Synthesis of (±) Prostaglandin-$F_{2\alpha}$ involving Photolytic Conversion of a Cyclobutanone to a γ-Lactol

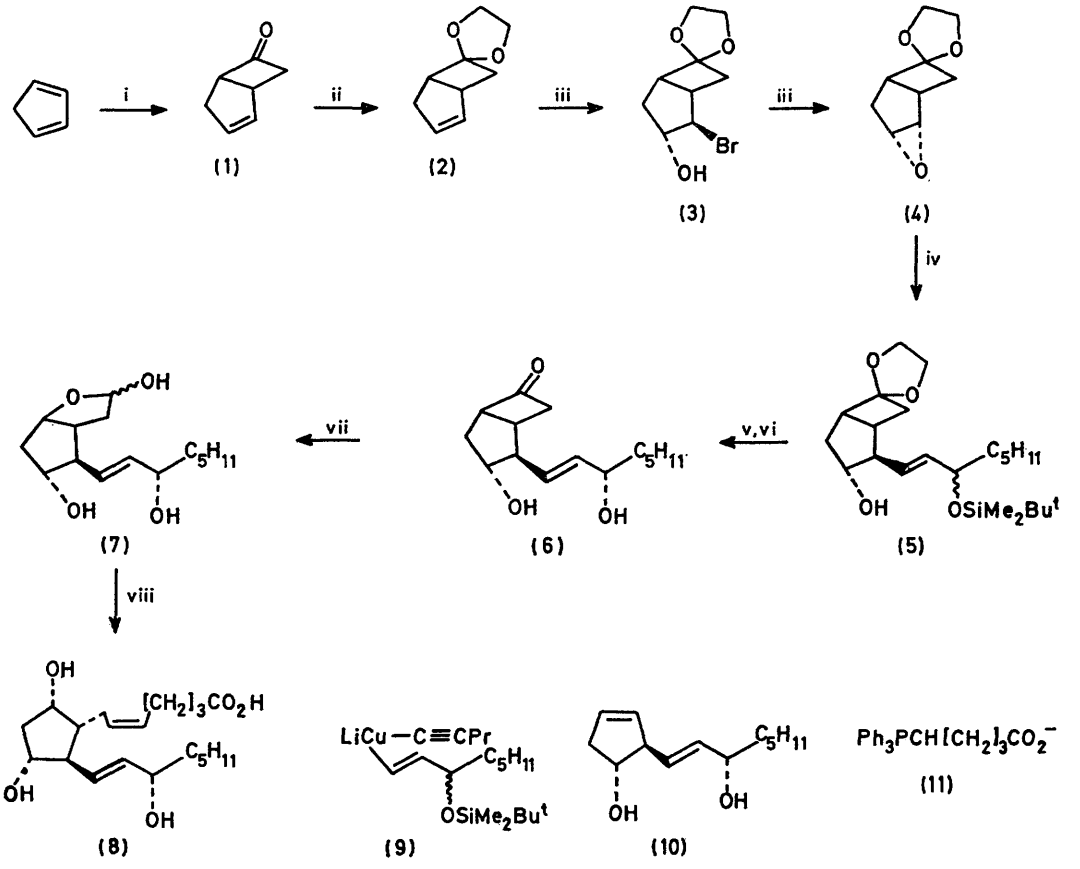
By ROGER F. NEWTON* and DEREK P. REYNOLDS
[*Chemical Research Department, Glaxo-Allenburys Research (Ware) Ltd., Ware, Herts.* SG12 0DJ]
and NOELLE M. CROSSLAND, DAVID R. KELLY, and STANLEY M. ROBERTS
(*The Ramage Laboratories, Department of Chemistry and Applied Chemistry, Salford University, Salford, Lancs.* M5 4WT)

Summary The acetal (**4**), prepared by a novel route, was converted into the ketone (**6**); this ketone furnished the known lactol (**7**) on photolysis in aqueous acetonitrile.

WE report a simple route from cyclopentadiene to (±)-prostaglandin $F_{2\alpha}$ (**8**) involving nine steps and a 10% overall yield based on a strategy that we have outlined previously.[1]

dehydrohalogenation *in situ* using aqueous potassium carbonate. In this way the epoxyacetal (**4**) was obtained from (**1**) in 72% yield (>99·5% pure by g.l.c.).

The acetal (**4**) reacted regioselectively with the cuprate reagent (**9**) to give the hydroxyacetal (**5**) in 65% yield after chromatography.[1] The ketone (**6**) is readily available from (**5**) (40% yield) by desilylation, chromatography, and deacetalization.



Reagents: i, CCl_2:C:O then Zn, HOAc. ii, $(CH_2OH)_2$, C_6H_6, H^+ with azeotropic removal of H_2O. iii, *N*-Bromoacetamide in H_2O–Me_2CO, pH 7, 18 h then add K_2CO_3. iv, (**9**), −30 °C, 18 h. v, F^-. vi, H^+. vii, *hν*, H_2O, MeCN. viii, (**11**), C_6H_6, 2 h.

Bicyclo[3.2.0]hept-2-en-6-one (**1**) can be prepared by cycloaddition of cyclopentadiene and dichloroketen followed by hydrodechlorination.[2] Treatment of the ketone (**1**) with ethylene glycol in benzene containing a catalytic amount of toluene-*p*-sulphonic acid gave the acetal (**2**). Regiospecific *endo*-epoxidation of the double bond in (**2**) was achieved by formation of the bromohydrin (**3**) followed by

Photolysis of the ketone (**6**) in aqueous acetonitrile[3] gave the lactol (**7**)[4] and the alkene (**10**). The photolysis products were separated by chromatography and identified by comparision with authentic samples. Since this isolation step led to some loss of lactol, it was found to be advantageous to extract the crude photolysis products into ethyl acetate, dry the solution, evaporate the solvent, and treat

the oily residue with the Wittig reagent (**11**). Using the latter procedure the ketone (**6**) gave (±)-prostaglandin-$F_{2\alpha}$ (**8**) (48%) and the alkene (**10**) (15%) after chromatography.

We thank Glaxo-Allenburys and the S.R.C. for a CASE award (to N. M. C.) and the Company for a Studentship award (to D. R. K.).

(*Received*, 30*th March* 1979; *Com.* 346.)

[1] R. F. Newton, C. C. Howard, D. P. Reynolds, A. H. Wadsworth, N. M. Crossland, and S. M. Roberts, *J.C.S. Chem. Comm.*, 1978, **662.**
[2] P. A. Grieco, *J. Org. Chem.*, 1972, **37**, 2363.
[3] N. M. Crossland, D. R. Kelly, S. M. Roberts, D. P. Reynolds, and R. F. Newton, preceding communication.
[4] *inter alia* E. J. Corey and R. Noyori, *Tetrahedron Letters*, 1970, 311; J. Fried, C. H. Lin, J. C. Sih, P. Dalven, and G. F. Cooper, *J. Amer. Chem. Soc.*, 1972, **94**, 4342; R. B. Woodward, J. Gosteli, I. Ernest, R. J. Friary, G. Nestler, H. Raman, R. Sitri, C. Suter, and J. K. Whitesell, *ibid.*, 1973, **95**, 6853.