EFFECT OF THE NATURE OF THE HALOGEN ATOM ON THE STRUCTURE AND REACTIVITY OF 5-HALO-2-NITROFURANS

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UDC 541.127:543.422.25.4.6:547.722.4.5

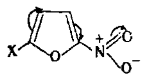
5-Chloro-2-nitrofuran was obtained for the first time. A comparative study of the properties (UV, IR, and NMR spectra) of 5-X-2-nitrofurans (X = Cl, Br, I) was made, and the kinetics of their reaction with diethylamine in dioxane were studied. The ratio of the rate constants in the indicated order is 29 : 23 : 1.

5-Bromo-2-nitrofuran (BNF) was obtained for the first time by Rinkes [1] by nitration of 5-bromopyromucic acid; after certain modifications [2-5], this method was solidly incorporated in chemical practice. 5-Bromo-2-nitrofuran is not only the starting preparation for the synthesis of compounds of the nitrofuran series [2-4, 6, 7] but has also been the subject for the investigation of the kinetics of nucleophilic substitution of halogen [8, 9]. We have previously proposed [2] a simple method for the preparation of 5-iodo-2-nitrofuran (INF), and 5-chloro-2-nitrofuran (CNF) was synthesized for the first time in the present reserach via a modification of the Rinkes method. Thus we obtained a sufficiently complete series of 5-X-2-nitrofurans (except for the 5-fluoro derivative, which has not yet been described), and opened up the possibility of making a comparison of the structures and reactivities of compounds of this series. In order to ascertain the effect of the nature of the halogen on the rate of its nucleophilic exchange in furan derivatives [10, 11], in the present research we studied the kinetics of the reaction of 5-X-2-nitrofurans with dimethylamine in dioxane. We also studied the spectral properties of the indicated compounds.

A definite regularity in the change in the properties is observed in the indicated series; this regularity is due to an increase in the polarizability of the halogen atom and intensification of its interaction with the nitro group.

In the UV spectrum this causes a bathochromic shift of the "charge-transfer" absorption band [12, 13]. In the IR spectrum one observes a shift to lower frequencies of both absorption bands of the nitro group — a similar phenomenon is characteristic for intramolecular "neutralization" of the nitro group and has been noted for aromatic nitro compounds that contain ring substituents with a positive mesomeric effect [14]. The NMR spectra of I-III contain two doublets; this corresponds to a system of two nonequivalent protons (the assignment of the bands was made on the basis of the literature data on the NMR spectra of 2,5-disubstituted furans [15]). From the chemical shifts it can be concluded that leveling of the degree of shielding of the protons in the 3 and 4 positions of the ring occurs in the I-III series. Whereas the difference in the chemical shifts $\Delta = \delta^{3H} - \delta^{4H}$ for I is 0.80 ppm, it is 0.62 ppm for II and 0.33 ppm for III, since the shielding of 3-H increases on passing from the chloro to the iodo derivative, whereas the shielding of 4-H weakens.

The "neutralizing" effect of the halogen atom, which removes the mesomeric effect of the nitro group to the diene system of the ring (shown in the scheme below), thus is reinforced in the indicated series.



I-III

Gavar and Stradyn' [16] on the basis of an analysis of the PMR spectra of furan derivatives arrived at the conclusion that polar interaction between the 2 and 5 positions of the ring is primarily transmitted through space

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Rostov State University, Rostov-on-Don. Translated from Khimiya Geterotsiklicheskikh Soedinenii, No. 10, pp. 1316-1318, October, 1976. Original article submitted December 31, 1975.

