indolyl isoquinuclidinol and the bicyclo[3.2.1]octane derivative. No material giving a negative Ehrlich test was obtained.[23]

B.—A solution of 0.48 g of tosylate in 15 ml of dry *t*-butyl alcohol in which 0.06 g of potassium had been dissolved was heated at reflux for 25 hr under nitrogen. The solvent was removed at reduced pressure, water was added, and the mixture was extracted with methylene chloride. After washing with water and drying, the solvent was removed at reduced pressure to give 0.17 g of waxy solid. This solid was dissolved in methylene chloride and chromatographed on 4 g of Merck alumina. The first fractions eluted with methylene chloride gave 0.01 g (3.8%) of the indolenine as a white solid. The infrared spectrum showed a carbonyl maximum at 6.03 μ and the nmr showed the following peaks: 2.73 (multiplet, CHCO), 3.82 (multiplet, CHNCO), 4.40 (multiplet, CH_2NCO), and the aromatic multiplet at *ca.* 7.3. The analytical sample, mp 249–251°, was obtained by recrystallization from benzene; λ_{max} 243 mμ (log ϵ 3.83), shifted in acid to λ_{max} 238 sh mμ (log ϵ 3.79) and λ_{max} 278 sh mμ (log ϵ 3.53).

Anal. Calcd for $C_{17}H_{18}N_2O$: C, 76.66; H, 6.81; N, 10.52. Found: C, 76.70; H, 6.99; N, 10.37.

Further elution of the column with methylene chloride gave 0.12 g of recovered tosylate.

When the reaction was carried out using 0.88 g of tosylate and 0.38 g of potassium *t*-butoxide in 10 ml of dimethyl sulfoxide at room temperature for 15 hr, followed by warming on the steam bath for 1.5 hr, there was obtained after chromatography and recrystallization from benzene 0.025 g (5%) of material, mp 249–251°.

A solution of 0.03 g of the indoleneine in 5 ml of methanol and 10 ml of 10% hydrochloric acid was allowed to stand at room temperature overnight. The mixture was evaporated to dryness at reduced pressure, and the residue was triturated with water. The solid material was collected, washed with water, and recrystallized from ethanol to give 0.01 g (33%)[24] of desethylibogamine lactam, mp 313–315° dec, identical with that of the material obtained in part A above.

Reaction of Ibogaine Lactam with Aluminum Chloride.—A solution of 0.2 g of ibogaine lactam[2a] was treated with 0.10 g of aluminum chloride in 0.10 ml of toluene under the reaction conditions described above for the cyclization. Upon isolation of the product there was obtained 0.18 g (90%) of recovered lactam, identical in all respects with the starting material.

(23) In view of the results obtained in model systems under similar conditions,[11] this reaction was not investigated in detail.

(24) Owing to the low yields in the cyclization step, no efforts were made to find the optimum conditions for this reaction.

Desethylibogamine.—To a suspension of 0.30 g of desethylibogamine lactam in 50 ml of dry tetrahydrofuran was added 0.60 g of lithium aluminum hydride. The reaction mixture was heated at reflux 8 hr and cooled, the excess hydride was decomposed with ethyl acetate, and 0.8 ml of water was added. The aluminum salts were filtered off and washed with tetrahydrofuran, and the combined filtrates were concentrated *in vacuo*. The oily residue was taken up in methylene chloride and filtered through a column of 4 g of neutral alumina. After evaporation of the solvent and recrystallization from methanol 0.23 g (81%) of material, mp 186–187°, was obtained. The nmr spectrum showed a high-field envelope centered about 1.8 and a complex series of peaks between 2.70 and 3.39 for the various protons adjacent to the aliphatic nitrogen and the indole nucleus. There was also an aromatic multiplet centered about 7.15. Electronic integration indicated the ratio of the three types of protons was 7:8:4. The nmr spectrum of ibogamine shows peaks at 0.93 (triplet CH_3CH_2), an envelope centered about 1.6, and a complex series of peaks between 2.55 and 3.60, plus the aromatic multiplet. The ultraviolet spectrum showed λ_{max} 226 mμ (log ϵ 3.41), 283 (3.89), and 293 (3.80).

