Synthesis of 1,3-Bishomoadamantane[1]

Judith S. Polley and Roger K. Murray, Jr.*

Department of Chemistry, University of Delaware, Newark, Delaware 19711

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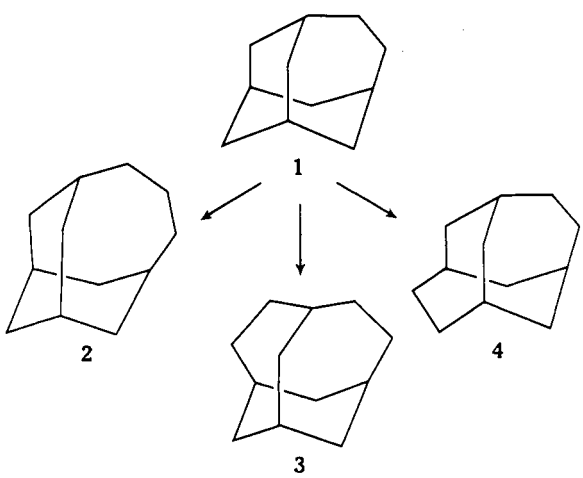
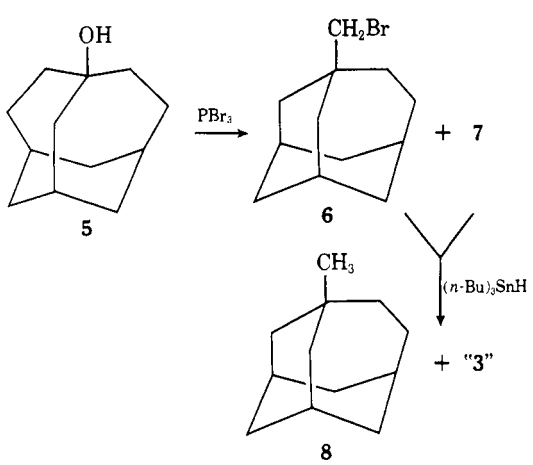
Three routes leading to 1,3-bishomoadamantane (**3**) have been developed. Homologation of homoadamant-4-en-2-one (**9**) by the Evans modification of the Tiffeneau–Demjanov ring expansion reaction gives a 90:10 mixture of tricyclo[4.4.1.1^{3,9}]dodec-7-en-4-one (**11**) and tricyclo[4.4.1.1^{3,9}]dodec-7-en-5-one (**12**), respectively. Reduction of **11**–**12** with sodium borohydride, followed by treatment of the resulting mixture of alcohols with phosphoryl chloride in pyridine, provides tricyclo[4.4.1.1^{3,9}]dodeca-4,7-diene (**23**). Catalytic hydrogenation of **23** affords **3**. Alternatively, homologation of 2-homoadamantanone by the same sequence of reactions employed for **9** → **11**–**12** gives a mixture of tricyclo[4.4.1.1^{3,9}]dodecan-4-one (**25**) and tricyclo[4.4.1.1^{3,9}]dodecan-5-one (**26**) which upon Wolff–Kishner reduction provides **3**. Finally, subjecting **25**–**26** to the same sequence of reactions utilized for **11**–**12** → **23** affords tricyclo[4.4.1.1^{3,9}]dodec-4-ene which gives **3** upon catalytic hydrogenation.

