of lithium diisopropylamide in 2 mL of THF, at −78 °C under nitrogen, was treated with 1,10-dibromodecane (0.396 g, 1.320 mmol) in 0.5 mL of THF and 0.4 mL of HMPA. The product was purified as usual to afford 77 mg (18.2% yield) of **24c**: mp 73–74.5 °C; ^{1}H NMR (250 MHz, $CDCl_3$) δ 1.2–1.7, 1.30 (m, bs, 16 H), 1.45 (d, 3 H, $J_{4,5}$ = 6.5), 1.85 (m, 2 H), 2.41 (d, 1 H, $J_{3OH,3}$ = 5.1), 2.57 (m, 1 H, $J_{2,3}$ = 8.5), 3.41 (t, 2 H $J_{14,15}$ = 6.8), 3.84 (ddd, 1 H), 4.21 (dq, 1 H, $J_{3,4}$ = 6.8); IR (KBr) 3320, 2860, 2800, 1730, 1460, 1355, 1340, 1320, 1300, 1280, 1270, 1205, 1190, 1180, 1085, 1050 cm^{-1}; HRMS (CI) calcd for $C_{15}H_{26}O_3Br$ ($M^+ - 1$), 333.1065; found, 333.1056.

Acknowledgment. We thank the Dow Chemical Company Foundation for generous support of this work.

Competitive Bridgehead Substitution in Electrophilic Oxidation Reactions of Ethanoadamantane

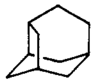
James J. Sosnowski and Roger K. Murray, Jr.*

Department of Chemistry, University of Delaware, Newark, Delaware 19716

Received November 22, 1983

In contrast to an earlier report, it is shown that oxidation of ethanoadamantane with lead tetraacetate, chromic acid, or a mixture of *tert*-butyl bromide and aluminum bromide occurs by competitive attack at the C-1, C-6, *and* C-8 bridgehead positions. The structure assignments of 6- and 8-ethanoadamantanol have been firmly established by ^{13}C NMR spectroscopy.

Although no quantitative study has been carried out, Schleyer has noted that the qualitative ease of ionic bromination of some polycyclic hydrocarbons seems to parallel the solvolysis rates of the resulting bromides.[1-3] These observations have led him to suggest that the relative proclivity for bromination at alternative intramolecular sites in these substrates can be related to the calculated change in strain energy (Δ strain) for carbocation formation at these positions. Since ionic bromination of hydrocarbons shows a strong preference for attack at tertiary C–H bonds, attention is directed to the bridgehead positions. For example, the ionic brominations of protoadamantane[1] (**1**) and diamantane[2] (**2**) take place exclusively at the bridgehead position in each compound which has the lowest calculated Δ strain value. In view of these results, it is striking that ionic bromination of ethanoadamantane (**3**) is reported to occur only at C-1 and C-6



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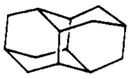

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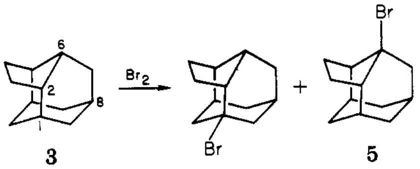

3 4 5 (1)

since the bridgehead position in **3** which is calculated by the Bingham–Schleyer force field to have the lowest Δ strain value is C-8.[3] When the more sophisticated Engler–Schleyer force field is employed and a correction term is included for the hyperconjugative stabilizing effect of β-alkyl branching, then the cation at C-6 in **3** is found to be the most stable and cations at C-1 and C-8 in **3** are calculated to be of equal stability.[3] The same relative stabilities of the ethanoadamantyl bridgehead cations are also obtained with MINDO/3.[3]

The relative amounts of **4** and **5** obtained in the ionic bromination of **1** are reported to vary with the reaction conditions.[3] However, even when the bromination is carried out in the presence of aluminum bromide to achieve thermodynamic control,[4] the only products isolated were **4** and **5**.[3] This is particularly surprising since calculations with Allinger's halide force field show that 8-bromoethanoadamantane should be the most stable isomer.[3] In view of these circumstances, we were prompted to investigate the relative reactivities of the bridgehead positions of ethanoadamantane in other electrophilic reactions.

