centration of free cysteine was negligible. The solution of adduct **7** (10^{-4} *M*) was placed in a cuvette and 2,2′-dipyridyl disulfide (36 μl., 10^{-2} *M* solution in tetrahydrofuran) was added to give an equimolar mixture. The ultraviolet absorption of the solution was then measured at various times. However, there was no change in the absorption; *i.e.*, there was no thiopyridone produced.

Registry No.—**1**, 497-23-4; **1a**, 25516-01-2; **2**, 22122-36-7; **2c**, 25516-03-4; **3**, 6124-79-4; **3c**, 25516-05-6; **4**, 591-11-7; **4a**, 25516-07-8; **4b**, 25516-08-9; **4c**, 6417-06-7; **4d**, 25516-10-3; 1-propanethiol, 107-03-9; α-toluenethiol, 100-53-8; L-cysteine, 52-90-4; N-acetyl-L-cysteine methyl ester, 7652-46-2.

Synthesis of D-1-Hydroxy-2-amino-3-ketooctadecane-4,5-^{3}H Hydrochloride[1a]

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N-Trifluoroacetyl- and N-carbobenzoxydihydrosphingosines were oxidized to their corresponding keto analogs with chromic anhydride in pyridine and converted to D-1-hydroxy-2-amino-3-ketooctadecane hydrochloride. It was found from the ease of removal of the N-protective groups that the N-carbobenzoxy compound provided the best yield of the ketoamine salt. N-Carbobenzoxydihydrosphingosine-4,5-^{3}H carried through the same reaction sequence yielded D-1-hydroxy-2-amino-3-ketooctadecane-4,5-^{3}H hydrochloride. The N-acetyl, O,N-diacetyl, and 2,4-dinitrophenylhydrazone derivatives of the ketoamine base were prepared for purposes of characterization. The presence of two forms of D-1-hydroxy-2-acetamido-3-ketooctadecane was suggested by the finding of one band on thin layer chromatography and two bands on gas–liquid chromatography.

During our investigation of the *in vitro* biosynthesis of long-chain bases by *Hansenula ciferri*, it was necessary to have D-1-hydroxy-2-amino-3-ketooctadecane[1b] which has been shown to be an intermediate in the biosynthesis of dihydrosphingosine.[2-4] The preparation of D-1-hydroxy-2-acetamido-3-ketooctadecane was reported[5] in which the secondary hydroxyl group of N-acetyldihydrosphingosine, D-*erythro*-1,3-dihydroxy-2-acetamidooctadecane,[6] was oxidized with chromic anhydride in pyridine.[7] It was thought that the free ketoamine or its salt could be obtained by this procedure if the oxidation were performed on the appropriate N-substituted base. N-Trifluoroacetyl- and N-carbobenzoxydihydrosphingosines were selected for this purpose because the trifluoroacetyl group could be cleaved easily under mild alkaline conditions at room temperature, whereas the carbobenzoxy function could be removed by hydrogenolysis.

Oxidation of N-trifluoroacetyldihydrosphingosine gave the expected D-1-hydroxy-2-trifluoroacetamido-3-ketooctadecane in about 35% yield. However, upon treatment with K_2CO_3, little or no free ketoamine was obtained, unlike reaction with the unoxidized parent compound which yielded the free base. The ketoamine hydrochloride was prepared in 24% yield from the N-trifluoroacetyl keto derivative by refluxing with 1.5 *N* HCl in aqueous ethanol. By comparison, oxidation of N-carbobenzoxydihydrosphingosine gave yields of about 45% of the respective keto analog (Scheme I, B, C); reduction over palladium in ethanol containing sufficient hydrochloric acid to neutralize the generated free base resulted in 95% yields of ketoamine hydrochloride. When the N-carbobenzoxy keto compound was reduced in glacial acetic acid, dihydrosphingosine was obtained whose identity was proved by infrared spectroscopy and by the melting point of its N-acetyl derivative. Thin layer chromatography of the ketoamine hydrochloride in chloroform:methanol (95:5) showed a single component, R_F 0.40; gas–liquid chromatography of the trimethylsilyl derivative was unsuccessful. The free ketoamine was obtained by treatment of the hydrochloride with $KHCO_3$ in aqueous methanol followed by extraction into ether and removal of solvent; it changed color rapidly from white to yellow after crystallization from petroleum ether. The yellow ketoamine melted at 49–54°. Thin layer chromatography disclosed one major component, R_F 0.42, along with five minor ones, R_F 0.69, 0.76, 0.83, 0.89, and 0.93. It was concluded that N-carbobenzoxydihydrosphingosine was the substrate of choice for preparation of the ketoamine hydrochloride because of the ease of removal of the protective group and the better overall yield.

