Synthesis and Reactions of 3- and 3,7-Substituted Bicyclo[3.3.1]nonanes[1]

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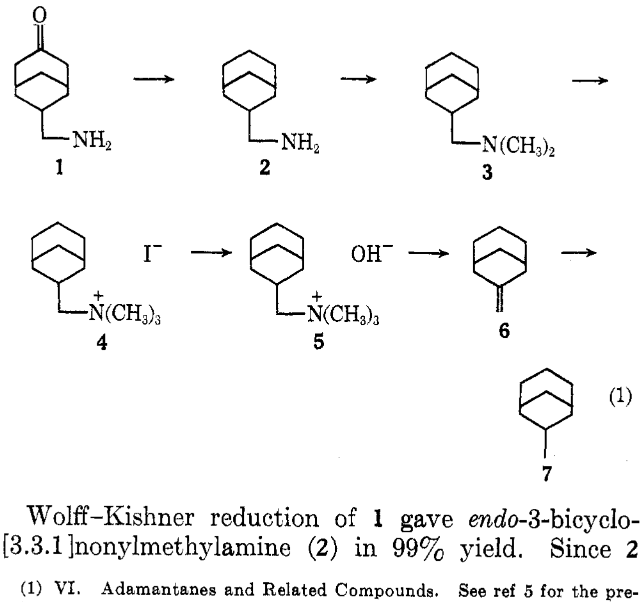
The readily available *endo*-7-aminomethylbicyclo[3.3.1]nonan-3-one serves as a convenient precursor for a variety of 3- and 3,7-substituted bicyclo[3.3.1]nonanes. The individual steps generally proceed in high yield. New compounds which are made available include *endo*-3-bicyclo[3.3.1]nonylmethylamine, *N*,*N*-dimethyl-7-methylene-*endo*-3-bicyclo[3.3.1]nonylamine, 7-methylenebicyclo[3.3.1]non-2-ene, and *endo*-3-bicyclo[3.3.1]-nonylcarbonitrile. 1-Methyl-2-oxaadamantane was also prepared. In addition, novel routes are provided for the indicated substances, 3-methylenebicyclo[3.3.1]nonane, *endo*-3-methylbicyclo[3.3.1]nonane, 3-methylbicyclo-[3.3.1]non-2-ene, and 3-bicyclo[3.3.1]nonylcarboxylic acid.

Various methods have been employed for the preparation of bicyclo[3.3.1]nonanes, in which acyclic or monocyclic materials serve as the immediate precursors.[2] Included in some of the newer approaches is the ring opening of suitably substituted adamantanes, which generally leads to 3,7-disubstituted derivatives.[2,3] Recently, in this category, 1-*N*,*N*-dichloroaminoadamantane was found[4] to provide *endo*-7-aminomethylbicyclo[3.3.1]nonan-3-one (**1**) in good yield from rearrangement by aluminum chloride with subsequent acid hydrolysis. The scope of this reaction has been investigated.[5,6] The present report is concerned with use of **1** as a versatile precursor for preparation of a variety of 3- and 3,7-substituted bicyclo[3.3.1]nonanes. New members of the series are made available, in addition to novel routes to previously reported compounds.

Results and Discussion

The first sequence of reactions involving the amino ketone is set forth in eq 1.



Wolff–Kishner reduction of **1** gave *endo*-3-bicyclo-[3.3.1]nonylmethylamine (**2**) in 99% yield. Since **2** is sensitive to carbon dioxide in air, characterization was accomplished mainly with the benzamide derivative; the nmr spectrum showed an indistinct triplet at δ 6.9 (1 H), attributed to NH (1 H) split by methylene protons, and another triplet at 3.3 (2 H) arising from CH_2N split by the bridgehead and NH protons. Compound **2** was converted to *N*,*N*-dimethyl-*endo*-3-bicyclo[3.3.1]nonylmethylamine (**3**) in 81% yield by formaldehyde in formic acid. Reaction with methyl iodide afforded the quaternary iodide **4** in 84% yield, which, in turn, gave rise to the quaternary hydroxide **5** on treatment with silver oxide. Hofmann elimination generated 3-methylenebicyclo[3.3.1]nonane[7] (**6**) (77% yield based on **4**). Exocyclic olefinic bands were present in the ir spectrum at 3100 and 875 cm^{-1}, in accord with the singlet at δ 4.6 (2 H) in the nmr spectrum. Hydrogenation of **6** with Pd/C gave 3-methylbicyclo[3.3.1]nonane (**7**) in 72% yield. Since **6** probably exists in the chair–chair conformation,[2] it is reasonable to assign the endo configuration to the major isomer on the basis of addition of hydrogen from the less hindered side. The minor component present is thought to be the exo isomer on the basis of a prior report[7] on hydrogenation of **16**. Our endo:exo ratio of 87:13 compares favorably with that, 86.5:13.5, reported for hydrogenation[7] of **16**.

