Registry No.—3-Fluorophenol, 372-20-3; *p*-toluenesulfonyl-chloride, 98-59-9; phenyl trifluoromethanesulfonate, 17763-67-6; phenol, 108-95-2; trifluoromethanesulfonic anhydride, 358-23-6; glycine benzyl ester *p*-toluenesulfonate, 1738-76-7.

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Secondary Deuterium Isotope Effects in the Solvolysis of *cis*- and *trans*-2-Acetoxycyclohexyl 2,2,2-Trifluoroethanesulfonates

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The 2,2,2-trifluoroethanesulfonates (tresylates) of specifically deuterated *cis*-2-acetoxycyclohexanol (*cis*-1βd, *cis*-1αd, *cis*-1$\beta' d_2$) and *trans*-2-acetoxycyclohexanol (*trans*-1βd, *trans*-1αd, *trans*-1$\beta' d_2$) were solvolyzed in 97 wt % trifluoroethanol at 93 and 55°C, respectively, and the secondary deuterium isotope effects were measured. The solvolysis products from the trifluoroethanolysis of the unlabeled isomeric tresylates *cis*-1 and *trans*-1 were also determined. The α effect in *trans*-1αd is similar in magnitude to the effects observed in SN2 reactions (k_H/k_D = 1.03). The β effects in *trans*-1βd and *trans*-1$\beta' d_2$ are also small (k_H/k_D = 0.98 and 1.04, respectively), reflecting the absence of significant hyperconjugative stabilization. These results are in agreement with a transition state structure closer to the oxonium ion intermediate than to the reactants. The results obtained in the solvolysis of the corresponding cis derivatives are significantly different. The α effect is large (k_H/k_D = 1.20) indicating that ionization to the solvent-separated ion pair is rate determining, while the β effects are "normal" but larger for *cis*-1βd (1.34) than for *cis*-1$\beta' d_2$ (1.23). On the basis of these results it was concluded that the cis derivative solvolyzes via a twist–boat transition state. The present work demonstrates the sensitivity of secondary deuterium isotope effects to structural changes of solvolytic transition states.

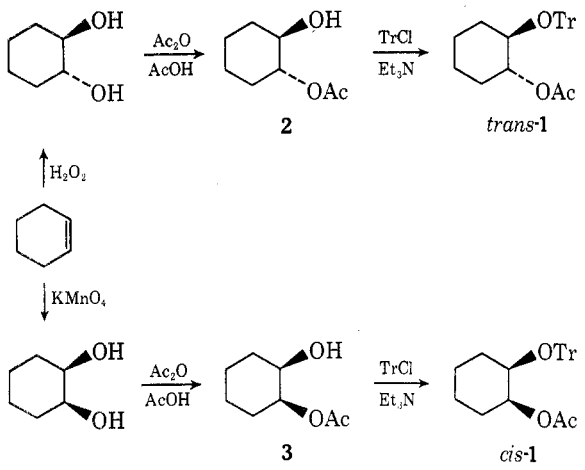
"The deuterium isotope effect has become one of the most important of the tools which physical organic chemists employ in the elucidation of the mechanisms of chemical reactions", but "a dilemma has plagued the interpretation of the experimental data". In 1961 when Westheimer wrote these lines,[1] the dilemma was associated with a spectrum of values of the ratio k_H/k_D. Regretfully, a lack of understanding of the meaning of differences in the magnitudes of observed isotope effects still pertains today.[2] In spite of a satisfactory theoretical treatment of isotope effects, primary[3] as well as secondary,[3,4] the interpretation of isotopic rate data rests mostly on the empirical comparison of these effects in systematically varied and closely related systems. The success of such an approach has been amply demonstrated by Shiner and co-workers[5] in their studies of nucleophilic substitution reactions.

We have shown[6] that the magnitude of secondary isotope effects changes in a predictable manner with the degree of bond breaking and bond making in the transition states of reactions proceeding with neighboring group participation. These studies involved mostly π and σ participation, whereas only a few data are known for n-participating systems.[7] In the present paper, we report kinetic and product studies on the trifluoroethanolysis of specifically deuterated *cis*- and *trans*-2-acetoxycyclohexyl 2,2,2-trifluoroethanesulfonates (tresylates). The solvolysis mechanism of the corresponding tosylates was elucidated in detail by Winstein,[8] which makes this substrate particularly appropriate for systematic studies of the mechanistic meaning of small differences in the k_H/k_D values.

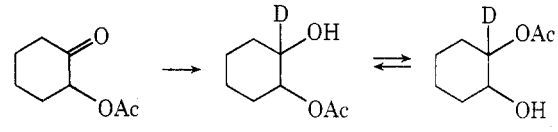
Results

Undeuterated *cis*- and *trans*-2-acetoxycyclohexyl tresylates (*trans*-**1**, *cis*-**1**) were prepared according to Scheme I using a slightly modified version of the published procedures.[9,10]

Scheme I



The synthesis of specifically deuterated substrates (*cis*-1βd, *trans*-1βd, *cis*-1αd, *trans*-1αd, *cis*-1$\beta' d_2$, *trans*-1$\beta' d_2$) could not be accomplished by the more convenient tresylation of deuterated 2-acetoxycyclohexanol, because preliminary examinations have shown that any method involving the preparation of sulfonate esters from 2-acetoxycyclohexanols leads to migration of the acetyl group.[11] In our case such a migration results in distribution of deuterium between positions 1 and 2 in the cyclohexane ring:



