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Resolution and Configurational Assignments of Methyl-3-hydroxy-5-oxo-cyclopent-1-eneheptanoate, an Important Prostaglandin Intermediate

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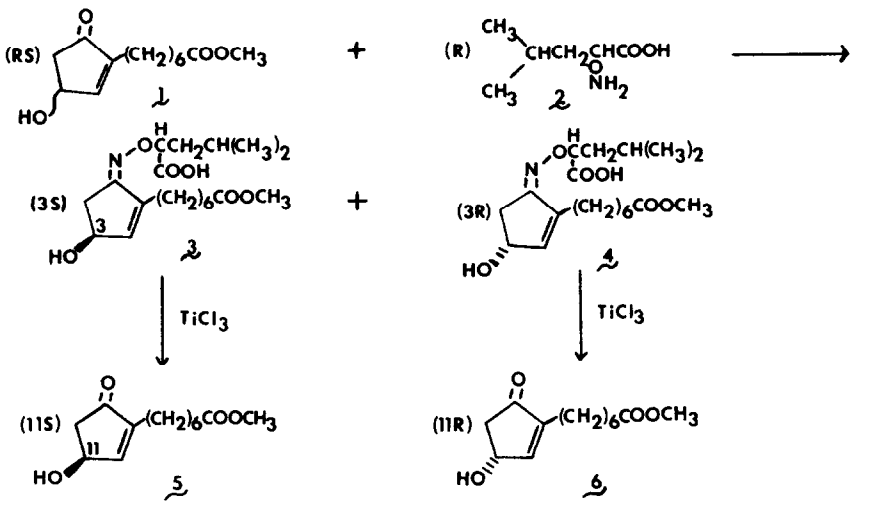
We wish to report the resolution and configurational assignments of methyl-3-hydroxy-5-oxocyclopent-1-eneheptanoate(1), a key intermediate in the synthesis of prostaglandins.[1-3] Treatment of 1 with (R)-2-aminooxy-4-methylvaleric acid(2)[4] in a methanol-pyridine mixture (10:1) at room temperature for 18 hours yielded a mixture of oximes (3) and (4). Although attempts at selective crystallization proved to be fruitless, chromatography on silicic acid (Mallinckrodt SilicAR CC-4) using 1% EtOH in $CHCl_3$ as eluent unexpectedly effected a clean separation of the two diastereoisomers 3 (eluted first) $[\alpha]_D$-61.9° ($CHCl_3$), m.p. 58-60° and 4 $[\alpha]_D$+55.7° ($CHCl_3$), m.p. 45-48°. Similar results were obtained with (R)-2-aminooxy-3,3-dimethylbutyric acid hydrochloride.[5]



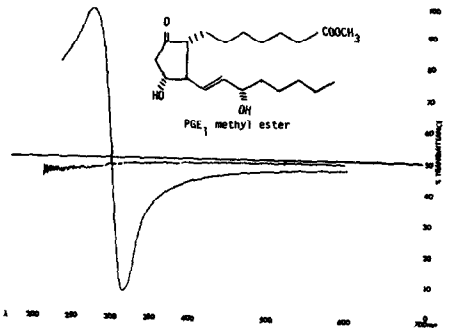


Fig. 1

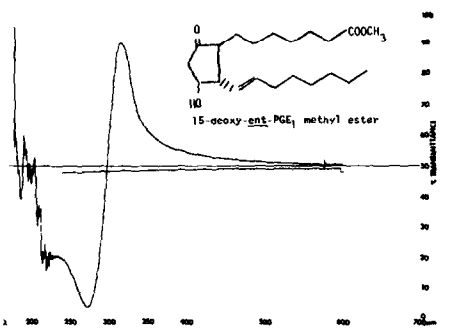


Fig. 2

Regeneration of the ketones 5 $[\alpha]_D$-17.2° (MeOH), m.p. 58-59°, and 6 $[\alpha]_D$+16.8° (MeOH), m.p. 58-59.5° was accomplished by treatment of 3 and 4 with titanium trichloride[6] at 60° for 3 hours in aqueous THF containing ammonium acetate.

The configurations of 5 and 6 were determined by converting each one to 15-deoxy PGE_1 methyl ester[3] and comparing the O.R.D. and C.D. curves of the products with those of authentic PGE_1 methyl ester.[7] Thus 15-deoxy PGE_1 methyl ester derived from 6 had O.R.D. and C.D. curves which were identical with those of PGE_1 methyl ester, whereas the product from 5 displayed the mirror image curves (Fig. 1 and Fig. 2).

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7. Prepared by diazomethane treatment of biosynthetically derived PGE_1; the configuration of PGE_1 at position 11 is R.