Neighboring Group Participation by the Carbon–Carbon Bond of an Epoxide. Synthesis and Solvolysis of Derivatives of 3-Oxa-*endo*-tricyclo[3.2.1.$0^{2,4}$]octan-*anti*-8-ol

Paul G. Gassman,* John G. Schaffhausen, and Peter W. Raynolds

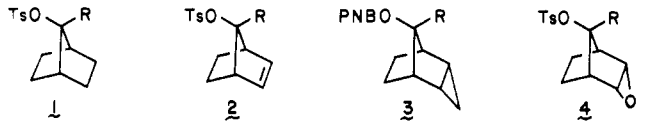
Contribution from the Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455. *Received October 9, 1981*

Abstract: α-Methyl/hydrogen rate ratios have been used to establish the presence of neighboring group participation by the carbon–carbon bond of epoxides in solvolysis reactions. As a model, the α-methyl/hydrogen rate ratio for the *endo*-tricyclo[3.2.1.$0^{2,4}$]oct-*anti*-8-yl system was determined to be 31. When the methylene of the cyclopropyl moiety was replaced by an oxygen, this α-CH_3/H rate ratio was found to be 1500. These ratios were compared to the value of 1.3×10^8 which was found for the bicyclo[2.2.1]hept-7-yl system and of 7.6×10^3 for the bicyclo[2.2.1]hept-2-en-*anti*-7-yl system. These ratios imply that the C–C bond of the epoxide function of 3-oxa-*endo*-tricyclo[3.2.1.$0^{2,4}$]oct-*anti*-8-yl derivatives is a powerful neighboring group in solvolysis reactions and is comparable to the double bond of the bicyclo[2.2.1]hept-2-en-*anti*-7-yl system as a neighboring group.

The carbon–carbon σ bond of the cyclopropyl group has been established as an extremely powerful neighboring group in certain solvolysis reactions.[1] Because of the similarities in ring strain between cyclopropanes and epoxides, attempts have been made to demonstrate that the carbon–carbon bond of an epoxide could participate in solvolysis reactions in a manner similar to that observed with cyclopropanes. Evidence gathered thus far[2] has been unconvincing. We now present data that firmly establish that the carbon–carbon bond of an epoxide can be a powerful neighboring group.

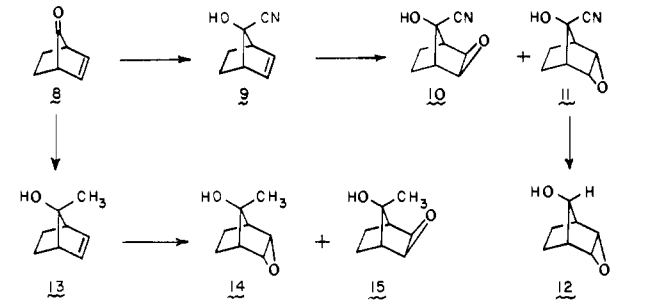
A major problem associated with any determination of neighboring group participation by a small heterocyclic ring such as an epoxide is an assessment of the rate retardation that will result from the relative electronegativity of the heteroatom. In the present study, this problem is manifest in determining the balance between the electron-withdrawing effect of the oxygen of the epoxide and the effect of the carbon–carbon σ bond as a neighboring group. In order to circumvent this dilemma, we chose to use α-CH_3/H rate ratios as a measure of neighboring group participation in the transition state for ionization. Our chosen substrate was the 3-oxa-*endo*-tricyclo[3.2.1.$0^{2,4}$]oct-*anti*-8-yl system. Methyl/hydrogen rate ratios had been determined previously for the bicyclo[2.2.1]heptyl system, **1** (Chart I), and for the bicyclo[2.2.1]hept-2-en-7-*anti*-yl system, **2**.[3,4] The 10^8 rate ratio observed for **1** was felt to be a reasonable measure of the methyl effect in a derivative of this system which lacked neighboring group participation,[3d] while the value of 10^3 observed for **2** indicated that the methyl substituent effect should be much smaller than 10^8 in the presence of major charge delocalization

Chart I



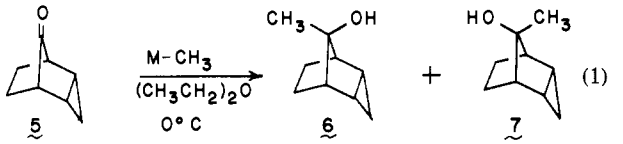
(a) R = H; (b) R = CH_3

Scheme I



through neighboring group participation.[3d,4]

In order to test the concept further, we needed to compare the rates of **3a** and **3b** (PNBO = *p*-nitrobenzoate). While rate data on **3a** existed,[1] **3b** was an unknown compound. Addition of methyllithium to **5**[1] (eq 1) gave predominantly the undesired



(1)

