6.61-6.51 (m, 1 H), 2.34 (s, 3 H), 2.31 (s, 3 H); ^{31}P (^1H) NMR δ -28.5. Anal. Calcd for $C_{24}H_{27}P$: C, 83.24; H, 7.80. Found: C, 83.16; H, 7.86.

Tris(2,5-dimethylphenyl)phosphine (7): stoichiometry ArMgBr (4.5 equiv), PCl_3 (1 equiv); yield 2.49 g (56%); white crytals; mp 148 °C (EtOH/C_6H_6); ^1H NMR δ 7.07 (br s, 2 H), 6.54 (d, ^3J(PH) = 4.1 Hz, 1 H), 2.32 (s, 3 H), 2.16 (s, 3 H); ^{31}P (^1H) NMR δ -29.9. Anal. Calcd for $C_{24}H_{27}P$: C, 83.24; H, 7.80. Found: C, 83.03; H, 7.80.

Tris(3,4-dimethylphenyl)phosphine (9): stoichiometry ArMgBr (4.7 equiv), PCl_3 (1 equiv); yield 0.82 g (22%); white needles; mp 89 °C (EtOH); ^1H NMR δ 7.32-6.90 (br m, 3 H), 2.25 (s, 3 H), 2.20 (s, 3 H); ^{31}P (^1H) NMR δ -8.4. Anal. Calcd for $C_{24}H_{27}P$: C, 83.24; H, 7.80. Found: C, 83.06; H, 7.62.

Tris(3,5-dimethylphenyl)phosphine (10): stoichiometry ArMgBr (4.5 equiv), PCl_3 (1 equiv); yield 1.96 g (52%); white needles; mp 162 °C (EtOH); ^1H NMR δ 6.97 (br s, 2 H), 6.90 (br s, 1 H), 2.26 (s, 6 H); ^{31}P (^1H) NMR δ -5.8. Anal. Calcd for $C_{24}H_{27}P$: C, 83.24; H, 7.80. Found: C, 83.18; H, 7.75.

Tris(2,4,5-trimethylphenyl)phosphine (12): stoichiometry ArMgBr (4 equiv), PCl_3 (1 equiv); yield 1.91 g (40%); white needles; mp 221 °C (EtOH/C_6H_6); ^1H NMR δ 6.97 (d, ^4J(PH) = 4.7 Hz, 1 H), 6.49 (d, ^3J(PH) = 4.4 Hz, 1 H), 2.28 (s, 3 H), 2.22 (s, 3 H), 2.06 (s, 3 H); ^{31}P (^1H) NMR δ -32.6. Anal. Calcd for $C_{27}H_{33}P$: C, 83.45; H, 8.56. Found: C, 83.54; H, 8.55.

Tris(2,6-dimethyl-4-methoxyphenyl)phosphine (22): stoichiometry ArMgBr (4 equiv), PCl_3 (1 equiv); yield 2.71 g (59%); white needles; mp 169 °C (EtOH); ^1H NMR δ 6.47 (d, ^4J(PH) = 2.6 Hz, 2 H), 3.75 (s, 3 H), 2.08 (s, 6 H); ^{31}P (^1H) NMR δ -39.5. Anal. Calcd for $C_{27}H_{33}O_3P$: C, 74.31; H, 7.57. Found: C, 74.22; H, 7.60.

Tris(2,3,4,5-tetramethylphenyl)phosphine (14): stoichiometry ArMgBr (5.3 equiv), PCl_3 (1 equiv); yield 2.45 g (61%); white crystals; mp 261 °C (EtOH/C_6H_6); ^1H NMR δ 6.39 (d, ^3J(PH) = 4.3 Hz, 1 H), 2.33 (s, 3 H), 2.21 (br s, 6 H), 2.08 (s, 3 H); ^{31}P (^1H) NMR δ -24.0. Anal. Calcd for $C_{30}H_{39}P$: C, 83.72; H, 9.07. Found: C, 83.49; H, 9.15.

Tris(2,4,6-tris(perdeuteriomethyl)phenyl)phosphine (11-d_{27}). A mixture of 225 mg (0.58 mmol) of tris(2,4,6-trimethylphenyl)phosphine (11), 140 mg of NaH (60% dispersion in mineral oil), and 8 g (95.0 mmol) of DMSO-d_6 (99.9%) was warmed at 130 °C for 48 h under argon. The reaction mixture was then carefully hydrolyzed with 30 mL of D_2O and extracted with benzene. The organic layer was dried over 4-Å molecular sieves and then evaporated to give a residual brown oil, which crystallized when triturated with methanol. The resulting solid was crystallized twice from absolute ethanol to yield 194 mg (80.6%) of a pale yellow powder. Sublimation (110-130 °C (10^{-2} mmHg)) yielded fine pale yellow needles: mp 182-187 °C; ^{31}P (^1H) NMR δ -37.05; ^1H NMR δ 6.72 (d, ^4J(PH) = 3.2 Hz, *m*-H), 2.22 (s, *o*-methyl), 2.07 (s, *p*-methyl). Assuming that no exchange has taken place with the meta hydrogens, a 95% exchange ratio was calculated from the ^1H NMR spectrum.

Acknowledgment. We are grateful to the Centre National de la Recherche Scientifique and the Centre d'Etudes Nucléaires de Grenoble (LETI) for support of this work.

Hydrogen Participation in the Solvolysis of 2-Methylcyclopentyl Arenesulfonates

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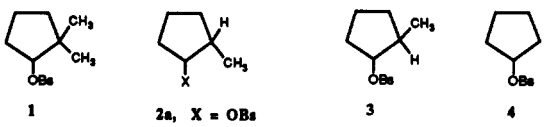
Received September 24, 1990

Solvolysis of *cis*- and *trans*-2-methylcyclopentyl arenesulfonates has been examined in several ethanol–water, trifluoroethanol–water, and hexafluoroisopropyl alcohol–water mixtures. Rates, α-d and β-d kinetic isotope effects, and product yields have been determined. The results indicate that *cis*-2-methylcyclopentyl *p*-toluenesulfonate reacts with rate-determining hydrogen participation after reversible formation of the intimate ion pair. In contrast, *trans*-2-methylcyclopentyl *p*-bromobenzenesulfonate reacts by varying proportions of rate-determining solvent nucleophilic attack, solvent-promoted elimination, and ion pair separation after reversible formation of the intimate ion pair. The details of these mechanisms are quantitatively described with the aid of a steady state analysis, and the results are correlated with the mechanisms previously proposed for cyclopentyl brosylate and 2,2-dimethylcyclopentyl brosylate.

Many years ago Winstein and Takahashi proposed that 3-methyl-2-butyl tosylate solvolyzed with hydrogen participation in aqueous ethanol, acetic acid, and formic acid.[1] Although 3-methyl-2-butyl tosylate showed only slight rate enhancement, the combination of predominantly rearranged products and large β-deuterium kinetic isotope effect convinced the authors that hydrogen migration occurred simultaneously with ionization. Since that time, the rearrangement of a tertiary hydrogen to a secondary carbon synchronous with ionization has been well documented in solvolytic reactions.[2,3] Unlike the acyclic systems, which show little rate enhancement, neomenthyl tosylate solvolyzes much faster than menthyl tosylate (170× in HOAc),[3d] and *cis*-4-*tert*-butyl-*cis*-2-methylcyclohexyl tosylate reacts faster than either of the 4-*tert*-butyl-*trans*-2-methylcyclohexyl tosylates.[3b] Clearly, in these cyclohexyl systems hydrogen participation is facilitated by the antiperiplanar relationship between the tertiary β hydrogen and the axial leaving group.



