Secondary Deuterium Isotope Effects in Solvolysis of Cyclopentyl *p*-Bromobenzenesulfonate. Stereochemistry of E1 and SN1 Reactions[1]

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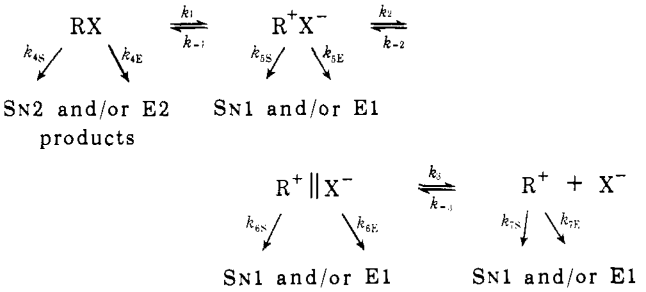
Abstract: Secondary α- and β-isotope effects in solvolysis of cyclopentyl-*1-d*, *cis*-cyclopentyl-*2-d*, *trans*-cyclopentyl-*2-d*, and cyclopentyl-*2,2,5,5-d*$_4$ brosylates were measured in different ethanol–water (E–W) and trifluoroethanol–water (TFE–W) mixtures. The magnitude of the effects indicates that in the E–W mixtures the products are derived by rate-determining substitution and elimination on the reversibly formed intimate ion pair. However, the change to TFE–W mixtures causes a change in mechanism; in these solvents the formation of the solvent separated ion pair is rate determining and the products are formed in fast subsequent attack on this intermediate. Consistent with this interpretation of the isotope effects, the elimination in E–W mixtures was found to be stereospecifically trans, while in TFE–W mixtures it is nonstereospecific. It was also determined that the configuration of the cyclopentanol formed in both types of solvents was inverted in comparison to the starting material. A detailed analysis provides an estimation of the isotope effects in each of the individual steps in the reaction.

Secondary deuterium isotope effects have become a very useful tool for reaction mechanism studies. Thus, the α effect can be used as a criterion for the solvolysis mechanism,[2] and the β effect has been shown to be very sensitive to participation of a neighboring group in solvolytic reactions.[3] The combination of secondary isotope effect data with a detailed product study can yield detailed information on a solvolytic reaction mechanism.

There is considerable evidence supplied by Winstein, *et al.*,[4] that at least three different carbonium ion type intermediates are involved in solvolytic substitution reactions. They are depicted as the tight (or intimate) ion pair, the solvent separated ion pair, and the free ion as indicated in Scheme I. Each of the steps from k_1 to k_7 can be rate determining. Substitution and elimination products can be derived from each of the intermediates in SN1 or E1 processes. It is assumed that products are formed irreversibly from the above intermediates and that no additional intermediates are involved. It is also assumed that the products are stable and that processes k_4 to k_7 are irreversible under reaction conditions favorable to substitution and elimination. Substitution and elimination products can be derived either from the same intermediate or from different intermediates. (It seems that the elimination may sometimes occur at an earlier stage of the reaction than substitution.[5])

Scheme I



Recent results show that the α effect is a function of the leaving group as well as of the mechanism.[6] Thus, it was found that for SN1 reactions the upper limit for the α effect (k_H/k_D) is 1.09 for iodides, 1.15 for chlorides, and 1.22 for sulfonate esters. This upper limit is characteristic of a particular leaving group and is fairly independent of changes in solvent polarity and nucleophilicity or substrate reactivity. It was concluded that these large effects are obtained when k_2 is the rate-determining step (conversion from the tight ion pair to the solvent separated ion pair).

Secondary β effects have been shown to be remarkably independent of changes in solvent composition when the quantity of the elimination product is constant.[7] The ratio k_{CH_3}/k_{CD_3} was 1.22 in the solvolysis of 1-phenylethyl chloride in ethanol–water mixtures ranging from 50 to 80 vol % of ethanol and in 97 wt % TFE–W. The yield of styrene was 1 to 3%. It was also found that the magnitude of the β effect may change when the quantity of the elimination product changes with the change of solvent[8] or the leaving group.[9]

Recently the results of solvolysis of 1,2-dimethyl-*exo*-2-norbornyl-*3,3-d*$_2$ *p*-nitrobenzoate in dioxane–water mixtures were published.[10] The isotope effect,

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[2] V. J. Shiner, Jr., "Isotope Effects in Chemical Reactions," C. J. Collins and N. S. Bowman, Ed., Van Nostrand Reinhold, New York, N. Y., 1970, Chapter 2.

[3] D. E. Sunko and S. Borčić, ref 2, Chapter 3.

[4] S. Winstein, B. Appel, R. Baker, and A. Diaz, *Chem. Soc., Spec. Publ.*, No. **19**, 109 (1965).

[5] H. L. Goering and K. Humski, *J. Amer. Chem. Soc.*, **90**, 6213 (1968).

[6] V. J. Shiner, Jr., and W. Dowd, *J. Amer. Chem. Soc.*, **93**, 1029 (1971); V. J. Shiner, Jr., M. W. Rapp, E. A. Halevi, and M. Wolfsberg, *ibid.*, **90**, 7171 (1968).

[7] V. J. Shiner, Jr., W. E. Buddenbaum, B. L. Murr, and G. Lamaty, *J. Amer. Chem. Soc.*, **90**, 418 (1968).

