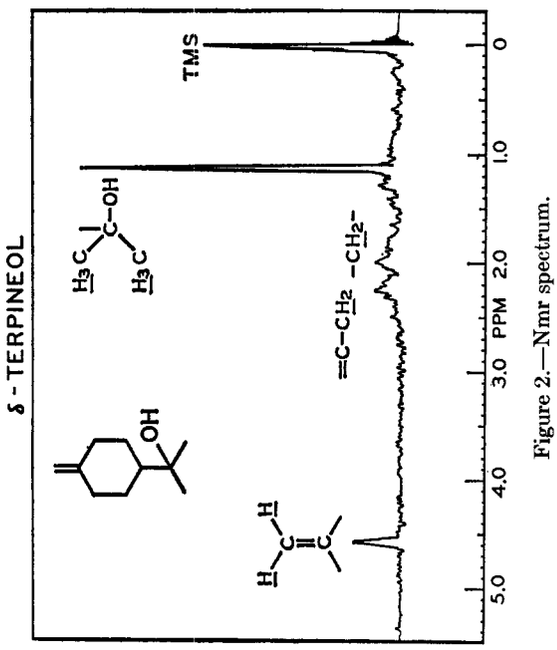

Figure 2.—Nmr spectrum.

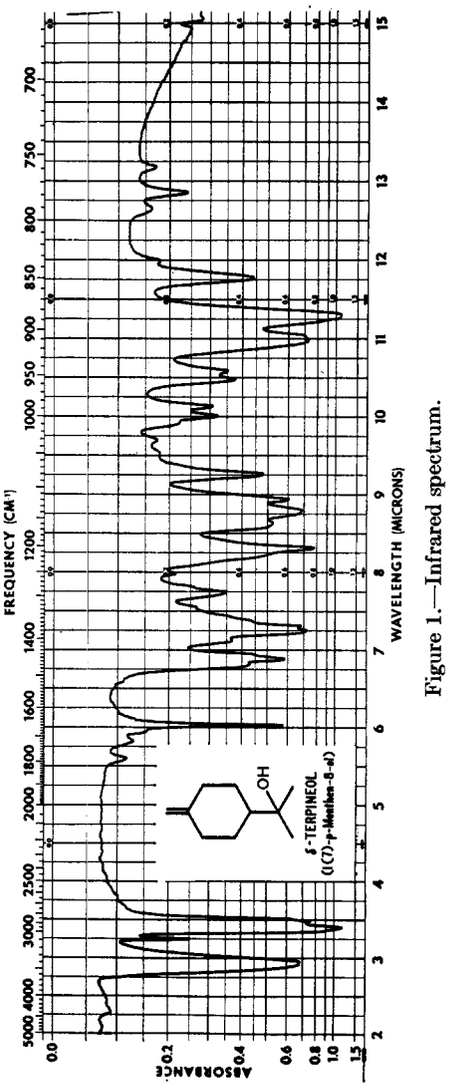

Figure 1.—Infrared spectrum.

Commercial terpineol was examined for Δ-terpineol content using a preparative gas chromatograph fitted with an 8-ft, $^3/_4$-in.-o.d. column containing Carbowax 20M on silane-treated Celite at 155° at a flow rate of 600 ml/min. *Ca.* 50 ml of the sample was passed through using 1-ml injections. That portion of the eluent was trapped where the Δ-terpineol was expected to elute; this is in the area just prior to where *trans*-β-terpineol emerges. *Ca.* 5 ml of material was thus obtained. Repeated injections, using identical experimental parameters, afforded 1 ml of material which, when passed through an 8-ft, $^3/_8$-in.-o.d. column containing 20% Carbowax 20M on silane-treated Celite at 150° with a flow rate of 200 ml/min, afforded 0.1 ml of material. Analysis on a 10-ft, $^1/_4$-in.-o.d., $^3/_{16}$-in.-i.d. column packed with 20% Carbowax 20M on silane-treated Celite at 150° at a flow rate of 60 cc/min gave a small amount of material consisting of *ca.* 60% Δ-terpineol and 40% *trans*-β-terpineol. Since it was fruitless to continue the attempted isolation of pure Δ-terpineol in the presence of β-terpineol, this method of isolating Δ-terpineol was abandoned. Calculations indicate that less than one-half of 1% of Δ-terpineol is present in commercial terpineol.

