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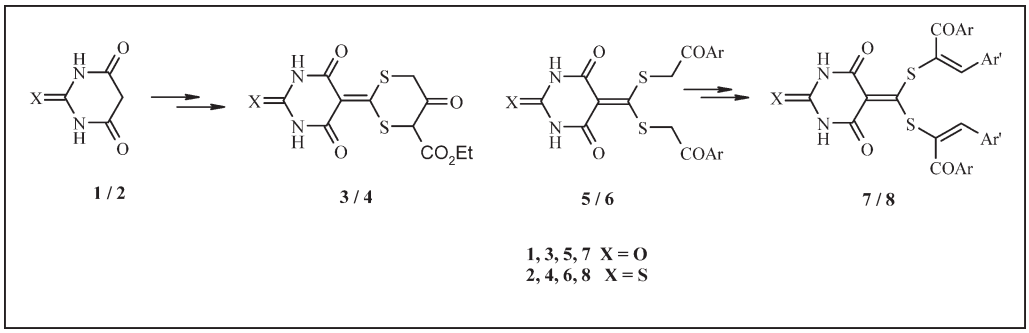

The reactivity of barbituric/thiobarbituric ketene dithiolates with bromoacetic ester and phenacyl bromide is studied.

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INTRODUCTION

The chemistry of activated olefins has gained importance because of their utility as synthons for the synthesis of a variety of carbocyclic and heterocyclic systems. In fact, we have reported a simple approach for the synthesis of *E*,*Z*-bis(styryl)sulfones [1]. We have also studied the reaction of vinyl chloride with aroyl and arylsulfonyl chlorides under Friedel-crafts conditions which afforded unsaturated oxosulfones and bissulfones [2]. This methodology has been extended to prepare bis unsaturated oxosulfones and bissulfones [3]. These activated mono and bis unsaturated olefins have been used to develop different heterocyclic systems [4]. In continuation of our interest on the synthesis of new activated olefins, the following Scheme 1 has been taken up.

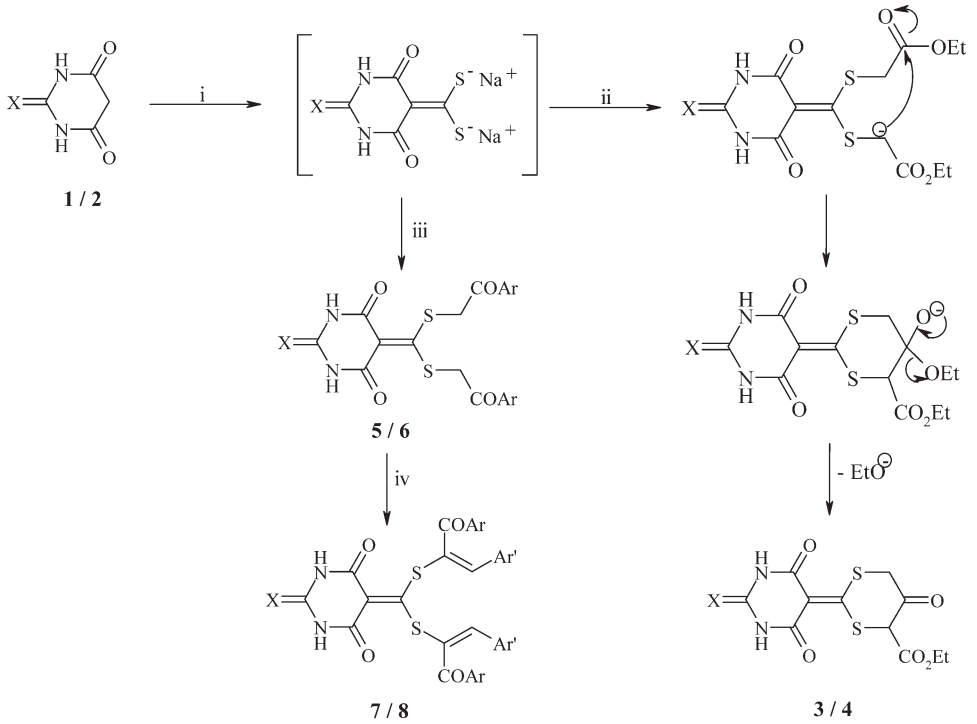
The reaction of active methylene compounds with carbon disulfide in the presence of a base followed by alkylation produced thioesters and ketene mercaptols [5]. Various acyclic and cyclic aliphatic and aromatic ketones have been utilized for this purpose. However, the reaction with less activated compounds like aliphatic aldehydes or ketones resulted in low yield [6] (10–25%). On the other hand, barbituric acid and thiobarbituric acid have not been explored as active methylene compounds to generate a variety of thioesters and ketene mercaptols. The present communication deals with the reactivity of barbituric acid and thiobarbituric acid with carbon disulfide in the presence of a base followed by alkylation with ethyl bromoacetate and phenacyl bromide.

