Tetrahedron Letters No. 12, pp 1059 - 1062, 1975. Pergamon Press. Printed in Great Britain.

VARIATIONS OF CARBON-14 KINETIC ISOTOPE EFFECTS IN THE MENSCHUTKIN TYPE REACTION OF BENZYL ARENESULFONATES

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(Received in Japan 25 January 1975; received in UK for publication 18 February 1975)

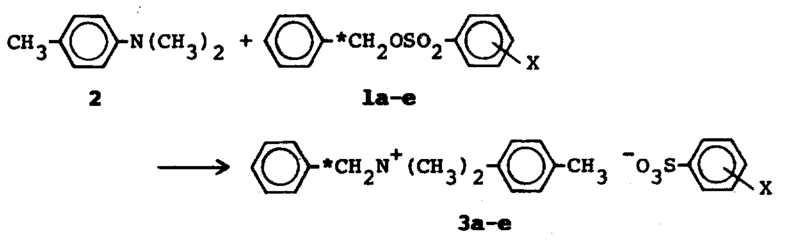
A large number of studies, both theoretical and experimental, have been focused in recent years on variations of primary hydrogen isotope effects in proton transfer reactions.[1] In 1961, Westheimer predicted that the isotope effect should go through a maximum when the transition state is symmetric in a vibrational sense.[2] The original reasoning involving the stretching frequencies of a three-center model was criticized, and revised calculations were presented.[3] No matter what the rationale might be, many examples have been reported on the primary hydrogen isotope effect which varies regularly through a maximum in a series of reactions.[4]

Similar behavior to that of the hydrogen isotope effect was predicted for the carbon-14 kinetic isotope effect in an S_N2 displacement reaction (eq 1).[5]

$$Y + R^{*}CH_2X \longrightarrow [Y\cdots R^{*}CH_2\cdots X] \longrightarrow R^{*}CH_2Y + X \qquad (1)$$

The results of theoretical calculations were conflicting[6-8] and, to our knowledge, no experimental approach to this prediction has been reported. We present here our observations that the carbon-14 isotope effect really changes through a maximum in a series of S_N2 reactions.

The Menschutkin type reaction of benzyl benzenesulfonate (**1**) with *N,N*-dimethyl-*p*-toluidine (**2**) was chosen as a model system (eq 2), in which the reactivity of the substrate can be varied by introducing the substituent X on the benzenesulfonate group.[9] The starting esters, especially **1b**, are



(2)

X : p-CH_3O (**a**), p-CH_3 (**b**), H (**c**), p-Cl (**d**), and m-NO_2 (**e**)

liable to decompose on exposure to air, but are stable in a refrigerator under the solvents used for recrystallization. The reaction was carried out in acetone at 35° with concentrations of 0.015 M in **1** and 0.015-0.06 M in **2**. The rate of the reaction was determined by following the concentrations of the salt (**3**) conductometrically.[10] The reaction obeyed good second order kinetics ($r = 0.9998$-0.9999) through at least 75% reaction in all cases. The mechanism of the reaction is, therefore, considered to be typical S_N2.

The reaction mixture was poured into cold petroleum ether six or seven times at appropriate intervals ranging from 20 to 75% reaction. The precipitated salts were purified by repeated crystallization until they showed constant radioactivities. Radioassay was undertaken by the dry combustion-ionization chamber counting method.[11]

Kinetic isotope effects were calculated according to eq 3, where x is

$$\log(A_\infty - A_x \cdot x) = k^{14}/k^{12} \log(1-x) + \log A_\infty \tag{3}$$

the fraction of reaction, A_x is the specific activity of the recovered **3** at x, and A_∞ is that at 100% reaction.[12] The results are summarized in Table I.

Two important characteristics are obvious from Table I. (1) The isotope effect, k^{12}/k^{14}, is quite large throughout the series; the value of 1.16 for **1c** is the largest one ever reported for an S_N2 reaction.[13] (2) The isotope effect goes through a maximum as the reactivity of **1** varies. This behavior is illustrated in figure 1. As a Hammett plot gives a straight line with $\rho = 2.08 \pm 0.03$, the mechanism of the reaction must remain unchanged through the series **1a-e**. This is the first illustration of the bell-shaped behavior of a heavy-atom kinetic isotope effect predicted by theoretical calculations, although the observed values of the effects are much larger than the calculated ones.[5-7] These results suggest that the transition state structure of an S_N2 reaction varies with the reactivity of a substrate and that the symmetry of the transition state is an important factor determining the magnitude of the kinetic isotope effect of the reacting carbon.

