Displacement and Cyclization in the Hofmann Degradation of Some Aminomethylnorbornene Quaternary Hydroxides

CHICITA F. CULBERSON AND PELHAM WILDER, JR.

Department of Chemistry, Duke University, Durham, North Carolina

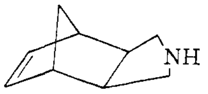
Received February 13, 1961

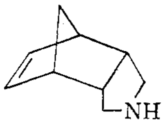
Thermal decomposition of the quaternary hydroxides of *endo*- and *exo*-2-aza-1,2-dihydrodicyclopentadiene proceeds by displacement at the α-carbon and at the quaternary methyl. β-Elimination is not observed. Displacement by hydroxide ion at the α-carbon gives an α,δ-amino alcohol which cyclizes to a tetrahydrofuran derivative upon decomposition of the quaternary ammonium hydroxide.

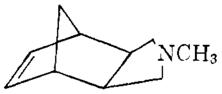
The Hofmann degradation has been the subject of numerous investigations and is widely used in proofs of structure, the normally observed β-elimination providing an excellent means for locating an amine function or for determining the number of intramolecular carbon–nitrogen bonds in cyclic amines. The reaction is of less general synthetic value, but in some cases where acids or high temperature pyrolysis must be avoided the Hofmann degradation yields products not readily prepared by other methods.[1] Theoretical implications of the course of the thermal decomposition of quaternary ammonium hydroxides are reviewed by Ingold.[2]

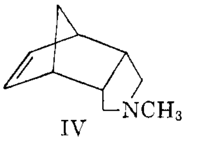
Recently we prepared the *exo* and *endo* isomers of 2-aza-1,2-dihydrodicyclopentadienes (I and II) and their N-methyl derivatives (III and IV).[3] Upon treatment with halogen acid and then base the *endo* amine II underwent cyclization to the tertiary amine V.[4]

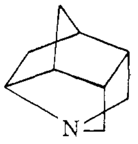
Important evidence supporting the structure of the tertiary amine was obtained through its Hofmann degradation which yielded primarily N-methylamine IV. This result led logically to an investigation of the products formed by decomposition of the quaternary ammonium hydroxide of the N-methylamine IV. Preliminary experiments indicated that the principal product of the Hofmann degradation of amine IV was also N-methylamine IV, formed in this case by displacement on methyl rather than by β-elimination. This coincidence demanded a rigorous proof of the purity of the tertiary amine V.[5] Contamination by starting material would invalidate the results of the Hofmann elimination since amine II on exhaustive methylation would yield the methiodide of amine IV.


I


II


III


IV


V

During this work, secondary products of the Hofmann degradation of the N-methylamine IV were noted. This reaction has now been studied in detail for both the *exo* and the *endo* systems. While anomalous results might be predicted by analogy with other highly strained or hindered systems, the complete absence of products resulting from β-elimination and the formation of methoxy amines were entirely unexpected.

The N-methyl-2-aza-1,2-dihydrodicyclopentadienes (III and IV) were quaternized with methyl iodide and converted to their methohydroxides in aqueous solution by means of silver oxide. The solutions were then evaporated and the residues were decomposed at temperatures not exceeding 160°, excessive heat being avoided to minimize any tendencies of the products to undergo thermal rearrangement or reverse Diels–Alder reactions.

Four compounds were detected after degradation of the *endo* N-methylamine methohydroxide. Fractional distillation of crude product yielded a low boiling material identified as the *endo* N-methylamine starting material. An intermediate boiling fraction, a solid and a high boiling viscous liquid were also isolated. The solid product was shown to be the *endo–cis* amino alcohol (VII). This amine readily forms a methiodide and absorbs one mole of hydrogen per mole of amine upon catalytic reduction. The structure of the amino alcohol was confirmed by synthesis. The *endo* anhydride (X) with methyl alcohol yields the acidic ester (XV) which reacts with thionyl chloride

