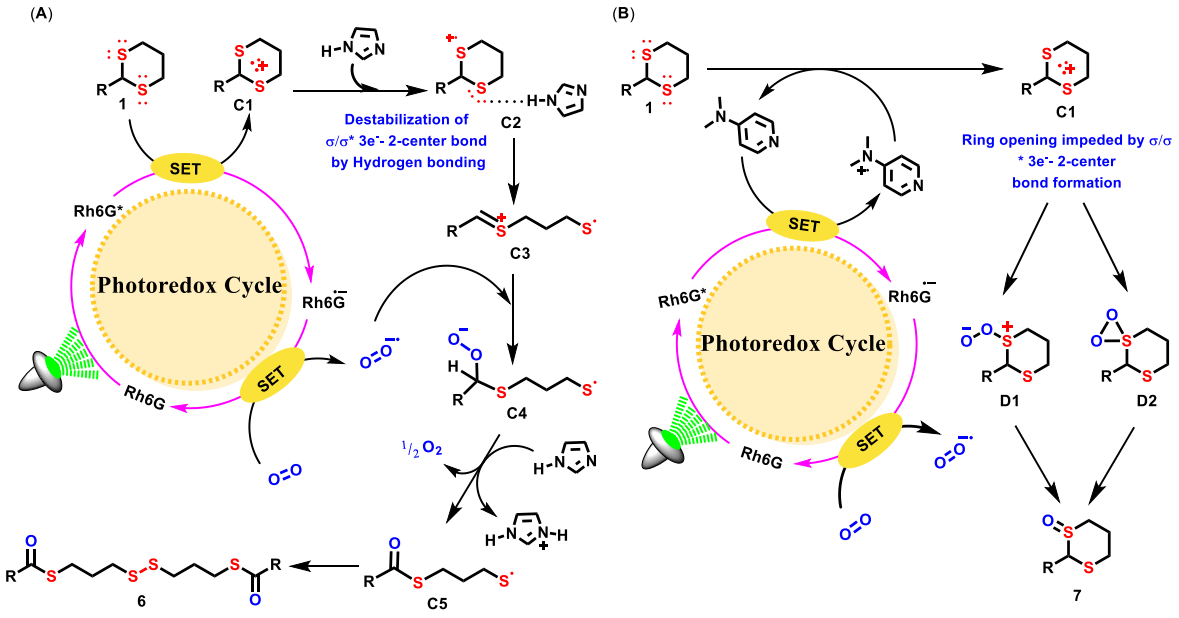


This oxidized $DMAP^{\bullet+}$ further involve in relay of SET with **3** (+1.26 V) to give intermediate **A1** and regenerates DMAP. This oxidized species of five membered dithiolane **A1** is unstable and would cleave to form the transient radical cationic intermediate **A2** (Fig 3.3A). This thionium ion intermediate **A2** reacts with the superoxide radical anion ($O_2^{\bullet-}$) to generate the intermediate **A3** (Fig 3.3A). This unstable **A3** would ultimately to furnish the thiyl radical intermediate **A4** by abstracting the proton and release of ½ O_2. Finally, the intermediate **A4** would form the S–S bond to accomplished the desired rearrangement product **4**.

On the other hand, in presence of Imd, due to the inefficient SET rate of the Rh6G* with Imd, the excited photocatalyst (Rh6G*) directly involves with SET process with dithiolane **1** to afford the oxidized dithiolane species **A1** (Fig 3.3B). This oxidized species **A1** is probably forms the hydrogen bonding with the imidazole and stabilized the oxidized dithiolane to form the intermediate **B1** (Fig. 3.3B). This intermediate **B1** further react with the superoxide

radical anion ($O_2^{\bullet-}$) to proceed for the final sulfoxide product **5** either through the reactive intermediate **B2** or **B3**.

Fig 3.4 Plausible Reaction Mechanism for Dithiane Rearrangement and Sulfoxidation.

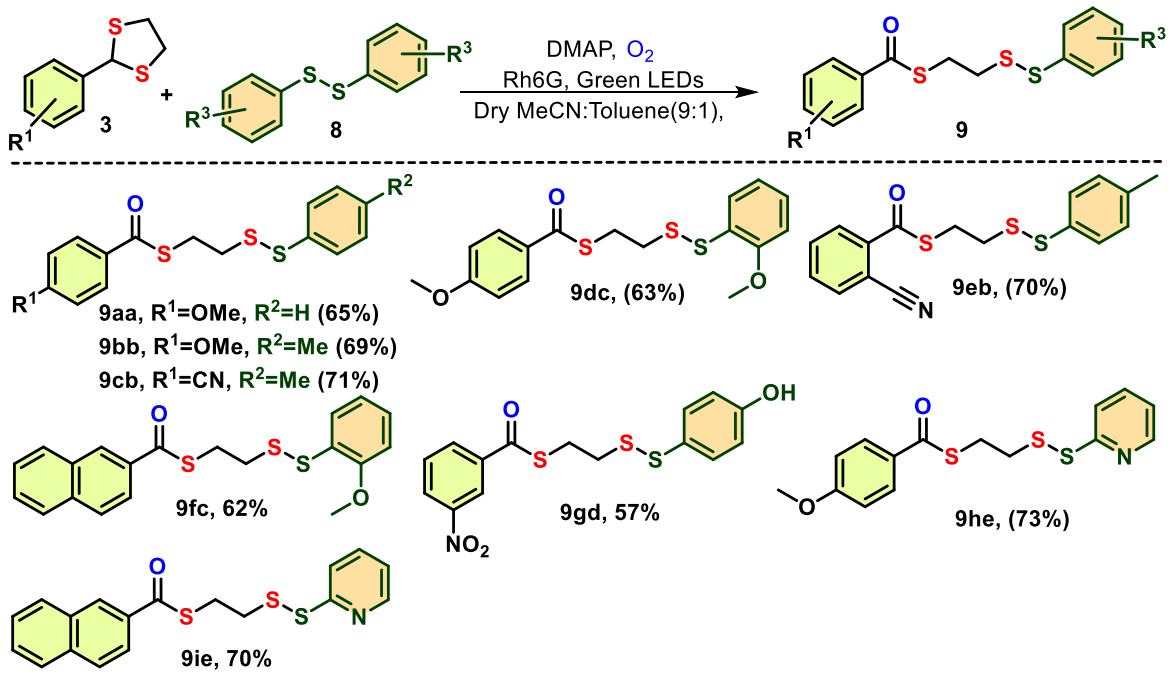


While in case of six membered cyclic dithioacetals (dithiane, **1**), upon treatment with Imd the excited photocatalyst Rh6G* reacts directly with dithioane **1** to generate the oxidized species **C1.** This intermediate **C1** is stabilized by transannular interaction between the two sulfur atoms (3e-2 center σ-σ* bond). However, it is believed that imidazole forms the hydrogen bonding with the intermediate **C1** and disturbs the 3e-2-center σ-σ* interaction to form intermediate **C2** (Fig, 3.4A). Hence, in destabilize the intermediate and facilitates the ring opening to generate the thionium-radical cation intermediate **C3**. This intermediate **C3** reacts with superoxide radical anion to generate the intermediate oxo-intermediate **C4**. This reactive and unstable intermediate **C4** will finally break down to give a radical intermediate **C5** by abstracting the proton and release of ½ O_2. The intermediate **C5** would finally dimerize to give rearrangement product **6**. While, in presence of DMAP via a relay of two SET events an intermediate **C1** is formed. At first single electron oxidation of DMAP takes place and then subsequently oxidizes the dithiane **4a** to form the intermediate **C1** (Fig 3.4B). This intermediate is well stabilized by transannular interaction (by the 3e-2-center σ-σ* interaction) and will persist relatively longer time in intermediate **C1**. Then, the superoxide radical anion ($O_2^{\bullet-}$) directly reacts with the oxidized sulfur atom of dithiane intermediate **C1** to afford the final product sulfoxide **7** via either reactive intermediate **D1** or **D2**.[43]

3.6 Application

Based on plausible reaction mechanistic pathways (Scheme 3.3A), we hypothesized that disulfide can be utilized to trap the *in situ* generated thiyl radical intermediate **A4** to access hetero-disulfide compounds. This would further confirm the formation of thiyl radical intermediate **A4** also it would give a novel strategy to access hetero-disulfides. The synthesis of hetero-disulfides is not very easy as most of the cases homo-disulfides are known to form.[44] In order to explore the application of this transformation, we set out for the synthesis of different hetero-disulfides (Table 3.5). Treatment of dithiolanes (**1**) with aromatic disulfides (**8a-8e,** little excess) under the optimized reaction conditions furnished the hetero-disulfides (**9aa-9ie**) in moderate to good yields respectively (up to 73%, Table 3.5). We realized that disulfides (**8**) substituted with electron rich aryl group as well as free hydroxyl substituted aryl worked well under the optimized reaction condition to afford the corresponding heterodisulfides **9**. While the disulfides with electron withdrawing groups and aliphatic disulfides did not proceed under the reaction conditions.

Table 3.5 Substrate Scope for the synthesis of Thioesters-heterodisulfide compounds



3.7 Conclusions

In summary, we have established a photoredox catalyzed base dependent rearrangement reaction of dithiolanes and dithianes to access rearrangement and sulfoxides under visible light. A variety of dithiolanes and dithianes reacted nicely under the standardized conditions to accomplished a wide variety of sulfoxides and rearrangement product. Further, we have demonstrated the usefulness of the reactivity for the synthesis of hetero-disulfides by trapping the *in situ* generated thiyl radical with diaryl disulfides. We have explored and successfully demonstrated the unique and unusual reactivity of dithiolanes and dithianes under different basic condition photooxidative reaction conditions for the very first time. This simple transformation does not require on any metal reagents or external oxidizing reagents. The transformations work well under visible light at room temperature and the rearrangement reaction gives an access to a molecule with two different functional groups in a single step from simple starting materials. The observed unique and novel reactivity of thioacetals reveals the new horizon for the synthesis of new molecules from dithioacetals by exploring the reactivity with different electrophiles and nucleophiles.

3.8 Experimental section:

3.8.1 General Information

(See the chapter 2, 2.7.1, page no. 38-39)

3.8.2 Synthesis of compounds 1 and 3: (1,3-dithiane and 1,3-dithiolane protection of aldehyde)[7f] (See Chapter 2, 3.7.2, page no. 39).

3.8.3 Synthesis of Disulfide-linked-dithioester 4 (General procedure A).

A highly dried glass RB was equipped with the magnetic bar, dithiolane **3** (1 equiv., 0.2 mmol), DMAP (2 equiv., 0.4 mmol), Rh6G (2 mol%) then the dry MeCN (1.8 mL) and dry toluene (0.2 mL) was added and reaction mixture was purged with oxygen for 5-10 min and continued the stirring under the green LEDs (15 W) irradiation and O_2 baloon at rt (6-12 h). After completion of reaction, the solvent was removed under reduced pressure using rotary evaporator and crude was purified by column chromatography to obtained the pure product **4** over silica gel using the percentage gradient of Hexane/Ethyl acetate. (**Note**- impurity of 1, 2-ethanedithiol in starting material and moisture drastically reduces the yield of product)

3.8.4 Synthesis of sulfoxide 5 (General procedure B).

A highly dried glass RB was equipped with the magnetic bar, dithiolane **3** (1 equiv., 0.2 mmol), imidazole (5 equiv., 1 mmol), Rh6G (2 mol%) then dry MeCN (1.5 mL) and dry ^{t}BuOH (0.5 mL) was added and reaction mixture was purged with oxygen for 5-10 min and stirring contined under the green LEDs (15 W) irradiation and O2 baloon at rt for 24 h. After completion of reaction, the mixture was passed through basic alumina. The filtrate was concentrated and the crude was purified by column chromatography to obtained the sulfoxide **5** over neutral alumina using percentage gradient of petroleum ether/EtOAc (**Note**- impurity of 1, 2-ethanedithiol in starting material and moisture drastically reduces the yield of product)

3.8.5 Synthesis of Disulfide-linked-dithioester 6 (General procedure C).

A highly dried glass RB was equipped with the magnetic bar, dithiolane **1** (1 equiv., 0.2 mmol), imidazole (5 equiv., 1 mmol), Rh6G (2 mol%) and dry MeCN (1.5 mL) and ^{t}BuOH

(0.5 mL) was added and mixture was purged for 10 min with oxygen stirred continueosly under green LEDs (15 W) and O_2 baloon at rt for 24 h. After completion, the solvent was removed by evaporation and the crude was purified by column chromatography over silica gel using hexane/ethyl acetate percentage gradiant to afford the rearranged product **6**. (**Note-** impurity of 1, 3-ethanedithiol in starting material and moisture drastically reduces the yield of product)

3.8.6 Synthesis of sulfoxide 7 (General procedure D).

A highly dried glass RB was equipped with the magnetic bar, dithiolane **1** (1 equiv., 0.2 mmol), DMAP (2 equiv., 0.4 mmol). Rh6G (2 mol%) and dry MeCN (1.8 mL) and dry *t*BuOH (0.2 mL) was added to the reaction mixture and purged with O_2 for 10 min and reaction stirred under green LEDs (15 W) and O_2 baloon at room temperature for 24 h (Monitored by TLC). After completion, reaction mixture was passed through basic alumina. The filtrate was concentrated and the crude was purified by column chromatography over neutral alumina using percentage gradient of hexane/ethyl acetate to obtained the sulfoxide **7**. (**Note**- impurity of 1, 3-ethanedithiol in starting material and moisture drastically reduces the yield of product)

3.8.7 Synthesis of Hetero disulfide 9 (General procedure E).

A highly dried glass RB was equipped with the magnetic bar, dithiolane **3** (1 equiv., 0.2 mmol), disulfide **8** (3 equiv., 0.6 mmol), DMAP (2 equiv., 0.4 mmol), Rh6G (2 mol%) then the dry MeCN (1.8 mL) and dry toluene (0.2 mL) was added and reaction mixture was purged with oxygen for 5-10 min and continued the stirring under the green LEDs (15 W) irradiation and O_2 baloon at rt (6-12 h). After completion of reaction, the solvent was removed under reduced pressure using rotary evaporator and crude was purified by column chromatography to obtained the pure product hetero-disulfide **9** over silica gel using the percentage gradient of Hexane/Ethyl acetate. (**Note-** impurity of 1, 2-ethanedithiol in starting material and moisture drastically reduces the yield of product)

3.8.8 Product Characterization data:

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(4-methoxybenzothioate) (4a)[12a]: White solid (32 mg, 70% yield), Mp: 81.5-82.5 °C; R_f = 0.4 (1:15 :: EA:pet ether).^{1}H NMR (400 MHz, $CDCl_3$): δ 2.99 (m, 4H), 3.40 (m, 4H), 3.86 (s, 6H), 6.91 (d, *J* = 8.8 Hz, 4H), 7.93 (d, *J* = 8.8 Hz, 4H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.2, 38.0, 55.3, 113.6, 129.6, 129.8, 163.6, 189.4,; HRMS (ESI-TOF) m/z calcd. For $C_{20}H_{23}O_4S_4$ $[M+H]^+$ 455.0479; found 455.0483.*S,S'*-

(disulfanediylbis(ethane-2,1-diyl)) dibenzothioate (4b): Colorless liquid (25 mg, 64%), R_f = 0.4 (1:39:: EA:pet ether). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.00 (m, 4H), 3.43 (m, 4H), 7.45 (t, *J* = 7.8 Hz, 4H), 7.58 (t, *J* = 7.4 Hz, 2H), 7.96 (d, *J* = 7.4 Hz, 4H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.6, 38.1, 127.4, 128.7, 133.7, 136.9, 191.3,; HRMS (ESI-TOF) m/z calcd. For $C_{18}H_{18}NaO_2S_4$ $[M+Na]^+$ 417.0087; found 417.0077.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(4-chlorobenzothioate) (4c)[12a] Colorless liquid, R_f = 0.4 (1:39 :: EA:pet ether) (38 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.99 (m, 4H), 3.43 (m, 4H), 7.43 (d, *J* = 8.5 Hz, 4H), 7.89 (d, *J* = 8.5 Hz, 4H),**;** $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.7 , 38.0, 128.7, 129.1, 135.2, 140.1, 190.2,; HRMS (ESI-TOF) m/z calcd. For $C_{18}H_{16}Cl_2NaO_2S_4$ $[M+Na]^+$ 484.9307; found 484.9307.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(4-(tert-butyl)benzothioate) (4d): White solid (Melting point- 64.6-65.3 °C), R_f = 0.5 (1:39 :: EA:pet ether) (34 mg, 67%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 18H), 3.04 – 2.92 (m, 4H), 3.47 – 3.33 (m, 4H), 7.46 (d, *J* = 8.7 Hz, 4H), 7.9 (d, *J* = 8.7 Hz, 4H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.5, 31.2, 35.3, 38.3, 125.7, 127.3, 134.3, 157.5, 190.9,; HRMS (ESI-TOF) m/z calcd. For $C_{26}H_{35}O_2S_4$ $[M+H]^+$ 507.1520; found 507.1529.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(4-(trifluoromethyl)benzothioate) (4e): White solid (Melting point- 92.7-94.0 °C), R_f = 0.5 (1:9 :: EA:pet ether) (42 mg, 79%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.03 – 3.00 (m, 4H), 3.49 – 3.45 (m, 4H), 7.72 (d, *J* = 8.4 Hz, 4H), 8.06 (d, *J* = 8.4 Hz, 4H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.9, 37.9, 123.6 (q, 555 Hz), 125.9 (q, 4 Hz), 127.7, 134.8, 135.0 (d, 32 Hz), 139.6, 190.5,; ^{19}F NMR (100 MHz, $CDCl_3$) δ 63.2. HRMS (ESI-TOF) m/z calcd. For $C_{20}H_{17}F_6O_2S_4$ $[M+H]^+$ 531.0016; found 531.0025.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(4-cyanobenzothioate) (4f): White solid (Melting point- 91.3- 94.7 °C), R_f = 0.4 (1:9 :: EA:pet ether) (32 mg, 73%). ^{1}H NMR (400 MHz,

$CDCl_3$) δ 3.05 – 2.81 (m, 4H), 3.46 (m, 4H), 7.76 (d, *J* = 8.7 Hz, 4H), 8.04 (d, *J* = 8.7 Hz, 4H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 29.0, 37.7, 117.0, 117.8, 127.8, 132.7, 139.9, 190.2,; HRMS (ESI-TOF) m/z calcd. For $C_{20}H_{17}N_2O_2S_4$ $[M+H]^+$ 445.0173; found 445.0171.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(4-(methylthio)benzothioate) (4g): White solid (Melting point- 85.1-86.9 ºC), R_f = 0.45 (1:14 :: EA:pet ether) (28 mg, 58%). ^1H NMR (400 MHz, $CDCl_3$) δ 2.52 (s, 6H), 3.03 – 2.94 (m, 4H), 3.45 – 3.35 (m, 4H), 7.24 (d, *J* = 8.7 Hz, 4H), 7.86 (d, *J* = 8.7 Hz, 4H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 14.9, 28.6, 38.2, 125.1, 127.7, 133.1, 146.7, 190.3,; HRMS (ESI-TOF) m/z calcd. For $C_{20}H_{23}O_2S_6$ $[M+H]^+$ 487.0022; found 487.0022.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(3-bromobenzothioate) (4h Yellow solid (Melting point- 71.3-72.5 ºC), R_f = 0.45 (1:39 :: EA:pet ether) (36 mg, 65%). ^1H NMR (400 MHz, $CDCl_3$) δ **8.08** (m, 2H), 7.88 (m, 2H), 7.70 (m, 2H), 7.33 (m, 2H), 3.51 – 3.39 (m, 4H), 3.03 – 2.94 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.8, 37.9, 123.1, 126.0, 130.3, 136.5, 138.6, 190.1,; HRMS (ESI-TOF) m/z calcd. For $C_{18}H_{17}Br_2O_2S_4$ $[M+H]^+$ 550.8478; found 550.8482.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(3-iodobenzothioate) (4i): White solid (Melting point- 61.0-62.2 ºC), R_f = 0.4 (1:99 :: EA:pet ether) (43 mg, 66%) ^1H NMR (400 MHz, $CDCl_3$) δ 3.02 – 2.92 (m, 4H), 3.46 – 3.36 (m, 4H), 7.98 – 7.81 (m, 4H), 7.19 (m, 2H), 8.26 (m, 2H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.7, 37.8, 94.23, 126.4, 130.3, 136.0, 138.4, 142.3, 189.8,; HRMS (ESI-TOF) m/z calcd. For $C_{18}H_{17}I_2O_2S_4$ $[M+H]^+$ 646.8201; found 646.8209.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(3-hydroxybenzothioate) (4j): White solid (Melting point- 96.7-97.9 ºC), R_f = 0.5 (3:7::EA:Pet ether) (18 mg, 44%). ^1H NMR (400 MHz, $CDCl_3$) δ 3.06 – 2.94 (m, 4H), 3.45 – 3.35 (m, 4H), 7.07 (m, 2H), 5.79 (s, 1H), 7.32 (m, 2H), 7.45 – 7.41 (m, 2H), 7.55 – 7.50 (m, 2H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.6, 38.0, 113.7, 119.8, 120.8, 130.0, 138.2, 155.9, 191.4,; HRMS (ESI-TOF) m/z calcd. For $C_{18}H_{19}O_4S_4$ $[M+H]^+$ 427.0166; found 427.0168.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(3,5-dimethoxybenzothioate) (4k):. White solid (Melting point- 85.9-86.7 ºC), R_f = 0.45 (1:9:: EA:pet ether) (37 mg, 71%). ^1H NMR (400 MHz, $CDCl_3$) δ 3.02 – 2.95 (m, 4H), 3.44 – 3.38 (m, 4H), 3.82 (s, 12H), 6.65 (t, *J* = 2.3 Hz, 2H), 7.09 (t, *J* = 2.7 Hz, 4H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.8, 38.0, 55.7,

105.1, 106.1, 138.8, 160.9, 191.2,; HRMS (ESI-TOF) m/z calcd. For $C_{22}H_{27}O_6S_4$ $[M+H]^+$ 515.0690; found 515.0695.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(2-chlorobenzothioate) (4l): Colorless liquid, R_f = 0.4 (1:19 :: EA:pet ether) (27 mg, 58%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.06 – 2.95 (m, 4H), 3.54 – 3.31 (m, 4H), 7.32 (m, 2H), 7.42 (m, 4H), 7.66 (m, 2H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 29.6, 37.8, 126.8, 129.4, 131.0, 131.0, 132.5, 137.2, 191.4,; HRMS (ESI-TOF) m/z calcd. For $C_{18}H_{16}Cl_2NaO_2S_4$ $[M+Na]^+$ 484.9307; found 484.9310.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(3,4-dimethoxybenzothioate) (4m): White solid (Melting point- 122.8-124.2 ^{o}C), R_f = 0.5 (2:8 :: EA:pet ether) (33 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.06 – 2.98 (m, 4H), 3.47 – 3.39 (m, 4H), 3.94 (s, 6H), 3.95 (s, 6H), 6.89 (d, J = 8.4 Hz, 2H), 7.47 (d, J = 2.1 Hz, 2H), 7.66 (dd, J = 8.4, 2.1 Hz, 2H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.5, 38.1, 56.0, 56.1, 109.4, 110.2, 121.8, 129.7, 148.9, 153.6, 189.8,; HRMS (ESI-TOF) m/z calcd. For $C_{22}H_{27}O_6S_4$ $[M+H]^+$ 515.0690; found 515.0695.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(naphthalene-2-carbothioate) (4n):. White solid (Melting point-94.7-96.2 ^{o}C), R_f = 0.4 (1:29 :: EA:pet ether) (31 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.06 (m, 4H), 3.56 – 3.43 (m, 4H), 7.57 (dd, J = 12.9, 8.5 Hz, 4H), 7.87 (d, J = 7.7 Hz, 4H), 7.96 (t, J = 7.1 Hz, 4H), 8.52 (s, 2H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.6, 38.1, 123.1, 126.9, 127.8, 128.5, 128.5, 128.8, 129.6, 132.4, 134.1, 135.8, 191.2,; HRMS (ESI-TOF) m/z calcd. For $C_{26}H_{23}O_2S_4$ $[M+H]^+$ 495.0581; found 495.0580.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(pyrene-1-carbothioate) (4o): Yellow viscus liquid, R_f = 0.4 (1:9 :: EA:pet ether) (26 mg, 41%), ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.84 (d, J = 9.4 Hz, 2H), 8.50 (d, J = 8.1 Hz, 2H), 8.23 – 8.18 (m, 2H), 8.17 – 8.06 (m, 8H), 8.01 (m, 4H), 3.64 – 3.59 (m, 4H), 3.24 – 3.18 (m, 4H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 193.6, 134.2, 131.1, 131.0, 130.5, 129.9, 129.7, 128.5, 127.1, 126.5, 126.5, 126.2, 124.7, 124.3, 124.2, 124.1, 38.4, 29.8. HRMS (ESI-TOF) m/z calcd. For $C_{38}H_{27}O_2S_4$ $[M+H]^+$ 643.0894; found 643.0888.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(benzo[d][1,3]dioxole-5-carbothioate) (4p): White solid (Melting point-93.1-94.6 ^{o}C), R_f = 0.5 (1:9 :: EA:pet ether) (31 mg, 64%), δ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (dd, J = 8.2, 1.7 Hz, 2H), 7.40 (d, J = 1.7 Hz, 2H), 6.83 (d, J = 8.2 Hz, 2H), 6.05 (s, 4H), 3.52 – 3.30 (m, 4H), 3.02 – 2.81 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 189.4, 152.1, 148.0, 131.3, 123.4, 108.1, 107.2,

