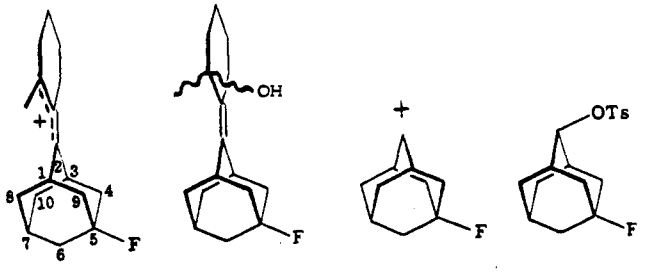
Absence of External π Assistance in the Generation of an Allylic Cation

Mary K. Boyd,[1a] Man-hua Lin,[1b] and W. J. le Noble*

Department of Chemistry, State University of New York, Stony Brook, New York 11794

Received April 27, 1993

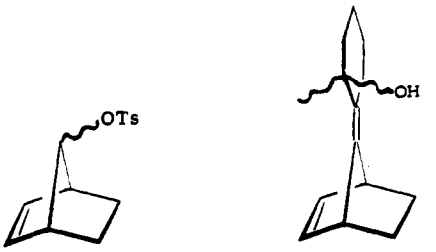
We reported[2] in 1989 that the rates of generation of allylic cation **1** from the diastereomeric percursor alcohols **2** were affected by the presence of the 5-fluoro substituent in a way just opposite to those of the simple 2-adamantyl cation **3**: whereas the *anti*-allyl alcohol reacts up to 45 times faster than the *syn*, the *Z*-tosylate **4** solvolyzes 200



1 **2** **3** **4**

times faster than the *E*-epimer. The latter observation[3] and others of a similar vein[4-6] cannot be understood without invoking σ assistance by the antiperiplanar C_1–C_8 and C_3–C_{10} bonds (hyperconjugation);[7] the former led to our hypothesis that the same bonds assist even in the formation of the allylic cation, but with opposite stereochemical results because of the node in the allylic π system (orbital symmetry control). We took note[2] of the question whether an even more dramatic inversion of stereochemistry might occur in systems in which π participation occurs, since such assistance sometimes leads to extremely large rate effects.

The archetypical example[8] of π participation is provided by the epimeric pair of 7-norbornenyl tosylates **5**, with the *E*-isomer solvolyzing faster than the *Z*-isomer by a factor of 10^7. We now report that in the acid-catalyzed dehydration of allylic alcohols **6**, there appears to be no π participation at all. This conclusion is, of course, subject to the unavoidable possibility that a remnant of such participation is present but coincidentally canceled by a minor involvement of the antiperiplanar σ electrons with the opposite effect.

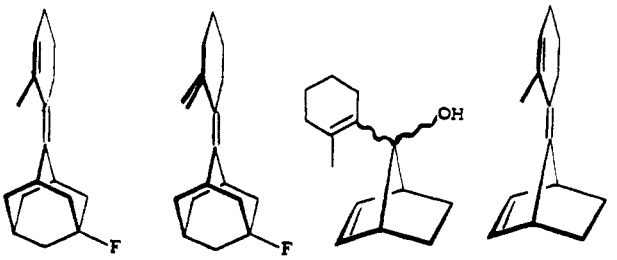


5 **6**

Results and Discussion

An equimolar mixture of alcohols **6** was prepared by condensation of a cyclohexanimine with 7-norbornenone, in a reaction analogous to that used before[2] in the preparation of (*E*)- and (*Z*)-**2**. The alcohols could not be chromatographically separated although the attempts did provide us with mixtures enriched in either isomer and a small sample of a single one. Upon dissolution of the mixtures at room temperature in moist acetonitrile with a sulfuric acid concentration of 10^{-4} M, both epimers vanished at identical rates; the composition of remaining mixture was the same as that of the initial sample throughout the reaction regardless of which isomer was in excess to begin with. This constancy in composition is clearly not the result of rapid equilibration. The norbornenyl double bond does not affect the relative heterolysis rates in this case.[9]

One additional, if more minor, difference was noted between the dehydration of **2** and that of **6**. Whereas (*E*)- and (*Z*)-**2** led directly to a mixture of exo- and endocyclic dienes **7** and **8**, mixtures of **6** decomposed by way of isomeric alcohols **9** which in turn led irreversibly to the same endocyclic triene **10**.



