Methyl 6-Deoxy-2,3-isopropylidene-α-D-mannoseenide.—Methyl 6-deoxy-6-iodo-α-D-mannoside (1 g.) was heated 4 hr. under reflux in absolute methanol (50 ml.) in which sodium (1.5 g.) has been dissolved. Most (40 ml.) of the methanol was removed by distillation under reduced pressure. The residue was taken up in chloroform (50 ml.), washed free of alkali with cold water, and dried over sodium sulfate. The chloroform was evaporated under reduced pressure and the remaining oil was distilled at 0.001 mm. with an oil bath temperature of 100–110°. The compound is extremely sensitive to acid-catalyzed hydrolysis; even carbonic acid or exposure to air resulted in hydrolysis, rearrangement, and crystallization of 6-deoxy-2,3-isopropylidene-5-keto-D-mannofuranose. This instability is responsible for an incorrect analysis.

The compound, when freshly prepared, showed the typical infrared absorption for C=C and decolorized bromine water instantaneously. The yield of mannoseenide was 0.50 g., 80% of theory, $[\alpha]^{24}D$ +51° (*c* 0.4, methanol–water, 2:1, v./v.). In 0.01 *N* hydrochloric acid in methanol–water (2:1, v./v.) containing 0.4% of the compound, the specific rotation decreased during 16 hr. from +45 to −23°.

Anal. Calcd. for $C_{10}H_{16}O_5$: C, 55.54; H, 7.46. Found: C, 54.23; H, 7.41.

The methyl 2,3-isopropylidene-α-D-mannoseenide was also prepared in lower yield by using silver fluoride in pyridine[9] for dehydroiodination of methyl 6-iodo-6-deoxy-2,3-isopropylidene-α-D-mannoside.

6-Deoxy-2,3-isopropylidene-5-keto-D-mannofuranose.—Methyl 6-deoxyisopropylidene-α-D-mannopyranoseenide (1 g.) was dissolved in 0.01 *N* hydrochloric acid (methanol–water, 2:1, v./v.) and left standing at room temperature for 16 hr. The acid was neutralized with sodium bicarbonate and the solution was evaporated to dryness under reduced pressure. The residue was extracted with boiling ether and the compound was induced to crystallize by addition of petroleum ether. It was recrystallized from ether–petroleum ether to give firm needles, m.p. 147–149°, $[\alpha]^{23}D$ −28° (*c* 0.5, methanol–water, 2:1, v./v.) in 0.6 g. yield.

Anal. Calcd. for $C_9H_{14}O_5$ (202.20): C, 53.44; H, 6.98. Found: C, 53.18; H, 7.07.

The compound did not decolorize bromine water but reduced ammoniacal silver nitrate solution. It showed typical infrared carbonyl absorption. It formed an amorphous bis (*p*-nitrophenylhydrazone).

Anal. Calcd. for $C_{21}H_{24}O_7N_6$ (470.30): C, 53.39; H, 5.12; N, 17.78. Found: C, 53.11; H, 5.62; N, 16.15.

6-Deoxy-L-gulitol.—6-Deoxy-2,3-isopropylidene-5-keto-D-mannofuranose (0.10 g.) was reduced with an excess of sodium borohydride in water. After standing 7 hr. at room temperature, the remaining borohydride was decomposed by addition of acetic acid. Sodium ions were removed by passing through a column of Dowex 50 H^+, and boric acid and acetic acid were driven off by repeatedly distilling absolute methanol from the residue. The remaining sirup crystallized from methanol; yield, 0.059 g. (73% of theory), m.p. 127°, m. m.p. with authentic compound, 127–128°. Müller and Reichstein[25] reported m.p. 127°. The infrared spectrum of the compound was identical with that of a reference sample of 1-deoxy-D-glucitol (or 6-deoxy-L-gulitol).[26] A trace of a second 6-deoxyhexitol was detected by paper chromatography. It showed the same chromatographic properties as L-rhamnitol. This demonstrated the position of the keto group in 6-deoxy-5-keto-2,3-isopropylidene-D-mannofuranose.

Acknowledgment.—We wish to express our appreciation to G. Cheniae, T. G. Traylor, P. Traylor, J. Bigeleisen, R. C. Fehey, and C. Perrin for helpful discussions and valuable advice.

(25) H. Müller and T. Reichstein, *Helv. Chim. Acta*, **21**, 251 (1938).
(26) Kindly provided by Dr. A. B. Foster, University of Birmingham.