RESULTS AND DISCUSSION

The barbituric acid (**1**) was treated with carbon disulfide in the presence of sodium hydride and was subsequently alkylated with ethyl bromoacetate. The reaction mixture was stirred for 8 h at room temperature and extracted with dichloromethane. The product obtained was identified as 5-oxo-2-(2,4,6-trioxopyrimidin-5-ylidene)-[1,3]dithiane-4-carboxylic acid ethyl ester (**3**) (Scheme 1). It seems that the initially formed [ethoxycarbonylmethylsulfanyl-(2,4,6-trioxopyrimidin-5-ylidene) methyl-sulfanyl]acetic acid ethyl ester undergoes Dieckmann cyclization resulting in the formation of **3**.

Similarly, the reaction of thiobarbituric acid (**2**) with carbon disulfide in the presence of sodium hydride followed by alkylation with ethyl bromoacetate produced 5-oxo-2-(4,6-dioxo-2-thioxopyrimidin-5-ylidene)-[1,3]dithiane-4-carboxylic acid ethyl ester (**4**). On the other hand, the reaction of barbituric acid/thiobarbituric acid **1/2** with carbon disulfide in the presence of sodium hydride followed by treatment with phenacyl bromide resulted in 5-[bis-(2-oxo-2-aryl-ethylsulfanyl)methylene]pyrimidine-2,4,6-trione (**5**)/5-[bis-(2-oxo-2-arylethyl-sulfanyl)methylene]-2-thioxopyrimidine-4,6-dione (**6**). The Knoevenagel reaction of **5** and **6** with araldehydes in the presence of benzylamine in acetic acid gave 5-[bis-(1-aroyl-2-arylvinylsulfanyl)-methylene]pyrimidine-2,4,6-trione (**7**) and 5-[bis-(1-aroyl-2-arylvinylsulfanyl)-methylene]-2-thioxo-pyrimidine-4,6-dione (**8**) (Scheme 1, Table 1). The structures of all the new

Scheme 1



1 / 2

5 / 6

7 / 8

3 / 4

i) NaH / CS_2 / DMSO
ii) $BrCH_2CO_2Et$
iii)$ArCOCH_2Br$
iv) Ar'-CHO / $PhCH_2NH_2$ / AcOH

1, **3**, **5**, **7** = X = O
2, **4**, **6, 8** = X = S

	Ar	Ar'
5a/6a	Ph	-
5b/6b	4-Me.Ph	-
5c/6c	4-Cl.Ph	-
7a/8a	Ph	Ph
7b/8b	4-Me.Ph	4-Me.Ph
7c/8c	4-Cl.Ph	4-Cl.Ph

Table 1

Physical and analytical data of compounds **3–8**.