[8] V. J. Shiner, Jr., W. Dowd, R. D. Fisher, S. R. Hartshorn, M. A. Kessick, L. Milakofsky, and M. W. Rapp, *J. Amer. Chem. Soc.*, **91**, 4838 (1969).

[9] S. G. Smith and D. J. W. Goon, *J. Org. Chem.*, **34**, 3127 (1969).

[10] K. Humski, *Croat. Chem. Acta*, **42**, 501 (1970).

k_H/k_{D_2}, changed from 1.28 to 1.35 with the change of dioxane content from 50 to 70 vol %, respectively, while at the same time the quantity of elimination products rose from 36 to 66 mol %. From the difference in the elimination product distribution for deuterated and undeuterated compounds, the primary isotope effect of 1.54 for the elimination was calculated. Assuming that the measured isotope effect is cumulative (primary and secondary) and that the elimination (k_{5E}) is the rate-determining process, it was possible to calculate the β-secondary isotope effect for the ionization which was remarkably constant (1.22) in all solvents used.[10]

In this paper the α-secondary and β-secondary deuterium isotope effects in the solvolysis of cyclopentyl *p*-bromobenzenesulfonate (brosylate) in different ethanol–water (E–W) and trifluoroethanol–water (TFE–W) mixtures are reported. We also report the results of a product analysis which was conducted in order to determine the contribution of the primary isotope effect for the elimination to the total measured isotope effect. It is shown that these results yield information about the intermediate from which products are derived and about the stereochemistry of the product formation processes.

Methods and Results

The required cyclopentanol, cyclopentanol-*1-d* (*α-d*), *cis*-cyclopentanol-*2-d* (*cis-β-d*), *trans*-cyclopentanol-*2-d* (*trans-β-d*), and cyclopentanol-*2,2,5,5-d*$_4$ (*β-d*$_4$) were prepared as described by Streitwieser, *et al.*[11] The corresponding brosylates were prepared by the usual Tipson procedure.[12] The deuterium content was determined by mass spectral analysis and was found in each case to be greater than 93% in all of the deuterated compounds. The positions of deuterium in each case were established by means of the paramagnetic shift reagent induced nmr spectra with tris(dipivalomethanato)praseodymium(III).[13]

Solvolysis in Ethanol–Water Mixtures. The titrimetric rates were obtained employing the automatic potentiometric titration method maintaining a constant pH setting at 6.8. The rate constants were calculated from the standard integrated first-order law using a nonlinear least-squares program. The rate constants and the isotope effects are presented in Table I. Each number represents the mean of at least eight kinetic measurements. No trend was observed in the rate constants between 20 and 80% of reaction. Neither common ion rate depression effect nor special salt effect was detected; added salt, $LiClO_4$ or NaOBs, in the range from 0.0025 to 0.030 *M*, caused only slight increases in the solvolysis rate of cyclopentyl brosylate in 70 vol % E–W at 40°, amounting at the highest concentration in the range to approximately 5–6%.

Table I. First-Order Rate Constants and Secondary Deuterium Isotope Effects in Solvolysis of Cyclopentyl Brosylates in Ethanol–Water Mixtures at 40°

Vol % ethanol	Isotope effects[a,b] α-d	cis-β-d	trans-β-d	β-d$_4$	$k \times 10^4$, sec^{-1} [c] all H
70	1.18	1.14	1.17	1.80	14.6 ± 0.1
80	1.15	1.13	1.18	1.73	7.23 ± 0.05
90	1.14	1.13	1.15	1.64	3.19 ± 0.01
96	1.15	1.13	1.16	1.50	1.545 ± 0.003
100	1.15	1.10	1.14	1.55	0.708 ± 0.005

[a] k_H/k_{D_n}; *n* is the number of deuterium atoms. [b] Standard errors are less than 1% of the value. [c] Uncertainties are standard errors.

The product yields were determined by glpc using 10% Ucon on Chromosorb and the flame ionization detector. The integrated peak areas were corrected by the factor obtained from the chromatogram of the standard mixture made from the pure compounds. The products were shown to be stable under the reaction conditions as well as on the glpc column. The results are presented in Table II.

Table II. Product Compositions[a] in Solvolysis of Cyclopentyl Brosylates in Ethanol–Water Mixtures at 40°

Vol % ethanol	Prod	Mol % All H	α-d	cis-β-d	trans-β-d	β-d$_4$
70	Alkene[b]	21.9	21.0	21.2	19.1	13.8
	Alcohol[c]	45.6	46.2	46.3	47.2	51.5
	Ether[d]	32.5	32.8	32.5	33.7	34.7
80	Alkene[b]	26.7	24.9	24.9	23.8	18.8
	Alcohol[c]	32.5	32.7	33.7	32.5	35.8
	Ether[d]	40.8	42.4	41.4	43.7	45.4
90	Alkene[b]	23.3	19.6	22.1	19.8	13.2
	Alcohol[c]	20.3	22.6	20.8	20.0	23.6
	Ether[d]	56.4	57.8	57.1	60.2	63.2
96	Alkene[b]	17.0	16.9	16.5	14.1	10.0
	Alcohol[c]	9.2	10.2	10.3	9.2	10.9
	Ether[d]	73.8	72.9	73.2	76.7	79.1
100	Alkene[b]	11.8	12.9	11.7	11.8	7.8
	Alcohol[c]					
	Ether[d]	88.2	87.1	88.3	88.2	92.2

[a] Compositions based on corrected capillary glpc peak areas. [b] Cyclopentene. [c] Cyclopentanol. [d] Cyclopentyl ethyl ether.

