Chemistry of Heterocyclic Compounds, Vol. 39, No. 1, 2003

AZOMETHINE DERIVATIVES ON THE BASIS OF 5-FORMYL-2,2'-BITHIENYL AND 5-FORMYL-2,2'-DITHIENYL SULFIDE

N. A. Korchevin, N. V. Russavskaya, E. P. Levanova, E. N. Sukhomazova, and E. N. Deryagina

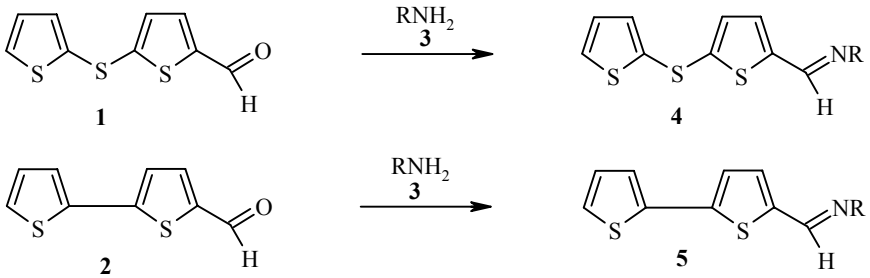
Six azomethine derivatives of 2,2'-dithienyl sulfide and five of 2,2'-bithienyl have been synthesized for the first time.

Keywords: azomethines, amines, 5-formyl-2,2'-bithienyl, 5-formyl-2,2'-dithienyl sulfide.

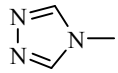
Azomethines of the thiophene and 2,2'-bithienyl series are promising antiseptic preparations [1,2]. Similar compounds are readily formed on condensing primary aromatic amines with appropriate aldehydes [2,3]. However there are no literature data on the preparation of azomethines of the 2,2'-dithienyl sulfide series. The introduction of a sulfur atom between the thiophene rings may possibly increase the conformational mobility of the latter, which may be displayed in specific physicochemical properties of compounds based on 2,2'-dithienyl sulfide. Azomethines are also starting materials for the synthesis of heterocyclic compounds [4], and extending their variety is a promising undertaking.

We have synthesized for the first time a series of azomethines from 5-formyl-2,2'-dithienyl disulfide (**1**), which were characterized by IR and ^{1}H NMR spectra. Azomethine analogs of 2,2'-bithienyl were synthesized and characterized for comparison. The majority of these were also obtained for the first time.

The reactions of aldehydes **1,2** with amines **3** were effected in the absence of solvent (in the case of liquid amines) or in ethanol. The exothermic reaction was carried out without supplying heat, but in certain cases a little heating (40-50°C) enabled an increase in the yield of the desired product (Table 1).



3a, **4a** R = Ph; **3b– 5b** R = 4-BrC_6H_4; **3c– 5c** R = $PhCH_2$; **3d– 5d** R = 4-MeC_6H_4;
3e– 5e R = 4-HOC_6H_4; **3f– 5f** R = $HOCH_2CH_2$; **3g**, **5g** R = 2-ClC_6H_4

3h, **5h** R = 

A. E. Favorsky Irkutsk Institute of Chemistry, Siberian Branch of the Russian Academy of Sciences, Irkutsk 664033, Russia; e-mail: vlad@irioch.irk.ru. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 1, pp. 60-64, January, 2003. Original article submitted April 21, 2000.

TABLE 1. Synthesis Conditions and Physicochemical Characteristics of Azomethines **4** and **5***

