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Abstract

Full Text

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Syntheses Based on Organolithium Compounds of the Furan Series

Alkyl-(α-furyl)-sulfides and Some of Their Transformations

(Presented by Academician B. A. Kazanskii, 1 IV 1963)

Furan, while displaying certain properties characteristic of dienes, in other respects, as an aromatic system, approaches thiophene in its behavior. In particular, like the latter, it is readily metalated by the action of butyllithium. However, this ability to form an organolithium compound is not equally expressed in these compounds: in an equimolecular mixture of furan with thiophene, one equivalent of butyllithium reacts almost exclusively with thiophene ([1]). The availability of lithium derivatives of furan and of some of its homologs can be widely used for obtaining compounds with diverse functions. In this connection, the experience acquired in our laboratory in studying transformations of thienyl-2-lithium is of interest ([1,2,4]).

The advantage of processes based on the use of the indicated organolithium compounds lies in the absence of a halogenation stage, which cannot be avoided if the intermediate product is an organomagnesium compound. Of considerable interest, in particular for further transformations, might be alkyl-(aryl)-furyl-2-sulfides; some compounds of this type have recently been described by Adams and co-workers ([3]). However, their method, based on the use of mercaptans of the fatty and aromatic series, is not very convenient. Simpler appears to be the method described here, analogous to that proposed for obtaining sulfides of the thiophene series ([4]). In this case, unsubstituted or substituted furyl-2-lithium, on interaction with elemental sulfur, forms the corresponding mercaptide, to which, without isolation from the mixture, an alkyl halide is added. To introduce the alkylmercapto group, a dialkyl disulfide may be used instead of sulfur and a halide. The yields of sulfides by this method range from 53 to 77%. By metalation of 2-alkylmercaptofuran followed by the action of sulfur and an alkyl halide, a bis-sulfide can be synthesized. From sylvan, by direct action of acid on the mercaptide, the corresponding mercaptan was obtained, but in 37% yield (it will be described later).

Sulfides of type I are readily formylated with substituted formamides ([5]), forming aldehydosulfides II, and are acetylated in the presence of phosphoric acid. The presence of a CHO group in position "3" of the ring is shown by conversion

of IIa into acid III and by desulfurization of its ester IV into the ester of the described acid V.

Transformations of the indicated type, leading from 2-alkylmercapto-5-alkylfuran to furan derivatives bearing a functional group in the β-position of the ring, are of independent interest as a route to 2,4-disubstituted furans. In such cases the alkylmercapto function plays the role of a group blocking the α-position. In essence, this route for the synthesis of 2,4-disubstituted furans is similar to that described

by one of us and L. D. Tarasova for the preparation of 2,3-disubstituted furans ([6]).

[reaction scheme]

Ia $R = H,\ R_1 = C_2H_5$; Ib $R = CH_3,\ R_1 = C_2H_5$; Iv $R = CH_3,\ R_1 = n\text{-}C_4H_9$; Ig $R =$ $R_1 = \text{iso-}C_4H_9$; Id $R = R_1 = C_2H_5$; Ie $R = SC_2H_5,\ R_1 = C_2H_5$.

IIa $R = CH_3,\ R_1 = C_2H_5$; IIb $R = CH_3,\ R_1 = n\text{-}C_4H_9$; III $R = CH_3,\ R_1 = C_2H_5$; IV $R = CH_3,\ R_1 =$

Experimental Part

Sulfides of the furan series. To 1 g-mole of a 1-1.5 N ethereal solution of *n*-butyllithium, under nitrogen at −35° and with stirring, 1.1 g-moles of freshly distilled furan or 2-alkylfuran were added over 10-15 min; cooling was removed and the mixture was boiled for 4-5 hr. At −5–0° there was added to the mixture, over 30 min, 1 g-atom of dry finely powdered sulfur, and then the cooling was removed. The mixture warmed up. After the temperature began to fall, the mixture was boiled for 50-60 min, cooled, and 1.1 g-moles of the distilled alkyl halide were added to it at −5–0°; it was then boiled again for 9-10 hr. The reaction product was cooled and, at 0-10°, 500 ml of 17% aqueous ammonium chloride solution was added. The ethereal layer was separated, and the aqueous layer was extracted with ether. The combined ethereal solution was washed with 3% caustic soda solution and with water, and dried with magnesium sulfate. The solvent was distilled off and the residue was distilled twice under nitrogen. Data for the alkylfuryl sulfides are given in Table 1.

