

# Kinetic Isotope Effect Study of the Borderline Solvolysis of Isopropyl $\beta$ -Naphthalenesulfonate

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**Abstract:** Carbon-14 and deuterium kinetic isotope effects have been determined for the solvolysis of isopropyl  $\beta$ -naphthalenesulfonate in ethanol, 20% ethanol-80% trifluoroethanol (v/v), trifluoroethanol, and 97% aqueous hexafluoroisopropyl alcohol (w/w). Deuterium isotope effects ( $^2k/^1k$ ) at  $\alpha$  ( $D_1$ ) and  $\beta$  ( $D_6$ ) increased in the order EtOH < 20EtOH-80TFE < TFE < 97HFIP, suggesting looser transition states in this order. Carbon isotope effects ( $^{12}k/^{14}k$ ) at  $\alpha$  (the reaction center) showed monotonic decrease in the above order while carbon effects at  $\beta$  (methyl groups) exhibited a bell shape variation with a maximum at TFE. These results, together with kinetic and product studies, suggest that the reactions in these solvents can be treated in terms of an  $S_N2$ - $S_N1$  mechanistic spectrum in which the rate-determining step shifts from substitution to ionization and then to dissociation when the solvent becomes more ionizing and less nucleophilic. Model calculations of the kinetic isotope effects were carried out in order to clarify the origin of the variation in the isotope effects. Reaction coordinate motion for the substitution model was the O-C-O asymmetric stretching vibration accompanied by the Walden inversion-type motion, while that for the ionization model was the C-O bond rupture assisted by the C-C-H hyperconjugation. The shift of the rate-determining step from ionization to dissociation was represented by decreasing the contribution of the hyperconjugative electron donation for the bond rupture; this describes the nature of the so-called "Lim" solvolysis. The calculations showed that  $\alpha$ - and  $\beta$ -deuterium isotope effects depend mainly on the tight-loose character of the transition state; carbon isotope effects were shown to be sensitive to the reaction coordinate. The trends in the  $\alpha$ - and  $\beta$ -carbon isotope effects could be reproduced by changing the nature of the reaction coordinate. A series of transition-state structures and reaction coordinate parameters are presented which reproduce all experimental isotope effects simultaneously.

Solvolytic reactions of isopropyl esters and halides are known to have borderline characters in which the mechanism varies between  $S_N1$  and  $S_N2$  extremes depending on nucleophilicity and ionizing power of the solvent.<sup>1</sup> The dependence of reaction rates on the properties of solvents is demonstrated by a linear free energy equation (eq 1),<sup>2</sup> where both  $l$  and  $m$  are of considerable magnitude. It follows that the reactions in trifluoroacetic acid (TFA)

$$\log(k/k_0) = lN_{OTs} + mY_{2-AdOTs} \quad (1)$$

and 97% (w/w) aqueous hexafluoroisopropyl alcohol (97HFIP) are close to the  $S_N1$  limit while the reaction in ethanol exhibits considerable  $S_N2$  character.

Although studies on solvent effects on rates provide information concerning the reaction mechanism in a macroscopic sense, they do not give information on details of the reaction mechanism, i.e., variation in the nature of the transition state with a change in solvent. An  $S_N1$ -like reaction should have a different transition state than an  $S_N2$ -like reaction. Kinetic isotope effects represent the best experimental method to obtain information on a transition state and its variation with solvent.

Earlier kinetic isotope effect studies by Shiner and his co-workers<sup>3</sup> on the mechanism of isopropyl solvolysis indicated that the dominant rate-controlling step varies from direct nucleophilic attack in aqueous EtOH to tight ion-pair formation in aqueous trifluoroethanol (TFE) and then to solvent separated ion-pair formation in TFA. These conclusions are mainly based on deuterium isotope effects. In the present investigation, both carbon-14 and deuterium kinetic isotope effects were measured for the reactions of isopropyl  $\beta$ -naphthalenesulfonate (**1**) in EtOH-TFE mixed solvents and in 97HFIP.<sup>4</sup> Model calculations for these observed isotope effects were then carried out to determine the variation of the nature of the transition state with the change in solvent.

## Results

Table I summarizes the rate constants at 65 °C together with the  $N$  and  $Y$  values of the solvents. It can be seen in Table I that the reaction rates are similar despite a large variation in the

nucleophilicity and the ionizing power of the solvents.

Product analysis was performed by recording  $^1H$  and  $^{13}C$  NMR spectra of a reaction solution sealed and allowed to react in an NMR tube. Both substitution and elimination products were observed in all solvents except for EtOH, in which ethyl isopropyl ether was the only product detected. For 80% TFE-20% ethanol (v/v) mixed solvent (80T) and 97HFIP, two substitution products were formed besides propene: ethyl isopropyl ether (44%) and trifluoroethyl isopropyl ether (56%) for the former, and isopropyl alcohol (ca. 60%) and hexafluoroisopropyl isopropyl ether (ca. 40%) for the latter.

The amount of propene was determined in two ways. The first was the direct observation of the methyl signal of propene by  $^1H$  NMR; in the presence of 2,6-lutidine, propene was stable under the reaction conditions and could be directly determined. Propene was unstable, however, in the absence of 2,6-lutidine, and only substitution products were detected. In this case, the amount of propene formed during the reaction was estimated by running the reaction with isopropyl- $d_6$  ester and measuring the degree of proton incorporation into the deuterated methyl groups of the substitution products. The results are summarized in Tables II and III. It is interesting that the amount of propene in HFIP is independent of the concentration of the added lutidine (Table II).

Kinetic isotope effects are listed in Tables I and IV. Values in parentheses in Table I are those for reactions without 2,6-lutidine. It can be seen that all kinetic isotope effects vary monotonically with change in solvent except for one, the  $\beta$ - $^{14}C$  isotope effect. Because the smaller  $\beta$ - $^{14}C$  isotope effect in 97HFIP compared with that in TFE was surprising, we repeated the isotope effect determination in these solvents using different batches of

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(2) Schadt, F. L.; Bentley, T. W.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1976**, *98*, 7667-7674.