Solvolysis in Trifluoroethanol–Water Mixtures. The isotope effects on the rates of solvolysis of deuterated cyclopentyl brosylates were also measured in TFE–W mixtures. The results are given in Table III. The rate-measurement technique and the number of experiments are identical as for solvolysis in E–W mixtures. Again no common ion rate depression and no special salt effect have been observed; added salt, $LiClO_4$ or NaOBs, in the range from 0.0025 to 0.030 *M*, caused only slight increases in the solvolysis rate of cyclo-

Table III. First-Order Rate Constants and Secondary Deuterium Isotope Effects in Solvolysis of Cyclopentyl Brosylates in Trifluoroethanol-Water Mixtures at 30°

Wt % TFE	Isotope effects[a,b] α-d	cis-β-d	trans-β-d	β-d$_4$	$k \times 10^4$, sec^{-1} [c] all H
70	1.23	1.21	1.23	2.15	5.83 ± 0.04
97.5	1.25	1.25	1.19	2.40	1.77 ± 0.01

[a] k_H/k_{D_n}; *n* is the number of deuterium atoms. [b] Standard errors are about 1% of the value. [c] Uncertainties are standard errors.

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(11) A. Streitwieser, Jr., R. H. Jagow, R. C. Fahey, and S. Suzuki, *J. Amer. Chem. Soc.*, **80**, 2326 (1958).

(12) R. S. Tipson, *J. Org. Chem.*, **9**, 235 (1944).

(13) K. Humski, L. Klasinc, D. Kovačević, and V. Kramer, *Croat. Chem. Acta*, **45**, 363 (1973).

pentyl brosylate in 70 wt % TFE–W at 30°, amounting at the highest concentration in the range to approximately 5–7%.

The product distribution studies were conducted in the same manner as for solvolysis in E–W mixtures and are given in Table IV. The products were shown to be stable under the reaction conditions for 10 half-lives of the reaction.

Table IV. Product Compositions[a] in Solvolysis of Cyclopentyl Brosylate in Trifluoroethanol–Water Mixtures at 30°

Wt % TFE	Product	Mol % All H	*α-d*	*cis-β-d*	*trans-β-d*	β-d_4
70	Alkene[b]	41.8	41.7	35.8	35.1	27.8
	Alcohol[c]	52.3	52.1	58.2	58.1	64.6
	Ether[d]	5.9	6.2	6.0	6.8	7.6
97	Alkene[b]	76.4	77.2	73.8	72.1	62.6
	Alcohol[c]					
	Ether[d]	23.6	22.8	26.2	27.9	37.4

[a] Compositions based on corrected capillary glpc peak areas. [b] Cyclopentene. [c] Cyclopentanol. [d] Cyclopentyl trifluoroethyl ether.

Stereochemistry of the SN1 Reaction. By means of nmr using a shift reagent it was possible to determine the configuration of the alcohol product relative to that of the starting material. When the *cis-β-d* brosylate was solvolyzed in different E–W mixtures and 70 wt % TFE–W cyclopentanol-*β-d* was isolated from the resulting products mixture by means of glpc (Carbowax), the position of deuterium relative to the hydroxyl group was established by nmr. The nmr chemical shift values and the corresponding integrals of previously prepared alcohols and alcohols isolated after 10 half-lives from the reaction mixtures are given in Table V. From the last three entries it is evident that the alcohol resulting either from E–W mixtures or from 70 wt % TFE–W was formed with at least 95% inversion of configuration on the reacting carbon. When starting with the *cis-β-d* brosylate in all three cases the *trans-β-d* alcohol was isolated as the major substitution product. Mass spectral deuterium analysis showed that alcohol products had the same deuterium content as *cis-β-d* alcohol from which the starting brosylate was prepared. Hence, there is no loss of deuterium during the formation of the alcohol. From the fact that deuterium is still in position 2 in the product it is evident that there is no hydride shift during the reaction.

Table V. Nmr[a] Chemical Shift[b] Values and Corresponding Integrals for Cyclopentanol[c] and Deuterated Cyclopentanols in the Presence of Pr(DPM)$_3$[d]

Compound	Deuterium content[e]	Integrals[f] 1- and 2,5-cis $\tau \sim 15$[b]	2,5-trans and 3,4-cis $\tau \sim 12$[b]	3,4-trans $\tau \sim 11$[b]
All H	0.00	3.02	4.03	1.94
α-d	0.99	2.03	3.97	2.01
cis-β-d	0.94	2.10	4.00	1.98
trans-β-d	0.97	3.05	3.07	1.92
β-d_4	3.85	1.02	2.10	2.02
From 70 wt % TFE–W[g]	0.93	2.99	3.12	1.94
From 70 vol % E–W[g]	0.93	2.96	3.20	1.91
From 80 vol % E–W[g]	0.93	3.01	3.09	1.97

[a] JEOL 100-MHz nmr. [b] In ppm with TMS as the external standard. It is an approximate value which depends on concentrations of alcohol and complex. [c] Concentrations of alcohols about 0.2 *M* and Pr(DPM)$_3$ 0.05 *M* in CCl$_4$. [d] Tris(dipivalomethanato)praseodymium(III) complex. [e] According to mass spectral analysis. [f] Average of four integrals; expressed as a number of protons normalized to the deuterium content. [g] Isolated by glpc after 10 half-lives of solvolysis. Starting material is *cis*-cyclopentyl-*2-d* brosylate.

