Organic & Biomolecular Chemistry

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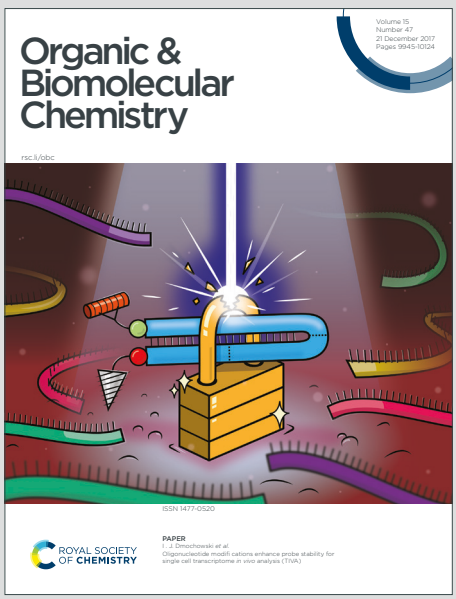

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DOI: 10.1039/D0OB00998A

ARTICLE

[5+1] Annulation strategy for the synthesis of multifunctional biaryls and *p*-teraryls from 1,6-Michael acceptor ketene dithioacetals

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

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A new type of ketene dithioacetal, 2-(3,3-bis-methylsulfanyl-1-arylallylidene)malononitriles containing 1,4 and 1,6-Michael acceptor was synthesized to study their reactivity for the synthesis of new molecular entity. We are reporting [5+1] annulation strategy for the construction of multifunctional biaryls and *p*-teraryls by selection of suitable nucleophile source. The reaction of *p*-nitrotoluene with 2-(3,3-bis-methylsulfanyl-1-aryl-allylidene)-malononitriles under basic conditions provides *p*-teraryls in good yields, while use of nitroethane as nucleophile source provides functionalized biaryls through cyclization followed by denitration. The reaction requires mild condition and exhibit good functional group tolerance.

Introduction

Ketene dithioacetals are important precursor in organic synthesis and broadly used as multifaceted synthone[1] for assembly of large class of carbocyclic and heterocyclic compound due to the presence of conjugated double bond, which can react with both nucleophiles and electrophiles.[2] Due to great synthetic potential of ketene dithioacetal, various researchers are involved in the exploration of their chemistry.[3] They can undergo addition, substitution and elimination reactions simultaneously and therefore used as promising precursor for the synthesis of different class of molecules.[4] Our research group had recently reported the assembly of imidazo[1,2-*a*]pyridines and aroylnaphthalenes moiety from ketene dithioacetals using the 4+2 and 5+1 annulation strategy.[5,6] There are a variety reactions reported from ketene dithioacetal, where reaction starts with 1,4-addition followed by cyclization and aromatization. Earlier our research group explored the synthesis of naphthalenes by [5+1] annulations using ketene dithioacetal of 2–cyanometylbenzonitrile (1,6-Michael acceptor). Therefore, we became interested to synthesized another ketene dithioacetal,[6] which can undergo 1,6-Michael addition and cyclization reaction and 2-(1-aryl-3,3-bis(methylthio)allylidene)malononitriles was design and synthesized.

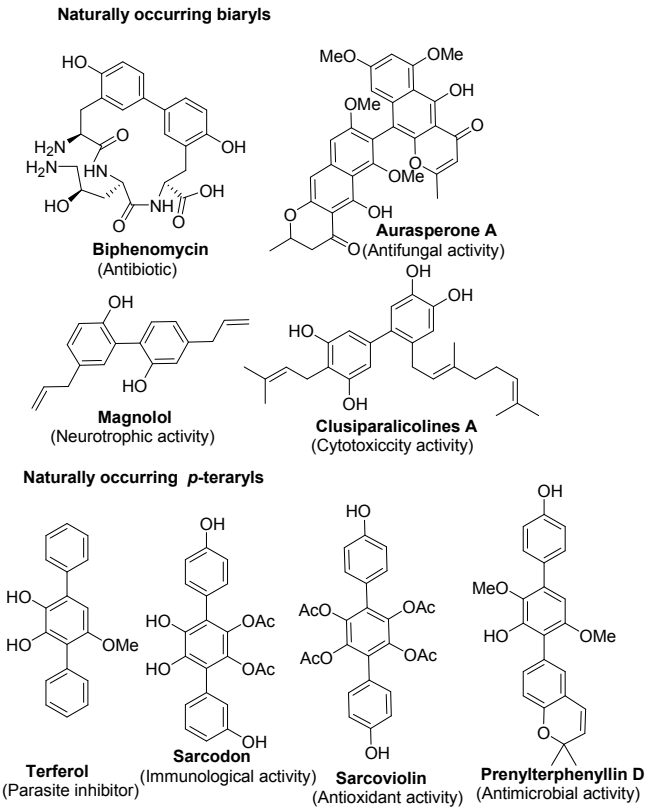

Figure 1. Structure of representative biaryl and *p*-teraryl derived natural compounds

Biaryls and teraryls are valuable structural moieties and various synthetic approaches have been established for their

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Electronic Supplementary Information (ESI) available: [details of any supplementary information available should be included here]. See DOI: 10.1039/x0xx00000x

assembly.[7] They are elite entities and present as substructure in various molecules of medicinal and material importance.[8] Biaryls and *p*-teraryls scaffolds are also present as substructure in various natural products, such as biphenomycin, aurasperone A, clusiparalicolines A, magnolol, terferol, sarcodan, sarcoviolin, prenylterphenyllin D and concrescens A (Figure 1).[9-10] Biaryls are also present as basic skeleton in pharmaceutically active compounds, light-emitting diodes, herbicides; liquid crystal and metal ligand.[11] Besides *p*-teraryl based compounds are reported for the industrial application as conducting polymers, liquid crystals, cation sensors, and dyes.[12]

Suitably aminated teraryls are also useful for the synthesis of biologically and pharmaceutically important compound like carbazoles, estrogen receptors, anti-HIV agent siamenol and antihyperglycemic agents.[13]

In general, synthesis of biaryls and teraryls are carried out by various transition metal catalyzed aryl-aryl bond formation reactions.[14] Another approach is assembly of benzene ring by cycloaddition reactions using aryl containing open chain precursors.[15] Various benzannulation strategies was developed for the construction of polyfunctionalized benzenes such as [3+2+1] Dötz reaction of Fisher carbene complexes, Danheiser alkyne-cyclobutenone [4+2] cyclization, [4+2] cycloaddition of metal cyclopentadiene and alkynes, transition-metal catalyzed [2+2+2] and [4+2] cycloadditions, [4+2] Yamamoto benzannulation of *o*-alkynyl benzaldehyde and alkyne, [3+3] cyclocondensation between biselectrophiles and bisnucleophiles, and 1,6-electrocyclization reaction.[16] However, these approaches suffer with some drawback with respect to environmental concern or atom economy, multi-steps and low yields of products. On the other hand metal-assisted cross-coupling reactions also suffer from the requirements for expensive organometallic reagents/catalysts, harsh reaction conditions and undesired side-products.

Herein, we used new ketene dithioacetal for generation of multifunctional biaryls and *p*-teraryls under mild condition.

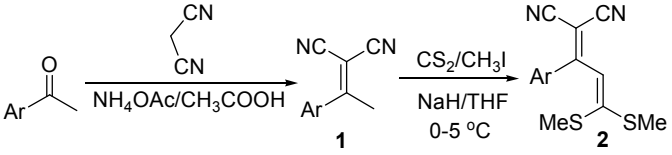
Results and discussion

Preparation of precursor 2-(3,3-bis(methylthio)-1-aryl-allylidene)malononitriles

To start our study, we synthesized the required precursors 2-(3,3-bis(methylthio)-1-aryl-allylidene)malononitriles. The first step was the synthesis of (1-arylethylidene)malononitriles by condensation reaction of aryl methyl ketone and malononitrile in presence of glacial acetic acid and ammonium acetate in toluene under reflux condition.[17] In the second step, 2-(1-arylethylidene)malononitriles was treated with carbon disulphide and methyl iodide under basic conditions to afford the desired precursor (**2**) in 60-98% yield (**Table 1**). Trial of many solvent and base combinations demonstrated that sodium hydride (NaH) in THF at 0-5 °C act as best combination (See ESI, Table 1).

In addition, we also tried to synthesize 1,6 Michael acceptor using dialkyl malonate and methyl/ethyl cyanoacetate instead of malononitrile but it was difficult to afford and their synthetic protocol are under investigation.

