

Disparate Pathways of Prostaglandin Biosynthesis in Coral and Mammalian Systems

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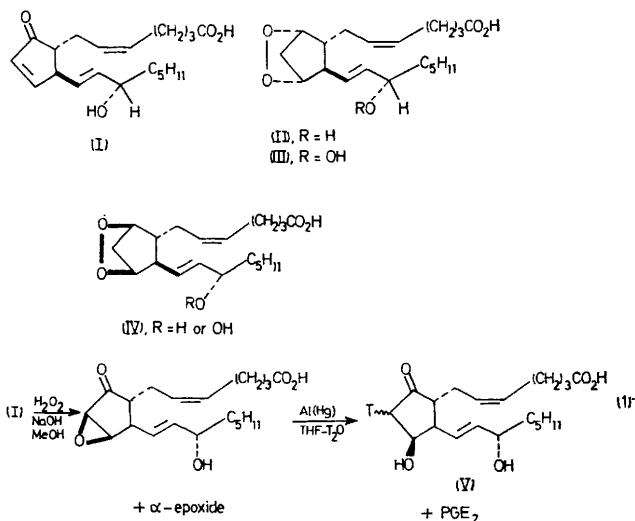
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Summary The biosynthetic pathway to prostaglandin A_2 (PGA_2) in the coral *P. homomalla* does not involve PGE_2 , PGH_2 , PGG_2 , or 11-*epi*- PGE_2 as intermediates and hence differs from that of mammalian systems.

THE discovery¹ that the Caribbean sea whip (or soft coral) *Plexaura homomalla* is a rich source of prostaglandin A_2 (I) (PGA_2) has provoked interest in coral prostaglandin biosynthesis. We now report that the biosynthetic pathway in this coral differs fundamentally from that for mammalian systems. It has been noted previously² that the coral and mammalian PG synthetases respond very differently to cofactors and inhibitors. For example, aspirin and indomethacin, powerful inhibitors of the mammalian synthetase,³ are without comparable effect on the coral PGA_2 synthetase.² In addition, the pathway of PGA_2 biosynthesis in the coral was found, surprisingly, not to involve PGE_2 .²

The endoperoxides (II) (PGH_2) and (III) (PGG_2) have been shown to be intermediates in the biosynthesis of prostaglandins from arachidonic acid by the mammalian synthetase from sheep (or bull) seminal vesicles.⁴ However, in numerous experiments with several different preparations of PGA_2 synthetase² of *P. homomalla* no formation of PGA_2 whatsoever could be detected starting either with [1-¹⁴C]-

PGH_2 ^{4b} or - PGG_2 ^{4b} (each *ca.* 15×10^6 d.p.m. mg^{-1}). The only products detected from PGH_2 and PGG_2 in these experiments are the non-enzymic decomposition products



observed in control experiments with denatured (boiled) enzyme. In other control runs it was demonstrated that the PGH_2 and PGG_2 used for these experiments were cleanly converted by a synthetase preparation from bull seminal vesicles to PGE_2 and PGF_{2a} . Thus it is clear that the endoperoxides PGH_2 and PGG_2 are not intermediates in PGA_2 synthesis by *P. homomalla*.

Another possible route of biosynthesis in *P. homomalla* was tested and ruled out, a process occurring *via* the endoperoxide structure (IV) and 11-*epi*- PGE_2 . A synthesis of

10-[3H]-11-*epi*- PGE_2 (V) was carried out from PGA_2 (equation 1).⁵ Incubation of chromatographically purified, labelled 11-*epi*- PGE_2 with active synthetase from *P. homomalla* gave no PGA_2 and essentially quantitative recovery of the counts as 11-*epi*- PGE_2 .

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⁵ See E. J. Corey and H. E. Ensley, *J. Org. Chem.*, 1973, **38**, 3187.