Anal. Calcd for $C_{17}H_{20}N_2$: C, 80.91; H, 7.99; N, 11.10. Found: C, 80.65; H, 7.90; N, 11.32.

Mercuric Acetate Oxidation of Desethylibogamine.—A solution of 0.03 g of desethylibogamine in 4 ml of 5% aqueous acetic acid containing 0.12 g of mercuric acetate was heated on the steam bath for 2 hr; the solution was saturated with hydrogen sulfide. The reaction mixture was filtered, made basic with sodium bicarbonate, and extracted with methylene chloride. Evaporation of the solvent and recrystallization from methanol gave 0.01 g of recovered desethylibogamine. Evaporation of the mother liquors gave a brown oil which by tlc consisted largely of starting material. The same reaction conditions applied to ibogamine gave similar results, while yohimbine gives an instantaneous precipitate of mercurous acetate.

Registry No.—Ia, 1630-03-1; III, 1630-02-0; IV, 1630-01-9; IIa, 10039-12-0; IIb, 10027-77-7; VII, 10043-41-1; IX, 1747-98-4; X, 10043-42-2.

Acknowledgment.—This work was supported by Grant NB-04589 from the National Institute of Neurological Diseases and Blindness, and in part by Public Health Service research career program award 1-K3-GM-5433. We wish to thank Dr. Neville Finch, of Ciba Pharmaceutical Co., for a sample of ibogamine

The Synthesis and Reactions of Some Isoquinuclidones[1,2]

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In the course of work directed at the total synthesis of the iboga alkaloids, the isoquinuclidones, 3-oxo-6-*endo*-hydroxy-2-azabicyclo[2.2.2]octane (Ia) and the corresponding N-benzyl compound (Ic), have been prepared. Acetolysis of the tosylate of the latter affords 2-benzyl-3-oxo-6-*endo*-acetoxy-2-azabicyclo[2.2.2]octane and 2-benzyl-3-oxo-7-*endo*-acetoxy-2-azabicyclo[3.2.1]octane with the latter predominating. Similarly, acetolysis of the bicyclo[3.2.1]octyl tosylate affords the same two products in the same ratio. This rearrangement proceeds with migration of a carboxamido group, apparently with participation of the amide nitrogen, a reaction for which there are few precedents.

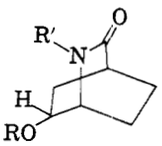
In the course of work directed at the synthesis of compounds related to the iboga alkaloids a new general synthesis of substituted isoquinuclidones was developed.[3] In the early phases of this work it was planned that a rather simple N-unsubstituted hydroxyisoquinuclidone (Ia) would be employed in the synthesis of desethylibogamine, with the indolyl ethyl moiety being added at a later stage.[4] Consequently, Ia was synthesized from the reaction of ammonia and 3-carbomethoxy-7-oxabicyclo[4.1.0]heptane, using the conditions described earlier.[3] Although the yields of

(1) A preliminary communication describing a portion of this work has been published by J. W. Huffman and T. Kamiya, *Tetrahedron Letters*, 1857 (1966).

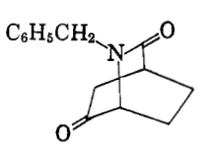
(2) This work was supported in part by Grant NB-04589 from the National Institute of Neurological Diseases and Blindness and in part by Public Health Service Career Program Award 1-K3-GM-5433.

(3) (a) J. W. Huffman, C. B. S. Rao, and T. Kamiya, *J. Am. Chem. Soc.*, **87**, 2288 (1965); (b) J. W. Huffman, C. B. S. Rao, and T. Kamiya, *J. Org. Chem.*, **32**, 697 (1967).

(4) This approach, and the one using the N-benzylisoquinuclidone, were explored initially, since it was felt that the conditions used in the isoquinuclidone synthesis would result in extensive decomposition of tryptamine. This is, however, not the case (see ref 3).



