

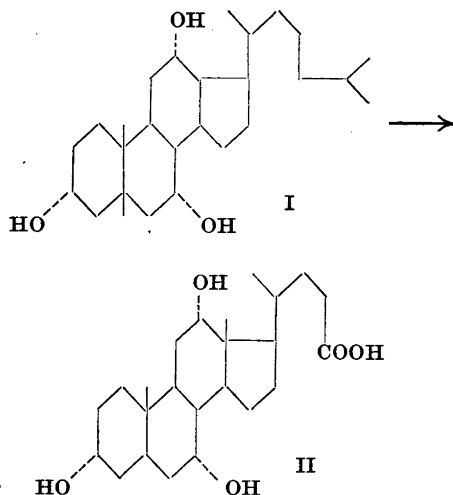
Synthesis and Metabolism of 3 α ,7 α ,12 α [4-¹⁴C] coprostane

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During the transformation of cholesterol into bile acids, the cholesterol side chain is presumably degraded through a ω - or methyl-oxidation followed by β -oxidation of an intermediary α -methyl-C₂₇ acid. It is not known when these reactions take place in relation to the various changes on the ring system.

We have now prepared 3 α -, 7 α -, 12 α -coprostane (I) *i.e.* a compound with the cholesterol side chain and the same configuration in the cyclic part as cholic acid.



It has been prepared by electrolysis of a mixture of cholic acid (II) and 2-methylbutyric acid; m.p. 186°. (Found: C 76.7; H 11.4. Calc. for C₂₇H₄₈O₃: C 77.1; H 11.5; $[\alpha]_D^{20} = 15.1^\circ \pm 2^\circ$ [0.9 ethanol]).

Starting from [4-¹⁴C] cholic acid and a large excess of 3-methylbutyric acid the corresponding ring labelled compound was obtained.

This compound has been administered intraperitoneally to rats with a bile fistula. Practically all activity was recovered in the bile during the following 10 hours. The isotope was to more than 90 per cent contained in taurocholic acid. A small amount of a labelled acidic compound was found in the chromato-

grams in the region where free trihydroxy acids appear but has not yet been identified.

Thus, when the ring system has the configuration of cholic acid, the sterol side chain is rapidly and completely degraded to that of a bile acid (I \rightarrow II).

In contradistinction, when ring labelled cholesterol is administered intraperitoneally in the same manner, it is distributed in the body and the isotope only slowly appears in the bile mainly as bile acids during the following weeks.

Metabolism of Bile Acids in Liver Slices and Homogenates

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The conjugation and 7 α -hydroxylation of desoxycholic acid to taurocholic acid found to take place in the rat *in vivo*, has also been demonstrated in rat liver slices ^{1,2}.

In continuing this work, these reactions have now been further studied in human and rat liver slices and homogenates. Carboxyl labeled bile acids have been used as substrate and the reaction products have mainly been characterized by paper chromatographic methods ³. Quantitative results have been obtained by measuring the radioactivity of the paper strips by means of an automatic scanner. The homogenizing medium contained 10.1 g sodium phosphate, 1.4 g potassium phosphate and 43 g sucrose per liter. The pH was 7.4. A short homogenizing time and a loose fitting pestle are essential. The conjugation with taurine in rat liver homogenates was inhibited at concentrations of bile acids in the range of 10–30 mg % (w/v, 30 % homogenate). However, the hydroxylation of taurodesoxycholic acid proceeds at much higher concentrations.

With the aid of the same technique we have investigated the metabolism of cholic, desoxycholic, chenodesoxycholic and lithocholic acid in human liver homogenates. The capacities to conjugate bile acids in these preparations were in the same range as for the rat liver homogenates. The average value for the conjugation of cholic acid without addition of any amino acids was 60 % taurocholic and 40 % glycocholic acid. The addition of 3 moles taurine changed the composition to 90 % taurocholic and 10 % glycocholic acid. Glycine (3–30 moles per mole bile acid) added to the homogenates of human liver caused smaller changes. Other substances such as cysteine

or cysteine-sulfonic acid had minor but distinct effect on this ratio.

1. Bergström, S., Rottenberg, M. and Voltz, J. *Hoppe-Seyler's Z. Physiol. Chem.* **295** (1953) 278.
2. Bergström, S., Dahlqvist, A. and Ljungqvist, U. *Kgl. Fysiograf. Sällskap. Lund. Förh.* **23** (1953) No. 12.
3. Sjövall, J. *Acta Chem. Scand.* **8** (1954) 329.

Synthesis and Metabolism of 2,2,17,17-Tetramethyloctadecanoic Acid

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Recently 2,2-dimethyl [1-¹⁴C] octadecanoic acid ¹ and 2-methyl [1-¹⁴C] octadecanoic acid ² have been prepared and administered to adult white rats. According to the activity recovered in the expired carbon dioxide, 2-methyloctadecanoic acid is metabolized in the same way as stearic acid. 2,2-Dimethyl [1-¹⁴C] octadecanoic acid was well absorbed, but the isotope was mainly excreted in the urine as 2,2-dimethyl [1-¹⁴C] adipic acid ¹.

We have now prepared 2,2,17,17-tetramethyl [1-¹⁴C] octadecanoic acid from 15,15-dimethylhexadecanoic acid and methyl hydrogen 2,2-dimethyl [1-¹⁴C] succinate (3-[3¹⁻¹⁴C] carbomethoxy-3-methylbutyric acid) by anodic synthesis. M.p. 46.6°–46.8°. (Found: C 77.5; H 12.9; equiv. wt. 341, Calc. for C₂₂H₄₄O₂ (340.6): C 77.6; H 13.0; equiv. wt. 341.)

When tetramethyl [1-¹⁴C] octadecanoic acid was fed to white rats no activity could be found in the urine.

The different metabolism of these branched fatty acids will be discussed.

1. Bergström, S., Borgström, B., Tryding, N. and Westöö, G. *Biochem. J.* *In press.*
2. Tryding, N. and Westöö, G. *To be published.*

Naturally Occurring *iso*Thiocyanates and their Possible Relationship with α -Amino Acids

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Systematic paperchromatographic investigations ¹ of seed and fresh parts of more than one hundred plant species, mainly belonging to the family *Cruciferae*, have indicated the presence of about 10 different, glucosidically bound, volatile *isothiocyanates*. In addition to the previously known allyl, *sec*-butyl, benzyl and β -phenylethyl *isothiocyanates*, the occurrence of 3-butenyl ², *isopropyl* ³ and ethyl ⁴ *isothiocyanate* in certain species has been definitely established in this laboratory. Three or four spots have been observed attributable to *isothiocyanates* of so far unrevealed structure.

Chemical similarities between naturally occurring *isothiocyanates* and the common α -amino acids suggest a possible biochemical relationship which will be briefly discussed.

1. Kjær, A., Conti, J. and Larsen, I. *Acta Chem. Scand.* **7** (1953) 1276.
2. Kjær, A., Conti, J. and Jensen, K. A. *Acta Chem. Scand.* **7** (1953) 1271.
3. Kjær, A. and Conti, J. *Acta Chem. Scand.* **7** (1953) 1011.
4. Kjær, A. and Larsen, I. *Acta Chem. Scand.* **8** (1954) 699.