7 **8** **9** **10**

The relative dehydration rates of mixed alcohols **9** were also of interest, but they could not be measured because both the ^1H and ^{13}C NMR spectra were very similar; in fact, we were not certain that we had a mixture until a

(1) (a) Present address: Chemistry Department, Loyola University, Chicago, IL 60626. (b) Present address: Plastics Research Department, Rohm and Haas Company, Box 219, Bristol, PA 19007.

(2) Lin, M.-h.; Boyd, M. K.; le Noble, W. J. *J. Am. Chem. Soc.* **1989**, *111*, 8746. When this manuscript was submitted, a referee astutely remarked that of the two allylic isomers of **2**, (*E*)- and (*Z*)-5-fluoro-2-hydroxy-2-(2-methyl-1-cyclohexenyl)adamantane, the latter should dehydrate faster than the former, in contrast to the behavior of isomers **2** themselves. We subsequently carried out this experiment and found the referee's prediction to be correct. The mixture of alcohols was obtained by the addition of 1-lithio-2-methylcyclohexene (Villemin, D.; Bouchta, L. *Synthesis* **1989**, 143. Cohen, T.; Doubleday, M. D. *J. Org. Chem.* **1990**, *55*, 4784.) to 5-fluoro-2-adamantanone; the *E*-isomer was predominant by roughly 10:1. It was recognized by the greater sensitivity to $Eu(fod)_3$ of $C_{8,10}$ (unsplit by F) than of $C_{4,9}$ ($J_{CF} \simeq 20$ Hz); the opposite is true of the minor isomer. Treatment of the mixture with dilute acid and monitoring by means of ^{19}F NMR showed that the minor isomer disappeared faster than the major one. We are indebted to Dr. Ashis Mukherjee for this experiment.

(3) Xie, M.; le Noble, W. J. *J. Org. Chem.* **1989**, *54*, 3839.

(4) Storegund, H. J.; Whiting, M. C. *J. Chem. Soc., Perkin. Trans. 2* **1975**, 1452.

(5) Adcock, W.; Coope, J.; Shiner, V. J.; Trout, N. A. *J. Org. Chem.* **1990**, *55*, 1411.

(6) Finne, E. S.; Gunn, T. R.; Sorensen, T. S. *J. Am. Chem. Soc.* **1987**, *109*, 7811.

(7) Cheung, C. K.; Tseng, L. T.; Lin, M.-h.; Srivastava, S.; le Noble, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 1598.

(8) Winstein, S.; Shatavsky, M.; Norton, C.; Woodward, R. B. *J. Am. Chem. Soc.* **1955**, *77*, 4183.

(9) A repeat experiment with (*E*)- and (*Z*)-**2** in this medium gave a reduced (but still clearly observable) ratio as compared with that used earlier.

0022-3263/93/1958-5541$04.00/0

reaction with methyl iodide under basic conditions procuded a mixture of methyl ethers in which the two methoxy and vinyl proton resonances could be clearly seen. Treatment of 9 with acetic anhydride under basic conditions also gave a product that was obviously a mixture of the two epimeric acetates. Examination of the mixture of ethers in aqueous acidic acetonitrile then showed that in this case also, elimination of the two epimers proceeded at identical rates to give 10.

The conclusion is that, their names notwithstanding, sigma and pi participation are very different phenomena - a point we have also made elsewhere.[10] The principal distinction is that in π participation, remote π electrons act through-space like an external nucleophile in a process that can be swamped[11] by the introduction of stabilizing σ substituents, while in σ participation, antiperiplanar σ electrons are involved through-bond in a hyperconjugative manner that cannot be suppressed by such substituents. Failure to recognize this difference[12] was a major cause of the inconclusive nature of the long debate about nonclassical ions.