M	6:7
Li	95:5
MgI	90:10
$(CuLi)_{1/2}$	8:92

isomer, **6**.[5] Similarly, addition of methylmagnesium iodide gave a 9:1 mixture of **6** and **7**, respectively. We felt that the use of a reagent that transferred methyl by an initial electron-transfer process might provide a change in product ratio. Our predictions were confirmed by the addition of lithium dimethylcuprate to **5** to yield an 8:92 mixture of **6**:**7**. The desired anti alcohol, **7**, was readily purified by recrystallization, mp 115–116 °C.[6] Treatment

(1) Haywood-Farmer, J. S.; Pincock, R. E. *J. Am. Chem. Soc.* **1969**, *91*, 3020. Battiste, M. A.; Deyrup, C. L.; Pincock, R. E.; Haywood-Farmer, J. *Ibid.* **1967**, *89*, 1954. Tanida, H.; Tsuji, T.; Irie, T. *Ibid.* **1967**, *89*, 1953. Haywood-Farmer, J.; Pincock, R. E.; Wells, J. I. *Tetrahedron* **1966**, *22*, 2007. Gassman, P. G.; Fentiman, A. F., Jr. *J. Am. Chem. Soc.* **1970**, *92*, 2551. Haywood-Farmer, J. *Chem. Rev.* **1974**, *74*, 315. Gassman, P. G., Chasman, J. N.; Reus, W. F., III; Battiste, M. A.; Haywood-Farmer, J. *J. Org. Chem.* **1979**, *44*, 2814.

(2) Hornback, J. M. *J. Org. Chem.* **1973**, *38*, 4122. David, F. *J. Chem. Soc., Chem. Commun.* **1979**, 553. David, F. *J. Org. Chem.* **1981**, *46*, 3512. For examples of epoxy carbinyl systems see: Peters, E. N. *J. Org. Chem.* **1978**, *43*, 4006. Whalen, D. L.; Brown, S.; Ross, A. M.; Russel, H. M. *Ibid.* **1978**, *43*, 428. Whalen, D. L.; Cooper, J. D. *Ibid.* **1978**, *43*, 432. Danen, W. C. *J. Am. Chem. Soc.* **1972**, *94*, 4835. Morita, H.; Oae, S. *Tetrahedron Lett.* **1969**, 1347. Richey, H. G., Jr.; Kinsman, D. V. *Ibid.* **1969**, 2505.

(3) (a) Lustgarten, R. K.; Lhomme, J.; Winstein, S. *J. Org. Chem.* **1972**, *37*, 1075. (b) Tanida, H.; Hata, Y.; Ikegami, S.; Ishitobi, H. *J. Am. Chem. Soc.* **1967**, *89*, 2928. (c) Tanida, H. *Acc. Chem. Res.* **1968**, *1*, 239. (d) Gassman, P. G.; Pascone, J. M. *J. Am. Chem. Soc.* **1973**, *95*, 7801.

(4) The rates listed involve solvent, temperature (25 °C), and leaving-group extrapolations. For the corresponding *p*-nitrobenzoates of **2a** and **2b**, an α-CH_3/H rate ratio of 1.0×10^2 was calculated at 135 °C and of 44 at 25 °C.[3d]

(5) The addition of methyllithium to **5** was reported previously to give exclusively **6**. Baird, M. S.; Reese, C. B. *J. Chem. Soc., Chem. Commun.* **1972**, 523.

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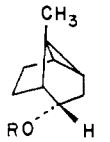
of **7** with *p*-nitrobenzoyl chloride and 4-(dimethylamino)pyridine in tetrahydrofuran gave the desired *p*-nitrobenzoate, **3b**.

The desired epoxides, **4a** and **4b**, were prepared from bicyclo[2.2.1]hept-2-en-7-one (**8**)[7] (Scheme I). Formation of the cyanohydrin gave only **9**.[8] Epoxidation of **9** with *m*-chloroperbenzoic acid gave a 55:45 mixture of **10** and **11**, respectively. This mixture was treated with potassium *tert*-butoxide and sodium borohydride. Column chromatography of the reaction mixture gave **12**. None of the syn alcohol related to **12** was observed. However, both the syn and anti alcohols that could be derived from **10** were observed. Since we have previously prepared both of the alcohols that could be derived from **10**, they were easily identified.[9] The structure and stereochemistry of **12** was readily established on the basis of its ^1H and ^{13}C NMR spectral data and on the basis of a lanthanide shift reagent study (see Experimental Section). Treatment of **12** with *p*-toluenesulfonyl chloride in pyridine gave **4a**.

