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F. M. WEINSTEIN and Academician of the Academy of Sciences of the Ukrainian SSR E. A. SHILOV

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Abstract

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F. M. WEINSTEIN and Academician of the Academy of Sciences of the Ukrainian SSR E. A. SHILOV

KINETIC ISOTOPE EFFECT IN THE IODINATION REACTIONS OF AROMATIC AMINES

It has recently been shown ([1]) that the iodination reactions of aromatic dialkylaminosulfonic acids are described by a trimolecular kinetic equation

$$-\frac{d(\mathrm{I})}{dt} = k_1[\mathrm{M}]^2[\mathrm{X}] + k_2[\mathrm{M}][\mathrm{X}][\mathrm{B}], \tag{1}$$

where M is the anion of a dialkylaminosulfonic acid, B is the basic component of the buffer mixture, and X is an iodine cation or molecular iodine. It follows from equation (1) that, in the iodination mechanism, the base B or a second molecule of the amine participates.

Two different explanations can be given for this phenomenon.

A. The base serves as a proton acceptor according to the scheme:

$$\mathrm{ArNR_2} + \mathrm{X} + \mathrm{B} \longrightarrow [\mathrm{ArNR_2} \cdots \mathrm{H} \cdots \mathrm{X} \cdots \mathrm{B}] \longrightarrow \mathrm{XArNR_2} + \mathrm{HB}$$

B. The iodinating agent is a complex of composition $\mathrm{X} \cdots \mathrm{NR_2Ar}$, or, in buffer solutions, $\mathrm{X} \cdots \mathrm{B}$:

$$\mathrm{ArNR_2} + \mathrm{X} \cdots \mathrm{NR_2Ar} \longrightarrow [\mathrm{ArNR_2} \cdots \mathrm{X} \cdots \mathrm{H} \cdots \mathrm{OH_2} \cdots \mathrm{ArNR_2}] \longrightarrow \mathrm{XArNR_2} + \mathrm{H_3O^+} + \mathrm{ArNR_2}$$

In this case the proton acceptor may be a water molecule (as accepted in the scheme) or another base.

Schemes A and B are kinetically indistinguishable, but a choice between them can be made by using determinations of the isotope effect upon replacement of hydrogen by iodine. Indeed, if the reaction follows mechanism A, then an isotope effect should be observed, since the removal of the proton corresponds to the stage that determines the overall reaction rate (because the second molecule of amine or the base B enters into the kinetic equation). If mechanism B is correct, then an isotope effect is not obligatory, because the stage of proton removal is

Figure 1

Figure 1: Figure 1

not reflected in the kinetic equation. However, iodination by mechanism B may also proceed with an isotope effect, provided that the rate of proton removal is comparable with the rate of formation of the intermediate quinoid complex.

In order to choose between the alternatives that had arisen, we studied the kinetics of iodination of several aromatic amines, aminocarboxylic and aminosulfonic acids (see Table 1), and in parallel determined the kinetic isotope effect by the method of comparing the rate constants for iodination of ordinary and deuterated amino compounds. It was established that the rate of iodination of the compounds studied, with the exception of certain special cases and conditions discussed below, generally follows equation (1). In this case, for primary amines and methylaniline: X is the iodine cation (hydrated or in a complex with the amine). Iodination of tertiary amino compounds proceeds by two pathways—via J^+ and via J_2 (or their complexes with amines).

Fig. 1. Rate of iodination of amino compounds
1 —light aniline; **2** —2,4,6-trideuteroaniline; **3** —light sodium salt of *m*-aminobenzoic acid; **4** —sodium salt of N,N-dimethylsulfanilic acid (open circles —light, dark circles —2,4,6-trideutero salt); **5** —sodium salt of 2,4,6-trideutero-*m*-aminobenzoic acid.

The principal experimental results are given in Table 1 and in Fig. 1. The table gives the experimental conditions, the percentage of hydrogen replacement in the deuterium compounds, the isotope effect (k_H/k_D), and the relative activity of the light amino compounds upon iodination (A_k). The value of A_k was taken relative to the iodination rate of the N,N-dimethylmetanilate ion, adopted as unity. The values of A_k should be regarded as approximate; exact comparison is made difficult by the fact that the iodination conditions of the different amino compounds necessarily differ greatly.

