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PROSTAGLANDINS III.[1] SYNTHESIS OF ($\pm$)-11-DEOXY-PGE$_1$

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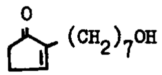
In an earlier communication[2] we described a prostaglandin synthesis based upon the cyclopentenone (I). We have now used this approach in a simple route to 11-deoxy-PGE$_1$.

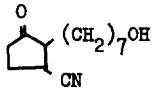
The nitrile (II),[2] prepared in 80% yield by reaction of I with acetone cyanohydrin, was converted with ethylene glycol into the ketal (IIIa) (90% yield): b.p. 196-216°/0.07 mm; which on treatment with diisobutylaluminium hydride in ether-benzene at 10-15° and subsequent work up with aqueous acetic acid afforded the aldehyde (IIIb) (90% yield). The latter underwent Wittig coupling with hexanoylmethylene triphenylphosphorane[2] to give the enone (IVa): ν max 1620, 1660 cm^{-1}, which was oxidised with chromium trioxide and sulphuric acid in dimethylformamide at 0° to the acid (IVb) (55% yield from IIIb): ν max 1620, 1660, 1700 cm^{-1}. Reduction of IVb with potassium borohydride in a citrate buffer at pH 8[3] and subsequent hydrolysis with 2N hydrochloric acid at 60° gave a 75% yield of an approximately equal mixture of ($\pm$)-11-deoxy-PGE$_1$ (V) and its 15-epimer (VI) which were separated by chromatography on silica gel, eluting with ethyl acetate-cyclohexane-formic acid (40:40:1); (V)[3] m.p. 82-84° (from ether-hexane) being the more polar compound.

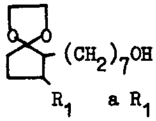
The convenience of this approach to prostaglandin synthesis has been enhanced by our finding that 7-hydroxyheptanal, our starting material for the preparation of enone (I),[2] can be readily obtained by sodium periodate cleavage of aleuritic acid**, thus permitting the synthesis of 11-deoxyprostaglandins in 7-8 steps from commercially available materials.

**9,10,16-trihydroxypalmitic acid

During our earlier studies in this series[2] we have assumed, by analogy with the findings of other workers,[4] that the trans-disposition of the side chains arose during the β-addition of the nitrile to the enone (I), and that this configuration was maintained throughout the subsequent stages in the synthesis. However, by using g.l.c. with a 3% OV17 Gas Chrom. Q column, it can be shown that the ketal (IIIa) consists of a mixture of two components (ratio approximately 65:35), and a shoulder on the g.l.c. peak of the ketonitrile (II) indicates that this is a similar mixture. The aldehyde (IIIb), however, gave mainly a single peak with only about 7% of the second component. It appears therefore that the nitrile may contain both cis- and trans-isomers and that most of the cis- is isomerised to the trans- form at the aldehyde stage.

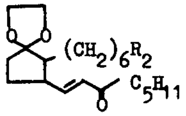

I


II


III

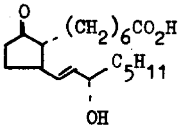
a $R_1 = CN$

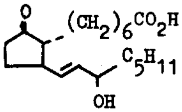
b $R_1 = CHO$


IV

a $R_2 = CH_2OH$

b $R_2 = CO_2H$


V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4) J.F. Bagli and T. Bogri, Tetrahedron Lett., 5, (1967).