Compound	Mp (°C)	Yield (%)	Ar	Ar′	Molecular formula	Analysis (%) calcd./found C	H	N
3	168–170	67	–	–	$C_{11}H_{10}N_2O_6S_2$ (330.34)	39.99	3.05	8.48
						39.92	2.98	8.52
4	182–184	65	–	–	$C_{11}H_{10}N_2O_5S_3$ (346.41)	38.14	2.91	8.09
						38.21	2.89	8.17
5a	182–184	76	C_6H_5	–	$C_{21}H_{16}N_2O_5S_2$ (440.49)	57.26	3.66	6.36
						57.22	3.63	6.41
5b	176–178	80	4-MeC_6H_4	–	$C_{23}H_{20}N_2O_5S_2$ (468.55)	58.96	4.30	5.98
						59.03	4.25	6.04
5c	230–232	85	4-ClC_6H_4	–	$C_{21}H_{14}Cl_2N_2O_5S_2$ (509.38)	49.52	2.77	5.50
						49.58	2.81	5.45
6a	175–177	75	C_6H_5	–	$C_{21}H_{16}N_2O_4S_3$ (456.56)	55.24	3.53	6.14
						55.30	3.55	6.08
6b	184–186	82	4-MeC_6H_4	–	$C_{23}H_{20}N_2O_4S_3$ (484.61)	57.00	4.16	5.78
						57.06	4.21	5.82
6c	192–194	77	4-ClC_6H_4	–	$C_{21}H_{14}Cl_2N_2O_4S_3$ (525.45)	48.00	2.69	5.33
						48.07	2.72	5.40
7a	159–161	71	C_6H_5	C_6H_5	$C_{35}H_{24}N_2O_5S_2$ (616.71)	68.16	3.92	4.54
						68.21	3.90	4.60
7b	164–166	76	4-MeC_6H_4	4-MeC_6H_4	$C_{39}H_{32}N_2O_5S_2$ (672.81)	69.62	4.79	4.16
						69.70	4.75	4.20
7c	197–199	80	4-ClC_6H_4	4-ClC_6H_4	$C_{35}H_{20}Cl_4N_2O_5S_2$ (754.49)	55.72	2.67	3.71
						55.76	2.70	3.76
8a	161–163	74	C_6H_5	C_6H_5	$C_{35}H_{24}N_2O_4S_3$ (632.77)	66.43	3.82	4.43
						66.37	3.86	4.48
8b	167–169	80	4-MeC_6H_4	4-MeC_6H_4	$C_{39}H_{32}N_2O_4S_3$ (688.88)	68.00	4.68	4.07
						68.07	4.65	4.01
8c	185–187	75	4-ClC_6H_4	4-ClC_6H_4	$C_{35}H_{20}Cl_4N_2O_4S_3$ (770.55)	54.55	2.62	3.64
						54.49	2.66	3.67

Table 2

IR data of compounds **3–8**.

Compounds	IR (KBr) cm^{-1}			
	C=S	C=C	C=O	NH
3	–	–	1752, 1735, 1710, 1685	3263
4	1485	–	1759, 1735, 1681	3216
5a	–	–	1720, 1703, 1685	3282
5b	–	–	1722, 1695, 1682	3274
5c	–	–	1733, 1702, 1686	3290
6a	1488	–	1726, 1712	3284
6b	1492	–	1720, 1704	3310
6c	1495	–	1712, 1725	3300
7a	–	1606	1672, 1680, 1730	3285
7b	–	1612	1724, 1682, 1675	3290
7c	–	1610	1720, 1684, 1677	3295
8a	1487	1588	1733, 1686	3251
8b	1498	1594	1730, 1680	3295
8c	1510	1610	1724, 1704	3300

compounds were confirmed by spectral parameters and elemental analyses which are depicted in Tables 2 and 3.

CONCLUSIONS

The reaction of barbituric acid/thiobarbituric acid with CS_2 followed by treatment with ethyl bromoacetate led to directly Dieckmann cyclized product. However, with phenacyl bromide bisalkylation takes place which are used as synthons to develop a new class of olefins by Knovenagel condensation with different araldehydes.

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

Table 3

^1H and ^{13}C NMR data of compounds **3–8**.