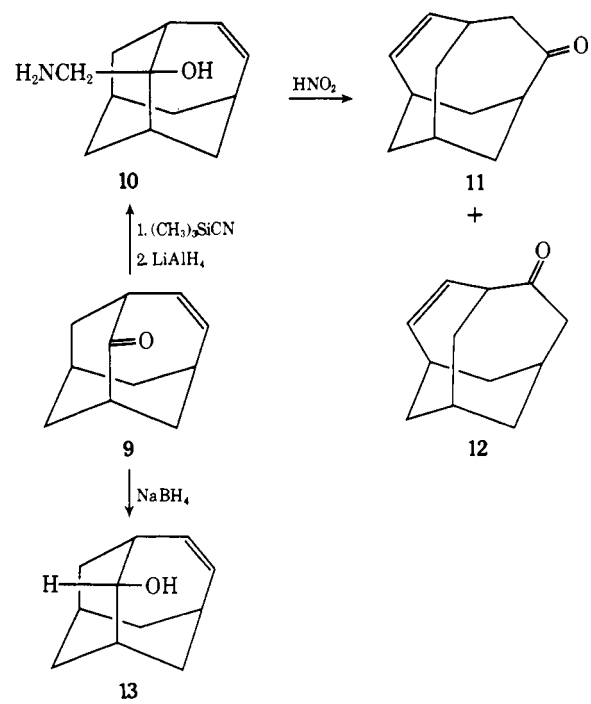
Insertion of a methylene group into any one of the carbon–carbon bonds in adamantane (T_d symmetry) gives but a single "homoadamantane" (**1**). By contrast, analogous homologation of **1** (C_{2v} or C_2 symmetry)[2] can afford three bishomoadamantanes (**2**–**4**). Sasaki has suggested the trivial names of 1,1-, 1,3-, and 1,5-bishomoadamantane, respectively, for these hydrocarbons.[3] Unequivocal syntheses of **2**[3] and **4**[4] have appeared and these compounds have been thoroughly characterized. However, the only reported synthesis of **3** is tenuous.[3] Treatment of an alcohol, presumed to have structure **5**, with phosphorus tribromide in *n*-hexane–benzene at 5–30 °C for 20 h gave in 25% yield a 6.5:1 mixture of 3-bromomethylhomoadamantane (**6**) and a "bridgehead bromide" (**7**), respectively. Subsequent reduction of this bromide mixture with tri-*n*-butyltin hydride in cyclohexane at 80–85 °C for 20 h and with Raney Ni catalyst at 40–50 °C for 2 days provided 3-methylhomoadamantane (**8**) and a minor product in a ca. 7.5:1 ratio, respectively. Since the minor product was not **2**, it was presumed to be **3**. However, the minor product was not isolated or characterized. We now wish to report an independent and unequivocal synthesis of 1,3-bishomoadamantane.





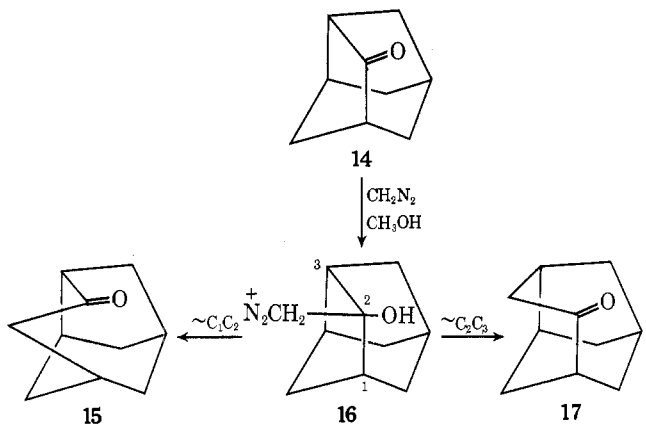
Results and Discussion

The skeletal framework of 1,3-bishomoadamantane was readily generated by Tiffeneau–Demjanov ring expansion of homoadamant-4-en-2-one (**9**).[5] Treatment of **9** with trimethylsilyl cyanide,[6] followed by reduction of the resulting trimethylsilyl cyanohydrin ether with lithium aluminum hydride, gave β-aminomethyl alcohol **10**. The stereochemical assignment of the substituents at C-2 in **10** follows from our earlier observation that sodium borohydride reduction of enone **9** gives 2-*endo*-homoadamant-4-enol (**13**) exclusively.[5] Treatment of **10** with nitrous acid provided in ca. 75% overall yield from **9** a 90:10 mixture of tricyclo[4.4.1.1^{3,9}]dodec-7-en-4-one (**11**) and tricyclo[4.4.1.1^{3,9}]dodec-7-en-5-one (**12**), respectively. Each of these enones shows a nonconjugated carbonyl absorption in the infrared at 1696 cm^{-1}. The assignment of the major product as the γ,δ-unsaturated ketone and the minor product as the β,γ-unsaturated ketone follows from the difference in chemical shift of the olefinic carbons in these compounds. As might well be expected, the difference