(3) Shiner, V. J., Jr. In "Isotope Effects in Chemical Reactions"; Collins, C. J., Bowmann, N. S., Eds.; Van Nostrand: New York, 1970; Vol. 2.

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**Table I.** Rate Constants and Kinetic Isotope Effects for the Solvolysis of Isopropyl  $\beta$ -Naphthalenesulfonate at 65 °C<sup>a</sup>

	$N_{OTs}$	$Y_{2-AdOTs}$	$10^5 k_2, s^{-1}$	$^{12}k/^{14}k$ $\alpha\text{-}^{14}C$	$H_k/D_k$ $\alpha\text{-}D_1$	$^{12}k/^{14}k$ $\beta\text{-}^{14}C$	$H_k/D_k$ $\beta\text{-}D_6$
EtOH	0.09 <sup>b</sup>	-2.033 <sup>b</sup>	7.05 ± 0.08	1.095 ± 0.004 <sup>d</sup>	1.07 ± 0.01	1.009 ± 0.002 <sup>d</sup>	1.22 ± 0.01
80T	-1.55 <sup>b</sup>	0.406 <sup>b</sup>	6.34 ± 0.03	1.089 ± 0.003 <sup>d</sup>	1.11 ± 0.01	1.015 ± 0.002 <sup>d</sup>	1.49 ± 0.01
TFE	-2.74 <sup>b</sup>	1.147 <sup>b</sup>	6.08 ± 0.07 (7.17 ± 0.10)	1.055 ± 0.002 <sup>d</sup>	1.15 ± 0.01 (1.16 ± 0.01)	1.017 ± 0.003 <sup>e</sup>	1.77 ± 0.01 (1.82 ± 0.02)
97HFIP	-3.93 <sup>c</sup>	2.46 <sup>c</sup>	11.5 ± 0.1 (10.8 ± 0.1)	1.044 ± 0.001 <sup>d</sup>	1.18 ± 0.01 (1.19 ± 0.02)	1.010 ± 0.002 <sup>e</sup>	2.22 ± 0.02 (2.25 ± 0.06)

<sup>a</sup> Reactions were carried out in the presence of 1.1 equiv of 2,6-lutidine. Values in parentheses are those without lutidine. Error limits are standard deviations for multiple measurements unless otherwise noted. <sup>b</sup> Kapsi, J.; Rappoport, Z. *J. Am. Chem. Soc.* **1980**, *102*, 3829–3837. <sup>c</sup> Schadt, F. L.; Bentley, T. W.; Schleyer, P. v. R. *Ibid.* **1976**, *98*, 7667–7674. <sup>d</sup> Errors are calculated as described in ref 16. <sup>e</sup> Average of three determinations.

**Table II.** Amount of Propene Produced during the Reactions at 65 °C

lutidine added	EtOH <sup>a</sup>	80T <sup>b</sup>	TFE	97HFIP
1.1 equiv	<i>c</i>	8%	15%	55%, 55% <sup>d</sup>
0			0%	0%

<sup>a</sup> EtOH-*d*<sub>6</sub>. <sup>b</sup> 20% EtOH-*d*<sub>6</sub>-80% TFE. <sup>c</sup> Not detected. <sup>d</sup> 2.5 equiv of 2,6-lutidine was added.

**Table III.** Amount of Proton Incorporation to the Final Products of the Reactions of Isopropyl-*d*<sub>6</sub> Ester at 65 °C

lutidine added	EtOH <sup>a</sup>	80T <sup>b</sup>	TFE	97HFIP
1.1 equiv	<i>c</i>	<i>c</i>	0%	1%
0	<i>c</i>	<i>c</i>	12%	56%

<sup>a</sup> EtOH-*d*<sub>6</sub>. <sup>b</sup> 20% EtOH-*d*<sub>6</sub>-80% TFE. <sup>c</sup> Impossible to determine due to the methyl signal of contaminated EtOH.

**Table IV.** Temperature Dependence of Deuterium Isotope Effects for the Reaction in 97HFIP

	65 °C	45 °C	25 °C <sup>a</sup>
$10^5 k, s^{-1}$	11.5 ± 0.09	1.51 ± 0.01	0.151
$H_k/D_k, \alpha\text{-}D_1$	1.18 ± 0.01	1.20 ± 0.01	1.22
$H_k/D_k, \beta\text{-}D_6$	2.22 ± 0.01	2.20 ± 0.08	2.18

<sup>a</sup> Extrapolated values.

reagents and solvents and using different methods of radioactivity measurement (liquid scintillation counting and ionization chamber counting) and obtained consistent results. Thus, we are confident that the values listed in Table I are correct.

**Mechanistic Implication.** The fraction of the alkene product was negligible in EtOH and small in TFE, and the addition of 1.1 equiv of 2,6-lutidine showed little effect on reaction rates and deuterium isotope effects in TFE. These suggest that elimination is not important in the EtOH-TFE solvent system. The finding that the kinetic plots without lutidine in TFE drifted upwards (see the Experimental Section) indicates that the role of the lutidine is to trap the sulfonic acid produced which otherwise catalyzes the reaction. This is in sharp contrast to the case in 97HFIP, in which the kinetic plots showed a sharp downward drift without lutidine. This suggests that in HFIP the added lutidine acts to suppress the backward reaction by trapping the sulfonic acid liberated. It may be concluded from these results that substitution and/or ionization steps are rate determining for the reactions in EtOH-TFE while an ion-pair return may be important in HFIP. The difference in mechanisms is reflected in the observed kinetic isotope effects.

