Steric and Conformational Effects in the Solvolysis of Ring-Fused Tertiary Cyclopropyl Derivatives

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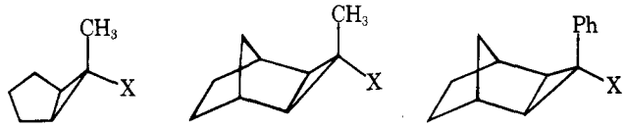
3-Methyl-*exo*-tricyclo[3.2.1.$0^{2,4}$]oct-*exo*-3-yl tosylate (**2**-OTs) and the methyl-d_3 analogue (**2**-OTs-d_3) have been prepared along with 3-phenyl-*exo*-tricyclo[3.2.1.$0^{2,4}$]oct-*exo*-3-yl trifluoroacetate (**3**-OTFA). Acetolysis of these substances gave only allylic acetates. Rate data suggest considerable steric rate enhancements for both **2**-OTs and **3**-OTFA. The β-deuterium isotope effect in the solvolysis of **2**-OTs was 1.33 ± 0.02, a value considered quite small in view of the large ($10^{8.42}$) α-methyl/α-hydrogen rate ratio. This was interpreted in terms of a sterically induced unfavorable transition-state conformation necessary for maximal hyperconjugative stabilization in the incipient cyclopropyl cation. Solvolysis of 1-phenylcyclopropyl derivatives was used as a model for the unassisted, k_c, formation of the 1-phenylcyclopropyl cation. Comparison of rate data with that of **3**-OTFA gave a steric rate enhancement for phenyl which was comparable to that of a methyl group. Conformational factors were suggested to account for a decreased phenyl steric effect.

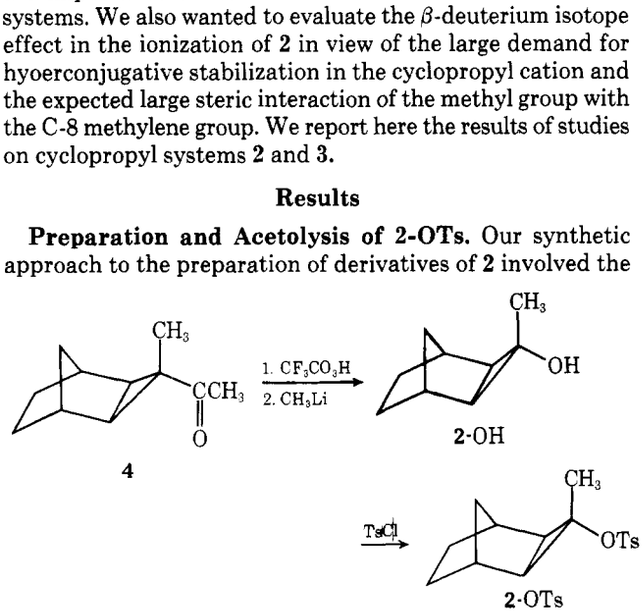
The solvolysis of cyclopropyl substrates has been an area of continuing interest.[2] Our interest in this area has led us to construct systems in which incipient cyclopropyl cation centers interact with adjacent olefinic centers.[3,4] We have also found that concerted ionization–electrocyclic opening to an allylic cation can be prevented by fusion of an *endo*-norbornyl system to a secondary cyclopropyl triflate.[3] Similarly the tertiary cyclopropyl system **1**, with the cyclopentyl ring fused to the cyclopropyl system and a leaving group in the exo position, undergoes stepwise processes giving a cyclopropyl cation, followed by rearrangement to an allylic cation.[5] The β-deuterium isotope effect in the solvolysis of **1** (X = OTf) was 1.42, a value not inconsistent with such a mechanism.[6] The importance of steric effects in the ionization of **1** was an unknown factor. We were therefore interested in preparing the tricyclo[3.2.1.$0^{2,4}$]octyl systems **2** and **3** in order to evaluate the importance of steric effects in the ionization of these systems. We also wanted to evaluate the β-deuterium isotope effect in the ionization of **2** in view of the large demand for hyoerconjugative stabilization in the cyclopropyl cation and the expected large steric interaction of the methyl group with the C-8 methylene group. We report here the results of studies on cyclopropyl systems **2** and **3**.



