# Reports of the Academy of Sciences of the USSR

Ya. L. Goldfarb, L. D. Tarasova

1965

SovietRxiv

## Abstract

## Full Text

**Reports of the Academy of Sciences of the USSR**

1965. Volume 163, No. 6

### CHEMISTRY

Ya. L. Goldfarb, L. D. Tarasova

# Synthesis of 2,4-Disubstituted Furans

*(Presented by Academician A. A. Balandin, January 29, 1965)*

Over the past two years a number of reports have appeared in print concerning the synthesis of various $\beta$-substituted furans ($^{1}$-$^{3}$) and selenophenes ($^{4}$). In some of these works ($^{2}$, $^{4}$), halogen-substituted derivatives of these heterocycles with a halogen in the $\beta$-position of the ring were used as starting compounds for further syntheses. It should be noted, however, that $\beta$-bromofuran, in contrast to its analogs in the thiophene ($^{5}$) and selenophene ($^{4}$) series, is relatively inaccessible. In any case, the route selected by Gronowitz and Sorlin ($^{2}$), presumably as the best way to obtain $\beta$-halofuran via $\beta$-chloromercury derivatives ($^{6}$), cannot be considered sufficiently satisfactory, at least because the yield reaches only 15%. Our attempt ($^{7}$) to obtain 4-bromo-2-acetylfuran (I) in one stage—by brominating 2-acetylfuran (III) in the presence of two and a half moles of aluminum chloride, in order thereby to proceed to 2,4-disubstituted furans—was unsuccessful: 4,5-dibromo-2-acetylfuran (II) was isolated.

In the present work it is shown that by selective reduction of the indicated dibromide it is possible to eliminate one bromine atom and in this way obtain 4-bromo-2-acetylfuran. The known reaction for the dehalogenation of bromo-substituted heterocyclic, in particular furan, compounds, which makes it possible to remove a bromine atom from the $\alpha$-position while preserving that in the $\beta$-position, proved difficult to carry out in the case of 4,5-dibromo-2-acetylfuran. For example, the action of zinc in ammonia ($^{8}$) led to a mixture of ketone (III) and a small amount of bromide (I); the action of butyllithium ($^{9}$) on the ketal of ketone II at −70° gave a poorly separable mixture of the starting ketal with the ketal of ketone I. As a result of the action of Raney nickel ($^{10}$), a mixture of ketones II and III was obtained; copper in quinoline ($^{11}$) gave too small a yield of I, and zinc dust in acetic acid under the conditions proposed by Gronowitz ($^{5}$) destroyed the product. A certain modification of this last method, consisting in the slow addition of zinc, regulating the reaction temperature within the range 35–50°, made it possible to obtain the desired compound (I). After one recrystallization from alcohol, the degree of purity of the product met the necessary requirements. The yield of ketone (I) was 78–80% of theory. The structure of ketone (I) was confirmed by its oxidation to the known 4-bromo-2-furancarboxylic acid (IV).

The melting point of a mixed sample of this acid with a specimen of it obtained by reduction of 4,5-dibromo-2-furancarboxylic acid (8) (V) showed no depression (see Scheme 1).

From ketone I, 4-bromo-2-ethylfuran (VI) was obtained by the Kishner reduction; from it, by the reaction of replacing bromine with lithium at −70° and subsequent treatment with dimethylformamide and diethyl disulfide, respectively, 5-ethyl-3-furaldehyde (VII) and 2-ethyl-4-ethylmercaptofuran (VIII) were synthesized. Aldehyde VII was oxidized to 5-ethyl-3-furancarboxylic acid (IX), which had also been obtained by another route by one of us,

Scheme 1

[chemical reaction scheme]

By Ya. L. Danyushevsky and M. A. Vinogradova, formylation of sulfide VIII gave 5-ethyl-3-ethylmercapto-2-furaldehyde (X), which is of interest as a starting material for the synthesis of chelates (cf. [6]).

## Experimental Part

**4-Bromo-2-acetylfuran (I).** To a mixture of 34 g (0.126 g-mol) of ketone (II) in 40 ml of acetic acid and 76 ml of water, 8.2 g (0.126 g-mol) of zinc dust was added at such a rate that the temperature of the mixture remained within 35–45°. On cooling the solution with ice and salt, a white precipitate formed, difficult to filter; after repeated grinding in a mortar with water it was filtered off and dried. Weight of dry product (I), 16.32 g. The filtrate was extracted with ether; the ethereal extract was washed with sodium bicarbonate solution and with water and dried over magnesium sulfate. After removal of the ether, a further 2.9 g of substance I was obtained. Yield of ketone (I), 80%; m.p. of the crude product, 57–64°. After two recrystallizations from aqueous alcohol, m.p. 69.5–70.5°.