101.9, 38.1, 28.6. HRMS (ESI-TOF) m/z calcd. For $C_{20}H_{19}O_6S_4$ $[M+H]^+$ 483.0064; found 483.0067.

dimethyl 4,4'-(((disulfanediylbis(ethane-2,1-diyl))bis(sulfanediyl))bis(carbonyl))dibenzoate (4q):. White solid (Melting point- 112.9-114.5 ^oC), R_f = 0.5 (2:8 :: EA:pet ether) (36 mg, 70%). ^1H NMR (400 MHz, $CDCl_3$) δ 3.06 – 2.95 (m, 4H), 3.50 – 3.41 (m, 4H), 3.95 (s, 6H), 7.99 (d, *J* = 8.7, 4H), **8.10** (d, *J* = 8.7, 4H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.9, 37.9, 52.6, 127.3, 130.0, 134.4, 140.1, 166.2, 190.9,; HRMS (ESI-TOF) m/z calcd. For $C_{22}H_{23}O_6S_4$ $[M+H]^+$ 511.0377; found 511.0373.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(2-methoxy-5-(trifluoromethoxy)benzothioate) (4r): White solid (Melting point- 76.6-77.9 ^oC), R_f = 0.5 (2:18 :: EA:pet ether) (40 mg, 65%). ^1H NMR (400 MHz, $CDCl_3$) δ 2.98 (ddd, *J* = 8.1, 5.7, 3.5 Hz, 4H), 3.43 – 3.30 (m, 4H), 3.94 (s, 6H), 6.99 (d, *J* = 9.1 Hz, 2H), 7.41 – 7.27 (m, 2H), 7.67 (dd, *J* = 3.0, 0.6 Hz, 2H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 29.2, 37.7, 56.3, 113.1, 120.5 (q, *J* = 767 Hz), 122.7, 126.5, 127.1, 142.2 (d, J = 2 Hz), 156.6, 189.1,; HRMS (ESI-TOF) m/z calcd. For $C_{22}H_{21}F_6O_6S_4$ $[M+H]^+$ 623.0125; found 623.0129.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(4-bromothiophene-2-carbothioate) (4s Yellow liquid, R_f = 0.5 (1:39 :: EA:pet ether) (42 mg, 73%). ^1H NMR (400 MHz, $CDCl_3$) δ 3.00 – 2.93 (m, 4H), 3.46 – 3.39 (m, 4H), 7.52 (d, *J* = 1.4 Hz, 2H), 7.69 (d, *J* = 1.4 Hz, 2H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.8, 37.8, 110.8, 130.1, 133.3, 142.2, 182.4,; HRMS (ESI-TOF) m/z calcd. For $C_{14}H_{13}Br_2O_2S_6$ $[M+H]^+$ 562.7607; found 562.7610.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(thiophene-2-carbothioate) (4t Yellow liquid, R_f = 0.4 (1:29 :: EA:pet ether) (27 mg, 66%). ^1H NMR (400 MHz, $CDCl_3$): δ 2.98 (m, 4H), 3.59 – 3.20 (m, 4H), 7.34 (d, 2H), 7.52 (d, 2H), 8.12 (s, 2H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.4, 38.1, 125.9, 126.5, 130.8, 140.7, 184.7,. HRMS (ESI-TOF) m/z calcd. For $C_{14}H_{15}O_2S_6$ $[M+H]^+$ 406.9396; found 406.9398.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(benzofuran-2-carbothioate) (4u): White solid (Melting point- 137.7-138.4 ^oC), R_f = 0.45 (1:18 :: EA:pet ether) (30 mg, 70%). ^1H NMR (400 MHz, $CDCl_3$) δ 3.17 – 2.88 (m, 4H), 3.49 (m, 4H), 7.33 (ddd, *J* = 8.0, 7.2, 1.0 Hz, 2H), 7.49 (ddd, *J* = 8.4, 6.2, 1.3 Hz, 2H), 7.55 (d, *J* = 0.8 Hz, 2H), 7.60 (dd, *J* = 8.4, 0.8 Hz, 2H), 7.74 – 7.68 (m, 2H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.1, 38.0, 111.7, 112.6, 123.3, 124.2, 127.0, 128.4, 151.0, 155.7, 181.7,; HRMS (ESI-TOF) m/z calcd. For $C_{22}H_{19}O_4S_4$ $[M+H]^+$ 475.0166; found 475.0167.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(2-phenylethanethioate) (4v Colorless liquid, R_f = 0.4 (1:49 :: EA:pet ether) (27 mg, 61%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.87 – 2.73 (m, 4H), 3.25 – 3.10 (m, 4H), 3.82 (s, 4H), 7.42 – 7.21 (m, 10H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.9, 37.8, 50.6, 127.6, 128.8, 129.7, 133.4, 196.9,. HRMS (ESI-TOF) m/z calcd. For $C_{20}H_{22}O_2S_4$ $[M+Na]^+$ 445.0400; found 445.0408.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(3-methylbutanethioate) (4w Colorless liquid, R_f = 0.3 (1:199 :: EA:pet ether) (21 mg, 60%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.95 (d, J = 6.6 Hz, 12H), 2.16 (dp, J = 7.1, 6.6 Hz, 2H), 2.44 (d, J = 7.1 Hz, 4H), 2.95 – 2.67 (m, 4H), 3.31 – 3.08 (m, 4H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 22.4, 26.6, 28.5, 38.2, 53.1, 198.5,; HRMS (ESI-TOF) m/z calcd. For $C_{14}H_{26}NaO_2S_4$ $[M+Na]^+$ 377.0713; found 377.0714.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) dicyclohexanecarbothioate (4x): Colorless liquid, R_f = 0.3 (1:199 :: EA:pet ether) (22 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.34 – 1.12 (m, 8H), 1.52 – 1.36 (m, 4H), 1.78 (dd, J = 9.6, 3.0 Hz, 4H), 1.91 (dd, J = 11.5, 3.0 Hz, 4H), 2.48 (tt, J = 11.5, 9.6 Hz, 2H), 2.84 (dd, J = 8.6, 6.5 Hz, 4H), 3.17 (dd, J = 8.6, 6.5 Hz, 4H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 25.6, 25.7, 28.1, 29.6, 38.2, 52.8, 202.5,; HRMS (ESI-TOF) m/z calcd. For $C_{18}H_{31}O_2S_4$ $[M+H]^+$ 407.1207; found 407.1207.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) didodecanethioate (4y):. White solid (Melting point-51.1-52.9 ^oC), R_f = 0.2 (1:199 :: EA:pet ether) (21 mg, 59%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 0.88 (t, J = 6.9 Hz, 6H), 1.36 – 1.19 (m, 32H), 1.65 (m, 4H), 2.54 (m, 4H), 2.89 – 2.80 (m, 4H), 3.23 – 3.15 (m, 4H).; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 14.1, 22.7, 25.6, 28.3, 28.9, 29.2, 29.3, 29.6, 31.9, 38.0, 44.2, 199.1,; HRMS (ESI-TOF) m/z calcd. For $C_{28}H_{55}O_2S_4$ $[M+H]^+$ 551.3085; found 551.3088.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(2-(prop-2-yn-1-yloxy)benzothioate) (4z): Colorless liquid, R_f = 0.5 (1:19 :: EA:pet ether) (33 mg, 65%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.49 (s, 2H), 2.93 (m, 4H), 4.76 (s, 4H); 3.33 (m, 4H), 7.00 (m, 2H), 7.14 – 7.02 (m, 2H), 7.50 – 7.26 (m, 2H), 7.88 – 7.59 (m, 2H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.9, 29.1, 29.7, 37.7, 37.9, 56.6, 76.4, 76.7, 77.0, 77.3, 77.9, 113.9, 121.5, 127.4, 129.9, 133.3, 133.6, 155.8, 190.1,; HRMS (ESI-TOF) m/z calcd. For $C_{24}H_{22}NaO_4S_4$ $[M+Na]^+$ 525.0299; found

Colorless liquid, R_f = 0.5 (1:19 :: EA:pet ether) (30 mg, 59%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.12 – 2.85 (m, 4H)¸ 3.47 – 3.20 (m, 4H), 4.67 (m, 4H), 5.32 (dd, J = 10.5, 1.3 Hz, 2H), 5.48

(dd, *J* = 17.2, 1.3 Hz, 2H), 6.10 (m, 2H), 7.04 – 6.81 (m, 2H), 7.44 (m, 2H), 7.91 – 7.59 (m, 2H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 29.1, 38.0, 69.8, 113.4, 118.1, 120.7, 126.9, 129.8, 132.5, 133.7, 157.1, 190.2,; HRMS (ESI-TOF) m/z calcd. For $C_{24}H_{26}NaO_4S_4$ $[M+Na]^+$ 529.0612; found 529.0615.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(4-(benzyloxy)benzothioate) (4ab): White solid (Melting point- 115.8-117.2 ^oC), R_f = 0.5 (1:39 :: EA:pet ether) (43 mg, 71%). ^1H NMR (400 MHz, $CDCl_3$) δ 2.98 (m, 1H), 3.40 (m, 4H), 5.12 (s, 4H), 6.99 (d, *J* = 8.8 Hz, 4H), 7.51 – 7.29 (m, 10H), 7.93 (d, *J* = 8.8 Hz, 4H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.5, 38.3, 70.3, 114.8, 127.6, 128.4, 128.8, 129.6, 130.0, 136.2, 163.17, 189.83,; HRMS (ESI-TOF) m/z calcd. For $C_{32}H_{31}O_4S_4$ $[M+H]^+$ 607.1105; found 607.1109.

S,S'-(disulfanediylbis(ethane-2,1-diyl)) bis(3-(tosyloxy)benzothioate) (4ac):. Colorless liquid, R_f = 0.5 (2:8 :: EA:pet ether) (41 mg, 63%). ^1H NMR (400 MHz, $CDCl_3$) δ 2.45 (s, 6H), 3.00 – 2.89 (m, 4H), 3.45 – 3.34 (m, 4H), 7.26 – 7.20 (m, 2H), 7.33 (d, *J* = 8.3 Hz, 4H), 7.40 (m, 2H), 7.55 – 7.48 (m, 2H), 7.72 (d, *J* = 8.3 Hz, 4H), 7.90 – 7.78 (m, 2H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 21.9, 28.8, 37.8, 121.3, 125.9, 127.6, 128.6, 130.1, 130.2, 132.1, 138.4, 145.9, 149.9, 190.0,; HRMS (ESI-TOF) m/z calcd. For $C_{32}H_{31}O_8S_6$ $[M+H]^+$ 735.0343; found 735.0350.

2-(4-methoxyphenyl)-1,3-dithiolane 1-oxide (5a)[29] White solid (Melting point- 115.8-117.2 ^oC), R_f = 0.3 (1:1 :: EA:pet ether) (38 mg, 83%). ^1H NMR (400 MHz, $CDCl_3$) δ 2.90 (m, 1H), 3.34 (m, 1H), 3.59 (m, 1H), 3.84 (m, 4H), 7.89 (d, *J* = 8.7 Hz, 2H), 7.40 (d, *J* = 8.7 Hz, 2H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 32.4, 53.1, 55.5, 77.3, 114.5, 124.9, 129.9, 160.2,; HRMS (ESI-TOF) m/z calcd. For $C_{10}H_{13}O_2S_2$ $[M+H]^+$ 229.0357; found 229.0358.

*2-phenyl-1,3-dithiolane 1-oxide (5b*colourless liquid, R_f = 0.35 (7:3 :: EA:pet ether) (30 mg, 76%). ^1H NMR (400 MHz, $CDCl_3$) δ 2.89 (m, 1H), 3.35 (m, 1H), 3.61 (m, 1H), 3.84 (m, 1H), 5.40 (s, 1H), 7.41 – 7.30 (m, 3H), 7.51 – 7.45 (m, 2H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) δ 32.59, 53.31, 77.94, 128.63, 129.14, 129.14, 133.20,; HRMS (ESI-TOF) m/z calcd. For $C_9H_{11}OS_2$ $[M+H]^+$ 199.0246; found 199.0251.

2-(4-(tert-butyl)phenyl)-1,3-dithiolane 1-oxide (5d): White solid, (Melting point- 112.7-114.1 ^oC), R_f = 0.35 (7:3 :: EA:pet ether) (41 mg, 81%). ^1H NMR (400 MHz, $CDCl_3$) δ 1.31 (s, 9H), 2.92 (m, 1H), 3.33 (m, 1H), 3.61 (m, 1H), 3.84 (m, 1H), 5.40 (s, 1H), 7.40 (d, *J* = 8.7 Hz, 4H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 31.3, 32.5, 34.8, 53.23, 77.5, 126.1, 128.4, 130.1, 152.4,. HRMS (ESI-TOF) m/z calcd. For $C_{13}H_{19}OS_2$ [M+

White solid (Melting point- 82.3-84.1 ^{o}C), R_f = 0.3 (7:3 :: EA:pet ether) (41 mg, 75%)^{1}H NMR (400 MHz, $CDCl_3$) δ 2.89 (m, 1H), 3.38 (m 1H), 3.63 (m, 1H), 3.85 (m, 1H), 5.34 (s, 1H), 7.29 – 7.22 (m, 1H), 7.43 (ddt, *J* = 8.0, 1.8, 0.8 Hz, 1H), 7.47 (ddd, *J* = 8.0, 1.9, 1.0 Hz, 1H), 7.66 – 7.63 (m, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) δ 32.76, 53.60, 77.30, 127.43, 130.01, 130.64, 131.59, 132.33, 135.65,; HRMS (ESI-TOF) m/z calcd. For $C_9H_{10}BrOS_2$ $[M]^+$ 276.9351; found 276.9351.

*2-(2-chlorophenyl)-1,3-dithiolane 1-oxide (5l*White solid (Melting point- 124.7-126.4 ^{o}C), R_f = 0.3 (7:3 :: EA:pet ether) (38 mg, 81%) ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.74 (m, 1H), 3.39 (m, 1H), 3.73 (m, 1H), 3.98 (m, 1H), 5.87 (s, 1H), 7.34 – 7.28 (m, 2H), 7.47 – 7.40 (m, 1H), 7.67 – 7.60 (m, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) δ 33.53, 52.62, 75.07, 127.54, 130.07, 130.34, 130.39, 130.39, 134.80,; 131.46, HRMS (ESI-TOF) m/z calcd. For $C_9H_{10}ClOS_2$ $[M]^+$ 232.9856; found 232.9853.

2-(3,4-dimethoxyphenyl)-1,3-dithiolane 1-oxide (5m): White solid (Melting point- 113.7-115.1 ^{o}C), R_f = 0.4 (9:1 :: EA:pet ether) (44 mg, 85%)^{1}H NMR (400 MHz, $CDCl_3$) δ 2.91 (m, 1H), 3.35 (m 1H), 3.59 (m 1H), 3.82 (m 1H), 3.88 (s, 3H), 3.89 (s, 3H), 5.36 (s, 1H), 6.85 (d, *J* = 8.3 Hz, 1H), 6.99 (d, *J* = 2.1 Hz, 1H), 7.07 (dd, *J* = 8.3, 2.1 Hz, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 32.4, 53.4, 56.1, 56.1, 77.8, 111.4, 121.2, 125.3, 149.3, 149.7,; HRMS (ESI-TOF) m/z calcd. For $C_{11}H_{14}O_3S_2$ $[M]^+$ 258.0384; found 258.0380.

2-(naphthalen-2-yl)-1,3-dithiolane 1-oxide (5n White solid (Melting point- 74.9-76.1 ^{o}C), R_f = 0.5 (1:1 :: EA:pet ether) (42 mg, 84%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.97 (s, 1H), 7.88 – 7.80 (m, 3H), 7.54 (m, 3H), 5.57 (s, 1H), 3.91 (td, *J* = 11.4, 5.4 Hz, 1H), 3.68 (ddd, *J* = 11.5, 6.9, 2.2 Hz, 1H), 3.38 (dddd, *J* = 13.5, 5.4, 2.2, 0.8 Hz, 1H), 2.95 (ddd, *J* = 13.4, 11.3, 6.9 Hz, 1H); $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 32.62, 53.36, 78.23, 125.66, 126.83, 126.96, 127.73, 128.11, 128.20, 128.92, 130.51, 133.17, 133.35,; HRMS (ESI-TOF) m/z calcd. For $C_{13}H_{13}OS_2$ $[M+H]^+$ 249.0408; found 249.0402.

2-(4-bromothiophen-2-yl)-1,3-dithiolane 1-oxide (5s): White solid (Melting point- 96.8-98.6 ^{o}C), R_f = 0.5 (2:1 :: EA:pet ether) (45 mg, 78%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.85 (m, 1H), 3.43 (m 1H), 3.65 (m, 1H), 3.89 (m, 1H), 5.57 (s, 1H), 7.10 (d, *J* = 1.4 Hz, 1H), 7.23 (d, *J* = 1.4 Hz, 1H),; $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 33.0, 53.2, 71.4, 110.9, 124.8, 129.7, 140.2,; HRMS (ESI-TOF) m/z calcd. For $C_7H_8BrOS_2$ $[M+H]^+$ 282.8921; found 282.8927.

2-(benzofuran-2-yl)-1,3-dithiolane 1-oxide (5u): White solid (Melting point- 84.8-86.6 ^{o}C), R_f = 0.5 (1:1 :: EA:pet ether) (34 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.05 (m, 1H), 3.54 (m, 1H), 3.73 (m, 1H), 3.96 (m, 1H), 5.52 (s, 1H), 6.83 (t, *J* = 0.9 Hz, 1H), 7.27 – 7.17 (m, 1H), 7.31 (ddd, *J* = 8.3, 7.2, 1.4 Hz, 1H), 7.45 (dq, *J* = 8.3, 0.9 Hz, 1H), 7.54 (ddd, *J* = 7.7, 1.4, 0.7 Hz, 1H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 33.15, 54.75, 70.02, 107.65, 111.44, 121.35, 123.37, 125.31, 127.57, 150.46, 155.56,; HRMS (ESI-TOF) m/z calcd. For $C_{11}H_{11}O_2S_2$ $[M+H]^+$ 239.0195; found 239.0192.

2-benzyl-1,3-dithiolane 1-oxide (5v White solid, R_f = 0.5 (2:1 :: EA:pet ether) (30 mg, 72%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.81 – 2.68 (m, 1H), 2.94 (dd, *J* = 14.3, 8.3 Hz, 1H), 3.22 (dd, *J* = 14.3, 6.4 Hz, 1H), 3.43 – 3.33 (m, 2H), 3.72 – 3.61 (m, 1H), 4.42 (dd, *J* = 8.3, 6.4 Hz, 1H), 7.25 – 7.21 (m, 2H), 7.36 – 7.28 (m, 3H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 31.64, 39.15, 54.60, 74.62, 127.41, 128.77, 129.09, 136.59,. HRMS (ESI-TOF) m/z calcd. For $C_{10}H_{13}OS_2$ $[M+H]^+$ 213.0402; found 213.0405.

S,S'-(disulfanediylbis(propane-3,1-diyl))dibenzothioate (6a): Colorless liquid, R_f = 0.5 (1:49 :: EA:pet ether) (15 mg, 37%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.10 (p, *J* = 7.1 Hz, 4H), 2.81 (t, *J* = 7.1 Hz, 4H), 3.18 (t, *J* = 7.1 Hz, 4H), 7.47 – 7.36 (m, 4H), 7.61 – 7.50 (m, 2H), 8.07 – 7.84 (m, 4H),. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 27.7, 29.1, 37.6, 127.4, 128.7, 133.5, 137.1, 191.8,; HRMS (ESI-TOF) m/z calcd. For $C_{20}H_{22}NaO_2S_4$ $[M+Na]^+$ 445.0400; found 445.0412.

S,S'-(disulfanediylbis(propane-3,1-diyl)) bis(3,4-dimethoxybenzothioate) (6b): White solid (Melting point- 62.3-63.4 ^{o}C), R_f = 0.5 (1:15 :: EA:pet ether) (18 mg, 32%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.09 (p, *J* = 7.1 Hz, 4H), 2.80 (t, *J* = 7.1 Hz, 4H), 3.16 (t, *J* = 7.1 Hz, 4H), 3.93 (s, 6H), 3.93 (s, 6H), 6.87 (d, *J* = 8.4 Hz, 2H), 7.46 (d, *J* = 2.1 Hz, 2H), 7.65 (dd, *J* = 8.4, 2.1 Hz, 2H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 27.6, 29.2, 37.6, 56.1, 56.2, 109.5, 110.3, 121.8, 130.1, 149.0, 153.6, 153.6, 190.5,; HRMS (ESI-TOF) m/z calcd. For $C_{24}H_{30}NaO_6S_4$ $[M+Na]^+$ 565.0822; found 565.0820.

S,S'-(disulfanediylbis(propane-3,1-diyl)) bis(4-chlorobenzothioate) (6c): White solid (Melting point- 40.4-41.2 ^{o}C), R_f = 0.45 (1:29 :: EA:pet ether) (23 mg, 47%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.09 (p, *J* = 7.1 Hz, 1H), 2.80 (t, *J* = 7.1 Hz, 1H), 3.18 (t, *J* = 7.1 Hz, 1H), 7.47 – 7.36 (m, 4H), 8.00 – 7.79 (m, 4H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 27.8, 29.1, 37.6, 128.7, 129.1, 135.4, 139.9, 190.6,; HRMS (ESI-TOF) m/z calcd. For $C_{20}H_{21}Cl_2O_2S_4$ $[M+H]^+$ 490.9801; found 490.9803.

S,S'-(disulfanediylbis(propane-3,1-diyl)) bis(4-(tert-butyl)benzothioate) (6d): White solid (Melting point- 57.3-57.8 ^{o}C), R_f = 0.4 (1:29 :: EA:pet ether) (18 mg, 34%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.33 (s, 18H), 2.08 (p, *J* = 7.1 Hz, 4H), 2.80 (t, *J* = 7.1 Hz, 4H), 3.17 (t, *J* = 7.1 Hz, 4H), 7.57 – 7.36 (m, 4H), 8.02 – 7.80 (m, 4H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 27.6, 29.2, 31.2, 35.3, 37.6, 125.7, 127.3, 134.5, 157.3, 191.3,; HRMS (ESI-TOF) m/z calcd. For $C_{28}H_{39}O_2S_4$ $[M+H]^+$ 535.1833; found 535.1836.

S,S'-(disulfanediylbis(propane-3,1-diyl)) bis(4-methylbenzothioate) (6e Colorless liquid, R_f = 0.4 (1:39 :: EA:pet ether) (28 mg, 30%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.08 (p, *J* = 7.1 Hz, 4H), 2.40 (s, 6H), 2.80 (t, *J* = 7.1 Hz, 4H), 3.16 (t, *J* = 7.1 Hz, 4H), 7.32 – 7.13 (m, 4H), 7.97 – 7.75 (m, 4H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 21.8, 27.6, 29.2, 37.6, 127.4, 129.4, 134.6, 144.4, 191.4,; HRMS (ESI-TOF) m/z calcd. For $C_{22}H_{27}O_2S_4$ $[M+H]^+$ 451.0894; found 451.0895.

*S,S'-(disulfanediylbis(propane-3,1-diyl)) bis(thiophene-3-carbothioate) (6f*Coloueless liquid, R_f = 0.4 (1:39 :: EA:pet ether) (14 mg, 35%). ^{1}H NMR (400 MHz, $CDCl_3$) δ2.08 (p, *J* = 7.1 Hz, 4H), 2.78 (t, *J* = 7.1 Hz, 4H), 3.16 (t, *J* = 7.1 Hz, 4H), 7.33 (dd, *J* = 5.1, 3.0 Hz, 2H), 7.52 (dd, *J* = 5.1, 1.3 Hz, 2H), 8.11 (dd, *J* = 3.0, 1.3 Hz, 2H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 27.5, 29.2, 37.5, 126.1, 126.6, 130.7, 141.0, 185.3,; HRMS (ESI-TOF) m/z calcd. For $C_{16}H_{19}O_2S_6$ $[M+H]^+$ 434.9709; found 434.9714.

2-phenyl-1,3-dithiane 1-oxide (7a)[30]White solid (Melting point- 138.5-140.8 ^{o}C), R_f = 0.5 (9:1 :: EA:pet ether) (38 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 – 2.31 (m, 1H), 2.56 – 2.47 (m, 1H), 2.79 – 2.65 (m, 2H), 2.92 – 2.84 (m, 1H), 3.58 – 3.54 (m, 1H), 4.55 (s, 1H), 7.43-7.35 (m, 5H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 29.3, 31.1, 54.5, 69.3, 128.5, 128.9, 129.1, 133.1, ; HRMS (ESI-TOF) m/z calcd. For $C_{10}H_{12}OS_2$ $[M+H]^+$ 213.0408; found 213.0410.

