Ketene Dithioacetals – Source for Different Heterocycles

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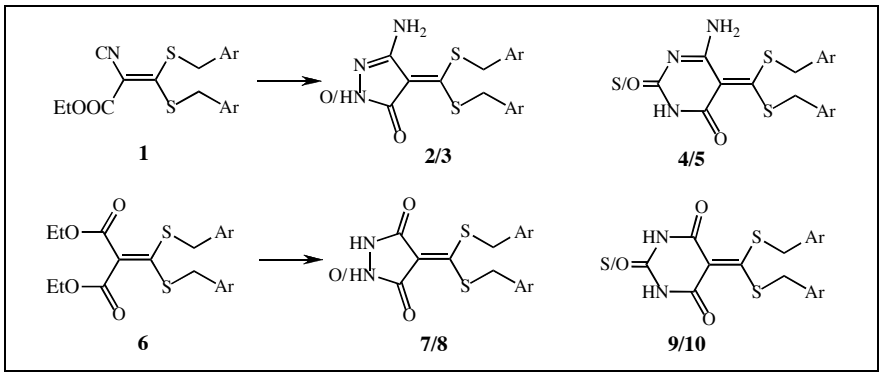

Some pyrazoline, isoxazoline and pyrimidine derivatives were synthesized from ketene dithioacetals using appropriate nucleophiles.

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INTRODUCTION

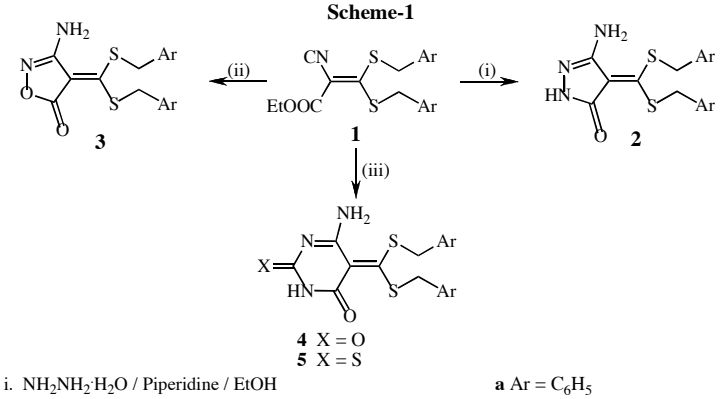
Among different heterocyclic systems the chemistry of five and six membered heterocycles *viz*., pyrazoles, isoxazoles and pyrimidines has gained importance. The pyrazole and isoxazole derivatives find applications as pharmaceutical agents. In fact, celecoxib and valdecoxib possess COX-1/ COX-2 inhibitory activity [1]. Apart from these, many barbiturates were assayed as therapeutic agents. Some barbituric and thiobarbituric acids were found to be hypnotics, convulsants, muscle relaxants, plant growth regulators [2] *etc*. The pyrazole, isoxazole and pyrimidine derivatives can be generated in a facile manner by cyclocondensation of Michael adducts with hydrazine, hydroxylamine, urea and thiourea. In fact, we have reported the synthesis of these heterocycles by the reaction of Michael adducts with different nucleophiles [3]. This methodology has also been used to develop spiro heterocycles [4].

Ketene dithioacetals synthesized by Freund [5] are versatile synthons for the development of a wide variety of heterocyclic systems [6]. The preparation of ketene dithioacetals is based on the condensation with carbon disulfide followed by *in situ* bis thioalkyation of the resultant ketene dithiolate anions. A number of reagents *viz*., potassium hydroxide, sodium hydride, potassium *tert*-butoxide, sodium *tert*-amylate, *n*-butyllithium, lithium diisopropylamide, lithium dicyclohexylamide, lithium hexamethyl disilazide, phase transfer catalysts *etc*. have been used for the condensation reaction [7]. Ketene dithioacetals are key intermediates for the preparation of a wide variety of heterocyclic compounds because the double bond present in them is amenable for both nucleophilic and electrophilic attack [8]. The alkylsulfonyl group is substituted by different nucleophiles to prepare oxazolidine [9], pyrazole [10], benzodiazepine [11], imidazolidine [12] *etc*. However, to our knowledge functionalization of *gem* cyanoester and diester functionalities in ketene dithiolates for the synthesis of heterocycles is hitherto not reported. The present communication deals with the synthesis of pyrazoline, isoxazoline and pyrimidine derivatives from ketene dithioacetals exploiting *gem* diester and *gem* cyano ester moieties.

