

## Asymmetric Synthesis of a Prostaglandin Intermediate using Micro-organisms

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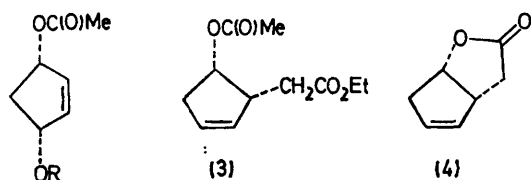
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**Summary** Asymmetric synthesis of a prostaglandin intermediate (**4**) from a simple non-chiral compound (**1**) was accomplished by using micro-organisms.

PARTRIDGE and his co-workers<sup>1</sup> have shown that the asymmetric induction of two chiral centres on the lactone (**4**) can lead to the asymmetric formation of prostaglandin F<sub>2α</sub>. We report an alternative asymmetric synthesis of the lactone (**4**) which possesses the two nuclear chiral centres needed to prepare natural prostaglandins.

† Optical rotation was taken in 0.5% MeOH solution at 25 °C.

Non-chiral *cis*-3,5-diacetoxycyclopentene (**1**)<sup>2,3</sup> was agitated aerobically with growing *Bacillus subtilis* var. *Niger*<sup>4</sup> 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,<sup>5,6</sup> 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,  $[\alpha]_D^{14} = -37.5^\circ$ , † in 20.8% overall yield [based on (**1**)] by heating in 2% ethanolic K<sub>2</sub>CO<sub>3</sub> solution.



(1) R = ClO)Me

(2) R = H

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

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<sup>2</sup> L. N. Owen and P. N. Smith, *J. Chem. Soc.*, 1952, 4035.

<sup>3</sup> T. Toru, S. Kurozumi, T. Tanaka, S. Miura, M. Kobayashi, and S. Ishimoto, *Synthesis*, 1974, **867**.

<sup>4</sup> T. Oritani and K. Yamashita, *Agric. and Biol. Chem. (Japan)*, 1975, **39**, 89.

<sup>5</sup> W. S. Johnson, L. Werthermann, W. R. Bartlett, T. J. Brocksom, T. -t. Li, D. J. Faulkner, and M. R. Petersen, *J. Amer. Chem. Soc.*, 1970, **92**, 741.

<sup>6</sup> K. Kondo, M. Matsumoto, and F. Mori, *Angew. Chem. Internat. Edn.*, 1975, **14**, 103.

Comparison of the optical rotation of (4) with that of an optically pure sample of the lactone ( $[\alpha]_D - 106^\circ$ )<sup>1</sup> indicated that (4) possessed the required absolute configuration with 35.0% optical purity.

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