All kinetic isotope effects showed smooth variation with change in solvent in the EtOH-TFE system;  $\alpha\text{-}D_1$ ,  $\beta\text{-}D_6$ , and  $\beta\text{-}^{14}C$  isotope effects increase while the  $\alpha\text{-}^{14}C$  isotope effect decreases when the solvent varies from EtOH to TFE. If we take the magnitude of the  $\alpha\text{-}D_1$  isotope effect as a measure of the tight-loose character of the transition state, it can be concluded that the transition state becomes looser as the solvent changes from EtOH to TFE. This is consistent with the trend of the  $\beta\text{-}D_6$  isotope effect which suggests that the degree of the hyperconjugative electron demand increases in this order. This is also consistent with the carbon-14 isotope effects; the  $\alpha\text{-}^{14}C$  isotope effects become smaller on going from EtOH to TFE, suggesting that the reaction has a larger  $S_N1$  character in TFE. The trend of the  $\beta\text{-}^{14}C$  isotope

effects may reflect a larger bonding change at the methyl groups in TFE compared with that in EtOH.

It is worth noting that the  $\beta\text{-}D_9$  kinetic isotope effect in ethanolysis of *tert*-butyl chloride is 2.33<sup>5</sup> which corresponds to 1.76 per  $D_6$ ; this value is similar to that observed in the present study for trifluoroethanolysis (1.77 per  $D_6$ ). This is in line with the idea that the reaction has a large  $S_N1$  character in TFE. However, the reaction is probably not limiting  $S_N1$  because the  $\alpha\text{-}D_1$  isotope effect is smaller than the limiting value.

In contrast to the case in EtOH-TFE, not all four isotope effects show expected magnitudes in HFIP; in particular the  $\beta\text{-}^{14}C$  isotope effect is smaller than expected compared with values in TFE and in 80T. Apparently the reaction mechanism in HFIP is different from those in the EtOH-TFE system discussed above. The most probable mechanism we can propose at present is a dissociation of a preformed ion-pair intermediate as the rate-determining step; product forming steps follow the dissociation step. The low nucleophilicity and high ionizing power of HFIP allows the dissociation step in HFIP to compete with the substitution and/or ionization steps which are rate-determining in EtOH-TFE. This mechanism is compatible with Shiner's conclusion<sup>3</sup> based on deuterium isotope effects if one assumes that HFIP and TFA solvents behave in similar ways.<sup>6</sup> The role of the added 2,6-lutidine is to trap  $\beta$ -naphthalenesulfonic acid and to suppress a backward reaction. This is consistent with the observation that the amount of propene is insensitive to the concentration of 2,6-lutidine (Table II).<sup>7</sup>

The proposed mechanism explains the trends of the kinetic isotope effects in HFIP. The  $\alpha\text{-}D_1$  and  $\beta\text{-}D_6$  isotope effects are larger because the transition state of the dissociation step is looser and has larger carbonium ion character than that of the ionization step. It should be noted that the deuterium isotope effects in HFIP at 25 °C are typical of values for a limiting  $S_N1$  solvolysis as can be seen in Table IV. The  $\alpha\text{-}D_1$  and  $\beta\text{-}D_6$  carbon kinetic isotope effects are small because the reaction coordinate in the transition state consists mainly of the translation of two heavy fragments, isopropyl cation and  $\beta$ -naphthalenesulfonate anion, and therefore little contribution from the reaction coordinate vibration to the carbon isotope effects is expected. The importance of the reaction coordinate contribution to carbon kinetic isotope effects is well documented<sup>8,9</sup> and is also shown in the model calculations described below. For the  $\beta\text{-}D_6$  effect in particular, it was found that little isotope effect is anticipated without the reaction coordinate contribution (*vide infra*).

(5) Shiner, V. J., Jr.; Murr, B. L.; Heinemann, G. *J. Am. Chem. Soc.* **1963**, *85*, 2413–2416.

(6) However, the magnitude of the  $\alpha\text{-}D_1$  isotope effect is different in these two solvents, and therefore, the mechanism should be somewhat different: Yamataka, H.; Tamura, S.; Hanafusa, T.; Ando, T. *J. Chem. Soc., Chem. Commun.* **1984**, 362–363.

(7) In the solvolysis of cyclopentyl brosylate in aqueous HFIP, it was concluded that elimination from the tight ion pair is in part rate-determining. Indeed, the  $\beta\text{-}D_9$  isotope effect for this reaction is larger (2.864 per  $D_4$ ) than the present case (2.22 per  $D_6$ ). The difference in mechanism between cyclopentyl brosylate and isopropyl  $\beta$ -naphthalenesulfonate is probably due to the difference in stability of olefins formed: Shiner, V. J., Jr.; Nollen, D. A.; Humski, K. *J. Org. Chem.* **1979**, *44*, 2108–2115.

(8) Yamataka, H.; Ando, T. *J. Phys. Chem.* **1981**, *85*, 2281–2286.

(9) Buddenbaum, W. E.; Shiner, V. J., Jr. In "Isotope Effects on Enzyme-Catalyzed Reactions", Cleland, W. W., O'Leary, M. H., Northrop, D. B., Eds.; University Park Press: Baltimore, 1977; Chapter 1.

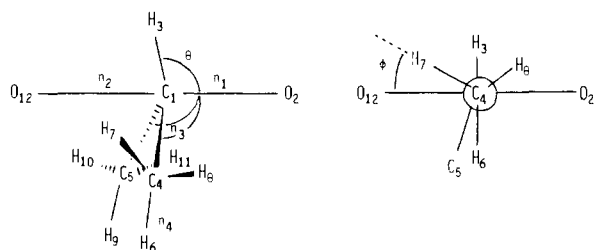


Figure 1. Transition-state geometrical model.

