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AN UNANTICIPATED, FACILE, REGIOSPECIFIC AND STEREOSPECIFIC A → F PROSTANOID TRANSFORMATION

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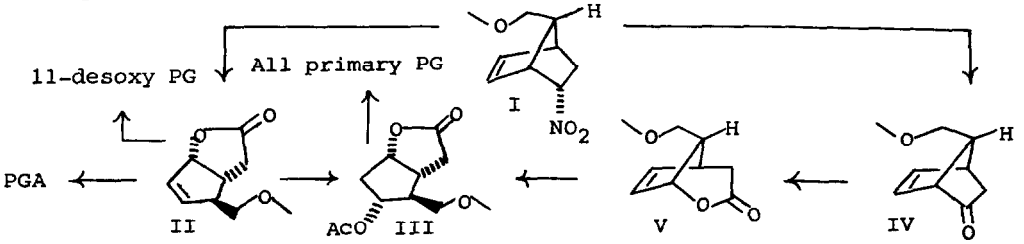
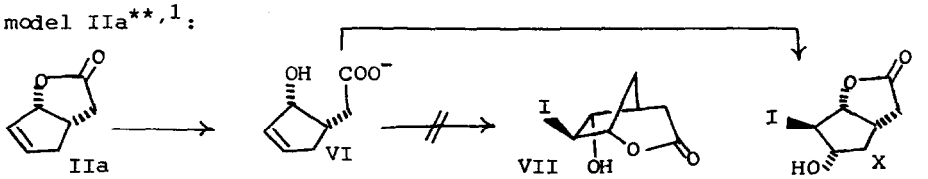
This communication presents, inter alia, the transformation of the versatile nitroethylene adduct I[1] to the Corey prostaglandin intermediate III.[2] This I→ III change, in our evaluation, constitutes the most practical entry to F prostaglandins and involves the particularly noteworthy II→ III change that takes place in a stereospecific and regiospecific fashion:

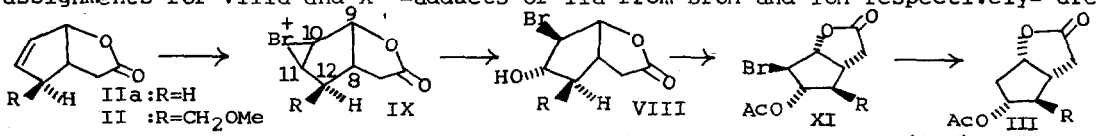


Compound I** has already been demonstrated as an excellent precursor to the ketone IV[1] and therefore the key intermediate III.[2] Surprisingly, the II→ III change constitutes the first A→ F prostanoid nucleus conversion. The practical, one-step preparation of the A prostanoid II from the readily available I,[1] made it attractive to explore the transformation of II to those related to the F series. The unanticipated, clean, II→ III change surfaced in attempts to introduce the additional asymmetric centre by a γ lactone → δ lactone change (VI→VII)[3] with model IIa**,[1]:



In the event, I_2/HCO_3^- treatment of VI, produced in situ, gave only one crystalline IOH adduct. Subsequent treatment of IIa with BrOH- generated in the medium from N-bromoacetamide and aqueous acetone[4] - gave exclusively one adduct in 93% yield to which structure VIIIa was given on the basis of conformational and steric considerations. Molecular models show clearly that the Br^+ could approach II only from the convex exo side and that the resulting ion IX would be preferentially opened from the 11 endo side; approach from 10 is unlikely because

of eclipsing interaction with the 9 substituent(prostaglandin numbering).[5] The assignments for VIIIa and X**-adducts of IIa from BrOH and IOH respectively- are



further confirmed by similar transformation of II** to adduct VIII(80%) and then to the known III,which was compared with an authentic sample. The BrOH adducts VIII and VIIIa were quantitatively transformed to their crystalline acetates XI** and XIa**, which were then hydrogenolyzed (Ni/H_2) in 70% yields to III** and IIIa**. Compound III was identical to an authentic sample.[6,7] The adduct I is nowwell connected with all prostaglandins and also the biologically active 11-desoxy prostaglandins.

