inobisbutyraldehyde tetraethyl diacetal (8 g, 26.4 mmol) was converted into the dialdehyde and allowed to self-condense.[18] Nine such runs were made simultaneously and after reduction the residues were pooled and distilled through a micro-spinning-band column. Four fractions were collected with the following boiling points (at 0.8 mm) and $n^{25}D$: (1) 97.5–98.5°, 1.4964; (2) 97.5°, 1.4969; (3) 97.5°, 1.4970; (4) 97.5–98.5°, 1.4970; total distilled material 7.76 g (23%). Paper chromatography (water–butanol–acetic acid) showed all four fractions to be identical and homogeneous: $\nu_{max}^{CHCl_3}$ 3400, 1625, 1610, 1565, 1362, 1317, 1270, 1160, and 1075 cm^{-1}.

The picrate was formed in 95% yield in ether and recrystallized several times from tetrahydrofuran–ether: mp 174–175° (lit. mp 174–175°,[15] 170.5°,[11] 172–173°[13,17]).

Anal. Calcd for $C_{14}H_{18}N_4O_8$: C, 45.40; H, 4.90; N, 15.13. Found: C, 45.20; H, 4.77; N, 15.26.

Picrolonate **17** was made in ether and recrystallized from ethanol, microcrystalline yellow solid, mp 161–162°.

Anal. Calcd for $C_{18}H_{23}N_5O_6$: C, 53.33; H, 5.72; N, 17.28. Found: C, 53.55; H, 5.91; N, 17.29.

Registry No.—**1,** 18944-80-4; **2,** 16853-08-0; **5,** 18927-50-9; **7,** 14129-07-8; **8,** 18927-52-1; **9,** 18968-32-6; **11,** 18927-53-2; **12,** 18929-90-3; 1-(4-methylcyclohexyl)-1-azacyclooctan-5-one picrate, 18927-74-7; 1-ethyl-1-azacyclononan-5-ol-6-one picrate, 18927-75-8; diethyl δ,δ′-benzyliminobisvalerate, 18944-93-9; 1-benzyl-1-azacyclodecan-6-one, 18944-94-0; 1-benzyl-1-azacyclodecan-6-one perchlorate, 18927-76-9; 1-benzyl-1-azacyclodecan-6-one picrate, 18927-77-0; **16,** 18929-91-4; **17,** 18929-92-5.

The Synthesis of *dl*-Deethylibogamine[1]

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The synthesis of deethylibogamine lactam (**22**) which was previously converted to deethylibogamine is described. Dihydrohomocarbostyril (**3**) was converted by acylation, reduction, and oxidation into the amido acid **12**. Further oxidation and hydrolysis gave the amino ketone **18**. Hydrogenation of the amino benzoic acids **13** and **18** over ruthenium gave the isoquinuclidones **14** and **19**, respectively. Oxidation of **19** followed by phenylhydrazone formation and Fisher indole synthesis gave **22**.

In recent years the efforts which have been expended on the synthesis of ibogamine (**1a**) have culminated in a number of reports of the preparation of this compound[3] and related species.[4] Prior to the publication of these results we had initiated a research program which was directed toward the syntheses of **1a** by way of the tricyclic ketone **2**.[5] The following discussion is concerned with the results of this work which led to the synthesis of deethylibogamine (**1b**) as well as the incorporation of an ethyl group onto a key reaction intermediate.

Homodihydrocarbostyril (**3**) was considered the ideal starting material for this synthesis since not only was it readily available from α-tetralone[6] but also the presence of the aromatic ring would permit the incorporation of a potential corboxylic acid function at a, oxidation of the benzylic position, b, and insertion of an ethyl group at c (Chart I). Hydrogenation of the aromatic ring would be expected to give the required all-*cis* product[7] and cyclization of the amino acid would give the desired tricyclic compound.

Friedel–Crafts acylation of **3** using aluminum chloride and acetyl chloride in carbon disulfide gave a 75% yield of the ketone **4**. The ultraviolet (uv) spectrum of **4** was essentially the same as that reported for *p*-acetamidoacetophenone but was quite different from those of the *ortho* and *meta* isomers.[8] Conjugation of the nitrogen with the ketone group lowered the reactivity of the latter and made the preparation of the ketal, **5**, more difficult than usual. Refluxing **4** in toluene with dry ethylene glycol and a trace of *p*-toluenesulfonic acid did not give any **5** under the common azeotropic distillation conditions. However, when **4** was treated with ethylene glycol in the presence of triethyl orthoformate and sulfuric acid, an 87% yield of **5** was obtained.

Lithium aluminum hydride reduction of **5** in tetrahydrofuran followed by acetylation of the crude amine gave a colorless oil, the infrared (ir) spectrum of which showed a single carbonyl stretching band at 1655 cm^{-1} but no adsorption in the 1040-cm^{-1} region which would be expected for a ketal.[9] The nmr spectrum of this product also showed that the doublet at δ 3.93 associated with the dioxolane protons was absent and, instead, a three-proton triplet at 1.26 and a two-proton quartet at 2.68 were observed. These data indicated that the ketal had been cleaved during the reduction of the lactam and that the product obtained was the ethyl tetrahydrobenzazepine, **7**. Since no other example of ketal cleavage by lithium aluminum hydride in the

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(2) Extracted from the dissertation submitted by W. G. P. to Seton Hall University in partial fulfillment of the requirements for the Ph.D. degree, 1968.

(3) (a) G. Büchi, D. L. Coffen, K. Kocsis, P. E. Sonnet, and F. E. Ziegler, *J. Amer. Chem. Soc.*, **87**, 2073 (1965); **88**, 3099 (1966). (b) J. P. Kutney, W. J. Cretney, P. LeQuesne, B. McKague, and E. Piers, *ibid.*, **88**, 4756 (1966). (c) S. I. Sallay, *ibid.*, **89**, 6762 (1967). (d) W. Nagata, S. Hirai, T. Okumura, and K. Kawata, *ibid.*, **90**, 1650 (1968).