The overall yield of D-1-hydroxy-2-amino-3-ketooctadecane-4,5-^{3}H hydrochloride was 30%; the radioactive yield based on N-carbobenzoxydihydrosphingosine-4,5-^{3}H was 15% (Scheme I). Since little or no tritium activity was observed on carbon atoms 1 to 3 in previous preparations[8] of dihydrosphingosine-4,5-^{3}H, the loss of 10.4 μCi after oxidation of N-carbobenzoxydihydrosphingosine (35.9 μCi/mg) to N-carbobenzoxy keto compound (25.5 μCi/mg) was attributed to an impurity of high specific activity which was removed from the keto compound but cochromatographed with N-carbobenzoxydihydrosphingosine-4,5-^{3}H during purification on the silicic acid column, and to removal of tritium on carbon atom 4 by exchange.

Proof that oxidation had occurred at the secondary hydroxyl group was obtained by treating an acetic acid

(1) (a) This investigation was supported in part by Public Health Service Research Grant No. NB 06300-04 from the National Institutes of Neurological Diseases and Stroke. (b) As this work was being prepared for publication, P. B. Mendershausen and C. C. Sweeley, *Biochemistry*, **8**, 2633 (1969), reported the micropreparation of the ketoamine free base from N-carbobenzoxydihydrosphingosine. However, the complete chemical characterization of this compound was not made. Since our efforts were directed at preparing sufficient material to be stored for varying periods of time during radioactive studies, it was decided to isolate the ketoamine as a salt.

(2) R. N. Brady, S. J. DiMari, and E. E. Snell, *J. Biol. Chem.*, **244**, 491 (1969).

(3) P. E. Braun and E. E. Snell, *ibid.*, **243**, 3775 (1968).

(4) (a) W. Stoffel, D. Le Kim, and G. Sticht, *Z. Physiol. Chem.*, **349**, 664 (1968); (b) *ibid.*, **349**, 1637 (1968).