Ia, R, R′ = H
b, R = COC_6H_5, R′ = H
c, R, R′ = COC_6H_5
d, R = H; R′ = $CH_2C_6H_5$
e, R = $O_2SC_7H_7$; R′ = $CH_2C_6H_5$
f, R = $COCH_3$; R′ = $CH_2C_6H_5$



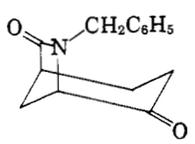
II

this compound were low (27%), the material was easily isolable. Attempted reduction of Ia to the amino alcohol failed, apparently owing to insolubility, and attempted preparation of the benzoate ester (Ib) gave two compounds. One product was a dibenzoyl derivative, which showed a split carbonyl band in the infrared with peaks at 5.82 and 5.98 μ and the nmr spectrum showed two quite low-field (δ 5.02 and 5.27) multiplets for the protons attached to carbons adjacent to oxygen and nitrogen. On the basis of these data, it was apparent that this material was the N,O-dibenzoyl derivative (Ic). The second compound obtained from the reaction was a monobenzoyl derivative, however it was not possible to determine by spectral methods whether this was the imide, or the simple benzoate ester. The compound was, however, stable to chromic acid–acetone for prolonged periods, and is, therefore, almost certainly the simple benzoate ester (Ib). Owing to the low yield of isoquinuclidone, and formation of the mixture of mono- and dibenzoyl derivatives when an attempt was made to block the hydroxyl group in Ia, an alternative approach to the iboga nucleus was explored.[5]

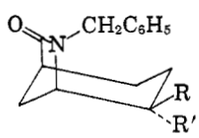
Repetition of the isoquinuclidone synthesis[3] using benzylamine rather then ammonia gave 2-benzyl-3-oxo-6-*endo*-hydroxy-2-azabicyclo[2.2.2]octane[6] (Id). Although this compound was not used in the synthesis of desethylibogamine,[3,5] it was found that acetolysis of its tosylate (Ic) proceeds in an unusual, and apparently novel fashion.[7]

When this tosylate (Ie) was heated at reflux in acetic acid, containing sodium acetate, two acetates were obtained in an over-all yield of 97%. The minor product (33%) was the *endo* acetate (If), while the major component (67%) was an isomer. By both thin layer chromatography and gas chromatography these are the only products of the acetolysis. The major product of the reaction showed carbonyl bands in the infrared at 5.80 and 5.97 μ, while the isoquinuclidone acetate (If) had absorption at 5.81 and 6.10 μ.

Basic hydrolysis of the isomer of If gave a hydroxy lactam, which on chromic acid oxidation gave a ketone which was isomeric with, but not identical with, 2-benzyl-3,6-dioxo-2-azabicyclo[2.2.2]octane (II), obtained by oxidation of Id. This ketone showed carbonyl absorption at 5.84 and 5.92 μ while II has carbonyl peaks at 5.82 and 6.10 μ. The nmr spectrum of the isomeric ketone was qualitatively somewhat similar to that of II, however the high-field aliphatic envelope was much less symmetrial than in II,[8] and the peak near δ 3.6, assigned to the proton attached to C_1 in II was a slightly broadened doublet (J = 5 cps) rather than a more or less diffuse peak. Based on these spectral data, the fact that this ketone was isomeric with II, and the mild reaction conditions employed in its formation, it was apparent that a rearrangement of the isoquinuclidine skeleton had occurred during the acetolysis. On the basis of the infrared spectrum of the product acetate, and also the corresponding ketone, it is apparent that the δ-lactam in I and II was now a γ-lactam. The splitting pattern of the proton at C_1 adjacent to nitrogen in the ketone was typical of the X proton of an ABX system where either J_{AX} or J_{BX} was quite small. On this basis, the ketone must be 2-benzyl-3,7-dioxo-2-azabicyclo[3.2.1]octane (III), and the original solvolysis product either the corresponding *exo* or *endo* acetate (IVa or IVb, respectively).