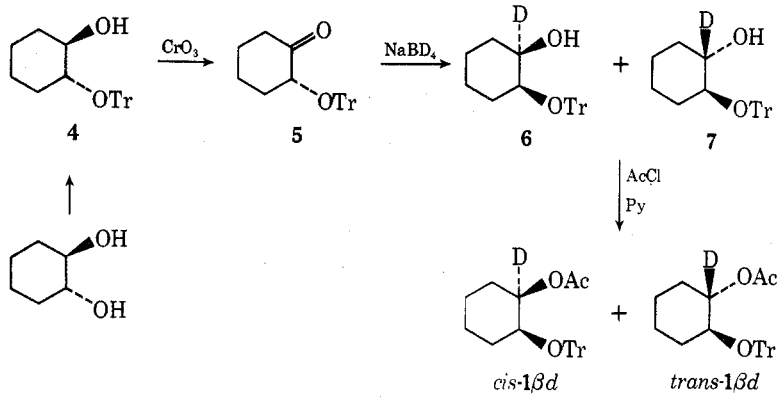
Therefore indirect synthetic routes, shown in Schemes II–IV, were developed for the preparation of specifically deuterated 2-acetoxycyclohexyl tresylates.

The synthetic scheme required the introduction of the tresyl group at an early stage of the synthesis. Fortunately no significant loss of material due to hydrolysis was observed during subsequent steps. However, some unavoidable loss of deuterium was observed during the conversion of **8** to **10**.

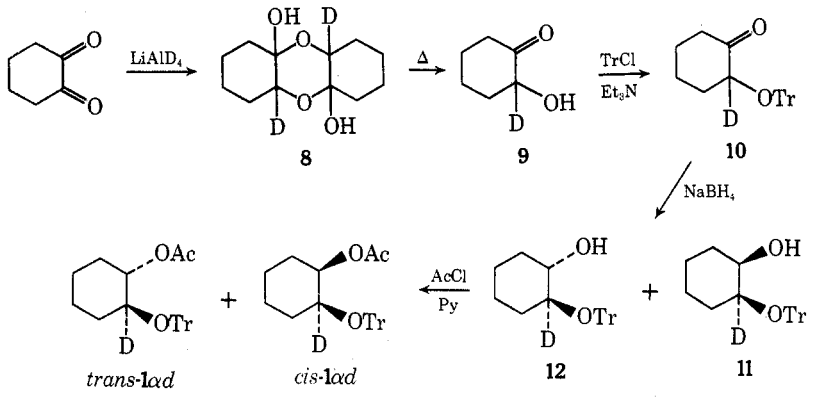
Solvolyses of *trans*-2-acetoxycyclohexyl tresylates (*trans*-**1**, *trans*-1βd, *trans*-1αd, *trans*-1$\beta' d_2$) were accomplished in 97 wt % 2,2,2-trifluoroethanol at 55 °C for 3 h (about 3 half-lives). The rates were measured potentiometrically at a constant pH.[12] Standard ampule technique in the presence of 2,6-lutidine had to be used for the less reactive tresylates *cis*-**1**, *cis*-1βd, *cis*-1αd, and *cis*-1$\beta' d_2$ (see Experimental Section for details). Clear first-order kinetic behavior was observed in all cases. The kinetic results are presented in Table I.

Table II gives the composition of solvolysis products as

Scheme II



Scheme III



Scheme IV

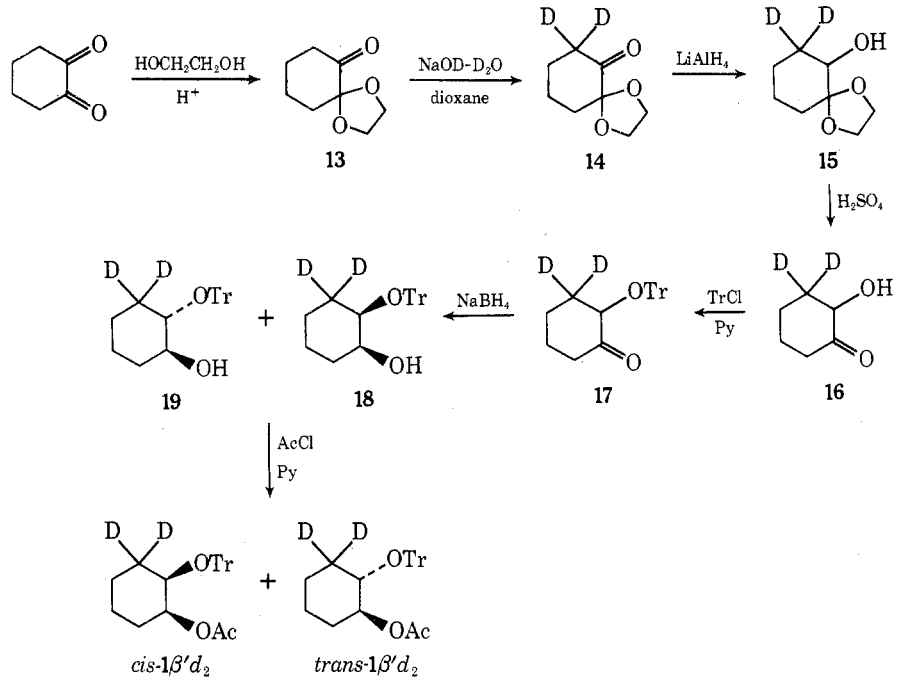
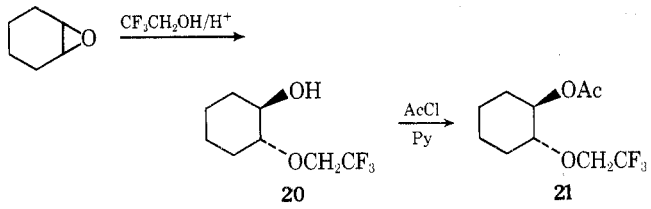


