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[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF THE UNIVERSITY OF ILLINOIS]

The Electrolytic Reduction of Tricyclic α-Aminoketones. Synthesis of Medium Rings Containing Nitrogen. III

BY NELSON J. LEONARD, SHERLOCK SWANN, JR., AND GLENN FULLER[1]

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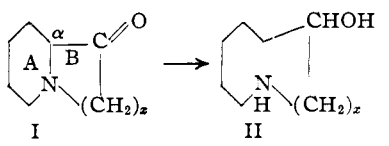
Our study of the electrolytic reduction of α-aminoketones has been extended to linear tricyclic α-aminoketones (V) in which one external ring is benzenoid and the other external ring, sharing a bridgehead nitrogen and containing the ketone group, is of varying ring size: 5, 6, 7 and 8 members. The extent of cleavage of the Cα–N bond and of rearrangement during electrolytic reduction at a lead cathode in 30% sulfuric acid at 60° has been found to be dependent upon the size of the ketone-containing ring. Moreover, when the latter is 7- or 8-membered, the process leads to a medium-size ring compound containing nitrogen and having a benzo grouping fused to the newly formed 11- or 12-membered ring.

The electrolytic reduction of bicyclic α-aminoketones (I), using a lead cathode in 30% sulfuric acid at 60°, is a unique method of making azacycloalkanols (II) of medium ring size.[2,3] It was of interest to determine whether the method would also apply to tricyclic α-aminoketones of the type in which a benzo grouping is fused to the A-ring (nonketonic) of I, especially since the additional benzenoid ring would be expected to induce certain steric restrictions on the conformations available to the *ortho* substituent groups.

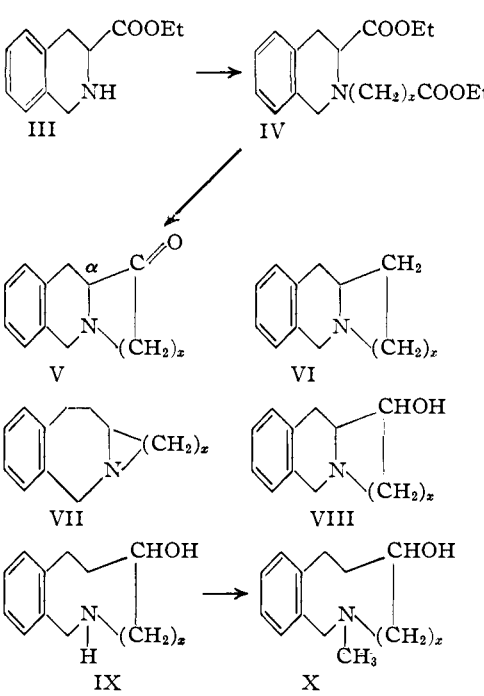


I II

	x
a	2
b	3
c	4
d	5

The common intermediate in the synthesis of four test compounds of the tricyclic α-aminoketone type was the aminoester, ethyl 1,2,3,4-tetrahydroisoquinoline-3-carboxylate (III), prepared from DL-phenylalanine by the method of Archer.[4] From this compound a series of aminodiesters of general formula IV were made. These diesters were subjected to Dieckmann cyclization reactions in order to obtain the corresponding α-aminoketones V. Closure of the seven- and eight-membered ring ketones (Vc,d) was effected under conditions of high dilution in xylene with potassium *t*-butoxide.[5] The products of the electrolytic reduction of each aminoketone V were separated and identified. In general, it was possible to account for 80–90% of the reduced material.

Three products are likely to be formed by the electrolytic reduction at a lead cathode of the first member of the linear tricyclic α-aminoketone series V, the six-six-five fused ring system, benzo[c]-7-keto-1-azabicyclo[4.3.0]nonane (Va). These products are benzo[c]-1-azabicyclo[4.3.0]nonane (VIa), and benzo[c]-7-hydroxy-1-azabicyclo[4.3.0]nonane (VIIIa) and benzo[c]-7-hydroxyazacyclononane (IXa). The ketone Va was unstable in 30% sulfuric acid, so that the reduction had to be carried out as quickly as possible in order to have any identifiable product result. The only product characterized unequivocally was VIa, which formed a picrate identical with the picrate of authentic benzo[c]-1-azabicyclo[4.3.0]nonane, prepared by the Wolff–Kishner reduction of Va. The residual product was contaminated with unreacted ketone, but infrared analysis indicated the presence of OH/NH. This product (or products) could not be purified for complete identification. In the bicyclic series, by contrast, the six-five fused ring system (Ia)



	x
a	2
b	3
c	4
d	5

(1) National Science Foundation Fellow, 1952–1953.