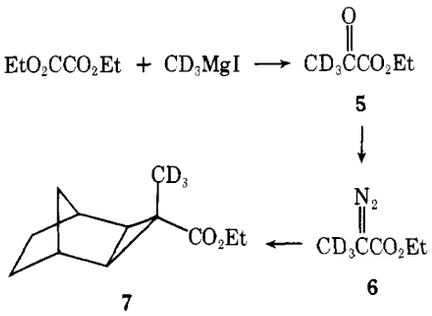
1 **2** **3**

Results

Preparation and Acetolysis of 2-OTs. Our synthetic approach to the preparation of derivatives of **2** involved the addition of methylcarboethoxycarbene to norbornene as previously described.[7] Further transformations previously described allowed the preparation of ketone **4**.[7] Baeyer–Villiger oxidation gave the corresponding acetate[8] which was converted to alcohol **2**-OH and tosylate 2-OTs. The preparation of the deuterated tosylate, **2**-OTs-d_3, required the preparation of ethyl diazopropionate-d_3, (**6**). Treatment of diethyl oxalate with methylmagnesium-d_3 iodide gave ethyl pyruvate-d_3 **5** which was converted to **6** via pyrolysis of the tosylhydrazone salt. Photosensitized addition of **6** to norbornene gave **7** which led subsequently to the preparation of **2**-OTs-d_3.

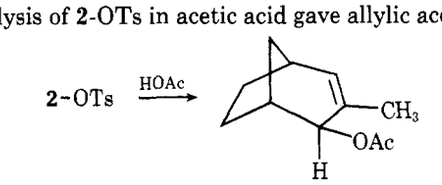


4 **2**-OH **2**-OTs



7 **6** **5**

Solvolysis of **2**-OTs in acetic acid gave allylic acetate **8** as the sole product. Kinetic data are also given in Table I. The β-deuterium isotope effect in **2** determined from the data in Table I is 1.33 ± 0.02. Comparison with **1**-OTs shows that **2**-OTs is 2.4 × 10^3 more reactive in acetic acid at 50 °C.



8

Preparation and Acetolysis of 3. The synthetic entry into the phenyl-substituted system, **3**, is shown below. Addition of phenylcarbene to norbornene gave a mixture of hydrocarbons **9** and **10**. Treatment of this mixture with butyllithium–TMEDA followed by oxygen led to alcohol **3**-OH. The exo isomer **10** does not react under these conditions and only the exo alcohol **3**-OH is formed. The tosylate derivative of **3**-OH was expected to be too reactive for convenient preparation and solvolysis. The *p*-nitrobenzoate derivative was expected to require an extremely high temperature to induce solvolysis. The trifluoroacetate derivative, **3**-OTFA, was therefore prepared since this derivative was expected to have intermediate reactivity.

Solvolysis of **3**-OTFA in acetic acid gave allylic acetate **11** as the sole product. Kinetic data are also given in Table I along with data for phenylcyclopropyl trifluroacetate (**12**), for comparison. Acetolysis of **3**-OTFA is 1.3 × 10^3 faster than **12**.

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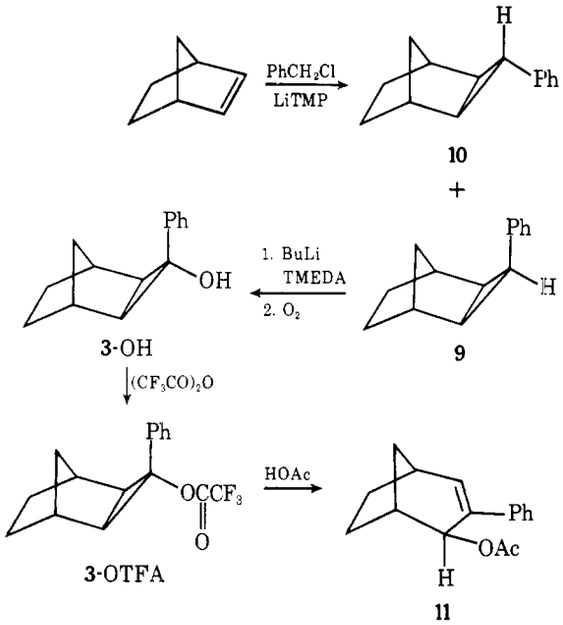
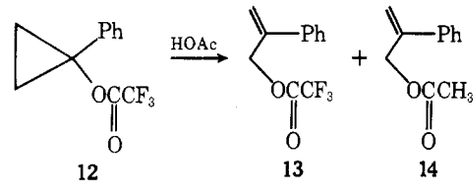


Phenyl trifluroacetate **12** gives mostly a product of internal return, allylic trifluoroacetate **13** along with about 20% allylic acetate **14** at low conversion of **12**. At higher conversion of **12**, concommitent solvolysis of **13** produces more of the allylic acetate **14**. These results parallel those of DePuy[9] in the solvolysis of phenylcyclopropyl tosylate.