Addition of methylmagnesium iodide to **8** gave **13**,[10] which on treatment with *m*-chloroperbenzoic acid gave a 78:22 mixture of **14** and **15**, respectively. Recrystallization from hexane gave pure **14**. The structure and stereochemistry of **14** was based primarily on ^1H and ^{13}C NMR data. It has been well established that the 2,3-endo protons occur at ca. δ 3.0 and are not coupled to the bridgehead protons while the 2,3-exo protons occur at ca. δ 3.5 and are coupled to the bridgehead protons in the epimeric 3-oxa-*exo*-tricyclo[3.2.1.$0^{2,4}$]octane and 3-oxa-*endo*-tricyclo-[3.2.1.$0^{2,4}$]octane, respectively.[11] The epoxide **14** showed a narrow multiplet a δ 3.44, while **15** exhibited a singlet at δ 3.20. This left no doubt about the relative stereochemistry of the epoxide moieties of **14** and **15**. Treatment of **14** with a slight excess of *n*-butyllithium followed by *p*-toluenesulfonyl chloride gave the desired *p*-toluenesulfonate, **4b**, mp 75 °C dec.

Solvolytic Studies of 3b. As shown in Table I, the rates of solvolysis of **3b** were determined at 65, 80, and 95 °C in 90% acetone–water buffered with 0.1 M 2,6-lutidine to give $k_{95°C} = (1.68 \pm 0.05) \times 10^{-3}$ s^{-1}. Using the measured[1,12] rate value of $k_{95°C} = (5.44 \pm 0.20) \times 10^{-5}$ s^{-1} for **3a**, under the same solvolytic conditions, gave an α-CH_3/H rate ratio for **3** of 31 at 95 °C.[4] This rate ratio is consistent with the well-established[1] ability of the cyclopropyl ring to participate in solvolysis reactions.

Product analysis showed that **3b** gave 57% of the internal return product, **16**, and 33% of the solvent-trapped product, **17**. Treatment of **7** with 10% perchloric acid also produced **17**.[5]



16 R = PNB
17 R = H

Solvolytic Studies of 4a and 4b. As listed in Table II, solvolysis of **4a** in 90% acetone–water buffered with 2,6-lutidine at 80, 95, and 110 °C gave $k_{95°C} = (7.71 \pm 0.11) \times 10^{-4}$ s^{-1} and $k_{25°C} = 6.20 \times 10^{-7}$ s^{-1}. Similar solvolysis of **4b** under the same conditions at 15, 30, and 45 °C gave $k_{95°C} = 1.16$ s^{-1}. Since **3a** and **3b** are

Table I. Rates of Solvolysis of *syn*-8-Methyl-*endo*-tricyclo[3.2.1.$0^{2,4}$]octan-*anti*-8-ol *p*-Nitrobenzoate in 90:10 v/v Acetone-Water Buffered with 0.1 M 2,6-Lutidine

compd	temp, ±0.05 °C	rate, s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
3b	95.00	$(1.68 \pm 0.05) \times 10^{-3}$		
	80.00	$(3.18 \pm 0.02) \times 10^{-4}$	24.8 ± 0.9	−4.5 ± 2.5
	65.00	$(7.59 \pm 0.23) \times 10^{-5}$		
	25.00[a]	4.38×10^{-7}		
3a	95.00[b]	$(5.44 \pm 0.20) \times 10^{-5}$		

[a] Extrapolated from higher temperatures. [b] Reference 12.

Table II. Rates of Solvolysis of 3-Oxa-*endo*-tricyclo[3.2.1.$0^{2,4}$]octan-*anti*-8-ol *p*-Toluenesulfonate and *syn*-8-Methyl-3-oxa-*endo*-tricyclo-[3.2.1.$0^{2,4}$]octan-*anti*-8-ol *p*-Toluenesulfonate in 90:10 v/v Acetone–Water Buffered with 0.1 M 2,6-Lutidine

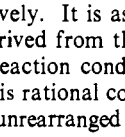
compd	temp, ±0.05 °C	rate, s^{-1}	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
4a	110.00	$(2.52 \pm 0.04) \times 10^{-3}$		
	95.00	$(7.71 \pm 0.11) \times 10^{-4}$	21.5 ± 0.5	−14.9 ± 1.2
	80.00	$(2.12 \pm 0.15) \times 10^{-4}$		
	25.00[a]	6.20×10^{-7}		
4b	95.00	1.16[a]		
	45.00	$(1.58 \pm 0.03) \times 10^{-2}$		
	30.00	$(3.38 \pm 0.03) \times 10^{-3}$	19.3 ± 0.1	−6.1 ± 0.4
	15.00	$(5.93 \pm 0.08) \times 10^{-4}$		
	25.00[a]	1.72×10^{-3}		

[a] Extrapolated from other temperatures.

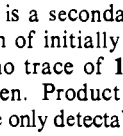
p-nitrobenzoates while **1a**, **1b**, **4a**, and **4b** are *p*-toluenesulfonates, direct rate comparisons involve considerable extrapolations. With standard *p*-nitrobenzoate to *p*-toluenesulfonate rate ratios, the relative rates of **1a**, **4a**, and **3a** would be 1.0, 10^8, and 10^{14}, respectively. The relative rates for **1b**, **4b**, and **3b** would be 1.0, 34, and 10^8. Clearly, in the nonmethylated examples of **1a** and **4a**, the endo epoxide provides a rate acceleration of ca. 10^8 in excess of any rate-retarding inductive effect of the epoxide oxygen.