Equation 2 summarizes the second sequence of reactions starting with **1**.

Exhaustive methylation was also performed with 4-azahomoadamantane (**8**) obtained from lithium aluminum hydride reduction[4] of **1**. The steps consisted of sequential formation of *N*-methyl-4-azahomoadamantane (**9**) in 83% yield, the iodide **10** in 98% yield, and then the hydroxide **11**. Decomposition of **11** gave *N*,*N*-dimethyl-7-methylene-*endo*-3-bicyclo[3.3.1]-nonylamine (**12**) in 64% yield (based on **10**). The structure of **12** was supported by the ir spectrum, indicating exocyclic olefinic CH at 3100 and 880 cm^{-1}, and the nmr spectrum, which also showed exocyclic olefin protons at δ 4.73 (s, 2 H). The tertiary proton CHN appeared at 3.0 (1 H). The direction of elimination is in accord with prior analogy.[8] The amino olefin **12** was subsequently converted to the iodide **13** (81% yield), and then to the hydroxide **14**. Pyrolysis of **14** provided 7-methylenebicyclo[3.3.1]non-2-ene (**15**) in 74% yield (based on **13**). Used in identification was the ir spectrum, displaying both exocyclic olefinic CH at 3100 and 878 cm^{-1} and endocyclic olefinic CH at 3050 and 720 cm^{-1}; alkene adsorption at 1645 cm^{-1} was also present. The nmr spectrum further

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[1] VI. Adamantanes and Related Compounds. See ref 5 for the preceding paper in the series.

[2] G. L. Buchanan in "Topics in Carbocyclic Chemistry," Vol. 1, D. Lloyd, Ed., Plenum Press, New York, N. Y., 1969, Chapter 3.

[3] (a) R. M. Black and G. B. Gill, *Chem. Commun.*, 972 (1970); (b) W. H. W. Lunn, *J. Chem. Soc. C*, 2124 (1970); (c) H. Stetter and P. Tacke, *Chem. Ber.*, **96**, 694 (1963); (d) F. N. Stepanov and V. D. Sukhoverkhov, *Angew. Chem., Int. Ed. Engl.*, **6**, 864 (1967); (e) H. Hamill, A. Karim, and M. A. McKervey, *Tetrahedron*, **27**, 4317 (1971); (f) A. R. Gagneux and R. Meier, *Tetrahedron Lett.*, 1365 (1969).

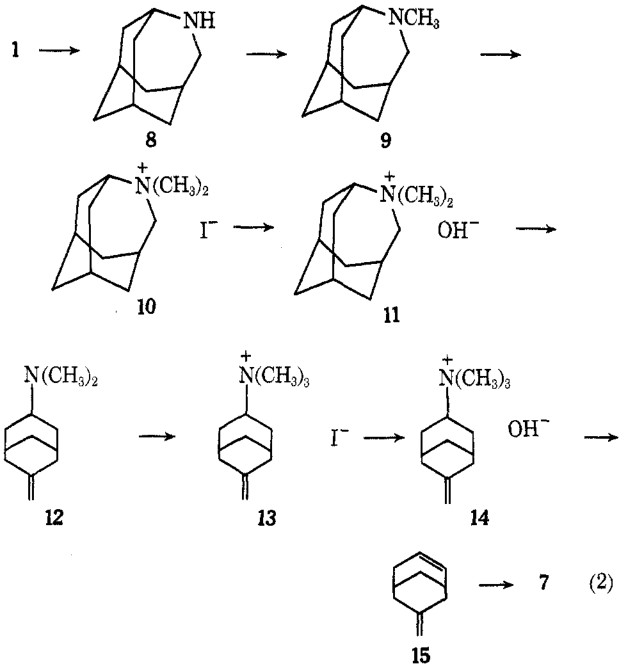
[4] P. Kovacic, J.-H. Liu, E. M. Levi, and P. D. Roskos, *J. Amer. Chem. Soc.*, **93**, 5801 (1971).