RESULTS AND DISCUSSION

The ethyl 3,3-bis(benzylthio)-2-cyanoacrylate (**1**) is prepared by the reaction of ethyl cyanoacetate with carbon disulfide in the presence of sodium ethoxide followed by *in situ* bis thioalkylation of the resultant ketene dithiolate anion with benzyl chloride. Similarly, condensation of diethyl malonate with carbon disulfide followed by bis thioalkylation resulted in diethyl 2-(bis(benzylthio)-methylene)malonate (**6**). The IR spectra of **1** and **6** showed absorption bands at 1730-1735 and 1620-1628 cm^{-1} for ester and olefinic moieties. An additional absorption band is observed in the IR spectrum of **1** at 2205-2208 cm^{-1} for the nitrile group. The ^1H NMR spectrum of **1a** displayed two singlets at δ 4.19 and 4.36 for benzylic protons indicating that they are in different chemical environments. However, **6a** exhibited a singlet at δ 4.21 for benzylic protons. Apart from this, a triplet

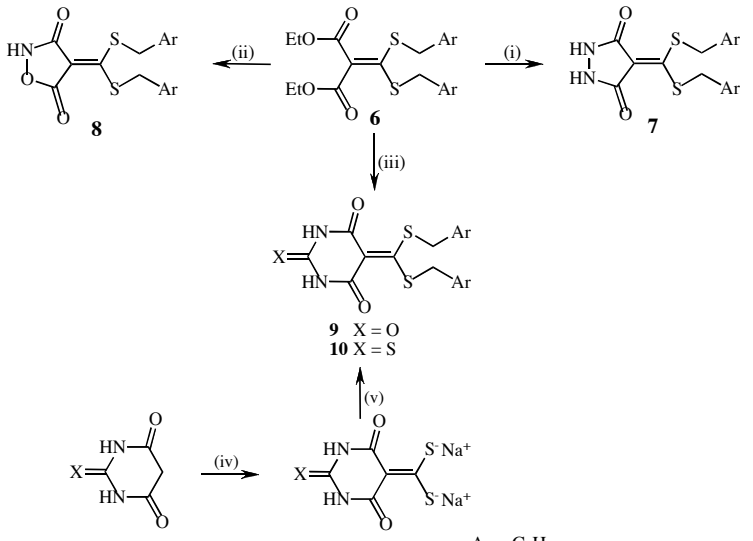
Scheme-1



i. $NH_2NH_2{\cdot}H_2O$ / Piperidine / EtOH
ii. $NH_2OH{\cdot}HCl$ / Piperidine / EtOH
iii. NH_2CXNH_2 / Piperidine / EtOH

a Ar = C_6H_5
b Ar = *p*-$CH_3C_6H_4$
c Ar = *p*-ClC_6H_4

Scheme-2



i. $NH_2NH_2{\cdot}H_2O$ / NaOEt / EtOH
ii. $NH_2OH{\cdot}HCl$ / NaOEt / EtOH
iii. NH_2CXNH_2 / NaOEt / EtOH
iv. CS_2 / NaOH / H_2O
v. $ArCH_2Cl$ / EtOH