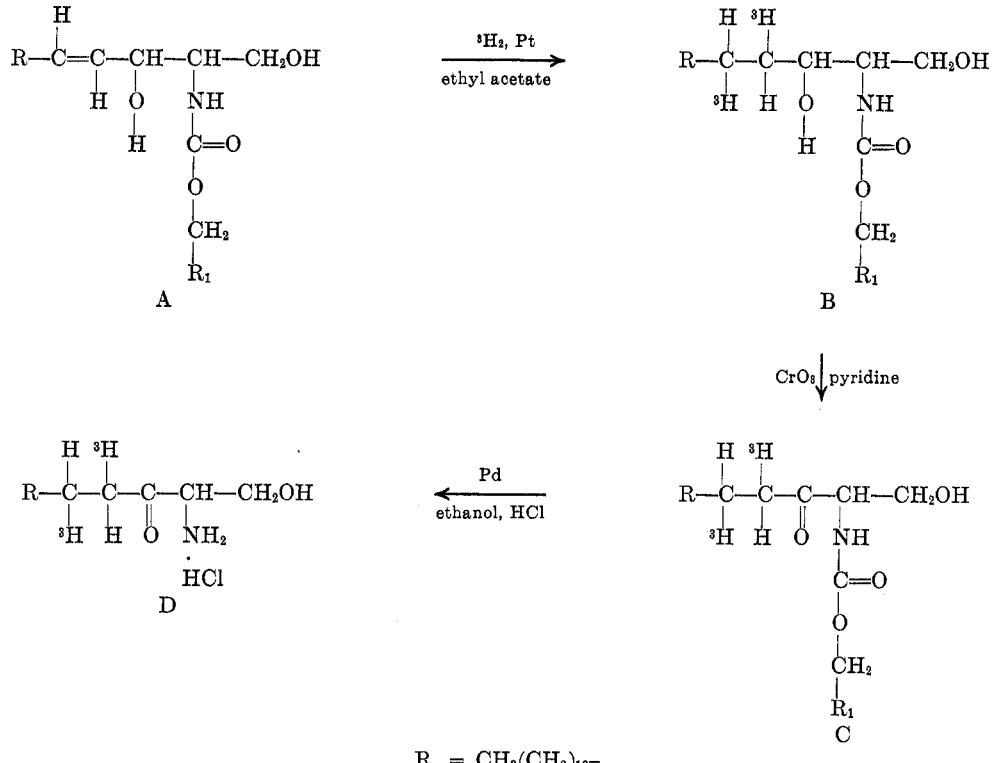
(5) R. C. Gaver and C. C. Sweeley, *J. Amer. Chem. Soc.*, **88**, 3643 (1966).

(6) H. E. Carter and Y. Fujino, *J. Biol. Chem.*, **221**, 879 (1956).

(7) G. I. Poos, G. E. Arth, R. E. Beyler, and L. H. Sarett, *J. Amer. Chem. Soc.*, **75**, 422 (1953).

(8) B. Weiss and R. L. Stiller, *J. Biol. Chem.*, **242**, 2903 (1966).

SCHEME I



solution of the ketoamine hydrochloride with lead tetraacetate. The major cleavage component was palmitic acid. This would be the product, along with a molecule each of formic acid and formaldehyde, if a vicinal ketoamine structure were present;[9] palmitaldehyde and two molecules of formic acid would be obtained if the primary hydroxyl had been oxidized. Treatment of the ketoamine hydrochloride with periodic acid gave an insoluble precipitate, with about 10% oxidation, similar to that which is obtained with dihydrosphingosine and periodic acid.

Thin layer chromatography in several solvent systems of D-1-hydroxy-2-acetamido-3-ketooctadecane showed one component, but gas–liquid chromatography of the trimethylsilyl derivative revealed two components, a major one at 12.5 min and a minor one at 25.5 min. The identity of the minor component could not be accounted for as the trimethylsilyl derivative of either N-acetylsphingosine or N-acetyldihydrosphingosine which had retention times of 27.5 and 31.5 min, respectively. Storage at room temperature under anhydrous conditions as well as successive passage through silicic acid columns disclosed, upon gas–liquid rechromatography, that the formerly minor component had increased to become the major one. A single component was still obtained by thin layer chromatography. Since gas–liquid chromatography–mass spectrometry was not available to aid in the determination of the structure of these components, it is postulated that gradual cyclization of the acetamido keto compound gives a substituted oxazolidine which would yield a ditrimethylsilyl derivative. Since ditrimethylsilyl-2-acetamidosphingosine has a retention time of 27.5 min, the oxazolidine may be the form that emerges at 25.5 min. The 12.5-min component, therefore, would be the monotrimethylsilyl derivative of the keto form.

(9) E. L. Jackson, *Org. React.*, **2**, 341 (1944).