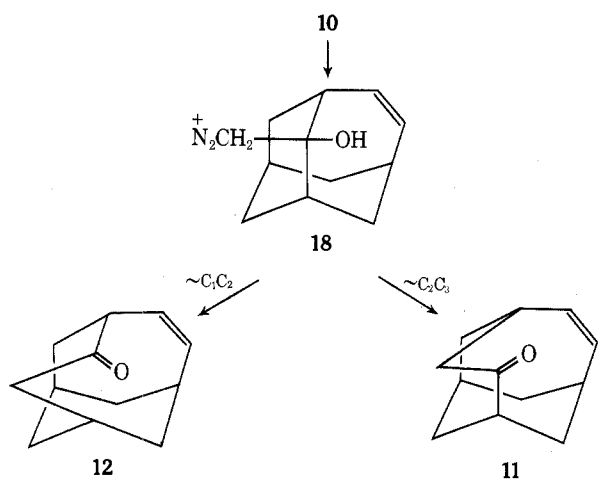


in chemical shift of the olefinic carbons in the γ,δ-unsaturated ketone (3.07 ppm) is significantly less than that for the β,γ-unsaturated ketone (10.14 ppm).[7] Moreover, the difference in chemical shift of the olefinic carbons in enone **9**, a β,γ-unsaturated ketone with a structure closely related to **12**, is 10.84 ppm.[7]

Recently, Schleyer and his co-workers have noted that homologation of 2-noradamantanone (**14**) with diazomethane proceeds with regioselective ring expansion of **14** to give 5-protoadamantanone (**17**) in 90–96% yield and 95% purity with no detectable amount of 4-protoadamantanone (**15**) present.[8]

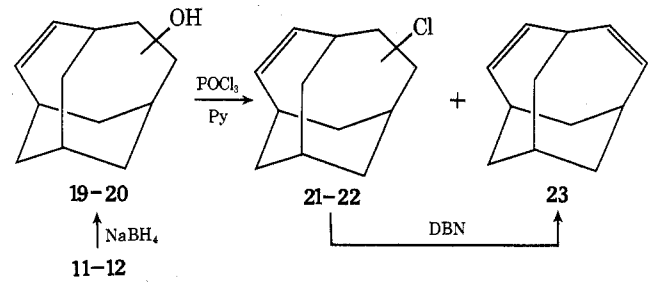


The complete migrational selectivity in intermediate **16** suggests a strong conformational preference of the two-carbon bridge in the protoadamantane products, i.e., migration of C_1–C_2 in **16** would lead to a transition state resembling ketone **15**, whereas C_2–C_3 bond migration in **16** would give **17**. Indeed, force field calculations on protoadamantane indicate that the conformation similar to **15** is ca. 6 kcal/mol higher in energy than the conformation resembling **17**.[8] It would appear that a similar analysis might explain the preferred migration of the C_2–C_3 bond in **18** to give **11** as the major product. It follows



that the preferred conformation of tricyclo[4.4.1.$1^{3,9}$]dodec-4-ene (**27**) probably resembles **11** rather than **12**.

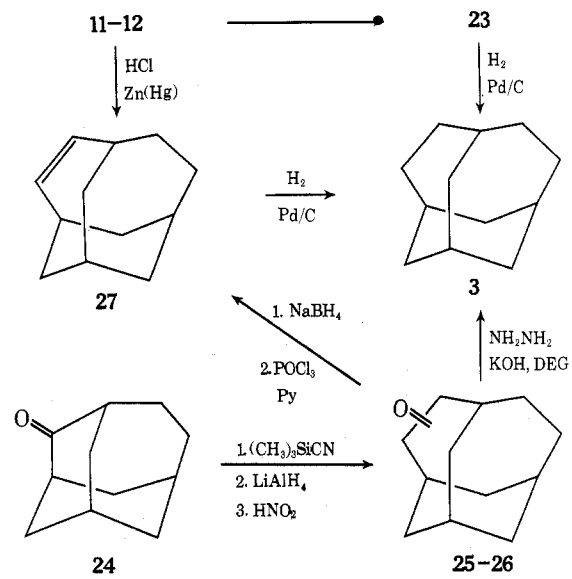
The synthesis of 1,3-bishomoadamantadiene (**23**) from **11–12** is straightforward. Sodium borohydride reduction of a 90:10 mixture of **11–12** gives a mixture of the corresponding alcohols (**19–20**) which when treated with phosphoryl chloride in pyridine at 5–15 °C affords a mixture of the corresponding chlorides (**21–22**) and diene **23** in a ratio of 45:55, respectively. If the mixture of reaction products is stirred with 1,5-diazabicyclo[4.3.0]non-5-ene (DBN) at 110 °C for 5 days,[9] the exclusive product is **23**. By this sequence of reactions, **23** can be obtained in ca. 40% overall yield from **11–12**. Consistent with the presence of a plane of symmetry in **23**, the ^{13}C NMR



spectrum of **23** contains only eight signals with four of the signals being twice as intense as the others.