Discussion

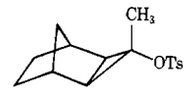
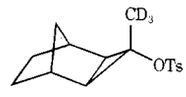
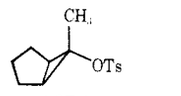
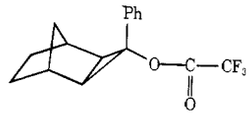
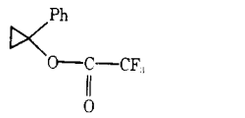
The solvolysis of **2**-OTs is best explained in terms of stepwise formation of a tertiary cyclopropyl cation, **15**, followed by opening to an allylic cation **16** and solvent capture. Similar behavior is seen in the solvolysis of **1**.[5] Initially apparent is the large rate enhancement in the acetolysis of **2**-OTs. A comparison with **1**-OTs shows a rate enhancement of 2.4×10^3. This is attributed to relief of ground state strain, due to an unfavorable methyl–C_8 interaction in **2**. Rate enhancement due to relief of ground state strain (B strain) is a well-documented phenomenon.[10] The actual magnitude of the steric rate acceleration in **2**-OTs is difficult to assess since steric effects could also be important in the solvolysis of **1**-OTs.

Considering the observed steric rate enhancement in **2**-OTs, the β-deuterium isotope effect is quite interesting. The value of 1.33 must be considered quite small in view of the large demand for hyperconjugative stabilization in the unstable cyclopropyl cation. The β-deuterium isotope effect in **1**-OTf[6] is 1.42, a value also considered relatively small. Any steric isotope effects[11] generated by steric crowding in **2**-OTs are not demonstrated in the measured isotope effect of only 1.33.

Servis, Borčić, and Sunko[12] have developed a correlation between the β-deuterium isotope effect and the α-methyl/α-hydrogen rate ratio. The α-methyl/α-hydrogen rate ratio for **2**-OTs is $10^{8.42}$, one of the largest yet determined[13] and indicative of a large demand for hyperconjugative stabilization.[12] The Servis, Borčić, Sunko (SBS) relationship predicts a β effect of 1.48, a value much larger than the observed value of 1.33. The conclusion based on the SBS relationship and comparison to the value for **1**-OTf is that the β-deuterium isotope effect for **2**-OTs is unusually small.

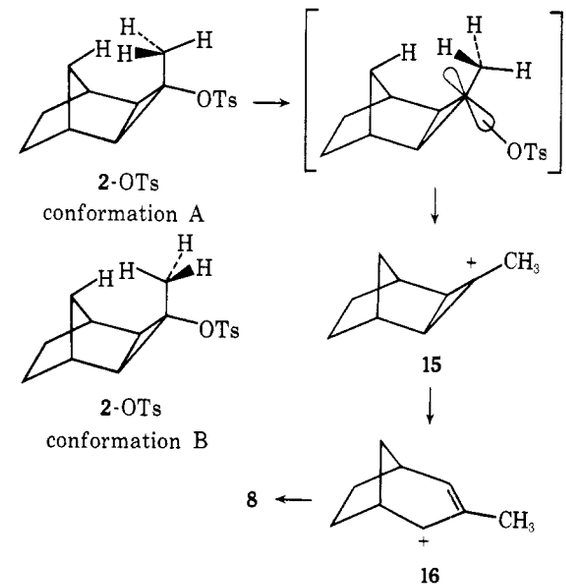
Examination of the possible methyl group conformations

Table I. Solvolysis Rates in Acetic Acid–0.1 M NaOAc

compd	registry no.	T, °C	$10^5 k$, s^{-1}
 2-OTs[e]	42856-12-2	70.0 50.0	54.3 5.48 ± 0.06
 2-OTs-d_3	66966-32-3	50.0	4.13 ± 0.00
 1-OTs[b]	66966-33-4	130.0 110.0 50.0[e]	26.3 3.65 2.28×10^{-3}
 3-OTFA[c]	66966-34-5	100.0 80.0	33.8 3.58
 12[d]	66966-35-6	160.0 142.0 100.0[e]	14.7 2.66 2.61×10^{-2}

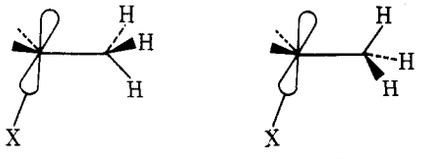
[a] $\Delta H^{\ddagger} = 24.6$ kcal, $\Delta S^{\ddagger} = -2$ eu. [b] $\Delta H^{\ddagger} = 29.6$ kcal, $\Delta S^{\ddagger} = -2$ eu. [c] $\Delta H^{\ddagger} = 29.9$ kcal, $\Delta S^{\ddagger} = 5$ eu. [d] $\Delta H^{\ddagger} = 33.1$ kcal, $\Delta S^{\ddagger} = 0$ eu. [e] Extrapolated value.