Pinacol Deamination Rearrangement of Dihydrosphingosine[1]

BENJAMIN WEISS AND RICHARD L. STILLER

Departments of Biochemistry, New York State Psychiatric Institute, and College of Physicians and Surgeons, Columbia University, New York, New York 10032

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The formation of an insoluble precipitate during the degradation of dihydrosphingosine with periodic acid was first observed by Carter and associates[2] in their classical studies of long-chain bases. A similar precipitate was formed when the radioactive long-chain bases from rat brain were degraded with periodate in aqueous methanol.[3] The use of various solvents during the oxidation appeared to have no effect on the formation of this precipitate. It was thought that quantitative degradation of the bases could be achieved if they were converted to the corresponding triols prior to treatment with periodate. The rearrangement of vicinal hydroxyamino compounds upon deamination with nitrous acid has been well documented,[4,5] but the nature and extent of a rearrangement in dihydrosphingosine has not been examined. The nitrite deamination of dihydrosphingosine in glacial acetic acid yielded <10% of 1,2,3-trihydroxyoctadecane. Although it was found, as this investigation was in progress, that dihydrosphingosine was easily degraded by lead tetraacetate in benzene–glacial acetic acid,[6] the study of the deamination of dihydrosphingosine was continued to determine the identity of the compounds formed in this reaction.

The deamination of the base was effected with $NaNO_2$ in glacial acetic acid and the products of the reaction

(1) This investigation was supported in part by Public Health Service Research Grant No. 03191-05 from the National Institute of Neurological Diseases and Blindness.

(2) (a) H. E. Carter, F. J. Glick, W. P. Norris, and G. E. Phillips, *J. Biol. Chem.*, **170**, 285 (1947); (b) H. E. Carter, W. P. Norris, F. J. Glick, G. E. Phillips, and R. Harris, *ibid.*, **170**, 269 (1947).

(3) B. Weiss, *ibid.*, **238**, 1953 (1963).

(4) Y. Pocker, in "Molecular Rearrangements," P. De Mayo, Ed., Interscience Publishers, Inc., New York, N. Y., 1963, Chapter 1.

(5) P. W. Kent, and M. W. Whitehouse, "Biochemistry of the Aminosugars," Academic Press Inc., New York, N. Y., 1955, p 213.

(6) B. Weiss, *Biochemistry*, **4**, 1576 (1965).