[5] S. J. Padegimas and P. Kovacic, *J. Org. Chem.*, **37**, 2672 (1972).

[6] T. Sasaki, S. Eguchi, T. Kiriyama, and H. Suzuki, *Syn. Commun.*, **1**, 267 (1971).

[7] R. A. Appleton and S. H. Graham, *Chem. Commun.*, 297 (1965).

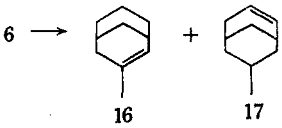
[8] A. C. Cope and E. R. Trumbull, *Org. React.*, **11**, 317 (1960).



(2)

substantiated the presence of two types of olefinic protons. Catalytic hydogenation of **15** also gave **7**, consisting mainly of the endo isomer.

The behavior of the unsaturates **6** and **15** on exposure to 97% formic acid was examined. Appleton and Graham have reported[7] the isomerization of 3-methylenebicyclo[3.3.1]nonane (**6**) to **16** (93%) and **17** (7%) from contact with formic acid at room temperature for some months (eq 3). We observed a similar result, namely a ratio of 96:4, after 12 hr at 100°. **16** was characterized and **17** was assumed to be the minor product. In contrast, the diene **15** gave, on refluxing with formic acid, a complex mixture containing 1-methyl-2-oxaadamantane (**18**) as the principal component (eq 4). Compound **18** was identified[9] by elemental analysis and spectral data (ir, nmr, and mass). A number of mechanistic pathways can be visualized for formation of the oxa compound, one of which is set forth in eq 5.



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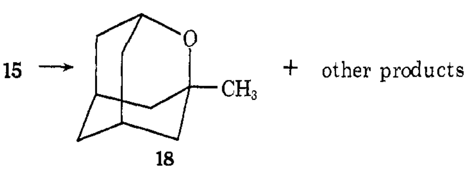

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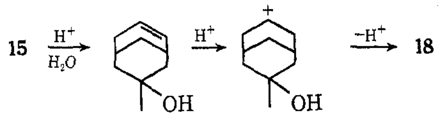

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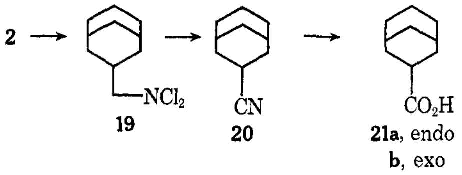
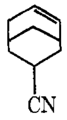


(6)

Another series of reactions based on **2** is shown in eq 6. The first step entailed conversion to the N,N-dichloro derivative **19** in 67% yield by exposure to calcium hypochlorite. Various reagents, quinoline, cesium fluoride, and potassium *tert*-butoxide, were examined for transformation of **19** to 3-bicyclo[3.3.1]-nonylcarbonitrile (**20**). The dehydrohalogenation was accomplished most effectively (65% yield) by quinoline. Only one nitrile product, presumably the endo isomer, was obtained under the various conditions, with no evidence for formation of the exo epimer. Structural confirmation for **20** was realized through synthesis by an alternate route. *endo*-3-Bicyclo[3.3.1]non-6-enecarbonitrile (**22**), prepared[10] from adamantanone under conditions of the Schmidt reaction, was subjected to catalytic hydrogenation in the presence of Pd/C catalyst. After 2 hr, reduction of the alkene functionality was incomplete. Additional exposure to the same conditions gave **20** along with basic material which was not characterized.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Hydrolysis of the saturated nitrile **20** to the carboxylic acid function was explored under both acidic and basic conditions. With aqueous sulfuric acid at reflux for 6 hr, a 66:34 mixture of exo:endo acids was formed. In the presence of caustic (reflux for 8 hr in methyl Cellosolve), the exo:endo ratio was 90:10. Prolonged exposure of the epimeric mixture of acids to caustic brought about isomerization to the exo form almost exclusively. Both isomers are reported in the literature.[11] Equilibration of the ester derivatives by methoxide is known[11] to favor the exo isomer to the extent of about 99%.

