A Dimer Alkaloid of 6,7β-Oxidodeoxynupharidine[1]

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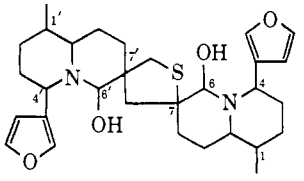
Abstract: A $C_{30}H_{42}N_2O_4$ alkaloid, corresponding in structure to a dimer of 6,7β-oxidodeoxynupharidine, was isolated from extracts of *Nuphar luteum* subsp. *macrophyllum*. The structure was elucidated by chemical and spectral means and was confirmed by the transformation of Δ⁶-dehydrodeoxynupharidine to the C_{30} dimer. A stereoisomeric C_{30} dimer corresponding to the 6,7α-oxidodeoxynupharidine was prepared and the existence of a mixed dimer was detected. Deoxynupharidin-7β-ol and 7-epideoxynupharidin-7α-ol were obtained in the metal hydride reductions of 6,7β-oxidodeoxynupharidine dimer and 7-epideoxynupharidine-6,7α-diol, respectively.

The aquatic macrophyte, *Nuphar luteum*, family Nymphaeaceae, produces a number of alkaloids possessing a 3-furyl group attached to quinolizidine or piperidine ring systems. These structural features all are incorporated within a regular sesquiterpenic framework.[2] Among the more structurally interesting alkaloids[3] discovered to date are the C_{30} compounds which consist of two C_{15}, (3-furyl)quinolizidine units fused in a somewhat symmetrical fashion through carbon and a third heteroatom, sulfur. This type of structure is exemplified by dihydroxythionuphlutine-*A* and -*B* (**1**), two stereoisomeric alkaloids which we



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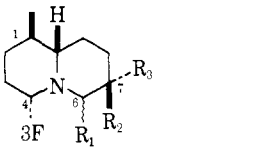
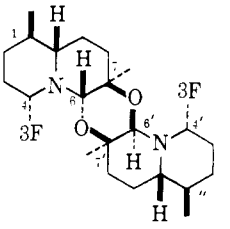
recently isolated from *N. luteum* subsp. *macrophyllum*.[4]

In continuing our investigation of various other chromatographic fractions obtained from the same extract from which the dihydroxythionuphlutines originated, we discovered in the more polar fractions a substance which on preliminary investigation appeared to possess properties consistent with either the 2-aminooxirane **2** or a dimer such as **3**. Our interest in the structure of this substance intensified when our search for reported 2-aminooxiranes revealed that although 2-aminooxiranes have been postulated for some time as intermediates in various reactions, they have been prepared only recently[5] and there is still relatively little known about the chemistry of this type of compound and its diol and dimer derivatives.[6,7] This paper describes the investigation which led to the isolation, establishment of structure and the preparation of the 2-aminooxirane dimer **3**.



3F = 3-furyl =



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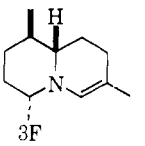
2, R_1,R_2 = β-oxido; $R_3 = CH_3$
4, $R_1 = R_2 = H$; $R_3 = CH_3$
7, $R_1 = OH$; $R_2 = OH$; $R_3 = CH_3$
8, $R_1 = H$; $R_2 = OH$; $R_3 = CH_3$
11, $R_1 = D$; $R_2 = OH$; $R_3 = CH_3$
12, $R_1 = OH$; $R_2 = CH_3$; $R_3 = OH$
13, $R_1 = H$; $R_2 = CH_3$; $R_3 = OH$



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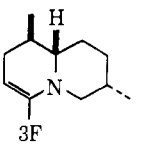

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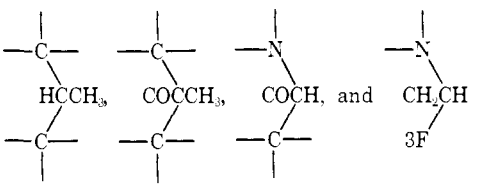
A 4.5-mg sample of the crystalline **3** was isolated by repeated column chromatography of one of the original more polar fractions obtained from the plant extract. The infrared spectrum revealed the presence of the 3-furyl group and several peaks in the C–O stretching region not found in the spectrum of deoxynupharidine (**4**). The nmr chemical-shift values and splitting patterns indicated the presence of structural features



The base peak in the mass spectrum was *m/e* 231 which corresponded to the molecular weight of a dehydrodeoxynupharidine. Also observed were very low intensity peaks at *m/e* 246 and 248 corresponding to 231 + 16 − 1 and 231 + 16 + 1, respectively. A very weak peak at *m/e* 493 corresponded to the dimer **3** less one hydrogen atom. Generally the mass spectrum appeared similar to that observed earlier for Δ⁶-dehydrodeoxynupharidine (**5**)[8] though the overall com-

(1) Support of this work by the National Institutes of Health, U. S. Public Health Service (Grant No. AI 10188), is gratefully acknowledged.
(2) (a) J. T. Wróbel, *Alkaloids*, **9**, 441 (1967); (b) O. E. Edwards, "Cyclopentanoid Terpene Derivatives," W. I. Taylor and A. R. Battersby, Ed., Marcel Dekker, New York, N. Y., 1968, Chapter 6.
(3) (a) O. Achmatowicz and J. T. Wróbel, *Tetrahedron Lett.*, 129 (1964); (b) O. Achmatowicz, H. Banazek, G. Spiteller, and J. T. Wróbel, *ibid.*, 927 (1964); (c) G. I. Birnbaum, *ibid.*, 4149 (1965).
(4) R. T. LaLonde, C. F. Wong, and W. P. Cullen, *ibid.*, 4477 (1970).
(5) (a) C. L. Stevens and P. M. Pillai, *J. Amer. Chem. Soc.*, **89**, 3084 (1967); (b) C. L. Stevens and P. M. Pillai, *J. Org. Chem.*, **37**, 173 (1972).
(6) K. Baum, *J. Amer. Chem. Soc.*, **90**, 7083 (1968).
(7) S. Laeuber and F. Lingens, *Z. Anal. Chem.*, **181**, 494 (1961).
(8) R. T. LaLonde, E. Auer, C. F. Wong, and V. P. Muralidharan, *J. Amer. Chem. Soc.*, **93**, 2501 (1971).

parison could not be made with a great deal of confidence because of the much lower intensities of the peaks of the isolated compound below *m/e* 231. However, both spectra showed peaks at *m/e* 216 (231 − CH_3) but no peak at *m/e* 214 (231 − CH_3 and H_2) where the base peak of Δ^3-dehydrodeoxynupharidine (**6**)[9] occurs. Thus the data obtained at this point suggested the presence of a deoxynupharidine skeleton with oxygenated carbons at C_6 and C_7.

The question of whether the isolated material was the 2-aminooxirane (**2**) or its dimer **3** was answered convincingly in a number of ways. First, the 100-MHz nmr when run in CCl_4 displayed two overlapping quartets corresponding to the C_4 H and $C_{4'}$ H. Second, the 60-MHz nmr when run in benzene showed two singlets in a 1:1 ratio corresponding to C_6 H and $C_{6'}$ H. These nmr properties clearly indicate that more than a single C_4 H and C_6 H are involved in the structure. Consequently, the oxirane structure could be dismissed. Moreover, the high-resolution mass spectra gave a satisfactory fit for the calculated value corresponding to $M^+ - 1$ and the isobutane chemical ion mass spectra gave adduct ions corresponding to $M \cdot C_4H_9^+$ and $M \cdot H^+$. Finally, the determination of the molecular weight in benzene solution was carried out by vapor phase osmometry. Values of 510 and 517 were obtained.