in **2**-OTs suggests a reason for this small isotope effect. It is suggested that conformation A is the preferred conformation of **2**-OTs, rather than conformation B in which there is a very unfavorable interaction with the C-8 proton. The hyperconjugative stabilization in the transition state derived from conformation A should be less than in the transition state derived from conformation B. A 0° dihedral angle between the developing p orbital and the adjacent proton, as in B, should



be preferred to the 60° angle in A for the observation of maximum isotope effects.[15] Similar arguments have been used by Shiner[16] to explain decreased isotope effects in conformationally rigid systems. While we do not suggest that **2**-OTs is held rigidly in conformation A, we do suggest that there is some barrier to attainment of a 0° dihedral angle in the transition state. This could account for the smaller than

normal isotope effect as seen in the solvolysis of 2-OTs. Hyperconjugative stabilization in the cationic intermediate de-

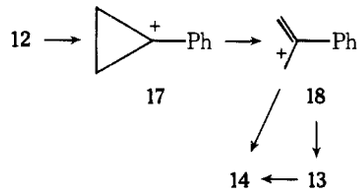


A B

rived from A should be the same as from B, but transition state stabilizations should differ.

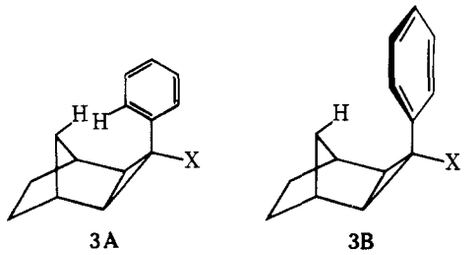
An alternative rationalization for the decreased isotope effect (suggested by a referee) involves the greater ability of 2-OTs-d_3 to populate conformation B due to the lesser steric demand in this substrate with solvolysis occurring preferentially from conformation B. While either of these two rationalizations would explain the reduced isotope effect, it appears clear that the effect is steric in origin.

Solvolysis of 3-OTFA can also be interpreted in terms of stepwise processes leading to a phenyl-substituted cyclopropyl cation and an allylic cation, respectively. Data for 1-phenylcyclopropyl trifluoroacetate (12) can be used to estimate the importance of steric acceleration in the acetolysis of 3-OTFA. We feel that solvolysis of 12 is a good model for the *unassisted* (k_c) stepwise formation of a 1-phenylcyclopropyl cation for the following reasons. It is not unreasonable to expect that the phenyl group could offset *all* of the participation due to concerted C_2–C_3 bond fragmentation during ionization of 12 in



view of the fact that a methyl group has been found to offset most of such participation in solvolysis of 1-methycyclopropyl triflate.[5] Additionally Brown has recently determined a ρ value for solvolysis of substituted phenylcyclopropyl dinitrobenzoates.[2] This rate data, along with DePuy's earlier data[9] indicate *no* abrupt change from a σ participation to a nonparticipating mechanism over a substituent range from *p*-methoxy to *p*-trifluoromethyl.[16] This is despite the fact that the *p*-methoxyphenyl derivative gives mostly ring retained products while the less activated substrates give solely allylic solvolysis products. This supports the stepwise mechanism over the entire aromatic substituent range despite the observation of only allylic products from 12. Finally, more direct evidence for the intermediacy of the 1-phenylcyclopropyl cation is its capture by borohydride in the solvolysis of 1-phenylcyclopropyl tosylate in aqueous diglyme.[5]

With these facts in mind, the steric enhancement in solvolysis rate of 3-OTFA is apparent. What is surprising is the fact that the magnitude (only a factor of 10^3) is less than steric acceleration in 2-OTs. Conformational effects again suggest a reason for this unexpected behavior. The "normal" conformation of a phenyl group bonded directly to a cyclopropane is as shown in **3A**.[18,19b] Due to an unfavorable steric interaction with the C-8 hydrogen, this conformation is unstable



3A 3B

relative to **3B**. It is not unreasonable to expect that a phenyl group held in conformation **3B** is less sterically demanding than the methyl group in **2**.

The NMR spectra of **9**, 3-OH, and 3-OTFA support the suggested conformation of **3B**. The aromatic region of **9** appears essentially as a singlet while that of **10** is complex. Closs[19] has discussed the reasons for this behavior in terms of phenyl conformations and anisotropic effects of the cyclopropane ring. This reasoning also supports **3B** as the preferred conformation of **9**. Additionally the syn C-8 protons in **9**, 3-OH, and 3-OTFA are shifted upfield, to δ 0.40, 0.37, and 0.40, respectively, due to the shielding effect of the aromatic ring in conformation **3B**. The corresponding syn C-8 proton of **10** appears at δ 1.20. The conclusion is that the preferred conformation of 3-OTFA is as in **3B** and that steric effects of the phenyl group in this conformation do not surpass those of the methyl group in 2-OTs.

In summary, this work shows the importance of steric effects in the ionization of tertiary cyclopropyl systems **2** and **3** as well as the importance of transition state conformation of a methyl group in determining β-deuterium isotope effects in **2**. The magnitudes of these steric effects are contrary to what is expected based on conformationally determined A values[20] of Taft E_s values[21] for phenyl vs. methyl.

