A study of the stereochemistry of this reaction has been reported separately.[21]

Experimental Section

All nmr spectra were run on a Varian A-60 instrument using $CDCl_3$ as solvent. Melting points were taken in sealed capillaries and are uncorrected. All reactions were carried out under an atmosphere of nitrogen.

General Procedure for Zn–HCl Reductions.—Acetic anhydride (40 ml) was saturated with HCl at −5 to −10° and 1 g of diketone was added; 10 g of activated zinc dust[22] was added slowly in portions over 3 hr with vigorous mechanical stirring so that the temperature of the reaction mixture remained below −5°. If the temperature was allowed to rise higher than this, the reaction became uncontrollable and the temperature rose rapidly to 40–50°. On completion of the addition the mixture was stirred for 2 hr longer at −5° and then filtered quickly through a prechilled funnel to remove the zinc residue, which was washed with cold acetic anhydride.

The diacetate was isolated by diluting the filtrate with 40 ml of water and adding solid Na_2CO_3 until the pH was neutral. The solution was extracted with three 100-ml portions of CH_2Cl_2, and the combined organic layers were washed with two 100-ml portions of water and dried over $MgSO_4$. Evaporation of solvents under reduced pressure gave the crude product.

This was converted to the free alcohol by stirring in 15 ml of methanol, 2 *N* in $NaOCH_3$, for 1 hr at room temperature. The solution was neutralized with excess Amberlite IR 120 (pyridinium form[23]), and the solution was decanted from the resin, which was washed with two 20-ml portions of methanol. Removal of the methanol under reduced pressure gave the crude alcohol, which was purified by chromatography, recrystallization, or sublimation.

Alternatively the alcohol could be isolated directly by adding the acetic anhydride filtrate to 200 ml of cold methanol and leaving the solution overnight. The solvents were removed under reduced pressure, and the oily residue was taken up in CH_2Cl_2 and washed with two 50-ml portions of H_2O, two 50-ml portions of 10% $NaHCO_3$, and 50 ml of H_2O. The organic layer was dried over $MgSO_4$ and evaporated under reduced pressure to give the crude alcohol.

Reactions using zinc amalgam in aqueous solution were carried out using the procedure of Wenkert and Yoder.[11]

Bicyclo[3.3.0]octane-1,5-diol.—The diol showed a symmetrical multiplet centered at δ 1.8 (12 H) and two exchangeable protons. An analytical sample, mp 61.5–62.0°, was obtained by recrystallization from hexane, mass spectrum *m/e* 142.

Anal. Calcd for $C_8H_{14}O_2$: C, 67.57; H, 9.92. Found: C, 67.61; H, 9.78.

$\Delta^{1,5}$-Bicyclo[3.3.0]octene.[10]—The benzaldehyde acetal of bicyclo[3.3.0]octane-1,5-diol was prepared by refluxing a solution of 426 mg (3 mmol) of the diol and 318 mg (3 mmol) of benzaldehyde in 15 ml of benzene with a catalytic amount (20 mg) of *p*-toluenesulfonic acid for 3 hr. The cooled solution was stirred with solid K_2CO_3 and the solvents were evaporated. The residue was chromatographed over 10 g of neutral alumina to remove trace amounts of unreacted starting material. Elution with hexane gave 620 mg (90% yield) of a straw-colored liquid, nmr δ 1–2.5 (m, 12 H), 5.80 (s, 1 H), and 7.4 (m, 5 H).

