

following manner. A 5.3-g. sample, m.p. 156–163°. was treated with a mixture of 15 cc. of carbon disulfide and 5 cc. of nitromethane, whereupon all but 1.92 g. of solid dissolved. The insoluble portion was crystallized twice from acetone to yield 0.70 g. of 2,2,5,5-tetraphenyltetrahydrofuran (I). Recrystallizations of the soluble portion of the original mix-

ture eventually yielded 0.12 g. of 1,1,4,4-tetraphenyl-1,3-butadiene (III) as the only other compound which could be isolated in pure condition.

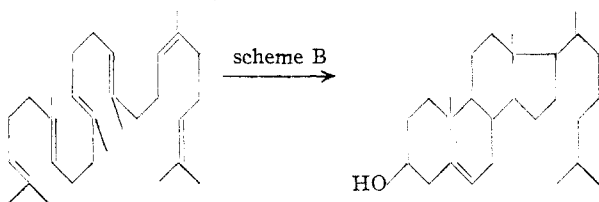
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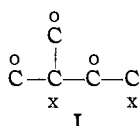
ON THE INCORPORATION OF ACETATE INTO CHOLESTEROL

Sir:

It has recently been demonstrated¹ that squalene is an efficient precursor of cholesterol and is most likely an intermediate in the conversion of acetate to this sterol. A pathway by which this hydrocarbon could be transformed into cholesterol was suggested by Robinson² in 1934 (route A). The recent findings^{3,4} that the sterols and tetracyclic triterpenes are most likely of the same absolute configuration have suggested an alternate mechanism for the utilization of squalene in the biosynthesis of cholesterol (scheme B).



Degradation of the side-chain⁵ and of ring A⁶ of cholesterol formed from C¹⁴-labeled acetate in biological experiments has indicated that such a biosynthesis might proceed by condensation of isoprenoid units labeled as shown in (I).⁷ Therefore, if route A was followed



carbon atoms 10, 13, 20 and 25 of cholesterol would be derived from a carboxyl carbon of acetate and carbon atoms 18, 19, 21 and 26 from the methyl carbon. Such would not be the case if the tetracyclic triterpenoid type of scheme (B) was followed since a migration of a carbon atom would be involved. Thus in route B, carbon atoms 10, 20 and 25 would be from carboxyl carbons and carbon atoms 13, 18, 19, 21 and 26 from methyl carbons.

(1) R. G. Langdon and K. Bloch, *J. Biol. Chem.*, **200**, 135 (1953).

(2) R. Robinson, *J. Soc. Chem. Ind.*, **53**, 1062 (1934).

(3) W. Klyne, *J. Chem. Soc.*, 2916 (1952).

(4) W. G. Dauben, D. F. Dickel, O. Jeger and V. Prelog, *Helv. Chim. Acta*, **36**, 325 (1953).

(5) J. Wüersch, R. L. Huang and K. Bloch, *J. Biol. Chem.*, **195**, 439 (1952).

(6) J. W. Cornforth, G. D. Hunter and G. Popják, *Biochem. J.*, **53**, xxiv (1953).

(7) The methyl carbon of acetate is denoted by o and the carboxyl carbon by x.

Hence, the acetic acid derived from a Kuhn–Roth oxidation of cholesterol which had been formed biosynthetically from C¹⁴-methyl-labeled acetic acid should contain C¹⁴ in the carboxyl group if route B was followed and not if route A was utilized.

Such an experiment was performed and the acetic acid so obtained was degraded by a Schmidt reaction. It was found that the acetic acid had a specific activity of 55,⁸ the carboxyl carbon had 35 and the methyl carbon had 74. It is seen that the carboxyl carbon atom of acetic acid derived from cholesterol possessed C¹⁴ as would be predicted by route B and thus would rule against the Robinson postulate (route A).

If one assumes that the ratio of methyl carbons to carboxyl carbons in cholesterol derived from acetate⁹ is 15/12 and that 5 of the 8 carbon atoms of the 4 molecules of acetic acid (from the angular positions as discussed above) obtained from the Kuhn–Roth oxidation of such a labeled cholesterol are, in turn, derived from the methyl carbons, then the specific activity of the carbon dioxide obtained by decarboxylation of acetic acid should have a value of only 22. The higher value, 35, can be reconciled by consideration of the involvement of the progenitor, methyl-labeled acetate, in the tricarboxylic acid cycle which would lead to some doubly-labeled acetate. This degree of randomization is of the same order of magnitude as recently reported by Cornforth, Hunter and Popják.⁶

These results strongly indicate that if squalene is directly utilized in the synthesis of cholesterol, a reaction scheme of the type B is strongly suggested.¹⁰

(8) All specific activities are expressed as dis./min./mg. BaCO₃.

(9) H. N. Little and K. Bloch, *J. Biol. Chem.*, **183**, 33 (1950).

(10) A recent report by Woodward and Bloch (*THIS JOURNAL*, **75**, 2023 (1953)) has suggested the same reaction scheme.

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POSSIBLE SIGNIFICANCE OF LACTONES AS INTERMEDIATES IN OXIDATION OF CARBONACEOUS MATERIALS

Sir:

Controlled oxidation of aqueous, alkaline suspensions of bituminous coals results in the conversion of about 50% of the carbon to a mixture of