REACTION OF AROMATIC AND HETEROAROMATIC COMPOUNDS BEARING ELECTRON-ACCEPTING SUBSTITUENTS

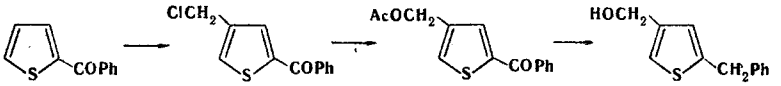
25.* SYNTHESIS OF (5-BENZYL-3-THIENYL)METHANOL FROM 2-BENZOYLTHIOPHENE

G. P. Gromova, L. I. Belen'kii, and Ya. L. Gol'dfarb

UDC 547.732'733.07

Under the action of paraformaldehyde and $AlCl_3$, 2-benzoylthiophene has been converted into 2-benzoyl-4-chloromethylthiophene, which on treatment with anhydrous sodium acetate has given 4-acetoxymethyl-2-benzoylthiophene. The reduction and simultaneous saponification of the latter under the conditions of the Kizhner reaction has yielded (5-benzyl-3-thienyl)methanol.

In recent years, a new class of pesticides has been discovered and is being widely investigated at the present time — synthetic analogs of natural pyrethrins, or pyrethroids, many of which possess an extremely high insecticidal activity [2]. In this connection, we have synthesized (5-benzyl-3-furyl)methanol [3], the ether of which with chrysanthemic acid is an effective insecticide of low toxicity for warm-blooded animals and has an activity approximately 50 times that of a mixture of natural pyrethrins [4]. A fundamental feature of the method developed is that, in contrast to known methods (see [2]), it does not include the stage of the closure of the furan ring, but is based on accessible furan compounds — pyromucic acid and its bromo derivatives. However, an attempt to realize a simpler scheme of synthesis of (5-benzyl-3-furyl)methanol from 2-benzoylfuran proved to be unsucessful, since it was impossible to obtain the key compound — 2-benzoyl-4-chloromethylfuran; the chloromethylation of 2-benzoylfuran took place with a very low yield and predominantly in position 5 of the furan ring [3]. Nevertheless, it has been found possible to perform a similar scheme of synthesis for (5-benzyl-3-thienyl)methanol (I).



It is known [4-8] that the carbinol (I) forms esters with a number of acids (including chrysanthemic acid) which are being studied as potential insectides, although they are less active from the furan analogs [2]. However, the possibility of obtaining fairly effective insecticides from carbinol (I) cannot be excluded.

The method that we have proposed permits the preparation of this carbinol in three stages from the readily available 2-benzoylthiophene (II). The chloromethylation of 2-benzoylthiophene under the action of paraformaldehyde and an excess of $AlCl_3$ in chloroform by the method proposed for the chloromethylation of 2-acetothienone [9] forms not only 2-benzoyl-4-chloromethylthiophene (III) but also 2-benzoyl-4,5-bischloromethylthiophene, diarylmethane derivatives, and a small amount of 2-benzoyl-5-chloromethylthiophene (according to PMR spectroscopy). Consequently, the conditions of chloromethylation were selected so as to avoid the formation of appreciable amounts of byproducts, but in these circumstances a considerable part of the initial ketone (II) was recovered unchanged. The chloromethyl ketone (III) was isolated with a yield of about 30% on the ketone (II) taken, but the sample obtained included, according to PMR, about 20% of the initial ketone (II) and about 2% of 2-benzoyl-4,5-bischloromethylthiophene as impurities; on the same basis, 2-benzoyl-5-chloromethylthiophene was absent. The 4-chloromethyl ketone (III) was characterized in the form of the crystal-

*For Communication 24, see [1].

N. D. Zelinskii Institute of Organic Chemistry, Academy of Sciences of the USSR, Moscow.
Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 4, pp. 472-474, April, 1980. Original article submitted September 26, 1979.