**Model Calculations.** The model calculations were carried out in order to clarify how the variation in the kinetic isotope effects can be rationalized in terms of the change in mechanism. Because of the ambiguity involved in the calculation procedures, we did not intend to obtain quantitative values of the transition-state parameters, but rather to focus on the trends of parameters and of the nature of the reaction coordinate.

**Calculation Method.** Model kinetic isotope effect calculations were carried out with program BEBOVIB-IV.<sup>10</sup> The general methods of constructing geometrical models and force fields are the same as those reported previously<sup>8,11</sup> and, therefore, will not be described in detail here.

In the present study, four kinetic isotope effects ( $\alpha$ -<sup>14</sup>C,  $\beta$ -<sup>14</sup>C,  $\alpha$ -D<sub>1</sub>, and  $\beta$ -D<sub>6</sub>) were calculated and compared with those observed. The geometrical model is shown in Figure 1, in which O<sub>2</sub> and O<sub>12</sub> are the oxygens of the leaving and the incoming groups, respectively. The four bond orders,  $n_1$ – $n_4$ , were related to each other as in eq 2 and 3; if  $n_2 = 0$  and  $n_1 = 1$  the model becomes the reactant, and if  $n_2 = 1$  and  $n_1 = 0$  the model becomes the product ether. The parameter  $p$  is a measure of the additional bonding to C <sub>$\alpha$</sub>  from the two methyl groups; when  $p = 0$ , there is no compensation of the decrease in bond order at C <sub>$\alpha$</sub>  in the transition state by additional hyperconjugative bonding; when  $p = 1$ , the decrease is completely compensated for by an increase in  $n_3$ . The angles  $\theta$  and  $\phi$  were related to the bond orders according to eq 4 and 5. In most calculations, the effect of solvation was represented by six oxygen atoms on the six  $\beta$ -hydrogens as shown

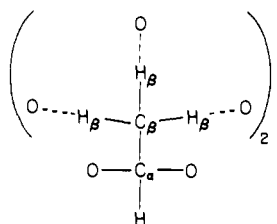
$$n_3 = 0.5p(1 - n_1 - n_2) + 1.0 \quad (2)$$

$$n_4 = 1 - (n_3 - 1)/3 \quad (3)$$

$$\theta = 30.0(1 - n_1 + n_2) \quad (4)$$

$$\phi = 90.0 + 19.5(n_1 - n_2) \quad (5)$$

below. This introduced another bond order  $n_{H-O}$ . Therefore, the



number of the independent geometrical parameters was three ( $n_1$ ,  $n_2$ , and  $p$ ) for the unsolvated model and four ( $n_1$ ,  $n_2$ ,  $p$ , and  $n_{H-O}$ ) for the solvated model.

Bond-stretching and angle-bending force constants were determined by eq 6 and 7 from the relevant bond orders and angles. Linear bending force constants for the solvated model were determined by eq 8, where  $F_{LB}^0 = 0.3$  mdyn A/rad<sup>2</sup>. Torsional force constants were set equal to 0.072 mdyn A/rad<sup>2</sup> for all cases.

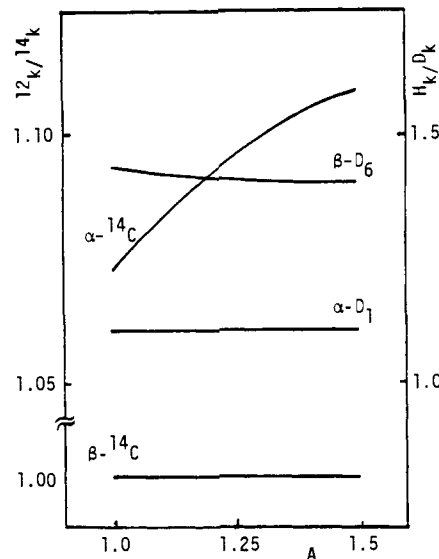


Figure 2. Calculated isotope effects vs. the magnitude of interaction constant  $A$ .  $n_1 = n_2 = 0.3$ ,  $p = 0.6$ ,  $B = C = E = 0.0$ .

Standard force constants for bond-stretching and angle-bending modes were the same as used previously.<sup>8,12</sup>

$$F_r = nF_r^0 \quad (6)$$

$$F_\alpha = (n_1n_2)g_\alpha F_\alpha^0; g_\alpha = 1.39 + 1.17 \cos \alpha \quad (7)$$

$$F_{LB} = (n_1n_2)^{1/2}F_{LB}^0 \quad (8)$$

A new, but somewhat complicated method of generating the reaction coordinate frequency was used in the present calculations. For a substitution-type reaction coordinate motion, two interaction constants,  $A$  and  $B$ , were used;  $A$  is the proportionality constant which couples the stretching modes of the two bonds, C<sub>1</sub>–O<sub>2</sub> and C<sub>1</sub>–O<sub>12</sub>, and  $B$  couples the C–O stretching modes to each of the three bending modes (OC<sub>1</sub>C<sub>4</sub>, OC<sub>1</sub>C<sub>5</sub>, and OC<sub>1</sub>H<sub>3</sub>). These two interaction constants generate an S<sub>N</sub>2-type asymmetric stretching motion with a contribution of the Walden-inversion type vibration as a reaction coordinate motion.<sup>8</sup> For an ionization-type reaction coordinate motion, two interaction constants,  $C$  and  $E$ , were used;  $C$  couples the C<sub>1</sub>–O<sub>2</sub> stretching mode to each of the two CC stretching modes and  $E$  couples the CC stretching modes to the CH stretching modes of the methyl groups. The two interaction constants generate a reaction coordinate motion in which the C<sub>1</sub>–O<sub>2</sub> bond rupture is assisted by the hyperconjugation of the two methyl groups.