Table I. Deuterium Isotope Effects in the Solvoylsis of Some 2-Acetoxycyclohexyl Tresylates in 97% TFE

Compd	Temp, °C	$k \times 10^5$, s^{-1}	k_H/k_D [a]
cis-1β*d*	93	1.81 (1)[b]	1.34 (3)[b]
trans-1β*d*	55	21.0 (1)	0.98 (1)
cis-1α*d*	93	2.01 (5)	1.20 (3)
	25[c]		1.25[c]
trans-1α*d*	55	20.00 (8)	1.03 (1)
	25[c]		1.033[c]
cis-1β'd_2	93	1.98 (5)	1.23 (6)
trans-1β'd_2	55	19.75 (8)	1.04 (1)

[a] The values are corrected to 100% deuterium content. Rate constants for undeuterated compounds *trans*-1 and *cis*-1 were 2.050 ± 0.006 × 10^{-4} s^{-1} at 55° C and 2.43 ± 0.04 × 10^{-5} s^{-1} at 93 °C, respectively. [b] The errors are given as standard errors, e.g., 1.34 (3) = 1.34 ± 0.03. The values of the isotope effects were calculated using three (for *cis*-1β*d*, *cis*-1α*d*, *cis*-1β'd_2) to six (for *trans*-1β*d*, *trans*-1α*d*, *trans*-1β'd_2) individual rate constants for both deuterated and undeuterated compounds. [c] Calculated from the observed values at higher temperatures assuming no isotope effect in the Arrhenius preexponential factor. For the relative temperature independence of β-deuterium effects see ref 5, p 148.

established by gas chromatography. For comparison the necessary trifluoroethyl ethers (**20, 21**) were synthesized as shown below:



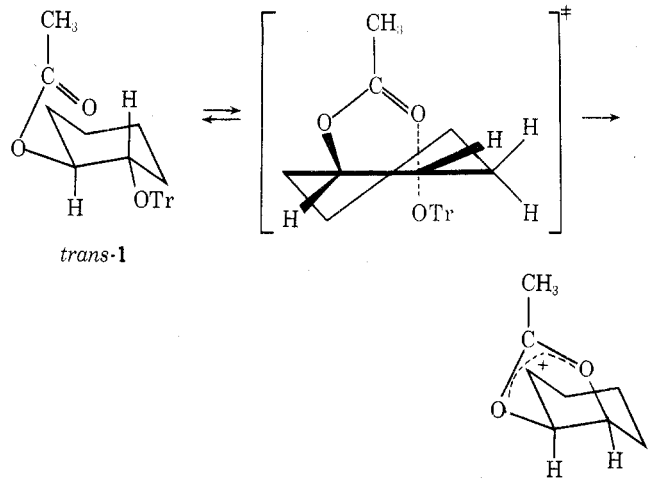
Discussion

The results obtained in the course of this work leave little doubt that in the solvolysis of *cis*- and *trans*-2-cyclohexyl tresylate small differences in the values of secondary deuterium isotope effects can be correlated with different transition state structures.

Only the trans isomer of the two isomeric acetoxy tresylates solvolyzes by acetoxy participation and the formation of a bridged intermediate.[8,13]

Table II. Solvolysis Products of *cis*- and *trans*-2-Acetoxycyclohexyl Tresylates in 97 wt % TFE

Substrate	Products			
trans-1	100%			
cis-1	55.6%	28.4%	4.4%	5.1% 6.5%



In concert with this mechanism the magnitude of the observed α effect is characteristic for direct displacement reactions involving partial bond formation with the entering internal nucleophile. Such small effects have been observed

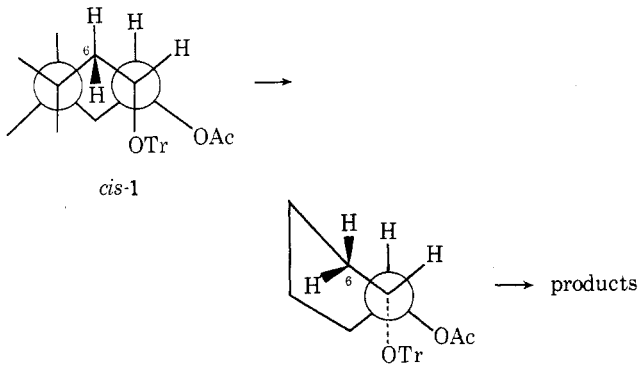
previously in SN2 reactions[14] and in n-participating solvolyses.[6] The rate effects of deuterium substitution in the β positions also support the established mechanistic pathway. The structure of the bridged cation, and consequently of the transition state leading to it, implies charge delocalization. In a delocalized bridged ion stereoelectronic factors render additional hyperconjugative stabilization by adjacent C–H(D) bonds superfluous.[12a,15] The β-isotope effects reflect this situation in detail. Labeling at C_2 affords a small rate increase indicative of greater inductive electron withdrawal from the C–D bond relative to the C–H bond.[16] The steric orientation of this bond also minimizes hyperconjugation. The rate effect of replacing deuterium for protium at C_6 is also small but positive (k_H/k_D = 1.04) revealing some hyperconjugative interaction with C_1. This is not surprising since bridging is probably not complete in the transition state and steric orientation of the C_6–D bonds does not preclude hyperconjugation. The observed effect parallels those in other delocalized transition states.[17] It is likely that here, as in *cis*-4-*tert*-butylcyclohexyl tosylate solvolysis,[5] only the axial C_6–D bond is properly oriented for interaction with the reaction center.

