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α-TRITIUM ISOTOPE EFFECTS IN THE MENSCHUTKIN-TYPE REACTION WITH VARIABLE TRANSITION STATES

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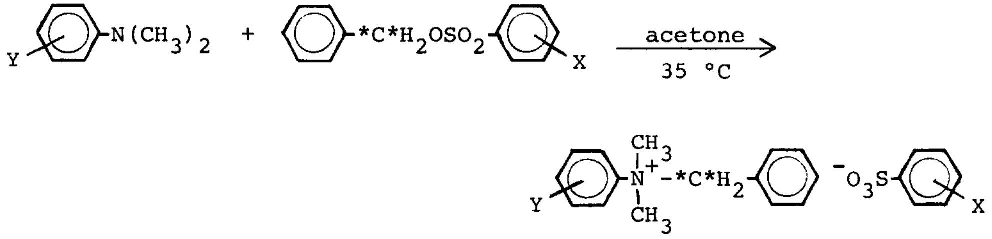
Abstract: Secondary α-tritium isotope effects in the series of the Menschutkin-type reaction of benzyl benzenesulfonates with *N,N*-dimethylanilines were all small and varied only slightly; it was concluded that the transition states vary mainly in the parallel direction to the reaction coordinate.

In previous papers from our laboratory,[1,2] we have reported the variation of carbon-14 kinetic isotope effects in the Menschutkin-type reaction of benzyl benzenesulfonates with *N,N*-dimethylanilines (Eq. 1).



(1)

The bell-shaped behavior of the carbon isotope effects at the S_N2 reaction center (*C) observed for a series of substituent X indicates that the transition-state structure varies with substituent and that the symmetry in terms of the force constants of two reacting bonds is important in determining the magnitude of the isotope effects.[1,3-8] Furthermore, variation of the bell shape observed for the second substituent Y gave clear-cut evidence for the validity of the theory concerning the variation of the transition-state structure with electronic perturbation.[2,9-11]

In connection with the recent debate on the variable *vs.* constant transition states and on the validity of the reactivity-selectivity principle,[12-16] further study of the reaction using another experimental probe is profitable. Here we report the results of secondary α-tritium isotope effects (Eq. 1, *H) measured for series of X and Y.

The experimental procedure employed was similar to that reported before.[1] Molar radioactivity of the products, quarternary ammonium salts, was determined by liquid scintillation counting.[17] Kinetic isotope effects were calculated by nonlinear regression analysis using Eq. 2,

$$A_x = A_\infty [\, 1 - (1 - x)^{{}^{\mathrm{T}}k/{}^{\mathrm{H}}k} \,] \,/\, x \qquad (2)$$

where x is the fraction of reaction, A_x is the molar radioactivity of the product at x, and A_∞ is that at 100% reaction.[2] The results are summarized in Table 1.

Table 1. α-Tritium Isotope Effects in the Reaction of Benzyl Benzenesulfonates and *N*,*N*-Dimethylanilines[a]

X	Y	${}^{\mathrm{H}}k/{}^{\mathrm{T}}k$	k_2^{rel} [b]
p-CH_3O	p-CH_3	1.035 ± 0.008[c]	0.302
p-CH_3	p-CH_3	1.033 ± 0.008	0.491
H	p-CH_3	1.043 ± 0.009	1.00
p-Cl	p-CH_3	1.055 ± 0.014	3.48
m-NO_2	p-CH_3	1.056 ± 0.011	32.2
p-Cl	p-Br	1.048 ± 0.009	0.496
p-Cl	H	1.042 ± 0.008	1.65
p-Cl	p-CH_3O	1.061 ± 0.012	8.01

[a] Initial concentration: 0.006-0.015 mol/l in ester and 0.015-0.060 mol/l in aniline. [b] Relative second-order rate constant.[2]
[c] Average of the results of two independent runs: ${}^{\mathrm{H}}k/{}^{\mathrm{T}}k = 1.043 \pm 0.014$ and 1.027 ± 0.013.