Catalytic hydrogenation of diene **23** affords 1,3-bishomoadamantane (**3**). The ^{13}C NMR spectrum of **3** is consistent with the assigned structure. Alternative synthetic routes to **3** are summarized in Scheme I. Tiffeneau–Demjanov ring

Scheme I



expansion of 2-homoadamantanone[5] (**24**) by the same sequence of reactions employed for **9** → **11–12** provides in ca. 70% yield a mixture of tricyclo[4.4.1.$1^{3,9}$]dodecan-4-one (**25**) and tricyclo[4.4.1.$1^{3,9}$]dodecan-5-one (**26**). Attempts to separate **25** and **26** by GLC were unsuccessful. However, it is apparent that the mixture is highly enriched in **25** as catalytic reduction of a 90:10 mixture of **11–12** gives a mixture of **25** and **26** that cannot be differentiated from the product mixture obtained upon homologation of **24**. Wolff–Kishner reduction of **25–26** gives **3**.

A third route to **3** is via 1,3-bishomoadamantene (**27**). Subjecting a mixture of **25** and **26** to the sequence of reactions employed for **11–12** → **23** gives **27** in ca. 50% yield. Olefin **27** can also be obtained by Clemmensen reduction of **11–12** or by dechlorination of **21–22** with lithium in *tert*-butyl alcohol–tetrahydrofuran.[10] Catalytic hydrogenation of **27** gives **3**.

Experimental Section

Infrared spectra were obtained on Perkin-Elmer 180 or 337 spectrophotometers and proton magnetic resonance spectra were recorded with Varian A-60A or Perkin-Elmer R-12B 60-MHz spectrometers. Carbon magnetic resonance spectra were taken at an operating frequency of 22.63 MHz on a Bruker HFX-90 spectrometer equipped for Fourier transform pulsed NMR with a Nicolet 1085 data system. Electron-impact mass spectra were obtained with a Du Pont CEC 21-110B mass spectrometer. Unless noted otherwise, yields were obtained by integration of appropriate signals in the ^1H NMR spectrum of the product(s) vs. the signal of a predetermined amount of added standard (generally trichloroethylene) and are regarded as being accurate to ca. ±10%. Elemental analyses were performed by Micro-Analysis, Inc., Wilmington, Del.

Tricyclo[4.4.1.1^{3,9}]dodec-7-en-4-one (11) and Tricyclo-[4.4.1.1^{3,9}]dodec-7-en-5-one (12). 18-Crown-6 (106 mg) and potassium cyanide (25 mg) were dissolved in 2 ml of anhydrous methanol. Evaporation of the solvent at reduced pressure gave a white, waxy solid. This catalyst and trimethylsilyl cyanide (4.3 g, 0.04 mol) were added to homoadamant-4-en-2-one[5] (**9**, 2.0 g, 12 mmol) and the reaction mixture was stirred at room temperature under nitrogen for 72 h. The excess trimethylsilyl cyanide was removed from the reaction mixture by evaporation at reduced pressure to give a rust-colored viscous oil which showed no carbonyl absorption in the infrared. The resulting unpurified α-silyloxynitrile was dissolved in 10 ml of anhydrous ether and added dropwise under nitrogen to a stirred slurry of 1.0 g (26 mmol) of lithium aluminum hydride in 30 ml of anhydrous ether at a rate which maintained a gentle reflux of the reaction mixture. Stirring was continued for 2 h after the addition had been completed. The excess lithium aluminum hydride present was destroyed by cautious dropwise addition of 1.0 ml of water, followed by 1.5 ml of 10% sodium hydroxide and 3.2 ml of water. Stirring was continued until a granular white precipitate formed. Filtration provided a clear yellow ether solution which was dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure provided the crude amino alcohol as an orange solid.