Table 1

Compound	% replacement of H by D	k_H/k_D	Relative activity, A_k	Initial concentrations (mol/l), pH, temperature
2,4,6-Trideutero-N,N-dimethylmetanilate ion	90	1	1	M 0.0758; J_2 0.008; KJ 0.04; 25°

Compound	% replacement of H by D	k_H/k_D	Relative activity, A_k	Initial concentrations (mol/l), pH, temperature
4-Deutero-N,N-dimethylmetanilate ion	61	1	1	M 0.0145; J_2 0.0072; KJ 0.073; phosphate 0.064; pH 6.9; 25°
2,6-Dideutero-N,N-dimethylsulfanilate ion	90	1	0.2	M 0.027; J_2 0.005; KJ 0.01; 25°
2,4,6-Trideutero-*m*-dimethylaminobenzoate ion	95	1.4	35	M 0.02; J_2 0.005; KJ 0.04; 30°
2,4,6-Trideuterometanilate ion	61	2*	0.02	M 0.133; J_2 0.015; KJ 0.036; 35°
2,4,6-Trideutero-*m*-aminobenzoate ion	90	4.8	0.22	M 0.045; J_2 0.005; KJ 0.05; 30°
Same	90	3.0	0.24	M 0.01; J_2 0.005; KJ 0.02; phosphate 0.1; pH 7.4; 30°
2,4,6-Trideuteroaniline	86	3.5	5.4	M 0.025; J_2 0.005; KJ 0.15; 25°

Compound	% replacement of H by D	k_H/k_D	Relative activity, A_k	Initial concentrations (mol/l), pH, temperature
Same	86	4.0	15	M 0.02; J_2 0.004; KJ 0.12; phosphate 0.025; NaCl 0.08; pH 8.0; 25°
2,4,6-Trideuteromethylaniline	95	3.2	110	M 0.01; J_2 0.002; KJ 0.3; acetate 0.05; pH 5.0; 25°
2,4,6-Trideuterodimethylaniline	89	3.0	120	M 0.01; J_2 0.002; KJ 0.15; lactate 0.5; pH 3.5; 30°

* This value of the isotope effect is apparently smaller than the true one because, in the preparation used, the percentage replacement of H by deuterium is small.

As the data in Table 1 and curve 4 in Fig. 1 show, the iodination reaction in some cases proceeds without any isotope effect ($k_H/k_D = 1$). This applies to the three dimethylaminobenzenesulfonic acids. The 2,4,6-trideutero-*m*-dimethylaminobenzoate ion is iodinated only slightly more slowly than the light compound. For the remaining amino compounds, iodination proceeds with a substantial isotope effect (from 3 to 4.8). This group includes various primary and secondary amines and salts of aminosulfonic and aminocarboxylic acids containing a primary amino group.

The fact that no isotope effect is observed for certain amino compounds proves, as indicated above, that the base participates in the reaction as part of the iodinating complex, and not as a proton acceptor. The presence of an isotope effect in other amines might be explained by a difference in the reaction mechanism; however, one must take into account the very great similarity of the kinetic dependences for the amines studied. We therefore believe that in all cases of iodination scheme B is valid, i.e., that the iodinating agents are complexes of the iodine cation and iodine with the amino compound or with base B.

Other considerations can also be adduced in support of this conclusion (1). In

particular, calculation shows that under conditions close to those of our experiments, the concentration of J^+ is 10^{-14}-10^{-15} M. Such a negligible concentration of the active agent probably cannot account for the observed rate of iodination. On the other hand, the formation of complexes between amines and halogens is a general rule (3), and cases are known in which the presence of amines in aqueous solution accelerates halogenation reactions (2).

It should be noted that a kinetic isotope effect of magnitude 4 was also found for the iodination reaction of deuterated phenol (4), analogous to the iodination of primary and secondary amines. Thus, iodination belongs to the small number of reactions of electrophilic substitution of hydrogen in aromatic systems for which a kinetic isotope effect has been found. As is known, nitration (5), bromination (6), and, for the most part, azo coupling (7) proceed at the same rate for light and heavy compounds. Sulfonation reactions (8) and cyclodehydration of anils (9) are associated with a small isotope effect. The substantial isotope effect established for the case of azo coupling of *p*-chlorophenyldiazonium with 2-naphthol-6,8-disulfonic acid in the presence of pyridine has been explained by steric hindrance (7).

At present it is unclear why iodination of amines is associated with an isotope effect in some cases and not in others. As can be seen from the data in Table 1, there is no general dependence between the reaction rate and the isotope effect. Thus, for example, an isotope effect is observed both for the very weakly active metanilic acid and for the highly active methylaniline and dimethylaniline. Meanwhile, the fairly active dimethylaminobenzenesulfonic salts are iodinated equally rapidly in the form of light and heavy compounds. It is possible that the relation between the rate of iodination and the isotope effect must be considered separately for the series of tertiary amines and for the series of primary and secondary amines.

Experimental Data*

Preparations. *m*- and *p*-Dimethylaminobenzenesulfonic acids were obtained by sulfonation of dimethylaniline (10). We prepared *m*-dimethylaminobenzoic acid from *m*-aminobenzoic acid by methylation with methyl iodide in alkaline medium (11). To separate the monomethyl pro–

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* With the participation of O. M. Grishina.

the derivative dimethylaminobenzoic acid was extracted with ether from the aqueous solution at pH $\sim$ 4; long thin needles, m.p. 154°. In the other cases, ready-made preparations were used after proper purification.

