Reaction of α-Keto Triflates with Sodium Methoxide

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Received May 17, 1977

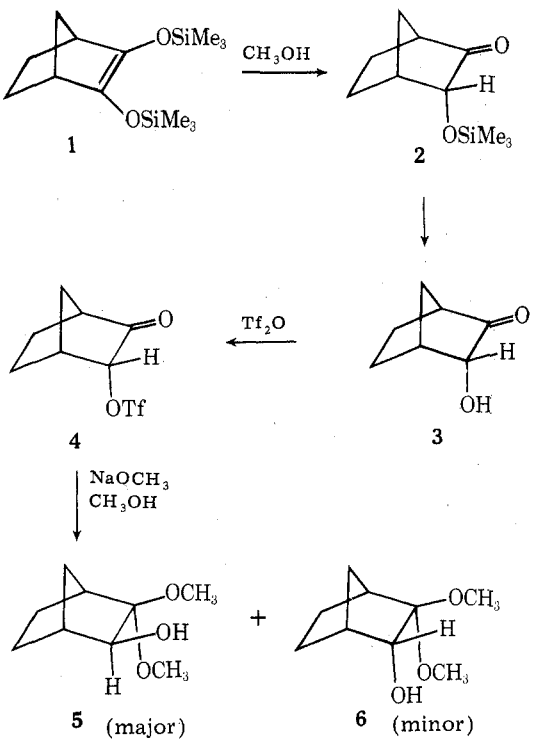
2-Oxo-*endo*-bicyclo[2.2.1]hept-3-yl triflate (**4**) reacts with sodium methoxide in methanol to give *exo*-2,2-dimethoxybicyclo[2.2.1]heptan-3-ol (**5**) as the major product along with smaller amounts of the endo epimer **6**. Complete deuterium incorporation was observed in the carbinyl position of these ketal alcohols when the reaction was carried out in the presence of methanol-d_1. These results were interpreted in terms of the intermediacy of an alkoxy epoxide intermediate which results from endo attack at the carbonyl center and intramolecular displacement of triflate. The epoxide intermediate could be independently generated, in situ, by epoxidation of 2-methoxybicyclo[2.2.1]hept-2-ene (**17**), but opened to give **5**. The reaction appears to be quite general for α-keto triflates. Opening of the methoxy epoxides derived from 2-oxo-*exo*-bicyclo[2.2.1]hept-3-yl triflate (**12**) and oxocyclohex-2-yl triflate (**32**) gave α-methoxy ketone products in addition to the ketal alcohols. Hydride migration in a zwitterionic intermediate is the suggested origin instead of direct S_N2 displacement of triflate. Triflate **32** gave no Favorskii ring contraction or deuterium incorporation in methanol-d_1, suggesting that epoxide formation is much more rapid than potential enolization processes.

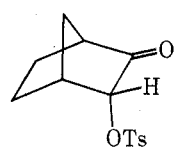
α-Hydroxy ketones are easily prepared via the Ruhlmann and Schrapler modification of the acyloin condensation[1] or epoxidation of silyl enol ethers.[2] The carbonyl function next to the hydroxyl group, in principle, should allow the preparation of secondary trifluoromethanesulfonate (triflate) esters without the problem of in situ solvolysis. It was also anticipated that the extreme lability of this leaving group could lead to unusual transformations of the α-keto triflates. We have prepared some of these triflate esters and have undertaken a study of their reaction with sodium methoxide with the goal of understanding the diverse mechanistic processes which can occur.

Results and Discussion

2-Oxo-*endo*-bicyclo[2.2.1]hept-3-yl Triflate. α-Hydroxy ketone **3** could be readily prepared from bis(trimethylsilyl) ether **1** in a methanolysis procedure. The intermediate keto silyl ether **2** can be isolated without significant amounts of the α-hydroxy ketone **3** if triethylamine is added. Conversion of **3** to 2-oxo-*endo*-bicyclo[2.2.1]hept-3-yl triflate (**4**) was straightforward. Treatment of triflate **4** with excess sodium methoxide in methanol at 0 °C led to formation of 3,3-dimethoxy-*exo*-bicyclo[2.2.1]heptan-2-ol (**5**) in 68% yield and 12% of 3,3-dimethoxy-*endo*-bicyclo[2.2.1]heptan-2-ol (**6**). Even under more strenuous conditions, keto tosylate **7** failed to undergo the analogous reaction. Chloro ketone **8** was epimerized under the attempted reaction conditions to a 1:1.6 mixture of exo and endo isomers,[3] while tosylate **7** gave none of the ketal alcohol. This is in line with the approximately 10^5 greater reactivity of triflates relative to tosylates.[5]

Scheme I





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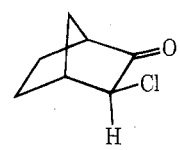

