

transfer involving 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene and 1,8-bis(diethylamino)-2,7-dimethoxynaphthalene in 60% Me₂SO-H₂O (v/v) is mostly due to a difference in entropies of activation. The value of the equilibrium constant for pre-equilibrium formation of the non-hydrogen-bonded intermediate from protonated 1,8-bis(diethylamino)-2,7-dimethoxynaphthalene ($K^* = \text{ca. } 2.0 \times 10^{-5}$) corresponds to an unfavorable free energy term of $\Delta G^\circ_{\text{HB}} = 27 \text{ kJ mol}^{-1}$. Hence according to the mechanism in eq 7 the overall free energy of activation for proton transfer to hydroxide ion from protonated 1,8-bis(diethylamino)-2,7-dimethoxynaphthalene in 70% Me₂SO-H₂O (v/v), $\Delta G^\ddagger = 67 \text{ kJ mol}^{-1}$, is composed of the term $\Delta G^\circ_{\text{HB}} = 27 \text{ kJ mol}^{-1}$ and the free energy of activation for the proton-transfer step ($\Delta G^\ddagger_{\text{PT}} = 40 \text{ kJ mol}^{-1}$). The proton-transfer step involves thermodynamically favorable proton removal by hydroxide ion from an ammonium ion and normally would be expected to occur at the diffusion limited rate. We have attributed the reduced rate

to a steric effect. Therefore the large free energy of activation for this step ($\Delta G^\ddagger_{\text{PT}} = 40 \text{ kJ mol}^{-1}$) may be the result of a small enthalpy term, $\Delta H^\ddagger_{\text{PT}} = \text{ca. } 16 \text{ kJ mol}^{-1}$, which is roughly the value expected for a diffusion-controlled reaction, and a large entropy contribution $T\Delta S^\ddagger_{\text{PT}} = \text{ca. } -24 \text{ kJ mol}^{-1}$. It follows that the enthalpy of activation for the overall reaction consists of two terms, $\Delta H^\circ_{\text{HB}} = \text{ca. } 19 \text{ kJ mol}^{-1}$ and $\Delta H^\ddagger_{\text{PT}} = \text{ca. } 16 \text{ kJ mol}^{-1}$, and the corresponding entropy terms are $T\Delta S^\circ_{\text{HB}} = \text{ca. } -8 \text{ kJ mol}^{-1}$ and $T\Delta S^\ddagger_{\text{PT}} = \text{ca. } -24 \text{ kJ mol}^{-1}$. These results show that the mechanism in eq 7 provides a reasonable explanation of the observed activation parameters.

Acknowledgment. We are grateful to the Royal Society and S.E.R.C. for support of this research.

Registry No. 1,8-Bis(diethylamino)-2,7-dimethoxynaphthalene, 67116-12-5; 1,8-bis(dimethylamino)-2,7-dimethoxynaphthalene, 67116-11-4.

Kinetic Isotope Effects in the Menschutkin-Type Reaction of Benzyl Benzenesulfonates with *N,N*-Dimethylanilines. Variation in the Transition-State Structure¹

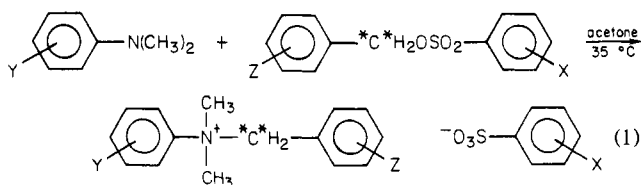
Takashi Ando,*[†] Hiroshi Tanabe, and Hiroshi Yamataka*

Contribution from the Institute of Scientific and Industrial Research, Osaka University, Ibaraki, Osaka 567, Japan. Received May 5, 1983. Revised Manuscript Received November 19, 1983

Abstract: Primary carbon-14 and secondary α -tritium isotope effects were measured for the Menschutkin-type reaction of *m*-bromobenzyl-methylene-¹⁴C X-substituted benzenesulfonates with Y-substituted *N,N*-dimethylanilines in acetone at 35 °C (eq 1; Z = *m*-Br). The large carbon-14 (¹²k/¹⁴k = 1.117-1.151) and small α -tritium (^Hk/^Tk = 1.026-1.041) isotope effects were consistent with the S_N2 mechanism of the reaction. A monotonous trend was observed when the carbon isotope effects were plotted against the relative rates for varied Xs and a fixed Y (*p*-CH₃), while a bell shape was observed for varied Ys and a fixed X (*p*-Cl). Comparison of the results with those obtained for the unsubstituted benzyl esters indicated that the substitution on the benzyl moiety with the electron-withdrawing *m*-Br group made the transition state more product-like. Smaller α -tritium isotope effects for the *m*-Br series than those for the unsubstituted series verified tighter transition states for the former. The variation in the three-centered S_N2 transition states caused by the substituents on the leaving group, the nucleophile as well as the benzyl moiety, is discussed in terms of Thornton's rules and described on a potential energy map.