A more useful comparison is provided by CH_3/H rate ratios, which are somewhat less complicated. Comparison of **1**, **2**, **3**, and **4** reveals α-CH_3/H rate ratios of 1.3×10^8, 7.6×10^3, 3.1×10^1, and 1.5×10^3, respectively. Thus, in terms of using CH_3/H rate ratios as a measure of neighboring group participation, the carbon–carbon bond of an epoxide is not quite as good as the carbon–carbon bond of a cyclopropane. However, depending on the α-CH_3/H rate ratio used for **2**, it would appear to be comparable to, or slightly weaker than, the carbon–carbon π bond of **2** in its ability to act as a neighboring group. Thus, it is clear that *the carbon–carbon bond of an epoxide group can serve as a powerful carbonium ion stabilizing function when properly situated.*

Product analysis showed that **4a** gave a 4:1 mixture of **18** and



18



19

12, respectively. It is assumed that **18** is a secondary product which is derived from the isomerization of initially formed **19** under the reaction conditions. Since no trace of **19** could be detected, this rational could not be proven. Product analysis of **4b** gave the unrearranged alcohol **14** as the only detectable product.

Experimental Section[13]

Tricyclo[3.2.1.$0^{2,4}$]octan-8-one (5). This ketone was prepared according to the literature procedure.[1]

(6) The essentially complete reversal of stereochemistry is interpreted to result from a dramatic change in the mechanism of the addition. For a discussion of electron-transfer reactions in the addition of Grignard reagents to carbonyls see: Ashby, E. C.; Goel, A. B. *J. Am. Chem. Soc.* **1981**, *103*, 4983. In the addition of lithium dimethylcuprate to **5**, we found that the ratio of **6** to **7** was extremely dependent on the concentration of the cuprate, with the formation of **7** being favored at very low concentrations of **5**.

(7) Gassman, P. G.; Marshall, J. L. "Organic Syntheses"; Wiley: New York, 1973; Collect. Vol. V, p 424.

(8) Gassman, P. G.; Talley, J. J. *J. Am. Chem. Soc.* **1980**, *102*, 4138.

(9) Gassman, P. G.; Pape, P. G. *J. Org. Chem.* **1964**, *29*, 160. Gassman, P. G.; Marshal, J. L., unpublished work.

(10) Warkentin, J. *Can. J. Chem.* **1970**, *48*, 1391.

(11) Zefirov, N. S.; Kasyan, L. I.; Gnedenkov, L. Y.; Shashkov, A. S.; Cherepanova, E. G. *Tetrahedron Lett.* **1979**, 949.

(12) Chasman, J. N., Ph.D. Thesis, University of Minnesota, Minneapolis, MN, 1978; p 53. See also: Gassman, P. G.; Chasman, J. N.; Reus, W. F., III; Battiste, M. A.; Haywood-Farmer, J. *J. Org. Chem.* **1979**, *44*, 2814.

(13) Melting points and boiling points are uncorrected. ^1H NMR spectra were recorded on either a Varian HFT-80 or a Hitachi Perkin-Elmer R24B nuclear magnetic resonance spectrometer. ^{13}C NMR spectra were recorded on a Varian CFT-20 nuclear magnetic resonance spectrometer. All chemical shifts are reported relative to tetramethylsilane. Elemental analyses were performed by the Scandinavian Microanalytical Laboratory, Herlev, Denmark.

Addition of Methyllithium to 5. Methyllithium was added to **5** according to the method of Baird and Reese.[5] While these workers reported that this reaction gave exclusively **6**, we found that a 95:5 mixture of **6**:**7**, respectively, was obtained.

Similarly, addition of methylmagnesium iodide to **5** at 0 °C in ether gave a 90:10 mixture of **6** and **7**, respectively.

Lanthanide Shift Reagent Studies. Relative stereochemistries of the two tertiary alcohols **6** and **7** were determined through lanthanide shift reagent studies using europium tris(1,1,1,2,2,3,3-heptafluoro-7,7-dimethyl-4,6-octanedionate) [Eu(fod)$_3$]. Chemical shifts vs. the [LSR]/[alcohol] ratios were plotted, and the slopes were determined.

The slopes for **6** were as follows: C_6-H_{exo}, 3.90; C_6-H_{endo}, 2.92. The slopes for **7** were as follows: C_6-H_{exo}, 14.38; C_6-H_{endo}, 7.22.

Addition of Lithium Dimethylcuprate to 5. Addition of 10 mg of **4** to a 10-fold excess of lithium dimethylcuprate at 0 °C in ether under high dilution gave an 8:92 ratio of **6**:**7**, respectively. When the reaction was scaled to a more preparative level and, of necessity, made more concentrated, this ratio changed to give a 45:55 mixture of **6** and **7**, respectively (see below).