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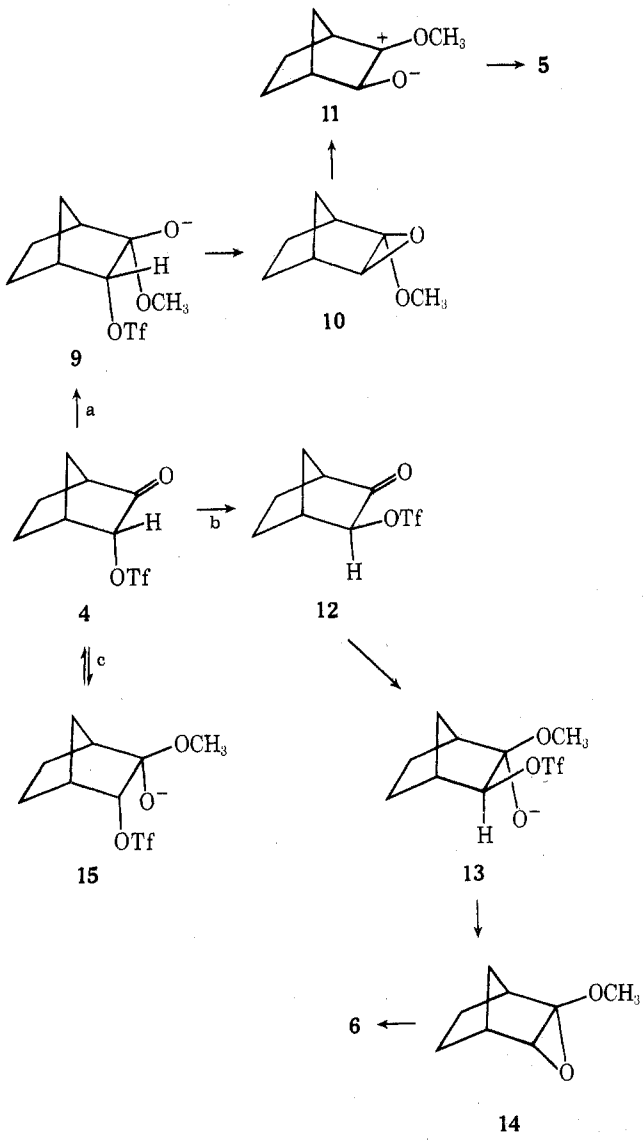
A mechanistic scheme to account for the formation of **5** is given in Scheme II. We envisage three competing reactions of triflate **4** with methoxide. Process a involves endo attack of methoxide at the carbonyl center leading to tetrahedral intermediate **9**. Collapse of **9** would lead to the exo epoxide **10**. Opening of epoxide **10** under the reaction conditions[4] via zwitterion **11** would lead to the observed 3,3-dimethoxy-*exo*-bicyclo[2.2.1]heptan-2-ol (**5**). This opening of epoxide **10** followed by methanol capture is preferred over a bimolecular process involving methoxide attack on epoxide **10**. That such processes can occur has been shown in the uncatalyzed opening of allylic epoxides via allylically stabilized cationic intermediates.[6]

The viability of the suggested mechanism has been supported by the in situ generation of epoxide **10** as shown in Scheme III. Ketalization of 3-chloronorcamphor (**8**) gave **16**. Attempted dechloromethoxylation with sodium in liquid ammonia gave norcamphor dimethyl ketal **18** and only traces of **17**. Treatment of **16** with magnesium–ethylene dibromide in refluxing tetrahydrofuran gave the desired, extremely acid sensitive, enol ether **17**. Reaction with *m*-chloroperbenzoic acid in methanol containing sodium carbonate gave none of epoxide **10**. The product of methanol addition, ketal alcohol **5**, along with norcamphor dimethyl ketal **18** were produced. This observation strongly supports the intermediacy of exo epoxide **10** in the reaction of keto triflate **4** with sodium methoxide.

The formation of alkoxy epoxides by such a mechanism is not unprecidented. Alkoxy epoxides intervene in the reaction of certain aromatic halo ketones, namely, **20**,[7] **21**,[7,8] and **22**,[9] with sodium methoxide. The reactions are overall second

Scheme II



order. With care, in certain cases the epoxide intermediates can be isolated.[10] The present example is of special interest in that the system is purely aliphatic and involves endo attack on a norbornyl system. The highly reactive triflate leaving

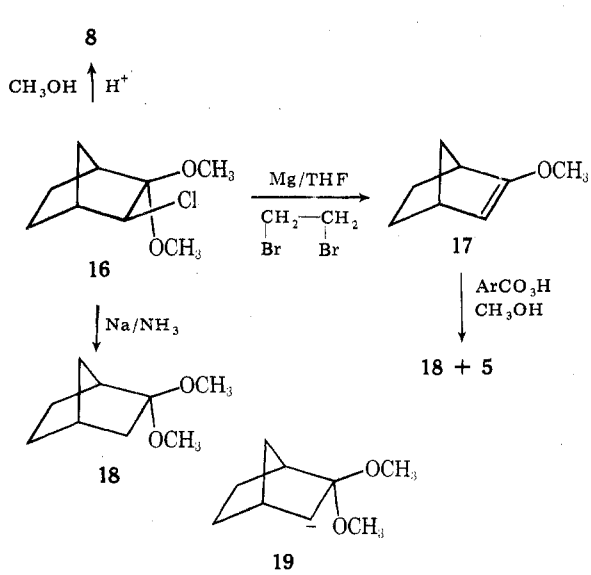
20 21 22

group is necessary to achieve the epoxide-forming reaction in this system, since direct rearward displacement of a leaving group in the intermediate methoxide complex in this rigid system is precluded.

