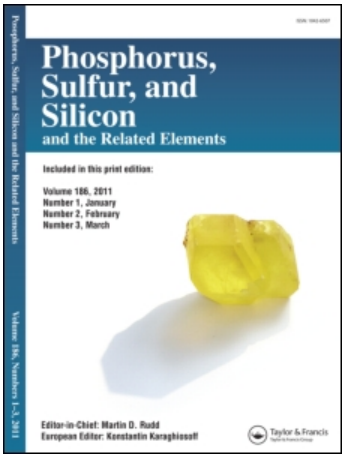

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Synthesis of 3,4-Biheterylthieno[2,3-b]-thiophenes. Part I: Synthesis of 3,4-Bi(1',3',4'-thiadiazolyl-, s-triazolyl-,1',3',4'-thiadiazinyl-, 1',3',4'-triazinyl-, thiazolyl-, 1',3'-thiazinyl- and primidinyl)-thieno[2,3-b]thiophenes

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SYNTHESIS OF 3,4-BIHETERYLTHIENO[2,3-b]-THIOPHENES. PART I: SYNTHESIS OF 3,4-Bi(1′,3′,4′-THIADIAZOLYL-, s-TRIAZOLYL-,1′,3′,4′-THIADIAZINYL-, 1′,3′,4′-TRIAZINYL-, THIAZOLYL-, 1′,3′-THIAZINYL- AND PRIMIDINYL)-THIENO[2,3-b]THIOPHENES

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*3,4-Diamino-2,5-dicarbethoxythieno[2,3-b]thiophene (**1**) was allowed to react with $NaNO_2$ and active methylenes to afford the corresponding azo compounds **2a–c**. Hydrazonyl chloride **2a** was treated with carbon disulfide, phenyl isothiocyanate, benzonitrile, benzyl cyanide, malononitrile, benzalaniline, ethyl mercaptoacetate, and ethyl glycinate to give 1,3,4-thiadiazolyl-, s-triazolyl-, 1,3,4-thiadiazinyl-, 1,3,4-triazinylthieno[2,3-b]thiophenes **3–6** respectively. The reaction of **2b,c** with urea, thiourea, and guanidine afforded pyrimidinyl- and thiazinylazothieno [2,3-b]thiophenes **7–10** respectively. Bithiazolylthieno[2,3-b]thiophenes **11** and **13** were synthesized by treating compound **1** with CS_2 along with halo compounds. The addition of S,S-, N,S-, and N,O-acetals to the Schiff base **14** afforded compounds **15–17** respectively.*

Keywords: 3,4-Bi[(carbethoxychloromethyl-, carbethoxycyanomethyl-, dicyanomethyl-) azo]-2,5-dicarbethoxythieno[2,3-b]thiophene; 3,4-Diamino-2,5-dicabethoxythieno[2,3-b]thiophene; PTC

The chemistry of 1,3-dipolar cycloadditionreaction is of great importance to organic chemists and considerable attention has been paid toward indepth studies of their synthetic potentials.[1,2] In addition to thiophenes[3–6] thiazoles[7–9] and s-triazoles[10–13] exhibit various biological activities. These observations motivated us to continue our previous work[14,15] on the synthesis of polyfused thienothiophenes.

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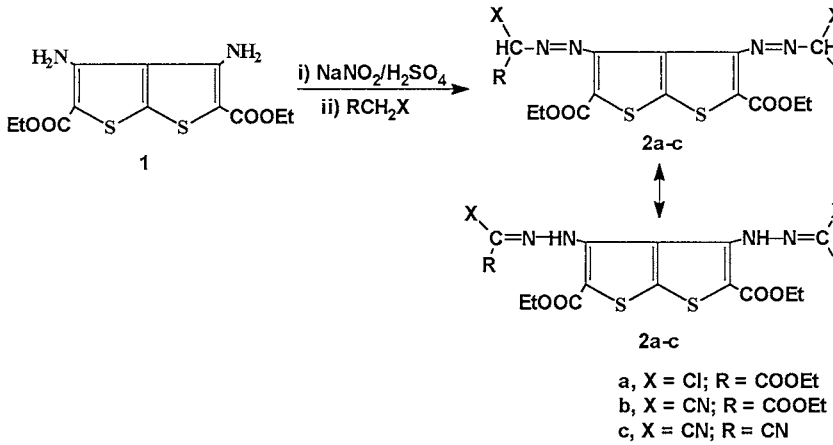
Thus, we report herein the synthesis of heterocyclic compounds containing these rings via the available starting material of 3,4-diamino-2,5-dicarbethoxythieno[2,3-b]thiophene[16] in our laboratory.

RESULTS AND DISCUSSION

3,4-Diamino-2,5-dicarbethoxythieno[2,3-b]thiophene **1** was dissolved in H_2SO_4 and treated with $NaNO_2$ at 0°C to afford the corresponding diazonium sulphate, which then was coupled with ethyl chloroacetate, ethyl cyanoacetate, or malononitrile to give 3,4-bi(carbethoxychloromethylazo)-2,5-dicarbethoxythieno[2,3-b]thiophene **2a**, 3,4-bi(carbethoxycyanomethylazo)-2,5-dicarbethoxythieno[2,3-b]thiophene **2b**, or 3,4-bi(dicyanomethylazo)-2,5-dicarbethoxythieno[2,3-b]thiophene **2c**. These compounds were proved to be good starting materials for the synthesis of 3,4-diheterylthieno[2,3-b]thiophene derivatives (cf. Scheme 1, Table I).



