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TERREIN, AN OPTICALLY ACTIVE PROSTAGLANDIN SYNTHON OF FUNGAL ORIGIN.

II.[1] CHEMICAL CONVERSION TO 4(R)-ACETOXY-2-CYCLOPENTENONE.

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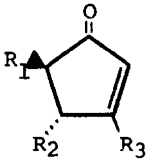
Synthetic approaches to the prostaglandins are still of high interest because natural sources are unable to supply the projected needs. Recent efforts in several laboratories have been devoted to chiral processes in an effort to avoid wasteful resolution steps. The recent establishment of 4(R)-acetoxy-2-cyclopentenone, 1, by Kurozumi, *et al*. (Table I) as a prostaglandin synthon by use of a combined chemical-microbiological process is a case in point.[2] Stork, *et al*. had previously published a prostaglandin synthesis based upon a similarly substituted but racemic intermediate.[3] We wish to report a convenient preparation of the optically active Kurozumi synthon from terrein, 2, a metabolite of *Aspergillus fischerii*[4-8] which has the correct absolute configuration for prostaglandin synthesis.

Terrein, 2, was converted selectively to its crystalline 5-acetyl derivative, 3, in 75% yield, by warming at 65° for 48 hr. in a THF, acetic anhydride (1 equivalent), sodium acetate (1.5 equivalents) slurry [mp 96.5-97°, $\lambda_{max}^{CHCl_3}$ 278 nm (ε=28,600), m/e 196 (M^+)]. Reduction of 3, in acetone with chromous chloride solution[10,11] afforded 4 as a clear yellow oil in 99% yield [$\lambda_{max}^{CHCl_3}$ 270 nm (ε=17,600); m/e 138 (M^+); pmr$_{CDCl_3}$ 2.3δ (dd, J = 2,20 Hz, 1H, H···C-C=O), 2.8δ(dd, J = 5,20 Hz, 1H, H▶C-C=O), and 5.2δ(dd, J = 5,2 Hz, H▶C-CH_2-C=O)]. Analogous reduction of diacetylterrein tended to remove both acetoxy functions.

TABLE I[9]



Structures	R_1	R_2	R_3
1	H	-OAc	H
2	-OH	-OH	$-CH=CHCH_3$ (trans)
3	-OAc	-OH	$-CH=CHCH_3$ (trans)
4	H	-OH	$-CH=CHCH_3$ (trans)
5	H	-OAc	$-CH=CHCH_3$ (trans)
6	H	-OAc	-CHO

Acetylation of 4 in THF with excess acetic anhydride and sodium acetate at 65° for 18 hr. produced 5 in 93% yield [mp 49-59°; $\lambda_{max}^{CHCl_3}$ 270 nm (ε=26,000); m/e 180 (M^+)]. Dieneone 5 was converted to aldehyde 6, in 86% yield, by osmium tetroxide/sodium periodate oxidation[12] in aqueous-acetone [mp 99-100°; $\lambda_{max}^{CHCl_3}$ 237 nm (ε=13,400); m/e 168]. Decarbonylation of 6 to 1 was accomplished in 56% yield by use of Wilkinson's reagent, $Rh(PPh_3)_3Cl$, in benzene-10%-butyronitrile at reflux for 5 min.[13,14] [$\lambda_{max}^{CHCl_3}$ 207 nm (ε=13,600); $[\alpha]_D^{20}$ MeOH = +95° (c = 0.061); m/e 140 (M^+); pmr$_{CDCl_3}$ 2.10δ(s, 3H, C_4-acetate), 2.25δ(dd, J = 3,19 Hz), 1H, H···C-C=O), 2.85δ(dd, J = 6,19 Hz, 1H, H▶C-C=O), 5.9δ(dddd, J = 1.5,3,3,6 Hz, 1H, H▶CCH_2=O), 6.4δ(dd, J = 1.5,6 Hz, 1H, HC=C$\underline{H}$C=O) and 7.65δ(dd, J = 3,6 Hz, 1H, $\underline{H}$C=CHC=O); ORD, λ_{max}^{MeOH} (c = 0.062, 27°): $[\phi]_{430}$ 0, $[\phi]_{350}$ - 1900, $[\phi]_{290}$ + 7,200, $[\phi]_{223}$ + 46,200, $[\phi]_{220}$ + 40,000*]. Kurozumi, *et al*. report a rotation of +84° for this compound resulting from transformation of a starting material which was 90% optically pure.[2]

Thus we have achieved a short (5 step) conversion to an optically active prostaglandin intermediate starting with a conveniently available and inexpensive natural product. An alternate to the use of the expensive Wilkinson's reagent for removal of the unwanted carbon or methods for the recovery of the rhodium would presumably have to be found before commercial application of this work could be made. In our hands, aldehyde 6 was not stable to the conditions (>200°) required for catalytic decarbonylation.[13] Additional routes to prostaglandin from terrein based upon this and other sequences are presently under investigation.

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14. The reported yield is the actual isolated yield after column chromatography The carbon monoxide complex, $Rh(Ph_3P)_2(CO)Cl$, was isolated in 90% yield. Considerable experimentation was required to find the optimal conditions for this step.