2-(3,4-dimethoxyphenyl)-1,3-dithiane 1-oxide (7b)[15a]: White solid (Melting point- 156.5-157.8 ^{o}C), R_f = 0.35 (9:1 :: EA:pet ether) (52 mg, 95%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 – 2.29 (m, 1H), 2.57 – 2.47 (m, 1H), 2.79 – 2.63 (m, 2H), 2.93 – 2.82 (m, 1H), 3.61 – 3.52 (m, 1H), 3.86 (s, 3H), 3.88 (s, 3H), 4.48 (s, 1H), 6.86 (d, *J* = 8.3 Hz, 1H), 6.89 (d, *J* = 2.1 Hz, 1H), 6.99 (dd, *J* = 8.3, 2.1 Hz, 1H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 29.7, 31.7, 54.9, 56.0, 56.0, 69.6, 111.3, 111.6, 121.5, 125.6, 149.4, 150.0,; HRMS (ESI-TOF) m/z calcd. For $C_{12}H_{17}O_3S_2$ $[M+H]^+$ 273.0619; found 273.0622.

2-(4-chlorophenyl)-1,3-dithiane 1-oxide (7c)[30]: White solid (Melting point- 144.5-146.2 °C), R_f = 0.45 (8:2 :: EA:pet ether) (43 mg, 87%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 – 2.31 (m, 1H), 2.60 – 2.50 (m, 1H), 2.81 – 2.65 (m, 2H), 2.94 – 2.84 (m, 1H), 3.62 – 3.53 (m, 1H), 4.52 (s, 1H), 7.40 – 7.33 (m, 4H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 29.6, 31.6, 54.9, 69.1, 129.5, 130.2, 132.0, 135.6,; HRMS (ESI-TOF) m/z calcd. For $C_{10}H_{12}ClOS_2$ $[M+H]^+$ 247.0018; found 247.0009.

2-(4-methylphenyl)-1,3-dithiane 1-oxide (7e)[30]: White solid (Melting point- 159.5-161.2 °C), R_f = 0.5 (8:2 :: EA:pet ether) (41 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.35 (s, 3H), 2.44 – 2.36 (m, 1H), 2.57 – 2.48 (m, 1H), 2.72 – 2.64 (m, 1H), 2.75 (m, 1H), 2.89 (m, 1H), 3.56 (m, 1H), 4.52 (s, 1H), 7.20 (m, 2H), 7.33 – 7.28 (m, 2H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) δ 21.36, 29.68, 31.62, 54.85, 69.61, 128.69, 129.98, 130.32, 139.54,; HRMS (ESI-TOF) m/z calcd. For $C_{11}H_{15}OS_2$ $[M+H]^+$ 227.0564; found 227.0565.

2-(thiophen-2-yl)-1,3-dithiane 1-oxide (7g)[30] White solid (Melting point- 159.8-161.1 °C), R_f = 0.45 (8:2 :: EA:pet ether) (39 mg, 91%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.42 – 2.28 (m, 1H), 2.54 (m, 1H), 2.80 – 2.70 (m, 2H), 2.96 – 2.83 (m, 1H), 3.57 – 3.45 (m, 1H), 4.84 (s, 1H), 7.04 (dd, *J* = 5.1, 3.6 Hz, 1H), 7.24 – 7.20 (m, 1H), 7.39 – 7.34 (m, 1H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 28.7, 31.7, 54.3, 64.7, 127.4, 127.6, 128.4, 135.1,; HRMS (ESI-TOF) m/z calcd. For $C_8H_{11}OS_3$ $[M+H]^+$ 218.9972; found 218.9965.

2-(4-methoxyphenyl)-1,3-dithiane 1-oxide (7h)[30]: White solid (Melting point- 169.7-171.3 °C), R_f = 0.45 (9:1 :: EA:pet ether) (40 mg, 82%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.43 – 2.29 (m, 1H), 2.56 – 2.45 (m, 1H), 2.69 – 2.63 (m, 1H), 2.77 – 2.69 (m, 1H), 2.87 (m, 1H), 3.55 (m, 1H), 3.79 (s, 3H), 4.50 (s, 1H), 6.94 – 6.88 (m, 2H), 7.36 – 7.30 (m, 2H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 29.6, 31.6, 54.9, 70.0, 125.6, 126.6, 126.8, 127.7, 128.2, 128.7, 129.1, 130.6, 133.3, 133.7,; HRMS (ESI-TOF) m/z calcd. For $C_{11}H_{15}O_2S_2$ $[M+H]^+$ 243.0508; found 263.0509.

2-(naphthalen-2-yl)-1,3-dithiane 1-oxide (7i)[30]: White solid (Melting point- 161.7 163-3 °C), R_f = 0.5 (7:3 :: EA:pet ether) (47 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.50 – 2.36 (m, 1H), 2.62 – 2.53 (m, 1H), 2.74 (m, 1H), 2.82 (m, 1H), 2.99 – 2.90 (m, 1H), 3.62 (m, 1H), 4.73 (s, 1H), 7.53 – 7.48 (m, 3H), 7.83 (dt, *J* = 12.2, 3.7 Hz, 2H), 7.88 (d, *J* = 8.6 Hz, 1H), 7.93 (d, *J* = 1.6 Hz, 1H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 29.6, 31.6, 54.9, 125.6, 126.6, 126.8, 127.7, 128.2, 128.7, 129.1, 130.6, 133.3, 133.7,; HRMS (ESI-TOF) m/z calcd. For $C_{14}H_{15}OS_2$ $[M+H]^+$ 263.0564; found 263.0567.

2-(3-bromophenyl)-1,3-dithiane 1-oxide (7j)[30]: White solid (Melting point- 142.9 144.3 °C), R_f = 0.4 (8:2 :: EA:pet ether) (52 mg, 90%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.44 – 2.27 (m, 1H), 2.58 – 2.47 (m, 1H), 2.72 – 2.65 (m, 1H), 2.76 (m, 1H), 2.88 (m, 1H), 3.57 (m, 1H), 4.50 (s, 1H), 7.30 – 7.23 (m, 1H), 7.35 (dt, *J* = 7.8, 1.3 Hz, 1H), 7.50 (ddd, *J* = 7.9, 2.0, 1.1 Hz, 1H), 7.57 (t, *J* = 1.8 Hz, 1H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 29.61, 31.54, 54.95, 69.12, 123.25, 127.65, 130.71, 131.85, 132.65, 135.69,; HRMS (ESI-TOF) m/z calcd. For $C_{10}H_{12}BrOS_2$ $[M+H]^+$ 290.9507; found 290.9507.

S-(2-(phenyldisulfanyl)ethyl) 4-methoxybenzothioate (9aa) Colorless liquid, R_f = 0.35 (1:19 :: EA:pet ether) (44 mg, 65 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.03 – 2.86 (m, 2H), 3.41 – 3.18 (m, 2H), 3.86 (s, 3H), 6.95 – 6.89 (m, 2H), 7.26 – 7.20 (m, 1H), 7.34 (m, 2H), 7.65 – 7.53 (m, 2H), 7.98 – 7.89 (m, 2H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 28.3, 38.5, 55.7, 113.9, 127.2, 128.1, 129.2, 129.6, 129.8, 137.2, 164.0, 189.8,; HRMS (ESI-TOF) m/z calcd. For $C_{16}H_{17}O_2S_3$ $[M+H]^+$ 337.0391; found 337.0399.

S-(2-(p-tolyldisulfanyl)ethyl) 4-methoxybenzothioate (9bb): Colorless liquid, R_f = 0.35 (1:19 :: EA:pet ether) (49 mg, 69%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.33 (s, 2H), 3.02 – 2.88 (m, 1H), 3.43 – 3.25 (m, 1H), 3.86 (s, 2H), 6.95 – 6.85 (m, 2H), 7.14 (m, 2H), 7.55 – 7.43 (m, 2H), 8.04 – 7.85 (m, 2H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 28.3, 38.34, 55.6, 113.9, 129.1, 129.6, 129.8, 130.0, 133.8, 137.6, 164.0, 189.8,; HRMS (ESI-TOF) m/z calcd. For $C_{17}H_{19}O_2S_3$ $[M+H]^+$ 351.0547; found 351.0554.

S-(2-(p-tolyldisulfanyl)ethyl) 4-cyanobenzothioate (9cb): Colorless liquid, R_f = 0.35 (1:9 :: EA:pet ether) (50 mg, 71%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3H), 3.00 – 2.95 (m, 2H), 3.45 – 3.40 (m, 2H), 7.18 – 7.11 (m, 2H), 7.50 – 7.45 (m, 2H), 7.78 – 7.72 (m, 2H), 8.06 – 7.99 (m, 2H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 28.8, 37.8, 77.1, 116.9, 117.9, 127.8, 129.3, 130.1, 132.6, 133.5, 137.9, 140.0, 190.2,; HRMS (ESI-TOF) m/z calcd. For $C_{17}H_{16}NOS_3$ $[M+H]^+$ 346.0394; found 346.0393.

S-(2-((2-methoxyphenyl)disulfanyl)ethyl) 4-methoxybenzothioate (9dc): . Colorless liquid, R_f = 0.4 (1:9 :: EA:pet ether) (46 mg, 63%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.01 – 2.96 (m, 2H), 3.37 (m, 2H), 3.86 (s, 3H), 3.90 (s, 3H), 6.87 (dd, *J* = 8.3, 1.1 Hz, 1H), 6.94 – 6.89 (m, 2H), 6.99 (td, *J* = 7.7, 1.1 Hz, 1H), 7.26 – 7.15 (m, 1H), 7.26 – 7.20 (m, 1H), 7.73 (dd, *J* = 7.7, 1.6 Hz, 1H), 8.01 – 7.86 (m, 2H),; ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ (ppm) 28.4, 38.1, 55.6, 56.1, 110.9, 113.9, 121.4, 125.0, 128.5, 129.0, 129.6, 129.8, 157.1, 164.0, 189.9,; HRMS (ESI-TOF) m/z calcd. For $C_{17}H_{19}O_3S_3$ $[M+H]^+$ 367.0496; found 367.0497.

S-(2-(p-tolyldisulfanyl)ethyl) 2-cyanobenzothioate (9eb): Colorless liquid, R_f = 0.45 (1:9 :: EA:pet ether) (49 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.34 (s, 3H), 3.04 – 2.96 (m, 2H), 3.50 – 3.41 (m, 2H), 7.18 – 7.12 (d, 2H), 7.51 – 7.47 (d, 2H), 7.70 – 7.66 (m, 2H), 7.84 – 7.80 (m, 1H), 8.05 – 8.01 (m, 1H),. $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 21.2, 29.3, 37.6, 110.3, 117.4, 129.3, 129.4, 130.1, 132.7, 132.9, 133.5, 135.2, 137.8, 139.2, 189.5,; HRMS (ESI-TOF) m/z calcd. For $C_{17}H_{15}NOS_3$ $[M]^+$ 345.0316; found 345.0315.

S-(2-((2-methoxyphenyl)disulfanyl)ethyl) naphthalene-2-carbothioate (9fc Colorless liquid, R_f = 0.4 (1:9 :: EA:pet ether) (48 mg, 62%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.07 – 3.01 (m, 2H), 3.49 – 3.43 (m, 2H), 3.92 (s, 3H), 6.88 (dd, *J* = 8.3, 1.0 Hz, 1H), 7.01 (td, *J* = 7.6, 1.1 Hz, 1H), 7.23 (dd, *J* = 7.7, 1.3 Hz, 1H), 7.58 (m, 2H), 7.75 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.88 (dd, *J* = 8.3, 4.4 Hz, 2H), 7.97 (dd, *J* = 8.6, 1.7 Hz, 2H), 8.51 (s, 1H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.7, 38.0, 56.0, 110.9, 121.4, 123.2, 125.0, 127.1, 127.9, 128.5, 128.6, 128.7, 128.9, 129.1, 129.7, 132.5, 134.3, 135.9, 157.2, 191.4,; HRMS (ESI-TOF) m/z calcd. For $C_{20}H_{19}O_2S_3$ $[M+H]^+$ 387.0547; found 387.0544.

S-(2-((4-hydroxyphenyl)disulfanyl)ethyl) 3-nitrobenzothioate (9gd): Colorless liquid, R_f = 0.5 (3:7 :: EA:pet ether) (42 mg, 57%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.01 (m, 3H), 3.69 – 3.24 (m, 3H), 5.20 (s, 1H), 7.50 (d, *J* = 8.7 Hz, 2H), 7.68 (m, 1H), 8.27 (dd, *J* = 1.6, 1.1 Hz, 1H), 8.42 (dd, *J* = 2.3, 1.1 Hz, 1H), 6.82 (d, *J* = 8.7 Hz, 2H), 8.77 (m, 1H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.7, 37.5, 116.3, 122.3, 127.7, 127.9, 129.9, 132.7, 132.8, 138.1, 148.4, 156.8, 189.4,; HRMS (ESI-TOF) m/z calcd. For $C_{15}H_{14}NO_4S_3$ $[M+H]^+$ 368.0085; found 368.0086.

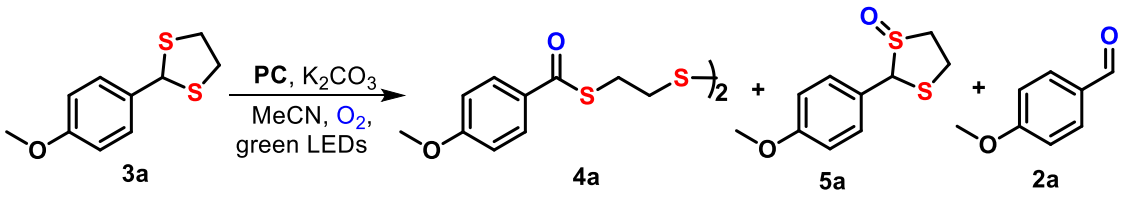
S-(2-(pyridin-2-yldisulfanyl)ethyl) 4-methoxybenzothioate (9he): White solid (Melting point-59.3-59.9 ^oC), R_f = 0.5 (1:9 :: EA:pet ether) (49 mg, 73%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.11 – 3.02 (m, 2H), 3.41 – 3.32 (m, 2H), 3.86 (s, 3H), 6.94 – 6.87 (m, 2H), 7.09 (ddd, *J* = 7.4, 4.8, 1.1 Hz, 1H), 7.64 (ddd, *J* = 8.1, 7.4, 1.8 Hz, 1H), 7.72 (dt, *J* = 8.1, 1.0 Hz, 1H), 8.02 – 7.82 (m, 2H), 8.47 (ddd, *J* = 4.8, 1.8, 0.9 Hz, 1H),; $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) 28.4, 38.6, 55.6, 113.9, 120.0, 120.9, 129.6, 129.7, 137.2, 149.8, 160.0, 164.0, 189.8,; HRMS (ESI-TOF) m/z calcd. For $C_{15}H_{16}NO_2S_3$ $[M+H]^+$ 338.0343; found 338.0347.

S-(2-(pyridin-2-yldisulfanyl)ethyl) naphthalene-2-carbothioate (9ie): Colorless liquid, R_f = 0.45 (2:8 :: EA:pet ether) (50 mg, 70%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.12-3.08 (m, 2H), 3.48-3.44 (m, 2H), 7.13 – 7.07 (m, 1H), 7.68 – 7.51 (m, 3H), 7.74 (d, *J* = 8.1 Hz, 1H), 7.88 (dd, *J* = 8.1, 4.3 Hz, 2H), 7.96 (d, *J* = 8.5 Hz, 2H), 8.53 – 8.46 (m, 2H),; $^{13}C\{^1H\}$ NMR (100

MHz, $CDCl_3$): δ (ppm) 28.6, 38.5, 120.1, 121.0, 123.2, 127.1, 127.9, 128.7, 128.7, 128.9, 129.7, 132.5, 134.1, 135.9, 137.2, 149.8, 159.9, 191.3,; HRMS (ESI-TOF) m/z calcd. For $C_{18}H_{16}NOS_3$ $[M+H]^+$ 358.0394; found 358.0398.

3.9 Appendix IIIA

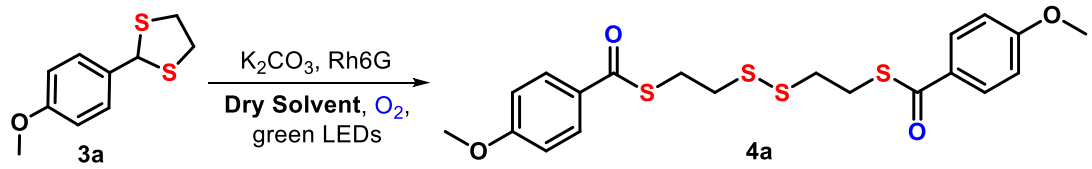
Table 1. Catalyst screening



Sr. No.	Photo Catalyst	Atmosphere & temperature	Base	Yield 4a (%)	Yield 5a (%)	Yield 2a (%)
1	Eosin Y	Open air	K_2CO_3	33	traces	50
2	Rhodamin6G	Open air	K_2CO_3	33	traces	52
3	Rhodamin6G	O_2	K_2CO_3	60	22	00
4	Eosin Y	O_2	K_2CO_3	60	25	00
5	Acr-Mes-perchlorate	O_2	K_2CO_3	51	25	00
6	TPP-tetrafluoroborate	O_2	K_2CO_3	53	29	00
7	Riboflavin	O_2	K_2CO_3	21	30	00
8	$Ru(II)(bpy)_3Cl_2$	O_2	K_2CO_3	48	27	00

[a]General reaction conditions: **3a** (0.2 mmol), K_2CO_3 (0.4 mmol), Acetonitrile (2 mL), PC (2 mol%), green/blue LEDs (15 W), under open air/O_2, 6 h. [b]Dry Acetonitrile, 6 h.

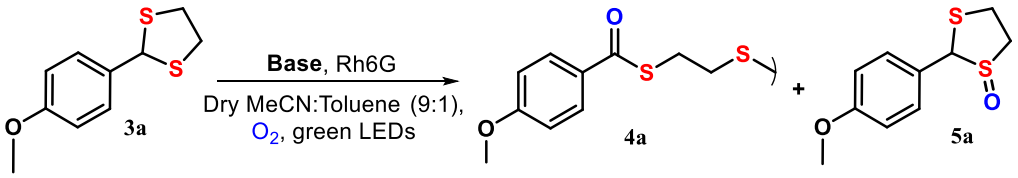
Table 2. Solvents screening



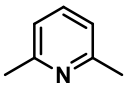
	Dry Solvent	Atmosphere & temp.	Base	Yield (%)
1	Acetonitrile	O_2, rt	K_2CO_3	60
2	Tetrahydrofuran	O_2, rt	K_2CO_3	46
3	1,4-dioxane	O_2, rt	K_2CO_3	41
4	Ethyl acetate	O_2, rt	K_2CO_3	35
5	Dichloromethane	O_2, rt	K_2CO_3	20
6	*tert*-butanol	O_2, rt	K_2CO_3	50
7	Dimethylsulfoxide	O_2, rt	K_2CO_3	30
8	Dimethylformamide	O_2, rt	K_2CO_3	30
9[c]	Acetonitrile:toluene (9:1)	O_2, rt	K_2CO_3	62
10[d]	Acetonitrile:toluene (9:1)	O_2, rt	K_2CO_3	62

[a]General reaction conditions: **3a** (0.2 mmol), Base (0.4 mmol), Solvent (2 mL), RG6G (2 mol%), green LEDs (15 W), under O_2. [b]Reaction without catalyst, 6 h, [c] 5 h, [d]Blue LEDs

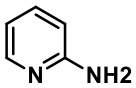
Table 3. Bases screening



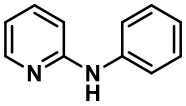
131
(4a, 60%)



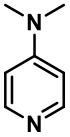
132
(4a, 57%)



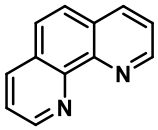
133
(4a, 35%)



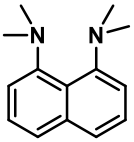
134
(4a, 39%)



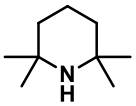
135
(4a, 70%)



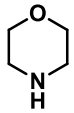
136
(4a, 59%)



137
(4a, 51%)

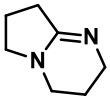


138
(4a, 41%)

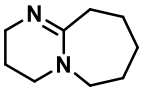


139
(4a, 41%)

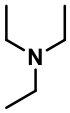
140
94a, 58%)



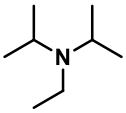
141
(4a, 59%)



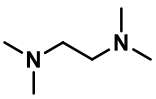
142
(4a, 55%)



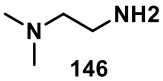
143
(4a, 34%)



144
(4a, 31%)



145
traces



146
(4a, 17%)

Na^tOBu

147
(4a, 37%)

KOAc

148
(4a, 38%)

Na_2CO_3

149
(4a, 48%)

K_2CO_3

150
(4a, 60%)

Cs_2CO_3

151
(4a, 57%)

Na_2PO_4

152
(4a, 44%)

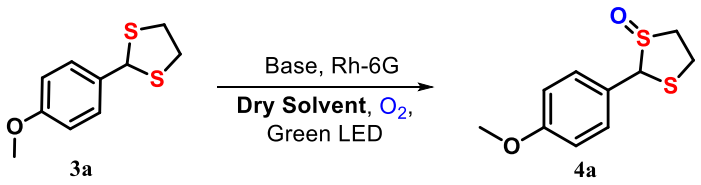
$NaHPO_4$

153
(4a, 47%)

154
(5a, 77%)

155
(4a, 60%)

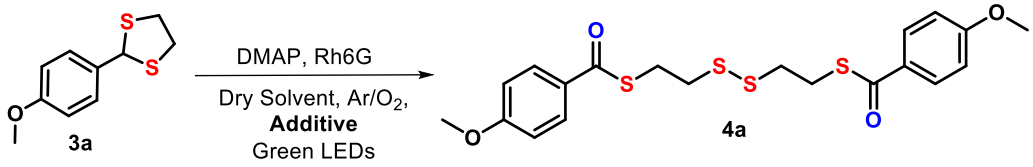
Table 4. Solvent screening



Sr. No.	Dry Solvent	Base	Atmosphere & temperature	Light source	Yield (%)
1	Acetonitrile	Imidazole	O_2, rt	Green LEDs	80
2	Tetrahydrofuran	Imidazole	O_2, rt	Green LEDs	73
3	1,4-dioxane	Imidazole	O_2, rt	Green LEDs	70
4	Ethyl acetate	Imidazole	O_2, rt	Green LEDs	68
5	Dichloromethane	Imidazole	O_2, rt	Green LEDs	58
6	*tert*-butanol	Imidazole	O_2, rt	Green LEDs	78
7	Dimethylsulfoxide	Imidazole	O_2, rt	Green LEDs	43
8	Dimethylformamide	Imidazole	O_2, rt	Green LEDs	71
9	Acetonitrile:*tert*-butanol(3:1)	Imidazole	O_2, rt	Green LEDs	83
10	Acetonitrile:*tert*-butanol(3:1)	Imidazole	O_2, rt	Blue LEDs	83
11	Acetonitrile:*tert*-butanol(3:1)	Imidazole	O_2, 50 °C	Green LEDs	traces

General reaction conditions: 3**a** (0.2 mmol), Base (1 mmol), Solvent (2 mL), Rh6G (2 mol%), green/blue LEDs (15 W), O_2 balloon, 12 h.

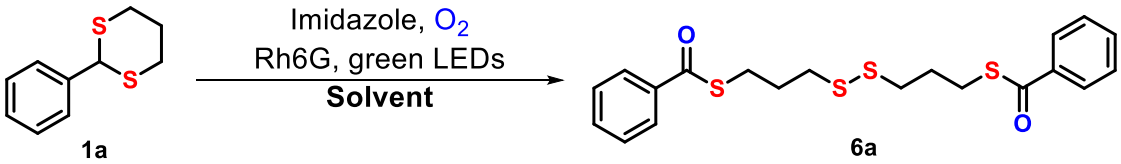
Table 5. Additives screening



Sr. No.	Additive (equiv.)	Atmosphere	Time (h)	Yield (%)
1	KNO_3 (4)	Argon	15	43
2	$NaNO_3$ (4)	Argon	15	41
3	$K_2S_2O_8$(4)	Argon	15	37
4	$(NH_4)_2S_2O_8$ (4)	Argon	15	35
5	Nitrobenzene (2)	O_2	12	49
6	2,4-dinitrobenzaldehyde (1)	O_2	12	52
7	Dimethylsulfide (1)	O_2	24	53
8	Thioanisol (1)	O_2	24	48
9	S_8 (0.2)	O_2	10	55
10	Se powder (0.2)	O_2	12	57

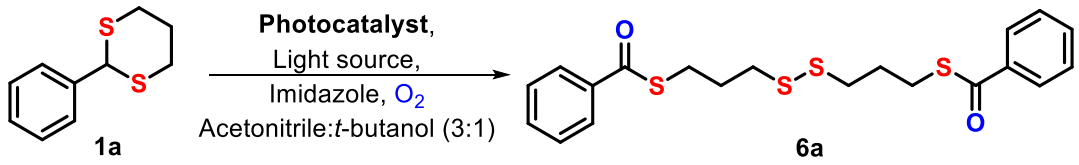
General reaction conditions: **3a** (0.2 mmol), DMAP (0.4 mmol), MeCN (1.8 mL), Toluene (0.2 mL), Rh6G (2 mol%), green LEDs (15 W), Argon/O_2 balloon.