Experimental Section

General. Gas chromatographic analyses were carried out on a Hewlett Packard Model 5750 using a 5 ft 5% SE 30 on Chromosorb G column. NMR spectra were recorded on a Varian A60A or a Varian XL-100 spectrometer in the Fourier transform mode and are reported vs. tetramethylsilane. Mass spectra were recorded on an AE1 Scientific Apparatus MS902 spectrometer.

Preparation of 2-OH. A solution of peroxytrifluoroacetic acid prepared from 811 mg of 90% hydrogen peroxide and 5.36 g of trifluoroacetic anhydride in 30 mL of methylene chloride was added slowly dropwise to a stirred solution of 1.25 g of ketone **4**[7] in 40 mL of methylene chloride containing 25 g of dibasic potassium phosphate. After completion of the addition the mixture was refluxed for 1.5 h. The entire solution was then taken up into ether and water, washed with sodium carbonate solution, and dried over sodium sulfate. Solvents were removed by distillation through a Vigreux column and the residue was distilled to give 1.03 g (75%) of previously reported *endo*-3-methyl-*exo*-tricyclo[3.2.1.$0^{2,4}$]oct-*exo*-3-yl acetate,[8] bp 60–63 °C (0.52 mm): NMR (CCl_4) δ 2.44 (2 H, m), 1.84 (3 H, s), 1.53 (3 H, s), 1.50–0.50 (8 H, m).

A solution of 0.88 g of the acetate obtained above in 7 mL of ether was cooled to 0 °C and 6.8 mL of 1.84 M methyllithium was added dropwise. After completion of the addition, the solution was cooled to −78 °C and 0.65 g of acetic acid in 5 mL of ether was added. After warming to approximately 10 °C, the organic phase was separated, washed with water and saturated sodium chloride solution, and dried over sodium sulfate. Solvent was removed on a rotary evaporator with the last traces being removed by vacuum pump. The yield of crude previously reported[8] alcohol 2-OH was 0.55 g (82%). Alcohol 2-OH was relatively unstable with respect to rearrangement to 2-acetylnorbornane.

Preparation of 2-OTs. A solution of 750 mg of *p*-toluenesulfonyl chloride in 5 mL of pyridine was cooled to 0 °C and 0.55 g of alcohol 2-OH was added. The solution was stored in a refrigerator for 29 h and an aqueous workup followed. Pyridine was removed by washing with cold, dilute hydrochloric acid. After drying the organic extract over anhydrous sodium sulfate, the solvent was removed by a rotary evaporator. The residue, which crystallized on cooling, was slurried with cold pentane and the solid (415 mg, 36%, mp 44–46 °C) was collected and washed with pentane: NMR (CCl_4) δ 7.85–7.15 (4 H, AA'BB' quartet), 2.45 (3 H, s), 1.72 (3 H, s), 1.55–1.10 (7 H, m), 0.74 (1 H, broad d, J = 11 Hz). Traces of unreacted *p*-toluenesulfonyl chloride in 2-OTs produced in certain runs were found to interfere with accurate determination of rate constants. To avoid this problem, the crude tosylate in pyridine was treated with a small amount of aqueous potassium hydroxide solution to remove the unreacted *p*-toluenesulfonyl chloride before crystallization.

Anal. Calcd for $C_{16}H_{20}O_3S$: C, 65.72; H, 6.89. Found: C, 65.90; H, 7.09.

Preparation of Ethyl Pyruvate-d_3 (5). Methylmagnesium-d_3 iodide was prepared from 25 g of methyl iodide (Aldrich Chemical Co.)

and 5.13 g of magnesium in 100-d_3 mL of ether. The Grignard reagent was added dropwise over a 2.5-h period to a solution of 68.8 g of diethyl oxalate in 140 mL of ether held at −78 °C. After completion of the addition, the mixture was warmed to 0 °C and then decomposed with ammonium chloride solution. The organic phase was separated and dried over sodium sulfate. Solvent was removed by distillation through a Vigreux column and the residue was distilled through a column packed with glass helices at 100 mm. The fraction boiling at 88–93 °C (9.49 g, 46%) was ethyl pyruvate-d_3 (**5**). NMR analysis shows no signal at δ 1.95 due to undeuterated ethyl pyruvate. A higher boiling fraction (115 °C) consisting of unreacted diethyl oxalate could also be collected.

Preparation of 2-OTs-d_3. The preparation of ethyl diazopropionate-d_3 (**6**) was accomplished by vacuum pyrolysis of the sodium salt of the tosylhydrazone of **5** as previously described for preparation of undeuterated ethyl diazopropionate. The addition of **6** to norbornene was as previously described for the undeuterated ethyl diazopropionate.[22] The remainder of the sequence for the preparation of 2-OTs-d_3 was completely analogous to the preparation of 2-OTs. The NMR spectrum of 2-OTs-d_3 showed no signal at δ 1.72.

