Foiled Electrocyclic Rearrangement of Cyclopropyl Cations

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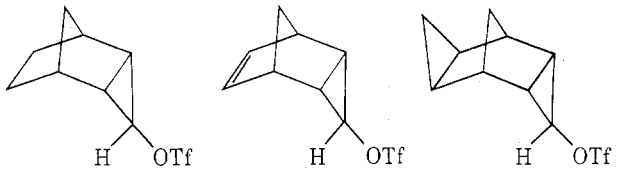
endo-Tricyclo[3.2.1.$0^{2,4}$]oct-*exo*-3-yl triflate (**1**), has been prepared along with the unsaturated and cyclopropyl analogs *endo*-tricyclo[3.2.1.$0^{2,4}$]oct-6-ene-*exo*-3-yl triflate (**2**) and *endo,exo*-tetracyclo[3.3.1.$0^{2,4}$.$0^{6,8}$]non-*exo*-3-yl triflate (**3**). Acetolysis rates and solvolytic product analyses indicate olefinic and cyclopropyl participation in the ionization of **2** and **3**, respectively. Relative rates are 1.0, 81, and 7.1, respectively. Rates of solvolysis of **1** are enhanced by steric repulsion due to the endo-6,7 hydrogens. Triflate **1** gave both *exo*- and *endo*-bicyclo[3.2.1]oct-3-en-2-yl acetate on solvolysis. These products suggest a descrete cyclopropyl cationic intermediate. Whereas **1** gave olefinic products, **2** and **3** gave only saturated products on solvolysis, consistent with long-range olefinic and cyclopropyl participation during ionization.

The phenomenon of neighboring group participation to incipient carbocationic centers is well documented.[1] When the center is cyclopropyl, the usual mode of assistance arises via the electrocyclic cyclopropyl to allylic cation rearrangement.[2] The unopened cyclopropyl cation is involved as a discrete intermediate only when strongly stabilizing groups are substituted on the cationic center.[3] It has been shown that a small ring fused to a cyclopropyl system and a leaving group in the exo position in such a system discourages electrocyclic cyclopropyl opening.[4] The smaller the fused ring, the more closely the intermediate should resemble the discrete cyclopropyl cation. In order to further test this hypothesis, the behavior of triflate **1** under solvolytic conditions has been examined.[5] Triflates **2** and **3** have also been prepared in an attempt to observe anchimeric assistance to the developing cationic center in the system where electrocyclic rearrangement has been blocked.

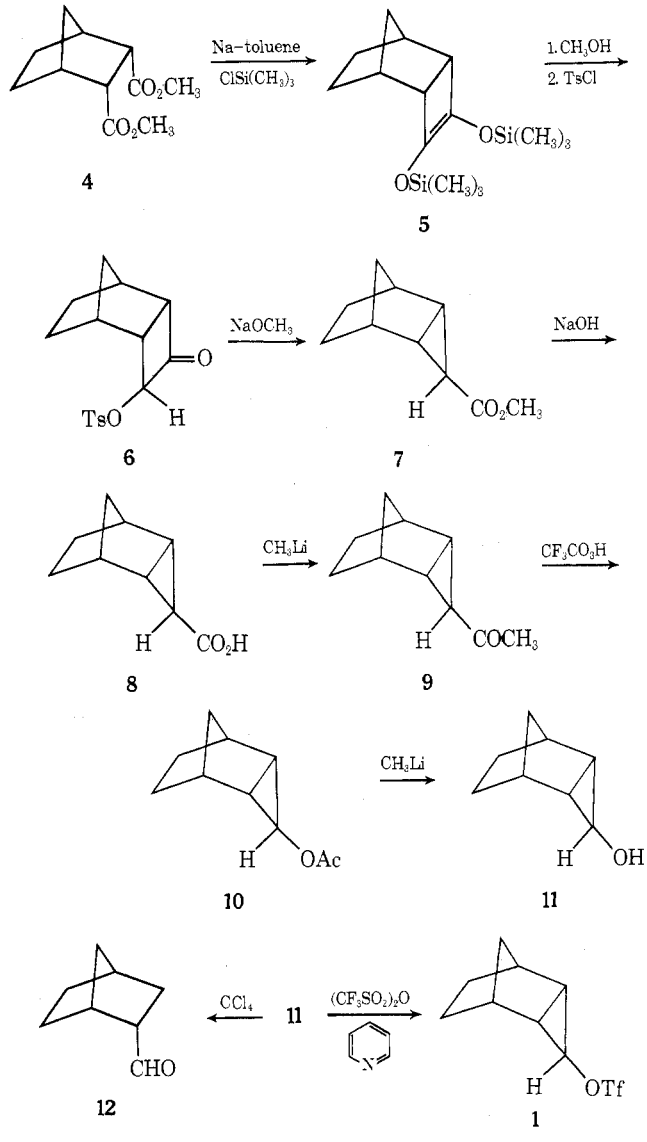


1 2 3

Syntheses. One of the major synthetic difficulties to be overcome was the incorporation of the endo-cyclopropyl group in **1**. Carbene additions to norbornene occur exclusively from the exo direction.[6] Hence the acyloin condensation was used to incorporate the endo ring system. Cyclization of diester **4** using the method of Schräpler and Rühlmann[7] gave bistrimethylsilyl ether **5** in 92% yield. Methanolysis was followed by conversion of the hydroxy ketone to tosylate **6**. Favorskii rearrangement gave the ring-contracted ester **7**.[8] The initial rearrangement product has the carbomethoxy group in the endo position. Epimerization to the desired ester **7** occurs readily under the reaction conditions. The completion of the synthesis was straightforward as outlined in Scheme I. Alcohol **11** (precursor to **1**) proved to be relatively unstable. Rearrangement to aldehyde **12** occurs when **11** is warmed in carbon tetrachloride. However treatment with triflic anhydride in pyridine successfully transformed **11** into **1**.