---

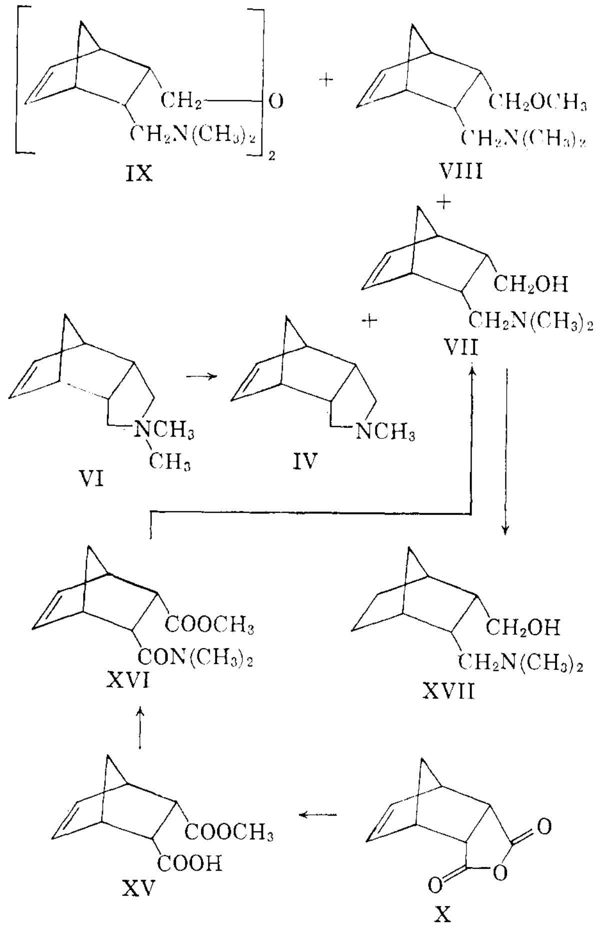
[1] For examples see: A. C. Cope and C. G. Overberger, *J. Am. Chem. Soc.*, **70**, 1433 (1948); A. C. Cope, R. J. Cotter, and G. C. Roller, *ibid.*, **77**, 3594 (1955); J. Meinwald and O. L. Chapman, *ibid.*, **80**, 633 (1958); Ya. M. Slobodin, *Zh. Obshch. Khim.*, **27**, 2473 (1957).

[2] C. K. Ingold, "Structure and Mechanism in Organic Chemistry," Cornell University Press, Ithaca, N. Y., 1953, pp. 419–472.

[3] Chicita F. Culberson and P. Wilder, Jr., *J. Org. Chem.*, **25**, 1358 (1960).

[4] P. Wilder, Jr., and Chicita F. Culberson, *J. Am. Chem. Soc.*, **81**, 2027 (1959).

[5] Chicita F. Culberson and P. Wilder, Jr., *ibid.*, **82**, 4939 (1960).

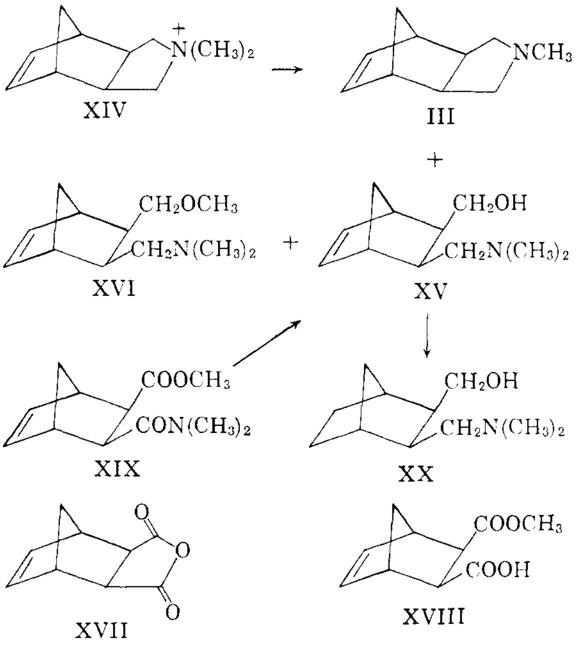


followed by dimethylamine to give the ester amide (XII). This product, on reduction with lithium aluminum hydride, yields the amino alcohol (VII) identical to the Hofmann product isolated.

Complete proof of the nature of the high boiling product was not obtainable with our small sample, but the evidence strongly supports the diamine ether structure (IX). Elemental analyses of the amine and its dipicrate agree with the calculated values as does the hydrogen absorption upon catalytic reduction. In addition, there is a strong band at 8.93 μ in the infrared spectrum and an absence of hydroxyl peaks.

The intermediate boiling fraction appeared to be a mixture of products and indeed gas chromatography revealed three components. The first peak was identified as that of the N-methylamine (IV) and the third as that of the amino alcohol (VII). Extraction of a small sample with dilute hydrochloric acid removed all peaks, thus proving that the central one was a basic component. The mixture was analyzed by gas chromatography using standard solutions of the N-methylamine and the amino alcohol and determining the amount of the unknown by difference. From the nature of the known products and their retention times, the course of degradation suggested by these products, and the presence of an ether band in the infrared spectrum of the mixture, the unknown was judged to be the methoxy amine (VIII). All attempts to prepare this compound failed, but a small pure sample was finally isolated by gas chromatography. Upon catalytic reduction, the amine absorbed the calculated volume of hydrogen and an elemental and methoxyl analysis of the methiodide of the reduced product also agreed. A small sample of this methiodide yielded the methiodide of the saturated *endo–cis* amino alcohol (VII) when treated with concentrated hydriodic acid.