[CONTRIBUTION FROM THE DANIEL SIEFF RESEARCH INSTITUTE, THE WEIZMANN INSTITUTE OF SCIENCE, REHOVOTH, ISRAEL]

Synthetic Studies on Sphingolipids. X.[1] Synthesis of Psychosine[2]

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The synthesis of psychosine (VIa) is described. N-Dichloroacetyl-3-O-benzoylsphingosine (IVa) was condensed with acetobromogalactose, and the resulting product deacylated by sodium methoxide to the N-dichloroacetylcerebroside (Va) which was hydrolyzed to VIa by warming with 0.3 *N* barium hydroxide at 70–80° for 90 min. By the same procedure glucopsychosine and dihydropsychosine were synthesized. The latter glycoside could also be obtained by hydrogenolysis of the N-benzyloxycarbonyl derivative Vc.

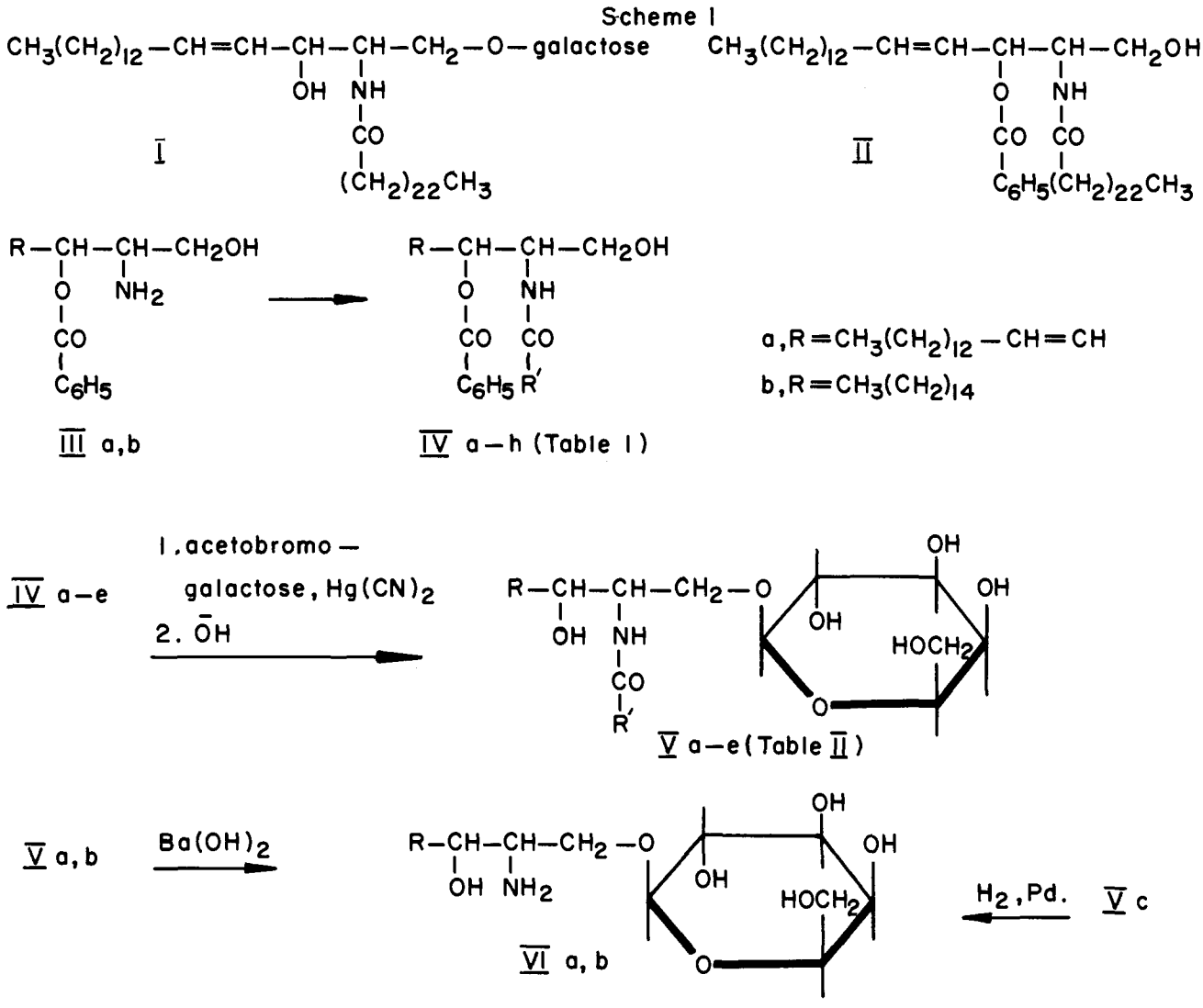
Psychosine (1-D-sphingosyl β-D-galactoside, VIa) is an alkaline hydrolysis product of the cerebrosides (I) in which the amino group forms an amide with a long-chain fatty acid.[3,4] On the basis of results obtained from enzymatic studies Cleland and Kennedy[5] have recently postulated that this galactoside is an intermediate in the biosynthesis of cerebrosides and other more complex glycosphingolipids. We wish to report the synthesis of psychosine and its dihydro derivative.

