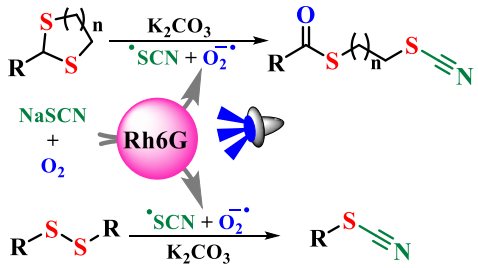
A Direct Access to Thiocyano-Thioesters from Cyclic Thioacetals via Photoredox Catalysis: An Introduction of Two Functional groups in One-Pot

Pankaj D. Dharpure[a], Mousumi Behera[a], Vikas V. Khade, Archana S. Thube[a] and Ramakrishna G. Bhat[a]*

The cyanation of organic compounds is an important and useful process as it directly provides nitriles which in turn can be utilized for different transformations. Although, thiocyanate salt has emerged as a very mild and environmentally friendly "source of CN" alternative to toxic and metal based cyanating reagents; its synthetic utility for the cyanation is highly limited to very few types of organic compounds. We have explored the reactivity of sodium thiocyanate for directly cyanating cyclic thioacetals for accessing thiocayano-thioesters with two different functional groups in one pot using photoredox catalysis under mild reaction conditions. Based on the reactivity of thiocyanate radical, the protocol has been further extended for the direct cyanation of disulfides and diselenides to access aryl thiocyanates and aryl selenocyanate. A series of control experiments and Stern-Volmer studies have been carried out to validate the mechanistic pathways.

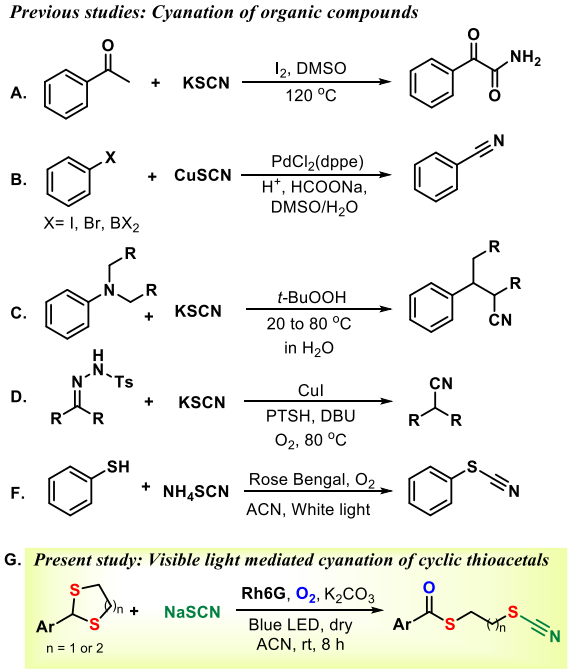


Key words: *Thioacetals, Cyanation, Thiocyanate, Thiocyano-thioesters, Aryl nitriles*

Introduction

Organic thiocyanates are very important and useful synthetic intermediates for the synthesis of tetrazoles and different functionalities such as thiols, disulfides, thioethers, trifuloromethyl thioethers, thiocarbamates, thioesters, and sulfonyl cyanides.[1-9] Likewise, thioesters are also important synthetic intermediates in many bio-synthetic pathways such as native chemical ligation, protein synthesis and nucleic acid synthesis.[10] Also, thioesters have been utilized in the drug delivery applications, biomolecules labelling.[11] Thioesters have also been employed as important building blocks alongside its synthetic utility as an acyl radical equivalent in many acyl transfer reactions.[12] Traditionally, the cyanation of organic molecules have been achieved using cyanating agents or by exploring the combined "CN source" starting from solvent (as a carbon source) and ammonium iodide/ammonium carbonate/ammonium bicarbonate/urea as nitrogen source under palladium catalysis or stoichiometric amount of copper at an elevated reaction temperature.[13] Most of these protocols relied on stoichiometric amount of oxidants, transition metals, ligands, costly reagents or more importantly usage of extremely toxic "CN sources" (CuCN) at an elevated reaction temperature. In order to overcome this, different thiocyanate salts have been explored as "CN source" that are inexpensive, easily available, comparatively non-toxic and bench-stable. Recently, thiocyanate salt has been used as a source of nitrogen for directly accessing phenylglyoxamides starting from acetophenone (Scheme 1a).[14] The cyanation of aromatic halides has been achieved by CuSCN via palladium catalysis to access a wide variety of aromatic nitriles (Scheme 1b).[15] The reaction of tertiary amines and KSCN under oxidizing reaction condition (*t*butoxide as an oxidant) at an elevated temperature afforded the corresponding nitriles (Scheme 1c).[16] The cyanation of *in situ* generated carbene from the tosylhydrazone has been reported using KSCN and CuI at 80 °C under alkaline reaction conditions (Scheme 1d).[17] Very recently for the first time, metal-free cyanation of thiophenol under visible light photoredox condition has been achieved by generating electrophilic thiocyanate radical as a "source of CN" to access a wide variety of aryl thiocyanates under oxygen atmosphere (Scheme 1e).[18]

Scheme 1: Application of thiocyanates in organic transformations



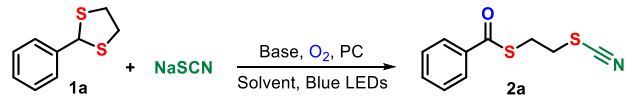
However, this useful and straightforward protocol for the cyanation using non-toxic ammonium thiocyanate salt is limited only to thiophenols. More importantly, the cyanation of thioethers has not

been achieved till date to the best of our knowledge. We have been working on photoredox catalysis and our continuous interest on thioacetals led us to focus on developing a protocol for the direct cyanation of organic molecules such as cyclic thioacetals under milder reaction conditions using inexpensive and environmentally benign cyanating reagents. Based on our experience, the formation and the cleavage of the dithioacetals is known to proceed via thiyl radical under photoredox condition.[19a-c] Recently our research group has achieved the disulphide-linked-dithioesters starting from dithioacetals using base dependent photoredox catalysis and this transformation has been proved to proceed via the cleavage of C–S bond.[19c] Based on the same concept, we have hypothesized that the *in situ* generated electrophilic thiocyanate radical can be trapped with dithioacetals to generate the molecules with the dual functional groups (thiocyano-thiosesters) in a single step under suitable reaction conditions. We envisaged that thiocyano-thioesters can be synthesized directly from dithioacetals by trapping the thyil radical with thiocyanate salt. Herein, we report the direct generation of two functional groups to access thiocayano-thioesters from dithioacetals under photoredox catalysis in one pot.