All four interaction constants were used for the intermediate region, where both S<sub>N</sub>2 and S<sub>N</sub>1 characters were to be considered. The curvature parameter  $D$  was given by

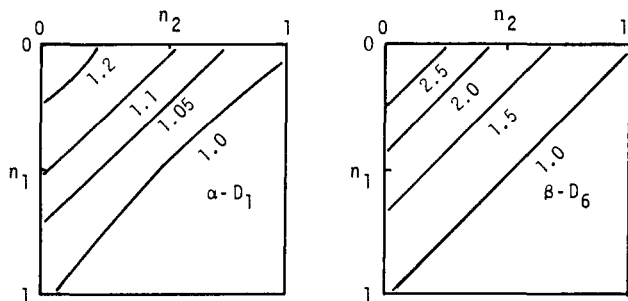
$$D = (1 - 3E^2)[(1 + A - 3B^2)(1 - A - 3B^2) \times (1 - 3E^2) - 2C^2(1 - B^2)] \quad (9)$$

The  $D$  function is the general equation for the treatment of the reaction coordinate in the S<sub>N</sub>2–S<sub>N</sub>1 spectrum. The  $D$  function for the substitution and ionization extremes are obtained by setting  $C = E = 0$  and  $A = B = 0$ , respectively; for the former  $D = (1 + A - 3B^2)(1 - A - 3B^2)$  and for the latter  $D = (1 - 3E^2)(1 - 2C^2 - 3E^2)$ . The conventional method to generate an S<sub>N</sub>1-type reaction coordinate, i.e.,  $F_{C-O}^* \leq 0$ , was investigated briefly and was found to give nearly the same results as those obtained for

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(11) (a) Melander, L.; Saunders, W. H., Jr. "Reaction Rates of Isotopic Molecules"; Wiley-Interscience: New York, 1980. (b) Sims, L. B.; Lewis, D. E. In "Isotopes in Organic Chemistry"; Buncl, E., Lee, C. C., Eds.; Elsevier: Amsterdam, 1984; Vol. VI, Chapter 4.

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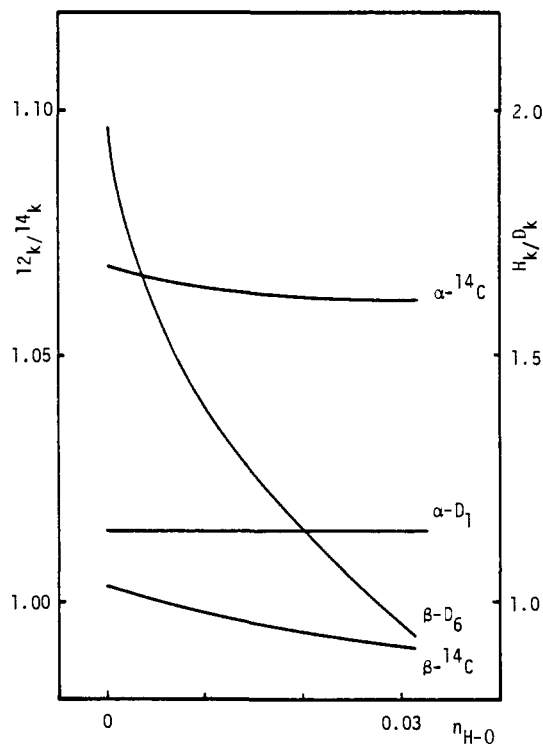
**Figure 3.** Contour maps for deuterium isotope effects.  $A = 1.05$ ,  $B = C = E = 0.0$ ,  $p = 0.85$ .

$C = 1.0$  and  $A = B = E = 0.0$ .

### Discussion

**Analysis of the Deuterium Isotope Effects.** It has previously been shown for the  $S_N2$  reactions of benzyl arenesulfonates that the carbon-14 kinetic isotope effects are sensitive to both the nature of the reaction coordinate and the transition-state geometry while the secondary deuterium isotope effects are not very sensitive to the reaction coordinate.<sup>8</sup> The same was found to be true in the present case as can be seen in Figure 2. The deuterium isotope effects are functions of only the geometrical parameters:  $n_1$ ,  $n_2$ , and  $p$ . Therefore, for a given value of  $p$ , it was possible to construct contour maps for the  $\alpha$ -D<sub>1</sub> and  $\beta$ -D<sub>6</sub> isotope effects as shown in Figure 3 for  $A = 1.05$  and  $p = 0.85$ . It is interesting to note that the constant isotope effect lines in Figure 3 are almost parallel to the diagonal between the upper-right and the lower-left corners for both isotope effects. This means that the  $\alpha$ -D<sub>1</sub> and  $\beta$ -D<sub>6</sub> isotope effects are sensitive to the tight-loose character ( $n_1 + n_2$ ) but not to the early-late character ( $n_1$  vs.  $n_2$ ) of the transition state. By making similar maps for different values of  $p$ , it was possible to determine a pair of ( $n_1 + n_2$ ) and  $p$  values which reproduced the experimentally observed  $\alpha$ -D<sub>1</sub> and  $\beta$ -D<sub>6</sub> isotope effects simultaneously. The values of ( $n_1 + n_2$ ) and  $p$  thus determined were 0.72, 0.50 for EtOH, 0.60, 0.65 for 80T, 0.44, 0.70 for TFE, and 0.34, 0.82 for 97HFIP. The variation in ( $n_1 + n_2$ ) is consistent with a looser transition state in a less nucleophilic and more ionizing solvent. The variation in  $p$ , on the other hand, suggests that the relative amount of positive charge on the methyl groups to that on the reaction center becomes greater for a looser transition state. Numerical calculations indicate that the positive charge on the central carbon is nearly constant at 0.14 while that on the methyl groups increases from 0.14 in EtOH to 0.54 in HFIP.