A solution of 940 mg (13.6 mmol) of sodium nitrite in 10 ml of water was added over 15 min to a solution of the crude amino alcohol in 110 ml of water and 4 ml of acetic acid which was maintained at 5 °C. The resulting reaction mixture was stirred at 5 °C for 1 h and then at 20 °C for 1 h and 60 °C for 2 h. The reaction mixture was quenched with water (100 ml), saturated with sodium chloride, and extracted with ether (5 × 75 ml). The combined ether extracts were washed with 5% aqueous sodium bicarbonate (2 × 50 ml) and saturated aqueous sodium chloride (2 × 50 ml) and then dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure gave 1.68 g of a yellowish solid which by ^{1}H NMR analysis contained a ca. 75% overall yield of olefinic products. GLC analysis (10 ft × 0.25 in. DC-550 column, 200 °C) showed the presence of three components in a ratio of ca. 1:1:8 with retention times of 7.2, 11.5, and 12.8 min, respectively. The products were purified by GLC (above conditions). The compound of shortest retention time proved to be unreacted **9**. The other minor component of the reaction mixture was isolated as a white solid and identified as **12**: δ_{Me_4Si} ($CDCl_3$) 6.5–5.55 (m, 2 H, CH=CH) and 3.65–1.2 (br m, 14 H); ν (CCl_4) 3020, 2925, 2850, 1696, 1655, 1440, 1275, 1245, 1150, 1115, 1080, 1015, and 930 cm^{-1}.

Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 82.04; H, 8.98.

The major product was also obtained as a white solid and identified as **11**: ^{1}H NMR δ_{Me_4Si} ($CDCl_3$) 6.19–5.69 (m, 2 H, CH=CH) and 3.24–1.27 (br m, 14 H); ^{13}C NMR δ_{Me_4Si} ($CDCl_3$) 217.0 (C-4), 136.2 (C-8), 133.0 (C-7), 51.7 (C-5), 44.9 (C-3), 39.5 (t), 35.5 (d), 34.5 (t), 33.2 (t), 32.7 (d), 31.4 (d), and 30.7 (t); ν (CCl_4) 3015, 2915, 2900, 2850, 1696, 1445, 1330, 1270, 1190, 1090, and 1035 cm^{-1}.

Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.78; H, 9.09.

Tricyclo[4.4.1.1^{3,9}]dodeca-4,7-diene (23). A solution of 1.53 g (8.7 mmol) of a ca. 90:10 mixture of **11–12** in 20 ml of methanol was added dropwise to a stirred solution of 1.64 g (42.6 mmol) of sodium borohydride in 75 ml of methanol at 0 °C. The reaction mixture was stirred for 2 h at 0 °C and then for 6 h at room temperature, at which point 150 ml of water was added. The resulting white suspension was saturated with sodium chloride and extracted with ether (5 × 100 ml). The combined ether extracts were dried over anhydrous magnesium sulfate and the solvent was evaporated at reduced pressure to give 1.52 g of a solid residue. Sublimation afforded 1.32 g (ca. 85% yield) of a white solid which was homogeneous by GLC analysis (10 ft × 0.25 in. DC-550 column, 200 °C). This material was purified by GLC to give a white solid which is presumed to be a mixture of **tricyclo[4.4.1.1^{3,9}]-dodec-7-en-4-ol (19) and tricyclo[4.4.1.1^{3,9}]dodec-7-en-5-ol (20)** that is highly enriched in **19**: δ_{Me_4Si} ($CDCl_3$) 6.38–5.77 (m, 2 H, CH=CH), 4.45–3.88 (br m, 1 H, CHOH), and 2.88–1.25 (br m, 15 H); ν (CCl_4) 3580, 3010, 2910, 2850, 1450, 1400, 1195, 1130, 1120, 1075, 1050, and 1015 cm^{-1}.

Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.79; H, 9.91.