Results and Discussion

In order to validate our hypthesis we commenced with the model reaction of dithiolane **1a** and ammonium thiocyanate in presence of K_2CO_3 as a base, Rhodamine 6G (2 mol%) as a photocatalyst, in dry acetonitrile under oxygen atmosphere by irradiating with blue LEDs for 8 h. The reaction afforded the corresponding desired product **2a** albeit in poor yield (15% Table 1, entry 1). Gratfyingly, the reaction of **1a** in presence of sodium thiocyanate under the reaction conditions afforded the desired product **2a** in very good yields (83%, Table 1, entry 2). In order to further optimize the reaction condition, we screened reaction using different photocatalysts such as Eosin Y, Rhodamine 6G (Rh6G), $Ru(bpy)_3Cl_2$, $Ir(bpy)_3$, Acridinium-perchlorate and Pyrillium-tetrafluroborate (Table 1, Entries 2 and 3-6). Among all the photocatalysts, Rh6G found to be optimum photocatalyst for the desired transformation by affording the desired product **2a** in very good yield (83% yield, Table 1, entry 2). Later, we screened different solvents and among all anhydrous acetonitrile proved to be advantageous for the smooth transformation of **1a** to thiocayano-thioester **2a** (Table 1, Entry 2 and 7-11). Among different bases screened, K_2CO_3 turned out to be most suitable base by providing the desired product **2a** in very good yield (83%) (Table 1. Entries 2 and 12-15). There was no significant change in the reactivity of sodium thiocyanate and potassium thiocyanate on the out come of desired product **2a** formation (83%, 82% yields respectively, see ESI 1.3, Entry 5 and 6). Later, we screened the desired reaction with variable stiochimetric amounts of sodium thiocyanate. We observed that excess sodium thiocyanate (5 equiv.) was essential for the smooth transformation to access the desired product **2a** in very good yield (See ESI, 1.3). The desired reaction did not work in the absence of light, photocatalyst and oxygen indicating these are very essential and ncessary requirement for the smooth and facile transformation (Table 1, entry 16, 18 and 19). While, the reaction in absence of base offered trace amount of desired product **2a** (Table 1, entry 17).

Table 1. Reaction optimization[a-f]



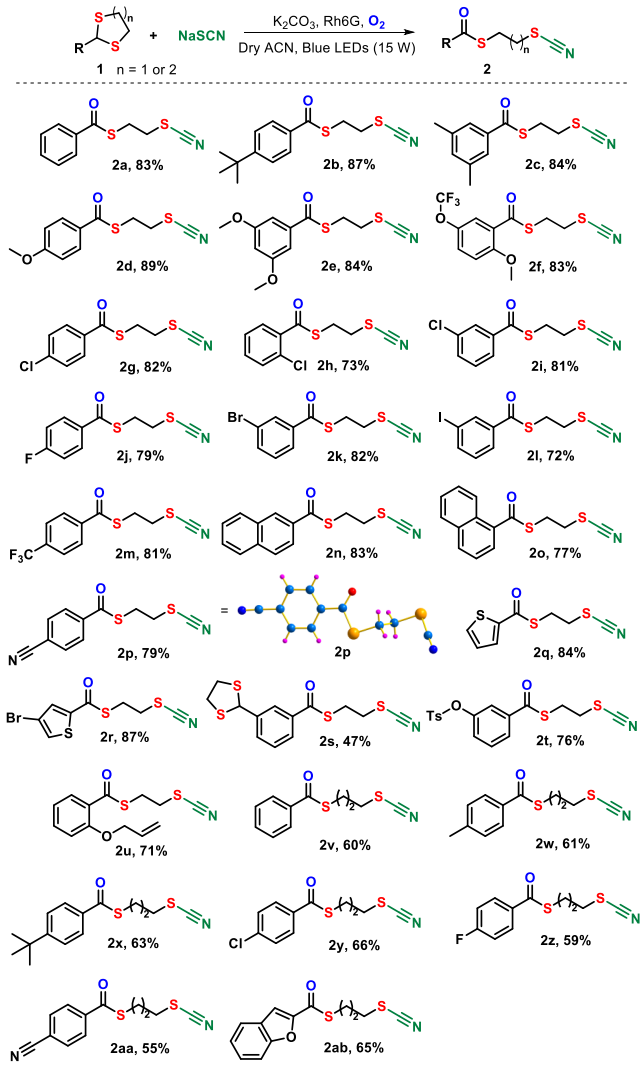
Entry	Catalyst	Solvent[#]	Base	Yield of **2a** in %
1[b]	Rh6G	MeCN	K_2CO_3	15
2	**Rh6G**	**MeCN**	**K_2CO_3**	**83**
3	Eosin Y	MeCN	K_2CO_3	67
4	Acr	MeCN	K_2CO_3	60
5	$Ru(bpy)_3Cl_2$	MeCN	K_2CO_3	49
6	Rose Bengol	MeCN	K_2CO_3	24
7	Rh6G	^{t}BuOH	K_2CO_3	61
8	Rh6G	DMSO	K_2CO_3	19
9	Rh6G	THF	K_2CO_3	43
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]	--	MeCN	K_2CO_3	N.R.
17	Rh6G	MeCN	--	Trace
18[d]	Rh6G (Argon)	MeCN	K_2CO_3	N.R.
19[e]	Rh6G (Without Light)	MeCN	K_2CO_3	N.R.
20[f]	Rh6G (open air)	MeCN	K_2CO_3	71

[a]0.1 mmol **1a**, 2 mol% catalyst, 0.2 equiv. base, 0.5 equiv. NaSCN, 2 mL solvent, O_2 baloon; [b]NH_4SCN; [c]Without catalyst at 60 ^oC [d]under argon; [e]Without light; [f]open air atmosphere, Blue LED (15 W), [#]-All solvents used were anhydrous.

In order to valiadate the necessity of anydrous solvent, we carried out the reaction in moist acetonitrile (undried). We observed the reduction in the yield of desired product **2a** (71%, Table 1, entry 20). Based on the exhaustive screening, dithiolane **1a** (1 equiv.), NaSCN (5 equiv.), K_2CO_3 (2 equiv.), Rh6G (2 mol%) in dry acetonitrile under O_2 atmosphere and blue LEDs (15 W) proved to be optimum reaction condition. Having optimized the reaction condition, we planned to explore diverse substrate scope of dithiolanes so as to generalize this protocol (Table 2). All the electronically neutral dithiolanes (**1a-c**) under the optimized reaction conditions offered the corresponding thiocyanao-thioesters (**2a-c**) in very good yields (upto 87%). Elelctron rich substrates (**1d-1f**) reacted smoothly to afford the desired products (**2d-2f**) in very good yields (upto 89%). Substrates (**1g-1m**) containing electron deactivating substituents at *o*/*m*/*p* positions also worked well under

optimized reaction conditions to furnish the desired products (**2g-m**) in a very good yields (upto 82%, Table 1). Naphthalene-1-dithiolane as well as naphthalene-2-dithiolane derivatives (**1n**, **1o**) also offerded the corresponding desired products **2n** and **2o** in very good yields (upto 83%). Further, dithiolane derived from aromatic aldehyde with electron withdrawing substituent (–CN) also afforded the desired product **2p** in good yield and the molecular structure of the **2p** was unambiguously confirmed by the single crystal X-ray analysis.[20] Even the dithiolanes derived heterocyclic aldehydes **1q**-**1r** also worked smoothly under the reaction conditions to afford corresponding products **2q-2r** in excellent yields (upto 87%, Table 1). Dithiolane substrates containing protecting groups afforded the corresponding products **2s-2u** in moderate to good yields (up to 76%) and the all protecting groups tolerated the reaction conditions. Later, reactivity of dithianes (six-membered cyclic thioacetals) have been explored to generalize this protocol. Gratifyingly, different dithianes **1v**-**1ab** derived from electron rich as well as electron difficeint aromatic aldehydes, and

Table 2. Substrate scope

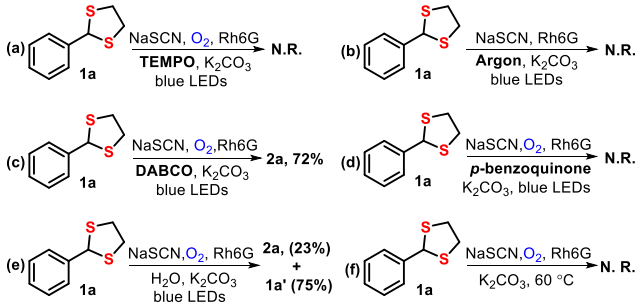


[a]0.1 mmol **1a**, 2 mol% Rh6G, 0.2 mmol K_2CO_3, 0.5 mmol NaSCN, 2 mL MeCN, O_2 baloon; 15 W Blue LEDs; isolated yields in percentage.