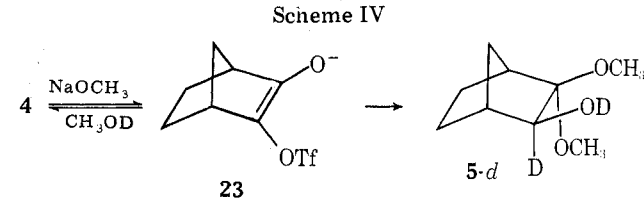
An alternate reaction pathway for triflate 4 (path b) involves isomerization to the exo epimer **12**. Addition of methoxide from the exo side of **12** would lead to the 3,3-dimethoxy-*endo*-bicyclo[2.2.1]heptan-2-ol (**6**) as shown in Scheme II. We believe that this process must be included to account for the small amount of **6** seen in this reaction. Process c, which involves exo attack of methoxide at the carbonyl center of **4**, is, no doubt, a more rapid process than the endo attack route. It is suggested that this process is nonproductive and reversible with the two products arising via paths a and b. The overall conversion of **4** to **5** represents a rare case of the major product of a reaction resulting from endo attack on an unencumbered bicyclo[2.2.1]heptyl system. In methanol-d_1, the ketal alcohol product **5d** was completely deuterated in the α position. Apparently, rapid reversible deprotonation of **4** giving enolate ion **23** occurs faster than the endo attack of methoxide at the carbonyl center.

2-Oxo-*exo*-bicyclo[2.2.1]hept-3-yl Triflate. The suggested origin of *endo*-3,3-dimethoxybicyclo[2.2.1]heptan-2-ol (**6**) in the reaction of triflate **4** with sodium methoxide involved the intermediacy of *exo*-triflate **12**. The independent preparation of **12** was accomplished by epoxidation–hydrolysis of silyl enol ether **24** which gave the dimer of **25**. Subsequent conversion to the triflate derivative **12** and treatment of **12** with sodium methoxide in methanol gave the endo ketal alcohol **6** and a small amount of *endo*-3-methoxybicyclo[2.2.1]-heptan-2-one (**27**). The inverted stereochemistry of **27** (relative to **12**) initially suggests an S_N2 type displacement as its origin. While we have not ruled out this possibility, we prefer the hydride shift mechanism shown in Scheme VI to account for the formation of **27**. This mechanism, in addition to accounting for the stereochemistry of **27**, also accounts for the fact that *endo*-triflate **4** gives none of the analogous *exo*-3-methoxybicyclo[2.2.1]heptan-2-one. Such a product would require an endo hydride migration in a norbornyl system. Such processes are quite unfavorable.[11] An S_N2 mechanism for the

