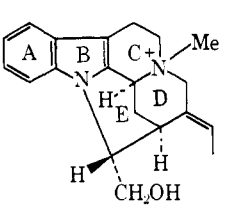
Calabash Curare Alkaloids. A Synthetic Study in the *C*-Fluorocurine–Mavacurine Series[1,2]

Dennis D. O'Rell,[3] Fred G. H. Lee, and V. Boekelheide*

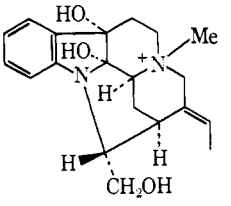
Contribution from the Department of Chemistry, University of Oregon, Eugene, Oregon 97403. *Received September 7, 1971*

Abstract: The syntheses of racemic 19,20-dihydronorfluorocurine (**22**) and racemic 19,20-dihydronormavacurine (**6**) have been accomplished starting with 3α-ethyl-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-*a*]quinolizin-2-one (**9**). The two key steps in the syntheses were (1) the Wittig reaction of **9** leading to the aldehyde **21** with inversion of configuration of the 3-ethyl group, and (2) the base-catalyzed cyclization of the epoxide **5** in the presence of oxygen to give racemic 19,20-dihydronorfluorocurine (**22**). In the absence of oxygen the base-catalyzed cyclization of **5** gave the apogeissoschizine derivative **7**. A model compound **29**, containing the same pentacyclic nucleus as *C*-mavacurine, has been converted to its corresponding Emde product **30**, and this Emde product has been shown to exhibit the same novel, transannular interactions on protonation and alkylation as had been discovered earlier for the Emde product **1** in the natural series. The oxidation of indole derivatives using nickel peroxide has been found in the case of **5** and **13** to give the corresponding hydroxyindolenine derivatives **25** and **27**, respectively. However, the reaction of tetrahydrocarbazole with nickel peroxide simply yields the corresponding dimer **35**.

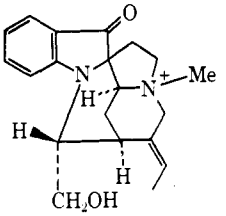
Crude calabash curare contains a great many alkaloids. Of these the physiologically potent C_{40} diquaternary alkaloids and their closely related derivatives have been thoroughly investigated chemically.[4] However, among the other alkaloids of calabash curare there are still many intriguing problems. Of especial interest to us has been the C_{20} monoquaternary series including *C*-fluorocurine,[5] *C*-mavacurine,[6] and *C*-alkaloid Y.[7] These three alkaloids, which have been interrelated to each other,[8,9] have also been interrelated to pleiocarpamine,[10] an alkaloid previously isolated from two apocyanaceae species, *Pleiocarpa mutica* Benth.[11] and *Hunteria eburnea* Pichon.[12] On the basis of their spectral properties and chemical behavior, structures have been assigned to each of these alkaloids as shown.



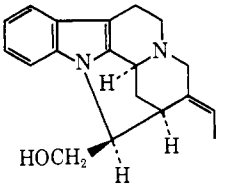
C-mavacurine



C-alkaloid Y



C-fluorocurine



pleiocarpaminol

These structures are, of course, closely related to those of corynantheine and the other members of the yohimbine series but with the notable difference that the 1 and 16 positions are joined giving an additional fused ring, ring E. Examination of molecular models shows that the effect of forming ring E is to give these molecules a pronounced hollow-sphere sort of geometry. The chemical properties of these molecules, particularly mavacurine and pleiocarpamine, are cited as supporting this interpretation. Thus, groups inside the sphere show the effects of strong transannular interactions. For example, the nmr signal for the β proton at C-21 is shifted upfield from that of tetramethylsilane due to the close proximity of the opposite indole nucleus with its accompanying deshielding ring current effect.[10]

Similarly, attack by chemical reagents occurs on the outside of the sphere giving derivatives in which the orientation of the substituents introduced is exclusively α. This is true for both hydrogenation as well as oxidation of the indole double bond.[9,13] However, the most remarkable behavior in this regard is found in the Emde derivative (**1**) of mavacurine. Presumably, the molecular structure of **1** is so rigid and the transannular interaction between N-(b) and the indole π cloud is so strong that normal protonation and alkylation of N-(b) do not occur. Instead, protonation and alkylation result in attack at C-3 leading to the quaternary structure shown by **2**. The action of acid is reversible but that of methylation is not. Further, treatment of **2** (R = Me) with base then yields the α-methyleneindole **3**, which again exhibits a strong transannular interaction, undergoing another methylation to give **4**.

(1) We thank the Public Health Service, National Heart Institute Grant 5-ROI-HE 09813, for financial support of this investigation.

(2) For the preceding communication in this series, see M. Grdinic, D. A. Nelson, and V. Boekelheide, *J. Amer. Chem. Soc.*, **86**, 3357 (1964).

(3) Abstracted from the doctoral dissertation of D. D. O'Rell, University of Oregon, 1970.

(4) For reviews, see K. Bernauer, *Fortschr. Chem. Org. Naturst.*, 17, 183 (1959); A. R. Battersby and H. F. Hodson, *Quart. Rev., Chem. Soc.*, **14**, 77 (1960).

(5) H. Schmid and P. Karrer, *Helv. Chim. Acta*, 30, 2081 (1947).

(6) Th. Wieland and H. Merz, *Chem. Ber.*, **85**, 731 (1952).

(7) H. Asmis, E. Bächli, E. Giesbrecht, J. Kebrle, H. Schmid, and P. Karrer, *Helv. Chim. Acta*, 37, 1968 (1954).

(8) H. Bickel, E. Giesbrecht, J. Kebrle, H. Schmid, and P. Karrer, *ibid.*, 37, 553 (1954).

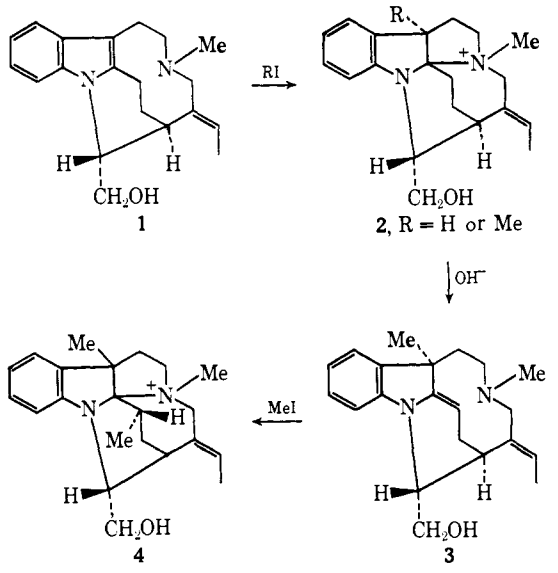
(9) H. Fritz, Th. Wieland, and E. Besch, *Justus Liebigs Ann. Chem.*, **611**, 268 (1957).

(10) M. Hesse, W. v. Philipsborn, D. Schumann, G. Spiteller, M. Spiteller-Friedmann, W. I. Taylor, H. Schmid, and P. Karrer, *Helv. Chim. Acta*, **47**, 878 (1964).

(11) W. G. Kump and H. Schmid, *ibid.*, **44**, 1503 (1961).

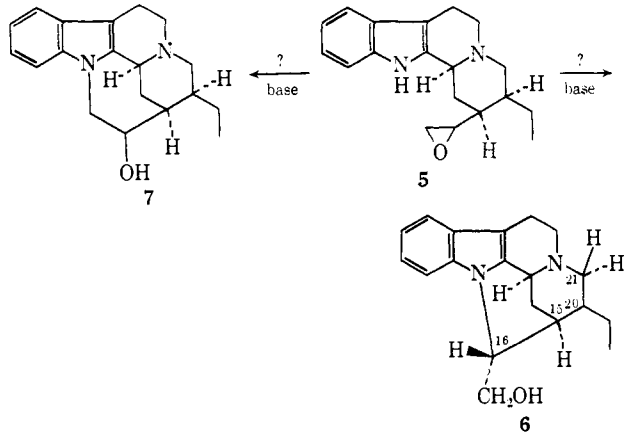
(12) M. F. Bartlett, R. Sklar, A. F. Smith, and W. I. Taylor, *J. Org. Chem.*, **28**, 2197 (1963).