Experimental Section

Materials and Analytical Procedures.—Methylene chloride was dried at reflux over calcium hydride and distilled. Methyl iodide (Matheson Coleman and Bell) was used as received. Ir spectra were obtained with a Beckman IR-8 spectrophotometer (calibrated with the 1601.8 cm^{-1} band of polystyrene). Varian T-60 and HA-100 instruments were used to obtain nmr data, which are reported in parts per million (δ) (in CDCl$_3$ unless otherwise indicated) relative to tetramethylsilane as internal standard. Microanalyses were performed by Galbraith Laboratories, Knoxville, Tenn., Micro-Tech Laboratories, Skokie, Ill., and by Mr. A. Gasiecki. Glpc was conducted on a Varian Aerograph 1800 instrument with the indicated columns: (I) 3% silicone DC 550, 3% Carbowax 20M on Chromosorb P (30/60 mesh), 10 ft × 0.25 in., copper: (II) 15% Carbowax 20M on Chromosorb W (45/60 mesh), 10 ft × 0.25 in., copper. Melting points and boiling points are uncorrected.

***endo*-7-Aminomethylbicyclo[3.3.1]nonan-3-one** (**1**).—A published procedure[4] was modified as indicated. The mixture obtained from addition of the acidic solution at about 10° to 1.4 l. of 50% sodium hydroxide was filtered and washed with water. The solid was extracted with warm (60–70°), 95% ethanol. After filtration, the residue, which contained inorganic solid, was extracted twice more with warm ethanol. The combined fil-

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[9] The independent synthesis will be reported in a forthcoming publication.

[10] T. Sasaki, S. Eguchi, and T. Toru, *J. Org. Chem.*, **35**, 4109 (1970).

[11] R. A. Appleton, C. Egan, J. M. Evans, S. H. Graham, and J. R. Dixon, *J. Chem. Soc. C*, 1110 (1968).

trate (about 900 ml) was gradually cooled to 0°, then left at −20° overnight. The crystals were collected by filtration and dried to give about 40 g of **1**, mp 161–162°. Concentration of the mother liquor provided another 3–5 g of product. Further purification should be carried out by sublimation (100°, 0.1 mm).

***endo*-3-Bicyclo[3.3.1]nonylmethylamine** (**2**).—**1** (16.7 g, 0.1 mol) and 64 g (2 mol) of 95% hydrazine were added to a mixture of 400 ml of diethylene glycol and 56 g of potassium hydroxide pellets.[12] While the mixture was slowly warmed to 143°, the caustic pellets gradually dissolved. After the mixture was refluxed at this temperature for 1 hr, the water and excess hydrazine were distilled until the pot temperature reached 190–200°. The viscous solution was refluxed for 3 hr, cooled to room temperature, and then poured into 500 ml of water. The aqueous solution was extracted portionwise with methylene chloride. The combined extract was washed several times with small portions of water and dried. Evaporation of solvent afforded 15.2 g (99% yield) of crude amine: bp 82–83.5° (1.3 mm); ir (neat) 3400, 2900, 2800, 1630, 1570, 1260, 1035, and 1020 cm^{-1}.

A literature procedure[13] provided 0.35 g of benzamide derivative, after crystallization from ethyl acetate, from 0.5 g of **2**. Two crystallizations from ethyl acetate–ether gave analytically pure material: mp 93.5–94.5°; ir ($CHCl_3$) 3500, 3010, 2930, 2860, 1650, 1560, 1520, 1470, and 1280 cm^{-1}; nmr ($CDCl_3$) δ 7.8 (m, 2 H), 7.45 (m, 3 H), 6.9 (indistinct t, 1 H), 3.3 (t, 2 H), 2.1–0.8 (m, 15 H).

Anal. Calcd for $C_{17}H_{23}NO$: C, 79.33; H, 9.00: N, 5.44. Found: C, 79.32; H, 8.96; N, 5.44.

The hydrochloride salt was obtained by passing HCl into an ethereal solution of **2**. A pure sample resulted after three crystallizations from ethanol–ether, mp >280° dec.

Anal. Calcd for $C_{10}H_{20}NCl$: C, 63.30; H, 10.62; N, 7.38; Cl, 18.68. Found: C, 63.54; H, 10.49; N, 7.11; Cl, 18.80.