A more sophisticated model may be constructed by considering specific solvation in the transition state. There are three positions to be solvated: the leaving and incoming oxygens, the  $\alpha$  carbon, and the  $\beta$  hydrogens. Among these, solvation to the oxygens has been shown to have little influence on kinetic isotope effects at the  $\alpha$  and  $\beta$  positions.<sup>13</sup> Solvation to the  $\alpha$  carbon is impossible because the carbon is already pentacoordinated; it may alternatively be regarded that the solvation is already incorporated into the model through the  $C_\alpha$ -O bonds. Thus, we investigated the effect of solvation to the  $\beta$ -hydrogens. Some of the results are illustrated in Figure 4. Among the four isotope effects, the  $\beta$ -D<sub>6</sub> effect is most sensitive to  $n_{H-O}$  because of the direct interaction of the hydrogens with the solvent molecules. The carbon-14 isotope effects show small dependence on  $n_{H-O}$ , due primarily to the difference in the reaction coordinate contribution between the solvated and unsolvated models; the contribution becomes smaller when  $n_{H-O}$  becomes larger because of the effective mass difference. As in the case of the unsolvated model, the values of two parameters, ( $n_1 + n_2$ ) and  $n_{H-O}$  in this case, were determined;  $n_1 + n_2 = 0.66$ ,  $n_{H-O} = 0.0045$  for EtOH, 0.52, 0.0040 for 80T, 0.40, 0.0034 for TFE, and 0.30, 0.0029 for 97HFIP;  $p = 0.85$  in all cases. Thus, the transition state is looser and the solvation is weaker for a less nucleophilic and more ionizing solvent.



**Figure 4.** Calculated isotope effects vs.  $n_{H-O}$ .  $n_1 = n_2 = 0.21$ ,  $p = 0.82$ ,  $A = 1.05$ ,  $B = C = E = 0.0$ .

**Analysis of the Carbon-14 Isotope Effects.** The tight-loose character of the transition state was determined from the analysis of the deuterium isotope effects. There remains the problem of analyzing the carbon-14 isotope effects in terms of the mechanistic change. Because the carbon-14 isotope effects are sensitive to both the transition-state geometry and the reaction coordinate vibration, not only the geometrical parameters but also the interaction constants should be varied.

An  $S_N2$ -type reaction coordinate motion can readily be generated by the interaction constants,  $A$  and  $B$ .<sup>8,9</sup> For  $S_N1$  on the other hand, the classical method of generating the reaction coordinate,  $F_{C-O}^* \leq 0$ , was found to be inadequate because this method did not yield  $\beta$ -<sup>14</sup>C isotope effects of the experimental magnitude. The only method by which  $\beta$ -<sup>14</sup>C isotope effects between 1.01 and 1.02 could be produced was to incorporate interaction constants  $C$  and  $E$ . These two interaction constants generate a reaction coordinate motion in which the  $C_\alpha$ -O bond rupture is accompanied by the  $C_\alpha$ - $C_\beta$  bond shortening and the  $C_\beta$ -H bond lengthening in the transition state. Thus, the methyl groups are dynamically involved in the reaction coordinate motion. Some of the calculated isotope effects are illustrated in Figure 5, in which the isotope effects calculated by using  $C + E$  are plotted against the relative magnitude of  $C$  and  $E$ . It is clear that the  $\beta$ -<sup>14</sup>C isotope effect becomes larger when the  $C_\beta$ -H hyperconjugation becomes important ( $E$  becomes larger) in the reaction coordinate.

Continuity between the  $S_N2$  and  $S_N1$  reaction coordinates is assured by eq 9. In the two extreme cases,  $C = E = 0$  (for  $S_N2$ ) and  $A = B = 0$  (for  $S_N1$ ); in the intermediate case, all four constants are between 1.0 and 0.0. One example is shown in Figure 6. In these calculations,  $D$  was set equal to  $-0.038$ , and the ratios,  $A^2/B^2$  and  $C^2/E^2$ , were fixed at 20 and 8, respectively. Under these constraints,  $B$ ,  $C$ , and  $E$  are completely determined by the choice of  $A$ . For example, if  $A = 0.9$ ,  $B = 0.20$  and  $C = E = 0.0$ ; if  $A = 0.5$ ,  $B$ ,  $C$ , and  $E = 0.11$ , 0.57, and 0.20, respectively; if  $A = B = 0.0$ ,  $C$  and  $E$  should be 0.66 and 0.23, respectively. It is important to point out that the experimental trends in the  $\alpha$ -<sup>14</sup>C and  $\beta$ -<sup>14</sup>C kinetic isotope effects in the EtOH-TFE solvent system are very well reproduced by changing only these interaction constants for a fixed geometry. This means that the variation of the  $\alpha$ - and  $\beta$ -carbon isotope effects comes

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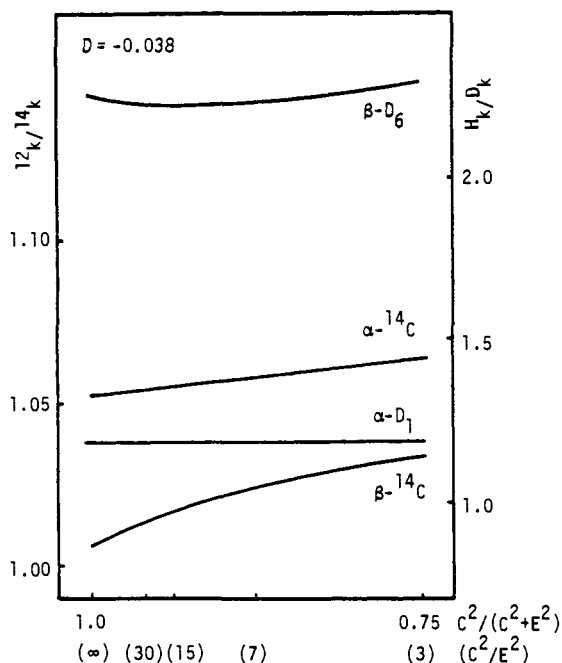


Figure 5. Calculated isotope effects vs. the nature of the reaction coordinate in  $S_N1$  model.  $n_1 = 0.3$ ,  $n_2 = 0.0$ ,  $p = 0.85$ ,  $n_{H-O} = 0.0009$ .

