2-(3-Indolyl)propan-1-ol (V). A.—Racemic V was prepared by lithium aluminum hydride reduction of methyl α-(3-indolyl)-propionate (prepared from (±)-VI and diazomethane) in tetrahydrofuran. Work-up gave (±)-V as a pink, viscous oil, bp 155° (0.1 mm). The *p*-nitrobenzoate melted at 117°.

Anal. Calc for $C_{18}H_{16}N_2O_4$: C, 66.65; H, 4.97; N, 8.64. Found: C, 66.66; H, 5.05; N, 8.59.

B.—A solution of 3.7 g of (+)-VI in tetrahydrofuran was reduced with 40 ml of a 1 *M* solution of diborane in tetrahydrofuran at room temperature for 2.5 hr. The mixture was poured onto ice and saturated with salt. The organic layer was washed with 5% sodium bicarbonate, dried, and distilled, yielding (+)-2-(3-indolyl)propan-1-ol:[17] bp 135° (0.1 mm); lit.[17] bp 145° (0.15 mm), $[\alpha]^{22}D$ +28.1° (*c* 2.5, CH_3OH).

C.—Following the procedure of Schach von Wittenau and Els,[3] 120 mg of (+)-α-indolmycenic acid, $[\alpha]D$ +7.8°, was reduced with lithium aluminum hydride in ether, and the resulting glycol (III) cleaved with sodium periodate. The crude α-(3-indolyl)-propionaldehyde(IV) showed carbonyl absorption at 1720 cm^{-1}. The aldehyde was not further characterized, but reduced directly with lithium aluminum hydride in ether. After the usual work-up, 55 mg of (+)-V was obtained, $[\alpha]^{25}D$ +20° (*c* 2.7, CH_3OH), which showed tlc behavior and infrared spectra identical with those of the alcohol obtained in parts A and B. The alcohols from both parts B and C showed plain positive ORD curves from 300–600 nm.

(17) R. A. Robinson, U. S. Patent 2,908,691; *Chem. Abstr.*, **56**, 3455 (1962).

Registry No.—(+)-II, 25834-21-3; (±)-V, 25834-22-4; (±)-V *p*-nitrobenzoate, 25834-23-5; (−)-VIII, 25834-24-6; (−)-VIII Ag salt, 25834-25-7; indolmycin, 23369-88-2.

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Synthesis of D-Dihydrosphingosine[1]

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A stereospecific synthesis of D-dihydrosphingosine is recorded. The reaction of 6-benzyloxycarbonylamino-2,2-dimethyl-5-formyl-3a,5,6,6a-tetrahydro-D-ribofuro[2,3-*d*]dioxolane (**6**), prepared in three steps from 3-amino-3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-allofuranose (**3**), with the Wittig reagent, prepared from tetradecyltriphenylphosphonium bromide (**2**) is described. The product, a mixture of cis and trans olefins (**8**), was deacetonated, and the resulting glycol was cleaved with sodium metaperiodate and then reduced with sodium borohydride to give crystalline 2-benzyloxycarbonylamino-D-*erythro*-Δ⁴-octadecene-1,3-diol (**11**). Hydrogenation of **11** over palladium on charcoal reductively deblocked the amine and saturated the olefin to give D-dihydrosphingosine (**12**).

D-Sphingosine (2-amino-1,3-dihydroxy-D-*erythro*-octadec-4-ene) and D-dihydrosphingosine (2-amino-1,3-dihydroxy-D-*erythro*-octadecane) are bases which serve as the backbone for the structures of cerebrosides, gangliosides, sphingomyelin, etc. Abnormal amounts of cerebroside derivatives have been observed in leukodystrophy,[2] Niemann–Pick and Tay–Sachs diseases,[3] etc. Unusual concentrations of sphingomyelin have been found in cataracts.[4]

Evidence is accumulating that sphingosine and dihydrosphingosine derivatives can act as prophylactics against certain laboratory induced diseases in animals. Thus intradermal injections containing cerebrosides offered significant protection against experimental allergic encephalomyelitis in rabbits.[5] Injection of ganglioside–cerebroside complexes offered relief from the symptoms of tetanus toxin in mice.[6] The suggestion was made[6] that such a technique might be of prophylactic value in human tetanus.

Biochemical studies using sphingosine derivatives isolated from natural sources were made difficult by the questionable purity of such materials. The syntheses of sphingosine[7] and dihydrosphingosine[8] reported have inevitably led to racemic mixtures which must then be resolved in order to obtain the desired optically active material.