Discussion

Recently Stoffer and Christen[14] reported that in 70 vol % E–W the *β-d* isotope effect for cyclopentyl brosylate is cumulative in nature. The value of 1.888 for the β-d_4 compound is very close to the square for mono-cis-deuterated derivative times the square for mono-trans-deuterated derivative (1.853). The difference between the values for the *cis-* and the *trans-β-d* compound was explained by the inability of the *trans*-hydrogen or -deuterium to obtain the desired coplanar orientation to the leaving group. In view of our results obtained in bicyclic systems[10] we thought that there is also a possibility that the elimination process is rate determining and that the product-forming process is k_5 (Scheme I). If such is the case then the discrepancy between the calculated and the experimentally obtained effect for the tetradeuterated derivative could be explained by the contribution of the primary deuterium isotope effect which is due to the C–D bond cleavage in the rate-determining olefin formation.

Results presented in Tables I and V for solvolysis in E–W mixtures indicate that in these solvents the elimination product (cyclopentene) as well as substitution products (cyclopentanol and cyclopentyl ethyl ether) are derived from the tight ion pair by rate-determining k_5 processes (Scheme I).

The k_5 processes are irreversible because the products are stable under the reaction conditions. The processes k_{-2} and k_{-3} from Scheme I can be excluded on the basis of the absence of the special salt effect and the common ion rate depression. There are several facts supporting this mechanism and indicating the absence of processes k_2 and k_3. These facts include α and β effects and the stereochemistry of elimination and substitution products.

The relatively low α effect (Table I) for cyclopentyl-*1-d* brosylate (1.15) is smaller than expected for a rate-determining k_2 process in the case of solvolysis of a sulfonate ester[6] (1.22). It seems that in 70 vol % E–W the k_2 process may begin to be important and the α effect rises to 1.18.

The measured β effect for the tetradeuterated compound changes with the change in water content of the solvent, while with monodeuterated derivatives it is somewhat higher for the *trans-* than for the *cis-β-d* compound (Table I). Not taking into account the effect obtained in 70 vol % E–W the decrease in the β effect for the β-d_4 derivative from 1.73 to 1.55 is accompanied by a decrease in olefin fraction in the all H compound from 26.7 to 11.8 mol % as the solvent is changed from 80 to 100 vol % E–W (Table II). This is consistent

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[14] J. O. Stoffer and J. D. Christen, *J. Amer. Chem. Soc.*, **92**, 3190 (1970).

with the elimination product-forming step (k_{5E}) being rate determining. No trend was observed in the β effect for the *cis-β-d* compound, while a slight trend is detectable for the *trans-β-d* derivative indicating that the trans-β deuterium is eliminated. For the *cis-β-d* compound there is no primary effect involved, whereas for the *trans-β-d* the competition for elimination between the trans positioned hydrogen and deuterium decreases the influence of the primary effect on the total measured effect. Thus, there is a small change in isotope effect from 1.18 to 1.14 with the change in the amount of the elimination product from 26.7 to 11.8 mol %, respectively.

The results also indicate that the substitution products are formed from the same intermediate in competition with elimination, both as rate-determining processes (all $k_5 < k_{-1}$). If the substitution products were mainly derived from the solvent separated ion pair then it could be expected that the decrease in the solvent ionizing power would decrease the relative amount of the substitution product since the competitive elimination occurs at an earlier stage of the reaction. Such is clearly not the case as can be seen from Table II, comparing the product composition in 70 and 100 vol % E–W. On the other hand if the substitution products are mainly derived from the tight ion pair then an increase in the basicity and a decrease in polarity caused by adding ethanol should favor substitution *vs.* elimination, in accord with the experimental facts.

Results presented in Tables III and V for solvolyses in TFE–W mixtures indicate that the products are mostly derived from the solvent separated ion pair by k_6 processes after rate-determining formation of the solvent separated ion pair.

Here, the α-secondary isotope effect reaches the maximum value for the solvolysis of sulfonate esters[6] ($\sim$1.22) which indicates that the step with rate constant k_2 is rate determining.

The β-secondary isotope effects are equal, within the experimental error, for the *cis-β-d* and the *trans-β-d* compounds. The change in the β effect for the β-d_4 derivative from 2.15 to 2.40 with a change of solvent from 70 to 97.5 wt % TFE–W is small compared with the large change in the amount of the elimination product (from 42 to 76 mol %, respectively). This shows that the elimination is not a rate-determining process.

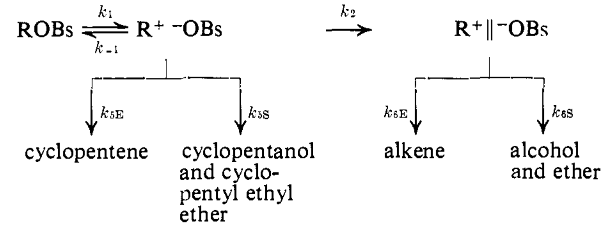
Elimination is mostly trans in E–W mixtures (that can be deduced from the second columns in Tables VII and VIII). The isotope effect on the product ratio r_{5E}/r_{5S} is 1.05 for *cis-β-d* and 1.17 for *trans-β-d*, indicating that mainly trans hydrogens (or deuterium) are eliminated. That would be expected for the olefin derived from a tight ion pair where the leaving group is still in the vicinity of the carbonium ion and thus hinders solvent attack from the cis side. The isotope effects on the product ratio in TFE–W were calculated in the same way giving values of 1.22 and 1.29 for *cis-β-d* and *trans-β-d*, respectively, indicating, within the experimental error, the equivalence of cis- and trans-β hydrogens in the elimination process. The stereoselectivity in the elimination with respect to the position of the β hydrogen is strongly diminished in comparison with the solvolysis in E–W mixtures.