Experimental Section

Thin layer chromatography was conducted as previously described[10] on plates coated with either Adsorbosil-1 (Applied Science Laboratories) or silica gel G (Brinkmann Instruments Company) and developed with chloroform:methanol (95:5) or chloroform:methanol:ammonia (40:10:1).[11] Bands were detected by exposure to iodine vapor. In experiments where the bands were to be analyzed by gas–liquid chromatography, or for radioactivity, a parallel run was made with exposure to iodine and used as a guide for removal of unexposed bands to avoid contamination of the sample by iodine. The silicic acid with the adsorbed compound was removed from the plate and was treated successively with 5-ml portions of chloroform:methanol (2:1) and twice with methanol at room temperature. After removal of solvent below 55° from the combined extracts, the residue was dried over phosphorus pentoxide and reacted with the trimethylsilyl reagent.[12]

Columns, 2.5 × 20 cm, were prepared with Mallinkrodt silicic acid which was washed several times with chloroform:methanol (2:1) and activated by heating 24 hr at 120°. The packed column was washed with several hundred milliliters of chloroform until the silicic acid showed no change in translucency.

The trimethylsilyl derivatives of the bases were analyzed by gas–liquid chromatography on 2.5% Se-30 on Gas Chrom Q, mesh 100–200. The column and injector and detector temperatures were maintained at 210, 270, and 240°, respectively. To 2.0 mg of base was added 0.5 ml of the trimethylsilyl reagent; after centrifugation of the reaction mixture, 1–2 μg samples of the supernatant were taken for analysis.

Infrared spectra were obtained on KBr disks with a Perkin-Elmer infrared spectrophotometer. Sphingosine was isolated as the sulfate from hydrolysates of bovine sphingolipids.[13] Dihydrosphingosine was prepared by hydrogenation of sphingosine over platinum in ethanol. The N-acetyl- and N-carbobenzoxy-

(10) B. Weiss and R. L. Stiller, *J. Lipid Res.*, **6**, 159 (1965).
(11) K. Sambasivarao and R. H. McCluer, *ibid.*, **4**, 437 (1963).
(12) H. E. Carter and R. C. Gaver, *ibid.*, **8**, 391 (1967).
(13) H. E. Carter, W. P. Norris, F. J. Glick, G. E. Phillips, and R. Harris, *J. Biol. Chem.*, **170**, 269 (1947).

dihydrosphingosines were prepared as previously described.[13,14] Fatty acids were esterified with diazomethane[15] and analyzed as reported earlier.[16]

Tritrifluoroacetyldihydrosphingosine (I).—Trifluoroacetic anhydride, 12.6 g (60 mmol), was added to 4.5 g (15 mmol) of dihydrosphingosine suspended in 150 ml of dry ethyl acetate; the base dissolved as the reaction proceeded. The organic layer was washed with water until neutral and the solvent removed. The residue, dried over phosphorus pentoxide, was crystallized from petroleum ether (Skellysolve B, bp 60–70°): yield 4.2 g; mp 104–106°; infrared absorption 1785 and 1220 (ester) (s), 1725 and 1535 (secondary amide) (s), and 1175 cm^{-1} (carbon–fluorine) (s); hydroxyl absorption was absent.

Anal. Calcd for $C_{24}H_{36}O_5NF_9$ (589.3): C, 48.87; H, 6.16. Found: C, 48.57; H, 6.01.

N-Trifluoroacetyldihydrosphingosine (II).—To 1.0 g of compound I in 75 ml of methanol was added 1.0 g of $KHCO_3$ in 48 ml of water. The mixture was stirred gently at 60° for 1 min, allowed to stand 12 hr at room temperature, and then treated twice with 125-ml portions of ether. The combined ether extracts were washed; the solvent was removed. The dried residue was crystallized from acetonitrile: yield 615 mg; mp 129–130° (The product gave a negative ninhydrin reaction in 95% ethanol.); infrared absorption 1700 and 1560 (secondary amide) (s), 1180 (carbon–fluorine) (s), 1115 (secondary hydroxyl) (m), 1075 and 1050 cm^{-1} (doublet, primary hydroxyl) (s).

Anal. Calcd for $C_{20}H_{38}O_3NF_3$ (397.3): C, 60.41; H, 9.64; N, 3.52; F, 14.35. Found: C, 60.42; H, 9.82; N, 3.58; F, 14.17.