(2) N. J. Leonard, S. Swann, Jr., and J. Figueras, Jr., THIS JOURNAL, **74**, 4620 (1952).

(3) N. J. Leonard, S. Swann, Jr., and E. H. Mottus, *ibid.*, **74**, 6251 (1952).

(4) S. Archer, *J. Org. Chem.*, **16**, 430 (1951).

(5) N. J. Leonard and R. C. Sentz, THIS JOURNAL, **74**, 1704 (1952).

gave predominantly the nine-membered-ring azacycloalkanol (IIa) on electrolytic reduction.[2]

The six-six-six fused ring system, benzo[c]-7-keto-1-azabicyclo[4.4.0]decane (Vb),[4] could produce any of four products under similar reduction conditions: benzo[c]-1-azabicyclo[4.4.0]decane (VIb), benzo[c]-1-azabicyclo-[5.3.0]decane (VIIb), benzo[c] - 7 - hydroxy - 1 - azabicyclo[4.4.0]decane (VIIIb) and benzo[c]-7-hydroxyazacyclodecane (IXb). The lower-boiling component of the reduction product was identified as VIIb (40% yield) by comparison of its picrate with the picrate of the product of Clemmensen reduction of Vb (reduction with rearrangement).[6] The isomeric amine, VIb, was prepared for comparison by the Wolff–Kishner reduction of Vb (reduction without rearrangement), and was found to differ from that obtained by both the electrolytic and the Clemmensen methods. The higher-boiling component of the mixture furnished by electrolytic reduction had an analysis and an infrared spectrum consistent with structure IXb (51% yield). However, attempted methylation with methyl iodide failed to produce a pure N-methyl derivative Xb, and accordingly the reduction product may have been a mixture of VIIIb and IXb. In the bicyclic series, the electrolytic reduction of the six-six fused ring system (Ib) gave the ten-membered ring azacycloalkanol (IIb) in major yield, and the rearranged amine, 1-azabicyclo[5.3.0]decane, in minor yield.[2]

The six-six-seven fused ring compound, benzo[i]-6-keto-1-azabicyclo[5.4.0]hendecane (Vc), was prepared by the Dieckmann cyclization[5] of IVc. Electrolytic reduction of Vc yielded two identifiable products, benzo[c]-1-azabicyclo[5.4.0]hendecane (VIIc) (29%) and benzo[c]-7-hydroxyazacyclohendecane (IXc) (47%), both resulting from scission of the C_α–N bond in the original α-aminoketone. Clemmensen reduction of Vc (reduction with rearrangement) also yielded VIIc, and this reaction was used to identify the rearranged product. The new eleven-membered ring compound IXc was identified by analysis, infrared spectrum and by methylation with formaldehyde–formic acid to benzo[c]-1-methyl-7-hydroxyazacyclohendecane (Xc).

Electrolytic reduction of the six-six-eight fused ring system, benzo[j]-7-keto-1-azabicyclo[6.4.0]dodecane (Vd), also produced two products. The first compound (15% yield) was identified tentatively as benzo[c]-1-azabicyclo[5.5.0]dodecane (VIId), a formulation which is to be preferred over the isomeric structure, benzo[j]-1-azabicyclo[6.4.0]-dodecane (VId). Ring cleavage of eight-membered ring α-aminoketones has been shown to occur during Clemmensen reduction in the monocyclic series[5] and electrolytic reduction in the bicyclic series,[3] so that "normal" reduction (Vd → VId) is unlikely in the tricyclic series, whereas products resulting from initial C_α–N cleavage are to be expected (VIId, IXd). The interesting feature of the electrolytic reduction of Vd is that, following scission of the C_α–N bond, a portion of the intermediate 2°-aminoketone is apparently able to undergo closure with the formation of two seven-membered rings (VIId). Since reclosure was not observed in the analogous bicyclic system (Id), it is attractive to assume that the cause of this difference lies in the element of fixity introduced by the presence of the benzene ring, *i.e.*, the coplanarity of the two *ortho* carbons with their substituent carbons bringing the >NH and >C=O in closer proximity. The other product of the electrolytic reduction of Vd was established as benzo[c]-7-hydroxyazacyclododecane (IXd) (48%) by analysis, infrared spectrum, and proof of the secondary nature of the amine by methylation (→ Xd).