In a recent communication[6] we have demonstrated that in order to assure an unequivocal synthesis of a sphingolipid involving substitution at carbon 1 of the sphingosine molecule it is necessary to block both the amino and the secondary hydroxyl group. Thus, the synthesis of cerasine (I) and other natural cerebrosides[7] was achieved by glycosidation of the disubstituted sphingosine (II).

The hydrolysis of cerebrosides of type I is known to proceed sluggishly giving psychosine in low yield and of poor quality.[8] In contradistinction to the synthesis of cerebrosides in which the amide grouping is retained as part of the molecule, the protecting N-acyl in the synthesis of psychosine must be such as to undergo mild hydrolysis. On the other hand, hydrolysis should not take place prior to the removal of the benzoyl group, since in such a case it would be difficult to avoid, during the course of the synthesis, O→N benzoyl migration which proceeds rapidly at a pH slightly above 7. We therefore undertook a systematic investigation of such protective groups which were likely to meet these requirements. To this end we prepared the 3-O-, N-protected bases IVa–h as possible aglucons in the proposed synthesis. Some of these protective groups are well known in the chemistry of amino acids.[9] Sphingosine is, however, a much stronger

(1) For part IX see D. Shapiro and E. S. Rachaman, *Nature*, **201**, 878 (1964).
(2) Taken from part of a thesis submitted by E. S. Rachaman to the Senate of the Hebrew University, Jerusalem, in partial fulfillment of the requirements for the Ph.D. degree, April, 1964.
(3) I. Pryde and R. W. Humphrey, *Biochem. J.* **18**, 661 (1924).
(4) I. Pryde and R. W. Humphrey, *ibid.*, **20**, 825 (1926).
(5) W. W. Cleland and E. P. Kennedy, *J. Biol. Chem.*, **235**, 45 (1960).
(6) See paper in ref. 1.
(7) D. Shapiro and H. M. Flowers, *J. Am. Chem. Soc.*, **83**, 3327 (1961).
(8) E. Klenk and R. Harle, *Z. Physiol. Chem.*, **178**, 221 (1928).

Scheme I



base, and its amides are expected to be more resistant to hydrolysis.

Following our previous practice in this series, we first studied the approach to dihydropsychosine as model compound employing the sulfate of the saturated monosubstituted base IIIb as starting material. The latter compound as well as its unsaturated counterpart IIIa resulted from an acid-catalyzed ring scission of a substituted oxazoline previously described.[7,10] The compounds IVa–f could be prepared by direct acylation of III in aqueous medium using acid chlorides or anhydrides. In order to avoid a possible O→N benzoyl migration the reaction was carried out at a pH of about 6 in a sodium acetate–acetic acid buffer solution. For the preparation of IVg *p*-nitrophenyl *t*-butyl carbonate was used as acylating agent in the presence of 40% potassium acetate solution, the optimum temperature being 60–65°. It is noteworthy that benzoyl migration took place, in part, under the influence of temperature even at a pH below 7. Approximately 15–20% of the sulfate were found to be converted into N-benzoyldihydrosphingosine whose quantity increased with elevation of temperature. Finally, IVh was obtained under anhydrous conditions by means of trifluoroacetic anhydride and sodium trifluoroacetate. The product gave, however, unsatisfactory analytical values, although its spectrum showed the expected bands.

Initially we encountered difficulties in the preparation of IVa and IVb by direct acylation of III. Since the dichloroacetyl group seemed the most promising one for masking the amine function, an effort was made to prepare IVb by a different route. It was finally synthesized by a sequence of reactions shown in Scheme II.

Treatment of dihydrosphingosine with methyl dichloroacetate gave the N-acyl derivative in almost quantitative yield. The primary hydroxyl was then protected by tritylation and finally the secondary hydroxyl was benzoylated. Removal of the trityl group with dilute acetic acid gave the desired disubstituted base. The high solubility of IX and X in most organic solvents made their purification difficult, and it was found more advantageous to introduce the *p*-nitrobenzoyl group in X. It is noteworthy that this scheme may be of interest in future synthetic work on sphingolipids, since it provides the possibility of a direct application of crude natural sphingosine.

The aglucons IV were condensed with tetraacetyl-α-D-galactosyl bromide in the presence of mercuric cyanide and in nitromethane–benzene as solvents.

(9) G. W. Anderson and A. C. McGregor, *J. Am. Chem. Soc.*, **79**, 6180 (1957).

(10) D. Shapiro, H. M. Flowers, and S. Spector-Shefer, *ibid.*, **81**, 4360 (1959).