The concept of variable transition states in S_N2 reactions has been studied extensively in recent years.²⁻¹² Among a variety of techniques so far employed for these studies, kinetic isotope effects are of great importance since they give us most direct information concerning the structure of a transition state. However, the majority of the isotope effect studies have been concerned only with secondary α -deuterium effects, except for a few cases in which heavy atom isotope effects were measured.^{3,12-17} Although secondary α -deuterium effects are generally accepted as a sensitive probe for detecting subtle changes in a transition-state structure, it is not safe to rely much on the results obtained from only one probe.

In previous papers from our laboratory, we have reported the usefulness of carbon-14 isotope effects in the study of variable S_N2 transition states.^{1a,b} In the Menschutkin-type reaction of benzyl benzenesulfonates (1) with *N,N*-dimethylanilines (2) (eq 1; X, Y = variable; Z = H)¹⁸ carbon-14 isotope effects at the



reaction center (*C) have been found to vary to a great extent. This variation has been discussed in connection with the symmetry

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[†] Present address: Department of Chemistry, Shiga University of Medical Science, Otsu, Shiga 520-21, Japan.

Table I. Rate Constants and Kinetic Isotope Effects in the Reaction of Z-Benzyl X-Bezenesulfonates with N,N-Dimethyl-Y-anilines in Acetone at 35 °C^a

X	Y	Z = m-Br			Z = H		
		10 ⁴ k ₂ , L mol ⁻¹ s ⁻¹	¹² k/ ¹⁴ k ^b	H _k /T _k	10 ⁴ k ₂ , L mol ⁻¹ s ⁻¹	¹² k/ ¹⁴ k ^c	H _k /T _k ^d
p-Cl	p-CH ₃ O	34.1 ± 0.4	1.130 ± 0.003	1.033 ± 0.009	62.6	1.142	1.061
H	p-CH ₃ O				17.1	1.140	
p-CH ₃	p-CH ₃ O				8.72	1.148	
m-NO ₂	p-CH ₃	141 ± 2	1.151 ± 0.004	1.041 ± 0.010	252	1.119	1.056
p-Cl	p-CH ₃	16.3 ± 0.2	1.148 ± 0.003	1.026 ± 0.012	27.2	1.149	1.055
H	p-CH ₃	4.55 ± 0.06	1.137 ± 0.005	1.030 ± 0.008	7.82	1.162	1.043
p-CH ₃	p-CH ₃	2.40 ± 0.06	1.141 ± 0.005	1.031 ± 0.008	3.84	1.156	1.033
p-CH ₃ O	p-CH ₃	1.34 ± 0.04	1.141 ± 0.005		2.36	1.147	1.035
m-NO ₂	H				101	1.158	
p-Cl	H	(6.89) ^e			12.9	1.143	1.042
H	H				3.41	1.135	
p-Cl	m-CH ₃	5.48 ± 0.03	1.129 ± 0.003				
p-Cl	p-Br	1.73 ± 0.05	1.117 ± 0.004	1.033 ± 0.010	3.88	1.139	1.048
m-NO ₂	m-NO ₂				8.60	1.127	

^a Initial concentration: 0.006–0.015 mol L⁻¹ in ester and 0.009–0.060 mol L⁻¹ in nucleophile. ^b For calculation of errors, see the Experimental Section. ^c Reference 1a,b. ^d Reference 1c. ^e Estimated from the substituent effect on the rate constants and used for plotting Figure 1b.

of the transition states.^{1a,b} We now report the results of carbon-14 and α-tritium isotope effects in the reaction series in which the substituent Z on the benzyl moiety is changed to a more electron-withdrawing group, m-Br. A detailed discussion concerning the results of the whole system will also be presented.