2-Ethylmercapto-5-methyl-3-furaldehyde (IIa). To a mixture of 74 g of Ib and 156 g of dimethylformamide there was added, over 1 hr at 0–5° and with stirring, 95 g of phosphorus oxychloride; cooling was then removed. After the temperature began to fall, the mixture was heated for 1 hr at 50–60° and left overnight. The viscous mass formed was poured into a mixture of ice and water, neutralized with soda, and left until morning. The organic layer was separated, and the aqueous layer was extracted with ether. The combined ethereal solution was washed with water and dried with magnesium sulfate. The solvent was distilled off in vacuo. The residue was distilled twice. Obtained: 39.6 g of IIa, yield 44.7%, b.p. 126–128° (13 mm), d_4^{20} 1.1267, n_D^{20} 1.5460.

Found, %:	C 56.60;	56.38;	H 5.95;	5.95;	S 18.91;	18.87
$C_8H_{10}O_2S$. Calculated, %:	C 56.44;		H 5.92;		S 18.83	

Semicarbazone: m.p. 211–212° with decomposition (from aqueous alcohol).

Found, %:	N 18.47;	18.22
$C_9H_{13}N_3O_2S$. Calculated, %:	N 18.49	

2-*n*-Butylmercapto-5-methyl-3-furaldehyde (IIb) was obtained from Iv under analogous conditions (see IIa). Yield 44.5%, b.p. 115.5–118° (3.5 mm), d_4^{20} 1.0697, n_D^{20} 1.5305.

Found, %:	C 60.35;	60.61;	H 7.13;	7.22;	S 16.19;	15.04
$C_{10}H_{14}O_2S$. Calculated, %:	C 60.56;		H 7.12;		S 16.17	

Semicarbazone: m.p. 188.5–189.5° with decomposition (from aqueous alcohol).

Found, %:	N 16.29;	16.11
$C_{11}H_{17}N_3O_2S$. Calculated, %:	N 16.46	

2-Ethylmercapto-5-methyl-3-acetylfuran. A mixture of 26.2 g of Ib, 28.2 g of acetic anhydride, and 2.2 g of 85% phosphoric acid

Table 1

Alkylfuryl sulfides

No.	Starting compound of the furan series and alkyl halide	Sulfide obtained	Gross formula	Yield of theoretical, %	B.p. at atmospheric pressure, °C/mm	d_4^{20}	n_D^{20}	MR_D^* found	MR_D^* calculated	Found, % C	Found, % H	Found, % S	Calculated, % C	Calculated, % H	Calculated, % S
Ia	Furan, C_2H_5I	2-Ethylmercaptofuran	C_6H_8OS	56	158–160 / 757					56.30	6.28	24.76	56.21	6.29	25.01
Ib	Sylvan, C_2H_5I	5-Ethylmercapto-2-methylfuran	$C_7H_{10}OS$	74.5	179–181 / 760	1.0251	1.5094	41.42	41.08	59.19	7.22	23.43	59.12	7.09	22.55
Iv	Sylvan, *n*-C_4H_9Br	5-*n*-Butylmercapto-2-methylfuran	$C_9H_{16}OS$	99	218–219 / 760	0.9831	1.4995	50.86	50.31	63.20	8.16	18.95	63.48	8.29	18.83
Ig	Sylvan, iso-C_4H_9Br	5-Isobutylmercapto-2-methylfuran	$C_9H_{16}OS$	96	209–210 / 747	0.9858	1.4994	50.75	50.31	63.12	8.22	18.94	63.48	8.29	18.83
Id	2-Ethylfuran, C_2H_5I	5-Ethylmercapto-2-ethylfuran	$C_8H_{12}OS$	90	91/20	1.0055	1.5064	46.16	45.69	61.23	7.73	20.65	61.49	7.74	20.52
Ie	2-Ethylfuran, C_2H_5I	2,5-Bis(ethylmercapto)furan	$C_8H_{12}OS_2$	112	115/9	1.0985	1.5540	—	—	51.15	6.48	34.31	51.02	6.42	34.06