(4) (a) J. W. Huffman, C. B. S. Rao, and T. Kamiya, *ibid.*, **87**, 2288 (1965); *J. Org. Chem.*, **32**, 697 (1967). (b) W. Nagata, S. Hirai, K. Kawata, and T. Okumura, *J. Amer. Chem. Soc.*, **89**, 5046 (1967). (c) Y. Ban, T. Wakamatsu, Y. Fujimoto, and T. Oishi, *Tetrahedron Lett.*, 3383 (1968).

(5) The utilization of this intermediate in the synthesis of ibogamine and epiibogamine has been recently reported.[3c,4c]

(6) E. C. Horning, V. L. Stromberg, and H. A. Lloyd, *J. Amer. Chem. Soc.*, **74**, 5153 (1952).

(7) R. P. Linstead, W. E. Doering, S. B. Davis, P. Levine, and R. R. Whetstone, *ibid.*, **64**, 1985, (1942).

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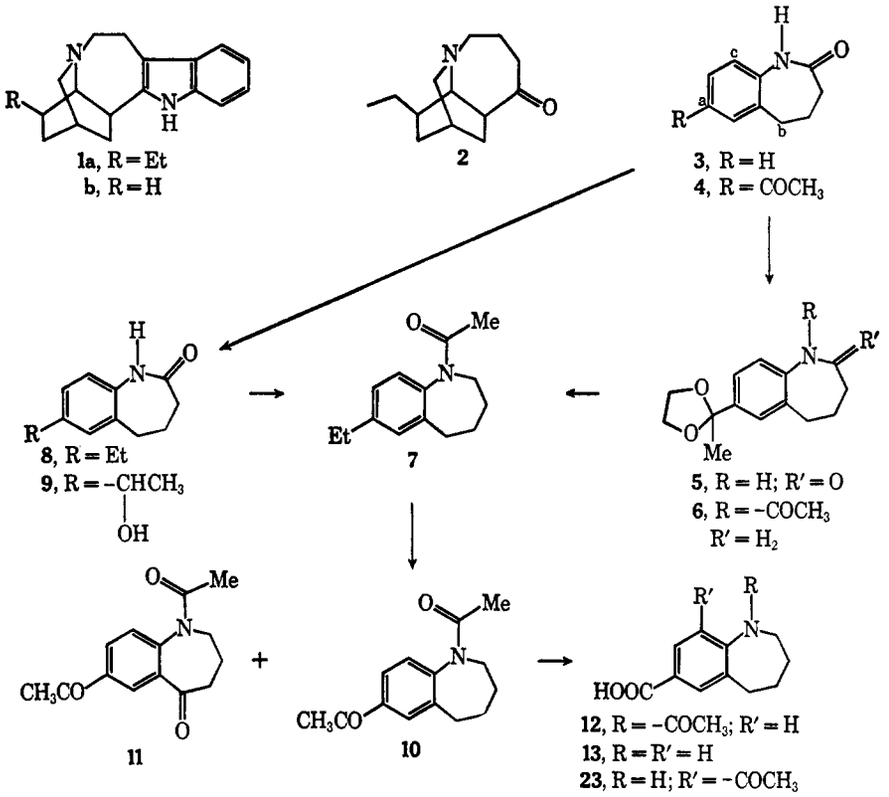
(9) R. T. Conley, "Infrared Spectroscopy," Allyn and Bacon, Inc., Boston, Mass., 1966, p 129.

CHART I



absence of Lewis acids could be found, **7** was synthesized by an alternate procedure to confirm these results.

Attempted hydrogenolysis of **4** in ethanol–ethyl acetate over palladium gave an extremely good yield of the hydroxylacatam **9.** The failure of **4** to be completely hydrogenolyzed under these conditions was attributed to catalyst deactivation by a trace of sulfur-containing impurity which conceivably originated from carbon disulfide decomposition during the Friedel–Crafts acylation. After repeated recrystallizations **4** was hydrogenolyzed in ethanol to the ethyllactam **8.** This poisoning effect was more conveniently eliminated by filtering an acetic acid solution of **4** through a pad of Norit. Hydrogenolysis of the resulting solution gave **8** in very good yield. Reduction of **8** followed by acetylation gave the amide **7,** which was identical with the material obtained by the lithium aluminum hydride reduction of **5.**

Attempted benzylic oxidations of **7** using chromic acid or chromium trioxide under a variety of conditions were unsuccessful with either unreacted **7** recovered or destruction of the ring system observed. However, with the use of potassium permanganate in a magnesium sulfate buffer[10] at low temperatures with a *t*-butyl alcohol cosolvent,[11] a mixture of the ketones **10** and **11** was obtained. Fractional recrystallization of the mixture afforded a 77% yield of **10** and an 8% yield of **11.** The ir spectrum of **10** had carbonyl adsorption bands at 1660 and 1680 cm^{-1} and its nmr spectrum exhibited singlet methyl peaks at δ 1.88 and 2.62 and integrated for eight methylene protons. The diketone **11,** however, had ir bands at 1662 and 1688 cm^{-1} and an nmr spectrum with singlet methyl adsorption at δ 1.84 and 2.45. The aromatic proton adsorptions of **11** were shifted further downfield than those of **10** with the strongest downfield shift exhibited by the proton at C-6 in **11.**

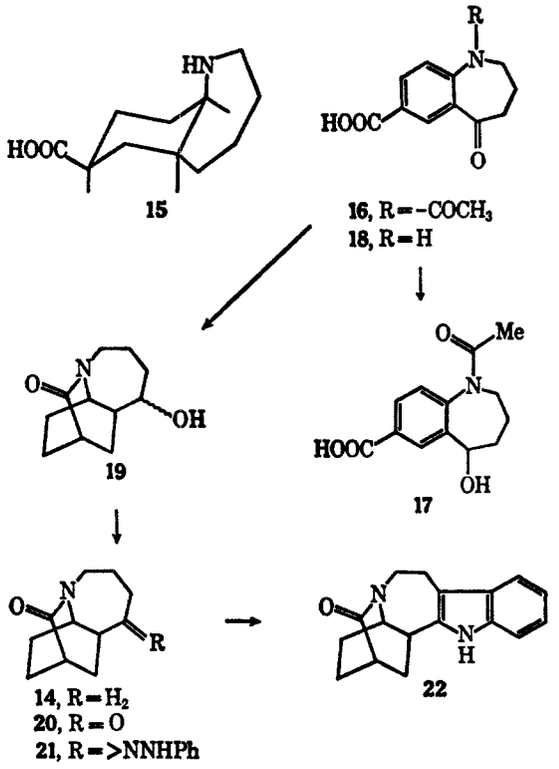
Sodium hypobromite oxidation of **10** gave the acid **12** in good yield. **12** was hydrolyzed in acid to the amine **13,** which was readily hydrogenated over ruthenium on charcoal at 160° to give directly the tricyclic lactam **14.** Ring closure under these conditions was not expected since it was reported that considerably higher temperatures were required to cyclize 4-aminocyclohexanecarboxylic acids to the isoquinuclidones.[12] It can be considered that the ring closure was facilitated by the favorable stereochemistry of the carboxy and amino group in the *cis*-fused intermediate **15** anticipated from hydrogenation of **13**[13] or, possibly, was catalyzed by the ruthenium metal either during or immediately following saturation of the ring. The ir spectrum of **14** exhibited a single carbonyl band at 1660 cm^{-1} which was in agreement with the position of the lactam bands reported for deethylibogamine lactam and ibogamine lactam.