 0009-3122/80/1604-0356$07.50

line 4-acetylaminomethyl-2-benzoylthiophene. The action of sodium acetate on the chloromethyl ketone (III) gave 4-acetoxymethyl-2-benzoylthiophene (IV) which, under the conditions of the Kizhner [Kishner] reaction (see [10]) was reduced with simultaneous saponification, being converted into the carbinol (I). The reaction product was readily freed from contaminating 2-benzylthiophene by chromatography on Al_2O_3. The total yield of the carbinol (I) was 28% on the 2-benzoylthiophene taken (38% when the recovery of the initial ketone is taken into account).

EXPERIMENTAL

The PMR spectra were recorded on a Tesla BS-497 instrument (100 MHz) in CCl_4 with TMS as internal standard. The compositions of the mixtures obtained were determined from the integral curves for the singlet signals of CH_2 groups in ketones: III, 4.54 ppm; 2-benzoyl-5-chloromethylthiophene, 4.72 ppm; 2-benzoyl-4,5-bischloromethylthiophene, 4.57 and 4.77 ppm; and diarylmethanes, 4.0 ppm (see [11-13]); and for ketone (II) from the 4-H signal, q, 7.08 ppm, $J_{4,5}$ = 5 Hz, $J_{3,4}$ = 4 Hz).

2-Benzoylthiophene (II) was obtained by the benzoylation of thiophene [14] or by the action of thiophene-2-carbonyl chloride on benzene in the presence of $AlCl_3$; yield 94%, bp 124-127°C (0.5 mm), mp 56-56.5°C.

2-Benzoyl-4-chloromethylthiophene (III). To 55.9 g (0.416 mole) of $AlCl_3$ in 30 ml of dry $CHCl_3$ was added 7.45 g (0.24 mole) of paraformaldehyde, and then, at 4-6°C over 1 h and 25 min, a solution of 30 g (0.16 mole) of the ketone (II) in 45 ml of dry $CHCl_3$. The mixture was kept cooling for 40 min and was then poured into a mixture of ice and hydrochloric acid and was extracted with chloroform, and the extract was washed with water and dried over $MgSO_4$. Distillation gave the following fractions: 1) the initial ketone (II), bp 120-160°C (0.9 mm), 9.75 g; and 2) bp 160-180°C (0.9 mm), 13.8 g, containing, according to PMR, 80% of 2-benzoyl-4-chloromethylthiophene (III), 18% of the initial ketone (II), and 2% of 2-benzoyl-4,5-bischloromethylthiophene. The yield of the chloromethyl ketone (III) was 29% on the ketone (II) taken and 44% on that consumed.

Under the conditions described for chloromethyl-2-acetothienone [15], 9.1 g (0.038 mole) of the chloromethyl ketone (III) and 5.6 g (0.04 mole) of hexamethylenetetramine gave 2-benzoyl-4-aminomethylthiophene, which, by the action of acetic anhydride in aqueous alkali was converted into 4-acetylaminomethyl-2-benzoylthiophene, mp 98-100°C (reprecipitated with benzene from ethereal solution). Found: C 64.6; H 5.1; N 5.6; S 12.2%. $C_{14}H_{13}NO_2S$. Calculated: C 64.8; H 5.0; N 5.4; S 12.4%.

4-Acetoxymethyl-2-benzoylthiophene (IV). A solution of 7 g (0.09 mole) of the chloromethyl ketone (III) in 35 ml of glacial AcOH was treated with 4.7 g (0.056 mole) of anhydrous AcONa and the mixture was boiled for 4 h and was then left at room temperature for 16 h, poured into water, and extracted with ether. The extract was washed with water, with $NaHCO_3$ solution, and with water again, and was dried over $MgSO_4$. Elimination of the solvent yielded 7.7 g of an oily substance which, without additional purification, was subjected to Kizhner reduction (see the following experiment). A sample for analysis was obtained as described above and was purified by chromatography on Al_2O_3 (using a mixture of heptane and ether as eluent), followed by molecular distillation at 1 mm (bath temperature 120-130°C), mp 33-39°C. Found: C 64.5; H 4.6; S 12.3%. $C_{14}H_{12}O_3S$. Calculated: C 64.6; H 4.6; S 12.3%.