Results and Discussion

Jones and Mellor have reported that bridgehead functionalization of bicyclic and polycyclic hydrocarbons can be achieved by oxidation of these substrates with lead tetraacetate and chloride ion in a solution of trifluoroacetic acid and methylene chloride.[5] Subsequent hydrolysis of the resulting trifluoroacetates gives the corresponding alcohols. The identity of the oxidizing agent in this reaction has not been established. However, it is clear that oxidation does not occur via a radical cation intermediate.[6] At present, a mechanism proceeding by electrophilic attack at a carbon–hydrogen bond is favored.[6] Oxidation of ethanoadamantane with lead tetraacetate under these conditions proceeds by competitive substitution at C-1, C-6, *and* C-8 in **3** to give alcohols **6**, **7**, and **8** in a ratio of 62:27:11, respectively (Scheme I).

We were not successful in separating these alcohols by chromatography. Our structure assignments for these compounds are based on the following observations. (1) Treatment of a mixture of **6**–**8** with concentrated hydro-

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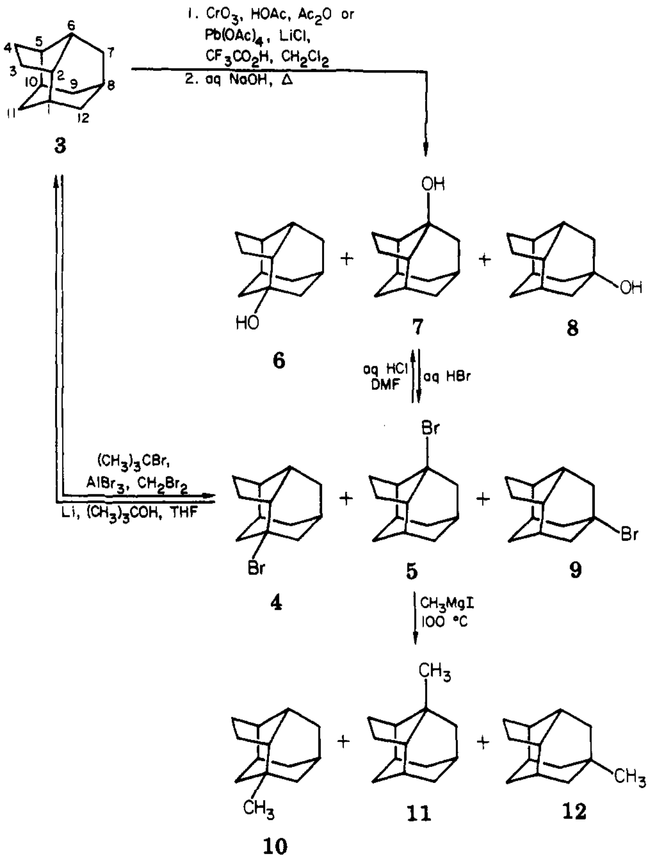
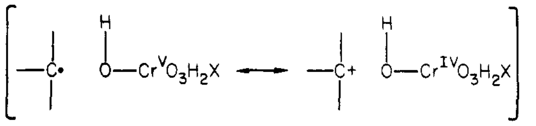
Scheme I