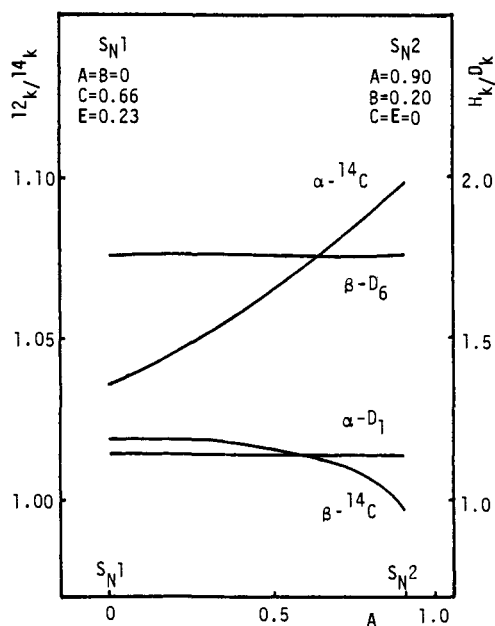


Figure 6. Calculated isotope effects vs. the nature of the reaction coordinate within the  $S_N2-S_N1$  spectrum.  $n_1 = n_2 = 0.2$ ,  $p = 0.85$ ,  $n_{H-O} = 0.034$ ,  $D = -0.038$ .

primarily from the difference in the nature of the reaction coordinate, in sharp contrast to the secondary deuterium isotope effects which are not very sensitive to the reaction coordinate vibration.

The variations in the  $\alpha$ - and  $\beta$ -carbon isotope effects in EtOH-TFE were thus rationalized in terms of the change in the nature of the reaction coordinate from  $S_N2$ -like (substitution) to  $S_N1$ -like (ionization). The question remains as to how to rationalize the  $\alpha$ - and in particular  $\beta$ -carbon isotope effects in HFIP. The mechanistic change from TFE to HFIP was assumed to be a shift of the rate-determining step from ionization to dissociation (vide supra). The shift should be accompanied by a change in the transition-state structure as well as in the reaction coordinate; the transition state becomes looser and the reaction coordinate becomes the translation of the two fragments; the nuclear reorganization within the isopropyl fragment becomes less important

Table V. Geometrical and Reaction Coordinate Parameters for the Transition States of the Solvolysis of Isopropyl  $\beta$ -Naphthalenesulfonate<sup>a</sup>

	EtOH <sup>b</sup>	80T <sup>b</sup>	TFE <sup>b</sup>	HFIP <sup>c</sup>
$n_1$	0.33	0.30	0.25	0.24
$n_2$	0.33	0.22	0.15	0.06
$n_{H-O}$	0.0045	0.0039	0.0034	0.0009
$p$	0.85	0.85	0.85	0.85
$A$	0.75	0.65	0.28	0.0
$B$	0.19	0.17	0.07	0.0
$C$	0.38	0.48	0.64	0.71
$E$	0.13	0.17	0.23	0.11

<sup>a</sup> $D = -0.038$ . <sup>b</sup> $A^2:B^2 = 15:1$ ,  $C^2:E^2 = 8:1$ . <sup>c</sup> $A = B = 0$ ,  $C^2:E^2 = 40:1$ .

for the reaction coordinate in HFIP. The change in the reaction coordinate can be expressed in terms of the change in relative importance of  $C$  and  $E$ . This is shown in Figure 5; both  $\alpha$ - and  $\beta$ -carbon isotope effects become smaller when  $E$  becomes smaller. Thus, the overall variation in the  $\alpha$ - and  $\beta$ -carbon isotope effects from EtOH to HFIP can be rationalized in terms of the change in the major interaction constants,  $A + B$  to  $C + E$  and then to  $C$  only. This corresponds to a change in the rate-determining step from substitution to ionization and then to dissociation.

**$S_N2-S_N1$  Spectrum and Transition-State Structures.** Based on the qualitative investigations of the dependence of calculated isotope effects on geometry and reaction coordinate motion, a series of transition states were determined for the four solvent systems within the  $S_N2-S_N1$  mechanistic spectrum. These transition states reproduce all of the kinetic isotope effects within experimental error limits. The geometrical and reaction coordinate parameters are listed in Table V. In all cases, the curvature parameter  $D$  was arbitrarily set constant at  $-0.038$ , which generates the reaction coordinate frequency of  $70-90i$   $cm^{-1}$ . The general trends of transition-state geometry and reaction coordinate parameters are in line with the idea that all of the reactions can be treated within the  $S_N2-S_N1$  spectrum, with the rate-determining step shifting from substitution to ionization and then to dissociation.

It is interesting to point out that in the case of EtOH, a reaction-coordinate frequency larger than  $500i$   $cm^{-1}$  can readily be generated by simply using a larger interaction constant  $C$  with the other geometrical and reaction-coordinate parameters unchanged. For example, the use of  $C = 0.80$  ( $D = -0.96$ ) instead of  $C = 0.38$  ( $D = -0.038$ ) raises  $\nu_L^*$  up to  $525i$   $cm^{-1}$  and still gives calculated isotope effects within the experimental error limits. In contrast, no attempt was successful to reproduce the experimental isotope effects with the reaction-coordinate frequency larger than  $100i$   $cm^{-1}$  in the case of HFIP. Any model which generates a large imaginary frequency gives too large  $\beta$ - and, in particular,  $\alpha$ -carbon isotope effects. These results may suggest that the barrier curvature for  $S_N2$  may be steep while that for  $S_N1$  should be nearly flat.