Degradation of the quaternized *exo* N-methylamine (XIV) gave three products. Two fractions were separated by distillation and each was analyzed by gas chromatography. The low boiling material proved to be pure *exo* N-methylamine (III). The second fraction contained three compounds: the *exo* N-methylamine (III), an intermediate material probably isomeric with the methoxy amine isolated in the *endo* case and a material of longer retention time. The last peak was proved to be due to the *exo–cis* amino alcohol (XV) by comparison with a known sample prepared by the same method used to obtain the *endo–cis* isomer; *exo* anhydride (XVII) yielded an acidic ester (XVIII) which formed an amide ester (XIX) readily reducible with lithium aluminum hydride. The mixture from the degradation was analyzed using pure samples of the two known components and determining the amount of the unknown by difference. No diamine ether analogous to the product (IX) obtained in the *endo* case was isolated, but a small yield of such an ether would not have been detected by the methods used here. The methoxy amine (XVI) was isolated chromatographically. Hydrogen uptake upon catalytic reduction and the elemental

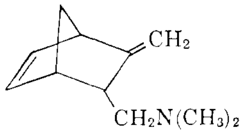


and methoxyl analyses of the methiodide of the reduced product agree with the formula assigned. Although our sample was too small for conclusive proof of the structure, all evidence and analogy with the *endo* case already described support the identification of this product as the methoxy amine (XVI).

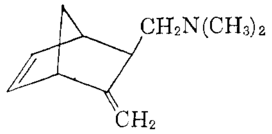
The total yield of all products was 77% in the *endo* case and 75% in the *exo* case. The yields calculated on the basis of the total product isolated are given below:

	N-Methylamine, %	Amino alcohol, %	Methoxy amine, %	Diamine ether, %
endo	55	26	8	12
exo	89	6	4	..

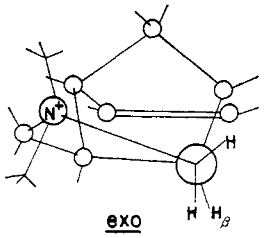
In these studies we have not detected the β-elimination products (XXI and XXII). These compounds are not known, but one would predict gas chromatograpic retention times just slightly higher than those of the N-methylamines. β-Elimination is probably inhibited by steric strain encountered in the *trans* coplanar transition state. The nearly eclipsed α- and β-carbons are illustrated in diagrams XXIII and XXIV for the *exo* and *endo* N,N-dimethylammonium ions. The α-carbon is indicated by the large circle and the β-hydrogen is labeled to show its position relative to the quaternary nitrogen.



XXI

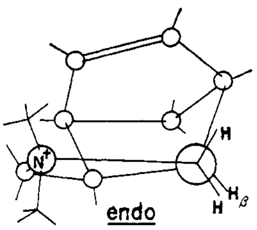


XXII



exo

XXIII



endo

XXIV

The principal reaction path in both the *endo* and *exo* systems is the displacement by hydroxyl ion on methyl, yielding the original N-methylamines. An attack on methyl is especially preferred in the *exo* compound where the N-substituted methyl groups are both exposed to attack. In the *endo* N,N-dimethyl quaternary ammonium ion, one methyl substituent is shielded by the norbornylene ring.

The amino alcohols (XIII and XV) can be formed by hydroxyl ion attack at an α-carbon in the pyrrolidine ring. The α-carbon is particularly open to attack by a nucleophile approaching from the side opposite the attachment of the quaternary ion (see the diagrams XXIII and XXIV).

The amino alcohol products distill very slowly during the degradation. In the strongly basic medium of the reaction, some alkoxide will be formed from the amino alcohol product and this nucleophile will then compete with the hydroxide ion in the displacement reactions. An attack by the alkoxide ion on a methyl yields the methoxy amines (XVI and VIII) and the N-methylamines (III and IV) while displacements by the alkoxide on the α-carbon yields a diamine ether (IX) isolated in the *endo* case only. The methoxy amines (XVI and VIII) might also form by reaction with methoxide, since methyl alcohol is generated during the degradation. But the volitility of methyl alcohol and the reversibility of its ionization would probably lessen its effectiveness as a reagent in this high-temperature degradation.

Amino alcohol and diamine ether products from the Hofmann degradation have been previously observed, especially in pyrrolidinium ion decomposition.[6-8] Such products are also possible in noncyclic amines, if the rotomer required for the *trans*-coplanar transition state for elimination is a high energy form.[9-12]

The *endo* amino alcohol (VII) was converted to its methiodide and treated with silver oxide to form the methohydroxide. The aqueous solution containing the quaternary hydroxide was concentrated on a steam bath at diminished pressure from an aspirator until decomposition was observed as the product began to sublime. Distillation was continued at atmospheric pressure. An excellent yield of 2-oxa-1,2-dihydro-*endo*-dicyclopentadiene (XXVI) was obtained. After one sublimation, the product was analyzed by gas chromatography and it gave a single peak with retention time identical to that of the *endo* ether (XXVI) from another source. The product yielded a phenyl azide adduct identified as that of the *endo* ether. All previous attempts to prepare a good analytical sample of the *endo* ether prepared from the diol (XXXII) by the action of toluenesulfonyl chloride and pyridine have failed[13-15] but after three sublimations the product of this Hofmann degradation gave an elemental analysis for carbon and hydrogen in excellent agreement with the calculated values.

---

(6) J. von Braun, *Ber.*, **49**, 2629 (1916).

(7) K. Jewers and J. McKenna, *J. Chem. Soc.*, 2209 (1958).