bromic acid provided a mixture of the corresponding bromides 4, 5, and 9. Reduction of this mixture with lithium–*tert*-butyl alcohol–tetrahydrofuran[7] afforded only 3. Thus, alcohols 6–8 all possess the carbon skeleton of ethanoadamantane. (2) Reaction of the mixture of bromides 4, 5, and 9 with excess methylmagnesium iodide[8] in ether at 100 °C gave a mixture of the corresponding methylethanoadamantanes 10–12. All of the resonances present in the ^{13}C NMR spectrum of this mixture and their couplings could be accounted for by the reported[3] ^{13}C NMR parameters of these compounds. However, we were somewhat concerned about the original structure assignments of 11 and 12 since they are primarily based on the perceived agreement between their measured and calculated ^{13}C NMR chemical shifts. Consequently, we have determined the lanthanide-induced chemical shifts with $Eu(fod)_3$ of the ^{13}C NMR resonances of alcohols 7 and 8. The signals due to 7 and 8 can be readily identified by comparison of the ^{13}C NMR spectrum of the 52:48 mixture of alcohols 6 and 7 resulting from hydrolysis of the mixture of bromides obtained in eq 1 with the ^{13}C NMR spectrum of the mixture of alcohols 6–8 produced in the lead tetraacetate oxidation of 3. With the exception of the carbon to which the hydroxyl group is attached, the greatest change in chemical shift of any of the resonances in 7 is for a methylene carbon of single intensity (C-7). The next largest shifts are for a methylene (C-3 and C-4) and a methine (C-2 and C-5) resonance with each being of double intensity. The only resonances in 8 which are shifted to a comparable extent are two signals for methylene carbons with one being of single intensity (C-7) and the other of double intensity (C-9 and C-12). These observations are consistent with the structures assigned to alcohols 7 and 8 and thus confirm the structures of 11 and 12.

We have also found that oxidation of ethanoadamantane with chromium trioxide in a mixture of acetic acid and acetic anhydride, followed by hydrolysis of the resulting acetates, gives alcohols 6, 7, *and* 8 in a ratio of 63:27:10, respectively. Chromic acid oxidations of polycyclic hydrocarbons are known to show a significant preference for substitution at the bridgehead positions.[9] These reactions are believed to proceed by way of a species that is best represented as the resonance hybrid shown below. This



intermediate may result from either hydrogen atom or hydride anion transfer from the hydrocarbon to a chromium(VI) complex.[10]

Since oxidation of ethanoadamantane with lead tetraacetate or chromic acid occurs competitively at C-1, C-6, and C-8, we were intrigued by the report[3] that thermodynamically controlled bromination of 3 with *tert*-butyl bromide and aluminum bromide in methylene bromide, followed by hydrolysis of the resulting mixture of bromides, afforded only alcohols 6 and 7 in a ratio of 96:4. We have repeated this reaction. An analysis of the resulting mixture of alcohols by quantitative ^{13}C NMR spectroscopy shows that 6, 7, *and* 8 are obtained in a ratio of 74:7:19, respectively. In the earlier study the reaction products were simply identified by comparison of their GLC retention times with authentic samples.[3] Perhaps alcohols 6 and 8 had identical or nearly identical retention times under the GLC conditions employed.

Experimental Section

Carbon magnetic resonance spectra were recorded with a Brüker WM 250-MHz spectrometer at 62.9 MHz and are referenced to an internal standard of tetramethylsilane.

Oxidation of Ethanoadamantane with Lead Tetraacetate. Ethanoadamantane (114 mg, 0.70 mmol) and lead tetraacetate (443 mg, 1.0 mmol, partially dried by suction filtration under dry nitrogen, then further dried over potassium hydroxide under vacuum, and stored in the dark in a dessicator over phosphorus pentoxide) were stirred with trifluoracetic acid (3 mL) that was 0.1 M in lithium chloride and methylene chloride (3 mL) for 24 h in the dark. The reaction mixture was then partitioned between ether (10 mL) and aqueous sodium hydroxide (0.5 g in 12 mL of water). The aqueous layer was extracted with ether (3 × 10 mL). The organic extracts were combined, then washed with saturated aqueous sodium bicarbonate (3 × 10 mL) and water (3 × 10 mL), and dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure provided a mixture of trifluoroacetates which were hydrolyzed by refluxing this material with 10% aqueous sodium hydroxide for 16 h. During this time, a considerable amount of white solid sublimed onto the condenser coils. This material was dissolved in ether. The crude reaction mixture was also extracted with ether (3 × 10 mL). The various ether extracts were combined and dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure provided a white solid residue which was sublimed to give 48 mg of a white solid. Analysis of this material by quantitative ^{13}C NMR indicated that the only compounds present were alcohols 6, 7, and 8, and unreacted 3 and that they were obtained in a ratio of 51:23:9:17, respectively.