Results

The reaction was followed by conductometry. Good second-order kinetics (*r* > 0.999) were obtained through at least 75% reaction in all cases. Second-order rate constants determined as the averages of three to four runs are shown in Table I. Carbon-14 and tritium isotope effects were determined by following the change in the molar radioactivity of the produced quaternary ammonium salts (3).¹ Radioactivity was measured by ion-chamber counting for carbon-14 and by liquid-scintillation counting for tritium. Kinetic isotope effects were calculated by nonlinear regression analysis by using eq 2, where *k is the rate constant

$$A_x = A_\infty [1 - (1 - x)^{*k/k}] / x \quad (2)$$

of a heavier isotope, *x* is the fraction of reaction, *A_x* is the molar radioactivity of the product at *x*, and *A_∞* is the molar radioactivity of the product at 100% reaction. The results are summarized in Table I together with the data for the series of Z = H.¹

Discussion

Table I reveals that the carbon-14 kinetic isotope effects obtained were all large while the secondary α-tritium isotope effects were rather small. These large carbon and small hydrogen isotope effects are strong evidence that the mechanism of the reaction is typical S_N2. This is in accord with the clean second-order

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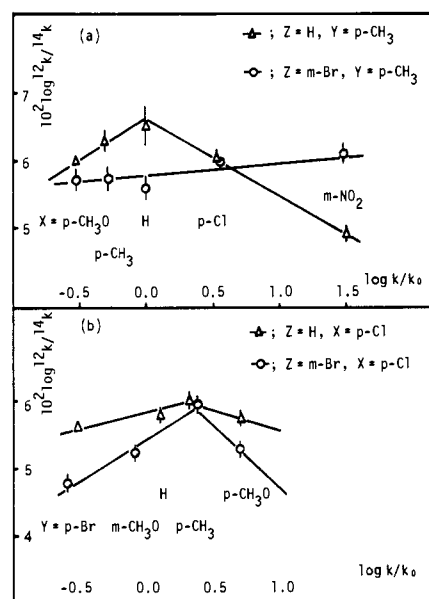


Figure 1. Variation of carbon-14 kinetic isotope effects in the Menshutkin-type reaction: (a) isotope effects vs. the substituent X on the leaving group; (b) isotope effects vs. the substituent Y on the nucleophile.

kinetics of the reaction throughout the series of X, Y, and Z.

Carbon-14 Isotope Effects. When Z was changed from H to m-Br, the carbon-14 isotope effects varied in a random fashion; most of them decreased, but one increased and one stayed unchanged. As a result, no apparent relation seemed to be present at first sight between the carbon isotope effects and the rate constants. However, when the effects were plotted against the relative rates for a single variation of either X or Y, the effects varied regularly (Figure 1). A monotonous trend was observed for X when Y was limited to p-CH₃, and a maximum appeared for Y when X was p-Cl. These features are quite similar to those observed when Z = H.^{1b,19}

The bell-shaped plot of the carbon-14 isotope effects recorded in Figure 1b is, as pointed out previously in four cases when Z = H,^{1b} the phenomenon that has been predicted theoretically for the three-centered transition state of an S_N2 reaction.^{20–25} This

(19) In the present paper, the isotope effects are plotted against the logarithms of the relative rates in contrast to Figure 1 of ref. 1b, in which the isotope effects were plotted against substituent constants, σ and σ° . Although we now think that the former is better because the discussion is concerned with the difference in free energy, the latter treatment does not cause serious trouble as the reaction constants (ρ) are almost the same for X and Y.

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observation verified that the symmetry of the transition state in terms of the force constants of the two reacting bonds is important in the determination of the isotope effects of the central carbon and that the electronic perturbation induced by the substituent does affect the transition-state structure.

In the previous paper,^{1b} we concluded that all the shifts of the maximum of the bell shape caused by changing X or Y when Z is H could be rationalized by means of the Hammond-type theories.²⁶⁻³⁰ In short, these theories predict that a transition-state structure of an S_N2 reaction becomes more reactant-like when a nucleophile becomes more nucleophilic or when a leaving group becomes a better one and that the opposite is expected when the case is reversed. Thus, our observation has proved that electronic perturbation on the nucleophile or the leaving group moves the S_N2 transition state in parallel (early-late) direction to the reaction coordinate and that this movement can be detected well by the primary carbon isotope effects.