The alcohol in the products is formed with inversion of configuration in E–W solvents (Table V) which is expected if the product is derived from the tight ion pair where the leaving group is still close to the substrate and hinders the nucleophilic attack from the front side.

The reason for the complete inversion of configuration in the alcohol obtained as a substitution product in TFE–W (Table V) is not clear.[15] One would expect less stereoselectivity in the product formation from the solvent separated ion pair than from the tight ion pair. The shielding of the front side by a leaving group cannot account by itself for these results, since the solvent is already between the leaving group and the carbonium ion in the external ion pair. However, it might be that only trifluoroethanol molecules separate the two counterions and thus block the front side from nucleophilic attack by water. The possibility of such "solvent sorting" is being currently investigated.

The qualitative analysis (*vide supra*) thus concludes that the abbreviated reaction Scheme II should apply.

Scheme II



In the more basic, more nucleophilic E–W solvent mixtures, k_{5E} and k_{5S} are sufficiently rapid that k_2 is relatively unimportant in these solvents. The evidence does, however, indicate that $k_{-1} > k_{5E}$. If we assume that the first step is in *equilibrium*, a number of equations can be derived to show the relationships among the isotope effects for the separate steps, the product yields, and the overall observed isotope rate effects. If $k_1/k_{-1} = K$, then the overall rate constant for the reaction of the hydrogen compound is

$$k_H = K(k_{5S} + k_{5E})$$

and the ratio for the hydrogen compound rate constant to the deuterium compound rate constant is

$$k_H/k_D = \frac{K(k_{5S} + k_{5E})}{K'(k'_{5S} + k'_{5E})} \qquad (1)$$

(where the primed values refer to the rate constants for the specific steps in Scheme II for the deuterium compound). The fractions of elimination (f_E) and substitution (f_S) obtained can be expressed as follows

$$f_{5E} = k_{5E}/(k_{5E} + k_{5S}) \qquad f_{5S} = k_{5S}/(k_{5E} + k_{5S})$$

$$f'_{5E} = k'_{5E}/(k'_{5E} + k'_{5S}) \qquad f'_{5S} = k'_{5S}/(k'_{5E} + k'_{5S})$$

The isotope effects on the separate steps (r) can be defined as follows

$$r_{5E} = k_{5E}/k'_{5E}, \text{ etc.}$$

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(15) This is contrary to the assumption of R. A. Sneen (R. A. Sneen, *Accounts Chem. Res.*, **6**, 46 (1973)) according to which the substitution product-forming step from external ion pair should presumably proceed with retention of configuration. It should also be mentioned that the α and β effects are significantly larger than unity if the product-forming step from the tight ion pair is part of the rate-determining process, as demonstrated in our work. Hence, nucleophilic displacement in which these isotope effects are nearly unity must proceed by a different mechanism. This appears to be an indirect proof of the classical SN2 mechanism.

Multiplying the right-hand side of eq 1 by $r_{5E}k'_{5E}/k_{5E}$ ($\equiv 1$) gives

$$k_H/k_D = \frac{K}{K'} r_{5E} \frac{(k_{5S} + k_{5E})}{k_{5E}} \times \frac{k'_{5E}}{(k'_{5S} + k'_{5E})} = \frac{K}{K'} r_{5E} \frac{f'_{5E}}{f_{5E}} \qquad (2)$$

Similarly, multiplying the right-hand side of eq 1 by $r_{5S}k'_{5S}/k_{5S}$ gives

$$k_H/k_D = \frac{K}{K'} r_{5S} \frac{f'_{5S}}{f_{5S}} \qquad (3)$$

Equating the right-hand side of eq 2 and 3 and rearranging

$$r_{5E}/r_{5S} = f'_{5S}f_{5E}/f_{5S}f'_{5E} \qquad (4)$$

The ratio of yields ("the isotope effect on the product ratio") is simply the ratio of isotope effects in the two competing product-forming steps. From the observed isotope effect on the reaction rate constant, and the product ratios from reaction of the hydrogen and deuterium compound, using eq 2 and 3 one can calculate the isotope effect on the formation of substitution product ($r_{5S}K/K'$) and elimination product ($r_{5E}K/K'$).

$$r_{5S}K/K' = k_Hf_{5S}/k_Df'_{5S} \qquad (5)$$

$$r_{5E}K/K' = k_Hf_{5E}/k_Df'_{5E} \qquad (6)$$

The values calculated from eq 4, 5, and 6 will be tabulated below for the reactions in E–W solvents.

In TFE–W solvents k_2 is rate determining and the isotope effect on the product ratio is simply

$$r_{6E}/r_{6S} = f'_{6S}f_{6E}/f_{6S}f'_{6E} \qquad (7)$$

and the observed isotope effect is

$$k_H/k_D = (K/K')r_2 \qquad (8)$$

Equations 7 and 8 will be applied below to the results in TFE–W mixtures.