SCHEME 1

It has been found that hydrazonyl chloride **2a** reacts with carbon disulfide and phenyl isothiocyanate as polarophiles in pyridine to yield 3,4-bi[5′-ethoxycarbonyl-1′,3′,4′-thiadiazol-3′-yl-2′-thione(phenylimine)azo]-2,5-dicarbethoxythieno-[2,3-b]thiophene **3a,b** respectively. The reaction pathway is assumed to proceed via the cycloaddition of the polarophiles with the nitrilimine, which is generated from the hydrazonyl chloride in basic medium. The regioselectivity of this reaction on C=S or C=N has been reported,[17] and cycloaddition reaction occurs

TABLE I Analytical and Spectral Data of the New Compounds

Comp. no.	m.p. (°C)[a] cryst. solvent	Yield (%)	Mol. form. (mol. wt.)	Analytical data[b] cal./found				IR (Cm^{-1})[c]	^{1}H-NMR ∂ (ppm)[d]
				C	H	N	S		
2a	151 Benzene	81	$C_{20}H_{22}N_4O_8S_2Cl_2$ (581.43)	41.31 41.01	3.81 3.67	9.63 9.49	11.03 10.71	3311 (NH), 1731–1752 (CO), 1609 (C=N), 741 (C—Cl)	11.2 (br, 2H, 2 NH), 4.4–4.2(q, 8H, $4CH_2$), 1.5–1.1 (m, 12H, $4CH_3$)
2b	173 Ethanol	86	$C_{22}H_{22}N_6O_8S_2$ (562.58)	46.96 46.81	3.94 3.77	14.93 14.71	11.39 11.59	3296 (NH), 2207 (CN) 1728–1755 (CO), 1613 (C=N)	11.9 (s, 2H, 2 NH), 4.4–4.2(q, 8H, $4CH_2$), 1.5–1.1 (m, 12H, $4CH_3$)
2c	192 Ethanol	91	$C_{18}H_{12}N_8O_4S_2$ (468.47)	46.14 46.34	2.58 2.76	23.92 23.79	13.68 13.41	3328 (NH), 2212 (CN), 1731 (CO), 1630(C=N)	9.1 (s, 2H, 2 NH), 4.4–4.2 (q, 4H, $2CH_2$), 1.5–1.1 (m, 6H, $2CH_3$)
3a	197 Ethanol	72	$C_{22}H_{20}N_4O_8S_6$ (660.79)	39.98 39.56	3.05 2.88	8.48 8.21	29.11 28.94	1730–1750(CO), 1617 (C=N), 1454 (C=S)	4.4–4.1 (q, 8H, $4CH_2$), 1.4–1.1 (m, 12 H, $4CH_3$)
3b	231 Dioxan	63	$C_{34}H_{30}N_6O_8S_4$ (778.87)	52.42 52.03	3.88 3.67	10.79 10.47	16.46 16.19	3071 (C-H arom.), 1729–1743 (CO), 1620 (C=N)	7.5–6.9 (m, 10H, arom.), 4.4–4.1 (q, 8H, $4CH_2$), 1.3–1.0 (m, 12H, $4CH_3$)
4a	259 Dioxan	69	$C_{34}H_{30}N_6O_8S_2$ (714.75)	57.13 56.89	4.23 4.11	11.75 11.59	8.97 8.79	3033 (C-H arom.), 1731–1748 (CO), 1613 (C=N)	7.7–7.1 (m, 10 H, arom.), 4.4–4.1 (q, 8H, 4 CH_2), 1.3–1.0 (m, 12H, $4CH_3$)
4b	210–2 Dioxan	80	$C_{36}H_{34}N_6O_8S_2$ (742.80)	58.20 57.99	4.61 4.48	11.31 11.07	8.63 8.55	3033 (C-H arom.), 1722–1745 (CO), 1626(C=N)	7.5–6.9 (m, 10 H, arom.), 4.4–4.1 (q, 8H, 4 CH_2 ester), 3.2 (s, 4H, 2 CH_2), 1.3–1.0 (m, 12H, $4CH_3$)
4c	186 Methanol	77	$C_{26}H_{24}N_8O_8S_2$ (640.63)	48.74 48.44	3.77 3.61	17.49 17.22	10.01 9.87	2211 (CN), 1728–1745 (CO), 1623(C=N)	4.4–4.1 (q, 8H, 4 CH_2 ester), 3.3 (s, 4H, 2 CH_2), 1.3–1.0 (m, 12H, $4CH_3$)
5	216 Chloroform	70	$C_{46}H_{42}N_6O_8S_2$ (870.96)	63.43 63.01	4.86 4.80	9.64 9.49	7.36 7.20	3071 (C=H arom.), 1736–1759 (CO), 1613 (C=N)	7.4–6.8 (m, 20 H, arom.), 6.0 (s, 2 H, 2 CH), 4.4–4.1 (q, 8H, 4 CH_2 ester), 1.3–1.0 (m, 12H, $4CH_3$)
6a	261 Ethanol	83	$C_{24}H_{24}N_4O_{10}S_4$ (656.71)	43.89 43.59	3.68 3.49	8.53 8.37	19.53 19.28	1728–1740 (CO_{ester}), 1683 (CO), 1611(C=N)	4.4–4.1 (q, 8H, 4 CH_2 ester), 3.9(s, 4H, 2 CH_2), 1.3–1.0 (m, 12H, $4CH_3$)
6b	229 Ethanol	61	$C_{24}H_{26}N_6O_{10}S_2$ (622.61)	46.29 45.91	4.21 4.30	13.49 13.68	10.30 10.26	3311 (NH), 1733–1749 (CO_{ester}), 1679 (CO), 1617 (C=N)	9.6 (s, 2H, 2 NH), 4.4–4.1 (q, 8H, 4 $CH_{2\,ester}$), 3.0 (s, 4H, 2 CH_2), 1.3–1.0 (m, 12H, $4CH_3$)