(8) F. E. King, D. M. Bovey, K. G. Mason, and R. L. St. D. Whitehead, *ibid.*, 250 (1953).

(9) R. B. Carlin and D. P. Carlson, *J. Am. Chem. Soc.*, **81**, 4673 (1959).

(10) J. von Braun, *Ann.*, **382**, 1 (1911).

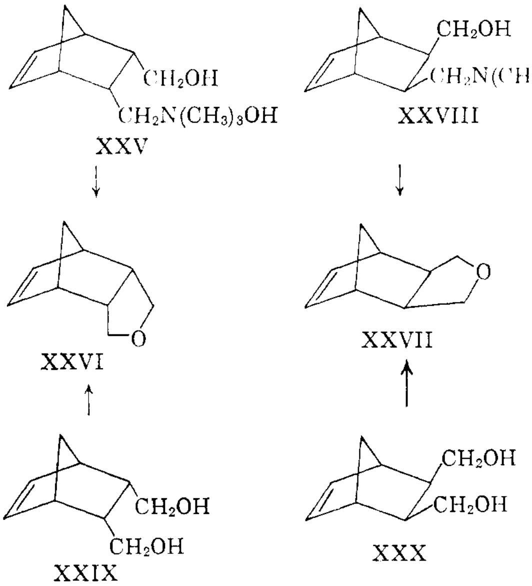
(11) H. R. Snyder and J. H. Brewster, *J. Am. Chem. Soc.*, **71**, 291 (1949).

(12) H. W. Bersch, R. Meyer, and G. Hubner, *Pharm. Zentralhalle*, **96**, 381 (1957).

(13) Chicita F. Culberson, J. H. Seward, and P. Wilder, Jr., *J. Am. Chem. Soc.*, **82**, 2541 (1960).

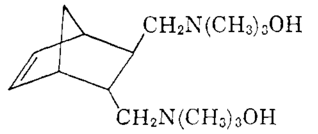
(14) K. Alder and W. Roth, *Ber.*, **88**, 407 (1955).

(15) E. L. Eliel and C. Pillar, *J. Am. Chem. Soc.*, **77**, 3600 (1955).

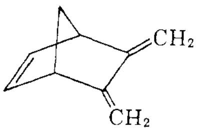


The *exo* amino alcohol was methylated with methyl iodide, converted to the hydroxide with silver oxide and distilled. Degradation proceeded smoothly as in the *endo* case and the only product, which was obtained in high yield, was the *exo* ether (XXVII). The *exo* ether was identified through its physical constants and its phenyl azide adduct which did not depress the melting point of an authentic sample. The purity of the *exo* ether (XXVII) obtained from the Hofmann degradation was verified by gas chromatography.

Unlike the cyclic N-methyl-2-aza-1,2-dihydrodicyclopentadienes, the quaternized amino alcohols (XXV and XXVIII) can assume the *trans* coplanarity required for elimination. In 1957, Alder *et al.*[16] reported the preparation of the olefin



XXXI



XXXII

XXXV in fair yield by a Hofmann degradation of the diamine quaternary hydroxide XXXI. Some bond opposition might be expected in the transition state in the case of the amino alcohols (XXV and XXVIII), in the *endo–cis* compound between the N-substituted methyl and the norbornylene double bond and in the *exo–cis* compound between the N-substituted methyl and the bridge methylene. But the products isolated indicate that the most energetically feasible route for the reaction is the intramolecular displacement by oxygen, even though the β-elimination process is possible. Intramolecular displacements of this type during Hofmann degradation reactions provide interesting synthetic routes to substituted oxygen heterocycles.[17]

Experimental

Analyses are by Galbraith Microanalytical Laboratories, Knoxville, Tennessee, and Dr. Ing. A. Schoeller, Mikroanalytisches Laboratorium, West Germany.

Methanolysis of *endo-cis*-Bicyclo[2.2.1]-5-heptene-2,3-dicarboxylic Acid Anhydride (X).—A mixture of 100 g. (0.61 mole) of *endo* anhyride and 500 ml. of absolute methyl alcohol was refluxed overnight and then the excess methyl alcohol was removed under diminished pressure. The product solidified and was recrystallized from benzene–ligroin (90–120°) yielding 96 g. (80%) of the half ester (XV), m.p. 101–102° (reported[18] m.p. 101–102°).

Methyl *endo-cis*-Bicyclo[2.2.1]-5-heptene-3-N,N-dimethylcarbamyl-2-carboxylate (XVI).—Fifty grams (0.25 mole) of the half ester (XI) was mixed with 100 g. of thionyl chloride and warmed gently. Hydrogen chloride was evolved exothermically. The solution was then refluxed for 20 min. and thionyl chloride was removed under diminished pressure. Dry gaseous dimethylamine from 50 g. of liquid amine was bubbled through a solution of the acid chloride residue in 500 ml. of dry benzene. The solution was stirred and cooled occasionally during the addition and finally cooled and filtered. The benzene solution was washed with 10% hydrochloric acid and with water and then dried over magnesium sulfate. Removal of benzene under diminished pressure and distillation of the residue yielded 37.5 g. (67%) of methyl *endo-cis*-bicyclo[2.2.1]-5-heptene-3-N,N-dimethylcarbamyl-2-carboxylate (XII), b.p. 136–138°/0.70 mm. A small sample was redistilled for analysis, b.p. 109°/0.15 mm., n^{24}_D 1.5108.