TABLE I

3-O-BENZOYL-N-ACYL DERIVATIVES OF SPHINGOSINE AND DIHYDROSPHINGOSINE (IVa–h)

IV	R	R′	Acylating agent	Crystn. solvent	M.p., °C.	Formula	Calcd.	Found
a	$CH_3(CH_2)_{12}CH{=}CH$	Cl_2CH	$(Cl_2CHCO)_2O$	Acetonitrile	75	$C_{27}H_{41}NO_4Cl_2$	C, 63.02; H, 8.03; N, 2.72; Cl, 13.78	C, 62.63; H, 8.15; N, 2.67; Cl, 13.19
b	$CH_3(CH_2)_{14}$	Cl_2CH	$(Cl_2CHCO)_2O$	Acetonitrile	77–78	$C_{27}H_{43}NO_4Cl_2$	C, 72.78; H, 8.39; N, 2.71; Cl, 13.73	C, 62.68; H, 8.40; N, 2.84; Cl, 13.58
c	$CH_3(CH_2)_{14}$	$C_6H_5CH_2O$	$C_6H_5CH_2OCOCl$	MeOH	58	$C_{33}H_{49}NO_5$	C, 73.43; H, 9.15; N, 2.6	C, 73.47; H, 9.20; N, 2.43
d	$CH_3(CH_2)_{14}$	CH_3	$(CH_3CO)_2O$	80% MeOH	65–67	$C_{27}H_{45}NO_4$	C, 72.44; H, 10.13; N, 3.35	C, 72.42; H, 10.11; N, 3.13
e	$CH_3(CH_2)_{14}$	C_6H_5	C_6H_5COCl	MeOH	90–91	$C_{32}H_{47}NO_4$	C, 75.70; H, 9.30; N, 2.76	C, 75.64; H, 9.38; N, 2.52
f	$CH_3(CH_2)_{12}CH$ CH	CH_3	$(CH_3CO)_2O$	Acetonitrile	75	$C_{29}H_{43}NO_4$	C, 72.77; H, 9.73; N, 3.14	C, 72.95; H, 9.75; N, 3.10
g	$CH_3(CH_2)_{14}$	$(CH_3)_3CO$	$(CH_3)_3C{-}O{-}CO{-}O_2N{-}C_6H_4{-}O$	Acetonitrile	89–90	$C_{30}H_{51}NO_5$	C, 71.30; H, 10.2; N, 2.8	C, 71.9; H, 10.01; N, 2.89
h	$CH_3(CH_2)_{14}$	CF_3	$(CF_3CO)_2O$	Nitromethane	75			

SCHEME II

Exploratory glycosidation reactions demonstrated that the compounds IVd–h could be eliminated as possible intermediates in the synthesis of psychosine or dihydropsychosine. Thus, the galactoside Vd was rather stable to hydrolysis and was recovered unchanged after refluxing with aqueous barium hydroxide for 8 hr. With Ve we had visualized the reduction of the benzoyl group with lithium aluminum hydride and a catalytic hydrogenation of the benzylamino derivative to dihydropsychosine. However, the amide proved to be stable to lithium aluminum hydride even on prolonged boiling in tetrahydrofuran. This is remarkable in view of the fact that N-benzoyldihydrosphingosine is reduced easily by this reagent.[11] We have observed with other amides of this type a similar stability which must be attributed to an effect of the carbohydrate moiety.

Glycosidation of IVg and IVh gave the corresponding galactosides only in negligible yields. However, whereas the trifluoroacetyl derivative could be hydrolyzed to dihydropsychosine, attempts to remove the *t*-butyloxycarbonyl group by means of trifluoroacetic acid under conditions described by Carpino[12] failed. At slightly elevated temperature splitting of the glycosidic bond occurred, apparently with simultaneous elimination of *t*-butyl alcohol and formation of an oxazolidone ring, as was indicated by the change in the infrared spectrum.

The use of the dichloroacetyl group for protection of the amine function provided a smooth route to psychosine and dihydropsychosine. The latter could also be obtained by catalytic hydrogenation of Vc. The crude tetraacetyl galactosides resulting from the condensation of IVa and IVb, respectively, with acetobromogalactose were saponified directly to Va and Vb which were obtained in yields up to 70%. To maintain these yields it was found essential to remove the mercury salts with hydrogen sulfide, *i.e.*, under slightly

(11) H. E. Carter, D. Shapiro, and J. B. Harrison, *J. Am. Chem. Soc.* **75**, 1007 (1953).

(12) L. A. Carpino, *ibid.*, **79**, 98 (1957).