Table 1. Synthesis of various 2-(3,3-bis(methylthio)-1-arylallylidene)malononitriles (2)



Entry	R	Yield of **2** (%)
2a	C_6H_5	96
2b	*p*-$CH_3.C_6H_4$	98
2c	*p*-$NH_2.C_6H_4$	96
2d	*p*-OMe.C_6H_4	98
2e	3,4-$(OCH_3)_2.C_6H_3$	94
2f	*o*-$OCH_3.C_6H_4$	83
2g	*p*-$F.C_6H_4$	92
2h	*p*-$Cl.C_6H_4$	91
2i	2,4-$Cl_2.C_6H_3$	78
2j	*o*-$Cl.C_6H_4$	85
2k	*p*-$Br.C_6H_4$	92
2l	*m*-$Br.C_6H_4$	90
2m	2-Furyl	70
2n	2-Thienyl	74
2o	1-Naphthyl	90
2p	2-Naphthyl	94
2q	*p*- $C_6H_5.C_6H_4$	92
2r	Cyclopropyl	60

For the synthesis of **2**; All reactions were performed by stirring **1** (10 mmol), CS_2 (11 mmol), CH_3I (22 mmol) and NaH (20 mmol) in THF (50.0 mL) at 0-5°C for 5 hours and yields are reported only for the second step of the reaction.

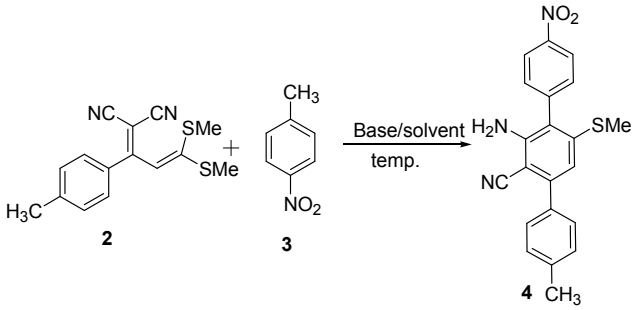
Synthesis of various multifunctional biaryls and p-teraryls

Once, we had precursors in our hand, reaction condition was optimized for the synthesis of *p*-teraryls. To optimize the reaction condition, 2-(3,3-bismethylsulfanyl-1-*p*-tolyl-allylidene)-malononitrile (**2b**) and 4-nitrotoluene were chosen as model substrates. We started the study using Et_3N, NaOH and KOH as a base in DMF at room temperature and both the starting materials were left unreacted (Table 2, entries 1-3). The use of KOH in DMF at 60 °C provides the desired *p*-teraryl in 65% yield (Table 2, entry 4), while increasing the temperature to 90 °C drop the yield to 50% (Table 2, entry 5). We further screened KOH in DMSO at room temperature and no product was obtained (Table 2, entry 6), while at 60 °C, the desired product was isolated in 45% yield (Table 2, entry 7). Then, we used NaH in DMSO and DMF at 60 °C and the product was obtained in 29 and 33% yield respectively (Table 3.1, entries 8 and 9). The use of Cs_2CO_3 and $NaNH_2$ in DMF at 60 °C provides no product and the starting materials were left unreacted (Table 2, entries 10 and 11). Furthermore, conducting the reaction using KOH in non-polar solvent such as dioxane, toluene and THF under reflux condition provided no product and the starting material (**2**) underwent hydrolysis (Table 2, entries 12-14). The optimization shows that, KOH in DMF at 60 °C is the best reaction conditions for the synthesis of multi-functionalized *p*-teraryls. With

DOI: 10.1039/D0OB00998A

optimal conditions in hand, the generality of the protocol was tested by using various functionalized ketene dithioacetals and commercially available 1-methyl-4-nitrobenzene, 2-bromo-1-methyl-4-nitrobenzene and 2-chloro-1-methyl-4-nitrobenzene (**Table 3**). It was found that, the reaction provides multi-functionalized *p*-teraryls in moderate yields in all cases, however a relatively lower yield was observed when 2-substituted-1-methyl-4-nitrobenzene (**4k, 4l and 4m**) and functionalized ketene dithioacetals bearing 2-substituted phenyl group (**4e**) was used probably due to steric hindrance effect. On the other hand, the reaction of 2-(1-furan/thiophen-2-yl)-3,3-bis(methylthio)allylidene)malononitriles with 1-methyl-4-nitrobenzene under same reaction conditions provides no product.

Table 2. Optimization of the reaction conditions 4[a]

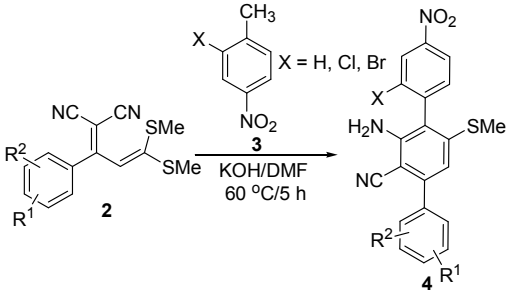


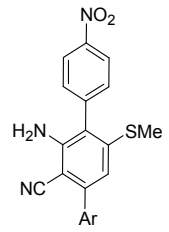
Entry	Base	Solvent	Temp.(°C)	Time (h)	Yield (%)[b]
1	Et_3N	DMF	r.t	24	-[c]
2	NaOH	DMF	r.t	24	-[c]
3	KOH	DMF	r.t	24	-[c]
4	KOH	DMF	60	5	65
5	KOH	DMF	90	7	50
6	KOH	DMSO	r.t	24	-[c]
7	KOH	DMSO	60	9	45
8	NaH	DMSO	60	18	29
9	NaH	DMF	60	18	33
10	Cs_2CO_3	DMF	60	24	-[c]
11	$NaNH_2$	DMF	60	24	-[c]
12	KOH	Dioxane	Reflux	12	-[d]
13	KOH	Toluene	Reflux	12	-[d]
14	KOH	THF	Reflux	12	-[d]

[a]All reaction were performed by stirring 2-(3,3-bis(methylthio)-1-arylallylidene)malononitrile (**2**) (0.5 mmol), 1-methyl-4-nitrobenzene (**3**) (0.5 mmol) and base (1 mmol) in solvent (4 mL) at room temperature and high temperature. (b) Room temperature was ranging between 40-45 °C and high temperature 60-90 °C; (c) Both the starting materials were left in the reaction mixture; (d) Compound **(2)** underwent hydrolysis.

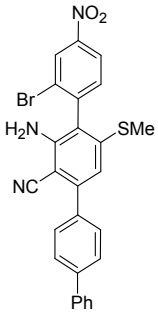
In addition, we tried the reaction of 2-(1-([1,1'-biphenyl]-4-yl)-3,3-bis(methylthio)allylidene)malononitrile (**2q**) with 1-methyl-4-nitrobenzene under optimized reaction condition and afforded linear quateraryl (**4k**) in 47% yield. The structure of 3'-amino-4-bromo-5'-(methylthio)-4''-nitro-[1,1':4',1''-terphenyl]-2'-carbonitrile (**4h)** was confirmed by single-crystal X-ray analysis.

Table 3. Synthesis of various multifunctional *p*-teraryls (**4**)[a]

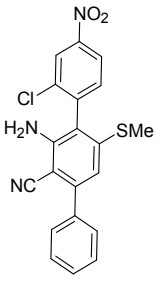




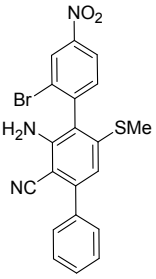
4a. Ar = C_6H_5; 60%
4b. Ar = 4-$CH_3C_6H_4$; 65%
4c. Ar = 4-$OCH_3C_6H_4$; 55%
4d. Ar = 3,4-$(OCH_3)_2C_6H_3$; 53%
4e. Ar = 2-$OCH_3C_6H_4$; 42%
4f. Ar = 4-FC_6H_4; 50%
4g. Ar = 4-ClC_6H_4; 50%
4h. Ar = 4-BrC_6H_4; 52%
4i. Ar = 3-BrC_6H_4; 48%
4j. Ar = 2-Naphthyl; 45%



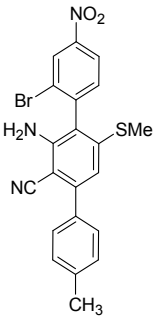
4k, 47%



4l, 41%



4m 40%



4n, 42%

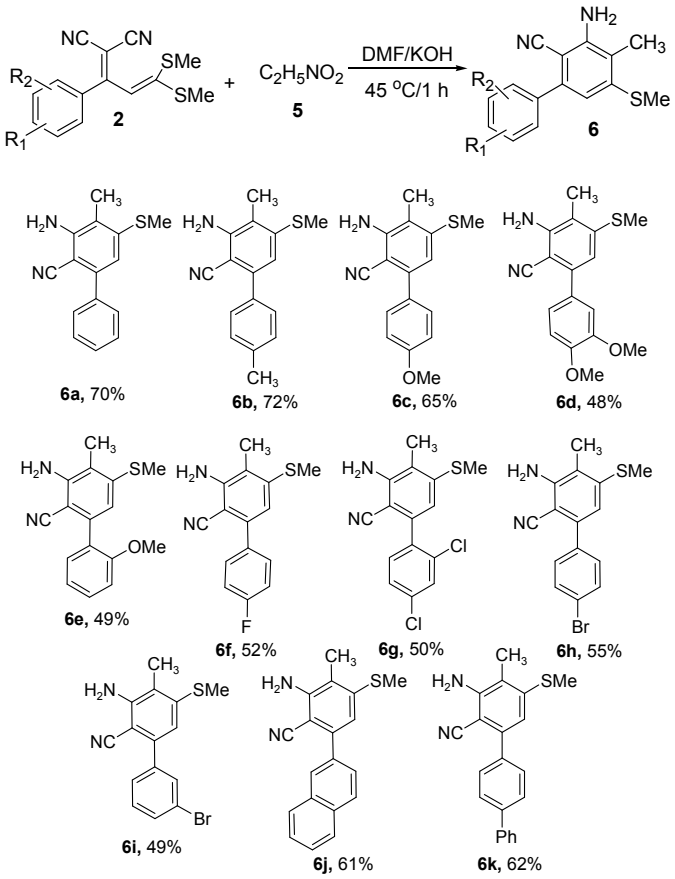
Reaction conditions:All reaction were carried out by stirring **2** (0.5 mmol), (0.5 mmol), KOH (1 mmol) in DMF (4.0 mL) at 60 °C

