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# SECONDARY ISOTOPE EFFECTS AND AROMATIC HYDROGEN EXCHANGE*

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IT has recently been demonstrated that secondary hydrogen isotope effects are absent from aromatic substitution by nitronium ion, mercuric ion, and molecular bromine.[1**] All evidence bearing on the mechanisms of these three reactions is consistent with a two-step reaction sequence having a single intermediate species for the actual substitution process.[3] Another type of aromatic substitution reaction, however, is thought to exist: the evidence concerning electrophilic substitution by hydrogen appears to

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[*] Work carried out under the auspices of the U.S. Atomic Energy Commission.

[**] The secondary isotope effect of 1.046 for bromination cited in this reference is now open to doubt: the expected large primary isotope effect in side chain bromination[2] could well account for all of the observed effect, even if only a relatively small amount of benzyl bromide were formed.

[1] C. G. Swain, T. E. C. Knee and A. J. Kresge, *J. Amer. Chem. Soc.* **79**, 505 (1957).

[2] K. B. Wiberg, *Chem. Rev.* **55**, 713 (1955).

[3] C. K. Ingold, *Structure and Mechanism in Organic Chemistry*, p. 279. Cornell Univ. Press, Ithaca, New York (1953); P. W. Robertson, *J. Chem. Soc.* 1267 (1954); P. B. D. de la Mare, T. M. Dunn and J. T. Harvey, *Ibid.* 923 (1957); H. Zollinger, *Experientia* **12**, 165 (1956); A. J. Kresge, unpublished work on mercuration.

demand a reaction sequence of at least three steps with at least two intermediate species along the reaction path.[4] We undertook to determine whether a secondary isotope effect would appear in this other type of aromatic substitution.

We measured the rate of exchange of tritium at 25° between 9.58 M sulfuric acid ( ~ 62 weight %) and both ordinary toluene and toluene-$\alpha$-$d_3$ (97 at.% deuterium in the methyl group). Tritium was present initially in the acid. Ortho- and para-substitution in this reaction are known to occur forty times as fast as meta-substitution.[5] The rates measured were, therefore, essentially those for ortho- and para-substitution.* Fig. 1 shows that substitution in both light and heavy toluene occurred at the same rate. Rate constants calculated by the usual least squares method are $k_H = 0.936$ cpm/min. $\sigma = 0.019$; $k_D = 0.935$ cpm/min. $\sigma = 0.018$ ( $\sigma$ is the standard deviation). This gives an isotope rate ratio of 1.002, $\sigma = 0.026$.

The absence of a secondary isotope effect in this reaction is consistent with data on other aromatic substitutions[1] and suggests the general absence of such effects in this large class of reactions. The usually accepted explanation[6] of secondary isotope effects is one involving hyperconjugation, and these effects would seem to be expected whenever hyperconjugative

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* The exchange was only taken to ca. 3% completion, the rate constants being obtained from direct plots of the amount of reaction vs. time. This procedure (valid for initial slopes only) avoids the necessity of knowing the position of exchange equilibrium.

[4] V. Gold and D. P. N. Satchell, J. Chem. Soc. 3609, 3619, 3622 (1955); Ibid. 1635 (1956).

[5] V. Gold and D. P. N. Satchell, J. Chem. Soc. 274 (1956).

[6] E. S. Lewis, Tetrahedron **5**, 143 (1959); V. J. Shiner, Jr., Ibid. **5**, 243 (1959).