Carbohydrates offer a wide assortment of extensively functionalized starting materials with known absolute configuration. By the attachment of a long alkyl chain to the appropriate amino sugar, the synthesis of optically pure sphingosine derivatives and analogs becomes a relatively simple procedure. A series of papers by Gigg, *et al.*,[9] describes the use of a Wittig condensation of an amino sugar derived from glucosamine with the ylide prepared from triphenylphosphine and tridecyl bromide to give D-phytosphingosine(4-hydroxydihydrosphingosine). The absence of a double bond in phytosphingosine circumvented the problem of cis *vs.* trans isomers of the Wittig product. For this same reason, the synthesis of D-dihydrosphingosine by a Wittig condensation was investigated initially and is reported here.

A logical starting material for the synthesis of D-dihydrosphingosine (and D-sphingosine) is the readily available 3-amino-3-deoxy-1,2:5,6-di-O-isopropylidene-

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(1) This investigation was supported by Public Health Service Research Grant No. NS-07776 from the National Institute of Neurological Diseases and Stroke.

(2) M. Sakai and T. Tano, *Yokohama Med. Bull.*, **16**, 57 (1965); *Chem. Abstr.*, **63**, 16935*h* (1965).

(3) G. Rouser, G. Feldman, and C. Galli, *J. Amer. Oil Chem. Soc.*, **42**, 411 (1965).

(4) G. L. Feldman and L. S. Feldman, *Invest. Ophthalmol.*, **4**, 162 (1965).

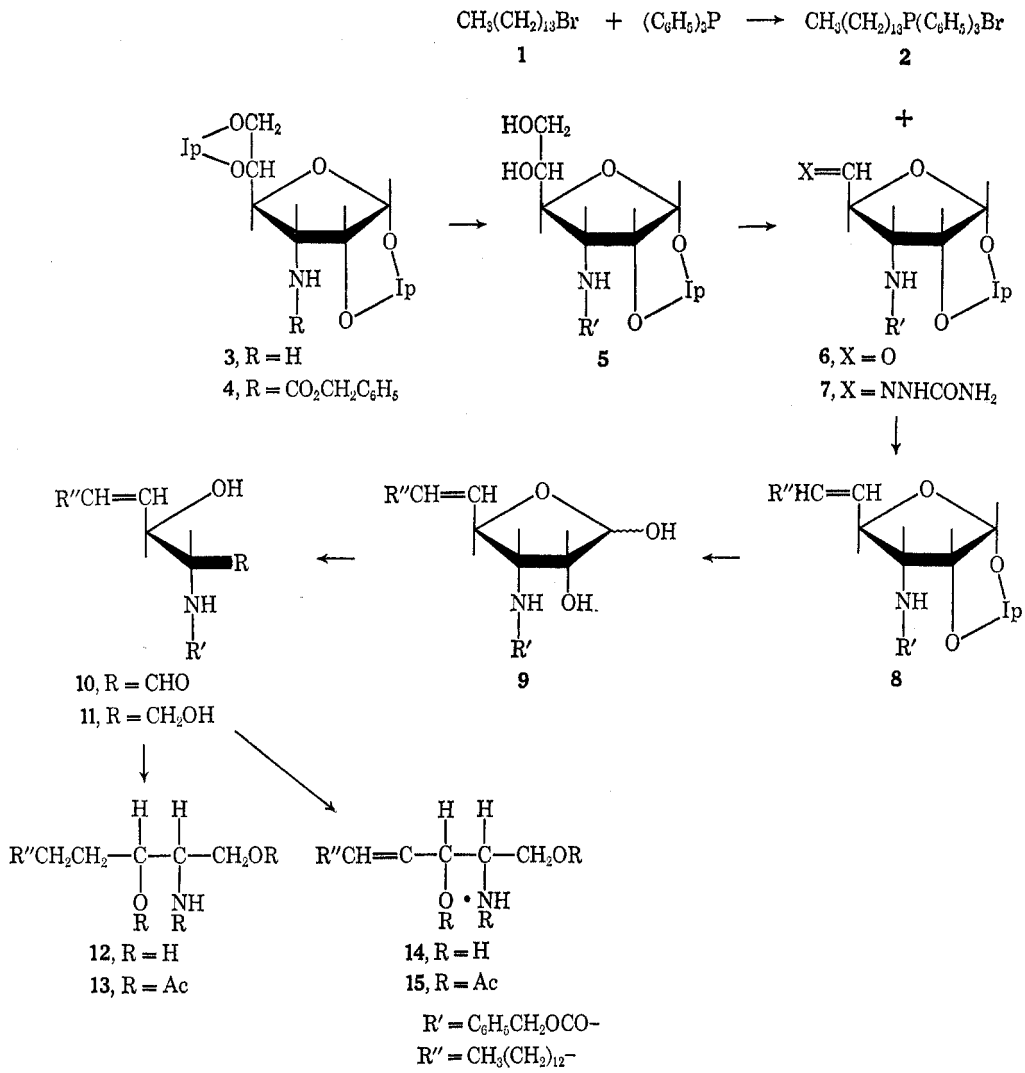
(5) B. Niedieck and U. Kuck, *Z. Immunitaetsforsch. Allerg. Klin. Immunol.*, **133**, 43 (1967).