Found, %: C 38.22; 38.25; H 2.76; 2.83; Br 42.03; 42.14
$C_6H_5BrO_2$. Calculated, %: C 38.12; H 2.67; Br 42.28

Semicarbazone, m.p. 189–190° (two recrystallizations from alcohol).

Found, %: N 16.97; 17.01
$C_7H_8BrN_3O_2$. Calculated, %: N 17.08

**4-Bromo-2-furancarboxylic acid (IV).** To a solution of sodium hypochlorite (from 5.75 g of caustic soda and 4.1 g of chlorine in 42 g of ice) at 50°, 2.8 g (0.014 g-mol) of ketone (I) was added. After heating at +70° for 45 min, at 0–5° there were added to the contents of the flask 2.5 ml of sodium bisulfite and 10% hydrochloric acid until an acid reaction to Congo was obtained. The product was filtered off and washed twice on the filter with cold water. Weight of product, 2.3 g (yield 97%), m.p. 123-125°. After two recrystallizations from heptane, m.p. 128.5-129.5°. Lit. (8): m.p. 128-129°.

Found, %: C 31.20; 31.31; H 1.56; H 1.56; Br 42.03; 42.09
$C_5H_3BrO_3$. Calculated, %: C 31.44; H 1.58; Br 41.85

**4-Bromo-2-ethylfuran (VI).** A mixture of 20 g (0.106 g-mol) of ketone (I), 26 g of 85% hydrazine hydrate, and 40 ml of ethylene glycol was heated to 90°. At 25°, 30 g of solid caustic potash was added to the solution, and, by heating the reaction flask on a burner, the mixture was distilled until a clear distillate was obtained, which was extracted with ether. The ethereal extract was dried with caustic potash. After removal of the ether, the product was distilled in vacuo. As a result of two distillations, 12 g of bromide VI was obtained (yield 65%), b.p. 56-57°/23 mm; $n_d^{20}$ 1.4918; $d_4^{20}$ 1.4284. $MR_D$ calculated 35.53; found 36.18.

Found, %: C 41.69; 41.38; H 4.29; 4.02; Br 45.60; 45.55
$C_6H_7BrO$. Calculated, %: C 41.17; H 4.03; Br 45.66

**5-Ethyl-3-furaldehyde (VII).** To 4.8 g (0.075 g-mol) of butyllithium (54 ml of ethereal solution) in a stream of nitrogen at −70° was added 11 g (0.063 g-mol) of bromide VI, and the solution was stirred at −70° for two hours; then, at this temperature, 14 ml (0.189 g-mol) of dimethylformamide in 20 ml of absolute ether was added. The mixture was left overnight in a stream of nitrogen. The contents of the flask were decomposed with 1% hydrochloric acid; the ethereal layer was separated, and the aqueous layer was extracted with ether. The combined ethereal extract was washed with 1% hydrochloric acid, water, and dried over magnesium sulfate. After removal of the ether, the residue was distilled twice in vacuo. 4.5 g of aldehyde VII* was isolated (yield 50%), with b.p. 90-95°/30 mm; $n_d^{20}$ 1.4872.

Found, %: C 67.00; 66.73; H 6.48; 6.54
$C_7H_8O_2$. Calculated, %: C 67.73; H 6.50

Semicarbazone, m.p. 178-179° (from alcohol).

Found, %: N 23.08; 23.35
$C_8H_{11}N_3O_2$. Calculated, %: N 23.19

Schiff base with β-naphthylamine—m.p. 126.5-127.5° (from alcohol).

Found, %: N 5.61; 5.80
$C_{17}H_{15}NO$. Calculated, %: N 5.62

**5-Ethyl-3-furancarboxylic acid (IX).** 0.5 g (0.004 g-mol) of aldehyde VII was oxidized with silver oxide obtained from 1.5 g (0.009 g-mol) of $AgNO_3$ and 1.1 g of caustic soda in 10 ml of water. After cooling of the mixture, the precipitate was filtered off, and the filtrate was acidified with 50% sulfuric acid and extracted with ether. After removal of the ether, 0.45 g was obtained (yield 79%) of acid IX, m.p. 106-107° (from heptane).