III



IVa, R = $OCOCH_3$; R′ = H
b, R = H; R′ = $OCOCH_3$
c, R = H; R′ = OH
d, R = H; R′ = $OSO_2C_7H_7$

Although mechanistic considerations (see below) indicate that the solvolysis product must be the *endo* acetate (IVb), this conclusion may also be reached on the basis of the nmr spectrum of IVb, and the corresponding alcohol (IVc). In both these compounds the C_7 proton appears as a rather narrow multiplet superimposed on the benzyl methylene signals. If these compounds were the *exo* isomers these protons would be axial and have a *trans*-diaxial relationship with one of the C_6 protons. This would give rise to the diffuse pattern normally observed for axial protons, rather than the sharp multiplet actually shown by these compounds.[9]

Also, in both the alcohol derived from IVb (IVc) and IVb itself the benzyl methylene protons appear as an AB quartet,[10] with $\Delta\delta$ being the same for both compounds (0.76). $\Delta\delta$ for the corresponding ketone (III) is, however, somewhat less (0.62). It would be expected that if the acetate group were *exo* (IVa), then anisotropic effects would cause $\Delta\delta$ for the acetate to be different than that of the corresponding alcohol.

To further investigate the nature of this rearrangement, the tosylate of the azabicyclo[3.2.1]octanol (IVd) was treated with acetic acid–sodium acetate and gave the same mixture of acetates obtained by acetolysis of Ie. Also, when either tosylate (Ie or IVd) was

(5) This approach to desethylibogamine was to have proceeded *via* reaction of Ib with indoleacetyl chloride, followed by reduction (lithium aluminum hydride) to an N-indolylethylisoquinuclidinol. Both this approach, and the one using the N-benzyllactam (Id) were dropped when it was found that tryptamine could be used in the isoquinuclidone synthesis.[3]

(6) The prefix *endo* is arbitrarily assigned to those compounds having substituents in a *trans* relationship to the nitrogen bridge.

(7) Following the appearance of the preliminary communication describing this reaction[1] a similar rearrangement was reported by G. Büchi, D. L. Coffen, K. Kocsis, P. E. Sonnet, and F. E. Ziegler, *J. Am. Chem. Soc.*, **88**, 3099 (1966).

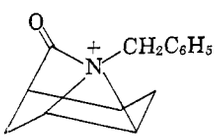
(8) In II the four aliphatic protons at C_7 and C_8 appear as a rather sharp pair of peaks at δ 1.82 and 1.88, and the protons at C_5 are clearly distinguishable. In the isomer, there is a continuous series of peaks from 1.7 to 2.3.

(9) N. S. Bhacca and D. H. Williams, "Applications of NMR Spectroscopy in Organic Chemistry" Holden-Day, Inc., San Francisco, Calif., 1954, pp 49–52.

(10) The benzyl protons in all compounds in both this series, and the original isoquinuclidones give rise to an AB pattern (J = 14–15 cps), with the exception of Id, where they are a broadened singlet.

heated to the melting point, and the pyrolysate was examined, it was found that a mixture of Ie and IVd had been formed, with the bicyclo[3.2.1]octanol derivative predominating by a factor of *ca.* 5:1.

Taking into consideration the over-all course of the above rearrangements, the observed stereospecificity, and the formation of the same mixture of products from similar reactions of both tosylates (Ie and IVd), it is apparent that the reactions in both series proceed *via* a common intermediate. The species which best agrees with these data is an acylaziridinium ion (V). Reaction of either tosylate to give V followed by attack of an appropriate nucleophile at either of the reactive sites on the carbocyclic ring will give the products observed in the above reactions.



V

These reactions, which involve neighboring group participation by amide nitrogen, appear to be the first examples of such participation under other than strongly basic conditions.[11] In addition to being a rather unusual example of neighboring group participation by amide nitrogen, these reactions belong to the small group of solvolytic skeletal rearrangements of saturated nitrogen heterocycles. The only other apparent example of this type of reaction is the racemization of L-(+)-2-α-tropanol,[12] which proceeds with participation of an amino nitrogen, a type of reaction for which there is considerable precedent.

