Asymmetric Synthesis of a Prostaglandin Intermediate using Micro-organisms

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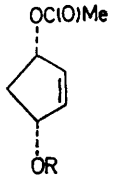
Summary Asymmetric synthesis of a prostaglandin intermediate (**4**) from a simple non-chiral compound (**1**) was accomplished by using micro-organisms.

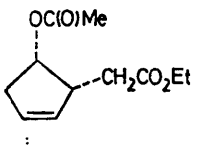
PARTRIDGE and his co-workers[1] have shown that the asymmetric induction of two chiral centres on the lactone (**4**) can lead to the asymmetric formation of prostaglandin $F_{2\alpha}$. We report an alternative asymmetric synthesis of the lactone (**4**) which possesses the two nuclear chiral centres needed to prepare natural prostaglandins.

Non-chiral *cis*-3,5-diacetoxycyclopentene (**1**)[2,3] was agitated aerobically with growing *Bacillus subtillis var. Niger*[4] for 15·5 h to give the crude chiral monoacetate (**2**) in 56·1% yield. On heating (**2**) with an excess of ethyl orthoacetate in the presence of a trace of pivalic acid for 18 h,[5,6] the rearranged product (**3**), b.p. 88—92 °C at 1 mmHg (Kuger Rohr), was obtained which was transformed into the lactone (**4**), b.p. 53—54 °C at 1·0 mmHg, $[\alpha]_D^{14}$ − 37·5°,† in 20·8% overall yield [based on (**1**)] by heating in 2% ethanolic K_2CO_3 solution.

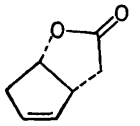
† Optical rotation was taken in 0·5% MeOH solution at 25 °C.



(1) R = C(O)Me
(2) R = H



(3)



(4)

The structures depicted above correspond to the absolute configuration of the natural prostaglandins.

Comparison of the optical rotation of (**4**) with that of an optically pure sample of the lactone ($[\alpha]_D$ — 106°)[1] indicated that (**4**) possessed the required absolute configuration with 35·0% optical purity.

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