(13) H. Bickel, H. Schmid, and P. Karrer, *Helv. Chim. Acta*, **38**, 649 (1955).



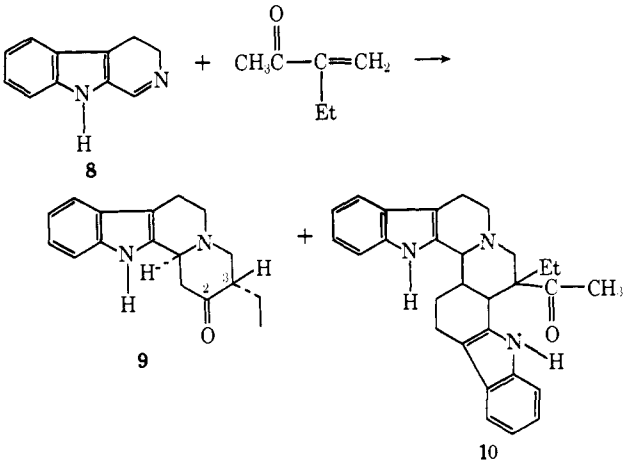
Although the chemical and spectroscopic evidence provided in support of these structural assignments is quite convincing,[10] the structures are sufficiently interesting and the transannular interactions sufficiently remarkable that it seemed desirable to undertake a synthetic study designed to provide further insight and possible confirmation of these structural deductions.

Of the possible synthetic objectives 19,20-dihydronormavacurine (**6**) was attractive from several points of view, but in particular it attracted us because we wished to test the concept of a base-catalyzed attack on an epoxide such as **5** as a one-step transformation for providing ring E with the hydroxymethyl group in place. It was clear, of course, that such a reaction might alternatively lead to a seven-membered ring E bearing a secondary hydroxyl, as in **7**. However, since structure



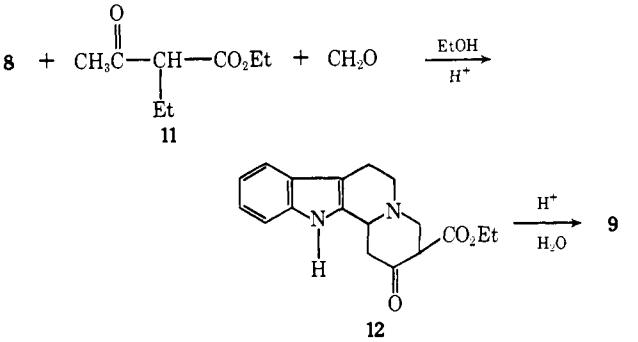
7 had been postulated earlier as a possible structure for 19,20-dihydronormavacurine,[13] such an outcome would also be of interest.[14]

For the preparation of **5**, 3,4-dihydro-β-carboline (**8**) was desired as starting material. Its standard preparation is by a Bischler–Napieralski cyclization of *N*-formyltryptamine. We found, as has also been noted recently by Whittaker,[15] that the reaction is much cleaner and proceeds in much higher yield when mild conditions are used rather than the standard vigorous conditions.[16] The conversion of **8** to the tetracyclic ketone **9** had been reported by Szántay and Töke to occur on reaction with the appropriate methyl vinyl ketone or its equivalent in what seemed a very convenient synthesis.[17] However, in our hands, this reaction gave both the desired ketone **9** plus the corresponding 2:1 adduct of structure **10**. The assignment of structure **10** is based on mass spectral and nmr evidence. After the completion of our studies Szántay, *et al.*, reported the same observation.[18] It should be noted that ketones **9** and **10** have similar melting points,



show no mixture melting point depression, and are difficult to separate.

In view of this, we looked to other possible routes for a synthesis of the tetracyclic ketone **9**. Previously, Tretter had reported that the reaction of 3,4-dihydroisoquinolines with acetoacetamides and formaldehyde gave the analogous benzoquinolizones in high yield.[19] Although it seemed likely that an α-alkyl substituent on the β-keto amide or β-keto ester would prevent this type of cyclization, the experiment was tried anyway. To our surprise and gratification, the reaction of 3,4-dihydro-β-carboline (**8**) with ethyl α-ethylacetoacetate (**11**) and formaldehyde proceeded smoothly in 60% yield to give the desired tetracyclic β-keto ester **12**. The spectral properties of **12** are fully in accord with its structural assignment and, on acid hydrolysis, **12** was



(14) It should be noted that a synthesis directed toward a molecule having the carbon skeleton of 7 has been reported by O. N. Tolkacher, V. G. Korobko, T. A. Shapiro, and N. A. Preobrazhenskii, *Khim. Geterotsikl. Soedin.*, 313 (1967); *Chem. Abstr.*, 67, 90974*f* (1967).

(15) N. Whittaker, *J. Chem. Soc. C*, 85 (1969).

(16) (a) E. Späth and E. Lederer, *Chem. Ber.*, **63**, 2102 (1930); (b) C. Schöpf and H. Steuer, *Justus Liebigs Ann. Chem.*, **558**, 124 (1947); (c) M. Onada and M. Sasamoto, *Chem. Pharm. Bull.*, **5**, 305 (1957); and (d) R. Gupta and J. Spencer, *Can. J. Chem.*, 40, 2049 (1962).

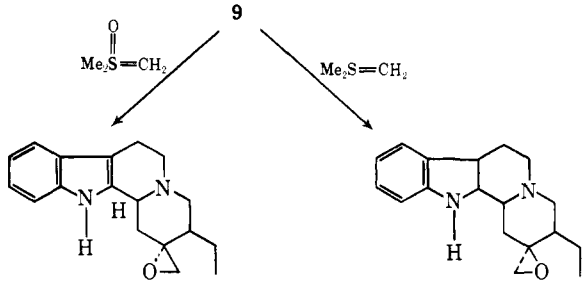
(17) Cs. Szántay and L. Töke, *Tetrahedron Lett.*, 251 (1963).

(18) Cs. Szántay, L. Töke, K. Honty, and Gy. Klaus, *J. Org. Chem.*, **32**, 423 (1967).

(19) J. Tretter, Belgium Patent 618,741 (Dec 10, 1962); *Chem. Abstr.*, **59**, 10007*e* (1963).

converted readily in 83% yield to **9**. Although the mechanism for the formation of **12** has not been elucidated, this route is clearly the one of choice for preparing **9**.

The next logical step in the synthesis was the conversion of **9** to the corresponding aldehyde **21**. As Corey and Chaykovsky have shown,[20] the reaction of cyclohexanone derivatives with dimethylsulfonium methylide gives predominantly a spiro epoxide with an axial carbon–carbon bond, whereas the similar reaction with dimethyloxosulfonium methylide gives predominantly a spiro epoxide with an equatorial carbon–carbon bond. In agreement with their findings, the reaction of **9** with dimethyloxosulfonium methylide gave in 88% yield an epoxide whose stereochemistry, as will be shown later, must be that given by **13**. Likewise, the reaction of **9** with dimethylsulfonium methylide gave in 88% yield an epimeric epoxide whose stereochemistry, by inference, is therefore that given by **14**. Unfortunately, attempts to effect an acid-

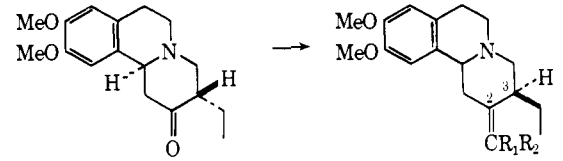


13 14

catalyzed rearrangement of either epoxide **13** or **14** to the corresponding aldehyde **21** (or its stereoisomer) were without success. Intractable tars were formed in each instance.