Having demonstrated the ease with which the isoquinuclidone **14** could be formed, it only remained to prepare this material with the appropriate oxygen function present for the incorporation of the indole ring. Buffered permanganate oxidation of the sodium salt of **12** gave the keto acid **16.** The ir spectrum of **16** showed three carbonyl bands at 1645, 1681, and 1713 cm^{-1} while integration of the aliphatic region of the nmr

(10) W. Winkler, *Chem. Ber.*, **81,** 256 (1948).
(11) B. J. Armitage, G. W. Kenner, and M. J. T. Robinson, *Tetrahedron*, **20,** 723 (1964).
(12) L. H. Werner and S. Ricca, Jr., *J. Amer. Chem. Soc.*, **80,** 2733 (1958).
(13) R. E. Ireland and P. W. Schiess, *J. Org. Chem.*, **28,** 6 (1963).

spectrum indicated the presence of only six methylene protons. The chemical shifts of the aromatic proton absorptions also reflected the presence of a new deshielding group on the ring. Hydrogenation of **16** over platinum gave the alcohol, **17**, (Chart II), while, over

CHART II



palladium, **12** was regenerated. Alkaline hydrolysis of **16** gave the amino acid **18** which was hydrogenated at high temperature over ruthenium on charcoal to give a very good yield of the epimeric alcohols **19**. The formation of an epimeric alcohol mixture was a clear indication that the ketone was reduced before the aromatic ring. A one-step hydrogenation of both systems would have resulted in the formation of a single epimer of the alcohol. Here again, the ring closure occurred at a temperature considerably lower than that required for thermal lactam formation so that the catalyst must have exerted some influence on this phase of the reaction. No evidence of lactone formation was observed.

Mild oxidation of **19** with chromic acid gave the tricyclic ketone **20** which was converted directly into the phenylhydroazone **21**. Heating crude **21** in polyphosphoric acid resulted in the formation of *dl*-deethylibogamine lactam (**22**), mp 311–315°, in 80% yield. This material was shown to be identical with a sample of the *dl*-deethylibogamine lactam prepared by Huffman[14] and subsequently converted into *dl*-deethylibogamine.

The only problem remaining was to determine whether a potential ethyl group could be incorporated into one of the intermediates used to prepare **22** so that this reaction sequence might be extended to the synthesis of ibogamine itself. Since it was shown that photolysis of acetanilide gave a mixture of aniline and *o*- and *p*-aminoacetophenone[15] it was felt that this photoanilide rearrangement[16] would provide the means whereby an acyl group could be attached to the benzene ring of one of the aromatic intermediates. Photolysis of the amide **12** in an ethanol solution using a 2537-Å light source[17] resulted in the desired rearrangement. While the uv spectrum of the reaction mixture indicated the presence of about 30% rearranged product only an 8% yield of **23** was actually isolated. The nmr spectrum of this material showed absorption for only two aromatic protons with each having only *meta* coupling. The ir spectrum of **23** had carbonyl bands at 1632 and 1670 cm^{-1} in contrast to the 1622 and 1712 cm^{-1} bands observed with **12**. The spectrum of **23** also had N–H adsorption at 3290 cm^{-1} which was unchanged on dilution, indicating intramolecular hydrogen bonding which is possible only in the *o*-aminoacetophenone-type structure. The uv spectrum of **23** is described in the Experimental Section.

In recent work on the photo Fries rearrangement it was found that, while the quantum yield for rearrangement was independent of solvent, that for cleavage was quite solvent dependent.[18] The quantum yield for cleavage was highest in ethanol but quite low in *t*-butyl alcohol. Since the photoanilide rearrangement is believed to occur by a mechanism similar to that of the photo Fries,[16] it was felt that the use of *t*-butyl alcohol in the irradiation of **12** would lead to higher yields of **23**. When this reaction was run, a 50% yield of rearranged product was indicated by uv analysis and a 33% yield of **23** was actually isolated.

In view of the recently reported stereospecific syntheses of ibogamine,[3c-e] further work directed toward the conversion of **23** into this material has been discontinued.

Experimental Section[19]

Homodihydrocarbostyril (3).—**3** was prepared by a modification of the procedure of Horning and coworkers.[6] A mixture of 50 g of tetralone-1 oxime (mp 102–104°) and 500 g of polyphosphoric acid was warmed with stirring on a steam bath until the reaction became exothermic. The flask was removed from the heat and the viscous liquid was stirred until it had cooled to 110°. Heating was resumed for an additional 30 min. The amber syrup was cooled and poured onto 1 kg of ice. The resulting white precipitate was extracted into methylene chloride and the extract was filtered through a pad of Norit, washed with water and saturated aqueous sodium chloride, and dried with sodium sulfate. Evaporative distillation of the solvent gave the white crystalline product, which was washed with cold ether, filtered, and dried. The pure product weighed 47 g (94%) and melted at 141–143° (lit.[6] mp 142.5–143°).

7-Acetyl-1,3,4,5-tetrahydro-2H-1-benzazepin-2-one (4).—To

(14) We wish to thank Professor Huffman for kindly supplying us with a sample of this material for comparison purposes.