Dihydrosphingosine.—Compound II, 50 mg in 4 ml of methanol, was treated with 50 mg of K_2CO_3 in 2 ml of water; the turbid reaction mixture was stirred gently at 60° for 1 min and allowed to stand 24 hr at room temperature. After removing the product with ether which was then washed and concentrated, the dried residue was crystallized from petroleum ether, yield 31 mg, mp 74–76°. The product gave a positive reaction with ninhydrin.

D-1-Hydroxy-2-trifluoroacetamido-3-ketooctadecane (III).—Dry chromic anhydride, 1.0 g (10 mmol), was added to a solution of 1.0 g (2.51 mmol) of compound II in 30 ml of dry pyridine surrounded by an ice bath; the reaction mixture was stirred magnetically. After 1 hr in the ice bath and another at room temperature, the reaction mixture was poured into an ice–water mixture and the product was removed by two extractions with 200-ml portions of ether:ethyl acetate (1:1). The organic layer was washed with water, filtered, and concentrated. The dried residue was dissolved in chloroform and loaded on a silicic acid column which was developed successively with 200 ml portions of chloroform, 1% methanol in chloroform, and methanol. The eluates were concentrated to dryness. The residue from chloroform was crystallized from petroleum ether (bp 60–70°): yield 355 mg; mp 72–74°; infrared absorption 1710 (carbonyl) (s), 1525 (secondary amide) (m), 1170 (carbon–fluorine) (s), and 1060 cm^{-1} (primary hydroxyl) (m).

Anal. Calcd for $C_{20}H_{36}O_3NF_3$ (395.3): C, 60.72; H, 9.18; N, 3.54; F, 14.42. Found: C, 60.03; H, 9.27; N, 3.65; F, 14.47.

Unreacted compound II, 180 mg, was recovered from the 1% methanol in chloroform eluate; the methanol eluate yielded an oil, 107 mg.

D-1-Hydroxy-2-amino-3-ketooctadecane Hydrochloride (IV).—Compound III, 100 mg, was refluxed 4 hr in 3 ml of 1.5 *N* HCl in 84% ethanol. The reaction mixture was lyophilized and dried over KOH and phosphorus pentoxide. The residue, washed several times by suspension in hot petroleum ether with centrifugation, was dissolved in 2 ml of ethanol; the precipitate that formed upon chilling the solution was collected by centrifugation after addition of 8 ml of petroleum ether: yield 19 mg; mp 97–98° (The product gave positive ninhydrin and chloride tests and reduced an alkaline copper tartrate solution.); infrared absorption 1725 (carbonyl) (s), 1615 and 1290 (NH_3^+) (m), and 1060 cm^{-1} (primary hydroxyl) (m).

Anal. Calcd for $C_{18}H_{36}O_2NCl$ (335.8): C, 64.32; H, 11.41; N, 4.17; Cl, 10.57. Found: C, 64.38; H, 11.16; N, 4.13; Cl, 10.78.

D-1-Hydroxy-2-carbobenzoxamido-3-ketooctadecane (V).—Dry chromic anhydride, 1.0 g (10 mmol), was added to 1.0 g (2.3 mmol) of N-carbobenzoxydihydrosphingosine in 30 ml of dry pyridine surrounded by an ice bath. The reaction mixture was processed as in the preparation of compound III and the product was separated on a silicic acid column. The residue from the chloroform eluate was crystallized from petroleum ether: yield 435 mg; mp 61–63°; infrared absorption 1720 (carbonyl) (s), 1690 and 1540 (secondary amide) (m), 1280 (ester) (s), and 1060 cm^{-1} (primary hydroxyl) (m). Thin layer and gas–liquid (retention time 127 min) chromatographies showed a single component.

Anal. Calcd for $C_{26}H_{43}O_4N$ (433.6): C, 71.95; H, 10.00; N, 3.23. Found: C, 71.61; H, 10.00; N, 3.18.