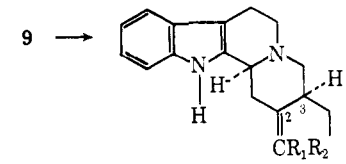
In seeking alternate methods of converting **9** to the analogous aldehyde **21**, we were very much concerned with choosing a method that would give not only the correct stereochemistry at C-15 but also at C-20, as shown by structure **6**. The naturally derived 19,20-dihydronormavacurine (**6**) has been obtained by catalytic hydrogenation of norfluorocurine followed by the usual pseudoindoxyl–indole conversion into the mavacurine series. Since the adsorption of norfluorocurine on a platinum catalyst should occur preferentially on the outside of the somewhat spherically shaped molecule, the addition of hydrogen to the C-19,20 double bond should occur with the introduction of hydrogens in the α configuration and so would result in the stereochemistry for 19,20-dihydronormavacurine shown by **6**. On the other hand, the ketone **9** can equilibrate through enolization and so the stereoisomer we have isolated should have the thermodynamically more stable configuration in which the hydrogen at C-3 is axial and the ethyl group is equatorial, as given by structure **9**. Thus, the conversion of ketone **9** to the desired aldehyde **21** requires an inversion of configuration at C-3 as well as the introduction of an equatorial aldehyde group at C-2.

In 1962 Brossi and Schnider in their studies on emetine observed that the benzoquinolizone **15** underwent a base-catalyzed condensation with methyl cyanoacetate to give the corresponding ethylidine derivative **16** in which the configuration at C-3 had inverted.[21] That this behavior is also common to the indoloquinolizone series has recently been shown by Szántay and Barczai-Beke, who proved that the condensation of **9** with methyl cyanoacetate caused inversion of configuration at C-3 and yielded **18**.[22] Furthermore, Open-



15

16, $R_1 = CO_2Me$; $R_2 = CN$
17, $R_1 = CO_2Me$; $R_2 = H$



18, $R_1 = CO_2Me$; $R_2 = CN$

shaw and Whittaker have studied the reaction of **15** with Wittig reagents and found that in the presence of base the ethylidine derivative **17** having an inverted configuration at C-3 is formed, whereas in the absence of base the normal ethylidine having the ethyl group α results.[23]

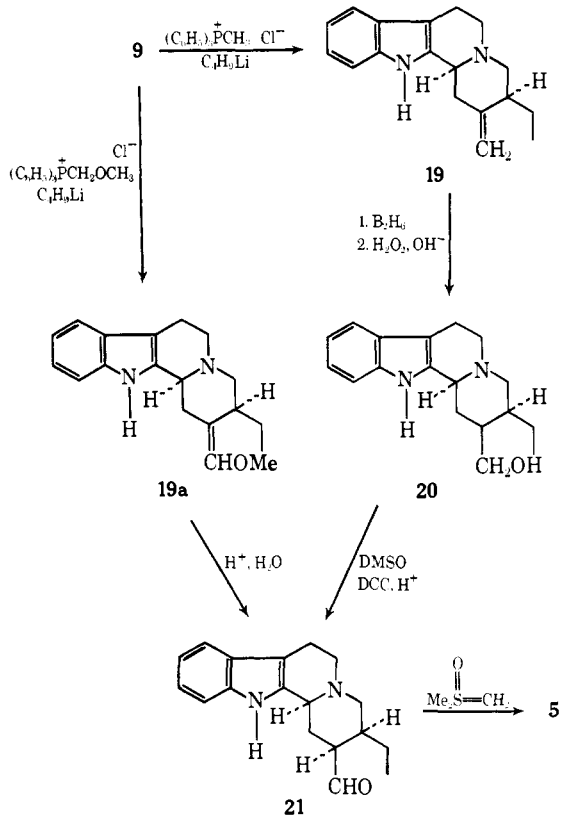
In view of this weight of evidence that base-catalyzed condensations, especially Wittig reactions, would effect inversion at C-3, we undertook the synthesis of **21** from **9** utilizing a Wittig reagent. The reaction of **9** with methylenetriphenylphosphorane proceeded in 80% yield to give **19** as white crystals. When **19** was treated with diborane followed by oxidation with alkaline hydrogen peroxide, the corresponding alcohol **20** resulted in 70% yield. Various reagents were investigated for the oxidation of **20** and the procedure of Albright and Goldman using *N,N*-dicyclohexylcarbodiimide proved to be the best,[24] although the yield of aldehyde **21** was only 35%. An alternative and improved procedure was then realized by condensing **9** with methoxymethylenetriphenylphosphorane to give **19a** in 66% yield which, on acid hydrolysis, gave **21**, identical in all respects with the sample prepared before.

Treatment of **21** with dimethyloxosulfonium methylide then gave **5**, in 88% yield. Presumably a mixture of two racemates should be formed in this reaction. However, thin layer chromatography indicated that one isomer predominated, and fractional crystallization gave a product of relatively sharp melting point.

When **5** was treated with sodium hydride in dimethyl sulfoxide under a nitrogen atmosphere, a new crystalline product, mp 223–224°, was formed in 62% yield. That this product did not have the desired cage structure of **6** could readily be seen from its ultraviolet absorption spectrum, which showed a fairly normal indole spectrum with maxima at 226 (ϵ 30,170), 282 (6240), and 289 nm (5060). By contrast caged structures such as **6**, having the chromophore of the norma-

(20) E. J. Corey and M. Chaykovsky, *J. Amer. Chem. Soc.*, 87, 1353 (1965).

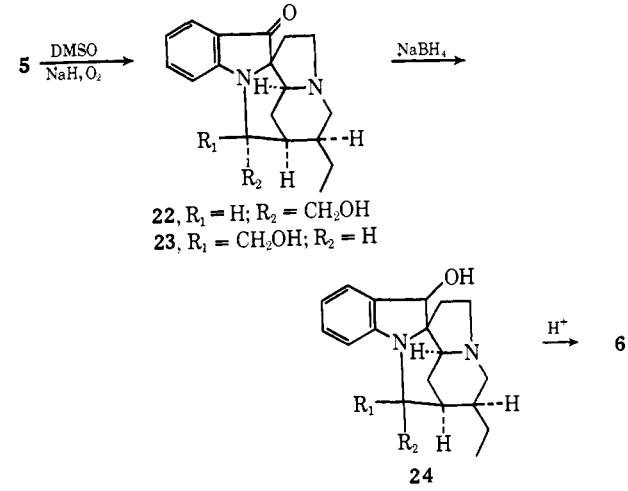
(21) A. Brossi and O. Schnider, *Helv. Chim. Acta*, **45**, 1899 (1962).
(22) Cs. Szántay and M. Barczai-Beke, *Chem. Ber.*, 102, 3963 (1969).
(23) H. T. Openshaw and N. Whittaker, *J. Chem. Soc.*, 1461 (1963).
(24) J. Albright and L. Goldman, *J. Amer. Chem. Soc.*, 87, 4214 (1965).



vacurine–pleiocarpaminol series, show two absorption bands, one at 232–234 nm and the other at 287–289 nm. On the other hand, the more normal indole ultraviolet spectrum of the product is in accord with structure **7** where the new ring being formed is seven-membered and so involves less strain than in **6**. Finally, the nmr signal for the hydroxyl proton appears as a doublet at τ −0.37 as would be expected for the secondary hydroxyl of **7** but is not in accord with structure **6**. Thus, we assign structure **7** to this product, an interesting addition to the family of derivatives of apogeissoschizine.[25]

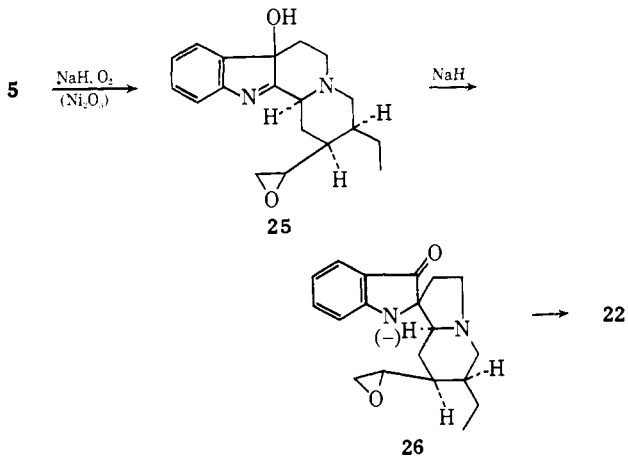
However, when **5** was treated with sodium hydride in dimethyl sulfoxide under an oxygen atmosphere instead of nitrogen, the reaction took a completely different course, giving a yellow, fluorescent, crystalline product in 62% yield. This product showed carbonyl absorption at 1686 cm^{-1} and a typical pseudoindoxyl ultraviolet absorption spectrum with maxima at 239 nm (ϵ 38,000), 260 (8560), and 405 (3430). These spectral properties are in very good agreement with those given for 19,20-dihydronorfluorocurine (**22**). Since our product had the correct elemental analysis and molecular weight and its nmr spectrum was in accord, it was apparent that we had in fact obtained either racemic 19,20-dihydronorfluorocurine (**22**) or its previously unknown epimer **23**.