Compound	Empirical formula	Found, % / Calculated, %					Reaction temp. °C	mp, °C*[3]	Yield, %
		C	H	N	Hal	S			
4a*[2]	$C_{15}H_{11}NS_3$	60.61 / 59.80	3.75 / 3.65	4.49 / 4.65	—	31.51 / 31.89	20-25	62-63	70
4b	$C_{15}H_{10}BrNS_3$	48.00 / 47.38	2.60 / 2.63	3.64 / 3.69	21.61 / 21.04	25.12 / 25.27	40-45	71-72	85
4c	$C_{16}H_{13}NS_3$	61.08 / 60.95	4.02 / 4.13	4.40 / 4.44	—	30.46 / 30.48	40	42	90
4d	$C_{16}H_{13}NS_3$	61.55 / 60.95	4.12 / 4.13	4.24 / 4.44	—	29.83 / 30.48	20-25	84-85	70
4e	$C_{15}H_{11}NOS_3$	56.26 / 56.78	3.58 / 3.47	4.45 / 4.42	—	29.86 / 30.28	45-50	136-137	80
4f	$C_{11}H_{11}NOS_3$	49.41 / 49.07	4.14 / 4.09	5.23 / 5.20	—	34.85 / 35.69	20-25	47-48	63
5b	$C_{15}H_{10}BrNS_2$	52.15 / 51.72	3.01 / 2.87	3.76 / 4.02	23.65 / 22.99	18.58 / 18.39	50	117-118	78
5c	$C_{16}H_{13}NS_2$	68.28 / 67.84	4.57 / 4.59	4.77 / 4.95	—	22.77 / 22.61	20-25	56-57	72
5d	$C_{16}H_{13}NS_2$	67.96 / 67.84	4.82 / 4.59	4.80 / 4.95	—	21.90 / 22.61	20-25	119-120	62
5e	$C_{15}H_{11}NOS_2$	63.58 / 63.16	3.91 / 3.86	4.75 / 4.91	—	22.19 / 22.46	50-55	231-232	97
5f	$C_{11}H_{11}NOS_2$	56.03 / 55.77	4.67 / 4.64	5.48 / 5.91	—	26.97 / 27.00	20-25	64-65	54
5g	$C_{15}H_{10}ClNS_2$	60.10 / 59.31	3.50 / 3.29	4.67 / 4.61	12.26 / 11.70	21.02 / 21.09	25-30	74-75	45
5h	$C_{11}H_8N_4S_2$	50.62 / 50.77	3.00 / 3.15	20.55 / 21.5	—	24.24 / 24.62	30-40	165-166	55

* Solvent was ethanol for compounds **4a,b,d,e 5b,d,e,h**.

*[2] Yield was 80% when carrying out the reaction at 40-45°C.

*[3] According to [2], compound **5d** has mp 126-128°C, and **5e** 228-229°C.

TABLE 2. The IR and ^{1}H NMR Spectral Characteristics of Azomethines **4** and **5**

Compound	IR spectrum, cm^{-1} (characteristic frequencies)	δ, ppm, *J* (Hz)			
		H_{Ar}	CH=N	N–CH_2 (OH)	$C\underline{H_2}$–OH(CH_3)
4a	3070 (w), 2960 (w), 2860 (w), 1600 (s), 1580 (s), 1490 (s), 1450 (m), 1420 (s)	7.44-6.95 (m)	8.38 (s)		
4b	3060 (w), 2910 (w), 2850 (w), 1600 (s), 1570 (s), 1480 (s), 1420 (s)	7.48-6.98 (m)	8.36 (s)		
4c	3070 (w), 3020 (w), 2920 (w), 2860 (w), 2810 (w), 1620 (s), 1500 (m), 1450 (m), 1420 (s)	7.36-6.84 (m)	8.25 (t, *J* = 1.46)	4.71 (d, *J* = 1.46)	
4d	3080 (w), 3010 (w), 2930 (w), 2900 (w), 1605 (s), 1580 (s), 1500 (m), 1420 (s)	7.44-6.97 (m)	8.40 (s)		2.34 (s)
4e	3400 (s), 3070 (w), 2980 (w), 2930 (w), 2800 (w), 1605 (s), 1590 (s), 1500 (s), 1440 (m), 1410 (s)	7.45-6.78 (m)	8.40 (s)	—*	
4f	3300 (s), 3080 (w), 2950 (w), 2915 (w), 2880 (w), 1610 (s), 1450 (w), 1415 (s)	7.80-6.28 (m)	8.30 (t, *J* = 1.2)	3.89 (m); 2.23 (s)	3.69 (m)
5b	3200 (s), 3090 (w), 2820 (w), 1600 (s), 1580 (s), 1540 (s), 1480 (s), 1440 (s), 1410 (s)	7.44-6.98 (m)	8.44 (s)		
5c	3300 (s), 3070 (m), 3030 (m), 2900 (m), 2880 (m), 1610 (s), 1598 (m), 1550 (w), 1450 (s), 1420 (s)	7.30-6.94 (m)	8.34 (t, *J* = 1.2)	4.77 (d, *J* = 1.2)	
5d	3440 (m), 3080 (w), 2910 (w), 1600 (s), 1590 (s), 1550 (m), 1500 (s), 1450 (s), 1410 (m)	7.42-6.94 (m)	8.42 (s)		2.33 (s)
5e	3410 (s), 3110 (w), 2910 (w), 1610 (s), 1540 (m), 1500 (m), 1370 (w), 1280 (s)	7.62-6.92 (m)	8.45 (s)	—*	
5f	3400, 3210 (w), 3080 (w), 3000 (w), 2930 (s), 2900 (m), 2870 (m), 2750 (m), 1610 (s), 1540 (m), 1450 (s), 1410 (s)	7.25-6.94 (m)	8.31 (t, *J* = 1.0)	3.89 (m); 2.36 (s)	3.66 (m)
5g	3500 (w), 3110 (s), 3060 (s), 1600 (s), 1590 (s), 1540 (m), 1480 (m), 1450 (s), 1420 (s), 1400 (m)	7.38-6.96 (m)	8.42 (s)		
5h	3420 (m), 3280 (m), 3115 (m), 1630 (m), 1620 (s), 1600 (m), 1510 (s), 1450 (s)	8.55 (s, $2H_{triazole}$); 7.48-7.07 (m)	8.63 (s)		