Unreacted starting material, 253 mg, was recovered from the 1% methanol in chloroform eluate. Thin layer and gas–liquid (retention time 15 min) chromatographies showed a single component.

D-1-Hydroxy-2-amino-3-ketooctadecane Hydrochloride (VI).—Compound V, 218 mg, was hydrogenated over 50 mg of palladium oxide in 125 ml of ethanol containing 0.5 ml of 1 *N* HCl (1 ml of concentrated HCl + 11 ml of ethanol); the solution was stirred magnetically 4 hr at room temperature. After filtration of the reaction mixture and washing of the catalyst with hot ethanol, the combined filtrates were concentrated and the residue, dissolved in a minimal volume of hot ethanol, was precipitated by addition of four volumes of petroleum ether, yield 146 mg, mp 97–98°. Tests for chloride, ninhydrin, and reduction of alkaline copper tartrate as well as the infrared spectrum and elementary analyses were the same as those obtained for compound IV. Thin layer chromatography showed a single component.

3-Hydroxy Diastereoisomers of Dihydrosphingosine Acetate.—Compound V, 218 mg, was hydrogenated over 50 mg of palladium oxide in 25 ml of glacial acetic acid in the same manner as described for the preparation of compound VI. After filtration of the reaction mixture and washing of the catalyst with hot ethanol, the combined filtrates were concentrated. Ethanol was added to the residue several times with distillation each time and the product, dried over KOH and phosphorus pentoxide, was washed by suspension in hot petroleum ether with centrifugation, yield 161 mg. Tests were positive for ninhydrin and acetate but negative for the reduction of alkaline copper tartrate. A portion of the acetate salt was converted to the N-acetyl derivative which melted at 128–131°; the same derivative of the natural *erythro* base melted at 125°.

Lead Tetraacetate Oxidation.—To 34 mg (0.1 mmol) of compound IV in 6 ml of glacial acetic acid was added with gentle warming 89 mg (0.2 mmol) of lead tetraacetate. After 2 hr at room temperature, 4 ml of methanol were added; 3 hr later, the reaction mixture was treated three times with 20-ml portions of ethyl acetate:*n*-heptane (1:1) after the addition of 5 ml each of water and 30% nitric acid. The combined extracts were washed with H_2O, filtered, and concentrated. The dried residue was crystallized from petroleum ether, yield 21 mg, mp 57°. Authentic palmitic acid melted at 58°. The infrared spectra of both samples were identical as were the retention times of their methyl esters on gas–liquid chromatography.

Derivatives of Compound VI. N-Acetyl (VII).—To 34 mg of compound VI in 6 ml of ether:ethyl acetate (1:1) was added 0.1 ml of acetic anhydride followed by 400 mg of $KHCO_3$ in 10 ml of water. After further addition of 50 ml of ether, the organic layer was washed and the solvent removed. The dried residue was crystallized from 10 ml of *n*-heptane, yield 32 mg, mp 104–105°. This product was identical with that obtained from the chromic anhydride oxidation of N-acetyldihydrosphingosine, as determined by thin layer and gas–liquid chromatographies and their infrared spectra.

Anal. Calcd for $C_{20}H_{39}O_3N$ (341.3): C, 70.32; H, 11.52; N, 4.10. Found: C, 70.79; H, 11.69; N, 4.04.

3-Hydroxy Diastereoisomers.—Compound VII, 30 mg, was treated with 8 mg of $NaBH_4$ in 10 ml of methanol containing 0.1 ml of NaOH. After 1 hr the reaction mixture was poured into an equal volume of ice water. The precipitate, removed by centrifugation, was dried and crystallized from *n*-heptane, yield 11 mg, mp 112–118°.

O,N-Diacetyl.—To 51 mg of compound VII in 2 ml of dry pyridine were added 0.1 ml of acetic anhydride; the product was removed with ether after addition of an equal volume of water. The organic layer was washed and concentrated and the residue was crystallized from petroleum ether, yield 48 mg, mp 95–96°. Infrared absorption for ester was present at 1750 and 1230 cm^{-1}.