(6) J. Mellanby, H. Mellanby, D. Pope, and W. E. Van Heyningen, *J. Gen. Microbiol.*, **54**, 161 (1969).

(7) (a) C. A. Grob and F. Gadient, *Helv. Chim. Acta*, **40**, 1145 (1957); (b) D. Shapiro, H. Segal, and H. M. Flowers, *J. Amer. Chem. Soc.*, **80**, 1194 (1958).

(8) (a) E. N. Zoonkova, K. I. Eller, V. I. Tsetlin, B. I. Mitsner, and N. A. Preobrazhenskii, *Zh. Org. Khim.*, **2**, 2184 (1966); (b) W. Stoffel, and G. Sticht, *Hoppe-Seyler's Z. Physiol. Chem.*, **348**, 1561 (1967).

(9) J. Gigg, R. Gigg, and C. D. Warren, *J. Chem. Soc.*, 1872 (1966), and subsequent papers.



α-D-allofuranose (**3**),[10] because the degradative removal of carbons 1 and 6 results in a 4-carbon fragment with the necessary functional groups in the desired D-erythro configuration. The amine function of **3** was blocked by a reaction with benzyl chloroformate in pyridine to give 3-benzyloxycarbonylamino-3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-allofuranose (**4**). Selective removal of the 5,6-isopropylidene group using aqueous acetic acid gave 3-benzyloxycarbonylamino-3-deoxy-1,2-O-isopropylidene-α-D-allofuranose (**5**) as a syrup. Cleavage of the glycol of **5** by means of sodium metaperiodate yielded 6-benzyloxycarbonylamino-2,2-dimethyl-5-formyl-3a,5,6,6a-tetrahydro-D-ribofuro[2,3-*d*]dioxolane (**6**) as an oil, characterized as the crystalline semicarbazone (**7**).

The Wittig reagent necessary for the condensation was prepared starting from the reaction of tetradecyl bromide (**1**) with triphenylphosphine to give crystalline tetradecyltriphenylphosphonium bromide (**2**). Treatment of **2** with 1 mol equiv of phenyllithium in ether–hexane generated the Wittig reagent. To this was added a solution of the aldehyde **6** in dry benzene and the reaction was refluxed for 21 hr to give, on work-up and chromatographic purification, a 30% yield of 6-benzyloxycarbonylamino-2,2-dimethyl-5-(1-pentadecenyl)-3a,5,6,6a-tetrahydro-D-ribofuro[2,3-*d*]dioxolane (**8**) of the mixed cis and trans configuration from which the cis isomer could be isolated pure by crystallization. The cis assignment was based on the fact that the infrared spectrum of the recrystallized Wittig product showed no absorption band at 10.3 μ.[11] It was not necessary to separate the cis from trans isomers, since the final hydrogenation would convert both to dihydrosphingosine (**12**)

Deacetonation of the mixed cis–trans olefin, **8**, using aqueous acetic acid gave a quantitative yield of 1,2 diol (**9**). Treatment of **9** with sodium metaperiodate cleaved the 1,2-glycol. Sodium borohydride reduction of the resulting aldehyde (**10**) gave crystalline 2-benzyloxycarbonylamino-D-*erythro*-Δ⁴-octadecene-1,3-diol (**11**). Hydrogenation of **11** using 10% palladium on charcoal yielded crystalline D-dihydrosphingosine (**12**), which was characterized as its sulfate. Acetylation of **12** using acetic anhydride in pyridine gave a crystalline triacetate (**13**) which had the same melting point, infrared spectrum, and optical rotation as a sample of D-dihydrosphingosine triacetate which was prepared from commercially available D-sphingosine. The mixture melting point of the two samples of triacetate showed no depression. This synthesis represents a more direct proof of structure by synthesis of dihydrosphingosine. The previous proof by synthesis de-

(10) (a) K. Freudenberg and F. Brauns, *Ber.*, **55**, 3233 (1922); (b) M. L. Wolfrom, F. Shafizadeh, and R. K. Armstrong, *J. Amer. Chem. Soc.*, **80**, 4885 (1958).