Our results indicate that at least four competing reactions may take place during the electrolytic reduction of tricyclic α-aminoketones (V) at a lead cathode: (1) complete reduction, without rearrangement, of carbonyl to methylene; (2) reduction, without rearrangement, to the tricyclic aminoalcohol; (3) initial scission of the C_α–N bond and subsequent condensation to form a rearranged tricyclic amine; (4) scission of the C_α–N bond and reduction of the ketone carbonyl to hydroxyl. The first reaction path is favored only in the reduction of the five-membered ring aminoketone Va, in which rearrangement is improbable, since the rearranged product would contain a four-membered ring (VIIa). No product was identified positively as resulting from the second reaction path, although such a compound may have been present in each of the mixtures of aminoalcohols isolated from the reduction of Va and Vb. The third path is the one favored during Clemmensen reduction of α-aminoketones.[6] It was proved that the six- and seven-membered ring α-aminoketones, Vb and Vc, underwent rearrangement in this manner during electrolytic reduction, and the eight-membered ring ketone Vd almost certainly did likewise (decreasing yields of VII: 40, 29, 15%, respectively). Some product from the fourth reaction path was probably present in all four of the reaction mixtures. However, positive identification was not realized in the mixtures resulting from the five- and six-membered ring aminoketones. New eleven- and twelve-membered rings were created by the electrolytic reduction of Vc and Vd, and this method of making medium rings is undoubtedly capable of further extension.

Experimental[7]

Preparation of the α-Aminoketones

Ethyl N-(β-Carbethoxyethyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylate (IVa).—A solution of 33 g. (0.161 mole) of ethyl 1,2,3,4-tetrahydroisoquinoline-3-carboxylate (III)[4] in 150 ml. of xylene, together with 22.2 g. (0.161 mole) of potassium carbonate, was stirred and heated to reflux. To this suspension was added 36.7 g. (0.161 mole) of ethyl β-iodopropionate over a 30-minute period. The reaction mixture was held at reflux temperature for 3 hours, then cooled. Water was added to dissolve the inorganic salts, and the organic layer was separated. The xylene solution was extracted with 200 ml. of 3 *N* hydrochloric acid. The acid solution was next treated with ether, and the ether extract was discarded. The aqueous solution was made basic with saturated aqueous potassium carbonate and extracted with

(6) N. J. Leonard and W. C. Wildman, THIS JOURNAL, **71**, 3089 (1949), and subsequent papers in that series.

(7) All melting points are corrected. Microanalyses were performed by Miss Emily Davis, Mrs. Katherine Pih, Mrs. Esther Fett and Mr. Joseph Nemeth. The infrared absorption spectra were determined by Miss Helen Miklas and Mrs. Rosemary F. Hill.

five 50-ml. portions of ether. The ether extracts were combined and dried. After removal of the solvent, the mixture was fractionally distilled *in vacuo*, b.p. 160–161° (4 mm.), $n^{20}D$ 1.5162, yield 12.6 g. (58% based on unrecovered starting material).

Anal. Calcd. for $C_{17}H_{23}NO_4$: C, 66.86; H, 7.59; N, 4.59. Found: C, 67.11; H, 7.31; N, 4.88.

The picrate, formed in 95% ethanol and recrystallized from absolute ethanol, separated as yellow prisms, m.p. 115–116°.

Anal. Calcd. for $C_{23}H_{26}N_4O_{11}$: C, 51.68; H, 4.90; N, 10.48. Found: C, 51.86; H, 4.89; N, 10.52.

Benzo[c]-7-keto-1-azabicyclo[4.3.0]nonane (Va).—A solution of sodium ethoxide in toluene was formed from 2.12 g. (0.092 gram atom) of sodium and 10 ml. of ethanol in 150 ml. of dry toluene. The excess ethanol was removed as the ethanol–toluene azeotrope. When the distillation temperature reached 110°, stirring was begun and a solution of 28.1 g. (0.092 mole) of IVa in 100 ml. of toluene was added over a period of 30 minutes. Ethanol formed during the reaction was removed as the azeotrope. Stirring and refluxing were continued for one hour and the mixture was then cooled. The toluene solution was added to 1.5 l. of 6 *N* hydrochloric acid. The mixture was stirred and heated on the steam-bath for 12 hours (negative ferric chloride test). The hydrochloric acid layer was separated from the toluene layer and concentrated *in vacuo* to a thin sirup. The sirup was made basic with saturated aqueous potassium carbonate and extracted with ether. The ether extracts were dried and the solvent was removed. The solid product was recrystallized from aqueous ethanol as light yellow-brown platelets, m.p. 85–86°; yield 8.3 g. (48%). The infrared spectrum (chloroform solution) showed the presence of a ketone carbonyl group in a 5-membered ring (1754 cm.$^{-1}$).

Anal. Calcd. for $C_{12}H_{13}NO$: C, 76.97; H, 7.00; N, 7.48. Found: C, 77.08; H, 7.27; N, 7.68.