Anal. Calcd. for $C_{12}H_{17}NO_3$: C, 64.55; H, 7.68. Found: C, 64.42; H, 7.52.

Lithium Aluminum Hydride Reduction of the Amide Ester (XII).—A solution of 12.5 g. (0.056 mole) of amide ester (XII) was added dropwise to a stirred solution of 5 g. (0.14 mole) of lithium aluminum hydride in 400 ml. of anhydrous ether. The reaction mixture was stirred under reflux for 36 hr. and then cooled to room temperature. Water saturated ether (100 ml.) was added slowly and then water was added dropwise with stirring until the exothermic reaction ceased and the oxides of lithium and aluminum formed a curdy filterable precipitate. The ether filtrate was dried over magnesium sulfate and the ether was removed under diminished pressure. The oily product crystallized from ligroin (b.p. 90–120°) yielding 8.4 g. (83%) of *endo-cis*-bicyclo[2.2.1]-5-heptene-3-N,N-dimethylaminomethyl-2-methylol, m.p. 98–99°.

Anal. Calcd. for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.73. Found: C, 73.03; H, 10.52; N, 7.70.

A methiodide, m.p. 227–228.5°, was recrystallized from absolute ethanol.

Anal. Calcd. for $C_{12}H_{22}INO$: C, 44.56; H, 6.86. Found: C, 44.77; H, 6.93.

Catalytic Reduction of the *endo-cis* Amino Alcohol (VII).—A mixture of 100 ml. of absolute ethanol and a small amount of Adams catalyst was saturated with hydrogen at 760.5 mm. of pressure and 29.5°. Then 0.1644 g. of amino alcohol was added. Hydrogen up-take ceased after 50 min., at which time 22.0 ml. (98%) had been adsorbed. The solution was filtered, ethanol was evaporated, and the residue was sublimed under reduced pressure yielding *endo-cis*-bicyclo[2.2.1]-heptane-2-N,N-dimethylaminomethyl-2-methylol, m.p. 55.5–56.5°, quantitatively.

Anal. Calcd. for $C_{11}H_{21}NO$: C, 72.08; H, 11.55. Found: C, 72.28; H, 11.46.

A methiodide, m.p. 222.5–223.5°, was recrystallized from absolute ethanol–anhydrous ether.

---

(16) K. Alder, S. Hartung, and O. Netz, *Ber.*, **90**, 1 (1957).

(17) H. W. Bersch and G. Hubner, *Arch. Pharm.*, **289**, 673 (1956); H. W. Bersch, R. Meyer, A. v. Mletzko, and K. H. Fischer, *ibid.*, **291**, 82 (1958); H. W. Bersch and G. Hubner, *ibid.*, **291**, 88 (1958).

(18) L. M. Rice and E. E. Reid, *J. Am. Chem. Soc.*, **74**, 3955 (1952).

Anal. Calcd. for $C_{12}H_{24}INO$: C, 44.31; H, 7.44. Found: C, 44.33; H, 7.42.

Methyl *exo-cis*-Bicyclo[2.2.1]-5-heptene-3-N,N-dimethylcarbamyl-2-carboxylate (XIX).—Fifty grams (0.30 mole) of *exo* anhydride (XVII) prepared by the method of Craig, was heated under reflux in 200 ml. of absolute methyl alcohol for 10 hr. Solvent was removed under diminshed pressure and the viscous liquid half ester was dried in a vacuum desiccator over phosphorus pentoxide for 3 days, during which time the product partially solidified. One hundred grams of thionyl chloride was added and the solution was boiled under reflux for about 10 min. Thionyl chloride was removed under diminished pressure and the straw-colored oily residue was dissolved in 500 ml. of dry benzene. Dry, gaseous dimethylamine from 50 g. of liquid reagent was bubbled through the benzene solution. The reaction mixture then was cooled and filtered, washed with excess 10% hydrochloric acid and with water, and finally dried over magnesium sulfate. Removal of benzene under diminished pressure yielded a viscous residue which was distilled rapidly, b.p. 102–105°/0.15 mm. with superheating to 110°/0.15 mm. The yield of product containing some solid but lower boiling impurity was 46.8 g. (69%). The liquid amide was separated by repeated fractional distillation yielding 34.9 g. (51%) of pure methyl *exo-cis*-bicyclo-[2.2.1]-5-heptene-3-N,N-dimethylcarbamyl-2-carboxylate (XVII), and 2.4 g. of the solid impurity which was not identified. A small sample of the product was distilled before analysis, b.p. 101–103°/0.12 mm., n^{25}D 1.5066.

Anal. Calcd. for $C_{12}H_{17}NO_3$: C, 64.55; H, 7.68. Found: C, 64.28; H, 7.60.