a Ar = C_6H_5
b Ar = *p*-$CH_3C_6H_4$
c Ar = *p*-ClC_6H_4

and a quartet are observed at δ 1.35 and 4.22 due to carboethoxy group. Treatment of 3,3-bis(benzylthio)-2-cyanoacrylate (**1**) and diethyl 2-(bis(benzylthio)methylene)malonate (**6**) with hydrazine hydrate resulted in 3-amino-4-(bis(benzylthio)methylene)-pyrazol-5-one (**2**) and 4-bis(benzylthio)methylene) pyrazolidine-3,5-dione (**7**). The cyclocondensation of **1** and **6** with hydroxylamine produced 3-amino-4-(bis(benzylthio)methylene)-isoxazol-5-one (**3**) and 4-(bis(benzylthio)methylene) isoxazolidine-3,5-dione (**8**). Adopting similar methodology, 6-amino-5-bis(benzylthio)methylene)-pyrimidine-2,4-dione (**4**), 6-amino-5-(bis(benzylthio)-methylene)-2,3-dihydro-2-thioxopyrimidine-4-one (**5**), 5-(bis(benzylthio)methylene) pyrimidine-2,4,6-trione (**9**) and 5-(bis(benzylthio)methylene)-2,3-dihydro-2-thioxo-pyrimidine-4,6-dione (**10**) are prepared by the reaction of **1** and **6** with urea and thiourea, respectively. However, the compounds, **2**-**5** and **7**-**10** are obtained in moderate yields (52-58 %). Compounds **9** and **10** are also obtained in good yield (66-68 %) using the one pot method by the treatment of barbituric acid and thiobarbituric acid with carbon disulfide followed by bis thioalkylation with benzyl chloride (Method B) (Schemes 1 and 2 and Table 1). The IR spectra of **2**-**5** displayed absorption bands at 1616-1628 (C=C), 1598-1614 (C=N) and 3320-3475 cm^{-1} (NH_2). Apart from these, absorption bands are observed at 1736-1748 cm^{-1} (CO-O) in compound **3**, 1654-1666 (*CO*-NH), 3200-3232 cm^{-1} (NH) in compounds **2, 4** and **5**, and 1490-1497 cm^{-1} (C=S) in compound **5**. On the other hand, compounds **7-10** showed absorption bands at 1621-1629 (C=C), 1656-1668 (CONH) and 3207-3236 cm^{-1} (NH). Besides, compound **8** exhibited a band at 1731-1738 cm^{-1} (CO-O) and compound **10** exhibited bands at 1491-1495 cm^{-1} (C=S) (Table 2). The ^1H NMR spectra of **2**-**5** showed

two singlets for benzylic protons at δ 4.06-4.21 and 4.18-4.33, and a broad singlet at δ 5.58-5.69 for NH_2. The compounds **2**,**4** and **5** also exhibited a broad singlet at δ 10.81-10.98 for NH. The signals due to NH and NH_2 disappeared on deuteration. The ^{13}C NMR spectra of **2**-**5** displayed six signals in the regions δ 39.4-42.2, 41.3-43.4 (CH_2-S), 102.9-104.7 (=*C*-CO), 154.5-156.0 (=C-S), 154.2-159.2 (C=N), 173.6-176.1 (C=O). Besides compound **4** showed another signal at δ 170.5-171.6 (C=O) whereas **5** at δ 164-7-166.3 (C=S). The ^1H NMR spectra of **7**-**10** exhibited a singlet at δ 4.15-4.31 for benzylic protons and a broad singlet at δ 10.44-10.91 for NH, which disappeared on deuteration. The ^{13}C NMR spectra of **7**-**10** exhibited four signals at δ 40.9-43.8 (CH_2-S), 102.7-104-9 (=*C*-CO), 154.4-157.3 (=C-S), 164.8-174.7 (C=O). Apart from these, compound **8** showed another signal at δ 171.4-171.9, **9** at δ 157.9-159.6 (C=O) and **10** at δ 172.2-174.1 (C=S) (Table 3).

