Synthesis of Prostaglandin-$F_{2\alpha}$ by Conjugate Addition of a Cuprate Reagent to 3-t-Butyldimethylsilyloxytricyclo[3.2.0.0^{2,7}]heptan-6-one[1]

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Summary A novel synthesis of (±)-prostaglandin-$F_{2\alpha}$ involves the stereospecific formation of 3-*endo*-t-butyldimethylsilyloxytricyclo[3.2.0.0.^{2,7}]heptan-6-one (**3**) and reaction of this strained cyclopropyl ketone with the organocuprate reagent (**4**).

WE disclose a novel route to (±)-prostaglandin-$F_{2\alpha}$ starting from cyclopentadiene. The pathway is described in the Scheme and entails the initial conversion of cyclopentadiene into bicyclo[3.2.0]hept-2-en-6-one (**1**).[2] Reaction of the alkenone (**1**) with *N*-bromoacetamide in aqueous acetone proceeded stereospecifically to yield the crystalline bromohydrin (**2**).[3] Protection as the t-butyldimethylsilyl-derivative followed by base-induced cyclisation gave the tricycloheptanone (**3**). The latter ring system is known to be susceptible to Michael-type attack by simple nucleophilic reagents.[4] However, conjugate addition with organometallic reagents had not been reported previously. We found that reaction of the ketone (**3**) with the mixed organocuprate reagent (**4**)[5] takes place smoothly at −78 °C to give the norbornanone (**5**) in 88% yield. Peracetic acid oxidation gave the lactone (**6**). Reduction of the lactone (**6**) to the lactol and subsequent Wittig reaction were conducted in the prescribed manner[6] to give the 9,15-diprotected prostaglandin-$F_{2\alpha}$ which was hydrolysed and chromatographed to give (±)-prostaglandin-$F_{2\alpha}$† and (±)-15-epi-prostaglandin-$F_{2\alpha}$.

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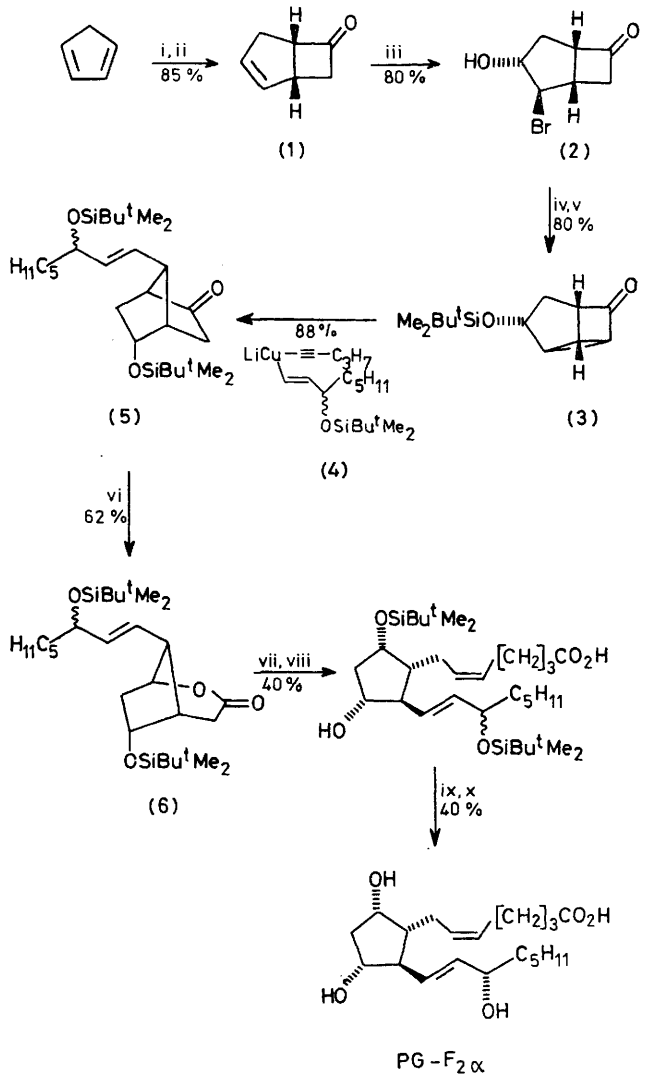

SCHEME. *Reagents:* (i) $Cl_2C{:}C{:}O$; (ii) Zn, HOAc; (iii) *N*-bromoacetamide, H_2O, Me_2CO; (iv) Me_2Bu^tSiCl, $HCONMe_2$, imidazole; (v) $KOBu^t$; (vi) $MeCO_3H$, $MeCO_2H$, $MeCO_2Na$; (vii) Bu^i_2AlH; (viii) $Ph_3\overset{+}{P}\text{-}\overset{-}{C}H(CH_2)_3CO_2^-$; (ix) H^+; (x) chromatography.

† Chromatographically and biologically identical to authentic material.

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