(11) L. J. Bellamy, "The Infrared Spectra of Complex Molecules," Wiley, New York, N. Y., 1954, p 31.

scribed by Gigg and coworkers[9] was indirect, in that they synthesized phytosphingosine and demonstrated the identity of their synthetic product with that of phytosphingosine prepared from naturally occurring sphingosine.

It is interesting to note that the Wittig reaction between the aldehyde (6) and the ylide derived from the phosphonium bromide (2) gave an olefin (8) which appeared to be a mixture of cis and trans isomers with the cis isomer predominant. There was undoubtedly a significant amount of the trans isomer, since the infrared spectrum of the material obtained after chromatography showed significant absorption at 10.3 μ. In the recrystallized samples of 8, this absorption was absent, hence the cis assignment.

For this synthesis to be useful in the synthesis of D-sphingosine, the Wittig reaction conditions must be altered so that the trans isomer of 8 will predominate. This aspect is currently under investigation.

Experimental Section[12]

3-Benzyloxycarbonylamino-3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-allofuranose (4).—A solution of 8.0 g (31 mmol) of 3-amino-3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-allofuranose (3)[10] in 130 ml of dry pyridine was cooled to 0° under nitrogen, and then 21.8 ml (124 mmol) of benzyl chloroformate was added dropwise with stirring and continued cooling. The mixture was stored at 0–5° for 18 hr, and then 4 ml of water was added dropwise with stirring to decompose the excess benzyl chloroformate. After *ca.* 0.5 hr at room temperature, the mixture was partitioned between 200 ml each of chloroform and saturated aqueous sodium bicarbonate. The layers were separated and the aqueous fraction was extracted with two additional portions of chloroform. The chloroform extracts were washed with water, combined, dried, and evaporated to dryness *in vacuo* to give 20.6 g of brown oil.

The oil was extracted with 100 ml of boiling cyclohexane. The cyclohexane solution was decanted and cooled to give 7.8 g (64%) of product as white crystals, mp 74–76°. The thin layer chromatography showed one spot at R_f 0.87 using solvent A. Recrystallization from 20 ml of cyclohexane gave the analytically pure product: mp 74–76°; λ_{max}^{Nujol} 5.80 (C=O), 8.60 μ (gem dimethyl); $[\alpha]^{20}D$ +55° (*c* 0.49, chloroform).

Anal. Calcd for $C_{20}H_{27}O_7N$: C, 61.1; H, 6.92; N, 3.56. Found: C, 61.1; H, 6.79; N, 3.54.

6-Benzyloxycarbonylamino-2,2-dimethyl-5-formyl-3a,5,6,6a-tetrahydro-D-ribofuro[2,3-*d*]dioxolane (6).—A solution of 5.9 g of 3-benzyloxycarbonylamino-3-deoxy-1,2:5,6-di-O-isopropylidene-α-D-allofuranose (4) in 145 ml of 75% aqueous acetic acid was heated at 60° under a nitrogen atmosphere for 20 min and then was cooled to −10° in an ice–salt bath. A solution of 5 *N* aqueous sodium hydroxide was added dropwise with vigorous stirring until pH 7 was obtained, and then the mixture was extracted with three 100-ml portions of chloroform. The combined chloroform extracts were washed with water, dried, and evaporated to dryness *in vacuo* to give a quantitative yield of 3-benzyloxycarbonylamino-3-deoxy-1,2-O-isopropylidene-α-D-allofuranose (5) as a colorless oil.

Thin layer chromatography showed one spot with R_f 0.30 and 0.19 in solvents A and B, respectively.