In the course of isolating the 2-aminooxirane dimer **3** we obtained a second more polar substance which was finally purified by arduous preparative layer chromatography. Storage of this substance neat in the cold under nitrogen for 2 days led to the formation of a contaminant having the properties similar to those of the first of the two substances isolated, the 2-aminooxirane dimer. Indeed, when the dimer was treated with aqueous acid and then base and the basified solution was extracted, the extract afforded a highly polar hydroxyl containing compound having the tlc and ir properties virtually identical with those of the second substance isolated. In time the hydroxylated compound reverted to the less polar dimer as evidenced by tlc and ir. These experiments indicated the two substances isolated were related by hydration–dehydration. On the basis of subsequent study which demonstrated the structure of the dehydrated form to be **3**, the hydrated form was deduced to be the hydrolysis product of **3**, the diol **7**. This deduction was supported by ir and nmr examinations of a freshly prepared sample of the hydrated form.

Since the dehydrated form was the more stable we decided it would be the more readily investigated. However, before proceeding with further studies on the limited amount of pure isolated material, we next investigated a fraction obtained from the first of the sequence of chromatographic separations. This fraction was examined through metal hydride and deuteride reductions in order to confirm the presence of a hemiaminal, or hemiaminal ether, in the plant extract and to ascertain the structure of the hemiaminal through a study of the products obtained by its reduction. As determined by tlc, the fraction examined contained a mixture of the 2-aminooxirane dimer and its hydrolysis product as well as other bases. Treatment of this fraction with sodium borohydride in methanol or lithium aluminum hydride in ether gave deoxynupharidin-7β-ol (**8**). The spectral properties and deduced structural features most pertinent to establishing the gross structure were the following. The ir showed hydroxyl bands at 2.8–3.2 μ and 3-furyl bands at 6.66 and 11.43 μ. The nmr revealed: (1) a doublet methyl characteristic of the $CH_3C(-C-)_2H$ group; (2) a singlet methyl, at slightly lower field, characteristic of $CH_3C(-C-)_2OH$; (3) a broad singlet attributable to an OH group since it disappeared on deuterium oxide addition; (4) a quartet at δ 2.53 (J = 11 and 2.5 Hz) assignable to the C_6 α-H (equatorial) on the basis of its splitting pattern, chemical shift, and known nmr properties of the same proton in deoxynupharidine (**4**);[10] (5) a quartet at δ 2.93 assignable to the C_4 β-H (axial) on the same basis applied in assigning the C_6 α-H. The δ 2.53 quartet was attributed to the C_6 equatorial proton being coupled to the geminal C_6 axial proton and to the C_8 equatorial proton. The orientation of C–C and C–H bonds separating C_6 and C_8 equatorial protons corresponds to the familiar W arrangement sufficient for long-range coupling.[11]

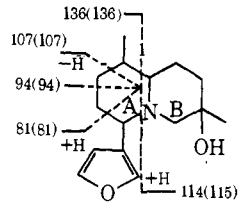
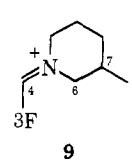


Figure 1. Principal mass spectral fragmentation modes of deoxynupharidin-7β-ol (**8**). Numbers in parentheses refer to *m/e* for deoxynupharidin-7β-ol-6-d_1.

The mass spectrum of deoxynupharidin-7β-ol (**8**) revealed a parent ion peak at *m/e* 249 which corresponded to the molecular weight of deoxynupharidine plus one oxygen atom. Intense ions at *m/e* 81, 94 (100%), 107, and 136 indicated that the tertiary OH group was not incorporated into ring A. The last given group of ions is also present in the mass spectrum of deoxynupharidine and high resolution mass spectral and deuterium labeling studies have demonstrated their origin as shown in Figure 1.[9] The presence of *m/e* 114, the second strongest peak in the mass spectrum of **8**, indicated that the tertiary OH group was located in ring B. This assignment was supported by the presence of *m/e* 178 (23%) whose intensity was much enhanced relative to that observed in the mass spectrum of deoxynupharidine. High-resolution and labeling studies show that *m/e* 178 should be represented largely by fragment **9** when generated from deoxynupharidine but by fragment **10** when generated from the thiospirane type alkaloids such as thionuphlutine-*A* and -*B* (**1**) (C_6 and $C_{6'}$ deoxy). Reasonably, the enhanced intensity of *m/e* 178 in the mass spectrum of deoxy-



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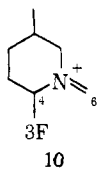

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(9) R. T. LaLonde, J. T. Woolever, E. Auer, and C. F. Wong, *Tetrahedron Lett.*, 1503 (1972).

(10) C. F. Wong, E. Auer, and R. T. LaLonde, *J. Org. Chem.*, **35**, 517 (1970).

(11) S. Sternhell, *Quart. Rev., Chem. Soc.*, **23**, 259 (1969).

nupharidin-7β-ol (**8**) can be ascribed to the presence of a C_7 tertiary hydroxyl group which preferentially facilitates fission of the C_6–C_7 bond through stabilization of the odd electron at C_7.

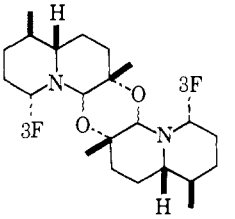
When the fraction containing the 2-aminooxirane dimer and its hydrolysis product was reduced with sodium borodeuteride, deoxynupharidin-7β-ol-*6*-d_1 resulted. The δ 2.53 signal, a quartet in the unlabeled sample, was observed as a broad singlet in the labeled sample. As for the mass spectrum, the parent ion was shifted to *m/e* 250 and *m/e* 136, 107, 94, and 81 were retained while *m/e* 114 was shifted to 115. *m/e* 178 was shifted to 179. Thus, on the basis of the structure assigned to deoxynupharidin-7β-ol the deuterium labeled alcohol must be deoxynupharidin-7α-ol-*6*-d_1 (**11**). Finally, a sample containing only the 2-aminooxirane dimer and its hydrolysis product was reduced with sodium borohydride to obtain as the only product the same tertiary alcohol formed by reduction of the fraction containing not only the 2-aminooxirane dimer and its hydrolysis product but other bases as well. Thus the metal hydride reduction series of experiments demonstrated the incorporation of one or more regular deoxynupharidine skeletal units in the structure of the 2-aminooxirane dimer and supported the preliminary spectral evidence which indicated that oxygen functions were located at C_6 and C_7.

To conclude the structure determination and to obtain a quantity large enough for a more extensive examination, a sample of the 2-aminooxirane dimer was prepared through the osmium tetroxide oxidation of Δ⁶-dehydrodeoxynupharidine (**5**). The diol **7** initially formed by this oxidation underwent dehydration on standing to afford the desired 2-aminooxirane dimer **3**, whose ir, nmr, mass spectral ORD, and tlc properties were identical with those of the 2-aminooxirane dimer originating from the plant extract. Moreover, the sodium borohydride reductions of two mixtures of 2-aminooxirane dimer and diol—the one obtained from the plant extract and the other by synthesis—gave two samples of crystalline 7β-ol **8** whose physical properties were identical with one another.