Table 6. Solvent screening



Sr. No.	Dry Solvent	Atmosphere	Light source	Yield (%)
1	Acetonitrile	O_2	Green LEDs	30
2	Tetrahydrofuran	O_2	Green LEDs	19
3	1,4-dioxane	O_2	Green LEDs	17
4	Ethyl acetate	O_2	Green LEDs	12
5	Dichloromethane	O_2	Green LEDs	Traces
6	*tert*-butanol	O_2	Green LEDs	28
7	Dimethyl sulfoxide	O_2	Green LEDs	20
8	Dimethylformamide	O_2	Green LEDs	18
9	Acetonitrile:*tert*-butanol (3:1)	O_2	Green LEDs	37
10	Acetonitrile:*tert*-butanol (3:1)	O_2	Blue LEDs	37

Table 7. Catalyst screening



Sr. No.	Catalyst	Atmosphere & temperature	Light source	Yield (%)
1	Rh6G	O_2, rt.	Green LED	37
2	Eosin Y	O_2, rt.	Green LED	10
3	Mes-Acr	O_2, rt.	Blue LED	31
4	$Ru(II)(bpy)_3Cl_2$	O_2, rt.	Blue LED	23

Table 8. Bases screening

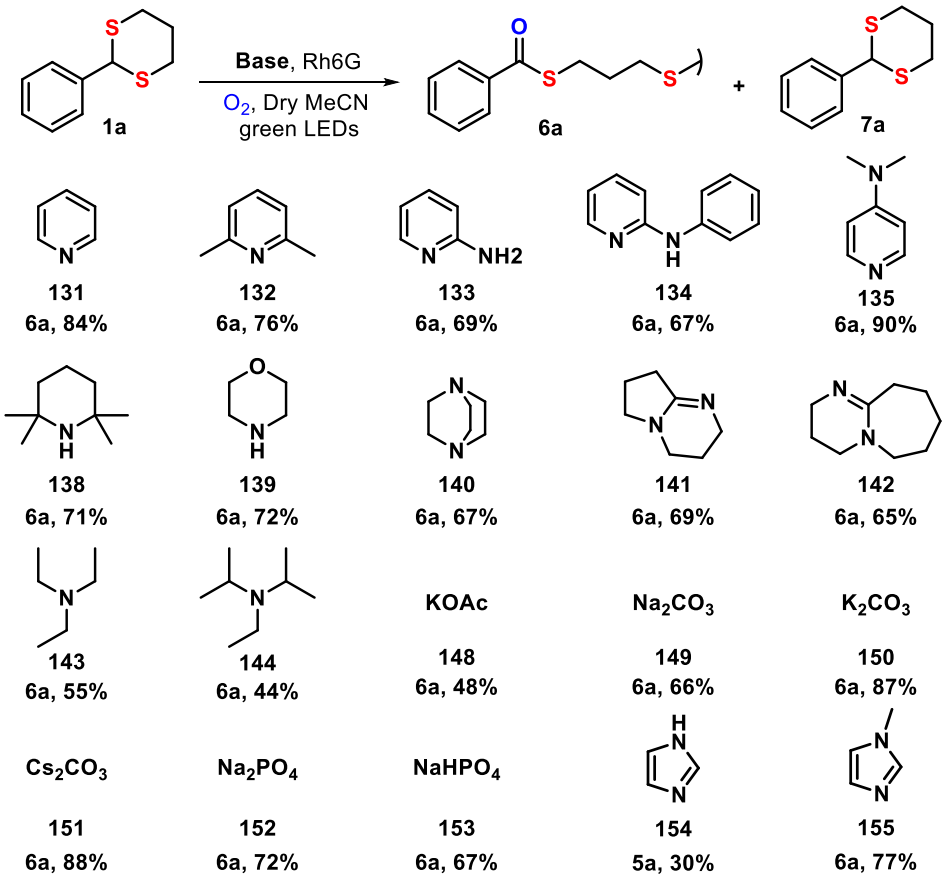
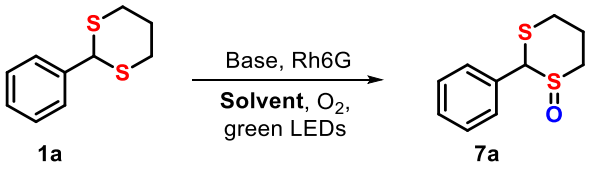


Table 9. Solvent screening



Sr. No.	Dry Solvent	Atmosphere & temperature	Base	Yield (%)
1	**Acetonitrile**	**O_2, rt.**	**DMAP**	**90**
2	Tetrahydrofuran	O_2, rt.	DMAP	70
3	1,4-dioxane	O_2, rt.	DMAP	75
4	Ethyl acetate	O_2, rt.	DMAP	60
5	Dichloromethane	O_2, rt.	DMAP	40
6	*tert*-butanol	O_2, rt.	DMAP	79
7	Dimethylsulfoxide	O_2, rt.	DMAP	72
8	Dimethylformamide	O_2, rt.	DMAP	73