Benzo[c]-7-keto-1-azabicyclo[4.4.0]decane (Vb).[4,8]—This compound was prepared by a modification of the method of Archer[4] in that sodium ethoxide was used in place of sodium hydride for the Dieckmann cyclization of IVb. The product crystallized from ethanol as yellow prisms, m.p. 98–99°. The infrared spectrum (chloroform solution) showed carbonyl absorption at 1719 cm.$^{-1}$. Analysis was also used as a test of purity.

Anal. Calcd. for $C_{13}H_{15}NO$: C, 77.58; H, 7.52; N, 6.96. Found: C, 77.38; H, 7.37; N, 6.92.

Ethyl N-(δ-Cyanobutyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylate.—To a solution of 41 g. (0.2 mole) of III in 200 ml. of dry xylene was added 27 g. (0.195 mole) of potassium carbonate. While the suspension was stirred and heated to reflux, 31.6 g. (0.195 mole) of δ-bromovaleronitrile (Columbia Chemicals) was added over a one-hour period. Heating and stirring were continued for 14 hours, and the mixture was cooled. The product was isolated in the same way as IVa (above). Distillation gave 27.6 g. (53% based on unrecovered starting material) of a yellow liquid, b.p. 175–180° (0.1 mm.), $n^{21.6}D$ 1.5229. The infrared spectrum showed the presence of nitrile (2260 cm.$^{-1}$) and ester carbonyl (1732 cm.$^{-1}$) groups.

Anal. Calcd. for $C_{17}H_{22}N_2O_2$: C, 71.30; H, 7.74; N, 9.78. Found: C, 71.44; H, 7.57; N, 9.89.

Ethyl N-(δ-Carbethoxybutyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylate (IVc).—A solution of 36.2 g. (0.126 mole) of ethyl N-(δ-cyanobutyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylate in 300 ml. of absolute ethanol was saturated with anhydrous hydrogen chloride. The mixture was stirred and heated on the steam-bath for one hour. After cooling, the solid ammonium chloride was removed by filtration, and the ethanol was removed *in vacuo* until the remaining material formed a thick paste. This paste was dissolved in water and made basic with saturated potassium carbonate solution. The mixture was extracted with ether, the ether extracts were dried and the solvent was removed. The product was distilled as a yellow liquid, b.p. 169–170° (0.1 mm.), $n^{20.5}D$ 1.5096, yield 32 g. (76%). The infrared spectrum showed ester carbonyl absorption (1730 cm.$^{-1}$).

Anal. Calcd. for $C_{19}H_{27}NO_4$: C, 68.44; H, 8.13; N, 4.20. Found: C, 68.68; H, 7.86; N, 4.51.

(8) G. R. Clemo and G. A. Swan, *J. Chem. Soc.*, 617 (1946).

Benzo[i]-6-keto-1-azabicyclo[5.4.0]hendecane (Vc).—This ketone was prepared by the high-dilution Dieckmann cyclization method.[5] A 1-liter 3-necked flask was equipped with stirrer, high-dilution apparatus with drip-tip condenser and a tube for introducing nitrogen above the reaction mixture. In this flask a solution of potassium *t*-butoxide was prepared from 5.63 g. (0.144 gram atom) of potassium and 21.3 g. of *t*-butyl alcohol in 400 ml. of dry xylene. The excess *t*-butyl alcohol was removed as the azeotrope, and more xylene was added to bring the volume to 400 ml. While the mixture was stirred and heated at reflux, a solution of 24 g. (0.072 mole) of IVc in 50 ml. of xylene was added over a period of 17 hours. The alcohol formed was removed periodically through the drip-tip condenser. After addition was complete, the product was poured into 1.2 l. of 6 *N* hydrochloric acid and treated exactly as the other Dieckmann cyclization mixtures. The product was dissolved in ethanol, treated with Darco, added to an equal volume of water and left in the refrigerator overnight. The product crystallized as light yellow platelets, m.p. 94–95°, yield 10.6 g. (69%).

The infrared spectrum (chloroform solution) showed ketone carbonyl absorption at 1707–1708 cm.$^{-1}$.

Anal. Calcd. for $C_{14}H_{17}NO$: C, 78.10; H, 7.96; N, 6.51. Found: C, 78.30; H, 7.92; N, 6.51.

Ethyl N-(ε-Carbethoxypentyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylate (IVd).—A solution of 30 g. (0.146 mole) of III in 250 ml. of xylene was treated with 35.5 g. (0.131 mole) of ethyl ε-iodocaproate[9] in the presence of 19.4 g. (0.14 mole) of potassium carbonate, in the same way as IVa was formed. Distillation of the product yielded 26.2 g. (58%) of a yellow liquid, b.p. 174–176° (0.3 mm.), $n^{22}D$ 1.5052. The infrared spectrum showed ester carbonyl absorption at 1732 cm.$^{-1}$ and *ortho* substituted benzene absorption at 745 cm.$^{-1}$.