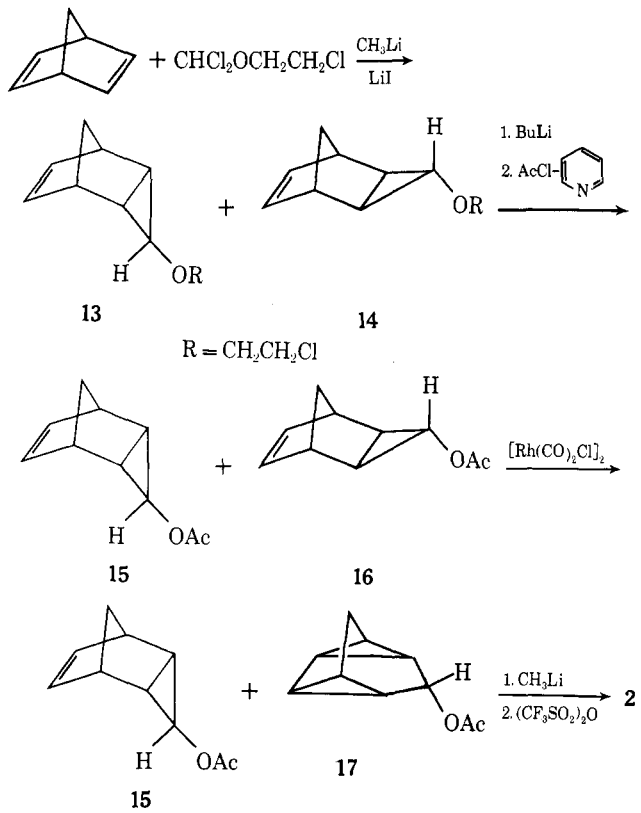
An analogous approach to unsaturated triflate **2** was not attempted owing to anticipated difficulties in maintaining unsaturation in the Baeyer–Villiger oxidation step. The procedure of Schöllkopf[9] was employed as shown in Scheme II. This procedure makes use of the fact that carbene additions to norbornadiene give some endo as well as exo adducts. Treatment of norbornadiene with dichloromethyl chloroethyl ether and methyllithium gave an unstable mixture of chloro ethers **13** and **14** (Scheme II). Cleavage of this mixture with butyllithium followed by treatment of the crude alcohol mixture with acetyl chloride–pyridine in ether gave a 50% yield (based on dichloromethyl chloroethyl ether) of acetates **15** and **16** in a ratio of 0.41:1. Treatment of the acetate mixture with rhodium dicarbonyl chloride dimer isomerizes exo isomer **16** to **17** while leaving **15** unscathed.[10] When this new acetate mixture (**15** and **17**) is converted to the corresponding triflates,

Scheme I

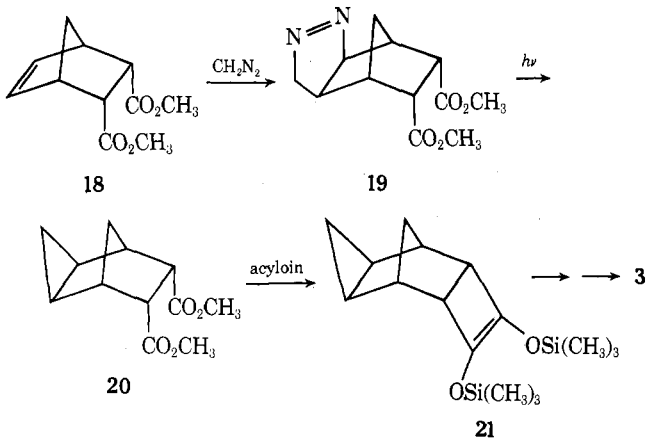


4 5 6 7 8 9 10 11 12 1

Scheme II



Scheme III



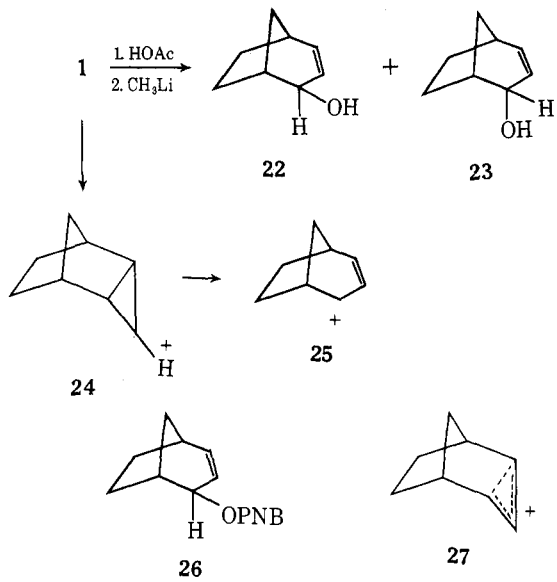
only **2** survives. The triflate derived from **17** is expected to be extremely reactive and no trace of this system is seen.

