The Microbial Transformation of Prostaglandins

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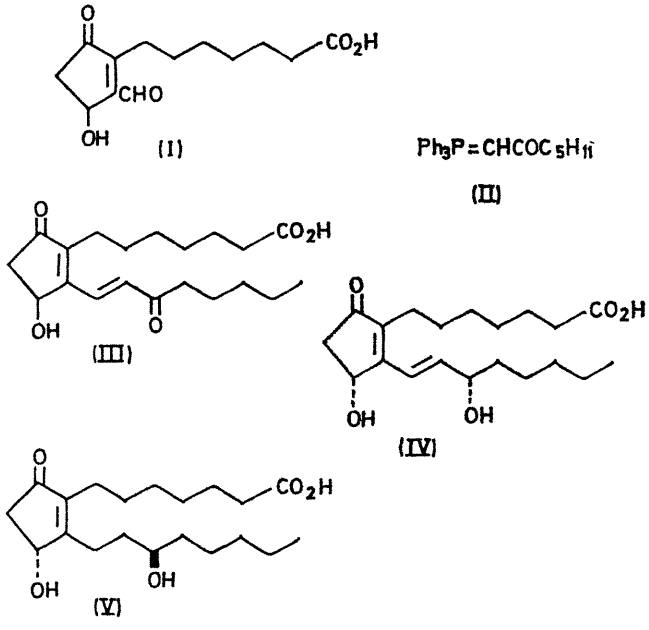
Summary (±)-$\Delta^{8(12)}$-15-Dehydro-PGE_1 (III), (±)-$\Delta^{8(12)}$-PGE_1 (IV), and (±)-15-*epi*-$\Delta^{8(12)}$-PGE_1 (V) have been synthesized from the readily available starting material (I), and compound (III) has been stereoselectively reduced by micro-organisms to either (+)- or (−)-(V).

THE Wittig condensation of 2-formyl-3-hydroxy-5-oxocyclopentene-1-heptanoic acid (I)[1] and n-hexanoylmethylenetriphenylphosphorane (II)[2] afforded an 85% yield of (±)-$\Delta^{8(12)}$-15-dehydro-PGE_1 (III), u.v. (MeOH) 291 nm (ε 21,900), dioxime, m.p. 211°. The keto-group at C-15 was reduced selectively with sodium borohydride to afford an 85% yield of approximately equal amounts of (±)-$\Delta^{8(12)}$-PGE_1 (IV) and (±)-15-*epi*-$\Delta^{8(12)}$-PGE_1 (V)†. These two new prostaglandins were readily separated by partition chromatography ‡ Compound (IV) was a glass and had a u.v. maximum (MeOH) at 276 nm (ε 28,200); the oxime, m.p. 115°. Compound (V) was also a glass, u.v. (MeOH) 276 nm (ε 26,500); the oxime: m.p. 138·5°. The biological properties of (IV) and (V) will be described in a separate publication.

Flavobacterium sp. NRRL B-3874 reduced the (−)-form of (±)-(III) stereoselectively, affording a 30% yield of the (−)-form of (V), $[\alpha]_D^{27}$ − 32 (0·964% in MeOH); m.p. 59·5°. The corresponding enantiomorph, (+)-(III), was not attacked by this organism. Neither (+)-(IV) nor (−)-(IV) was formed in this reduction. On the other hand, *Pseudomonas sp.* NRRL B-3875 reduced the (+)-form of (±)-(III) stereoselectively producing exclusively the (+)-form of (V) in a yield of 24%; $[\alpha]_D^{27}$ + 26 (1·01% in MeOH); m.p. 58° while leaving (−)-(III) intact. The enantiomorph which was not used up in each reduction was optically active and could be separated from (V) by partition chromatography. Stereoselective reductions and an optical resolution were thus achieved by these microbial processes.



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[1] M. Miyano and C. R. Dorn, *Tetrahedron Letters*, 1969, 1615.
[2] P. F. Beal, tert., J. C. Babcock, and F. H. Lincoln, *J. Amer. Chem. Soc.*, 1966, **88**, 3131.

† The stereochemical assignment (tentative) of (IV) and (V) is based upon the further chemical transformation and the biological properties which will be discussed in detail in the full publication.
‡ The stationary phase is made of Mallinckrodt SilicAR CC-4 and the lower phase of benzene (15)–methanol (5)–water (2) mixture; the upper phase was used as the moving phase.