Heteroaromatic aldehydes afforded the corresponding desired products **2v**-**2ab** in good yields (upto 66%, Table 1).

In order to have an insight into the reaction mechanism, we carried out few control experiments systematically. The reaction of dithiolane **1a** in presence of TEMPO did not work thus confirming the radical nature of the transformation (Scheme 2a). The reaction in absence of oxygen (under argon atmosphere) did not work indicating the necessary requirement of oxygen for this reaction (Scheme 2b). Later, in order to investigate the involvement of singlet oxygen if any in the reaction pathway, reaction of **1a** was carried out in presence of DABCO (singlet oxygen quencher). We observed that reaction worked smoothly and DABCO did not have any impact in the yield of **2a** thus indicating that singlet oxygen has no significant role in the reaction pathway (Scheme 2c).[21] While, the reaction of **1a** in presence of *p*-benzoquinone under standard optimized reaction conditions did not work. This result confirmed the involvment of superoxide radical anion in the reaction mechanism (Scheme 2d).[22] The reaction in presence of water led to significant reduction in the yield of desired product **2a** along with the corresponding benzaldehyde as a side product **1a'** (scheme 2e).

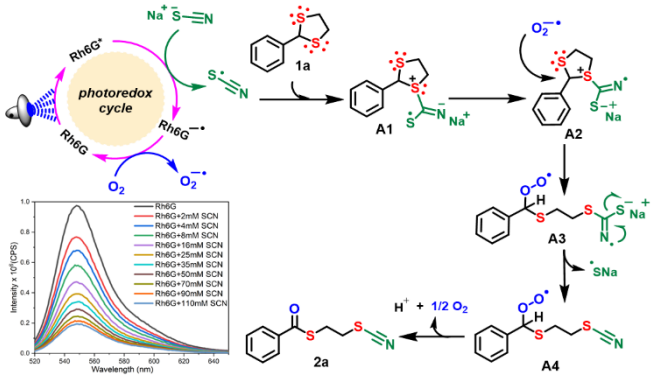
Scheme 2. Control experiments



While, the reaction in dark but in presence of photocatalyst under standard reaction conditions at an elavated reaction temperature (60 °C) did not work (Scheme 2f). This indicated that not only the photocatalyst but also the light is absolutely essential for this transformation and the temperature do not have any role for the desired product fromation. Further, in order to confirm the possible single electron transfer (SET) event of Rh6G* with dithioacetal or NaSCN, we carried out the Stern-Volmer experiment. This study revealed that the efficiency of the SET of Rh6G* with the NaSCN is much higher than that of **1a** (see ESI 1.4). The efficiency of SET of NaSCN with the Rh6G* was further supported by the oxidation potential of NaSCN (E^{ox} = +0.66 V vs SCE) which is less than the reduction potential of Rh6G* (E^{red} = +1.39 V vs SCE).[23,24] Based on the control experiments, Stern-Volmer plot and preceeding literature,[19b] we have depicted the plausible reaction mechanism (Fig 1). Upon irradiation of blue light, the photocatalyst Rh6G gets excited to Rh6G*. This excited species Rh6G* (E^{red} = +1.39 V vs SCE)[23] takes part in SET process with sodium thiocyanate (E^{ox} = +0.66 V vs SCE)[24] instead of **1a** (E^{ox} =

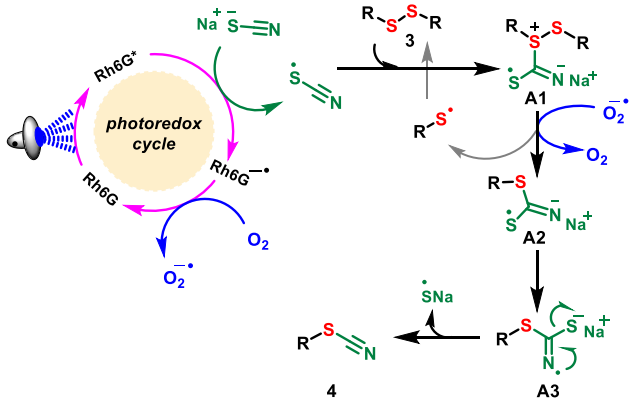
+1.26 V vs SCE) by the reductive quenching pathway to generate the photocatalyst radical anion ($Rh6G^{\bullet -}$, reduced form) and thiocyanate radical (oxidized form $^{\bullet}SCN$).

Fig. 1. Plausible reaction mechanism



This SET event was unambiguously confirmed by the Stern Volmer experimental studies (ESI 1.4). Further, $Rh6G^{\bullet -}$ takes part in another SET event with oxygen to generate superoxide radical anion and the ground state Rh6G thus completing the photocatalyitic cycle. (Fig 1). Simultaneously, highly reactive thiocyanate radical species reacts with the dithiolane **1a** to form an intermediate **A1**. This would further form the corresponding intermediate **A2** by shifting of electron from nitrogen to sulfur. Highly nucleophilic superoxide radical anion attacks the intermediate **A2** at the electrophilic carbon to generate intermediate **A3**. This intermediate would further collapse to form hydroperoxide intermediate **A4**. This unstable intemediate ultimately breaks down to form the desired product **2a.**

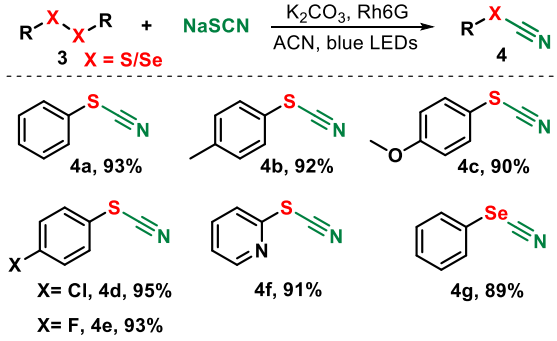
Fig. 1. Plausible reaction mechanism



Based on the plasuible reaction mechanism, it is evident that after SET process, the *in situ* generated oxidized thiocyanate radical is more likely to be electrophilic and has high possibility to be attacked by the nucleophilic sulfur atom of dithioacetal followed by the cleavage of bond (with the neighbouring carbon atom). In order to explore the reactivity of thiocyanate radical and to validate this hypothesis, we planned to trap this using suitable compounds such as aryl disulfides (Fig 2).

In this regard, we commenced with a model reaction of diphenyl disulfide **3a**, sodium thiocyanate (5 equiv.) under standard optimum reaction conditions used for obtaining thiocyano-thioesters. Gratifyingly, we obtained the corresponding desired phenyl thiocyanate **4a** in excellent yield (93%, Table 3). Encouraged by this initial success, we planned to generalise this protocol as further application and for the wider applicability (Table 3).

Table 3. Substate scope



[a]**3** (0.1 mmol), Rh6G (2 mol%), K_2CO_3 (0.2 mmol), NaSCN (0.5 mmol), MeCN (2 mL), O_2 baloon, Blue LEDs (15W)

Reaction of differen diaryl disulfides **3b-3f**, reacted smoothly with sodium thiocyanate under the reaction conditions to afford the corresponding aryl thiocyanates **4b-4f** in excellent yields (up to 95%, Table 3). Even diphenyl diselenide **3g** reacted smoothly with sodium thiocyanate under the reaction conditions to afford the corresponding phenyl selenocyante **4g** in very good yield (89%). This protcol also proved to be very efficient in synthesizing thiocyantes from easily accessible diaryl disulfides in one pot.