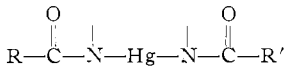
TABLE II

N-ACYL-DL-SPHINGOSYL- (AND DIHYDROSPHINGOSYL-) β-D-GALACTOPYRANOSIDES (Va–e), DERIVED FROM THE AGLUCONS IV

Aglucons	V	M.p., °C.	Crystn. solvent	$[\alpha]^{26}D$ (pyridine)	Formula	Calcd.	Found[a]
IVa	a	172	Ethanol	+6.6°	$C_{26}H_{47}NO_8Cl_2$	C, 54.54; H, 8.27; N, 2.45; Cl, 12.39	C, 54.60; H, 8.35; N, 2.54; Cl, 12.02
IVb	b	155	MeOH–acetonitrile (1:1)	+1.6°	$C_{26}H_{49}NO_8Cl_2$	C, 54.36; H, 8.59; N, 2.44; Cl, 12.34	C, 54.28; H, 8.74; N, 2.68; Cl, 11.71
IVc	c	125	Chloroform	+13.7°	$C_{32}H_{55}NO_8$	C, 64.29; H, 9.27; N, 2.34	C, 63.69; H, 9.30; N, 2.58
IVd	d	148–150	MeOH–acetonitrile (1:1)	+4.6°	$C_{26}H_{51}NO_8$	C, 61.75; H, 10.17; N, 2.77	C, 61.05; H, 10.03; N, 2.53
IVe	e	138	MeOH	+16.5°	$C_{31}H_{53}NO_8$	C, 65.58; H, 9.41; N, 2.46	C, 64.98; H, 9.27; N, 2.34

[a] % galactose found: a, 29.5; b, 29.5; c, 30; d, 36; e, 30.

acidic conditions, prior to deacylation with sodium methoxide. The viscous oil remaining after evaporation of the reaction solvents formed a clear solution in petroleum ether although it was found to contain appreciable amounts of mercury. Direct treatment with alkali, even with sodium bicarbonate, reduced the yields considerably, apparently as a result of cleavage of the glycosidic linkage. We have no explanation for this behavior, except the suggestion that it involves, at least in part, a covalently bound mercury in the form of



Amides are known to form complexes of this type which are easily split by sulfides.[13]

With the hydrolysis of Va,b we encountered an interesting observation. Hydrolysis of natural cerebrosides is usually carried out by means of barium hydroxide in the presence of dioxane to facilitate *solution*.[14] Following this method we found that the reaction was accompanied by a cleavage of the glycosidic bond giving a low yield of VI. This result was even more distinct with the trifluoroacetyl derivative. However, treatment of a *suspension* in aqueous barium hydroxide yielded 80% of VI. We attribute this behavior to the strong negative nature of the dichloroacetyl group which places these cerebrosides into the class of alkali-sensitive glycosides. It is well established that alkali sensitivity of glycosides is a function of the aglucon. It may withdraw electrons from the glycosidic bond as a result of activation by substituents in the β-position. The electron attraction inherent in the dichloroacetamido group may be expected to exercise such an effect.

The molecule of a cerebroside consists of a hydrophobic and a hydrophilic part. In analogy to the behavior of higher fatty acids on water it may form a solid and a liquid film consisting of a unimolecular layer of the lipid portion floating on the surface with the sugar moiety in the surface of water. Such a situation may arise in an aqueous suspension of VI. It will impede ionic interaction between the two parts of the molecule and thus facilitate hydrolysis without affecting the glycosidic linkage.

Psychosine is a potential key intermediate in the synthesis of fatty acid labeled cerebrosides and other glycosphingolipids, and it seemed appropriate to study the acylation of its amino group. The reaction of dihydropsychosine with lignoceroyl chloride in the presence of sodium acetate under the conditions described for the preparation of the disubstituted sphingosines was accompanied by partial acylation of the hydroxyl groups and resulted in low yield. It was found that acylation could be effected conveniently and in a satisfactory yield by employing an activated ester such as *p*-nitrophenyl lignocerate.

(13) H. Ley and K. Shaefer, *Ber.*, **35**, 1309 (1902).

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

Experimental

Acylation of III. A. Preparation of IVa–f.—The racemic sulfate of III (4.5 g.) obtained by an acid-catalyzed ring scission of the corresponding substituted oxazoline[7] was dissolved in a mixture of tetrahydrofuran (75 ml.) and 2 *N* acetic acid (15 ml.). To the rapidly stirred solution were added simultaneously, during 20–30 min., 50% sodium acetate solution (80 ml.) and the acylating agent dissolved in dry ether (ten volumes). Eight grams of the anhydride and 30% excess of the acid chloride were used, respectively, for the acylation of 0.01 mole of the sulfate. After stirring for 4 hr., the ethereal extract was washed several times, dried, and evaporated *in vacuo*. The oily residue was recrystallized from methanol or acetonitrile. The physical properties and analytical data are summarized in Table I.