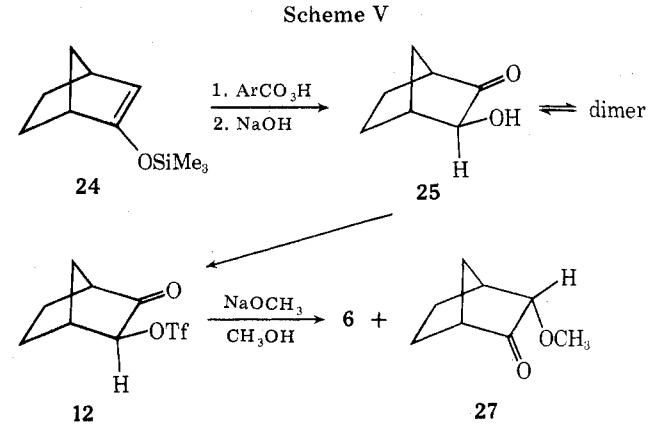
Scheme III



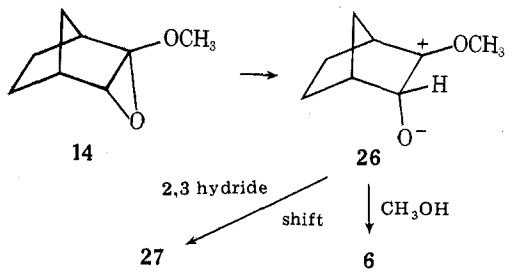
Scheme IV



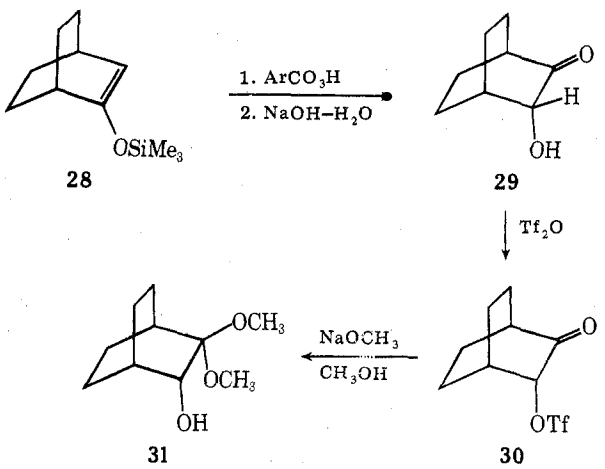
Scheme V



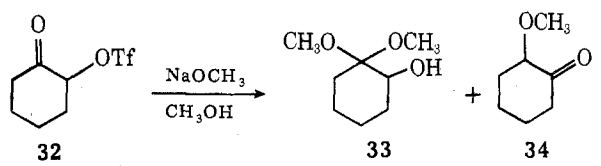
Scheme VI



Scheme VII



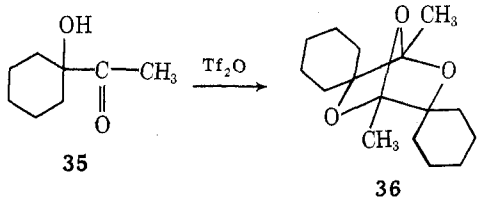
Scheme VIII



formation of **27** would also require an endo approach of methoxide on **12**. This process should be less favorable than an exo approach to triflate **4**. The relative amounts of keto ethers formed in reaction of triflates **4** and **12** with sodium methoxide are therefore not consistent with an S_N2 process.[12]

Generality of the Reaction. Attention was next turned to an evaluation of the generality of the reaction of α-keto triflates with sodium methoxide. Hydroxy ketone **29** could be prepared by epoxidation–hydrolysis of silyl enol ether **28**. Reaction of the triflate derivative **30** with sodium methoxide gave ketal alcohol **31**. The triflate derivative **32** of 2-hydroxycyclohexanone also gave a ketal alcohol product **33** along with 2-methoxycyclohexanone (**34**). It is interesting to note that *none* of the Favorskii product, methyl cyclopentanecarboxylate, is formed under the reaction conditions. The reaction of **32** truely contrasts with the reaction of 2-chlorocyclohexanone with methoxide[13] and demonstrates the generality of the alkoxy epoxide forming reaction even when the Favorskii ring contraction is a mechanistic alternative. The triflate leaving group is undoubtedly the key which allows rapid epoxide formation while bypassing the Favorskii product. The keto ether product could arise by a direct displacement of triflate by methoxide as well as by a variety of processes involving the alkoxy epoxide intermediate. In contrast to triflate **4**, reaction of **32** with sodium methoxide in methanol-d_1 gave *no* deuterium incorporation in the carbinyl position of ketal alcohol product **33**. This attests to the rapidity of the epoxide-forming reaction to the complete exclusion of enolate-forming reactions of **32**.

Although the preparation of certain triflate derivatives of α-hydroxy ketones was quite straightforward, all attempted preparations were not uniformly successful. Attempted conversion of 2-hydroxycyclopentanone to the triflate derivative by usual procedures gave no isolable products. The triflate derivative of 2-hydroxycyclohexanone (**32**) decomposed readily when inpure. Also attempts to prepare **32** in pyridine as solvent were unsuccessful. Also unsuccessful was an attempt to prepare the triflate derivative of **35**. In addition to recovered starting alcohol, only a product of dehydration, **36**, was isolated.[14]



Experimental Section

NMR spectra were recorded on a Varian A-60A or XL-100 spectrometer. Mass spectra were recorded on an AEI Scientific Apparatus MS902 spectrometer. Infrared spectra were recorded on a Perkin-Elmer 455 or Infracord spectrometer.

Methanolysis of 1. Bis(trimethylsilyl) ether **1** (5.0 g), prepared as previously described,[15] was dissolved in 25 mL of dry methanol under nitrogen. After refluxing for 15 min, the solvent was removed under vacuum leaving 2.2 g of crude **3**. The residue was slurried with pentane and 1.66 g (71%) of crystalline **3** was collected: mp 137–143 °C (lit.[16] mp 143–151 °C); IR (neat) ν_{O-H} 2.88 μm, $\nu_{C=O}$ 5.71 μm; NMR (CCl_4) δ 4.0–4.2 (1 H, br s, exchanges with D_2O), 3.88 (1 H, d of d, J = 1.5 and 5 Hz), 2.25–2.85 (2 H, m), 1.1–2.3 (6 H, m).

