[CONTRIBUTION FROM THE INSTITUTE OF CHEMISTRY, MEDICAL FACULTY, UNIVERSITY OF ZAGREB]

STUDIES IN THE SPHINGOLIPIDS SERIES. III. PREPARATION OF SPHINGINE BY THE CATALYTIC REDUCTION OF TRIBENZOYLSPHINGOSINE[1]

M. MUNK-WEINERT, D. E. SUNKO, AND M. PROŠTENIK

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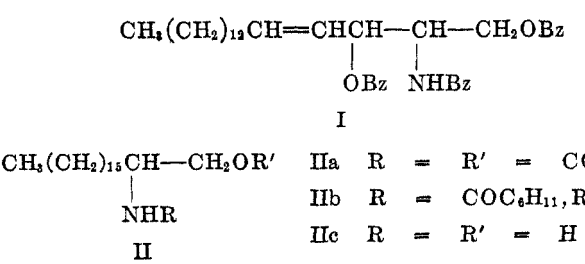
Recently Carter, *et al.* (1, 2) discovered that, by the catalytic reduction of triacetylsphingosine in ethanol solution in the presence of Adams platinum catalyst, 1.5–1.8 moles of hydrogen were taken up with the formation of an amorphous solid. This was purified by acetylation and subsequent hydrolysis of the crystalline diacetyl derivative, giving D(−)-sphingine (1-hydroxy-2-amino-octadecane). They discussed and cleared up the mechanism of the reduction. Carter, Norris, Glick, Phillips, and Harris (3) also reduced tribenzoylsphingosine in glacial acetic acid. Over 2 moles of hydrogen were consumed during the reduction, but no defined product could be obtained.

In attempting to prepare some sphingine, we reduced the ethanol solution of tribenzoylsphingosine (I) in the presence of Adams platinum catalyst at room temperature and atmospheric pressure. In a rapid reaction 11 moles of hydrogen were taken up (Fig. 1). This amount of hydrogen is required for the hydrogenolysis of the benzoyloxy group in the allylic position, the saturation of the double bond, and the complete reduction of three benzene rings. A nicely crystalline O,N-dicyclohexanoylsphingine (IIa), $[\alpha]_D^{22}$ +21.36° (in chloroform), and cyclohexanecarboxylic acid were obtained in a good yield. The alkaline hydrolysis of IIa with *N* methanolic potassium hydroxide gave N-cyclohexanoylsphingine (IIb). The specific rotation of IIb was not determined due to the low solubility of the compound in different organic solvents. Attempts to carry out the hydrolysis of IIa and IIb to sphingine with 5 % methanolic potassium hydroxide failed. Even after very prolonged refluxing, the reaction mixtures contained considerable amounts of unhydrolyzed or partially hydrolyzed material. However, both IIa and IIb were hydrolyzed completely with 10% methanolic sulphuric acid giving D(−)-sphingine (IIc), $[\alpha]_D^{22}$ −5.10° (in chloroform). Thus, starting from I, sphingine could readily be obtained in an over-all yield of more than 60%.



[1] Paper II, Sunko and Prošteník, *J. Org. Chem.*, **18**, 1523 (1953).

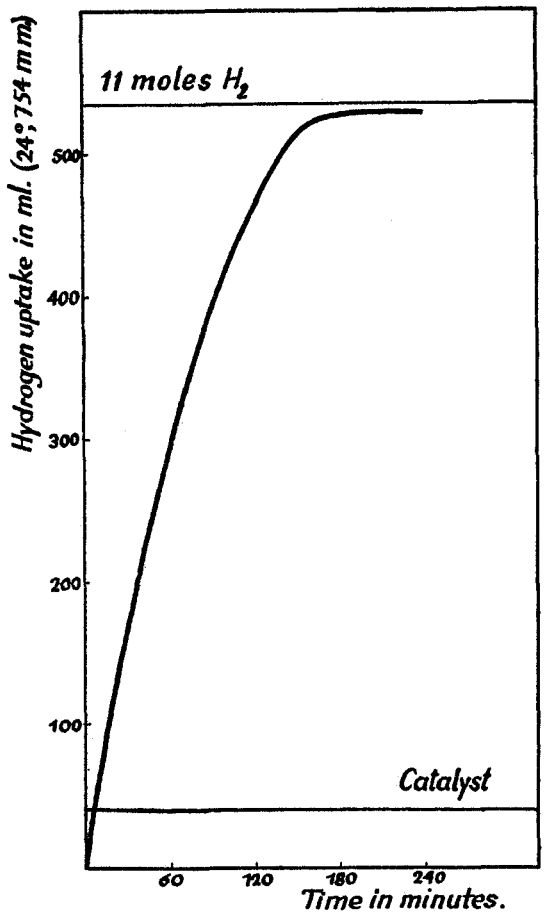


FIG. 1. HYDROGENATION OF TRIBENZOYLSPHINGOSINE

EXPERIMENTAL

The melting points are uncorrected.