To the dimethylcopper lithium prepared from 3.8 g (20 mmol) of cuprous iodide and 28 mL of 1.4 M methyllithium in 500 mL of ethyl ether was added, at 5 °C, 1.0 g (8.2 mmol) of neat **5** over 2 min. The solution was stirred in the cold for 2 h and quenched with water. GLC analysis (Carbowax 20 M, 190 °C) indicated the presence of **7** and **6** in the ratio of 55:45, with **6** having the shorter retention time. The solvent was removed, and the residue was recrystallized six times from hexane, yielding 0.22 g (19%) of **7** with less than 0.5% contamination by **6**; mp 115–116 °C; ^{1}H NMR ($CDCl_3$) δ 1.96–1.5 (3 H, m), 1.56 (3 H, s), 1.3–0.6 (8 H, m); ^{13}C NMR ($CDCl_3$) δ 94.2, 43.5, 25.4, 20.1, 18.3, 13.6; IR (KBr) 1375, 1317, 1278, 1130, 1046, 936 cm^{-1}; mass spectrum 138.1049, calcd for $C_9H_{14}O$ 138.1044.

Anal. Calcd for $C_9H_{14}O$: C, 78.21; H, 10.21. Found: C, 78.02, H, 10.15.

***syn*-8-Methyl-*endo*-tricyclo[3.2.1.0^{2,4}]oct-*anti*-8-yl *p*-Nitrobenzoate (3b).** A solution of 0.24 g (1.74 mmol) of **7**, 0.33 g (3 mmol) of 4-(dimethylamino)pyridine, and 0.55 g (2.9 mmol) of *p*-nitrobenzoyl chloride in 10 mL of tetrahydrofuran was stirred overnight at room temperature. The solvent was removed and the residue partitioned between water and methylene chloride. The organic portion was dried over anhydrous magnesium sulfate and filtered, and the solvent was removed. The residue was passed through 10 g of basic alumina to remove a minor impurity. The product was recrystallized from hexane yielding 0.34 g (68%) of **3b** as a light yellow solid: mp 130–132 °C; ^{1}H NMR ($CDCl_3$) δ 8.29 (2 H, A of an AB q, J = 10 Hz), 8.10 (2 H, B of an AB q, J = 10 Hz), 2.52 (2 H, m), 1.82 (3 H, s), 1.9–0.9 (8 H, m); IR (KBr) 1718, 1528, 1350, 1304, 1271, 1121, 1101, 840, 715 cm^{-1}; mass spectrum, *m/e* 287.

Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.88; H, 5.97; N, 4.88. Found: C, 66.76; H, 5.98; N, 4.71.

Bicyclo[2.2.1]hept-2-en-7-one (8). This ketone was prepared according to the literature procedure.[7]

***syn*-7-Cyanobicyclo[2.2.1]hept-2-en-*anti*-7-ol (9).** This cyanohydrin was prepared according to the literature procedure.[8]

Epoxidation of 9. Formation of 10 and 11. A solution of 3.3 g (24.2 mmol) of **9**, 0.07 g of 2,6-di-*tert*-butyl-4-methylphenol,[14] 6.6 g (ca. 33 mmol) of *m*-chloroperbenzoic acid, and 4 mL of ethanol-free chloroform was heated at 55–60 °C for 14 h. An additional 3.3 g of the peracid in 3 mL of chloroform was added to the mixture, which was thick and white due to the precipitation of *m*-chlorobenzoic acid. After 25 h, an additional 2.0 g of the peracid in 5 mL of chloroform was added. Olefin consumption was complete after 38 h, whereupon the mixture was diluted with 25 mL of methylene chloride and added to a solution of 10 g of sodium bicarbonate and 5 g of sodium thiosulfate in 100 mL of water. The aqueous layer became orange when stirred. The organic layer was filtered through anhydrous sodium sulfate, and the solvent was removed under reduced pressure. The residue was taken up in 4 mL of benzene, and a small amount of a white solid was removed by filtration. Removal of benzene under reduced pressure yielded 2.6 g of an orange semisolid containing a mixture of **10** and **11** as well as small amounts of other unidentified products. Although the ratio of **10** to **11** in the early stages of the reaction was ca. 1:1 as determined by ^{1}H NMR, the ratio changed with time as **10** suffered acid-catalyzed decomposition faster than **11**. An attempt to separate the isomers by column chromatography (alumina, 50% ether–hexane) gave partially purified samples of **11** as an extremely waxy solid and **10**, a liquid, each in ca. 90% purity; **11** could not be readily freed of the impurities by crystallization. **11**: ^{1}H NMR ($CDCl_3$) δ 3.62 (2 H, br s), 2.05 (2 H, br s), 1.61 (4 H, br s). **10**: 3.36 (2 H, s), 2.79 (2 H, s), 2.1–1.0 (4 H, m). The assignment of stereochemistry rests on the fact that the epoxide proton is a sharp singlet for **10** and is a broad singlet for **11**.[11] Since **11** could not be obtained pure in reasonable yield, the crude mixture was used in the next reaction since both components would be initially converted into a keto epoxide.