Anal. Calcd. for $C_{20}H_{29}NO_4$: C, 69.13; H, 8.41; N, 4.03. Found: C, 69.18; H, 8.24; N, 4.25.

Benzo[j]-7-keto-1-azabicyclo[6.4.0]dodecane (Vd).—Dieckmann condensation of 16.4 g. (0.047 mole) of IVd was carried out under the same high-dilution conditions as that of IVc. Addition of the diester to the potassium *t*-butoxide solution took 32 hours. The product, weighing 4.47 g. (42%) formed orange-brown prisms when recrystallized from aqueous ethanol, m.p. 77–78°. The infrared spectrum (chloroform solution) showed ketone carbonyl absorption at 1703 cm.$^{-2}$.

Anal. Calcd. for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11. Found: C, 78.71; H, 8.25; N, 6.29.

Clemmensen Reduction of the α-Aminoketones

Clemmensen Reduction of Benzo[c]-7-keto-1-azabicyclo[4.4.0]decane (Vb).—Zinc amalgam was formed by addition of 15 ml. of water and 1 ml. of concentrated hydrochloric acid to a mixture of 7 g. of granulated zinc and 1 g. of mercuric chloride. The liquid was decanted and the amalgam was washed once with water. The amalgamated zinc, with 1.5 g. (7.5 millimoles) of Vb, was treated with 50 ml. of 20% hydrochloric acid. The mixture was heated under reflux for 2 hours. After 20 minutes the original red color of the solution had disappeared. After cooling, the solution was decanted from the mercury remaining in the flask and was made basic with 50% potassium hydroxide solution. The solid was removed by filtration, and both solid and liquid were treated with several small portions of ether. The ether extracts were combined and dried. Most of the ether was removed by distillation and ethanolic picric acid was added. A **picrate** formed almost immediately, m.p. 177–182°, yield 2.08 g. (67%). After one recrystallization from ethanol it separated as elongated yellow platelets, m.p. 190–191°, which had the correct analysis for the picrate of benzo[c]-1-azabicyclo[5.3.0]decane (VIIb).

Anal. Calcd. for $C_{19}H_{20}N_4O_7$: C, 54.80; H, 4.84; N, 13.46. Found: C, 55.03; H, 4.79; N, 13.42.

Clemmensen Reduction of Benzo[i]-6-keto-1-azabicyclo[5.4.0]hendecane (Vc).—Zinc amalgam was made in the usual manner from 4 g. of granulated zinc and 1 g. of mercuric chloride. To this amalgam was added a solution of 0.15 g. (0.74 millimole) of Vc in 25 ml. of 20% hydrochloric acid. The mixture was heated at reflux for 2 hours, then cooled, and the product was isolated in the same way as de-

(9) N. J. Leonard and W. E. Goode, THIS JOURNAL, **72**, 5404 (1950).

scribed above. The crude picrate melted at 185–187° and weighed 0.15 g. (48%). After five recrystallizations from ethanol, the picrate formed yellow platelets, m.p. 193–194°. This picrate had the correct analysis for the picrate of benzo[c]-1-azabicyclo[5.4.0]hendecane (VIIc).

Anal. Calcd. for $C_{20}H_{22}N_4O_7$: C, 55.81; H, 5.15; N, 13.02. Found: C, 55.85; H, 5.37; N, 12.86.

Wolff–Kishner Reduction of the α-Aminoketones

Wolff–Kishner Reduction of Benzo[c]-7-keto-1-azabicyclo[4.3.0]nonane (Va).—To a solution of 0.5 g. (2.7 millimoles) of Va in 15 ml. of triethylene glycol was added 1 ml. of hydrazine hydrate. The solution was heated at 120° for 2 hours. After addition of 1.5 g. of potassium hydroxide, the solution was heated to 180° for 45 minutes. A considerable amount of gas was evolved and a small amount of material distilled. The remaining triethylene glycol solution was diluted with 100 ml. of water and extracted with four 10-ml. portions of ether. The combined ether extracts were dried and the ether was removed. Addition of ethanolic picric acid caused a picrate to precipitate immediately; yield 0.63 g. (59%). Recrystallized from ethanol, it formed yellow needles; m.p. 186.5–188° dec. The product had the correct analysis for the picrate of benzo[c]-1-azabicyclo[4.3.0]nonane (VIa).

Anal. Calcd. for $C_{18}H_{18}N_4O_7$: C, 53.75; H, 4.51; N, 13.93. Found: C, 53.82; H, 4.21; N, 13.87.