1 2a, X = OBs 2b, X = OTs 3 4

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0022-3263/91/1956-3542$02.50/0

Table I. First-Order Solvolysis Rates for *p*-Bromobenzenesulfonate Esters at 25 °C

	compounds and rate constants[a]				rate ratios		
solvent[b]	1	2a (cis)	3 (trans)	4	2a/3	2a/1	3/4
90E	0.750	19.6	1.78	7.9	11.0	26.1	0.23
80E	2.72	57.4	4.67	14.0	12.3	21.1	0.33
70E	7.07	127	9.86	27.8	12.9	18.0	0.35
70T	51.7	293[c]	25.6	32.7	11.6	5.7	0.78
97T	42.4	180[c]	16.2	10.5	11.1	4.2	1.54
90H	275		227[d]	27.5			

[a] *k*'s are in units of 10^{-5} s^{-1} measured spectrophotometrically (1) or conductometrically (2, 3). [b] 90E is 90 vol % ethanol–10 vol % water, etc.; 70T is 70% trifluoroethanol–30% water, etc.; 90H is 90% 1,1,1,3,3,3-hexafluoro-2-propanol–10% water. [c] Calculated from tosylate rate constant assuming OBs/OTs ratio = 3.0 in TFE. Verified from measurements of both tosylates and brosylates of 3 in 97T. [d] Rate constant in 98H.

Table II. Yields[a] of Products from the Solvolysis of *cis*-2-Methylcyclopentyl-*1-d* *p*-Toluenesulfonate at 25 °C

	products						%
solvent[b]	*trans*-5-*1-d*	6-*2-d*	7-*2-d*	7	7-*5-d*	8-*2-d*[c]	rearr
70E	8[d]	2	13	2	7	68	82
97T	0	2	6	12	32	47	98

[a] Expressed as a percentage of the total product mixture. [b] See footnote *b* in Table I. [c] Mixture of 8-*cis*-2-*d* and 8-*trans*-2-*d*. [d] 5% alcohol, 3% ether.

In an earlier study we reported an unusual example of methyl participation in the solvolysis of 2,2-dimethylcyclopentyl brosylate (1).[4] Unlike previous examples, methyl participation in 1 occurs after reversible formation of the intimate ion pair. We attributed the reluctance of the methyl group to migrate to the strain energy required in the cyclopentyl system for the methyl group to become aligned parallel with the vacant p orbital of the α carbon. In an analogous cyclopentyl system, *cis*-2-methylcyclopentyl tosylate was shown to solvolyze 10 times faster than *trans*-2-methylcyclopentyl tosylate,[5] but since the rate enhancement was small the authors discounted the importance of hydrogen participation in the cis isomer. Because of the structural similarities to 2,2-dimethylcyclopentyl 1, we undertook a study of *cis*-2-methylcyclopentyl 2, with a view toward the possibility of hydrogen participation *after* reversible intimate ion pair formation.[6] To this end, we now report rate data, product studies, and isotope effects for *cis*- and *trans*-2-methylcyclopentyl arenesulfonates measured in a range of solvents.

Results and Discussion

Table I lists the solvolysis rate constants for *cis*-2-methylcyclopentyl brosylate (2a) and *trans*-2-methylcyclopentyl brosylate (3) in solvents arranged in order of decreasing nucleophilicity and increasing ionizing power from 90% by volume aqueous ethanol (90E) to 90% aqueous 1,1,1,3,3,3-hexafluoro-2-propanol (90H). As expected, the cis isomer 2a was more reactive than the trans isomer 3 in all solvents. Surprisingly, the rate ratio is fairly constant (11.0–12.4) and shows no trend over this broad range of solvent nucleophilicities. The constancy of this ratio is probably due to the fortuitous operation of two parallel effects, which we will discuss later. For purposes of later comparisons, we included the rate constants for both 2,2-dimethylcyclopentyl brosylate (1) and cyclopentyl brosylate (4).

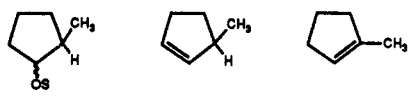
Table III. Yields[a] of Products from the Solvolysis of *trans*-2-Methylcyclopentyl-*1-d* *p*-Bromobenzenesulfonate at 25 °C

	products						%
solvent[b]	*cis*-5-*1-d*	6-*2-d*	7-*2-d*	7	7-*5-d*	8-*2-d*[c]	rearr
70E	42[d]	7	16	2	3	31	37
70T	14[e]	5	28	3	7	42	57
97T	2[f]	5	34	3	13	43	66
98H	0	8	41	5	26	21	64

[a–c] See Table II. [d] 31% alcohol, 11% ether. [e] 12% alcohol, 2% ether. [f] 1% alcohol, 1% ether.

Tables II and III report the product yields from solvolyses in various solvents of *cis*-2-methylcyclopentyl-*1-d* tosylate and *trans*-2-methylcyclopentyl-*1-d* brosylate, respectively. The reactions were carried out at 25 °C in 0.1 M solutions buffered with 2,6-lutidine in sealed NMR tubes and allowed to proceed for more than 10 half-lives, after which the product yields were determined from ^2H NMR spectra. The product yields from the α deuterium labeled compounds should closely resemble those from the nondeuterated compounds since the α-d isotope effects are expected to perturb only slightly the product distributions. Deuterium labeling offered us the advantage of distinguishing between 1-methylcyclopentene derived from the unrearranged secondary cation from that which came from the rearranged tertiary ion. Also, from the deuterium chemical shifts, we were able to assign the stereochemistry of the various formed substitution products.

From Table II, cis tosylate 2-*1-d* gives primarily rearranged products in both solvents studied, and the unrearranged substitution products have inverted configuration. Only *trans*-2-methylcyclopentanol-*1-d* and the ethyl ether (*trans*-5-*1-d*), and 3-methylcyclopentene-*2-d* (6-*2-d*) can occur exclusively from the unrearranged ion. On the other hand, 1-methylcyclopentene-*2-d* (7-*2-d*) can be derived from either the unrearranged secondary or the rearranged tertiary ion resulting from hydrogen migration. The remaining products, 1-methylcyclopentene (7), 1-



5 6 7

methylcyclopentene-*5-d* (7-*5-d*), *cis*-1-methylcyclopentanol-*2-d* (8-*cis*-2-*d*), *trans*-1-methylcyclopentanol-*2-d* (8-*trans*-2-*d*), and the corresponding ethers can only come from the rearranged tertiary cation. Based on conclusions from a steady state analysis (vide infra) of the proportion of 7-*2-d* that is derived from the rearranged ion, we estimate that 82% of the product mixture in 70E and 98% in 97T comes from rearrangement.