TABLE 1. UV, IR, and NMR Spectra of 5-X-2-Nitrofurans (I-III)

N	X	UV		IR		NMR		k_2, liter • mole^{-1} • sec^{-1}
		λ_{max}, nm	lg ε	$\nu_s^{NO_2}$, cm^{-1}	$\nu_{as}^{NO_2}$, cm^{-1}	δ^{3H}, ppm	δ^{4H}, ppm	
I	Cl	313	5,01	1347	1538	7,18	6,38	$6{,}6 \cdot 10^{-3}$
II	Br	315	4,04	1346	1537	7,12	6,50	$5{,}4 \cdot 10^{-3}$
III	I	328	4,09	1342	1532	7,05	6,73	$2{,}3 \cdot 10^{-4}$

and through the ring oxygen atom and that only a small fraction of the effect is due to the diene system. The increase in the polarizability of the halogen atom in the Cl, Br, I series evidently also affects the overall distribution of electron density primarily due to transmission of the effect via the shortest pathway – through space and through the oxygen atom. Suppression of the inductive effect of the nitro group also weakens its mesomeric effect, and this leads to equalization of the electron densities in the 3 and 4 positions.

The reactivities of I-III were estimated from the second-order rate constants in their reaction with dimethylamine in dioxane. It follows from the data in Table 1 that CNF and BNF differ only slightly with respect to their reactivities, whereas a sharp decrease in the rate is observed for INF – the ratio of the rate constants in the indicated series is 29 : 23 : 1. These results can be compared with similar data on the effect of the nature of the halogen atom on the rate of nucleophilic substitution in the benzene ring. It is not possible to predict the overall order of reactivities of the halogens for reactions of this type [17]. The only thing that is known is that in all cases the iodo derivatives react more slowly than the chloro and bromo derivatives, as we observed in our study, and the rates of the latter two are commensurable and can be interchanged in this series. For example, the ratio of the rate constants in the reaction of 2,4-dinitrohalobenzenes with piperidine in methanol is 4.3 : 4.3 : 1, whereas the ratio changes to 3.84 : 4.50 : 1 in the reaction of 4-nitrohalobenzenes with piperidine in DMSO [17]. It is interesting to note that there is not such a sharp drop in the reactivities between the chloro and iodo derivatives as that observed in our study in any one of the cases analyzed in [17].

It follows from Table 1 that the order of the reactivities corresponds to the order of the change in the spectroscopic properties of I-III, although the limited number of compounds does not make it possible to make a more rigorous correlation here. A qualitative comparison shows that the physical parameters of the chloro and bromo derivatives differ only slightly, whereas there is a sharp change in these values on passing to the iodo derivative. This is especially the case with regard to the UV spectra ($\Delta\lambda_{Cl \to Br} = 2$ nm, $\Delta\lambda_{Br \to I} = 13$ nm) and the NMR spectra ($\Delta\delta^{4H}_{Cl \to Br} = 0.12$ ppm, $\Delta^{4H}_{Br \to I} = 0.23$ ppm). The change in the electron density in the ring, which is characterized by the spectral properties, also regulates in this way the general tendency toward a change in the reactivities of the compounds, although one also should not observe a complete analogy here because of the effect on the free energy of activation of specific factors due to the geometry and energy of the transition state.

EXPERIMENTAL

Synthesis of the Compounds. 5-Bromo-2-nitrofuran and 5-iodo-2-nitrofuran were obtained by methods described in [2, 5].

5-Chloro-2-nitrofuran. Acetic anhydride (20 ml) was placed in a three-necked 100-ml flask equipped with a stirrer, a dropping funnel, and a thermometer, and the flask was cooled to −10°. A 21-g sample of nitric acid (sp. gr. = 1.5) was added dropwise with stirring, during which the rate of addition was regulated in such a way that the temperature in the flask was maintained at ~−10°. A 4.6-g sample of 5-chloropyromucic acid was dissolved separately in 25 ml of acetic anhydride, and the solution was added from the dropping funnel with vigorous stirring in the course of 1 h to the nitrating mixture while maintaining the same temperature. Stirring was continued for another hour, after which the temperature was gradually raised to 0° in the course of 2 h, and the mixture was stirred at 0° for another hour. The solution was poured over ice, and the aqueous mixture was saturated with sodium chloride and extracted five times with ether. The ether extracts were combined and steam distilled. After removal of the ether by distillation, the CNF was removed by distillation in the form of an oil that solidified after cooling. The CNF crystals were removed by filtration with a cooled Buchner funnel, dried in a desiccator, and stored in a refrigerator. The yield of product with mp 23° was 1.05 g (23%). Found: Cl 24.18%. Calculated: Cl 24.12%.

