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PREPARATION OF 2-(4-HYDROXY-1-OXOCYCLOPENT-2-ENE)HEPTANOIC ACID AN IMPORTANT PROSTAGLANDIN SYNTHON

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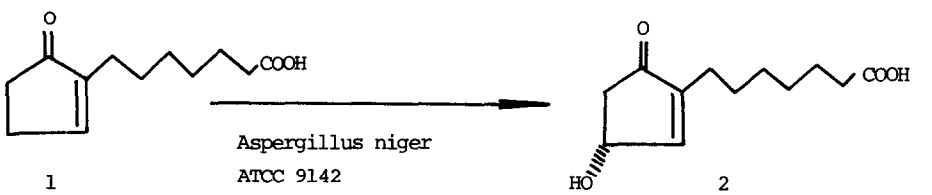
We wish to report an efficient preparation of 2-(4-hydroxy-1-oxocyclopent-2-ene)heptanoic acid 2 (1-5), a key intermediate of prostaglandin synthesis, by microbial hydroxylation (6-8) of readily avialable 2-(1-oxocyclopent-2-ene)heptanoic acid 1 (9,10).
Aspergillus niger ATCC 9142 was found to transform effectively to 2 with partial asymmetric induction.

Compound 1 (263 mg), mp 39°, was dissolved in the fermentation medium which had the same composition as reported by Tabenkin et al. (8) and was adjusted to PH 7.
The fermentation medium (300 ml) was inoculated with a well-sporulated Aspergillus niger ATCC 9142 and incubated at 29° for 24 hr. The cell was filtered and the filtrate was saturated with ammonium sulfate and extracted with ethyl ether, dried (Na_2SO_4) and evaporated in vacuo to leave oily residue. This residue was purified by preparative thin layer chromatography (silica-gel; Et_2O-isoPr$_2$O-AcOH 70:35:3) to give 2 (177 mg, 67% yield) (11), mp 15-20°; $[\alpha]_D^{20}$ + 8.0° (c 0.071, CH_3OH), and a small amount of 2-(1-oxocyclopent-2-ene)butanoic acid; υ 3400-3000, 1720, 1680, 1620 cm^{-1}; λ_{max}^{MeOH} 227 mμ ; $\delta_{TMS}^{CDCl_3}$ 1.50-2.70 (8H), 4.20 (1H), 7.14 (2H), 7.40 (1H); m/e 154,



1 2

136, 123, 108, 95, 94, 80, 79; which was presumably derived via β-fission of the fatty acid 1. Compound 2 was treated with diazomethane in ether to afford the methyl ester 3, (90% yield from 2), $[\alpha]_D^{20}$ + 6.1° (c 0.046 CH_3OH) (13).

The studies for increasing the optical yield of 2 are currently in progress by utilizing other culture conditions or by screening other microorganisms capable of such hydroxylations.

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10. Cyclopentenone 1 was prepared from methyl 2-oxocyclopentaneheptanoate by the sequence bromoacetalization, dehydrobromination, deacetallization, and hydrolysis, and will be the subject of a forthcoming publication from our laboratories.
11. Satisfactory infrared, ultraviolet, nuclear magnetic resonance and mass spectra were obtained.
12. The melting point of racemic 2 reported in the reference (1) was 37.6-38.5°.
13. The specific rotation of the optically pure 3 reported in the references (3,4) was + 16.8° and + 17.8°, respectively.