Lacking natural material for comparison, we sought additional chemical information for aid in deciding between **22** and **23**. The conversion of 19,20-dihydronorfluorocurine (**22**) to 19,20-dihydronormavacurine (**6**) has been described, and the spectral properties of 19,20-dihydronormavacurine are given in great detail.[10] Therefore, we subjected our product to a similar sequence: reduction with sodium borohydride to give **24**



followed by warming with acid. Isolation of the product gave an oil whose ultraviolet spectrum showed maxima at 233 and 288 nm, as would be expected for **6**.[10] Furthermore, its nmr spectrum was in close correspondence with that recorded for 19,20-dihydronormavacurine, including the signal at τ 10.27 for the β-H at C-21.[10] Finally, the mass spectrum of this product showed the same parent ion and the same nine fragmentation peaks as recorded for 19,20-dihydronormavacurine, with even the relative intensities of the fragmentation peaks being closely similar (see Experimental Section). The coincidences between the spectral properties of our product and those recorded for 19,20-dihydronormavacurine are so strong that we conclude that our pseudoindoxyl derivative is indeed racemic 19,20-dihydronorfluorocurine (**22**) and its transformation product is racemic 19,20-dihydronormavacurine (**6**). However, the possibility of some contamination of our products by the corresponding epimers cannot be ruled out.

The one-step conversion of **5** to **22** is unusual and, because of its possible generality, deserves further comment. The air oxidation of indoles to give hydroxyindolenines is a well-known conversion.[26] We propose that the first step in our example is the reaction of oxygen with the indole anion of **5** to give the hydroxyindolenine **25**. Further, hydroxyindolenines are known to undergo base-catalyzed rearrangement to the corresponding pseudoindoxyl, and we would propose the rearrangement of **25** to **26** as being the next step.



(25) M.-M. Janot, *Tetrahedron*, **14**, 113 (1961).

(26) B. Witkop and J. B. Patrick, *J. Amer. Chem. Soc.*, 73, 2188 (1951).

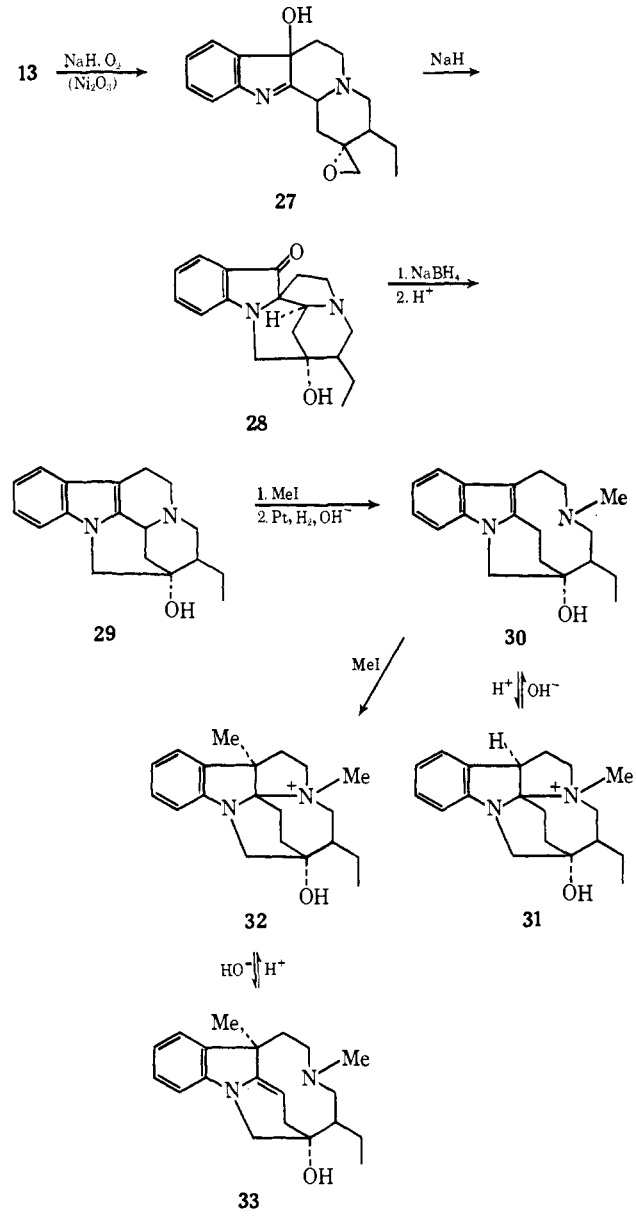
At this stage attack of the pseudoindoxyl nitrogen anion on the epoxide would be expected to occur to give **22**. The reason why the indole nitrogen of **5** attacks the epoxide to form a seven-membered ring whereas the pseudoindoxyl nitrogen attacks the epoxide to form a six-membered ring is readily apparent from examination of molecular models.

As one test of this hypothesis we prepared the pseudoindoxyl **25** separately, and then subjected it to reaction with sodium hydride in dimethylformamide. Again, as expected, the product was **22**. Because of the presence of the epoxide function, we chose not to use the standard platinum catalyst plus oxygen for preparing **25** from **5**.[10] Instead, we elected to try nickel peroxide, a convenient reagent introduced by Nakagawa, *et al.*, for oxidation of alcohols.[27] The conversion of **5** to **25** using nickel peroxide proceeded smoothly, although in relatively poor yield.

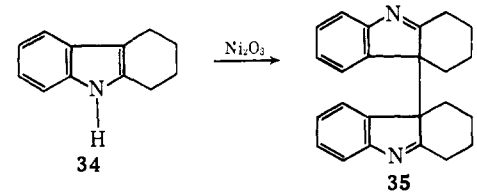
Having available then a method for preparing the pentacyclic nucleus of the mavacurine system, we wished to investigate the corresponding Emde products and the unusual transannular interactions reported for them. For this purpose we selected a derivate more readily available in quantity than **6**. The epoxide **13** was allowed to react with sodium hydride and oxygen in dimethyl sulfoxide as solvent, giving in 68% yield the corresponding pseudoindoxyl **28**. As before, **13** could be converted stepwise to the hydroxyindolenine **27** which, with sodium hydride in DMF, again yielded the pseudoindoxyl **28**. However, the former procedure is preferable both from the point of view of convenience and yield. Reduction of **28** with sodium borohydride followed by an acid-catalyzed Wagner–Meerwein rearrangement led in 89% yield to the corresponding crystalline, normavacurine derivative **29**.

Since ring closure of **27** to form the pentacyclic nucleus **28** can only occur if the carbon–carbon bond of the epoxide has the β configuration, the formation of **28** establishes in turn the configurations assigned to the two epoxides **13** and **14**. It should be noted that the spectral properties of **29** are very similar to those of 19,20-dihydronormavacurine, as would be expected. The ultraviolet absorption spectrum of **29** shows maxima at 232 nm (ϵ 29,700) and 287 (7120), and the nmr signal for the β proton at C-21 appears as a quartet centered at τ 10.07.