To a solution of 230 mg (1 mmol) of the benzaldehyde acetal in 20 ml of ether at 0° was added 1.6 ml of 1.3 *M* *n*-butyllithium in pentane (2.1 mmol). The solution was stirred for 24 hr at 0° and then 2 ml of H_2O was added. The organic layer was separated, the water was washed with two 2-ml portions of ether, and the combined ether washings were washed with 2 ml of H_2O and 2 ml of brine. After drying over $MgSO_4$, most of the solvent was removed by distillation through a 25-cm Vigreux column. Then 1 ml of CH_2Cl_2 was added, the stillhead was attached directly to the pot, and the distillation was continued until no more solvent was collected at a pot temperature of 80°. The pot was allowed to cool to room temperature and the distillation was continued under vacuum (water aspirator ≈15 mm) while cooling the receiver in liquid nitrogen. The pot was briefly heated to 60° before the distillation was discontinued; 170 mg of volatile material was collected and analyzed by nmr, which showed three singlets, one for CH_2Cl_2, one for cyclohexane (present in the commercial *n*-butyllithium solution), and one at δ 2.18 from the $\Delta^{1,5}$-bicyclo[3.3.0]octenes.[10b] A pure sample of this material was isolated by glc and had an ir spectrum identical with that reported by Block.[10c]

Tricyclo[3.3.1.0^{3,7}]nonane-3,7-diol (2, *n* = 1).—Prepared by the general procedure described above, the crude diol was stirred with ether and filtered to give a granular solid, mp 301–303° (lit. 297–298°), mass spectrum *m/e* 154.

Anal. Calcd for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.05; H, 9.19.

3,7-Dimethyltricyclo[3.3.0.0^{3,7}]octan-1-ol (4).—The crude alcohol obtained by the general procedure described above was purified by chromatography on silica gel (25 g/g). Elution with 7:3 pentane–ether removed the ketone 5 from the column. The alcohol 4 eluted with 1:1 pentane–ether. Sublimation at 55–60° (15 mm) gave a 50% yield of pure alcohol, mp 108–109°, mass spectrum *m/e* 152.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 79.15; H, 10.68.

Tosylate of 4.—To a solution of 1.0 g (6.5 mmol) of the alcohol in 5 ml of dry pyridine at 0° was added 1.4 g (7.2 mmol) of tosyl chloride in 5 ml of pyridine. The solution was stirred for 16 hr, after which 0.5 ml of H_2O was added and the solution was stirred for an additional hour. Most of the pyridine was removed under reduced pressure, and the residue was taken up in CH_2Cl_2 and washed with 15 ml of 1 *M* HCl, 15 ml of H_2O, and 15 ml of 10% $NaHCO_3$. The CH_2Cl_2 was evaporated under reduced pressure to give 1.6 g (80% yield) of spectroscopically pure tosylate. Recrystallization from pentane afforded an analytical sample, mp 75.5–76.5°.

Anal. Calcd for $C_{17}H_{22}O_3S$: C, 66.65; H, 7.24; S, 10.46. Found: C, 66.57; H, 7.15; S, 10.54.

1,5-Dimethylbicyclo[3.3.0]octan-3-one (5).—A solution of 152 mg (1 mmol) of 4 and 168 mg (1.5 mmol) of potassium *t*-butyl alcohol was refluxed for 4 hr. After cooling it was diluted with 7 ml of H_2O, neutralized with 1 *M* HCl, and extracted with three 20-ml portions of ether. The ether extracts were washed with two 10-ml portions of water and with saturated brine, and dried over $MgSO_4$. Evaporation of the solvent gave 130 mg (85%) of the ketone 5 (ir 1740 cm^{-1}), pure by nmr [δ 1.06 (s, 6 H), 1.73 (s, 6 H), and 2.20 (d, 4 H)]. An analytical sample was prepared by sublimation.

Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.65: H, 10.45.

Registry No.—2 (*n* = 1), 29898-26-8; 4, 32139-02-9; 4 tosylate, 32256-06-7; 5, 32139-03-0; bicyclo[3.3.0]-octane-1,5-diol, 32139-04-1.

Acknowledgment.—We wish to thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the Research Corporation for partial support of this work. We also wish to thank Messrs. Richard Weinberg and Conrad Schmidt for some experimental assistance.

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(23) Prepared by washing the resin with 10% aqueous pyridine followed by distilled water and then methanol.