The monotonous trend observed for X when Z was *m*-Br (Figure 1a) suggests that the maximum would be found at a more electron-withdrawing area of X, where the three-centered transition state is symmetrical. Since a good leaving group with an electron-withdrawing substituent is expected to make the transition state more reactant-like,²⁶⁻³⁰ substitution on the benzyl moiety with *m*-Br must have the opposite effect of keeping the balance in that area. This means that the effect of electronic perturbation on the central carbon of the three-centered transition state of S_N2 does have a parallel component to the reaction coordinate and that an electron-withdrawing substituent makes the transition state more product-like. If this interpretation is correct, then how does this observation reconcile with the theories?

Thornton predicted that electron withdrawal from the central carbon of the S_N2 reaction should make the perpendicular stretching difficult and have a small effect on the parallel vibration.²⁶ Thus, a tighter transition state is expected as the overall primary effect. The parallel effect can become important, however, when the nucleophile and the leaving group are distinctly different. In the present reaction (eq 1), the nucleophile and the leaving group are different in their charges. For such a case, Thornton stated that the electronegativity of the atom "in the molecule" should be considered.²⁶ The nitrogen atom in eq 1 becomes positively charged in the transition state in contrast to the negatively charged oxygen atom. Since the central carbon becomes positively charged in the transition state, an electron-withdrawing substituent on this carbon should make the C-O bond stretching and the C-N bond compression difficult. As the force constant for the parallel motion is negative, a later transition state with a longer C-O bond and a shorter C-N bond is expected for this particular case. This is in harmony with what we observed.

The difference in charge of nucleophiles was considered more explicitly by Harris and Kurz.²⁷ According to their "q rule", an electron-withdrawing substituent on the central atom will tend to decrease the order of the reacting bond to the negative nucleophile and increase the order of the reacting bond to the uncharged nucleophile.²⁷ This exactly follows Thornton's rule as shown above. Thus, the late transition state caused by the *m*-Br substituent on the benzyl moiety is consistent with the theoretical predictions.^{26,27}

It is interesting that the shift of the bell shape can be detected only when the isotope effects are plotted against X (Figure 1a) and that the maximum stays at the same substituent, *p*-CH₃, when

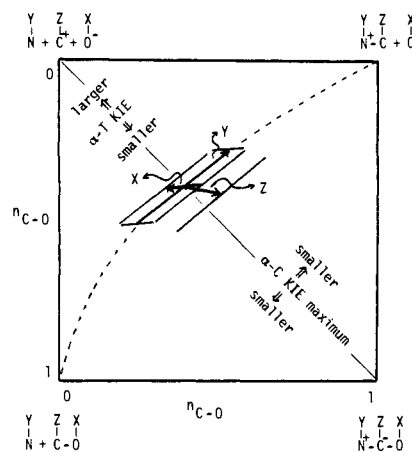


Figure 2. Schematic transition-state map of reaction 1.

the effects are plotted against Y (Figure 1b). Similar behavior was also observed for the series of Z = H;^{1b} the bell shape shifted to a large extent when the isotope effects were plotted against X, while it shifted only slightly when the effects were plotted against Y (Figure 1a,b of ref 1b). These facts indicate that substituent Y on the nucleophile has a larger effect on the magnitude of the isotope effect than substituent X on the leaving group has. The reason is not clear at present, but it might be characteristic of S_N2, the reaction brought about by the attack of a nucleophile.³¹

Elaborate model calculations of kinetic isotope effects on the present reaction system³² have suggested that, in contrast to the sharp variation of the carbon isotope effects for the parallel movement of the transition state, they are almost insensitive to the perpendicular movement; primary carbon isotope effects do not give any information on the tight-loose character of the transition state. However, α -hydrogen isotope effects should be a very sensitive probe of the tightness of the transition state.³²

α -Tritium Isotope Effects. Table I shows that each α -tritium isotope effect for the *m*-Br series is always smaller than that for the corresponding unsubstituted derivative. Thus, the tight transition state is brought about by an electron-withdrawing substituent on the central carbon of the S_N2 reaction. The same conclusion has been drawn in the related studies of the α -deuterium isotope effects in the benzyl substitution.^{3,5,7,12}

As described above, a tighter transition state was predicted by Thornton for electron withdrawal from the central carbon, but the effect of the difference in charge of the nucleophile and the leaving group on the tightness of the transition state was not explicitly considered. The present observation indicates that the prediction is also effective for the case of a neutral nucleophile and a negative leaving group. This indicates that attractive interaction between the central carbon and the leaving group dominates over the repulsive interaction between the central carbon and the nucleophile in the benzyl substitution.