Found, %: C 59.70; 59.70; H 5.58; 5.64
$C_7H_8O_3$. Calculated, %: C 59.99; H 5.75

**2-Ethyl-4-ethylmercaptofuran (VIII).** To 40 g (0.22 g-mol) of bromide VI in a stream of nitrogen at −70° was added 16 g (0.25 g-mol) of butyllithium (205 ml of ethereal solution). The solution was stirred for two hours at −70°, after which 27.0 g (0.22 g-mol) of diethyl disulfide was added to the mixture. On the next day the mixture was decomposed with cold water; the ethereal layer was separated, washed with 10% caustic soda solution and with water, and dried over magnesium sulfate.

After removal of the ether, the residue was distilled twice in vacuo. 21.5 g of sulfide VIII was obtained (yield 60%) with b.p. 105–107°/32 mm, $n_d^{26}$ 1.4987.

Found, %: C 61.29; 61.53; H 7.82; 7.97; S 20.46; 20.34
$C_8H_{12}SO$. Calculated, %: C 61.50; H 7.74; S 20.52

* The carbon content is low by ~1%. For the analogously constructed 5-methyl-3-thiophenaldehyde, elementary analysis is not given (12).

**5-Ethyl-3-ethylmercapto-2-furaldehyde (X).** To a mixture of 20 g (0.15 g-mol) of sulfide VIII and 44 g (0.6 g-mol) of dimethylformamide, at $t = 0 \div 10°$, 28 g (0.18 g-mol) of $POCl_3$ was added over 45 min. The solution changed color from yellowish to red. It was left for 17 h, after which it was decomposed with a mixture of 200 g of ice and 200 ml of water. The solution was neutralized with 60 g of soda and left for 3 h, then extracted three times with ether. The ether layer was washed with water and dried over magnesium sulfate. After distilling off the ether, the residue was distilled twice in vacuo. 17 g of aldehyde (X) was obtained (yield 72%), b.p. 136.5–137°/5 mm, $n_d^{20}$ 1.5711.

| | | | |
|---|---|---|---|
| Found, %: | C 58.47; 58.30; | H 6.70; 6.55; | S 17.35; 17.49 |
| $C_9H_{12}SO_2$. Calculated, %: | C 58.68; | H 6.56; | S 17.40 |

**Semicarbazone:** m.p. 194.5–195.5° (two recrystallizations from alcohol).

| | |
|---|---|
| Found, %: | N 17.30; 17.39 |
| $C_{10}H_{15}N_3SO_2$. Calculated, %: | N 17.41 |

N. D. Zelinsky Institute of Organic Chemistry
Academy of Sciences of the USSR

Received
15 I 1965

## CITED LITERATURE

1. a) Ya. L. Gol' d farb, Ya. L. Danyushevskii, M. A. Vinogradova, DAN, **151**, 332 (1963). b) Ya. L. Gol' d farb, Ya. L. Danyushevskii, Izv. AN SSSR, ser. khim., 1964, No. 7, 1345.
2. S. Gronowitz, G. Sorlin, Ark. Kemi, **19**, 515 (1963).
3. M. Valenta, M. Janda, Coll., **29**, 1577 (1964).
4. Yu. K. Yur' ev, N. K. Sadovaya, E. A. Grekova, ZhOKh, **34**, 847 (1964).
5. S. Gronowitz, Acta chem. scand., **13**, 1045 (1959).
6. H. Gilman, G. F. Wright, J. Am. Chem. Soc., **55**, 3302 (1933).
7. Ya. L. Gol' d farb, L. D. Tarasova, Izv. AN SSSR, OKhN, 1960, No. 7, 1304.
8. H. B. Hill, C. R. Sanger, Ann., **232**, 46 (1886).
9. S. O. Lawesson, Acta chem. scand., **10**, 1020 (1956).
10. H. Kämmerer, L. Horner, Ber., **91**, 1376 (1958).
11. R. Motoyama, S. Nishimura, E. Imoto, J. Chem. Soc., **78**, 950 (1957); RZhKhim, 57468 (1958); Bull. Univ. Osaka Prefect, Ser. A, **6**, 127 (1958); Chem. Abstr., **53**, 4248e (1959).
12. Ya. L. Gol' d farb, Yu. B. Vol' kenshtein, B. V. Lopatin, ZhOKh, **34**, 969 (1954).

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

*Source: Math-Net.Ru and CyberLeninka. Machine translation. Verify with the original.*