SYNTHESIS OF A PHOSPHATIDALETHANOLAMINE, A CEPHALIN PLASMALOGEN

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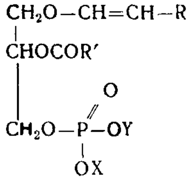
Up to the present time, no synthesis of cephalin plasmalogens (I), which are the main form of natural aldehydogenic lipids [1], has been effected. We have developed basic methods for the synthesis of phosphorus-containing plasmalogens [2] which provide the possibility for obtaining individual classes of these compounds. The main difficulty in the synthesis of the cephalin plasmalogens (I) is due to the necessity for using specific N-protective groups which must be eliminated under conditions excluding acid and alkaline hydrolysis and also catalytic hydrogenation. The transtritylation reaction for the elimination of a N-trityl group, performed with N-tritylalkylamines [3], has shown that it can be used in the synthesis of the cephalin plasmalogens.

The present paper describes the preparation of cephalin plasmalogens, the basic scheme for this having been put into effect with racemic compounds and mixtures of cis and trans isomers.



$$\begin{array}{l} CH_2O-CH=CH-R \\ | \\ CHOCOR' \\ | \qquad\quad O \\ | \qquad\;\; /\!\!/ \\ CH_2O-P-OY \\ \qquad\quad\;\; | \\ \qquad\quad\;\; OX \end{array}$$

I. $X=H$, $Y=CH_2CH_2NH_2$ III. $X=CH_2C_6H_5$, $Y=CH_2CH_2NHT_2$
II. $X=Ag$, $Y=CH_2C_6H_5$ IV. $X=Na$, $Y=CH_2CH_2NHT_2$
$R=H-C_{14}H_{29}$, $R'=H-C_{15}H_{31}$.

The cephalin plasmalogen (I) was synthesized in two variants. According to one of them, silver benzyl 1-O-(hexadec-1'-enyl)-2-palmitoyl-3-glyceryl phosphate (II) was condensed with N-trityl-β-chloroethylamine [4] (boiling in benzene for 6 h), and after chromatography on silica, benzyl 1-O-(hexadec-1'-enyl)-2-palmitoyl-3-glyceryl N-tritylaminoethyl phosphate (III) was obtained. Yield 68%, mp 16-18°C, R_f 0.26 [here and below in a fixed layer of silica, petroleum ether–ether (2:1)]. IR spectrum (thin layer), cm^{-1}: 3290-3310, 3030, 3060, 1740, 1655-1672 (doublet), 1595, 1460, 1375, 1270, 1160, 1020, 930, 900, 740, 705. In addition, (III) was obtained by condensing 1-O-(hexadec-1'-enyl)-3-iodo-2-palmitoyl-3-deoxyglycerol with silver benzyl N-tritylaminoethyl phosphate (mp 190-192°C) [4] (boiling in benzene, 6 h) with a yield of 58%.

The anionic debenzylation of (III), performed by boiling with NaI in acetone (5 h) gave sodium 1-O-(hexadec-1'-enyl)-2-palmitoyl-3-glyceryl N-tritylaminoethyl phosphate (IV). Yield 83%, mp 30-31°C, R_f 0.51 [acetone–methanol (9:1)]; IR spectrum (paraffin oil), cm^{-1}: 3200-3400, 1735, 1655-1670 (doublet), 1580-1590 (doublet), 1470, 1370, 1230, 1170, 1060, 930, 900, 840, 740, 705. The N-trityl group in (IV) was eliminated by boiling with allyl alcohol (2-2.5 h) with a yield of 81%.

Substance (I) was obtained in the form of the Na salt, which was recrystallized from methanol–chloroform–acetone (1:1:3), mp 80-91°C; R_f 0.35 [chloroform–methanol–acetone (13:5:1)]. IR spectrum (chloroform), cm^{-1}: 3200-3400, 1735, 1655-1670 (doublet), 1640 (shoulder), 1550, 1470, 1370, 1235, 1170, 1070, 930, 820, 720. Substance (I) was identified chromatographically and spectroscopically with synthetic and natural preparations of cephalin with an ester bond.

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Thus, we have for the first time effected the synthesis of a cephalin plasmalogen and have proposed the use in lipid chemistry of the transtritylation reaction for the elimination of a N-trityl protective group.

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