* The atomic refraction for sulfide sulfur was taken as 7.921, and for oxygen as 1.764 (*).

heated for 1.5 hours at 90–95°; after the addition of 100 ml of water, it was stirred for 1 hour and extracted with ether. The aqueous layer was neutralized with soda and extracted with ether. The ethereal solution was washed with an aqueous solution of sodium bicarbonate, with water, and then dried over

magnesium sulfate. The ether was distilled off and the residue was distilled. This gave 15.5 g of ketone, yield 45.7%, b.p. 87–89° (2 mm), n_D^{20} 1.5416 (crystallizes on cooling).

Found, %:	C	58.35;	58.39;	H	6.59;	6.57;	S 17.67; 17.49
$C_9H_{12}O_2S$. Calculated, %:	C	58.67;		H	6.53;		S 17.40

Semicarbazone: m.p. 139.5–141.5° (from aqueous alcohol).

Found, %:	N 17.25; 17.50
$C_{10}H_{15}N_3O_2S$. Calculated, %:	N 17.41

2-Ethylmercapto-5-methylfuran-3-carboxylic acid (III) and its methyl ester (IV). Acid III was obtained by oxidation of 10.2 g of aldehyde IIa with silver oxide according to the method proposed for the oxidation of 3-thiophenealdehyde (7). This gave 10.3 g (yield 92%) of acid III, m.p. 157.7–158.7° (from aqueous alcohol). Neutralization equivalent 185.21; calculated 186.22.

Found, %:	C	51.49;	51.54;	H	5.23;	5.47;	S 17.25; 17.15
$C_8H_{10}O_3S$. Calculated, %:	C	51.60;		H	5.41;		S 17.22

Methyl ester IV was obtained by boiling 10 g of acid III in 100 ml of methanol in the presence of 2 ml of conc. sulfuric acid for 6 hours. This gave 8.6 g of ester IV, yield 80.3%, b.p. 104–104.5° (3 mm), m.p. about 25–28°.

Found, %:	C	54.27;	54.10;	H	5.93;	5.95;	S 15.95; 15.66
$C_9H_{12}O_3S$. Calculated, %:	C	53.98;		H	6.04;		S 16.01

5-Methylfuran-3-carboxylic acid (V). A solution of 5 g of methyl ester IV in 400 ml of methanol was heated for 1 hour with ~15 g of skeletal nickel at 50–60°. The solution was decanted from the catalyst, and the latter was washed with methanol. The combined solution was filtered, and the methanol was almost completely distilled off. To the residue was added a fivefold volume of water, and the oil that separated was extracted with ether. The extract was dried over magnesium sulfate, the solvent was distilled off, and the residue was distilled. This gave 2 g of the methyl ester of acid V, b.p. 80–83° (29 mm), yield 57%. By boiling with a 20% aqueous solution of caustic soda and ordinary work-up, 1.5 g (yield 86%) of acid V was obtained, m.p. 116–116.5° (from water). Literature data: m.p. 119° (8). Neutralization equivalent 125.15; calculated 126.11.

Found, %:	C 57.45; 57.14; H 4.59; 4.76
$C_6H_6O_3$. Calculated, %:	C 57.17; H 4.80

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Note: Figure translations are in progress. See original paper for figures.