To further expand the scope of this methodology, we have employed nitroethane as nucleophile source. He reaction condition was optimized by using different base and solvent combinations (see ESI, Table 2). It was observed that use of potassium hydroxide in DMF at 45 °C act as best reaction condition. The generality of protocol was tested by using diferent 2-(3,3-bis(methylthio)-1-arylallylidene)malononitriles **(2)** to afford 3-amino-4-methyl-5-(methylthio)-[1,1'-biphenyl]-2-carbonitriles **(6)** in moderate to

good yields (**Table 4**). It was observed that, substituents such as Me, OMe, F, Cl and Br on the phenyl ring of the ketene dithioacetals are well tolerated during the reaction.

2-Naphthyl and biphenyl containing ketene dithioacetals were also examined and the desired products obtained in 61% and 62% yields respectively. Interestingly, when nitromethane was used as a nucleophile source in lieu of nitroethane, a complex mixture was obtained. Nitromethane might be involved in other side reactions (interact at other double bond) probably due to its small size and higher reactively as compared to nitroethane.

Table 4. Synthesis of multifunctional biaryls[a]

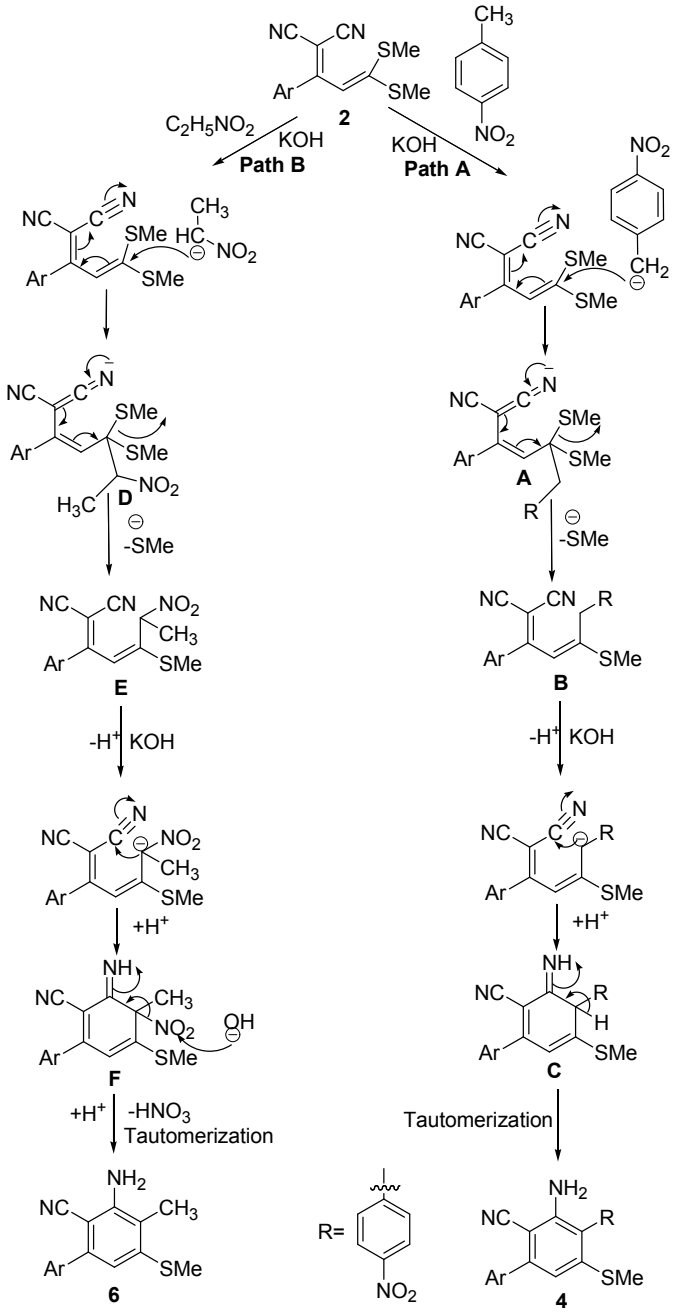


[Reaction conditions: All reaction was carried out by stirring **2** (0.5 mmol), **5** (0.5 mmol) and KOH (1 mmol) in DMF (4.0 mL) at 45°C].

Mechanistic Investigation

On the basis of the product formed, we proposed that the formation of both biaryl and teraryl by the reaction of nitroethane and *p*-nitrotoluene follows two different pathways (**Scheme 1**). The precursor 2-(3,3-bis(methylthio)-1-arylallylidene)malononitriles has two electrophilic centers at the C-1 and C-3 position. Among them C-3 is highly vulnerable in case of using large nucleophiles. For the synthesis of teraryls, reaction starts with generation of carbanion from *p*-nitrotoluene under basic conditions. Mechanistically, reaction is possibly initiated through attack of nucleophile at the C-3 position of 2-(3,3-bis(methylthio)-1-arylallylidene)malononitriles (**2**) to form intermediate **A**, which was converted to intermediate **B** by reversal of the charge and elimination of SMe group. In presence of excess of base, intermediate **B** generates the carbanion which intramolecularly attacks at one of the nitrile group with the formation of imine **C**. Intermediate **C** undergoes tautomerization to afford the desired teraryl **4**.

Scheme 1. Plausible mechanism for the synthesis of multifunctional *p*-teraryls and biaryls



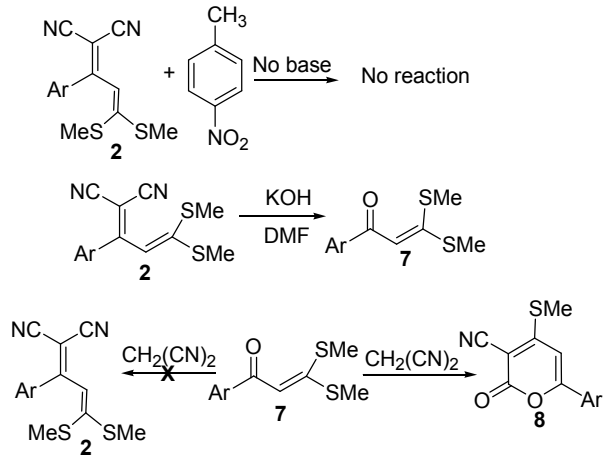
If nitroethane is used as nucleophile source, reaction follows path B. Under basic condition carbanion generated from nitroethane undergoes 1,6-addition reaction to form intermediate **D**, which was converted to intermediate **E** by loss of methanthiol group. In presence of excess of base carbanion generated at carbon adjacent to nitro group, which cyclize intramolecularly using nitrile group to afford imine **F**. At last, excess of hydroxide ion attacks at nitrogen of

nitro group of intermediate **F** to afford aromatization by loss of nitric acid.

To understand the role of base, we perform the control reaction between 2-(3,3-bis(methylthio)-1-phenyl-allylidene)malononitrile and *p*-nitrotoluene without base and no product was observed and starting material was left unconsumed (**Scheme 5**). This suggests that base is required for the reaction. In another reaction, 2-(3,3-bis(methylthio)-1-phenyl-allylidene)malononitrile was treated with KOH in DMF and afforded 3,3-bis-methylsulfanyl-1-phenyl-propenone in good yield. This suggests that C-1 position is also reactive and interact with nucleophile depending on their nature. In another trial 3,3-bis-methylsulfanyl-1-phenyl-propenone was treated with malononitrile under basic condition provides 1,6-Michael acceptor 2*H*-pyran-2-ones instead of compound **2**. This reaction suggests that compound **2** can be exclusively synthesized from 2-(1-phenyl-ethylidene)-malononitrile obtained by reaction of acetophenone with malononitrile, which on treatment with carbon disulfide and methyl iodide provides compound **2**.

Further reaction of this compound is under investigation with various other nucleophiles.

