insure that all the hydrogen selenide was absorbed by the ascarite.) The rate of gas evolution remained almost constant during the 30-min. period with the copper-chromium catalyst, indicating that at least a rapid rate of poisoning did not occur. The platinum catalyst was much more susceptible to poisoning and at the end of 20 min. the rate of hydrogen evolution was less than one third of an initial rate more rapid than that of the copper-chromium catalyst. Running the benzeneselenol over the catalyst at slower rates or higher or low temperatures did not increase the yield. In a typical experiment (using 10 g. of *o*-ethylbenzeneselenol) with the copper-chromium catalyst, the ascarite tube gained 0.355 g. which would indicate that about 80% of the benzeneselenol underwent hydrogenolysis to give hydrogen selenide. After the run the catalyst tube was washed with benzene which was allowed to run down into the condensate. The benzene solution was then washed with dilute sodium hydroxide and then water. After the solution was dried over magnesium sulfate most of the benzene was removed by distillation through an efficient column. The residue which still contained some benzene was flash distilled to give first a forerun of benzene with some selenonaphthene. The material which boiled above 200° was collected and after crystallization from methanol, 1.72 g. of material of m.p. 50–51° was obtained. The picrate of this material melted at 155–157°. When the forerun from the distillation was treated with picric acid, 0.4 g. of picrate of m.p. 151–153° was obtained. The melting point of selenonaphthene has been reported as 50–51° and its picrate as 156–157°.[11]

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III. Synthesis of Dihydrosphingosine-1,3-cyclophosphate[1]

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In a previous communication,[2] it was reported that in the preparation of dihydrosphingosine-1-phosphate from sphingosine which is D-erythro-1,3-dihydroxy-2-amino-4-trans-octadecene,[3] *N*-carbobenzoxydihydrosphingosine reacted with only 1 mole of diphenylphosphoryl chloride to yield *N*-carbobenzoxy-1-diphenylphosphoryl dihydrosphingosine. It was thought that knowledge of this reaction would possibly be utilized in the synthesis of several phosphate diesters in which the primary hydroxyl group of dihydrosphingosine and another nitrogen-containing moiety, such as ethanolamine, choline, or serine, are esterified with phosphoric acid. In a series of reactions under a variety of conditions, *N*-carbobenzoxydihydrosphingosine-1-phenylphosphoryl *N*-carbobenzoxyethanolamine, the desired intermediate in the preparation of dihydrosphingosine-1-phosphoryl-ethanolamine, could not be obtained by the addition of *N*-carbobenzoxyethanolamine to *N*-carbobenzoxydihydrosphingosine and phenylphosphoryl dichloride. Similar results were obtained when choline chloride was substituted for the protected ethanolamine in the above reaction. However, from each reaction mixture a crystalline derivative was isolated in reasonable yield. These derivatives had the same melting point and similar contents of nitrogen and phosphorus. Removal of the protective groups by catalytic hydrogenolysis over platinum yielded a monophosphate ester of dihydrosphingosine. Since this compound consumed no periodic acid under conditions that cleaved dihydrosphingosine-1-phosphate, it was concluded to be dihydrosphingosine-1,3-cyclophosphate and its immediate precursor thus was *N*-carbobenzoxydihydrosphingosine-1,3-phenylcyclophosphate. Further confirmation of this structure was provided by its conversion to the phosphate monoester by opening of the diester ring after acid hydrolysis. This yielded essentially the 1-isomer, the 3-isomer being undetected, which was ascertained by the finding of palmitaldehyde after periodic acid oxidation of the isolated phosphate monoester.

EXPERIMENTAL

N-Carbobenzoxydihydrosphingosine-1,3-phenylcyclophosphate (I). A chilled solution of 6.5 g. of *N*-carbobenzoxydihydrosphingosine[2] in 30 ml. of anhydrous pyridine was added with vigorous stirring for 3–5 min. to 3.2 g. of phenylphosphoryl dichloride[4] in 10 ml. of pyridine surrounded by an ice bath. After standing for 30 min. at 0°, the reaction mixture, upon attaining room temperature, was poured into 500 ml. of crushed ice water. When the precipitate aggregated, it was removed by suction filtration, dried over phosphorus pentoxide *in vacuo*, and crystallized from 200 ml. of n-heptane; yield 3.1 g. (36% of theory); m.p., 81–82°.

Anal. Calcd. for $C_{32}H_{48}O_6NP$ (573.4): C, 66.87; H, 8.44; N, 2.44; P, 5.40. Found: C, 66.86; H, 8.72; N, 2.45; P, 5.47.

