

Mechanism and Stereochemistry of Vinyl Group Formation in Haem Biosynthesis

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Summary It is shown that both vinyl groups of haem are formed through the loss of *S* hydrogen atoms located at β -positions of the propionic acid side chains; the hydrogen atoms at the α -positions of the side chains are not involved in the biosynthesis of haem.

β -hydrogen is retained. A mechanism of the latter type is suggested by the work of Sano.³

The presence of vinyl groups as well as intact propionic acid side chains within the same molecule (5) may serve as reliable indicators for giving information on the reaction, $-\text{CH}_2-\text{CH}_2-\text{CO}_2\text{H} \rightarrow -\text{CH}=\text{CH}_2$, in isotopic studies.

When 5-amino-[3,5-³H₄]laevulinic acid [(2a), 5 mg, 13×10^6 c.p.m./mg], containing 43% of the total radioactivity at C-5 and the remainder at C-3, was incubated for 8 h at 37° with a haemolysed preparation⁴ of anaemic† chick

CONTINUING studies on the mechanisms of enzymic reactions involved in porphyrin biosynthesis,^{1,2} we now

TABLE

Substrate	³ H: ¹⁴ C in (7)	³ H: ¹⁴ C in (6)	
		Found	Predicted for conclusions drawn
[2 <i>RS</i> - ³ H ₂]Succinic acid	1.00	0.85	0.83
[2 <i>R</i> - ³ H ₁]Succinic acid	1.00	0.94-0.96	1.00
[2 <i>S</i> - ³ H ₁]Succinic acid	1.00	0.70	0.67

report results on the decarboxylation reactions involved in the formation of vinyl groups in haem (5) biosynthesis. Analogies suggest that conversion of the propionic acid portion of a precursor porphyrinogen, such as coproporphyrinogen (4), into a vinyl group may occur by one of at least two broad mechanisms, (a) and (b). Mechanism (a) requires that both β -hydrogens of the propionic acid side chain are removed, while mechanism (b) predicts that one

blood (25 ml), 1.35×10^6 c.p.m. of tritium were incorporated into haem.⁵ The C-3 of (2a) with its associated hydrogen atoms occupies the position indicated by (▲) in haem (5). The tritiated haem was mixed with another sample of haem biosynthesised from [4-¹⁴C](2a). The doubly labelled material was subjected to removal of iron to give protoporphyrin-IX^{6a} (5a). The latter, after reduction^{6b} to mesoporphyrin-IX (5b), was oxidised with

† Chickens were made anaemic by subcutaneous injections of phenylhydrazine (5 mg/kg body weight) every alternate day for a week.