Lithium Aluminum Hydride Reduction of the Amide Ester (XIX).—A solution of 22.3 g. (0.10 mole) of the *exo-cis* amide ester in 100 ml. of anhydrous ether was added dropwise to a vigorously stirred solution of 8 g. (0.22 mole) of lithium aluminum hydride in 600 ml. of anhydrous ether. When addition was complete, the reaction mixture was stirred under reflux for 36 hr. and then cooled to room temperature. About 100 ml. of water saturated ether was added slowly with stirring and then enough water was added dropwise to yield a filterable solution. The reaction mixture was filtered and the filtrate was dried over magnesium sulfate. Removal of ether and distillation of the residue yielded 17.3 g. (96%) of *exo-cis*-bicyclo[2.2.1]-5-heptene-3-N,N-dimethylaminomethyl-2-methylol (XV), b.p. 76°/0.30 mm.—75.5°/0.22 mm. A small sample was redistilled for analysis, b.p. 75–76°/0.22 mm, n^{25}D 1.4972.

Anal. Calcd. for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.73. Found: C, 71.44; H, 10.23; N, 7.69.

A methiodide was prepared and recrystallized from absolute ethanol, m.p. 187–189°.

Anal. Calcd. for $C_{12}H_{22}INO$: C, 44.59; H, 6.86. Found: 44.78; H, 6.88.

Catalytic Reduction of the *exo-cis* Amino Alcohol (XV).—A mixture of 100 ml. of absolute ethanol and a small quantity of platinum oxide catalyst was saturated with hydrogen at 750.6 mm. of pressure and 30°. The *exo-cis* amino alcohol (0.6320 g., 0.00349 mole) was added. Hydrogen up-take was complete in 45 min. and 90.4 ml. (98.5%) of hydrogen was absorbed. The solution was filtered, the ethanol was evaporated, and the residue was distilled, yielding 0.4929 g. (77%) of *exo-cis*-bicyclo[2.2.1]heptane-3-N,N-dimethylaminomethyl-2-methylol; b.p. 86–87°/0.40 mm., $n^{25.5}$D 1.4877.

Anal. Calcd. for $C_{11}H_{21}NO$: C, 72.08; H, 11.55. Found: C, 71.76; H, 11.28.

The methiodide, m.p. 179–180°, was recrystallized from absolute ethanol.

Anal. Calcd. for $C_{12}H_{24}INO$: C, 44.31; H, 7.44; Found: C, 44.50; H, 7.59.

Hofmann Degradations.—Each methiodide was converted to the methohydroxide by mixing a concentrated aqueous solution of the quaternary salt with an excess of freshly prepared and thoroughly washed silver oxide. The mixing was carried out in a large mortar and the lumps of silver oxide coated with silver iodide were broken up by grinding. The slurry was then filtered and the solid was washed several times with distilled water. The combined aqueous filtrate and washings were distilled using a Woods Metal bath. The temperature was held at about 120° during the initial distillation but allowed to rise as high as 150–160° by the end of the degradation. The distillate was extracted with ether and the extract was dried over magnesium sulfate. The residue obtained by evaporation of the ether was treated further as described for each case below.

1. **N,N-Dimethyl-2-aza-1,2-dihydro-*endo*-dicyclopentadiene Ammonium Iodide (VI).**—An aqueous solution of the methohydroxide was prepared from 29.1 g. (0.10 mole) of methiodide (VI) and silver oxide from 34.0 g. (0.20 mole) of silver nitrate and 8.0 g. (0.20 mole) of sodium hydroxide. The portion of the product which steam distilled during the 5-hr. degradation was fractionated under reduced pressure yielding 5.12 g. of the *endo* N-methylamine (IV), b.p. 77–81°/14.5 mm. (fraction A) and 1.49 g. of a mixture, b.p. 77–91°/3 mm. (fraction B). Solid amino alcohol remaining in the column and distillation flask (fraction C) was taken up in 60–90° ligroin.

The pot residue from the degradation reaction was shaken with water and ether and the aqueous layer was extracted further with ether. The ether extracts were combined and dried over magnesium sulfate. Removal of ether left a viscous residue from which solid amino alcohol separated on standing. The solid was removed and combined with fraction C (see above). The liquid supernatant product was distilled yielding 1.26 g. of a mixture, b.p. 57–84°/2.3 mm., which was added to fraction B, solid amino alcohol, b.p. 87–92°/2.3 mm, which was added to fraction C and 1.56 g. of the amino ether (IX), b.p. 155–157°/0.35 mm., n^{24}D 1.5089.

Anal. Calcd. for $C_{22}H_{36}N_2O$: C, 76.69; H, 10.53; N, 8.13; mol. wt. 344. Found: C, 76.78; H, 10.35; N, 8.26; mol. wt. 372 (19).

A picrate of the diamine ether was prepared using excess picric acid and the product was recrystallized from absolute ethanol, m.p. 196–198°.