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Lanthanide-Induced Shifts of Alcohols 6–8. A 52:48 mixture of alcohols **6** and **7** was prepared as described previously by hydrolysis of the mixture of bromides **4** and **5** obtained from stirring **3** with bromine at 3 °C for 4 h.[3] The chemical shifts of the ^{13}C NMR resonances of **6** and **7** were identified by comparison of the ^{13}C NMR spectrum of this mixture with the ^{13}C NMR spectrum of the 62:27:11 mixture of alcohols **6**, **7**, and **8** resulting from the lead tetraacetate oxidation of **3**. The ^{13}C NMR spectrum of the mixture of **6** and **7** in $CDCl_3$ was then obtained after the cumulative addition of 0.25, 0.50, 0.75, and 1.00 molar equivalents of Eu(fod)$_3$. Following is a summary of the chemical shifts of the ^{13}C NMR resonances of alcohols **6** and **7**. Indicated in parentheses are the induced downfield shift in ppm for each signal for a 1:1 molar ratio of the shift reagent to substrate and the particular atom to which each chemical shift is assigned. These assignments are consistent with the observed proton-coupled ^{13}C NMR spectrum of a mixture of **6** and **7** and with the relative intensities of the resonances.

6: δ 70.2 (C-1), 49.6 (5.5, C-2), 44.7 (8.4, C-12), 41.5 (2.8, C-5), 40.8 (3.0, C-6), 39.5 (6.6, C-11), 35.5 (2.4, C-9), 34.9 (3.0, C-10), 32.4 (2.5, C-7), 29.8 (3.1, C-8), 29.6 (2.7, C-4), 25.4 (4.7, C-3).

7: δ 77.8 (C-1), 48.6 (5.0, C-2 and C-5), 41.1 (8.2, C-7), 36.3 (2.2, C-9 and C-12), 35.6 (2.5, C-1 and C-10), 29.8 (3.4, C-8), 29.6 (2.7, C-11), 27.4 (5.1, C-3 and C-4).

With this information in hand, the resonances due to alcohol **8** in the ^{13}C NMR spectrum of the mixture of **6**–**8** could be clearly identified. A $CDCl_3$ solution of the mixture was treated with Eu(fod)$_3$ as described above. The results are as follows:

8: δ 67.9 (C-8), 44.8 (7.0, C-9 and C-12), 42.8 (3.1, C-6), 41.5 (6.4, C-7), 40.9 (2.6, C-2 and C-5), 35.9 (3.0, C-1 and C-10), 30.9 (2.7, C-11), 28.9 (1.3, C-3 and C-4).

1-, 6-, and 8-Bromoethanoadamantanes from a Mixture of 1-, 6-, and 8-Hydroxyethanoadamantanes. A suspension of a 62:27:11 mixture of alcohols **6**, **7**, and **8** (200 mg, 1.12 mmol) obtained above in 47% hydrobromic acid (28 mL) was sealed in an aerosol bottle and heated at 100 °C for 2.5 h. After the reaction mixture had cooled, it was poured onto water (50 mL) and then extracted with ether (3 × 20 mL). The combined ether extracts were dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure provided 172 mg of a white solid which was sublimed (80 °C, 0.6 mm) to give 140 mg (52% yield) of a mixture of bromides **4**, **5**, and **9**.