Methanolysis of 1 with Triethylamine Present. Bis(trimethylsilyl) ether **1** (10 g) was dissolved in 50 mL of dry methanol containing five drops of triethylamine. After a 2-h reflux, the solvent was removed under vacuum, and the infrared and NMR spectra of the residue were recorded: IR (neat) no OH, $\nu_{C=O}$ 5.68 μm, $\nu_{C=C}$ 5.95 μm (m, unreacted **1**); NMR (CCl_4) δ 3.78, (d of d, J = 1.3 and 4.5 Hz, C-3 H of **2**), and multiplets at 2.4–2.65, 0.75–2.3, 0.05–0.25 consistent with a mixture of **2** and **1**. After addition of 50 mL of dry methanol and another 2-h reflux, the solvent was again removed by vacuum. The residue had an infrared spectrum consistent with a mixture of **1**, **2**, and **3**. Even longer reflux times with more methanol consumed **1** and gave mixture of **2** and **3**.

Preparation of 4. Pyridine (30 mL) was cooled in an ice–water bath and 8.46 g of trifluoromethanesulfonic anhydride was added slowly dropwise with stirring. The ice bath was removed until the white precipitate dissolved completely and the solution was recooled in the ice bath. Keto alcohol **3** (3.15 g) was added slowly in small portions, and the resulting solution was stored at −15 °C for 2.5 h. The solution was then diluted with 30 mL of ether and extracted with water. The water layer was separated and extracted with ether, and the combined ether extracts were washed with water, cold dilute hydrochloric acid until acidic, and brine. After standing over sodium sulfate, the solvent was removed through a Vigreux column on a steam bath and the residue was distilled to give 5.31 g (82%) of **4**: bp 62–64 °C (0.05 mm); IR (neat) C=O 5.64 μm; NMR (CCl_4) δ 4.89 (1 H, d, J = 5 Hz), 2.87–3.15 (1 H, m), 2.65–2.87 (1 H, m), 1.0–2.5 (6 H, m); mass spectroscopic molecular weight, 258.0191 (calcd for $C_8H_9F_3O_4S$, 258.0173).

Reaction of 4 with Sodium Methoxide in Methanol. Sodium (0.96 g) was dissolved in 25 mL of dry methanol under nitrogen and the solution was cooled to 0 °C. Triflate **4** (1.88 g) was added dropwise and the solution was refluxed for 1.8 h. After diluting with ether, the solution was extracted with water. The water layer was extracted with another portion of ether. The combined ether extracts were washed with water and brine, and dried over sodium sulfate. The solvents were removed through a Vigreux column and the residue was distilled to give 0.85 g (80%) of a 5.7 to 1 mixture of **5** and **6**,[11c] bp 67–69 °C (1.5 mm). In a separate run, gas chromatographic analysis on 5 ft, 5% SE30 on chromsorb G (column A), showed immediate consumption of **4** when added to sodium methoxide in methanol at 0 °C. Ketal alcohol **5** had the following spectral properties: NMR (CCl_4) δ 3.1–3.4 (7 H, m with sharp s at 3.18 and 3.29), 2.7–3.0 (1 H, br s, exchanges with D_2O), 1.87–2.40 (8 H, m); mass spectroscopic molecular weight 172.1076 (calcd for $C_9H_{16}O_3$, 172.1099).

Reaction of 4 with Sodium Methoxide in Methanol-d_1. The procedure was the same as that above, except the reaction time was 10 min at 25 °C after addition of **4**. Sodium (0.16 g), 7 mL of methanol-d_1, and 0.79 g of **4** gave 0.42 g (79%) of **5**-*d*: bp 69 °C (2 mm). Complete deuteration at C-3 was confirmed by conversion of **5**-*d* to its acetate[11c] followed by NMR analysis. The NMR of the acetate of **5** shows the C-3 H cleanly separated from all other absorptions.[11c]

Preparation of 7. Keto alcohol **3** (1.34 g) was dissolved in 15 mL of pyridine and cooled to 0 °C in an ice–water bath. *p*-Toluenesulfonyl chloride (2.13 g) was added in small portions and the solution was stored at −5 °C for 24 h. The reaction mixture was diluted with 50 mL of ether and extracted with water, dilute hydrochloric acid until acidic, brine, and dried over sodium sulfate. The solvent was removed by a rotary evaporator, leaving 2.36 g (79%) of **7** which was recrystallized from methanol: mp 102.5–103.5 °C; IR (neat) $\nu_{C=O}$ 5.69 μm; NMR ($CDCl_3$) δ 7.75–8.0 (2 H, m), 4.58 (1 H, d, J = 5 Hz), 2.55–3.05 (2 H, m), 2.45 (3 H, s), 1.2–2.2 (6 H, m).

Anal. Calcd for $C_{14}H_{16}O_4S$: C, 59.98; H, 5.75. Found: C, 60.09; H, 5.77.

Preparation of 16. Chloro ketone **8**[17] (8.0 g) was dissolved in 40 mL of dry methanol and 7.4 g of trimethyl orthoformate. *p*-Toluenesulfonic acid monohydrate (250 mg) was added and the solution was refluxed for 10.5 h. After cooling, the acid was neutralized with sodium methoxide and the solvents were removed at 140 mm. The residue was distilled to give 10.12 g (96%) of **16**: bp 73–75 °C (0.85 mm); NMR (100 MHz, $CDCl_3$) δ 3.69 (1 H, d, J = 2.5 Hz), 3.34 (3 H, s), 3.25 (3 H, s), 2.25–2.55 (2 H, m), 1.1–2.25 (6 H, m); mass spectroscopic molecular weight 190.0752 (calcd for $C_9H_{15}O_2Cl$, 190.0760).