(15) D. Elad, D. V. Rao, and V. I. Stenberg, *J. Org. Chem.*, **30**, 3252 (1965).

(16) (a) V. I. Stenberg in "Organic Photochemistry," O. L. Chapman, Ed., Marcel Dekker, Inc., New York, N. Y., 1967, pp 142–145. (b) D. Bellus and P. Hrdlovič, *Chem. Rev.*, **67**, 599 (1967).

(17) Photolyses were carried out in a Rayonet Photochemical Reacter, Model RPR-100, having a battery of sixteen 2537-Å lamps (35 W) surrounding the reaction vessel.

(18) M. R. Sandner and D. J. Trecker, *J. Amer. Chem. Soc.*, **89**, 5725 (1967).

(19) Boiling points and melting points are uncorrected. The ir spectra were obtained on a Beckman IR-10 recording double-beam ir spectrophotometer. Nmr spectra were obtained in deuteriochloroform, unless otherwise indicated, using tetramethylsilane as the internal standard. Spectra were recorded on a Varian Associates Model A-60A spectrometer. The spectral data are reported in units of δ and the multiplicity of the resonance signal and the number of protons integrated for the peak are given in parentheses. The uv spectra were measured in methanol on a Beckman DB spectrophotometer. Wavelengths are expressed in millimicrons (mμ) and extinction coefficients as ϵ are given in parentheses.

a stirred suspension of 480 mg of **3**, 15 ml of carbon disulfide, and 2.25 g of anhydrous aluminum chloride was slowly added 0.56 ml of acetyl chloride. The mixture was refluxed for 1 hr and the carbon disulfide was removed by distillation. The red, oily complex was decomposed by addition to 25 g of ice and the white precipitate was extracted into methylene chloride. The extract was washed with water and saturated aqueous sodium chloride, dried with sodium sulfate, filtered through a pad of Norit, and evaporated to a tan, crystalline solid. Recrystallization from 1:1 benzene–cyclohexane with hot filtration through a pad of Norit gave 460 mg (75.4%) of the white, crystalline product, mp 159.5–162°. Further recrystallizations gave pure **4**: mp 164–166°; uv spectrum, λ_{max} 216–220 mμ (ε 14,520) and 274–276 (16,720); ir spectrum (Nujol), 1675 (ketone) and 1630 cm^{-1} (lactone).

Anal. Calcd for $C_{12}H_{13}NO_2$: C, 70.91; H, 6.45; N, 6.89. Found: C, 70.82; H, 6.58; N, 6.82.

The Ketal (5) of 7-Acetyl-1,3,4,5-tetrahydro-2H-1-benzazepin-2-one.—A mixture of 8.12 g of **4**, 10 g of triethyl orthoformate, 8 g of freshly distilled ethylene glycol, and 2 drops of sulfuric acid was stirred until all of the solid had dissolved. On standing, the crystalline product separated. The mixture was chilled in an ice bath and filtered and the crystals were washed with cold ethanol and ether. The product weighed 8.60 g (87%), mp 187–189.5°. Recrystallizations from ethanol and from benzene gave pure **5**: mp 188–189.5°; uv spectrum λ_{max} 249 mμ (ε 7910) and 280 (333, sh); ir spectrum (Nujol), 1663 (C=O) and 1040 cm^{-1} (ketal); nmr spectrum, $-OCH_2CH_2O-$ at δ 3.93 (complex doublet, 4) and $-CH_3$ at 1.66 (singlet, 3).

Anal. Calcd for $C_{14}H_{17}NO_3$: C, 67.99; H, 6.92; N, 5.66. Found: C, 68.10; H, 6.88; N, 5.85.

7-(1′-Hydroxyethyl)-1,3,4,5-tetrahydro-2H-1-benzazepin-2-one (9).—A suspension of 16.2 g of crude **4**, 3 g of 5% palladium on carbon, 200 ml of ethyl acetate, and 50 ml of ethanol was shaken in a Parr apparatus under 45 psig of hydrogen for 46 hr. Another 2 g of catalyst was added and shaking was continued for 7 hr longer. The catalyst was removed by filtration and evaporation of the filtrate gave a fluffy, white solid which was stirred in ether, filtered, and dried. The crude product weighed 15.26 g (94%), mp 173–176°. Recrystallization from acetonitrile gave pure **9**: mp 177–179°; ir spectrum (Nujol), OH at 3440, NH at 3200, and C=O at 1660 cm^{-1}; uv spectrum, λ_{max} 240 mμ (ε 17,730) and 280 (2220, sh); nmr spectrum, OH at δ 8.15 (singlet, 1), methinyl CH at 4.88 (quartet, 1, J = 6.5 Hz), and CH_3 at 1.49 (doublet, 3, J = 6.5 Hz).

Anal. Calcd for $C_{12}H_{15}NO_2$: C, 70.30; H, 7.36; N, 6.82. Found: C, 70.23; H, 7.38; N, 6.97.

7-Ethyl-1,3,4,5-tetrahydro-2H-1-benzazepin-2-one (8). Method A. Hydrogenolysis of Pure 4.—A solution of 260 mg of **4** in 25 ml of 95% ethanol was stirred in the presence of 100 mg of 10% palladium on carbon under 1 atm of hydrogen pressure for 90 min. The theoretical amount of hydrogen was absorbed in the first 40 min. Filtration and evaporation of the solvent gave 230 mg (95%) of crude **8** as a white solid, mp 160–163.5°.

Method B. Hydrogenolysis of Crude 4.—A solution of 20.3 g of crude **4** in 100 ml of glacial acetic acid was filtered through a pad of Norit, diluted with an additional 50 ml of solvent, and shaken in a Parr apparatus at 50 psig of hydrogen for 3 hr in the presence of 3 g of 5% palladium on carbon. The catalyst was removed by filtration and evaporation of the filtrate gave a white, crystalline solid which was washed with ether and dried. Recrystallization from acetonitrile with hot filtration through Norit gave 17.2 g (91%) of pure **8**: mp 166.5–168°; uv spectrum, λ_{max} 240 mμ (ε 14,650) and 280 (1290, sh); ir spectrum (Nujol), NH at 3040 and 3180, C=O at 1668 cm^{-1}; nmr spectrum, CH_3 at δ 1.20 (triplet, 3, J = 7.5 Hz, CH_2 at 2.60 (quartet, 2, J = 7.5 Hz).