Purification of the Solvent and Preparation of the Solutions. Dioxane was purified by the usual method [18]. A solution of dimethylamine in dioxane was prepared by bubbling dried (over potassium hydroxide) dimethylamine gas through dioxane. The amine concentration in solution was determined by titration with 0.1

N H_2SO_4 with an LPU-01 potentiometer, after which the solution was diluted with dioxane to the required concentration.

Kinetic Measurements. The kinetics of the reaction were studied at 50°; the substrate concentration was 0.05 M, and the reagent concentration was 0.15 M. The reaction was carried out in Landolt vessels in an ultrathermostat and was stopped by dilution of the mixture with water and acidification with nitric acid. The course of the reaction was monitored from the percentage of ionic halogen, which was determined by potentiometric titration by the usual method [10].

Spectral Measurements. The UV spectra of dioxane solutions of the compounds were recorded with an SF-4a spectrophotometer. The IR spectra of carbon tetrachloride solutions were recorded with a UR-20 spectrometer. The NMR spectra of carbon tetrachloride solutions of the compounds were obtained with a Tesla spectrometer (operating frequency 80 MHz).

LITERATURE CITED

1. I. J. Rinkes, Rec. Trav. Chim., 50, 981 (1931); Chem. Zentralblatt, 1, 65 (1932).
2. Z. N. Nazarova and V. N. Novikov, Zh. Obshch. Khim., 31, 263 (1961).
3. B. R. Balaguer and G. M. Garcia-Marquina, An. Real. Acad. Farmac., 27, 47 (1961); Ref. Zh. Khim., 5Zh209 (1962).
4. V. N. Novikov and Z. N. Nazarova, Zh. Obshch. Khim., 1, 2022 (1965).
5. Z. N. Nazarova and V. N. Novikov, Methods for the Synthesis of Chemical Reagents and Preparations [in Russian], Vol. 17, IREA, Moscow (1968), p. 20.
6. Z. N. Nazarova, V. N. Novikov, and V. Ts. Bukhaeva, Zh. Obshch. Khim., 34, 705 (1964).
7. O. Dann and E. F. Möller, Chem. Ber., 80, 23 (1947).
8. V. N. Novikov and Z. N. Nazarova, Zh. Org. Khim., 2, 1901 (1966).
9. D. Spinelli, G. Guanti, and C. Dell'Erba, Boll. Scient. Fac. Chim. Industry, Bologna, 25, 71 (1967).
10. V. N. Novikov and Z. N. Nazarova, Khim. Geterotsikl. Soedin., No. 1, 3 (1967).
11. V. N. Novikov, V. Ts. Bukhaeva, F. T. Pozharskii, and A. M. Simonov, Khim. Geterotsikl. Soedin., No. 2, 252 (1971).
12. O. V. Sverdlova, Electronic Spectra in Organic Chemistry [in Russian], Khimiya, Leningrad (1973), p. 214.
13. J. C. Brand and G. Eglinton, Application of Spectroscopy in Organic Chemistry [Russian translation], Mir, Moscow (1967), p. 210.
14. L. B. Bellamy, Infrared Spectra of Complex Molecules, Methuen (1958).
15. Physical Methods in the Chemistry of Heterocyclic Compounds [in Russian], Khimiya, Moscow–Leningrad (1966), p. 432.
16. R. A. Gavar and Ya. P. Stradyn', Khim. Geterotsikl. Soedin., No. 1, 15 (1965).
17. T. J. De Bur and I. P. Dirsk, in: Chemistry of Nitro and Nitroso Groups [Russian translation], Vol. 1, Mir, Moscow (1972), p. 371.
18. Preparative Organic Chemistry [Russian translation], Inostr. Lit., Moscow (1959).