It is also apparent in Table I that the range of the variation in the tritium isotope effects is smaller for the *m*-Br series than for the H series; the effects varied only 1.5% for the former but 2.8% for the latter. This is in contrast to the rate constants which varied about 10² for both series (Table I). This indicates that the transition state for the *m*-Br series is not only tighter but also less plastic than that for the H series. This phenomenon is not predicted explicitly by Thornton,²⁶ but it is reasonably expected from his rule.

Transition-State Map. It is clear from the present results that the successive labeling method, that is, measurement of the kinetic isotope effects at as many different atoms as possible,²⁰ is essential

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(31) It may be worth noting that, according to Tsuno and his co-workers,¹⁸ the reaction is enthalpy dependent for a change in the nucleophile and is entropy dependent for a change in the leaving group, although ρ_Y (-1.7 to -1.9) and ρ_X (2.1-2.3) are of the same order. This may be evidence that the kinetic isotope effects are primarily determined by the transition-state structure itself and not affected much by the difference in solvation.

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for unequivocal discussion of the variations in the transition state. These variations can be mapped on a three-dimensional potential energy surface (Figure 2), in which energy contour lines are omitted. In this diagram, the carbon-14 kinetic isotope effect becomes maximum when the transition state is symmetrical around the diagonal between the upper left and the lower right corners. The α -tritium isotope effect increases as a general trend when the transition state becomes loose by coming close to the upper left corner.

The effects of three substituents, X, Y, and Z, are shown as vectors in the diagram. The length of the vector represents the magnitude of the effect, and the direction of the vector reflects the parallel and perpendicular character of the effect. The point of the arrow corresponds to an electron-withdrawing substituent. The diagram shows that the effects of perturbation X and Y are mainly parallel to the reaction coordinate with a slight contribution of the perpendicular component; between them Y has a greater effect than X. On the other hand, perturbation Z moves the transition state in both perpendicular and parallel directions. The vector $Y(X)$ and solid lines parallel to the vector correspond to and of the variation of the kinetic isotope effects plotted against Y (X). Thus, four lines along vector Y (three for Z = H and one for Z = *m*-Br) crossing the diagonal correspond to the four bell shapes observed in the plots of the carbon-14 isotope effects against Y (Figure 1b and also Figure 1b of ref 1b). On the other hand, only one line along vector X goes across the diagonal, which refers to the observation of only one bell shape and three monotonous trends in the plots against X (Figure 1a and also Figure 1a of ref 1b). Thus, all the behavior of the variation in the isotope effects, including the slight decrease in the α -tritium effects when Z is changed to *m*-Br, is illustrated in a consistent manner in this transition-state map. It is worth noting that, as discussed above, this map is consistent with Thornton's rules in every respect; the More O'Ferrall-type analysis of the potential energy surfaces also gives the same conclusion.

An Affirmative Epilogue. In a recent publication, Arnett and Reich have critically reviewed the present status of the study on the transition-state structure of an S_N2 reaction by the use of free energy analysis.³³ Two possible pitfalls have been pointed out by them. The first is the fact that the transition state is usually far removed in structure and energy from both the initial and final states, so that the rigorous use of a Hammond-type approach is dangerous. The second is the ignorance about solvation dynamics which govern the energetics of the reaction in solution. The kinetic isotope effect is within the framework of the transition-state theory, and many assumptions and approximations are used for its application. Nevertheless, we believe that the kinetic isotope effect is the approach with the least risk of falling into such pitfalls among those approaches used for the elucidation of the transition-state structure provided that it is used with great care together with the successive labeling method. A problem unsettled yet is how to rationalize the cases where the Thornton-type analysis is ineffective.^{3,13,34} Further study along this line from experimental and theoretical viewpoints is now in progress.