Treatment of **29** with methyl iodide followed by catalytic hydrogenation over platinum in the presence of base led smoothly to the Emde product **30**. Again, in analogy with the Emde product from *C*-mavacurine, the Emde product **30** on protonation or methylation showed a change in its ultraviolet spectrum indicating the transformation of the indole chromophore to that of an indoline. In the case of protonation this is a reversible reaction and is best represented by the equilibrium **30** $\rightleftharpoons$ **31**. The methylation product **32** is likewise formulated as the result of a transannular reaction. Although **32** does not revert to **30**, its ultraviolet spectrum is pH dependent, indicating an equilibrium between the indoline **32** and the α-methylene indole **33**. Thus, with our synthetic model **30**, we have confirmed the occurrence of the same type of transannular behavior postulated earlier for the Emde product derived from mavacurine.



One final point should be made regarding the use of nickel peroxide with indole derivatives. As described earlier, the reaction of nickel peroxide with **13** and with **5** gave the corresponding hydroxyindolenines. In attempting to explore the generality of this reaction, we examined the behavior of tetrahydrocarbazole (**34**) toward nickel peroxide. To our surprise the products in this case were the meso and racemic diastereoisomers of the tetrahydrocarbazole dimer **35**. This behavior



suggests that nickel peroxide oxidation may involve intermediate free radicals. Why, on the one hand, hydroxyindolenines are produced and, on the other hand, tetrahydrocarbazole dimerizes, is not clear. However, the yield of the dimers is good and this type

(27) K. Nakagawa, R. Konaka, and T. Nakata, *J. Org. Chem.*, 27, 1597 (1962).

of dimerization could be synthetically valuable, as, for example, in syntheses directed toward calycanthine derivatives.[28]

Experimental Section[29]

3,4-Dihydro-β-carboline (8). To a solution of 20.0 g of tryptamine in 200 ml of ethyl acetate was added 6.9 g of formic acid. The resulting solid was collected by filtration, washed with ethyl acetate, and air-dried to give 24.6 g (99%) of the formate salt of tryptamine as white crystals. These, on heating at 200° for 0.5 hr, gave *N*-formyltryptamine as a pale yellow oil. This was cooled to 0° and 100 ml of freshly distilled phosphoryl chloride was added. Solution was effected by careful warming but while maintaining the temperature of the reaction mixture below 40°. After the solution had stood at room temperature for 1.5 hr, it was concentrated under reduced pressure. The residue was extracted with four 250-ml portions of an aqueous 10% acetic acid solution, the combined extracts were made basic, and the product was extracted with dichloromethane. Concentration of the dichloromethane extract gave 19.4 g (95%) of solvated crystals, mp 93–97°.[15]

3-Carbethoxy-3-ethyl-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-*a*]quinolizin-2-one, 12. To a solution of 1.017 g of ethyl α-ethylacetoacetate and 600 mg of a 37% aqueous formaldehyde solution in a mixture of 0.5 ml of glacial acetic acid and 50 ml of ethanol there was added 1.015 g of 3,4-dihydro-β-carboline, and the resulting solution was boiled under reflux for 24 hr under a nitrogen atmosphere. After the mixture had cooled, it was made basic with dilute aqueous potassium hydroxide and extracted with four 50-ml portions of chloroform. The combined extracts were washed with water, dried, and concentrated. The residue was taken up in a 4:1 mixture of benzene–ether and chromatographed over silica gel. The residue from the main eluate fraction was recrystallized from an acetone–petroleum ether (bp 30–60°) mixture to yield 1.22 g (60%) of colorless crystals: mp 160–162°; ir (KBr) 3390 (NH), 1715 (C=O, ketone), and 1695 cm^{-1} (C=O, ester); nmr ($CDCl_3$) τ 1.54 (s, 1 H, NH), 2.40–3.00 (m, 4 H, ArH), 5.72 (q, 2 H, J = 7 Hz, OCH_2CH_3), 5.9–8.89 (m, 14 H), and 9.08 (t, 3, OCH_2CH_3); uv (EtOH) 225 nm (ε 37,100), 282 (7580), and 289.5 (6340); and mass spectrum, *m/e* (rel intensity) 340 (100), 339 (77), 311 (12), 297 (25), 267 (31), 237 (15), 184 (58), 170 (100), 169 (85), and 156 (89).

Anal. Calcd for $C_{20}H_{24}N_2O_3$: C, 70.57; H, 7.11; N, 8.23. Found: C, 70.69; H, 6.93; N, 8.40.

3α-Ethyl-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-*a*]quinolizin-2-one, 9. A solution of 500 mg of **12** in a mixture of 10 ml of ethanol and 50 ml of an aqueous 15% sulfuric acid solution was boiled under reflux for 12 hr under a nitrogen atmosphere. The solution was then cooled, made basic, and extracted with chloroform. The chloroform extracts were washed with water, dried, and concentrated. The resulting residue was taken up in chloroform and chromatographed over alumina (Woelm, basic, activity III). From the main eluate fraction there was isolated 326 mg (83%) of colorless crystals: mp 208–209°; ir (KBr) 3356 (NH) and 1701 cm^{-1} (C=O); nmr ($CDCl_3$) τ 1.66 (s, 1 H, NH), 2.50–3.20 (m, 4 H, ArH), and 6.20–9.20 (m, 15 H); and uv (EtOH) 225 nm (ε 39,000), 282 (8150), and 289.5 (6740). This sample was identical in all respects with samples of **9** prepared as described by Szántay, *et al.*[18]

Anal. Calcd for $C_{17}H_{20}N_2O$: C, 76.09; H, 7.51; N, 10.44. Found: C, 76.00; H, 7.38; N, 10.43.

Spiro-2α-oxiranyl-3α-ethyl-1,2,3,4,6,7,12,12b-octahydroindolo-[2,3-*a*]quinolizine (13). Under a nitrogen atmosphere with careful exclusion of oxygen, 393 mg of a 55% sodium hydride suspension and 1.98 g of trimethylsulfoxonium iodide were dissolved in 25 ml of dry dimethyl sulfoxide. Hydrogen began evolving immediately and the solution was stirred for 45 min to complete the process. Then a solution of 2.00 g of **9** in 25 ml of dry dimethyl sulfoxide was added with stirring. The solution was stirred at room temperature for 45 min, heated at 60° for 45 min, and then poured into 200 ml of cold water. The solid, which separated, was extracted with four 50-ml portions of chloroform. After the chloroform extracts had been washed with water, they were dried and concentrated. The resulting solid was recrystallized from a chloroform–hexane mixture to give 1.87 g (88%) of colorless crystals: mp 197–202°; uv_{max} (EtOH) 225 nm (ε 36,800), 282 (7440), and 290 (6260); ir (KBr) 3378 cm^{-1} (NH), 855 and 825 (oxiranyl ring H's); nmr ($CDCl_3$) τ 1.92 (s, 1 H, NH), 2.35–3.15 (m, 4 H, ArH), and 6.60-9.30 (m, 17 H).

Anal. Calcd for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92. Found: C, 76.45; H, 7.65; N, 10.06.

Spiro-2β-oxiranyl-3α-ethyl-1,2,3,4,6,7,12,12b-octahydroindolo[2,-3-*a*]quinolizine (14). Under a nitrogen atmosphere and with careful exclusion of oxygen, 80.5 mg of a 56.8% sodium hydride suspension was dissolved in 10 ml of dimethyl sulfoxide and heated at 60° for 1 hr to generate the dimsyl anion. After the solution had been cooled to −10°, a solution of 388 mg of trimethylsulfonium iodide in 10 ml of dry dimethyl sulfoxide was added with stirring. Then, a solution of 500 mg of **9** in 20 ml of dry tetrahydrofuran was added with stirring. After 2 hr, the mixture was allowed to warm to room temperature over another 2-hr period and poured into 200 ml of cold water. The resulting mixture was extracted with chloroform and the chloroform extracts were washed with water, dried, and concentrated. The resulting solid was taken up in dichloromethane and chromatographed over alumina (Woehm, neutral, activity III). The solid from the main fraction of eluate was recrystallized from a chloroform–hexane mixture to give 463 mg (88%) of colorless crystals: mp 217–220°; uv_{max} (EtOH) 225 nm (ε 37,000), 282 (7500), and 290 (6340); ir (KBr) 3375 cm^{-1} (NH); nmr ($CDCl_3$) τ −0.3 (s, 1 H, NH), 2.40–3.15 (m, 4 H, ArH), and 6.20–9.50 (m, 17 H).