Preparation of 17. Chloro ketal **16** (2.02 g) was dissolved in 15 mL of dry tetrahydrofuran (THF) and 0.84 g of magnesium was added. After refluxing for 1.5 h under nitrogen, 4 g of 1,2-dibromoethane in 5 mL of THF was added dropwise over 3 h to the refluxing mixture. The mixture was cooled, filtered, and diluted with ether. The organic phase was extracted with dilute sodium carbonate and brine, and dried over sodium sulfate. Two drops of triethylamine were added and the solvents were removed through a Vigreux column. The residue was distilled to give 0.34 g of a mixture of three products containing 60% of **17** or 15% overall yield of **17** from **16**. Enol ether **17** had spectra consistent with those previously reported.[18]

Reaction of 17 with *m*-Chloroperbenzoic Acid in Methanol. Sodium acetate (94 mg) and sodium carbonate (122 mg) were suspended in 3 mL of dry methanol. *m*-Chloroperbenzoic acid (284 mg) was added. The enol ether **17** (170 mg, 60% of the mixture as prepared above) was added in 1 mL of methanol at 0 °C. After the addition of **17**, the reaction was warmed to 25 °C and stirred for 1 h. Ether and water were added, and the phases were separated. The ether layer was washed with dilute sodium thiosulfate and brine, and dried over sodium sulfate. The solvents were removed through a Vigreux column and the residue was distilled (1–2 mm) to give 70.3 mg of a mixture of **5** (60%) and **18**[18] (40%).

Reaction of 16 with Sodium in Liquid Ammonia. Liquid ammonia (10 mL) was condensed into a mixture of 1 g of **16** in 2 mL of dry ether. Sodium was then added in small pieces under nitrogen until a blue color persisted, and the solution was stirred for another 15 min. Water was carefully added. After the ammonia had evaporated, the aqueous phase was extracted with two portions of ether. The combined ether extracts were washed with brine and dried over sodium sulfate. The solvent was removed through a Vigreux column and the residue was distilled to give 0.56 g of a 4 to 1 mixture of **18**[18] and **17**.

Preparation of 24. Methyl lithium (138 mL of 1.84 M) was added slowly dropwise to 27.6 g of diisopropylamine dissolved in an equal volume of dry ether under nitrogen. The resulting solution was cooled to −78 °C in a dry ice–acetone bath and 19.7 g of norcamphor in 20 mL of ether was slowly added dropwise. After stirring for 10 min, the solution was warmed to 0 °C and 46 mL of chlorotrimethylsilane was added all at once. The solution was warmed to 25 °C and stirred for 30 min. The mixture was then extracted with cold dilute sodium bicarbonate and brine, and dried over sodium sulfate. The solvents were removed through a Vigreux column and the residue was distilled to give 26.08 g (80%) of **24**: bp 58–63 °C (14 mm); IR (neat) $\nu_{C=C}$ 6.20 μm; NMR (CCl_4) δ 4.50 (1 H, d, J = 3 Hz), 2.3–2.8 (2 H, m), 0.7–1.9 (6 H, m), 0.07 (9 H, s); mass spectroscopic molecular weight 182.1109 (calcd for $C_{10}H_{18}OSi$, 182.1127).

Reaction of 24 with *m*-Chloroperbenzoic Acid. *m*-Chloroperbenzoic acid (6.12 g of Aldrich 85% peracid) was suspended in 130 mL of dry hexane and the mixture was cooled in an ice–methanol bath. Silyl ether **24** (5 g) was dissolved in 50 mL of hexane and was added dropwise over 15 min. After stirring for another hour, the *m*-chlorobenzoic acid was removed by filtration, and the filtrate was concentrated under reduced pressure. The residue was dissolved in 60 mL of ether and 50 mL of 15% aqueous sodium hydroxide was added. After vigorously stirring the system for 11.5 h, the phases were separated and the aqueous phase was extracted with a 20-mL portion of ether. The combined ether phases were washed with a small portion of water and brine, and dried over sodium sulfate. The solvent was removed by a rotary evaporator, leaving an oil which consisted mostly of noncamphor and **25**. Upon standing, the dimer crystallized from the oil and was collected in several crops. The yield was 0.28 g (8%) which could be cleaved to monomer **25** by heating to its melting point or by sublimation at 1–2 mm. The dimer of **25** melted at 139–145 °C. Previously reported **25**[19] had the following properties: IR (neat) ν_{O-H} 2.84 μm, $\nu_{C=O}$ 5.79 μm; NMR ($CDCl_3$) δ 3.52 (1 H, d, J = 2.8 Hz), 2.98 (1 H, br s, exchanges with D_2O), 2.5–2.7 (2 H, m), 1.1–2.4 (6 H, m).

