Application of the Thorpe—Ziegler reaction for the synthesis of functionalized thiophenes, thienopyrimidines, and thienotriazines

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Approaches to the synthesis of 3-aminothiophene-2,4-dicarboxylic acid derivatives and to their conversions into thieno[3,4-*d*]pyrimidines, thieno[3,4-*d*]-1,2,3-triazines, and thieno[3,2-*d*]pyrimidines are developed.

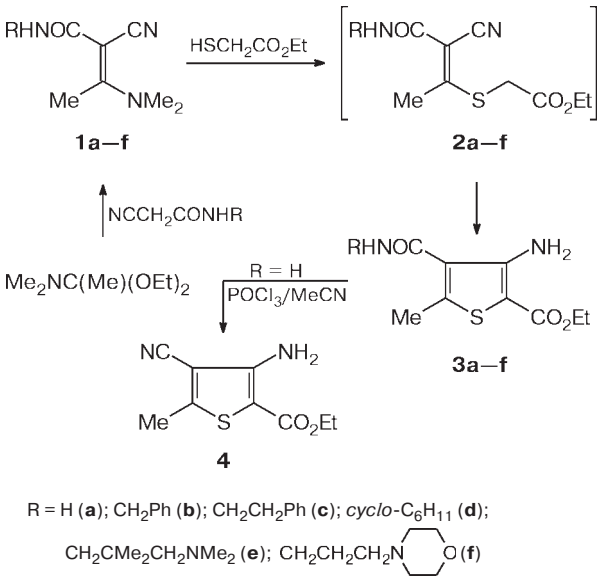
Key words: enamines, the Thorpe—Ziegler cyclization, thiophenes, pyrimidines, 1,2,3-triazines.

The Thorpe—Ziegler reaction is one of the most promising lines in the chemistry of five-membered heterocycles, which makes it possible to obtain variously substituted 3-aminofurans, -pyrroles, and -thiophenes.[1,2] Recently,[3] we have used this reaction to convert β-enamino nitriles into 3-aminopyrrole derivatives. The goal of the present work was the search for a general approach to the synthesis of functionalized 3-aminothiophenes and studies of their transformations into fused heterocyclic systems containing a thiophene fragment.

Results and Discussion

2-Cyano-3-dimethylaminobut-2-enamide derivatives **1a—f** were chosen as the starting compounds. These are obtained by reactions of the corresponding cyanoacetamides with *N*,*N*-dimethylacetamide diethyl acetal. There are some data indicating that (1-ethoxyethylidene)malononitrile[4] and enamino ketones of the 3-[(dimethylamino)methylidene]tetrahydrofuran-2-one series[5] react with alkanethiols to give the corresponding substituted 2-alkylthio olefins. Based on these data, we studied the reactions of compounds **1a—f** with ethyl thioglycolate in the presence of K_2CO_3, which probably occur *via* intermediates **2a—f**. The latter undergo the Thorpe—Ziegler cyclization into ethyl 3-amino-4-*N*-R-carbamoyl-5-methylthiophene-2-carboxylates **3a—f** (Scheme 1). The first member of this series, namely, compound **3a**, is smoothly dehydrated upon heating with $POCl_3$ in MeCN to form the known[4] ethyl 3-amino-4-cyano-5-methylthiophene-2-carboxylate (**4**).

Scheme 1



R = H (**a**); CH_2Ph (**b**); CH_2CH_2Ph (**c**); *cyclo*-C_6H_{11} (**d**); $CH_2CMe_2CH_2NMe_2$ (**e**); $CH_2CH_2CH_2N\langle O\rangle$ (**f**)

Derivatives of 3-aminothiophene-2,4-dicarboxylic acid **3a—f** are very interesting as precursors of fused heterocycles. Thus with HCO_2H as a one-carbon component for the closure of the pyrimidine ring, one can obtain substituted ethyl 3,4-dihydrothieno[3,4-*d*]pyrimidine-7-carboxylates **5a—d** from thiophenes **3a,b,d,f** (Scheme 2). Compounds **5b,c,e** were also synthesized by alkylation of thienopyrimidine **5a**. The structures of *N*-alkyl derivatives **5b,c** were confirmed by their independent synthesis from compounds **3b,d** and HCO_2H.