***N*,*N*-Dimethyl-*endo*-3-bicyclo[3.3.1]nonylmethylamine** (**3**).[14]—Formaldehyde (37%, 30 ml, 0.55 mol) was added to a mixture of 30 g (0.63 mol) of 97% formic acid and 15.2 g (0.1 mol) of **2**. On heating the mixture at 95° for 8 hr, gas evolution occurred. The dark solution was cooled, mixed with 60 ml of 4 *N* HCl, and then concentrated to a viscous liquid. After water (60 ml) was added, the solution was made basic with 50% NaOH at 0°. The ether extract was washed with water, dried, and freed of solvent. The residue weighed 14.7 g (81% yield): ir (neat) 2950, 2870, 2830, 2780, 1450, 1280, 1260, 1100, 1070, 1050, 1040, 1030, 1025, 850, 828, and 735 cm^{-1}; nmr δ 2.18 (s, 6 H), 2.15–0.70 (m, 17 H).

***N*,*N*,*N*-Trimethyl-*endo*-3-bicyclo[3.3.1]nonylmethylammonium Iodide** (**4**).—Methyl iodide (20.4 g, 0.144 mol) was added to a mixture of 13 g (0.072 mol) of **3** in 75 ml of absolute ether. Salt immediately precipitated. After the mixture was allowed to stand overnight, the salt was filtered and dried, 19.5 g (84% yield) of **4**, mp 291–292° dec after three crystallizations from ethanol–ether.

Anal. Calcd for $C_{13}H_{26}NI$: C, 48.30; H, 8.10; N, 4.33; I, 39.26. Found: C, 48.18; H, 8.10; N, 4.22; I, 39.34.

***N*,*N*,*N*-Trimethyl-*endo*-3-bicyclo[3.3.1]nonylmethylammonium Hydroxide** (**5**).—A mixture of 14.2 g (0.044 mol) of **4** and 60 ml of distilled water was cooled to 0°, whereupon precipitation occurred. After addition of 40 ml of ethanol, silver oxide (23 g, 0.1 mol) was added to the solution at 0°, and the mixture was stirred at this temperature for 5 hr. Following filtration, evaporation provided a viscous liquid, 8 g, after standing under high vacuum.

3-Methylenebicyclo[3.3.1]nonane (**6**).[7,15]—**5** (4 g) was placed in a 10-ml, round-bottom flask connected through a short-path distillation head to a 5-ml receiver cooled in an acetone–Dry Ice bath. Residual water was removed under high vacuum. Then degradation gradually took place at 95° during 1 hr. The ether extract of the olefin product was washed with water and dried. Removal of ether provided 2.3 g (77% yield overall from **4**) of **6**. The analytical sample was collected by glpc at 90° (column I): $n^{30}\text{D}$ 1.4947; ir (neat) 3100, 3020, 2960, 2840, 1645, 1440, 1110, 905, 875, and 750 cm^{-1}; nmr δ 4.6 (s, 2 H), 2.50–0.90 (m, 14 H).

Anal. Calcd for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.18; H, 11.76.

3-Methylbicyclo[3.3.1]nonane[7] **(7) from 6.**—**6** (1.6 g, 1.17 mmol) was hydrogenated overnight at room temperature in 50 ml of absolute ethanol with 0.5 g of 5% palladium on charcoal in a Parr apparatus. After filtration, removal of solvent afforded 1.3 g (72% yield) of **7**. The analytical sample was obtained as described for **6**: $n^{30}\text{D}$ 1.4735; ir (neat) 3040, 2930, 1460, 1375, 1360, 1130, 1110, and 696 cm^{-1}; nmr δ 2.10–0.60 (m, sharp d at 1.80).

Anal. Calcd for $C_{10}H_{18}$: C, 86.87: H, 13.12. Found: C, 86.86; H, 12.97.

The crude product contained 13% of a second component.

***N*-Methyl-4-azahomoadamantane** (**9**).—Methylation (adapted from **3**) of 16.1 g (0.106 mol) of **8**[4] gave 14.5 g (83% yield) of **9**: ir (neat) 2900, 2860, 2780, 1440, 1390, 1275, 1205, 1135, 1120, and 1035 cm^{-1}; nmr δ 2.98 (s, 1 H), 2.85 (d, 2 H), 2.50 (s, 3 H), 2.18–1.20 (m, 13 H). The hydrochloride was obtained as described for **2**·HCl.

Anal. Calcd for $C_{11}H_{20}NCl$: C, 65.49; H, 9.99; N, 6.94; Cl, 17.57. Found: C, 65.48; H, 10.00; N, 6.87; Cl, 17.75.

***N*,*N*-Dimethyl-4-azoniatricyclo[4.3.1.1^{3,8}]undecane Iodide** (**10**).—**9** (14.5 g, 0.088 mol), on treatment (see **4**) with methyl iodide, gave 26.5 g (98% yield) of product, mp 311–312° dec.