* The signal of the OH group proton is in the region of the multiplet signals of the aromatic and heterocyclic protons.

In the majority of cases the yield of azomethines **4** and **5** was 70-93%. Azomethine **4g** was not obtained. Even with a twofold excess of 2-chloroaniline **3g** and maintaining at 40-50°C for 8 h unreacted aldehyde **1** remained in the reaction mixture (check by GLC). The analogous azomethine **5g** was formed from 2,2'-bithienyl in less than 45% yield. Azomethines **4f, 5f**, and **5h** were also formed in low yields. Aldehyde **1** did not react with amine **3h** under analogous conditions.

The synthesized azomethines **4** and **5** are solid substances, bright yellow to brown in color. The melting points of compounds **4** were significantly lower than the melting points of the corresponding azomethines **5**. A similar regularity was also observed for unsubstituted 2,2'-dithienyl sulfide [5] and 2,2'-bithienyl [6] and also for their 5-formyl derivatives. This may be caused by the more ordered structure of the molecules of 2,2'-bithienyl derivatives compared with the structure of the analogous 2,2'-dithienyl sulfide derivatives, for which evidently there is a larger number of conformers with different disposition of thiophene rings relative to one another.

Analysis of the spectral characteristics of compounds **4** and **5** (Table 2) enabled the assumption that only one geometric isomer is formed for azomethines **4** and **5,** analogous to the formation of only the anti form of the Schiff's bases in the reaction of aromatic aldehydes with substituted anilines [7].

There was an intense absorption band at 1600-1620 cm^{-1} in the IR spectra of all the compounds obtained. This band corresponds to the stretching vibrations of the azomethine group (C=N) [2]. Besides this band the band for the stretching vibrations of associated hydroxyl group appears in the spectra of compounds **4f** and **5f** at 3300 and 3400 cm^{-1} respectively. These data and also the data of ^1H NMR spectra indicate the absence of cyclization of azomethines into oxazolidines, which frequently accompanies the reaction of carbonyl compounds with 2-aminoethanol (**3f**) [8]. The appropriate set of frequencies for the stretching vibrations of the OH group was observed in the IR spectra at 3200-3400 cm^{-1}, also the bands assigned to the stretching vibrations of C–H at 2800-3100 cm^{-1}, the C–H deformation vibrations at 800-1200 cm^{-1}, and the stretching vibrations of the C–S bond at 500-600 cm^{-1} were observed.