Conclusions

In summary, we have successfully developed the safe and environmentally benign protocol for the cyanation of cyclic thioacetals and disulfides to access thiocyano-thioesters and aryl thiocyanates respectively using commercially viable and nontoxic sodium thiocyanate as a cyanating source under visible light conditions. The protocol offers the direct access to a wide range of thiocyano-thioesters and aryl thiocyantes starting from dithioacetals and aryl disulfides respectively for the first time using the photoredox-catalysis under ambient reaction condition. The protocol proved to be efficient and worled under ambient reaction condition using clear energy source and do not require external oxidizing reagent.

EXPERIMENTAL SECTION

General Information: Reagent Information: All reactions were carried out with distilled and dried solvents using oven-dried glass

wares under dry Argon atmosphere, unless otherwise stated. All reagents were purchased from commercial sources and used as received, unless otherwise indicated. Thin layer chromatography (TLC) was performed using silica gel 60 GF254 pre-coated aluminum backed plates (2.5 mm) with detection by UV light. Visualization was accomplished by irradiation with a UV light at 254 nm and vanillin staining agent. Column chromatography was performed using silica gel (100-200 mesh) eluting with petroleum ether and ethyl acetate. Petroleum ether and ethyl acetate mixture was used as gradient elution for column chromatography. Analytical Information: All isolated compounds were characterized by Proton (^{1}H) and carbon (^{13}C) NMR spectra were recorded on a 400 MHz Jeol ECS-400 and Bruker Avance III HD Ascend 400 MHz spectrometer. All Nuclear Magnetic Resonance spectra were recorded in $CDCl_3$. The NMR spectra were recorded using tetramethyl silane (TMS) as the internal standard. ^{1}H NMR spectra were recorded at 400 MHz and ^{13}C NMR spectra were recorded at 100/150 MHz (Bruker and Jeol), unless otherwise noted. Chemical shifts (δ) are reported in ppm downfield from $CDCl_3$ (δ = 7.26 ppm) for ^{1}H NMR and relative to the central $CDCl_3$ resonance (δ = 77.16 ppm) for ^{13}C NMR spectroscopy. For 1H NMR, data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, s = sextet, h = heptet, m = multiplet, br = broad), coupling constants (*J*) and integration. Coupling constants (*J*) are reported in Hertz (Hz). Carbon chemical shifts are reported in ppm from tetramethyl silane (TMS) with the solvent resonance as the internal standard ($CDCl_3$ δ 77.0 ppm). coupling constants (J) are given in Hz and integration. ^{13}C NMR spectra were recorded with complete proton decoupling. ^{19}F NMR spectra were recorded at 377 MHz. Mass samples were analyzed by high resolution mass spectrometry (HRMS) using ESI TOF. Melting points were measured in an open glass capillary and values are uncorrected. Mass samples were analyzed by High-Resolution Mass Spectrometry (HRMS) using ESI-TOF. Melting points were measured in capillary tubes on a Büchi B-540 apparatus, are uncorrected. Fluorescence emission spectra were obtained on a Fluoromax-4 spectrofluorometer from Horiba Jobin-Yvon, with xenon light source in a 3 mL, Hellma fluorescence cuvette (path length 1.0 cm).

General procedure A for the synthesis of compounds 1: (1,3-dithiane and 1,3-dithiolane protection of aldehyde)[25]

To a round bottom flask containing SiO_2, PPA (6.5 w/w %) was added DCM (10 mL) and stirred well for 15 min. After that DCM was evaporated to obtain a well mixed SiO_2-PPA mixture. To this mixture, DCM (15 mL), aldehyde (1 equiv.; 1.5 mmol) and 1, 2-dithiane (1.2 equiv.), or 1,3-dithiane (1.2 equiv.) were added, and stirred for 6 h at room temperature. After completion of the reaction (monitored by TLC) the solution was filtered through cotton. The filtrate was treated with saturated KOH solution (5 mL) and stirred for 30 min to quench excess dithiane. After which, solution was extracted with dichloromethane (3 x 20 mL). The combined extracts was dried over anhydrous sodium sulfate, filtered and concentrated under reduced pressure. The crude product was further purified by column chromatography over silica gel to afford the corresponding compound **1**.

General procedure B for the synthesis of thioester-thiocyanate 2.

An oven-dried round bottom flask equipped with a stir bar and rubber septum is charged with dithiolane **1** (0.1 mmol, 1 equiv.), K_2CO_3 (0.2 mmol, 2 equiv.), NaSCN (0.5 mmol, 5 equiv.) Rhodamin6G (2 mol%), dry MeCN (2 mL). The reaction mixture was initially purged with O_2 for 5 min and the oxygen atmosphere was maintained throughout the reaction (using a Oxygen balloon). The reaction mixture was stirred under the irradiation of blue LEDs (15 W) at room temperature for 6-12 h (monitored by TLC). After completion of the reaction, the solvent was removed under reduced pressure and the crude residue was purified by column chromatography over silica gel using mixture of petroleum ether/EtOAc as an eluent to afford the corresponding **2**. (Note-The presence of moisture and the impurity of 1, 2-ethanedithiol in dithiolane (**1**) greatly influences the yield of reaction. Dry solvent is must to avoid the deprotection to corresponding aldehyde. The reaction temperature is 25-30 ^{o}C).

General procedure C for the synthesis of aryl thiocyanate 4.

An oven-dried round bottom flask equipped with a stir bar and rubber septum is charged with diaryl disulfide **3** (0.1 mmol, 1 equiv.), K_2CO_3 (0.2 mmol, 2 equiv.), NaSCN (0.5 mmol, 5 equiv.) Rhodamin 6G (2 mol%), MeCN (2 mL). The reaction mixture was initially purged with O_2 for 5 min and the oxygen atmosphere was maintained throughout the reaction (using a Oxygen balloon). The reaction mixture was stirred under the irradiation of blue LEDs (15 W) at room temperature for 6-12 h (monitored by TLC). After completion of the reaction, the solvent was removed under reduced pressure and the crude residue was purified by column chromatography over silica gel using mixture of petroleum ether/EtOAc as an eluent to afford the corresponding **2**. (Note-The presence of moisture and the impurity of 1, 2-ethanedithiol in dithiolane (**1**) greatly influences the yield of reaction. Dry solvent is must to avoid the deprotection to corresponding aldehyde. The reaction temperature 25-28 ^{o}C).

Product Characterization data:

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

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

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

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

*S-(2-thiocyanatoethyl) 3,5-dimethoxybenzothioate (**2e**)*: The compound **2e** was prepared following the General Procedure **B**. colourless liquid (24 mg, 84% yield); R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 (d, *J* = 2.3 Hz, 2H), 6.68 (t, *J* = 2.3 Hz, 1H), 3.83 (s, 6H), 3.51 – 3.34 (m, 2H), 3.26 – 3.08 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 190.60, 161.02, 138.20, 111.54, 106.35, 105.16, 55.75, 33.48, 29.20. HRMS (ESI-TOF) m/z calcd. For $C_{12}H_{14}NO_3S_2$ $[M+H]^+$ 284.0410; found 284.0413.

*S-(2-thiocyanatoethyl) 2-methoxy-5-(trifluoromethoxy)benzothioate (**2f**)*: The compound **2f** was prepared following the General Procedure **B**. colourless liquid (28 mg, 83% yield); R_f = 0.4 (3:20 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (d, *J* = 3.0 Hz, 1H), 7.38 (dd, *J* = 9.1, 3 Hz, 1H), 7.02 (d, *J* = 9.1 Hz, 1H), 3.97 (s, 3H), 3.40 (m, 2H), 3.22 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 188.38, 157.15, 142.41, 127.26, 126.27, 124.38, 122.82, 121.82, 119.26, 113.36, 111.64, 56.40, 33.29, 29.72. HRMS (ESI-TOF) m/z calcd. For $C_{12}H_{11}F_3NO_3S_2$ $[M+H]^+$ 338.0127; found 338.0131.