2-Benzoyl-4-hydroxymethylthiophene (I). To 7.7 g (0.03 mole) of compound (IV) in 130 ml of ethylene glycol was added 5.4 g (0.108 mole) of hydrazine hydrate and the mixture was boiled for 30 min and was cooled, after which 7.1 g (0.127 mole) of powdered KOH was added and it was boiled again for 30 min, cooled, poured into water, and extracted with ether, and the extract was washed with water and dried over $MgSO_4$. Distillation of the ether yielded 5.3 g of an oil which was purified by chromatography on Al_2O_3, the impurities being eluted, first, with heptane–ether (10:1) after which the carbinol (I) was eluted with ethanol. After elimination of the ethanol, the residue was subjected to molecular distillation at 0.2 mm and a bath temperature of 100-120°C. This gave 4.4 g of the oily carbinol (I), yield 78%. Found: C 71.0; H 5.9; S 15.5%. $C_{12}H_{12}OS$. Calculated: C 70.6; H 5.9; S 15.7%. PMR spectrum (in CCl_4), ppm: 2.80 (s, br., 1 H, OH), 4.00 (s, 2 H, CH_2R), 4.38 (s, 2 H, CH_2O), 6.63 (d, 1 H, 3-H), 6.83 (d, 1 H, 5-H), 7.17 (s, br. 5 H, R), $J_{3,5}$ = 1.5 Hz. α-Naphthylurethane, mp 121-123°C (from heptane). Found: C 73.9; H 5.5; S 8.7%. $C_{23}H_{19}NO_2S$. Calculated: C 74.0; H 5.1; S 8.6%.

LITERATURE CITED

1. L. I. Belen'kii, V. S. Bogdanov, and I. B. Karmanova, Izv. Akad. Nauk SSSR, Ser. Khim., No. 8, 1735 (1979).
2. M. Elliott and N. F. Janes, Chem. Soc. Rev., 7, 473 (1978).
3. L. I. Belen'kii, G. P. Gromova, and Ya. L. Gol'dfarb, Khim. Geterotsikl. Soedin., No. 3, 306 (1978).
4. M. Elliott, N. F. Janes, and B. C. Pearson, J. Chem. Soc., C, No. 14, 2551 (1971).
5. K. Ueda, T. Mizutani, N. Itatani, T. Fujimoto, and Y. Okuno, Japanese Patent No. 05385 (1969); Chem. Abstr., 71, 3260 (1969).
6. Y. Okuno, M. Hirano, J. Ohno, H. Takeda, O. Magara, N. Itaya, and I. Nishioka, GFR Patent No. 2,436,462 (1975); Chem. Abstr., 83, 114678 (1975).
7. Sumitono Chem. Co. Ltd., GFR Patent No. 2,335,347 (1974); Chem. Abstr., 80, 120746 (1974).
8. M. Matsui, K. Ueda, T. Mizutani, N. Itaya, S. Kitamura, K. Fujikami, K. Fufimoto, and Y. Okuno, Japanese Patent No. 10538 (1969); Chem. Abstr., 72, 66798 (1970).
9. Ya. L. Gol'dfarb, I. B. Karamanova, Yu. B. Vol'kenshtein, and L. I. Belen'kii, Khim. Geterotsikl. Soedin., No. 11, 1474 (1978).
10. A. F. Oleinik, G. A. Modnikova, K. Yu. Novitskii, T. I. Zykova, T. A. Gus'kova, and G. N. Pershin, Khim.-Farm. Zh., No. 9, 41 (1976).
11. L. I. Belen'kii, I. B. Karamanova, Yu. B. Bol'kenshtein, and Ya. L. Gol'dfarb, Izv. Akad. Nauk SSSR, Ser. Khim., No. 5, 956 (1971).
12. L. I. Belen'kii, I. B. Karamanova, and Ya. L. Gol'dfarb, Zh. Org. Khim., 7, 1743 (1971).
13. L. I. Belen'kii, I. B. Karmanova, and Ya. L. Gol'dfarb, Zh. Org. Khim., 9, 1514 (1973).
14. G. L. Stadnikoff and J. L. Goldfarb, Ber., 61, 231 (1928).
15. A. P. Yakubov, L. I. Belen'kii, and Ya. L. Gol'dfarb, Zh. Org. Khim., 7, 525 (1971).