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HALOGEN REACTIVITIES. VI. THE REACTIVITIES OF SEVERAL α-BROMOFURANS. THE ISOLATION OF 2-METHOXYFURAN

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Previous papers (1) in this series have described kinetic studies of a variety of aromatic halogen compounds, both carbocyclic and heterocyclic. The present paper is a preliminary report of the reaction of 2-bromofuran with methoxide ion and piperidine and of methyl 5-bromo-2-furoate with methoxide. We also disclose the first isolation of a simple alkoxyfuran.

2-Bromofuran has rightfully earned the reputation of being a very inert halide. For example, it has been reported (2) that the halogen-carbon bond is not split by treatment with aqueous sodium hydroxide and sodium cyanide, metallic sodium, dimethylzinc, nor activated magnesium. Consequently it was somewhat surprising to find that both piperidine and sodium methoxide can bring about the removal of the bromine relatively easily. Some discoloration was noted in all reactions in which bromofuran was used although it was more severe with piperidine than with methoxide.

In Table I are given the pseudounimolecular reaction rate constants for the bromofuran and piperidine reaction and the second order reaction[2] rate constants for bromofuran and methyl 5-bromo-2-furoate with sodium methoxide in methanol.

Since the reaction of methoxide with the bromoester appeared to be quite clean it seemed possible that the reaction might provide a feasible route to the hitherto unknown methoxyfuran. Saponification of the methoxy ester isolated from the reaction mixture afforded 5-methoxy-2-furoic acid. Both of these compounds are stable in the laboratory for some days after which they gradually liquefy. Methyl 5-methoxy-2-furoate did not form an adduct with maleic anhydride in ether solution. The acid on gentle heating lost carbon dioxide to produce 2-methoxyfuran. This ether proved to be a colorless sweet-smelling liquid boiling at 106–108°. On standing in the air for some hours it gradually became viscous, finally turning into a straw-colored glassy resin. Under nitrogen however, in the refrigerator, it appears to be stable for some weeks. On exposure to the vapors of hydrochloric acid the ether acquired a deep violet-red color which faded in about 15 minutes.

The structure of the methoxyfuran was proved by the method suggested by VanCampen and Johnson (3). By reaction with maleic anhydride the unstable 3-methoxy-3,6-endoxy-1,2,3,6-tetrahydrophthalic anhydride was formed, which,

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[1] Taken from the M.S. Thesis of Robert J. Petfield, Quaker Oats Co. Fellow in Organic Chemistry, 1953–1954.

[2] Difficulty in attaining the concentrated solutions of sodium methoxide required for the pseudounimolecular determinations necessitated our turning to the second order determinations.

TABLE I

PSEUDOUNIMOLECULAR REACTION RATE CONSTANTS

Compound	Reagent	T,°C.	k(hrs^{-1})
Bromofuran	Piperidine	207.66 ± .1	0.0330 ± .0006
		216.30 ± .05	.05020 ± .0011
		199.28 ± .05	.0232 ± .0004
$\Delta E^* = 22.0 \pm .98$			
$\Delta S^* = -47.3$			

BIMOLECULAR REACTION RATE CONSTANTS

			k(m^{-1} lhr^{-1})
Bromofuran	Sodium methoxide	187.62 ± .05	.0426 ± .0011
		191.19 ± .05	.0553 ± .0014
		193.33 ± .05	.0666 ± .0042
		196.86 ± .1	.0906 ± .0052
		211.08 ± .05	.2564 ± .0057
$\Delta E^* = 36.8 \pm 1.5$			
$\Delta S^* = -4.48$			
Methyl 5-bromo-2-furoate	Sodium methoxide	66.05 ± .1	.0646 ± .0006
		75.10 ± .1	.1583 ± .0021
		80.75 ± .1	.2870 ± .0044
		84.90 ± .1	.4439 ± .0174
$\Delta E^* = 24.5 \pm 1.1$			
$\Delta S^* = -10.3$			

It is interesting to note that the presence of the carbomethoxy1 group "*para*" to the bromine lowers the $E_{act.}$ in reaction with methoxide by about 12 Kcal.

on treatment with an acetic acid solution of 48% hydrobromic acid produced the known 3-hydroxyphthalic anhydride. Its identity was proved by comparison of melting point and mixture melting point with an authentic specimen.

The investigation of the alkoxyfurans is continuing and future papers will deal with their chemistry as well as the relationship of the kinetics of nucleophilic substitution of halofurans with similar systems.

EXPERIMENTAL

Preparation of reagents. Piperidine was purified in the manner previously described (4).