Table III shows that *trans*-2-methylcyclopentyl-*1-d* brosylate (3-*1-d*) yields significantly more unrearranged substitution (*cis*-5-*1-d*) and elimination (6-*2-d*) products than cis isomer 2-*1-d* and that unrearranged substitution occurs exclusively with inversion of configuration. As in the case of the cis compound, 1-methylcyclopentene-*2-d* (7-*2-d*) may be formed from either the rearranged tertiary or unrearranged ions. Note, however, that trans isomer 3-*1-d* gives much larger yields of 7-*2-d* than 2-*1-d* under the same conditions. The remaining products can only

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(6) A similar study has been reported for 2-phenylcyclopentyl tosylates.[7] The analysis, however, is complicated by phenyl migration in the trans isomer.

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Table IV. Yields[a] of Products from the Solvolysis of *cis*-2-Methylcyclopentyl-*2-d* *p*-Toluenesulfonate at 25 °C

	products					
solvent[b]	*trans*-5-2-*d*	6-3-*d*	7	7-2-*d*	7-5-*d*	8-2-*d*[c]
70E		1	13	4	10	71[d]
97T	0	3	2	21	29	45

[a-c] See Table II. [d] Includes any 5-2-*d* produced, ^{2}H NMR lines not separated.

Table V. Yields[a] of Products from the Solvolysis of *trans*-2-Methylcyclopentyl-*2-d* *p*-Bromobenzenesulfonate at 25 °C

	products					
solvent[b]	*cis*-5-2-*d*	6-3-*d*	7	7-2-*d*	7-5-*d*	8-2-*d*[c]
70E		9	9	1	3	77[d]
70T		8	17	1	10	64[d]
97T		8	22	2	20	48[d]
98H	0	12	17	8	40	25

[a-c] See Table II. [d] Includes any 5-2-*d* produced, ^{2}H NMR lines not separated.

arise from the rearranged tertiary ion. Using the yields of 7 and 7-5-*d* to estimate the proportion of 7-2-*d* that originates from the tertiary ion, we conclude that in 70E 37% of the product comes from rearrangement and that the proportion increases to 66% in 97T.

Tables IV and V report the product studies from the solvolysis of *cis*- and *trans*-2-methylcyclopentyl-2-*d* arenesulfonates, respectively. Because the deuterium label was β in both the unrearranged and rearranged substitution products, the ^{2}H NMR absorptions overlapped and in this study we were unable to determine confidently the relative amounts of those two products. Nevertheless, the alkene products, 6-3-*d* (unrearranged), 7-2-*d* and 7-5-*d* (rearranged), and 7 (both rearranged and unrearranged) could be determined easily from their unique chemical shifts. It is significant that the cis-β-deuterated isomer (Table IV) shows only a small loss of deuterium in the form of 1-methylcyclopentene (7) (13% in 70E and 2% in 97T). The trans-β-deuterated isomer (Table V), on the other hand, gives somewhat larger amounts of 7 ranging from 9% in 70E to 22% in 97T.

In summary, both *cis*- and *trans*-2-methylcyclopentyl compounds undergo substitution with inversion of configuration, and the cis isomer **2b** gives mostly rearranged products while the trans compound **3** yields nearly equal amounts of rearranged and unrearranged products. The studies from the β-deuterated compounds (Tables IV and V) show that only a minor amount of 1-methylcyclopentene results from direct elimination of the tertiary β hydrogen.

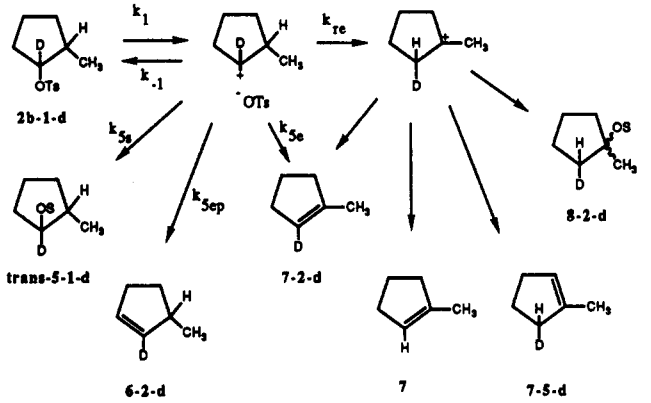
Table VI summarizes the secondary kinetic isotope effects in the various solvents used. For both the cis and trans isomers, the α-d effect is greater than 20%, indicating that in all solvents *reversible* ionization precedes the rate-determining step.[8] For *cis*-2-methylcyclopentyl tosylate (**2b**) the β-d effect is large (1.904–2.304), indicating along with the product studies that hydride shift (rearrangement) of the tertiary hydrogen occurs in the rate-determining step.[9] In contrast, the β-d effect for the trans

Table VI. Secondary Deuterium Isotope Rate Effects[a] in Solvolysis of *cis*- and *trans*-2-Methylcyclopentyl Arenesulfonates at 25 °C

isomer and label[b]		solvent[c]			
		70E	70T	97T	98H
2b[d]	α-d	1.239		1.233	
	β-d	1.904		2.034	
	β'-d_2[e]	1.255		1.234	
	β,β'-d_3	2.389		2.513	
	γ-d_3	1.000	0.986	0.975	
3[f]	α-d	1.200	1.215	1.224	
	β-d	1.330	1.464	1.515	1.470
	β'-d_2[e]	1.462	1.486	1.500	
	β,β'-d_3	1.974	2.176	2.273	
	γ-d_3	0.963	0.969	0.975	

[a] The reproducibilities of the isotope effects are 0.005 and less. [b] α is at C1, β is at C2, β' at C5, and γ is on the methyl group. [c] See footnote *b*, Table II. [d] Rate constants (in units of 10^{-5} s^{-1}) for **2b** are 22.21 ± 0.04 in 70E; 97.79 ± 0.06 in 70T; and 59.17 ± 0.11 in 97T. [e] Calculated from β,β'-d_3/β-d. [f] The rate constants (in units of 10^{-5} s^{-1}) for **3** are 9.863 ± 0.006 in 70E; 25.62 ± 0.01 in 70T; and 16.16 ± 0.01 for 97T.

Scheme I



isomer **3** is never higher than 1.5, even in the most nonnucleophilic solvents. This suggests that in spite of 93% of the product mixture in 97T coming from direct elimination and rearrangement, only a small proportion occurs by rate-determining loss or migration of the β hydrogen.

Scheme I describes the mechanism for solvolysis of *cis*-2-methylcyclopentyl-*1-d* tosylate (2-*1-d*). After reversible formation of the intimate ion pair, most of the reaction proceeds by *rate-determining* hydrogen migration (82% in 70E and 98% in 97T) to convert the secondary cation into the more stable tertiary ion. In 70E, 8% substitution at the intimate ion pair competes with rearrangement to slightly depress the β-d effect (1.904). Comparing the results for **2b** with 2,2-dimethylcyclopentyl brosylate (**1**), the α-d effect for **2b** (1.23) is larger than the value of 1.20 observed for **1**, where methyl migration at the intimate ion pair is rate-determining.[4] This suggests that in the transition state for hydrogen migration there is less bonding to the cationic center than there is for methyl migration. In fact, it generally appears that in the transition state for hydrogen migration the stiffness of the α hydrogen is unaffected by any partial bond between the β hydrogen and the α carbon. In the case of neomenthyl tosylate where hydrogen participation is synchronous with ionization, the α-d effect is 1.15 and 1.17 in 70T and 97T, respectively.[3d] These are the same α-d values that one would expect from unassisted ionization.[10] Therefore, it is not surprising that in a case where hydrogen partici-