The synthesis of **3** was analogous to that of **1**. The prerequisite ester, **20**, necessary for cyclization was prepared by photolysis of the pyrazoline **19** derived from the unsaturated diester **18** (Scheme III). (Various Simmons–Smith procedures using **18** gave only small amounts of **20** in a very slow reaction. This lack of Simmons–Smith reactivity is apparently due to an electron-deficient olefinic linkage in **18**, a feature which leads to enhanced rates of pyrazoline formation.) Acyloin cyclization of **20** gives a 75% yield of the tetracyclic system **22**. The remainder of the synthetic sequence to **3** was completely analogous to Scheme I.

Results and Discussion

Solvolysis of 1. Acetolysis of **1** gave, after cleavage of the acetate products with methyllithium, a 91% yield of alcohols **22** and **23** in a ratio of 2.3:1 with exo alcohol **22** predominating.[11,12] No trace of acetate with retained tricyclic structure could be detected. The unexpected appearance of endo alcohol **23** is in contrast to the behavior of **26**, which gives exclusive exo alcohol **22** on solvolysis.[13] A product stability study showed that the exo acetate (precursor to **22**) isomerized under the reaction conditions[14] to give an identical acetate mixture with that obtained in the solvolysis study.

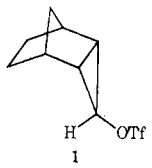
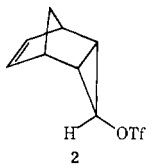
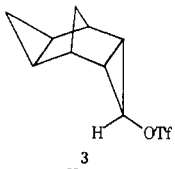
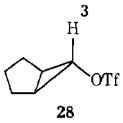
The lack of formation of acetate **10** (which was not convertible to the acetate derivatives of **22** and **23** under the reaction conditions) argues against a "partially opened allylic cation"[4b,15] as suggested by Schleyer, Schöllkopf, Pople et al. in the solvolysis of *exo*-bicyclo[4.1.0]hept-7-yl tosylate and bicyclo[3.1.0]hex-6-yl triflate (**28**). If solvent capture of such a cation, **27**, occurred, substantial amounts of product with retained tricyclic structure should be produced. This is due to the significant positive charge localized on carbon 3 in the partially opened ion **27**. This process would be analogous to the formation of *exo*-bicyclo[4.1.0]hept-7-yl acetate from *exo*-bicyclo[4.1.0]hept-7-yl tosylate. The allylic alcohol products suggest that one actually attains the cyclopropyl cation **24** as a descrete intermediate.[16] The rearrangement of **24** to **25**, which accounts for the observed products, is now allowed, and is expected to occur rapidly.[17] The acetolysis of **1** hence points to an extremely rare case of a solvolytically generated unsubstituted cyclopropyl cation.[19]



Consider next the rates of acetolysis of **1**. Kinetic data (Table I) imply that solvolysis of **1** is enhanced. The basis of this conclusion is the following. Triflate **1** undergoes acetolysis 4.6 times faster than *exo*-bicyclo[3.1.0]hex-6-yl triflate (**28**)[4c] despite the greater ring strain in the former. Because of the effectively "smaller" fused ring in **1**,[20] acetolysis is expected to be slower than in **28**. Additionally, **28** solvolyses *faster* than predicted on the basis of the carbonyl stretching frequency of cyclopropanone.[21] This fact, along with the fact that **28** leads to a partially opened ion, suggests that the acetolysis rate of **28** is enhanced relative to its "unassisted rate". Since **1** solvolyses even faster than **28**, the conclusion must be that **1** is considerably enhanced. The source of this rate enhancement is thought to be steric repulsion[22] due to the endo 6,7 hydrogens which is relieved as **1** proceeds to **24**.

Solvolysis of 2. Acetolysis rates indicate that ionization of **2** is greatly assisted by long-range olefinic participation. Because **1** is itself largely enhanced, its absolute rate is not a good model for the unassisted solvolysis of **2**. Triflate **2** undergoes acetolysis 81 times faster than **1** despite the ex-

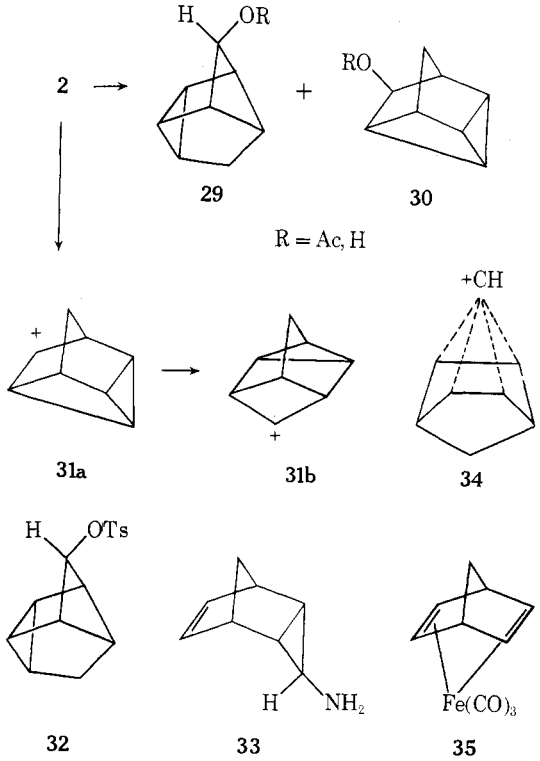
Table I
Rates of Solvolysis in Acetic Acid–0.1 *M* Sodium Acetate