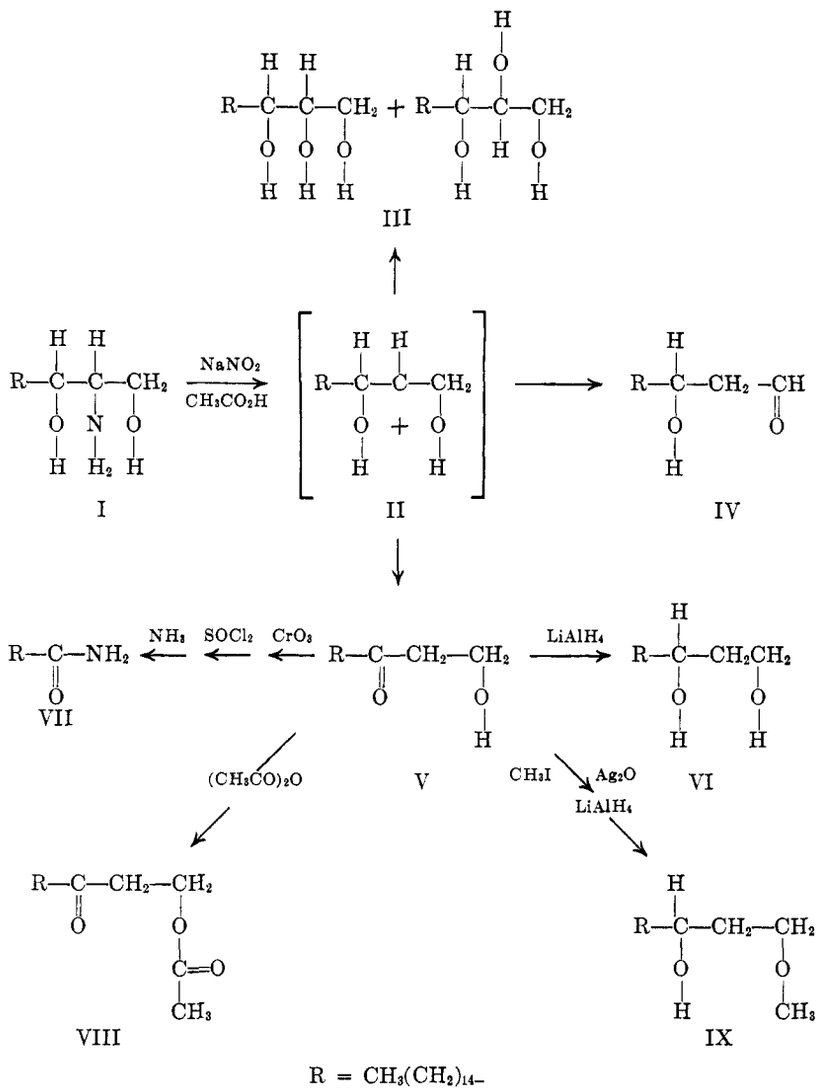

Figure 1.—The nitrite deamination of dihydrosphingosine (I) yielded *ca.* 8% of the mixture of diastereoisomeric 1,2,3-trihydroxyoctadecanes (III). The major product, 1-hydroxy-3-ketooctadecane (V), was accounted for by rearrangement of the carbonium ion intermediate (II). Its structure was proven by the following sequence of reactions: (a) reduction with $LiAlH_4$ to the diol (VI); (b) CrO_3 oxidation to palmitic acid and its identification as the amide (VII); (c) esterification with acetic anhydride (VIII); and (d) methylation and reduction to the hydroxy ether (IX). See text for details.

were separated on a silicic acid column by elution with chloroform–petroleum ether (bp 60–70°) (55:45 v/v) and methanol chloroform (10:90 v/v). The chloroform–petroleum ether eluate yielded the major product of the reaction, 79% (Figure 1, V). It could not be crystallized from a variety of solvents and did not yield a thiosemicarbazone or 2,4-dinitrophenylhydrazone. Reduction with $LiAlH_4$ gave an octadecanediol which was not susceptible to periodate oxidation (Figure 1, VI). Oxidation of compound V with CrO_3 in glacial acetic acid yielded palmitic acid which was identified as the amide (Figure 1, VII). The acetyl ester (Figure 1, VIII) and methyl ether of compound V were essentially unaffected by the CrO_3 treatment. These reactions suggest that the major compound from the rearrangement of dihydrosphingosine is 1-hydroxy-3-ketooctadecane (Figure 1, V) which may be formed from a carbonium ion intermediate (Figure 1, II) by a hydride shift from carbon atom 3 to carbon atom 2. 3-Hydroxyoctadecanal (Figure 1, IV) would have been formed had the hydride shift occurred from carbon atom 1 to carbon atom 2; this possibility was eliminated because oxidation of the acetylated and methylated derivatives of compound V, which were recovered unchanged, did not give 3-acetoxy- or 3-methoxyoctadecanoic acid. The nuclear magnetic resonance spectra of the acetyl ester and methyl ether compounds revealed no aldehyde function. The yields of the various derivatives were affected by the sensitivity of the molecule to oxidation and to acid. In contrast to the present rearrangement which involves a carbon atom bearing a secondary hydroxyl group, the deamination rearrangement of glucosaminol occurs *via* the carbon atom bearing the primary hydroxyl group to give 2-deoxyglucose.[5,7]