Compound	^1H NMR ($CDCl_3$/DMSO-d_6) δ (ppm)	^{13}C NMR ($CDCl_3$/DMSO-d_6) δ (ppm)
3	1.25 (t, 3H, —CH_2—C*H*$_3$, J = 7.2 Hz), 3.25 (s, 2H, —SCH_2—CO), 4.14 (q, 2H, —C*H*$_2$—CH_3, J = 7.2 Hz), 4.44 (s, 1H, [—SCH—CO(CO)], 10.25 (bs, 2H, NH)	13.8 (—CH_2—*C*H_3), 40.5 (—S*C*H_2—CO), 59.6 (O*C*H_2—CH_3), 65.3 (—S*C*H—CO), 104.6 (C-5), 159.4 (C-2), 168.6 (C-4 and C-6), 173.4 (*C*O—O), 175.2 [=C—S(S)], 205.4 (CO)
4	1.19 (t, 3H, —CH_2—C*H*$_3$, J = 6.9 Hz), 3.23 (s, 2H, —SCH_2—CO), 4.18 (q, 2H, —C*H*$_2$—CH_3, J = 6.9 Hz), 4.39 (s, 1H, [—SCH—CO(CO)], 9.86 (bs, 2H, NH)	13.5 (—CH_2—*C*H_3), 39.8 (—S*C*H_2—CO), 58.9 (—O*C*H_2—CH_3), 64.5 (—S*C*H—CO), 105.5 (C-5), 169.3 (C-4 and C-6), 172.6 (*C*O—O), 174.5 [=C—S(S)], 181.6 (C-2), 207.2 (C=O)
5a	3.89 (s, 4H, —S*C*H_2—CO), 7.35–7.84 (m, 10H, Ar-H), 10.32 (s, 2H, NH)	46.2 (—S*C*H_2—CO), 113.4 (C-5), 156.7 (C-2), 168.3 (C-4 and C-6), 174.6 [C=*C*—S(S)], 198.4 (C=O)
5b	2.24 (s, 6H, Ar-CH_3), 3.85 (s, 4H, —S*C*H_2—CO), 7.24–7.85 (m, 8H, Ar-H), 11.29 (s, 2H, NH)	21.4 (Ar-CH_3), 45.9 (—S*C*H_2—CO), 112.8 (C-5), 156.5 (C-2), 167.5 (C-4 and C-6), 175.3 [C=*C*—S(S)], 197.9 (C=O)
5c	3.81 (s, 4H, —S*C*H_2—CO), 7.41–7.95 (m, 8H, Ar-H), 11.22 (s, 2H, NH)	47.5 (—S*C*H_2—CO), 114.2 (C-5), 158.4 (C-2), 166.5 (C-4 and C-6), 175.5 [C=*C*—S(S)], 196.8 (C=O)
6a	3.85 (s, 4H, —S*C*H_2—CO), 7.26–7.52 (m, 10H, Ar-H), 9.98 (s, 2H, NH)	48.4 (—S*C*H_2—CO), 112.4 (C-5), 168.5 (C-4 and C-6), 176.4 [C=*C*—S(S)], 188.4 (C-2), 198.3 (C=O)
6b	2.26 (s, 6H, Ar-CH_3), 3.87 (s, 4H, —SCH_2—CO), 7.19–7.43 (m, 8H, Ar-H), 9.89 (s, 2H, NH)	21.2 (Ar-CH_3), 47.6 (-S*C*H_2-CO), 112.8 (C-5), 168.8 (C-4 and C-6), 175.8 [C=*C*-S(S)], 187.9 (C-2), 197.6 (C=O)
6c	3.86 (s, 4H, —SCH_2—CO), 7.24–7.80 (m, 8H, Ar-H), 9.96 (s, 2H, NH)	48.5 (—S*C*H_2—CO), 114.3 (C-5), 168.2 (C-4 and C-6), 175.3 [C=*C*—S(S)], 189.3 (C-2), 197.5 (C=O)
7a	6.94 (s, 2H, Ar-CH=C), 7.19-7.78 (m, 20H, Ar-H), 9.87 (s, 2H, NH)	120.5 (C-5), 136.8 (Ar-*C*H=C), 138.5 (Ar-CH=*C*), 157.5 [C=*C*—S(S)], 159.2 (C-2), 168.4 (C-4 and C-6), 186.9 (CO)
7b	2.21 (s, 12H, Ar-CH_3), 6.89 (s, 2H, Ar-CH=C), 7.14–7.26 (m, 16H, Ar-H), 9.88 (s, 2H, NH)	21.5 (Ar-CH_3), 121.2 (C-5), 136.3 (Ar-*C*H=C), 139.2 (Ar-CH=*C*), 156.2 [C=*C*—S(S)], 158.5 (C-2), 169.3 (C-4 and C-6), 188.2 (CO)
7c	6.98 (s, 2H, Ar-CH=C), 7.25–7.80 (m, 16H, Ar-H), 9.85 (s, 2H, NH)	121.2 (C-5), 136.3 (Ar-*C*H=C), 138.9 (Ar-CH=*C*), 158.4 [C=*C*—S(S)], 159.8 (C-2), 167.5 (C-4 and C-6), 185.8 (CO)
8a	6.96 (s, 2H, Ar-CH=C), 7.22–7.81 (m, 20H, Ar-H), 9.79 (s, 2H, NH)	120.2 (C-5), 135.9 (Ar-*C*H=C), 139.4 (Ar-CH=*C*), 156.8 [C=*C*—S(S)], 166.8 (C-4 and C-6), 182.4 (C-2), 186.5 (CO)
8b	2.18 (s, 12H, Ar-CH_3), 6.92 (s, 2H, Ar-CH=C), 7.19–7.82 (m, 16H, Ar-H), 9.75 (s, 2H, NH)	21.3 (Ar-CH_3), 121.5 (C-5), 136.2 (Ar-*C*H=C), 139.8 (Ar-CH=*C*), 156.2 [C=*C*—S(S)], 167.2 (C-4 and C-6), 181.8 (C-2), 185.9 (CO)
8c	6.90 (s, 2H, Ar-CH=C), 7.25–7.79 (m, 16H, Ar-H), 9.79 (s, 2H, NH)	122.2 (C-5), 136.9 (Ar-*C*H=C), 138.4 (Ar-CH=*C*), 157.2 [C=*C*—S(S)], 166.9 (C-4 and C-6), 182.2 (C-2), 185.5 (CO)