Compd	Temp, °C	k, sec^{-1}	$\Delta H^{\ddagger}$, kcal	$\Delta S^{\ddagger}$, eu	k_{rel} (100°)
 1	140.0	$(4.20 \pm 0.01) \times 10^{-5}$	32.7	−0.1	
	150.0	$(1.10 \pm 0.03) \times 10^{-4}$			
	160.0	$(2.73 \pm 0.04) \times 10^{-4}$			1
	100.0[a]	5.31×10^{-7}			
 2	100.0	$(4.32 \pm 0.02) \times 10^{-5}$	28.1	−3.6	81
	110.0	$(1.19 \pm 0.03) \times 10^{-4}$			
	120.0	$(3.13 \pm 0.01) \times 10^{-4}$			
 3	120.0	$(3.52 \pm 0.03) \times 10^{-5}$	31.8	1.4	
	130.0	$(9.73 \pm 0.02) \times 10^{-5}$			
	140.0	$(2.66 \pm 0.03) \times 10^{-4}$			7.1
	100.0[a]	3.75×10^{-6}			
 28	150.0[b]	2.23×10^{-5}	32.3	−4.3	
	175.0[b]	2.01×10^{-4}			
	100.0[a,b]	1.15×10^{-7}			0.22

[a] Calculated from data at other temperatures. [b] Data of Su, Sliwinski, and Schleyer, ref 4c.

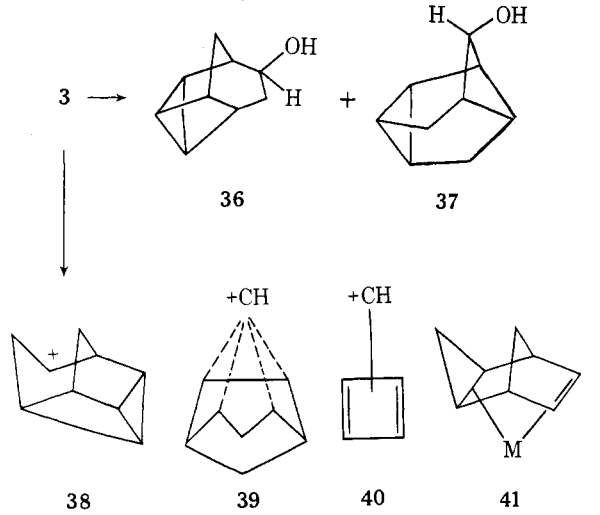
pected rate-retarding inductive effect of the double bond[23] and the lack of steric acceleration in **2**. Anchimeric assistance in **2** is therefore *much greater than*[24] the observed 81 difference in rate between **1** and **2**.

Product studies also bear out the involvement of the unsaturated center in the ionization of **2**. Acetolysis leads to a 55% yield of acetates **29**-OAc and **30**-OAc in a ratio of 1:1. In 65% aqueous acetone, **2** gives a 77% yield of the corresponding alcohols **29**-OH and **30**-OH in a ratio of 1.1:1.[25] No olefinic products were obtained. The same products were found by Coates[26] in acetolysis of **32** and recently by Masamune[27] in the aqueous deamination of **33**. The similarity in products implies a common intermediate or series of intermediates, represented by **31**. The more delocalized ion conceptically derived from **2**, ion **34**, has been generated by Masamune[27] under stable ion conditions. This ion and derivatives[28] can be considered cationic analogs of the well known norbornadiene–iron tricarbonyl complex, **35**.[29]



Solvolysis of 3. Significant long-range cyclopropyl participation in the ionization of **3** is also inferred by rate data. Despite the expected decrease in steric acceleration (relative to **1**) and the rate-retarding cyclopropyl inductive effect,[30] **3** still solvolyzed 7.1 times faster than **1**. Cyclopropyl enhancements in **3**, although slightly less than olefinic enhancements in **3**, must therefore be a real and large factor.

For product studies, solvolysis of **3** was carried out in 65% aqueous acetone containing triethylamine to neutralize liberated triflic acid. Structural assignment of the hydrolysis products proved to be quite formidable. A mixture of at least four alcohols was produced. Spectral data showed the lack of olefinic linkages in the two major isomeric alcohols produced and the presence of cyclopropyl hydrogens. Only alcohols **36** and **37** have structures consistent with the spectral properties of these two major alcohols. Of these two, the major alcohol is assigned structure



36 on the basis of the observed triplet at δ 4.00 (J = 8 Hz) in the carbinyl region of the NMR spectrum. The minor alcohol, assigned structure **37**, shows a broad singlet at δ 3.94 in the carbinyl region. The other products, produced in minor amounts, remained uncharacterized.

The two major products, as well as kinetic evidence, point to a long-range cyclopropyl-assisted ionization, leading to **38**. The more delocalized ion, **39**, conceptionally derived from **3**, is the trishomo analog of square pyrimidal cation **40**,[31] and the cationic analog of metal–tricyclo[3.2.1.$0^{2,4}$]octene complexes, **41**.[10a,b]

Experimental Section

NMR spectra were recorded on a Varian A-60A spectrometer. Data are reported in δ (parts per million) relative to tetramethylsilane. Mass spectra were recorded on an AEI Scientific Apparatus MS902 spectrometer. Infrared spectra were recorded on a Perkin-Elmer Infracord spectrometer. Elemental analyses were performed by Midwest Microlab, Ltd.