Experimental Section[13]

3-Oxo-6-*endo*-hydroxy-2-azabicyclo[2.2.2]octane. A.—A mixture of 10.0 g of the mixture of *cis* and *trans* epoxides from methyl 3-cyclohexene-1-carboxylate, 40 ml of ammonium hydroxide, and 20 ml of methanol was allowed to stand at room temperature for 4 hr and then heated at reflux for 50 min. The solvent was evaporated at reduced pressure and the residual mixture of ester and amide was heated at 150–160° for 1 hr in a sublimation apparatus. The sublimation apparatus was then evacuated with an oil pump (*ca.* 1 mm) and heating was continued for 5 hr at the same temperature. The sublimate was washed with acetone and dried to give 2.47 g (27%) of pale tan crystals, mp 243–245° (sublimes). Recrystallization from isopropyl alcohol or methanol–ethyl acetate gave white crystals, mp 246–247° (sublimes).

Anal. Calcd for $C_7H_{11}NO_2$: C, 59.56; H, 7.85; N, 9.92. Found: C, 58.77, 58.99;[14] H, 7.58, 7.96; N, 9.96.

B.—A mixture of 5 g of the epoxy ester, 5 ml of methanol, and 50 ml of aqueous ammonia was heated at 110° for 24 hr. The solvent was removed *in vacuo*, and the crude solid was taken up in 10% ethanolic sodium hydroxide, and heated at reflux for 15 hr. The solution was acidified to pH 7, the solvent was removed at reduced pressure, and the residue was pyrolyzed as described above to give 0.87 g (19%) of material identical with that prepared by method A.

Benzoylation of the Isoquinuclidone.—To a solution of 2.66 g of the lactam in 1.8 ml of dry pyridine was added with cooling 3.0 g of benzoyl chloride. The reaction was allowed to stand at room temperature overnight and poured into water, and the resulting solid was filtered off, washed with water, and recrystallized from methanol to give 1.05 g of dibenzoate, mp 174–175°. This compound showed infrared maxima (C=O) at 5.82 and 5.98 μ, and nmr peaks at δ 2.62, 5.02, and 5.27 (all one-proton multiplets) in addition to aromatic and saturated aliphatic multiplets.

Anal. Calcd for $C_{21}H_{19}NO_4$: C, 72.19; H, 5.46; N, 4.01. Found: C, 72.14; H, 5.48; N, 4.09.

Concentration of the mother liquors gave a monobenzoate (1.74 g, mp 171–172°) which showed infrared absorption at 5.81 and 5.94 μ and nmr peaks at δ 2.58, 3.89, and 5.20 (all one-proton multiplets) plus aromatic and saturated aliphatic multiplets.

Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.56; H, 6.16; N, 5.71. Found: C, 68.31; H, 6.16; N, 5.74.

Reaction of 0.2 g of the monobenzoate with 0.7 ml of benzoyl chloride in pyridine under the usual conditions gave 0.21 g of material, mp 173–175°, identical with the dibenzoyl compound. When 0.53 g of the monobenzoate was dissolved in 15 ml of reagent grade acetone and treated with excess Kiliani's reagent,[15] there was no apparent consumption of chromate. After 2 weeks the reaction mixture was poured into water, concentrated on a hot plate, and cooled, giving 0.26 g (49%) of recovered monobenzoate as the only isolable product.