Scheme 5. Control reaction for the reactivity of compound **2**



Conclusions

In summary, we used 1,6-Michael acceptor ketene dithioacetals for developing a new methodology to synthesize highly substituted biaryls and *p*-teraryls. The reaction of *p*-nitrotoluene and nitroethane with 2-(3,3-bis-methylsulfanyl-1-aryl-allylidene)-malononitriles under basic conditions provides *p*-teraryls and biaryls respectively in good yields. This reaction requires mild condition and shows good functional group tolerance. We also tried to explained the mechanism. We have exclusively perform 1,6-addition over 1,4-Michael addition. In addition we also demonstrated that hydroxide ion act as nucleophile in absence of proton source ad provides 1,4-Michael addition to afford loss of malononitrile. Further chemistry of the ketene dithioacetals are under investigation.

Experimental

General: Commercially available reagents from Sigma Aldrich, Alfa Aesar and Spectrochem were used directly. ^{1}H and ^{13}C NMR spectra were recorded using 400 MHz NMR and 100 MHz NMR spectrometer and $CDCl_3$ was used as solvent. Chemical shifts for all the compounds are reported in parts per million shifts (δ-value) from $CDCl_3$ (δ 7.26 ppm for ^{1}H and 77.00 ppm for ^{13}C NMR) as an internal standard. In ^{1}H NMR signal patterns are reported as s, singlet; d, doublet; dd, double doublet; t, triplet and m, multiplet. Coupling constant (J) for protons are reported in hertz (Hz). Infrared (IR) spectra of all the compounds was recorded on a Perkine Elmer AX-1 spectrophotometer and reported in wave number (cm^{-1}). HRMS reported are showing the peak for MH^+.

General procedure for the synthesis of 2-(3,3-bis(methylthio)-1-arylallylidene)malononitriles 2a-r: To a vacuum dried RB flask sodium hydride (20.0 mmol) was taken in dry THF (50.0 mL) and cooled to 0-5 °C over an ice bath. Then 2-(1-arylethylidene)malononitriles (10.0 mmol) was added slowly within 45 minutes with constant stirring at 0-5 °C and the reaction mixture was further stirred for 25-30 minutes. To this solution carbon disulfide (11 mmol) was added drop-wise within 25-30 minutes and the mixture was again stirred for 25-30 minutes. Further, methyl iodide (22 mmol) was added drop-wise at 0-5 °C and continued the stirring for another 30 minutes. Then, the reaction mixture was warmed slowly to room temperature and stirred for 3 hours. After completion of the reaction (determined by TLC), excess of THF was removed under reduced pressure and crushed ice was added to the reaction mixture. The obtained precipitate was filtered, dried and recrystallized with cold ethanol.

2-(3,3-Bis(methylthio)-1-phenylallylidene)malononitrile (2a)
Brown solid; yield: 2.62 g, (96%); **mp =** 180–182 °C; **IR** (KBr): 2921, 2215, 1429-1607 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.32 (s,3H, -SMe), 2.60 (s, 3H, -SMe), 6.48 (s, 1H, ArH), 7.27-7.30 (m, 2H, ArH), 7.43-7.46 (m, 3H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 16.4, 17.7, 77.7, 113.1, 113.8, 114.2, 129.5, 130.0, 132.7, 137.5, 165.8, 166.4; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{13}N_2S_2$: 273.0515; found: 273.0519.

2-(3,3-Bis(methylthio)-1-(*p*-tolyl)allylidene)malononitrile (2b)
Yellow solid; yield: 2.80 g (98%); **mp =** 92–95 °C; **IR** (KBr): 2921, 2215, 1429-1607 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.30 (s,3H, -CH_3), 2.41 (s, 3H, -SMe), 2.59 (s, 3H, -SMe), 6.49 (s, 1H, ArH), 7.22-7.30 (m, 4H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 16.5, 17.6, 21.6, 77.4, 114.0, 114.2, 114.5, 128.6, 129.8, 131.5, 142.0, 164.4, 168.1; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd for $C_{15}H_{15}N_2S_2$: 287.0671; found: 287.0666.

2-(1-(4-Aminophenyl)-3,3-bis(methylthio)allylidene)-malononitrile (2c)
Yellow solid; yield: 2.77 g (96%); **mp** = 100–105 °C; **IR** (KBr): 2925, 2215, 1435-1568 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.28 (s, 3H, -SMe), 2.54 (s, 3H, -SMe), 4.13 (s, 2H, -NH_2), 6.39 (s, 1H, ArH), 6.66 (d, *J* = 8 Hz, 2H, ArH), 7.24 (s, 2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 16.8, 17.7, 75.1, 114.7, 115.0, 115.5, 123.7, 130.5, 131.4, 150.6, 161.8, 168.3; **HRMS** (ESI): *m/z* $[M + H]^+$ calcd for $C_{14}H_{14}N_3S_2$: 288.0624; found: 288.0629.

DOI: 10.1039/D0OB00938A

2-(1-(4-Methoxyphenyl)-3,3-bis(methylthio)allylidene)-malononitrile (2d)

Brown solid; yield: 2.98 g (98%); **mp** = 105–107 °C; **IR** (KBr): 2925, 2215, 1435-1568 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.31 (s,3H, -SMe), 2.59 (s, 3H, -SMe), 3.87 (s, 3H, -OMe), 6.46 (s, 1H, ArH), 6.97 (d, J = 8 Hz, 2H ArH), 7.34 (d, J = 8 Hz, 2H ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 16.6, 17.6, 55.3, 72.7, 114.3, 114.4, 114.5, 114.8, 126.4, 130.7, 162.4, 163.8, 167.8; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{15}H_{15}N_2OS_2$: 303.0620; found: 303.0626.

2-(1-(3,4-Dimethoxyphenyl)-3,3-bis(methylthio)allylidene)-malononitrile (2e)

Brown solid; yield: 3.14 g (94%); **mp** = 120–122 °C; **IR** (KBr): 3002, 2959, 2213, 1423-1596 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.32 (s,3H, -SMe), 2.60 (s, 3H,- SMe), 391 (s, 3H, -OMe), 3.95 (s, 3H, -OMe), 6.47 (s, 1H, ArH), 6.88-7.01 (m, 3H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 16.6, 17.6, 55.9, 56.1, 79.4, 111.2, 111.7, 114.0, 114.4, 115.0, 122.5, 126.5, 149.3, 152.0, 164.0, 167.6; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{16}H_{17}N_2O_2S_2$: 333.0726; found: 333.0726.

2-(1-(2-Methoxyphenyl)-3,3-bis(methylthio)allylidene)-malononitrile (2f)

Brown solid; yield: 2.51 g (83%); **mp** = 115–117 °C; **IR** (KBr): 3002, 2925, 2214, 1429-1599 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.31 (s,3H, -SMe), 2.60 (s, 3H, -SMe), 3.86 (s, 3H, -OMe), 6.55 (s, 1H, ArH), 6.97 (d, J = 8 Hz, 1H, ArH), 7.01-7.08 (m, 2H, ArH), 7.45 (t, J = 8 Hz, 1H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 16.3, 17.6, 55.8, 78.1, 111.7, 113.5, 114.1, 114.4, 121.2, 123.6, 129.3, 132.3, 156.4, 164.1, 164.6; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{15}H_{15}N_2OS_2$: 303.0620; found: 303.0624.

2-(1-(4-Fluorophenyl)-3,3-bis(methylthio)allylidene)-malononitrile (2g)

Brown solid; yield: 2.67 g (92%); **mp =** 95–97 °C; **IR** (KBr): 2923, 2216, 1435-1568 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.42 (s,3H, -SMe), 2.54 (s, 3H, -SMe), 6.27 (s, 1H, ArH), 6.64 (dd, J = 1.2 Hz, J = 3.6 Hz, 2H,ArH), 7.21 (d, J = 4 Hz, 1H,ArH), 7.71 (d, J = 1.6 Hz, 1H,ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 16.4, 17.7, 77.7, 113.4, 114.0, 114.2, 116.5 (d, $J_{C\text{-}F}$ = 20 Hz), 130.3, 130.8 (d, $J_{C\text{-}F}$ = 20 Hz), 163.2, 165.6 (d, $J_{C\text{-}F}$ = 20 Hz), 166.6; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{14}H_{12}FN_2S_2$: 291.0420; found: 291.0422.

2-(1-(4-Chlorophenyl)-3,3-bis(methylthio)allylidene)-malononitrile (2h)

Brown solid; yield: 2.80 g (91%); **mp** = 100–102 °C; **IR** (KBr): 2922, 2215, 1428-1588 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.33 (s,3H, -SMe), 2.60 (s, 3H, -SMe), 6.48 (s, 1H, ArH), 7.22 (d, J = 8.8 Hz, 1H,ArH), 7.29 (d, J = 8.8 Hz, 1H,ArH), 7.45 (d, J = 8.8 Hz, 1H, ArH), 7.61 (d, J = 8.8 Hz, 1H,ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 16.5, 17.7, 77.7, 113.1, 113.8, 114.1, 129.5, 130.0, 130.1, 132.5, 165.8, 166.4; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{14}H_{12}ClN_2S_2$: 307.0125; found: 307.0135.