Table VI. Isotope Effects in Solvolysis of Cyclopentyl-*2,2,5,5-d*$_4$ Brosylate in E–W Mixtures

	β-d_4 isotope effects		
Vol % ethanol	Elim *vs.* sub in R$^+$OBs$^-$ [a]	Sub on R$^+$OBs$^-$ [b]	Elim from R$^+$OBs$^-$ [c]
70	1.74	1.63	2.83
80	1.57	1.56	2.45
90	2.00	1.45	2.90
96	1.84	1.47	2.70
100	1.58	1.48	2.34
Av	1.74	1.52	2.64
Per D		1.11	

[a] r_{5E}/r_{5S}. [b] $r_{5S}K/K'$. [c] $r_{5E}K/K'$.

Applying the equations derived above, we calculate for the β-d_4 compound solvolyzing in E–W mixtures the values shown in Table VI. The figures in the second and fourth columns of Table VI involve isotope effects in elimination of a single β-*d* and, therefore, are composites of primary and secondary effects. We return to their analysis below. The third column is simply the overall secondary effect when the step labeled k_{5S}, nucleophilic attack on the tight ion pair, is the rate-determining step and is, of course, the product of the secondary effect on the equilibrium times the secondary effect on the nucleophilic attack step.

For the *cis-β-d* compound reacting in E–W solvents the isotope effects are all secondary because only trans hydrogens are eliminated. Using the equations derived above the results shown in Table VII are calculated for the *cis-β-d* compound. These results demonstrate that the secondary β effect is about 5% greater in the elimination reaction than in the substitution reaction.

Table VII. Isotope Effects in the Solvolysis of *cis*-Cyclopentyl-*2-d* Brosylate in E–W Mixtures

	cis-β-d isotope effects		
Vol % ethanol	Elim *vs.* sub in R$^+$OBs$^-$ [a]	Sub on R$^+$OBs$^-$ [b]	Elim from R$^+$OBs$^-$ [c]
70	1.04	1.11	1.18
80	1.10	1.10	1.21
90	1.07	1.11	1.19
96	1.04	1.12	1.17
100	1.01	1.10	1.11
Av	1.05	1.11	1.17

[a] r_{5E}/r_{5S}. [b] $r_{5S}K/K'$. [c] $r_{5E}K/K'$.

For the *trans-β-d* compound in E–W solvents the calculated isotope effects are shown in Table VIII.

Table VIII. Isotope Effects in the Solvolysis of *trans*-Cyclopentyl-*2-d* Brosylate in E–W Mixtures

	trans-β-d isotope effects		
Vol % ethanol	Elim *vs.* sub in R$^+$OBs$^-$ [a]	Sub on R$^+$OBs$^-$ [b]	Elim from R$^+$OBs$^-$ [c]
70	1.19	1.13	1.34
80	1.16	1.14	1.32
90	1.23	1.10	1.35
96	1.25	1.12	1.40
100	1.00	1.14	1.14
Av	1.17	1.13	1.31

[a] r_{5E}/r_{5S}. [b] $r_{5S}K/K'$. [c] $r_{5E}K/K'$.

The elimination reaction involves a mixture of two processes, one eliminating a trans hydrogen and the other eliminating a trans deuterium. Comparing column 3 with the same column in Table VII, it can be seen that the cis and trans (secondary) β effects are about the same when nucleophilic attack on the tight ion pair (k_{5S}) is rate determining (1.13 *vs.* 1.11).

For solvolysis in TFE–W mixtures (Table III) the *cis-* and *trans-β-d* effects do not appear significantly different and the square of their product is within experimental error the same as the effect observed for the β-d_4 compound. This is expected if the rate-determining step is that labeled k_2 in the scheme. The average of all of the observed β-*d* effects in 70 and 97.5 wt % TFE–W is 1.22 per D or 2.21 for four β-deuterium atoms, and we conclude that these are the values for r_2K/K'. The value r_{6E}/r_{6S} derived from the isotope effect on the product ratio for the β-d_4 compound is 1.87 in 70 wt % TFE–W and 1.93 in 97.5 wt % TFE–W.

Applying the equations derived above we calculate for the α-*d* compound solvolyzing in E–W mixtures the results shown in Table IX. Although the scatter is

Table IX. Isotope Effects in Solvolysis of Cyclopentyl-*1-d* Brosylate in E–W Mixtures

	α-*d* effects		
Vol % ethanol	Elim *vs.* sub in R^+OBs^{-} [a]	Sub on R^+OBs^{-} [b]	Elim from R^+OBs^{-} [c]
70	1.05	1.17	1.23
80	1.10	1.12	1.23
90	1.25	1.09	1.36
96	1.01	1.15	1.16
100	0.90	1.16	1.05
Av	1.06	1.14	1.21

[a] r_{5E}/r_{5S}. [b] $r_{5S}K/K'$. [c] $r_{5E}K/K'$.

large compared with the average value it seems reasonable to conclude from the results in column 2 that the α-*d* isotope effect in elimination is about 6% larger than it is for substitution. This is similar to the conclusion reached above that the secondary β-*d* effect was about 5% larger for elimination than for substitution.