2-Benzyl-3-oxo-6-*endo*-hydroxy-2-azabicyclo[2.2.2]octane.—A solution of 16.0 g of the mixture of *cis*- and *trans*-epoxy ester and 11.0 g of benzylamine in 40 ml of ethanol was heated at reflux for 12 hr. After removing the ethanol *in vacuo*, the residue was heated at 150° for 2 hr, then at 190° for 1 hr, leaving a brown gum. This residue was taken up in 50 ml of methanol and 50 ml of 10% aqueous sodium hydroxide and heated at reflux for 1 hr. The ethanol was removed at reduced pressure and the aqueous residue was extracted with methylene chloride. The extracts were washed with water and dried, and the solvent was removed, leaving 17.0 g (71%) of clear oil which crystallized on standing. Recrystallization from benzene gave material, mp 97–99°, which showed an infrared band at 6.12 μ (C=O) and nmr peaks at δ 2.40, 3.36, 3.80 (one-proton multiplets), 4.38 (two protons, broadened singlet), and 7.16 (singlet).

Anal. Calcd for $C_{14}H_{17}NO_3$: C, 72.70; H, 7.41; N, 6.06. Found: C, 73.00; H, 7.46; N, 6.13.

The acetate was formed in the usual manner by heating the alcohol overnight in acetic anhydride. This compound, mp 124–125° from hexane, had infrared peaks at 5.81 and 6.10 μ (ester and lactam C=O). The nmr spectrum showed one-proton multiplets at δ 2.59, 3.62, and 4.68 and an AB quartet (J = 14 cps) centered at 4.53 in addition to aromatic and saturated aliphatic protons.

Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.12. Found: C, 70.44; H, 7.14; N, 5.12.

2-Benzyl-3-oxo-7-*endo*-hydroxy-2-azabicyclo[3.2.1]octane.—To a solution of 0.20 g of the isomeric acetate from the acetolysis was added 0.3 ml of 10% aqueous sodium hydroxide and 4 ml of methanol. The reaction mixture was allowed to stand overnight at room temperature, concentrated *in vacuo*, diluted with water, and extracted with methylene chloride. After drying, the methylene chloride was removed leaving 0.17 g of alcohol as a clear oil which crystallized on standing. Recrystallization from hexane gave white crystals, mp 85–86°.

Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41; N, 6.06. Found: C, 72.78; H, 7.26; N, 5.98.

The infrared spectrum showed absorption at 5.93 μ (C=O) and the nmr spectrum showed peaks at δ 2.42 (one proton, multiplet), 3.46 (one proton, quartet, J = 5 cps), 3.83 (one proton, multiplet), 4.35 (AB quartet, J = 14 cps), and 7.29 (five protons, singlet), plus saturated aliphatic protons.

2-Benzyl-3,7-dioxo-2-azabicyclo[3.2.1]octane.—To a solution of 0.17 g of the rearranged alcohol in 20 ml of reagent grade acetone was added Kiliani's reagent until a permanent orange color was present. After 12 hr at room temperature, the reaction mixture was concentrated *in vacuo*, taken up in water, and ex-

(11) (a) B. Capon [*Quart. Rev.* (London), **18**, 45 (1964)] cites a number of examples of this type of reaction, and also a number of references to the well-known participation by amide oxygen, see also, J. Hine, "Physical Organic Chemistry, 2nd ed, McGraw-Hill Book Co., Inc., New York, N. Y., 1962, pp 146–148. (b) The isoquinuclidine ring system seems to be particularly well suited to rearrangements of this sort as noted by Büchi.

(12) S. Archer, T. R. Lewis, M. R. Bell, and J. W. Schulenberg, *J. Am. Chem. Soc.*, **83**, 2386 (1961); see also however ref 7.

(13) Melting points were determined on a Hershberg melting point apparatus and are uncorrected. Infrared spectra were carried out as liquid films or potassium bromide pellets using a Perkin-Elmer Model 137 spectrophotometer. Nmr spectra were determined in deuteriochloroform using a Varian A-60 spectrometer and all values are reported in parts per million (ppm) relative to tetramethylsilane. Microanalyses were carried out by Galbraith Laboratories, Knoxville, Tenn.

(14) Adequate analytical data could not be obtained.