*S-(2-thiocyanatoethyl) 4-chlorobenzothioate (**2g**)*: The compound **2g** was prepared following the General Procedure **B**. colourless liquid (21 mg, 82% yield); R_f = 0.4 (3:20 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H), 3.53 – 3.33 (m, 2H), 3.24 – 3.17 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 189.60, 140.63, 134.67, 129.28, 128.83, 111.52, 33.48, 29.21. HRMS (ESI-TOF) m/z calcd. For $C_{10}H_9ClNOS_2$ $[M+H]^+$ 257.9809; found 257.9811.

*S-(2-thiocyanatoethyl) 2-chlorobenzothioate (**2h**)*: The compound **2h** was prepared following the General Procedure **B**. colourless liquid (19 mg, 73% yield); 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). $^{13}C\{^1H\}$ 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 calcd. For $C_{10}H_9ClNOS_2$ $[M+H]^+$ 257.9809; found 257.9810.

*S-(2-thiocyanatoethyl) 3-chlorobenzothioate (**2i**)*: The compound **2i** was prepared following the General Procedure **B**. colourless liquid (19 mg, 73% yield); R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91 (t, *J* = 2.1 Hz, 1H), 7.83 (dt, *J* = 7.9, 1.3 Hz, 1H), 7.58 (ddd, *J* = 8.0, 2.1, 1.0 Hz, 1H), 7.42 (t, *J* = 7.9, 1.0 Hz, 1H), 3.49 – 3.45 (m, 2H), 3.24 – 3.20 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 189.63, 137.81, 135.27, 134.02, 130.26, 127.47, 125.61, 111.48, 33.42, 29.26. HRMS (ESI-TOF) m/z calcd. For $C_{10}H_9ClNOS_2$ $[M+H]^+$ 257.9809; found 257.9810.

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

*S-(2-thiocyanatoethyl) 3-bromobenzothioate (**2k**)*: The compound **2k** was prepared following the General Procedure **B**. colourless liquid (25 mg, 82% yield); R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (t, *J* = 1.9 Hz, 1H), 7.88 (dt, *J* = 7.9, 1.4 Hz, 1H), 7.74 (ddd, *J* = 8.0, 2.0, 1.0 Hz, 1H), 7.36 (t, *J* = 7.9 Hz, 1H), 3.60 – 3.37 (m, 2H), 3.28 – 3.07 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 189.50, 137.96, 136.91, 130.46, 130.35, 126.03, 123.15, 111.43, 33.39, 29.23. HRMS (ESI-TOF) m/z calcd. For $C_{10}H_9BrNOS_2$ $[M+H]^+$ 301.9303; found 301.9309.

*S-(2-thiocyanatoethyl) 3-iodobenzothioate (**2l**)*: The compound **2l** was prepared following the General Procedure **B**. colourless liquid (25 mg, 72% yield); R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (q, *J* = 1.7 Hz, 1H), 8.02 – 7.87 (m, 2H), 7.33 – 7.19 (m, 1H), 3.51 (m, 2H), 3.24 (m, 2H).$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 189.40, 142.84, 137.96, 136.20, 130.57, 126.65, 111.48, 94.47, 33.43, 29.24. HRMS (ESI-TOF) m/z calcd. For $C_{10}H_9INOS_2$ $[M+H]^+$ 349.9165; found 349.9171.

*S-(2-thiocyanatoethyl) 4-trifluorobenzothioate (**2m**)*: The compound **2m** was prepared following the General Procedure **B**. white solid (25 mg, 81% yield), Mp: 89.5-91.1 °C; R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 – 7.84 (m, 2H), 7.81 – 7.63 (m, 2H), 3.65 – 3.37 (m, 2H), 3.32 – 3.08 (m, 2H).$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 189.97, 139.08, 139.06, 135.55, 135.22, 130.61, 127.87, 126.12, 126.08, 126.04, 126.00, 124.87, 122.16, 111.43, 33.36, 29.36. HRMS (ESI-TOF) m/z calcd. For $C_{11}H_9F_3NOS_2$ $[M+H]^+$ 292.0072; found 292.0078.

*S-(2-thiocyanatoethyl) naphthalene-2-carbothioate (**2n**)*: The compound **2n** was prepared following the General Procedure **B**. yellow solid (23 mg, 83% yield), Mp: 79.1-80.6 °C; R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.52 (s, 1H), 8.01 – 7.94 (m, 2H), 7.93 – 7.86 (m, 2H), 7.61 (m, 2H), 3.52 (m, 2H), 3.27 (m, 2H).$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 190.64, 136.15, 133.67, 132.52, 129.78, 129.22, 129.02, 128.90, 128.01, 127.30, 123.07, 111.63, 33.69, 29.24. HRMS (ESI-TOF) m/z calcd. For $C_{14}H_{12}NOS_2$ $[M+H]^+$ 274.0355; found 274.0353.

*S-(2-thiocyanatoethyl) naphthalene-1-carbothioate (**2o**)*: The compound **20** was prepared following the General Procedure **B**. colourless liquid (21 mg, 77% yield); R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.64 – 8.44 (m, 1H), 8.09 (m, 1H), 8.05 (m, 1H), 7.90 (m, 1H), 7.65 – 7.54 (m, 2H), 7.52 (m, 1H), 3.63 – 3.37 (m, 2H), 3.37 – 3.11 (m, 2H).$^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 192.76, 134.33, 133.91, 133.88, 129.28, 128.60, 128.51, 126.98, 125.17, 124.59, 111.67, 33.62, 29.97. HRMS (ESI-TOF) m/z calcd. For $C_{14}H_{12}NOS_2$ $[M+H]^+$ 274.0355; found 274.0357.

*S-(2-thiocyanatoethyl) 4-cyanobenzothioate (**2p**)*: The compound **2p** was prepared following the General Procedure **B**. white solid (20 mg, 79% yield) Mp: 84.1-85.6 °C; R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 – 8.02 (m, 1H), 7.81 – 7.76 (m, 1H), 3.55 – 3.48 (m, 1H), 3.26 – 3.20 (m, 1H).^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 189.57, 139.33, 132.76, 127.90, 117.69, 117.35, 111.26, 33.23, 29.42. HRMS (ESI-TOF) m/z calcd. For $C_{11}H_9N_2OS_2$ $[M+H]^+$ 249.0151; found 249.0155.

*S-(2-thiocyanatoethyl) thiophene-2-carbothioate (**2q**)*: The compound **2q** was prepared following the General Procedure **B**. colourless liquid (19 mg, 84% yield); R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 – 7.80 (m, 1H), 7.70 – 7.66 (m, 1H), 7.16 – 7.12 (m, 1H), 3.48 – 3.44 (m, 2H), 3.25 – 3.21 (m, 2H).^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 182.55, 141.18, 133.74, 131.96, 128.23, 111.47, 33.64, 29.24. HRMS (ESI-TOF) m/z calcd. For $C_8H_8NOS_3$ $[M+H]^+$ 229.9763; found 229.09766.