Synthesis of 1-Methyladamantano[1,2-*b*]pyrrolidine, a Novel Heterocyclic System

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The interesting chemistry of adamantane[1] and the biological activity of aminoadamantane and its de-

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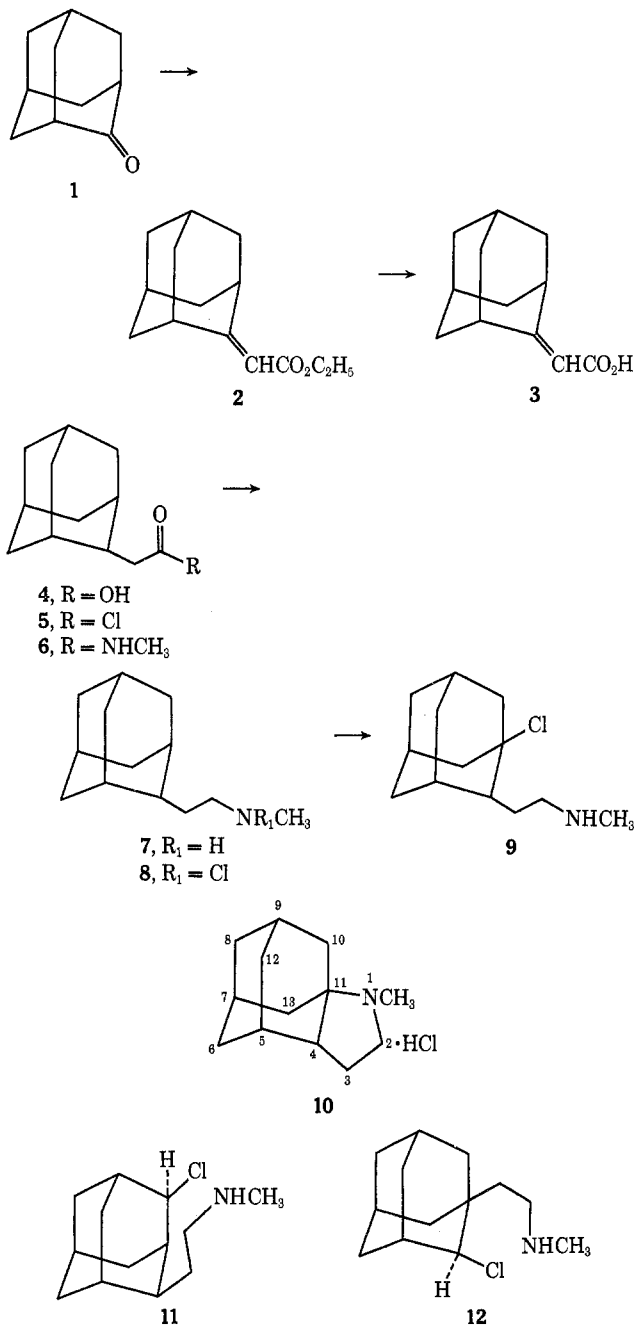
rivatives[2] have stimulated an interest in the syntheses of 1,2-disubstituted adamantanes.[3] The recent report on the syntheses of compounds containing heterocyclic ring systems fused onto the 1 and 2 positions of adamantane[4] prompts us to report our synthesis of 1-methyladamantano[1,2-*b*]pyrrolidine (**10**), a novel heterocyclic system.

The successful route to the synthesis is based on the reaction sequence shown in Scheme I. The reaction

SCHEME I



of 2-adamantanone with triethyl phosphonoacetate and sodium hydride gave Δ^2,α-adamantaneacetic acid ethyl ester (**2**). It was determined that, by using 1.5 equiv of triethyl phosphonoacetate to 1 equiv of 2-adamantanone and allowing the reaction to proceed at 45°, a nearly quantitative yield of **2** could be realized. Base hydrolysis of **2** furnished Δ^2,α-adamantaneacetic acid (**3**) in 98% yield. Catalytic hydrogenation of **3** over palladium on charcoal gave a quantitative yield of 2-adamantaneacetic acid (**4**). Compound **4** was converted to its acid chloride **5** by reaction with thionyl chloride. Treatment of **5** with 40% aqueous monomethylamine furnished an 86% yield of *N*-methyl-2-adamantaneacetamide (**6**). Reduction of **6** with lithium aluminum hydride in tetrahydrofuran gave a 90% yield of *N*-methyl-2-adamantaneethylamine (**7**). Treatment of **7** with aqueous sodium hypochlorite solution[5] yielded the desired *N*-chloroamine **8**.