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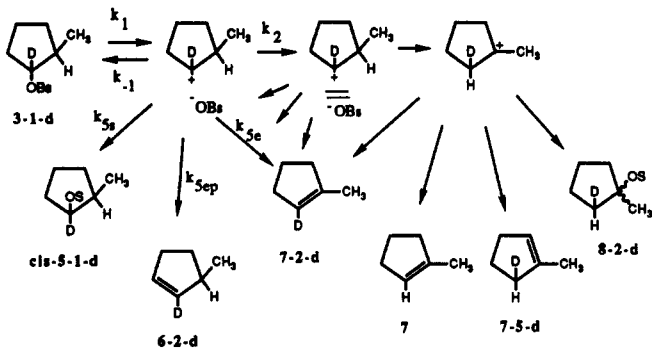
Scheme II



pation occurs after reversible formation of the intimate ion pair that we observe a maximum α-d effect.[8c] Thus, from the α-d effects it appears that resonance structure **9** is more important in describing hydrogen rearrangement[8b,11] in contrast to structure **10**, which is relatively more important for methyl migration.[12] The γ-d_3 effects from *cis*-2-(methyl-d_3)cyclopentyl tosylate, which are mostly inverse, again support the view that although hydrogen migration is rate-determining there is little charge development on the β carbon.

The β'-d_2 effects[13] for *cis*-2-methylcyclopentyl tosylate (**2b**) of 1.26 (70E) and 1.23 (97T) are very similar to the β-d_2 effects for the dimethyl compound **1**, which range from 1.25 (70E) to 1.30 (90H).[4] These values suggest that in both compounds some orbital vacancy is lost at the α carbon of the intimate ion pair. For cis compound **2b**, resonance structure **9** as a transition state accounts for a maximum α-d effect and a β'-d_2 effect lowered from a maximum value of 1.48.[4] In the case of dimethyl compound **1**, partial bond formation of the migrating methyl group in transition state **10** predicts a slightly lowered α-d effect and a lowered β-d_2 effect.

Both 2,2-dimethyl **1** and *cis*-2-methylcyclopentyl **2** react by mechanisms in which participation for conformational reasons does not occur simultaneously with ionization, but instead after reversible formation of the intimate ion pair. In both cases small proportions of the other reactions (2–10%) of the intimate ion pair compete with slowed rearrangement as the rate-determining step. The secondary to tertiary cationic rearrangements of both hydrogen and methyl in cyclopentyl systems are estimated to be an additional 1.5 kcal/mol higher in activation energy than those in acyclic systems.[14] This is attributed to the unfavorable orbital orientations in the ion.[15]

As expected,[16] the relative rates (Table I) of solvolysis of *cis*-2-methylcyclopentyl brosylate (**2a**) to 2,2-dimethylcyclopentyl brosylate (**1**) show that hydrogen migration occurs faster than methyl migration. In ethanolic solvents the cis compound **2a** ranges from 18 to 26 times faster than dimethyl compound **1**, whereas in TFE solvents the rate ratio drops to 5.7 (70T) and 4.2 (97T). Apparently, hydrogen rearrangement with a transition-state structure similar to **9** is assisted by hydrogen bonding to the more basic solvent, ethanol, while methyl migration as in **10** is not.[17]

Scheme II describes the mechanism for solvolysis of *trans*-2-methylcyclopentyl-*1-d* brosylate (**3-1-d**). After reversible formation of the intimate ion pair, rate-determining substitution and elimination of either the secondary or tertiary β hydrogens compete with rate-determining dissociation to the solvent-separated ion pair. The partitioning of the intimate ion pair depends upon the solvent; for example, in 70E more than 40% of the reaction goes by substitution on the intimate ion pair, whereas in less nucleophilic solvents a higher proportion reacts via the solvent-separated ion pair, up to 70% in 97T. In all cases, however, the secondary-to-tertiary rearrangement occurs *after* the rate-determining step.

The α-d effects, which range from 1.200 in 70E to 1.224 in 97T (Table VI), reflect the decreasing amounts of rate-determining substitution (Table III) at the intimate ion pair. The remaining pathways from the intimate ion pair, elimination and leaving group dissociation, do not affect the hybridization at the α carbon and thus do not depress the α-d effect. The *observed* β-d effect from *trans*-2-methylcyclopentyl-*2-d* brosylate, which ranges from 1.330 in 70E to 1.515 in 97T, is a composite of the isotope effects for the various competing rate-determining pathways. The β-d effect of 1.48 for reversible formation of an intimate ion pair[4] is lowered by substitution (k_{5s}) and elimination of hydrogens from the β' position (k_{5ep}), which serve to reduce the orbital vacancy at the α carbon. On the other hand, elimination of the tertiary β hydrogen (k_{5e}), a primary isotope effect, increases the observed β-d effect. Formation of the solvent-separated ion pair (k_2) does not affect the β-d effect. The trend of increasing observed β-d effects in Table VI correlates primarily with a decrease in the amount of substitution (k_{5s}) at the intimate ion pair. Since the observed β-d effect is in a range consistent with a secondary isotope effect, it is apparent that only small amounts of elimination (k_{5e}) and no rearrangement, both of which would contribute primary isotope effects, are occurring at the intimate ion pair.

The unusually high β-d effect for a nonparticipating hydrogen[9b] is due to the favorable conformation of the tertiary β hydrogen to the vacant p orbital and reflects the maximum hyperconjugative effect for a β hydrogen.[19] Usually such orientation results in hydrogen migration, but in this case the leaving group at the intimate ion pair hinders rearrangement. Only after dissociation to the solvent-separated ion pair does hydride shift occur.

Surprising to us, however, is that we do not observe more rate-determining syn elimination from the intimate ion pair in 97T. This is the dominant pathway for cyclopentyl

(11) Shiner, V. J., Jr.; Buddenbaum, W. E.; Murr, B. L.; Lamaty, G. *J. Am. Chem. Soc.* **1968**, *90*, 418–426.
(12) Shiner, V. J., Jr.; Fisher, R. D. *J. Am. Chem. Soc.* **1971**, *93*, 2553–2554.
(13) The β'-d_2 effects are the calculated isotope effects for *cis*-2-methylcyclopentyl-*5,5-d*$_2$ tosylate, which were determined from the observed isotope effects for *cis*-2-methylcyclopentyl-*2,5,5-d*$_3$ and *cis*-2-methylcyclopentyl-*2-d* tosylates, β-d_3/β-d_1.
(14) Brouwer, D. M.; Hogeveen, H. In *Progress in Physical Organic Chemistry*; Streitwieser, A., Jr., Taft, R. W., Eds.; Wiley; New York, 1972; Vol. 9, pp 211–218.
(15) (a) Brouwer, D. M.; Hogeveen, H. *Recl. Trav. Chim. Pays-Bas* **1970**, *89*, 211–224. (b) Schleyer, P. v. R. *Angew Chem.* **1969**, *81*, 539–540.
(16) Hogeveen, H.; Gaasbeek, C. J. *Recl. Trav. Chim.* **1969**, *88*, 1305–1312.
(17) It is estimated that hydrogen migration is 2.5 kcal/mol lower in activation energy than methyl migration in secondary to tertiary cationic rearrangements.[16] Assuming at 25 °C the relative rate of migration, k^H/k^{Me} = 70, we estimate that in 97T the relative rate of ionization of 2,2-dimethyl **1** to *cis*-2-methyl **2**, $k_1^1/k_1^2 \leq 16$ (assuming that the relative rate of internal return, $k_{-1}^1/k_{-1}^2 \leq 1$ due to some steric hindrance in **1** to internal return). The relative rate of ionization is in the range expected from the inductive/hyperconjugative effect of the additional β methyl group in **1**.[18]
(18) Bentley, T. W. *Ann. Rep. Prog. Chem., Sect. B* **1974**, *71*, 120.
(19) Richter, S.; Bregovec, I.; Sunko, D. E. *J. Org. Chem.* **1976**, *41*, 785–790.

brosylate in 97T,[8c] and we expected the syn tertiary hydrogen in 3 to eliminate readily to give 1-methylcyclopentene. However, neither the products nor the β-d effect support that mechanistic path.