Table 1

Physical and Analytical Data of Compounds **2-10**

Compound	Mp (°C)	Ar	Yield %	Molecular Formula	Analysis % Calcd. /Found		
					C	H	N
2a	122-124	C_6H_5	58	$C_{18}H_{17}N_3OS_2$	60.82	4.82	11.82
					60.64	4.87	11.91
2b	137-139	*p*-$CH_3C_6H_4$	55	$C_{20}H_{21}N_3OS_2$	62.63	5.52	10.96
					62.71	5.50	10.90
2c	132-134	*p*-ClC_6H_4	57	$C_{18}H_{15}N_3\ Cl_2OS_2$	50.94	3.56	9.90
					50.84	3.58	9.98
3a	146-148	C_6H_5	52	$C_{18}H_{16}N_2O_2S_2$	60.65	4.52	7.86
					60.75	4.49	7.93
3b	153-155	*p*-$CH_3C_6H_4$	57	$C_{20}H_{20}N_2O_2S_2$	62.47	5.24	7.29
					62.53	5.28	7.34
3c	164-166	*p*-ClC_6H_4	56	$C_{18}H_{14}N_2\ Cl_2O_2S_2$	50.83	3.32	6.59
					50.76	3.30	6.52
4a	182-184	C_6H_5	55	$C_{19}H_{17}N_3O_2S_2$	59.51	4.47	10.96
					59.60	4.52	10.90
4b	169-171	*p*-$CH_3C_6H_4$	58	$C_{21}H_{21}N_3O_2S_2$	61.29	5.14	10.21
					61.18	5.17	10.28
4c	195-197	*p*-ClC_6H_4	54	$C_{19}H_{15}N_3\ Cl_2O_2S_2$	50.45	3.34	9.29
					50.52	3.32	9.37
5a	169-171	C_6H_5	56	$C_{19}H_{17}N_3OS_3$	57.11	4.29	10.52
					57.20	4.33	10.60
5b	144-146	*p*-$CH_3C_6H_4$	57	$C_{21}H_{21}N_3OS_3$	58.99	4.95	9.83
					59.04	4.90	9.90
5c	182-184	*p*-ClC_6H_4	55	$C_{19}H_{15}N_3\ Cl_2OS_3$	48.72	3.23	8.97
					48.79	3.20	8.93
7a	133-135	C_6H_5	58	$C_{18}H_{16}N_2O_2S_2$	60.65	4.52	7.86
					60.69	4.55	7.82
7b	140-142	*p*-$CH_3C_6H_4$	57	$C_{20}H_{20}N_2O_2S_2$	62.47	5.24	7.29
					62.41	5.28	7.23
7c	146-148	*p*-ClC_6H_4	55	$C_{18}H_{14}N_2\ Cl_2O_2S_2$	50.83	3.32	6.59
					50.92	3.30	6.65
8a	154-156	C_6H_5	53	$C_{18}H_{15}NO_3S_2$	60.48	4.23	3.92
					60.53	4.26	3.88
8b	149-151	*p*-$CH_3C_6H_4$	54	$C_{20}H_{19}NO_3S_2$	62.31	4.97	3.63
					62.34	5.00	3.67
8c	160-162	*p*-ClC_6H_4	58	$C_{18}H_{13}N\ Cl_2O_3S_2$	50.71	3.07	3.29
					50.79	3.12	3.33
9a	216-218	C_6H_5	57	$C_{19}H_{16}N_2O_3S_2$	59.35	4.19	7.29
			65*		59.42	4.15	7.25
9b	198-200	*p*-$CH_3C_6H_4$	56	$C_{21}H_{20}N_2O_3S_2$	61.14	4.89	6.79
			68*		61.10	4.91	6.83
9c	214-216	*p*-ClC_6H_4	55	$C_{19}H_{14}Cl_2N_2O_3S_2$	50.34	3.11	6.18
			67*		50.39	3.10	6.23
10a	201-203	C_6H_5	56	$C_{19}H_{16}N_2O_2S_3$	56.97	4.03	6.99
			68*		56.92	4.08	7.04
10b	196-198	*p*-$CH_3C_6H_4$	55	$C_{21}H_{20}N_2O_2S_3$	58.85	4.70	6.54
			66*		58.89	4.67	6.59
10c	214-216	*p*-ClC_6H_4	58	$C_{19}H_{14}Cl_2N_2O_2S_3$	48.61	3.01	5.97
			65*		48.64	3.00	6.03

* Yield obtained in method B.