Reaction of Norbornene with Benzyl Chloride and LiTMP. A solution of LiTMP[23] prepared from 17.5 mL of 1.84 M methyllithium and 5.02 g of tetramethylpiperidine in 4 mL of ether was added dropwise to a solution of 3.46 g of benzyl chloride and 19.9 g of norbornene in 8 mL of ether at −10 °C over a 1-h period. After completion of the addition, the mixture was warmed to room temperature and stirring was continued for 3.2 h. The mixture was quenched with water and the organic phase was separated and washed with dilute hydrochloric acid until the aqueous phase remained acidic. After washing with saturated sodium chloride solution and drying over sodium sulfate, the solvent and norbornene were removed by distillation through a Vigreux column at atmospheric pressure. The residue was distilled through a short path condenser and collected in two fractions. Fraction 1, bp 62–69 °C (0.04 mm), weighed 0.96 g and was enriched in the *endo*-phenyl isomer **9**. Fraction 2, bp 69–95 °C (0.04 mm), weighed 0.96 g and was enriched in the *exo*-phenyl isomer **10**. The total yield of **9** and **10** was 1.92 g (38%). A previous run showed a 1.2 to 1 ratio of 9:10 as determined by gas chromatography. Samples of each product were isolated by preparative gas chromatography. NMR of **9** (CCl_4) δ 7.17 (5 H, bs), 2.40 (2 H, m), 1.78 (1 H, t, J = 7.5 Hz), 1.36 (4 H, m), 1.11 (2 H, d, J = 7.5 Hz), 0.40 (2 H, m); mass spectroscopic molecular weight 184.1254 (calcd. for $C_{14}H_{16}$, 184.1252). NMR of **10** (CCl_4) δ 7.3–6.7 (5 H, m), 2.42 (2 H, m), 1.77 (1 H, t, J = 3 Hz), 1.40 (4 H, m), 1.20 (1 H, br d, J = 11 Hz), 0.98 (2 H, d, J = 3 Hz), 0.75 (1 H, br d, J = 11 Hz); mass spectroscopic molecular weight 184.1254 (calcd. for $C_{14}H_{16}$, 184.1252).

Preparation of 3-OH. A mixture of phenylcyclopropanes **9** and **10** (0.96 g of the first fraction previously described) was added to a solution of 3.25 mL of 2.4 M *n*-butyllithium in hexane containing 1.01 g of tetramethylethylenediamine and 3 mL of ether at 0 °C. The solution turned light red upon addition of the mixture of **9** and **10**. The solution was then stirred at room temperature for 1 h after which time the solution was a deep red color. The mixture was then cooled to −35 °C and the flask was equipped with a gas bubbler. Oxygen was continuously added at this temperature for 40 min. The red color had significantly faded. The mixture was warmed to −20 °C and 0.97 g of acetic acid was added to the reaction mixture. Water was then added and the organic phase was separated, washed with water and saturated sodium chloride solution, and dried over sodium sulfate. The solvent was removed by rotary evaporation. Crystals of 3-OH formed on removal of the solvent. The residue was slurried in cold pentane and the solid was collected to give 0.17 g of 3-OH: mp 146–146.5 °C; NMR (CCl_4) δ 7.30 (5 H, br s), 2.33 (2 H, m), 1.47 (1 H, s, exchange with D_2O), 1.38 (4 H, br s), 1.24 (2 H, s), 0.37 (2 H, m); mass spectroscopic molecular weight, 200.1276 (calcd. for $C_{14}H_{16}O$, 200.1201).

Preparation of 3-OTFA. A solution of 140 mg of trifluoroacetic anhydride in 1.5 mL of pyridine was cooled to 0 °C and 81 mg of 3-OH was added. The mixture was stored in a refrigerator overnight. After an aqueous workup with ether extraction, pyridine was removed by washing the organic phase with dilute hydrochloric acid. The organic phase was dried over sodium sulfate and the solvent was removed by distillation through a Vigreux column. The residue was distilled to give 81 mg (67%) of 3-OTFA, bp 60–65 °C (0.04 mm). Gas chromatographic analysis showed a single product. On storage in a refrigerator, 3-OTFA crystallized: mp 50–51 °C; NMR ($CDCl_3$) δ 7.60–7.20 (5 H, m), 2.52 (2 H, br s), 1.58 (4 H, br s), 1.41 (2 H, br s), 0.40 (2 H, br s); mass spectroscopic molecular weight 296.1064 (calcd. for $C_{16}H_{15}F_3O_2$, 296.1024).