Appendix IIIB: ^{1}H and ^{13}C NMR spectral data of representative compounds

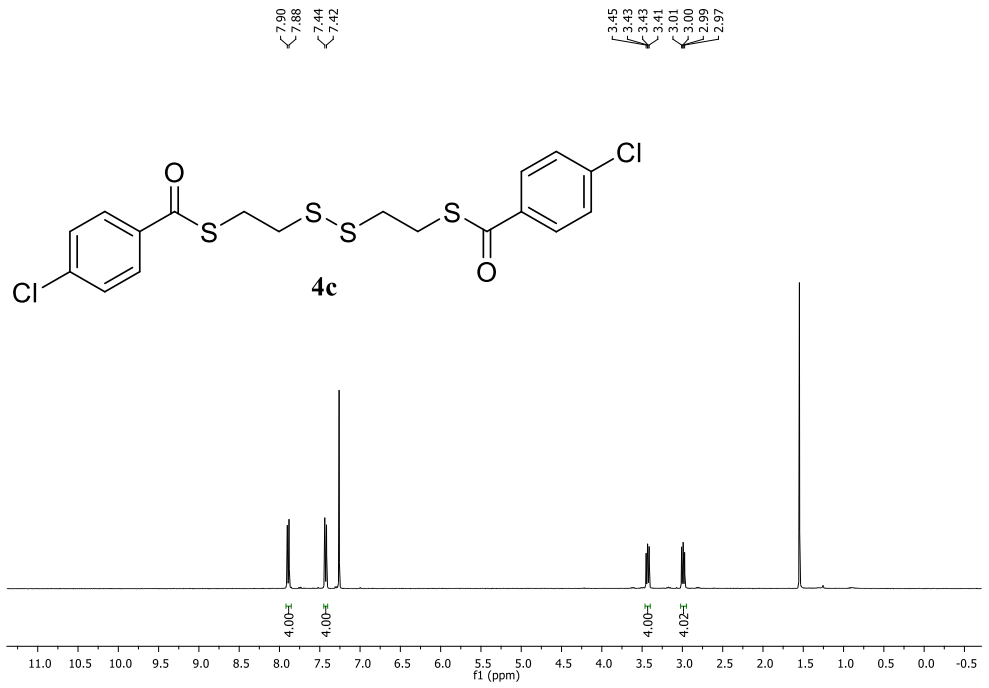


Fig. III. 1: ^{1}H NMR spectrum of **4c**, $CDCl_3$, 400 MHz

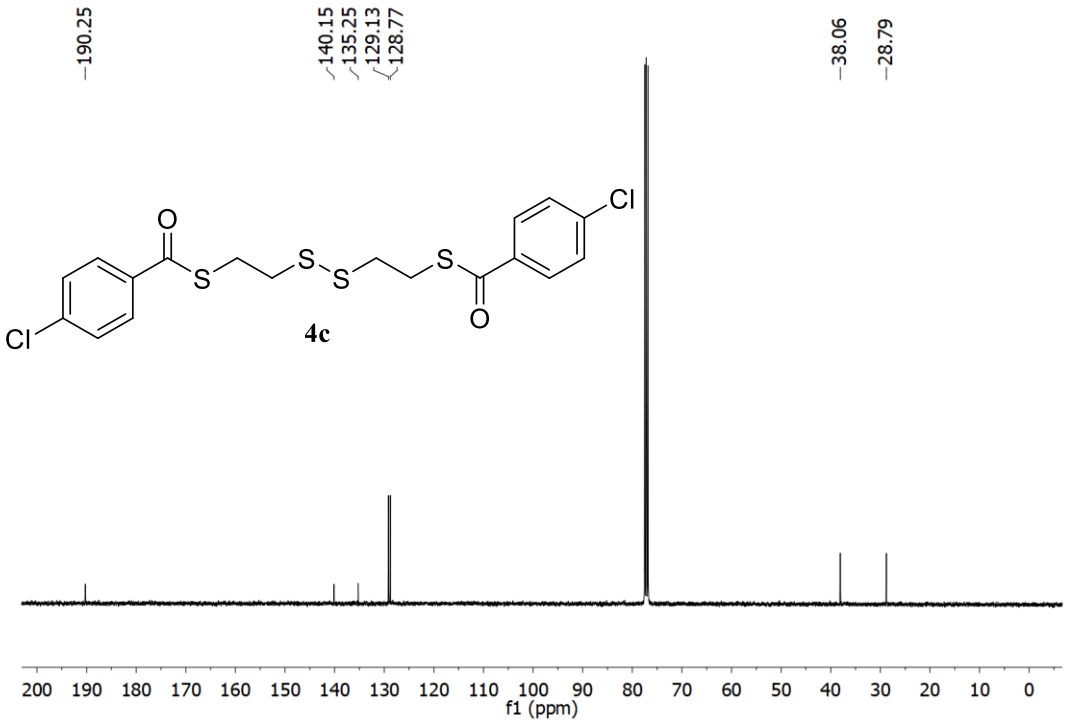


Fig. III. 2: ^{13}C {^{1}H} NMR spectrum of **4c**, $CDCl_3$, 100 MHz

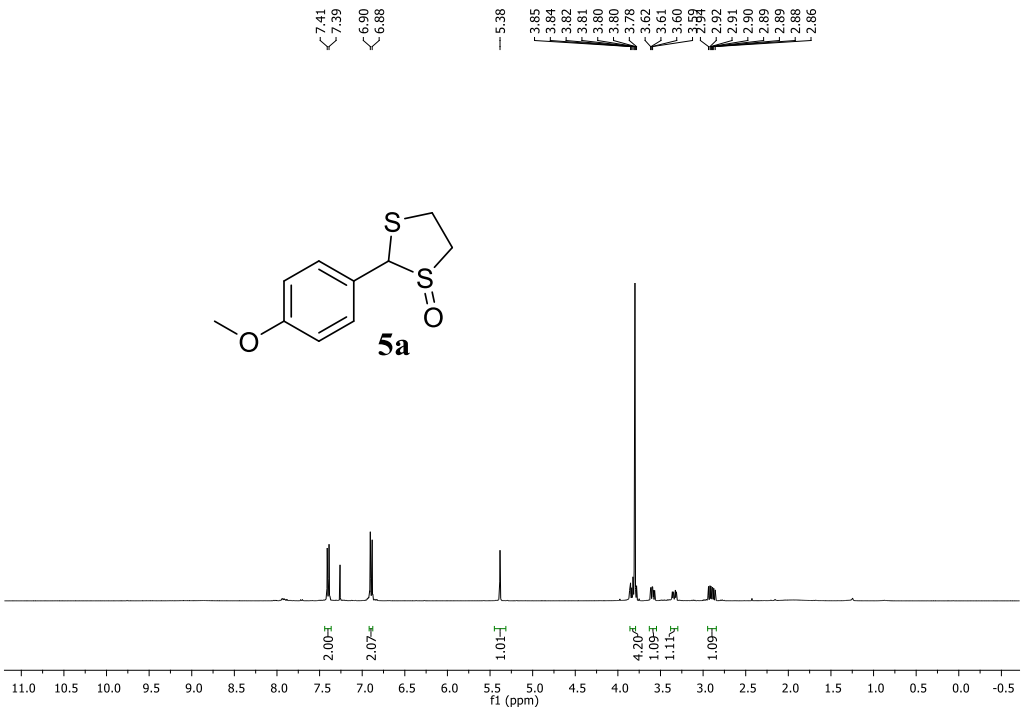


Fig. III. 3: ^{1}H NMR spectrum of **5a**, $CDCl_3$, 400 MHz

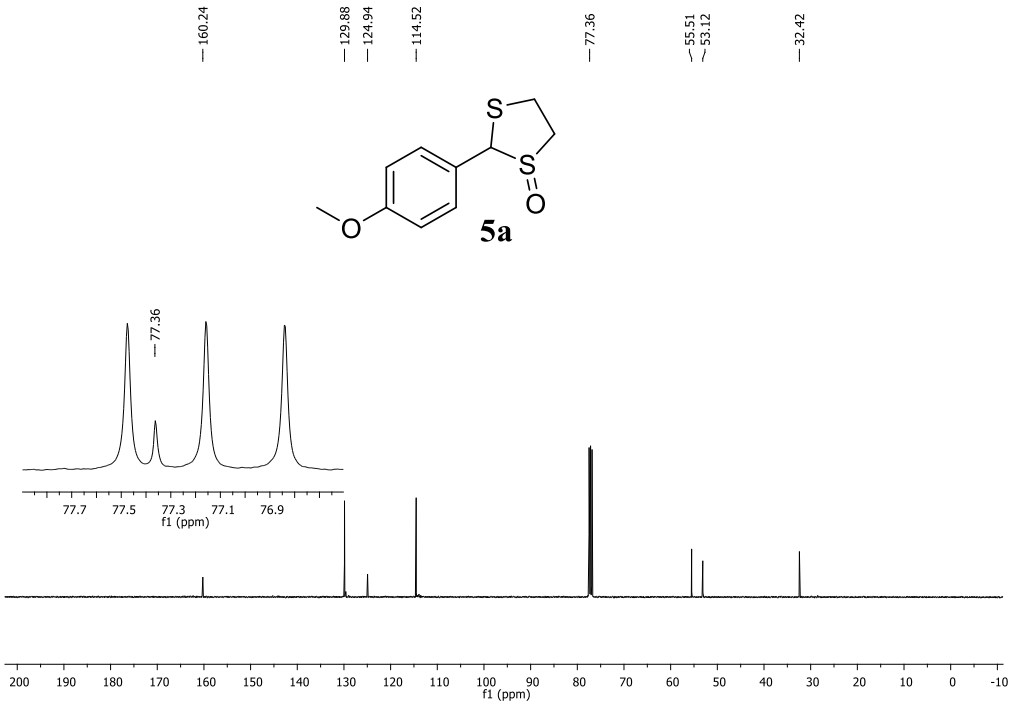


Fig. III. 4: $^{13}C\{^{1}H\}$ NMR spectrum of **5a**, $CDCl_3$, 100 MHz

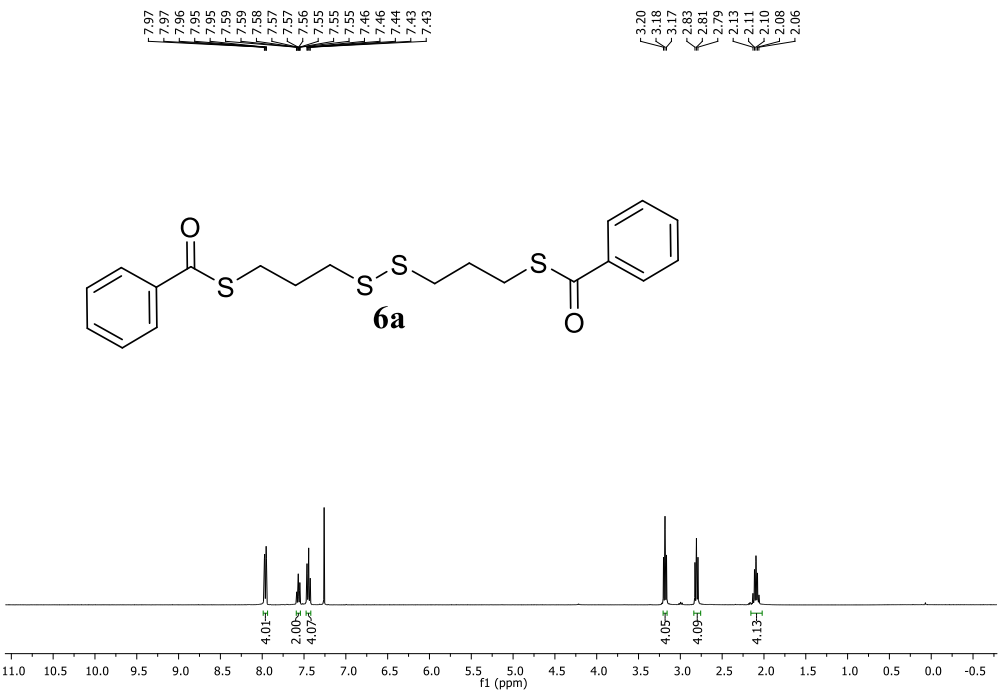


Fig. III. 5: ^{1}H NMR spectrum of **6a**, $CDCl_3$, 400 MHz

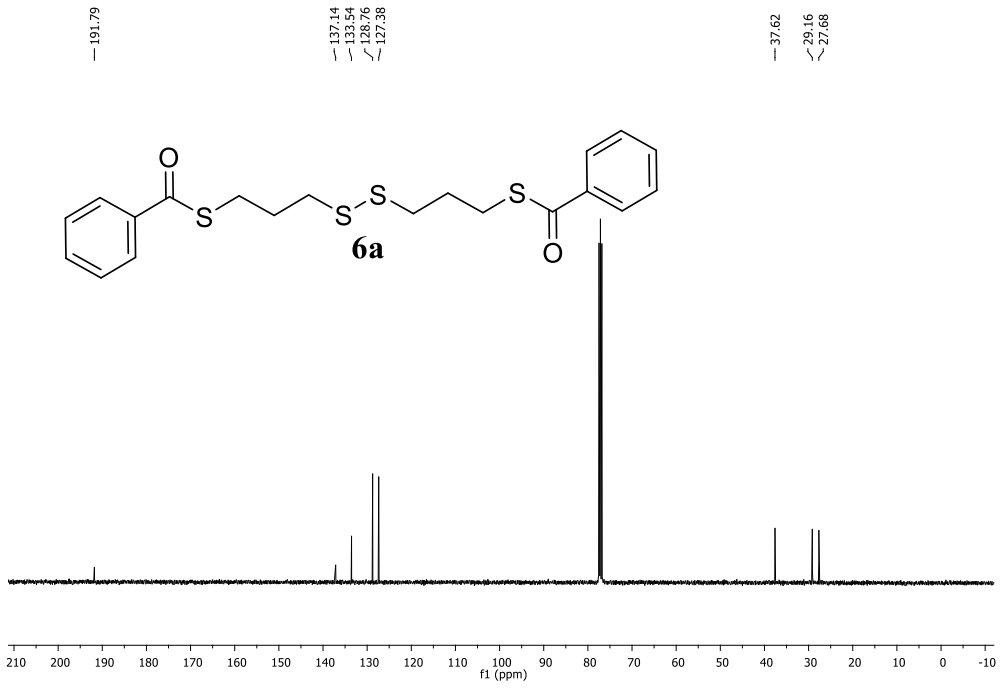


Fig. III. 6: ^{13}C {^{1}H} NMR spectrum of **6a**, $CDCl_3$, 100 MHz

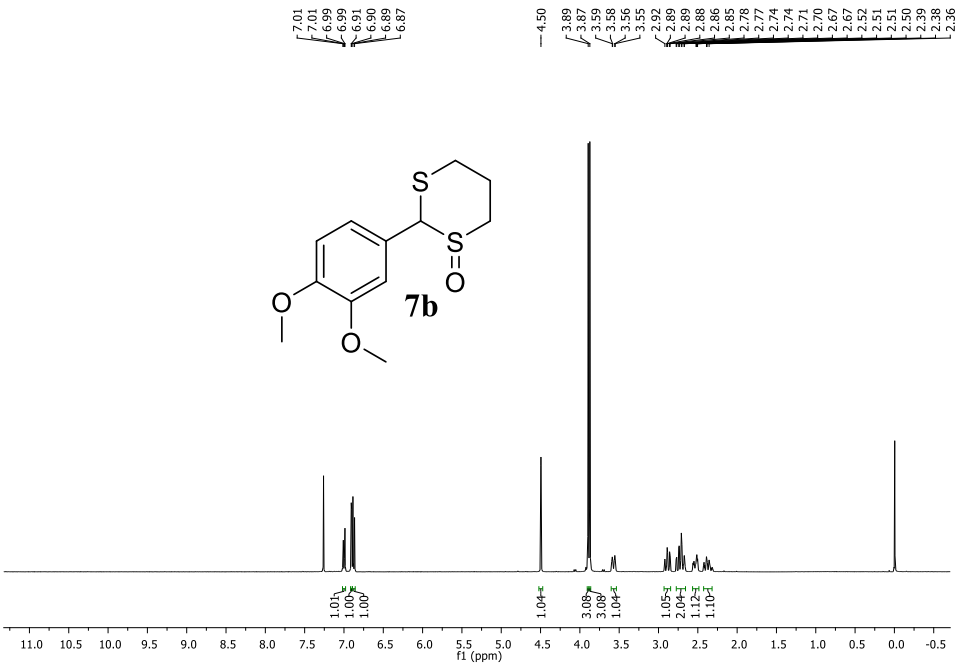


Fig. III. 7: ^{1}H NMR spectrum of **7b**, $CDCl_3$, 400 MHz

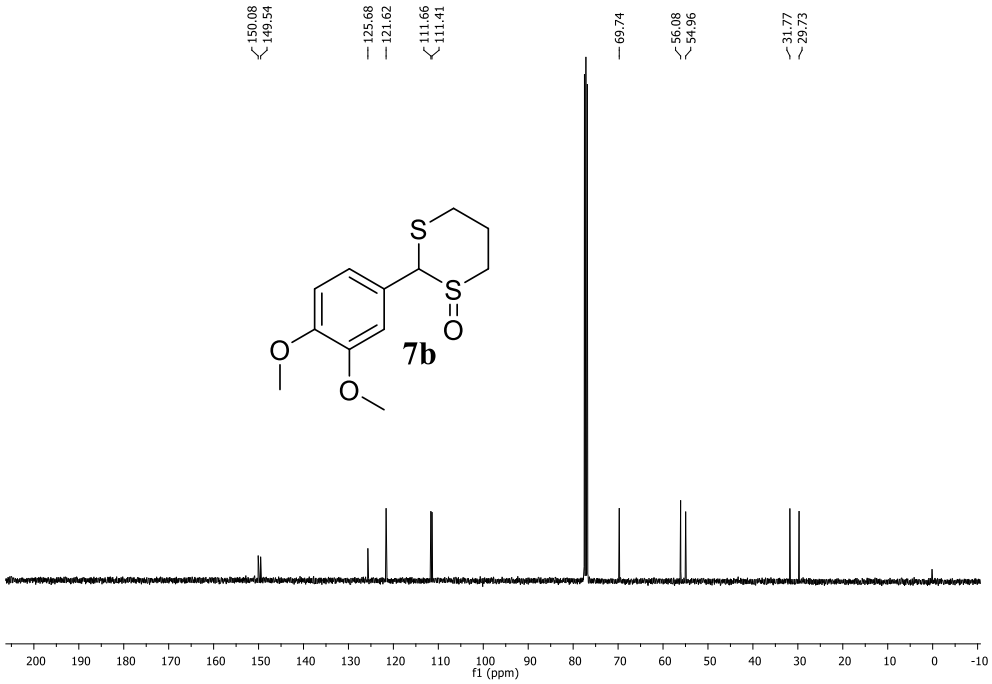


Fig. III. 8: ^{13}C {^{1}H} NMR spectrum of **7b**, $CDCl_3$, 100 MHz

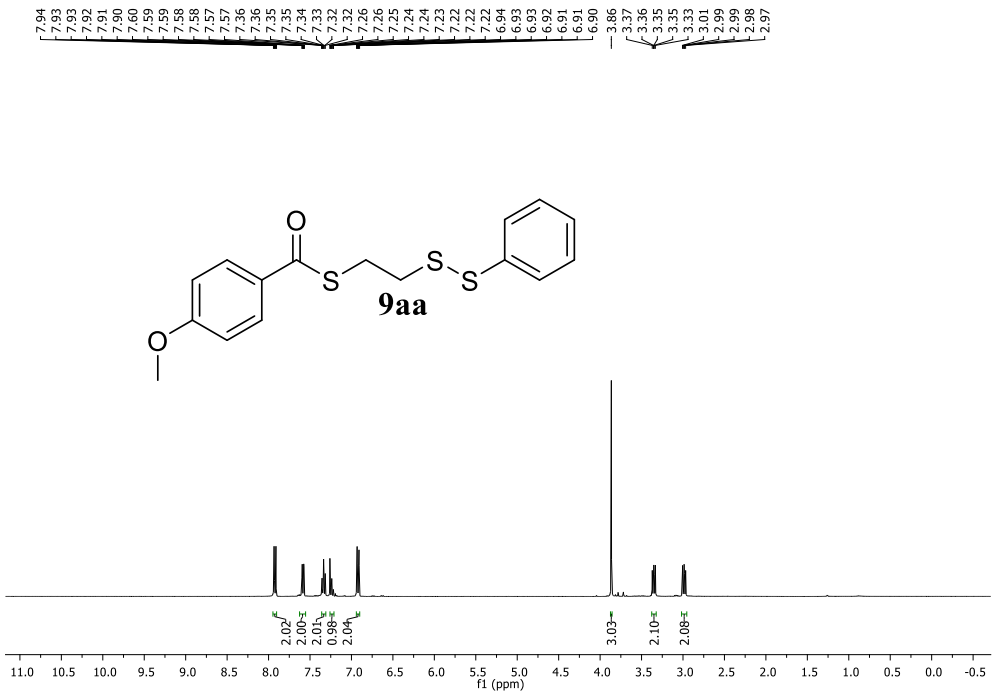


Fig. III. 9: ^{1}H NMR spectrum of **9aa**, $CDCl_3$, 400 MHz

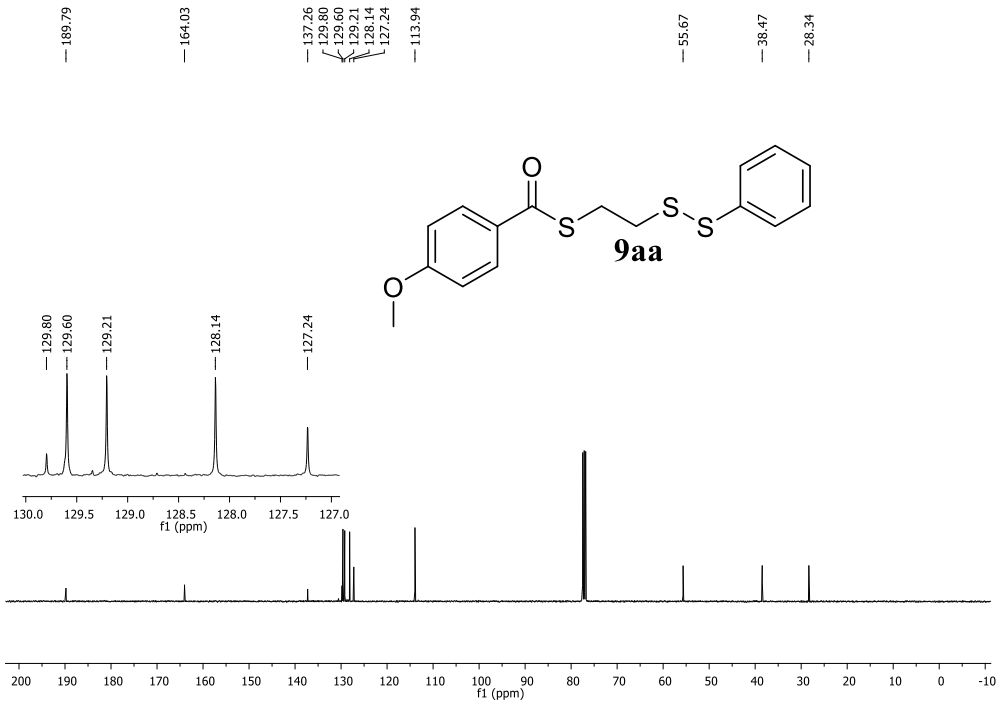


Fig. III. 10: ^{13}C {^{1}H} NMR spectrum of **4c**, $CDCl_3$, 100 MHz

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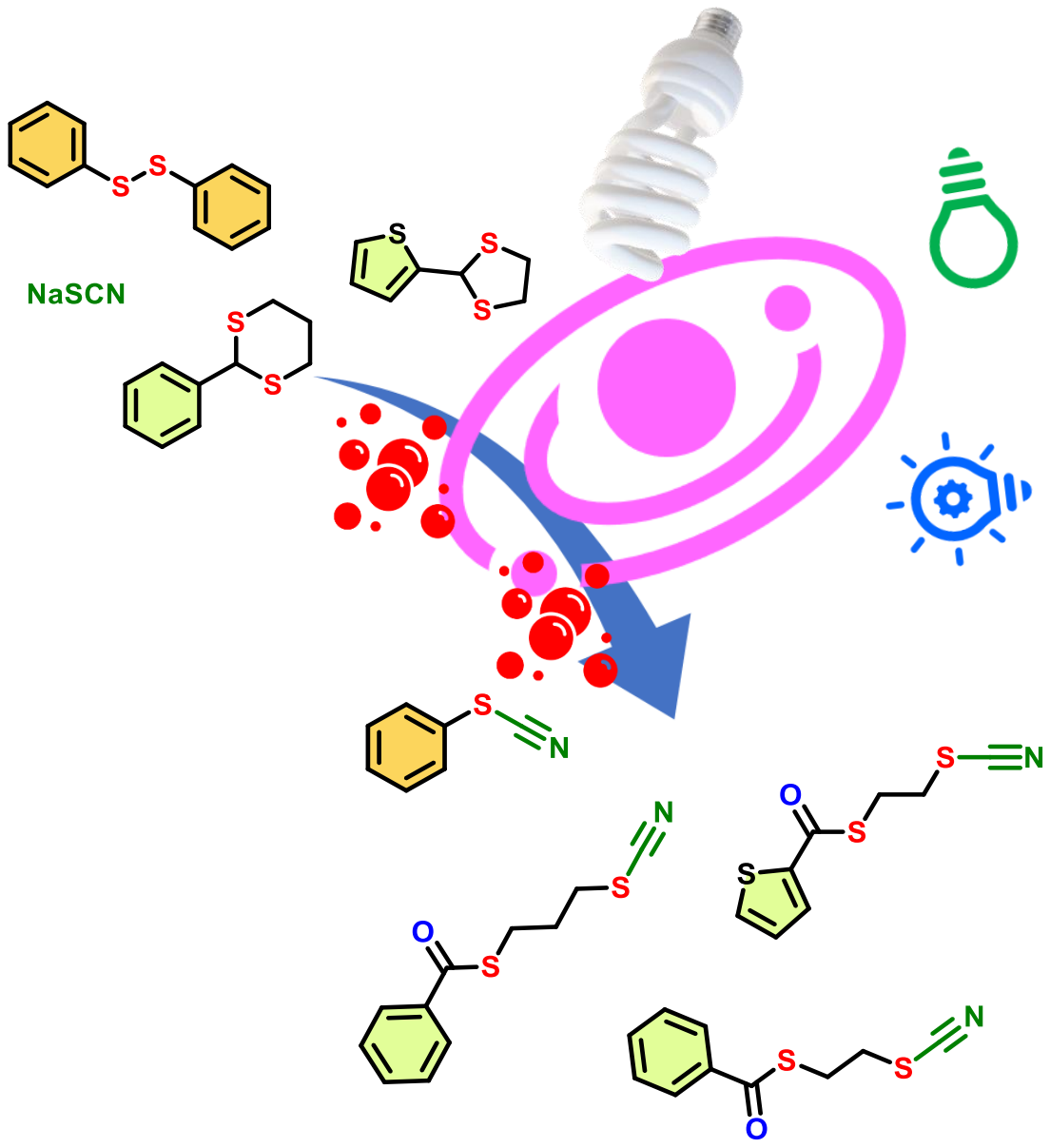
Chapter 4: A Direct Synthesis of Thiocyano-Thioesters from Cyclic Thioacetals via Visible Photoredox Catalysis



Chapter 4

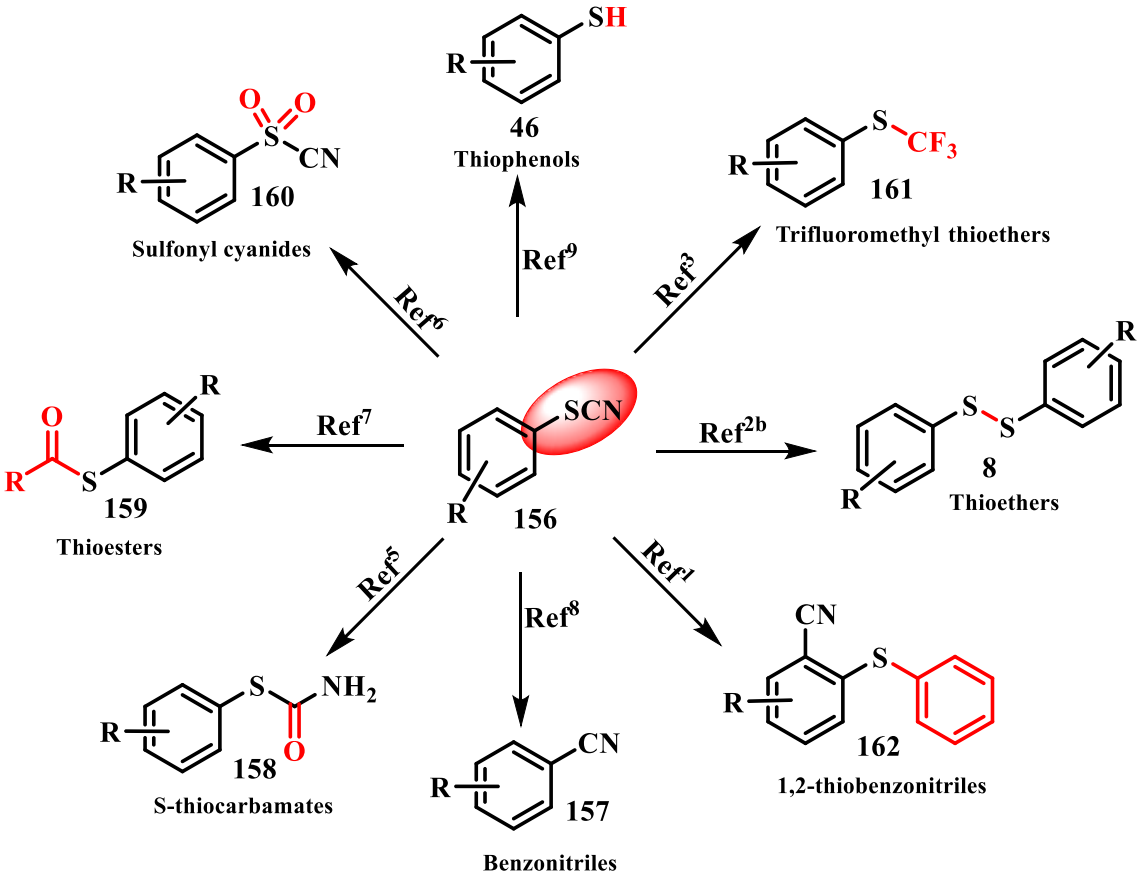
A Direct Synthesis of Thiocyano-Thioesters from Cyclic Thioacetals via Visible Photoredox Catalysis

4.1 ***Abstract:*** *Cyanation is one of the highly important and useful transformation to access the nitrile functionality in organic molecules. However, the cyanation of organic molecules is highly limited to a very few reactive substrates and cyantion of organic compounds generally requires highly toxic reagents as "CN source". Undoubdetly, the cyanation using mild and environmentally benign reagent is highly desirable and thiocynate salt has been eomloyed as a safer alterntaive to cyanide reagent. We have developed a protocol for the cyanation of cyclic dithioacetals as well as disulfides using sodium thiocyanate under visible light photoredox catalysis to access thiocyano-thioesters in an efficient manner. This protocol proved to highly effective to introduce two functional groups in one pot to access thioester-thiocynates and alkyl thiocyanates respectively.*

4.2 Introduction

Thiocyanate has been proven as a central building block for the synthesis of different functional moieties such as nitriles **157,** thiocarbamates **158**, thioesters **159**, sulfonyl cyanides **160** thiols **46**, thioethers **161 (**trifuloromethyl thioethers), disulfides **8**, thiobenzonitriles **162** etc (Scheme 4.1).[1-9] Similarly, even thioester also plays a significant and vital role as an important intermediate in many biological processes such as; protein synthesis, native chemical ligation (NCL) and nucleic acid synthesis.[10] More prominently, thioesters have been widely utilized in biomolecules labelling as well as in drug delivery applications.[11] Additionally, thioesters have been widely employed in many synthetic transformations and often used as an important surrogate of acyl radical for the acylation reactions.[12] Apart from this, thioesters have great synthetic utility in the synthesis of alcohols, aldehydes, ketones, esters, amides.[12]

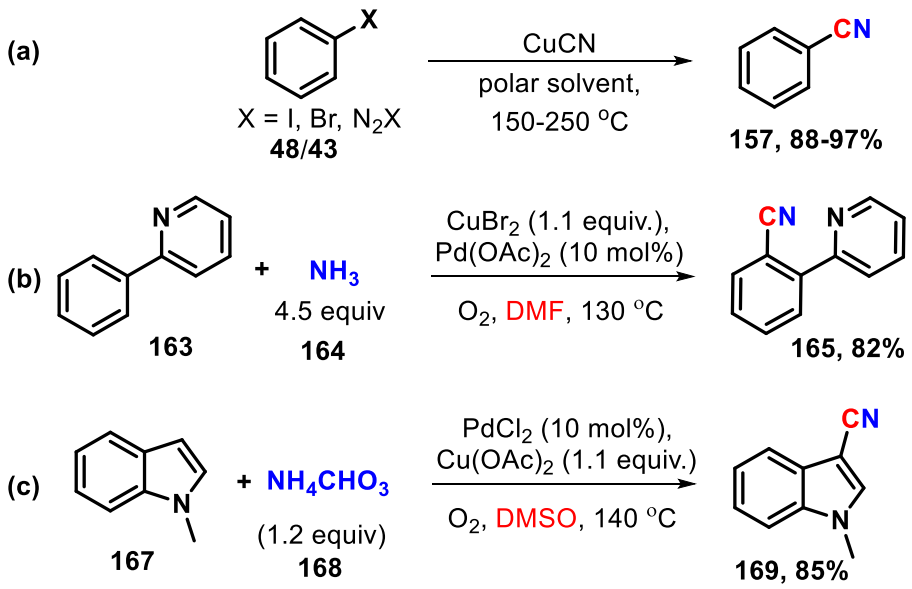
Scheme 4.1: Aryl thiocyanate as a building block for constructing useful different functionalities.



Traditionally, cyanation is accomplished by using a "CN source" (toxic cyanide reagents) or by using metal catalysts along with other necessary ligands, oxidants for the *in situ* generation of cyanide (cyanide source) at an elevated reaction temperature.[13] The cyanation of the aromatic halides **48**/diazonium salts **43** has been achieved using CuCN (as a toxic CN source) at an elevated temperature (125-150 ^{o}C) to access the corresponding nitriles **157** in good to very good yields (up to 97%, Scheme 4.2a).[13a] The cyanation of an pyridine substituted benzene **163** has been also achieved using the palladium catalyst (10 mol%) along with copper reagent (stoichiometric amount) and ammonia **164** under oxygen atmosphere via the *in situ* generation of CN in DMF at an elevated temperature to afford the corresponding nitrile **165** (82%, Scheme 4.2b).[13b] Likewise, heteroarene such as *N*-methyl indole **167** on treatment with $PdCl_2$ (10 mol%), copper acetate (1.1 equiv.) and ammonium bicarbonate (NH_4CO_3) **168** under oxygen atmosphere in DMSO at an elevated temperature 140 ^{o}C

furnished the corresponding 3-cyano *N*-methyl indole **169** in good yield (85%, Scheme 4.2c).[13c]

Scheme 4.2 Cyanation using the toxic metal cyanide and metal catalysts at high temperature

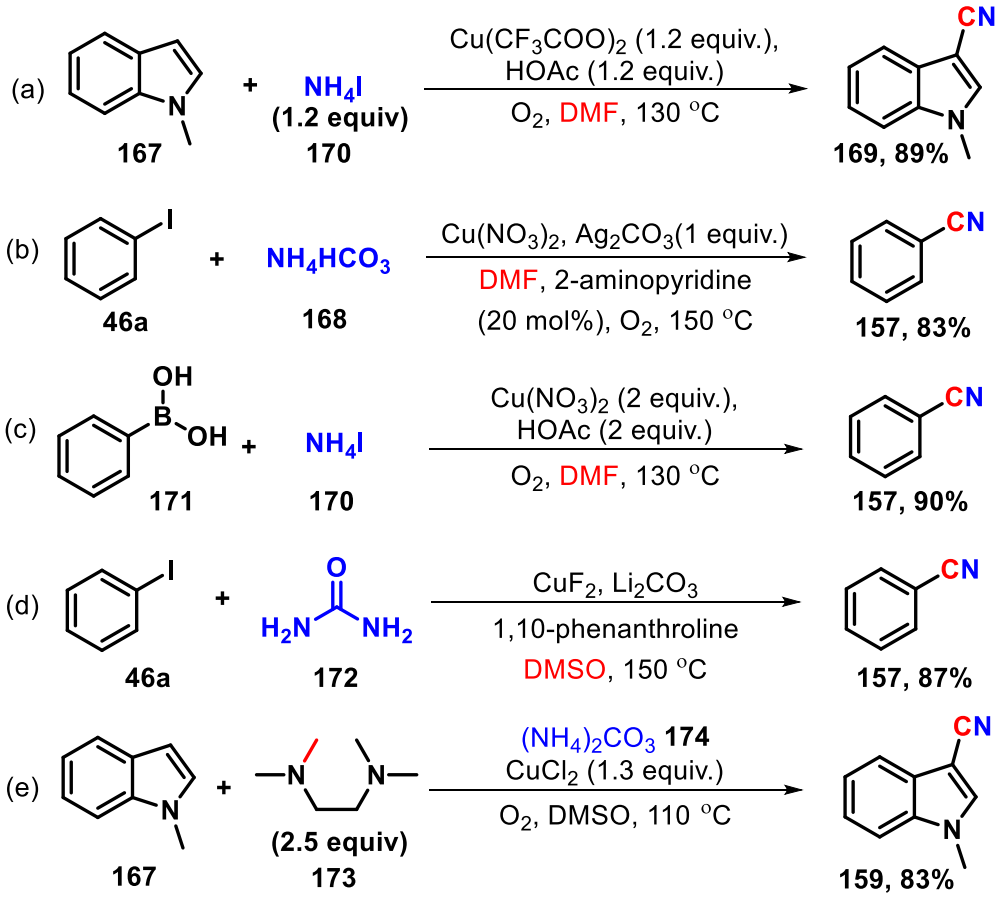


The cyanation has been also achieved using different copper reagents under oxidizing reaction conditions and these protocols successfully avoided the use of toxic cyanating reagents such as CuCN and expensive palladium catalysts. However, these protocols relied on the usage of an excess amount of copper reagent at elevated temperatures (110-150 °C) (Scheme 4.3a-e).

The cyanation of *N*-methyl indole **167** has been achieved by using the stoichiometric amount of copper triflate reagent under oxygen atmosphere by generating *in situ* "CN source" by the reactions of ammonium iodide **170** and DMF to afford the corresponding 3-cyano *N*-methyl indole **169** in good yield (89%, Scheme 4.3, a).[13d] The cyanation of aryl iodide **46a** has been also achieved by utilizing the ammonium bicarbonate **168** in presence of copper and silver reagents under oxidizing reaction conditions in DMF to access the corresponding nitrile **157** in good yield (83%, Scheme 4.3b).[13e] The reaction of ammonium iodide **170** with DMF in presence of copper nitrate (2 equiv.) at high reaction temperature has been achieved for the direct cyanation of boronic acids **171** to a corresponding nitrile **157** (Scheme 4.3c).[13f] Alternatively, the cyanation of aryl iodide **46a** has been also achieved using the mixture of urea **172** and DMSO at an elevated temperature in presence of copper fluoride and the 1,10-phenanthroline ligand to access the corresponding nitrile **157** (87%, Scheme 4.3 d).[13g] The

cyanation of N-methyl indole **167** has been also achieved using ammonium carbonate **174** and tetramethylethylene diamine TMEDA **173 (**as nitrogen source) in DMSO (as carbon source) in presence of stoichiometric amount of copper chloride under oxygen atmosphere at 130 ℃ (83%, Scheme 4.3e).[13h]

Scheme 4.3 Cyanation using the copper reagents at elevated temperature

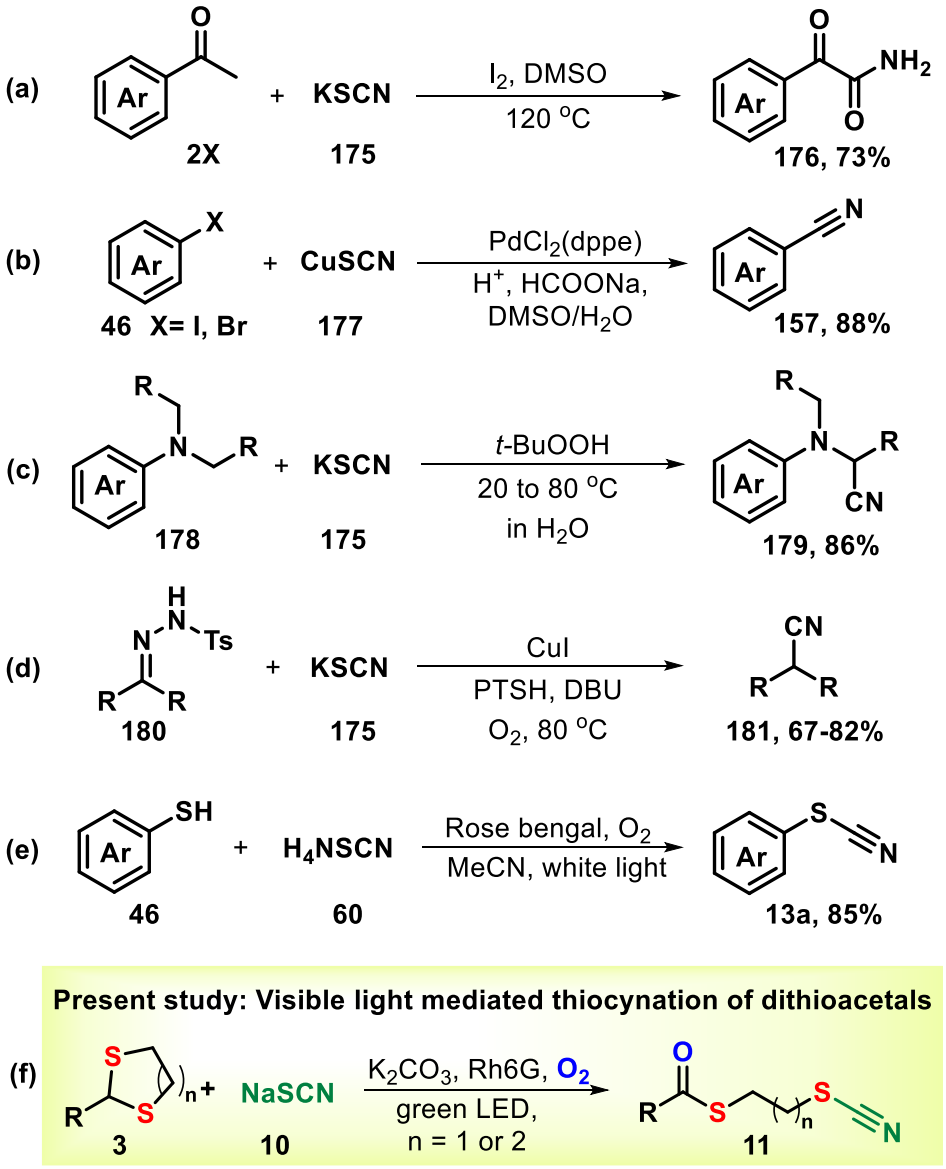


Some of these useful methods successfully avoided the usage of highly toxic CuCN reagent, but unfortunately required the equimolar or the excess amount of metal catalysts/reagents at very high reaction temperatures. Some of these reaction conditions limit their practical utility for wider substrates scope especially for the sensitive compounds and also it generates metal waste and consumes energy.

