notes on methodology

A simplified procedure for the preparation of 2,3-*O*-isopropylidene-*sn*-glycerol from L-arabinose

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Summary A new procedure for the preparation of 2,3-*O*-isopropylidene-*sn*-glycerol is described. L-arabinose is converted to its 4,5-monoisopropylidene diethyl mercaptal derivative. This compound is then subjected to periodate oxidation and borohydride reduction. Following neutralization, the acetone-glycerol is extracted from the aqueous solution into chloroform. Evaporation of the chloroform and subsequent distillation yielded pure 2,3-*O*-isopropylidene-*sn*-glycerol ($[\alpha]_D^{22} = -14.5°$ (in substance)) in an overall yield of 15–25%.—**Kanda, P., and M. A. Wells.** A simplified procedure for the preparation of 2,3-*O*-isopropylidene-*sn*-glycerol from L-arabinose. *J. Lipid Res.* 1980. **21:** 257–258.

Supplementary key words periodate oxidation · optical purity

Naturally occurring phospholipids, as well as mono-, di-, and triglycerides generally exist in optically active forms. In cases where they are not isolable, studies requiring these compounds or their optical antipodes in pure form necessitate chemical syntheses. Likewise, the determination of the absolute configuration of these molecules often rests on comparison with pure synthetic counterparts.

One of the key intermediates in the preparation of glycerides and phosphoglycerides of known configuration is an optically pure isopropylidene glycerol. The two isomers of this species have been obtained from the enantiomeric mannitols (1–5) or serines (6). The 1,2-*O*-isopropylidene-*sn*-glycerol is readily prepared from D-serine or D-mannitol. The preparation of 2,3-*O*-isopropylidene-*sn*-glycerol from L-mannitol is complicated by the circumstance that L-mannitol, being unavailable commercially, must be synthesized from L-arabinose through a lengthy series of reactions (4). The use of L-serine for this purpose, while more straightforward, has in our hands yielded an isopropylidene glycerol of low optical rotation. We describe here a new synthesis of optically pure 2,3-*O*-isopropylidene-*sn*-glycerol from L-arabinose, as shown in **Fig. 1.**

MATERIALS AND METHODS

L-(+)-arabinose (Aldrich, Milwaukee, WI) was recrystallized according to Bates (7) to give $[\alpha]_D^{22} = +104.5°$ (4% aqueous solution, 24 hr). All other materials and solvents were reagent grade. The 4,5-monoisopropylidene-L-arabinose diethyl mercaptal was synthesized according to English and Griswold (8) and gave $[\alpha]_D^{22} = +7.3$ (C, 8.5 in methanol, mp = 75°C (lit. (8), $[\alpha]_D^{22} = +7.6$, mp 75.6°C).

Preparation of 2,3-*O*-isopropylidene-*sn*-glycerol

The sodium periodate oxidation of 4,5-monoisopropylidene-L-arabinose diethyl mercaptal was carried out essentially according to the procedure of LeCocq and Ballou (5). Fifty-eight g of sodium periodate was dissolved in 550 ml of water and chilled in ice to about 5°C. With stirring, 26.6 g of 4,5-monoisopropylidene-L-arabinose diethyl mercaptal was added in portions, maintaining the temperature between 10 and 15°C. After a further 15 min at this temperature, 1400 ml of absolute ethanol was added, and the solution filtered to remove sodium iodate. To the cold cherry red filtrate was added cautiously 14.5 g of sodium borohydride in water. The solution was stirred an additional 2 hr at room temperature, then neutralized with acetic acid. The volume was reduced in vacuo to approximately 350 ml to remove ethanol, and the aqueous solution extracted six times with chloroform. The combined chloroform extracts were dried over sodium sulfate, and then magnesium sulfate. The chloroform was evaporated in vacuo, and the resulting syrup distilled in vacuo to yield 6.2 g of pure 2,3-*O*-isopropylidene-*sn*-glycerol (52% yield); bp 94–95°C (15 mm); $[\alpha]_D^{22} = -14.5°$ (in substance). Overall yield from L-arabinose = 15–25%.

RESULTS AND DISCUSSION

The procedure described here for preparing 2,3-*O*-isopropylidene-*sn*-glycerol represents an alternate route to that using L-mannitol (4). The overall yield here from L-arabinose ranged from 15 to 25% in several preparations. Although this is slightly lower

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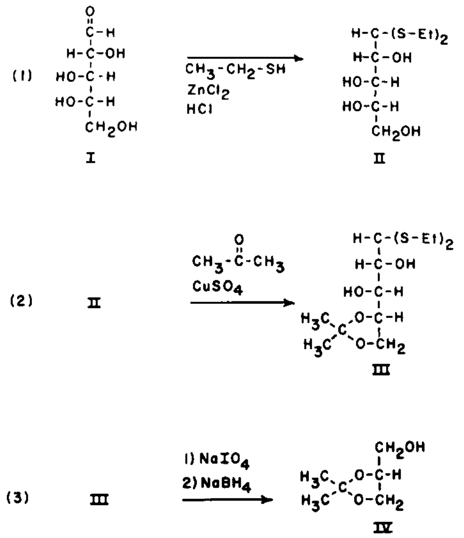

Fig. 1. Reaction scheme for the preparation of 2,3-*O*-isopropylidene-*sn*-glycerol (IV). Reaction 1), formation of 1,1-diethyl mercaptal L-arabinose (II) from L-arabinose (I) and ethyl mercaptan in HCl with $ZnCl_2$ catalyst. In reaction 2), (II) is converted to its 4,5-monoisopropylidene derivative (III) by condensation with acetone in presence of copper sulfate ($CuSo_4$) catalyst. The ketal (III) is then cleaved with sodium periodate ($NaIO_4$) and reduced with sodium borohydride ($NaBH_4$) to yield the 2,3-*O*-isopropylidene-*sn*-glycerol (IV).

than the yield (~30%) from L-arabinose through the intermediate L-mannitol, one can avoid the lengthy series of reactions in preparing L-mannitol (4). The preparation of 2,3-*O*-isopropylidene-*sn*-glycerol from L-serine (6) is somewhat more facile with higher yield (45%), but we have been unable to obtain a product with a $[\alpha]_D^{22}$ higher than −13.3°. This may be due to the difficulty of obtaining optically pure L-serine. In the procedure reported here, the $[\alpha]_D^{22}$ varied from −14.2° to −14.5° in different preparations, compared to +14.5° reported for the optical isomer (5). The specific rotation of the 2,3-*O*-isopropylidene-*sn*-glycerol is dependent on the optical purity of the 4,5-monoisopropylidene-L-arabinose diethyl mercaptal, and often, two or more recrystallizations of this compound from ether-petroleum ether are necessary to achieve the desired purity (8). Furthermore, moisture in the final product may lower the optical rotation (2). It should be noted that the 2,3-*O*-isopropylidene-*sn*-glycerol is configurationally unstable upon standing, and should be used immediately. Finally, it was determined in this procedure that 3 molar equivalents of sodium periodate relative to the 4,5-monoisopropylidene-L-arabinose diethyl mercaptal gave the best yield of product, probably due to the consumption of periodate by one or more of the sulfur atoms (9, 10).

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