3-Oxa-*endo*-tricyclo[3.2.1.0^{2,4}]octan-*anti*-8-ol (12). A solution mixture of 1.6 g of a crude mixture of **10** and **11** in 150 mL of tetrahydrofuran at −60 °C was treated with 5 mL of 1.78 M potassium *tert*-butoxide in tetrahydrofuran (Callery Chemical Co.). After the mixture was stirred at −60 °C for 15 min, 1.0 g of sodium borohydride and 20 mL of methanol were added, and the reaction was allowed to warm to 25 °C over a 0.5-h period. The solvent was removed under reduced pressure, and the residue was partitioned between methylene chloride and water. The organic phase was dried over anhydrous sodium sulfate and filtered, and the solvent was removed under reduced pressure. Analysis of the crude residue by ^{1}H NMR indicated the presence of **12**, 3-oxa-*exo*-tricyclo[3.2.1.0^{2,4}]octan-*syn*-8-ol, and 3-oxa-*exo*-tricyclo[3.2.1.0^{2,4}]octan-*anti*-8-ol in the ratio of 4:1:5, respectively. No indication of the presence of any 3-oxa-*endo*-tricyclo[3.2.1.0^{2,4}]octan-*syn*-8-ol was obtained.

Chromatography of the crude residue on activity III basic alumina gave **12** contaminated with **10**. Recrystallization from hexane gave 0.17 g (8% from **9**) of **12**: mp 185–186 °C; ^{1}H NMR ($CDCl_3$) δ 4.04 (1 H, br s), 3.36 (2 H, narrow m), 2.20 (2 H, br s), 1.48 (4 H, br s); ^{13}C NMR ($CDCl_3$) δ 84.0, 55.1, 41.5, 22.4; mass spectrum 126.0686, calcd for $C_7H_{10}O_2$ 126.0681.

Anal. Calcd for $C_7H_{10}O_2$: C, 66.64; H, 7.99. Found: C, 66.14; H, 7.96.

Lanthanide Shift Reagent Study of 12. With Eu(fod)$_3$, the slopes of the various protons of **12** were as follows: H_1, 13.19; H_2, 16.04; $H_{5\text{-exo}}$ and $H_{5\text{-endo}}$, 13.44; H_8, 20.22. The shifts observed indicate that the Eu(fod)$_3$ is complexing with both the hydroxyl and epoxide moieties. The similar shifts of the exo and endo protons at C_5 and C_6 are only consistent with the hydroxyl group being in the anti configuration.

3-Oxa-*endo*-tricyclo[3.2.1.0^{2,4}]oct-*anti*-8-yl *p*-Toluenesulfonate (4a). The alcohol **12** was allowed to react with *p*-toluenesulfonyl chloride in pyridine at room temperature for 13 h. Water and methylene chloride were added, and the organic phase was separated and dried over anhydrous sodium sulfate. After filtration, the solvent was removed under reduced pressure, and the residue was crystallized from ether–hexane to give a 92% yield of large yellow plates: mp 46.5–48.0 °C; ^{1}H NMR ($CDCl_3$) δ 7.77 (2 H, A of an AB q, J = 8 Hz), 7.22 (2 H, B of an AB q, J = 8 Hz), 4.45 (1 H, m), 3.33 (2 H, m), 2.44 (3 H, s), 2.35 (2 H, br s), 1.49 (2 H, s), 1.44 (2 H, br s); ^{13}C NMR ($CDCl_3$) δ 144.7, 133.7, 129.7, 127.4, 86.8, 53.02, 40.3, 22.4, 21.3.

Anal. Calcd for $C_{14}H_{16}O_4S$: C, 59.99; H, 5.75. Found: C, 59.95; H, 5.82.

***syn*-7-Methylbicyclo[2.2.1]hept-2-en-*anti*-7-ol (13).** The procedure of Warkentin[10] was used to prepare **13** from **8**.

***syn*-8-Methyl-3-oxa-*endo*-tricyclo[3.2.1.0^{2,4}]octan-*anti*-8-ol (14).** To a stirring solution of 5.7 g (46 mmol) of **13** in 50 mL of dry methylene chloride was added dropwise a solution of 11.9 g (69 mmol) of *m*-chloroperbenzoic acid in 100 mL of dry methylene chloride. The reaction was allowed to stir for 18 h, then 10% sodium carbonate solution was added, and the resulting solution was stirred for 0.5 h. The organic layer was separated, washed with 20 mL of brine, dried over anhydrous magnesium sulfate, filtered, and concentrated to give 5.6 g (87%) of a semisolid residue. Recrystallization from pentane–benzene gave a white solid which contained **15** and **14** in a 22:78 ratio (as determined by ^{1}H NMR analysis). Four additional recrystallizations from hexane gave **14** as white needles containing less than 2% of **15**. Two sublimations gave analytically pure **14**: mp 100.5–101.5 °C; IR (KBr) 3300, 3040 (db), 3020, 2950, 1470, 1433, 1377, 1310, 1273, 1218, 1135, 1040, 981, 970, 940, 928, 855 (db), 843, 768, 722, 661, 552, 521, 395, 340 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.44 (2 H, n m), 1.9 (2 H, m), 1.83 (1 H, s), 1.5 (7 H, m). The narrow multiplet at δ 3.44 was replaced by a singlet at δ 3.20 for **15**.