Acyloin Condensation of *endo-cis*-2,3-Dicarbomethoxynorbornane (4). Sodium (37 g) was dispersed in 1300 ml of dry refluxing toluene using a wire stirrer and 170 g of chlorotrimethylsilane was added. A solution of 60.6 g of diester **4** in 700 ml of toluene was added dropwise to the stirred, refluxing solution over a 14-hr period. Refluxing was continued for an additional 8 hr. The mixture was cooled and filtered through Celite, and solvent was removed from the filtrate by distillation through a Vigreux column at reduced pressure. The residue was distilled through a Vigreux column to give 78.5 g (92%) of bistrimethylsilyl ether **5**: bp 75–80° (0.3 mm); NMR (CCl_4) δ 0.15 (18 H, s), 1.31 (4 H, broad s), 1.58 (2 H, m), 2.08 (2 H, m), 2.67 (2 H, doublet of doublets).

Anal. Calcd for $C_{15}H_{28}O_2Si_2$: C, 60.75; H, 9.52. Found: C, 60.61; H, 9.62.

Methanolysis of 5. Absolute methanol (160 ml, distilled from magnesium) was added to 32 g of bistrimethylsilyl ether **5** under nitrogen. The solution was refluxed for 7 hr. Solvent was removed under vacuum and the crude residue was slurried in pentane. The product was collected, washed well with pentane, and air dried. A white solid weighing 15.6 (95%) was obtained: mp 105–140°; NMR ($CDCl_3$) δ 1.60 (6 H, m), 2.58 (2 H, m), 3.16 (2 H, m), 4.16 (1 H, s, exchanges with D_2O), 4.81 (1 H, doublet of doublets, J = 9, 4 Hz).

Anal. Calcd for $C_9H_{12}O_2$: m/e 152.0837. Found: m/e 152.0858.

Preparation of 6. The crude hydroxy ketone obtained above (15.6 g) was dissolved in 80 ml of pyridine and the solution was cooled to 0°. With stirring, 21.9 g of *p*-toluenesulfonyl chloride was added in portions. The mixture was stored at 0° for 24 hr and then taken up in water and methylene chloride. The methylene chloride extract was washed with dilute hydrochloric acid to remove pyridine and with sodium carbonate solution, and dried over anhydrous sodium sulfate. The solvent was removed by rotary evaporator. The yield of crude tosylate **6** was 28.5 g (91%), mp 96–100°. An analytical sample was recrystallized from methanol: mp 100–102°; NMR ($CDCl_3$) δ 1.50 (6 H, br s), 2.30 (2 H, m), 2.46 (3 H, s), 3.12 (2 H, m), 5.28 (1 H, doublet of doublets, J = 9, 3 Hz), 7.66 (4 H, doublet of doublets, aromatic).

Anal. Calcd for $C_{16}H_{18}O_4S$: C, 62.72; H, 5.92; S, 10.47. Found: C, 62.44; H, 6.07; S, 10.68.

Favorskii Rearrangement of 6. Sodium methoxide was prepared by dissolving 7.26 g of sodium in 145 ml of absolute methanol. The solution was cooled in ice under nitrogen while 9.07 g of tosylate **6** was added in portions. The mixture was brought to reflux and heating was continued for 2 hr. The mixture was then cooled and 19 g of acetic acid was added. The mixture was then taken up in low-boiling petroleum ether and water. The aqueous phase was extracted with an additional portion of petroleum ether. The combined extracts were washed with water and dried over anhydrous sodium sulfate. The solvent was removed by distillation through a glass helice packed column and the residue was distilled through a short-path condenser. The yield of ester **7** was 1.98 g (40%): bp 67–69° (0.7 mm); NMR (CCl_4) δ 1.0–1.6 (6 H, m), 1.8–2.1 (3 H, m), 2.40 (2 H, m), 3.57 (3 H, s).

Anal. Calcd for $C_{10}H_{14}O_2$: m/e 166.0994. Found: m/e 166.1019.

Saponification of 7. A 2.24-g sample of ester **7** was dissolved in 10 ml of methanol and a solution of 1.84 g of potassium hydroxide in water was added. The mixture was refluxed for 2 hr and the volume was reduced to 10 ml by distillation at reduced pressure. The residue was acidified with dilute hydrochloric acid and the solid acid **8** was collected, washed with water, and dried under vacuum. The yield of crude acid **8** was 1.66 g (81%). A sample was purified by sublimation at 0.3 mm, mp 114–116°.

Anal. Calcd for $C_9H_{12}O_2$: m/e 152.0837. Found: m/e 152.0829.

Preparation of 9. A 1.66-g sample of acid **8** was dissolved in 40 ml of dry ether. A 14-ml aliquot of 1.7 M methyllithium in ether was diluted to 25 ml with ether and added dropwise to the stirred solution. Upon completion of the addition, the mixture, from which salts had precipitated, was refluxed for 1 hr. The mixture was then cooled and poured into ice water and the ether phase was separated. After washing with saturated sodium chloride solution, the ether phase was dried over anhydrous sodium sulfate and filtered and the solvent was removed by distillation through a Vigreux column. The residue was distilled to give 1.39 g (84%) of ketone **9**, bp 57–59° (0.6 mm), which crystallized on standing: NMR ($CDCl_3$) δ 0.9–1.7 (6 H, m), 1.75–2.1 (3 H, m), 2.17 (3 H, s), 2.37 (2 H, m).

Anal. Calcd for $C_{10}H_{14}O$: m/e 150.1045. Found: m/e 150.1047.