Anal. Calcd for $C_{12}H_{15}NO$: C, 76.16; H, 7.99; N, 7.40. Found: C, 75.82; H, 7.80; N, 7.67.

1-Acetyl-7-ethyl-2,3,4,5-tetrahydro-1H-1-benzazepine (7). Method A. Reduction and Acetylation of 8.—A solution of 30.24 g of **8** in 600 ml of dry tetrahydrofuran was added over a 1-hr period to a stirred suspension of 18.40 g of lithium aluminum hydride in 200 ml of tetrahydrofuran. The mixture was stirred and refluxed for 20 hr. Excess hydride was decomposed by slow addition of 150 ml of ethyl acetate followed by an additional 1 hr of reflux. The mixture was cooled and 60 ml of water was added carefully. The alumina was removed by filtration and washed with ether and with methylene chloride. The combined filtrate was evaporated to a turbid, yellow oil which was dissolved in 100 ml of methylene chloride, filtered through a pad of Norit, dried with sodium sulfate, and evaporated to a clear, yellow oil.

The crude amine was dissolved in 300 ml of acetic anhydride and allowed to stand overnight. Evaporative distillation of the solvent *in vacuo* left a turbid amber oil which was dissolved in ether and stirred with 5% hydrochloric acid for 15 min. The ether layer was separated and washed successively with 5% sodium bicarbonate solution, water, and saturated aqueous sodium chloride. After drying with magnesium sulfate, the ether solution was filtered through a pad of Norit and evaporated to 31.1 g of yellow oil which was purified by distillation at reduced pressure to give 28 g (81%) of a colorless oil, bp 128–130° (0.45 mm). Redistillation in a short-path, bulb-to-bulb, distilling tube at 0.04 mm gave pure **7**: bath temperature 120°; ir spectrum (film), C=O at 1655 cm^{-1}; uv spectrum, λ_{max} 265 mμ (ε 400), 274 (290), and 226 (9840, sh); nmr spectrum, CH_3 at δ 1.26 (triplet, 3, J = 7.5 Hz), CH_3 at 1.83 (singlet, 3), $-CH_2-$ at 2.68 (quartet, 2, J = 7.5 Hz), and aromatic protons at 7.06 (singlet, 3).

Anal. Calcd for $C_{14}H_{19}NO$: C, 77.38; H, 8.81; N, 6.45. Found: C, 77.29; H, 9.14; N, 5.92.

Method B. Reduction and Acetylation of 5.—A solution of 2.50 g of **5** in 50 ml of dry tetrahydrofuran was added over 15 min to a stirred suspension of 1.15 g of lithium aluminum hydride in 30 ml of tetrahydrofuran. The mixture was stirred and refluxed for 19 hr and the excess hydride was decomposed with 10 ml of ethyl acetate. The mixture was cooled and 4.5 ml of water was added carefully. After stirring for 30 min longer, the alumina was removed by filtration and washed with ether. The combined filtrate was evaporated to a cloudy yellow oil which was dissolved in 50 ml of 1:1 benzene–*n*-hexane, decanted from the water layer, dried with potassium carbonate, and evaporated to give 2.08 g of yellow oil.

A solution of the oil in 50 ml of acetic anhydride was allowed to stand for 1 hr, warmed on a steam bath for 15 min, and cooled, and the solvent was removed by evaporative distillation. The residual yellow oil was purified by distillation *in vacuo* in a Hickman still to give 1.47 g (53.5%) of pure **7** as a colorless oil, bp 105° (0.1 mm).

1,7-Diacetyl-2,3,4,5-tetrahydro-1H-1-benzazepine (10) and 1,7-Diacetyl-2,3,4,5-tetrahydro-1H-1-benzazepin-5-one (11).—A solution of 45 g of potassium permanganate in 1750 ml of water was added with stirring to a mixture of 30 g of **7**, 500 ml of *t*-butyl alcohol, 100 ml of water, and 90 g of anhydrous magnesium sulfate. The reaction mixture was stirred at 23° for 24 hr. After heating on a steam bath and hot filtration through Celite, the manganese dioxide was washed well with 95% ethanol. The wash was combined with the colorless filtrate and evaporated *in vacuo* to a volume of 1000 ml. Extraction with methylene chloride followed by drying and evaporative distillation of the solvent gave 32.2 g of amber oil. The oil was dissolved in 110 ml of ether. Scratching induced the crude diketone, **11**, to crystallize slowly. After refrigeration overnight, the crystals were removed by filtration, washed with ether, and dried. Recrystallization from 1:1 benzene–cyclohexane gave 2.82 g (8.4%) of crude **11**, mp 134–138°.

The filtrates were combined and evaporated *in vacuo* to a yellow oil which crystallized slowly in petroleum ether (bp 30–60°). Filtration gave 24.7 g (77.4%) of crude **10**, mp 71–78°. The monoketone was purified by recrystallization from *n*-hexane to give pure **10**: mp 84–86°; ir spectrum (Nujol), amide C=O at 1660, ketone C=O at 1680 cm^{-1}; uv spectrum, λ_{max} 262 mμ (ε 11,600); nmr spectrum CH_3 at δ 1.88 (singlet, 3) and at 2.62 (singlet, 3), aromatic CH at 7.28 (doublet, 1, J = 9 Hz), at 7.81 (multiplet, 1), and at 7.92 (singlet, 1), total integration indicated eight methylene protons.

Anal. Calcd for $C_{14}H_{17}NO_2$: C, 72.70; H, 7.41. Found: C, 72.76; H, 7.39.

Recrystallization of the diketone from 1:2 benzene–cyclohexane gave pure **11**: mp 142–143°; ir spectrum (Nujol), C=O at 1662 and at 1688 cm^{-1}; uv spectrum, λ_{max} 231 mμ (ε 18,540) and 270 (8040); nmr spectrum, CH_3 at δ 1.84 (singlet, 3) and at 2.45 (singlet, 3), aromatic CH at 7.19 (doublet, 1, J = 8.5 Hz), at 7.97 (doublet of doublets, 1, J_1 = 8.5, J_2 = 2 Hz), and at 8.25 (doublet, 1, J = 2 Hz), total integration indicated six methylene protons.