Table 2

IR Data of Compounds **2-10**

Compound	IR (cm^{-1})							
	C=C	C=S	C=N	*CO*NH	*C*O-O	NH	NH_2	
2a	1622	-	1602	1661	-	3209	3369	3475
2b	1628	-	1611	1654	-	3200	3355	3449
2c	1619	-	1605	1659	-	3204	3364	3471
3a	1623	-	1599	-	1736	-	3325	3468
3b	1626	-	1607	-	1742	-	3320	3465
3c	1628	-	1611	-	1748	-	3326	3470
4a	1616	-	1614	1661	-	3212	3331	3472
4b	1627	-	1609	1664	-	3217	3329	3469
4c	1624	-	1598	1656	-	3232	3323	3467
5a	1620	1493	1613	1662	-	3208	3332	3470
5b	1625	1497	1611	1666	-	3225	3334	3473
5c	1622	1490	1609	1658	-	3213	3336	3471
7a	1624	-	-	1659	-	3219	-	-
7b	1627	-	-	1666	-	3207	-	-
7c	1625	-	-	1662	-	3222	-	-
8a	1622	-	-	1664	1738	3225	-	-
8b	1628	-	-	1658	1731	3231	-	-
8c	1624	-	-	1661	1736	3218	-	-
9a	1629	-	-	1656	-	3234	-	-
9b	1623	-	-	1663	-	3226	-	-
9c	1620	-	-	1657	-	3229	-	-
10a	1623	1495	-	1664	-	3224	-	-
10b	1621	1493	-	1656	-	3236	-	-
10c	1623	1491	-	1661	-	3230	-	-

CONCLUSION

The functionalization of *gem* diester and *gem* cyano ester functionalities in ketene dithioacetals with different nucleophiles led to a new class of biologically potent heterocycles pyrazoline, isoxazoline pyrimidine and their derivatives.

EXPERIMENTAL

Melting points were determined in open capillaries on a Mel-Temp apparatus and are uncorrected. The purity of the compounds was checked by TLC (silica gel H, BDH, ethyl acetate/hexane, 1:3). The IR spectra were recorded on a Thermo Nicolet IR 200 FT-IR spectrometer as KBr pellets and the wave numbers were given in cm^{-1}. The ^1H NMR spectra were recorded in $CDCl_3$ / DMSO-d_6 on a Varian EM-360 spectrometer (300 MHz). The ^{13}C NMR spectra were recorded in $CDCl_3$ / DMSO-d_6 on a Varian VXR spectrometer operating at 75.5 MHz. All chemical shifts are reported in δ (ppm) using TMS as an internal standard. The microanalyses were performed on a Perkin-Elmer 240C elemental analyzer. The starting compounds ethyl 3,3-bis(benzylthio)-2-cyanoacrylate (**1**) and diethyl 2-(bis(benzylthio)methylene)malonate (**6**) were prepared by the literature procedure [13].

3-Amino-4-(bis(benzylthio)methylene)-pyrazol-5-one (2) / 3-amino-4-(bis(benzylthio)methylene) isoxazol-5-one (3): General Procedure. To a solution of **1** (1 mmol) in ethanol, hydrazine hydrate (1.5 mmol) / hydroxylamine hydrochloride (1.2 mmol) and piperidine (3 mL) were added and refluxed for 7-10 hours. The solution was cooled and poured into crushed ice containing conc. HCl. The solid obtained was collected by filtration, dried, and recrystallized from ethanol.

6-Amino-5-(bis(benzylthio)methylene)pyrimidine-2,4-dione (4) / 6-amino-5-(bis(benzylthio)methylene)-2,3-dihydro-2-thioxopyrimidine-4-one (5): General Procedure. The compound **1** (1 mmol) was dissolved in ethanol (10 mL). To this, urea / thiourea (1.5 mmol) in ethanol (10 mL) and piperidine (3 mL) was added and refluxed for 10-12 hours. The contents were cooled and poured into crushed ice containing conc. HCl. The separated solid was collected by filtration, dried and recrystallized from ethanol.

4-(Bis(benzylthio)-methylene) pyrazolidine-3,5-dione (7) / 4-(bis(benzylthio) methylene) isoxazolidine-3,5-dione (8): General Procedure. To a solution of **6** (1 mmol) in ethanol, hydrazine hydrate (1.5 mmol) / hydroxylamine hydrochloride (1.2 mmol) and sodium ethoxide (3 mL) were added and refluxed for 6-8 hours. The solution was cooled and poured into crushed ice containing conc. HCl. The solid obtained was collected by filtration, dried, and recrystallized from ethanol.