The *N*-chloroamine **8** was then subjected to Hofmann–Loeffler–Freytag reaction. The reaction is customarily run in strong sulfuric acid or sulfuric acid–acetic acid mixtures, with heat or ultraviolet light used to initiate the free-radical reaction.[6] The use of strong acid and heat, in our case, led to the formation of 2-adamantanone.[7] However, photolysis of **8** in the sulfuric acid–acetic acid mixture, using a low-pressure mercury lamp at 25° for 1 hr, gave a good yield (85%) of a single product (tlc). It has been assigned structure **9**: nmr τ 6.05–6.30 (br, 1, NH), 7.44–7.58 (m, 2-$CH_2N<$), 7.75–7.87 (d, 3, CH_3NH), 7.87–8.09 (2, CH_2), 8.09–8.5 (s, 14 H). The alternate isomeric structure **11** is ruled out, since the characteristic upfield absorption (doublet at τ 8.5–8.7) of the hydrogen on the carbon bearing the chlorine in compounds of type **12**[8] is absent in our product. The much greater stability of the tertiary adamantane radical, together with the preferential formation of six-atom cyclic transition states, generally noted in Hofmann–Loeffler–Freytag reactions,[9] would explain the exclusive formation of **9**.

The cyclization of **9** presented considerable difficulties. Compound **9** was found to be particularly resistant to solvolytic displacement under a variety of reaction conditions. Clearly, no "back-side" attack is possible at the tertiary center through the cage compound. Even the aluminum halide catalyzed substitution reaction conditions involving the bridgehead "carbonium ion," so generally successful in the adamantane field,[1] failed. The cyclization was finally achieved in 34% yield by heating at 290° for 10 min. The structure of **10** is supported by microanalysis and the spectral data: ir 3.70–4.4 μ (>NH^+); nmr τ −2.17 to −1.50 (br, 1, N^+H), 5.83–6.42 (m, 2, $CH_2N<$), 6.90–7.30 (m, 2, CH_2), 7.35–7.45 (d, 3, >N^+H-CH_3), 7.65–8.5 (m, 14 H); mass spectrum *m/e* 191 (M^+ − HCl).

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Experimental Section

Melting points were determined on a Thomas-Hoover "Uni-Melting" apparatus and are uncorrected. Infrared spectra were determined on a Perkin-Elmer 21 spectrometer in Nujol. Nmr spectra were obtained on a Varian A-60 spectrometer in $CDCl_3$, with $(CH_3)_4Si$ as the internal standard. Mass spectra were determined on an AEI-MS-902 mass spectrometer.

Δ^2,α-Adamantaneacetic Acid (3).—To a well-stirred suspension of 21.8 g (0.45 mol) of sodium hydride (NaH) in 300 ml of dry 1,2-dimethoxyethane (DME), 100.9 g (0.45 mol) of triethyl phosphonoacetate was added slowly at 20°. After stirring for 2 hr at room temperature, a solution of 45.0 g (0.3 mol) of **1** in 450 ml of dry DME was added rapidly. The reaction mixture was maintained at 45° for 2 hr and then stirred overnight at room temperature. The mixture was concentrated, diluted with water, and extracted with ether. The ether extract was washed with water, dried ($MgSO_4$), and concentrated to give 65.5 g (99%) of **2** as a thick yellow liquid, ir 5.83 (C=O), 6.08 μ (conjugated C=C).