A stirred solution of 5.6 g (16 mmol) of 5,6-diol (5) in 85 ml of 50% aqueous methanol was treated with 3.45 g (16 mmol) of sodium metaperiodate under a nitrogen atmosphere. The reaction was stirred at room temperature for 1 hr by which time a white precipitate had separated. The reaction was filtered and the filtrate was extracted with three 200-ml portions of chloroform. The chloroform layers were washed with water, and then dried and evaporated to dryness *in vacuo* to give a quantitative yield of product 6 as a colorless oil: λ_{max}^{film} 5.85 (C=O), 8.60 μ (gem dimethyl).

Thin layer chromatography using solvent B showed one spot at R_f 0.37.

The semicarbazone 7 prepared by the procedure of Shriner and Fuson,[13] was recrystallized from ethanol and had mp 197–198°, $[\alpha]^{22}D$ +59° (*c* 0.50, methanol).

Anal. Calcd for $C_{17}H_{23}N_4O_6$: C, 54.0; H, 5.86; N, 14.8. Found: C, 54.3; H, 5.97; N, 14.7.

Tetradecyltriphenylphosphonium Bromide.—A mixture of 10.0 g (0.36 mol) of 1-bromotetradecane and 9.5 g (0.36 mol) of triphenylphosphine was heated at 140° under a nitrogen atmosphere for 5 hr. The reaction formed a solid gel when it was cooled. The gel was dissolved in 50 ml of dried (over molecular sieves) acetone and 120 ml of dry diethyl ether was added. The solution was cooled at 0° and then filtered to give 15.3 g (78%) of product (2) as white crystals, mp 91–94°. The analytical sample was prepared by recrystallization from acetone–ether to give white crystals with mp 94–96°.

Anal. Calcd for $C_{32}H_{44}BrP$: C, 71.2; H, 8.22; Br, 14.8. Found: C, 71.5; H, 8.36; Br, 14.7.

6-Benzyloxycarbonylamino-2,2-dimethyl-5-(1-pentadecenyl)-3a,5,6,6a-tetrahydro-D-ribofuro[2,3-*d*]dioxolane (8).—To a stirred solution of 9.44 g (17.5 mmol) of tetradecyltriphenylphosphonium bromide in 625 ml of dry benzene under a nitrogen atmosphere was added 8.93 ml of phenyllithium solution (17.6 mmol). The mixture was stirred for 10 min, and then a solution of 5.2 g (16.2 mmol) of fresly prepared aldehyde 6 in 50 ml of dry benzene was added. The reaction was heated at reflux for 21 hr, and then the benzene was evaporated to dryness *in vacuo* to yield 19.9 g of residue as a brown oil. Thin layer chromatography (solvent B) showed no trace of aldehyde (6) and the oil gave a negative test for reducing sugar using Benedict's reagent.

The residue was dissolved in 10 ml of dry benzene and was applied to a column which contained 143 g of silica gel. The column was developed with 275 ml of benzene and then 1000 ml of 10% diethyl ether in benzene. The ether–benzene fraction was evaporated to dryness *in vacuo* to give 2.4 g (30%) of product (8) as an oil which crystallized on standing and was satisfactory for the next step.

Thin layer chromatography using solvent C showed two spots at R_f 0.75 and 0.70, presumably the cis and trans isomers of 8: λ_{max}^{film} 5.85 (carbonyl), 6.65 (amide II), 8.6 (gem dimethyl), 10.3 μ (weak, trans-disubstituted olefin).

Recrystallization of the crystalline mixture from 30 ml of methanol gave 444 mg of product, mp 72–73°, which was homogeneous on thin layer chromatography in solvent C with R_f 0.75: λ_{max}^{Nujol} 5.85 (carbonyl), 6.6 (amide II), 8.6 μ (gem dimethyl).

The absence of infrared absorption at 10.3 μ is consistent with the assignment of a cis configuration, $[\alpha]^{20}D$ −4° (*c* 0.48, chloroform).

Anal. Calcd for $C_{30}H_{47}NO_6$: C, 71.8; H, 9.44; N, 2.79. Found: C, 72.1; H, 9.46; N, 2.89.

2-Benzyloxycarbonylamino-D-*erythro*-Δ⁴-octadecene-1,3-diol (11).—A solution of 2.0 g of mixed cis–trans isomers (8) in 100 ml of 80% aqueous acetic acid was heated at reflux under a nitrogen atmosphere for 3 hr. The solution was evaporated to dryness *in vacuo* to give 1.68 g of crude diol 9 as a brown oil. Thin layer chromatogaphy in solvent C showed no trace of starting material.