acetate/hexane-2:1). The IR spectra were recorded on a Nicolet IR 200 FTIR spectrometer using KBr pellets (ν in cm^{-1}). The ^1H NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a Jeol JNM λ-300 MHz. The ^{13}C NMR spectra were recorded in $CDCl_3$/DMSO-d_6 on a Jeol JNM spectrometer operating at 75.5 MHz. All chemical shifts were reported in δ (ppm) using TMS as an internal standard. The microanalyses were performed on Perkin-Elmer 240C elemental analyzer. All the solvents and reagents were obtained from commercial sources and purified before use if necessary. Column chromatography was performed in silica gel (60–120 mesh).

5-Oxo-2-(2,4,6-trioxopyrimidin-5-ylidene)-[1,3]dithiane-4-carboxylic acid ethyl ester (3)/5-oxo-2-(4,6-dioxo-2-thioxo-pyrimidin-5-ylidene)-[1,3]dithiane-4-carboxylic acid ethyl ester (4): general procedure. To a solution of barbituric acid/thiobarbituric acid (**1**, 1.28 g/**2**, 1.44 g, 10 mmol) dissolved in DMSO (15 mL), sodium hydride (0.46 g, 20 mmol) was added slowly while stirring at room temperature. To this carbon disulfide (1.14 g, 15 mmol) in DMSO (4 mL) was added and the stirring was continued for 1 h. Then ethyl bromoacetate (5.01 g, 30 mmol) was added dropwise to the stirred solution. After stirring at room temperature for 7–8 h, the reaction mixture was diluted with water and extracted with dichloromethane. The organic layer was washed with water followed by brine solution and dried over an. sodium sulfate. Removal of the solvent under vacuum gave **3/4**.

5-[Bis-(2-oxo-2-arylethylsulfanyl)methylene]-pyrimidine-2,4,6-trione (5)/5-[bis-(2-oxo-2-arylethylsulfanyl)methylene]-2-thioxopyrimidine-4,6-dione (6): general procedure. To a solution of barbituric acid/thiobarbituric acid (**1**, 1.28 g/**2**, 1.44 g, 10 mmol) in DMSO (15 mL), sodium hydride (0.46 g, 20 mmol) was added slowly while stirring at room temperature. To this carbon disulfide (1.14 g, 15 mmol) in DMSO (4 mL) was added at the same temperature. The solution was stirred for 1 h. Then, phenacyl bromide (3.98 g, 20 mmol) was added in portions and continued stirring for 10–12 h. The reaction mixture was diluted with water and extracted with dichloromethane. The organic layer was washed with water followed by brine solution and dried over an. sodium sulfate. Removal of the solvent *in vaccuo* gave a solid which was purified by column chromatography and identified as **5/6**.

5-[Bis-(1-aroyl-2-arylvinylsulfanyl)methylene]pyrimidine-2,4,6-trione (7)/5-[bis-(1-aroyl-2-aryl-vinylsulfanyl)methylene]-2-thioxopyrimidine-4,6-dione (8): general procedure.. A mixture of **5/6** (4.40 g/4.56 g, 10 mmol), araldehyde (2.12 g, 20 mmol), benzylamine (0.5 mL), and glacial acetic acid was refluxed for 7–8 h. The reaction mixture was cooled, treated with dry ether (50 mL), and refrigerated overnight. Any product separated was collected by filtration. The filtrate was extracted with ether, washed with sodium bisulfite solution, dilute hydrochloric acid, and finally with water. Evaporation of the ethereal layer gave yellow solid product **7/8** which was recrystallized from 2-propanol.

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