(15) Y. Sato and N. Ikekawa, *J. Org. Chem.*, **24**, 1367 (1959).

tracted with methylene chloride. Upon removing the solvent a colorless oil remained which was redissolved in methylene chloride and filtered through 3 g of neutral alumina to give 0.11 g (66%) of solid which upon recrystallization from hexane gave material, mp 73–74°, with infrared bands (C=O) at 5.84 and 5.92 μ. The nmr spectrum showed peaks at δ 2.67 and 3.62 (one-proton multiplet) and an AB pattern (J = 15 cps) centered at 4.41.

Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.51; H, 6.69; N, 6.01.

2-Benzyl-3,6-dioxo-2-azabicyclo[2.2.2]octane. A.—To a solution of 1.57 g of alcohol in 60 ml of acetone was added sufficient Kiliani's reagent to impart a permanent orange color. After 15 min at room temperature the solution was poured into water, concentrated on the steam bath, and extracted with three portions of methylene chloride. After washing with water and drying, the solvent was removed leaving 1.45 g of oil, the infrared spectrum of which showed a weak band at 5.82 μ (C=O) in addition to the amide carbonyl at *ca.* 6.10 μ. The oil was dissolved in benzene and chromatographed on 45 g of Merck alumina. Elution with 1:1 benzene–ether gave 0.44 g (28%) of ketone as a colorless oil which crystallized on standing. Recrystallization from ethyl acetate gave white crystals, mp 98–99°. The nmr spectrum showed an AB quartet (J = 14 cps) at δ 4.54, one-proton multiplets at 2.95 and 3.65, and a two-proton multiplets as 2.40.

Anal. Calcd for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.54; H, 6.58; N, 6.01.

The dinitrophenylhydrazone formed yellow needles, mp 191–193°, from methanol–ethyl acetate.

Anal. Calcd for $C_{20}H_{19}N_5O_5$: C, 58.68; H, 4.78; N, 17.11. Found: C, 58.57; H, 4.85; N, 17.05.

B.[16]—To a solution of 0.69 g of the hydroxyisoquinuclidone in 5 ml of dimethyl sulfoxide, 10 ml of benzene and 0.25 ml of pyridine containing 1.68 g of dicyclohexyl carbodiimide were added to 0.15 ml of trifluoroacetic acid. The reaction mixture was allowed to stand at room temperature overnight, the dicyclohexylurea was filtered off, and the solvents were evaporated. The residual oil (0.7 g) was taken up in warm ethyl acetate and on cooling there was obtained 0.41 g (60%) of material, mp 96–99°, identical with that obtained in part A. Tlc of the mother liquors indicated that the bicyclo[3.2.1]octanone was also obtained in this reaction but it could not be isolated.

2-Benzyl-3-oxo-7-*endo*-tosyloxy-2-azabicyclo[3.2.1]octane.—To a solution of 0.5 g of the 2-azabicyclo[3.2.1]octanol in 1 ml of pyridine was added 0.5 g of tosyl chloride. The reaction mixture was stirred at room temperature 16 hr and poured into water, and the precipitated solid (0.71 g, 85%), mp 123–124°, was collected. Recrystallization from methanol gave the analytical sample, mp 124–125°.

Anal. Calcd for $C_{21}H_{23}NO_4S$: C, 65.44; H, 6.02; N, 3.63. Found: C, 65.63; H, 6.22; N, 3.59.

2-Benzyl-3-oxo-6-*endo*-tosyloxy-2-azabicyclo[2.2.2]octane.—To a solution of 3.00 g of *p*-toluenesulfonyl chloride in 6 ml of pyridine at room temperature, was added 3.00 g of the N-benzylisoquinuclidone. The reaction mixture was allowed to stand at room temperature for 20 hr and then poured into water, and the precipitated solid (4.3 g, 86%) was collected. The analytical sample, mp 152–154°, was recrystallized from methanol.

Anal. Calcd for $C_{21}H_{23}NO_4S$: C, 65.44; H, 6.02; N, 3.63. Found: C, 65.22; H, 6.04; N, 3.53. The nmr showed peaks at δ 2.40 (one proton, singlet), 2.54, 3.67, 4.25 (one proton, multiplets), 4.45 (two protons, AB quartet, J = 14), plus aromatic and saturated aliphatic multiplets.