(Continued on next page)

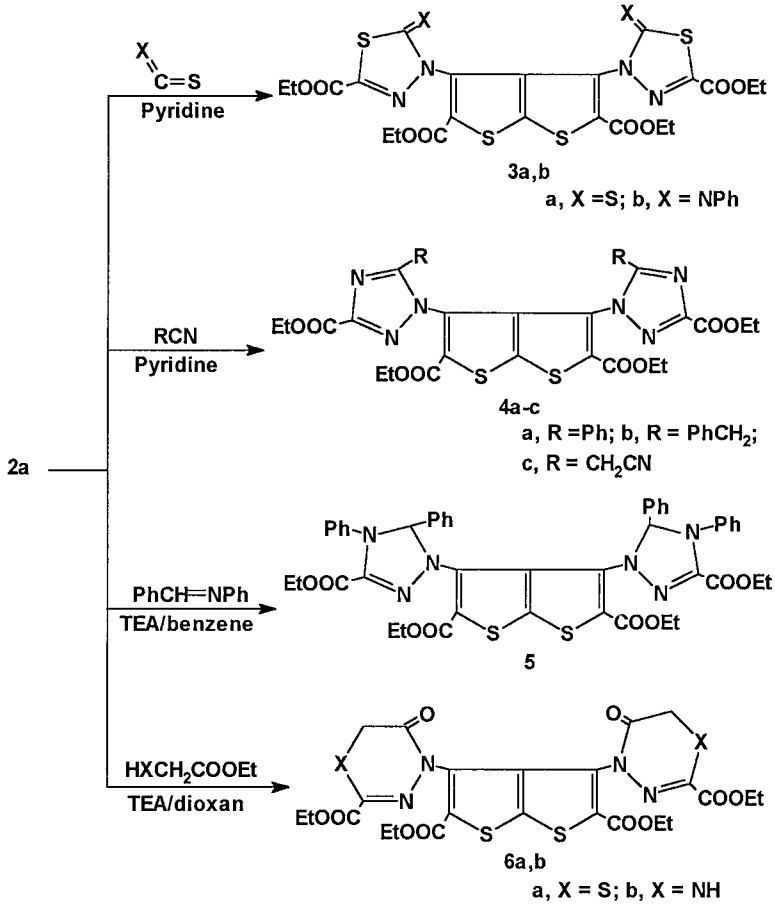
TABLE I Analytical and Spectral Data of the New Compounds *(Continued)*

Comp. no.	m.p. (°C)[a] cryst. solvent	Yield (%)	Mol. form. (mol. wt.)	Analytical data[b] cal./found C	H	N	S	IR (Cm^{-1})[c]	^{1}H-NMR ∂ (ppm)[d]
7	289 Ethanol	59	$C_{20}H_{18}N_{10}O_8S_2$ (590.54)	40.67 40.50	3.07 3.11	23.71 23.50	10.86 10.69	3435, 3341, 3290 (NH, NH_2), 1731, (CO), 1695 (CO), 1589 (N=N)	11 (s, 2H, 2NH), 9.3 (s, 2H, 2NH), 5.0–4.7 (br, 4H, $2NH_2$), 4.4–4.1 (q, 4H, $2CH_2$), 1.3–1.0 (m, 6H, $2CH_3$)
8a	307 Ethanol	68	$C_{20}H_{18}N_{10}O_6S_4$ (622.67)	38.57 38.48	2.91 2.77	22.49 22.32	20.59 20.38	3449, 3350, 3291 ($2NH_2$), 1738 (CO), 1688 (CO), 1603 (N=N)	5.5–5.2 (br, 4H, $2NH_2$), 4.8–4.5 (br, 4H, $2NH_2$), 4.4–4.1 (q, 4H, $2CH_2$), 1.3–1.0 (m, 6H, $2CH_3$)
8b	273–5 Ethanol	72	$C_{20}H_{20}N_{12}O_6S_2$ (588.57)	40.81 40.61	3.42 3.27	28.55 28.81	10.89 10.70	3449, 3350, 3310, 3279 (NH, NH_2), 1730 (CO), 1689 (CO), 1611 (N=N)	9.3 (s, 2H, 2 NH), 5.4–5.1 (br, 4H, $2NH_2$), 4.8–4.5 (br, 4H, $2NH_2$), 4.4–4.1 (q, 4H, $2CH_2$), 1.3–1.0 (m, 6H, $2CH_3$)
9a	311–313 Dioxan	55	$C_{20}H_{20}N_{12}O_6S_2$ (588.57)	40.81 40.55	3.42 3.29	28.55 28.39	10.89 10.73	3431, 3329, 3300, 3211 (NH, H_2), 1736 (CO), 1695 (CO), 587 (N=N)	9.9 (s, 2H, 2NH), 5.4–4.8 (br, 8H, 4 NH_2), 4.4–4.1 (q, 4H, $2CH_2$), 1.3–1.0 (m, 6H, $2CH_3$)
9b	297–299 Dioxan	59	$C_{20}H_{20}N_{12}O_4S_4$ (620.70)	38.70 38.92	3.24 3.29	27.08 27.49	20.66 20.73	3300, 3279, 3232, 3198 (NH, H_2), 1732 (CO), 1591 (N=N)	10.7 (s, 2H, 2NH), 5.5–4.8 (br, 8H, 4 NH_2), 4.4–4.1 (q, 4H, $2CH_2$), 1.3–1.0 (m, 6H, $2CH_3$),
10	286–288 Ethanol	67	$C_{20}H_{22}N_{14}O_4S_2$ (586.60)	40.94 40.59	3.78 3.61	33.43 33.59	10.93 10.73	3446, 3339, 3317, 3293 (NH_2), 1730 (CO), 1601 (N=N)	5.5–5.0 (br, 8H, 4 NH_2), 4.8–4.6 (br, 4H, $2NH_2$), 4.4–4.1 (q, 4H, $2CH_2$), 1.3–1.0 (m, 6H, $2CH_3$)
11a	311 $CHCl_3$	66	$C_{18}H_{16}N_4O_4S_6$ (544.72)	39.68 39.29	2.96 2.87	10.28 10.03	35.31 35.11	3211, 3120 (NH_2), 1740 (CO), 1433(CS)	6.3 (s, 2H,2=CH), 6.0–5.5 (br, 4H, $2NH_2$), 4.4–4.1 (q, 4H, $2CH_2$), 1.3–1.0 (m, 6H, $2CH_3$)
11b	266 Ethanol	50	$C_{20}H_{14}N_6O_4S_6$ (594.73)	40.38 40.03	2.37 2.21	14.13 13.98	32.34 32.11	3321, 3200 (NH_2), 2100 (CN), 1732 (CO), 1433 (CS)	6.1–5.4 (br, 4H, $2NH_2$), 4.4–4.1 (q, 4H, $2CH_2$), 1.3–1.0 (m, 6H, $2CH_3$)
11c	288 Dioxan	70	$C_{30}H_{22}N_2O_4S_6$ (666.87)	54.02 53.79	3.32 3.17	4.20 4.02	28.84 28.59	1740 (CO), 1432 (CS)	7.8–7.0 (m, 10H, arom), 6.0 (s, 2H, 2=CH) 5.8–5.5 (br, 4H, $2NH_2$), 4.4–4.1 (q, 4H, $2CH_2$), 1.3–1.0 (m, 6H, $2CH_3$)