Experimental Section

Synthesis. 7-Norbornenone was prepared by the procedures of Gassman and Marshall.[13] The condensation of this ketone with *N*-*n*-butylcyclohexanimine followed procedures described previously;[2] it produced 7-(2-oxocyclohexyl)-7-norbornenol (possibly a mixture of two diastereomers) as a pale yellow oil in 55% yield: ^{1}H NMR ($CDCl_3$) δ 5.87 (s, 2H), 3.50 (s, 2H), 3.0–1.5 (m, 12H), 0.83 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 217.24, 136.06, 133.24, 91.48, 50.35, 48.89, 46.18, 43.22, 30.77, 28.09, 25.12, 22.80, 22.57. Treatment of the alcohol(s) with *p*-toluenesulfonic acid in benzene in a Dean–Stark apparatus furnished the single (racemic) enone 7-(2-oxocyclohexylidene)norbornene; after aqueous workup and silica gel chromatography with 10% ethyl acetate–hexane, an 87% yield was obtained as a colorless oil: ^{1}H NMR, δ 6.08 (s, 2H), 3.91 (s, 1H), 3.21 (s, 1H), 2.35–1.08 (m, 12H); ^{13}C NMR δ 202.36, 163.20, 136.10, 134.09, 114.96, 41.86, 41.81, 28.96, 24.36, 24.16, 23.88, 23.58. The ketone (0.71 g, 3.8 mM) in THF (15 mL) was treated with methyllithium in hexane (10 mL, 1.4 M); after aqueous workup and column chromatography, a white solid mixture of alcohols 6 was obtained with approximately equimolar composition as judged by the methyl ^{1}H peaks: mp 58–60 °C; ^{1}H NMR, δ 6.10 (m, 2H), 4.01 (m, 1H), 3.38 (m, 1H), 2.4–1.0 (m, 11H); 1.29 and 1.28 (2s, 3H), 1.05 (d, 2H). Repeated attempts at chromatographic separation led to enriched mixtures ($\geq$2:1) which allowed us to group the ^{13}C NMR signals: isomer "1" (^{1}H methyl at δ 1.29) δ 147.51, 136.47, 135.02, 120.44, 74.57, 43.26, 42.75, 41.75, 28.98, 27.24, 26.88, 24.60, 24.13, 23.65; isomer "2" (^{1}H methyl at δ 1.28) δ 147.17, 136.16, 135.52, 120.91, 74.15, 43.15, 42.92, 41.67, 28.50, 27.39, 26.44, 24.60, 24.13, 23.55. A small pure sample of isomer "1" was obtained eventually, and the peak assignments were confirmed.

Reaction of Alcohols 6 with Acid. An equimolar mixture of alcohols 6 (95 mg, 0.05 mM) in acetonitrile (10 mL) was treated with 0.05 mL of 0.02 M aqueous sulfuric acid at room temperature. After 30 minutes, neutralization and workup gave 85 mg (93%) of alcohol(s) 9 as a colorless oil: ^{1}H NMR δ 5.92 (s, 2H), 2.86 (bs, 2H), 2.05–1.45 (m, 11H), 1.78 (s, 3H), 0.92 (2s, 2H); ^{13}C NMR, δ 134.04, 132.72, 132.60, 93.50, 48.16, 33.25, 30.74, 23.60, 22.81, 22.65, 21.54. Instead, use of a 1-mL sample of 0.04 M aqueous sulfuric acid and a reaction time of 2 days gave a 77% yield (30 mg) of the triene 7-[1-(2-methylcyclohex-2-enylidene)]norbornene (10) as a pale yellow oil. ^{1}H NMR, δ 6.22 (s, 2H), 5.48 (s, 1H), 3.71 (s, 1H), 3.41 (s, 1H), 2.24–1.55 (m, 8H), 2.10 (s, 3H), 1.07 (m, 2H). ^{13}C NMR, δ 150.30, 136.30, 135.57, 133.26, 127.46, 114.41, 43.09, 42.75, 28.84, 26.35, 24.95, 24.38, 23.65, 23.23. A kinetic study of the isomerization of 6 (2 mg) was done in CD_3CN (0.5 mL) containing a trace amount of cyclohexane standard. This solution was treated with 0.025 mg of H_2SO_4 in 0.25 μL D_2O (prepared by repeated dilutions) at room temperature; ^{1}H NMR spectra were measured at 1-min intervals. Two mixtures were so studied with epimeric compositions 38:62 and 53:47, as judged by the ratio of the δ 1.29 and 1.28 ^{1}H NMR signals. In both experiments, the original ratio remained unchanged during more than 90% of the reaction.