(14) B. Weiss, *J. Amer. Chem. Soc.*, **79**, 5553 (1957).

(15) K. S. Tenny, S. C. Gupta, R. F. Nystrom, and F. A. Kummerow, *J. Amer. Oil Chem. Soc.*, **40**, 172 (1963).

(16) B. Weiss, *Biochemistry*, **3**, 1288 (1964).

Anal. Calcd for $C_{22}H_{41}O_4N$ (383.3): C, 68.87; H, 10.78; N, 3.65. Found: C, 68.99; H, 10.72; N, 3.75.

2,4-Dinitrophenylhydrazone.—Compound VI, 34 mg, was refluxed 5 min with 30 mg of 2,4-dinitrophenylhydrazine in 4 ml of methanol containing 0.1 ml of 6 *N* HCl. After cooling to room temperature the reaction mixture was centrifuged. The precipitate was crystallized from methanol, yield 27 mg, mp 138–141°.

Anal. Calcd for $C_{24}H_{42}O_5N_5Cl$ (515.3): C, 55.86; H, 8.22; N, 13.58. Found: C, 55.55; H, 8.21; N, 13.43.

Compound VII, 51 mg, treated in the same manner as compound VI with 2,4-dinitrophenylhydrazine, yielded 38 mg of derivative, mp 165°. The anticipated hydrazone corresponding to $C_{26}H_{43}O_6N_5$ (521.3) with calculated values for C, 59.85, H, 8.31, and N, 13.43 was not obtained; instead, the values for C, 55.37, H, 6.53, and N, 17.59 were found suggesting an empirical formula of $C_{26}H_{36}O_7N_7$ (557.3). The product showed one component on thin layer chromatography.

D-1-Hydroxy-2-carbobenzoxamido-3-ketooctadecane-4,5-^{3}H (VIII).—To 1.4 mg (22.8 mC) of N-carbobenzoxydihydrosphingosine-4,5-$^3H^8$ in 50 ml of methanol were added 434 mg of N-carbobenzoxydihydrosphingosine; the solution was concentrated and the residue was dried over phosphorus pentoxide. The product was dissolved in 30 ml of pyridine, chilled and treated with 435 mg of dry chromic anhydride. The remainder of the procedure, including column chromatography on silicic acid, was the same as that employed in the preparation of compound V, yield 138 mg (32%), mp 63°; recovered radioactivity 3.5 mCi, 15%; specific activity 25.5 μCi/mg (11.1 mCi/mmol).

The yield of N-carbobenzoxydihydrosphingosine-4,5-^{3}H recovered from the 1% methanol in chloroform was 150 mg (35%), mp 105–106°. Radioactive yield 5.4 mCi, 24%; specific activity 35.9 μCi/mg.

D-1-Hydroxy-2-amino-3-ketooctadecane-4,5-^{3}H Hydrochloride.[17]—Compound VIII, 138 mg, was hydrogenated and the product was isolated in the same manner as that described for the preparation of compound VI, yield 93.4 mg (87%), mp 96–98°; Recovered radioactivity 3.3 mCi, 14%; specific activity 35.7 μCi/mg (11.9 mC/mmol). The product was stored in the dark *in vacuo* over phosphorus pentoxide.

Registry No.—I, 25515-49-5; II, 25515-50-8; dihydrosphingosine, 764-22-7; III, 25515-52-0; IV, 25515-53-1; V, 25515-54-2; VI (2,4-dinitrophenylhydrazone), 25515-57-5; dihydrosphingosine acetate (diastereoisomers), 25528-34-1; VII, 25515-55-3; VII (3-hydroxy diastereoisomers), 13552-12-0; VII (O,N-diacetyl), 25515-56-4; VIII, 25568-74-5; D-1-hydroxy-2-amino-3-ketooctadecane-4,5-^{3}H (HCl), 25515-58-6.