From the product composition it can be inferred that 97% TFE behaves similar to wet acetic acid. For this solvent Winstein proposed[9] the intermediacy of orthoacetate which is formed from the initial acetoxonium ion by attack of water and loss of proton. This reaction affords *cis*-2-acetoxycyclohexanol, which was in our case the only product formed.

Inspecting the results obtained with the cis isomer an entirely different picture emerges. Here acetoxy participation is absent and the solvolysis is $\sim 10^3$ times slower (at 50 °C). The α effect is close to its maximum value for the solvolysis of sulfonate esters (~1.23) which is characteristic for rate-determining formation of the solvent separated ion pair.[18]

The stereochemistry of the substitution products (90% inversion and 10% retention) also supports the formation of the solvent separated ion-pair intermediate. The substitution pathway should in this case be similar to the one observed in reactions of simple cyclohexyl derivatives in solvents of high ionizing power and low nucleophilicity.[19]

Both β effects are normal in magnitude and direction. However the C_6-d_2 compound *cis*-1$\beta'd_2$ shows a smaller effect than the C_2-d_1-tresylate *cis*-1βd (1.23 vs. 1.34). This, we believe, can be rationalized as follows. In a chair conformation the axial and equatorial deuteriums at C_6 are not equivalent for hyperconjugation[20] and the effects should be 0.944 (equatorial) and 1.174 (axial), respectively.[21] The maximal effect in this configuration should be 0.94 × 1.174 = 1.11, which is considerably less than observed. However, *cis*-2-acetoxycyclohexyl tresylate, with two bulky groups cis to each other, should prefer a twist-boat conformation. In this conformation the dihedral angles between the C_6–D bonds and the developing p orbital at C_1 are not optimal for hyperconjugation but both deuteriums can interact partially, leading to an effect of intermediate value.[22]



The larger effect with the d_1 compound can be ascribed to rate-determining elimination in combination with hyperconjugation. The elimination product, acetoxycyclohexene, was shown to be unstable under the reaction conditions. It affords cyclohexanone, which could be detected among the reaction products (6% from the unlabeled tresylate). Thus, this relatively large β effect could be ascribed to a partial rate-determining elimination in addition to hyperconjugation. Although the hydrogen participation cannot be precisely assessed,[23] an alternative rationalization based on hyperconjugation only is also conceivable. Shiner[16] reported β effects as high as 1.30 for cases where the dihedral angle between the C–D bond and the vacant p orbital is close to zero. In our particular case owing to the presence of an electron-withdrawing group a conformation favoring maximal C–H(D) hyperconjugation should be preferred[24] and the β effect could be even larger as to account entirely for the observed value of 1.34. However, the present set of experimental data does not allow us to distinguish between these two interpretations.

Experimental Section

Melting points are uncorrected. The progress of all reactions was followed by thin layer chromatography on silica gel. Infrared spectra were recorded on a Perkin-Elmer Infracord 137 spectrometer. For NMR spectra a Varian A-60 instrument was used. Chemical shifts are quoted in δ values against tetramethylsilane as internal standard. Mass spectra were taken on a Varian MAT CH7 mass spectrometer. Gas chromatography was performed on a Pye Unicam 104 instrument. A 5 ft × 0.25 in. column of 20% PEG 20M on 60–80 mesh Chromosorb W HP was used. Kinetic measurements were made on a Radiometer, Copenhagen, automatic titrator TTT2 with autoburette ABU11 and titrigraph SBR3. The deuterium content was determined by integration of the proton signals obtained on a Varian A-60, and the deuterium signals on a Varian HR-220 spectrometer and confirmed by mass spectrometry.

Materials. 2,2,2-Trifluoroethanesulfonyl chloride (tresyl chloride) (Willow Brook Laboratories, Inc., for synthetic purpose) and silica gel Merck (0.08–0.2 mm) for column chromatography were used. Lithium aluminum deuteride was Fluka A.G. (>99 atom % D).

***trans*-2-Acetoxycyclohexanol (2).** This material was prepared from *trans*-1,2-cyclohexanediol according to the method previously described.[9] The original procedure was modified insofar as isolation and purification were carried out by chromatography on a column of silica gel with ether–chloroform (4:1) as the eluent. In addition to **2** (31% yield) the corresponding diacetate (32%) was also obtained: ir (neat) 3500, 1740 cm^{-1}; NMR (CCl_4) δ 0.90–2.15 (m, 8 H), 1.97 (s, 3 H), 3.10 (s, 1 H), 3.17–3.64 (m, 1 H), 4.24–4.70 (m, 1 H).