B. 3-O-Benzoyl-N-*t*-butyloxycarbonyldihydrosphingosine (IVg).—To a solution of the sulfate of IIIb (9 g.) in tetrahydrofuran (150 ml.) and 1 *N* acetic acid (50 ml.) were added *p*-nitrophenyl *t*-butyl carbonate (3 g.) and a 40% solution of potassium carbonate (70 ml.). The mixture was stirred at 55–65° for 8 hr. The upper layer was then poured into ice–water (300 ml.) containing 3 *N* sulfuric acid (50 ml.). The oily material which separated was taken up in ether and the ether was dried and evaporated. The residue (10.5 g.) was digested with hot acetonitrile (100 ml.). The insoluble part (3 g.) was unreacted sulfate. From the filtrate a product melting at 74–76° (3 g.) precipitated upon cooling. It was dissolved in ether (90 ml.) and the insoluble part (1.5 g.) was filtered and crystallized from methanol. It melted at 110° and was identified as N-benzoyldihydrosphingosine. The ethereal filtrate was evaporated and the residue was crystallized from acetonitrile (40 ml.), yielding 3.15 g., m.p. 89–90°.

Anal. Calcd. for $C_{30}H_{51}NO_5$ (505.7): C, 71.3; H, 10.2; N, 2.8. Found: C, 71.9; H, 10.01; N, 2.89.

C. 3-O-Benzoyl-N-trifluoroacetyldihydrosphingosine.—A mixture of the sulfate (4.05 g.), sodium trifluoroacetate (1.8 g.), and trifluoroacetic anhydride (15 ml.) was stirred at 40–50° for 2 hr. Most of the anhydride was then evaporated *in vacuo* and the residue was poured into ice–water and extracted with ether. The ether solution was washed with sodium bicarbonate solution until neutral and the solvent was dried and evaporated. The oily residue (6 g.) was dissolved in dry methanol and the solution was refluxed for 1 hr. Addition of ice–water precipitated the product which was dried and recrystallized from nitromethane. The pure compound weighed 2.5 g. and melted at 75°.

N-Dichloroacetyldihydrosphingosine (VIII).—A mixture of dihydrosphingosine (5 g.) and methyl dichloroacetate (50 ml.) was heated in a gently boiling water bath for 2 hr. The clear solution was cooled, petroleum ether (200 ml., b.p. 60–90°) was added, and the precipitate was filtered and washed. Crystallization from methanol yielded 5.5 g. (88%), m.p. 142–144°. The amide was identical with the product obtained by hydrolysis of IVb with sodium methoxide.

Anal. Calcd. for $C_{20}H_{39}Cl_2NO_3$: C, 58.25; H, 9.59; Cl, 17.20; N, 3.40. Found: C, 58.50; H, 9.44; Cl, 17.09; N, 3.63.

N-Trichloroacetyldihydrosphingosine, prepared similarly in 80% yield, melted at 114–115°.

Anal. Calcd. for $C_{20}H_{38}Cl_3NO_3$: C, 53.75; H, 8.57; Cl, 23.80; N, 3.14. Found: C, 53.52; H, 8.33; Cl, 23.14; N, 3.44.

N-Dichloroacetyl-1-O-trityldihydrosphingosine (IX).—To a solution of N-dichloroacetyldihydrosphingosine (8 g.) in dry tetrahydrofuran (160 ml.) were added freshly prepared trityl

chloride (6 g.) dissolved in tetrahydrofuran (6 ml.) and dry pyridine (1.6 g.). After stirring for 30 min., the mixture was allowed to stand at room temperature (about 30°) for 48 hr. Most of the solvent was evaporated *in vacuo* under reduced pressure and the residue was taken up in ether. The ethereal solution was washed with dilute hydrochloric acid, then with water to neutral, and was dried and evaporated. The residue was dissolved in warm petroleum ether (50 ml.), and the solution was allowed to stand at room temperature for 2–3 hr. and filtered from trityl carbinol. The filtrate was cooled and the collected product was washed with a little cold petroleum ether, giving 9 g. (68%), m.p. 88–90°. Two more recrystallizations at room temperature from a little petroleum ether and from a little methanol, respectively, raised the melting point to 94–95°.

Anal. Calcd. for $C_{10}H_{51}Cl_2NO_3$: C, 71.53; H, 8.16; Cl, 10.82; N, 2.14. Found: C, 71.40; H, 8.30; Cl, 10.33; N, 1.94.

3-O-Benzoyl-N-dichloroacetyl-1-trityldihydrosphingosine (X).—To a cooled solution of IX (6.65 g.) in dry pyridine (70 ml.) was added benzoyl chloride (2 ml.) and the mixture was left at room temperature overnight. The oily product which separated upon addition of ice–water was taken up in ether, the solution was washed successively with cold 2 *N* hydrochloric acid, 5% sodium bicarbonate, and water, dried, and evaporated. The residue was recrystallized twice from absolute ethanol, yielding 6 g. (80%), m.p. 72–74°.