Preparation of 12. Pyridine (3 mL) was cooled in an ice–water bath and 0.29 g of triflic anhydride was added dropwise. Monomer **25** (0.100 g), prepared by heating the dimer to the melting point, was added rapidly using a small amount of methylene chloride as solvent. The resulting solution was stored at −15 °C for 55 min. Ether (10 mL) was added, and the mixture was extracted with water, cold dilute hydrochloric acid until acidic, and brine, and dried over sodium sulfate. The solvent was removed through a Vigreux column, the last traces by rotary evaporator. Pentane (5 mL) was added to the residue and the solution was stored at −15 °C overnight. The solid which had formed was separated by decantation of the solvent and washing with another portion of fresh pentane. The solid was unreacted dimer (0.04 g). The pentane solution was concentrated by rotary evaporator and the residue was distilled to give 0.076 g (62% based on unrecovered **25**) of **12**: bp 65–72 °C (0.07 mm); IR (neat) $\nu_{C=O}$ 5.64 μm; NMR (CCl_4) δ 4.43 (1 H, d, J = 2.8 Hz), 2.6–3.0 (2 H, m), 1.4–2.4 (6 H, m); mass spectroscopic molecular weight, 258.0198 (calcd for $C_8H_9F_3O_4S$, 258.0173).

Reaction of 12 with Sodium Methoxide in Methanol. Triflate **12** (0.0511 g) was dissolved in 0.4 mL of dry methanol at 25 °C, and 0.3 mL of 1 M sodium methoxide in methanol was immediately added all at once. After stirring for 1 h, the solution was diluted with 7 mL of ether. The ether phase was extracted with water and brine, and dried over sodium sulfate. Gas chromatographic analysis on column A indicated two products, **6** and **27**, which were identified by spectral comparison with authentic samples[11c] after separation by preparative gas chromatography on 6 ft, 5% SE30 on chromosorb G (column B). The yields of **6** and **27** were 70 and 22% as determined by gas chromatography using napthalene as an internal standard.

Preparation of 28 The procedure was identical to that used for the preparation of **24**. Diisopropylamine (1.80 g), 1.84 M methyllithium (9.2 mL), bicyclo[2.2.2]octan-2-one (2.00 g), and chlorotrimethylsilane (3.5 g) gave 2.87 g (88%) of **28**: bp 85–87 °C (12 mm); IR (neat) $\nu_{C=C}$ 6.08 μm; NMR (CCl_4) δ 4.98 (1 H, d of d, J = 2 and 7 Hz), 2.0–2.3 (2 H, m), 1.1–1.9 (8 H, m), 0.14 (9 H, s); mass spectroscopic molecular weight, 196.1277 (calcd for $C_{11}H_{20}OSi$, 196.1283).

Reaction of 28 with *m*-Chloroperbenzoic Acid in Hexane. The procedure was identical to that used for the reaction of **24** with with *m*-chloroperbenzoic acid. Silyl ether **28** (1.70 g) dissolved in 12 mL of hexane was added to a cooled suspension of 1.57 g of *m*-chloroperbenzoic acid in 35 mL of hexane. After filtration and solvent removal, the residue was partitioned between 13 mL of ether and 25 mL of 10% aqueous sodium hydroxide for 12 h. Workup gave a mixture of bicyclo[2.2.2]octan-2-one and the desired hydroxy ketone **29** in a ratio of about 2 to 1 as determined by gas chromatographic analysis (column A). The hydroxy ketone dimer was separated by slurrying the mixture with petroleum ether and filtering off the insoluble dimer. The yield of dimer was 0.33 g (27%). The monomeric **29** could be obtained by heating the dimer to the melting point as previously described.[20]

Preparation of 30. Pyridine (2.5 mL) was cooled in an ice–water bath and 0.33 g of triflic anhydride was added slowly dropwise. The dimer of **29** (0.13 g) was melted (sealed tube) and transferred to the cooled solution with 1.5 mL of pyridine. After storing at −15 °C for 2 h, 10 mL of ether was added, and the organic phase was extracted with cold water, cold dilute hydrochloric acid until acidic, cold water, and brine, and dried over sodium sulfate. The solvents were removed through a Vigreux column on a steam bath, with the last traces being removed by a rotary evaporator, leaving 0.21 g (87%) of offwhite unstable solid triflate **30**, mp 48–51 °C; IR (KBr pellet) $\nu_{C=O}$ 5.73 μm; NMR (CCl_4) δ 4.88 (1 H, d, J = 2.7 Hz) 2.3–2.6 (2 H, m), 1.5–2.3 (8 H, m); mass spectroscopic molecular weight, 272.0340 (calcd for $C_9H_{11}F_3O_4S$, 272.0330).