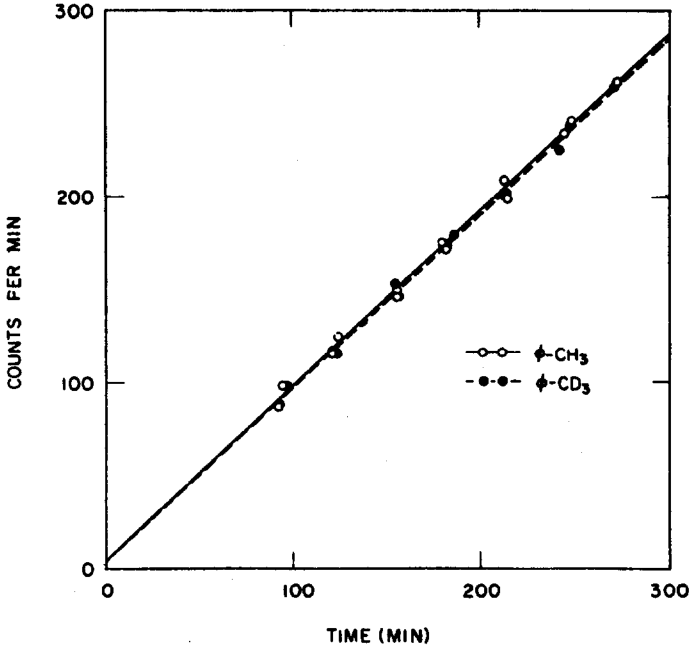

FIG. 1. Rates of nuclear hydrogen exchange of toluene and toluene-α-$d_3$ with 9.58 M sulfuric acid-t at 25°.[5]

effects are important. And yet, it can be demonstrated that carbon-hydrogen hyperconjugation is at least as important an activating influence in aromatic substitution as it is in those solvolytic reactions where most secondary isotope effects have been found.*

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* For example, application of a method recently developed by Taft and Lewis[7] which permits quantitative estimate of the hyperconjugative

An attempt has recently been made to rationalize this anomaly by invoking different degrees of electron release for C-H and C-D bonds.[8] This leads to an inductive contribution to the secondary isotope effect of a methyl group opposite in sign to the hyperconjugative contribution, and these two effects are said to be nicely balanced in aromatic substitution. It has recently been demonstrated, however, that any difference in inductive electron release between C-H and C-D bonds cannot possibly be large enough to accomodate this explanation.[**9]

The anomaly, therefore, remains. And the fact that it exists at all makes it desirable to emphasize the danger of a too facile identification of secondary isotope effects with hyperconjugative phenomena, for it appears that the latter may be present without necessarily giving rise to the former.

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effect of a methyl group on a reaction, and which expresses the magnitude of this effect in terms of a parameter, R, discloses that aromatic bromination by molecular bromine has the remarkably high R value of 2.9. R values for aromatic hydrogen exchange, nitration, and mercuration are 1.8, 1.5, and 1.4 respectively, whereas R values for solvolytic reactions of benzhydryl and dimethylbenzyl chlorides range from 1.2 to only 1.4.

** Moreover, when Taft's method for quantitative evaluation of inductive effects[7,10] is applied to the cases in question, I values ranging from 0.10 to 0.19 are obtained for the solvolytic reactions, and 0.10 to 0.45 (bromination), for the aromatic substitutions. The ratios of the R values cited above to these I values will measure the relative contribution of hyperconjugative to inductive effects. These ratios are not significantly different for the two classes of reactions: 6.5 to 14 for solvolysis and 6.3 to 18 (hydrogen exchange) for aromatic substitution. Any small difference, in fact, points to the greater relative importance of hyperconjugation in aromatic hydrogen exchange.

[7] R. W. Taft, Jr. and I. C. Lewis, Tetrahedron 5, 210 (1959).

[8] E. A. Halevi and M. Nusim, Bull. Res. Counc. Israel 5A, 263 (1956); Abstrs. 16th Intl. Cong. Pure Appl. Chem. II, p. 27 (1957); E. A. Halevi, Tetrahedron 1, 174 (1957); Trans. Faraday Soc. 54, 1441 (1958).

[9] R. E. Weston, Jr., Tetrahedron 6, 31 (1959).

[10] R. W. Taft, Jr., Steric Effects in Organic Chemistry (Edited by M. S. Newman) Chap. 13. John Wiley, New York (1956).