In addition to the 6,7β-diol **7** the osmium tetroxide oxidation of the Δ⁶-enamine also furnished the epimeric 7-epideoxynupharidin-6,7α-diol (**12**) whose elemental analysis and spectral properties were consistent with the structure assigned (see Expeimental Section). Sodium borohydride reduction of the diol **12** gave 7-epideoxynupharidin-7α-ol whose configuration at C_7 was established by the concentration independence of the intramolecular hydrogen-bonded OH group absorbing at 3520 cm^{-1} in the ir. In contrast, the ir of deoxynupharidin-7β-ol displayed a hydrogen-bonded OH group (3520–3300 cm^{-1}) which disappeared completely at the lower concentration level where the band of the 7α-ol persisted. It follows that the configuration of C_7 in the 6,7β-diol **7** and related 2-aminooxirane dimer **3** must be the same as that in deoxynupharidin-7β-ol. Significantly, both 7β-, and 7α-ols show strong Bohlmann absorption.[12] Therefore, both alcohols possess trans-fused quinolizidine ring systems. Interestingly, neither of the two diols nor the 2-aminooxirane dimer **3** exhibit Bohlmann bands.

(12) (a) F. Bohlmann, *Chem. Ber.*, **91**, 2157 (1958); (b) M. W. Wiewiorowski and J. Skolick, *Bull. Acad. Pol. Sci., Ser. Sci. Chim.*, 10, 1 (1962).

Contrasting with the spontaneous dehydration of the 6,7β-diol, the 6,7α-diol **12** remained in the diol form but could be dehydrated by azeotropic distillation of the water of dehydration. Water absorbed by tlc plates was sufficient to convert the dehydrated form back to the diol **12**. As for the structure of the dehydrated form, the low- and high-resolution electron impact mass spectrum gave no evidence for a parent ion at *m/e* 494, though a low intensity peak was observed at *m/e* 493. However, the isobutane chemical ion mass spectrum gave adduct ions corresponding to $M \cdot C_4H_9^+$ and $M \cdot H^+$. Therefore, the product resulting from the 6,7α-diol would be the dimer **14**.



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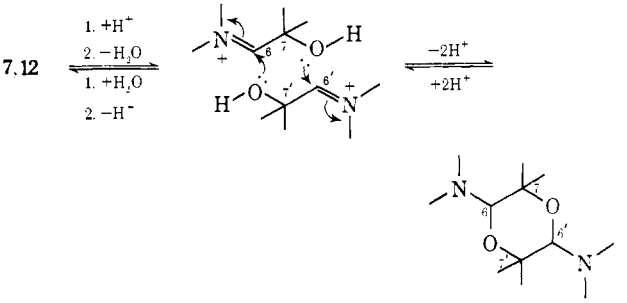
The difficulty with which the 6,7α-diol undergoes 2-aminooxirane dimer formation, relative to the 6,7β-diol, would seem to be the result of the increased steric demands of the 7α axial hydroxyl group in nucleophilic attack on $C_{6'}$. Reasonably, the electrophile in the dimerization is the iminium ion which may be formed by the loss of protonated OH from C_6.

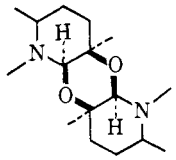


A mixed dimer was formed by mixing the 6,7α-diol **12** and the 2-aminooxirane dimer **3**. The existence of the mixed dimer was detected by tlc experiments, the details of which are given in the Experimental Section. Sodium borohydride reduction of the mixed dimer gave a mixture of deoxynupharidin-7β-ol (**8**) and 7-epideoxynupharidin-7α-ol (**13**).

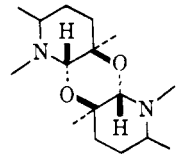
The two most important questions pertaining to the stereochemistry of the dimer **3** centered on the mode of quinolizidine ring fusion and the configuration at C_6 and $C_{6'}$. We observed that the nmr signal for the angular C_7 methyl groups was shifted downfield while the signal for the secondary C_1 methyl groups was shifted upfield on changing the solvent from deuteriochloroform to benzene. These benzene-induced shifts are consistent with both angular methyl groups being axial and both secondary methyl groups being equatorial in two quinolizidine systems each of which contains two trans-fused, six-membered rings in chair conformations. The result and its interpretation are in agreement with the previously observed, benzene-induced shift behavior of axial and equatorial methyl groups in quinolizidine *Nuphar* alkaloids.[13,14]

(13) C. F. Wong and R. T. LaLonde, *Photochemistry*, **9**, 659 (1970).
(14) Similar benzene-induced shift behavior of methyl groups in 1,3-dioxanes and steroidal sapogenins has been observed; see (a) J. E.

The detection of chemical shift nonequivalent C_4 and $C_{4'}$ protons and C_6 and $C_{6'}$ protons, as referred to earlier, was of utmost importance in deducing the configurations of C_6 and $C_{6'}$. Accepting the above conclusion about the nature of the quinolizidine ring stereochemistry restricts the possible structures to three stereoisomeric 2-aminooxirane dimers differing in configuration at C_6 and $C_{6'}$. These are **3**, **3a**, and **3b**.



3a



3b

Molecular models reveal that **3b** would have the central dioxane ring locked in a twist-boat conformation[15] and would belong to molecular symmetry point group C_2. Consequently, **3b** would have equivalent groups.[16] Of primary significance relative to the nmr results, C_4 and $C_{4'}$ protons would be chemical-shift equivalent as would the C_6 and $C_{6'}$ protons. Since the nmr studies show these sets of protons to be chemical-shift nonequivalent, **3b** can be dismissed.

The central dioxane ring of **3a** may possess a twist-boat conformation and thereby give a structure belonging to point group C_2. Such a structure can be dismissed for the same reason that **3b** was dismissed. Alternatively, **3a** may possess a dioxane ring possessing a chair conformation and thereby give a structure belonging to point group C_1. However, one or the other rings fused to the chair dioxane ring must assume a twist-boat conformation. Molecular models reveal such a structure to be a prohibitively high energy form. Therefore, we prefer structure **3** (point group C_1). Only in stereoisomer **3** is it possible to combine the two quinolizidine systems possessing trans-fused chair rings to a chair dioxane ring.