Preparation of 1-Phenylcyclopropyl Trifluoroacetate (12). A solution of 4.7 g of trifluoroacetic anhydride in 15 mL of pyridine was cooled to 0 °C and 2.00 g of 1-phenylcyclopropanol[24] was added. After 3.5 h at 10 °C, an aqueous workup followed. The product was isolated by distillation giving 3.06 g (89%) of **12**: bp 56–58 °C (1.6 mm); NMR (CCl_4) δ 8.60–8.18 (5 H, m), 1.50–1.20 (4 H, m); mass spectroscopic molecular weight 230.0553 (calcd. for $C_{11}H_9F_3O_2$, 230.0555).

Solvolysis of 1-OTs and 2-OTs. Kinetic Method. The kinetic procedure for solvolysis of tosylates involved the titrimetric method already described.[3]

Solvolysis of 3-OTFA. Kinetic Method. Solvolysis rates of 3-OTFA were measured using the sealed tube method and were monitored by ultraviolet spectroscopy by observing the appearance of the styrene chomophore at 250 nm. At given time intervals, 1-mL aliquots of a solution of 3-OTFA in acetic acid were diluted to 25 mL with methanol and the absorbance at 250 nm was recorded. Rate constants were calculated by the usual method and agreed well with rates estimated by gas chromatographic analysis.

Solvolysis of 1-Phenylcyclopropyl Trifluoroacetate (12). Kinetics Method. Solvolysis of **12** was done using the sealed tube method and was monitored by gas chromatography using biphenyl as an internal standard. At given time intervals, 1-mL aliquots of a solution of **12** in acetic acid were diluted with 2.5 mL of ether. Extractions were done with 2.5 mL of water, 3.0 mL of water, and 1.0 mL of Na_2CO solution, respectively. A solution of biphenyl (1.0 mL) prepared from 0.451 g in 25 mL of ether was added followed by Na_2SO_4. The solutions were then analyzed for remaining **12** by gas chromatography at 100 °C. Rate constants were calculated in the usual manner by the least-squares method and had minimum correlation coefficients of 0.9996.

Solvolysis of 2-OTs, 3-OTFA, and 12. Product Analyses. A sample of substrate in acetic acid–0.1 M NaOAc was heated (sealed tube) for 10 half-lives. Trifluoroacetate **12** was only heated for 2 half-lives. An aqueous workup followed. Gas chromatographic analysis of the products from 2-OTs and 3-OTFA showed single products, **8** and **11**, respectively. Similar analysis of the solvolysis of **12** showed the presence of **13** and **14**. Samples of all products were isolated by preparative gas chromatography and structures were confirmed by NMR and infrared and mass spectroscopy. NMR of **8** ($CDCl_3$) δ 5.88 (1 H, doublet of quartets, J = 7, 1.5 Hz), 4.80 (1 H, d, J = 3 Hz), 2.46 (2 H, m), 2.07 (3 H, s), 1.95–1.08 (9 H, m with doublet, J = 1.5 Hz at 1.58); mass spectroscopic molecular weight 180.1165 (calcd. for $C_{11}H_{16}O_2$, 180.1150). NMR of **11** ($CDCl_3$) δ 7.3 (5 H, m), 6.57 (1 H, d, J = 7 Hz), 5.60 (1 H, d, J = 3 Hz), 2.88–2.48 (2 H, m), 1.96 (3 H, s), 1.86–1.18 (6 H, m); mass spectroscopic molecular weight 242.1293 (calcd. for $C_{16}H_{18}O_2$, 242.1307). NMR of **13**[9] ($CDCl_3$) δ 7.42 (5 H, bs), 5.67 (1 H, s), 5.47 (1 H, s), 5.25 (2 H, s). NMR of **14** ($CDCl_3$) δ 7.6–7.2 (5 H, m), 5.58 (1 H, bs), 5.40 (1 H, bs), 2.08 (3 H, s).

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Registry No.—2-OH, 66966-36-7; 3-OH, 66966-37-8; **4**, 42856-10-0; **5**, 66966-38-9; **8**, 66966-39-0; **9**, 67010-34-8; **10**, 66966-40-3; **11**, 66966-41-4; **13**, 66966-42-5; **14**, 7534-40-9; *endo*-3-methyl-*exo*-tricyclo[3.2.1.$0^{2,4}$]oct-*exo*-3-yl acetate, 67010-35-9; MeI-d_3, 865-50-9; diethyl oxalate, 95-92-1; benzyl chloride, 100-44-7; norbornene, 498-66-8; 1-phenylcyclopropanol, 29526-96-3.

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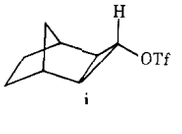

i

for i at 50 °C[14] and a triflate:tosylate rate ratio of $10^{4.76}$. This is the measured rate ratio of 1-OTf/1-OTs at 50 °C. See ref 5 and 14 and Table I.