***N*,*N*-Dimethyl-4-azoniatricyclo[4.3.1.1^{3,8}]undecane Hydroxide** (**11**).—The hydroxide was obtained as a syrup (see **5**).

***N*,*N*-Dimethyl-7-methylene-*endo*-3-bicyclo[3.3.1]nonylamine** (**12**).—Crude **11**, generated from 26.5 g of **10**, on pyrolysis (see **6**) provided 10 g (64% yield based on **10**) of product: ir (neat) 3100, 2940, 2830, 2780, 1645, 1450, 1380, 1365, 1300, 1260, 1175, 1145, 1100, 1080, 1030, and 880 cm^{-1}; nmr δ 4.73 (s, 2 H), 3.00 (s, 1 H), 2.40–0.80 (m, 18 H, sharp s at 2.20).

***N*,*N*,*N*-Trimethyl-7-methylene-*endo*-3-bicyclo[3.3.1]nonylammonium Iodide** (**13**).—Compound **13** (12.3 g, 81% yield) was formed by treating 8.5 g (0.048 mol) of **12** with methyl iodide (see **4**), mp 287–288° dec (purified as for **4**).

Anal. Calcd for $C_{13}H_{24}NI$: C, 48.61; H, 7.53; N, 4.36; I, 39.50. Found: C, 48.88; H, 7.65; N, 4.51; I, 39.30.

***N*,*N*,*N*-Trimethyl-7-methylene-*endo*-3-bicyclo[3.3.1]nonylammonium Hydroxide** (**14**).—The hydroxide was isolated as a syrup from 10.3 g (0.032 mol) of **13**.

7-Methylenebicyclo[3.3.1]non-2-ene (**15**).—The diolefin **15** was obtained by pyrolysis of **14** (see **6**): 3.2 g (74% yield based on **13**); $n^{30}\text{D}$ 1.5037; ir (neat) 3100, 3050, 2900, 2850, 1645, 1430, 1045, 980, 910, 878, 726, and 705 cm^{-1}; nmr δ 5.62 (s, 2 H), 4.72 (s, 1 H), 4.52 (s, 1 H), 2.60–1.20 (m, 10 H).

Anal. Calcd for $C_{10}H_{14}$: C, 89.47; H, 10.53. Found: C, 89.40; H, 10.85.

***endo*-3-Methylbicyclo[3.3.1]nonane**[7] **(7) from 15.**—Hydrogenation of **15** (as described for **7** from **6**) afforded **7** (83% yield), identical with material obtained from **6**. A minor component was present (13% of total).

3-Methylbicyclo[3.3.1]non-2-ene[7] (**16**).—A mixture of olefin **6** (0.25 g, 1.84 mmol) in a small amount of ether (used for transfer) and 2 ml of 97% formic acid was refluxed for 12 hr at 100°. After extraction with ether, the ether layer was washed in succession with water, 5% sodium carbonate, and water. Evaporation of ether from the dried solution gave 0.1 g (40% yield) of product. Glpc analysis (column I, isothermal at 90°, 60 ml/min) showed a ratio of 96:4 for **16** *vs.* the minor component. **16**: ir (neat) 3015, 2950, 2850, 1440, 915, 850, 818, and 725 cm^{-1}; nmr δ 5.4 (vague d, 1 H), 2.5–1.2 (m, 15 H).

1-Methyl-2-oxaadamantane (**18**).—A mixture of diolefin **15** (1 g, 7.5 mmol) in a small amount of ether (used for transfer) and 3 ml of 97% formic acid was refluxed for 10 hr at 100°. The color turned dark, and a light brown solid separated. Liquid was decanted from the solid, which was dissolved in ether, washed with water, dried, and freed of solvent, wt 0.2 g of gummy material. The original liquid was extracted with ether. The organic solution was washed in succession with water, 5% sodium hydroxide, and water. The combined aqueous fraction was extracted with ether which was combined with the main portion of the ether solution. After a water wash, removal of ether from the dried solution gave 0.7 g of residue which was analyzed by glpc (column II, 110° for 10 min, then to 180°, 100 ml/min). The seven-component mixture contained about 39% of **18** as the principal ingredient: ir (CCl_4) 2940, 2890, 1440, 1390, 1320, 1205, 1130, 1090, 1040, 1010, and 870 cm^{-1}; nmr (CCl_4) δ 4.05 (s, 1 H), 2.15–1.3 (m, 12 H), 1.10 (s, 3 H); mass spectrum *m/e*

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(13) R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds," 5th ed, Wiley, New York, N. Y., 1964, p 260.