The crude ester **2** was hydrolyzed by refluxing with 300 ml of 5 *N* alcoholic KOH for 4 hr. The basic solution was cooled, acidified with 5 *N* HCl, and extracted with $CHCl_3$. The $CHCl_3$ solution was dried ($MgSO_4$) and evaporated *in vacuo* to give 56.6 g (98%) of **3** as brownish-white powder. Crystallization from dilute acetone gave an analytical sample: mp 136–138°; ir 3.70–4.00 (bonded OH), 5.90 (C=O), 6.10 μ (conjugated C=C); nmr τ 4.38 (s, 1, vinyl H), 5.83–6.05 (br, 1, OH), 7.37–7.66 (br, 2, CH adjacent to C=C), 7.83–8.25 (s, 12 H).

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 75.19; H, 8.49.

2-Adamantaneacetic Acid (4).—A solution of 9.6 g (0.05 mol) of **3** in C_2H_5OH containing 1 equiv of 5 *N* NaOH was hydrogenated over 5% Pd/C. After acidification, the solvent was removed *in vacuo* and the residue was extracted with $CHCl_3$, dried ($MgSO_4$), and evaporated *in vacuo* to give 9.5 g (94%) of white solid, mp 118–120°. Recrystallization from pentane gave an analytical sample as white crystals: mp 118–120°; ir 3.70–4.00 (bonded OH), 5.92 μ (C=O); nmr τ 5.34 (s, 1, OH), 7.55 (br, 2, CH_2), 8.07–8.38 (s, 15H).

Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.05; H, 9.32.

***N*-Methyl-2-adamantaneacetamide (6).**—The reaction of 8.9 g (0.046 mol) of **4** with thionyl chloride gave 9.4 (97%) of the acid chloride **5**, ir 5.50 μ (C=O). It was dissolved in 50 ml of dry tetrahydrofuran (THF) and added dropwise to 10 ml of 40% aqueous solution of monomethylamine. The THF was evaporated *in vacuo*, and the residue was extracted with $CHCl_3$, dried ($MgSO_4$), and concentrated to give 7.9 g (86%) of **6** as a white solid, mp 142–149°. Crystallization from CH_3CN gave an analytical sample as white needles: mp 147–150°; ir 3.05–3.25 (NH), 6.02–6.12 μ (C=O); nmr τ 4.00–4.30 (br, 1, NH), 7.14–7.22 (d, 2, CH_2), 7.70 (br, 3, NCH_3), 8.05–8.40 (s, 15H).

Anal. Calcd for $C_{13}H_{21}NO$: C, 75.31; H, 10.21; N, 6.76. Found: C, 75.21; H, 10.15; N, 6.76.

***N*-Methyl-2-adamantaneethylamine (7).**—To a well-stirred suspension of 3.0 g of lithium aluminum hydride in 100 ml of dry THF cooled in ice, a solution of 7.4 g (0.36 mol) of **6** in 100 ml of dry THF was added dropwise. The reaction mixture was then refluxed overnight. Working up the reaction yielded 6.5 g (90%) of **7** as an oil: ir 3.00 μ (NH); nmr τ 4.30–4.55 (NH), 7.16–7.55, 8.08–8.45. The hydrochloride of **7** was crystallized from CH_3CN to give an analytical sample, mp >270°, ir 3.30–4.10 μ (NH_2^+ and CH).

Anal. Calcd for $C_{13}H_{23}N \cdot HCl$: C, 67.99; H, 10.53; N, 6.10. Found: C, 68.11; H, 10.81; N, 6.02.