5-(bis(benzylthio)methylene)pyrimidine-2,4,6-trione (9) / 5-(bis(benzylthio) methylene)-2,3-dihydro-2-thioxopyrimidine-4,6-dione (10): General Procedure. The compound **6** (1 mmol) was dissolved in ethanol (10 mL). To this, urea / thiourea (1.5 mmol) in ethanol (10 mL) and sodium ethoxide (3 mL) was added and refluxed for 8-10 hours. The contents were cooled and poured into crushed ice containing conc. HCl. The separated solid was filtered, dried and recrystallized from ethanol.

Method B. A mixture of barbituric acid / thiobarbituric acid (1 mmol), 30% sodium hydroxide solution (10 mL) and carbon disulfide (1.5 mmol) was stirred for 20-24 hours. To this, 1 N

Table 3

^{1}H and ^{13}C NMR Data of Compounds **2-5 and 6-10**

Compound	^{1}H NMR (δ, ppm)	^{13}C NMR (δ, ppm)
2a	4.19 (s, 2H, CH_2), 4.33 (s, 2H, CH_2), 5.62 (s, 2H, NH_2), 7.12-7.76 (m, 10H, Ar-H), 10.91 (bs, 1H, NH)	40.3 (CH_2-S), 41.3 (CH_2-S), 104.7 (=*C*-CO), 155.2 (=C-S), 157.4 (C=N), 174.3 (C=O), 128.2, 129.2, 130.4, 131.6, 131.9, 132.4 (aromatic carbons)
2b	2.32 (s, 3H, Ar-CH_3), 4.13 (s, 2H, CH_2), 4.28 (s, 2H, CH_2), 5.69 (s, 2H, NH_2), 7.15-7.72 (m, 8H, Ar-H), 10.98 (bs, 1H, NH)	24.5 (Ar-CH_3), 41.1 (CH_2-S), 42.5 (CH_2-S), 103.9 (=*C*-CO), 155.0 (=C-S), 159.2 (C=N), 173.6 (C=O), 128.4, 130.0, 130.6 131.4, 132.7, 133.6. (aromatic carbons)
2c	4.09 (s, 2H, CH_2), 4.22 (s, 2H, CH_2), 5.64 (s, 2H, NH_2), 7.11-7.79 (m, 8H, Ar-H), 10.94 (bs, 1H, NH)	40.6 (CH_2-S), 42.1 (CH_2-S), 104.2 (=*C*-CO), 155.5 (=C-S), 156.7 (C=N), 174.0 (C=O), 129.6, 129.9, 130.4, 133.4, 134.6, 135.8 (aromatic carbons)
3a	4.21 (s, 2H, CH_2), 4.30 (s, 2H, CH_2), 5.58 (s, 2H, NH_2), 7.03-7.27 (m, 10H, Ar-H)	40.2 (CH_2-S), 42.4 (CH_2-S), 104.1 (=*C*-CO), 155.5 (=C-S), 154.2 (C=N), 174.8 (C=O), 128.4, 129.4, 129.7, 131.8, 134.2, 135.2 (aromatic carbons)
3b	2.35 (s, 3H, Ar-CH_3), 4.16 (s, 2H, CH_2), 4.27 (s, 2H, CH_2), 5.63 (s, 2H, NH_2), 7.08-7.36 (m, 8H, Ar-H)	23.9 (Ar-CH_3), 42.2 (CH_2-S), 43.4 (CH_2-S), 103.6 (=*C*-CO), 155.2 (=C-S), 155.8 (C=N), 175.2 (C=O), 129.4, 129.8, 130.7, 131.4, 134.3, 134.7 (aromatic carbons)
3c	4.11 (s, 2H, CH_2), 4.23 (s, 2H, CH_2), 5.67 (s, 2H, NH_2), 7.02-7.31 (m, 8H, Ar-H)	40.9 (CH_2-S), 42.9 (CH_2-S), 104.0 (=*C*-CO), 155.7 (=C-S), 159.2 (C=N), 174.0 (C=O), 128.7, 130.4, 132.3, 133.6, 134.0, 136.9 (aromatic carbons)