The protons of the aromatic and thiophene rings of azomethines **4** and **5** give a multiplet signal in the ^1H NMR spectra of azomethines at 6.9-7.8 ppm. The signal of the azomethine proton is displayed at low field at 8.3-8.6 ppm under the anisotropic influence of the nitrogen atom. Its displacement towards low field is also aided by such substituents at nitrogen atom in the aromatic ring as chlorine, bromine, methyl, and hydroxyl groups (**4d,e, 5b,d,e,g**). 1,3,4-Triazole group on nitrogen atom displaces the signal of the azomethine proton even more towards low field (**5h**), but benzyl substituent at the carbon atom of the azomethine bond displaces it towards high field (**4c, 5c**).

So, six azomethine derivatives of 2,2'-dithienyl sulfide and five derivatives of 2,2'-bithienyl have been synthesized and characterized for the first time. Due to the simple method of synthesizing 2,2'-dithienyl sulfide developed in [9], its potentially biologically active azomethine derivatives become available substances like the analogous compounds of the thiophene and bithienyl series. In addition these substances possess high synthetic potential for obtaining new compounds with a broad spectrum of biological activity.

EXPERIMENTAL

The IR spectra were taken on a Specord IR-75 spectrometer in KBr disks. The ^1H NMR spectra were recorded on a Jeol FX 90 Q (90 MHz) instrument for 15-20% solutions of substances in $CDCl_3$, internal standard was HMDS. The completion of reaction was determined by the disappearance of the initial aldehyde from the reaction mixture using a LKhM-80-1 gas-liquid chromatograph (column 3 × 2000 mm, liquid phase silicone XE-60 (5%) on support Chromaton XE-60 N-AW HMDS, linear temperature programming at 12 deg/min).

Aldehydes **1** and **2** were obtained by the formylation of 2,2'-dithienyl sulfide and 2,2'-bithienyl by the method of [10].

N-R-N-{(*E*)-[5-(2-Thienylthio)-2-thienyl]methylene}amines (4) and N-R-N-{(*E*)-[5-(2-Thienyl)-2-thienyl]methylene}amines (5). The reaction of aldehydes **1** and **2** with amines **3** was carried out in a flask fitted with a reflux condenser under stirring on a magnetic stirrer. Reactants were used in stoichiometric quantities. After completion of the reaction (2-4 h) the reaction mixture was cooled. This caused crystallization of the product, which was purified by recrystallization from ethanol. The synthetic conditions and characteristics of the synthesized compounds are given in Table 1.

REFERENCES

1. P. I. Buchin and A. E. Lipkin, *Derivatives of Thiophene and Bithienyl as Promising Antiseptics of a New Group* [in Russian], Izd. Sarat. Univ., Saratov (1974).
2. K. I. Vakhreeva, M. G. Viderker, P. I. Buchin, A. E. Lipkin, and T. B. Ryskina, *Khim.-farm. Zh.*, No. 1, 24 (1972).
3. V. S. Egorova, V. N. Ivanova, and H. I. Putokhin, *Khim. Geterotsikl. Soedin.*, 829 (1967).
4. S. V. Kessar, P. S. Pahwa, Pawanjit, Paramjit Singh, and Y. P. Gupta, *Indian J. Chem.*, **16B**, 92 (1978).
5. M. G. Voronkov, E. N. Deryagina, L. K. Papernaya, E. N. Sukhomazova, N. A. Korchevin, and G. G. Efremova, *Khim. Geterotsikl. Soedin.*, 1614 (1986).
6. M. G. Voronkov, E. N. Deryagina, E. N. Sukhomazova, O. I. Randin, V. V. Keiko, and I. D. Kalikhman, *Khim. Geterotsikl. Soedin.*, 1186 (1976).
7. V. M. Potapov, *Stereochemistry* [in Russian], Khimiya, Moscow (1976).
8. E. D. Bergmann, *Chem. Rev.*, **53**, 309 (1953).
9. M. G. Voronkov, E. N. Deryagina, L. G. Klochkova, and A. S. Nakhmanovich, *Zh. Org. Khim.*, **12**, 1515 (1976).
10. B. P. Fedorov and F. M. Stoyanovich, *Zh. Obshch. Khim.*, **33**, 2251 (1963).