In this regard, there is a growing interest for the development of cyanation strategies that uses relative less toxic and environmentally safer reagent at an ambient reaction condition. Over the last few years thiocyanate salt has emerged as safer and useful “CN source” for the cyanation of different organic compounds. Thiocyanates are easily available, inexpensive and

significantly non-toxic in nature. Potassium thiocyanate **175** and iodine have been employed to access phenylglyoxamides **176** starting from aryl ketones **2x** in good yield (Scheme 4.4a).[14] The cyanation of aromatic halides **46** accomplished by using CuSCN **177** and palladium catalyst (5 mol%) to furnished different nitriles in good to very good yields (up to 88%, Scheme 4.4b).[15]

Scheme 4.4. Cyanation of organic compounds using thiocyanates



Even the cyanation of tertiary amines **178** has been demonstrated using potassium thiocyanate **175** under oxidizing reaction conditions at 80 ℃ to afford the corresponding nitriles **179** (up to 86% yields, Scheme 4.4c).[16] Similarly, the cyanation of tosyl hydrazones

180 has been disclosed using potassium thiocyanate **175** and copper iodide through the *in situ* generated carbene intermediate to access the corresponding nitriles **181** (Scheme 4.4d).[17] Very recently, an elegant metal-free cyanation of thiophenol **46** has been achieved using ammonium thiocyanate **60** via photoredox catalysis under oxygen atmosphere to furnish the corresponding phenyl thiocyante **13a** via the generation of thiocyanate radical in good yield (85% Scheme 4.4e).[18] However, this simple and straightforward strategy for cyanation using potassium thiocyanate is explored for thiophenols derivatives only. Hitherto, to the best of our knowledge the cyanation of thioethers has not been realized using thiocyanates. Another important and useful compounds such thioesters have been synthesized by developing different protocols relying on acid, aldehydes, acid chlorides, acid anhydrides or by thiocarbonylation.[19, 20]

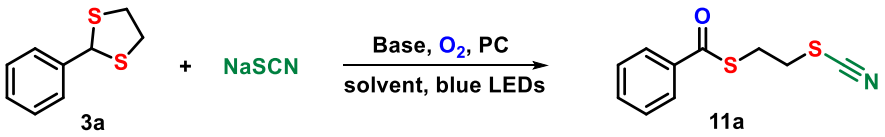
As discussed earlier, the compounds containing both thiocyano and thioster moieties are very important intermediates and there no reports on the synthesis of compounds containing both thioesters and thiocyano moieties in one pot. Owing to the importance of this framework and looking at the complexity involved in the synthesis of thiocyano-thioesters in single step we became interested in exploring further. Our research group has been working in the field of photoredox catalysis and we have been working on the reactivity of cyclic dithioacetals under visible light photoredox catalysis. After gleaned through the literature, we became interested in establishing a strategy for direct cyanation of cyclic thioethers such as cyclic dithioacetals using benign and mild reactive cyanating reagents. Having expertise in the field and working with cyclic dithioacetals, earlier we had disclosed that the cleavage of C–S bond in cyclic dithioacetals is known to generation of thiyl radical intermediate under visible light irradiation.[19a-c] Very, recently we have developed a novel synthetic route to access rearrangement of cyclic dithioacetals under basic photoredox catalytic conditions through the controlled cleavage of single C–S bond.[19c] To explore this reactivity by considering the mechanistic pathway for disulphide-linked-dithioesters, we hypothesized that compound containing dual functional groups such as thiocyano-thiosesters can be synthesized in one pot by using the reactivity of electrophilic thiocyanate radical with cyclic dithioacetals under suitable photoredox conditions (Scheme 4.4f).

In this chpater, we describe the development of a novel startegy to access thicyano-thiosters directly from via cyclic dithioacetals by the introduction of two functional groups in single step visible light photoredox catalytic conditions.

4.3 Results and Discussion

4.3.1 Reaction optimization

Table 4.1. Reaction optimization



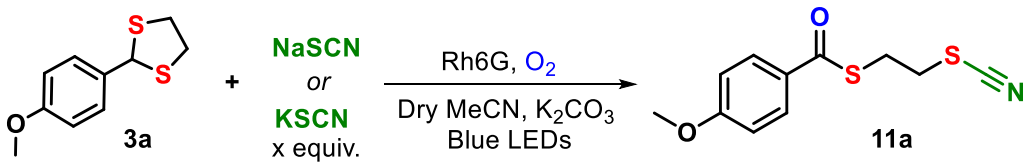
Entry	Catalyst	Solvent	Base	Yield of 11a in %
1[b]	Rh6G	MeCN	K_2CO_3	15
2	Rh6G	MeCN	K_2CO_3	83
3	Eosin Y	MeCN	K_2CO_3	67
4	Acr	MeCN	K_2CO_3	60
5	$Ru(bpy)_3Cl_2$	MeCN	K_2CO_3	49
6	Rose Bengal	MeCN	K_2CO_3	24
7	Rh6G	^{t}BuOH	K_2CO_3	61
8	Rh6G	DMSO	K_2CO_3	19
9	Rh6G	THF	K_2CO_3	43
10	Rh6G	Dioxane	K_2CO_3	51
11	Rh6G	$CHCl_3$	K_2CO_3	33
12	Rh6G	MeCN	DMAP	70
13	Rh6G	MeCN	TEA	41
14	Rh6G	MeCN	Na_2CO_3	62
15	Rh6G	MeCN	$NaHCO_3$	58
16[c]	Rh6G	MeCN	K_2CO_3	82
17	--	MeCN	K_2CO_3	N.R.
18[d]	Rh6G(without Light)	MeCN	K_2CO_3	N.R.
19[e]	Rh6G (Argon)	MeCN	K_2CO_3	N.R.
20	Rh6G	MeCN	--	Traces
21[f]	Rh6G (open air)	MeCN	K_2CO_3	71

[a]**3a** (0.1 mmol), Catalyst (2 mol%), K_2CO_3 (0.2 mmol), NaSCN (0.5 mmol), MeCN (2 mL), O_2 baloon, blue LEDs (15 W), isolated yields in %; [b]NH_4SCN, [c]KSCN, [d]without light, [e]under argon, [f]open air

To substantiate our hypthesis, we began with the dithiolane **3a** and ammonium thiocyanate (NH_4SCN) **60** using Rh6G (2 mol%) as a PC, K_2CO_3 as a base under oxygen atmosphere in dry acetonitrile with the irradiation of visible light (Blue LEDs, 15 W) for 8 h. Interestingly, the model reaction furnished the anticipated product: thiocyano-thioester **11a** in 15% yield (Table 4.1, entry 1). Surprisingly, the sodium thiocyanate **10** (instead of NH_4SCN **60**) under the intial reaction conditions (Table 4.1 Entry 2) furnished the corresponding desired thiocyano-thioester **11a** in 83% yield (Table 1, Entry 2). Encouraged by the initial results we varied the various parameter to increase the yield of reaction condition. Sequentially, we screened several well known PC such as; Rh6G **30**, EY **33**, Acr-Mes **27**, $Ru(bpy)_3Cl_2$ **14**, $Ir(ppy)_3$ **15**, and TPT (Pyrillium-BF_4) **18** while maintaining other reaction conditions (Table 4.1, Entries 2 and 3-6). We observed that Rh6G proved to be more efficient and optimum PC for the desired transformation of **3a** to furnish the corresponding thiocyano-thioester **11a** in very good yield (83%, Table 1, Entry 2) and while the other PC catalyzed the desired transforamtion but did not furnish the **11a** in higher yields. Next to examine, the role of solvent on the outcome of the reaction, we further performed the reaction of dithiolane **3a** and sodium thiocyanate **10**, Rh6G (2 mol%) in different solvents while maintaining other optimized conditions so far (Table 4.1, Entry 2 and 7-11). We observed that among all solvents screened, anhydrous acetonitrile found to be helpful for the facile transformation of **3a** to thiocayano-thioester **11a** in good yield (83%, Table 4.1, Entry 2). Later, to optimise the suitable base, we carried out the reaction of **3a** using different bases under the standardized reaction conditions so far (Table 4.1, Entries 12-15). We observed that among all the bases evaluated, K_2CO_3 proved to be the efficient base for the facile transformation to afford thiocayano-thioester **11a** in very good yield (83%, Table 4.1. Entries 12-15). Later, in order to evaluate the role of counter cation if any on the outcome of the transformation, we screened the reaction of **3a** in presence of potassium thiocyanate **175** while keeping constant the other standardized condition (Table 4.1. Entry 16). Potassium thiocyanate **175** reacted smoothly with **3a** to afford the desired product **11a** in 82% yield and we observed that there was no remarkable change in the reactivity of KSCN in compasriosn to that of NaSCN (83%, Table 4.1, Entry 2). In order to optimise the amount of NaSCN, we screened the reaction of **1a** with different stiochimetric amounts of sodium thiocyanate while maintaining the standard conditions (Table 4.2). Based on these experiements, it was evident that an excess stoichiometric amount of sodium thiocyanate (5 equiv.) is

very much required for the rapid conversion of **3a** to the corresponding thiocayano-thioester **11a** in very good yield (Table 4.2, Entries1-5).

Table 4.2 Screening for stiochiometry of thiocyanate salt



Sr. no.	Catalyst	NaSCN (equiv.)	Base	Yield of 2a in %
1	Rh6G	1	K_2CO_3	55
2	Rh6G	2	K_2CO_3	65
3	Rh6G	3	K_2CO_3	73
4	Rh6G	4	K_2CO_3	79
5	Rh6G	5	K_2CO_3	83

Reaction Condition: 0.1 mmol **3a**; 0.2 mmol K_2CO_3; Rh6G (2 mol%); 2 mL Dry MeCN; 15 W blue LEDs

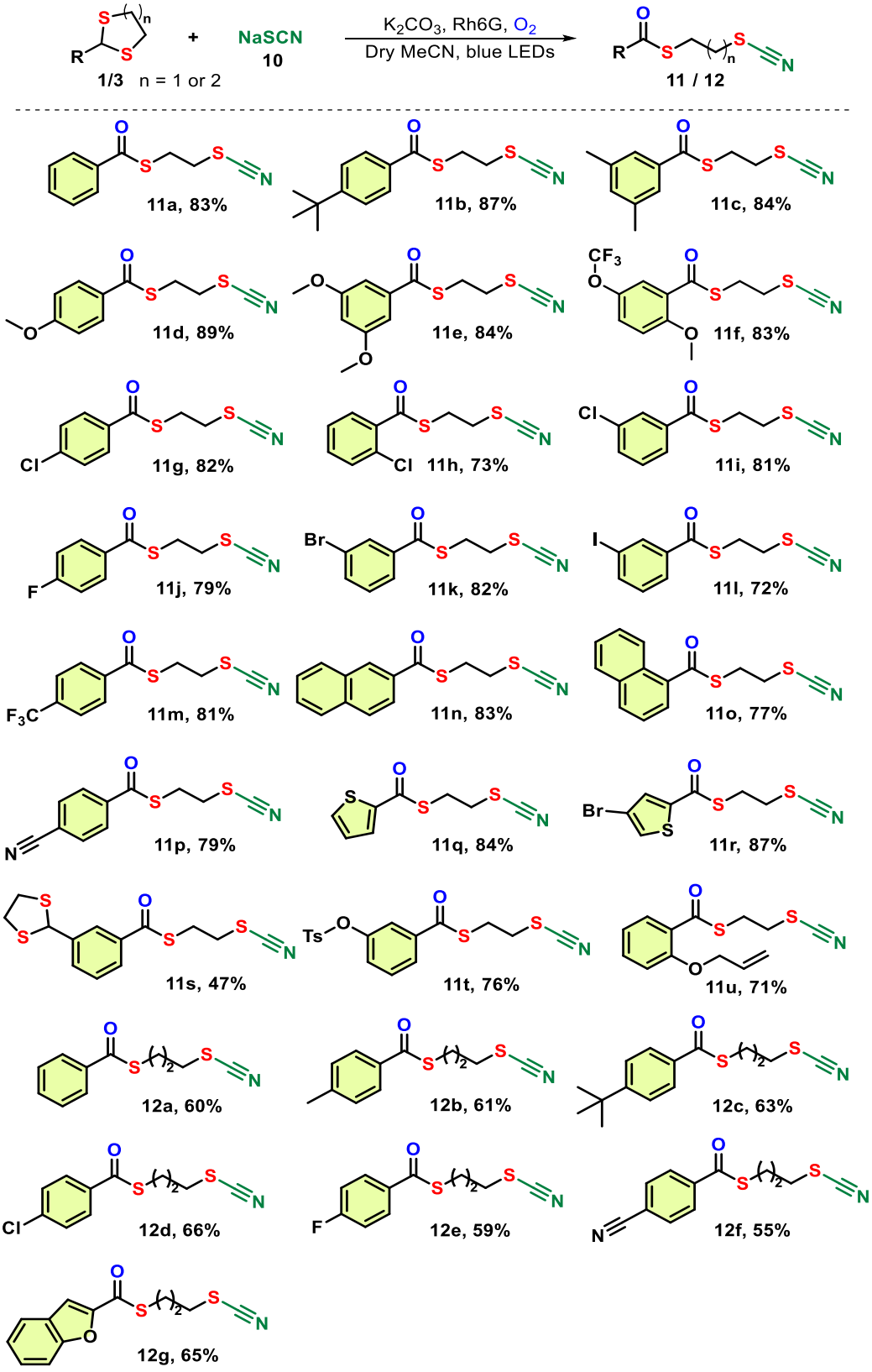
Later, in order to evaluate the necessity and role of visible light, PC and oxygen we carried out the reaction in the absence of each of these independently. We observed that reaction of **3a** did not afford the desired product **11a** in the absence of light, PC and oxygen (Table 4.1, entries 17, 18 and 19). These results clearly revealed that visible light, PC as well oxygen are absolutely necessary for the facile conversion and they play significant role in the mechanistic pathway. We also noticed that in absence of base (K_2CO_3), transformation afforded just trace amount of thiocayano-thioester **11a** (Table 4.1, entry 20). This result indicated that K_2CO_3 has an important role in mechansitic pathway. In order to verify the requirement of anydrous solvent or role of water on the overall transformation, we explore the reaction of **3a** under the satndard conditons optimsied so far in moist acetonitrile (undried). Interstingly, the presence of water (moist MeCN) lowered the yield of **11a** significantly in comparision to dry acetonitrile (71%, Table 4.1, Entry 21). Based on the deatiled and systematic screening we observed that dithiolane **3a** (1 equiv.), NaSCN (5 equiv.), Rh6G (2 mol%) as PC, K_2CO_3 (2 equiv.) as base O_2 atmosphere, in dry acetonitrile under the irradiation of

blue LEDs (15W) turned out to be beneficial reaction condition to obtain the corresponding thiocayano-thioester **11a** in maximum yield.

4.3.2 Substrate Scope of dithiolanes and dithianes

Having obtained the optimize reaction condition, we further set out for generalizing the protcol for the wider substrate scope using different dithiolanes as well as dithianes (Table 4.3). In this reagrd, we prepared various dithiolans **3** and dithianes **1** starting from different aldehydes by reactions with mercaptans following the literature procedures (See Experiental section).[20] To begin we screened different dithiolanes and we observed that under optimum reaction conditions, electronically neutral dithiolanes (**3a-3c**) reacted smoothly with NaSCN **10** to afford the thiocyanao-thioesters (**11a-c**) respectively (upto 87% yields, Table 4.3). The dithiolanes derived from electron rich aldehydes (**3d-3f**) also reacted smoothly under the optimum reaction conditions to furnished the respective products (**11d-11f**) (upto 89% yields). Dithiolanes derived from aldehydes substituted with electron deactivating substitution at *o*/*m*/*p* positions (**3g-3m**) reacted without difficulty under the standerdized reaction conditions to afford the corresponding thiocayano-thioesters (**11g-11m**) (upto 82% yields, Table 4.3). Highly aromatic substrates such naphthalene-1-dithiolane and naphthalene-2-dithiolane **(3n, 3o)** under the same reaction conditions also afforded the corrsponding thiocayano-thioesters (**11n**, **11o)** in excellent yields (upto 83%, Table 4.3). The dithiolane obtained from aromatic aldehyde having strong electron withdrawing group (–CN) also reacted well under the reaction conditions to furnsih the desired thiocayano-thioester **11p** in good yield (79%, Table 4.3). The dithiolanes derived from heteroaromatic aldehydes **3q-3r** underwent smooth transformation to furnsih the corresponding products thiocayno-thioesters **11q-11r** (upto 87% yield, Table 4.3). Dithiolane substrates derived from aromatic aldehydes having protecting groups on phenyl ring furnished the corresponding **11s-11u** thiocyano-thioesters in moderate to good yields (up to 76%) and we observed that under rection condtions all protecting groups remains untouched in the product. Interestingly, we observed that only one dithiolane moiety of the substrate having two dithiolane moities (**3s**) reacted with sodium thiocyanate to afford the corresponding thiocyano-thioester (**11s**)

Table 4.3 Substrate scope of dithiolanes and dithianes cyanation



0.1 mmol **3**/**1**, 2 mol% Rh6G, 0.2 equiv. K_2CO_3, 0.5 equiv. NaSCN, 2 mL MeCN, O_2 baloon, 15W blue LEDs

albeit in a low yield (47%) within the time span of 8 h. In order to generalize the strategy, we subjected different dithianes **1** (six-membered cyclic dithioacetals) under optimum reaction conditions. Dithianes derived from aromatic aldehydes substituted with electron rich as well as electron difficient functionalities and heteroaromatic aldehydes (**1a-1g**) furnished the corresponding desired thiocyano-thioester products **12a-12g** in good yields (upto 66%, Table 4.3).

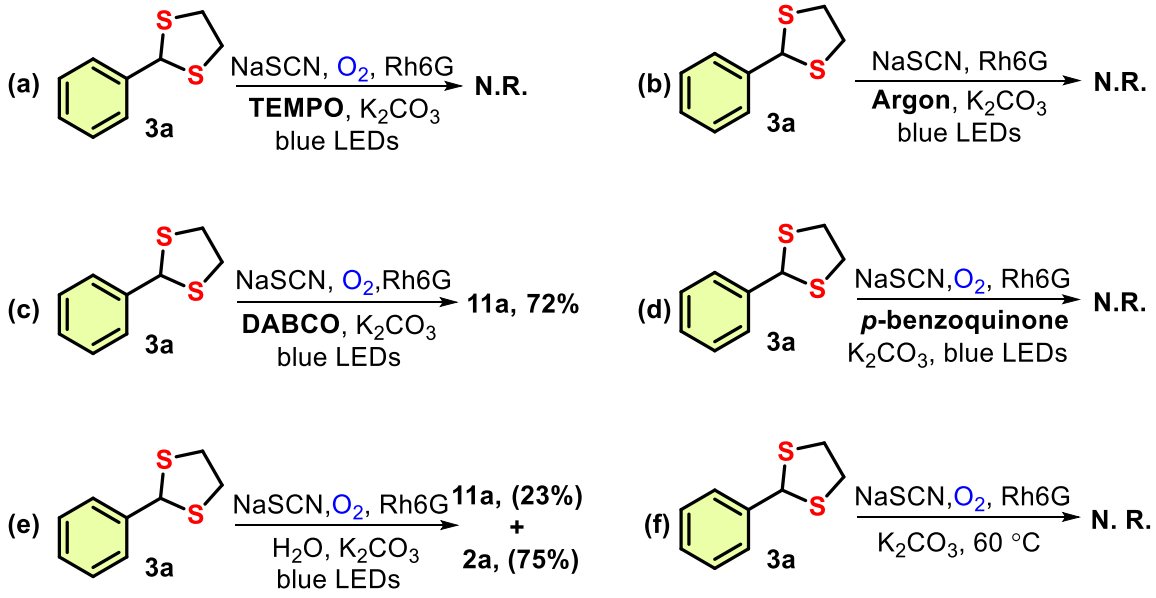
4.4 Mechanistic study

4.4.1 Control experiments

To investigate the plausible reaction route, we systematically checked a series of control experiments. To begin with we treated dithiolane **3a** with TEMPO under optimum reaction condition and we observed that reaction did not work (Scheme 4.5a). This result unambiguosly confirmed that reaction must be involving a radical intermediate (Scheme 4.5a). Later, the reactiom of **3a** in the absence of oxygen (under argon atmosphere) while maintaining other optimum reaction conditions did not furnsih the desired product thus, indicating the essential role of oxygen during the reaction pathway (Scheme 4.5b). Based on the previous control experiment, we learnt that oxygen is having a key role and to investigate whether or not singlet oxygen in the reaction we monitored the reaction of **3a** in presence of DABCO (singlet oxygen quencher) We observed that DABCO did not interfere with the overall transformation and we obtain the corresponding product **11a** in good yield (Scheme 4.5c). This result revealed that singlet oxygen has no role in the reaction pathway and has no significant role to hindered the product formation (Scheme 4.5c).[21] Treatment of **3a** with *p*-benzoquinone under optimum reaction condition did not furnsih the desired product **11a** (Scheme 4.5d). This result clearly indicated that superoxide radical anion is involved during the reaction pathway (Scheme 4.5d).[22] Later, the reaction of **3a** in presence of water (10% v/v, 0.2 mL) furnish the product **11a** in poor yield and corresponding benzaldehyde **2a** as side product was formed predominently (Scheme 4.5e). Later we performed the reaction of **3a** in absence of light (under dark conditions) while maintaining other optimized reaction condition but at an elavated reactio temperature (60 ^{o}C) to check the role of heat and light (Scheme 4.5f). The reaction did not work and starting remain as it is thus indicating that light is

undeniably necessary for the initiation of reaction and the temperature have no impact on driving the reaction.

Scheme 4.5. Control experiments



[a]0.1 mmol **1**, 2 mol% catalyst, 0.2 mmol K_2CO_3, 0.5 mmol NaSCN, 2 mL Dry ACN, O_2 baloon.

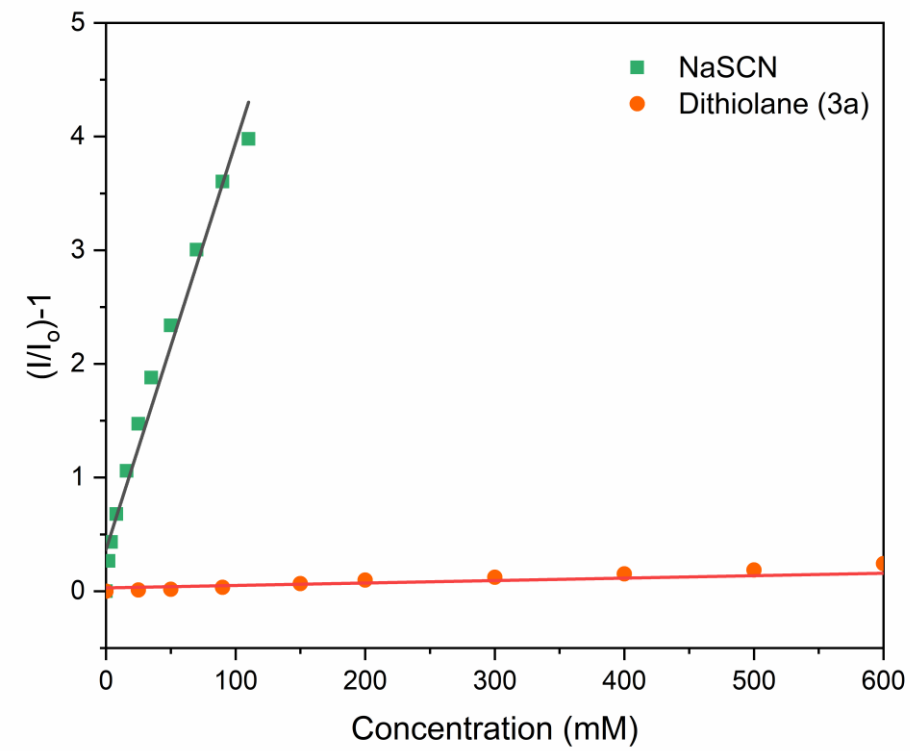
4.4.2 Stern-Volmer experiment

In order to have further insight into the mechanism and to validate the single electron transfer (SET) process of Rh6G* with sodium thicyanante (NaSCN) or dithiolane, Stern-Volmer experiment were carried out. These studies clearly revealed Rh6G* has a higher SET rate with NaSCN than that with dithioacetal **3a** and **1a** (see Fig. 4.1, Stern-Volmer graph). The efficiency of SET process from Rh6G* to NaSCN was additionally validated by the oxidation potential of NaSCN (E_{ox} = +0.66 V vs SCE) that is less than the reduction potential of Rh6G* (Ered = +1.39 V vs SCE) and the oxidation potential of dithiolane **3a** is (E_{ox} = +1.21 V vs SCE).[22,23]

Experiments were performed using a 1 µM solution of Rh6G in acetonitrile and variable concentrations of quencher (NaSCN and **3a**) in a Hellma fluorescence cuvette (3 mL, path length 1.0 cm). Samples were excited at 515 nm and the intensity of emission was monitored at 548 nm and expressed as the (I_0/I)-1 where I_0 is the emission intensity of Rh6G at 548 nm

in the absence of a quencher and I is the observed intensity, as a function of the quencher concentration. $I_0/I-1$ (548nm Intensity maximum) versus the quencher concentration was mapped, and the subsequent Stern-Volmer plot was calculated for comparison from the linear fit.