12a	229 Ethanol	61	$C_{22}H_{26}N_2O_8S_6$ (638.82)	41.36 41.55	4.10 4.24	4.38 4.55	30.11 30.33	3211 (NH), 1744–1730 (CO), 1400 (CS)	9.6 (s, 2H, 2 NH), 4.4–4.1 (q, 8H, 4 $CH_{2\,ester}$), 4.0 (s, 4H, 2 CH_2), 1.3–1.0 (m, 12H, 4CH_3)
12b	289 Ethanol	52	$C_{28}H_{34}N_2O_{12}S_6$ (782.95)	42.95 42.66	4.37 3.11	3.57 3.23	24.57 24.77	3200 (NH), 1740–1720 (CO), 1420 (CS)	9.3 (s, 2H, 2NH), 4.4–4.1 (m, 12H, 6$CH_{2\,ester}$), 3.9 (s, 2H, 2CH), 1.3–1.0 (m, 18H, 6CH_3)
13a	307 Ethanol	68	$C_{18}H_{14}N_2O_6S_6$ (546.69)	39.54 39.77	2.58 2.77	5.12 5.33	35.19 35.31	3112 (NH), 1750 1734 (CO), 1422 (CS)	4.4–4.1 (m, 4H, 2 CH_2 ester), 4.0 (s, 4H, 2CH_2), 1.6–1.0 (m, 6H, 2CH_3)
13b	273–275 Ethanol	70	$C_{24}H_{22}N_2O_{10}S_6$ (690.81)	41.72 41.55	3.21 3.37	4.05 4.22	27.85 27.66	1750–1720 (CO), 1420 (CS)	4.4–4.1 (m, 8H, 4CH_2 ester), 4.0 (s, 2H, 2 CH), 1.5–1.0 (m, 12H, 4CH_3)
14	311–313 Dioxan	52	$C_{26}H_{20}N_4O_8S_2$ (580.57)	53.78 53.55	3.47 3.29	9.65 9.59	11.04 11.22	1741 (CO), 1600 (C=N)	9.9 (s, 2H, 2=CH), 8.0–7.5 (m, 8H, arom.), 4.4–4.1 (q, 4H, 2CH_2), 1.3–1.0 (t, 6H, 2CH_3)
15	297–299 Dioxan	58	$C_{34}H_{24}N_8O_8S_6$ (864.97)	47.20 47.44	2.79 2.55	12.95 12.80	22.24 22.44	3211, 3143 (NH_2), 2134 (CN), 1745 (CO), 1432 (CS)	8.1–7.5 (m, 8H, arom.), 6.5 (s, 2H, 2CH), 5.7–5.4 (br, 4H, 2NH_2), 4.4–4.1 (q, 4H, 2CH_2), 1.3–1.0 (m, 6H, 2CH_3)
16a	286–288 Ethanol	63	$C_{46}H_{34}N_{10}O_8S_4$ (983.05)	56.19 56.33	3.48 3.21	14.24 14.00	13.04 13.22	3211, 3143 (NH_2), 2114 (CN), 1745 (CO)	8.1–7.2 (m, 18H, arom.), 6.5 (s, 2H, 2CH), 5.4–5.0 (br, 4H, 2NH_2), 4.4–4.1 (q, 4H, 2CH_2), 1.4–1.1 (m, 6H, 2CH_3)
16b	188 Ethanol	94	$C_{46}H_{34}N_{10}O_{10}S_2$ (950.93)	58.09 58.22	3.60 3.77	14.73 14.60	6.74 6.66	3211, 3143 (NH_2), 2100 (CN), 1745 (CO)	8.5–7.0 (m, 18H, arom.), 6.4 (s, 2H, 2CH), 5.6–5.3 (br, 4H, 2NH_2), 4.4–4.1 (q, 4H, 2CH_2), 1.5–1.0 (m, 6H, 2CH_3)
17a	308 Dioxan	90	$C_{46}H_{34}N_{10}O_8S_4$ (983.05)	56.19 56.33	3.48 3.21	14.24 14.00	13.04 13.22	3211, 3143 (NH_2), 2120 (CN), 1745 (CO), 1433 (CS)	8.8–7.2 (m, 18H, arom.), 6.5 (s, 2H, 2CH), 5.4–5.0 (br, 4H, 2NH_2), 4.4–4.0 (q, 4H, 2CH_2), 1.5–1.2 (m, 6H, 2CH_3)
17b	277 Ethanol	79	$C_{46}H_{34}N_{10}O_{10}S_2$ (950.93)	58.09 57.90	3.60 3.47	14.73 14.82	6.74 6.85	3211, 3143 (NH_2), 2200 (CN), 1745 (CO_{ester}), 1690 (CO)	8.8–7.2 (m, 18H, arom.), 6.0 (s, 2H, 2CH), 5.8–5.5 (br, 4H, 2NH_2), 4.3–4.0 (q, 4H, 2CH_2), 1.5–1.0 (m, 6H, 2CH_3)