Phosphoryl chloride (1.604 g, 10.45 mmol) was added in five portions to a stirred solution of 1.24 g (6.97 mmol) of a mixture of **19** and **20** in 5.8 ml of pyridine. The temperature of the reaction mixture was lowered to ca. 5 °C before each addition of phosphoryl chloride and was raised to ca. 15 °C after each addition. When the addition was complete, the suspension was stirred for 12 h at 25 °C and then for 9 h at 60 °C. The reaction mixture was then cooled, diluted with 250 ml of water, and extracted with ether (4 × 100 ml). The combined ether extracts were washed with water and saturated aqueous sodium chloride, and then dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure gave a yellowish oil which formed a precipitate when added to water. This precipitate was filtered and sublimed (60 °C, 5 mm) to afford 611 mg of a white solid. GLC analysis (10 ft × 0.25 in. DC-550 column, 200 °C) indicated two major products with retention times of 4.0 and 10.2 min and some very minor components of intermediate retention times. Purification by GLC (above conditions) gave **23** (shorter t_R) as a white solid: ^{1}H NMR δ_{Me_4Si} ($CDCl_3$) 6.74–5.92 (m, 4 H, CH=CH) and 3.3–1.3 (br m, 12 H); ^{13}C NMR δ_{Me_4Si} ($CDCl_3$) 137.4, 134.5, 39.5, 35.2, 33.8, 32.9, 32.1, and 27.2 in the ratio of 2:2:1:2:1:1:2:1, respectively; ν (CCl_4) 3015, 2905, 2840, 1650, 1430, 950, and 865 cm^{-1}.

Anal. Calcd for $C_{12}H_{16}$: C, 89.94; H, 10.06. Found: C, 90.10; H, 9.76.

The product with t_R 10.2 min was also isolated by GLC (above conditions) as a white solid and is presumed to be a mixture of **7-chlorotricyclo[4.4.1.1.^{3,9}]dodec-4-ene (21) and 8-chlorotricyclo[4.4.1.1^{3,9}]dodec-4-ene (22)** that is highly enriched in **21**: δ_{Me_4Si} ($CDCl_3$) 6.48–5.68 (m, 2 H, CH=CH), 4.74–4.34 (m, 1 H,CHCl), and 3.22–1.08 (br m, 14 H); ν (CCl_4) 3010, 2920, 2850, 1445, 1195, and 945 cm^{-1}; *m/e* 196/198 = P/P + 2 = 3/1. Treatment of this material with lithium in *tert*-butyl alcohol–tetrahydrofuran (see below) gave **27**.

Analysis of the sublimed material by ^{1}H NMR showed that the ratio of **21–22:23** was 45:55.

The mixture of **21–22** and **23** (715 mg) and 1,5-diazabicyclo[4.3.0]-non-5-ene (1.362 g, 10.98 mmol) was stirred under a nitrogen atmosphere at 110 °C for 5 days. The reaction mixture was cooled, quenched in 250 ml of water, and then extracted with ether (6 × 75 ml). The combined ether extracts were washed with water (2 × 50 ml) and saturated aqueous sodium chloride (2 × 50 ml) and dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure provided a white solid which by GLC analysis (10 ft × 0.25 in. DC-550 column, 200 °C) contained only **23**. Sublimation (60 °C, 4 mm) of the residue gave 484 mg (3.03 mmol, 74% yield) of **23**.

Tricyclo[4.4.1.1^{3,9}]dodecan-4-one (25) and Tricyclo-[4.4.1.1^{3,9}]dodecan-5-one (26). A. A solution of 60 mg (0.34 mmol) of a 90:10 mixture of **11–12** in 50 ml of ethanol was stirred with 20 mg of 10% palladium on charcoal under an atmosphere of hydrogen for 24 h. The reaction mixture was then filtered to remove the catalyst. The catalyst was washed several times with methanol and the filtrate and washings were combined. Evaporation of the solvent at reduced pressure gave 56 mg (93% yield) of a white solid. This material appeared to be homogeneous under a variety of GLC conditions: 10 ft × 0.25 in. DC-550 column at 225, 200, and 175 °C; 10 ft × 0.25 in. SE-30 column at 225 °C; 5 ft × 0.25 in. OV-1 column at 225, 200, and 170 °C; and 5 ft × 0.25 in. Porapak Q column at 260, 225, and 200 °C. The ketone mixture was purified by GLC (10 ft × 0.25 in. DC-550 column, 190 °C) to give a mixture of **25** and **26** as a white solid which was highly enriched in **25**: δ_{Me_4Si} ($CDCL_3$) 2.88–2.54 (m, 2 H, —CH_2C=O)and 2.54–1.28 (br m, 16 H); ν (CCl_4) 2910, 2850, 1686, 1445, 1405, 1355, 1180, 1075, 1025, and 930 cm^{-1}.