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(rel intensity) 153 (8), 152 (58), 109 (10), 96 (10), 95 (100), 94 (85), 93 (9), 84 (23), 79 (21), 67 (13), 45 (24), 43 (14), and 41 (10).

Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 78.57; H, 10.77.

***N,N*-Dichloro-*endo*-3-bicyclo[3.3.1]nonylmethylamine** (19).—An adaptation of a published procedure[16] was followed. A solution of 11.1 g (0.05 mol) or 2, 45 ml of water, and 15 ml of concentrated HCl (warmed to effect solution) was added dropwise to a cooled (5–10°) mixture of 45 ml of water, 90 ml of methylene chloride, and 20.4 g (0.1 mol) of calcium hypochlorite (70% pure). The mixture was stirred for 15 min, after which the organic phase was separated, washed twice with water, and dried, yielding 11.5 g (67%) of product which titrated for 94% of the theoretical amount of positive chlorine. Sublimed product (100% of theory for positive chlorine) gave mp 37–39.5°.

***endo*-3-Bicyclo[3.3.1]nonylcarbonitrile** (20). **A. Quinoline Route.**—According to a literature procedure,[17] a solution of 2 g (0.009 mol) of 19 (98% pure) and 15 ml of quinoline was heated with stirring under nitrogen at 160° for 18 hr. The reaction mixture was poured into 60 ml of cold 2 *N* HCl, and then extracted with ether. Solvent evaporation from the dried organic layer provided 1.3 g of a dark red-brown oil. Sublimation (35°, 0.01 mm) and crystallization from petroleum ether (bp 30–60°) yielded 0.9 g (65%) of 20, mp 59–60°. The ir spectrum showed nitrile absorption at 2337 cm^{-1}.

B. CsF Route.—The method of Sharts[18] was used. A solution of 9.4 g (0.034 mol) of 19 (91% pure) and 12.7 g (0.084 mol) of cesium fluoride in 70 ml of acetonitrile was heated at 50° with stirring for 48 hr. After the solution was filtered, solvent removal yielded 7.6 g of dark brown, viscous liquid. Sublimation and crystallization from petroleum ether afforded 20 as a white, crystalline solid, 2.7 g (52% yield), mp 59–60°.

Anal. Calcd for $C_{10}H_{15}N$: C, 80.48; H, 10.13; N, 9.39. Found: C, 80.27; H, 10.34; N, 9.40.

C. *t*-BuOK Route.—A literature route[19] was modified. A solution of 2 g (7.9 mmol) of 19 (94% pure) dissolved in 20 ml of *tert*-butyl alcohol was added dropwise with stirring to 1.9 g (0.017 mol) of potassium *tert*-butoxide in 25 ml of *tert*-butyl alcohol. The reaction mixture was protected by a drying tube. The temperature rose to 60° and then dropped to 25° during the 3-hr reaction period. A white precipitate formed. After the *tert*-butyl alcohol was removed, the residue was treated with 25 ml of ether and 10 ml of water. The organic layer was separated and the aqueous phase was extracted with portions of ether. The combined organic phase was dried and freed of solvent. Sublimation and crystallization from petroleum ether yielded 0.4 g (33%) of 20, mp 59–60°.

***endo*-3-Bicyclo[3.3.1]non-6-enecarbonitrile**[10] **(22).**—To a stirred solution of 16 ml of acetic acid, 12 ml of methanesulfonic acid, and 4 g (0.027 mol) of adamantanone was added 2 g (0.031 mol) of NaN_3 portionwise over a period of 50 min. After being stirred for an additional 20 min, the mixture was poured over crushed ice, forming a precipitate which was washed with water and dried, 1.3 g (33% yield), mp 171–181° (lit.[20] mp 176.5–181.5°). The ir spectrum was essentially identical with that of authentic material.[21]

***endo*-3-Bicyclo[3.3.1]nonylcarbonitrile (20) from Hydrogenation[22] of *endo*-3-Bicyclo[3.3.1]non-6-enecarbonitrile (22).**—22 (1 g) was dissolved in 50 ml of ethanol and placed in a Parr apparatus along with 0.25 g of 10% Pd on carbon. After 2 hr of agitation at 42 psi, the catalyst was removed by filtration and the solvent was evaporated. The product was taken up in 20 ml of ether and extracted three times with 10-ml portions of cold 7.5% HCl. Solid from evaporation of the ether solution was sublimed, yielding 0.9 g of product. Ir analysis indicated that a minor amount of 22 was still present. Therefore, the product was hydrogenated for another 2 hr. The resulting neutral product (0.2 g, 15% yield), mp 60–61°, displayed an ir spectrum identical with that of the nitrile from 19. Glpc analysis indicated a purity greater than 99%. Amine product, 0.7 g of the hydrochloride, from the second hydrogenation, was not characterized.