Some comment regarding the origin of the 6,7β-diol and the corresponding 2-aminooxirane dimer would seem appropriate in concluding this report. A plausible source of the 6,7β-diol is air oxidation of the Δ^6-dehydrodeoxynupharidine (**5**). In fact, air oxidation of the latter in ether at room temperature for 5 days produces, among several other products, both the 6,7β- and the 6,7α-diols 7 and **12**, respectively. Evidence for their formation is the isolation of deoxynupharidin-7β-ol (**8**) and 7-epideoxynupharidin-7α-ol (**13**) from a mixture of bases obtained by sodium borohydride reduction of the air oxidation mixture. Subsequent to obtaining this result, a small amount of the plant material was re-examined for the presence of the 6,7α-diol. The re-examination involved the following sequence: extraction of freshly ground plant material under nitrogen, chromatographic separation of fractions which would contain the 6,7α- and 6,7β-diols, sodium borohydride reduction of each of the two fractions considered to contain diols, but determined to be free of 7α- and 7β-ols, and chromatographic and spectrometric examination of each of the two reduction products. As expected, one reduction product was identified as deoxynupharidin-7β-ol (**8**). The other was 7-epideoxynupharidin-7α-ol (**13**), the detection of which indicates the presence of the 6,7α-diol **12** in the extract. Whether the 6,7β- and 6,7α-diols are true plant metabolites or are formed by air oxidation of plant-produced Δ^6-enamine in the course of preparing the plant material for extraction is still an open question. We are attempting to answer this question by a search for the Δ^6-enamine in the plant and by further studies of its oxidation.

Experimental Section

Spectra were obtained as follows: nmr in solution as indicated, 2% TMS (δ 0.0), on Varian A-60 and HA-100 spectrometers, time averaged spectra using a Varian-Data 620I computer, by M. L. Green, H. Jennison, and A. Vulcano, symbols s, d, t, q, m, and br refer to singlet, doublet, triplet, quartet, multiplet, and broad, respectively; ir in solution as indicated, Perkin-Elmer, Models 137 and 621, symbols, s, m, w, sp, and br refer to strong, moderate, weak, sharp, and broad, respectively; low-resolution mass spectrum at 70 eV, direct inlet at 110°, Hitachi-Perkin-Elmer Model RMU6E by H. Jennison; high-resolution and chemical ion mass spectra by R. Foltz, the High Resolution Mass Spectrometry Laboratory, Battelle's Columbus Laboratories, Columbus, Ohio, AEI MS-9 with SRIC Model CIS-2 combined chemical ionization and electron impact ion source, high resolution mass spectra by direct insertion probe at 120°, source temperature 200°; ORD in solution as indicated using a Durrum-Jasco spectropolarimeter-5. Melting points were determined on a Köfler micro hot stage and Mel-Temp apparatus and are uncorrected. Optical rotations were determined in solution as indicated on a Perkin-Elmer Model 141 polarimeter. Tlc was performed on 20-cm plates coated with the adsorbent specified at a uniform thickness of 0.25 mm, unless otherwise indicated, and using the solvents specified; microscope slides were uniformly coated with 0.25 mm of adsorbent for tlc. Assignment of R_f values to specific compounds was made by comparison with an authentic sample on the same plate. Spots were developed by uv and Drangendorff spray reagent. Glc was carried out on an F & M Research Chromatograph, Model 810, equipped with a flame ionization detector and using He as the carrier gas. The elemental analyses and the determination of molecular weights by vapor phase osmometry were carried out by Galbraith Laboratories, Knoxville, Tenn.

Isolation of 6,7β-Oxidodeoxynupharidine Dimer and Deoxynupharidine-6,7-β-diol. Powdered rhizomes of *Nuphar luteum* subsp. *macrophyllum* (2.7 kg) were soaked with 5.4 l. of 10% aqueous NH_3 for 24 hr. The resulting material was shaken with 10.8 l. of CH_2Cl_2 for 3 hr. The CH_2Cl_2 extract was siphoned off and shaken twice with 2 l. of 10% H_2SO_4. The combined acid solution was cooled and basified to pH 10 with about 500 ml of concentrated aqueous NH_3 in ice. The basic solution was extracted with CH_2Cl_2 several times. The combined CH_2Cl_2 extract was dried (Na_2SO_4). Removal of the solvent at the rotary evaporator gave 29.7 g of residue, 24 g of which was treated in the following manner in order to facilitate chromatographic separation. The residue sample was mixed with 250 ml of benzene and 20 g of alumina (activity III) and the resulting mixture was shaken vigorously. The suspension was allowed to settle and the benzene solution decanted. The alumina was washed with small quantities of benzene and air dried. The combined benzene washings and original benzene solution were added to a column (75 × 5 cm) of 720 g of alumina packed in hexane. Finally the air-dried alumina was added to the top of the column. The column was eluted with 1 l. of hexane and then with hexane–CH_2Cl_2 in the proportions and amounts in liters as follows: 99:1, 1.4; 95:5, 2.8; 95:5, 2.4; 8:2, 0.7; 1:1, 2.5; 1:3, 1.6. Thereafter the column was eluted with 5.8 l. of CH_2Cl_2, 1.2 l. of CH_2Cl_2–MeOH (99:1), and finally with 2.3 l. of MeOH. The CH_2Cl_2–MeOH (99:1) fraction afforded 2.5 g of residue A which was stored in a refrigerator for 8 months prior to examination. A 600-mg sample of residue A was added to a column of alumina (45 g, activity II) which was eluted with 500 ml of CH_2Cl_2 (fraction 1, 10 mg), 200 ml of CH_2Cl_2–0.4% MeOH (fraction 2, 96 mg), and 75 ml of CH_2Cl_2–0.4% MeOH (fraction 3, 174 mg). Fraction 1 was rechromatographed on alumina (ac-

Anderson, *Tetrahedron Lett.*, 4713 (1965), and (b) D. H. Williams and N. S. Bhacca, *Tetrahedron*, **21**, 1641 (1964).

(15) For comparison, the necessity of a boat dioxane in **3b** is also a requirement of the central six-membered ring in the *trans-anti-trans*-perhydrophenanthrene system; see W. G. Dauben and K. S. Pitzer, "Steric Effects in Organic Chemistry," M. S. Newman, Ed., Wiley, New York, N. Y., 1956, Chapter 1.

(16) K. Mislow and M. Raban, *Top. Stereochem.*, **1**, 1 (1967).

tivity III) using hexane–5% ether (100 ml) to obtain 4.5 mg of the dimer **3**: mp 165–170°; tlc (alumina) R_f (C_6H_6) 0.72, (ether–CCl_4, 1:9) 0.68, (ether–hexane, 15:85) 0.49; admixture with synthetic dimer tlc (alumina) R_f values are the same as for the natural dimer, mp 165–172°; $[\alpha]^{25}D$ −93° ± 5 (*c* 0.26 g/100 ml, CH_2Cl_2,); ir (CH_2Cl_2) 6.08 (w), 6.29 (w), 6.68 (m, sp), 7.36 (m), 8.10 (w), 8.24 (w), 8.55 (s), 8.69 (s), 8.91 (s), 9.14 (w), 9.32 (s, sp), 9.43 (m, sp), 9.67 (s, sp), 9.82 (s, sp), 9.94 (s, sp), 10.08 (s, sp), 11.47 (s, sp), 12.39 (m), 12.68 μ (s, br) and identical with the ir of the synthesized sample; nmr (100 MHz, time averaged, CCl_4) δ 0.87, 0.89, 0.91 (m, ~12 H, $HCCH_3$ and $ROCCH_3$), 3.75–4.10 (m, C_4 and $C_{4'}$ H), 3.89 (s, C_6 and $C_{6'}$ H), 6.08 (br s, 2 H, β-furyl H), 7.11 (d, 4 H, α-furyl H), and identical with the nmr of the synthesized sample; mass spectrum *m/e* (% rel intensity) 493 ($M^+ - 1$) (0.5), 231 (100); ORD (*c* 240 mg/100 ml, hexane, *l* = 0.1 dm) $[\Phi]_{400}$ − 1040°, $[\Phi]_{350}$ − 1300°, $[\Phi]_{300}$ − 1560°, $[\Phi]_{284}$ −1600°, $[\Phi]_{260}$ −1520°, $[\Phi]_{244}$ −1340°, $[\Phi]_{240}$ −1440°, $[\Phi]_{231}$ −3630°, $[\Phi]_{230}$ −2970°.