Additional support for Scheme II comes from the β′-d_2 effects and the γ-d_3 effects of *trans*-2-(methyl-d_3)cyclopentyl brosylate. The β′-d_2 values, which range from 1.462 (70E) to 1.500 (97T), are consistent with solvent separation as a dominant rate-determining step.[4] The values of 0.963 to 0.971 for γ-d_3 indicate that there is no orbital vacancy development on the β carbon and only the inductive effect of the C–H(D) bonds of the methyl group is operative in stabilizing the 2-methylcyclopentyl cation.[9,20]

The relative rates for *cis*- and *trans*-2-methylcyclopentyl brosylates in several solvents can be interpreted nicely by using the proposed mechanisms. Both cis and trans isomers undergo reversible ionization, but the cis compound follows with facile rate-determining 1,2-hydride shift, whereas the intimate ion pair from the trans isomer more slowly undergoes a combination of rate-determining capture by solvent (k_{5s}), elimination to form alkene (k_{5e} and k_{5ep}), and formation of solvent-separated ion pair (k_2). Once the solvent-separated ion pair has been formed, about 80 to 95% of it rearranges to the tertiary ion. The intimate ion pair from the trans isomer reacts slowly because the trans methyl group hinders attack by solvent, and the syn tertiary hydrogen is not readily eliminated and is sterically hindered by the leaving group from rearranging. We believe that the constant cis/trans rate ratio (11.0–12.4) over the solvents studied results from a coincidental parallel operation of two effects. In ethanolic solvents, hydride shift in the cis compound is assisted by hydrogen bonding at the intimate ion pair stage, while in these same solvents, nucleophilic attack on the intimate ion pair (k_{5s}) of the trans isomer is also accelerated. On the other hand, in TFE solvents neither hydride transfer nor nucleophilic attack is enhanced and the rate ratio remains about the same.

The chemistry of *trans*-2-methylcyclopentyl brosylate (3) resembles cyclopentyl brosylate (4) with some significant differences due to the β methyl group. Although the rate of ionization (k_1) of 3 is probably faster than that of 4,[18] the observed relative rate, $k(3)/k(4)$, in 70E is 0.355. The slower rate of 3 reflects the steric inhibition by the β methyl group to nucleophilic attack on the intimate ion pair (k_{5s}). Consequently, 3 yields only 42% unrearranged substitution product, whereas cyclopentyl 4 gives 78% substitution in 70E[8b,21] mostly via k_{5s}. The relative rates in nonnucleophilic 97T (1.54) and 97H (2.12),[22] on the other hand, reflect the greater stability of the 2-methylcyclopentyl cation and the unimportance of the k_{5s} path in the fluorinated alcohols.

Although there has been some success in correlating solvolysis rates in HFIP of β-methyl-substituted cyclopentyl tosylates with calculated changes in strain energy,[22] we feel that the analysis does not adequately explain the difference in rates of the particular compounds described in this work. From isotope effects and product studies it is clear that *cis*-2-methylcyclopentyl and *trans*-2-methylcyclopentyl arenesulfonates react by different mechanisms with different rate-determining steps. Thus, satisfactory predictions based *only* on linear free energy relationships (LFER)[23] may be fortuitous. For example, different transition states with similar charge distributions may be affected similarly by changes in solvent ionizing power.

For reactions occurring by mechanisms involving a single pathway, the experimentally observed kinetic isotope effects along with product studies can be used to test quantitative predictions about the reaction and offer insight about the structure of the transition state of the rate-determining step. However, in branched mechanisms such as Schemes I and II, the observed isotope effects are a combination of the isotope effects for the preequilibrium steps and for the competing rate-determining steps. Analyses of such complex mechanisms based on product studies and observed isotope effects are at best "semiquantitative" and are not easily tested. However, application of our data to a steady state analysis allowed us, first, to describe the mechanism quantitatively and, second, to see if our mechanism was consistent with the constraints of accepted single-step isotope effects used in the analysis.

A steady state analysis using the Simplex method of optimization has been successfully used to correlate overall experimental kinetic isotope effects and solvent-independent single-step isotope effects with product yields.[8c,24] For a branching mechanism the technique works by adjusting partition factors among the competing pathways using single-step isotope effects until the errors between the experimental observations (product yields and experimental isotope effects) and the corresponding calculated quantities have been minimized. In our study, a rigorous application of this procedure to the proposed mechanisms described in Schemes I and II is partially compromised because 1-methylcyclopentene is derived from more than one pathway. Consequently, the observed yield of that product cannot be assigned to a single specific path and used to check the fit of the calculation with the experimental observation. More specifically, in Scheme I 1-methylcyclopentene-2-*d* (7-2-*d*) can be formed either by rate-determining elimination (k_{5e}) from the intimate ion pair or from elimination from the tertiary ion *after* rate-determining rearrangement. Thus, the calculated partition factor (f_{5e}) for elimination from the intimate ion pair is not expected to equal the yield of 7-2-*d*. However, based upon observed yields of 1-methylcyclopentene (7) and 1-methylcyclopentene-5-*d* (7-5-*d*), which come only from the rearranged tertiary ion, one can estimate the fractions of 7-2-*d* that are derived from the tertiary ion and from the unrearranged intimate ion pair.

In the case of *cis*-2-methylcyclopentyl tosylate (Scheme I), the partition factors (Table VII) indicate that the intimate ion pair has a much greater preference for rearrangement than elimination. In 70E, 82% of the intimate ion pair undergoes rearrangement and only 11% eliminates to form 1-methylcyclopentene, the remainder of which comes by elimination from the rearranged tertiary ion. In 97T, 98% of the intimate ion pair rearranges. The analysis requires that the single-step isotope effect for elimination of the tertiary hydrogen from the intimate ion pair equals 1.99 and the single-step isotope effect for rearrangement of that hydrogen be 1.67 to accommodate the fit to the overall experimental isotope effects and product yields.