Tritium isotope effects were determined fairly precisely.[18] Reproducibility was also confirmed for one case, X = p-CH_3O and Y = p-CH_3.

It is obvious in Table 1 that the observed tritium isotope effects are all small; ${}^{\mathrm{H}}k/{}^{\mathrm{T}}k = 1.03$-$1.06$ corresponds to ${}^{\mathrm{H}}k/{}^{\mathrm{D}}k = 1.02$-$1.04$.[19] This result, in accord with the large primary carbon-14 isotope effects,[1,2] clearly supports the S_N2 mechanism of the reaction. There is a distinct tendency that a larger tritium effect accompanies a faster reaction. However, this variation is rather small and in contrast to the large variation of the primary carbon-14 isotope effects.[1,2]

As mentioned above, the magnitude of the primary carbon isotope effects is mainly governed by the early-late character of the transition state. On the other hand, it is generally thought that the secondary α-hydrogen isotope effects arise from changes in out-of-plane bending frequencies of the isotopic bonds in reaching the transition state. Thus, the α-hydrogen effects give us the information concerning the tightness of the transition state. The present observation of a small tendency in the α-tritium isotope effects may indicate a looser transition state for a faster reaction. A similar tendency, a larger α-deuterium isotope effect for a faster reaction, has been observed by Harris and his coworkers in the Menschutkin reaction of methyl iodide with substituted pyridines,[21] while the reverse has been reported by Westaway and Ali in the reaction of substituted phenylbenzyldimethylammonium ions with thiophenoxide ion.[22] These conflicting results imply that the mechanism of the transition-state variation is not unique but dependent on each reaction system. However, further discussion on this mechanism is risky at present because the differences in the isotope effects observed in this study are barely outside the limit of experimental errors.

Theoretical calculations carried out for the present reaction system have shown that even a small variation of the transition state in the tightness/looseness direction can cause a much larger variation of the α-hydrogen isotope effects than that observed here.[20] Furthermore, it has been predicted by the calculations that the symmetry of the transition state or the nature of the reaction coordinate motion may affect the magnitude of the secondary α-hydrogen isotope effects at least to a small extent.[20] Thus, it is concluded that the variation of the transition-state structure of this reaction system detected by the variation of kinetic isotope effects, large in carbon-14 and small in α-tritium, should mainly be parallel (early-late) to the reaction coordinate.[21-24] The variation perpendicular (tight-loose) to the reaction coordinate may occur but only to a limited extent. It is important to point out here that this conclusion is in accord with the theory,[9-11] which predicts that the perturbation on the nucleophile or the leaving group should induce the variation of the transition state in the parallel direction.

Kinetic isotope effects are regarded as one of the most effective probes to detect the variation of the transition-state structure.[21-24] The present investigation gives us an example of a further elaborate application of kinetic isotope effects; namely, combination of the results obtained from different types of isotope effects enables us to look into further details of variable transition states.

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(17) The product salts were isolated at seven different fractions of reaction, ranging from 20 to 75% completion, purified by recrystallization, and then assayed with a Beckman LS 9000 instrument. Molar radioactivity of each sample salt was determined as the average of three to six measurements with the standard deviation less than 0.7%; each measurement was carried out with *ca.* 5 mg of the salt (1.1-4.7 mCi/mol) dissolved in a mixture of 14 ml of Aquasol-2 (New England Nuclear) and 1 ml of methanol. Counting efficiency was determined for each measurement by external standardization (H-number method, Beckman) and was in the range of 30-35%.

(18) Precision of radioactivity measurement of tritium by liquid scintillation counting was less than that of carbon-14 by ionization-chamber counting,[1,2] and the standard deviations of the tritium isotope effects (< ±1.4%) were larger than those of the carbon-14 effects (< ±0.8%). However, this precision should still be better than that expected for the deuterium isotope effects of this reaction which would be determined by direct comparison of the rate constants of independent runs with stadard deviations of ±2%.[1,2]

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