***trans*-2-Acetoxycyclohexyl Tresylate (*trans*-1).** To a cooled (0 °C) solution of 550 mg (3.5 mmol) of *trans*-2-acetoxycyclohexanol and 430 mg (4.3 mmol) of triethylamine in 30 ml of dry dichloromethane, 680 mg (3.7 mmol) of tresyl chloride was added dropwise with stirring. The temperature of the reaction mixture was kept below 0 °C during the addition. The mixture was then washed with water followed by cold 10% sulfuric acid, water, saturated sodium bicarbonate, and saturated sodium chloride solution. After drying ($MgSO_4$) and removal of the solvent in vacuo, recrystallization from petroleum ether afforded 409 mg (38%) of pure product: mp 66–67 °C; ir (KBr) 1740, 1380, 1250, 1185, 1095, 930 cm^{-1}; NMR (CCl_4) δ 1.10–2.40 (m, 8 H), 1.98 (s, 3 H), 3.78 (q, 2 H, J = 9 Hz), 4.50–4.73 (m, 2 H).

Anal. Calcd for $C_{10}H_{15}F_3O_5S$: C, 42.35; H, 5.28. Found: C, 42.60; H, 5.39.

***cis*-2-Acetoxycyclohexanol (3).** This compound was prepared from *cis*-1,2-cyclohexanediol according to the same procedure[9] described above for the trans isomer, **2**. In addition to the corresponding diacetate (32%) 26% of the desired product was obtained: ir (neat) 3500, 1750 cm^{-1}; NMR (CCl_4) δ 1.10–2.15 (m, 8 H), 2.04 (s, 3 H), 3.65–3.94 (m, 1 H), 4.67–4.95 (m, 1 H).

***cis*-2-Acetoxycyclohexyl Tresylate (*cis*-1).** Following the same procedure described for the corresponding trans isomer, *trans*-1, 40% of pure product was obtained; mp 68–69 °C; ir (KBr)

1760, 1370, 1340, 1250, 1185, 1140, 1095, 1060, 985, 945, 920 cm^{-1}; NMR (CCl_4) δ 1.42–2.20 (m, 8 H), 2.01 (s, 3 H), 3.90 (q, 2 H, J = 9 Hz), 4.54–5.23 (m, 2 H).

***trans*-2-Hydroxycyclohexyl Tresylate (4).** *trans*-1,2-Cyclohexanediol (5.7 g, 49 mmol) and 3.0 g (30 mmol) of triethylamine were dissolved in 350 ml of dry dichloromethane and the solution cooled to −5 °C. Tresyl chloride (4.5 g, 25 mmol) was then added dropwise with stirring, keeping the temperature of the reaction mixture below 0 °C. The resulting solution was then washed with water followed by saturated sodium bicarbonate solution and dried ($MgSO_4$). The solvent was evaporated in vacuo, and the crude product chromatographed on a column of silica gel with benzene–ether (4:1) yielding 3.7 g (57%) of pure product: mp 61–65 °C; ir (KBr) 3480, 1375, 1270, 1195, 1140, 1095, 980, 935 cm^{-1}; NMR ($CDCl_3$) δ 1.00–2.59 (m, 8 H), 2.50 (s, 1 H), 3.47–3.93 (m, 1 H), 4.18 (q, 2 H, J = 9 Hz), 4.47–4.85 (m, 1 H).

2-Oxocyclohexyl Tresylate (5). To a solution containing 400 mg (1.5 mmol) of 2-hydroxycyclohexyl tresylate in 15 ml of acetone, Jones reagent (CrO_3–H_2SO_4) was added with stirring at room temperature until the TLC control showed the absence of starting material (6 h). The reaction mixture was then diluted with 25 ml of ether and 20 ml of water, and the ethereal layer was separated, washed twice with water, and dried ($MgSO_4$). The evaporation of the solvent in vacuo left 330 mg (85%) of product which recrystallized from petroleum ether showed mp 88–90 °C; ir (KBr) 1730, 1390, 1280, 1260, 1190, 935 cm^{-1}; NMR ($CDCl_3$) δ 1.50–2.72 (m, 8 H), 4.27 (q, 2 H, J = 9 Hz), 5.00–5.40 (m, 1 H).

***cis*- and *trans*-2-Hydroxycyclohexyl-*2*-d_1 Tresylate (6, 7).** To a cooled (0 °C) solution of 600 mg (2.3 mmol) of 2-oxocyclohexyl tresylate in 25 ml of methanol, 50 mg (1.2 mmol) of sodium borodeuteride was added. After the reaction was complete, 100 ml of ether and 40 ml of water was added to the reaction mixture. The ethereal layer was separated and the aqueous layer extracted with ether. The combined ethereal extracts were washed with water and dried ($MgSO_4$). Evaporation of the solvent in vacuo left 580 mg (96%) of a mixture of isomeric alcohols: ir (neat) 3600, 1380, 1325, 1255, 1180, 1140, 935 cm^{-1}.

The isomers were not separated at this stage but used as such in the next step.

***cis*- and *trans*-2-Acetoxycyclohexyl-*2*-d_1 Tresylate (*cis*-1βd, *trans*-1βd).** To a cooled (0 °C) solution of 580 mg of the mixture of *cis*- and *trans*-2-hydroxycyclohexyl-*2*-d_1 tresylate, dissolved in 15 ml of dry pyridine, excess of acetyl chloride (2.0 ml) was added dropwise, with stirring. After 6 h, 100 ml of ether and 20 g of crushed ice were added to the reaction mixture. The organic layer was separated, washed with cold 10% sulfuric acid followed by water, and dried ($MgSO_4$) and ether removed in vacuo. The resulting 596 mg of crude solid (99%) was purified by chromatography on a column of silica gel with benzene–ether (4:1) as the eluent.

