A Facile Synthesis of Some Thieno/Furo-[2,3-*d*]pyrimidine-2-yl-thioacetic Acid Derivatives Seref Demirayak* and Usama Abu Mohsen

Department of Pharmaceutical Chemistry, Faculty of Pharmacy, University of Anadolu, Eskişehir 26470, Turkey Received March 1, 2000

The reaction of 2-(α -chloroacetamido)-3-cyano-4,5-disubstituted thiophenes/furanes with ammonium thiocyanate in methanol or ethanol afforded methyl or ethyl (4-amino-5,6-disubstituted thieno/furo[2,3-*d*]-pyrimidine-2-yl)thioacetates in good yields.

J. Heterocyclic Chem., 38, 507 (2001).

Thieno/furopyrimidines, which are well known bioisosteres of quinazolines, are of great importance because of their remarkable effects on the central nervous system as well as a wide variety of other biological activities [1,2]. The chemistry of thieno/furopyrimidines have also received attention because their starting materials, 2-amino-3-carboxy/cyanothiophenes/furanes, can conveniently be synthesised [3,4].

It has been reported that the reaction of *N*-aryl or heteroaryl- α -halogenoacetamides with ammonium thiocyanate in ethanol gives 4-thiazolinone derivatives [5-10]. Obviously a rearrangement reaction takes place during the reaction. The mechanism of this reaction was investigated by Knotz [7,8]. However, we obtained condensed pyrimidine derivatives **3** instead of **2** using the 2-(α -haloacetylamino)- 3-cyano compounds **1** as starting

materials. It can be supposed that 4-thiazolinone derivatives 2 is formed as an intermediate and that the reaction continues *via* the rearrangement shown, where intermediate 2 initially reacts with the solvent (*i.e.* methanol, ethanol) to form compounds 3.

Compound **3e** has been previously synthesised by reacting ethyl chloroacetate with a derivative of 4-amino-5,6-tetramethylenethieno[2,3-d]pyrimidine-2-(1H)thione that was obtained from a derivative of 2-benzoylthioureido-3-carbonitrilethiophene [11]. As described above, this report provides a convenient one-pot reaction for the synthesis of compounds **3a-i**.

Spectroscopic methods confirm the structure of compounds 3. The characteristic stretching bands at approximately 2220 cm⁻¹ originated from cyano groups of the starting compounds 1 are not observed in the IR

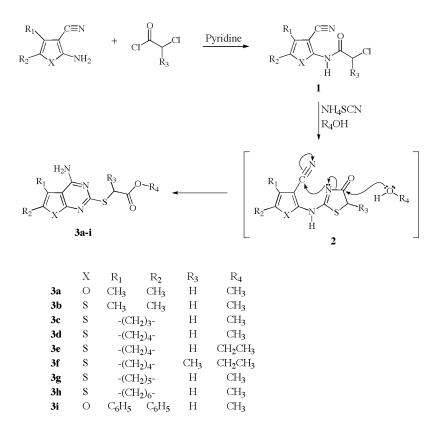


Table 1 Some Physicochemical Properties of **3a-i**

No	Yield	Mp	Formula	Analysis(%) Calcd./Found		
	(%)	(°C)		С	анса./гоц Н	na N
3a	63	193	C ₁₁ H ₁₃ N ₃ O ₃ S	49.42	4.90	15.72
3b	57	188	$C_{11}H_{13}N_3O_2S_2$	49.26 46.53	5.18 4.61	16.06 14.80
3c	75	169	$C_{12}H_{13}N_3O_2S_2$	46.30 48.79	4.85 4.43	15.10 14.22
3d	70	145	$C_{13}H_{15}N_3O_2S_2$	48.56 50.46	4.40 4.88	14.00 13.58
3e	72	127	$C_{14}H_{17}N_3O_2S_2$	50.26 51.99	5.10 5.29	13.25 12.99
3f	72	126[a]	$C_{15}H_{19}N_3O_2S_2$	52.15 53.33	4.98 5.67	13.25 12.44
3g	48	112	$C_{14}H_{17}N_3O_2S_2$	53.12 51.99	5.35 5.29	12.75 12.99
3h	42	150	$C_{15}H_{19}N_3O_2S_2$	51.69 53.33	5.40 5.67	13.10 12.44
3i	72	164	$C_{21}H_{17}N_3O_3S$	53.65 64.43	5.92 4.37	12.20 10.73
				64.25	4.60	11.00

[a] Reported literature mp 139-141°C [7].

spectra of compounds **3**. Also the expected peaks in the NMR spectra are observed, including the alkyl groups from the alcohol used as solvent. In their MS spectra, peaks were observed corresponding to molecular ions and the base peaks correspond to ions generated by loss of COOR groups.