Wolff–Kishner Reduction of Benzo[c]-7-keto-1-azabicyclo[4.4.0]decane (Vb).—The Wolff–Kishner reduction of Vb was carried out in the same manner as described above on 1.5 g. (7.5 millimoles) of the ketone. The picrate of the product weighed 1.73 g. (55%). After four recrystallizations from ethanol, the picrate formed yellow prisms, m.p. 161–162°. The analysis was correct for the picrate of benzo[c]-1-azabicyclo[4.4.0]decane (VIb) (von Braun and Pinkernelle[10] reported 177°).

Anal. Calcd. for $C_{19}H_{20}N_4O_7$: C, 54.80; H, 4.84; N, 13.48. Found: C, 54.54; H, 5.06; N, 13.50.

Electrolytic Reductions of the α-Aminoketones

General Method.—The lead cathode (of 99.95% purity or better) was cast in a graphite mold at 270°. The cathode was cleaned in dilute nitric acid and prepared by the modified Tafel procedure.[11] This cathode was in the form of twin bars, having a total surface area of 100 cm.^{2}. The anode was a sheet of lead which surrounded the porous alundum cup holding the catholyte solution. This solution was formed by dissolving the aminoketone in enough 30% sulfuric acid to make 100 ml. of solution. The anolyte was also 30% sulfuric acid. The reduction procedure employed has been described by Swann.[11] The electrolytic reductions were carried out at the lead cathode at a current density of 0.05 amp./cm.^{2} and a temperature of 60°. In all cases the time of reduction was 20% longer than the theoretical required for four faradays of electricity per mole of compound.

After reduction, the catholyte solution was made strongly basic with excess 50% aqueous potassium hydroxide while the temperature was held at 10–20°. The mixture was then extracted with ether. The ether extracts were dried and the ether was removed. The products were isolated by distillation.

Electrolytic Reduction of Benzo[c]-7-keto-1-azabicyclo[4.3.0]nonane (Va).—This compound began to decompose almost immediately in 30% sulfuric acid, but reduction was carried out on 6.7 g. (0.036 mole) of Va. Distillation of the product through a Holzman column[12] yielded a low-boiling fraction, b.p. 87–92° (0.06 mm.), $n^{20}D$ 1.5582, yield 0.538 g.; and a high-boiling product, b.p. 140–145° (0.06 mm.), $n^{20}D$ 1.5779, yield 1.666 g.

The lower-boiling substance showed weak infrared absorption in the 3300 cm.$^{-1}$ region indicating slight NH or OH contamination. There was also some carbonyl absorption at 1752 cm.$^{-1}$. A picrate, formed in ethanol and recrystallized from the same solvent, separated as yellow needles; m.p. 186.5–188°. The melting point was not depressed when this picrate was mixed with the picrate of the product of Wolff–Kishner reduction of Va. Infrared spectra (Nujol mull) of the two picrates were identical.

Anal. Calcd. for $C_{18}H_{18}N_4O_7$: C, 53.73; H, 4.51; N, 13.93. Found: C, 53.98; H, 4.63; N, 14.03.

The infrared spectrum of the higher-boiling product (chloroform solution) showed carbonyl absorption at 1752 cm.$^{-1}$ (probably Va). However, OH and/or NH absorption (3610 cm.$^{-1}$) indicated possible reduction to benzo[c]-7-hydroxyazacyclononane (IXa) or to benzo[c]-7-hydroxy-1-azabicyclo[4.3.0]nonane (VIIIa).

Anal. Calcd. for $C_{12}H_{17}NO$ (IXa): C, 75.35; H, 8.96; N, 7.32. Calcd. for $C_{12}H_{15}NO$ (VIIIa): C, 76.15; H, 7.99; N, 7.40. Found: C, 75.48; H, 8.57; N, 7.17.

Electrolytic Reduction of Benzo[c]-7-keto-1-azabicyclo[4.4.0]decane (Vb).—Reduction of 5.4 g. (0.027 mole) of this aminoketone and distillation of the reaction products yielded two distinct fractions. The lower-boiling material was a colorless liquid, weighing 2.0 g. (40%); $n^{20.8}D$ 1.5565, b.p. 100–102° (0.6 mm.). The infrared spectrum showed no NH, OH or carbonyl absorption bands. The liquid had an analysis correct for benzo[c]-1-azabicyclo[5.3.0]decane (VIIb).

Anal. Calcd. for $C_{13}H_{17}N$: C, 83.37; H, 9.15; N, 7.48. Found: C, 83.16; H, 9.27; N, 7.50.

The picrate, formed in 95% ethanol and recrystallized from absolute ethanol, separated as yellow platelets, m.p. 191–192°. No depression in melting point was observed when this picrate was mixed with the picrate of the product of Clemmensen reduction of Vb. The infrared spectra (Nujol mull) of the two picrates were identical.