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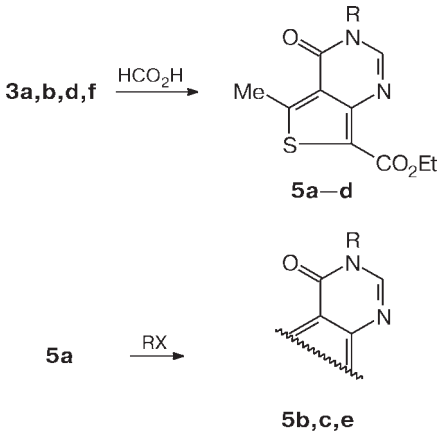
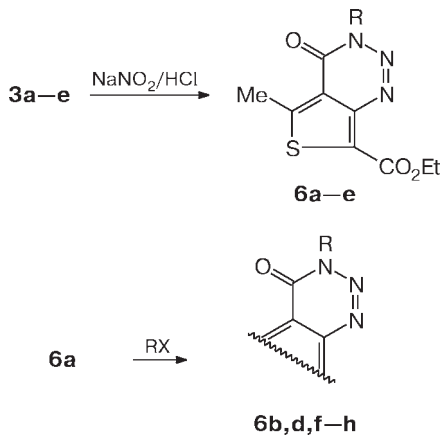
Scheme 2



5: R = H (**a**); CH_2Ph (**b**); *cyclo*-C_6H_{11} (**c**); $CH_2CH_2CH_2N\langle\rangle O$ (**d**); CH_2COPh (**e**)

Scheme 3



6: R = H (**a**); CH_2Ph (**b**); CH_2CH_2Ph (**c**); *cyclo*-C_6H_{11} (**d**); $CH_2CMe_2CH_2NMe_2$ (**e**); CH_2CO-1-Ad (**f**); $CH_2COC_6H_4$-*p*-Br (**g**); $CH_2CONHC_6H_4$-*p*-Me (**h**)

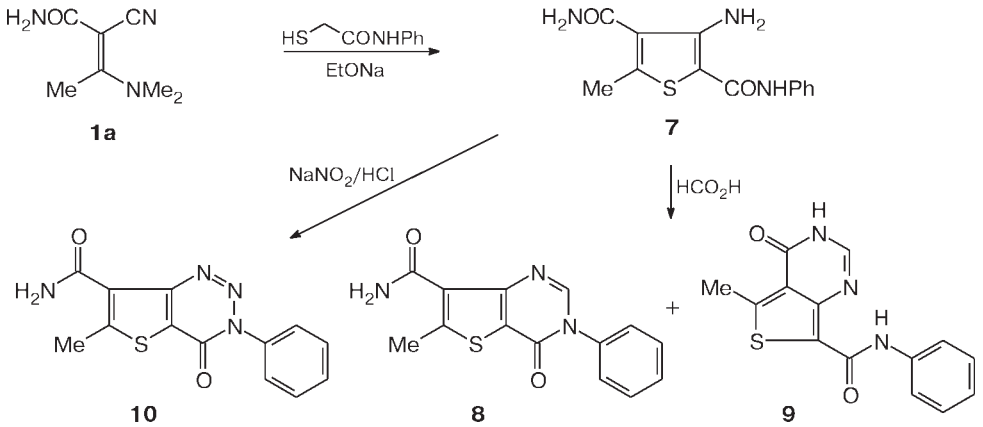
Diazotization of thiophenes **3a—e** ($NaNO_2$, AcOH, HCl, 20 °C) yielded thieno[3,4-*d*]-1,2,3-triazines **6a—e** (Scheme 3). Bicyclic compound **6a** was alkylated in DMF in the presence of K_2CO_3 to give derivatives **6b,d,f—h**.

Compounds **6b,d** obtained by both methods are identical, which suggests the selective *N*-alkylation of thienotriazine **6a**.