Baeyer–Villiger Oxidation of 9. Peroxytrifluoroacetic acid was prepared from 1.08 g of 90% hydrogen peroxide and 10.1 g of trifluoroacetic anhydride in 10 ml of methylene chloride. A 1.6-g sample of ketone **9** was dissolved in 23 ml of methylene chloride and 18.7 g of dibasic potassium phosphate was added. The peracid solution was added dropwise to the cooled mixture with vigorous stirring. Upon completion of the addition, the mixture was refluxed for 1.75 hr. The mixture was taken up into ether and water. The organic phase was washed with potassium carbonate solution and saturated sodium chloride solution and dried over anhydrous sodium sulfate. Solvents were removed by distillation through a Vigreux column. The residue was distilled to give 1.27 g (72%) of acetate **10**: bp 49–50° (0.4 mm); NMR (CCl_4) δ 1.0–1.4 (6 H, m), 1.4–1.7 (3 H, m) 1.90 (3 H, s), 2.39 (2 H, m), 4.00 (1 H, s).

Anal. Calcd for $C_{10}H_{14}O_2$: m/e 166.0994. Found: m/e 166.0975.

Formation and Isomerization of 11. A 1.15-g sample of acetate **10** was dissolved in 10 ml of ether and 10 ml of 1.7 M methyllithium in ether was added dropwise to the solution cooled in an ice bath. The mixture was stirred at 15° for 15 min and cooled to −78°, and 15 ml of water was added dropwise. The ice was allowed to melt and the ether phase was separated, washed with water and saturated sodium chloride solution, and dried over sodium sulfate. After filtration, the solvent was removed under vacuum. The crude residue showed the following NMR (CCl_4): δ 1.0–1.8 (8 H, m), 2.33 (2 H, m), 3.29 (1 H, s). No trace of the aldehyde proton of **12** at δ 10.02 was detected. When the NMR sample was warmed at 65° for 15 min, no trace of the carbinyl proton at δ 3.29 remained. A sharp singlet appeared at δ 10.02. A sample of aldehyde **12** was isolated by distillation of the NMR sample. The infrared showed an aldehydic C–H stretch at 3.64 μ and a carbonyl stretch at 5.80 μ.

Formation of 1. The above procedure for the preparation of alcohol **11** was followed using 0.90 g of acetate **10** and 7 ml of 1.7 M methyllithium. The crude alcohol **11** was dissolved in 3 ml of ether and added to a solution of 3.1 g of trifluoromethanesulfonic anhydride in 9 ml of pyridine held at 0°. The mixture was stored at 0° for 8 hr. The mixture was then poured into water and extracted with two portions of pentane. The combined organic extracts were washed with acetic acid solution to remove pyridine, with water, and with potassium carbonate solution and dried over anhydrous sodium sulfate. The pentane was removed by distillation through a Vigreux column and the residue was distilled to give 0.923 g (67%) of colorless triflate **1**: bp 48–50° (0.45 mm); NMR (CCl_4) δ 1.1–1.8 (6 H, m), 1.95 (2 H, m), 2.55 (2 H, m), 4.25 (1 H, s).

Anal. Calcd for $C_9H_{11}F_3O_3S$: m/e 256.0381. Found: m/e 256.0366.

Formation of 15 and 16. A 10-g sample of dichloromethyl chloroethyl ether and 69 g of norbornadiene were placed in a flask and cooled to 0°. Methyllithium (84 ml of 1.08 M solution) prepared from methyl iodide in ether was added dropwise to the stirred solution over a 20-min period. After stirring at 0° for 15 min under nitrogen, ice water was added. The organic phase was separated rapidly and washed with cold sodium thiosulfate solution and sodium hydroxide solution. The organic phase was dried over sodium sulfate and filtered and solvents were removed under vacuum. The entire procedure was carried out rapidly under nitrogen. The crude residue (**13** and **14**) was dissolved in 60 ml of ether and 80 ml of 2.3 M butyllithium in hexane was added to the cold solution over 15 min. After stirring for 15 min, the solution was cooled to −78° and 1.5 g of methanol in 20 ml of ether was added. This cold mixture was then added via syringe to a slurry of 20 g of acetyl chloride and 33 g of pyridine in 200 ml of ether at 0°. The mixture was then stirred at room temperature for 8 hr. After filtering through Celite, the filtrate was poured into water and worked up in a standard

manner. The solvents were removed by distillation through a Vigreux column. The residue was distilled and the fraction of bp 55–59° (0.45 mm) was collected. The yield of the acetate mixture (**15** and **16**) was 4.99 g (50%). The NMR spectrum of **16** (CCl_4) shows an olefinic triplet at δ 6.35 (J = 2 Hz) and a carbinyl broad singlet at δ 4.66. Acetate **15** shows an olefinic triplet at δ 5.83 (J = 2 Hz) and a carbinyl broad singlet at δ 3.48. The ratio of **16** to **15** determined by NMR integration was 2.4:1.

Rhodium(I)-Catalyzed Isomerization of 16. A solution of 4.7 g of acetates **15** and **16** and 0.64 g of rhodium dicarbonyl chloride dimer in 3 g of carbon tetrachloride was heated (sealed tube) at 80° for 2 hr. The mixture was diluted with pentane and filtered through Celite and the filtrate was washed with potassium carbonate solution. The pentane extract was dried over sodium sulfate and filtered and the solvent was removed by distillation. The residue was distilled to give 3.38 g (72%) of recovered acetates, bp 52–55° (0.7 mm). The NMR spectrum shows no trace of **16.** The carbinyl proton of **17** appears at δ 4.29. Small amounts of olefinic products are present along with **15.**

Formation of 2. A 3.39-g sample of acetate mixture **15** and **17** was dissolved in 25 ml of ether and cooled in an ice bath. Methyllithium (26 ml, 1.7 M in ether) was added dropwise and stirring was continued for 15 min. The work-up procedure was the same as in the preparation of **11.** The crude mixture of alcohols was dissolved in 5 ml of ether and added dropwise to a cold solution of 11.45 g of trifluoromethanesulfonic anhydride in 35 ml of pyridine. The mixture was kept at 0° for 10 hr. Isolation of **2** was accomplished in the same manner as **1.** The yield of **2** was 1.212 g (23% based on starting acetates): bp 47–50° (0.45 mm); NMR (CCl_4) δ 1.65 (2 H, q, J = 1.5 Hz), 2.00 (2 H, t, J = 2 Hz), 3.11 (2 H, m), 5.87 (2 H, t, J = 2 Hz).