Experimental Section

Materials. Z-substituted benzyl X-substituted benzenesulfonates (**1**) were prepared from benzyl chloride or *m*-bromobenzyl bromide with silver X-benzenesulfonates in acetonitrile according to the procedure described in the literature.³⁵ Most of the esters were recrystallized from anhydrous ether, but benzene-hexane was used for *m*-nitrobenzenesulfonates and ligroin for benzyl *p*-chlorobenzenesulfonate. The esters are labile when exposed to air, but they can be stored without decomposition in a refrigerator under the solvent for recrystallization. Melting points (uncorrected) were as follows [X, Z, mp (°C)]: *p*-CH₃O, H, 73–74; *p*-CH₃, H, 57–58 (lit.³⁶ mp 58.5–58.9 °C); H, H, 57–58 (lit.³⁷ mp 59 °C); *p*-Cl, H, 58.5–59.0; *m*-NO₂, H, 67.5–68.0; *p*-CH₃O, *m*-Br,

66.2–66.7; *p*-CH₃, *m*-Br, 104.0–104.2; H, *m*-Br, 62.0–62.5; *p*-Cl, *m*-Br, 84.0–84.2; *m*-NO₂, *m*-Br, 51.9–52.3.

Benzoic-carbonyl-¹⁴C acid (Radiochemical Center, Amersham and New England Nuclear) was reduced by lithium aluminum hydride and chlorinated by thionyl chloride to give benzyl-methylene-¹⁴C chloride, which gave the ¹⁴C-labeled esters of the Z = H series. Bromination of benzoic-carbonyl-¹⁴C acid (Radiochemical Center, Amersham), followed by reduction with diborane³⁸ and bromination with hydrobromic acid, gave *m*-bromobenzyl-methylene-¹⁴C bromide, which gave the ¹⁴C-labeled esters of the Z = *m*-Br series. Molar radioactivities of both series of the esters were about 3.5 mCi mol⁻¹. Benzyl-methylene-³H alcohol and its *m*-bromo derivative were obtained by reduction of the corresponding benzaldehydes with sodium borohydride-³H (Commissariat a l'Energie Atomique). These benzyl alcohols, after the same sequence of steps as above, gave each series of the esters labeled with ³H. Molar radioactivity was 1.1–4.5 mCi mol⁻¹.

N,N-Dimethyl-*m*-anisidine and *N,N*-dimethyl-*p*-anisidine were prepared according to the known methods.^{39,40} Other *N,N*-dimethylanilines were commercially available and purified before use.

N-Benzyl-*N,N*-dimethylanilinium benzenesulfonates (**3**) were prepared from the reaction of the esters (**1**) and anilines (**2**) in dry acetone under reflux. Melting points (uncorrected) were as follows [X, Y, Z, mp (°C), solvent for recrystallization (unless otherwise mentioned ethanol-hexane was used)]: *p*-Cl, *p*-CH₃O, H, 172.0–173.0; H, *p*-CH₃O, H, 172.0–173.0; *p*-CH₃, *p*-CH₃O, H, 174.0–175.0; *m*-NO₂, *p*-CH₃, H, 148.5–149.0; *p*-Cl, *p*-CH₃, H, 184.5–185.5; H, *p*-CH₃, H, 145.5–146.5; *p*-CH₃, *p*-CH₃, H, 154.0–154.5; *p*-CH₃O, *p*-CH₃, H, 146.5–147.0; *m*-NO₂, H, H, 156.0–157.0; *p*-Cl, H, H, 203.0–204.0; H, H, H, 137.5–139.0, acetone-hexane; *p*-Cl, *p*-Br, H, 179.0–180.0; *m*-NO₂, *p*-Br, H, 147.5–149.0; *m*-NO₂, *m*-NO₂, H, 147.5–148.0, 2-propanol-benzene; *p*-Cl, *p*-CH₃O, *m*-Br, 186.8–187.0, acetone-hexane; *m*-NO₂, *p*-CH₃, *m*-Br, 172.5–173.0; *p*-Cl, *p*-CH₃, *m*-Br, 166.4–167.0; H, *p*-CH₃, *m*-Br, 160.5–161.0; *p*-CH₃, *p*-CH₃, *m*-Br, 174.0–175.0; *p*-CH₃O, *p*-CH₃, *m*-Br, 180.5–181.2; *p*-Cl, *m*-CH₃O, *m*-Br, 149.6–150.0, acetone-hexane; *p*-Cl, *p*-Br, *m*-Br, 171.6–172.0.

The elemental analyses of all compounds cited above and of their precursors gave satisfactory results for C, H, N, S, Cl, and Br. Acetone was refluxed with potassium permanganate, distilled, treated with anhydrous potassium carbonate, and then fractionally distilled from molecular sieves.