Study of Alcohol 9. Although alcohol(s) 9 seemed to be a single epimer as judged by its NMR spectra, epimeric mixtures of both acetate esters and methyl ethers were obtained, as follows. Alcohol 9 (40 mg, 0.020 mM) and 4-(dimethylamino)pyridine (23 mg, 0.021 mM) were dissolved in triethylamine (freshly distilled from CaH_2) under nitrogen, and acetic anhydride (0.1 mL) was added by syringe at room temperature. The reaction was 60% complete at 40 h, as judged by TLC. Silica gel column chromatography with CH_2Cl_2 served to remove the pyridine; subsequent chromatography with 10% ethyl acetate in hexane gave 10 mg of unreacted 9 and 25 mg of acetate as a yellow oil. Its ^{1}H NMR spectrum showed it to be a mixture: δ 6.02 and 5.80 (s and s), 3.40 and 3.20 (s and s), 1.94 (s), 1.88–0.98 (m). Alcohol 9 (30 mg, 0.015 mM) in THF (2 mL) was added by syringe to sodium hydride (35 mg, as 50% dispersion in oil, rinsed twice with hexane and covered with THF (2 mL)), followed by methyl iodide (40 μL, 0.06 mM) under nitrogen. After the mixture was stirred overnight, methanol was added. After further workup, 22 mg (63%) of an ether product was analyzed by ^{1}H NMR which gave similar evidence of the presence of a mixture: δ 6.0 (s), 5.88 (s), 3.04 (s), 3.02 (s), 2.96 (s), 2.10–0.89 (m). Treatment of this mixture with dilute H_2SO_4 in CD_3CN (CH_2Cl_2 as internal standard) and ^{1}H NMR monitoring showed that both ethers hydrolyzed at equal rates to give alcohol 9.

Acknowledgment. M.K.B. is pleased to acknowledge the Postdoctoral Fellowship support by the National Sciences and Engineering Council of Canada. The National Science Foundation supported this investigation. We are also pleased to acknowledge our indebtedness to Professors R. G. Bergman for a conversation which stimulated this work, and P.G. Gassman for a sample of 1,2-dichloro-1-methylcyclohexane. Dr. A. Mukherjee carried out the experiment mentioned in footnote 2.

Supplementary Material Available: ^{1}H and ^{13}C NMR spectra of mixtures of 6, 9, and the methyl ethers of 9, of a single isomer of 6, and of 10 (13 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead for ordering information.

(10) Lin, M.-h.; Cheung, C. K.; le Noble, W. J. *J. Am. Chem. Soc.* **1988**, *110*, 6562.
(11) (a) Gassman, P. G.; Zeller, J.; Lumb, J. T. *J. Chem. Soc., Chem. Commun.* **1968**, 69. (b) Gassman, P. G.; Fentiman, A. F. *J. Am. Chem. Soc.* **1970**, *92*, 2549.
(12) le Noble, W. J. *Croat Chem. Acta* (special issue) **1992**, 1968.
(13) Gassman, P. G.; Marshall, J. L. *Org. Synth.* **1968**, *48*, 25, 68.