[a]Uncorrected.
[b]Satisfactory microanalysis obtained C; ±0.41, H; ±0.3, N; ±0.3, S; ±0. 3.
[c]Measured by Nicolet FT-IR 710 spectrophotometer.
[d]Measured by a Varian EM 360 L spectrometer at 60 MHZ using TMS as internal standard and DMSO as a solvent.

on C=S to yield the thiadiazole structure and not the isothermic structure 1,2,4-triazole (cf. Scheme 2, Table I).



SCHEME 2

The reaction of hydrazonyl chloride **2a** with active nitriles, namely benzonitrile, benzyl cyanide, and malononitrile, using pyridine as a solvent affords 3,4-bi[(3′-carbethoxy-5′-phenyl(benzyl, cyanomethyl)-1′,2′,4′-triazol-1′-yl)azo]-2,5-dicarbethoxythieno[2,3-b]thiophene **4a–c** respectively. The formation of these compounds is assumed to proceed via the dipolar cycloaddition of the nitrileimine to the cyano group.

Similarly, treatment of compound **2a** with benzalaniline in presence of triethylamine gives 3,4-bi[(3′-carbethoxy-4′,5′-diphenyl-1′,2′,4′-triazol-1′-yl)azo]-2,5-dicarbethoxythieno[2,3-b]thiophene **5**. The

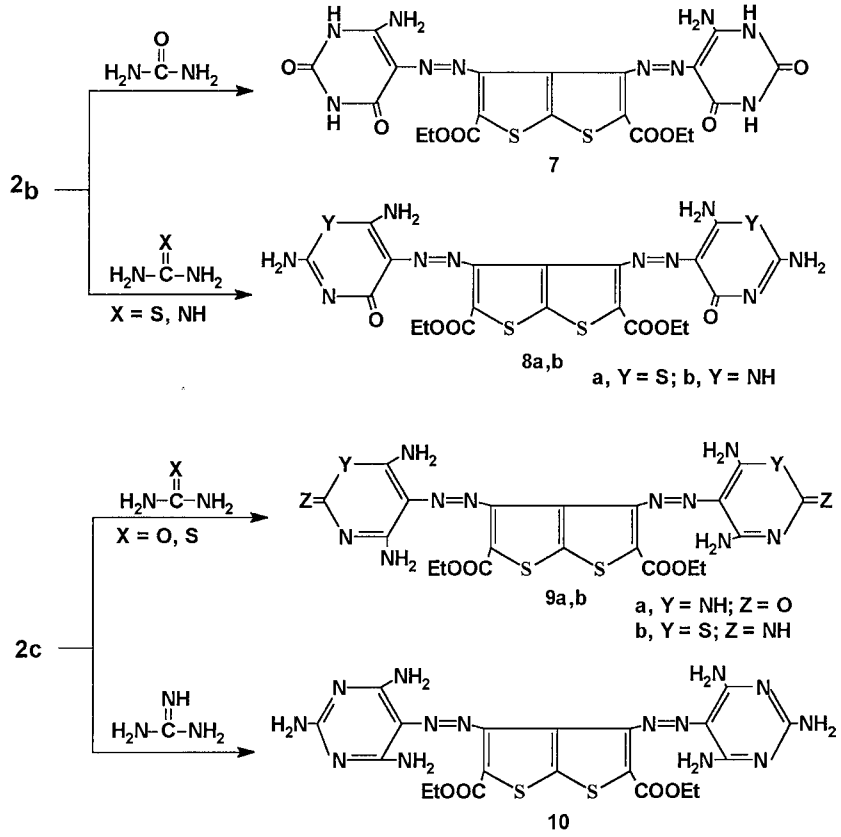
reaction mechanism is suggested to proceed via the dipolar cycloaddition of the formed nitrileimine to the C=N (cf. Scheme 2, Table I).

Moreover, on treating compound **2a** with ethyl mercaptoacetate and ethyl glycinate in presence of triethylamine, 3,4-bi[(2′-ethoxycarbonyl-5′,6′-dihydro-1′,3′,4′-thiadiazin-4′-yl-5′-one)azo]-2,5-diethoxycarbonylthieno[2,3-b]thiophene **6a** and 3,4-bi[(2′-ethoxycarbonyl-1′,5′,6′-trihydro-1′,3′,4′-triazin-4′-yl-6′-one)azo]-2,5-diethoxycarbonylthieno-[2,3-b] thiophene **6b**, respectively, are obtained. The reaction pathway is assumed to proceed via the addition of the SH or NH_2 group to the nitrileimine followed by intramolecular cyclization with elimination of ethanol molecule.