From the average of the results of solvolysis in 70 and 97.5 wt % TFE–W mixtures it is calculated that r_2K/K' is about 1.24 and that r_{6E}/r_{6S} is 0.98.

The effects estimated using the equations derived above all involve products or ratios of isotope effects in the individual steps. In order to compare figures for individual steps one must first estimate the effect in a particular step. The most straightforward way of doing this appears to be to assume that the isotope effects in step k_2 are unity. It has been argued that this should be at least approximately true because the covalent bond between alkyl and leaving groups has already been broken before this step and the k_2 process merely involves increasing the length of the ionic bond.[6] In Table X the derived isotope effects on the equilibrium in the first step (K/K') and on the rate constants k_{5E} and k_{5S} are given.

Table X. Estimated Isotope Effects for the Separate Steps in Solvolysis of Cyclopentyl Brosylate in E–W and TFE–W Solvents

	Isotope effects			
Reaction step	α-*d*	*cis*-β-*d*	*trans*-β-*d*	β-d_4
$R^+OBs^- \xrightarrow{k_2} R^+\|\|OBs^-$ [a]	(1.00)	(1.00)	(1.00)	(1.00)
Equil formation of R^+OBs^- [b]	1.24	1.23	1.21	2.28
Sub on R^+OBs^- [c]	0.92	0.90	0.93	0.67
Elim from R^+OBs^- [d]	0.98	0.95	1.08	1.16

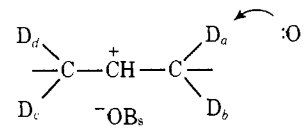
[a] r_2, assumed value. [b] K/K'. [c] r_{5S}. [d] r_{5E}.

The results indicate that the α-*d* effect on the equilibrium formation of the tight ion pair is large and that the α-*d* effect (r_{5S}) for nucleophilic attack on the tight ion pair (k_{5S}) is inverse. One would expect a similar effect on the recombination of the tight ion pair because both of these reactions involve nucleophilic attack on a carbonium ion by an oxygen base and the basicities in the two cases (BsO^- and H_2O) are not much different. Thus, the overall α-*d* effect when the step with rate constant k_{5S} is rate determining is 1.24 × 0.92 or 1.14, essentially the same as has been proposed for reactions of sulfonate esters when the step labeled k_1 is rate determining.

On the other hand, elimination from the tight ion pair *via* rate constant k_{5E} does not involve increasing the coordination number at the α-carbon atom and therefore is not expected to show a significant inverse α-*d* effect. The derived value of r_{5E}, 0.98, is not appreciably different from unity and the overall α-*d* effect when k_{5E} is rate determining is essentially that in the equilibrium formation of the tight ion pair.

The β-*d* effects on the equilibrium formation on the tight ion pair are, within experimental error, the same for *cis*- and *trans*-β-*d* and as expected the value for the β-d_4 compound is within experimental error the square of the product of the values for *cis*- and *trans*-β-*d* compounds. As in the α-*d* effect example cited above the β-*d* effects on *nucleophilic attack* on the tight ion pair are inverse and about the same order of magnitude for both *cis*- and *trans*-β-*d*. The value for the β-d_4 compound is again within experimental error of the square of the product of the values for *cis*- and *trans*-β-*d*.

The interpretation of the β effect on the elimination from the tight ion pair (r_{5E}) is complicated because there are four, in principle different, isotope effects involved. The situation is illustrated in the partial formula for the β-d_4 compound below.



One of the trans deuterium atoms (D_a) is eliminated and gives rise to a primary isotope effect which we refer to as "*a*." Similarly, the other deuterium atoms give rise to secondary isotope effects "*b*," "*c*," and "*d*." Assuming the cumulative character of isotope free energy effects[16] the observed value of $(k_{5E}/k'_{5E})_{\beta\text{-}d_4}$ is expected to be the product of the individual isotope effect.

$$(k_{5E}/k'_{5E})_{\beta\text{-}d_4} = abcd = 1.16$$

Under the same assumption

$$(k_{5E}/k'_{5E})_{cis\text{-}\beta\text{-}d} = 2bc/(b + c) = 0.95$$

and in the same way

$$(k_{5E}/k'_{5E})_{trans\text{-}\beta\text{-}d} = 2ad/(a + d) = 1.08$$

Thus, for the four unknown isotope effects we have only three experimental observations and three equations. The simplest way of proceeding is not to try and separate the "*b*" and "*c*" isotope effects but to estimate their product and use this to derive isotope effects "*a*" and "*d*." Rearranging the equation for the *cis*-β-*d* effect we obtain

$$bc = 0.95(b + c)/2$$

Examination of the equations shows that if either "*b*" or "*c*" is larger than 0.95 then the other ("*c*" or "*b*") must be smaller and their average, $(b + c)/2$, cannot be much different from 0.95. Thus, *bc* can be approximated quite closely as $(0.95)^2$. This *bc* product gives 0.83 for "*d*," and 1.54 for "*a*," the primary isotope effect on elimination from the tight ion pair. The inverse secondary β-isotope effect in the elimination process, 0.83, is as expected similar to those found in the competing substitution. The *bc* product is somewhat larger than $(0.83)^2$ probably because "*b*" includes an

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[16] V. J. Shiner, Jr., B. L. Murr, and G. Heinemann, *J. Amer. Chem. Soc.*, **85**, 2413 (1963).

"α-effect" contribution from the breaking of the C–H_a bond.