Anal. Calcd. for $C_{46}H_{57}Cl_2NO_4$: C, 72.80; H, 7.57; Cl, 9.34; N, 1.85. Found: C, 72.42; H, 7.34; Cl, 9.67; N, 1.67.

3-O-(*p*-Nitrobenzoyl)-N-dichloroacetyl-1-trityldihydrosphingosine.—To a cooled solution of *p*-nitrobenzoyl chloride (1.2 g.) in dry chloroform (15 ml.) were added pyridine (0.6 ml.) and the disubstituted base IX (3.6 g.). The mixture was stirred at room temperature until solution ensued and kept for 15–16 hr. at 35°. The oily residue obtained after working up as described above was recrystallized from methanol (35 ml.) in the cold and a second time from 40 ml. at room temperature, yielding 2.6 g., m.p. 87–90°.

Anal. Calcd. for $C_{46}H_{56}Cl_2N_2O_6$: C, 68.66; H, 7.02; Cl, 8.8; N, 3.48. Found: C, 68.59; H, 6.96; Cl, 8.82; N, 3.80.

3-O-Benzoyl-N-dichloroacetyldihydrosphingosine (IVb) by Detritylation of X.—A suspension of X (7.5 g.) in 90% acetic acid (75 ml.) was warmed on a boiling water bath with occasional shaking for 10–15 min. The clear solution was poured into ice–water (200 ml.), and the precipitate was filtered and washed with water. The dry product was dissolved in hot hexane (40 ml.), the solution was cooled, and the separated tritylcarbinol was filtered off. The filtrate was concentrated *in vacuo* and the residue was crystallized from ethanol (20 ml.), yielding 3.4 g. (61%), m.p. 71–72°.

Anal. Calcd. for $C_{27}H_{43}Cl_2NO_4$: C, 62.79; H, 8.39; Cl, 13.73; N, 2.71. Found: C, 62.78; H, 8.32; Cl, 13.42; N, 2.56.

3-O-(*p*-Nitrobenzoyl)-N-dichloroacetyldihydrosphingosine was prepared similarly from the *p*-nitro derivative of X; yield 86%, m.p. 107–108°.

Anal. Calcd. for $C_{27}H_{42}Cl_2N_2O_6$: C, 57.75; H, 7.4; Cl, 12.64; N, 4.99. Found: C, 58.02; H, 7.63; Cl, 12.29; N, 5.19.

Glycosidation.—A solution of the benzoylceramide IV (0.004 mole) in dry nitromethane (60 ml.) and dry benzene (60 ml.) was heated with stirring and exclusion of moisture to 100–110° until 25–30 ml. of the solvent distilled off slowly. The mixture was allowed to cool to room temperature and tetraacetylgalactosyl bromide (0.004 mole) and mercuric cyanide (0.004 mole) were added quickly. The weighed materials had been dried *in vacuo* overnight. The solution was stirred at 80° for 8–10 hr., cooled, and, after addition of ether, shaken several times with cold saturated hydrogen sulfide solution. The black precipitate was filtered off and the filtrate was shaken several times with cold 2.5% sodium bicarbonate solution. The organic layer was washed with water to neutral, dried, and evaporated *in vacuo* at a temperature not exceeding 55°. The remaining viscous oil was dissolved in absolute methanol (60 ml.), a catalytic amount of sodium dissolved in a few milliliters of methanol was added, and the solution was allowed to stand at room temperature overnight. Neutralization with 2 *N* acetic acid was followed by the addition of water, and the mixture was cooled to complete precipitation. The product was filtered, washed thoroughly with distilled water, and dried. The raw cerebroside thus obtained was dissolved in a mixture of chloroform and methanol (9:1) and passed over a silicic acid column. Elution with the same solvent mixture gave the cerebrosides in yields ranging from 50–70%.

Glycosidation of 3-O-(*p*-Nitrobenzoyl)-N-dichloroacetyldihydrosphingosine proceeded according to the general method except that 80% of the aglucon was recovered unchanged, even after a reflux of 18 hr. However, the yield of the cerebroside Vb was 50%, based on the amount which entered the reaction.

Psychosine (DL-Sphingosyl β-D-Galactopyranoside, VIa).—A suspension of the cerebroside Va (1.45 g.) in 5% aqueous barium hydroxide solution (40 ml.) was rapidly stirred at 65–70° for 1 hr. The temperature was then raised and maintained at 75–80° for an additional hour. The reaction mixture was cooled, filtered, and the precipitate was washed with distilled water. The dried product was dissolved in a mixture of chloroform and methanol (2:1) and passed through a silicic acid column. Chloroform–methanol (4:1), followed by a 2:1 mixture, removed traces of unchanged cerebroside. Elution with methanol yielded pure psychosine (930 mg., 80%). It was recrystallized from a little ethanol or from a mixture of methanol and acetonitrile (1:1). It softened at 130°, turned yellow at about 150°, and melted with decomposition at 195–200°, $[\alpha]^{20}D$ −12.5° (pyridine); R cytolipin H = 0.4.