The separation of isomers was achieved mechanically. After slow crystallization from petroleum ether two different types of crystals of convenient size were obtained. Careful separation with the aid of a microscope gave 312 mg of massive blocks (cis isomer, *cis*-βd) and 60 mg of fine clustered needles (trans isomer, *trans*-1βd) with the following characteristics. Cis isomer: mp 68–69 °C; ir (KBr) 1740, 1370, 1360, 1255, 1190, 1140, 1100, 970, 945, 925 cm^{-1}; NMR (CCl_4) δ 1.36–2.16 (m, 8 H), 1.98 (s, 3 H), 3.91 (q, 2 H, J = 9 Hz), 4.92–5.12 (m, 1 H). Trans isomer: mp 66–67 °C; ir (KBr) 1740, 1370, 1250, 1185, 1145, 1095, 930 cm^{-1}; NMR (CCl_4) δ 1.14–2.43 (m, 8 H), 1.98 (s, 3 H), 3.87 (q, 2 H, J = 9 Hz), 4.43–4.81 (m, 1 H); deuterium content 0.85 atom D per molecule (NMR).

2-Hydroxycyclohexanone-*2*-d_1 (9). To a suspension of 3.0 g (70 mmol) of lithium aluminum deuteride in 50 ml of dry ether, 11.2 g (100 mmol) of 1,2-cyclohexanedione was added at such a rate that gentle boiling was maintained. The resulting mixture was refluxed with stirring for 30 min, 15 ml of water was then added, and the precipitate was filtered and washed with ether. The aqueous layer of the filtrate was separated and extracted thoroughly with ether, the ethereal layers were combined and dried (Na_2SO_4) and ether was removed in vacuo. On standing for 24 h from 6.3 g of a crude oily product, 0.6 g of crystalline hemiketal 8 was filtered off and washed with ether. The oily residue was then chromatographed on a column of silica gel with ether–benzene (4:1) yielding 1.5 g of the solid dimer 8: mp 148–150 °C; ir (KBr) 3400, 1220, 1130, 1100, 985, 950, 860 cm^{-1}. As by-products 2.0 g of 1,2-cyclohexanediol and 1.1 g of a product whose identity was not examined were obtained.

On heating in a sealed tube under nitrogen to the melting point the dimeric product 8 was converted into the liquid monomer 9, which was immediately used in the next step: ir (neat) 3500, 1710, 1100, 890 cm^{-1}.

2-Oxocyclohexyl-*1*-d_1 Tresylate (10). To a cooled (0 °C) solution of 1.5 g (13 mmol) of freshly prepared 2-hydroxycyclohexanone-*2*-d_1 and 1.5 g of triethylamine in 40 ml of dry dichloromethane, 2.4 g (13 mmol) of tresyl chloride was added dropwise with stirring during 15 min. Stirring was prolonged for 15 min, and the resulting solution was washed with water, followed by 10% sulfuric acid, water, saturated sodium bicarbonate, and saturated sodium chloride solution, and dried (Na_2SO_4). After the removal of solvent, chromatography on a column of silica gel with benzene–ether (7:3) as eluent gave 1.5 g (44%) of pure product: mp 89–90 °C; ir (KBr) 1715, 1390, 1330, 1260, 1190, 1140, 1095, 965 cm^{-1}; NMR ($CDCl_3$) δ 1.40–2.65 (m, 8 H), 4.28 (q, J = 9 Hz), 5.00–5.40 (m, 1 H).

***cis*- and *trans*-2-Hydroxycyclohexyl-*1*-d_1 Tresylate (11, 12).** 2-Oxocyclohexyl-*1*-d_1 tresylate (1.3 g, 5 mmol) was reduced with 0.15 g (4 mmol) of sodium borohydride under the same conditions as described above for the preparation of isomeric alcohols 6 and 7. The chromatography on a column of silica gel with benzene–ether (7:3) yielded 0.9 g (69%) of the mixture of isomeric alcohols 11 and 12 which was used as such in the next step.

***cis*- and *trans*-2-Acetoxycyclohexyl-*1*-d_1 Tresylate (*cis*-1αd, *trans*-1αd).** The mixture of *cis*- and *trans*-2-hydroxycyclohexyl-*1*-d_1 tresylate (0.9 g) was esterified with 3.0 ml of acetyl chloride in 20 ml of dry pyridine following the procedure described above for corresponding β-deuterated compounds *cis*-1βd and *trans*-1βd. After careful separation of the crystals 250 mg of the cis and 50 mg of the trans isomer were obtained. Cis isomer: ir (KBr) 1740, 1390, 1340, 1250, 1185, 1140, 1095, 1055, 925 cm^{-1}; NMR ($CDCl_3$) δ 1.37–2.15 (m, 8 H), 2.05 (s, 3 H), 3.97 (q, 2 H, J = 9 Hz), 4.73–5.17 (m, 1 H); deuterium content 0.70 atom D per molecule. Trans isomer: ir (KBr) 1740, 1380, 1250, 1180, 1145, 1090, 925 cm^{-1}; deuterium content 0.70 atom D per molecule.