Ethanoadamantane from a Mixture of 1-, 6-, and 8-Bromoethanoadamantanes. Lithium metal (220 mg, 31 mmol) was added to a solution of the mixture of bromides **4**, **5**, and **9** (65 mg, 0.27 mmol) obtained above in anhydrous *tert*-butyl alcohol (4 mL) and anhydrous tetrahydrofuran (20 mL) and the mixture was stirred at room temperature for 5 h. At this point water (10 mL) was added and stirring was continued for 0.5 h. The resulting solution was extracted with ether (2 × 20 mL) and the combined ether extracts were dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure gave 32 mg (73% yield) of an oily solid. Analysis of this material by GLC (5 ft × 0.25 in. QF-1 column) showed a single component to be present. Its ^{13}C NMR spectrum was identical with that of an authentic sample of **3**.

1-, 6-, and 8-Methylethanoadamantanes from a Mixture of 1-, 6-, and 8-Bromoethanoadamantanes. A solution of the mixture of bromides **4**, **5**, and **9** (75 mg, 0.31 mmol) obtained above and methylmagnesium iodide (31 mmol) in ether (10 mL) was sealed in an aerosol bottle and heated at 100 °C for 20 min. The reaction vessel was then cooled in an ice–water bath and the excess Grignard reagent present was destroyed by the slow addition of 5% aqueous hydrochloric acid. The ether layer present was separated, washed with water (2 × 5 mL), and dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure afforded 41 mg (75% yield) of a white solid. Analysis of this material by ^{13}C NMR showed that **10**, **11**, and **12** were the only components of this material.

Chromic Acid Oxidation of Ethanoadamantane. Chromium trioxide (120 mg, 1.2 mmol) was added in small portions to a stirred solution of **3** (100 mg, 0.62 mmol) in acetic acid (2 mL) and acetic anhydride (2 mL) at room temperature. After the addition was complete, the reaction mixture was stirred for 6 h at room temperature. At this point the reaction mixture was diluted with ice water (20 mL) and it was then extracted with ether (3 × 20 mL). The combined ether extracts were washed with 10% aqueous sodium carbonate (3 × 20 mL) and water (2 × 20 mL) and then dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure provided an oil which was hydrolyzed by refluxing this material with a mixture of water (10 mL), methanol (10 mL), and potassium hydroxide (400 mg) for 16 h. During this time, a white solid sublimed onto the condenser coils. This material was dissolved in ether. The crude reaction mixture was also extracted with ether (3 × 20 mL). The various ether extracts were combined and dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure provided a white solid residue which was sublimed to afford 41 mg of a white solid. Analysis of this material by quantitative ^{13}C NMR showed that the only compounds present were alcohols **6**, **7**, and **8** and unreacted **3** and that they were obtained in a ratio of 59:25:9:7, respectively.

Bromination of Ethanoadamantane with *tert*-Butyl Bromide and Aluminum Bromide. Ethanoadamantane (303 mg, 1.87 mmol) was stirred with *tert*-butyl bromide (510 mg, 3.72 mmol) and a trace of aluminum bromide in methylene bromide (30 mL) at room temperature for 24 h. At this point the reaction mixture was washed with water (2 × 20 mL) and then dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure gave a residue which was hydrolyzed by refluxing it with stirring with 0.67 N aqueous hydrochloric acid (3 mL) and *N*,*N*-dimethylformamide (2.6 mL) for 20 h. During this time, a white solid sublimed onto the condenser coils. This material was dissolved in ether. The reaction mixture was also extracted with ether (3 × 20 mL). The various ether extracts were combined and dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure provided a white solid residue. Analysis of this material by quantitative ^{13}C NMR showed that alcohols **6**, **7**, and **8** were the only products of this reaction and that they were obtained in a ratio of 74:7:19, respectively.

Acknowledgment. This work was supported by grants from the United Parkinson Foundation and the University of Delaware Research Foundation.

Registry No. **3**, 15002-90-1; **4**, 72708-40-8; **5**, 72708-42-0; **6**, 72708-44-2; **7**, 72725-70-3; **8**, 89922-31-6; **9**, 72708-43-1; **10**, 72708-45-3; **11**, 72708-47-5; **12**, 81012-63-7.