Anal. Calcd for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92. Found: C, 76.44; H, 7.87; N, 10.07.

2-Methylene-3β-ethyl-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-*a*]-quinolizine (19). To a solution of 1.32 g of methyltriphenylphosphonium bromide in 100 ml of dry tetrahydrofuran under a nitrogen atmosphere there was added dropwise with stirring 3.7 mmol of *n*-butyllithium in hexane. After the deep red mixture had been stirred for 30 min, a solution of 935 mg of **9** in 25 ml of dry tetrahydrofuran was added dropwise with stirring. The mixture was then allowed to stir at room temperature for an additional 8 hr before being concentrated under reduced pressure. The yellow residue was then taken up in a 1:1 mixture of dichloromethane–petroleum ether and chromatographed over alumina (Woelm, neutral, activity III). The residue from concentration of the main eluate fraction was recrystallized from aqueous methanol to give 770 mg (80%) of white crystals: mp 138–140°; uv_{max} (EtOH) 226 nm (ε 35,400), 282 (7450), and 290 (6320); ir (KBr) 3425 cm^{-1} (NH) and 1642 (C=CH_2); nmr ($CDCl_3$) τ 2.25 (s, 1 H, NH), 2.50–3.20 (m, 4 H, ArH), 5.17 (d, 2 H, =CH_2), and 6.60–9.10 (m, 15 H); mass spectrum (70 eV) *m/e* (rel intensity) 266 (75), 265 (93), 251 (30), 237 (82), 183 (50), 182 (95), and 169 (100).

Anal. Calcd for $C_{18}H_{22}N_2$: C, 81.16; H, 8.32; N, 10.52. Found: C, 80.97; H, 8.29; N, 10.63.

2-Hydroxymethyl-3β-ethyl-1,2,3,4,6,7,12,12b-octahydroindolo-[2,3-*a*]quinolizine (20). To a solution of 1.20 g of **19** and 93 mg of sodium borohydride in 50 ml of dry diglyme there was added dropwise with stirring 0.42 ml of freshly distilled boron trifluoride etherate. After the mixture had been stirred at room temperature for 2 hr, 5.0 ml of an aqueous 3 *N* solution of sodium hydroxide was added, followed by 5.0 ml of aqueous 30% hydrogen peroxide, and the resulting solution was stirred overnight. The reaction mixture was then poured into cold water and extracted with dichloromethane. The combined extracts were washed with water, dried, and concentrated. The resulting solid was recrystallized from chloroform to give 897 mg (70%) of colorless crystals: mp 211–214°; uv_{max} (EtOH) 225 nm (ε 36,000), 282 (7600), and 290 (6400); ir (KBr) 3438 cm^{-1} (NH), 3311 (OH), and 1000 (CH_2O); nmr (DMSO-d_6) τ −0.40 (s, 1 H, NH), 2.50–3.20 (m, 4 H, ArH), 6.20–9.35 (m, 19 H).

Anal. Calcd for $C_{18}H_{24}N_2O$: C, 76.02; H, 8.51; N, 9.85. Found: C, 75.94; H, 8.53; N, 9.96.

2-Methoxymethylene-3β-ethyl-1,2,3,4,6,7,12,12b-octahydroindolo-[2,3-*a*]quinolizine (19a). To a solution of 11.5 g of methoxymethyltriphenylphosphonium chloride in 125 ml of tetrahydrofuran, cooled in an ice bath, there was added with stirring 33.6 mmol of phenyllithium in a benzene–ether mixture. The deep red mixture was stirred for 20 min before adding dropwise a solution of 3.00 g of **9** in 25 ml of tetrahydrofuran. The mixture was then slowly al-

(28) E. S. Hall, F. McCapra, and A. I. Scott, *Tetrahedron*, **23**, 4131 (1967).

(29) Microanalyses were performed by A. Bernhardt and Micro-Tech Laboratories. Infrared spectra were measured with an Beckman IR-5a or IR-7 spectrometer; nmr spectra with Varian A-60 or HA-100 instruments using deuteriochloroform or hexadeuteriodimethyl sulfoxide as solvents and with tetramethylsilane as an internal standard; ultraviolet and visible spectra with a Cary Model 15; and mass spectra with a Consolidated Model 21-110 spectrometer. We thank the National Science Foundation for funds used toward the purchase of the Varian A-60 and C.E.C. 110-21b.

lowed to warm to room temperature with stirring and concentrated under reduced pressure. The residue was taken up in a 1:4 ethyl acetate–hexane mixture and chromatographed over silica gel. Concentration of the main eluate fraction gave a solid which was recrystallized from a chloroform–hexane mixture to yield 2.19 g (66%) of colorless crystals: mp 139–146°; uv_{max} (EtOH) 225 nm (ϵ 34,300), 282 (6750), and 290 (5720); ir (KBr) 3413 cm^{-1} (NH) and 1667 (>C=CHOMe); nmr ($CDCl_3$) τ 2.00 (s, 1 H, NH), 2.50–3.20 (m, 4 H, ArH), 4.18 (s, 1 H, >C=C*H*OMe), 6.40 (s, 3 H, OCH_3), and 6.60–9.20 (m, 15 H); mass spectrum (70 eV) *m/e* (rel intensity) 296 (41), 281 (48), 265 (17), 169 (22), 58 (100), and 43 (100).

Anal. Calcd for $C_{19}H_{24}N_2O$: C, 76.99; H, 8.16; N, 9.45. Found: C, 77.18; H, 7.82; N, 9.37.

2β-Formyl-3β-ethyl-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-*a*]quinolizine (21). A. Oxidation of 20. To a mixture of 200 mg of **20** and 500 mg of *N,N'*-dicyclohexylcarbodiimide in 5 ml of dimethyl sulfoxide there was added 2.4 ml of a 1 *M* solution of anhydrous phosphoric acid in dimethyl sulfoxide. After the solution had been stirred at room temperature for 12 hr, a solution of 100 mg of oxalic acid in 1.0 ml of water was added to destroy any remaining *N,N'*-dicyclohexylcarbodiimide. The solution was then poured into 50 ml of water containing 2.0 ml of 85% phosphoric acid and extracted with ether to remove *N,N'*-dicyclohexylurea. The aqueous solution was then made basic and extracted with dichloromethane. After concentration of the dichloromethane extracts, the residual solid was purified by thin layer chromatography over silic gel–PF_{254} using a 19:1 ethyl acetate–triethylamine mixture for elution. This gave 75 mg (35%) of colorless crystals: mp 169–171°; uv_{max} (EtOH) 225 nm (ϵ 36,200), 282 (7730), and 290 (6560); ir (KBr) 3472 cm^{-1} (NH) and 1720 (CH=O); nmr ($CDCl_3$) τ 0.37 (d, 1 H, CHC(=O)*H*), 2.50–3.20 (m, 4 H, ArH), 6.20–9.40 (m, 15 H); mass spectrum, *m/e* (rel intensity) 282 (100), 281 (85), 253 (75), 184 (95), and 170 (38).

Anal. Calcd for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92. Found: C, 76.76; H, 7.80; N, 10.08.

B. Hydrolysis of 19a. A solution of 2.19 g of **19a** in a mixture of 25 ml of 3 *N* aqueous hydrochloric acid and 25 ml of methanol was stirred at room temperature for 1 hr. The mixture was diluted with water, made basic, and extracted with chloroform. The combined chloroform extracts were washed with water, dried, and concentrated. The residual solid was chromatographed over silica gel using a 1:4 ether–hexane mixture for elution. Concentration of the main eluate fraction gave 910 mg (43%) of colorless crystals, mp 169–171°. These crystals showed no melting point depression with a sample of crystals as prepared in A and in all respects were identical with the crystals from A.

