[CONTRIBUTION FROM THE WM. H. CHANDLER CHEMISTRY LABORATORY, LEHIGH UNIVERSITY]

Halogen Reactivities. VIII.[1] 2-Halofurans

DONALD G. MANLY[2] AND E. D. AMSTUTZ

Received July 10, 1956

The kinetics of nucleophilic displacement with piperidine of 2-halofurans, 5-methyl-2-iodofuran, and 5-chloro-2-furoylpiperidide have been investigated. The reactivity is compared with the benzene analogs and an unexpected reaction of 2-iodofuran with piperidine is discussed.

The general nonreactivity of the carbon to halogen bond in the halofurans has long been a source of difficulty in preparative reactions as evidenced by recent attempts to prepare 2-methoxyfuran directly from the halofurans.[3] Recent interest in the kinetics of halocompounds has made available the data necessary for a comparison of the halofurans with other well known compounds. Because of the difficulty in using methoxide as a nucleophilic reagent, piperidine has been used as an alternate not only for convenience but also to permit comparisons with other preciously investigated compounds. The method and apparatus used in these determinations was that previously reported.

Table 1 lists the values obtained in this work and those necessary for comparative purposes.

TABLE I

Compound	ΔE* (kcal.)	ΔF* (kcal.)[a]	ΔS* (e.u.)[a]	log PZ[a]
2-Chlorofuran	21.89 ± 0.36	41.23 ± 0.03	−42.1 ± 1.5	7.8
Chlorobenzene[1]	26.8 ± 1.4	43.3 ± .05	−42.4 ± 3.0	7.71
2-Bromofuran[4]	21.69 ± 0.33	39.08 ± .02	−39.1 ± 1.3	8.4
Bromobenzene[1]	24.1 ± 0.4	41.4 ± .02	−42.3 ± 1.0	7.73
Iodobenzene[5]	23.6	40.7	−38.2	8.75
2-Iodofuran	30.85 ± 0.38	38.74 ± .02	−18.8 ± 1.2	12.9
5-Methyl-2-iodofuran	26.65 ± 0.75	39.47 ± .03	−29.1 ± 2.4	10.6
5-Chloro-2-furoyl-piperidide	17.22 ± 0.85	31.05 ± .03	−37.1 ± 2.8	—

[a] Calculated from rate constants at 200°C.

From a comparison of the results on chloro and bromo furans and benzenes it is apparent that both types of compounds have essentially the same steric requirements. Although the benzene compounds have a slightly higher activation energy, the rate controlling free energy of activation shows that the furans have a slightly more reactive carbon to halogen bond than the benzene analogues. Chlorofuran has the same reactivity as bromobenzene and chloro- and bromofuran have about a tenfold greater rate of reaction than the corresponding benzene compounds.

The slightly greater reactivity of the halofurans is attributed to the oxygen atom which could increase the positive character of the carbon bearing the halogen by an inductive effect. The over-all effect would be expected to be slight because of the opposed mesomeric effect and the possible repulsion of a nucleophilic reagent by the basic oxygen. A study[6] of carboxypiperidide substituted halogen compounds showed that the furans have a lower free energy of activation by 4.8 kcal and 500 fold greater reactivity. Reactivity of the halogen would be expected to be greatly enhanced by the mesomeric effect caused by the electron withdrawal of the carboxypiperidide group in addition to the inductive effect of the oxygen atom.

In an attempt to compare the kinetics of the various halogen substituted furoylpiperidides, the results shown in Table I were obtained for 5-chloro-2-furoylpiperidide. The rate constants were erratic showing a definite increase with time which was shown not to be due to piperidine hydrochloride catalysis as indicated in Table 3. Because definite trends were observed, valid comparative results probably cannot be obtained.

The results obtained for 2-iodofuran did not fit in with the expected trends as may be seen by comparing the other 2-halofurans and the halobenzenes. The tremendous increase in activation energy and the large difference in entropy of activa-

(1) Paper VII: Richardson, Brower, and Amstutz, *J. Org. Chem.*, **21**, 890 (1956).

(2a) Taken from the Ph.D. Thesis of Donald G. Manly, Quaker Oats Fellow in Organic Chemistry 1954–56. (2b) Present address, Research Laboratories, The Quaker Oats Co., Barrington, Ill.

(3) Manly and Amstutz, *J. Org. Chem.*, **21**, 516 (1956).

(4) Recalculated values; see Petfield and Amstutz, *J. Org. Chem.*, **19**, 1944 (1954).

(5) Berliner, Quinn, and Edgerton, *J. Am. Chem. Soc.*, **72**, 5305 (1950).

(6) Paper IX, to be published.