Also, the reacion of compounds **2b,c** with urea, thiourea, and guanidine was investigated. Treatment of compound **2b** with these reagents affords 3,4-bi[(6′-amino-1′,2′,3′,4′-tetrahydroprimidin-5′-yl-2′,4′-dione) azo]-2,5-diethoxycarbonylthieno[2,3-b]thiophene **7**, 3,4-bi[(2′,6′-diamino-1′,3′,4′-thiazin-5′-yl-4′-one)azo]-2,5-diethoxycarbonylthieno[2,3-b]thiophene **8a**, and 3,4-bi[(2′,6′-diamino-1′ (H)-primidin-5′-yl-4′-one)azo]-2,5-diethoxycarbonylthieno[2,3-b]thiophene **8b** respectively. The formation of these compounds is assumed to be via the addition of the NH_2 group or SH group to the cyano group followed by cyclization with elimination of ethanol molecule.

On the other hand, the reaction of compound **2c** with urea, thiourea, and guanidine yields 3,4-bi[(4′,6′-diamino-1′-3′-oxazin-5′-yl-2′-one)azo]-2,5-diethoxycarbonylthieno[2,3-b]thiophene **9a**, 3,4-bi[(4′,6′-diamino-2′-imino-1′,3′-thiazin-5′-yl)azo]-2,5-diethoxycarbonylthieno[2,3-b]thiopophene **9b**, and 3,4-bi[(2′,4′,6′-triaminoprimidin-5′-yl)azo]-2,5-diethoxycarbonylthieno[2,3-b]thiophene **10** respectively. The formation mechanism is assumed to proceed through the addition of the NH_2 group or SH group to the cyano group followed by cyclization via the addition of the second NH_2 group to the other cyano group (cf. Scheme 3, Table I).

Bithiazolylthieno[2,3-b]thiophene derivatives **11a–c** and **13a–c** are obtained from the reaction of compound **1** with CS_2 along with halo compounds namely chloroacetonitrile, bromomalononitrile, phenacyl bromide, ethyl chloroacetate, and diethyl bromomalonate in presence of KOH using DMF as a solvent. The reaction pathway is suggested to proceed via the addition of the NH_2 of compound **1** to CS_2, forming the corresponding potassium dithiocarbamate which reacts with the halo compound to afford the corresponding dithioester. This dithioester undergoes intramolecular cyclization through the addition of the NH group to the cyano group to give compounds **11a,b** or elimination of either water molecule to yield compound **11c** or ethanol molecule to afford compounds **13a,b**.



SCHEME 3

On treating compound **1** with *p*-nitrobenzaldehyde in a mixture of acetic anhydride and acetic acid, the corresponding Schiff base **14** is obtained. The addition of S-,S-, N-,S-, and N-,O- acetals to compound **14** was investigated. The reaction of compound **14** with S-,S-acetal obtained by treating malononitrile with CS_2 using solid-liquid phase-transfer catalysis (PTC) technique [dioxan/K_2CO_3/tetrabutylammonium bromide (TBAB)] affords 3,4-bi(4′-amino-5′-cyano-2′,6′-dihydro-2′-*p*-nitrophenyl-1′,3′-thiazin-1′-yl-6′-thione)-2,5-dicarbethoxythieno[2,3-b]thiophene **15**. Treatment of compound **14** with N-,S-acetal synthesized from the reaction of malononitrile with phenyl isothiocyanate under the same experimental conditions yields 3,4-bi(4′-amino-5′-cyano-6′-phenylimino-2′-*p*-nitrophenyl-1′,3′-thiazin-3′-yl)-2,5-dicarbethoxythieno[2,3-b]thiophene **16a** and 3,4-bi (4′-amino-5′-cyano-2′-*p*-nitrophenyl-1′-phenylprimidin-3′-yl-6′-thione)-2,5-dicarbethoxythieno[2,3-b]thiophene **17a**. Also, the reaction of compound

14 with N-,O- acetal obtained by treating malononitrile with phenyl isocyanate using the same PTC technique gives 3,4-bi(4′-amino-5′-cyano-6′-phenylimino-2′-*p*-nitrophenyl-1′,3′-oxazin-3′-yl)-2,5-dicarbethoxythieno[2,3-b]thiophene **16b** and 3,4-bi(4′-amino-5′-cyano-2′-*p*-nitrophenyl-1′-phenylprimidin-3′-yl-6′-thione)-2,5-dicarbethoxythieno[2,3-b]thiophene **17b**. The reaction mechanism was postulated to proceed through the nucleophilic attack of the SH, NH, or OH group of the S,S-, N,S- or N,O-acetal at the active C=N followed by cyclization through the addition of the NH group to the CN group (cf. Scheme 4, Table I).