2β-Oxiranyl-3β-ethyl-1,2,3,4,6,7,12,12b-octahydroindolo[2,3-*a*]quinolizine (5). A solution of 154 mg of a 56.8% sodium hydride dispersion and 792 mg of trimethylsulfoxonium iodide in 25 ml of dry dimethyl sulfoxide was stirred for 30 min under a nitrogen atmosphere with rigid exclusion of oxygen. Then a solution of 1.00 g of **21** in 20 ml of dimethyl sulfoxide was added dropwise with stirring. After 15 min, the mixture was warmed to 60° and maintained at that temperature for 30 min. It was then cooled and poured into 150 ml of water. The white solid, which separated, was extracted with chloroform, washed with water, and dried, and the chloroform was removed under reduced pressure. The residue was taken up in dichloromethane and chromatographed over alumina (Woelm, neutral, activity III). The solid, obtained from the main fraction of eluate, was recrystallized from a chloroform–hexane mixture to give 905 mg (87%) of white crystals: mp 178–180°; uv_{max} (EtOH) 225 nm (ϵ 37,200), 282 (7590), and 289 (6400); ir (KBr) 3322 cm^{-1} (NH), 911 and 895 (oxiranyl ring); nmr ($CDCl_3$) τ 2.25 (s, 1 H, NH), 2.40–3.15 (m, 4 H, ArH), 6.78–9.10 (m, 20 H); mass spectrum (70 eV) *m/e* (rel intensity) 296 (95), 295 (100), 170 (48), 169 (53), and 156 (33).

Anal. Calcd for $C_{19}H_{24}N_2O$: C, 76.99; H, 8.16; N, 9.45. Found: C, 76.85; H, 7.96; N, 9.62.

Decarbomethoxy-16-hydroxytetrahydroapogeissoschizene (7). A solution of 30.1 mg of prewashed sodium hydride and 301 mg of **5** in 50 ml of dry dimethyl sulfoxide was prepared at room temperature under a nitrogen atmosphere and then warmed to 50° for 5 hr. The solution was then poured into 250 ml of cold water, and the solid, which separated, was extracted with chloroform. The chloroform extract was washed with water, dried, and concentrated. The residual solid was taken up in a 19:1 chloroform–methanol mixture and chromatographed over silica gel. The solid, obtained from the main fraction of eluate, was recrystallized from a chloroform–methanol–hexane mixture to give 230 mg (62%) of white crystals: mp 223–224°; uv_{max} (EtOH) 226 nm (ϵ 30,170), 282 (6240), and 289 (5060); ir (KBr) 3425 cm^{-1} (OH); nmr (DMSO-d_6), τ −0.37 (d, 1 H, CHO*H*), 2.50–3.15 (m, 4 H, ArH), 6.40–9.40 (m, 19 H).

Anal. Calcd for $C_{19}H_{24}N_2O$: C, 76.99; H, 8.16; N, 9.45. Found: C, 76.62; H, 7.43; N, 9.82.

19,20-Dihydronorfluorocurine (22). A. By Reaction of 5 with Sodium Hydride in the Presence of Oxygen. A solution of 68 mg of prewashed sodium hydride and 418 mg of **5** in 50 ml of dimethyl sulfoxide was stirred for 12 hr at room temperature while oxygen was being bubbled through the reaction mixture. The bright red solution was then poured into 250 ml of cold water. After the yellow, fluorescent aqueous solution had been extracted with chloroform, the combined chloroform extracts were washed with water, dried, and concentrated. The residual oil was chromatographed on silica gel using a 7:2:1 benzene–ethyl acetate–diethylamine mixture. The material obtained from the main eluate fraction was recrystallized from an acetone–hexane mixture to give 272 mg (62%) of yellow crystals: mp 176–179°; uv_{max} (EtOH) 238.5 nm (ϵ 38,000), 259.5 (8560), and 405 (3430); ir (KBr) 3390 cm^{-1} (OH) and 1686 (>C=O); nmr ($CDCl_3$) τ 2.35–3.50 (m, 4 H, ArH) and 5.80–9.30 (m, 20 H); mass spectrum (70 eV) *m/e* (rel intensity) 312 (56), 281 (100), 200 (16), 186 (17), and 168 (10).

Anal. Calcd for $C_{19}H_{24}N_2O_2$: C, 73.05; H, 7.74; N, 8.97. Found: C, 72.84; H, 7.75; N, 8.91.

B. Oxidation of 5 by Nickel Peroxide Followed by Reaction with Sodium Hydride. A mixture of 1.02 g of nickel peroxide[29] and 400 mg of **5** in 40 ml of glyme was stirred at room temperature for 1 hr. After removal of the precipitated nickel oxides, the solution was concentrated to give a red solid whose spectral properties (λ_{max} 262 nm (ϵ 4000)) were in accord with those of known hydroxyindolenines.[30,31] The crude solid was dissolved in 20 ml of dimethylformamide and, maintaining a nitrogen atmosphere, an excess of sodium hydride was added. The solution was heated at 70° for 1 hr, cooled, and poured into cold water. The aqueous solution was extracted with chloroform; the chloroform extracts were washed with water, dried, and concentrated. The residual oil was chromatographed over silica gel using a 7:2:1 mixture of benzene–ethyl acetate–diethylamine, as before. Recrystallization of the product from acetone–hexane gave 60 mg (14%) of yellow crystals, mp 176–179°, identical in all respects with the sample of **22** prepared in A.

19,20-Dihydronormavacurine (6). A solution of 100 mg of sodium borohydride and 20 mg of **22** in 50 ml of ethanol was boiled under reflux for 2 hr, during which the yellow, fluorescent color disappeared. The excess borohydride was destroyed by addition of acid, the aqueous solution was made basic, and the resulting mixture was extracted with ether. The ether extract was washed with water, dried, and concentrated. The residual oil was taken up in 20 ml of 0.5 *N* sulfuric acid and heated on a steam bath for 2 hr. The solution was cooled, made basic with aqueous potassium hydroxide, and extracted with chloroform. The chloroform extract was washed with water, dried, and concentrated. The residual oil was subjected to thin layer chromatography over silica gel using a 19:1 mixture of ethyl acetate–triethylamine. The main fraction was preceded by a small amount of a faster moving spot, which may be the epimeric 19,20-dihydropleiocarpaminol. Elution of the main spot followed by concentration of the eluate gave a colorless oil. The ultraviolet absorption spectrum of this oil showed absorption maxima at 233 and 288 nm as expected, and its nmr spectrum duplicated very closely that recorded for 19,20-dihydronormavacurine.[10] However, probably the most informative spectral property is that of the mass spectrum and its fragmentation pattern. Both natural and synthetic materials show exactly the same fragmentation pattern. The relative intensities are summarized in Table I and are compared with the relative intensities in the mass spectrum of natural 19,20-dihydronormavacurine as previously recorded.[10]

16-Dehydroxymethyl-15α-hydroxy-19,20-dihydronorfluorocurine (28). A. By Reaction of 13 with Sodium Hydride in the Presence of Oxygen. A mixture of 1.70 g of **13** and 410 mg of prewashed sodium hydride in 50 ml of dimethyl sulfoxide was stirred for 18 hr at room temperature while oxygen was bubbled through the reaction mixture. It was then poured into 250 ml of cold water, and the yellow solid which separated was extracted with chloroform. The

(30) A. I. Scott, "Ultraviolet Spectra of Natural Products," Macmillan, New York, N. Y., 1964, p 175.

(31) B. Witkop, J. B. Patrick, and H. Kissman, *Chem. Ber.*, **85**, 949 (1952).