The reaction of enamine **1a** with thioglycolanilide in the presence of EtONa afforded 3-aminothiophene **7** containing two carbamoyl fragments (Scheme 4). To compare their reactivities in closing the pyrimidine ring, we made to react compound **7** with HCO_2H. The reaction products were 6-methyl-4-oxo-3-phenyl-3,4-dihydrothieno[3,2-*d*]pyrimidine-7-carboxamide (**8**) and 5-methyl-4-oxo-3,4-dihydrothieno[3,4-*d*]pyrimidine-7-carboxanilide (**9**) in 81 and 7% yields, respectively. The ^1H NMR spectrum of thieno[3,2-*d*]pyrimidine **8** contains two symmetrically broadened singlets of equal intensity at δ 7.52 and 8.56 for the amido group, whereas isomeric thieno[3,4-*d*]pyrimidine **9** gives differently shaped singlets at δ 10.98 (narrow signal) and 12.10 (strongly broadened signal) for the NH protons of the pyrimidine fragment and the CONHPh group, respectively.

The structures of compounds **8** and **9** were confirmed by ^{13}C NMR spectroscopy using heteronuclear resonance technique. Signals for the C=O groups in isomers **8** and **9** differ in shape. Thus a signal at δ 163.4 for the C(7′) atom in compound **8** is significantly broadened, probably, because of the conformational mobility of its amide fragment. A signal for the C(4) atom appears at δ 155.5 (d, $^3J_{C(4),C(2)H}$ = 5.8 Hz). The ^{13}C NMR spectrum of compound **9** shows a narrow signal at δ 159.1 for the C(7′) atom and a doublet at δ 158.4 for the C(4) atom ($^3J_{C(4),C(2)H}$ = 6.1 Hz).

Scheme 4



In the spectrum of compound **9**, a signal for the C atom of the methyl group is substantially shifted upfield (δ 16.0) compared to the analogous signal for bicycle **8** (δ 26.9). This shift is due to a "steric compression" effect in compound **9** (the so-called "γ-*gauche* effect"[6] between the MeC(5) and C(4)=O groups), which is absent for the analogous MeC(6) and C(7′)=O groups in compound **8**. This effect is also observed for the C(4) atom in compound **9** (δ 158.4), as distinct from the C(7′) atom in compound **8** (δ 163.4, $\Delta\delta = \delta_{C(7'),\mathbf{8}} - \delta_{C(4),\mathbf{9}} = 5$). These data indicate that the C(4) atom of the carbonyl group in thienopyrimidine **9** belongs to the cyclic fragment and is close to the Me group in the thiophene ring, whereas it is the C(6)Me and $CONH_2$ groups that are close to each other in bicycle **8**. Hence, one can conclude that bicycles **8** and **9** contain [3,2-*d*]- and [3,4-*d*]-fused rings, respectively.

Thus, the cyclization of compound **7** mainly involves the amide fragment in position 2 of the thiophene ring. Such a tendency for heterocyclization with possible involvement of α- and β-substituents has been found earlier for thiophene[4] and pyrrole derivatives.[7]

In this case, the *N*-phenylcarbamoyl group in position 2 of the thiophene ring seems to be more basic, which was confirmed by the diazotization of compound **7** resulting in thieno[3,2-*d*]-1,2,3-triazine **10** (see Scheme 4). The structure of compound **10** was determined using ^{1}H NMR spectroscopy. The NH_2 protons of the amide fragment in compound **10** give two equally broadened singlets at δ 7.85 and 8.10.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Varian Unity Plus-400 spectrometer (400 MHz) in DMSO-d_6 with Me_4Si as the internal standard. IR spectra were recorded on a Perkin—Elmer 457 instrument (Nujol). Mass spectra (EI, 70 eV) were recorded on a Finnigan SSQ-710 spectrometer (direct inlet of a sample). The course of the reaction was monitored and the purity of the products was checked by TLC on Kieselgel 60 F_{254} plates (Merck) in MeOH or MeOH—AcOEt. Melting points were determined on a Boetius hot stage.

Compound **1a** was prepared according to the known procedure.[8]

***N*-Alkyl-2-cyano-3-dimethylaminobut-2-enamides 1b—d,f (general procedure).** *N*,*N*-Dimethylacetamide diethyl acetal (21 mL, 120 mmol) was added at 60 °C to a solution of *N*-alkylcyanoacetamide[9—11] (100 mmol) in 100 mL of anhydrous EtOH. The reaction mixture was stirred for 30 min and cooled. The precipitate that formed was filtered off to give compounds **1b—d,f**. Their yields, melting points, and elemental analysis data are given in Table 1.