Tlc (alumina, ether–0.4% MeOH) of fraction 2 showed three spots, R_f 0.35, 0.53, and 0.73. Tlc separation (alumina, ether–0.4% MeOH) of the component corresponding to R_f 0.53 gave 22 mg of a sticky oil, supposedly deoxynupharidin-6,7β-diol: ir 2.8–3.1 (w, br), 6.0 (w), 6.69 (s, sp), 11.45 μ (s, sp); nmr (CCl_4) δ 0.91 (m, $HCCH_3$), 1.28 (s, $HOCCH_3$), 4.0–3.3 (m, C_6H and C_4H), 6.39 (br s, 1 H, β-furyl H), 7.34 (m, 2 H, α-furyl H). After storage for 2 days in the refrigerator under nitrogen, a sample gave a tlc (alumina, ether–0.4% MeOH) showing R_f 0.53 and 0.95.

Another fraction, 5.7 mg containing the dimer (tlc, alumina, C_6H_6, R_f 0.72) but also containing a uv-active impurity, was treated with 5 ml of methanol, 0.5 ml of 0.12 *M* aqueous HCl, and 5 ml of water. The methanol was removed by evacuating the mixture at 30° for 1 hr. The remaining mixture was extracted with ethyl ether. The water layer was basified to pH 12 and then extracted with CH_2Cl_2. The extract was dried and evaporated to dryness to obtain 2.9 mg of colorless residue presumably deoxynupharidin-6,-7β-diol: tlc alumina (C_6H_6) R_f 0.0; ir (CH_2Cl_2) 2.8 μ. After storing neat at 0° for 2 days under nitrogen the tlc spot corresponding to the dimer (R_f 0.72) emerged. The ratio of diol to dimer appeared to be 1:1 judging from the intensities of the two spots. After 7 days of storage neat at 0° only the spot corresponding to the dimer was observed. The ir showed no band at 2.8 μ.

Detection of the 6,7α- and 6,7β-Diols. A 270-g quantity of freshly ground slices of air-dried plant material was extracted according to essentially the same procedure described above except that proportionately smaller quantities of solvents purged with nitrogen were employed. The 119 mg of crude extract was chromatographed on 10 g of neutral alumina (activity I) previously purged with nitrogen. The column was eluted with 50 ml of 10% Et_2O in hexane (fraction A1, 17 mg), 50 ml of 10% Et_2O in C_6H_6 (fraction A2, 9.3 mg), 50 ml of Et_2O–C_6H_6, 1:3 (fraction A3, 6.0 mg), 20 ml of Et_2O–C_6H_6, 1:1 (fraction A4, 1.7 mg), 20 ml of Et_2O (fraction A5, 0 mg), and 50 ml of MeOH (fraction A6, 41.6 mg).

Fraction A3 contained at least five components, three of which had R_f values corresponding to deoxynupharidin-7β-ol (R_f 0.36), 7-epideoxynupharidin-7α-ol (R_f 0.51), and 7-epideoxynupharidin-6,7α-diol (R_f 0.63) on tlc (alumina GF_{254}, CH_2Cl_2–MeOH (200:1)). Material corresponding to the 6,7α-diol was separated by preparative tlc (alumina GF_{254}, CH_2Cl_2–MeOH (200:1)) and thereafter was treated with 100 mg of $NaBH_4$ in 2 ml of MeOH for 12 hr at 25°. The solid residue was filtered off. To the filtrate was added 5 ml of H_2O and the bulk of the MeOH was removed at the rotary evaporator. Thereafter the aqueous mixture was extracted with CH_2Cl_2. The extract was dried (Na_2SO_4). Vacuum evaporation of solvent gave about 0.2 mg of residue containing 7-epideoxynupharidin-7α-ol: tlc (microscope slide, alumina GF_{254}, 10 ml of CH_2Cl_2–1 drop of MeOH) R_f 0.51; tlc (microscope slide, alumina GF_{254}, Et_2O–C_6H_6 (1:2)) R_f 0.69; glc (10% Carbowax 20M, 6 ft × 1/8 in., 220°) 3.3 min; glc (10% SE-30 silicone rubber, 6 ft × 1/8 in., 170°) 8.0 min; mass spectrum *m/e* (% rel intensity) 249 (25.5), 178 (21.5), 136 (45), 114 (61), 94 (100).

Fraction A6, containing no deoxynupharidin-7β-ol by tlc, in 0.5 ml of MeOH was treated with 64 mg of $NaBH_4$ at 25° for 12 hr. Water (10 ml) was added and the bulk of the MeOH was removed at the rotary evaporator. The resulting mixture was extracted with CH_2Cl_2. The extract was dried (Na_2SO_4) and the solvent was evaporated to obtain 38.3 mg of residue which was chromatographed on 5 g of neutral alumina (activity II). Fractions B1 (20 ml of C_6H_6, 0.3 mg), B2 (20 ml of Et_2O–C_6H_6 (1:1), 1.2 mg), and B3 (20 ml of Et_2O–C_6H_6 (1:1), 0.2 mg) were obtained. Fraction B2 contained deoxynupharidin-7β-ol: tlc (microscope slide alumina GF_{254}, 10 ml of CH_2Cl_2–1 drop of MeOH) R_f 0.43; tlc (microscope slide, alumina GF_{254}, Et_2O–C_6H_6 (1:2)) R_f 0.55; glc (10% Carbowax 20M, 6 ft × 1/8 in., 220°) 6.1 min; glc (10% SE-30 silicone rubber, 6 ft × 1/8 in., 170°) 9.5 min; ir identical with that of authentic sample (see below); mass spectrum *m/e* (% rel intensity) 249 (26), 178 (23), 136 (52), 114 (77), 94 (100).

Deoxynupharidin-7β-ol from $LiAlH_4$, $NaBH_4$, and $NaBD_4$ Reduction of Residue A. A 165-mg sample of residue A in 4 ml of methanol was treated overnight at 25° with 50 mg of $NaBH_4$. Water was added and the mixture was extracted with CH_2Cl_2. The solvent was removed by vacuum evaporation and the semisolid residue (160 mg) was chromatographed on alumina (activity III) with CH_2Cl_2–C_6H_6 (12:88) to obtain 19 mg of deoxynupharidin-7β-ol: mp 101.5–102.5°; $[\alpha]^{25}D$ − 121° (*c* 0.5 g/100 ml, $CHCl_3$); ir (CCl_4) 2.8–3.2 (br, w), 3.66 (m), 6.66 (m, sp), 6.86 (m), 6.95 (m), 7.26 (m), 8.62 (br, m), 9.40 (m), 9.63 (br, s), 11.43 μ (sp, s); nmr (CCl_4) δ 0.92 (d, *J* = 6.5 Hz, 3 H, $HCCH_3$), 1.11 (s, 3 H, $HOCCH_3$), 1.30 (br s, OH), 2.53 (q, *J* = 11 and 2.5 Hz, 1 H, C_6 equatorial H), 2.93 (q, *J* = 7.5 and 5 Hz, 1 H, C_4 axial H), 6.2 (m, 1 H, β-furyl H), 7.23 (m, 2 H, α-furyl H); mass spectrum *m/e* (% rel intensity) 249 (26) (M^+), 234 (7), 232 (13), 220 (9), 206 (14), 178 (23), 164 (10), 136 (50), 114 (64), 107 (29), 96 (37), 94 (100), 81 (30).