TABLE II

Compound	T_{corr} (°C.)	k (hr.$^{-1}$)
2 Chlorofuran	202.50	0.00285 ± 0.00005
	222.19	.00731 ± .00100
	231.29	.01064 ± .00048
	235.90	.01336 ± .00041
2-Bromofuran[4]	199.3	.02234 ± .00037
	207.7	.03171 ± .00054
	216.3	.04937 ± .00090
	231.2	.09735 ± .00254
2-Iodofuran	175.24	.00756 ± .00033
	179.57	.01053 ± .00034
	182.81	.01474 ± .00100
	188.49	.02033 ± .00017
	196.31	.03572 ± .00078
	214.38	.12093 ± .00075
5-Methyl-2-iodofuran	183.96	.00183 ± .00012
	192.06	.01326 ± .00048
	197.25	.01795 ± .00077
	202.30	.02428 ± .00081
5-Chloro-2-furoyl-piperidide	90.60	.01015 ± .00059
	95.73	.01599 ± .00057
	97.84	.01666 ± .00122
	102.45	.02091 ± .00223
	109 04	.03213 ± .00193

TABLE III

KINETICS OF 5-CHLORO-2-FUROYL PIPERIDIDE CONTAINING PIPERIDINE HYDROCHLORIDE

Time (Hr.)	k (hr.$^{-1}$) A[a]	B[b]	Δk[c]
0.5	0 01820	0.00932	0.00888
1 0	.01801	.01618	.00183
1 5	.01881	.01753	.00128
2.0	.01924	.01861	.00063

[a] A N = 0.1999. Not containing piperidine hydrochloride. [b] B containing piperidine hydrochloride at a concentration of 0.00451N. [c] T_{corr} = 101.10°C.

tion or PZ factor was entirely unexpected whereas the lower free energy of activation was consistent with the faster rate of reaction. The fact that the rate of reaction is faster while the activation energy is higher is quite unusual and implies a different reaction mechanism. The well known ability of furan compounds to undergo 2,5 addition[7] suggests the possibility of a similar type reaction with piperidine.

To provide evidence for a preliminary addition of piperidine, the kinetics of 5-methyl-2-iodofuran were investigated. With the 5-position blocked, a 2,5 addition would be highly improbable. The entropy of activation or PZ factor of 5-methyl-2-iodofuran appears to be consistent with nucleophilic displacement and the free energy of activation is likewise consistent with the previously reported[8] deactivation by a methyl group. The results also eliminate the possibility of a 2,3 addition. Since the data are in agreement with the expected values, it is quite probable that 2-iodofuran did undergo a multistage reaction rather than nucleophilic displacement.

(7) Rinkes, *Rec. trav. chim.*, **50**, 981 (1931). Clauson-Kaas, *Kgl. Danske Videnskab. Selskab. Mat.-fys. Medd*, **24**, 18 (1947); *C. A.*, **42**, 1930 (1948).

EXPERIMENTAL

Apparatus, techniques, and calculations were the same as in previous papers.[1]

2-Chlorofuran, b.p. 77.1–77.6° was prepared by decarboxylation of 5-chloro-2-furoic acid.

2-Iodofuran, b.p. 61–62°/57 mm. was prepared by iodination of 2-furylmercuric chloride.[9]

5-Methyl-2-iodofuran, b.p. 56–57°/20 mm. was prepared in 46% yield by iodination of 5-methyl-2-furylmercuric chloride.[10]

5-Chloro-2-furoylchloride was prepared in 89% yield from the acid and thionyl chloride, b.p. 85–86°/16 mm. and m.p. 29–30°.

5-Chloro-2-furoylpiperidide: Piperidine (17.9 g.) in 22 ml. of ether was added dropwise to a rapidly stirred solution of 16.5 g. of 5-chloro-2-furoylchloride in 40 ml. of ether. After an additional hour the mixture was filtered and the ether filtrates were evaporated and distilled to give 18 g. (89%) of the product, b.p. 137–139°/3 mm.

Anal. Calc'd for $C_{10}H_{12}ClO_2N$: C, 56.3; H, 5.67; N, 6.58. Found: C, 56.5; H, 5.87; N, 6.32.

Acknowledgement. The authors wish to express their appreciation to Mr. Andrew P. Dunlop and The Quaker Oats Co. for the financial support of this work.

BETHLEHEM, PA.

(8) Berliner and Monack, *J. Am. Chem. Soc.*, **74**, 1574 (1952).

(9) Gilman, Mallory, and Wright, *J. Am. Chem. Soc.*, **54**, 733 (1932).

(10) Gilman and Wright, *J. Am. Chem. Soc.*, **55**, 3302 (1933).