1,4-Dioxa-6-oxospiro[4.5]decane (13). A solution of 10 g of 1,2-cyclohexanedione in 300 ml of benzene, an equimolar amount of 1,2-dihydroxyethane, and 100 mg of *p*-toluenesulfonic acid was heated at reflux for 8 h. Water was continuously separated. The resulting solution was washed with sodium hydroxide solution, and dried ($MgSO_4$) and the solvent evaporated in vacuo. Ten grams (62%) of a crude oily product was obtained. The crude product containing a certain amount of the diketal was used without further purification in the next step: ir (neat) 1740, 1200, 1100, 1028, 957, 905 cm^{-1}; NMR ($CDCl_3$) δ 1.4–2.05 (m, 6 H), 2.34–2.72 (m, 2 H), 3.94 (s, 4 H).

1,4-Dioxa-6-oxospiro[4.5]decane-*7,7*-d_2 (14). A reaction mixture containing 5 g (32 mmol) of the crude monoketal 13 and 20 mg of sodium deuteroxide in 50 ml of D_2O–dioxane (1:1 mixture) was heated at 50 °C for 10 h. Solvent was then removed in vacuo and the oily residue was treated twice as described before. After final removal of the solvent 50 ml of benzene was added to the residue, and the resulting solution was washed with 5 × 5 ml of D_2O. After drying ($MgSO_4$) and the removal of benzene in vacuo 4.5 g (89%) of an oily product was obtained: ir (neat) 2220, 2130, 1735, 1190, 1100, 1050, 1030, 955 cm^{-1}; NMR ($CDCl_3$) δ 1.4–2.05 (m, 6 H), 3.92 (s, 4 H); deuterium content better than 1.90 atoms D per molecule (by ^1H NMR).

1,4-Dioxa-6-hydroxyspiro[4.5]decane-*7,7*-d_2 (15). To a suspension of 540 mg (14 mmol) of lithium aluminum hydride in 60 ml of dry ether, 4.5 g (28 mmol) of crude ketone 14 dissolved in 5 ml of ether was added dropwise. Then 0.6 ml of water followed by 0.6 ml of 15% sodium hydroxide solution and 2 ml of water were added to the reaction mixture. The inorganic precipitate was filtered off, the ether layer separated, and the water layer extracted with ether. The combined ethereal extracts were dried ($MgSO_4$), ether removed in vacuo, and the crude product chromatographed on silica gel with benzene–ether (1:1); 2.9 g (64%) of pure oily product was obtained, ir (neat) 3140, 2220, 2130, 1165, 1100, 1030, 955, 985 cm^{-1}.

2-Hydroxycyclohexanone-*3,3*-d_2 (16). Ketal 15 (1.8 g) was dissolved in 15 ml of acetone, 15 ml of 20% sulfuric acid was added, and the resulting solution kept at 50 °C for 30 min. Acetone was then removed in vacuo and the residual aqueous solution extracted with dichloromethane (4 × 25 ml). The combined extracts were washed with sodium bicarbonate solution followed by water and dried ($MgSO_4$) and the solvent was evaporated in vacuo to a volume of ca. 40 ml. Complete removal of solvent was avoided because it causes the formation of the dimeric product 8. The identity of the product was checked by TLC using the corresponding nondeuterated compound as a standard.

2-Oxocyclohexyl-6,6-d_2 Tresylate (17). To a cooled (0 °C) dichloromethane solution of the keto alcohol **16** from the previous step an equimolar amount of dry pyridine was added calculated on the basis of a 100% yield in the preceding ketal hydrolysis. An equimolar amount of tresyl chloride was then added dropwise with stirring. Isolation and purification as described for compound **10** afforded 1.1 g of crystalline product: ir (KBr) 1740, 1395, 1335, 1265, 1190, 1020, 935, 840 cm^{-1}; NMR ($CDCl_3$) δ 1.40–2.75 (m, 6 H), 4.25 (q, 2 H, J = 9 Hz), 5.17 (s, 1 H).

***cis*- and *trans*-2-Hydroxycyclohexyl-6,6-d_2 Tresylate (18, 19).** Using the procedure described for the preparation of compounds **11** and **12** (Scheme III), 1.1 g of keto tresylate **17** gave 0.8 g (73%) of a mixture of isomeric alcohols, which was used without further purification in the next step.

***cis*- and *trans*-2-Acetoxycyclohexyl-6,6-d_2 Tresylate (*cis*-1$\beta'd_2$, *trans*-1$\beta'd_2$).** Applying the same method of preparation and separation as described for corresponding compounds *cis*-1αd and *trans*-1αd in Scheme III, 293 mg (32%) of pure cis and 70 mg (8%) of trans product was obtained. Cis isomer: ir (KBr) 2220, 2130, 1780, 1390, 1250, 1175, 1145, 1080, 915 cm^{-1}; NMR ($CDCl_3$) δ 1.15–2.00 (m, 6 H), 2.02 (s, 3 H), 3.92 (q, 2 H, J = 9 Hz), 4.65–5.25 (m, 1 H); deuterium content 1.95 atoms D per molecule (NMR). Trans isomer: ir (KBr) 2220, 2130, 1745, 1380, 1250, 1185, 1145, 1095, 930 cm^{-1}; NMR ($CDCl_3$) δ 1.20–2.00 (m, 6 H), 2.00 (s, 3 H), 3.85 (q, 2 H, J = 9 Hz), 4.45–4.80 (m, 1 H); deuterium content 1.95 atoms D per molecule (NMR).