The octadecanetriol fraction, which consisted predominantly of the 2-acetyl ester, was obtained from the methanol–chloroform eluate. Crystallization of the triol was accomplished after mild alkali treatment. If the original deamination product were subjected to alkali prior to placement on the column, separation of triol and 1-hydroxy-3-ketooctadecane was sharper,

(7) Y. Matsushima, *Bull. Chem. Soc. Japan*, **24**, 144 (1951).

but yields of the latter were reduced by formation of polymeric side products. Proof of the structure of this compound as 1,2,3-trihydroxyoctadecane was obtained by periodate oxidation. The long-chain aldehyde was identified as palmitaldehyde by vapor phase chromatography and from the 2,4-dinitrophenylhydrazone; formaldehyde was characterized as the dimedon derivative.

The supernatant liquid from the crystallization of the octadecanetriol yielded a yellow wax (10%). It contained *ca.* 3% triol and decolorized bromine and permanganate solutions, and its infrared spectrum resembled that of 1-hydroxy-3-ketooctadecane. This fraction was not characterized further.

Experimental Section

Deamination of Dihydrosphingosine.—Sphingosine was isolated from beef brain and spinal cord according to the procedure of Carter, *et al.*[2] The free base was hydrogenated over platinum in ethanol to the dihydro form. To 2.0 g of base in 50 ml of glacial acetic acid, two 1.0-g portions of $NaNO_2$ were added with a 30-min interval between additions. The reaction mixture was stirred magnetically in an amber bottle at room temperature. *Ca.* 30 min after the last addition of nitrite, four volumes of water were added. The reaction products were removed with ether which was washed with 10% $NaHCO_3$ and water. The syrup obtained after removal of the ether was dried over P_2O_5 to an amorphous yellowish solid: yield 1.80 g; mp 38–50°. It gave a negative reaction with ninhydrin in 95% ethanol.

Column Chromatography.—A silicic acid (Mallinckrodt) column, 2.5 × 20 cm, was prepared as previously described[8] except that the final chloroform wash was followed by one with petroleum ether. After loading with 3.6 g of the deaminated product in warm petroleum ether, the column was developed successively with 500 ml each of chloroform–petroleum ether (55:45, v/v) and methanol–chloroform (10:90, v/v). The eluates were concentrated to dryness, and the residues were stored over P_2O_5 until further use.

Chloroform–Petroleum Ether Fraction, 1-Hydroxy-3-ketooctadecane (V).—An amorphous, yellowish wax was obtained from the chloroform–petroleum ether eluate: yield 2.8 g; mp 39–41°. It gave a positive Tollens' reaction and decolorized a solution of $KMnO_4$ but not of bromine. The infrared absorption bands in chloroform were at 3500 cm^{-1} (m), 1710 cm^{-1} (m), 1510 cm^{-1} (w), 1470 cm^{-1} (s), 1380 cm^{-1} (w), 1210 cm^{-1} (s), and doublet 1080 and 1050 cm^{-1} (s).

Anal. Calcd for $C_{18}H_{36}O_2$ (284.3): C, 75.98; H, 12.76; O, 11.26. Found: C, 75.57; H, 12.66; O, 11.13.

Reduction to DL-1,3-Dihydroxyoctadecane (VI).—Compound V, 2.6 g in 75 ml of dry ether containing 500 mg of $LiAlH_4$, was refluxed for 4 hr. The product was isolated as described previously[9] and was crystallized from petroleum ether: yield 1.4 g; mp 62–65°. It gave a positive Tollens' reaction (3 hr) and decolorized a solution of $KMnO_4$ but not of bromine.

Anal. Calcd for $C_{18}H_{38}O_2$ (286.3): C, 75.44; H, 13.38; O, 11.18. Found: C, 75.20; H, 13.17; O, 11.24.

Oxidation to Palmitic Acid (VII).—To a magnetically stirred solution of 2.5 g of compound V in 50 ml of cold glacial acetic acid, surrounded by an ice bath, was added 1.5 g of CrO_3. The bath was removed after 15 min, and the reaction mixture was stirred for an additional 2 hr. After dilution of the reaction mixture with four volumes of water, the product was isolated and converted to the amide as described previously:[3] yield 566 mg; mp 104–106°.