Anal. Calcd for $C_{14}H_{15}NO_3$: C, 68.55; H, 6.16; N, 5.71. Found: C, 68.65; H, 6.16; N, 5.90.

1-Acetyl-2,3,4,5-tetrahydro-1H-1-benzazepine-7-carboxylic Acid (12).—A solution of 6.49 g of **10** in 85 ml of dioxane was slowly added with stirring to a cold (0–5°) solution of sodium hypobromite (prepared from 10.1 g of sodium hydroxide and 13.5 g of bromine in 140 ml of water). The reaction mixture was stirred in an ice bath for an additional 60 min. After the addition of 10 ml of acetone followed by another 30 min of stirring in the cold, the mixture was evaporated *in vacuo* in a 40° water bath to a volume of 90 ml. The turbid solution was washed with methylene chloride, filtered through a pad of Norit, chilled in an ice bath, and slowly acidified with concentrated hydrochloric acid. The white precipitate was collected and recrystallized from aqueous acetone with hot filtration through Norit to give 5.05 g (78%) of the crystalline acid, mp 199.5–202°. Recrystallizations from acetonitrile gave pure **12**: mp 200–201.5°; ir spectrum (Nujol), acid OH at 2600, acid C=O at 1712, and amide C=O at 1622 cm^{-1}; uv spectrum, λ_{max} 213 mμ (ε 7630) and 246 (3900); nmr spectrum, CH_3 at δ 1.97 (singlet, 3), aromatic CH at 7.28 (doublet, 1, J = 8 Hz), at 7.96 (doublet, 1, J = 8 Hz), and at 8.09 (singlet, 1), COOH at 11.62 (singlet, 1).

Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 67.13; H, 6.60; N, 6.13.

2,3,4,5-Tetrahydro-1H-1-benzazapine-7-carboxylic Acid (13).—A solution of 1 g of **12** in 20 ml of 20% sulfuric acid was refluxed for 44 hr, filtered through a pad of Norit, and neutralized to pH 4.5 with 10% sodium hydroxide solution. The precipitate was filtered and dried to give 500 mg of white crystals, mp 168–170°. Extraction of the aqueous filtrate with methylene chloride, followed by drying and evaporation of the extract, gave an additional 250 mg of the solid. Recrystallization from aqueous ethanol gave 550 mg (67%) of the white crystalline product, mp 171.5–174°. Sublimation at 0.3 mm in a 140–150° bath for 1 hr gave pure **13**: mp 173–174.5°; ir spectrum (Nujol), NH at 3375 and 3410, OH at 2450 and 2550, C=O at 1670 cm^{-1}; uv spectrum, λ_{max} 230 mμ (ε 2000) and 287 (13,800); nmr spectrum, aromatic CH at δ 6.67 (doublet, 1, J = 8 Hz), at 7.78 (doublet of doublets, 1, J_1 = 8, J_2 = 2 Hz), and at 7.83 (singlet, 1).

Anal. Calcd for $C_{11}H_{13}NO_2$: C, 69.09; H, 6.85; N, 7.32. Found: C, 69.34; H, 6.80; N, 7.23.

1-Azatricyclo[6.3.1.0^{6,11}]dodecan-12-one (14).—A mixture of 400 mg of **13**, 500 mg of 5% ruthenium on carbon, and 50 ml of 95% ethanol was stirred in a stainless steel autoclave at 150° and 2200 psig of hydrogen for 24 hr. Filtration, followed by evaporative distillation of the alcohol, gave a viscous oil which was boiled in benzene, filtered through a pad of Norit, and evaporated to give 330 mg of a yellow oil. Infrared (film) absorption at 3410 cm^{-1} showed water to be present in the oil. (This band was still present after boiling a 50-mg sample of the oil in 20 ml of anhydrous benzene with 50 mg of calcium hydride for 15 hr followed by filtration and evaporation.)

The oil was dissolved in petroleum ether (bp 30–60°), stirred with anhydrous potassium carbonate for 1 hr, filtered through a pad of Norit, and evaporated to give 270 mg of a colorless oil having the same ir spectrum. Short-path distillation in a Hickman still gave 260 mg (69.4%) of crude **14**, bp 70–75° (0.5 mm). Redistillation at 0.02 mm in a bulb-to-bulb distilling tube (bath temperature 125–130°) gave pure **14**: ir spectrum (film), lactam at 1660 and water at 3450 cm^{-1}; nmr spectrum, complex, water at δ 5.29 (singlet, 1), no change after treatment with deuterium oxide.

Anal. Calcd for $C_{11}H_{17}NO \cdot 0.5H_2O$: C, 70.20; H, 9.36; N, 7.44. Found: C, 70.24; H, 9.62; N, 7.27.

1-Acetyl-2,3,4-5-tetrahydro-1H-1-benzazepin-5-one-7-carboxylic Acid (16).—A solution of 6.75 g of potassium permanganate in 400 ml of water was added with stirring to a cold solution of 5.0 g of **12**, 0.88 g of sodium hydroxide, and 15 g of anhydrous magnesium sulfate in 200 ml of water. The reaction mixture was stirred in a 24° water bath for 69 hr. The manganese dioxide was removed by filtration and washed thoroughly with ethanol. The alcohol wash was evaporated to a yellow oil which was dissolved in methylene chloride and shaken with the aqueous filtrate. After separation, the aqueous layer was acidified with hydrochloric acid to pH 6 and extracted thoroughly with methylene chloride. The extract was washed with saturated aqueous sodium chloride, dried with sodium sulfate, and evaporated *in vacuo* to a colorless glass which crystallized in ether. Filtration gave 3.07 g (58%) of the crude product, mp 162–178°. Recrystallizations from acetonitrile gave pure **16**: mp 187–188°; ir spectrum (Nujol), acid OH at 3200, acid C=O at 1713, ketone C=O at 1681, amide C=O at 1645 cm^{-1}; uv spectrum, λ_{max} 231 mμ (ε 14,200), 261 (5240), and 305 (1180); nmr spectrum, CH_3 at δ 2.09 (singlet, 3), aromatic CH at 7.44 (doublet, 1, J = 8 Hz), at 8.32 (doublet of doublets, 1, J_1 = 8, J_2 = 2.5 Hz), and at 8.68 (doublet, 1, J = 2.5 Hz), acidic H at 7.29 (singlet, 1).