Anal. Calcd for $C_9H_9F_3O_3S$: m/e 254.0224. Found: m/e 254.0253.

Formation of 20. Diazomethane was prepared from 200 g of Diazald (Aldrich Chemical Co.) in 1 l. of ether, 52 g of potassium hydroxide, and 250 ml of 95% ethanol.[32] Unsaturated diester **18** (60 g) was added to the diazomethane solution and the mixture was stored at room temperature for 50 hr. Gas chromatographic analysis shows only a trace (less than 1%) of starting ester **18.** The excess diazomethane was removed by distillation and an additional 30 g of **18** was added to the recovered diazomethane. After 3 days, most of the diester **18** had reacted. Solvents were removed from the pyrazoline **19** under reduced pressure with the last traces being removed under a vacuum of 0.5 mm. Pyrazoline **19** shows $\nu_{N=N}$ at 6.47 μ in the infrared.

Approximately 15-g portions of the crude **19** were dissolved in 350 ml of acetone and irradiated with a 450-W Hanovia lamp using a quartz immersion well. Irradiation was continued until nitrogen evolution ceased (approximately 8 hr for each portion). At the end of the irradiation, acetone was removed by rotary evaporator. The combined photolytes were distilled at 0.3 mm. The distillate contained unsaturated diester **18,** tricyclic diester **20,** and small amounts of other lower boiling impurities. The entire distillate was dissolved in 250 ml of methanol and ozonized exhaustively at −78°. The mixture (from which **20** had crystallized) was warmed to room temperature and a solution of 20 g of sodium carbonate, 50 ml of 30% hydrogen peroxide, and 150 ml of water was added. After stirring for 5 min, the mixture was taken up into ether and water. After a standard work-up, the residue was distilled to give 37.2 g (39%) of solid diester **20,** bp 108–112° (0.3 mm). A sublimed sample gave mp 69–73°; NMR (CCl_4) δ −0.19 to 0.65 (2 H, m), 0.80 (1 H, m), 1.06–1.33 (3 H, m), 2.59 (2 H, m), 2.95 (s H, m), 3.60 (6 H, s).

Anal. Calcd for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19. Found: C, 64.49; H, 7.34.

Acyloin Condensation of 20. The procedure was analogous to the cyclization of diester **4.** Diester **20** (37.0 g), 22.5 g of sodium, and 99 g of chlorotrimethylsilane gave 38.17 g (75%) of bistrimethylsilyl ether **21:** bp 86–88° (0.2 mm); NMR (CCl_4) δ 0.17 (18 H, s), 0.17–0.95 (4 H, m), 0.95–1.5 (2 H, m), 2.05 (2 H, m), 2.61 (2 H, d, J = 3 Hz).

Anal. Calcd for $C_{16}H_{28}O_2Si_2$: m/e 308.1628. Found: m/e 308.1653.

Kinetics Procedure. A known amount (80–100 mg) of a given triflate was diluted to 10 ml with 0.10 M sodium acetate in anhydrous acetic acid containing 1% acetic anhydride. The solution was divided into eight aliquots and heated in sealed tubes at a particular temperature. One-milliliter aliquots were titrated at given times with 0.02 M perchloric acid in anhydrous acetic acid using either a Metrohm E576 automatic recording titrator or manual potentiometric titration for end-point determinations. All rate constants were determined using an infinity titer which agreed well with calculated values. Rate constants were determined by the method of least squares as calculated by computer. All solvolytic runs gave excellent first-order plots through greater than 75% reaction.

Solvolysis of 1. Product Analysis. A 0.309-g sample of **1** was dissolved in 15 ml of 0.1 M sodium acetate in acetic acid–1% acetic anhydride and the mixture was heated (sealed tube) for 16 hr at 150–153°. The mixture was taken up into ether and water. After a standard work-up, excess methyllithium was added to the acetates dissolved in ether. Samples of alcohols **22** and **23** were isolated by preparative gas chromatography using a 6-ft, 15% Carbowax 20M on Chromosorb P column at 130°. Identification was made by NMR and infrared spectral comparison with authentic samples. In a separate run, the yield of acetates was determined by gas chromatography vs. an internal standard. The ratio of alcohols **22** to **23** was also determined by gas chromatography, after cleavage of the acetates with excess methyllithium.

Solvolysis of 2. Product Analysis. A 0.3005-g sample of **2** was dissolved in 14 ml of 0.1 M sodium acetate in acetic acid–1% acetic anhydride and the mixture was heated (sealed tube) at 110° for 16 hr. After a standard work-up, the products were isolated by distillation. The yield of **29**-OAc and **30**-OAc was 0.1067 g (55%). In addition, 0.037 g of higher boiling products (probably diacetates) was obtained. The carbinyl proton of **29**-OAc is a singlet at δ 4.67, in **30**-OAc a doublet (J = 2.6 Hz) at δ 4.49.