EXPERIMENTAL

Synthesis of Compounds 2a–c: General Procedure

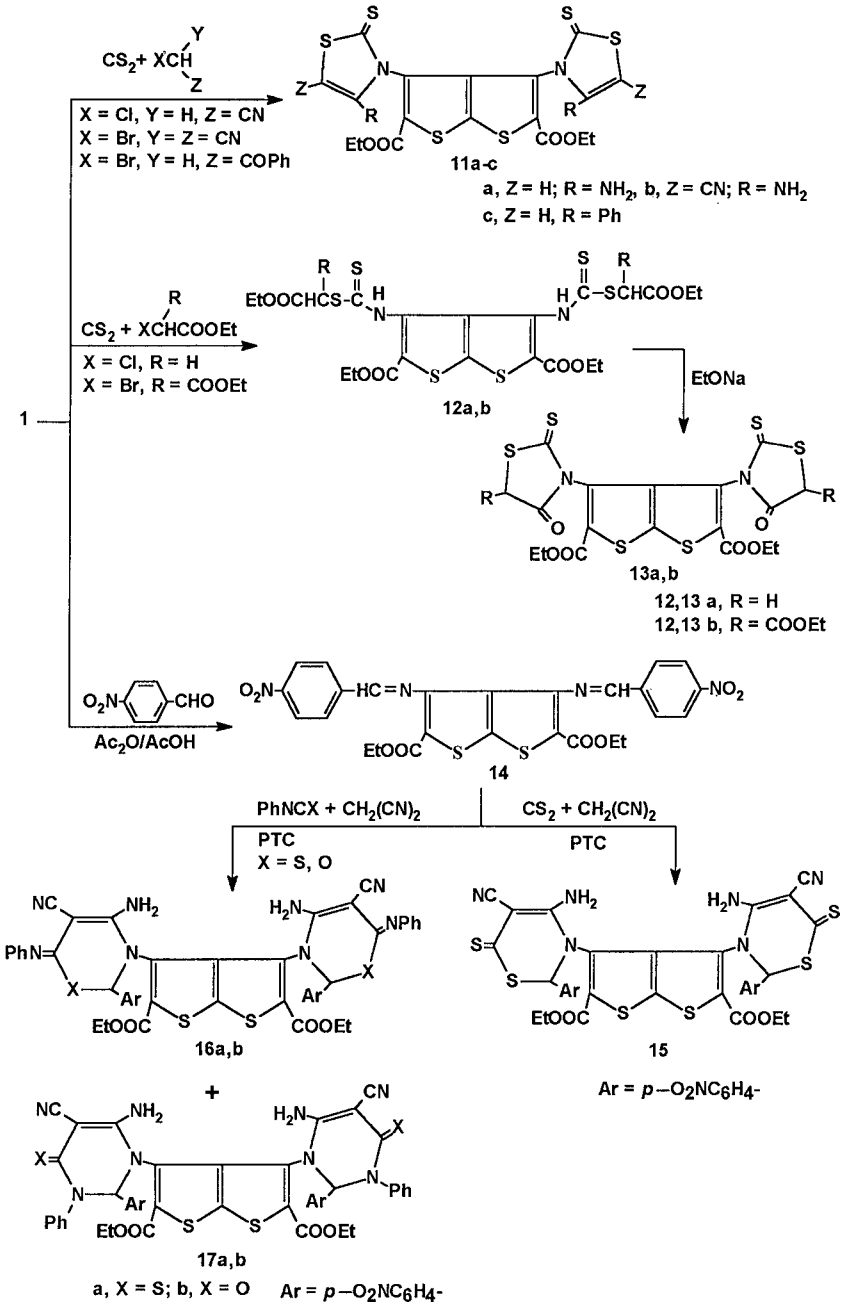
A solution of compound **1** (1.96 g, 0.01 mmol) in conc. H_2SO_4 (10 ml) was cooled in an ice bath at 0–5°C, whereupon a cold solution of sodium nitrite (1.4 g, 0.02 mmol) in conc. H_2SO_4 (5 ml) was added dropwise during stirring. The reaction mixture was set aside for 30 min at 5°C, and then treated with a stirred solution of (0.02 mmol) of ethyl chloroacetate (2.36 ml), ethyl cyanoacetate (2.26 ml), or malononitrile (1.32 g) at the same temperature in the presence of sodium acetate (3.5 g, 0.04 mmol). The reaction mixture was stirred for 1 h at room temperature. The separated solid was collected by filtration and crystallized from a suitable solvent (cf. Table I).

Synthesis of Compounds 3a,b and 4a–c: General Procedure

A mixture of compound **2a** (2.9 g, 0.005 mmol) and (0.01 mmol) of carbondisulfide (0.76 ml), phenyl isothiocyanate (1.19 ml), benzonitrile (1.03 ml), benzyl cyanide (1.17 ml), or malononitrile (0.66 ml) was refluxed in dry pyridine (50 ml) for 3 h. The reaction mixture was cooled and poured into ice/HCl mixture. The resulting solid was collected by filtration and crystallized from a suitable solvent (cf. Table I).

Synthesis of Compound 5

To a solution of compound **2a** (2.9 g, 0.005 mmol) and benzalaniline (1.81 g, 0.01 mmol) in dry benzene (80 ml) was added TEA (1 ml, 0.01 mmol). The reaction mixture was refluxed for 4 h and evaporated in vacuo. The residual solid was washed with water and crystallized from a proper solvent (cf. Table I).



SCHEME 4

Synthesis of Compounds 6a,b: General Procedure

To a solution of compound **2a** (2.9 g, 0.005 mmol) and (0.01 mmol) of ethyl mercaptoacetate (1.1 ml) or ethyl glycinate (1.4 g) in dry dioxan (70 ml) was added TEA (2 ml, 0.02 mmol), The reaction mixture was refluxed for 5 h and evaporated in vacuo. The residual solid was washed with water and crystallized from a suitable solvent (cf. Table I).

Synthesis of Compounds 7–10: General Procedure

To a mixture of (0.005 mmol) of compound **2b** (2.8 g) or **2c** (2.34 g), the proper amino compound (0.01 mmol) (urea 0.06 g, thiourea 0.76 g, or guanidine 0.96 g) and absolute ethanol (50 ml), sodium ethoxide (0.23 g of Na in 8 ml ethanol) was added. The reaction mixture was refluxed for 7 h, concentrated, and cooled. The separated solid was filtered off, washed with water, and crystallized from a proper solvent (cf. Table I).

