A Completely Non-hydrolyzable Synthetic Analogue of Lecithin

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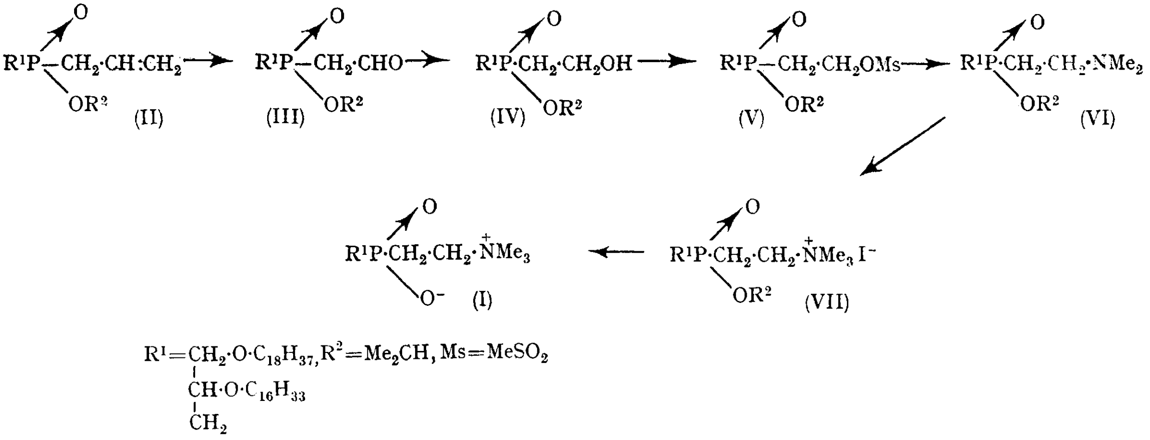
RECENTLY[1] various synthetic glycerophospholipids containing a phosphonic acid group have been described and the natural occurrence of such substances has also been reported.[2]

We report the synthesis of the first phosphinate-containing phosphatide analogue (I) which contains ether rather than ester groups and thus possesses no hydrolyzable moieties. The synthetic route used is shown in the Scheme.



2-Hexadecoxy-3-octadecoxyiodopropane[3] by Arbuzov condensation with di-isopropyl allylphosphonite[4] gave the isopropyl (dialkoxypropyl)-allylphosphinate (II), m.p. 31—32°. Periodate–osmate oxidation afforded the phosphinate aldehyde (III), which was readily reduced by sodium borohydride to the corresponding alcohol (IV), whose methanesulphonate (V) with dimethylamine gave the tertiary amine (VI). Quaternization yielded the methiodide (VII), m.p. 166—167°, which on acid hydrolysis or treatment with trimethylchlorosilane[5] yielded the lecithin analogue (I) as a monohydrate, m.p. 202—203° (decomp.) (34%). The racemic diastereoisomers (II)—(VII) were not resolved during the isolation procedures and both yielded the same racemic lecithin when the possibility of optical isomerism about phosphorus was removed in the final hydrolysis.

The phosphinate lecithin was homogeneous on silica gel plates in chloroform–methanol–water (64 : 25 : 4), chloroform–methanol–7N-ammonium hydroxide (64 : 25 : 4), and chloroform–formic acid (98%)-methanol (70 : 2·5 : 2). The i.r. spectrum showed a rather diffuse hydrogen-bonded P→O band at 1175 cm.$^{-1}$ and the absence of the strong P–O–C band around 1000 cm.$^{-1}$ found in all previously reported phosphatides.

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