Anal. Calcd for $C_{12}H_{18}O$: C, 80.85; H, 10.18. Found: C, 80.75; H, 10.21.

B. Treatment of 1.0 g (6.1 mmol) of 2-homoadamantanone[5] (**24**) by the sequence of reactions described for **9** → **11–12** gave in ca. 70% yield (by ^{1}H NMR analysis) a white solid whose infrared and ^{1}H NMR spectra were identical with those obtained for the 90:10 mixture of **25–26** generated in A.

Tricyclo[4.4.1.1^{3,9}]dodec-4-ene (27). A. Reduction of a mixture of 250 mg of **25** and **26** with sodium borohydride by the procedure described for **11–12** → **19–20** gave 253 mg of a white solid which was homogeneous by GLC analysis (10 ft × 0.25 in. DC-550 column, 200 °C). This material was purified by GLC to give a white solid which is presumed to be a mixture of **tricyclo[4.4.1.1^{3,9}]dodecan-4-ol (28) and tricyclo[4.4.1.1^{3,9}]dodecan-5-ol (29)** that is highly enriched in **28**: δ_{Me_4Si} ($CDCl_3$) 4.21–3.80 (m, 1 H, CHOH) and 2.77–1.18 (br m, 19 H); ν (CCl_4) 3630, 3400 (br), 2905, 1450, 1050, and 1020 cm^{-1}.

Anal. Calcd for $C_{12}H_{20}O$: C, 79.95; H, 11.18. Found: C, 80.03; H, 11.01.

Treatment of 187 mg of a mixture of **28** and **29** according to the conditions employed for **19–20** → **23** afforded 87 mg (51% yield) of **27** which was isolated by GLC (10 ft × 0.25 in. DC-550 column, 175 °C) as a white solid: δ_{Me_4Si} ($CDCl_3$) 6.30–5.46 (m, 2 H, CH=CH) and 2.93–1.25 (br m, 16 H); ν (CCl_4) 3010, 2900, 2845, 1445, 1190, 1155, 1000, 950, 940, and 930 cm^{-1}.

Anal. Calcd for $C_{12}H_{18}$: C, 88.82; H, 11.18. Found: C, 89.07; H, 10.98.

B. A solution of 50 mg of a 90:10 mixture of **11–12** in 1 ml of toluene was added to a mixture of 400 mg of amalgamated zinc, 0.5 ml of water,

and 1 ml of hydrochloric acid. The resulting mixture was vigorously refluxed for 4 days with portions of HCl and amalgamated zinc being added every 6 h. After cooling, the reaction mixture was diluted with 40 ml of water and extracted with ether (6 × 25 ml). The combined ether extracts were washed several times with 5% aqueous sodium bicarbonate, then with saturated aqueous sodium chloride (2 × 25 ml), and finally dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure gave a white solid which GLC analysis (10 ft × 0.25 in. DC-550 column, 200 °C) showed contained some unreacted starting material, a minor component which was not identified, and a major component with a relatively short retention time. Purification of the major product by GLC (above conditions) gave a white solid whose ir spectrum was identical with that of **27** obtained by procedure A.

C. Lithium (54 mg, 7.7 mmol) was added to a stirred solution of 19 mg (0.1 mmol) of a mixture of **21** and **22** in 2 ml of *tert*-butyl alcohol and 10 ml of dry tetrahydrofuran. The reaction mixture was stirred at room temperature for 3.5 h. Water (10 ml) was then added and stirring was continued for 30 min. The resulting solution was extracted with ether (3 × 40 ml) and the combined ether extracts were dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure gave a white solid which by GLC analysis (10 ft × 0.25 in. DC-550 column, 200 °C) contained a trace of starting material and a single major product. Purification of the product by GLC provided 3.5 mg of a white solid whose mass spectrum was identical with that of **27** obtained by procedure A.