2,4,6-Trideuteroaniline, -methylaniline, and -dimethylaniline, as well as 2,4,6-trideutero-*m*-amino- and -*m*-dimethylaminobenzoic acids, were obtained by exchange in an acidic medium of the light amino compounds with 99% D_2O on heating to 100° for 60–100 hours. 2,4,6-Trideutero-*m*-

Figure 2. Iodination of dimethylaniline. Initial concentrations (mol/l): dimethylaniline 0.0039, J_2 0.0015, KJ 0.4, phosphate 0.04; pH 6.1; 30°. 1 — light dimethylaniline; 2 —2,4,6-trideuterodimethylaniline

Figure 2: Figure 2. Iodination of dimethylaniline. Initial concentrations (mol/l): dimethylaniline 0.0039, J_2 0.0015, KJ 0.4, phosphate 0.04; pH 6.1; 30°. 1 —light dimethylaniline; 2 —2,4,6-trideuterodimethylaniline

and *p*-dimethylaminobenzenesulfonic acids were prepared by sulfonation of 2,4,6-trideuterodimethylaniline with 30% deuteroleum, obtained from SO_3 and D_2O. 4-Deutero-N,N-dimethylmetanilic acid was obtained by sulfonation of 4-deuterodimethylaniline, prepared from *p*-bromodimethylaniline via *p*-lithiodimethylaniline ([12]). The deuterium content in the preparations obtained was determined from the water after combustion by flotation, mass-spectrometric, or drop methods.

Fig. 2. Iodination of dimethylaniline. Initial concentrations (mol/l): dimethylaniline 0.0039, J_2 0.0015, KJ 0.4, phosphate 0.04; pH 6.1; 30°. 1 —light dimethylaniline; 2 —2,4,6-trideuterodimethylaniline.

The rate of iodination was measured at various concentrations of the amino compounds, iodine, and potassium iodide, without additives and in the presence of phosphate, acetate, or lactate as buffer salts. The drop in the iodine titer was observed by microtitration of samples with thiosulfate.

The results of the kinetic experiments are for the most part well reproduced and make it possible to establish exact dependences of the reaction rate on the concentration of the components of the mixture. These data will be set forth in detail elsewhere. In this article we shall note only that, in the iodination of methylaniline and dimethylaniline, the reaction under certain definite conditions has an autocatalytic character, as is seen from Fig. 2. The reaction proceeds normally according to equation (1) if it is carried out at low concentrations of free amine and iodine. The values of k_H/k_D given for these two amines in Table 1 were obtained under conditions in which autocatalysis did not occur, in particular at low pH. Fig. 2 shows, however, that the autocatalytic reaction also proceeds with an isotope effect equal to 3-4. The nature of the autocatalytic reaction is not yet entirely clear.

Institute of Organic Chemistry
Academy of Sciences of the Ukrainian SSR

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REFERENCES

1. A. N. Kurakin, E. A. Shilov, *Ukr. Khim. Zhurn.*, **23**, 31 (1957).

2. E. A. Shilov, A. I. Slyadneva, G. V. Kupinskaya, *ZhOKh*, **22**, 1499 (1952); L. Brown, F. Soper, *J. Chem. Soc.*, 1953, 3576.

3. Ya. A. Fialkov, *Usp. Khim.*, **15**, 486 (1946).

4. E. Grovenstein, D. Kilby, *J. Am. Chem. Soc.*, **79**, 2972 (1957).

5. L. Melander, *Ark. Kemi*, **2**, 211 (1950); T. Bonner, F. Bowyer, G. Williams, *J. Chem. Soc.*, 1953, 2650; W. Lauer, W. Noland, *J. Am. Chem. Soc.*, **75**, 3689 (1953); K. Halvarson, L. Melander, *Ark. Kemi*, **11**, 77 (1957).

6. L. Melander, l.c.; P. de la Mare, T. Dunn, J. Harvey, *J. Chem. Soc.*, 1957, 923.

7. H. Zollinger, *Helv. Chim. Acta*, **38**, 1597, 1617 (1955).

8. L. Melander, l.c.; U. Berglund-Larsson, L. Melander, *Ark. Kemi*, **6**, 219 (1953).

9. T. Bonner, J. Wilkins, *J. Chem. Soc.*, 1955, 2358.

10. A. N. Kurakin, *ZhOKh*, **18**, 2089 (1948).

11. R. Willstätter, W. Kahn, *Ber.*, **37**, 411 (1904).

12. W. Davies, F. Mann, *J. Chem. Soc.*, 1944, 279.

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