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

*S-(2-thiocyanatoethyl) 3-(1,3-dithiolan-2-yl)benzothioate (**2s**)*: The compound **2s** was prepared following the General Procedure **B**. colourless liquid (15 mg, 47% yield); R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.08 (d, *J* = 1.9 Hz, 1H), 7.85 (dt, *J* = 7.8, 1.4 Hz, 1H), 7.77 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.42 (t, *J* = 7.8 Hz, 1H), 5.65 (s, 1H), 3.53 (ddd, *J* = 7.0, 5.9, 3.8 Hz, 2H), 3.49 – 3.43 (m, 2H), 3.39 (ddd, *J* = 8.1, 6.2, 3.8 Hz, 2H), 3.21 (dd, *J* = 8.6, 6.2 Hz, 2H).^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 190.37, 142.17, 136.57, 133.72, 129.19, 127.14, 126.97, 111.59, 55.59, 40.55, 33.55, 29.15. HRMS (ESI-TOF) m/z calcd. For $C_{13}H_{14}NOS_4$ $[M+H]^+$ 327.9953; found 327.9960.

*S-(2-thiocyanatoethyl) 3-(tosyloxy)benzothioate (**2t**)*: The compound **2t** was prepared following the General Procedure **B**. colourless liquid (29 mg, 76% yield); R_f = 0.4 (1:9 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87 – 7.82 (m, 0H), 7.73 (d, *J* = 8.3 Hz, 1H), 7.54 – 7.50 (m, 0H), 7.43 (t, *J* = 8.0 Hz, 0H), 7.34 (d, *J* = 8.0 Hz, 1H), 7.29 – 7.24 (m, 1H), 3.45 (dd, *J* = 8.3, 6.4 Hz, 1H), 3.20 (dd, *J* = 8.3, 6.4 Hz, 1H), 2.46 (s, 1H.^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 189.26, 149.82, 145.87, 137.70, 131.99, 129.98, 128.52, 127.90, 125.89, 121.27, 111.29, 33.27, 29.16, 21.79. HRMS (ESI-TOF) m/z calcd. For $C_{17}H_{16}NO_4S_3$ $[M+H]^+$ 394.0236; found 394.0242.

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

*S-(3-thiocyanatopropyl) benzothioate (**2v**)*: The compound **2v** was prepared following the General Procedure **B**. colourless liquid (14 mg, 60% yield); R_f = 0.4 (1:19 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 – 7.94 (m, 2H), 7.62 – 7.57 (m, 1H), 7.49 – 7.45 (m, 2H), 3.23 (m, 2H), 3.07 (m, 2H), 2.26 – 2.20 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$): δ 191.46, 136.74, 133.87, 128.87, 127.44, 112.06, 32.75, 30.12, 26.84. HRMS (ESI-TOF) m/z calcd. For $C_{11}H_{12}NOS_2$ $[M+H]^+$ 238.0355; found 238.0361.

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

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

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

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

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

*S-(3-thiocyanatopropyl) benzofuran-2-carbothioate (**2ab**)*: The compound **2ab** was prepared following the General Procedure **B**. colourless liquid (14 mg, 55% yield); R_f = 0.4 (2:15 :: EA:pet ether), ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.71 (dt, *J* = 8.0, 1.0 Hz, 1H), 7.59 (dq, *J* = 8.5, 0.9 Hz, 1H), 7.55 (d, *J* = 1.0 Hz, 1H), 7.49 (ddd, *J* = 8.5, 7.2, 1.3 Hz, 1H), 7.33 (ddd, *J* = 8.0, 7.1, 1.0 Hz, 1H), 3.27 (t, *J* = 6.8 Hz, 2H), 3.08 (t,

J = 7.1 Hz, 2H), 2.26 (p, *J* = 6.9 Hz, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 181.73, 155.63, 150.79, 128.49, 126.90, 124.25, 123.37, 112.53, 111.91, 111.78, 32.60, 29.99, 26.21. HRMS (ESI-TOF) m/z calcd. For $C_{13}H_{12}NOS_2$ $[M+H]^+$ 278.0304; found 278.0309.

*thiocyanatobenzene (**4a**)*: The compound **4a** was prepared following the General Procedure **C**. colourless liquid (25 mg, 93% yield); R_f = 0.4 (1:99 :: EA:pet ether), ^1H NMR (400 MHz, $CDCl_3$): δ 7.54 (dd, *J* = 6.4, 3.0 Hz, 2H), 7.49 – 7.37 (m, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 130.30, 130.15, 129.61, 124.50, 110.62. HRMS (ESI-TOF) m/z calcd. For C_7H_6NS $[M+H]^+$ 136.0215; found 136.0217.

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

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

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

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

*2-thiocyanatopyridine (**4f**)*: The compound **4f** was prepared following the General Procedure **C**. colourless liquid (24 mg, 91% yield); R_f = 0.4 (1:9 :: EA:pet ether), ^1H NMR (400 MHz, $CDCl_3$): δ 8.50 (ddd, *J* = 4.8, 2.0, 0.9 Hz, 1H), 7.75 (td, *J* = 7.8, 1.9 Hz, 1H), 7.58 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.26 (ddd, *J* = 7.5, 4.8, 1.1 Hz, 1H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 150.65, 150.09, 138.58, 122.87, 122.11, 109.13. HRMS (ESI-TOF) m/z calcd. For $C_6H_5N_2S$ $[M+H]^+$ 137.0168; found 137.0172.

*selenocyanatobenzene (**4g**)*: The compound **4g** was prepared following the General Procedure **C**. yellow liquid (32 mg, 89% yield); R_f = 0.4 (1:9 :: EA:pet ether), ^1H NMR (400 MHz, $CDCl_3$): δ 7.65 – 7.60 (m, 2H), 7.43 – 7.36 (m, 3H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$): δ 132.87, 130.50, 129.89, 121.93, 101.60. HRMS (ESI-TOF) m/z calcd. For C_7H_6NSe $[M+H]^+$ 183.9660; found 183.9667. (Note – **4f** causes vomiting sensation if inhilaed for long)

ASSOCIATED CONTENT

Supporting Information-Reaction optimization details, Mechanistic study, Experimental procedures, characterization data of compounds and Copies of ^1H and ^{13}C NMR spectra.

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Conflicts of interest

In There are no conflicts to declare

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Notes and references

(1) Pawliczek, M.; Garve, L. K. B.; Werz, D. B. Activation of Aryl Thiocyanates Followed by Aryne Insertion: Access to 1,2-Thiobenzonitriles. *Org. Lett*. **2015**, *17*, 1716−1719.

(2) (a) Zhang, T.; Deng, G.; Li, H.; Liu, B.; Tan, Q.; Xu, B. Cyclization of 2-Biphenylthiols to Dibenzothiophenes under PdCl2/DMSO Catalysis. *Org. Lett*. **2018**, *20*, 5439−5443. (b) Hoggarth, E. Sexton, W. A. New Reactions of Thiocyanic Esters. *J. Chem. Soc.* **1947**, 815– 818.