A 130-mg sample of residue A was treated in 30 ml of ether with 160 mg of $LiAlH_4$ under nitrogen for 2 hr at 25°. The ether was evaporated and the residue was treated with water and the mixture extracted with CH_2Cl_2. Evaporation of CH_2Cl_2 left 75 mg of oil which on elution chromatography (CH_2Cl_2–C_6H_6 (1:10)) on alumina (activity III) gave 40 mg of crystalline deoxynupharidin-7β-ol whose physical properties were identical with those reported in the paragraph above.

A 140-mg sample of residue A in 5 ml of methanol was treated with 150 mg of $NaBD_4$ for 2.5 hr at 25°. The mixture was processed as in the experiment using $NaBH_4$ to obtain 38 mg of deoxynupharidin-7β-ol-6-d_1: nmr (CCl_4) δ 2.53 (br s, 1 H); ir (CCl_4) 4.8 μ (w); mass spectrum *m/e* (% rel intensity) 250 (12), 235 (6), 232 (10), 231 (10), 221 (8), 207 (12), 179 (21), 164 (9), 136 (52), 115 (66), 114 (23), 107 (16), 97 (27), 96 (17), 95 (22), 97 (100), 81 (30).

Deoxynupharidin-7β-ol from the Reduction of a Mixture of Deoxynupharidine-6,7β-diol and 6,7β-Oxidodeoxynupharidine Dimer. A 3.3-mg mixture containing diol and dimer in 0.2 ml of MeOH was treated with 10 mg of $NaBH_4$ at 25° for 30 min. The alumina tlc of the product was identical with the alumina tlc (R_f 0.45, CH_2Cl_2–CH_3OH (150:1)) of deoxynupharidin-7β-ol obtained by reduction of residue A and synthesis and different from the alumina tlc of 7-epideoxynupharidin-α-ol (R_f 0.59, CH_3Cl_2–CH_3OH (150:1)).

Osmium Tetroxide Oxidation of Δ^6-Dehydrodeoxynupharidine. A 545-mg sample of the title enamine[6] and 645 mg of osmium tetroxide in 25 ml of anhydrous ether was stirred under nitrogen for 6 days at 25°. The solvent was evaporated at reduced pressure. The residue was dissolved in aqueous methanol and to the resulting solution was added 6 g of sodium sulfite. After 2 hr the mixture was extracted with CH_2Cl_2 and the extract was dried. Evaporation of the solvent at reduced pressure gave 621 mg of green-colored oil which was chromatographed on alumina (50 g, activity II) using 100 ml of hexane, 500 ml of hexane–ether (1:1), 300 ml of ether, and 200 ml of 2% MeOH–CH_2Cl_2. The ether fraction yielded 246 mg of colorless, crystalline 7-epideoxynupharidin-6,7α-diol: mp 176–177° (1°/min). The optical rotation was observed to change with time. Therefore, the rotation (α) was measured over the course of 6.5 hr and a straight line plot of log α against time gave an extrapolated value of $[\alpha]^{25}D$ −64° (*c* 0.5 g/100 ml, $CHCl_3$) for time zero. Tlc (alumina, Et_2O–CH_2Cl_2 (2:13)) R_f 0.47; ir (CH_2Cl_2) 2.81 (w, sp), 2.88 (w, sp), 6.24 (w), 6.70 (m, sp), 7.30 (m), 7.58 (w), 8.70 (m), 8.86 (m), 9.74 (s), 11.49 (s, sp); nmr ($CDCl_3$) δ 0.96 (d, *J* = 4 Hz, 3 H, $HCCH_3$), 1.14 (s, 3 H, $HOCCH_3$), 1.87 (d, *J* = 5.5 Hz, 1 H, HC_6OH), 3.04 (br s, 1 H, CH_3COH), 3.68 (q, *J* = 6 and 7.5 Hz, 1 H, C_4H), 4.10 (d, *J* = 5.5 Hz, 1 H, HOC_6H), 6.41 (m, 1 H, β-furyl H), 7.42 (m, 2 H, α-furyl H); mass spectrum *m/e* (% rel intensity) 265 (13) (M^+), 248 (7), 247 (24), 232 (13), 219 (48), 204 (100), 191 (29), 176 (35), 136 (20), 107 (23), 94 (61).

Anal. Calcd for $C_{15}H_{23}NO_3$: C, 67.92; H, 8.74; N, 5.28. Found: C, 67.76; H, 8.80; N, 5.17.

The 2% MeOH–CH_2Cl_2 fraction yielded 138 mg of sticky oil which on tlc (alumina, Et_2O–CH_2Cl_2 (2:13)) revealed three spots (R_f 0.07, 0.47, 0.92). Further chromatography on alumina (activity III) with 40 ml each of hexane, 10% CH_2Cl_2–C_6H_6, and CH_2Cl_2 and 200 ml of Et_2O gave fractions 1 (19.5 mg), 2 (0 mg), 3 (0 mg), 4 (16 mg), and 5 (21.3 mg), respectively. Fraction 1 was the pure dimer of 6,7β-oxidodeoxynupharidine (**3**): tlc alumina