O,N-Dicyclohexanoylsphingine (IIa). A suspension of 1.1 g. of tribenzoylsphingosine (I) (m.p. 118–120°, prepared by hydrolysis of a crude beef brain sphingolipids mixture and subsequent benzoylation) and 200 mg. of freshly prepared Adams platinum oxide (4) in 90 ml. of 95% ethanol were hydrogenated at 24° and 754 mm. After 3 hours the reduction was complete. The hydrogen uptake was 531 ml. (Calc'd 537 ml.) or 98%. Thus, excluding the hydrogen absorbed for the reduction of platinum oxide, 11 moles of hydrogen were taken up. The catalyst was filtered off and the solution was evaporated *in vacuo* to dryness. In order to remove the liberated acid, the crude product (1.12 g.) was dissolved in ether and the solution was washed successively with saturated aqueous sodium bicarbonate and water. After drying and evaporation of the solvent, there remained 950 mg. of crude, crystalline product, m.p. 84–86°. One crystallization from 10 ml. of 95% ethanol gave 660 mg. of colorless needles, m.p. 89–90°, 72.4% yield. For analysis the substance was recrystallized once more, m.p. 90–91°, $[\alpha]_D^{22}$ +21.36° (*c*, 2.336, in chloroform).

Anal. Calc'd for $C_{32}H_{59}NO_3$: C, 75.98; H, 11.76; N, 2.77.

Found: C, 75.62; H, 11.57; N, 2.84.

The aqueous solution obtained by washing the crude reduction product with sodium bicarbonate, was evaporated *in vacuo* to a small volume, acidified with dilute sulphuric acid, and extracted with ether. The solvent was removed giving 180 mg. of a viscous oil, which was distilled in a glass tube at 12 mm. and 95–100° (heating block temperature). The distillate gave colorless crystals, m.p. 29–30°, which is in agreement with the melting point of cyclohexanecarboxylic acid (30–31°) given in the literature.

N-Cyclohexanoylsphingine (IIb). A solution of 300 mg. of IIa in 15 ml. of *N* methanolic potassium hydroxide was heated on the water-bath at 40° for one hour. During the reaction the N-cyclohexanoyl derivative partly crystallized. After cooling with ice, the crystals were collected, washed thoroughly with water, and dried. Thus 210 mg. (89.4% yield) of colorless platelets, m.p. 114°, were obtained. For the analysis the substance was recrystallized from 95% ethanol, and melted at 115.5–116°.

Anal. Calc'd for $C_{25}H_{49}NO_2$: C, 75.89; H, 12.48; N, 3.54.
Found: C, 75.96; H, 12.42; N, 3.51.

D-*Sphingine* (IIc). *A. By hydrolysis of IIa.* A solution of 250 mg. of IIa in 5 g. of 10% methanolic sulphuric acid was refluxed for 24 hours. The solution was made alkaline with aqueous potassium hydroxide, and the resulting solid was filtered off, washed with water, and dried. Thus 120 mg. of a colorless product (85.1% yield), m.p. 84–85°, was obtained. One crystallization from ether did not change the melting point.

B. By hydrolysis of IIb. A solution of 90 mg. of IIb in 5 g. of 10% methanolic sulphuric acid was hydrolyzed and worked up in the same manner as described above. Thereby 63 mg. (97% yield) of colorless crystals, m.p. 85–87°, were obtained. One crystallization from ether raised the m.p. to 86–87°; $[\alpha]_D^{22}$ −5.10° (*c*, 3.14, in chloroform). Carter and Humiston gave m.p. 84–89° and $[\alpha]_D$ −5.5°.

Anal. Calc'd for $C_{18}H_{39}NO$: C, 75.72; H, 13.77; N, 4.91.
Found: C, 75.26; H, 13.58; N, 5.06.

SUMMARY

1. The preparation of sphingine by the catalytic reduction of tribenzoylsphingosine (I) was effected.

2. Two new intermediates, dicyclohexanoylsphingine (IIa) and N-cyclohexanoylsphingine (IIb) were described.

ZAGREB, ŠALATA, YUGOSLAVIA

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