NEW METHOD FOR SYNTHESIZING OPTICALLY ACTIVE DIGLYCERIDES

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UDC 542.91+535.56+547.426.21/23

Optically active α,β-diglycerides are key intermediate products in the synthesis of biologically important phospholipids. They have themselves been synthesized either through L-O-benzylglycerol [1] or through γ-monotrityl derivatives of α-monoglycerides [2]. The first of these methods, however, becomes very complex when synthesizing unsaturated diglycerides, since a bromination–debromination stage must be included to protect the double bonds; in practice, the second method is suitable for producing only L-isomers, which are not constituents of natural phospholipids (D-α,β-diglycerides can be obtained by this method only from difficult to get D-α-monoglycerides). Synthesis of α,β-diglycerides from α-O-monotritylglycerol has also been described, but only racemic compounds have been produced by this method [3,4].

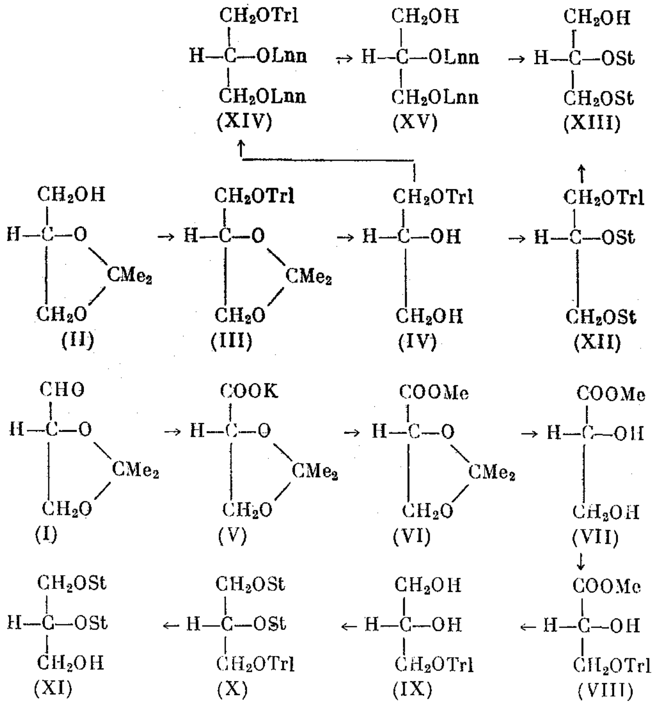
EXPERIMENTAL

This article described the synthesis of optically active L- and D-α-tritylglycerols (IV) and (IX) and of D- and L-α,β-diglycerides from them. The starting materials for synthesis of (IV) and (IX) were readily available D-α,β-O-isopropylideneglyceraldehyde (I) and D-α-β-O-isopropylideneglycerol produced from it (II) [5]. Tritylation of the latter led to D(R)-α-O-trityl-β,γ-O-isopropylideneglycol (III) with a melting point of 89-90° (hexane and an $[\alpha]_D^{20}$ +15.5° (C 8.4; dioxane); according to the data in [6], the melting point is 85-86° and the $[\alpha]_D^{23}$ -13.0° (C 10; dichloroethane). Found %: C 80.22; H 6.99. $C_{25}H_{26}O_3$. Calculated %: C 80.18; H 7.06. Both protected groups in (III) (trityl and isopropylidene) were split off by acidic hydrolysis, but special experiments showed that the former was more stable. The greatest selectivity was achieved when a 5% solution of (III) was hydrolyzed in a 5 : 1 mixture of dioxane and water with the aid of an equal weight of trichloroacetic acid at room temperature for 3-4 days. The hydrolysis was approximately 50% complete (checked by thin-layer chromatography [TCL] on Al_2O_3). After separation of the reaction products by chromatography on Al_2O_3, the unreacted (III) was again hydrolyzed. This produced a yield of 31% of L(R)-α-O-tritylglycerol (IV) with a melting point of 95-96° ($CHCl_3$; hexane) and $[\alpha]_D^{20}$ 9.55° (C 5.6; dioxane). Found %: C 78.60; H 6.65. $C_{22}H_{22}O_3$. Calculated %: C 79.01; H 6.63. (see scheme on next page).