Ethyl 3-amino-4-*N*-R-carbamoyl-5-methylthiophene-2-carboxylates 3a—d,f (general procedure). The ester $HSCH_2CO_2Et$ (120 mmol) and K_2CO_3 (1 g, 7 mmol) were added to a suspension of an enamine **1a—d,f** (100 mmol) in 100 mL of anhydrous EtOH. The reaction mixture was refluxed for 16 h, diluted with water, and cooled. The precipitate that formed was filtered off and washed with water to give aminothiophenes **3a—d,f**. The structure of compound **3a** was proved by elemental analysis data (see Table 1) and mass spectrum (m/z (I_{rel} (%)): 228 $[M]^+$ (74), 211 $[M - NH_3]^+$ (91), 183 $[M - CO - NH_3]^+$ (60), 166 $[M - NH_3 - OEt]^+$ (49)). The yields and physicochemical and spectroscopic characteristics of compounds **3b—d,f** are given in Tables 1 and 2.

Table 1. Yields, melting points, and elemental analysis data for *N*-alkyl-2-cyano-3-dimethylaminobut-2-enamides **1b—d,f** and ethyl 3-amino-4-*N*-R-carbamoyl-5-methylthiophene-2-carboxylates **3a—f**

Compound	Yield (%)	M.p.*/°C	Found / Calculated (%) C	H	N	S	Molecular formula
1b	79	108—111	69.23 / 69.11	7.21 / 7.04	17.18 / 17.27	—	$C_{14}H_{17}N_3O$
1c	75	95—98	70.23 / 70.01	7.31 / 7.44	16.51 / 16.33	—	$C_{15}H_{19}N_3O$
1d	81	131—133	66.19 / 66.35	8.75 / 8.99	17.76 / 17.86	—	$C_{13}H_{21}N_3O$
1f	81	93—95	60.11 / 59.98	8.71 / 8.63	19.77 / 19.98	—	$C_{14}H_{24}N_4O_2$
3a	50	188—190	47.35 / 47.36	5.20 / 5.30	12.12 / 12.27	14.31 / 14.20	$C_9H_{12}N_2O_3S$
3b	49	120—122	60.11 / 60.36	5.80 / 5.70	8.91 / 8.80	10.30 / 10.07	$C_{16}H_{18}N_2O_3S$
3c	40	105—106	61.22 / 61.42	6.19 / 6.06	8.27 / 8.43	9.88 / 9.65	$C_{17}H_{20}N_2O_3S$
3d	48	146—147	58.01 / 58.04	7.02 / 7.14	9.21 / 9.02	10.55 / 10.33	$C_{15}H_{22}N_2O_3S$
3e	60	67—68	56.42 / 56.28	8.14 / 7.97	12.54 / 12.31	9.52 / 9.39	$C_{16}H_{27}N_3O_3S$
3f	30	101—102	54.06 / 54.02	7.09 / 7.11	11.82 / 11.85	9.02 / 9.03	$C_{16}H_{25}N_3O_4S$

* Recrystallization from EtOH (**1b—d,f** and **3a—d**), Pr^iOH (**3e**), or aqueous EtOH (**3f**).

Ethyl 3-amino-4-[*N*-(3-dimethylamino-2,2-dimethyl)propylcarbamoyl]-5-methylthiophene-2-carboxylate (3e). *N*,*N*,2,2-Tetramethylpropane-1,3-diamine (Aldrich) (6.35 g, 49 mmol) was added to a solution of $NCCH_2CO_2Et$ (5.52 g, 48.7 mmol) in 75 mL of EtOH. The reaction mixture was stirred for 2 h, *N*,*N*-dimethylacetamide diethyl acetal (8.9 mL, 49 mmol) was added, and the mixture was left for 20 h. Then $HSCH_2CO_2Et$ (7.6 g, 58.8 mmol) and K_2CO_3 (2.0 g, 14 mmol) were added and the resulting mixture was stirred at 75 °C for 16 h, cooled, and poured into 100 mL of water. The reaction product was extracted with 80 mL of AcOEt and the extract was dried with $CaCl_2$ and concentrated *in vacuo*. The residue was triturated with water and the precipitate that formed was filtered off to give compound **3e** (see Tables 1 and 2).