Anal. Calcd for $C_{16}H_{33}ON$ (255.3): C, 75.22; H, 13.03. Found: C, 75.86; H, 12.97.

Preparation of 1-Acetoxy-3-ketooctadecane (VIII).—Compound V, 2.5 g, was treated with 4 ml of acetic anhydride in 30 ml of dry pyridine. The reaction mixture was poured into ice water and the product was extracted into ether which was washed with water and removed under reduced pressure. The syrup, dried over P_2O_5, was placed on a 1.5 × 9.0 cm silicic acid column in the same manner as described for the resolution of the deamination mixture. The column was developed with 75 ml of petroleum ether which was discarded and with 100 ml of chloroform–petroleum ether (55:45, v/v) which was concentrated and dried: yield of light yellow syrup, 1.3 g. The infrared and nuclear magnetic resonance spectra showed strong carbonyl but no hydroxyl group absorption and no aldehyde function, respectively.

Anal. Calcd for $C_{20}H_{38}O_3$ (326.3): C, 73.55; H, 11.74; O, 14.71. Found: C, 73.15; H, 11.55; O, 14.54.

Preparation of 1-Methoxy-3-hydroxyoctadecane (IX).—To 2.1 g of compound V in 30 ml of dimethylformamide, surrounded by an ice bath, were added 3.5 ml of methyl iodide and 3.5 g of Ag_2O. The reaction mixture was stirred magnetically overnight at room temperature in an amber bottle, and the product was isolated as described previously.[10] The syrupy residue, after removal of solvent and drying over P_2O_5, was fractionated on a small silicic acid column similar to that used for the purification of compound VIII. The first 100 ml of petroleum ether eluate was concentrated and the dried syrup was reduced with $LiAlH_4$ and isolated in the same manner as described for the preparation of compound VI: yield of light yellow syrup, 1.1 g. Infrared absorption bands were present at 1105 cm^{-1} (s) and 3500 cm^{-1} (m) for the ether and hydroxyl groups, respectively.

Anal. Calcd for $C_{19}H_{40}O_2$ (300.3): C, 75.92; H, 13.43; OCH_3, 10.33. Found: C, 75.39; H, 13.23; OCH_3, 10.14.

Methanol–Chloroform Fraction, 1,2,3-Trihydroxyoctadecane (III).—The residue was treated with 1 ml of saturated aqueous KOH in 50 ml of ethanol for *ca.* 4 hr at room temperature. After dilution of the reaction mixture with several volumes of water, the product was removed with ether which was washed until neutral. The dried residue obtained after removal of solvent was crystallized several times from chloroform–petroleum ether (1:15): yield, 289 mg. The triol reduced Tollens' reagent and decolorized a solution of $KMnO_4$ but not of bromine.

Anal. Calcd for $C_{18}H_{38}O_3$ (302.3): C, 71.45; H, 12.67; O, 15.88. Found: C, 71.49; H, 12.61; O, 15.94.

Degradation of 1,2,3-Trihydroxyoctadecane.—A solution of 150 mg of triol and 300 mg of periodic acid in 15 ml of methanol was warmed at 50° for 1 hr and the reaction products were isolated as described previously.[3] The long-chain aldehyde was identified as palmitaldehyde by vapor phase chromatography[11] and as the 2,4-dinitrophenylhydrazone: yield, 104 mg; mp 105–106°. The short-chain aldehyde was characterized *via* the dimedon derivative as formaldehyde: yield, 30 mg; mp 190°.

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Rearrangement of Amides with Iodine Pentafluoride[1]

TRAVIS E. STEVENS

Rohm and Haas Company, Redstone Research Laboratories, Huntsville, Alabama

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The mild fluorinating agent, iodine pentafluoride, is known to dehydrogenate amines to produce nitriles, imines, and azo compounds,[2] and to dehydrate formamides to isonitriles.[3] Now, primary amides, when

(1) This research was carried out under Army Ordnance Contract DA-01-021 AMC-11536 (Z).
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