## Conclusions

The present combined experimental-theoretical isotope effect study provides the following conclusions. (1) The transition state is of looser character in the order EtOH < 80T < TFE < HFIP. (2) The magnitude of the  $\alpha$ -D<sub>1</sub> and  $\beta$ -D<sub>6</sub> isotope effects depends mainly on the tight-loose character of the transition state. (3) Solvation to the methyl groups is important for the  $\beta$ -D<sub>6</sub> isotope effect. (4) The variation of the  $\alpha$ - and  $\beta$ -carbon-14 isotope effects in the present reactions can be reproduced by a change in the nature of the reaction coordinate within the  $S_N2-S_N1$  mechanistic spectrum. In EtOH, two interaction constants,  $A$  and  $B$ , are important to generate an  $S_N2$ -type reaction coordinate motion, while in TFE two interaction constants,  $C$  and  $E$ , become important in order to obtain  $\beta$ -carbon isotope effects within experimental range. These interaction constants generate an ionization-type reaction coordinate motion in which C-O bond rupture is assisted by hyperconjugation of the methyl groups. In HFIP where dissociation becomes the rate-determining step, interaction constant  $C$  mainly determines the reaction coordinate. And finally (5) an  $S_N1$ -type reaction coordinate is required for

the reaction in EtOH and an  $S_N2$ -type reaction coordinate is required for the reaction in TFE. No  $S_N2$ -type contribution is necessary in HFIP.

### Experimental Section

**Materials.** Isopropyl- $\alpha$ - $^{14}C$   $\beta$ -naphthalenesulfonate was prepared from isopropyl-2- $^{14}C$  alcohol (New England Nuclear) by the usual method.<sup>14</sup> Isopropyl- $\beta$ - $^{14}C$   $\beta$ -naphthalenesulfonate was synthesized by reduction of acetone-1,3- $^{14}C_2$  (New England Nuclear) with lithium aluminum hydride, followed by esterification of the alcohol.<sup>15</sup> Esters labeled with deuterium at the  $\alpha$  and  $\beta$  positions were prepared by using lithium aluminum deuteride and acetone- $d_6$ , respectively, as deuterium sources. The chemical purity of the labeled compounds was verified by comparison of their physical constants with those for the unlabeled compounds. Isopropyl  $\beta$ -naphthalenesulfonate was recrystallized from *n*-hexane: **1**, mp 54.5–55.0 °C (lit.<sup>16</sup> mp 55–56 °C). The elementary analyses of all the protio and deuterio compounds gave satisfactory results for C, H (D), N, Cl, and S. Solvents were purified according to the standard methods described in the literature.<sup>17,18</sup>

**Reaction of Isopropyl  $\beta$ -Naphthalenesulfonate.** Reactions were carried out in the presence of 1.1 equiv of 2,6-lutidine unless otherwise noted. Product analysis was performed by recording  $^1H$  and  $^{13}C$  NMR spectra on a JEOL JNM-FX 100 spectrometer. A solution of isopropyl  $\beta$ -naphthalenesulfonate (0.04–0.12 M) with or without 2,6-lutidine was sealed in an NMR tube and allowed to react for more than 10 half-lives. The amount of propene formed was calculated from the relative intensity of the methyl signal ( $\delta = 0.48$  ppm relative to the methyl signal of an isopropyl ether) to those of the  $\alpha$ -hydrogen of the  $\beta$ -naphthalenesulfonyl moiety and the methyl hydrogens of 2,6-lutidine ( $\delta = 1.41$  ppm relative to the methyl signal of an isopropyl ether). In the absence of lutidine, propene was unstable and converted to substitution products or the starting ester. The amount of propene formed during the reaction was estimated by running the reaction of isopropyl- $\beta$ - $d_6$   $\beta$ -naphthalenesulfonate to completion and measuring the amount of proton incorporation into the methyl groups of the substitution products.

For 80% TFE–20% water (v/v) mixed solvent and 97% (w/w) aqueous HFIP, two substitution products were detected besides propene: ethyl isopropyl ether and trifluoroethyl isopropyl ether for the former and isopropyl alcohol and hexafluoroisopropyl isopropyl ether for the latter. Relative amounts of the substitution products were determined by  $^{13}C$  NMR for the former and by  $^1H$  NMR for the latter.

**Determination of Rate Constants and Kinetic Isotope Effects.** Rate constants were determined by a UV method in which the absorbance of isopropyl  $\beta$ -naphthalenesulfonate at 325 nm was used to follow the reactions. The initial concentration of the ester was 0.0362 M. Reactions in the presence of 2,6-lutidine showed good first order rate plots with correlation coefficients better than 0.9997 without any systematic drift. Reactions without lutidine, however, showed sharp downward drift in 97HFIP and upward drift in TFE, and therefore, the rate constants are less reliable.

Kinetic isotope effects were determined as described earlier.<sup>19</sup> All carbon-14 kinetic isotope effects were measured by ionization chamber counting.<sup>19,20</sup> For the  $\beta$ - $^{14}C$  isotope effects in TFE and 97HFIP, both ionization chamber counting and liquid scintillation counting<sup>21</sup> were used to assure the reliability of the results. The molar radioactivities of the starting materials were 3.0–4.0 mCi/mol for the former and ca. 0.5 mCi/mol for the latter counting method. Precision of the radioactivity measurement of  $^{14}C$  by liquid scintillation counting (Beckman LS 9000) was better than that for tritium<sup>17</sup> with the standard deviation of  $\pm 0.4\%$ ; this precision is similar to that obtained by ionization chamber counting. The scintillation solution used in this study was Aquasol-2 (New England Nuclear) and the counting efficiency determined by external standardization (H-number method) was about 95%.

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**Registry No.** D<sub>2</sub>, 7782-39-0;  $^{14}C$ , 14762-75-5; isopropyl  $\beta$ -naphthalenesulfonate, 67199-42-2.

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