2-(1-(2,4-Dichlorophenyl)-3,3-bis(methylthio)allylidene)-malononitrile (2i)

Brown solid; yield: 2.65 g (78%); **mp** = 93–95 °C; **IR** (KBr): 3083, 2922, 2215, 1427-1586 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.39 (s,3H, -SMe), 2.62 (s, 3H, -SMe), 6.54 (s, 1H, ArH), 7.15 (d, J = 8.4 Hz, 1H,ArH), 7.37 (d, J = 8.0 Hz, 1H,ArH), 7.50 (s, 1H,ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 16.5, 17.8, 78.3, 112.3, 113.5, 113.7, 128.3, 130.5, 130.5, 132.4, 133.6, 137.5, 162.7, 166.6; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{14}H_{11}Cl_2N_2S_2$: 340.9735; found: 340.9733.

2-(1-(2-Chlorophenyl)-3,3-bis(methylthio)allylidene)-malononitrile (2j)

Brown solid; yield: 2.62 g (85%); **mp** = 93–95 °C; **IR** (KBr): 3088, 2925, 2207, 1427-1585 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.33 (s,3H, -SMe), 2.60 (s, 3H, -SMe), 6.55 (s, 1H, ArH), 7.19 (dd, J = 1.2 Hz, J = 7.2 Hz, 1H, ArH), 7.36 (td,J = 2.0 Hz, J = 7.6 Hz, 1H,ArH), 7.41 (dd, J = 1.6 Hz, J = 8.0 Hz, 1H,ArH), 7.43-7.47 (m, 1H,ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 16.5, 17.8, 78.1, 112.5, 113.7, 114.0, 127.8, 129.7, 130.4, 132.0, 132.6, 134.0, 164.0, 166.0; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{14}H_{12}ClN_2S_2$: 307.0125; found: 307.0129.

2-(1-(4-Bromophenyl)-3,3-bis(methylthio)allylidene)-malononitrile (2k)

Brown solid; yield: 3.22 g (92%); **mp** = 98–100 °C; **IR** (KBr): 3054, 2923, 2215, 1427-1587 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.33 (s,3H, -SMe), 2.61 (s, 3H, -SMe), 6.48 (s, 1H, ArH), 7.22 (d, J = 8.4 Hz, 2H, ArH), 7.61 (d, J = 8.4 Hz, 2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 16.0, 16.5, 77.7, 113.1, 113.8, 114.1, 126.0, 130.1, 132.5, 133.3, 165.8, 166.4; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{14}H_{12}BrN_2S_2$: 350.9620; found: 350.09607.

2-(1-(3-Bromophenyl)-3,3-bis(methylthio)allylidene)-malononitrile (2l)

Brown solid; yield: 3.15 g (90%); **mp** = 120–122 °C; **IR** (KBr): 2958, 2854, 2214, 1425-1557 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.34 (s,3H, -SMe), 2.61 (s, 3H, -SMe), 6.48 (s, 1H, ArH), 7.29 (d, J = 8.4 Hz, 1H, ArH), 7.36 (t, J = 7.6 Hz, 1H,ArH), 7.46 (s, 1H, ArH), 7.64 (d, J = 7.6 Hz, 1H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 16.6, 17.7, 78.0, 113.0, 113.7, 114.0, 123.0, 127.1, 130.7, 131.2, 134.0, 136.3, 165.6, 166.3; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{14}H_{12}BrN_2S_2$: 350.9620; found: 350.9628.

2-(1-(Furan-2-yl)-3,3-bis(methylthio)allylidene)malononitrile (2m)

Brown solid; yield: 1.52 g (70%); **mp =** 45–47 °C; **IR** (KBr): 3054, 2213, 1427-1650 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.42 (s,3H, -SMe), 2.54 (s, 3H, -SMe), 6.27 (s, 1H, ArH), 6.57 (dd, J = 2 Hz, J = 3.6 Hz, 1H, ArH), 7.22 (d, J = 3.6 Hz, 1H,ArH), 7.71-7.71 (m, 1H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 17.1, 17.6, 75.2, 113.6, 114.1, 114.3, 114.7, 120.3, 147.5, 148.0, 153.3, 158.5; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{12}H_{11}N_2OS_2$: 263.0307; found: 263.0314.

2-(3,3-Bis(methylthio)-1-(thiophen-2-yl)allylidene)malono-nitrile (2n)

Brown viscous; yield: 1.72 g (74%); **mp** = 53–55 °C; **IR** (KBr): 2923, 2213, 1410-1596 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.39 (s,3H, -SMe), 2.55 (s, 3H, -SMe), 6.39 (s, 1H, ArH), 7.18-7.20 (m, 1H, ArH), 7.69 (dd, J = 5.6 Hz, J = 13.2 Hz, 2H ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 17.0, 17.5, 76.2, 114.0, 114.4, 116.5, 128.7, 133.0, 133.4, 136.6, 159.8, 160.3; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{12}H_{11}N_2S_3$: 279.0079; found: 279.0083.

2-(3,3-Bis(methylthio)-1-(naphthalen-1-yl)allylidene)malono-nitrile (2o)

Brown solid; yield: 2.90 g (90%); **mp =** 103–105 °C; **IR** (KBr): 3054, 2924, 2213, 1427-1650 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.22 (s,3H, -SMe), 2.63 (s, 3H, -SMe), 6.59 (s, 1H, ArH), 7.40

DOI: 10.1039/D0OB00998A

(d, *J* = 8 Hz, 1H, ArH), 7.55-7.61 (m, 2H, ArH), 7.88-7.94 (m, 4H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 17.0, 17.8, 78.1, 113.3, 114.2, 114.3, 123.8, 125.7, 126.6, 126.8, 127.5, 128.7, 130.6, 131.1, 132.4, 133.7, 166.2, 166.4; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{18}H_{15}N_2S_2$: 323.0671; found: 323.0677.

2-(3,3-Bis(methylthio)-1-(naphthalen-2-yl)allylidene)malononitrile (2p)

Brown solid; yield: 3.05 g (94%); **mp** = 110–112 °C; **IR** (KBr): 3054, 2924, 2213, 1427-1650 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.21 (s,3H, -SMe), 2.63 (s, 3H, -SMe), 6.59 (s, 1H, ArH), 7.40 (d, *J* = 12 Hz, 1H,ArH), 7.35-7.60 (m, 2H, ArH), 7.88-7.94 (m, 4H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 16.5, 17.7, 77.8, 113.8, 114.2, 114.5, 124.1, 125.1, 126.8, 127.8, 128.8, 129.0, 129.1, 131.8, 133.0, 134.3, 165.2, 166.7; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{18}H_{15}N_2S_2$: 323.0671; found: 323.0675.

2-(1-([1,1'-Biphenyl]-4-yl)-3,3-bis(methylthio)allylidene)-malononitrile (2q)

Brown solid; yield: 3.20 g (92%); **mp** = 125–127 °C; **IR** (KBr): 2923, 2214, 1428-1603cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.30 (s,3H, -SMe), 2.60 (s, 3H, -SMe), 6.51 (s, 1H, ArH), 7.38 (t, *J* = 7.2 Hz, 1H,ArH), 7.42-7.47 (m, 4H, ArH), 7.64 (d, *J* = 8.8 Hz, 2H, ArH), 7.69 (d, *J* = 8.4 Hz, 2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 16.7, 17.8, 77.7, 114.1, 114.2, 114.6, 127.2, 127.7, 128.2, 129.0, 129.3, 133.3, 139.7, 144.2, 165.0, 167.7; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{17}N_2S_2$: 349.0828; found: 349.0820.

2-(1-Cyclopropyl-3,3-bis(methylthio)allylidene)malononitrile (2r)

Brown liquid; yield: 1.42 g (60%); **mp** = 40-42 °C; **IR** (KBr): 2924, 2217, 1426-1512 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 0.93-0.97 (m,2H), 1.23-1.28 (m, 3H), 2.42 (s,3H, -SMe), 2.51 (s, 3H, -SMe), 5.73 (s, 1H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 10.4, 11.2, 16.4, 17.3, 18.5, 82.5, 113.4, 113.5, 114.1, 154.3, 177.0; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{11}H_{13}N_2S_2$: 237.0515; found: 237.0510.

General procedure for the synthesis of 3'-amino-5'-(methylthio)-4''-nitro-[1,1':4',1''-teraryl]-2'-carbonitriles 4a-n: A mixture of 2-(3,3-bis(methylthio)-1-arylallylidene)malono nitriles **2** (0.5 mmol), 2-substituted-1-methyl-4-nitrobenzenes**3** (0.5 mmol) and KOH (1.0 mmol) in DMF (4.0 mL) was stirred at 60 °C for 5 hours. When reaction was completed (monitored by TLC), the crude mixture was poured onto the ice-water with constant stirring. The mixture was then neutralized with 10% HCl. The resulting precipitate was collected by filtration, washed with water and dried. The crude was purified by silica gel column chromatography (hexane/ethylacetate: 85/15) to afford the desired products.