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Steric Relief Control of Solvolysis Rates of 1-Alkyl-2-adamantyl Substrates. Empirical Force-Field Calculations

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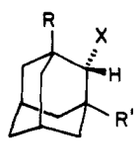
8-Cyano-4-*exo*-protoadamantanol (*exo*-**3**) isolated from the solvolysis of 1-cyano-2-adamantyl tresylate (**1g**-OTres) was oxidized to 8-cyano-4-protoadamantanone (**4**), which was reduced by sodium borohydride to a 5:4 mixture of 8-cyano-4-*endo*-protoadamantanol (*endo*-**3**) and *exo*-**3**. No *endo*-**3** was evidenced in the original solvolysis mixture from **1g**-OTres, so that solvolysis of **1g**-OTres is as stereoselective as the solvolysis of the 1-methyl analogue (**1b**-OTs). The variation of steric strain in the ionization of 1-alkyl-2-adamantyl substrates (**1b–e**) was evaluated by force-field calculations. A significant relief of steric strain [Δ(strain)] was found for this process, and it was correlated with the rates of solvolysis (k) by the equation: $\log k = 0.63\Delta(\text{strain}) - 6.73$ ($r = 0.9693$, SD = 0.271). Thus, the rate increase produced by 1-alkyl substituents in the solvolysis of 2-adamantyl substrates is fully accounted for by the steric strain relief (which can be adjusted for a more refined treatment by a smaller polar effect of 1-substituents), and no other mechanistic assumption is necessary.

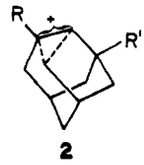
Empirical force field calculations[1] have been used to solve various problems in physical organic chemistry.[2] Recent applications permitted estimation of the most stable conformations of known[3] or as yet unsynthesized compounds;[4] calculation of barriers and pathways for conformer interconversions;[5] determination of the most stable member of a (usually large) family of isomeric hydrocarbons;[6] predictions or rationalizations of pathways in carbocationic isomerizations;[6a,7] and hydrogenolysis reactions of strained polycycles.[8] Examples of rationalization of products obtained in cyclizations[9] and in ring enlargements of carbocations[10] can also be noted. A special group of applications consists of the calculations of steric strain variations in reactions involving a change of hybridization at the reaction center and the correlation of reaction rates with the variations in strain energy. Thus, ester hydrolysis[11] and oxidation of secondary alcohols[12] were successfully correlated. The most useful results, however, were obtained for the solvolytic reactions involving carbocations by Schleyer, who pioneered the use of force field calculations for mechanistic studies of chemical reactions.[13]

It is the purpose of this paper to report on the application of this approach to the solvolysis of 1-alkyl-2-adamantyl substrates and to present new experiments in the study of the 1-cyano analogue.[14]

Studies of the solvolysis of the parent (**1a**) and 1-alkyl-substituted 2-adamantyl bromides (**1b–e**-Br) and sulfonates (**1b–e**-OSO_2Ar) have been interpreted to indicate that the ionization of **1b–e** is anchimerically assisted (K_Δ process[15]) and involves σ-bridged ions (**2b–e**) as intermediates.[16] It was stated that **1b** provides a "textbook" example of "nonclassical" ion, . . . "free from the many anomalies of the 2-norbornyl system".[16c] A subsequent investigation of related substrates carrying deactivating substituents (**1f,g**)[17] led the present writer to question[14] some of the conclusions expressed by previous workers.[16] Such a viewpoint elicited interest[18] as well as criticism.[19] Most of the latter concerned the existence[14] of a relationship between rearrangement and rate enhancement in the solvolysis of 1-substituted 2-adamantyl substrates (**1**). It was considered[14] that, if the formation of rearranged product is due to bridging, then the measured solvolysis rate is faster than the value expected in the absence of bridging. A precise mathematical relationship between rates and amount of rearrangement for **1** could not be deduced,[20] but in the same solvent and under the same conditions a larger amount of rearranged product possibly reflects a larger acceleration.[14] In other words, if two phenomena (rate enhancement and rearrangement) are produced by the same cause (bridging) they are necessarily related. As this point was also recognized by the previous workers,[21] it needs no further elaboration. One valid observation remained, however: In the solvolysis of the cyano derivative (**1g**-OTres), a rearranged product, 8-cyanotricyclo[4.3.1.$0^{3,8}$]decan-4-*exo*-ol (8-cyano-4-*exo*-protoadamantanol) (*exo*-**3**) was formed (38%) along with the starting alcohol (**1g**-OH).[14] The absence of the



1 (X = OH, Br, OTs, OTres)



2

a R=R'=H
b R=Me, R'=H
c R=Et, R'=H
d R=*i*-Pr, R'=H
e R=*t*-Bu, R'=H
f R=H, R'=COO Me
g R=H, R'=CN

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