Tricyclo[4.4.1.1^{3,9}]dodecane (3). A. A solution of 110 mg of **23** in 50 ml of ethanol was stirred at room temperature with 660 mg of 10% palladium on charcoal under an atmosphere of hydrogen for 24 h. The reaction mixture was filtered to remove the catalyst and the catalyst was washed several times with methanol. The filtrate and washings were combined and the methanol was removed by distillation to leave a solid residue which by GLC analysis (10 ft × 0.25 in. DC-550 column, 175 °C) contained a single component. Isolation of the product by GLC (above conditions) gave 47 mg of **3** as a white solid: ^{1}H NMR δ_{Me_4Si} ($CDCl_3$) 2.5–1.4 (br m); ^{13}C NMR δ_{Me_4Si} ($CDCl_3$) 44.65 (t), 40.99 (t), 36.62 (d), 34.35 (t), 32.57 (d), 31.76 (t), 31.06 (t), and 29.55 (d) in the ratio of 1:1:1:2:1:2:2:2, respectively; ν (CCl_4) 2910, 1450, 1260, 1200, 1140, 1110, and 1060 cm^{-1}.

Anal. Calcd for $C_{12}H_{20}$: C, 87.73; H, 12.27. Found: C, 87.84; H, 12.09.

B. Hydrogenation of **27** under the conditions employed for **23** → **3**, followed by purification of the product by GLC, provided a white solid whose mass spectrum was identical with that of **3** obtained by procedure A.

C. A solution of 50 mg of **25–26**, 264 mg of potassium hydroxide, and 230 mg of 95% hydrazine in 1.5 ml of diethylene glycol was heated with stirring at 110 °C for 30 min, and then for 3 h at 180 °C. During this time, a white solid appeared on the water-cooled condenser. The system was cooled and the material on the condenser was dissolved in ether and then dried over anhydrous magnesium sulfate. Evaporation of the solvent at reduced pressure afforded 30 mg of a white solid which by GLC analysis (10 ft × 0.25 in. DC-550 column, 175 °C) was homogeneous. Isolation of the product by GLC gave a white solid whose ir spectrum was identical with that of **3** obtained by procedure A.

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Registry No.—**3**, 36071-59-7; **9**, 55638-05-6; **11**, 59839-97-3; **12**, 59839-98-4; **19**, 59839-99-5; **20**, 59840-00-5; **21**, 59840-01-6; **22**, 59840-02-7; **23**, 59840-03-8; **24**, 55638-10-3; **25**, 59840-04-9; **26**, 59840-05-0; **27**, 59840-06-1; **28**, 59840-07-2; **29**, 59840-08-3; phosphoryl chloride, 10025-87-3.

References and Notes

(1) A preliminary report of this work was presented at the 10th Middle Atlantic Regional Meeting of the American Chemical Society, Philadelphia, Pa., Feb 25, 1976.
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Kinetics and Mechanism of Acidic and Alkaline Hydrolysis of Hindered *N*-Methylarylhydroxamic Acids

D. C. Berndt* and I. E. Ward

Department of Chemistry, Western Michigan University, Kalamazoo, Michigan 49008

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Thg kinetics of acidic and basic catalyzed hydrolysis of ortho-substituted *N*-methylbenzohydroxamic acids have been investigated at moderate acidity and high basicity. The results are interpreted in terms of a bimolecular mechanism for acidic catalysis and as reaction of the hydroxamic acid conjugate base with water and hydroxide ion for basic catalysis in the catalytic range investigated. Specific salt effects are reported.

We have investigated the kinetics and mechanism of the acidic and basic catalyzed hydrolysis of hindered benzohydroxamic acids in order to learn the effect of this increased hindrance upon the mechanisms of the reactions, the range of catalyst concentration required, and the importance of salt effects at these higher concentrations. The increased hindrance is provided by use of ortho-substituted *N*-methylbenzohydroxamic acids in comparison to unsubstituted benzohydroxamic acid. Smith and Yates[1] have studied the acid-catalyzed hydrolysis of benzamide, *N*-methyl- and *N,N*-dimethylbenzamide and have inferred from their data that all three compounds probably do not react via the oxygen protonated form *or* that benzamide does hydrolyze via oxygen protonation while the other N-substituted compounds do not. McClelland's[2] recent report of small but detectable ^{18}O exchange for the acidic hydrolysis of benzamide supports the latter conclusion.

Our present results indicate that there is no mechanism change in the acid-catalyzed hydrolysis upon introduction of an *N*-methyl and ortho groups in hydroxamic acids. There appears to be a significant rate of reaction in the absence of added acid or alkali at high salt concentrations. Specific salt effects are also observed.

Acidic Catalysis. Equation 1 expresses the reaction under