A 0.2570-g sample of **2** was dissolved in 7.5 ml of acetone, and 4 ml of water and 0.155 g of triethylamine were added. The mixture was heated (sealed tube) at 100° for 35 hr. After a standard work-up, the alcohol products were isolated by distillation which gave 0.095 g (77%) of alcohols **29**-OH and **30**-OH. The alcohols were inseparable by gas chromatography. Identification of the components of the mixture was made by infrared and NMR spectral comparison with authentic samples.[21] The carbinyl proton of **29**-OH is a singlet at δ 4.11, in **30**-OH, a doublet (J = 2.6 Hz) at δ 3.77. The alcohol ratio was 1.1:1 by integration of the carbinyl protons.

Solvolysis of 3. Product Analysis. A 0.3024-g sample of **3** was dissolved in 7.5 ml of acetone, and 3.7 ml of water and 0.221 g of triethylamine were added. The mixture was heated (sealed tube) at 130° for 20 hr. After a standard work-up, the sample was analyzed by gas chromatography using a 6-ft, 15% Carbowax 20M on Chromosorb P column at 160°. Four products were observed. The two major products were isomeric alcohols (calcd m/e for $C_9H_{12}O$: 136.0888. Found: 136.0884) and were isolated by preparative gas chromatography using a 6-ft, 15% Carbowax 20M on Chromosorb P column at 160°. NMR analysis of each alcohol showed no olefinic protons and the presence of cyclopropyl protons. The major product, **36,** showed a triplet at δ 4.00 (J = 8 Hz) in the carbinyl region of the spectrum. The minor alcohol, **37,** showed a broad singlet at δ 3.94 in the carbinyl region.

Registry No.—**1,** 56514-04-6; **2,** 56514-05-7; **3,** 56514-06-8; **4,** 4098-47-9; **5,** 56514-07-9; **6,** 56514-08-0; **6** free alcohol, 56514-09-1; **7,** 56514-10-4; **8,** 56552-96-6; **9,** 56552-97-7; **10,** 56514-11-5; **11,** 56514-12-6; **12,** 3574-54-7; **15,** 56514-13-7; **16,** 56552-98-8; **17,** 56514-14-8; **18,** 832-56-4; **19,** 56086-40-9; **20,** 56514-15-9; **21,** 56514-16-0; **22,** 4802-43-1; **23,** 32222-49-4; **28,** 25327-17-7; **29** (R = Ac), 38311-35-2; **29** (R = OH), 38311-30-7; **30** (R = Ac), 38311-36-3; **30** (R = H), 56613-90-1; **36,** 56514-17-1; **37,** 56514-18-2; chlorotrimethylsilane, 75-77-4; p-toluenesulfonyl chloride, 98-59-9; methyllithium, 917-54-4; peroxytrifluoroacetic acid, 359-48-8; trifluoromethanesulfonic anhydride, 358-23-6; norbornadiene, 121-46-0; rhodium dicarbonyl chloride dimer, 14523-22-9; diazomethane, 334-88-3.

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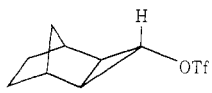

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Substituent, Reagent, and Solvent Effects on the Steric Course of Additions Initiated by Electrophilic Bromine to 3-Bromocyclohexene. A Comparison with the Stereoselectivity of Epoxidation and the Regioselectivity of Ring Opening of Epoxides

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The steric course of the addition of bromine, pyridine perbromide, and acetyl hypobromite to 3-bromocyclohexene in several low polarity nonprotic solvents has been investigated. The bromination always produces nonequilibrium mixtures of two 1,2,3-tribromocyclohexanes resulting from anti addition, in ratios which are markedly affected by the solvent. The addition of pyridine perbromide gives, besides the same tribromo derivatives, a bromo–pyridinium adduct arising from electrophilic attack by bromine anti to the allylic substituent followed by nucleophilic attack by pyridine at C_1. The addition of acetyl hypobromite affords three isomeric anti bromo–acetate adducts, whose distribution is almost solvent independent. The comparison of the stereo- and regioselectivity of the last addition reaction with those of the epoxidation of 3-bromocyclohexene and of the hydrogen bromide opening of its cis and trans epoxides shows a stringent analogy. In both cases the electrophilic attack occurs preferentially (80–90%) anti to the allylic bromine atom; moreover, both the nucleophilic attack by bromide on the protonated epoxides and that by acetate on the epibromonium ions, which are assumed as intermediates for the addition reaction, occur exclusively or with very high preference at the ring carbon which is farther from the substituent. The steric course of the addition of bromine in the presence of bases (like pyridine or ethyl ether) is rationalized on the basis of a ionic two-stage mechanism involving product control by steric, electronic, and conformational factors during the nucleophilic rather than the electrophilic step.

The steric course of halogen additions to 3-substituted cyclohexenes has been shown to markedly depend both on the reagent and solvent employed and on the nature of the allylic substituent.[1-3] Whereas alkyl groups exert mainly a steric effect in both the electrophilic and nucleophilic step of the additions, a polar substituent may also affect the stereo- and regioselectivity in several additional ways. For instance, the product distribution found in the bromination of some 2-cyclohexen-1-ol derivatives has been interpreted[3] on the basis of a syn directive effect of a hydroxy (or methoxy) group, operating in the electrophilic step, in conjunction with an inductive effect, operating in the nucleophilic one. As a part of a research program concerning the stereochemistry and the mechanism of electrophilic additions to alkenes, we extended our investigation to 3-halogenocyclohexenes, starting with the bromo derivative **1**.