Although the general trend has been noted before, this is the first example of a reaction that shifts cleanly from rate-determining attack on the tight ion pair to rate-determining formation of the solvent separated ion pair on changing from ethanol–water to TFE–W solvent. It is also the first example in which the stereochemistry of the elimination and substitution reactions from the tight and solvent separated ion pairs is observed for the same reactant. The correlation of these results with *α-d* and *β-d* effects on the rates and product ratios is very satisfying.

Experimental Section

Deuterated Cyclopentyl Brosylates. Cyclopentanol, cyclopentanol-*1-d*, *cis*-cyclopentanol-*2-d*, *trans*-cyclopentanol-*2-d*, and cyclopentanol-*2,2,5,5-d*$_4$ were prepared by previously published methods.[11,14] The deuterium contents were established by mass spectrometry and were better than 93% in all cases. The purity of alcohols was better than 98% in all cases according to glpc analysis (10% Ucon). The corresponding brosylates were prepared by the usual Tipson procedure.[12]

Kinetic Measurements. The titrimetric rates were obtained employing the automatic potentiometric titration method using the pH-Stat Radiometer, SBR-2/TTT11, Copenhagen, maintaining a constant pH of 6.8. The concentration of brosylate esters was about 0.0015 *M* (10 mg in 20 ml of solvent) in all kinetic experiments. The samples of esters titrated were taken at random in order to minimize the influence of the temperature variation, or any other variations, on the rate of solvolysis. The double jacketed titrimetric cell with solvent was allowed to stabilize 20 min at the corresponding temperature prior to addition of ester. At least eight measurements were conducted for each of the esters in the particular solvent and temperature. The rate constants were calculated from the standard integrated first-order law using a nonlinear least-squares program. No trend was observed in the rate constants between 20 and 80% of reaction completion.

The rate measurements needed to detect a possible common ion rate depression effect were performed as described above with added sodium brosylate in concentrations from 0.0025 to 0.03 *M*. Only one rate measurement for the corresponding salt concentration was taken.

The possibility of the special salt effect was tested by addition of lithium perchlorate (from 0.025 to 0.03 *M*) into the reaction mixture.

Product Study. In a typical experiment, cyclopentyl brosylate (64.4 mg) and 1 ml of 80 vol % E–W were sealed in an ampoule (2 ml) and heated at 40° for 2.7 hr (10 half-lives of the reaction). The ampoule was opened and a small quantity of sodium bicarbonate and magnesium sulfate was added in order to neutralize the acid and to remove most of the water from the solvent. After 1 hr the solution was injected into the gas chromatograph (Varian 1800) equipped with a digital integrator (Varian 480). The column was 10 ft long with 10% Ucon on Chromosorb P 45/60. The temperature was changing from 70 (3.3 min) to 110° (20° per min). Peak areas obtained were multiplied by the correction number calculated from the chromatogram of the mixture containing known quantities of pure samples of each product.

The product study of each compound in a particular solvent was conducted in two ampoules in an identical way. From each sample at least three injections into a gas chromatograph were performed giving a total of six injections for each of the compounds in a particular solvent.

The products were proven to be stable under the solvolytic conditions as well as on the glpc column. Samples of the separate pure products with an adequate quantity of *p*-bromobenzoic acid added were treated in the same way as samples in the product study. The gas chromatogram revealed in all cases only the compound tested.

Nmr Study. In a typical experiment, *cis*-cyclopentyl-*2-d* brosylate (3 g) was solvolyzed for 3.3 hr (10 half-lives) in 50 ml of 70 wt % TFE–W mixture at 30°. After 3.3 hr (10 half-lives) the resulting acid was neutralized ($NaHCO_3$) and dried ($MgSO_4$). Cyclopentanol-*2-d* was separated from the mixture by means of glpc (Autoprep A-700) at 170° using a 20-ft column with 20% Carbowax 20 M on Chromosorb P 60/80. By repeating the separation procedure twice, 200 mg of 99.8% pure product was obtained. Cyclopentanol-*2-d* (~6 mg) was added into the nmr tube containing 0.4 ml of CCl_4 and ~14 mg of tris(dipivalomethanato)praseodymium(III) complex. The spectra were recorded on a JEOL 100-MHz nmr spectrometer.

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Fluorine Magnetic Resonance Spectra of Some *p*-Fluorophenylcarbonium Ions. A Possible Solvation Entropy Effect[1]

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Abstract: The fluorine magnetic resonance spectra of a number of tertiary *p*-fluorophenylcarbonium ions have been determined. The chemical shifts fall into three main groups: acyclic at lowest field, monocyclic at intermediate field, and bicyclic at highest field. The total range is 8 ppm, representing about 6 kcal energy difference. A possible interpretation in terms of steric restriction of rotation by solvation is discussed.

In earlier papers we presented some evidence in support of the intuitively reasonable proposal that the para proton nuclear magnetic resonance chemical shift of phenylcarbonium ions (**1**) could serve as a measure of the π-electron demands of the carbonium ion center.[2] Although a linear correlation of the chemical shift values with the log of the calculated delocalization energies was observed over a range of carbonium ion stabilities, the chemical shift was too insensitive to energy differences to be useful (in the

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[1] This work was supported by the National Science Foundation under Grant GP 10734.

[2] D. G. Farnum, *J. Amer. Chem. Soc.*, **86**, 934 (1964); **89**, 2970 (1967).