Ethyl 3-amino-4-cyano-5-methylthiophene-2-carboxylate (4). Phosphoryl chloride (2.0 g, 13 mmol) was added to a solution of thiophene **3a** (2.28 g, 10 mmol) in 20 mL of dry MeCN. The reaction mixture was refluxed with stirring for 1 h and poured into 200 mL of cold water. The precipitate that

Table 2. Chemical shifts (δ) in the ^{1}H NMR spectra of compounds **3b—f**

Compound	δ (*J*/Hz)					
	$CH_2\underline{Me}$ (t)	C(5)Me (s)	$C\underline{H}_2Me$ (q)	NH_2 (s)	NH (t)	Other protons
3b	1.22 (*J* = 7.2)	2.48	4.19 (*J* = 7.2)	6.41	8.61 (*J* = 6.0)	4.45 (d, 2 H, $NHC\underline{H}_2$, $J_{CH_2,NH}$ = 5.6); 7.22—7.38 (m, 5 H, Ph)
3c	1.22 (*J* = 7.2)	2.30	4.16 (*J* = 7.2)	6.34	8.13 (*J* = 6.0)	2.84 (t, 2 H, $C\underline{H}_2Ph$, $^3J_{CH_2,CH_2}$ = 7.2); 3.53 (q, 2 H, $NHC\underline{H}_2$, $^3J_{CH_2,NH}$ = 7.3); 7.20—7.30 (m, 5 H, Ph)
3d	—*	2.44	4.18 (*J* = 7.2)	6.31	7.97 (*J* = 5.6)**	1.23—1.80 (m, 13 H, $\underline{Me}CH_2$ + 5 CH_2); 3.70 (m, 1 H, CH)
3e	1.24 (*J* = 7.2)	2.51	4.18 (*J* = 7.2)	6.42	8.09 (*J* = 6.0)	0.87 (s, 6 H, CMe_2); 2.14 (s, 2 H, NCH_2); 2.22 (s, 6 H, NMe_2); 3.15 (d, 2 H, $C\underline{H}_2NH$, $^3J_{CH_2,NH}$ = 5.6)
3f	1.23 (*J* = 6.8)	2.46	4.18 (*J* = 6.8)	6.37	8.09 (*J* = 5.6)	1.65 (quint, 2 H, CH_2); 2.32 (m, 6 H, 3 CH_2); 3.24 (q, 2 H, CH_2); 3.55 (t, 4 H, 2 CH_2, $^3J_{CH_2,CH_2}$ = 5.0)

* Overlap with signals for the CH_2 groups of the cyclohexyl fragment.
** Doublet.

formed was filtered off to give compound **4** (0.63 g, 30%), m.p. 139—140 °C (from aqueous MeCN). Found (%): C, 51.59; H, 4.99; N, 13.20; S, 15.09. $C_9H_{10}N_2O_2S$. Calculated (%): C, 51.41; H, 4.79; N, 13.32; S, 15.25.

Ethyl 5-methyl-4-oxo-3,4-dihydrothieno[3,4-*d*]pyrimidine-7-carboxylates 5a—e (general procedure *A*). A solution of thiophene **3a** (1.82 g, 8 mmol) in 40 mL of HCO_2H was refluxed for 7—9 h (TLC). The reaction mixture was diluted with water and the precipitate that formed was filtered off to give compound **5a** (1.52 g, 80%), m.p. >250 °C (from DMF). Found (%): C, 50.67; H, 4.35; N, 11.82; S, 13.68. $C_{10}H_{10}N_2O_3S$. Calculated (%): C, 50.41; H, 4.23; N, 11.76; S, 13.46. IR, ν/cm^{-1}: 1670 (C=O), 1570 (C=C).

Compounds **5b—d** were obtained analogously from thiophene derivatives **3b,d,f**. Their yields and physicochemical and spectroscopic characteristics are given in Tables 3 and 4.

General procedure *B*. Compounds **5b,c,e** were synthesized by alkylating compound **5a** under the alkylation conditions for bicycle **6a** (see below) (see Tables 3 and 4).