Dihydrosphingosine-1,3-cyclophosphate (II). 2.0 g. of I were dissolved in 50 ml. of glacial acetic acid containing 200 mg. of platinum oxide and hydrogenated under slightly above atmospheric pressure and room temperature. When the uptake of hydrogen ceased, the reaction mixture was filtered; the filtrate was diluted with 6 volumes of water and brought to *p*H 4.0–5.0 (*p*H paper) with 5*N* NaOH. After chilling the solution in an ice bath, the precipitate was removed, dried over phosphorus pentoxide, and crystallized from 100 ml. of 85% ethanol. The moist precipitate obtained after crystallization was washed successively on the filter with 20 ml. portions of ethanol (twice), acetone, and ether; yield 0.45 g. (35% of theory). Dihydrosphingosine-1,3-cyclophosphate is insoluble in water and most organic solvents but soluble in glacial acetic acid and acid or alkaline ethanol. It consumed no periodic acid.

Anal. Calcd. for $C_{18}H_{38}O_4NP$ (363.3): C, 59.45, H, 10.54, N, 3.85, P, 8.53. Found: C, 59.72, H, 10.63, N, 3.78, P, 8.56.

Conversion of dihydrosphingosine-1,3-cyclophosphate to dihydrosphingosine-1-phosphate (III). 151. 8 mg. of dihydrosphingosine-1,3 cyclophosphate were heated under reflux for 18 hr. in a solvent mixture consisting of 5 ml. of glacial acetic acid, 15 ml. of 34% hydrobromic acid, and 5 ml. of

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water. After cooling to room temperature, the reaction mixture was diluted with 2 volumes of water and chilled in an ice bath. The flocculent white precipitate was removed by suction filtration and washed successively on the filter with 75 ml. portions of water, acetone, and ether; yield 142.7 mg. The entire 142.7 mg. of dihydrosphingosine-1-phosphate, 0.418 mM, were oxidized with periodic acid as previously described.[2] The consumption of periodate was 0.384 mM. This result indicates 92% completion of the reaction. The palmitaldehyde, isolated as the 2,4-dinitrophenylhydrazone, melted at 105–106°; yield 42 mg.

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Some Observations on the Iodoform Test

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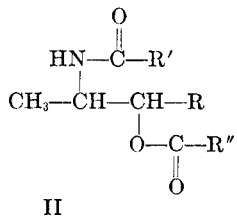
The reactivity of various hypohalite solutions on organic compounds and the scope of this reactivity



II

IIa. R = CH_2OCH_3; R′, R″ = CH_3

IIb. R, R′, R″ = C_2H_5

IIc. R, R′, R″ = CH_3

was adequately reviewed by Fuson and Bull[3] in 1934, and since that time relatively few new structure types have been found to give a positive iodoform test (Lieben's Reaction). These new structures which gave the iodoform test could nevertheless always be explained by hydrolysis, cleavage, or oxidation. Thus α,β-unsaturated ketones not having the requisite methyl ketone or methyl carbinol grouping, could yet yield iodoform if they are capable of forming acetaldehyde or saturated methyl ketones upon a reverse aldol condensation.[4] Upon treatment with sodium hypoiodite 5-methyl-2-furoic acid also yielded iodoform.[5]

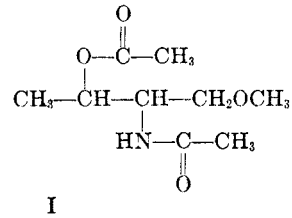
In the course of an investigation on the structure of Elaiomycin,[6] the iodoform test was used in an attempt to distinguish between two possible structures of a degradation product, *N*-(2-hydroxy-1-methylenemethoxypropyl)acetamide, acetate ester (I) and *N*-(2-hydroxy-3-methoxy-1-methylpropyl)-acetamide, acetate ester (IIa).

Distinction between these two structures by the iodoform test was discovered impossible when synthetic IIa yielded iodoform.

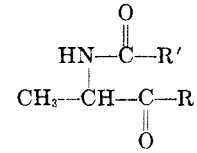
While systems which contain the group CH_3-$CHNH_2$— are known to give a positive test,[3] the conditions of the iodoform test employed in this work were not vigorous enough to hydrolyze an acylated amine. Alanine and isopropylamine which gave a positive test were acetylated to *N*-acetylalanine and *N*-isopropylacetamide, respectively, and the iodoform test failed.

That the esterified methyl carbinol system was hydrolyzed under the standard conditions to give the requisite grouping for iodoform formation was demonstrated by positive tests on *O*-acetyl lactic acid and *N*-(2-hydroxy-1-methylpropyl)acetamide, acetate ester (IIc).

Treatment of *N*-(3-methoxy-1-methylacetonyl)-



I



III

IIIa. R = CH_2OCH_3; R′ = CH_3
IIIb. R, R′ = C_2H_5

acetamide (IIIa) with sodium hypoiodite also resulted in the formation of iodoform. The ketone IIIa would be formed in the hydrolysis and oxidation of IIa with sodium hypoiodite. Further, *N*-(1-

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