To a solution of the above diol (1.68 g, *ca.* 3.64 mmol) in 400 ml of methanol under a nitrogen atmosphere was added 1.07 g (5.0 mmol) of sodium metaperiodate. The mixture was stirred at room temperature for 16 hr and then was filtered. The filter cake was washed with methanol and the combined filtrate and washings were evaporated to dryness *in vacuo*. The residue was partitioned between chloroform and water. The chloroform extract was washed with water, dried, and evaporated to dryness *in vacuo* to give a 100% yield of the aldehyde 10 as an oil.

A solution of 1.25 g (2.9 mmol) of the above aldehyde (10) in 180 ml of methanol was cooled to 0° under a nitrogen atmosphere, and then a solution of 109 mg (2.9 mmol) of sodium borohydride in 60 ml of methanol was added dropwise with stirring. The reaction was stirred for 16 hr and then was evaporated to dryness *in vacuo* to yield a brown oily residue which was partitioned be-

(12) Melting points are corrected. Organic solutions were dried using anhydrous magnesium sulfate. Thin layer chromatograms were run on silica gel HF (E. Merck A. G. Darmstadt). Spots were detected using iodine vapor. Solvent systems used for developing the chromatograms were: A, ethyl acetate–diethyl ether (1:3); B, ethyl acetate–chloroform (1:1); C, 10% diethyl ether in benzene; D, 10% benzene in ether. Silica gel chromatography was carried out using Gallard Schlesinger reagent grade silica gel (90–200 mesh).

(13) R. L. Shriner and R. C. Fusion, "The Systematic Identification of Organic Compounds," Wiley, New York, N. Y., 1948, p 170.

tween 200 ml each of water and chloroform. The layers were separated and the aqueous phase was extracted with three additional portions of chloroform. The chloroform layers were washed with water, dried, and evaporated to dryness *in vacuo* to yield 0.98 g of an oil which solidified. Thin layer chromatography in solvent D showed a number of spots with a major one at R_f 0.75.

Trituration of the oil with cold hexane gave 123 mg of product with mp 63–66°, $[\alpha]^{20}D$ −6° (*c* 0.26, chloroform). Thin layer chromatography in solvent D showed one spot at R_f 0.75: λ_{max}^{Nujol} 5.95 (carbonyl), 6.5 (amide II), 10.3 μ (weak, trans-disubstituted olefin).

Anal. Calcd for $C_{26}H_{43}NO_4$: C, 72.0; H, 10.0; N, 3.23. Found: C, 71.8; H, 10.2; N, 3.39.

2-Amino-D-*erythro*-octadecane-1,3-diol (12) (D-Dihydrosphingosine).—A solution of 105 mg (0.24 mmol) of 2-benzyloxycarbonylamino-D-*erythro*-Δ^4-octadecene-1,3-diol (**11**) in 2.7 ml of glacial acetic acid was hydrogenated at atmospheric pressure and room temperature using 68 mg of 10% palladium on charcoal for 20 hr. The hydrogenation mixture was filtered and the filtrate was evaporated to dryness *in vacuo* to yield 82 mg of product as a white solid which was characterized as the sulfate.[14] Recrystallization from glacial acetic acid gave crystals, mp 150° dec, λ_{max}^{Nujol} 6.5 μ (NH).

Anal. Calcd for $C_{36}H_{80}N_2O_8S$: C, 61.7; H, 11.5; N, 4.0. Found: C, 61.7; H, 11.3; N, 4.12.

Lesuk, *et al.*,[14] reported that the sulfate slowly darkened on heating and finally melted at 265° dec. Thus the melting point does not appear to be a reliable criterion for identification.

D-Dihydrosphinogosine Triacetate (13).—Acetylation of crude D-dihydrosphingosine using acetic anhydride in pyridine gave crystals, mp 90–93°, $[\alpha]^{19}D$ +16° (*c* 0.5 in chloroform), which had the same infrared spectrum as authentic dihydrosphingosine triacetate[8b] and which gave no melting point depression when a mixture melting point was determined with a sample of authentic dihydrosphingosine triacetate which had been prepared from commercially available D-sphingosine sulfate. D-dihydrosphingosine triacetate is reported to have mp 98°, $[\alpha]D$ +17° (*c* 1.4, chloroform).[15]

Registry No.—**2**, 25791-20-2; **4**, 25791-21-3; **6**, 25834-61-1; **7**, 25791-22-4; **8**-*cis*, 25791-23-5; **8**-*trans*, 25834-62-2; **11**, 25834-63-3; **12**, 764-22-7; **12** sulfate, 25791-25-7.