The mechanism for solvolysis of *trans*-2-methylcyclopentyl brosylate (Scheme II) involves three separate in-

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(21) Steady state analysis of the product mixture and isotope effects for cyclopentyl brosylate suggests that in 70E only 57% of the total product mixture comes via k_{5s} path.[8c]

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Table VII. Reaction Parameter Values Which Give the Best Fit

solvent	f_{5s}	f_{5e}	f_{5ep}	f_{re}
Partitioning Factors[a]				
cis-2-Methylcyclopentyl *p*-Toluenesulfonate Ester				
70E	0.05	0.11	0.02	0.82
97T	0.01	0.00	0.01	0.98
trans-2-Methylcyclopentyl *p*-Bromobenzenesulfonate Ester				
				f_2
70E	0.40	0.11	0.08	0.41
70T	0.11	0.16	0.05	0.68
97T	0.02	0.23	0.05	0.70
98H	0.00	0.23	0.08	0.69

	α-d	β-d	β'-d_2
Single-Step Isotope Effects[b]			
cis-2-Methylcyclopentyl *p*-Toluenesulfonate Ester			
r_1	1.150	1.230	1.230
r_{-1}, r_{5s}	0.916	0.846	0.846
r_{5e}	0.996	1.990	0.905
r_{5ep}	1.000	0.690	1.637
r_2	1.000	1.000	1.000
r_{re}	1.000	1.674	0.820
trans-2-Methylcyclopentyl *p*-Bromobenzenesulfonate Ester			
r_1	1.145	1.202	1.280
r_{-1}, r_{5s}	0.916	0.846	0.846
r_{5e}	0.996	2.151	0.905
r_{5ep}	0.996	0.693	1.637
r_2	1.00	1.00	1.00

[a] f refers to the "fraction" in one branch relative to the total forward reaction; subscripts refer to the reaction step. For example in *trans*-2-methylcyclopentyl brosylate, $f_{5s} = k_{5s}/(k_{5s} + k_{5e} + k_{5ep} + k_2)$. [b] r refers to single-step isotope effects and is solvent independent. The single-step isotope effects are defined relative to the effect on k_2. For example, $r_{5e} = (k^H_{5e}/k^D_{5e})(k^D_2/k^H_2)$.

Table VIII. Reaction Results[a]

	trans-2-methylcyclopentyl				*cis*-2-methylcyclopentyl	
solvent	70E	70T	97T	98H	70E	97T
$k_H/k_{\alpha d}$						
obsd	1.200	1.215	1.224	1.230	1.239	1.233
calcd	1.203	1.227	1.228	1.222	1.213	1.222
R	−0.003	−0.012	−0.004	0.008	0.026	0.011
$k_H/k_{\beta d}$						
obsd	1.350	1.464	1.515	1.470	1.904	2.034
calcd	1.357	1.461	1.515	1.472	1.905	2.035
R	−0.007	0.003	0.000	−0.002	−0.001	−0.001
$k_H/k_{\beta d3}$						
obsd	1.974	2.176	2.273		2.389	2.510
calcd	1.956	2.174	2.270	2.219	2.389	2.503
R	0.018	0.002	0.003		0.000	0.007
F^{α}_{5s}						
obsd	0.420	0.140	0.020	0.000	0.080	0.000
calcd	0.422	0.115	0.017	0.000	0.054	0.013
R	−0.002	0.025	0.003	0.000	0.026	−0.013
F^{α}_{5ep}						
obsd	0.070	0.050	0.050	0.080	0.020	0.020
calcd	0.073	0.048	0.049	0.077	0.022	0.006
R	−0.003	0.002	0.001	0.003	−0.002	0.014
F^{α}_{5e}						
obsd[b]	0.119	0.145	0.230	0.247	0.100	0.000
calcd	0.113	0.163	0.239	0.237	0.107	0.000
R	0.006	−0.018	−0.009	0.010	−0.007	0.000
F^{β}_{5ep}						
obsd	0.090	0.080	0.080	0.120	0.030	0.030
calcd	0.104	0.073	0.079	0.122	0.051	0.014
R	−0.014	0.007	0.001	−0.002	−0.021	0.016
F^{β}_{5e}						
obsd[b]	0.060	0.085	0.145	0.111	0.080	0.000
calcd	0.052	0.080	0.124	0.121	0.085	0.000
R	0.008	0.005	0.021	−0.010	−0.005	0.000

[a] Comparison of values calculated with the parameters from Table VII with observed product yields and kinetic isotope effects. F refers to product yields as the fraction of the total product. For example, F^{α}_{5s} refers to the fraction of product via k_{5s} for the α-d reactant. [b] The observed product yield by this pathway is estimated by subtracting from the total product yield that which was estimated to be formed from the rearranged tertiary ion.

termediates, all of which may yield products. Because the substitution product from the unrearranged ion was inverted, we made the initial simplifying assumption that products from the unrearranged ion came exclusively from the intimate ion pair and *not* from the solvent-separated ion pair. Thus, as in the case with the cis isomer **2-*1-d***, yields of *cis*-**5-*2-d*** and **6-*2-d*** could be used to test the fit of the optimization program, while the yield of **7-*2-d*** from the intimate ion pair had to be estimated. Later, we found it necessary to modify our initial assumption in order to significantly improve the fit. We partitioned the amount of **7-*2-d*** that comes from the *unrearranged* ions, 85% from the intimate ion pair and 15% from the solvent-separated ion pair. Thus, for this complex mechanism where it was not possible to obtain rate–product correlations, the steady state analysis offered additional insight by requiring adjustments in the mechanism in order to achieve optimization.

From the results of Table VIII, the program gave an excellent fit (<1%) for all experimental isotope effects, and the partition factors from Table VII offer several quantitative insights. In 70E, only 41% of the intimate ion pair reacts by rate-determining solvent separation (f_2), with the remainder undergoing substitution or elimination. In the less nucleophilic solvents (70T, 97T, and 98H), the major pathway for the intimate ion pair is rate-determining solvent separation (68–70%). Subsequently, the solvent-separated ion pair undergoes 85 to 95% rearrangement, which supports the idea that the leaving group in the intimate ion pair of **3** hinders rearrangement. Interestingly, the percentage rearrangement of the solvent-separated ion pair from **3** is approximately the same as that from the intimate ion pair from cis isomer **2b**. The amount of rate-determining syn elimination of the tertiary hydrogen (f_{5e}) from the intimate ion pair of **3** increases only slightly from 11% in 70E to 23% in 97T and 98H. Based on results from cyclopentyl brosylate,[8b,c] we had expected more leaving group promoted syn elimination in the fluorinated alcohols.

The corresponding single-step isotope effects (Table VII) for the α-d compounds are the same for **2b** and **3** and equal those reported for cyclopentyl brosylate.[8c] The isotope effects for the β-d compounds are conformation dependent, and, therefore, it is not surprising that the single-step isotope effects, which gave the best fit, show some slight variation between the cis and trans isomers. For example, r_1 for β-d compounds is 1.230 for the cis isomer and 1.202 for the trans compound, suggesting that conformationally there is slightly better overlap between the developing p orbital and adjacent tertiary C–H(D) bond in **2b**. Significantly, for both **2b** and **3** the r_1 values for the β'-d_2 compound closely approximate those for the β-d compound, indicating that either only one of the β' hydrogens can hyperconjugatively stabilize the cation or that both β' hydrogens, due to less than optimal dihedral angles, stabilize the cation to a lesser extent, giving a cumulative effect equal to the β-d value. The single-step isotope effect for rearrangement (r_{re}) in **2b** is 1.674, which is small for a primary isotope effect. Consistent with our observations (vide supra), this isotope effect suggests an unsymmetrical transition state and most likely one in which there is little C–H bond breaking.