1-Chloro-*N*-methyl-2-adamantaneethylamine (9).—A solution of 15.4 g (0.08 mol) of **7** in CH_2Cl_2 was stirred at room temperature with 200 ml of 5% NaOCl for 2 hr. The aqueous layer was removed, 200 ml of fresh NaOCl was added, and the mixture was stirred overnight at room temperature. The organic layer was separated, washed with water, dried ($MgSO_4$), and evaporated *in vacuo* to give 16.4 g (90%) of **8** as an oil. Compound **8** was dissolved in 190 ml of acid solution (16.7 ml of 95–98% H_2SO_4, 4.3 ml of H_2O, and 160 ml of CH_3CO_2H) and photolyzed at 25° in a Hanovia photochemical reactor with a low-pressure mercury lamp. After 1 hr exposure, the reaction mixture gave a negative halogen test with KI solution. After cooling, the solution was made basic with 10% NaOH, extracted with $CHCl_3$, washed with water, dried ($MgSO_4$), and evaporated *in vacuo* to give 15.5 g (85%) of **9** as a yellow oil: ir 2.85–3.20 μ (NH); nmr τ 6.05–6.30 (br, 1, NH), 7.44–7.58 (m, 2, $CH_2N<$), 7.75–7.87 (d, 3, CH_3NH), 7.87–8.5 (br, 2, CH_2), 8.09–8.5 (s, 14 H). The hydrochloride of **9** was crystallized from CH_3CN to give an analytical sample, mp >270°.

Anal. Calcd for $C_{13}H_{22}NCl \cdot HCl$: C, 59.10; H, 8.77; N, 5.31. Found: C, 59.23; H, 8.92; N, 5.13.

1-Methyladamantano[1,2-*b*]pyrrolidine (10).—Compound **9** (4.5 g, 0.02 mol) was heated under nitrogen at 290° (previously heated oil bath) for 10 min. After cooling, the residue, ir 3.70–4.4 μ (N^+H-), was triturated with 10% NaOH. The oil that formed was extracted with $CHCl_3$, washed with water, dried ($MgSO_4$), and evaporated to give 3.2 g of residue. It was dissolved in 20 ml of acetic anhydride and stirred overnight at room temperature. The excess acetic anhydride was removed *in vacuo* and the residue was partitioned between $CHCl_3$ and 5 *N* HCl. The aqueous layer was separated, basified, extracted with $CHCl_3$, dried ($MgSO_4$), and evaporated *in vacuo* to give 1.3 g (34%) of **10** as a pale yellow oil. The hydrochloride of **10** was crystallized from dioxane to give white crystals: mp 231–236°; ir 3.70–4.44 μ ($>N^+H-$); nmr τ −2.17 to −1.50 (br, 1, N^+H), 5.83–6.42 (m, 2, $CH_2N<$), 6.90–7.30 (m, 2, CH_2), 7.35–7.45 (d, **3**, $>N^+HCH_3$), 7.65–8.5 (m, 14 H); mass spectrum *m/e* 191 (M^+ − HCl).

Anal. Calcd for $C_{13}H_{21}N \cdot HCl$: C, 68.55; H, 9.74; N, 6.15; Cl, 15.57. Found: C, 68.30; H, 9.61; N, 6.18; Cl, 15.38.

Registry No.—**3**, 25220-07-9; **4**, 26082-22-4; **6**, 32132-60-8; **7** HCl, 32132-61-9; **9** HCl, 32132-63-1; **10**, 32139-10-9.

Reevaluation of α-Alkyl Substituent Kinetic Effects on Acid- and Base-Catalyzed Enolization

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Recently published work indicates that a controversy still exists regarding the exact nature of the influence exerted by α-alkyl groups on the rates of enolization of carbonyl compounds. According to Warkentin, *et al.*,[1] "the usual effect of an α-alkyl substituent is to accelerate acid-catalyzed enolization and to retard base-catalyzed enolization relative to the corresponding rates for unsubstituted ketone." This statement appears to be well authenticated for the case of base-catalyzed enolization[1,2] but appears to be less definite for acid-catalyzed enolization.[3] The above generalization arises essentially from studies of the preferential enolization rates of ketones containing two reaction sites, which of course constitutes a slightly different problem from that encountered in the comparative studies of alkyl- and nonalkyl-substituted ketones. Actually this generalization is in contradiction with results obtained for phenyl alkyl ketones[4] and dialkyl

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