3'-Amino-5'-(methylthio)-4''-nitro-[1,1':4',1''-terphenyl]-2'-carbonitrile (4a)

Brown solid; yield: 110 mg (60%); **mp** = 145–148 °C; **IR** (KBr): 3408, 2925, 2215, 1431-1568 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.39 (s,3H, -SMe), 4.27 (s, 2H, -NH_2), 6.66 (s, 1H, ArH), 7.47-7.55 (m, 5H, ArH), 7.57 (d, *J* = 8 Hz, 2H, ArH), 8.39 (d, *J* = 8.4 Hz, 2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 14.01, 92.1, 114.2, 118.1, 121.7, 124.4, 127.3, 129.3, 131.6, 135.2, 138.7, 141.0, 143.1, 145.1, 147.6, 149.0; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{16}N_3O_2S$: 362.0958; found: 362.0958.

3'-Amino-4-methyl-5'-(methylthio)-4''-nitro-[1,1':4',1''-terphenyl]-2'-carbonitrile (4b)

Brown solid; yield: 123 mg (65%); **mp =** 110–112 °C; **IR** (KBr): 3480, 2925, 2215, 1425-1560 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.39 (s,3H, -CH_3), 2.43 (s, 3H, -SMe), 4.26 (s, 2H, -NH_2), 6.65 (s, 1H, ArH), 7.31 (d, *J* = 12 Hz, 2H, ArH), 7.49 (d, *J* = 8 Hz, 2H, ArH), 7.53 (d, *J* = 12 Hz, 2H, ArH), 8.40 (d, *J* = 8 Hz, 2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 15.2, 21.2, 114.1, 117.5, 120.2, 124.8, 128.3, 129.4, 131.7, 135.6, 139.0, 141.7, 145.1, 145.2, 146.0, 147.0, 148.0; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{18}N_3O_2S$: 376.1114; found: 376.1118.

3'-Amino-4-methoxy-5'-(methylthio)-4''-nitro-[1,1':4',1''-terphenyl]-2'-carbonitrile (4c)

Brown solid; yield: 108 mg (55%); **mp** = 115–118 °C; **IR** (KBr): 3474, 2925, 2205, 1462-1599 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.39 (s,3H, -SMe), 3.87 (s, 3H, -OMe), 4.25 (s, 2H, NH_2), 6.63 (s, 1H, ArH), 7.03 (d, *J* = 12 Hz, 2H, ArH), 7.53 (dd, *J* = 1.2 Hz, *J* = 8.4 Hz, 4H, ArH), 8.40 (d, *J* = 8.8 Hz, 2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 15.2, 55.3, 92.5, 114.0, 114.1, 120.0, 124.2, 124.8, 129.7, 130.6, 130.8, 131.8, 141.8, 145.2, 147.0, 148.0, 160.2; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{18}N_3O_3S$: 392.1063; found: 392.1059.

3'-Amino-3,4-dimethoxy-5'-(methylthio)-4''-nitro-[1,1':4',1''-terphenyl]-2'-carbonitrile (4d)

Brown solid; yield: 117 mg (53%); **mp** = 113–115 °C; **IR** (KBr): 3408, 2925, 2215, 1435-1568 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.40 (s,3H, -SMe), 3.94 (s, 3H, -OMe), 3.96 (s, 3H, -OMe), 4.27 (s, 2H, -NH_2), 6.56 (s, 1H, ArH), 6.99 (d, *J* = 8.4 Hz, 1H, ArH), 7.12-7.16 (m, 2H, ArH), 7.52 (d, *J* = 8.4 Hz, 2H, ArH), 8.39 (d, *J* = 8.0 Hz, 2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 15.3, 56.0, 56.1, 92.7, 111.3, 111.8, 114.1, 117.7, 120.2, 121.1, 125.0, 132.0, 132.0, 142.0, 145.3, 146.0, 147.0, 148.1, 149.0, 149.8; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{22}H_{20}N_3O_4S$: 422.1169; found: 422.1178.

3'-Amino-2-methoxy-5'-(methylthio)-4''-nitro-[1,1':4',1''-terphenyl]-2'-carbonitrile (4e)

Brown solid; yield: 117 mg (42%); **mp** = 113–115 °C; **IR** (KBr): 3408, 2925, 2215, 1435-1568 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.36 (s,3H, -SMe), 3.90 (s, 3H, -OMe), 4.19 (s, 2H, -NH_2), 6.63 (s, 1H, ArH), 7.04-7.09 (m, 2H, ArH), 7.30 (dd, *J* = 1.6 Hz, *J* = 7.2 Hz, 1H, ArH), 7.44 (td, *J* = 2.0 Hz, *J* = 8.4 Hz, 1H, ArH), 7.55 (d, *J* = 11.2 Hz, 2H, ArH), 8.40 (d, *J* = 8.8 Hz, 2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 15.3, 55.7, 94.8, 111.4, 115.2, 117.3, 120.5, 121.0, 125.0, 127.5, 130.5, 130.7, 132.0, 142.0, 143.1, 145.0, 146.3, 148.1, 156.5; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{18}N_3O_3S$: 392.1063; found: 392.1062.

3'-Amino-4-fluoro-5'-(methylthio)-4''-nitro-[1,1':4',1''-terphenyl]-2'-carbonitrile (4f)

Brown solid; yield: 95 mg (50%); **mp** = 230–233 °C; **IR** (KBr): 3460, 2924, 2208, 1429-1597 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.39 (s, 3H, -SMe), 4.27 (s, 2H, -NH_2), 6.61 (s, 1H, ArH), 7.19 (t, *J* = 8.4 Hz,

2H, ArH), 7.52-7.58 (m, 4H, ArH), 8.40 (dd, *J* = 2 Hz, *J* = 6.8 Hz, 2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ*14.3, 92.3, 115.7 (d, $J_{C\text{-}F}$ = 20 Hz), 118.0, 121.2, 124.0, 125.0, 128.6, 129.0 (d, $J_{C\text{-}F}$ = 60 Hz), 132.0, 138.2, 141.0, 145.0, 146.1, 147.0, 163.2 (d, $J_{C\text{-}F}$ = 270 Hz);**HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{15}FN_3O_2S_2$: 380.0864; found: 380.0870.

3'-Amino-4-chloro-5'-(methylthio)-4''-nitro-[1,1':4',1''-terphenyl]-2'-carbonitrile (4g)

Brown solid; yield: 100 mg (50%); **mp =** 110–112 °C; **IR** (KBr): 3480, 2924, 2209, 1426-1521 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.38 (s, 3H, -SMe), 4.27 (s, 2H, -NH_2), 6.60 (s, 1H, ArH), 7.45-7.50 (m, 2H, ArH), 7.50-7.58 (m, 4H, ArH), 8.39 (d, *J* = 8.0 Hz, 2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ*15.3, 92.1, 114.1, 117.2, 120.0, 125.0, 125.6, 128.0, 129.8, 131.8, 135.2, 137.0, 141.6, 144.8, 147.1, 148.2; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{15}ClN_3O_2S$: 396.0568; found: 396.0580.

3'-Amino-4-bromo-5'-(methylthio)-4''-nitro-[1,1':4',1''-terphenyl]-2'-carbonitrile (4h)

Brown solid; yield: 115 mg (52%); **mp =** 101–103 °C; **IR** (KBr): 3479, 2924, 2205, 1424-1571 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.13 (s, 3H, -SMe), 4.04 (s, 2H, -NH_2), 6.35 (s, 1H, ArH), 7.00 (d, *J* = 1.2 Hz, 2H, ArH), 7.19 (d, *J* = 8.4 Hz, 2H, ArH), 7.37 (d, *J* = 14 Hz, 2H, ArH), 8.14 (d, *J* = 8 Hz, 2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 15.2, 92.3, 114.0, 117.2, 120.7, 123.4, 125.0, 130.0, 131.7, 132.0, 137.3, 141.5, 144.7, 145.6, 147.0, 148.1; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{15}BrN_3O_2S_2$: 440.0063; found: 440.0060.

3'-Amino-3-bromo-5'-(methylthio)-4''-nitro-[1,1':4',1''-terphenyl]-2'-carbonitrile (4i)

Brown solid; yield: 107 mg (48%); **mp =** 185–187 °C; **IR** (KBr): 3474, 2925, 2207, 1427-1567 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.40 (s, 3H, -SMe), 4.29 (s, 2H, -NH_2), 6.61 (s, 1H, ArH), 7.38 (t, *J* = 8 Hz, 1H, ArH), 7.53 (d, *J* = 8.4 Hz, 3H, ArH), 7.59-7.61 (m, 1H, ArH), 7.68-7.69 (m, 1H, ArH), 8.41 (d, *J* = 8.0 Hz, 2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 14.0, 92.1, 117.6, 118.1, 120.0, 122.0, 124.4, 127.3, 128.7, 129.3, 131.6, 134.7, 138.7, 141.0, 143.1, 145.1, 147.6, 149.0; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{15}BrN_3O_2S_2$: 440.0063; found: 440.0068.