5-Bromo-2-furoic acid was prepared by the method of Whittaker (5), m.p. 186–187°. *Methyl 5-bromofuroate* was distilled (b.p. 88–89° at 3 mm.) and recrystallized from methanol and aqueous dioxane, m.p. 62.5–63.5°.

2-Bromofuran was freshly distilled from quinoline before use, b.p. 101.5–102.5°.

The procedure followed in the kinetic studies as well as the estimation of the precision of the activation energies was that described in previous papers (6, 4).

Methyl 5-methoxy-2-furoate. A solution of 19.5 g. of methyl 5-bromo-2-furoate in 125 ml. of 2.5 *M* sodium methoxide in absolute methanol was heated at 90° for one-half hour in a citrate bottle. Since, at this time a light-brown coloration had developed, the bottle was cooled, opened, and the contents filtered. Most of the alcohol then was removed by distillation and the residue was treated with dil. hydrochloric acid and extracted with ether.

On drying the ether extracts and distilling under diminished pressure there were obtained several fractions boiling in the vicinity of 100–102° at 6 mm. These were combined (8.7 g. from 2 runs) and recrystallized from petroleum hexane. The colorless crystalline ester melted at 51–52°. After standing for some weeks in a stoppered bottle it gradually became semi-liquid and no longer recrystallized well from petroleum hexane.

Anal. Calc'd for $C_7H_8O_4$: C, 53.8; H, 5.16.
Found: C, 53.8; H, 5.34.

5-Methoxy-2-furoic acid. A solution of 8 g. of methyl 5-methoxy-2-furoate in 50 ml. of 8% aqueous sodium hydroxide was refluxed for 2½ hours, cooled, acidified, and filtered. The white crystalline acid so obtained, weighed 5.9 g. when air-dried and melted at 136–138° (dec.). On standing for several weeks in a stoppered bottle in the laboratory it became quite pasty.

Anal. Calc'd for $C_5H_5O_2 \cdot CO_2H$: Neut. Equiv., 142. Found: Neut. Equiv., 144.

2-Methoxyfuran. On heating 2 g. of methoxyfuroic acid in a small distilling flask flushed with carbon dioxide a yellow distillate was obtained. Redistillation yielded 0.5 g. of colorless, mobile liquid which boiled at 110–111°; n_D^{25} 1.4468, d_4^{25} 1.0646. MR_D (calc'd) 25.439. MR_D (Found) 25.14.

Anal. Calc'd for $C_5H_6O_2$: C, 61.21; H, 6.17.
Found: C, 61.12, 61.12; H, 6.32, 6.40.

3-Methoxy-3,6-endoxy-1,2,3,6-tetrahydrophthalic anhydride. A few drops of 2-methoxyfuran was dissolved in dry ether and permitted to react with an ethereal solution of maleic anhydride. After about three hours the crystalline precipitate was removed and washed with ether. It then melted at 120–121°. After a few days the colorless crystals had become semi-liquid.

Anal. Calc'd for $C_9H_8O_5$: C, 55.11; H, 4.11.
Found: C, 55.38; H, 4.17.

3-Hydroxyphthalic anhydride. A sample of approximately 1 g. of adduct was heated at reflux a total of about 4 hours in 10 ml. of glacial acetic acid and 5 ml. of 48% hydrobromic acid. The liquid then was removed by vacuum distillation and the residue was extracted several times with boiling xylene, much hydrogen bromide being evolved in the process and considerable tar being left behind. The solid which separated from the cold xylene was filtered off and sublimed under diminished pressure. The sublimate (about 0.15 g.) softened at about 180° and melted at 198–200° alone and when mixed with authentic 3-hydroxyphthalic anhydride (m.p. 198–199.5°; reported (7), 198–199°.

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REFERENCES

(1) Paper V, BROWER, WAY, SAMUELS, AND AMSTUTZ, *J. Org. Chem.*, **19**, 1830 (1954).
(2) DUNLOP AND PETERS, *The Furans*, Reinhold Publishing Corp, New York, 1953, p. 85.
(3) VANCAMPEN AND JOHNSON, *J. Am. Chem. Soc.*, **55**, 430 (1933).
(4) BROWER AND AMSTUTZ, *J. Org. Chem.*, **18**, 1075 (1953).
(5) WHITTAKER, *Rec. trav. chim.*, **52**, 352 (1933).
(6) BROWER, SAMUELS, WAY, AND AMSTUTZ, *J. Org. Chem.*, **18**, 1648 (1953).
(7) PRATT AND PERKINS, *J. Am. Chem. Soc.*, **40**, 219 (1918).