Ethyl 5-methyl-4-oxo-3,4-dihydrothieno[3,4-*d*]-1,2,3-triazine-7-carboxylates 6a—h (general procedure *A*). Concentrated HCl (5 mL) was added to a solution of thiophene **3a** (2.28 g, 10 mmol) in a mixture of DMF (10 mL) and AcOH (15 mL). Then a solution of $NaNO_2$ (0.83 g, 12 mmol) in 3.0 mL of water was added at 20 °C. The precipitate that formed was filtered off to give compound **6a** (2.0 g, 84%), m.p. 189—190 °C (from EtOH—DMF, 3 : 1). Found (%): C, 45.53; H, 3.86; N, 17.58; S, 13.56. $C_9H_9N_3O_3S$. Calculated (%): C, 45.18; H, 3.79; N, 17.56; S, 13.40. ^{1}H NMR, δ: 1.34 (t, 3 H, $CH_2\underline{Me}$, ^3J = 6.9 Hz); 2.91 (s, 3 H, Me); 4.36 (q, 2 H, $C\underline{H}_2Me$); 14.60 (s, 1 H, NH).

Compounds **6b—e** were obtained analogously from thiophene derivatives **3b—e**. Their yields and physicochemical and spectroscopic characteristics are given in Tables 3 and 4.

General procedure *B*. Potassium carbonate (1.1 g, 8 mmol) and an alkyl halide ($PhCH_2Cl$, *cyclo*-$C_6H_{11}Cl$, 1-Ad-$COCH_2Br$, *p*-$BrC_6H_4COCH_2Br$ (each from Aldrich), and *p*-Me-$C_6H_4CONHCH_2Br$ [12]) (7.5 mmol) were added to a solution of thienotriazine **6a** (6.3 mmol) in 40 mL of DMF. The reaction mixture was stirred at 60 °C for 1.5 h and diluted with water. The precipitate that formed was filtered off to give compounds **6b,d,f—h** (see Tables 3 and 4).

3-Amino-4-carbamoyl-5-methyl-2-(*N*-phenylcarbamoyl)thiophene (7). A mixture of enamine **1a** (2.0 g, 13 mmol), $HSCH_2CONHPh$ (3.34 g, 20 mmol), and EtONa (1.36 g, 20 mmol) in 60 mL of anhydrous EtOH was refluxed with stirring for 8 h and poured into water. The precipitate that formed was filtered off to give compound **7** (0.75 g, 21%), m.p. 249—251 °C (from EtOH—acetone, 2 : 1). Found (%): C, 56.80; H, 4.65; N, 15.35; S, 11.40. $C_{13}H_{13}N_3O_2S$. Calculated (%): C, 56.71; H, 4.76; N, 15.26; S, 11.65. MS, *m/z* (I_{rel} (%)): 275 $[M]^+$ (54), 258 $[M - NH_2]^+$ (33), 183 $[M - PhNH - NH_3]^+$ (100), 166 $[M - PhNH - 2\ NH_3]^+$ (59).

6-Methyl-4-oxo-3-phenyl-3,4-dihydrothieno[3,2-*d*]pyrimidine-7-carboxamide (8) and 5-methyl-4-oxo-3,4-dihydrothieno[3,4-*d*]pyrimidine-7-carboxanilide (9). Thiophene **7** (2.0 g, 7.3 mmol) was added to a DMF—HCOOH—$HCONH_2$ mixture (15 : 5 : 2, 70 mL). The reaction mixture was refluxed for

Table 3. Yields, melting points, and elemental analysis data for ethyl 5-methyl-4-oxo-3,4-dihydrothieno[3,4-*d*]pyrimidine-7-carboxylates **5b—e** and ethyl 5-methyl-4-oxo-3,4-dihydrothieno[3,4-*d*]-1,2,3-triazine-7-carboxylates **6b—h**