***trans*-2-Hydroxycyclohexyl 2,2,2-Trifluoroethyl Ether (20).** A solution of 0.98 g (10 mmol) of cyclohexene oxide in 30 ml of 2,2,2-trifluoroethanol and one drop of sulfuric acid was heated to reflux for 1 h. Barium carbonate was added to the cooled reaction mixture to neutralize the acid and the resulting precipitate filtered off. The filtrate was concentrated in vacuo and the residue chromatographed on column of silica gel with benzene–ether (4:1) yielding 0.4 g (50%) of oil: ir (neat) 3460, 1280, 1180, 1160, 1120, 970 cm^{-1}.

***trans*-2-Acetoxycyclohexyl 2,2,2-Trifluoroethyl Ether (21).** *trans*-2-Hydroxycyclohexyl trifluoroethyl ether (197 mg, 0.1 mmol) in 10 ml of dry pyridine was treated with excess of acetyl chloride following the procedure for preparation of *cis*-1βd and *trans*-1βd described above. The chromatography on a column of silica gel with benzene–ether (9:1) as the eluent afforded 150 mg (63%) of pure oil: ir (neat) 1745, 1280, 1245, 1160, 1125, 1060, 1045, 974 cm^{-1}; NMR (CCl_4) δ 1.77–2.18 (m, 8 H), 1.97 (s, 3 H), 3.10–3.58 (m, 1 H), 3.85 (q, 2 H, J = 9 Hz), 4.43–4.98 (m, 1 H). A small amount of the corresponding cis ether was also isolated and characterized by ir. It was used as a standard in the GLC analysis of solvolysis products.

Acetoxycyclohexene. This compound was prepared from cyclohexanol and acetic anhydride according to the published procedure.[25]

Kinetic Measurements. 2,2,2-Trifluoroethanol, 97 wt % (Fluka), was used as solvent in solvolyses. Measurements of the titrimetric rates for the trans derivatives *trans*-**1**, *trans*-1βd, *trans*-1αd, and *trans*-1$\beta'd_2$ were carried out by means of a pH-Stat Radiometer, Copenhagen, TTT2 titrator with ABU11 autoburette and SBR3 recorder.

The titrimetric cell with solvent was allowed to stabilize at the desired temperature (55 °C) prior to addition of substrates. The concentration of substrate was 6–7 mg/15 ml of solvent in all experiments. The titration solution was 0.02 N sodium hydroxide in 97 wt % TFE.

Six kinetic measurements were performed for each compound alterating the solvolysis of labeled and unlabeled substance.

Rate measurements for cis tresylates *cis*-**1**, *cis*-1βd, *cis*-1αd, and *cis*-1$\beta'd_2$ were accomplished by the usual ampule technique at 93° using 6 mg of substrate, 2 equiv of 2,6-lutidine, and 5 ml of solvent (97% TFE) in each ampule. The titration was accomplished potentiometrically with 0.02 N sulfuric acid as titration solution.

Rate data were evaluated by a nonlinear least-square sum-fitting program.

Product Studies. *trans*-2-Acetoxycyclohexyl tresylate (470 mg) in 180 ml of 97 wt % trifluoroethanol was solvolyzed at 55° under the same conditions as in the kinetic runs for at least 8 half-lives. GLC analysis showed only one product with identical retention time with *cis*-2-acetoxycyclohexanol. After dilution of the reaction mixture with water and subsequent ether extraction, the solvolysis product was isolated and identified as 2-acetoxycyclohexanol by ir spectroscopy.

cis-2-Acetoxycyclohexyl tresylate (608 mg) was solvolyzed in 130 ml of 97 wt % trifluoroethanol in the presence of 321 mg of 2,6-lutidine in sealed ampules at 93 °C. The products were identified by GLC and the major products isolated by column chromatography over silica gel and identified as *trans*-2-acetoxycyclohexyl trifluoroethyl ether (28.4%) by ir, NMR, and comparison with authentic samples. By separate experiments the stability of all products under the solvolytic conditions was determined. With the exception of acetoxycyclohexane all were found to be stable.

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Registry No.—*trans*-**1**, 57573-63-4; *cis*-**1**, 57573-64-5; *trans*-1*d*, 57573-65-6; *cis*-1*d*, 57573-66-7; *trans*-1βd, 57573-67-8; *cis*-1βd, 57573-68-9; *trans*-1$\beta'd_2$, 57573-69-0; *cis*-1$\beta'd_2$, 57573-70-3; **2**, 20520-69-8; **3**, 13858-62-3; **4**, 57573-71-4; **5**, 57573-72-5; **6**, 57573-73-6; **7**, 57573-74-7; **8**, 57573-75-8; **9**, 57573-76-9; **10**, 57573-77-0; **11**, 57573-78-1; **12**, 57573-79-2; **13**, 4746-96-7; **14**, 57573-80-5; **15**, 57573-81-6; **16**, 57573-82-7; **17**, 57573-83-8; **18**, 57573-84-9; **19**, 57573-85-0; **20**, 57573-86-1; **21**, 57573-87-2; *trans*-1,2-cyclohexanediol, 1460-57-7; tresyl chloride, 1648-99-3; *cis*-1,2-cyclohexanediol, 1792-81-0; 1,2-cyclohexanedione, 765-87-7; 1,2-dihydroxyethane, 107-21-1; cyclohexene oxide, 286-20-4; trifluoroethanol, 75-89-8.

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