Kinetic Procedures. Reactions were carried out in acetone at 35.00 ± 0.02 °C with 0.006–0.015 mol L⁻¹ of the ester (**1**) and 0.009–0.060 mol L⁻¹ of the nucleophile (**2**).⁴¹ The molar ratio of **1** to **2** was varied from 1:1 to 1:10 depending on the reactivity. The reactions were followed by conductometry. Since the conductance is not linearly related to the concentration of **3**, a calibration curve was predetermined for each **3** by using 8 to 10 solutions of various concentrations of **3**. The curve was approximated with a cubic equation (eq 3) by regression analysis, in which *y* is the concentration of **3** and *x* is the conductance. Equation 3 reproduced the actual concentration of **3** within an error of ±0.3%.

$$y = ax^3 + bx^2 + cx + d \quad (3)$$

Determination of Kinetic Isotope Effects. Reactions of the labeled compounds were carried out with solutions of the same concentrations of the reactants as those used for the respective kinetic runs. We recovered the product salts at several, usually seven, different fractions of reaction, ranging from 20 to 75% completion, by pipetting out adequate amounts of the reaction solutions and pouring them into cold petroleum ether. Crude salts, usually 60 to 70 mg, were purified by recrystallization until they showed constant radioactivities.

Accurate radioactivity measurement of the purified samples of the ¹⁴C-labeled salts was carried out by ion-chamber counting according to the procedure described earlier.⁴² Radioactivity measurement of the ³H-labeled salts was carried out by liquid-scintillation counting on a Beckman LS 9000 instrument. Each counting solution was made from ca. 5 mg of a purified salt, 1 mL of methanol, and 14 mL of Aquasol-2 (New England Nuclear). Counting efficiency (30–35%) was determined by automatic external standardization (H-number method) for each solution. The standard deviation of the molar radioactivity for ³H was

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less than 0.7%, which was worse than that for ^{14}C (<0.3%).

Kinetic isotope effects were then calculated by nonlinear regression analysis with use of eq 2 in the text. Error limits shown in Table I are the standard deviations of the isotope effect values calculated for each x with use of eq 4, in which A_∞ was the value determined by regression analysis with use of eq 2.

$$^{\text{H}}k/{}^{\text{T}}k = \frac{\log(1-x)}{\log[1-(xA_x/A_\infty)]} \quad (4)$$

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Registry No. 1 (Z = *m*-Br; X = *p*-Cl), 88801-92-7; 1 (Z = *m*-Br; X = H), 88801-93-8; 1 (Z = *m*-Br; X = *p*-CH₃), 88801-94-9; 1 (Z = *m*-Br; X = *m*-NO₂), 88801-95-0; 1 (Z = *m*-Br; X = *p*-CH₃O), 88801-96-1; 1 (Z = H; X = *p*-CH₃O), 53226-51-0; 1 (Z = H; X = CH₃), 1024-41-5;

1 (Z = H; X = H), 38632-84-7; 1 (Z = H; X = *p*-Cl), 13086-79-8; 1 (Z = H; X = *m*-NO₂), 55735-65-4; 2 (Y = *p*-CH₃O), 701-56-4; 2 (Y = *p*-CH₃), 99-97-8; 2 (Y = H), 121-69-7; 2 (Y = *m*-CH₃O), 15799-79-8; 3 (X = *p*-Cl; Y = *p*-CH₃O; Z = H), 88801-97-2; 3 (X = H; Y = *p*-CH₃O; Z = H), 88801-98-3; 3 (X = *p*-CH₃; Y = *p*-CH₃O; Z = H), 88825-18-7; 3 (X = *m*-NO₂; Y = *p*-CH₃; Z = H), 88825-19-8; 3 (X = *p*-Cl; Y = *p*-CH₃; Z = H), 88801-99-4; 3 (X = H; Y = *p*-CH₃; Z = H), 88802-00-0; 3 (X = *p*-CH₃; Y = *p*-CH₃; Z = H), 88802-01-1; 3 (X = *p*-CH₃O; Y = *p*-CH₃; Z = H), 88802-02-2; 3 (X = *m*-NO₂; Y = H; Z = H), 88802-03-3; 3 (X = *p*-Cl; Y = H; Z = H), 88802-04-4; 3 (X = Y = Z = H), 88802-05-5; 3 (X = *p*-Cl; Y = *p*-Br; Z = H), 88802-07-7; 3 (X = *m*-NO₂; Y = *p*-Br; Z = H), 88802-08-8; 3 (X = *m*-NO₂; Y = *m*-NO₂; Z = H), 88825-21-2; 3 (X = *p*-Cl; Y = *p*-CH₃O; Z = *m*-Br), 88802-10-2; 3 (X = *m*-NO₂; Y = *p*-CH₃; Z = *m*-Br), 88802-12-4; 3 (X = *p*-Cl; Y = *p*-CH₃; Z = *m*-Br), 88802-13-5; 3 (X = H; Y = *p*-CH₃; Z = *m*-Br), 88802-14-6; 3 (X = *p*-CH₃; Y = *p*-CH₃; Z = *m*-Br), 88802-15-7; 3 (X = *p*-CH₃O; Y = *p*-CH₃; Z = *m*-Br), 88825-22-3; 3 (X = *p*-Cl; Y = *m*-CH₃O; Z = *m*-Br), 88802-17-9; 3 (X = *p*-Cl; Y = *p*-Br; Z = *m*-Br), 88802-19-1; tritium, 10028-17-8; carbon-14, 14762-75-5; 2 (Y = *p*-Br), 586-77-6; 2 (Y = *m*-NO₂), 619-31-8.