(14) A. Lesuk and R. J. Anderson, *J. Biol. Chem.*, **139**, 457 (1941).

(15) C. A. Grob, E. F. Jenny, and H. Utzinger, *Helv. Chim. Acta*, **34**, 2249 (1951).

12α-Etiojerva-1,4-diene-3,17-dione

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Microbiological oxidation of the 12α-pregnajervane **1f** produces the title compound **4a** whose structure was proven unambiguously by an alternate synthesis from the same starting material. This route involves successive Baeyer–Villiger oxidation, oxidation of the 3-hydroxyl group (→ **2e**, R′ = Ac), selenium dioxide oxidation of the A ring (→ **4e**, *R′* = Ac), saponification of the acetate, and oxidation of the resulting 17-hydroxyl group. The stereochemistry of the C-17 substituents is discussed.

Microbiological oxidation of saturated pregnanes has proved a useful method to prepare the corresponding A ring unsaturated derivatives.[1] Since analogous compounds in the 12α-etiojervane series were of interest for biological evaluation, the 12α-pregnajervane[2,3] (**1f**) (R = H) was submitted to bacterial oxidation. The chief product (~30%) was not the dienone **4f** although the desired A ring grouping was present (uv and nmr analysis). An overoxidation (Scheme I) of a type familiar in the pregnanes[1] had occurred, yielding a tetracycle in which the 17-acetyl group had been degraded to the 17 ketone (without epimerization at C-13). The gross structure **4a** was suggested by the presence of a saturated carbonyl band at 5.83 μ and the absence of the acetyl signal near 125 Hz.

Structural confirmation of the fermentation product was accomplished without difficulty since a similar compound, the 17β-hydroxy-1,4-diene (**4e**, R′ = H, 13α-CH_3) had been prepared earlier in the 12α,13α-etiojervane series by an unambiguous chemical synthesis.[3a] Oxidation of the hydroxyl group in the latter compound afforded a material spectrally very similar to the fermentation product, but differing in its optical rotation (+162° *vs.* −86°). The difference between the two compounds, a result of the stereochemistry at C-13, was resolved by treating the less stable 13β-methyl derivative (**4a**) with base, generating the more stable 13α-methyl compound **4b**.[4]

When the activity of the unstable dienone **4a** as an aldosterone-blocking agent was discovered,[5] additional supplies of this compound and its derivatives were required. The moderate yields of the dienedione **4a** from fermentation and the limited success of early attempts to utilize it chemically led to the exploration of its chemical synthesis.

Although the starting ketone **1c** has the 13-methyl in the desired configuration, side chain degradation by Beckmann rearrangement of its oxime, even under carefully controlled conditions, caused epimerization at C-13.[3a] Attempted utilization of this accessible 13α epimer **1b** by hydrogenation of its enol diacetate (Δ^{17}) yielded, after saponification, largely hydrogenolyzed materials containing little of the desired 17β-diol **1e** (R = R′ = H).

Conversion of the unsaturated ketone **1a** (Δ^{12})[3a] to the desired 13β-methyl compound was attempted by hydrogenation over several palladium catalysts; however, the preponderant product in each case was the stable 13α-methyl derivative.[6] Use of platinum catalysts, in an effort to reduce both the olefinic and the car-

(1) W. Charney and H. L. Herzog, "Microbial Transformations of Steroids," Academic Press, New York, N. Y., 1967.

(2) The term "etiojervane" and "pregnajervane" represent 17aβ-methyl-*C*-nor-D-homo-18-nor-5α,13β-androstane and its pregnane analog, respectively. See F. C. Chang and R. C. Ebersole, *Tetrahedron Lett.*, 3521 (1968).

(3) (a) W. F. Johns and I. Laos, *J. Org. Chem.*, **30**, 123 (1965); (b) W. F. Johns, *ibid.*, **29**, 2545 (1964).

(4) A similar epimerization of the 13-methyl group is described in ref 3a.

(5) Private communication from Dr. L. Hofmann of these laboratories. The activities of this and related compounds will be included in a future communication.

(6) A recent communication reports formation of the 13β-methyl derivatives in this way, success apparently a result of the difference in catalysts employed: *cf.* H. Mitsuhashi and N. Kawahara, *Tetrahedron*, **21**, 1215 (1965).