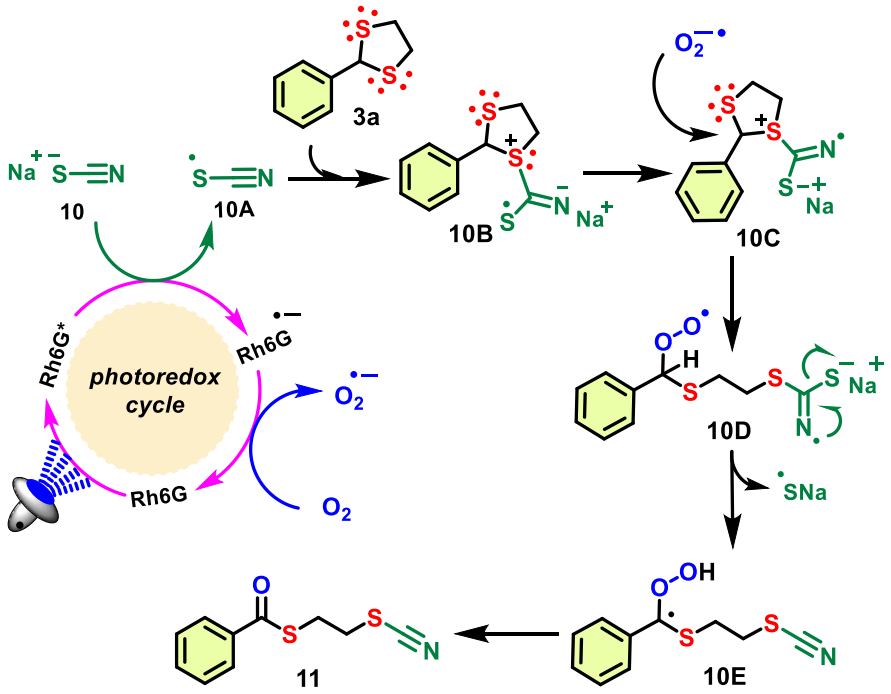
Fig. 4.1 Stern-Volmer graph



4.5 Plausible reaction mechanism

By corelating information obtained from the control experiments, Stern-Volmer studies (Fig 4.1) and earlier literature,[21] we have proposed a plausible reaction pathway (Fig 4.2). The PC, Rh6G gets excited to Rh6G* upon irradiation of visible light (blue LEDs). Further, this excited PC, Rh6G* (E_{red} = +1.39 V vs SCE)[22] upon interaction with electron rich donor sodium thiocyanate (E_{ox} = +0.66 V vs SCE)[23] goes for SET via reductive quenching photocatalytic cycle to generate the corresponding reduced PC ($Rh6G^{\bullet-}$) and one electron oxidized thiocyanate radical ($^{\bullet}SCN$) **10A**. This efficient SET was substantiated by the Stern-Volmer experiment, suggesting that SET rate of Rh6G* is

Fig. 4.2 Plausible reaction Mechanism

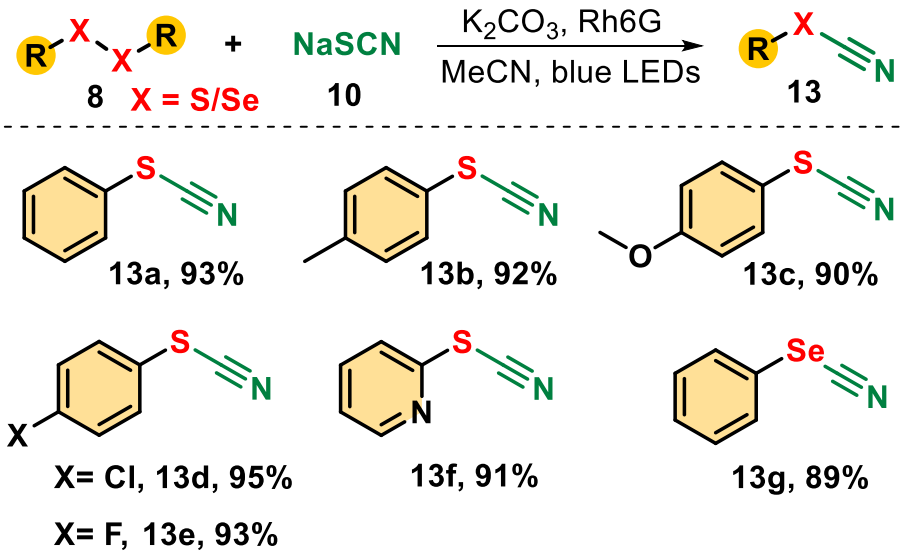


much higher for NaSCN compare to the dithiolane **3a** at a lower concentration (Fig. 4.1). Further, Rh6G•− gets involved in second SET process with oxygen molecule to form superoxide radical anion along with the regeneration of ground state Rh6G, thus completing the photocatalytic cycle. (Fig 4.2). Later, dithiolane **3a** reacts with the highly reactive thiocyanate radical species to offer an intermediate **10B**. This intermediate **10B** further form the intermediate **10C** by intramolecular one electron transfer (from nitrogen to sulfur). This intermediate **10C** would be attacked by the highly reactive nucleophilic superoxide radical anion at the carbon center to form intermediate **10D**. This intermediate **10D** would eventually form hydroperoxide intermediate **10E** having thiocyano group by release of NaS• radical. To confirmed the the release of NaS• radical species, we have done the reaction of **3a** with phenylthiocyanate **13a** and carried out the reaction under same reaction condition. We observed the desired product **11a** formation and a release of phenylthyil radical which on dimerizarion delived diphenyldisulfide **8a,** this esperiment indiretly support the release sulfur radical species during the reaction pathways. This unstable peroxy radical intemediate **10E** would ultimately breaks dow to form the corresponding thiocyano-thioester **11.**

4.6 Utility of thiocynation for cyanation of aryl disulfide 8

Looking into the Fig 4.2B reaction mechanism to obtained thioester-thiocyanate, it is quite clear that single electron oxidized thiocynate radical is more likely to be behave as an electrophile. This thiocynate radical will be attacked by the nucleophilic sulfur of dithioacetals leads to the C–S bond cleavage. In order to utilize the reactivity of thiocyanate radical and to substatntiate our mechanism further, we set out to utilized this thiocyanate radical reactivity with other sulfur compounds such as diaryl disulfides instead of thioacteals (Scheme 4.6).

Scheme 4.6 Substrate scope for cynation of diaryl disulfide



[a]0.1 mmol **8**, 2 mol% Rh6G, 0.2 mmol K_2CO_3, 0.5 mmol NaSCN, 2 mL MeMeCN; 15W blue LEDs

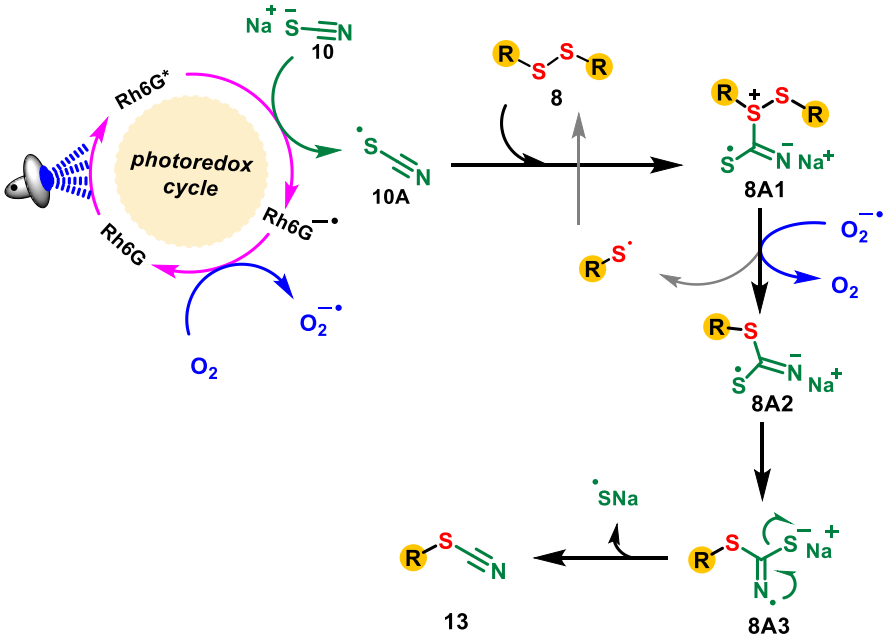
To corroborate this, we treated diphenyl disulfide **8a** with NaSCN (5 equiv.) under the standerized reaction conditions of thiocyanate-thioester. Pleasantly, this model reacion afforeded the desired phenyl thiocyanate **13a** under mild reaction condition in excellent yield (93%, Scheme 4.6). With this initial success, we further planned to explore the substrate scope to generalise the protocol and for the wider applicability (Scheme 4.6) We then explored the reaction of diaryl disulfides (**8b-8f**) with NaSCN **10** under same reaction conditions to afford the corresponding aryl-thiocynates (**13b-13f**) (up to 95% yields, Scheme 4.6). Later we explored the reactivity of diphenyl diselenide with NaSCN **10** and under the same reaction conditions to obtained the phenyl selenocyante **13g** (89% yield). This simple methodology has demonstrated the

synthesis of aryl thiocyantes starting from simple diaryl disulfides and sodium thiocynate in a single step.

4.7 Plausible reaction mechanism for the cyanation of diaryl disulfide 8

The plausible reaction mechanism initiate with the oxidation of thiocynate salt **10** by excited state PC, Rh6G* to generate the electrophillic **•SCN** (**10A**) and Rh6G$^{\bullet-}$(**Fig. 4.2**). This *in situ* generated electrophillic radical **10A** reacts with diaryl disulfide **8** to genate the intermediate **8A1.** This intermediate **8A1** further reacts with superoxide radical anion to form intermediate **8A2**. This intermediate would form intermediate ultimately form the final product aryl thiocynate **13** through the intermediate **8A3**.

Fig. 4.1 Plausible reaction mechanism for aryl thiocyanate



4.8 Conclusions

we have unravels an efficient and environmentally benign method for the cyanation of cyclic dithioacetals and disulfides to access thioester-thiocynates and alkyl thiocyanates. The protol relied on commercially viable, easily available and sodium thiocyanate as a cynating reagent. The protocol offered direct access to a thiocyanate-thioesters and alkyl cyanates starting from the dithioacetals and disulfides for the first time by the irradiation of visible light using mild and nontoxic NaSCN salt. A series of control experiments have been performed to have insights into the mechanism, The protocol worked smoothly under ambient reaction

conditions and did not require any external oxidizing agents for the ring opening of dithioacetals.

4.9 Experimental section:

4.9.1 General remark

(See Chapter 2, 3.7.1, page no. 38)

4.9.2 Synthesis of compounds 1 and 3:

(See Chapter 2, 3.7.2, page no. 39)

4.9.3 Synthesis of thioester-thiocyanate 11 or 12 (General procedure 4A).

In a oven dried glass RB equipped with the magnetic bar, dithiolane **3** or dithiane **1** (0.1 mmol, 1 equiv.), NaSCN (0.5 mmol, 5 equiv.), K_2CO_3 (0.2 mmol, 2 equiv.) and (Rh6G 2 mol%) was added and then charged with dry MeCN. Further reaction mixture was purged with molecular oxygen for 5 min and kept for stirring under the irradiation of blue LEDs (15 W) and oxygen atmosphere (oxygen balloon) until the reaction complete (6-12 h). After completion the solvent was evaporated and the crude was purified by column chromatography using the hexane and ethyl acetate percentage gradient system. Purified product **11**/ **12** are polar than the starting materials. (**Reaction requirement**- pure starting material, dry solvent and normal reaction temperature 25-30 ℃)

4.9.4 Synthesis of arylthiocynate 13 (General procedure 4B).

In a glass RB equiped with a stir bar, disulfide **8** (0.1 mmol, 1 equiv.), NaSCN (0.5 mmol, 5 equiv.) K_2CO_3 (0.2 mmol, 2 equiv.), Rh6G (2 mol%) was added and next MeCN (2 mL) was added reaction mixture was purged with oxygen (5 min) and continued stirring till the reaction completes under oxygen atmosphere and blue LEDs (15 W) at room temperature for 6-12 h. After completion, the solvent was evaporated using rotary evaporator and crude residue was further purified by column chromatography to access **13** over silica gel using percentage gradient of hexane/ethyl acetate.

4.9.5 Product Characterization data:

*S-(2-thiocyanatoethyl) benzothioate (**11a**)*: (18 mg, 83% yield), colourless liquid, R_f = 0.4 (1:15 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.27 – 3.10 (m, 2H), 3.57 – 3.35 (m, 2H), 7.52 – 7.38 (m, 2H), 7.71 – 7.52 (m, 1H), 8.06 – 7.83 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) δ 29.11, 33.61, 111.62, 127.52, 128.96, 134.16, 136.37, 190.75. HRMS (ESI-TOF) m/z calculated for $C_{10}H_{10}NOS_2$ $[M+H]^+$ 224.0198; found 224.0197.

*S-(2-thiocyanatoethyl) 4-(tert-butyl)benzothioate (**11b**)*: (24 mg, 87% yield), White solid, Mp: 92.5-91.5 ^oC; R_f = 0.4 (1:15 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.34 (s, 9H), 3.25 – 3.06 (m, 2H), 3.69 – 3.34 (m, 2H), 7.49 (d, *J* = 8.5 Hz, 2H), 7.89 (d, *J* = 8.4 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) δ 29.00, 31.17, 33.67, 35.39, 111.68, 125.91, 127.44, 133.74, 158.12, 190.27. HRMS (ESI-TOF) m/z calculated for $C_{14}H_{18}NOS_2$ $[M+H]^+$ 280.0824; found 280.0827.

*S-(2-thiocyanatoethyl) 3,5-dimethylbenzothioate (**11c**):* (21 mg, 84% yield), colourless liquid, R_f = 0.4 (1:15 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.38 (s, 6H), 3.21 (m, 2H), 3.45 (m, 2H), 7.24 (s, 1H), 7.56 (s, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) δ 21.65, 29.40, 34.02, 111.97, 125.55, 136.14, 136.76, 139.07, 191.29. HRMS (ESI-TOF) m/z calculated for $C_{12}H_{14}NOS_2$ $[M+H]^+$ 252.0511; found 252.0517.

*S-(2-thiocyanatoethyl) 4-methoxybenzothioate (**11d**)*: (22 mg, 89% yield), White solid, Mp: 99.2-97.5 ^oC; R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.22 – 3.18 (m, 2H), 3.43 (m, 2H), 3.87 (s, 3H), 6.93 (d, *J* = 8.8 Hz, 2H), 7.92 (d, *J* = 8.8 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ (ppm) δ 29.00, 33.77, 55.73, 111.73, 114.11, 129.20, 129.76 164.38, 189.09. HRMS (ESI-TOF) m/z calculated for $C_{11}H_{12}NO_2S_2$ $[M+H]^+$ 254.0304; found 254.0309.

*S-(2-thiocyanatoethyl) 3,5-dimethoxybenzothioate **11e**)*: (24 mg, 84% yield); colourless liquid, R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.26 – 3.08 (m, 2H), 3.51 – 3.34 (m, 2H), 3.83 (s, 6H), 6.68 (t, *J* = 2.3 Hz, 1H), 7.08 (d, *J* = 2.3 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 29.20, 33.48, 55.75, 105.16, 106.35, 111.54, 138.20, 161.02, 190.60. HRMS (ESI-TOF) m/z calculated for $C_{12}H_{14}NO_3S_2$ $[M+H]^+$ 284.0410; found 284.0419.

*S-(2-thiocyanatoethyl) 2-methoxy-5-(trifluoromethoxy)benzothioate (**11f**)*: (28 mg, 83% yield); colourless liquid, R_f = 0.4 (3:20 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.22

(m, 2H), 3.40 (m, 2H), 3.97 (s, 3H), 7.02 (d, *J* = 9.1 Hz, 1H), 7.38 (dd, *J* = 9.1, 3 Hz, 1H), 7.71 (d, *J* = 3.0 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 29.72, 33.29, 56.40, 111.64, 113.36, 119.26, 121.82, 122.82, 124.38, 126.27, 127.26, 142.41, 157.15, 188.38. HRMS (ESI-TOF) m/z calculated for $C_{12}H_{11}F_3NO_3S_2$ $[M+H]^+$ 338.0127; found 338.0131.

*S-(2-thiocyanatoethyl) 4-chlorobenzothioate (**11g**)*: (21 mg, 82% yield); colourless liquid, R_f = 0.4 (3:20 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.24 – 3.17 (m, 2H), 3.53 – 3.33 (m, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 7.88 (d, *J* = 8.4 Hz, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 29.21, 33.48, 111.52, 128.83, 129.28, 134.67, 140.63, 189.60. HRMS (ESI-TOF) m/z calculated for $C_{10}H_9ClNOS_2$ $[M+H]^+$ 257.9809; found 257.9813.

*S-(2-thiocyanatoethyl) 2-chlorobenzothioate (**11h**)*: (19 mg, 73% yield); colourless liquid, R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 – 7.67 (m, 1H), 7.49 – 7.43 (m, 2H), 7.36 (ddd, *J* = 7.7, 6.3, 2.3 Hz, 1H), 3.50 – 3.45 (m, 2H), 3.28 – 3.24 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 190.76, 136.54, 133.02, 131.26, 129.50, 127.04, 111.54, 33.34, 30.09. HRMS (ESI-TOF) m/z calculated for $C_{10}H_9ClNOS_2$ $[M+H]^+$ 257.9809; found 257.9810.

*S-(2-thiocyanatoethyl) 3-chlorobenzothioate (**11i**)*: (19 mg, 73% yield); colourless liquid, R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.24 – 3.20 (m, 2H), 3.49 – 3.45 (m, 2H), 7.42 (t, *J* = 7.9, 1.0 Hz, 1H), 7.58 (ddd, *J* = 8.0, 2.1, 1.0 Hz, 1H), 7.91 (t, *J* = 2.1 Hz, 1H), . $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 29.26, 33.42, 111.48, 125.61, 127.47, 130.26, 134.02, 135.27, 137.81, 189.63. HRMS (ESI-TOF) m/z calculated for $C_{10}H_9ClNOS_2$ $[M+H]^+$ 257.9809; found 257.9810.

*S-(2-thiocyanatoethyl) 4-fluorobenzothioate (**11j**)*: (19 mg, 79% yield); colourless liquid, R_f = 0.5 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.47 (m, 2H), 3.22 (m, 2H), 7.22 – 6.99 (m, 2H), 8.09 – 7.83 (m, 2H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 29.10, 33.44, 111.41, 115.93, 116.15, 129.95, 130.05, 132.59, 132.62, 164.98, 167.53, 189.08. HRMS (ESI-TOF) m/z calculated for $C_{10}H_9FNOS_2$ $[M+H]^+$ 242.0104; found 242.0106.

*S-(2-thiocyanatoethyl) 3-bromobenzothioate (**11k**)*: (25 mg, 82% yield); colourless liquid, R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.28 – 3.07 (m, 2H), 3.60 – 3.37 (m, 2H), 7.36 (t, *J* = 7.9 Hz, 1H), 7.74 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1H), 7.88 (dt, *J* = 7.9, 1.4 Hz, 1H), 8.07 (t, *J* = 1.9 Hz, 1H),. $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$): δ 29.23, 33.39, 111.43, 123.15, 126.03, 130.35, 130.46, 136.91, 137.96, 189.50. HRMS (ESI-TOF) m/z calculated for $C_{10}H_9BrNOS_2$ $[M+H]^+$ 301.9303; found 301.9311.

*S-(2-thiocyanatoethyl) 3-iodobenzothioate (**11l**)*: (25 mg, 72% yield); colourless liquid, R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.51 (m, 2H), 3.24 (m, 2H), 7.33 – 7.19 (m, 1H), 8.02 – 7.87 (m, 2H), 8.30 (q, J = 1.7 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 29.24, 33.43, 94.47, 111.48, 126.65, 130.57, 136.20, 137.96, 142.84, 189.40. HRMS (ESI-TOF) m/z calculated for $C_{10}H_9INOS_2$ $[M+H]^+$ 349.9165; found 349.9172.

*S-(2-thiocyanatoethyl) 4-trifluorobenzothioate (**11m**)*: (25 mg, 81% yield), white solid, Mp: 91.1-89.5 ^oC; R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.32 – 3.08 (m, 2H), 3.65 – 3.37 (m, 2H), 7.81 – 7.63 (m, 2H), 8.14 – 7.84 (m, 2H).$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 29.36, 33.36, 111.43, 122.16, 124.87, 126.00, 126.04, 126.08, 126.12, 127.87, 130.61, 135.22, 135.55, 139.06, 139.08, 189.97. HRMS (ESI-TOF) m/z calculated for $C_{11}H_9F_3NOS_2$ $[M+H]^+$ 292.0072; found 292.0081.

*S-(2-thiocyanatoethyl) naphthalene-2-carbothioate (**11n**)*: (23 mg, 83% yield), yellow solid, Mp: 80.6-79.1 ^oC; R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.27 (m, 2H), 3.52 (m, 2H), 7.61 (m, 2H), 7.93 – 7.86 (m, 2H), 8.52 (s, 1H), 8.01 – 7.94 (m, 2H).$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 29.24, 33.69, 111.63, 123.07, 127.30, 128.01, 128.90, 129.02, 129.22, 129.78, 132.52, 133.67, 136.15, 190.64. HRMS (ESI-TOF) m/z calculated for $C_{14}H_{12}NOS_2$ $[M+H]^+$ 274.0355; found 274.0363.

*S-(2-thiocyanatoethyl) naphthalene-1-carbothioate (**11o**)*: (21 mg, 77% yield); colourless liquid, R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.37 – 3.11 (m, 2H), 3.63 – 3.37 (m, 2H), 7.52 (m, 1H), 7.65 – 7.54 (m, 2H), 7.90 (m, 1H), 8.05 (m, 1H), 8.09 (m, 1H), 8.64 – 8.44 (m, 1H).$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 29.97, 33.62 , 111.67, 124.59, 125.17, 126.98, 128.51, 128.60, 129.28, 133.88, 133.91, 134.33, 192.76. HRMS (ESI-TOF) m/z calculated for $C_{14}H_{12}NOS_2$ $[M+H]^+$ 274.0355; found 274.0357.

*S-(2-thiocyanatoethyl) 4-cyanobenzothioate (**11p**)*: (20 mg, 79% yield); white solid, Mp: 85.6-84.1 ^oC; R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.26 – 3.20 (m, 1H), 3.55 – 3.48 (m, 1H), 7.81 – 7.76 (m, 1H), 8.07 – 8.02 (m, 1H).$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 29.42, 33.23, 111.26, 117.35, 117.69, 127.90, 132.76, 139.33, 189.57. HRMS (ESI-TOF) m/z calculated for $C_{11}H_9N_2OS_2$ $[M+H]^+$ 249.0151; found 249.0158.

*S-(2-thiocyanatoethyl) thiophene-2-carbothioate (**11q**)*: (19 mg, 84% yield); colourless liquid, R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.25 – 3.21 (m, 2H), 3.48 – 3.44 (m, 2H), 7.16 – 7.12 (m, 1H), 7.70 – 7.66 (m, 1H), 7.84 – 7.80 (m, 1H).$^{13}C\{^1H\}$ NMR (100

MHz, $CDCl_3$): δ 29.24, 33.64, 111.47, 128.23, 131.96, 133.74, 141.18, 182.55. HRMS (ESI-TOF) m/z calculated for $C_8H_8NOS_3$ $[M+H]^+$ 229.9763; found 229.09766.

S-(2-thiocyanatoethyl) 4-bromothiophene-2-carbothioate ***(11r)***: (19 mg, 84% yield); colourless liquid, R_f = 0.4 (1:9 :: EA:pet ether), ^1H NMR (400 MHz, $CDCl_3$): δ 3.28 – 3.09 (m, 3H), 3.56 – 3.37 (m, 2H), 7.56 (d, *J* = 1.5 Hz, 1H), 7.70 (d, *J* = 1.4 Hz, 1H).$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 29.40, 33.49, 111.23, 130.84, 133.94, 141.63, 181.89. HRMS (ESI-TOF) m/z calculated for $C_8H_7BrNOS_3$ $[M+H]^+$ 307.8868; found 307.8872.

S-(2-thiocyanatoethyl) 3-(1,3-dithiolan-2-yl)benzothioate ***11s)***: (15 mg, 47% yield); colourless liquid, R_f = 0.4 (1:9 :: EA:pet ether), ^1H NMR (400 MHz, $CDCl_3$): δ 3.21 (dd, *J* = 8.6, 6.2 Hz, 2H), 3.39 (ddd, *J* = 8.1, 6.2, 3.8 Hz, 2H), 3.49 – 3.43 (m, 2H), 3.53 (ddd, *J* = 7.0, 5.9, 3.8 Hz, 2H), 5.65 (s, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 7.77 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.85 (dt, *J* = 7.8, 1.4 Hz, 1H), 8.08 (d, *J* = 1.9 Hz, 1H).$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 29.15, 33.55, 40.55, 55.59, 111.59, 126.97, 127.14, 129.19, 133.72, 136.57, 142.17, 190.37. HRMS (ESI-TOF) m/z calculated for $C_{13}H_{14}NOS_4$ $[M+H]^+$ 327.9953; found 327.9961.

S-(2-thiocyanatoethyl) 3-(tosyloxy)benzothioate ***(11t)***: (29 mg, 76% yield); colourless liquid, R_f = 0.4 (1:9 :: EA:pet ether), ^1H NMR (400 MHz, $CDCl_3$): δ 2.46 (s, 1H), 3.20 (dd, *J* = 8.3, 6.4 Hz, 1H), 3.45 (dd, *J* = 8.3, 6.4 Hz, 1H), 7.29 – 7.24 (m, 1H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.43 (t, *J* = 8.0 Hz, 0H), 7.54 – 7.50 (m, 0H), 7.73 (d, *J* = 8.3 Hz, 1H), 7.87 – 7.82 (m, 0H).$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 21.79, 29.16, 33.27, 111.29, 121.27, 125.89, 127.90, 128.52, 129.98, 131.99, 137.70, 145.87, 145.87, 149.82, 189.26. HRMS (ESI-TOF) m/z calculated for $C_{17}H_{16}NO_4S_3$ $[M+H]^+$ 394.0236; found 394.0243.