Conformation of a Saturated 13-Membered Ring

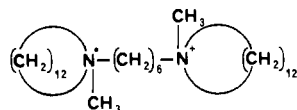
B. H. Rubin,*† M. Williamson,† M. Takeshita,† F. M. Menger,† F. A. L. Anet,‡
B. Bacon,‡ and N. L. Allinger§

Contribution from the Department of Chemistry, Emory University, Atlanta, Georgia 30322, Department of Chemistry, University of Georgia, Athens, Georgia 30602, and Department of Chemistry and Biochemistry, University of California, Los Angeles, California 90024.

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Abstract: The synthesis and X-ray structure elucidation of α,ω -bis(methyldodeca-1,12-diylammonio)hexane dibromide permitted an examination of the conformation of a 13-atom macrocycle. Such rings are of interest because they lie on the borderline between "medium" and "large" ring systems and are generally considered very complex with a variety of conformational possibilities. It is shown that the ring assumes a [33331] geometry in agreement with force-field calculations carried out on cyclotridecane and 1,1-dimethylcyclotridecane. Disorder in one portion of the molecule was resolved by a combination of molecular mechanics and crystallographic least-squares refinement.

In the course of synthesizing space-encompassing molecules,¹ we secured a crystalline bolaform electrolyte² bearing two saturated 13-membered rings.



This substance afforded us an opportunity to determine the conformation of a 13-atom heteromacrocycle for which the "conformational situation is very complex, with a variety of conformational candidates".³ A diamond-lattice model has been used for defining idealized geometries for macrocyclic rings; however, only rings containing an even number of atoms can be made to superimpose on a diamond lattice, since all bonds must occur in pairs.⁴ It has been suggested, on these grounds, therefore, that these odd-membered macrocyclic rings must be distorted with respect to their bond lengths, bond angles, dihedral angles, or combinations thereof.⁴ In these odd-membered macrocycles bonding distortion is expected to be minimized when the rings exist as three- or five-cornered conformations.⁵ Anet and Rawdah⁶ and Dale⁷ have calculated the energy for a number of cyclotridecane conformations and find the three- and five-cornered conformations depicted in Figure 1 to be among those of lowest

energy. A crystal structure of a hydroxylcyclotridecylphosphonate containing two independent molecules in the asymmetric unit has been reported in which each of the molecules has a strikingly different conformation.⁸

Much more is known about rings with 12 and 14 atoms. Cyclododecane assumes a "square" [3333] conformation in preference to the diamond lattice configuration since the latter possesses three unfavorable H/H repulsions. Both X-ray data and low-temperature ^{13}C NMR confirm this picture.^{9,10} Cyclotetradecane, on the other hand, is a totally strain-free diamond-lattice system (the smallest saturated ring above six atoms so endowed).¹¹ The 14-membered ring has a "rectangular" [3434] geometry with two parallel chains held at roughly van der Waals distances.¹¹ Unfortunately, cyclotridecane (on the borderline between the

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* Emory University.

† University of California.

‡ University of Georgia.