Anal. Calcd for $C_{13}H_{13}NO_4$: C, 63.15; H, 5.30; N, 5.66. Found: C, 63.11; H, 5.64; N, 5.83.

1-Acetyl-2,3,4,5-tetrahydro-1H-1-benzazepin-5-ol-7-carboxylic Acid (17).—A solution of 2 g of **16** in 100 ml of 95% ethanol was shaken under 50 psig of hydrogen in the presence of 200 mg of platinum oxide catalyst for 1 hr. The theoretical amount of hydrogen was absorbed in the first 25 min. The catalyst was removed by filtration and the filtrate was evaporated *in vacuo* to a white froth which crystallized in ether. Recrystallization from acetonitrile gave 1.50 g (75%) of pure **17**: mp 184.5–185.5°; ir spectrum (Nujol), OH at 3440, acid C=O at 1698, amide C=O at 1628 cm^{-1}; uv spectrum, λ_{max} 244 mμ (ε 9880); nmr spectrum (DMSO-d_6), CH_3 at δ 1.92 (singlet, 3), aromatic CH at 7.26 (doublet, 1, J = 7 Hz), at 7.98 (doublet of doublets, 1, J_1 = 7, J_2 = 2 Hz), and at 8.46 (doublet, 1, J = 2 Hz).

Anal. Calcd for $C_{13}H_{15}NO_4$: C, 62.60; H, 6.08; N, 5.62. Found: C, 62.68; H, 6.03; N, 5.11.

Hydrogenolysis of 16.—A mixture of 4.0 g of **16**, 1.0 g of 5% palladium on carbon, 6 drops of 70% perchloric acid, and 100 ml of glacial acetic acid was shaken under 50 psig of hydrogen for 91 hr. The catalyst was removed by filtration and the mineral acid was neutralized by addition of an aqueous solution of sodium acetate. Evaporative distillation of the solvent *in vacuo* gave a viscous white oil which was stirred with water and evaporated again to remove the last traces of acetic acid. The residue was dissolved in water and the solution was saturated with sodium chloride and extracted with methylene chloride. The extract was washed with saturated aqueous sodium chloride, dried with sodium sulfate, and evaporated to a colorless syrup which crystallized in ether. Filtration and washing gave crude **12**, mp 187–192°.

2,3,4,5-Tetrahydro-1H-1-benzazepin-5-one-7-carboxylic Acid (18).—A solution of 500 mg of **16** and 300 mg of sodium hydroxide in 10 ml of water was refluxed for 21 hr, cooled, filtered through a pad of Norit, and treated with Dry Ice to neutralize excess base. The solution was then slowly acidified with 5% hydrochloric acid and chilled in an ice bath and the white precipitate was filtered and dried. Recrystallization from 95% ethanol with hot filtration through a pad of Norit gave 250 mg (61%) of pure **18**: mp 286–287.5° dec; ir spectrum (Nujol), NH at 3370, acid C=O at 1675, ketone C=O at 1650 cm^{-1}; uv spectrum, λ_{max} 242 mμ (ε 13,100), 288 (14,500), and 345 (287); nmr spectrum (DMSO-d_6), aromatic CH at δ 6.98 (doublet, 1, J = 9 Hz), at 7.77 (doublet of doublets, 1, J_1 = 9, J_2 = 2 Hz), and at 8.17 (doublet, 1, J = 2 Hz), exchangeable protons at 3.20 (multiplet, 1) and at 7.45 (singlet, 0.8).

Anal. Calcd for $C_{11}H_{11}NO_3$: C, 64.38; H, 5.40; N, 6.83. Found: C, 64.24; H, 5.51; N, 6.94.

1-Azatricyclo[6.3.1.0^{6,11}]dodecan-5-ol-12-one (19).—A solution of 880 mg of **18** in 100 ml of 95% ethanol was stirred in the presence of 1.5 g of 5% ruthenium on carbon in a stainless steel autoclave at 160° under 2000 psig of hydrogen for 41 hr. The catalyst was removed by filtration and the ethanol was distilled *in vacuo* to leave a clear, colorless oil which was boiled in benzene, filtered through a pad of Norit, and evaporated to give 680 mg (81%) of crude **19**. Short-path distillation at 0.05 mm in a bulb-to-bulb distilling tube gave pure **19** (bath temperature 130°): ir spectrum (film), OH at 3390, C=O at 1648 cm^{-1}; nmr spectrum, OH at δ 2.69 (singlet, 1) exchangeable with deuterium oxide, H_2O at 5.33 (singlet, 0.2) not exchangeable with deuterium oxide, aliphatic region complex. Thin layer chromatography on silica gel (ethyl acetate) exhibited two overlapping spots of approximately equal intensity after detection with iodine vapor. This material was used directly for the preparation of **22** by the following reaction sequence.

1-Azatricyclo[6.3.1.0^{6,11}]dodecane-5,12-dione (20).—To a cold (0–5°), stirred solution of 345 mg of crude **19** in 25 ml of acetone was slowly added 1 ml of 4 *M* chromic acid solution (prepared from 100 g of chromium trioxide and 90 ml of sulfuric acid in 400 ml of water). After stirring in the cold for 45 min, the reaction mixture was permitted to warm to room temperature. After 15 min at room temperature, the excess chromic acid was destroyed with 6 drops of isopropyl alcohol. Water was added

to dissolve the green precipitate and the acetone was removed by evaporative distillation *in vacuo* in a 35° bath. The aqueous solution was washed with ether and saturated with sodium chloride and extracted repeatedly with methylene chloride. The extract was washed with saturated brine, dried with sodium sulfate, filtered through a pad of Norit, and evaporated to 190 mg (56%) of crude **20** as a colorless oil: ir spectrum (film), ketone C=O at 1698, lactam C=O at 1660 cm^{-1}.