Solvolysis of 2-benzyl-3-oxo-6-*endo*-tosyloxy-2-azabicyclo[2.2.2]-octane.—A solution of 1.0 g of the tosylate in 10 ml of acetic acid containing 0.31 g of anhydrous sodium acetate was heated at reflux for 2 hr. The solvent was removed at reduced pressure and the residue was taken up in water and extracted with methylene chloride. The organic extract was washed with aqueous sodium bicarbonate and water and dried, and the solvent was removed to leave 0.67 g (93%) of a mixture of acetates. Thin layer chromatography (alumina-G) indicated a two-component mixture, and vapor phase chromatography (0.25 in × 6 ft column of silicone grease on diatomaceous earth at 245°) showed that the mixture consisted of 33% of the original isoquinuclidone acetate and 67% of a second component. In order to isolate the new compound, 1.40 g of the mixture was dissolved in methylene chloride and chromatographed on 40 g of neutral alumina. The first fractions eluted with methylene chloride gave 0.70 g of an isomeric acetate, mp 92–94° from benzene–hexane.

Anal. Calcd for $C_{16}H_{19}NO_3$: C, 70.31; H, 7.01; N, 5.12. Found: C, 70.24; H, 7.12; N, 5.13. The infrared spectrum showed bands at 5.80 and 5.97 μ (C=O) and the nmr showed peaks at δ 2.48, 3.59, and 4.81 (all one-proton multiplets) and an AB system centered at 4.42.

Further elution with the same solvent gave 0.27 g of a mixture of the two acetates, and finally 0.14 g of acetate, mp 124–125°, identical with that obtained by direct acetylation of the isoquinuclidone.

Solvolysis of 2-Benzyl-3-oxo-7-*endo*-tosyloxy-2-azabicyclo-[3.2.1]octane.—A solution of 0.015 g of the 2-azabicyclo-[3.2.1]octyl tosylate in 3 ml of acetic acid, containing 0.01 g of sodium acetate, was heated at reflux for 3 hr. The reaction product (0.01 g) was isolated as described in the solvolysis of the bicyclooctyl tosylate. Thin layer chromatography (silica gel G, benzene–acetone, 8:1) showed two components, the R_f values of which coincided with those of the 2-azabicyclo[3.2.1]- and -[2.2.2]octyl acetates. The infrared spectrum of the mixture was identical with that of the solvolysis product of the 2-azabicyclo[2.2.2]octyl tosylate. Vapor phase chromatography of the mixture under the conditions described above, showed that the mixture consisted of 67% of the bicyclo[3.2.1]octyl acetate and 33% of the isoquinuclidine derivative.

Thermal Rearrangement of 2-Benzyl-3-oxo-6-*endo*-tosyloxy-2-azabicyclo[2.2.2]octane.—The isoquinuclidone tosylate (0.70 g) was heated at 170° for 5 min and the pale amber pyrolysate was taken up in methanol. Fractional crystallization from this solvent gave 0.15 g of recovered azabicyclo[2.2.2]octyl tosylate, melting point, and mixture melting point 150–151°, and 0.40 g of the -[3.2.1]octyl tosylate, mp 124–125°. Integration of the nmr spectrum of the crude reaction product indicated that the two tosylates were originally present in a ratio of *ca.* 1 to 5.

When 0.03 g of the 2-azabicyclo[3.2.1]octyl tosylate was treated similarly, the infrared and nmr spectra of the crude product were identical with those obtained from the isoquinuclidone derivative.

Registry No.—Ia, 10028-27-0; Ic, 10028-28-1; Ib, 10028-29-2; Id, 5906-38-7; If, 5906-39-8; IVc, 10028-32-7; III, 5906-41-2; II, 10028-34-9; dinitrophenylhydrazone of II, 10028-35-0; IVd, 5906-43-4; Ie, 7421-56-9; isomer of If, 10028-38-3.

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