In summary, the steady state analysis applied to Schemes I and II reinforces the distinctive differences of these two mechanisms, and, using accepted single-step

isotope effects, the analysis supports mechanisms in which the rate-determining steps occur after reversible formation of the intimate ion pair. Additionally, in cases where rate–product correlations cannot be used to account for all product yields, the steady state treatment may be used to test mechanistic assumptions to obtain a quantitative description of the reaction.

Experimental Section

Boiling points and melting points are uncorrected. NMR spectra were recorded on Varian Assoicates EM-360, T60, and HR220 and Nicolet 360 spectrometers, and in all cases spectra agreed with structural assignments. Chemical shifts are recorded in parts per million (ppm = δ) from tetramethylsilane (TMS) for ^{1}H NMR spectra. Mass spectral data were obtained on a Hewlett-Packard 5995 GC/MS instrument. High-performance liquid chromatography (HPLC) separations were performed on a Rainin HP Rabbit instrument equipped with a silica packed, stainless steel column. Brosylates and tosylates were purified by HPLC on a preparative silica column, eluting with hexane–ethyl acetate mixtures.

***trans*-2-Methylcyclopentyl *p*-Bromobenzenesulfonate (3).** Following the procedure of Tipson,[25] to a solution of 1.03 g (0.0103 mol) of *trans*-2-methylcyclopentanol (Aldrich) in 10 mL of dry pyridine at 0 °C was added 2.84 g (0.0111 mol) of *p*-bromobenzenesufonyl chloride. The solution was stirred for 40 min and stored at 0 °C for 2 days. The solution was poured into a mixture of ether and ice water, extracted with 2 N H_2SO_4 and saturated $NaHCO_3$, and dried over anhydrous $MgSO_4$. The solvent was removed and the brosylate crystallized from pentane at −78 °C, but melted on warming to room temperature (79% yield). The brosylate oil was purified by preparative HPLC, eluting with 2% ethyl acetate–98% hexane on silica gel. NMR ($CDCl_3$): δ 0.95 (d, 3 H), 1.74 (m, 7 H), 4.45 (m, 1 H), 7.70 (s, 4 H).

All brosylates and tosylates were prepared by using the above procedure and were either recrystallized or chromatographed by preparative HPLC before kinetics.

***trans*-2-Methylcyclopentanol-*1-d*.** A mixture of 76% *trans*-2-methylcyclopentanol-*1-d* and 24% *cis*-2-methylcyclopentanol-*1-d* was prepared by the reduction of 12.0 g (0.123 mol) of 2-methylcyclopentanone (Aldrich) with 2.86 g (0.068 mol) of $LiAlD_4$ in ethyl ether at 0 °C. The mixture of alcohols was converted to the corresponding 3,5-dinitrobenzoates, which were separated by five successive fractional crystallizations from methanol,[26] yielding 6.3 g of *trans*-2-methylcyclopentyl-*1-d* 3,5-dinitrobenzoate, mp 85–87.5 °C. The dinitrobenzoate was converted back to the alcohol by refluxing in 35 mL of 2.5 M NaOH for $2^1/_2$ h. The product was isolated by steam distillation and then by saturating the distillate with anhydrous K_2CO_3 to induce separation of the alcohol from water. Distillation of the final product yielded 1.2 g of 96% pure *trans*-2-methylcyclopentanol-*1-d* with 4% contamination by the cis isomer as determined by GC/MS. Small contamination by the cis isomer, as the brosylate, was removed by HPLC, eluting with 2% ethyl acetate–98% hexane.

***trans*-2-Methylcyclopentanol-*2-d*.** To a mixture of 5.0 g (61 mmol) of 1-methylcyclopentene and 0.89 g (21 mmol) of $NaBD_4$ in 30 mL of anhydrous THF at 5 °C was added a solution of 3.6 g (25 mmol) of boron trifluoride etherate in 5 mL of THF.[27] After 4 h of stirring, the reaction was worked up with 7 mL of 3 M NaOH, followed by 7 mL of 30% H_2O_2. The reaction mixture was saturated with K_2CO_3, and the THF phase was dried and distilled at 75 °C (51 mm), yielding 3.9 g of alcohol.

***cis*-2-Methylcyclopentyl *p*-Toluenesulfonate (2b).** Following the procedure of Krishnamurthy and Brown,[28] 6.4 g of distilled *cis*-2-methylcyclopentanol (bp 134–136 °C) was prepared from 9.6 g of 2-methylcyclopentanone (Aldrich), using L-Selectride (Aldrich). Using the Tipson procedure, the tosylate (mp 24–26 °C) was prepared in 72% yield. NMR ($CDCl_3$): δ 0.93 (d, 3 H), 1.72 (m, 7 H), 2.38 (s, 3 H), 4.77 (m, 1 H), 7.30 (d, 2 H), 7.75 (d, 2 H).

***cis*-2-Methylcyclopentanol-*1-d*.** A solution of $LiAl(OMe)_3D$ was prepared by adding 7.23 g (226 mmol) of MeOH in 15 mL of THF to a slurry of 3.16 g (75.2 mmol) of $LiAlD_4$ in 30 mL of THF at 0 °C. To this mixture at room temperature was added 75 mL of 1 M (*s*-Bu)$_3$B.[29] After 45 min of stirring, the mixture was cooled to −78 °C and 5.14 g (52.4 mmol) of 2-methylcyclopentanone was slowly added. The reaction was allowed to stir at room temperature for 12 h and then worked up in a manner similar to the procedure using L-Selectride for the preparation of *cis*-2-methylcyclopentanol. Distillation gave 4.3 g (85% yield) of *cis*-2-methylcyclopentanol-*1-d*.

***cis*-2-Methylcyclopentanol-*2-d*.** A solution of 5.30 g (16.5 mmol) of *trans*-2-methylcyclopentyl-*2-d* brosylate, which had been prepared from the corresponding alcohol, in 50 mL of a 1.3 M tetramethylammonium acetate–DMSO solution was stirred at room temperature for 4 h. The reaction mixture was poured into 150 mL of petroleum ether, washed three times with 100-mL portions of water and once with saturated NaCl, and dried over anhydrous K_2CO_3. The solvent was removed by distillation, yielding 3 mL of liquid identified as *cis*-2-methylcyclopentyl-*2-d* acetate. ^{1}H NMR (60 MHz, $CDCl_3$) showed absorption at δ 5.00 (m, 1 H) for the proton at C(1), which is diagnostic of the cis isomer. The corresponding proton in the trans isomer, which occurs at δ 4.59, was not present. The acetate was converted to *cis*-2-methylcyclopentanol-*2-d* by treating 1.72 g (12 mmol) of acetate with 0.485 g (12.7 mmol) of $LiAlH_4$ in ethyl ether at 0 °C. Distillation gave a final yield of 882 mg (73%).