3-Bicyclo[3.3.1]nonylcarboxylic Acid (21a and 21b). A. By Acid Hydrolysis.[23]—A solution of 2 g (8.8 mmol) of 20, 15 ml of water, and 12.5 ml of concentrated H_2SO_4 was refluxed for 6 hr. During this time, product which crystallized in the condenser was returned to the reaction flask. The mixture was diluted with 25 ml of cold water and filtered. The solid residue was dissolved in 15% NaOH and treated with activated charcoal. The acid was recovered by neutralization followed by sublimation (90°, 0.01 mm) and crystallization from petroleum ether, wt 2.1 g (92% yield), mp 112–113°. Differential scanning calorimetry gave a melting endotherm of 111°.

Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.54; neut equiv, 168.2. Found: C, 71.23; H, 9.45; neut equiv, 168.7.

Preparation of the methyl esters[11] was accomplished by addition of ethereal diazomethane to a solution of 0.5 g (0.003 mol) of 21a and 21b (from acid hydrolysis) in 10 ml of anhydrous ether. Addition was continued until a slight yellow color remained for 5 min, indicating excess diazomethane. A blank containing only ether was used for comparison. Glpc of the methyl esters at 175° on 15% Carbowax 20M Chromosorb W indicated a composition of 66% exo and 34% endo.

B. By Basic Hydrolysis.[24]—A solution of 1.2 g (0.008 mol) of 20, 10 ml of ethylene glycol monomethyl ether, and 2 g (0.036 mol) of KOH was refluxed under nitrogen for 8 hr. Progress of the reaction was followed by passing the evolved ammonia into a bromcresol green solution[25] (HCl). The reaction mixture was cooled, filtered, and neutralized with HCl. After filtration of the precipitate, sublimation and crystallization from petroleum ether yielded 0.9 g (65% yield) of the epimeric acids, mp 123–126°. Differential scanning calorimetry gave a melting endotherm of 127°, neut equiv 169.6 (calcd 168.2). Esterification was effected as described in the preceding section. Glpc analysis indicated a mixture of 90% exo and 10% endo.

***exo*-3-Bicyclo[3.3.1]nonylcarboxylic Acid (21b) by Isomerization.**—A solution of 200 mg (1.2 mmol) of a mixture of 21a and 21b (from basic hydrolysis of 20), 0.33 g (0.006 mol) of KOH, and 5 ml of ethylene glycol monomethyl ether was refluxed (116°) under nitrogen for 24 hr. Work-up, as described for the basic hydrolysis of 20, yielded 178 mg (89% yield) of 21b, mp 130–131° [lit.[11] for 21b (99% pure), mp 132–133.5°]. Differential scanning calorimetry gave a melting endotherm of 134°; ir (KBr) 3100–2500 (OH), 1675 (C=O), 1405, 1250, and 940 cm^{-1}; nmr δ 12.22 (s, 1, CO_2H), 3.02 (m, 1, $CHCO_2H$), 1.77 (m, 14, remaining protons).

Registry No.—**1**, 34650-78-7; **2**, 37445-20-8; **2** benzamide derivative, 37445-21-9; **2** HCl, 37445-22-0; **3**, 37445-23-1; **4**, 37445-24-2; **5**, 37445-25-3; **6**, 19437-17-3; **7**, 37439-64-8; **8**, 22776-74-5; **9**, 37439-66-0; **9** HCl, 37439-67-1; **10**, 37439-68-2; **11**, 37439-69-3; **12**, 37445-26-4; **13**, 37445-27-5; **14**, 37445-28-6; **15**, 37439-70-6; **16**, 2721-36-0; **18**, 6508-22-1; **19**, 37445-29-7; **20**, 37445-30-0; **21a**, 19489-18-0; **21b**, 19489-16-8; **22**, 26768-57-0.

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