4a	4.07 (s, 2H, CH_2), 4.20 (s, 2H, CH_2), 5.64 (s, 2H, NH_2), 7.10-7.39 (m, 10H, Ar-H), 10.89 (bs, 1H, NH)	40.1 (CH_2-S), 42.0 (CH_2-S), 102.9 (=*C*-CO), 154.7 (=C-S), 159.2 (C=N), 170.5, 176.1 (C=O), 128.2, 129.4, 130.2, 130.8, 131.4, 131.9 (aromatic carbons)
4b	2.29 (s, 3H, Ar-CH_3), 4.14 (s, 2H, CH_2), 4.27 (s, 2H, CH_2), 5.61 (s, 2H, NH_2), 7.11-7.42 (m, 8H, Ar-H), 10.86 (bs, 1H, NH)	24.7 (ArCH_3), 39.4 (CH_2-S), 41.9 (CH_2-S), 103.7 (=*C*-CO), 154.5 (=C-S), 158.7 (C=N), 170.5, 174.8 (C=O), 128.6, 129.1, 129.7, 130.9, 131.2, 132.4 (aromatic carbons)
4c	4.18 (s, 2H, CH_2), 4.26 (s, 2H, CH_2), 5.64 (s, 2H, NH_2), 7.08-7.66 (m, 8H, Ar-H), 10.82 (bs, 1H, NH)	41.3 (CH_2-S), 42.8 (CH_2-S), 104.1 (=*C*-CO), 154.9 (=C-S), 159.2 (C=N), 171.6, 174.1 (C=O), 128.8, 129.4, 131.4, 131.8, 132.4, 132.8 (aromatic carbons)
5a	4.06 (s, 2H, CH_2), 4.18 (s, 2H, CH_2), 5.68 (s, 2H, NH_2), 7.10-7.64 (m, 10H, Ar-H), 10.85 (bs, 1H, NH)	39.5 (CH_2-S), 41.6 (CH_2-S), 103.2 (=*C*-CO), 155.4 (=C-S), 157.4 (C=N), 164.7 (C=S), 173.9 (C=O), 128.5, 129.8, 130.6, 131.7, 132.1, 132.5 (aromatic carbons)
5b	2.34 (s, 3H, Ar-CH_3), 4.17 (s, 2H, CH_2), 4.22 (s, 2H, CH_2), 5.63 (s, 2H, NH_2), 7.15-7.68 (m, 8H, Ar-H), 10.81 (bs, 1H, NH)	25.5 (Ar-CH_3), 40.6 (CH_2-S), 42.5 (CH_2-S), 103.7 (=*C*-CO), 154.9 (=C-S), 158.2 (C=N), 165.3 (C=S), 174.6 (C=O), 128.8, 129.6, 130.8, 131.6, 132.7, 133.2 (aromatic carbons)
5c	4.13 (s, 2H, CH_2), 4.21 (s, 2H, CH_2), 5.61 (s, 2H, NH_2), 7.08-7.62 (m, 8H, Ar-H), 10.88 (bs, 1H, NH)	41.4 (CH_2-S), 43.3 (CH_2-S), 104.1 (=*C*-CO), 156.0 (=C-S), 157.9 (C=N), 166.3 (C=S), 174.3 (C=O), 128.6, 129.1, 129.5, 129.8, 131.1, 132.4, 134.7, 134.9 (aromatic carbons)
7a	4.15 (s, 4H, CH_2), 7.11-7.67 (m, 10H, Ar-H), 10.85 (bs, 2H, NH)	41.9 (CH_2-S), 102.9 (=*C*-CO), 155.5 (=C-S), 172.7 (C=O), 128.2, 129.2, 131.4, 132.7, 132.9 (aromatic carbons)
7b	2.32 (s, 3H, Ar-CH_3), 4.23 (s, 4H, CH_2), 7.12-7.69 (m, 8H, Ar-H), 10.79 (bs, 2H, NH)	23.9 (Ar-CH_3), 42.4 (CH_2-S), 103.7 (=*C*-CO), 155.1 (=C-S), 172.1 (C=O), 128.4, 129.5, 131.5, 132.6, 133.4 (aromatic carbons)