Anal. Calcd. for $C_{34}H_{42}N_8O_{15}$: C, 50.86; H, 5.27. Found: C, 51.18; H, 5.21.

The diamine ether (0.728 g., 0.00212 mole) was reduced in the presence of Adams catalyst in 120 ml. of absolute ethanol, with 1 atm. of hydrogen. Exactly 0.00444 mole (105%) of hydrogen was absorbed. Catalyst and ethanol were removed and the product was converted to its picrate, m.p.206.5–207.5°.

Anal. Calcd. for $C_{34}H_{44}N_8O_{15}$: C, 50.74; H, 5.51. Found: C, 50.44; H, 5.54.

Fraction C was recrystallized from ligroin (b.p. 60–90°) yielding 3.07 g. of the amino alcohol (VII), m.p. 97–98°; a mixed melting point with synthetic material was not depressed and the infrared spectra were identical.

Fractions A and B were analyzed by gas chromatography, using pure samples of the *endo* N-methylamine (IV) and the amino alcohol (VII) as standards (for the conditions of these analyses and the retention times observed see part 2 below). Fraction A consisted entirely of *endo* N-methyl amine (IV). Fraction B contained 44% by weight N-methyl amine (IV), 12% by weight amino alcohol (VII), and (by difference) 44% by weight of another material subsequently shown to be most probably the methoxy amine (VIII). The total yields of the four products detected in the Hofmann degradation were 42% *endo* N-methyl amine (IV), 20% *endo-cis* amino alcohol (VII),

---

(19) The molecular weight was determined by the boiling point elevation of benzene. A determination by the Rast method (Dr. Carl Tiedcke, Laboratory of Microchemistry, Teaneck, N. J.) gave a value of 240, perhaps because of thermal decomposition at the higher temperature of this determination.

6% *endo-cis* methoxy amine (VIII) and 9% diamine ether (IX).

A sample (about 0.450 g.) of the *endo-cis* methoxy amine was isolated from the mixed product by gas chromatography, $n^{21}\text{D}$ 1.4796. The infrared spectrum showed no hydroxyl peaks, and strong absorption at 8.80–9.35 μ in the ether region. Most of the sample (0.4141 g., 0.00212 mole) was reduced under 1 atm. pressure of hydrogen in the presence of Adams catalyst. The hydrogen uptake was 102% of that calculated for the methoxy amine (VIII). The product was converted directly to its methiodide which crystallized from absolute ethanol, m.p. 208.5–209.0°.

Anal. Calcd. for $C_{13}H_{26}INO$: C, 46.02; H, 7.73; N, 4.13; OCH_3, 9.15. Found: C, 46.16; H, 7.73; N, 4.18; OCH_3, 8.83.

Two hundred and thirty milligrams (6.8×10^{-4} mole) of the *endo-cis* saturated methoxy amine methiodide was digested on a steam bath with 3.5 ml. of conc. hydriodic acid for 15 min. Some acid was removed under diminished pressure and then 150 ml. of absolute ethanol was added, the solution was cooled in an ice bath and the solid precipitate was collected by filtration. The product was recrystallized three times from absolute ethanol yielding 0.20 g. (91%) of the methiodide of the saturated *endo-cis* amino alcohol XVII, m.p. 221–222°; a mixed melting point with an authentic sample was not depressed and the infrared spectra were identical.

2. **N,N-Dimethyl-2-aza-1,2-dihydro-*exo*-dicyclopentadiene Ammonium Iodide (XIV).**—The methohydroxide was prepared from 29.1 g. (0.10 mole) of the methiodide (XIV) and silver oxide from 34.0 g. (0.20 mole) of silver nitrate and 8.0 g. (0.20 mole) of sodium hydroxide. The distillate from the degradation yielded 3.7 g. of liquid product (fraction A), b.p. 76–77°/14.5 mm. (reported for the *exo* N-methyl amine (III)[3] b.p. 77–78°/14 mm.). The pot residue from the degradation yielded 5.6 g. of liquid, b.p. 75–77°/13.5 mm., which was combined with fraction A (see above) and 2.1 g. of a mixture of products, b.p. 77–128°/3.5 mm. (fraction B). Only a small amount of resinous material remained in the pot after this distillation.

The two fractions (A and B) were analyzed by gas chromatography as described for the *endo* case. Fraction A was found to be pure *exo* *N*-methyl amine (X), identified by its retention time and by its infrared spectrum. Fraction B consisted of a mixture of 30% by weight *exo* N-methyl amine (III), 40% by weight *exo-cis* amino alcohol (XV) and (by difference) 30% by weight of a component believed to be the *exo-cis* methoxy amine (XVI). The total yields of the three products detected from the Hofmann degradation were 68% *N*-methyl amine (III), 3% *exo-cis* amino alcohol (XV) and 4% *exo-cis* methoxy amine (XVI).