(17) Preliminary studies showed that this compound was an efficient precursor in the biosynthesis of phytosphingosine by growing cultures of the yeast *Hansenula ciferrii*.

Carbodiimide–Sulfoxide Reactions. VIII.[1] Reactions of Oximes and Hydroxylamines[2]

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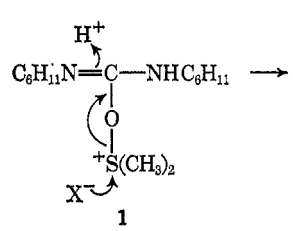
The reaction of benzophenone oxime with dimethyl sulfoxide and dicyclohexylcarbodiimide in the presence of trifluoroacetic acid leads to formation of α,α-diphenyl-*N*-(thiomethoxymethyl)nitrone (**5**) and the isomeric *O*-(thiomethoxymethyl)benzophenone oxime (**6**). The relative amounts of **5** and **6** depend upon the reaction conditions and, using pentadeuterio-**5**, intramolecular rearrangement into pentadeuterio-**6** has been demonstrated. Similar formation of a nitrone and oxime ether occurred using fluoren-9-one oxime, but certain aliphatic oximes led to complex reaction mixtures. Reactions of several 17-oximino steroids led to the formation of D-homolactams and of unsaturated nitriles *via* first- and second-order Beckmann rearrangements, the latter being unusual with these compounds. Both *syn* and *anti* isomers of *p*-bromobenzaldoxime gave *p*-bromobenzonitrile and α-*p*-bromophenyl-*N*-(thiomethoxymethyl)nitrone in different proportions. *N*-Phenylhydroxylamine gave azoxybenzene, presumably *via* oxidation to nitrosobenzene, and *N*,*N*-dibenzylhydroxylamine gave α-phenyl-*N*-benzylnitrone in high yield. Mechanisms for these reactions are presented.

Previous papers in this series have described mild acid-catalyzed reactions of dimethyl sulfoxide (DMSO) and dicyclohexylcarbodiimide (DCC) with alcohols,[4] phenols,[5] and active methylene compounds.[1] In each case the observable reactions can be explained by nucleophilic attack of the functional group upon an initial DMSO–DCC adduct (**1**), giving an oxysulfonium salt, or related derivative, (**2**) which can readily lose a proton



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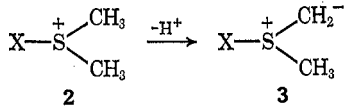

2 **3**

giving a sulfonium ylide (**3**). The latter can then directly rearrange or undergo further reactions.

The mildness of these reactions suggests that other nucleophilic functional groups might also react with **1** leading to many possible types of reaction. In this paper we describe the reactions of several different types of oximes and hydroxylamines while in subsequent publications a wide range of other functional groups are considered.[6]

Benzophenone oxime (**4**) was found to react rapidly with DMSO and DCC in the presence of 0.5–1.0 equiv of anhydrous orthophosphoric acid, omission of any of these reagents blocking the reaction. Unlike the reactions described previously, however, free trifluoro

(1) For part VII, see A. F. Cook and J. G. Moffatt, *J. Amer. Chem. Soc.*, **90**, 740 (1968).

(2) This and related work was presented as part of the Eleventh National Medicinal Chemistry Symposium of the American Chemical Society, Quebec, Canada, June 1968.

(3) Syntex Postdoctoral Fellow, 1964–1965.

(4) (a) K. E. Pfitzner and J. G. Moffatt, *J. Amer. Chem. Soc.*, **87**, 5661, 5670 (1965); (b) A. H. Fenselau and J. G. Moffatt, *ibid.*, **88**, 1762 (1966).

(5) (a) M. G. Burdon and J. G. Moffatt, *ibid.*, **88**, 5855 (1966); (b) M. G. Burdon and J. G. Moffatt, *ibid.*, **89**, 4725 (1967).

(6) U. Lerch and J. G. Moffatt, unpublished results.