***trans*-2-Methylcyclopentanol-*2,5,5-d*$_3$.** To a vigorously stirred mixture of 75 mL of anhydrous ethyl ether and 20 mL of D_2O at 0 °C was added slowly 3 g of sodium metal. After stirring for 2 h to insure complete reaction of sodium, 12.4 g (0.13 mol) of 2-methylcyclopentanone was added. The reaction was stirred vigorously for 18 h at room temperature, after which the ether solution was separated from the aqueous phase, dried ($MgSO_4$), and concentrated to about 15 mL by distillation. This ethyl ether solution containing partially exchanged 2-methylcyclopentanone was added to a newly prepared mixture of ethyl ether and OD^-/D_2O, and the procedure was repeated. After four cycles of the above procedure 12 g of 2-methylcyclopentanone-*2,5,5-d*$_3$ was isolated by distillation. MS(EI): *m/e* (rel intensity) 99 (0.9), 100 (3.9), 101 (58.1), 102 (3.8), 103 (0.5). The ketone was converted to a 75/25 mixture of *trans*- and *cis*-2-methylcyclopentanols by reduction with $LiAlH_4$ as described above. The alcohols were converted to 3,5-dinitrobenzoates and separated and converted back to alcohols as described above. Final yield of *trans*-2-methylcyclopentanol-*2,5,5-d*$_3$ after distillation was 1.8 g.

***cis*-2-Methylcyclopentanol-*2,5,5-d*$_3$.** Following the procedure of Krishnamurthy and Brown,[28] 2-methylcyclopentanone-*2,5,5-d*$_3$ was converted to *cis*-2-methylcyclopentanol-*2,5,5-d*$_3$ using L-Selectride reagent.

***trans*-2-(Methyl-*d*$_3$)cyclopentanol.** Following the procedure of Sato et al.,[30] 20.5 g of 2-carbethoxy-2-(methyl-*d*$_3$)cyclopentanone was prepared from 25.0 g of methyl iodide-*d*$_3$ and 20.3 g of 2-carbethoxycyclopentanone (Aldrich). The product was diluted with 130 mL of 25% HCl and refluxed gently to induce decarboxylation. After 8 h the reaction was worked up, and 14.5 g of 2-(methyl-*d*$_3$)cyclopentanone was isolated after distillation. Following a procedure of Umland and Jefraim,[26] 4.1 g of 2-(methyl-*d*$_3$)cyclopentanone was converted to 3.2 g of 2-(methyl-*d*$_3$)cyclopentanol, 95% trans isomer and 5% cis isomer. As indicated above the slight contamination by cis isomer was removed by HPLC.

***cis*-2-(Methyl-*d*$_3$)cyclopentanol.** Following the procedure of Krishnamurthy and Brown,[28] 4.8 g of 2-(methyl-*d*$_3$)cyclopentanone was converted to 1.9 g of *cis*-2-(methyl-*d*$_3$)cyclopentanol using L-Selectride.

Solvolytic Product Determination. The product studies were carried out as described above. The ^{2}H NMR spectra were

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recorded on Varian Associates 220-MHz and Nicolet 360-MHz spectrometers operating at 33 and 55.4 MHz, respectively. Product yields were determined by comparison of peak areas by using either the cut and weigh technique or by using a programmed curve-fitting routine. Estimated errors using these methods is 2–3%. Chemical shifts (δ) were determined relative to tetramethylsilane-d_{12} and were as follows: 3-methylcyclopentene-2-*d* (**6**-2-*d*), 5.9; 1-methylcyclopentene-2-*d* (**7**-2-*d*), 5.6; 3-methylcyclopentene-3-*d* (**6**-3-*d*), 3.0; 1-methylcyclopentene-5-*d* (**7**-5-*d*), 2.5; *cis*-2-methylcyclopentanol-1-*d* (*cis*-**5**-1-*d*), 4.3; *cis*-2-methylcyclopentyl-1-*d* ethyl ether (*cis*-**5**-1-*d*), 4.0; *cis*-2-methylcyclopentyl-1-*d* 2,2,2-trifluoroethyl ether (*cis*-**5**-1-*d*), 4.1; *trans*-2-methylcyclopentanol-1-*d* (*trans*-**5**-1-*d*), 4.0; *trans*-2-methylcyclopentyl-1-*d* ethyl ether (*trans*-**5**-1-*d*), 3.7; *trans*-1-methylcyclopentanol-2-*d* (**8**-*trans*-2-*d*), 1.8; *cis*-1-methylcyclopentanol-2-*d* (**8**-*cis*-2-*d*), 2.1; 2-methylcyclopentanol-2-*d* (**5**-2-*d*), and 2-methylcyclopentyl-2-*d* ethyl ether (**5**-2-*d*), 1.8–2.1.

Solvent Preparation. UV and Conductance Kinetic Procedures. The procedures were the same as those that have been previously reported.[8b,31]

Acknowledgment. This material is based upon work supported by the National Science Foundation under grants CHE 85-06682 (project support) and CHE 81-05004 (Nicolet 360 NMR). M.A.I. also wished to acknowledge The Robert A. Welch Foundation and the W. M. Keck Foundation (HP 5995 GC/MS) for support.

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Vinyl Sulfonyl Esters and Amides in the Synthesis of Substituted δ-Sultams and δ-Sultones

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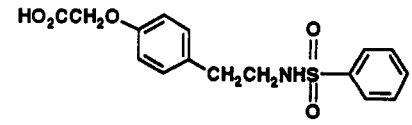
Received October 19, 1990

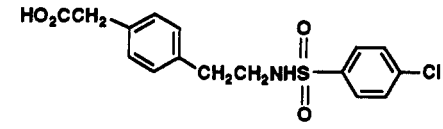
The Michael reaction of phenyl vinyl sulfonate (**3**) or vinyl sulfonamide **12** with phenylacetic esters was the key step in a general synthesis of 4-phenyl-substituted 1,2-thiazane 1,1-dioxides (sultams) and 5-phenyl-1,2-oxathiane 1,1-dioxides (sultones). This methodology was applied to the synthesis of some cyclic sulfonamide and sulfonate derivatives (I and II) of the potent TXA_2 receptor antagonists BM.13177 and BM.13505.

Vinyl sulfonyl esters and amides have served as substrates in a variety of reactions analogous to their carbonyl counterparts including epoxidation,[1] aziridination,[2] and Diels–Alder[3] and nitrone[4] cycloadditions. In addition, these versatile compounds have been utilized as acceptors in Michael reactions, primarily with oxygen and nitrogen nucleophiles.[5] Very few examples of Michael reactions of vinyl sulfonyl derivatives with active methylene compounds have been reported.[5]

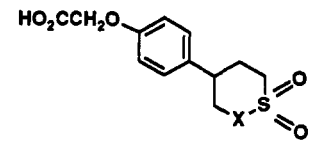
As part of a search for novel antithrombotic agents related to the thromboxane A_2 (TXA_2) receptor antagonists BM.13177 and BM.13505,[6] we were led to propose a series of cyclic sulfonamides and sulfonates as potential substrates.[7] Herein, we describe the utilization of the Michael reactions of vinyl sulfonates and sulfonamides with phenylacetic esters as the key steps in a general synthesis of 4-phenyl-substituted 1,2-thiazane 1,1-dioxides (δ-sultams) and 5-phenyl-1,2-oxathiane 2,2-dioxides (δ-sultones).[8] The application of this methodology to the synthesis of some derivatives (sultams and sultones, I and II) of these potent TXA_2 antagonists is also presented.



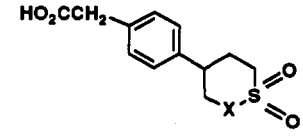
BM.13177



BM.13505



I X = NH, O



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