(3) Danoun, G.; Bayarmagnai, B.; Gruenberg, M. F.; Goossen, L. J. Sandmeyer Trifluoromethylthiolation of Arenediazonium Salts with Sodium Thiocyanate and Ruppert−Prakash Reagent. *J. Chem. Sci*. **2014**, *5*, 1312−1316.
(4) Segalovich-Gerendash, G.; Rozenberg, I.; Alassad, N.; Nechmad, N. B.; Goldberg, I.; Kozuch, S.; Lemcoff, N. G. Imposing Latency in Ruthenium Sulfoxide-Chelated Benzylidenes: Expanding Opportunities for Thermal and Photoactivation in Olefin Metathesis. *ACS Catal.* **2020**, *10*, 4827−4834.
(5) Chen, J.; Wang, T.; Wang, T.; Lin, A.; Yao, H.; Xu, J. Copper Catalyzed C5-selective Thio/Selenocyanation of 8-aminoquinolines. *Org. Chem. Front.* **2017**, *4*, 130−134.
(6) Yang, L.; Tian, Z.-Y.; Zhang, C.-P. Transition-Metal-Free Selective Synthesis of (Z)-1,2-Diarylthio-1-arylalkenes, (2-Arylethene-1,1,2-triyl)tris(arylsulfane)s and Alkynyl Sulfides from Thiocyanates and Terminal Arylalkynes. *ChemistrySelect* **2019**, *4*, 311−315.
(7) Grieco, P. A.; Yokoyama, Y.; Williams, E. Aryl Selenocyanates and Aryl Thiocyanates: Reagents for the Preparation of Activated Esters. *J. Org. Chem.* **1978**, *43*, 1283−1285.
(8) Vaghasiya, B. K.; Satasia, S. P.; Thummar, R. P.; Kamani, R. D.; Avalani, J. R.; Sapariya, N. H.; Raval, D. K. Oxidative Cyanide-free Cyanation on Arylboronic Acid Derivatives using Aryl/Heteroaryl Thiocyanate using Novel IL-PdCl4 Catalyst under Mild Condition. *J. Sulfur Chem.* **2018**, *39*, 507−515.
(9) Kellly, T. R.; Kim, M. H.; Curtis, A. D. M. Structure Correction and Synthesis of the Naturally Occurring Benzothiazinone BMY 40662. *J. Org. Chem.* **1993**, *58*, 5855−5857.
(10) (a) Echelman, D. J.; Lee, A. Q.; Fernández, J. M. Mechanical forces regulate the reactivity of a thioester bond in a bacterial adhesion. *J. Biol. Chem*. **2017**, *292*, 8988–8997. (b) Folikumah, M. Y.; Behl, M.; Lendlein, A. Thiol–Thioester Exchange Reactions in Precursors Enable pH-Triggered Hydrogel Formation. *Biomacromolecules* **2021**, *22*, 1875–1884. (c) Xuan, W.; Collins, D.; Koh, M.; Shao, S.; Yao, A.; Xiao, H.; Garner, P. P.; Schultz, P.G. Site-specific Incorporation of a Thioester Containing Amino Acid into Proteins. *ACS Chem. Biol.* **2018**, *13*, 578–581. (d) Schuler, B.; Pannell, L. K. Specific Labeling of Polypeptides at Amino-Terminal Cysteine Residues Using Cy5-benzyl Thioester. *Bioconjug. Chem.* **2002**, *13*, 1039−1043. (e) Sletten E. M.; Bertozzi, C. R. Bioorthogonal Chemistry: Fishing for Selectivity in a Sea of Functionality. *Angew. Chem., Int. Ed*. **2009**, *48*, 6974–6998. (f) Rinalducci, S.; Murgiano. L.; Zolla, L. Redox proteomics: basic principles and future perspectives for the detection of protein oxidation in plants. *J. Exp. Bot.* **2008**, *59*, 3781–3801. (g) Trang Le, N. T.; Quynh Nguyen, T. N.; Cao, V. D.; Hoang, D. T.; Ngo, V. C.; Hoang Thi, T. T. Recent Progress and Advances of Multi-Stimuli-Responsive Dendrimers in Drug Delivery for Cancer Treatment. *Pharmaceutics*. **2019**, *11*, 591.
(11) (a) Franke, J.; Hertweck, C. Biomimetic Thioesters as Probes for Enzymatic Assembly Lines: Synthesis, Applications, and Challenges. *Cell Chem. Bio.* **2016**, *23*, 1179-1192; (b) Burke, H. M.; Sweeney, L. and Scanlan, E. M. Exploring chemoselective S-to-N acyl transfer reactions in synthesis and chemical biology. *Nat. Comm.* **2017**, *8*, 15655; (c) Chen,B.; Sun, Y.; Niu, J.; Jarugumilli, G. K. and Wu, X. Protein Lipidation in Cell Signaling and Diseases: Function, Regulation, and Therapeutic Opportunities. *Cell Chem. Bio.*, **2018**, *25*, 817-831; (d) Yang, W. and Xia, S-H. Mechanisms of regulation and function of G-protein-coupled receptor kinases. *World J. Gastroenterol*. **2006**, *12*, 7753–7757.
(12) (a) Rossi, S.; Benaglia, M.; Cozzi, F.; Genoni A.; and Benincori, T. Organocatalytic Stereoselective Direct Aldol Reaction of Trifluoroethyl Thioesters. *Adv. Synth. Catal.* **2011**, *353*, 848–854; (b) D. Crich and I. Sharma, Iterative *In Situ* Click Chemistry Creates Antibody-like Protein-Capture Agents. *Angew. Chem., Int. Ed.* **2009**, *48*, 2355–2358; (c) Crich, D.; and Sasaki, K.; On the Reaction of Thioacids with Isocyanates and Isothiocyanates: A Convenient Amide Ligation Process
Org. Lett. **2009**, *11*, 3514–3517; (d) Benaglia, M.; Cinquini, M. and Cozzi, F. The S-Thioester Enolate/Imine Condensation: A Shortcut to β-Lactams. *Eur. J. Org. Chem*. **2000**, 563–572; (e) Matsuo, K. and Sindo, M. Cu(II)-Catalyzed Acylation by Thiol Esters Under Neutral Conditions: Tandem Acylation-Wittig Reaction Leading to a One-Pot Synthesis of Butenolides. Org. Lett. **2010**, *12*, 5346–5349; (f) Iimura, S.; Manabe, K. and Kobayashi, S. Hydrophobic Polymer-Supported Catalyst for Organic Reactions in Water: Acid-Catalyzed Hydrolysis of Thioesters and Transprotection of Thiols. Org. Lett. **2003**, *5*, 101–103; (g) Fukuyama T. and Tokuyama, H. Palladium-mediated synthesis of aldehydes and ketones from thiol esters. *Aldrichimica Acta*, **2004**, *37*, 87–96; (h) Yang, H.; Li, H.; Wittenberg, R.; Egi, M.; Haung, W.; and Liebeskind, L. S. Ambient Temperature Synthesis of High Enantiopurity *N*-Protected Peptidyl Ketones by Peptidyl Thiol Ester−Boronic Acid Cross-Coupling. *J. Am. Chem. Soc.* **2007**, *129*, 1132–1140; (i) Li, H.; Yang, H. and Liebeskind, L. S. Synthesis of High Enantiopurity *N*-Protected α-Amino Ketones by Thiol Ester-Organostannane Cross-Coupling using pH-Neutral Conditions. *Org. Lett.* **2008**, *10*, 4375–4378; (j) Kunchithapatham, K.; Eichman, C. C. and Stambuli, J. P. Synthesis of Diaryl Ketones *via* a Phosphine-free Fukuyama Reaction. *Chem. Commun*., **2011**, *47*, 12679–12681; (k) Yost, J. M.; Zhou, G. and Coltart, D. M. A Facile and Efficient Direct Aldol Addition of Simple Thioesters. *Org. Lett.* **2006**, *8*, 1503–1506; (l) Utsumi, N.; Kitagaki, S. and Barbas III, C. F. Organocatalytic Mannich-Type Reactions of Trifluoroethyl Thioesters. *Org. Lett.* **2008**, *10*, 3405–3408; (m) Alonso, D. A.; Kitagaki, S.; Utsumi, N. and Barbas III, C. F. Towards Organocatalytic Polyketide Synthases with Diverse Electrophile Scope: Trifluoroethyl Thioesters as Nucleophiles in Organocatalytic Michael Reactions and Beyond. *Angew. Chem., Int. Ed*. **2008**, *47*, 4588–4591; (n) Iida, A.; Osada, J.; Nagase, R.; Misaki, T. and Tanabe, Y. Mild and Efficient Pentafluorophenylammonium Triflate (PFPAT)-Catalyzed C-Acylations of Enol Silyl Ethers or Ketene Silyl (Thio)Acetals with Acid Chlorides. *Org. Lett.* **2007**, *9*, 1859–1862.
(13) (a) Kim, J.; Chang, S. A New Combined Source of "CN" from *N*,*N*-dimethylformamide and Ammonia in the Palladium-catalyzed Cyanation of Aryl C-H bonds. *J. Am. Chem. Soc.* **2010**, *132*, 10272–10274. (b) Xu, S.; Teng, J.; Yu, J-T; Sun, S. and Cheng, J. Copper-Mediated Direct Cyanation of Heteroarene and Arene C–H Bonds by the Combination of Ammonium and DMF. *Org. Lett*. **2019**, *21*, 9919–9923. (c) Li, X.; Wang, S.; Zang, J.; Liu, M.; Jiang, G. and Ji, F. Copper- and DMF-mediated switchable oxidative C–H cyanation and formylation of imidazo[1,2-a]pyridines using ammonium iodide. *Org. Biomol. Chem*., **2020**, *18*, 9100-9108. (d) Ren, X.; Chen, J.; Chen F. and Cheng, J. The palladium-catalyzed cyanation of indole C–H bonds with the combination of NH_4HCO_3 and DMSO as a safe cyanide source. *Chem. Commun.,* **2011**, *47*, 6725-6727. (e) Liu, B.; Wang, J.; Zhang, B.; Sun,Y.; Wang, L.; Chena, J. and Cheng, J. Copper-mediated C3-cyanation of indoles by the combination of amine and ammonium. *Chem. Commun.,* **2014**, 50, 2315-2317. (f) Zhang, L.; Ping Lu, P. and Wang, Y. Copper-mediated cyanation of indoles and electron-rich arenes using DMF as a single surrogate. *Org. Biomol. Chem*., **2015**,*13*, 8322-8329. (g) Zheng, K.; Liu, B.; Chen, S. and Chen,