Table I. Relative Intensities of Peaks in the Mass Spectra of Synthetic and Natural 19,20-Dihydronormavacurine

m/e	Natural material (ref 10)	Synthetic material
296 (M^+)	63	79
266 (M − 30)	22	28
265 (M − 31)	100	100
236	9	10
222	22	30
206	12	20
194	10	13
182	24	22
181	10	17
180	38	53

combined chloroform extracts were washed with water, dried, and concentrated. The residual oil was chromatographed over silica gel using a 17:2:1 mixture of benzene–ethanol–triethylamine as eluent. The material from the main fraction of eluate was recrystallized from a chloroform–hexane mixture to give 860 mg (68%) of yellow crystals: mp 212–214°; uv_{max} (EtOH) 240.5 nm (ε 24,750), 260.5 (10,640), and 410 (3675); ir (KBr) 1672 cm^{-1} (>C=O); nmr ($CDCl_3$) τ 2.30–3.50 (m, 4 H, ArH), and 5.90–9.20 (m, 18 H); mass spectrum (70 eV) *m/e* (rel intensity) 298 (71), 281 (18), 213 (20), 151 (78), 139 (100), and 110 (26).

Anal. Calcd for $C_{18}H_{22}N_2O_2$: C, 73.05; H, 7.74; N, 8.97. Found: C, 72.84; H, 7.75; N, 8.91.

B. Oxidation of 13 with Nickel Peroxide Followed by Reaction with Sodium Hydride. A mixture of 1.50 g of nickel peroxide and 500 mg of **13** in 60 ml of glyme was heated at 60° with stirring for 1 hr. After removal of the precipitated nickel oxides, the solution was concentrated to give 480 mg of a red solid whose ultraviolet spectrum showed a single absorption maximum at 262 nm in accord with the hydroxyindolenine structure **27**.[30,31] To a solution of this red solid in 30 ml of dimethylformamide there was added 74 mg of prewashed sodium hydride and the mixture was heated at 60° for 10 min. The bright red solution was then poured into cold water, and the yellow solid which separated was extracted with chloroform. The chloroform extract was washed with water, dried, and concentrated. Chromatography of the residual oil over silica gel using a 17:2:1 mixture of benzene–ethanol–triethylamine as eluent gave a yellow solid which, on recrystallization from a chloroform–hexane mixture, yielded yellow crystals, mp 212–214°. A mixture of these crystals with a sample of those prepared in A showed no melting point depression and in all respects these crystals were identical with those prepared in A.

16-Dehydroxymethyl-15α-hydroxy-19,20-dihydronormavacurine (29). A solution of 50 mg of **28** and 100 mg of sodium borohydride in 60 ml of ethanol was boiled under reflux for 2 hr. After addition of acid to destroy excess borohydride, the solution was concentrated to a volume of 2 ml, 20 ml of 5 *N* aqueous sulfuric acid was added, and the resulting solution was heated on a steam bath for 2 hr. It was then made basic and extracted with dichloromethane. After the dichloromethane extract had been washed with water, dried, and concentrated, the residual oil was chromatographed over alumina (Woelm, basic, activity III) using a 1:1 mixture of chloroform–ether for elution. The solid obtained from the main fraction of eluate was recrystallized from a dichloromethane–hexane mixture to give 40 mg (89%) of white crystals: mp 85–95°; uv_{max} (EtOH) 232 nm (ε 29,700) and 287 (7120); ir (KBr) 3448 cm^{-1} (OH); nmr ($CDCl_3$) τ 2.20–2.90 (m, 4 H, ArH), 5.70–9.30 (m, 16 H), and 10.07 (q, 1 H, J = 12 Hz and J' = 4 Hz); mass spectrum (70 eV) *m/e* (rel intensity) 282 (100), 264 (30), 235 (44), 222 (37), 221 (21), 220 (64), 208 (78), 207 (68), 206 (81), 196 (36), and 180 (45).

Anal. Calcd for $C_{18}H_{22}N_2O$: C, 76.56; H, 7.85; N, 9.92. Found: C, 76.43; H, 7.86; N, 9.79.

Emde Product (30). A solution of 35 mg of **29** and 1.5 ml of methyl iodide in 25 ml of methanol was allowed to stand overnight at room temperature. Concentration of the solution gave a yellow solid which was dissolved in 75 ml of 1 *N* aqueous potassium hydroxide solution containing a suspension of 100 mg of a platinum oxide catalyst. The mixture was subjected to hydrogenation at 1 atm and room temperature for 12 hr. After removal of the catalyst and concentration of the filtrate, the residue was chromatographed over silica gel using a 50:48:2 mixture of benzene–ethyl acetate–triethylamine for elution. The main fraction gave 27 mg (75%) of a colorless oil, presumably a mixture of epimers, which showed no tendency to crystallize: uv_{max} (EtOH) 234 nm (ε 27,800) and 286 (6260), whereas in acidic ethanol the maxima were at 205, 243, and 295 nm; nmr ($CDCl_3$) τ 2.40–3.00 (m, 4 H, ArH), 6.00–6.25 (m, 2 H), 6.30–7.50 (m, 5 H), 7.63 (s, 3 H, NCH_3), 7.75–9.70 (m, 11 H), and 10.01 (s, 1 H, C_{21}-H_α); mass spectrum (70 eV) *m/e* (rel intensity) 298 (25), 280 (9), 222 (47), 156 (15), 144 (11), and 59 (100).

Anal. Calcd for $C_{19}H_{26}N_2O$: C, 76.47; H, 8.78; N, 9.39. Found: C, 76.34; H, 8.67; N, 9.51.

Methylation of the Emde Product. A solution of 20 mg of **30** and 0.5 ml of methyl iodide in 5 ml of methanol was allowed to stand at room temperature for 5 hr. After concentration, the residual oil was taken up in acetone and addition of ether caused the separation of 18 mg of white crystals: mp 224–229°; uv_{max} (EtOH) 205 nm (ε 37,900), 246 (12,500) and 297 (2920). When the solution was made basic, it showed a single absorption maximum at 287 nm (8540) in accord with the α-methyleneindole structure **33**.[10]

Anal. Calcd for $C_{20}H_{29}N_2OI$: C, 55.11; H, 6.63; N, 6.36. Found: C, 55.59; H, 6.75; N, 6.36.

Nickel Peroxide Oxidation of Tetrahydrocarbazole. A mixture of 1.00 g of tetrahydrocarbazole (**34**) and 3.50 g of nickel peroxide[27] in 50 ml of glyme was stirred at room temperature for 1 hr. After removal of the precipitate of nickel oxides, the solution was concentrated to give a brown oil. This was chromatographed over silica gel using a 5:1 mixture of hexane–ethyl acetate for elution. The first main fraction of eluate, on cencentration, gave an oil which crystallized from an acetone–hexane mixture to yield 150 mg (15%) of white crystals: mp 158–160°; uv_{max} (EtOH) 223 nm (ε 37,000), 272 (21,160), sh 280 (19,800), and sh 292 (14,120); ir (C_6H_6) 1567 cm^{-1} (>C=N); nmr ($CDCl_3$) τ 2.00–3.30 (m, 8 H, ArH) and 6.00–9.20 (m, 16 H); mass spectrum (70 eV) *m/e* (rel intensity) 340 (65), 171 (100), 170 (89), and 143 (83). These spectral data are in accord with structure **35**.

Anal. Calcd for $C_{24}H_{24}N_2$: C, 84.76; H, 7.11; N, 8.23. Found: C, 84.51; H, 6.94; N, 8.37.

The second fraction of eluate also gave an oil which, on sublimation, yielded 600 mg (60%) of white crystals: mp 141–147°; uv_{max} (EtOH) 223 nm (ε 36,600), 278 (23,300), sh 289 (17,380); ir (C_6H_6) 1565 cm^{-1} (C=N); nmr ($CDCl_3$) τ 2.00–3.30 (m, 8 H, ArH) and 6.00–9.20 (m, 16 H); mass spectrum (70 eV) *m/e* (rel intensity) 340 (25), 171 (100), 170 (71), and 143 (75). These data are likewise in accord with structure **35**.

Anal. Calcd for $C_{24}H_{24}N_2$: C, 84.76; H, 7.11; N, 8.23. Found: C, 84.53; H, 7.02; N, 8.36.