Reaction of 30 with Sodium Methoxide in Methanol. Sodium (0.10 g) was dissolved in 4 mL of dry methanol and the solution was cooled in an ice–water bath. Keto triflate **30** (0.13 g) was dissolved in

dry ether and added dropwise. The solution was refluxed for 30 min, cooled, and diluted with 20 mL of ether. The organic phase was extracted with water and brine, and dried over sodium sulfate. The solvent was removed through a Vigreux column and the residue was distilled to give 0.05 g (56%) of **31**, contaminated with traces of two lower boiling unidentified components: bp 80–83 °C (2.0 mm); IR (neat) ν_{O-H} 2.73 μm; NMR (CCl_4) δ 3.50–3.65 (1 H, m), 3.26 (3 H, s), 3.20 (3 H, s), 2.8–3.1 (1 H, br s, exchanges with D_2O), 1.0–2.0 (10 H, m); mass spectroscopic molecular weight, 186.1252 (calcd for $C_{10}H_{18}O_3$, 186.1256).

Preparation of 32. Pyridine (0.68 g) was dissolved in 22 mL of methylene chloride and the solution was cooled in an ice–water bath. 2-Hydroxycyclohexanone dimer (0.70 g) was heated to its melting point (sealed tube) and quickly transferred to the cooled solution. Triflic anhydride (2.25 g) was added dropwise and the solution was stored at −15 °C for 1 h. A cold, rapid workup was necessary to prevent decomposition of **22**. The solution was diluted with 50 mL of ether, extracted with cold water, cold dilute hydrochloric acid until acidic, and cold saturated sodium chloride (brine), and dried over sodium sulfate. The organic phase was decanted from the drying agent into a flask containing a small amount of sodium bicarbonate, and the solvent was removed on a rotary evaporator. The crude residue crystallized to give 1.76 g (118%) of **32** as an unstable offwhite solid: mp 59–62 °C dec; IR (neat) $\nu_{C=O}$ 5.81 μm; NMR (CCl_4) δ 4.9–5.3 (1 H, m), 1.3–2.8 (8 H, m).

Reaction of 32 with Sodium Methoxide in Methanol. Keto triflate **32** (0.50 g) was dissolved with stirring in 3 mL of 1 M sodium methoxide in methanol. After stirring at room temperature for 30 min, the solution was diluted with ether and extracted with water and brine, and dried over sodium sulfate. The solvent was removed on a steam bath through a Vigreux column and the residue distilled to give 0.10 g of a 3.5 to 1 mixture of **33** and **34**, identified by spectral comparison with authentic samples. Gas chromatographic analysis confirmed the absence of both 2-cyclohexen-1-one and methyl cyclopentanecarboxylate. In a duplicate reaction, crude triflate **32**, prepared from 0.56 g of 2-hydroxycyclohexanone, gave 0.24 g of **33** and **34**.

Reaction of 35 with Triflic Anhydride. Pyridine (0.80 g) and 1 g of **35** were dissolved in 10 mL of methylene chloride. The solution was cooled in an ice–water bath and 2.6 g of triflic anhydride was slowly added dropwise. Precipitation of a white solid was observed. After standing at −15 °C for 30 min, the mixture was diluted with ether and extracted with water and brine, and dried over sodium sulfate. The solvents were removed on a steam bath through a Vigreux column, leaving an unstable residue which discolored rapidly upon standing. Addition of 10 mL of 1 M sodium methoxide in methanol followed by a standard aqueous workup and removal of solvent gave a residue which was distilled in two fractions. Fraction one contained 0.37 g (37%) of **35**, bp 35 °C (0.06 mm). Fraction two contained 0.34 g (36%) of **36**,[14] bp 80–82 °C (0.07 mm). When pyridine was used as solvent for this reaction, only unreacted **35** and 1-acetylcyclohexene was recovered in 1 to 2.2 ratio.

Acknowledgment. Financial support from the Research Corp. is gratefully acknowledged.

Note Added in Proof. Epoxidation of 1-methoxycyclohexene in methanol has recently been found to also give 33.[21]

Registry No.—**1**, 63715-72-0; **2**, 63715-73-1; **3**, 5164-68-1; **4**, 63715-74-2; **5**, 63703-36-6; **6**, 63703-35-5; **7**, 10464-71-8; **12**, 63715-76-4; **16**, 63715-77-5; **24**, 57722-40-4; **25**, 5164-67-0; **28**, 63715-78-6; **29** dimer, 63715-71-9; **30**, 63715-79-7; **31**, 63715-80-0; **32**, 63715-81-1; trifluoromethanesulfonic anhydride, 358-23-6; sodium methoxide, 124-41-4; *p*-toluenesulfonyl chloride, 98-59-9; norcamphor, 497-38-1; chlorotrimethylsilane, 75-77-4; bicyclo[2.2.2]octan-2-one, 2716-23-6; 2-hydroxycyclohexanone dimer, 30282-14-5.

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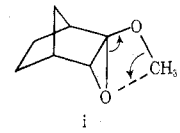
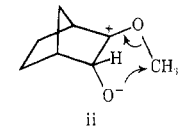


i



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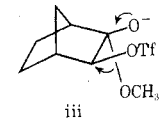

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