S-(2-thiocyanatoethyl) 2-(allyloxy)benzothioate ***(11u)***: (20 mg, 71% yield); colourless liquid, R_f = 0.4 (1:9 :: EA:pet ether), ^1H NMR (400 MHz, $CDCl_3$): δ 3.25 – 3.05 (m, 2H), 3.49 – 3.25 (m, 2H), 4.69 (dt, *J* = 5.2, 1.5 Hz, 2H), 5.34 (dq, *J* = 10.5, 1.4 Hz, 1H), 5.49 (dq, *J* = 17.2, 1.5 Hz, 1H), 6.12 (ddt, *J* = 17.2, 10.5, 5.3 Hz, 1H), 7.10 – 6.90 (m, 2H), 7.48 (ddd, *J* = 8.5, 7.4, 1.8 Hz, 1H), 7.84 (dd, *J* = 7.8, 1.8 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 29.67, 33.54, 70.01, 111.88, 113.54, 118.56, 120.94, 126.03, 130.11, 132.46, 134.51, 157.70, 189.47. HRMS (ESI-TOF) m/z calculated for $C_{13}H_{14}NO_2S_2$ $[M+H]^+$ 280.0460; found 280.0464.

S-(3-thiocyanatopropyl) benzothioate ***(12a)***: (14 mg, 60% yield); colourless liquid, R_f = 0.4 (1:19 :: EA:pet ether), ^1H NMR (400 MHz, $CDCl_3$): δ 2.26 – 2.20 (m, 2H), 3.07 (m, 2H), 3.23 (m, 2H), 7.49 – 7.45 (m, 2H), 7.62 – 7.57 (m, 1H), 7.98 – 7.94 (m, 2H). $^{13}C\{^1H\}$ NMR

(100 MHz, $CDCl_3$): δ 26.84, 30.12, 32.75, 112.06, 127.44, 128.87, 133.87, 136.74, 191.46. HRMS (ESI-TOF) m/z calculated for $C_{11}H_{12}NOS_2$ $[M+H]^+$ 238.0355; found 238.0361.

*S-(3-thiocyanatopropyl) 4-methylbenzothioate (**12w**)*: (15 mg, 61% yield); colourless liquid, R_f = 0.4 (1:19 :: EA:pet ether), ^1H NMR (400 MHz, $CDCl_3$): δ 2.25 – 2.19 (m, 2H), 2.42 (s, 3H), 3.06 (m, 2H), 3.21 (m, 2H), 3.21 (m, 2H), 7.27 – 7.24 (m, 2H), 7.87 – 7.83 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 21.87, 26.74, 30.17, 32.76, 112.10, 127.50, 129.52, 134.23, 144.82, 191.04. HRMS (ESI-TOF) m/z calculated for $C_{12}H_{14}NOS_2$ $[M+H]^+$ 252.0511; found 252.0518.

*S-(3-thiocyanatopropyl) 4-(tert-butyl)benzothioate (**12b**)*: (18 mg, 63% yield); colourless liquid, R_f = 0.4 (1:19 :: EA:pet ether), ^1H NMR (400 MHz, $CDCl_3$): δ 1.34 (s, 9H), 2.22 (m, 2H), 3.06 (m, 2H), 3.22 (m, 1H), 7.49 – 7.35 (m, 2H), 7.94 – 7.81 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 26.72, 30.18, 31.20, 32.75, 35.36, 112.11, 125.82, 127.36, 134.13, 157.78, 191.04. HRMS (ESI-TOF) m/z calculated for $C_{15}H_{20}NOS_2$ $[M+H]^+$ 294.0981; found 294.0985.

*S-(3-thiocyanatopropyl) 4-chlorobenzothioate (**12c**)*: (18 mg, 66% yield); colourless liquid, R_f = 0.4 (1:9 :: EA:pet ether), ^1H NMR (400 MHz, $CDCl_3$): δ 2.23 (m, 2H), 3.06 (m, 2H), 3.23 (m, 2H), 7.53 – 7.30 (m, 2H), 7.98 – 7.70 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 26.97, 30.04, 32.71, 111.97, 128.78, 129.19, 135.07, 140.31, 190.29. HRMS (ESI-TOF) m/z calculated for $C_{11}H_{11}ClNOS_2$ $[M+H]^+$ 271.9965; found 271.9966.

*S-(3-thiocyanatopropyl) 4-fluorobenzothioate (**12d**)*: (15 mg, 59% yield); colourless liquid, R_f = 0.4 (1:9 :: EA:pet ether), ^1H NMR (400 MHz, $CDCl_3$): δ 2.22 (m, 1H), 3.06 (m, 1H), 3.23 (m, 1H), 7.17 – 7.11 (m, 2H), 8.02 – 7.95 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 26.96, 30.09, 32.71, 112.00, 115.93, 116.15, 129.96, 130.06, 133.07, 133.10, 164.96, 167.50, 189.93. HRMS (ESI-TOF) m/z calculated for $C_{11}H_{11}FNOS_2$ $[M+H]^+$ 256.0261; found 256.0267.

*S-(3-thiocyanatopropyl) 4-cyanobenzothioate (**12e**)*: (14 mg, 55% yield); colourless liquid, R_f = 0.4 (2:15 :: EA:pet ether), ^1H NMR (400 MHz, $CDCl_3$): δ 2.28 – 2.22 (m, 1H), 3.06 (t, J = 7.1 Hz, 1H), 3.27 (t, J = 6.9 Hz, 1H), 7.79 – 7.76 (m, 1H), 8.07 – 8.03 (m, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 27.25, 29.89, 32.65, 111.84, 117.10, 117.86, 127.87, 132.75, 139.77, 190.24. HRMS (ESI-TOF) m/z calculated for $C_{12}H_{11}N_2OS_2$ $[M+H]^+$ 263.0307; found 263.0311.

*S-(3-thiocyanatopropyl) benzofuran-2-carbothioate (**12f**)*: (14 mg, 55% yield); colourless liquid, R_f = 0.4 (2:15 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.26 (p, *J* = 6.9 Hz, 2H), 3.08 (t, *J* = 7.1 Hz, 2H), 3.27 (t, *J* = 6.8 Hz, 2H), 7.33 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H), 7.49 (ddd, *J* = 8.5, 7.2, 1.3 Hz, 1H), 7.55 (d, *J* = 1.0 Hz, 1H), 7.59 (dq, *J* = 8.5, 0.9 Hz, 1H), 7.71 (dt, *J* = 8.0, 1.0 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 26.21, 29.99, 32.60, 111.78, 111.91, 112.53, 123.37, 124.25, 126.90, 128.49, 150.79, 155.63, 181.73. HRMS (ESI-TOF) m/z calculated for $C_{13}H_{12}NOS_2$ $[M+H]^+$ 278.0304; found 278.0309.

*thiocyanatobenzene (**13a**)*: (25 mg, 93% yield); colourless liquid, R_f = 0.4 (1:99 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 – 7.37 (m, 3H), 7.54 (dd, *J* = 6.4, 3.0 Hz, 2H). ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$): δ 110.62, 124.50, 129.61, 130.15, 130.30. HRMS (ESI-TOF) m/z calculated for C_7H_6NS $[M+H]^+$ 136.0215; found 136.0217.

*1-methyl-4-thiocyanatobenzene (**13b**)*: (27 mg, 92% yield); colourless liquid, R_f = 0.4 (1:99 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.37 (s, 3H), 7.25 – 7.20 (m, 2H),7.44 – 7.40 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 21.27, 111.15, 120.64, 130.81, 131.06, 140.36. HRMS (ESI-TOF) m/z calculated for C_8H_8NS $[M+H]^+$ 150.0372; found 150.0375.

*1-methoxy-4-thiocyanatobenzene (**13c**)*: (30 mg, 90% yield); colourless liquid, R_f = 0.4 (2:98 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.82 (s, 3H), 7.04 – 6.77 (m, 2H), 7.62 – 7.35 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 55.64, 111.73, 113.86, 115.93, 133.93, 161.40. HRMS (ESI-TOF) m/z calculated for C_8H_8NOS $[M+H]^+$ 166.0321; found 166.0328.

*1-chloro-4-thiocyanatobenzene (**13d**)*: (32 mg, 95% yield); colourless liquid, R_f = 0.4 (2:98 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 – 7.41 (m, 2H), 7.49 – 7.46 (m, 2H),. ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 110.15, 122.86, 130.61, 131.62, 136.35. HRMS (ESI-TOF) m/z calculated for C_7H_5ClNS $[M+H]^+$ 169.9826; found 169.9831.

*1-fluoro-4-thiocyanatobenzene (**13e**)*: (28 mg, 93% yield); colourless liquid, R_f = 0.4 (2:98 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.18 – 7.11 (m, 2H), 7.60 – 7.51 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 110.60, 117.52, 117.74, 119.21, 119.25, 133.22, 133.31, 162.39, 164.89. HRMS (ESI-TOF) m/z calculated for C_7H_5FNS $[M+H]^+$ 154.0121; found 154.0125.

*2-thiocyanatopyridine (**13f**)*: (24 mg, 91% yield); colourless liquid, R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.26 (ddd, *J* = 7.5, 4.8, 1.1 Hz, 1H), 7.58 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.75 (td, *J* = 7.8, 1.9 Hz, 1H), 8.50 (ddd, *J* = 4.8, 2.0, 0.9 Hz, 1H). ^{13}C{^{1}H}

NMR (100 MHz, $CDCl_3$): δ 109.13, 122.11, 122.87, 138.58, 150.09, 150.65. HRMS (ESI-TOF) m/z calculated for $C_6H_5N_2S$ $[M+H]^+$ 137.0168; found 137.0172.

*selenocyanatobenzene (**13g**)*: (32 mg, 89% yield); yellow liquid, R_f = 0.4 (1:9 :: EA:pet ether), ^1H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.36 (m, 3H), 7.65 – 7.60 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 101.60, 121.93, 129.89, 130.50, 132.87. HRMS (ESI-TOF) m/z calculated for C_7H_6NSe $[M+H]^+$ 183.9660; found 183.9667. (**Note** – **13g** is toxic, causes omitting inhalation inhalation)

4.10 Appendix IV: ^1H and ^{13}C spectral data of representative compounds

Compound No.	Figure II.X	Data	Page No.
11a	Fig. IV. 1 and IV. 2	^1H and ^{13}C	148
12d	Fig. IV. 3 and IV 4	^1H and ^{13}C	149
13b	Fig. IV.5 and IV. 6	^1H and ^{13}C	150

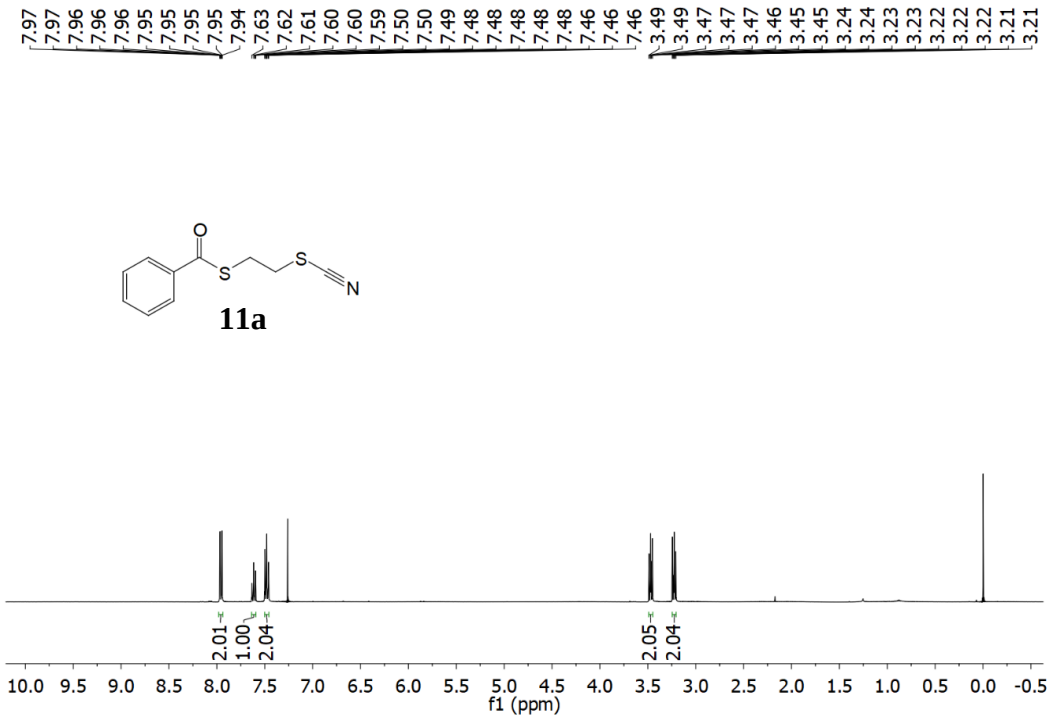


Fig. IV. 1: ^{1}H NMR spectrum of **11a**, $CDCl_3$, 400 MHz

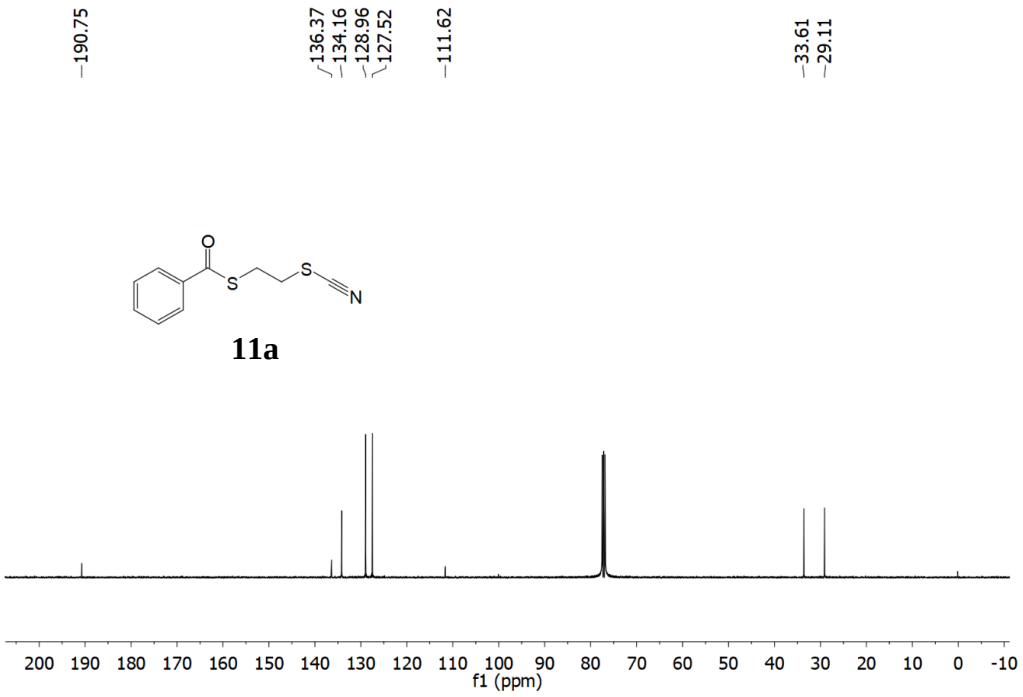


Fig. IV. 2: ^{13}C {^{1}H} NMR spectrum of **11a**, $CDCl_3$, 100 MHz

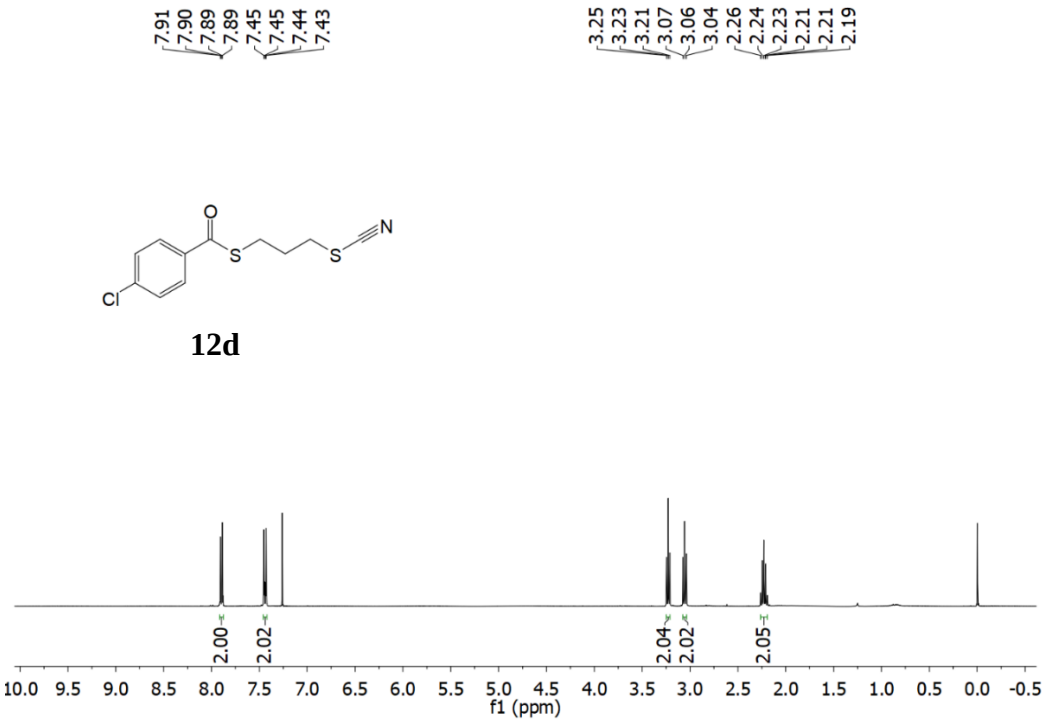


Fig. IV. 3: ^{1}H NMR spectrum of **12d**, $CDCl_3$, 400 MHz

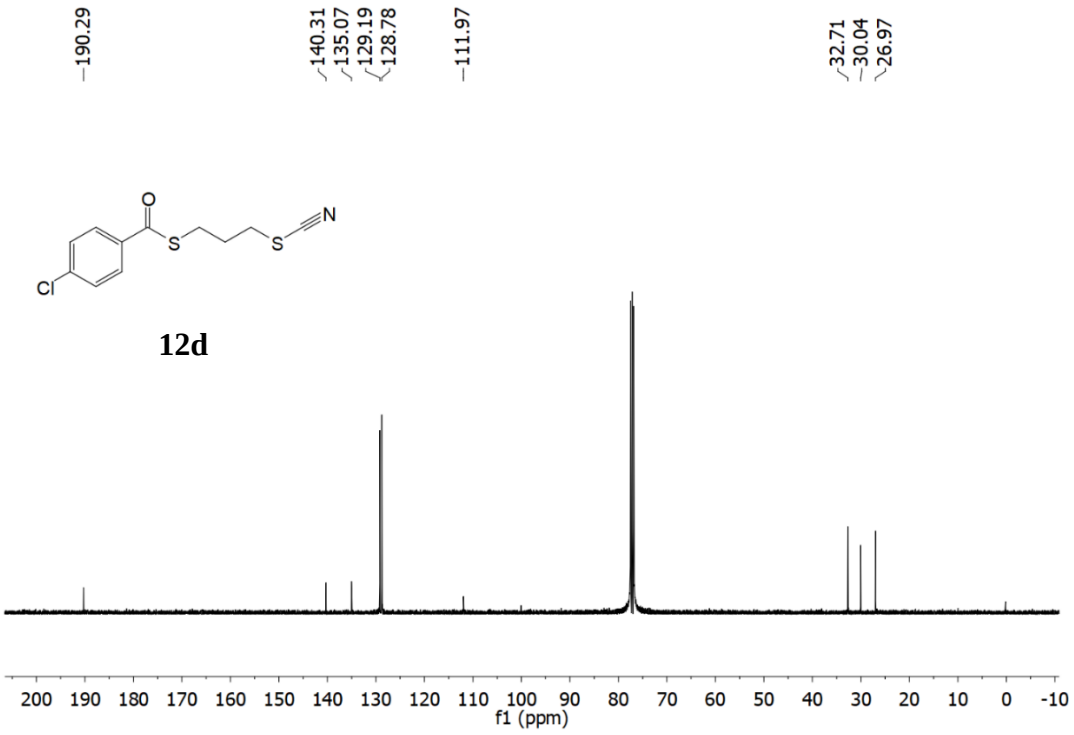


Fig. IV. 4: ^{13}C {^{1}H} NMR spectrum of **12d**, $CDCl_3$, 100 MHz

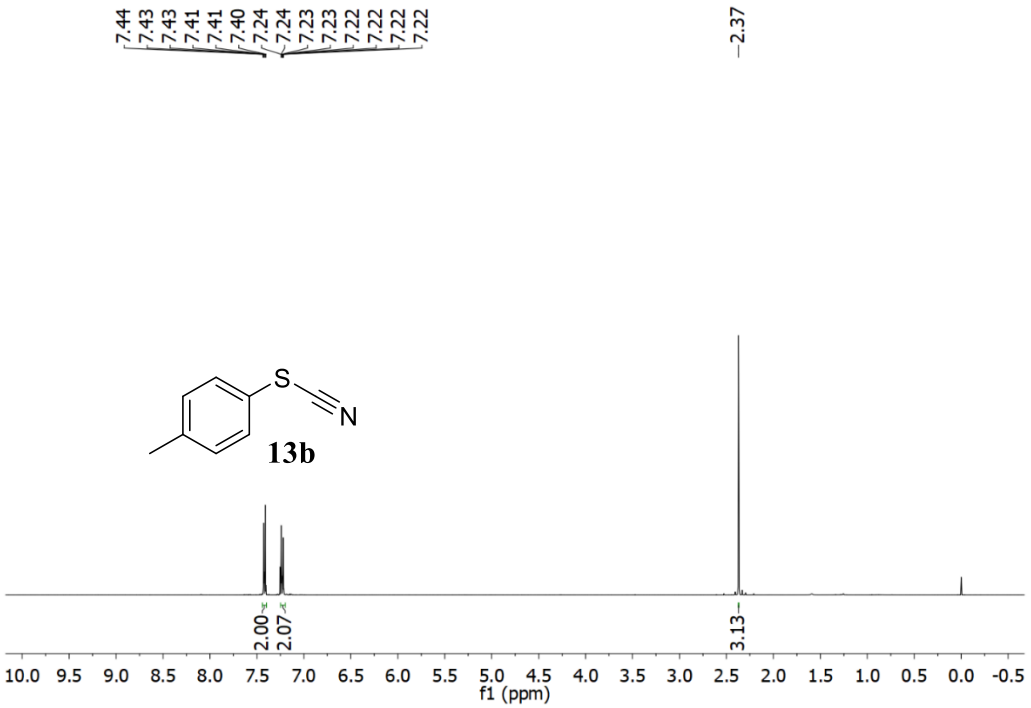


Fig. IV. 5: ^{1}H NMR spectrum of **13b**, $CDCl_3$, 400 MHz

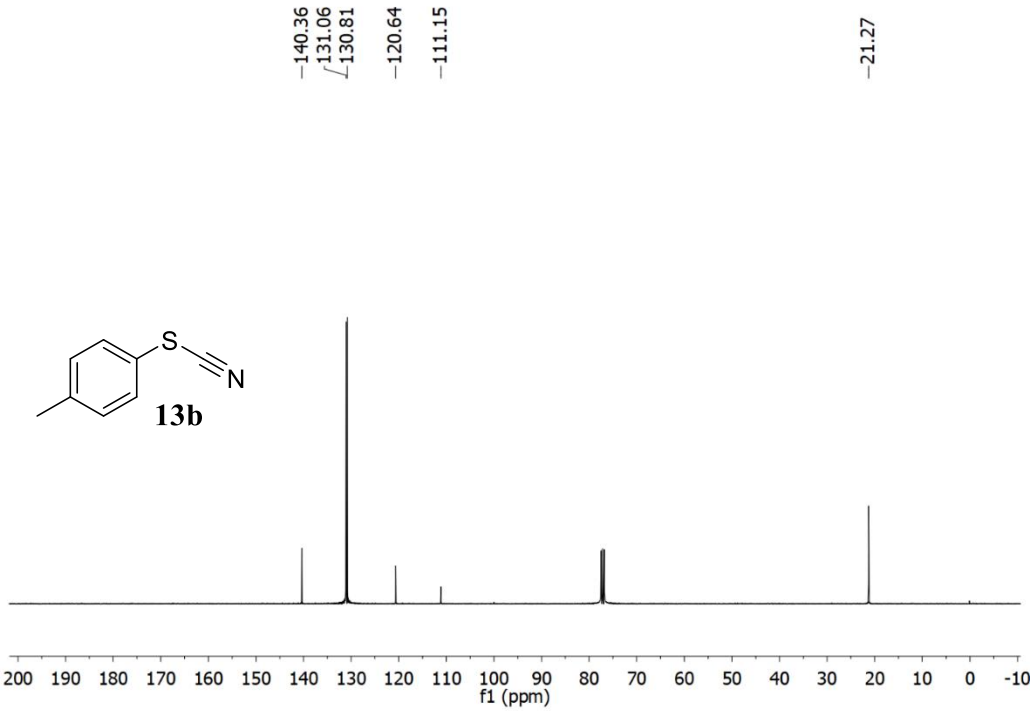


Fig. IV. 6: ^{13}C {^{1}H} NMR spectrum of **13b**, $CDCl_3$, 100 MHz

4.11 Notes and references

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