

## Studies on the biosynthesis of bile acid

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Cholic acid biosynthesis from cholesterol involves C-24/C-25 bond cleavage. A precursor of the bond cleavage reaction is 3 $\alpha$ , 7 $\alpha$ , 12 $\alpha$ -trihydroxycoprostan-26-oic acid (THCA) and this acid is converted into cholic acid by a mechanism similar to that of the  $\beta$ -oxidation of fatty acids. This research has focused on the stereochemical aspects of this C-C bond cleavage reaction and led to the following findings.

Evidence of the enzymatic formation of 24-oxo-THCA from  $\Delta^{24}$ -THCA has been obtained for the first time by the use of  $^{13}\text{C}$  as a tracer. All of the four stereoisomers of 3 $\alpha$ , 7 $\alpha$ , 12 $\alpha$ , 24-tetrahydroxycoprostan-26-oic acid (TeHCA) were formed when THCA was incubated with rat liver mitochondrial fraction. In contrast, (24R, 25R) THCA was formed when 700 g supernatant fraction was used for incubation. The (25R) stereochemistry is noteworthy, since (3S)-hydroxy intermediate is known for  $\beta$ -oxidation of fatty acids. 27-Nor analogs of THCA and  $\Delta^{24}$ -THCA were also incubated with the mitochondrial fraction to give a mixture of (24R)- and (24S)-24-nor-TeHCA.