Anal. Calcd. for $C_{24}H_{47}NO_7 \cdot 0.5H_2O$: C, 61.24; H, 10.28; galactose, 38.3. Found: C, 61.40; H, 10.10; galactose, 38.0.

Psychosine Sulfate.—The base (120 mg.) was dissolved in absolute ethanol (4 ml.) and the solution was treated with 1 equiv. of 0.2 *N* absolute alcoholic sulfuric acid, care being taken that it is only slightly acidic to congo red. The mixture was allowed to stand overnight and the precipitate was filtered and washed with ether. After drying *in vacuo* over phosphorus pentoxide, the sulfate was recrystallized from absolute ethanol (25 ml.). It melted with decomposition at 205–210°, after softening at 150–160°; $[\alpha]^{25}D$ −5.7° (pyridine).

Anal. Calcd. for $C_{24}H_{47}NO_7 \cdot 0.5H_2SO_4 \cdot 0.5H_2O$: C, 55.46; H, 9.50. Found: C, 55.30; H, 9.45.

Dihydropsychosine was prepared either by hydrolysis of Vb as described above or by hydrogenolysis of Vc with 10% palladium on charcoal at 70 p.s.i. After recrystallization from ethanol it melted at 190°, with softening at 145°; $[\alpha]^{25}D$ −7° (pyridine).

Anal. Calcd. for $C_{24}H_{49}NO_7$: C, 62.17; H, 10.65; N, 3.02. Found: C, 62.19; H, 10.42; N, 3.03.

N-Dichloroacetyl-1-DL-Sphingosyl β-L-glucopyranoside was prepared by the general procedure, m.p. 160° with previous sintering at 130°; $[\alpha]^{18}D$ +5° (pyridine).

Anal. Calcd. for $C_{26}H_{47}Cl_2NO_8 \cdot H_2O$: C, 52.87; H, 8.36; Cl, 12.05. Found: C, 52.52; H, 8.45; Cl, 12.17.

Glucopsychosine (1-DL-sphingosyl β-L-glucopyranoside), prepared by hydrolysis of the preceding cerebroside with aqueous barium hydroxide, melted at 190° with decomposition; $[\alpha]^{20}D$ −5.7°.

Anal. Calcd. for $C_{24}H_{47}NO_7 \cdot H_2O$: C, 60.09; H, 10.29. Found: C, 60.14; H, 10.20.

N-Benzyloxycarbonyldihydrosphingosine.—To a cooled solution of 3-O-benzoyl-N-benzyloxycarbonyldihydrosphingosine (IVc, 0.1 g.) in methanol (9 ml.) was added 1 *N* sodium hydroxide (1 ml.) and the mixture was allowed to stand at room temperature for 3 hr. The crystalline product which separated was washed with cold methanol–water (1:1) and recrystallized from ethyl acetate (40 ml.); yield 70 mg. (80%), m.p. 110–112°.

Anal. Calcd. for $C_{26}H_{45}NO_4$: C, 71.7; H, 10.30; N, 3.21. Found: C, 71.44; H, 10.28; N, 3.13.

2-Phenyl-4-hydroxymethyl-5-pentadecyl-2-oxazolidone.—A solution of 3-O-benzoyl-N-benzyloxycarbonyldihydrosphingosine (IVc, 1 g.) in methanol (60 ml.) was treated with 1 *N* sodium hydroxide (10 ml.). The precipitate formed was dissolved by slight warming and the solution was left overnight at room temperature. Addition of water (40 ml.) completed the precipitation. The raw product (0.62 g., 95%) melted at 95°. Crystallization from ethyl acetate raised the melting point to 96°.

Anal. Calcd. for $C_{19}H_{37}NO_3$: C, 63.68; H, 11.39; N, 4.28. Found: C, 63.69; H, 11.35; N, 4.36.

Acylation of Dihydropsychosine.—A solution of dihydropsychosine (0.10 g.) and *p*-nitrophenyl lignocerate (0.11 g.) in chloroform and methanol 1:1 (10 ml.) was refluxed for 2 hr. The solvent was removed *in vacuo* and the residue was digested twice with boiling ether to remove the *p*-nitrophenol. The insoluble part (120 mg., 70%) was recrystallized from methanol and melted at 184–189°. The infrared spectrum was identical with that of an authentic sample.[5]