Synthesis of Compounds 11a–c and 12a,b: General Procedure

To a solution of compound **1** (1.96 g, 0.01 mmol) in DMF (30 ml), a solution of KOH (1.12 g, 0.02 mmol) in 10 ml H_2O was added followed by addition of CS_2 (1.32 ml, 0.02 mmol). The reaction mixture was refluxed in a water bath at 80°C for 2 h and left to cool to 20°C. To the reaction mixture (0.02 mmol) of the appropriate halogen compound chloroacetonitrile (1.26 ml), bromomalononitrile (2.9 g), phenacyl bromide (3.98 g), ethyl chloroacetate (2.36 ml), and diethyl bromomalonate (4.70 ml) was added. The reaction mixture was stirred at 20°C for 1 h and the solid product formed upon pouring onto ice containing few drops of hydrochloric acid (pH = 6), was collected by filtration, and crystallized from the suitable solvent (cf. Table I).

Synthesis of Compounds 13a,b: General Procedure

A solution of (0.005 mmol) of compound **12a** (3.19 g) or **12b** (3.91 g) in ethanol (50 ml) contaning sodium ethoxide (0.23 g of Na in 10 ml ethanol) was refluxed for 3 h, the separated product formed upon pouring onto ice/water containing hydrochloric acid (pH = 6) was collected by filtration and crystallized from a proper solvent (cf. Table I).

Synthesis of Compound 14

To a solution of compound **1** (1.96 g, 0.01 mmol) in glacial acetic acid (20 ml), and acetic anhydride (10 ml), *p*-nitrobenzaldehyde (3.02 g,

0.02 mmol) was added. The reaction mixture was treated with sodium acetate (3 g, 0.03 mmol), refluxed for 5 h, evaporated in vacuo and the residual solid was washed with water, dried, and crystallized from ethanol.

Synthesis of Compounds 15, 16a,b, and 17a,b: General Procedure

To a suspension of anhydrous potassium carbonate (3 g) in dry dioxan (20 ml), malononitrile (0.66 g, 0.01 mmol), and CS_2 (0.76 ml, 0.01 mmol), PhNCO (1.1 ml) or PhNCS (1.2 ml) was added. The reaction mixture was treated with a catalytic amount of TBAB and vigorously stirred at 30°C for 30 min. After the addition of compound **14** (2.9 g, 0.005 mmol), the reaction mixture was stirred at 60°C for 3 h (TLC). The reaction mixture was filtered off and the filtrate was evaporated in vacuo. The residual solid was washed with water and crystallized from the appropriate solvent, where compounds **15** and **16a,b** were obtained (cf. Table I). The solid potassium carbonate was dissolved in distilled water (50 ml). The separated solid was collected by filtration and crystallized from the proper solvent, where compounds **17a,b** were obtained. (cf. Table I).

REFERENCES

[1] A. Padwa, *Angew Chem. Int. Ed. Engl.*, **15,** 123 (1976).
[2] A. Padwa (Ed.), *1,3-Dipolar Cycloaddition Chemistry* (John Wiley & Sons, New York, 1984), vols. 1 and 2.
[3] J. K. Chakrabarti, L. Horsman, T. M. Hotten, I. A. Pullar, D. E. Tupper, and F. C. Wright, *J. Med. Chem.*, **23,** 878 (1980).
[4] V. J. Ram, H. K. Pandey, and A. J. Vlietinck, *J. Heterocyclic Chem.*, **18,** 1277 (1981).
[5] A. E. Abdel-Rahman, I. M. A. Awad, and E. A. Bakhite, *Phosphorus, Sulfur, and Silicon*, **60,** 189 (1991).
[6] I. M. A. Awad, A. E. Abdel-Rahman, and E. A. Bakhite, *Coll. Czch. Chem. Commun.*, **56,** 1749 (1991).
[7] S. K. Mallick, A. R. Martin, and R. G. Lingard, *J. Med. Chem.*, **14,** 53 (1971).
[8] A. Andolsek, B. Stanoumik, M. Tisler, M. Likar, and P. Schauer, *J. Med. Chem.*, **14,** 53 (1971).
[9] W. H. Burton, W. L. Budde, and C. C. Cheng, *J. Med. Chem.*, **13,** 1009 (1970).
[10] H. N. Dogan, S. Buyuktimkin, S. Rollas, E. Yemni, and A. Cevikba, *Farmaco*, **52,** 565 (1997).
[11] A. M. Dhiman, K. N. Wadodkar, and S. D. Patil, *Indian J. Chem.*, **40B(7),** 636 (2001).
[12] A. M. Dhiman, K. N. Wadodkar, and S. D. Patil, *Indian J. Chem.*, **40B(7),** 640 (2001).
[13] U. V. Laddi, M. B. Talawar, S. R. Desai, R. S. Bennur, and S. C. Bennur, *Indian J. Chem.*, **40B(7),** 828 (2001).

[14] A. Khodairy and H. Abdel-Ghany, *Phosphorus, Sulfur, and Silicon*, **162,** 259 (2000).
[15] H. Abdel-Ghany and A. Khodairy, *Phosphorus, Sulfur, and Silicon*, **166,** 45 (2000).
[16] A. K. El-Shafei, H. A. Abdel-Ghany, A. A. Sultan, and A. M. M. El-Saghier, *Phosphorus, Sulfur, and Silicon*, **73,** 15 (1992).
[17] M. K. A. Ibrahim, A. H. H. El-Ghandour, S. M. M. El-Shikh, and S. A. Mishael, *Indian J. of Chemistry*, **36B,** 91 (1997).