Chemistry of Heterocyclic Compounds, Vol.35, No. 6, 1999

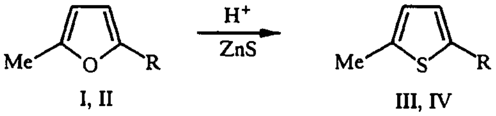
NEW METHOD FOR SYNTHESIS OF 2,5-DISUBSTITUTED THIOPHENES

T. I. Gubina, B. I. Drevko, L. N. Fedina, S. M. Rogacheva, and V. G. Kharchenko

The use of hydrogen sulfide at the moment of formation is proposed for the recyclization of furans into thiophenes in acidic media. The advantages of this method are shown.

We previously developed a method for synthesis of 2,5-disubstituted thiophenes and selenoles comprising reaction of the appropriate furan with hydrogen sulfide or selenide in acidic media [1,2]. A solution of the furan compound in ethanol (methanol or propanol) is saturated with hydrogen sulfide or selenide and subjected to the action of 30 or 57% perchloric, or 36% hydrochloric acid, or gaseous hydrogen chloride at 30-60°C depending on the structure of the substrate [3].

A new method for synthesis of 2,5-disubstituted thiophenes is proposed in the present communication and is the reaction of the appropriate furan compound with hydrogen sulfide at the moment of formation. Zinc sulfide was used as the sulfide reagent.



I, III R = Me; II, IV R = $CH_2CH_2CH(OH)Me$

The reaction was carried out in an ethanolic solution of concentrated hydrochloric acid or under the action of hydrogen chloride in abs. ethanol. The effect of various factors on the yield of the desired product was studied using the reaction of 2,5-dimethylfuran with zinc sulfide (Tables 1 and 2).

The following conditions were determined as optimal when using hydrochloric acid in ethanol: ratio of substrate to zinc sulfide 1:1.2-1.4, initial concentration of acid reagent 3.3-4.0N, reaction temperature 30-40°C, reaction time 1-2.5 h. Optimum conditions for the absolute medium were reactant ratio 1:1.2, HCl concentration 2.0-2.4N, temperature 50°C, and reaction time 1-1.5 h.

The process was characterized by its selectivity and the high yield of the desired products, the lower reaction time, the ease of isolating the desired product, and the absence of toxic gaseous hydrogen sulfide (the latter point guarantees the ecological purity of the synthesis). The high yield of the desired product is possibly explained by the influence of specific salt effects arising from the formation of zinc chloride in the reaction medium [4].

N. G. Chernyshevskii Saratov State University, Saratov 410026, Russia. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 6, pp. 736-738, June, 1999. Original article submitted January 6, 1999.

0009-3122/99/3506-0650$22.00©1999 KluwerAcademic/Plenum Publishers

TABLE 1. Effect of Various Factors on the Yield of 2,5-Dimethylthiophene in the Reaction of 2,5-Dimethylfuran with Zinc Sulfide in Hydrochloric Acid Solution

T, °C	c_0, HCl, N	Initial concentration of I and ZnS in mixture, M	Ratio of substrate I:ZnS	Reaction time, h	Yield, %
20	2.4	0.01:0.012	1:1.2	13	40
	3.3	0.01:0.012	1:1.2	6	75
30	2.0	0.01:0.012	1:1.2	6	65
	2.4	0.01:0.012	1:1.2	3	67
	3.3	0.01:0.012	1:1.2	2	73
	4.0	0.01:0.012	1:1.2	1.5	78
40	2	0.01:0.012	1:1.2	5	75
	2.4	0.01:0.012	1:1.2	4	70
	3.3	0.01:0.012	1:1.2	0.8	85
	3.3	0.01:0.01	1:1	1	68
	3.3	0.01:0.014	1:1.4	0.8	83
	3.3	0.01:0.015	1:1.6	1	63
	3.3	0.01:0.011	1:1.1	1	65
	3.3	0.01:0.012	1:1.2	2	40
	3.3	0.01:0.012	1:1.2	2.5	85
	3.3	0.01:0.012	1:1.2	1	85

TABLE 2. Effect of Various Factors on the Yield of 2,5-Dimethylthiophene in the Reaction of 2,5-Dimethylfuran with Zinc Sulfide in Abs. Ethanol Saturated with HCl*

T, °C	c_0, HCl, N	Reaction time, h	Yield, %
50	2.4	1.0	70
	2.0	1.5	77
	3.3	0.5	60
	4.0	0.5	69
60	2.4	0.5	51
	3.3	0.25	40

EXPERIMENTAL

A check on the progress of reactions and identification of products was effected on a Tsvet 101 chromatograph with a flame-ionization detector. The stationary phase was Apiezon L (15%) supported on Chromaton N-AW-DMCS. Column size was 1 m × 3 mm. Thermostat temperature was 160°C, carrier gas was helium supplied at 2 liter/h. The IR spectra of the synthesized compounds taken on a Specord M 80 instrument were analogous to standard samples.

Compounds I and II were synthesized by the known procedure [2].

2,5-Dimethylthiophene (III). Hydrochloric acid (11.8N, 83 ml) was poured into a solution of compound I (5.2 g, 0.04 mol) and zinc sulfide (6.5 g, 0.065 mol) in ethanol (220 ml). The reaction was conducted with constant stirring and heating at 40°C. Depending on the consumption of the initial compound fresh portions of substrate, zinc sulfide, and acid were added at intervals of 20-30 min. The acid was added to the reaction mixture in the amount necessary to maintain the acidity of the medium within the limits 3.0-3.3N. In all, compound I (126 g, 1.3 mol), zinc sulfide (153 g, 1.56 mol), and acid (300 ml) were put into the reaction. 2,5-Dimethylthiophene separated during the reaction as a bright yellow oil in the upper part of the reactor. At the end of the reaction it was separated and distilled. The fraction with bp 135-137°C was collected, n_D^{20} 1.5145. Yield 117.5 g (80%). Literature data [5]: bp 137.5°C, n_D^{20} 1.5142.

2-(3-Hydroxybutyl)-5-methylthiophene (IV). This reaction was carried out analogously using as initial charge compound II (7.5 g, 0.05 mol) and zinc sulfide (5.8 g, 0.06 mol) in ethanol (220 ml) and hydrochloric acid (11.8N, 87 ml). In all, compound II (154 g, 1 mol), zinc sulfide (117 g, 1.2 mol), and hydrochloric acid (240 ml) were fed into the reaction. After separation, the upper layer was washed with water, extracted with ether, dried over calcined $MgSO_4$, and redistilled in vacuum. The fraction with bp 100-102°C (2 mm) was collected, n_D^{20} 1.5196. Literature data [2]: bp 100-101°C (2 mm), n_D^{20} 1.5200.

REFERENCES

1. V. G. Kharchenko, I. A. Markushina, and T. I. Gubina, *Dokl. Akad. Nauk SSSR*, **255**, 1144 (1980).
2. V. G. Kharchenko, T. I. Gubina, and I. A. Markushina, *Zh. Org. Khim.*, **18**, No. 2, 394 (1982).
3. V. G. Kharchenko, T. I. Gubina, S. P. Voronin, and I. A. Markushina, *Khim. Geterotsikl. Soedin.*, No. 11, 1144 (1986).
4. A. Lupi and B. Chubar, *Salt Effects in Organic and Organometallic Chemistry* [Russian translation], Mir, Moscow.
5. H. D. Hartough, *Thiophene and Its Derivatives*, Interscience, New York (1952).