Anal. Calcd for $C_8H_{12}O_2$: C, 68.55; H, 8.63. Found: C, 68.55; H, 8.64.

***syn*-8-Methyl-3-oxa-*endo*-tricyclo[3.2.1.0^{2,4}]oct-*anti*-8-yl *p*-Toluenesulfonate (4b).** A solution of 50 mg of **14** in 2 mL of tetrahydrofuran was cooled in a dry ice–isopropanol bath and treated with 0.20 mL of 2.5 M *n*-butyllithium. After 5 min, 95 mg of solid *p*-toluenesulfonyl chloride was added, and the reaction mixture was stirred for 15 min, followed by warming to 0 °C and stirring at that temperature for 45 min. The reaction mixture was poured into cold methylene chloride (−30 °C) and washed quickly with one 5-mL portion of saturated sodium bicarbonate solution. The organic layer was filtered through anhydrous sodium sulfate, and the solvent was removed under reduced pressure in

(14) The addition of 2,6-di-*tert*-butyl-4-methylphenol has been reported to inhibit adverse radical reactions that can complicate epoxidations. Kishi, Y.; Aratani, M.; Tanino, H.; Fukuyama, T.; Goto, T. *J. Chem. Soc., Chem. Commun.* **1972**, 64.

the cold to give a solid residue. Recrystallization from ether–hexane in the cold gave 45 mg (42%) of **4b** as white, well-formed crystals: mp 75 °C dec; ^{1}H NMR ($CDCl_3$) δ 7.76 (2 H, A of AB q, J = 9 Hz), 7.25 (2 H, B of AB q, J = 9 Hz), 3.41 (2 H, m), 2.40 (5 H, m), 1.73 (3 H, s), 1.50 (4 H, m); ^{13}C NMR ($CDCl_3$) δ 129.4, 126.8, 55.1, 45.2, 24.0, 18.1. Although this material could be stored safely at −30 °C, it slowly decomposed at room temperature and underwent extensive fragmentation on attempted analysis by mass spectroscopy. Therefore neither an elemental analysis nor an exact mass molecular weight was obtained for **4b**. Upon solvolysis in 90:10 v/v acetone–water buffered with 0.01 M 2,6-lutidine, **4b** liberated 100 ± 2% of the theoretical amount of *p*-toluenesulfonic acid.

Kinetic Procedure. Solvolyses were run in 90% acetone–10% water (v/v) containing 0.01 M 2,6-lutidine. Rates were determined conductometrically. The conductivity cell could be sealed by a high-vacuum stopcock equipped with O-rings that permitted measurements above the normal boiling point of acetone. The runs at 45 °C and lower were made by adding the substrate to the solvent in a thermally preequilibrated cell.

Product Studies of 3b. Preparative solvolysis of 0.168 g of **3b** in 90:10 (v/v) acetone–water followed by removal of the solvent gave a residue to which water was added. The organic products were extracted with methylene chloride and chromatographed on 15 g of activity III basic alumina. Elution with 50% ether–50% hexane gave 0.095 g (57%) of 1-methyltricyclo[3.3.0.0^{2,8}]oct-*endo*-4-yl *p*-nitrobenzoate (**16**) as a white solid after recrystallization from ether–hexane: mp 104–105 °C (lit.[5] mp 100–101 °C); ^{1}H NMR ($CDCl_3$) δ 8.19 (4 H, br s), 5.34 (1 H, br q, J = 7 Hz),[15] 2.7–2.4 (2 H, m), 1.36 (3 H, s), 2.4–0.7 (7 H, br m); mass spectrum 287.1135, calcd for $C_{16}H_{17}NO_4$ 287.1156.

Anal. Calcd for $C_{16}H_{17}NO_4$: C, 66.88; H, 5.97; N, 4.88. Found: C, 66.86; H, 6.20; N, 5.00.

Further elution yielded 26.5 mg (33%) of 1-methyltricyclo[3.3.0.0^{2,8}]octan-*endo*-4-ol (**17**)[5] as a clear, colorless oil which was homogeneous by GLC analysis: ^{1}H NMR ($CDCl_3$) δ 4.32 (1 H, br q, J = 6 Hz), 2.5–0.7 (9 H, m), 1.30 (3 H, s); mass spectrum 138.1054, calcd for $C_9H_{14}O$ 138.1044.