7c	4.21 (s, 4H, CH_2), 7.08-7.72 (m, 8H, Ar-H), 10.81 (bs, 2H, NH)	43.1 (CH_2-S), 104.2 (=*C*-CO), 154.7 (=C-S), 173.7 (C=O), 128.1, 129.4, 131.4, 131.9, 132.6 (aromatic carbons)
8a	4.20 (s, 4H, CH_2), 7.14-7.70 (m, 10H, Ar-H), 10.84 (bs, 1H, NH)	42.1 (CH_2-S), 103.5 (=*C*-CO), 155.2 (=C-S), 171.4, 174.4 (C=O), 129.4, 129.6, 130.5, 131.1, 132.0 (aromatic carbons)
8b	2.30 (s, 3H, Ar-CH_3), 4.28 (s, 4H, CH_2), 7.11-7.71 (m, 8H, Ar-H), 10.81 (bs, 1H, NH)	25.1 (Ar-CH_3), 43.7 (CH_2-S), 104.2 (=*C*-CO), 155.6 (=C-S), 171.6, 174.0 (C=O), 128.2, 129.2, 131.4, 131.8, 132.0 (aromatic carbons)
8c	4.31 (s, 4H, CH_2), 7.19-7.70 (m, 8H, Ar-H), 10.83 (bs, 1H, NH)	43.0 (CH_2-S), 104.4 (=*C*-CO), 154.4 (=C-S), 171.9, 174.7 (C=O), 129.3, 129.9, 132.3, 134.6, 137.3 (aromatic carbons)
9a	4.23 (s, 4H, CH_2), 7.12-7.74 (m, 10H, Ar-H), 10.86 (bs, 2H, NH)	42.1 (CH_2-S), 103.9 (=*C*-CO), 155.8 (=C-S), 159.6, 166.6 (C=O), 128.9, 129.2, 132.6, 133.9 (aromatic carbons)
9b	2.33 (s, 3H, Ar-CH_3), 4.28 (s, 4H, CH_2), 7.09-7.81 (m, 8H, Ar-H), 10.84 (bs, 2H, NH)	24.3 (Ar-CH_3), 43.3 (CH_2-S), 104.2 (=*C*-CO), 156.0 (=C-S), 158.4, 165.2 (C=O), 128.9, 129.1, 129.6, 131.6, 135.5 (aromatic carbons)
9c	4.25 (s, 4H, CH_2), 7.11-7.69 (m, 8H, Ar-H), 10.91 (bs, 2H, NH)	43.8 (CH_2-S), 104.9 (=*C*-CO), 155.3 (=C-S), 157.9, 164.8 (C=O), 128.5, 129.4, 129.8, 130.4, 134.7 (aromatic carbons)
10a	4.19 (s, 4H, CH_2), 7.10-7.77 (m, 10H, Ar-H), 10.89 (bs, 2H, NH)	40.9 (CH_2-S), 102.7 (=*C*-CO), 154.9 (=C-S), 165.9 (C=O), 172.2 (C=S), 128.2, 129.0, 131.4, 132.3, 133.6 (aromatic carbons)
10b	2.35 (s, 3H, Ar-CH_3), 4.27 (s, 4H, CH_2), 7.08-7.49 (m, 8H, Ar-H), 10.85 (bs, 2H, NH)	23.8 (Ar-CH_3), 42.3 (CH_2-S), 103.2 (=*C*-CO), 167.3 (=C-S), 168.2 (C=O), 173.5 (C=S), 127.4, 128.4, 129.6, 130.1, 132.4 (aromatic carbons)
10c	4.29 (s, 4H, CH_2), 7.12-7.48 (m, 8H, Ar-H), 10.44 (bs, 2H, NH)	43.2 (CH_2-S), 103.5 (=*C*-CO), 156.2 (=C-S), 166.1 (C=O), 174.1 (C=S), 129.1, 129.5, 129.8, 131.1, 133.6 (aromatic carbons)

hydrochloric acid (10 mL) was added followed by benzyl chloride (2 mmol) in ethanol (5 mL). Stirring was continued for 15-17 hours. The yellow precipitate that separated was collected by filtration, dried and recrystallized from DMF.

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