Anal. Calcd. for $C_{19}H_{20}N_4O_7$: C, 54.80; H, 4.84; N, 13.46. Found: C, 55.02; H, 4.93; N, 13.46.

The higher-boiling product was a viscous yellow-green liquid, weighing 2.81 g. (51%), b.p. 142–145° (0.5 mm.), $n^{20}D$ 1.5744. The infrared absorption spectrum (chloroform solution) showed an absorption band at 3600 cm.$^{-1}$ and general absorption in the 3300 cm.$^{-1}$ region, indicating the presence of OH and/or NH groups. The spectrum showed that the product was possibly a mixture of benzo[c]-7-hydroxyazacyclodecane (IXb) and benzo[c]-7-hydroxy-1-azabicyclo[4.4.0]decane (VIIIb).

Anal. Calcd. for $C_{13}H_{17}NO$ (VIIIb): C, 76.81; H, 8.43; N, 6.89. Calcd. for $C_{13}H_{19}NO$ (IXb): C, 76.05; H, 9.33; N, 6.82. Found: C, 76.23; H, 9.29; N, 6.62.

Electrolytic Reduction of Benzo[i]-6-keto-1-azabicyclo[5.4.0]hendecane (Vc).—Reduction of 9 g. (42 millimoles) of Vc yielded two products. The first was a colorless liquid, b.p. 120° (0.3 mm.), $n^{20}D$ 1.5580, yield 2.4 g. (29%). Its infrared spectrum showed no NH, OH or carbonyl absorption. This liquid formed a picrate in ethanol which was recrystallized from the same solvent in the form of yellow platelets, m.p. 194–195°. Mixed melting points and infrared spectra (Nujol mull) showed this picrate to be identical with that of the product of Clemmensen reduction of Vc. The analysis was consistent with the proposed formula, benzo[c]-1-azabicyclo[5.4.0]hendecane (VIIc).

Anal. Calcd. for $C_{20}H_{22}N_4O_7$: C, 55.81; H, 5.15; N, 13.02. Found: C, 55.72; H, 5.33; N, 12.94.

The high-boiling product of the reduction was an extremely viscous yellow-green liquid, b.p. 152–154° (2.5 mm.), $n^{20}D$ 1.5668, yield 4.3 g. (47%). The infrared spectrum (chloroform solution) showed OH and/or NH absorption (a strong band at 3620 cm.$^{-1}$ and general absorption in the 3300 cm.$^{-1}$ region) and no carbonyl absorption. The analysis was consistent with the 11-membered ring aminoalcohol structure (IXc) rather than that of the tricyclic aminoalcohol.

Anal. Calcd. for $C_{14}H_{21}NO$: C, 76.67; H, 9.65; N, 6.39. Found: C, 76.94; H, 9.85; N, 6.52.

A picrate was formed in ether and recrystallized from ether–ethanol as yellow prisms, m.p. 156.5–158°.

Anal. Calcd. for $C_{20}H_{24}N_4O_8$: C, 53.57; H, 5.39; N, 12.50. Found: C, 53.71; H, 5.23; N, 12.68.

Electrolytic Reduction of Benzo[j]-7-keto-1-azabicyclo[6.4.0]dodecane (Vd).—Reduction at a lead cathode of 4.17 g. (18 millimoles) of Vd led to the isolation of two products. The lower-boiling material, a colorless liquid, weighed 0.586 g. (15%), b.p. 120–130° (0.7 mm.), $n^{20}D$

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1.5508. The infrared absorption spectrum showed that no alcoholic hydroxyl or secondary amine group was present, but it did disclose some carbonyl impurity (1699 cm.$^{-1}$). A **picrate**, formed in ethanol and recrystallized from the same solvent, separated as yellow prisms, m.p. 165°, with the correct analysis for either the picrate of benzo[c]-1-azabicyclo[5.5.0]dodecane (VIId) or the picrate of benzo-[j]-1-azabicyclo[6.4.0]dodecane (VId).

Anal. Calcd. for $C_{21}H_{24}N_4O_7$: C, 56.75; H, 5.44; N, 12.61. Found: C, 57.04; H, 5.68; N, 12.61.

When triturated with absolute ether, the higher-boiling product crystallized as colorless prisms, m.p. 92–93°, yield 2.031 g. (48%). The infrared spectrum showed OH and/or NH absorption (a sharp band at 3615 cm.$^{-1}$ and a broad band in the 3400 cm.$^{-1}$ region). Analysis was consistent with the proposed formula, benzo[c]-7-hydroxyazacyclododecane (IXd), and not with the tricyclic aminoalcohol formula, benzo[j]-7-hydroxy-1-azabicyclo[6.4.0]dodecane (VIIId).

