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SYNTHESIS OF A "MIXED-ACID" α-LECITHIN*

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SINCE naturally occurring glycerolphosphatides as a rule contain two different fatty acids, we have synthesized several "mixed-acid" α-lecithins. These synthetic lecithins may become valuable substrates for biochemical model studies.

The preparation of a number of L-α-lecithins containing two identical acyl groups by acylating L-α-glycerylphosphorylcholine with acyl chlorides of varying chain length (C_2 to C_{24}), has been reported.[1] The corresponding conversion of β-lysolecithins to lecithins with two different acyl groups proved possible as well.[2]

During our attempts to prepare defined "mixed-acid" lecithins from lysolecithins we succeeded in synthesizing γ-octadecanoyl-β-dodecanoyl-α-lecithin (IV) by another route.

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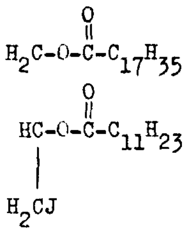
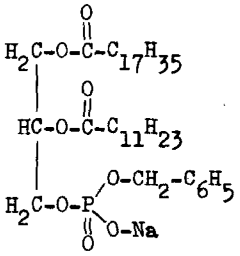
[*] This work is part of a study into the field of phosphatides initiated by the late Prof. F. Kögl.

[1] N.H. Tattrie and C.S. McArthur, Canad. J. Biochem. Physiol. **35**, 1165 (1957); E. Baer and D. Buchnea, Ibid. **37**, 953 (1959); F. Kögl, G.H. de Haas and L.L.M. van Deenen, Rec. Trav. Chim. In press (1960).

[2] G.H. de Haas and L.L.M. van Deenen, To be published.



I



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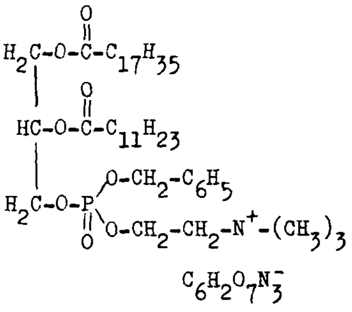
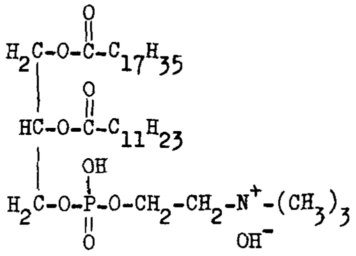


III



IV

γ-Octadecanoylglycerol[3] was converted with p-toluene-sulphonyl chloride in anhydrous pyridine into γ-octadecanoyl-α-(p-toluenesulphonyl)-glycerol, which upon treatment with sodium iodide in acetone provided γ-octadecanoyl-α-iodohydrin, as colourless crystals from methanol (yield 70%; m.p. 61.5°); (Found: C, 53.59; H, 8.80. $C_{21}H_{41}O_3J$ requires C, 53.84; H, 8.82). The melting point is identical with that of γ-octadecanoyl-α-iodohydrin prepared according to Wohl,[4] by acylating α-iodohydrin directly with octadecanoyl chloride.

This compound upon acylation with dodecanoyl chloride in anhydrous

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[3] E. Baer and H.O.L. Fischer, J. Amer. Chem. Soc. **67**, 2031 (1945).

[4] H. Wohl, Inaug.-Diss. Techn. Hochschule München (1927).

pyridine yielded γ-octadecanoyl-β-dodecanoyl-α-iodohydrin (I), as colourless crystals from methanol (yield 95%; m.p. 33.5°); (Found: C, 61.06; H, 9.90. $C_{33}H_{63}O_4J$ requires C, 60.94; H, 9.73).

By treatment with silver dibenzylphosphate, according to Hessel *et al.*,[5] I was converted in nearly quantitative yield into dibenzyl γ-octadecanoyl-β-dodecanoylglycerol phosphate; colourless crystals from methanol (m.p. 39°); (Found: C, 70.40; H, 9.82; P, 3.71. $C_{47}H_{77}O_8P$ requires C, 70.46; H, 9.69; P, 3.86).

Monodebenzylation of this dibenzylester with sodium iodide in acetone according to Gielkens *et al.*,[6] furnished the corresponding sodium salt (II), as a white powder (yield 90%);(Found: C, 65.38; H, 9.68; P, 4.20. $C_{40}H_{70}O_8PNa$ requires C, 65.55; H, 9.63; P, 4.23). This sodium salt was readily converted in a 90% yield into the corresponding silver salt; colourless crystals from acetone (m.p. 54°); (Found: C, 59.01; H, 8.26; P, 3.70. $C_{40}H_{70}O_8PAg$ requires C, 58.74; H, 8.63; P, 3.67).

The silver salt thus obtained, was allowed to react with 2-bromo-ethylene trimethylammonium picrate[7] (100% excess) by refluxing in tetrahydrofurane for 24 hr in the dark. After removal of the precipitated silver bromide and the excess 2-bromo-ethylene trimethylammonium picrate, the benzyl γ-octadecanoyl-β-dodecanoyl-glycerol-α-phosphorylcholinepicrate (III) was obtained as a waxy, yellow solid in a yield of 96%.

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[5] L.W. Hessel, I.D. Morton, A.R. Todd and P.E. Verkade, *Rec. Trav. Chim.* **73**, 150 (1954).

[6] J.W. Gielkens, M.A. Hoefnagel, L.J. Stegerhoek and P.E. Verkade, *Rec. Trav. Chim.* **77**, 656 (1958).

[7] I. Kabashima, *Ber.* **71**, 1073 (1938).

Decomposition of this picrate in acetone with Amberlite IR-45 yielded the corresponding free base. After removal of the benzyl group by hydrogenolysis in absolute ethanol, using a palladium-active carbon catalyst,[6] we obtained in a 96% yield the "mixed-acid" lecithin (IV), a colourless powder from ether with m.p. 211-212°.

The lecithin was analysed as cadmium chloride adduct (Found: C, 45.31; H, 7.76; N, 1.49; P, 3.02. $(C_{38}H_{78}O_9NP)_2(CdCl_2)_3$ requires: C, 45.68; H, 7.87; N, 1.40; P, 3.10).

Saponification of the free lecithin and analysis of the fatty acids by gas-liquid chromatography ascertained the presence of equimolar amounts of octadecanoic acid (recovered: 99%) and dodecanoic acid (recovered: 98%).

The foregoing procedure was also employed for the synthesis of the structural isomer γ-dodecanoyl-β-octadecanoyl-α-lecithin. Both isomers, and corresponding "mixed-acid" α-lecithins obtained by acylating lysolecithins, will be further characterized by physical and biochemical analysis. The synthesis of lecithins containing two identical acyl groups was also achieved, but in this case the described method appeared to be more elaborate than the preparation of these lecithins by the direct acylation of L-α-glycerylphosphorylcholine.[1] The lecithins obtained by both procedures proved to be identical, indicating once more the validity of the present method. The synthesis of optically pure "mixed-acid" L-α-lecithins and lecithins containing both a saturated and an unsaturated fatty acid, is in progress. Full details will be reported elsewhere.

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