2-Amino-6-(methylthio)-4-(naphthalen-2-yl)-4'-nitro-[1,1'-biphenyl]-3-carbonitrile (4j)

Brown solid; yield: 98 mg (45%); **mp =** 180–183 °C; **IR** (KBr): 3470, 2925, 2215, 1435-1568 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.32 (s, 3H, -SMe), 4.30 (s, 2H, -NH_2), 6.71 (s, 1H, ArH), 7.49-7.55 (m, 3H, ArH), 7.56-7.62 (m, 3H, ArH), 7.76 (d, *J* = 8 Hz, 1H, ArH), 7.95 (t, *J* = 6.8 Hz, 2H, ArH), 8.42-8.46 (m, 2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 15.1, 95.0, 115.7, 120.6, 125.0, 125.1, 125.3, 126.1, 126.6, 127.1, 128.5, 129.2, 131.3, 131.7, 131.8, 133.6, 136.1, 141.7, 144.8, 145.0, 146.5, 148.1; **HRMS** (ESI): *m/z* [M + NH_4]$^+$ calcd for $C_{24}H_{21}N_4O_2S$: 429.1385; found: 429.1380.

3''-Amino-5''-(methylthio)-4'''-nitro-[1,1':4',1'':4'',1'''-quaterphenyl]-2''-carbonitrile (4k)

Brown solid; yield: 103 mg (47%); **mp** = 80–82 °C; **IR** (KBr): 3478, 2924, 2207, 1435-1569 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 2.41 (s, 3H, -SMe), 4.29 (s, 2H, NH_2), 6.71 (s, 1H, ArH), 7.40 (d, *J* = 8 Hz, 1H, ArH), 7.48 (t, *J* = 8.4 Hz, 2H, ArH), 7.55 (d, *J* = 8 Hz, 2H, ArH), 7.62-7.74 (m, 6H, ArH), 8.41 (d, 2H, ArH); ^{13}C NMR (100 MHz, $CDCl_3$): *δ* 15.2, 92.4, 114.1, 117.4, 120.4, 124.8, 127.1, 127.3, 127.4, 127.5, 127.6, 128.8, 131.7, 137.3, 140.2, 141.7, 141.8, 145.5, 147.0, 148.8; HRMS (ESI): *m/z* [M + H]$^+$ calcd for $C_{26}H_{20}N_3O_2S$: 438.1271; found: 438.1270.

3'-Amino-2''-chloro-5'-(methylthio)-4''-nitro-[1,1':4',1''-terphenyl]-2'-carbonitrie (4l)

Brown solid; yield: 82 mg (41%); **mp** = 188–190 °C; **IR** (KBr): 3462, 2924, 2211, 1430-1573 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.42 (s, 3H, -SMe), 4.24 (s, 2H, -NH_2), 6.68 (s, 1H, ArH), 7.47-7.54 (m, 4H, ArH), 7.60 (d, *J* = 7.2 Hz, 2H, ArH), 8.29 (dd, *J* = 2.4 Hz, *J* = 8.4 Hz, 1H, ArH), 8.48 (d, *J* = 2.4 Hz, 1H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 15.2, 93.0, 114.5, 117.3, 118.3, 123.0, 125.8, 128.5, 128.7, 129.0, 133.6, 136.5, 138.5, 140.4, 145.5, 146.6, 147.0, 149.0; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{15}ClN_3O_2S$: 396.0568; found: 396.0573.

3'-Amino-2''-bromo-5'-(methylthio)-4''-nitro-[1,1':4',1''-terphenyl]-2'-carbonitrile (4m)

Brown solid; yield: 88 mg (40%); **mp** = 170–172 °C; **IR** (KBr): 3369, 2925, 2208, 1459-1572 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.42 (s, 3H, -SMe), 4.21 (s, 2H, -NH_2), 6.68 (s, 1H, ArH), 7.47-7.53 (m, 4H, ArH), 7.61 (dd, *J* = 1.2 Hz, *J* = 8.4 Hz, 2H, ArH), 8.34 (dd, *J* = 2.4 Hz, *J* = 8.0 Hz, 1H, ArH), 8.65 (d, *J* = 1.6 Hz, 1H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 15.1, 92.7, 114.3, 117.2, 120.0, 123.5, 126.0, 128.5, 128.7, 129.0, 129.0, 133.4, 138.3, 142.5, 145.3, 146.4, 146.6, 148.5; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{20}H_{15}BrN_3O_2S$: 440.0063; found: 442.0055.

3'-Amino-2''-bromo-4-methyl-5'-(methylthio)-4''-nitro-[1,1':4',1''-terphenyl]-2'- carbonitrile (4n)

Brown solid; yield: 95 mg (42%); **mp** = 200–202 °C; **IR** (KBr): 3468, 2925, 2215, 1435-1568 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): *δ* 2.41 (s, 3H, -SMe), 2.43 (s, 3H, -CH_3), 4.19 (s, 2H, -NH_2), 6.67 (s, 1H, ArH), 7.31 (d, *J* = 8.0 Hz, 2H, ArH), 7.50 (d, *J* = 8.4 Hz, 3H, ArH), 8.33 (dd, *J* = 2.4 Hz, *J* = 8.4 Hz, 1H, ArH), 8.65 (d, *J* = 6.0 Hz, 1H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): *δ* 15.2, 21.4 92.8, 114.3, 117.5, 120.0, 123.6, 126.1, 128.4, 129.0, 129.5, 133.5, 135.6, 139.1, 145.2, 145.2, 146.6, 146.7, 148.6; **HRMS** (ESI): *m/z* [M + H]$^+$ calcd for $C_{21}H_{17}BrN_3O_2S$: 454.0219; found: 454.0223.

Synthesis of 3-amino-2-aryl-5-(methylthio)-[1,1'-biphenyl]-4-carbonitriles 6a-k: A mixture of 2-(3,3-bis(methylthio)-1-arylallylidene)malononitrile **2** (0.5 mmol), nitroethane **5** (0.5 mmol), and KOH (1.0 mmol) in DMF (4.0 mL) was stirred at 40-45 °Cfor 1 hour. After the completion, the reaction mixture was poured onto crushed ice with vigorous stirring followed by neutralization with 10% hydrochloric acid. The precipitate obtained was filtered, washed with H_2O and dried. The crude was purified by silica gel column chromatography using

hexane/ethylacetate (90:10) as an eluent to afford biaryl product.

3-Amino-4-methyl-5-(methylthio)-[1,1'-biphenyl]-2-carbonitrile (6a)

White solid; yield: 90 mg (70%); **mp** = 80–82 °C; **IR** (KBr): 3483, 3383, 2923, 2854, 2216, 1734, 1441-1628 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.20 (s, 3H, -SMe), 2.48 (s, 3H, $-CH_3$), 4.49 (s, 2H, $-NH_2$), 6.60 (s, 1H, ArH), 7.40-7.48 (m, 3H, ArH), 7.51-7.52 (m, 1H, ArH), 7.53-7.54 (m, 1H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.3, 15.3, 92.3, 114.6, 117.1, 118.1, 128.5, 128.6, 128.6, 139.0, 143.3, 145.0, 148.0**;** **HRMS** (ESI): *m/z* [M + H]$^+$calcd for $C_{15}H_{15}N_2S$: 255.0950; found: 255.0942.

3-Amino-4,4'-dimethyl-5-(methylthio)-[1,1'-biphenyl]-2-carbonitrile (6b)

White solid; yield: 97 mg (72%); **mp** = 93–95 °C; **IR** (KBr): 3476, 3381, 2923, 2208, 1703, 1427-1628 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.12 (s, 3H, $-CH_3$), 2.33 (s, 3H, -SMe), 2.40 (s, 3H, $-CH_3$), 4.41 (s, 2H, $-NH_2$), 6.51 (s, 1H, ArH), 7.19 (d, *J* = 9.2 Hz,2H, ArH), 7.35 (d, *J* = 8.4 Hz,2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.1, 15.2, 21.2, 92.2, 114.4, 116.7, 118.1, 128.3, 129.2, 136.0, 138.4, 143.2, 144.7, 147.7; **HRMS** (ESI): *m/z* [M + H]$^+$calcd for $C_{16}H_{17}N_2S$: 269.1107; found: 269.1099.

3-Amino-4'-methoxy-4-methyl-5-(methylthio)-[1,1'-biphenyl]-2-carbonitrile (6c)

White solid; yield: 93 mg (65%);**mp =** 95–97 °C; **IR** (KBr): 3461, 3374, 2924, 2207, 1731, 1459-1635 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.19 (s, 3H, $-CH_3$), 2.48 (s, 3H, -SMe), 3.85 (s, 3H, -OMe), 4.48 (s, 2H, $-NH_2$), 6.57 (s, 1H, ArH), 6.99 (d, *J* = 8.8 Hz,2H, ArH), 7.47 (d, *J* = 8.4 Hz,2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.1, 15.2, 55.3, 92.1, 114.0, 114.3, 116.5, 118.2, 129.6, 131.3, 143.0, 144.7, 147.7, 159.8; **HRMS** (ESI): *m/z* [M + H]$^+$calcd for $C_{16}H_{17}N_2OS$: 285.1056; found: 285.1049.