Anal. Calcd. for $C_{15}H_{23}NO$ (IXd): C, 77.20; H, 9.94; N, 6.00. Calcd. for $C_{15}H_{21}NO$: C, 77.88; H, 9.15; N, 6.05. Found: C, 76.92; H, 10.03; N, 6.09.

Methylations of the Aminoalcohols

Benzo[c]-1-methyl-7-hydroxyazacyclohendecane (Xc).—The formaldehyde–formic acid procedure[2] was used. Distillation of the product from 0.668 g. of benzo[c]-7-hydroxyazacyclohendecane (IXc) yielded 0.490 g. (69%) of a substance which solidified after standing for several days at room temperature. This material was recrystallized from petroleum ether in the form of colorless prisms, m.p. 82.5–84°. The infrared absorption spectrum (chloroform solution) showed strong OH absorption (3610 cm.$^{-1}$) and showed new absorption peaks indicative of the introduction of a methyl group (1345 and 2770 cm.$^{-1}$).

Anal. Calcd. for $C_{15}H_{23}NO$: C, 77.20; H, 9.94; N, 6.00. Found: C, 77.08; H, 9.71; N, 5.81.

Benzo[c]-1-methyl-7-hydroxyazacyclododecane (Xd).—A 1.137-g. (4.9 millimoles) sample of benzo[c]-7-hydroxyazacyclododecane (IXd) was methylated with methyl iodide in the presence of potassium bicarbonate.[3] The product distilled as a viscous yellow-green liquid, b.p. 151–155° (1 mm.), $n^{20}D$ 1.5484, yield 0.659 g. (55%). The infrared spectrum (chloroform solution) still showed OH absorption (a sharp band at 3610 cm.$^{-1}$ and a wide band about 3420 cm.$^{-1}$), and new methyl absorption (1350 and 2770 cm.$^{-1}$). A trace of carbonyl impurity was also indicated (1700 cm.$^{-1}$).

Anal. Calcd. for $C_{16}H_{25}NO$: C, 77.68; H, 10.19; N, 5.66. Found: C, 77.41; H, 10.31; N, 5.68.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF CALIFORNIA]

The Chlorination of *trans*-Decalin

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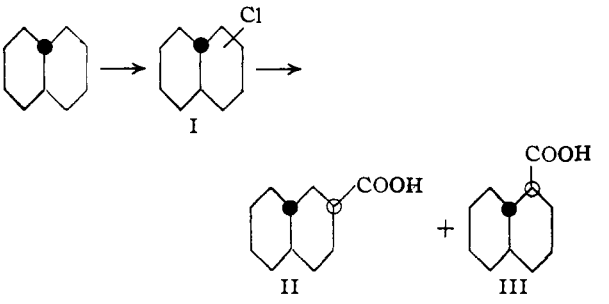
trans-Decalin was chlorinated and the product was shown to consist of approximately equal amounts of the 1- and 2-isomers.

In the course of a study related to the determination of the steric relationship existing between the various decalols and decalylamines,[2] the chlorination of decalin was investigated as a possible route for starting materials. This reaction has been widely utilized for the past 50 years[3–9] for the preparation of *trans*-decalin derivatives and in all cases only products derived from a 2-chlorodecalin have been reported. Recently, Zlatkis and Smith[9] published an improved method of chlorination of this decalin and claimed the material formed could be separated, by distillation, into two isomeric *trans*-2-chlorodecalins, identified by conversion to known *trans*-2-decalols, m.p. 53.5° and 74°.[10,11]

The chlorination of *trans*-decalin has been repeated utilizing the procedure of Tsatsas[8] and a 58% yield of chlorodecalins (I) was obtained (based upon recovered decalin). The product was converted to the Grignard reagent which upon carbonation gave a mixture of acids in 41% yield. By recrystallization, the known *trans*-decahydro-2-naphthoic acid (II),[12] m.p. 105–106° (lit.[8] 109°), was readily obtained. Fractional crystallization of the acids in the mother liquor gave no pure acid.



In an attempt to separate this remaining isomeric mixture, partition chromatography was investigated. Using the method of Ramsey and Patterson[13] it was found that the material could be separated into two fractions. The faster moving fraction was found to consist of the *trans*-2-acid (II) while the slower moving fraction yielded the previously unreported *trans*-1-acid (III), m.p. 102.0–102.8°. The structures of these acids were established by degradation to known decalylam-

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(12) In formulas II and III, the open circles denote that the configuration of the carboxyl group with respect to the nearest ring juncture hydrogen atom is not known at present. In all formulas, the hydrogen at carbon 9 of the decalin nucleus has arbitrarily been written as above the plane of the paper.

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