A small sample (about 200 mg.) of the *exo-cis* methoxy amine (XVI) was separated from fraction B by gas chromatography. The pure compound, $n^{21}\text{D}$ 1.4805, gave an infrared absorption spectrum almost identical to that of the *endo-cis* methoxy amine (VIII) from 2.0 μ to 8.0 μ, but differing conspicuously at higher wave lengths while still retaining strong peaks at 8.85–9.35 μ in the region of ether absorption. Most of the product (0.1509 g., 0.000774 mole) was reduced under 1 atm. of hydrogen in the presence of Adams catalyst, absorbing 99.5% of the amount of hydrogen calculated for the methoxy amine (XVI). The entire product was converted to the methiodide which was crystallized from absolute ethanol, m.p. 190–191°.

Anal. Calcd. for $C_{13}H_{26}INO$: C, 46.02; H, 7.73; N, 4.13; OCH_3, 8.73. Found: C, 46.24; H, 7.59; N, 3.96; OCH_3, 9.15.

A Perkin-Elmer Model 154C Vapor Fractometer was used for all chromatographic analyses. The 6 mm. × 1 mm. column was packed with one part Union Carbide polypropylene glycol to four parts of Johns-Manville Chromasorb W (30/60 mesh) by weight. The column was heated to 149° and a helium flow of 56 cc./min. was maintained. The retention times of the products detected in these studies are given in the table below:

	N-Methyl amine	Methoxy amine	Amino alcohol
endo	3.8 min.	9.6 min.	26.0 min.
exo	3.1	9.0	25.8

The retention times of the amino alcohols were very close, but the identities of these compounds were verified by comparing small collected fractions with known samples. The retention times of the ethers (XXVI and XXVII) were almost identical to those of the N-methyl amines (IV and III), respectively, and a prepared mixture of the *exo* ether (XXVII) and the *exo* N-methyl amine (III) gave a single peak with no shoulders at 3.2 min. It was thus necessary to demonstrate further the purity of the N-methyl amine fractions. Titrations with 0.1 N hydrochloric acid of samples of the A fractions, supposed to be pure N-methyl amines (*endo* in one case and *exo* in the other), agreed with titrations of known pure *exo* N-methyl amine (III). Samples of the B fractions were extracted with 0.1 N hydrochloric acid and rechromatographed. No peaks were retained after acid extraction.

3. ***endo-cis*-Bicyclo[2.2.1]-5-heptene-3-N,N-dimethylaminomethyl-2-methylol Methiodide (XXV).**—Silver oxide from 10.4 g. (0.061 mole) of silver nitrate and 2.44 g. (0.061 mole) of sodium hydroxide was used to prepare the methohydroxide from 19.4 g. (0.060 mole) of the methiodide of the *endo-cis* amino alcohol (VII). Degradation yielded 7.3 g. (90%) of crude 2-oxa-1,2-dihydro-*endo*-dicyclopentadiene (XXVI). A chromatograph (140°, 42 cc./min. helium flow and 2 m. × 6 mm. column) of the semisolid pale yellow product showed a single peak at 16.8 min. When admixed with a sample of the *exo* ether (XXVII), there were two peaks, one at 13.1 min. for the *exo* isomer and one at 16.9 min. for the *endo* isomer. A portion of the product was sublimed before analysis, m.p. 90–92° in a sealed tube (reported[14] m.p. 94°,[15] m.p. 91°).

Anal. Calcd. for $C_9H_{12}O$: C, 79.37; H, 8.88. Found: C, 79.49; H, 8.97.

One gram of the sublimed product in 5 ml. of approximately 25% phenyl azide in ether deposited 1.66 g. (88%) of adduct, m.p. 174–178°, after 4 days. The adduct was recrystallized from acetone yielding 1.5 g., m.p. 176–178°; a mixed melting point with a known sample of the phenyl azide adduct of the *endo* ether was not depressed.

4. ***exo-cis*-Bicyclo[2.2.1]-5-heptene-3-N,N-dimethylaminomethyl-2-methylol Methiodide (XXVIII).**—An aqueous solution of the methohydroxide was prepared from 14.5 g. (0.045 mole) of the methiodide of the *exo-cis* amino alcohol (XV) and silver oxide from 7.8 g. (0.046 mole) of silver nitrate and 1.8 g. (0.046 mole) of sodium hydroxide. Degradation yielded 5.3 g. (87%) of 2-oxa-1,2-dihydro-*exo*-dicyclopentadiene (XXVII) after one distillation; b.p. 79–80°/25 mm, $n^{26}\text{D}$ 1.4949 (reported[14] b.p. 82°/24 mm., $n^{20}\text{D}$ 1.4973). The product was chromatographed at 140° with a helium flow of 42 cc./min. through a 2 m. × 6 mm. column. A single peak was observed at 13.0 min. The phenyl azide adduct was prepared and recrystallized from acetone, m.p. 126–127° (reported[5] m.p. 126–127°); a mixed melting point with a sample of the adduct from the *exo* ether prepared by a different method was not depressed.

Acknowledgment.— This research was supported in part by a grant from the Petroleum Research Fund administered by the American Chemical Society. Grateful acknowledgment is hereby made to the donors of this fund. This research also was supported in part by a Research Grant (CY-4298C2) of the National Institutes of Health, Public Health Service.