Table I. Rates and Kinetic Isotope Effects for the Reaction of Benzyl Arenesulfonates ($PhCH_2OSO_2C_6H_4$-X, **1a-e**) with *N,N*-Dimethyl-*p*-toluidine in Acetone at 35°

X		k_2 ($l.mol^{-1}sec^{-1}$)	k_{rel}	k^{12}/k^{14}
p-CH_3O	(**1a**)	$(2.36\pm0.07)\times10^{-4}$	0.302	1.140±0.001
p-CH_3	(**1b**)	$(3.84\pm0.06)\times10^{-4}$	0.491	1.145±0.003
H	(**1c**)	$(7.82\pm0.01)\times10^{-4}$	1.00	1.160±0.005
p-Cl	(**1d**)	$(2.72\pm0.07)\times10^{-3}$	3.48	1.139±0.001
m-NO_2	(**1e**)	$(2.52\pm0.04)\times10^{-2}$	32.2	1.110±0.001

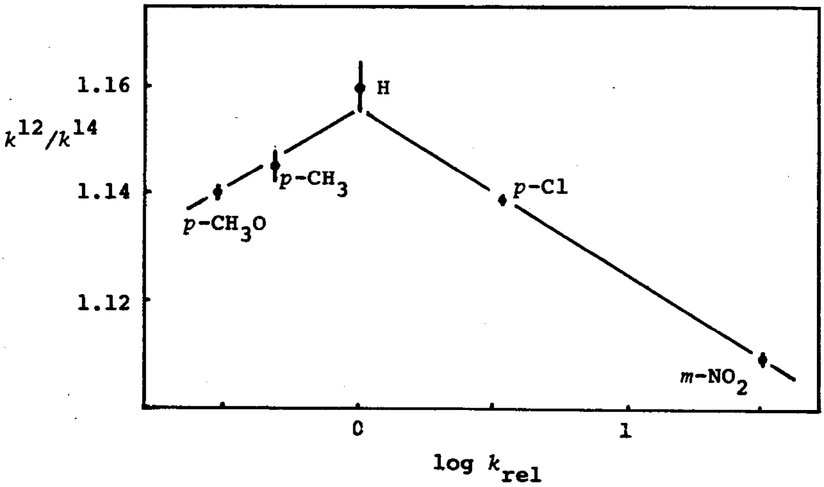


Figure 1. k^{12}/k^{14} *vs.* log k_{rel}; the reaction of benzyl arenesulfonates with *N,N*-dimethyl-*p*-toluidine.

Acknowledgment. We thank Professors Y. Yukawa and Y. Tsuno for helpful discussions. Support by the Scientific Research Grant from the Ministry of Education is gratefully acknowledged.

References and Footnotes

1. For a recent review of this subject, see R. P. Bell, "The Proton in Chemistry," 2nd ed, Chapman and Hall Ltd, London, 1973, pp 250-296.
2. F. H. Westheimer, *Chem. Rev.*, **61**, 265 (1961).
3. R. P. Bell, W. H. Sachs, and R. L. Tranter, *Trans. Faraday Soc.*, **67**, 1995 (1971), and references cited therein.
4. See, for example, R. P. Bell and B. G. Cox, *J. Chem. Soc. B*, 783 (1971).
5. A. Fry, *Pure Appl. Chem.*, **8**, 409 (1964).
6. A. V. Willi, *Z. Naturforsch.*, **21a**, 1385 (1966).
7. L. B. Sims, A. Fry, L. T. Netherton, J. C. Wilson, K. D. Reppond, and S. W. Crook, *J. Amer. Chem. Soc.*, **94**, 1364 (1972).
8. J. Bron, *Can. J. Chem.*, **52**, 903 (1974).
9. Substituent effects on the rates of the reaction were determined and discussed: S. D. Yoh, M. Sawada, Y. Tsuno, and Y. Yukawa, Abstracts of the 28th Spring Meeting of the Chemical Society of Japan, Tokyo, 1973, p 1288.
10. Due to nonlinearity of the conductance to the concentration of **3**, calibration curves were prepared for individual salts and used for the kinetics.
11. V. F. Raaen, G. A. Ropp, and H. P. Raaen, "Carbon-14," McGraw-Hill, New York, N. Y., 1968, pp 235-247.
12. In order to obtain accurate values of A_∞, which were often difficult to be determined experimentally, the linear regression technique was applied repeatedly for eq 3 using observed x and A_x until the results became self-consistent. The calculated values of A_∞ were 1-2% larger than the observed ones. In the case when **1** was stable enough for radioassay, the calculated A_∞ was confirmed to agree with the specific activity of **1**.
13. The value decreases slightly ($k^{12}/k^{14} = 1.142$) when the experimentally observed A_∞ is used.