TECHNICAL PAPERS

Synthesis of Enantiomeric α-Lecithins[1]

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Lecithins containing only saturated fatty acids, known as hydrolecithins, have been shown to occur in nature (*3, 4, 6, 7*). Although numerous attempts have been made to synthesize hydrolecithins, none of these syntheses has yielded the desired product. We have recently accomplished the synthesis of several pure α-hydrolecithins of known spatial arrangement. An α,β-diglyceride in its D-, L-, or racemic form is phosphorylated with monophenylphosphoryl dichloride in the presence of pyridine. The reaction product, without isolation, is immediately esterified with choline chloride. The diacyl-α-glycerylphenylphosphorylcholine chloride is isolated and purified via the reineckate. The reineckate is converted to the sulfate and the protective phenyl group removed by catalytic hydrogenolysis. After elimination of the sulfate ion the resulting hydrolecithin is isolated and is purified by crystallization from a suitable solvent such as diisobutyl ketone.

The following three L-α-hydrolecithins have been synthesized by using as starting materials the corresponding D-α,β-diglycerides, which were prepared according to the procedure described by Sowden and Fischer (*5*):

L-α-distearoyl lecithin (DSL): $C_{44}H_{90}O_9NP$—*Found.* C, 64.6; H, 10.84; N, 1.85; P, 3.81. $[\alpha]^{26}_{D}+6.1°$ in chloroform-methanol 1:1, c 4.2; $M_D+49.3°$.

L-α-dipalmitoyl lecithin (DPL): $C_{40}H_{82}O_9NP$—*Found.* C, 63.9; H, 11.1; N, 1.87; P, 4.13. $[\alpha]^{23}_{D}+6.7°$ in chloroform-methanol 1 : 1, c 4.2; $M_D+50.2°$.

L-α-dimyristoyl lecithin (DML): $C_{36}H_{74}O_9NP$—*Found.* C, 62.0; H, 11.1; N, 1.97; P, 4.43. $[\alpha]^{23}_{D}+7.0°$; $M_D+48.5°$.

The molecular ratio of choline : phosphoric acid : fatty acids in the synthetic lecithins was found to be very close to 1 : 1 : 2. The three synthetic lecithins, after crystallization from diisobutylketone, gave distinct X-ray diffraction patterns which establish their crystalline structure.

The solubilities of the crystalline lecithins in various solvents were determined. The following values, while not precise, indicate the approximate magnitude of solubility of DSL, DPL, and DML at 22–23° expressed as g/100 ml of solution: dry acetone, 0.01, 0.02, and 0.06, respectively; dry ether, 0.02, 0.02, and 0.03; dry ethanol, 0.8, 1.5, and > 15. In addition, all three lecithins are readily soluble both in glacial acetic acid and in chloroform at room temperature, as well as in hot diisobutyl ketone.

The synthetic L-α-dipalmitoyl lecithin was found to be identical with dipalmitoyl lecithin isolated from natural sources (Thannhauser and associates). Thus, the optical purity of the synthetic product and the stereochemical classification of the natural product are established (L-series). The close similarity of the molecular rotation of DPL to those of DSL and DML is a reasonable assurance that both DSL and DML have also been obtained as pure enantiomers and that the synthesis described is one of general application.

Because of the peculiar kind of stereochemistry of asymmetrically substituted glycerol derivatives an unusual situation presents itself: if we consider any particular lecithin as having been derived from the corresponding diglyceride, it would be assigned to one particular stereochemical series, whereas if we consider the same compound as a derivative of the glycerylphosphorylcholine moiety, it would be assigned to the opposite stereochemical series. The reason for this unusual situation is fully discussed elsewhere (*2*). Confronted with the necessity of assigning a stereochemical designation to the synthetic lecithins, an arbitrary choice had to be made between the two possibilities mentioned above. Since the diglyceride portion of the molecule varies from lecithin to lecithin, it seemed logical to choose as a reference compound the glycerylphosphorylcholine moiety, because it is common to all lecithins. The stereochemical relationship of the α-glycerylphosphorylcholines to the glyceraldehydes, the final reference compounds, has already been established (*1*). Thus, by definition, synthetic and natural lecithins containing the L-α-glycerylphosphorylcholine belong to the L-series.

The synthetic procedure described above makes available for the first time individual lecithins of proven configuration and constitution upon which to conduct systematic zymological and other biochemical and physiological studies.

The experimental details will be reported shortly.

References

1. Baer, E., and Kates, M. *J. Amer. chem. Soc.*, 1948, **70**, 1394.
2. Fischer, H. O. L., and Baer, E. *Chem. Rev.*, 1941, **29**, 287.
3. Lesuk, A., and Anderson, R. J. *J. biol. Chem.*, 1941, **139**, 457.
4. Merz, O. *Z. physiol. Chem.*, 1931, **196**, 10.
5. Sowden, J., and Fischer, H. O. L. *J. Amer. chem. Soc.*, 1941, **63**, 3244.
6. Thannhauser, S. J., Benotti, J., and Boncoddo, N. F. *J. biol. Chem.*, 1946, **166**, 669.
7. Thannhauser, S. J., and Boncoddo, N. F. *J. biol. Chem.*, 1948, **172**, 135.

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