Compound	Yield (%) (method)	M.p./°C (solvent)	Found / Calculated (%)				Molecular formula
			C	H	N	S	
5b	78 (A) 56 (B)	219—220 (toluene—DMF, 3 : 1)	62.21 62.18	4.72 4.91	8.81 8.53	9.67 9.76	$C_{17}H_{16}N_2O_3S$
5c	84 (A) 69 (B)	204—205 (MeCN—DMF, 2 : 1)	60.00 59.98	6.19 6.29	8.92 8.74	9.98 10.01	$C_{16}H_{20}N_2O_3S$
5d	75 (B)	171—173 (aqueous DMF)	59.21 59.32	6.48 6.64	7.57 7.69	8.69 8.80	$C_{18}H_{24}N_2O_4S$
5e	65 (A)	>260 (aqueous DMF)	60.85 60.66	4.65 4.53	7.96 7.86	9.31 9.00	$C_{18}H_{16}N_2O_4S$
6b	62 (A) 90 (B)	150—151 (EtOH)	58.19 58.35	4.48 4.59	12.51 12.76	9.59 9.73	$C_{16}H_{15}N_3O_3S$
6c	83 (A)	149—150 (EtOH—DMF, 2 : 1)	59.43 59.46	5.01 4.99	12.22 12.24	9.37 9.34	$C_{17}H_{17}N_3O_3S$
6d	71(A) 82 (B)	206—207 (DMF)	56.08 56.06	6.00 5.96	13.03 13.07	9.96 9.98	$C_{15}H_{19}N_3O_3S$
6e	51 (B)	84—85 (aqueous Pr^iOH)	54.35 54.53	6.76 6.86	15.97 15.90	9.10 9.10	$C_{16}H_{24}N_4O_3S$
6f	51 (A)	151—153 (Pr^iOH—acetone, 1 : 1)	60.61 60.70	6.18 6.06	10.07 10.11	7.45 7.72	$C_{21}H_{25}N_3O_4S$
6g	57 (A)	171—173 (Pr^iOH—acetone, 1 : 1)	47.05 46.80	3.31 3.23	9.84 9.63	7.60 7.35	$C_{17}H_{14}BrN_3O_4S$
6h	82 (A)	>260 (DMF—water, 2 : 1)	56.11 55.95	4.59 4.70	14.63 14.50	8.20 8.30	$C_{18}H_{18}N_4O_4S$

Table 4. Chemical shifts (δ) in the ^1H NMR spectra of compounds **5c,e** and **6b—e,g,h**

Compound	δ (*J*/Hz)				Compound	δ (*J*/Hz)			
	$CH_2\underline{Me}$ (t)	C(5)Me (s)	$C\underline{H}_2Me$ (q)	Other protons		$CH_2\underline{Me}$ (t)	C(5)Me (s)	$C\underline{H}_2Me$ (q)	Other protons
5e	1.28 (*J* = 7.2)	2.88	4.28 (*J* = 7.2)	5.09 (s, 2 H, $C\underline{H}_2Ph$); 7.25—7.38 (m, 5 H, Ph); 8.42 (s, 1 H, CH)	**6d**	—*	2.95	4.39 (*J* = 7.2)	1.20—1.98 (m, 13 H, 5 CH_2 + $\underline{Me}CH_2$); 4.80 (m, 1 H, CH)
5c	—*	2.88	4.28 (*J* = 7.2)	1.17—1.90 (m, 13 H, $\underline{Me}CH_2$ + 5 CH_2); 4.50 (m, 1 H, CHN); 8.24 (s, 1 H, C(2)H)	**6e**	1.33	2.94	4.37	0.87 (s, 6 H, CMe_2); 2.21 (s, 2 H, $Me_2NC\underline{H}_2$); 2.27 (s, 6 H, NMe_2); 4.22 (s, 2 H, $C\underline{H}_2CMe_2$)
6b	1.37 (*J* = 7.2)	2.91	4.38 (*J* = 7.2)	5.48 (s, 2 H, CH_2); 7.25—7.40 (m, 5 H, Ph)	**6g**	1.35 (*J* = 7.2)	2.93	4.39 (*J* = 7.2)	5.95 (s, 2 H, CH_2CO); 7.82, 8.05 (both d, 2 H each, BrC_6H_4)
6c	1.33 (*J* = 6.8)	2.94	4.37 (*J* = 7.2)	3.11 (t, 2 H, $CH_2C\underline{H}_2$, *J* = 7.2); 4.51 (t, 2 H, $C\underline{H}_2CH_2$, *J* = 7.2); 7.18—7.28 (m, 5 H, Ph)	**6h**	1.33 (*J* = 7.2)	2.94	4.39 (*J* = 7.2)	2.24 (s, 3 H, $\underline{Me}C_6H_4$); 5.12 (s, 2 H, CH_2CO); 7.10, 7.42 (both d, 2 H each, MeC_6H_4)

* Overlap with signals for the CH_2 groups of the cyclohexyl fragment.