EXPERIMENTAL

Melting points were determined by using an Electrothermal digital melting point apparatus and are uncorrected. Spectroscopic data were recorded on the following instruments: IR, Shimadzu IR 435 Spectrophotometer; ¹H-NMR, Jeol JNM-EX 90A FT Spectrometer; MS, VG Platform Mass Spectrometer. 2-Amino-3-cyano-4,5-disubstituted thiophene or furan derivatives were prepared by literature methods[12,13].

General Procedure for the Synthesis of Methyl or Ethyl (4-Amino-5,6-disubstituted Thieno / Furo[2,3-*d*]pyrimidine-2-yl)thioacetates 3a-i.

A mixture of the suitable 1 (5 mmol) (which were obtained by reacting 2-amino-3-cyano-4,5-disubstituted thiophene/furan with α -chloroacetyl/propionyl chloride in pyridine) and ammonium thiocyanate (10 mmol) in methanol or ethanol (100 ml) was refluxed for 6 hours. The solvent was evaporated. The residue was washed with water and recrystallised from ethanol.

Spectroscopic Data of 3a-i No Ir (KBr) cm-1 ¹H nmr (δ ppm) Ms (m/z) 3434, 3295, 3176 (N-H), 2.16 (s, 3H, CH₃), 2.23 (s, 3H,), 3a 267.0, (M, 37 %), 1723 (C=O) 3.63 (s, 3H,), 3.95 (s, 2H,), 6.95 238.0 (100 %) (bs, 2H,) 3450, 3285, 3120 (N-H), 2.35 (6H, s), 3.65 (3H, s), 283.1 (M, 32 %), 3b 1744 (C=O) 3.96 (2H, s), 6.88 (2H, bs) 224.1 (100 %) 3425, 3250, 3125 (N-H), 2.30-2.60 (2H, m), 2.75-3.10 3c 1735 (C=O) (4H, m), 3.65 (3H, s), 3.97 (2H, s), 6.92 (2H, bs) 3d 3415, 3270, 3120 (N-H), 1.80-2.10 (4H, m), 2.65-3.15 1727 (C=O) (4H, m), 3.67(3H, s), 3.96(2H, s), 6.92 (2H, bs) 3e 3450, 3284, 3114 (N-H), 1.21 (3H, t); 1.80 (4H, bs); 324 (M+1, 10 %), 1745 (C=O) 2.6-3.0 (4H, m); 3.93 (2H, s); 323 (M, 42 %), 6.81 (2H, bs) 250 (100 %) 3f 3410, 3265, 3120 (N-H), 1.21 (3H, t), 1.57 (3H, d), 1.80-2.10 1725 (C=O) (4H, m), 2.75-3.10 (4H, m), 4.19 (2H, q), 4.54 (2H, q), 6.97 (2H, bs) 3425, 3270, 3177 (N-H), 3g 1.10-1.80 (6H, m), 2.65-3.15 1730 (C=O) (4H, m), 3.67 (3H, s), 3.96 (2H, s), 6.92 (2H, bs) 3434, 3290, 3170 (N-H), 3h 1.10-1.80 (8H, m), 2.70-3.02 1724 (C=O) (4H, m), 3.64 (3H, s), 3.97 337(M, 46 %), (2H, s), 6.98 (2H, bs) 278(100 %) 3i 3430, 3290, 3160 (N-H), 3.66 (3H, s), 3.94 (2H, s), 6.25 1730 (C=O) (2H, bs), 7.20-7.52 (10H, m)

Table 2

REFERENCES AND NOTES

[1] Y. A. Ibrahim, A. H. Elwahy and A. M. Kadry, *Adv. Heterocyclic Chem.*, **65**, 235 (1996).

[2] G. Varvounis, and T. Giannopoulos, *Adv. Heterocyclic Chem.*, **66**, 193 (1996).

[3] S. Gronowitz, Thiophene and its Derivatives, Part 1, John Wiley & Sons, NY, 1985, p 1-213.

[4] R. W. Sabnis, D. W. Rangnekar and N. D. Sonawane, J. Heterocyclic Chem., **36**, 333 (1999).

[5] R. Adams, P. H. Long, and A. Jeanes, *J. Am. Chem. Soc.*, **58**, 2544 (1936).

[6] H. Taniyama, and S. Takemura, J. Pharm. Soc. Japan, 73,

- 167 (1953); Chem Abst., 47, 12360h (1953).
 - [7] F. Knotz, Sci. Pharm., 35, 215 (1967).
 - [8] F. Knotz, Sci. Pharm., 35, 300 (1967).

[9] A. Gürsoy, and Z. Cesur, J. Fac. Pharm. Istanbul, 18, 79 (1982).

[10] Z. Cesur, Pharmazie, 42, 716 (1987).

[11] S. Leistner, M. Gütschow and G. Wagner, Arch. Pharm.

(Weinheim), 322, 227 (1989).

[12] K. Gewald, Chem. Ber. 99, 1002 (1966).

[13] K. Gewald, E. Schinke and H. Böttcher, *ibid.* 99, 94 (1966).