When **7** was dissolved in ether and treated with a small amount of 10% perchloric acid for 10 min at room temperature, it was completely converted to **17**.

Product Studies of 4a. A solution of 0.172 g of **4a** and 0.070 g of 2,6-lutidine in 4.0 mL of 90% acetone–10% water (v/v) was heated at 95–100 °C for 3.5 h in a sealed ampoule. Workup involved removal of the solvent under reduced pressure, extraction of the product with methylene chloride, and drying over anhydrous magnesium sulfate. Filtration followed by removal of the solvent under reduced pressure gave 0.080 g of a 4:1 mixture of **18** and **12** which was contaminated by a small amount of 2,6-lutidine (as determined by NMR analysis). Preparative HPLC on porosil with ethyl acetate as eluant gave pure **18**: ^{1}H NMR ($CDCl_3$) δ 4.91 (1 H, s, $H_{4\text{-endo}}$),[16] 4.01 (1 H, br t, J = 6 Hz), 2.70 (1 H, br m), 2.30 (1 H, t, J = 6 Hz), 2.1–1.2 (5 H, complex m); ^{13}C NMR ($CDCl_3$) δ 109.6, 64.3, 50.3, 35.5, 29.8, 26.3, 25.7, 22.1; mass spectrum 126.0679, calcd for $C_7H_{10}O_2$ 126.0678.[17]

Lanthanide Shift Study of 18. The slopes obtained for **18** were as follows: H_1, 10.5; H_2, 20.73; H_4, 28.30; H_5, 11.90; H_6, H_7, H_8 (5 H total), ca. 6.5.

Product Studies of 4b. The solvolysis of 67 mg of **4b** in 90% acetone–10% water (v/v) was carried out for 10 half-lives to give 34.7 mg of material which consisted of only **14** contaminated by trace amounts of acetone and methylene chloride. Integration of the ^{1}H NMR sample vs. an internal standard indicated a yield of 97 ± 10% of **14**. No trace of the ring-opened product could be detected by NMR.

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Registry No. 3a, 16384-95-5; **3b**, 83153-08-6; **4a**, 83153-09-7; **4b**, 83153-10-0; **5**, 14224-86-3; **6**, 38310-50-8; **7**, 83198-89-4; **9**, 74816-10-7; **10**, 83153-11-1; **11**, 83198-87-2; **12**, 83198-88-3; **14**, 83153-12-2; **16**, 38310-53-1; **17**, 38310-52-0; **18**, 83153-13-3.

(15) This peak could also be described as a doublet of doublets with $J_{H_{4\text{-ex}}\text{-}H_5} = J_{H_{4\text{-ex}}\text{-}H_3}$ = ca. 7 Hz. It has been well established that a hydrogen in the exo position at C_4 couples to the bridgehead hydrogen at C_5 with a J = 6–7 Hz while the corresponding hydrogen in the endo position at C_4 has J = 0 Hz.[1,5,12] See also: Buckeridge, R. G.; Frayne, K. J.; Johnson, B. L. *Aust. J. Chem.* **1965**, *28*, 1311.

(16) The singlet nature of this absorption requires that the hydroxyl group be in the exo position.[15]

(17) Compound **18** was quite unstable, and much of the material was lost on a single pass through an HPLC. No attempt was made to obtain an elemental analysis.

Synthesis and Solvolysis of Sulfonate Esters of 3-Phenyl-3-aza-*endo*-tricyclo[3.2.1.0^{2,4}]octan-*anti*-8-ols. Identification of the Carbon–Carbon Bond of Aziridines as a Powerful Neighboring Group in Solvolysis Reactions

Paul G. Gassman,* John G. Schaffhausen, Frank D. Starkey, and Peter W. Raynolds

Contribution from the Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455. *Received October 9, 1981*

Abstract: 3-Phenyl-3-aza-*endo*-tricyclo[3.2.1.0^{2,4}]octan-*anti*-8-ol and *syn*-8-methyl-3-phenyl-3-aza-*endo*-tricyclo[3.2.1.0^{2,4}]-octan-*anti*-8-ol have been synthesized and converted to the corresponding *p*-toluenesulfonate esters. Solvolysis of these two sulfonates in acetone–water buffered with 2,6-lutidine gave an α-methyl/hydrogen rate ratio of 1.0 × 10^3. This established that the carbon–carbon bond of aziridines can be a powerful neighboring group in solvolysis reactions when properly oriented. In an absolute rate comparison, 3-phenyl-3-aza-*endo*-tricyclo[3.2.1.0^{2,4}]oct-*anti*-8-yl *p*-toluenesulfonate solvolyzes about 10^9 times faster than bicyclo[2.2.1]hept-7-yl *p*-toluenesulfonate. Product studies were carried out.

We have demonstrated that α-methyl/hydrogen rate ratios are a very useful measure of the presence of neighboring group participation by the carbon–carbon bonds of cyclopropanes and of epoxides.[1,2] We were particularly intrigued by the observation

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