F. Copper-catalyzed cyanation of aryl iodide with the combined cyanide source of urea and DMSO. *Tetrahedron letters*, **2013**, *54*, 5250-5252. (h) Cristau, H-J.; Ouali, A.; Spindler, J-F.; and Taillefer, M. Mild and Efficient Copper-Catalyzed Cyanation of Aryl Iodides and Bromides. *Chem. A Eur. J.* **2005**, *11*, 2483-2492. (i) Saikia, R.; Park, K.; Masuda, H.; Itoh, M.; Yamada, T.; Sajiki, H.; Mahanta, S.; Thakur, A. and Bora, U. Revisiting the synthesis of aryl nitriles: a pivotal role of CAN. *Org. Biomol. Chem.*, **2021**, *19*, 1344-1351. (j) Kim, J.; Kim, H. and Chang, S. Copper-Mediated Selective Cyanation of Indoles and 2-Phenylpyridines with Ammonium Iodide and DMF. *Org. Lett.* **2012**, *14*, 3924–3927. (k) Kim, J.; Choi, J.; Shin, K. and Chang, S. Copper-Mediated Sequential Cyanation of Aryl C–B and Arene C–H Bonds Using Ammonium Iodide and DMF. *J. Am. Chem. Soc.* **2012**, *134*, 2528–2531.

(14) Wang, C.; Geng, X.; Zhao, P.; Zhou, Y.; Wu, Y-D and Wu, A-X. Employing Thiocyanate Salts as a Nitrogen Source via CN Bond Cleavage: Divergent Synthesis of α-Ketoamides and 2-Acyloxazoles. *Org. Chem. Front.,* **2019**, *6*, 2534-2538.

(15) Zhang, G-Y.; Yu, J-T.; Hu, M-L. and Cheng, J. Palladium-Catalyzed Cyanation of Aryl Halides with CuSCN. *J. Org. Chem*. **2013**, *78*, 2710–2714.

(16) Wagner, A and Ofial, A. R. Potassium Thiocyanate as Source of Cyanide for the Oxidative α-Cyanation of Tertiary Amines. *J. Org. Chem*. **2015**, *80*, 2848–2854.

(17) Huang, Y.; Yu, Y.; Zhu, Z.; Zhu, C.; Cen, J.; Li, X.; Wu, W. and Jiang, H. Copper-Catalyzed Cyanation of N-Tosylhydrazones with Thiocyanate Salt as the "CN" Source. *J. Org. Chem*. **2017**, *82*, 7621–7627.

(18) Guo, W.; Tan, W.; Zhao, M.; Zheng, L.; Tao, K.; Chen, D. and Fan, X. Direct Photocatalytic S–H Bond Cyanation with Green "CN" Source. *J. Org. Chem*. **2018**, *83*, 6580–6588.

(19) (a) Khade, V. V.; Thube, A, S.; Dharpure, P. D. Direct Synthesis of 1,3-dithiolanes from Terminal Alkynes via Visible Light Photoredox Catalysis. *Org. Biomol. Chem.*, **2022**, *20*, 1315–1319. (b) Dharpure, P. D.; Bhowmic, A.; Warghude, P. K.; Bhat, R. G. *Tetrahedron Lett*. **2020**, *61*, 151407-151415. (c) Dharpure, P.; Behera, M.; Thube, A. and Bhat, R. G. Base Dependent 1,3-dithioacetals Rearrangement over Sulfoxidation under Visible-Light Photocatalysis to Access Disulfide-Linked-Dithioesters. **2021**, DOI:10.26434/chemrxiv-2021-x9kht.

(20) CCDC 2175599 (compound **2p**) contain the supplementary crystallographic data. These data can be obtained free of charge by The Cambridge Crystallographic Data Centre.

(21) Guo, J.-T.; Yang, D.-C.; Guan, Z.; He, Y.-H. Chlorophyll-Catalyzed Visible-Light-Mediated Synthesis of Tetrahydroquinolines from *N,N*-Dimethylanilines and Maleimides. *J. Org. Chem.* **2017**, *82*, 1888-1894.

(22) Pelaez, M.; Falaras, P.; Likodimos, V.; O'shea, K.; De la Cruz, A.; Dunlop, P. S. M.; Byrne, J. A.; Dionysiou, D. D. Use of Selected Scavengers for the Determination of NF-TiO2 Reactive Oxygen Species During the Degradation of Microcystin LR under Visible Light Irradiatio. *J. Mol. Catal. A Chem.* **2016**, *15*, 183-189.

(23) (a)Dietrich, A.; Buschmann, V.; Müller, C.; Sauer, M. Fluorescence resonance energy transfer (FRET) and competing processes in donor–acceptor substituted DNA strands: a comparative study of ensemble and single-molecule data. *Rev. Mol. Biotechno.* **2002**, *82*, 211-231. (b) Sören Doose, S.; Neuweiler, H.; Sauer, M. Fluorescence Quenching by Photoinduced Electron Transfer: A Reporter for Conformational Dynamics of Macromolecules. *ChemPhysChem*. **2009**, *10*, 1389-1398.

(24) Mitra, S.; Ghosh, M.; Mishra, S. and Hajra, A. Metal-Free Thiocyanation of Imidazoheterocycles through Visible Light Photoredox Catalysis. *J. Org. Chem*. **2015**, *80*, 8275–8281.

(25) Shaterian, H. R.; Azizi, K.; Fahimi, N. Silica-supported phosphorus pentoxide: a reusable catalyst for S,S-acetalization of carbonyl groups under ambient conditions. *J. Sulfur Chem*. **2011**, *32*, 85-91.