REFERENCES AND FOOTNOTES

1. S. Ranganathan, D. Ranganathan and A.K. Mehrotra, J. Am. Chem. Soc., 96,5261 (1974).
2. E.J. Corey, N.M. Weinshenker, T.K.Schaaf and W. Huber, J.Am.Chem.Soc., 91, 5675 (1969); E.J. Corey, T.K. Schaaf, W. Huber, U. Koelliker and N.M. Weinshenker, J.Am.Chem.Soc., 92, 397 (1970); E.J. Corey, R. Noyori and T.K. Schaaf, J.Am.Chem.Soc., 92, 2586 (1970).
3. Interestingly, the classical V→III change involves a reverse δ-lactone→γ-lactone transformation (ref.2).
4. Reagents for Organic Synthesis, Fieser and Fieser, Vol.I, John Wiley, New York, 1967, p.74.
5. The trans addition associated with N-bromoacetamide- aqueous acetone reagent is well recognized: A Lardon and T. Reichstein, Helv.Chim.Acta, 26, 747 (1943); H. Reich and T. Reichstein, Helv.Chim.Acta, 26, 562 (1943); G.H. Ott and T. Reichstein, Helv.Chim.Acta, 26, 1799 (1943).
6. We are most grateful to Professor C. Gandolfi for a generous gift of (+)III (C.Gandolfi, G.Doria and P.Gaio, Tetrahedron Letters, 4303 (1972)).
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** Analytical data in excellent accord with that expected have been obtained for this substance.

I: oil, bp 90°/0.1 mm; ir(neat) 1540, 1366 cm^{-1}(nitro); nmr δ($CDCl_3$) 3.3(d,-CH_2-O-), 3.31(CH_3-O-), 5.1(m, H-C-NO_2), 5.91(q), 6.39(q)(olefinic); II:oil, bp 140°/0.3 mm; ir(neat) 1770 cm^{-1}(lactone); nmr δ($CDCl_3$) 3.35(5H,-CH_2-O-CH_3),5.55 (m, H-C-O-), 6.04(m, olefinic); IIa: oil, bp 80°/1 mm; ir(neat) 1767 cm^{-1}(lactone); nmr δ($CDCl_3$)5.5(m, H-C-O-), 5.9(m),6.1(m)(olefinic); III: oil, bp 110°/0.05 mm; ir(neat) 1770(lactone), 1740(ester) cm^{-1}; nmr δ(CCl_4) 1.94(-OCOCH_3), 3.32(d, -CH_2-O-),3.28(-O-CH_3), 4.88(m, 2x H-C-O-); IIIa: mp 66-67°; ir(KBr)1770 (lactone), 1740(ester) cm^{-1}; nmr δ($CDCl_3$) 2.04(-OCOCH_3) 5.2(m, 2x H-C-O-); X: mp 116-117°; ir(KBr) 3448(OH), 1770(lactone) cm^{-1} nmr δ($CDCl_3$) 4.44 (br, H-C-I), 4.63(b, H-C-OH), 5.4(d, H-C-O-); XI: mp 84-85°; ir(KBr) 1770(lactone), 1740 (ester) cm^{-1}; nmr δ($CDCl_3$) 2.08(-OCOCH_3), 3.32(-OCH_3), 3.5(d, -CH_2-O-), 4.25(m, H-C-Br), 5.08(m, H-C-O-), 5.3(m, H-C-O-); XIa: mp 87-88°; ir(KBr) 1770(lactone), 1740(ester) cm^{-1}; nmr δ($CDCl_3$) 2.0(-OCOCH_3), 4.38(b, H-C-Br), 5.23(m, 2x H-C-O-).