R_f (ether–CH_2Cl_2 (2:13)) 0.92, (ether–CCl_4 (1:9)) 0.68, (ether–hexane (15:85)) 0.49, (C_6H_6) 0.72; mp 164–174°; $[\alpha]^{25}D$ −83° (CH_2Cl_2, *c* 1.98 g/100 ml); ir (CH_2Cl_2) OH absent, 3.41, 3.50, 5.80 (w), 6.30 (w), 6.78, 6.88, 7.32, 8.52, 8.90, 9.75, 9.80, 9.92, 11.45 μ; nmr ($CDCl_3$) δ 0.92 (br s, 12 H, HCCH_3 and ROCCH_3), 3.94 (m, 2 H, C_4 and $C_{4'}$ H), 4.06 (br s, 2 H, C_6 and $C_{6'}$ H), 6.25 (m, 2 H, β-furyl H), 7.30 (m, 4 H, α-furyl H); nmr (C_6H_6) 0.83 (6 H, m, HCCH_3), 1.14 (s, 6 H, ROCCH_3), 3.90 (m, 2 H, C_4 and $C_{4'}$ H), 4.28 (br s, 1 H, C_6 or $C_{6'}$ H), 4.40 (br s, 1 H, $C_{6'}$ or C_6 H); nmr (100 MHz, CCl_4) 0.87 (m, 12 H, HCCH_3 and ROCCH_3); δ 3.59 (q, *J* = 2 and 6 Hz, 1 H, C_4 or $C_{4'}$ H), 3.68 (q, *J* = 2 and 6 Hz, 1 H, $C_{4'}$ or C_4H), 3.86 (br s, 2 H, C_6 and $C_{6'}$ H), 6.06 (br s, 2 H, β-furyl H), 7.06 (br s, 2 H, α-furyl H), 7.19 (m, 2 H, α-furyl H); mass spectrum *m/e* (% rel intensity) 493 (0.5), 248 (2), 247 (0.8), 246 (2), 233 (1), 232 (17), 231 (100), 230 (3), 216 (2), 204 (1), 176 (0.5), 136 (2), 107 (2), 96 (5), 95 (2), 94 (6), 81 (2); high-resolution mass spectrum obsd/calcd (formula), 493.3106/493.3066 ($C_{30}H_{41}N_2O_4$), 248.1646/248.1650 ($C_{15}H_{22}NO_2$), 231.1643/231.1623 ($C_{15}H_{21}NO$); isobutane chemically induced mass spectra *m/e* (% rel intensity formula) 551 (14, M + $C_4H_9^+$), 495 (16, M + H^+), 369 (2), 355 (4), 304 (7), 248 (100), 232 (4), 231 (3), 230 (5); ORD (*c* 246 mg/100 ml, hexane, *l* = 0.1 dm) $[\Phi]_{400}$ −965°, $[\Phi]_{350}$ −1190°, $[\Phi]_{300}$ −1480°, $[\Phi]_{284}$ −1520°, $[\Phi]_{244}$ −1400°, $[\Phi]_{240}$ −1510°, $[\Phi]_{231}$ −3860°, $[\Phi]_{230}$ −2750°.

Anal. Calcd for $C_{30}H_{42}N_2O_4$: C, 72.85; H, 8.56; N, 5.67. Found: C, 72.77; H, 8.60; N, 5.69.

An 8-mg sample of the dimer was treated at 25° with 1.7 ml of aqueous $HClO_4$ and sufficient acetone to obtain a homogeneous solution. The solvents were removed by vacuum evaporation and the residue was recrystallized from acetone to obtain a crystalline solid: decomposition point 235° with no melting; ir (KBr) 5.9 μ; mass spectrum (% rel intensity) 248 (17), 247 (15), 232 (50), 231 (62), 219 (15), 204 (100), 176 (27), 107 (27), 94 (98).

As determined by alumina tlc (CH_2Cl_2–Et_2O (13:2)), elution fraction 4 contained the 6,7α-diol (R_f 0.47) and the 6,7β-diol (R_f 0.07). Elution fraction 5 (mp 60–65°) contained the 6,7β-diol (R_f 0.07) and the dimer of 6,7β-oxidodeoxynupharidine (R_f 0.92).

Air Oxidation of Δ⁶-Dehydrodeoxynupharidine. A solution of 72 mg of the Δ⁶-enamine in 10 ml of ether was stirred at 25° for 5 days. Evaporation of the solvent left a brown oil which on tlc (alumina G F_{254}, 10% Et_2O in hexane) gave R_f 0.77 (6,7β-oxido dimer), R_f 0.33 (6,7α-diol), and R_f 0.0. The brown oil in 2% MeOH in Et_2O solution was filtered through 2 g of alumina (activity III). Evaporation of the solvent from the filtrate gave 49 mg of residue which was dissolved in 20 ml of MeOH and treated with 100 mg of $NaBH_4$ for 26 hr at 25°. Water (10 ml) was added and the bulk of the MeOH was removed at the rotary evaporator. The aqueous mixture was extracted with CH_2Cl_2 and the extract washed with 0.20 *N* aqueous HCl. The aqueous solution was basified with 5 ml of 2 *N* NaOH and extracted with CH_2Cl_2. The CH_2Cl_2 extract was dried (Na_2SO_4). Evaporation of solvent and elution chromatography of the residue on 3 g of alumina (activity III) with C_6H_6 left 2.7 mg of a mixture of two bases: tlc (alumina GF_{254}, CH_2Cl_2–MeOH (150:1)) R_f 0.57 (deoxynupharidin-7β-ol) and 0.86 (7-epideoxynupharidin-7α-ol); ir (CCl_4) 2.83, 3.6, and 11.45 μ; mass spectrum *m/e* (% rel intensity) 249 (26) (M^+), 232 (3), 231 (5), 230 (2), 206 (12), 178 (22), 136 (51), 114 (82), 107 (27), 94 (100); glc (10% SE-30 silicone rubber, 6 ft × 1/8 in., 175°) 7.3 (7-epideoxynupharidin-7α-ol) and 8.4 min (deoxynupharidin-7β-ol); glc (10% Carbowax 20 M, 6 ft × 1/8 in., 220°) 3.3 (7-epideoxynupharidin-7α-ol) and 6.1 min (deoxynupharidin-7β-ol).

Dimer of 6,7α-Oxidodeoxynupharidine from 7-Epideoxynupharidine-6,7α-diol. An 18-mg sample of the 6,7α-diol in dry benzene was heated to reflux under nitrogen for 2 days with azeotropic removal of the water. Vacuum evaporation of the solvent gave 18 mg of the dimer: mp 176–177°; $[\alpha]^{25}_{546}$ +9.6° (*c* 0.54 g/100 ml, $CHCl_3$); $[\alpha]^{25}_{588}$ +3.1° (*c* 0.54 g/100 ml, $CHCl_3$,); ir ($CHCl_3$), OH absent, 6.24 (w), 6.69 (m), 8.51 (s), 8.73 (s), 9.11 (m), 9.41 (s), 9.7 (m), 9.82 (s), 10.08 (s), 10.2 (s), 11.47 (s, sp); nmr ($CDCl_3$) δ 0.71 (s, 6 H, ROCCH_3), 4.79 (s, 6 H, C_6 and $C_{6'}$ H), 6.27 (br s, 2 H, β-furyl H), 7.23 (m, 2 H, α-furyl), 7.37 (m, 2 H, α-furyl); nmr (C_6H_6) 0.79 (d, *J* = 6 Hz, 6 H, HCCH_3), 0.92 (s, 6 H, ROCCH_3), 3.75 (d of m, *J* = 12 Hz, 2 H, C_4 and $C_{4'}$ H), 4.04 (s, 2 H, C_6 and $C_{6'}$ H); mass spectrum *m/e* (% rel intensity) 493 (0.2), 248 (2), 257 (2), 246 (1), 233 (2), 232 (17), 231 (100), 230 (3), 219 (2), 218 (1), 216 (3), 204 (5), 176 (3), 136 (1), 107 (2), 97 (1), 96 (5), 95 (2), 94 (8), 81 (2); high-resolution mass spectrum calcd/obsd (formula), 248.1677/248.1650 ($C_{15}H_{22}NO_2$), 231.1631/231.1623 ($C_{15}H_{21}NO$); isobutane chemically induced mass spectrum *m/e* (% rel intensity, formula) 551 (20, M + $C_4H_9^+$), 495 (30, M + H^+), 304 (35), 248 (100), 232 (8), 231 (5), 230 (4); ORD (*c* 263 mg/100 ml, hexane, *l* = 0.1 dm) $[\Phi]_{400}$ + 188°, $[\Phi]_{350}$ +188°, $[\Phi]_{300}$ +70°, $[\Phi]_{293}$ 0°, $[\Phi]_{250}$ −1245°, $[\Phi]_{230}$ −3240°, $[\Phi]_{225}$ −4390°, $[\Phi]_{221}$ −3480°.