5 h and cooled. The precipitate that formed was filtered off to give compound **8** (1.68 g, 81%), m.p. 326—328 °C (from DMF). Found (%): C, 58.87; H, 3.78; N, 14.59; S, 11.00. $C_{14}H_{11}N_3O_2S$. Calculated (%): C, 58.93; H, 3.89; N, 14.73; S, 11.24. MS, *m/z* (I_{rel} (%)): 285 $[M]^+$ (31), 268 $[M - NH_3]^+$ (100), 240 $[M - CO - NH_3]^+$ (23). ^{1}H NMR, δ: 2.89 (s, 3 H, Me); 7.50—7.60 (m, 5 H, Ph); 7.62, 8.60 (both br.s, each 1 H, NH_2); 8.52 (s, 1 H, C(2)H). ^{13}C NMR, δ: 26.9 (CH_3, $^1J_{C,H}$ = 132.6 Hz); 119.8 (s, C(4a)); 125.6 (m, C(7)); 127.5 (2 C); 129.1, 129.3 (2 C); 136.8 (Ph); 149.1 (d, C(2), $^1J_{C(2),H}$ = 210 Hz); 153.8 (d, C(7a), $^3J_{C(7a),C(2)H}$ = 12.7 Hz); 155.5 (d, C(4), $^3J_{C(4),C(2)H}$ = 5.8 Hz); 156.6 (q, C(6), $^2J_{C(6),CH_3}$ = 6.9 Hz); 163.4 (br.s, C(7′)).

The mother liquor was diluted with water (100 mL) and the precipitate (0.2 g) that formed was filtered off and dissolved in 10% NaOH. The solution was filtered and neutralized with conc. HCl to pH 7. The precipitate that formed was filtered off to give compound **9** (0.15 g, 7%), m.p. >260 °C. Found (%): C, 58.81; H, 3.72; N, 14.51; S, 11.01. $C_{14}H_{11}N_3O_2S$. Calculated (%): C, 58.93; H, 3.89; N, 14.73; S, 11.24. ^{1}H NMR, δ: 2.88 (s, 3 H, Me); 7.10 (t, 1 H, C(4′)H, Ph); 7.36 (t, 2 H, C(3′)H, Ph); 7.63 (d, 2 H, C(2′)H, Ph); 8.07 (s, 1 H, CH); 10.98 (s, 1 H, NH); 12.10 (br.s, 1 H, NH). ^{13}C NMR, δ: 16.0 (q, CH_3, $^1J_{C,H}$ = 132.0 Hz); 122.7 (q, C(4a), $^3J_{C(4a),CH_3}$ = 3.8 Hz); 122.9 (s, C(7)); 119.6 (2 C); 124.0, 129.3 (2 C); 138.4 (Ph); 147.0 (d, C(7a), $^3J_{C(7a),C(2)H}$ = 12.9 Hz); 147.5 (d, C(2), $^1J_{C(2),H}$ = 205.3 Hz); 150.7 (q, C(5), $^2J_{C(5),CH_3}$ = 6.8 Hz); 158.4 (d, C(4), $^3J_{C(4),C(2)H}$ = 6.1 Hz); 159.1 (s, C(7′)).

7-Carbamoyl-6-methyl-3-phenyl-3,4-dihydrothieno[3,2-*d*]-1,2,3-triazin-4-one (10) was obtained by the diazotization of thiophene **7** as described for compound **6a**. The yield was 62%, m.p. 286—288 °C (from DMF). Found (%): C, 54.69; H, 3.71; N, 19.32; S, 11.09. $C_{13}H_{10}N_4O_2S$. Calculated (%): C, 54.54; H, 3.52; N, 19.57; S, 11.20. MS, *m/z* (I_{rel} (%)): 286 $[M]^+$ (91), 258 $[M - CO]^+$ (100), 241 $[M - CO - NH_3]^+$ (17). ^{1}H NMR, δ: 2.86 (s, 3 H, Me); 7.52—7.68 (m, 5 H, Ph); 7.85, 8.10 (both br.s, each 1 H, NH_2).

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