***dl*-Deethylibogamine Lactam (21).**—A solution of 60 mg of **20**, 50 mg of phenylhydrazine hydrochloride, and 30 mg of anhydrous sodium acetate in 10 ml of water and 1 ml of 95% ethanol was stirred for 1 hr, chilled in an ice bath, and filtered to give 40 mg (46%) of the crude phenylhydrazene, **21**, as a tan powder: mp 141–182°; ir spectrum (Nujol), NH at 3285, C=O at 1658, C=N at 1650 cm^{-1}; uv spectrum, λ_{max} 273 mμ (ε 8200).

A mixture of 20 mg of **21** and 690 mg of polyphosphoric acid was stirred under nitrogen and heated to 135–140° for 30 min. The mixture was cooled and 10 g of ice was added. Filtration gave a gray powder which was recrystallized from ethanol with hot filtration through a pad of Norit to give 15 mg (80%) of **21**: mp 311–315° dec (lit.[4a] mp 313–315°); the ir spectrum of this material was identical with that of an authentic sample;[14] infrared spectrum, NH at 3180, C=O at 1645 cm^{-1} (Nujol); uv spectrum, λ_{max} 225 mμ (ε 31,100), 275 (6610, sh), 283 (7320), 291 (6370) [lit.[4a] λ_{max} 225 mμ (ε 31,600), 283 (6460), 291 (6030)]. Ibogamine lactam[20] had λ_{max} 223 mμ (ε 34,500), 283 (7600), and 291 (6650).

(20) M. F. Bartlett, D. F. Dickel, and W. I. Taylor, *J. Amer. Chem. Soc.*, **80**, 126 (1958).

9-Acetyl-2,3,4,5-tetrahydro-1H-1-benzazepine-7-carboxylic Acid (23).—A solution of 2.13 g of **12** in 600 ml of *t*-butyl alcohol in a quartz reaction vessel was photolyzed under nitrogen with 2537-Å light for 66 hr at 50°. After evaporation of the alcohol, the residual yellow froth was dissolved in ether and filtered to remove 240 mg of high melting point powder. Evaporation of the ether gave a froth which was dissolved in 5 ml of acetonitrile and allowed to stand in the cold. Filtration gave 340 mg of crude **23**, mp 198–206°. Successive crops of the crude product were obtained from acetonitrile and from acetone to give a total of 710 mg (33%). Recrystallization from acetone gave pure **23** as yellow crystals: mp 224–225.5°; ir spectrum (Nujol), NH at 3270, acid OH at 2600, acid C=O at 1670, ketone C=O at 1632 cm^{-1}; uv spectrum, λ_{max} 230 mμ (ε 15,500, sh), 245 (21,150), 302 (15,130), 373 (4900); nmr spectrum, CH_3 at δ 2.63 (singlet, 3), aromatic CH at 7.75 (doublet, 1, J = 2 Hz) and at 8.43 (doublet, 1, J = 2 Hz), COOH at 9.43 (singlet, 1), NH at 2.95 (multiplet, 1). The last two protons were exchangeable with deuterium oxide.

Anal. Calcd for $C_{13}H_{15}NO_3$: C, 66.94; H, 6.48; N, 6.00. Found: C, 66.78; H, 6.77; N, 6.09.

Registry No.—**1b**, 19034-53-8; **4**, 19029-01-7; **5**, 19029-02-8; **7**, 19029-03-9; **8**, 19029-04-0; **9**, 19029-05-1; **10**, 19029-06-2; **11**, 19029-07-3; **12**, 19029-08-4; **13**, 19029-09-5; **14**, 19034-54-9; **16**, 19029-10-8; **17**, 19029-11-9; **18**, 19029-12-0; **21**, 19034-55-0; **22**, 19034-56-1; **23**, 19029-13-1.

Catalytic Hydrogenation of α,β-Unsaturated Ketones. IV.[1,2] The Effect of the Medium on Product Stereochemistry

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The hydrogenation of $\Delta^{1,9}$-octalone-2 has been run in a number of different solvents and under a variety of conditions. In neutral medium it has been found that the product stereochemistry was dependent not only on the polarity but also on the type of solvent used. In aprotic media it is proposed that a nonpolar solvent promotes a 1,2-adsorption process and a polar solvent favors one occurring through 1,4 adsorption. In hydroxylic media hydrogen bonding to the carbonyl group or hemiketal formation is thought to occur in solvents of high polarity thus forcing the reaction to take place by way of 1,2 adsorption while in less polar hydroxylic solvents such solvation is not important and the reaction proceeds through a 1,4-adsorption process. The product stereochemistry not only depends on the nature of the adsorption process but also on the "hydrogen availability" to the catalyst. In acidic media product stereochemistry is dependent on the strength of the acid, the mode of adsorption of the substrate and the "hydrogen availability" to the catalyst. These data are shown to be compatible with a protonation–hydride ion transfer mechanism or with a process involving hydrogenation of the enol but not with one in which the acid serves only to increase the polarity of the solvent. In basic solutions the product stereochemistry obtained was markedly dependent on the amount of base present, particularly in the very dilute region. These results are interpreted as indicating that the reaction proceeds by way of kinetically and thermodynamically controlled enolate ion formation. It is proposed that these enolates are very strongly adsorbed on the catalyst surface and that the product stereochemistry can best be explained by way of a hydride ion transfer from the catalyst followed by protonation of the adsorbed species from the solution.

While the mechanistic aspects of the hydrogenation of simple olefins has been the subject of extensive investigation for the past 30 years,[4] little work has been done on the mechanism of the hydrogenation of polarized double bonds such as carbonyl groups and the double bonds of α,β-unsaturated ketones. Those mechanistic proposals which have been made concerning these latter hydrogenations have been essentially attempts to rationalize the marked effect which the reaction medium has on the stereochemistry of the products obtained.

For instance, Brewster[5] has proposed a mechanism for the hydrogenation of substituted cyclohexanones to account for the influence which the reaction medium has on the product stereochemistry. In acid, initial protonation of the carbonyl oxygen to give a carbonium ion was proposed. This ion was then adsorbed on the

(1) Paper III in this series: R. L. Augustine, *J. Org. Chem.*, **28**, 152 (1963).

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(3) Taken in part from the Doctoral Dissertations submitted by D.C.M. and R.E.F. (1966) and the Master's Thesis submitted by C.S.S. (1963) to Seton Hall University in partial fulfillment of the requirements for the respective degrees.

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