3-Amino-3',4'-dimethoxy-4-methyl-5-(methylthio)-[1,1'-biphenyl]-2-carbonitrile (6d)

White solid; yield: 76 mg (48%); **mp** = 120–122 °C; **IR** (KBr): 3468, 3381, 2924, 2852, 2206, 1708, 1442-1708 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.19 (s, 3H, $-CH_3$), 2.48 (s, 3H, -SMe), 3.92-3.93 (s, 6H, -OMe), 4.49 (s, 2H, $-NH_2$), 6.59 (s, 1H, ArH), 6.95 (d, *J* = 8.0 Hz,1H, ArH), 7.06-7.09 (m,2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.2, 15.4, 56.0, 56.1, 92.3, 111.2, 112.0, 114.5, 116.8, 118.3, 121.1, 131.7, 143.1, 144.8, 148.0, 148.8, 149.4; **HRMS** (ESI): *m/z* [M + H]$^+$calcd for $C_{17}H_{19}N_2O_2S$: 315.1162; found: 315.1155.

3-Amino-2'-methoxy-4-methyl-5-(methylthio)-[1,1'-biphenyl]-2-carbonitrile (6e)

White solid; yield: 70 mg (49%); **mp** = 95–93 °C; **IR** (KBr): 3461, 3374, 2924, 2207, 1731, 1459-1635 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.19 (s, 3H, $-CH_3$), 2.45 (s, 3H, -SMe), 3.84 (s, 3H, -OMe), 4.42 (s, 2H, $-NH_2$), 6.56 (s, 1H, ArH), 7.00-7.05 (m,2H, ArH), 7.23 (m,1H, ArH), 7.37-7.41 (m,1H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.3, 15.3, 55.6, 94.3, 111.3, 115.4, 117.2, 118.0, 120.7, 128.0, 130.1, 130.8, 140.2, 144.6, 147.2, 156.6; **HRMS** (ESI): *m/z* [M + H]$^+$calcd for $C_{16}H_{17}N_2OS$: 285.1056; found: 285.1049.

3-Amino-4'-fluoro-4-methyl-5-(methylthio)-[1,1'-biphenyl]-2-carbonitrile (6f)

White solid; yield: 71 mg (52%);**mp** = 188–190 °C; **IR** (KBr): 3473, 3378, 2922, 2211, 1739, 1424-1696 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.19 (s, 3H, $-CH_3$), 2.48 (s, 3H, -SMe), 4.51 (s, 2H, $-NH_2$), 6.55 (s, 1H, ArH), 7.14 (t, *J* = 8.4 Hz,2H, ArH), 7.49 (dd, *J* = 5.6 Hz, *J* = 8.8 Hz, 2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.1, 15.2, 92.1, 114.4, 115.6 (d, $J_{C\text{-}F}$ = 32 Hz), 117.1, 118.0, 130.1 (d, $J_{C\text{-}F}$ = 10 Hz), 135.0, 142.1, 145.0, 147.8, 162.8 (d, $J_{C\text{-}F}$ = 248.8 Hz); **HRMS** (ESI): *m/z* [M + H]$^+$calcd for $C_{15}H_{14}FN_2S$: 273.0856; found: 273.0848.

3-Amino-2',4'-dichloro-4-methyl-5-(methylthio)-[1,1'-biphenyl]-2-carbonitrile (6g)

White solid; yield: 81 mg (50%); **mp** = 165–167 °C; **IR** (KBr): 3480, 3383, 2924, 2212, 1737, 1455-1630 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.20 (s, 3H, $-CH_3$), 2.45 (s, 3H, -SMe), 4.48 (s, 2H, $-NH_2$), 6.49 (s, 1H, ArH), 7.28 (s,1H, ArH), 7.33 (dd, *J* = 2.4 Hz, *J* = 8.4 Hz, 1H, ArH), 7.52 (d, *J* = 1.6 Hz,1H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.3, 15.3, 93.5, 115.1, 117.1, 118.0, 127.3, 128.3, 129.8, 132.0, 135.2, 136.2, 139.5, 145.0, 147.7; **HRMS** (ESI): *m/z* [M + H]$^+$calcd for $C_{15}H_{13}Cl_2N_2S$: 323.0171; found: 323.0158.

3-Amino-4'-bromo-4-methyl-5-(methylthio)-[1,1'-biphenyl]-2-carbonitrile (6h)

White solid; yield: 92 mg (55%);**mp** = 175–177 °C; **IR** (KBr): 3468, 3375, 2923, 2854, 2209, 1712, 1461-1637 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.20 (s, 3H, $-CH_3$), 2.48 (s, 3H, -SMe), 4.50 (s, 2H, $-NH_2$), 6.55 (s, 1H, ArH), 7.41-7.47 (m,4H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.3, 15.3, 92.0, 114.4, 117.4, 118.0, 129.0, 130.0, 134.7, 137.7, 142.0, 145.2, 148.0; **HRMS** (ESI): *m/z* [M + H]$^+$calcd for $C_{15}H_{14}BrN_2S$: 333.0056; found: 333.0067.

3-Amino-3'-bromo-4-methyl-5-(methylthio)-[1,1'-biphenyl]-2-carbonitrile (6i)

White solid; yield: 82 mg (49%);**mp =** 180–185 °C; **IR** (KBr): 3376, 2921, 2206, 1703, 1445-1637 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.20 (s, 3H, $-CH_3$), 2.49 (s, 3H, -SMe), 4.52 (s, 2H, $-NH_2$), 6.55 (s, 1H, ArH), 7.33 (t, *J* = 8.0 Hz, 1H, ArH), 7.45-7.48 (m, 1H, ArH), 7.53-7.56 (m,1H, ArH), 7.63 (t, *J* = 2.0 Hz, 1H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.3, 15.4, 92.1, 114.5, 117.7, 122.6, 122.7, 127.4, 130.1, 131.5, 131.6, 141.0, 141.6, 145.2, 148.0; **HRMS** (ESI): *m/z* [M + H]$^+$calcd for $C_{15}H_{14}BrN_2S$: 333.0056; found: 333.0047.

2-Amino-3-methyl-4-(methylthio)-6-(naphthalen-2-yl)benzonitrile (6j)

White solid; yield: 93 mg (61%); **mp** = 167–169 °C; **IR** (KBr): 3486, 3376, 2924, 2208, 1705, 1436-1629 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.22 (s, 3H, $-CH_3$), 2.50 (s, 3H, -SMe), 4.53 (s, 2H, $-NH_2$), 6.70 (s, 1H, ArH), 7.51-7.53 (m,2H, ArH), 7.64 (dd, *J* = 1.6 Hz, *J* = 8.4 Hz, 1H, ArH), 7.86-7.95 (m, 3H, ArH), 8.00 (s, 1H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.3, 15.4, 92.5, 115.0, 117.2, 118.2, 126.4, 126.5, 126.6, 127.8, 128.4, 133.1, 133.2, 136.4, 143.3, 145.0, 148.0;

HRMS (ESI): *m/z* [M + H]$^+$calcd for $C_{19}H_{17}N_2S$: 305.1107; found: 305.1104.

3-Amino-4-methyl-5-(methylthio)-[1,1':4',1''-terphenyl]-2-carbonitrile (6k)

White solid; yield: 103 mg (62%); **mp** = 90–92 °C; **IR** (KBr): 3382, 3376, 2925, 2208, 1705, 1462-1629 cm^{-1}; **^{1}H NMR** (400 MHz, $CDCl_3$): δ 2.21 (s, 3H, -CH_3), 2.50 (s, 3H, -SMe), 4.53 (s, 2H, -NH_2), 6.65 (s, 1H, ArH), 7.37 (t, *J* = 7.2 Hz,1H, ArH), 7.47 (t, *J* = 7.6 Hz,2H, ArH), 7.59-7.63 (t, *J* = 8.8 Hz, 4H, ArH), 7.69 (d, *J* = 8.4 Hz, 2H, ArH); **^{13}C NMR** (100 MHz, $CDCl_3$): δ 13.3, 15.4, 92.2, 114.6, 117.2, 118.2, 127.2, 127.4, 127.6, 129.0, 129.0, 138.0, 140.5, 141.4, 142.8, 145.0, 148.0; **HRMS** (ESI): *m/z* [M + H]$^+$calcd for $C_{21}H_{19}N_2S$: 331.1263; found: 331.1247.

Conflicts of interest

There are no conflicts of interest to declare.

Acknowledgements

We are grateful to acknowledge Indian Council of Medical Research (ICMR), New Delhi for financial support. RP is thankful to the University of Delhi for providing instrument facilities to accomplish this work. S. is thankful to UGC, New Delhi for providing research fellowship.

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