Detection of the Mixed Dimer. One milligram each of 6,7β-oxidodeoxynupharidine dimer and 7-epideoxynupharidine-6,7α-diol in 20 ml of methanol was treated with 2 ml of 0.12 *N* aqueous HCl. The methanol was evaporated, the resulting aqueous mixture was saturated with NaCl, and the pH was adjusted to 12 with aqueous NaOH and extracted with CH_2Cl_2. The CH_2Cl_2 extract was dried (Na_2SO_4) and the solvent was evaporated. The residue (2.4 mg) was stored in the refrigerator for 4 days. Tlc (silica gel on a microscope slide, $GF_{254-366}$, twice developed with CH_3CN–benzene (1:5)) showed R_f 0.0, 0.68, and 0.85, (alumina GF_{254}, 1.8% CH_3CN–hexane) R_f 0.0, 0.48, and 0.58, the first two spots having R_f values identical with the R_f values of 7-epideoxynupharidine-6,7α-diol and 6,7β-oxidodeoxynupharidine dimer, respectively. Material corresponding to R_f 0.48 was extracted from the alumina and was reduced with $NaBH_4$ in 10 drops of MeOH at 25° for 30 min. The solvent was evaporated and the residue was extracted to obtain a residue: tlc (alumina GF_{254}, CH_2Cl_2–MeOH (15:1.0)) R_f 0.40, identical with the R_f of deoxynupharidin-7β-ol and different from 7-epideoxynupharidin-7α-ol (R_f 0.55).

Material corresponding to R_f 0.58 on the original plate was extracted from the alumina and was reduced with $NaBH_4$ in the manner described above to obtain a residue: tlc (alumina GF_{254}, on a microscope slide, CH_2Cl_2–MeOH (15:0.1)) R_f 0.40 and 0.55 and identical with R_f values of deoxynupharidin-7β-ol and epideoxynupharidin-7α-ol, respectively.

Next the original plate was developed with CH_2Cl_2–Et_2O (15:2). The R_f 0.0 present originally was absent and R_f 0.37 appeared. The latter spot was identical with the R_f value of 7-epideoxynupharidine-6,7α-diol. Tlc of 6,7α-oxido-7-epideoxynupharidine dimer also gave R_f 0.37 under the same conditions.

7-Epideoxynupharidin-7α-ol from 7-Epideoxynupharidine-6,7α-diol. A 110-mg sample of the 6,7α-diol in 10 ml of MeOH was treated with 300 mg of $NaBH_4$ for 10 hr. The MeOH was evaporated and the residue was mixed with water and the mixture was extracted with CH_2Cl_2. The combined CH_2Cl_2 extract was dried. Evaporation of CH_2Cl_2 gave 91 mg of oil which was eluted from neutral alumina (5 g, activity III) with benzene to obtain 75 mg of 7-epideoxynupharidin-7α-ol: mp 35–37°; $[\alpha]^{25}D$ −105° (*c* 0.62 g/100 ml, 95% EtOH); ir (CH_2Cl_2) 2.86 (s), 3.6–3.8 (w), 6.24 (w), 6.64 (m), 7.14 (m), 8.22 (m), 7.33 (m), 7.48 (m), 7.52 (m), 8.62 (s), 8.84 (s), 11.49 (s), 12.6 μ (br, s); ir (CCl_4, 0.21 *M*) 3520 cm^{-1}; ir (CCl_4, 0.01 *M*) 3520 cm^{-1}; nmr ($CDCl_3$) δ 0.99 (d, *J* = 6 Hz, HCCH_3), 1.02 (s, 6 H with 0.99, HOCCH_3), 2.70 (q, *J* = 11.5 and 2.5 Hz, 1 H, C_6 equatorial H), 3.07 (q, *J* = 5 and 7.5 Hz, C_4 H), 6.38 (br s, 1 H, β-furyl H), 7.36 (m, 2 H, α-furryl H); mass spectrum *m/e* (% rel intensity) 249 (M^+, 45), 248 (14), 234 (8), 232 (6), 220 (13), 206 (29), 194 (7), 178 (32), 164 (10), 148 (12), 136 (60), 121 (12), 114 (80), 107 (29), 96 (31), 94 (100), 81 (28).

Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 72.44; H, 9.29; N, 5.50.

Deoxynupharidin-7β-ol from Deoxynupharidine-6,7β-diol and 6,7β-Oxidodeoxynupharidine Dimer. Elution fraction 5 (20 mg; see the last paragraph of the subsection dealing with the OsO_4 oxidation for fraction identification) in 1 ml of EtOH was treated with 20 ml of $NaBH_4$ at 60° for 3 hr. Alumina tlc (CH_2Cl_2–Et_2O (13:2)) showed two spots (R_f 0.6 and 0.8). Vacuum evaporation of solvent gave a residue which was mixed with water. The mixture was extracted with CH_2Cl_2 and the combined extracts were dried. Vacuum evaporation of the solvent left 22 mg of residue which was eluted from 3 g of neutral alumina (activity III) with four 20-ml portions of *n*-hexane, to obtain fractions 1 (2.3 mg), 2 (1.9 mg), 3 (0.2 mg), and 4 (0 mg). Continued elution with 40 ml of CH_2Cl_2–20% Et_2O gave 12.2 mg of deoxynupharidin-7β-ol, mp 99–100°. Rechromatography in the manner described gave the 7β-ol: mp 101.5–102.5°; $[\alpha]^{25}D$ −120° (*c* 0.635 g/100 ml, 95% EtOH); ir (CCl_4, 0.204 *M*) 3610 (free OH), 3520–3300 cm^{-1} (bonded OH); ir (CCl_4, 0.01 *M*) 3610 (free OH), 3520–3300 cm^{-1} absent; ir and nmr were identical with spectra of the sample obtained from $LiAlH_4$ and $NaBH_4$ reduction of residue A; mass spectrum *m/e* (% rel intensity) 249 (M^+, 59), 248 (16), 234 (8), 232 (11), 220 (10), 206 (13), 194 (5), 178 (28), 164 (7), 148 (7), 126 (74), 121 (8), 114 (100), 107 (23), 96 (27), 94 (90), 81 (22); high-resolution mass spectrum [obsd (calcd), (formula)] 249.1720 (249.1729) ($C_{15}H_{23}NO_2$), 136.0885 (136.0888) ($C_8H_{12}O$), 114.0921 (114,0919) ($C_6H_{11}NO$), 107.0495 (107.0497) (C_7H_7O), 96.0808 (96.0813) ($C_6H_{10}N$), 94.0415 (94.0419) (C_6H_6O).

Anal. Calcd for $C_{15}H_{23}NO_2$: C, 72.25; H, 9.30; N, 5.62. Found: C, 72.09; H, 9.23; N, 5.44.