In order to synthesize D(S)-α-O-tritylglycerol (IX), we proceeded from the acetonide of D-glyceraldehyde (I) [5]. The latter was oxidized with aqueous $KMnO_4$ in D-glyceric acetonide isolated in the form of its K salt (V), a solution of which in absolute methanol was neutralized with dry HCl at -5° and immediately treated with etheric CH_2N_2. The unpuritied oily methyl ester formed (VI) was hydrolyzed with dilute HCl in methyl-D-glycerate (VII). The latter is highly resinified during distillation, so that a small amount was isolated in pure form as a colorless oil with a d_4^{20} 1.2792, n_D^{20} 1.4468, and $[\alpha]_D^{20}$ -4.7° (without solvent). The majority of the unpurufied (VII) was converted to pyridine by triphenylchloromethane. According to the data yielded by TCL on silica gel, the mixture of reaction products contained the methyl ester of β-O-trityl-D(R)-glyceric acid (VIII) and triphenylcarbinol. Chromatography of part of this mixture on low-activity silica gel yielded pure (VII) with a melting point of 127-128° (ether) and $[\alpha]_D^{18}$ -5.3° (C 5.7; dioxane). Found %: C 76.36; H 6.22. $C_{23}H_{22}O_4$. Calculated %: C 76.22; H 6.12. The mixture of (VIII) and triphenylcarbinol was subjected to alumohydride reduction. Chromatography of the reaction product on Al_2O_3 yielded D(S)-α-O-tritylglycerol (IX) with a melting point of 93-94° ($CHCl_3$; hexane) and $[\alpha]_D^{20}$ -9.6° (C 5.2; dioxane); according to the data in [6], the melting point is 97° and $[\alpha]_D^{20}$ -17.7° (C 8; pyridine). Found %: C 78.78; H 6.71; $C_{22}H_{22}O_3$. Calculated %: C 79.01; H 6.63.

Esterification of (IV) and (IX) with stearoylchloride in pyridine yielded D(S)-α-O-trityl-β,γ-distearoylglycerol (XII) with a melting point of 52-52.5° (acetone) and $[\alpha]_D^{20}$ +7.0° (C 6.4; dioxane) (found %: C 80.23; H 10.53. $C_{58}H_{90}O_5$. Calculated %: C 80.13; H 10.46 and the corresponding L-isomer (X) with a melting point of 51-52° (acetone) and an $[\alpha]_D^{20}$ of -7.2° (C 1.1; dioxane) (found %: C 80.36; H 10.77. $C_{58}H_{90}O_5$. Calculated %: C 80.13; H 10.46

Institute of Natural–Compound Chemistry, Academy of Sciences of the USSR. Translated from Izvestiya Akademii Nauk SSSR, Seriya Khimicheskaya, No. 4, pp. 927-929, April, 1967. Original article submitted October 7, 1966.



Trl = triphenylmethyl, Lnn = linolenoyl, St = stearoyl

In order to detritylate (X) and (XII), we made use of the ability of active silica gel to split off the trityl group without causing acyl migration [3, 7]. When chromatographed on active silica gel, (X) and (XII) respectively yielded L(R)-α,β-distearin (XI) with a melting point of 75-76° ($CHCl_3$; hexane) and $[\alpha]_D^{20}$ +2.5° (C 8.8; $CHCl_3$) and D(S)-α,β-distearin (XIII) with a melting point of 71.5-72° ($CHCl_2$; hexane) and $[\alpha]_D^{20}$ -2.6° (C 8.6; $CHCl_3$) (compare [1]). The agreement of the absolute angles of rotation of the enantiomeric pairs (IV-IX), (X-XII), and (XI-XIII) indicates that they were optically pure.

Esterification of L(R)-α-O-tritylglycerol (IV) with linolenoylchloride in pyridine produced D(S)-α-O-trityl-β,γ-dilinolenoylglycerol (XIV) in the form of an oil with $[\alpha]_D^{20}$ +7.15° (C 1.26; dioxane). Found %: C 81.74; H 9.31. $C_{58}H_{78}O_5$. Calculated %: 81.45; H 9.19. Detritylation of (XIV) on active silica gel was accompanied by partial acyl migration, which did not occur in the synthesis of (XII). Chromatography of the resultant mixture of 1,2- and 1,3-diglycerides on silica gel yielded D(S)-α,β-dilinolenin (XV) in the form of an unstable colorless oil with $[\alpha]_D^{20}$ -4.0° (C 1.37; $CHCl_3$). On hydration over Pt in heptane, (XV) formed optically pure D(S)-α,β-distearin (XIII).

CONCLUSIONS

1. A method has been developed for synthesizing L-α-O-tritylglycerol and D-α-O-tritylglycerol, which are intermediate products in glyceride synthesis, from D-mannitol.

2. D-α,β-distearin, L-α,β-distearin, and D-α,β-dilinolenin were obtained from tritylglycerols.

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