Synthesis of Prostaglandin A_2 from 3-*endo*-Bromotricyclo[3.2.0.$0^{2,7}$]heptan-6-one

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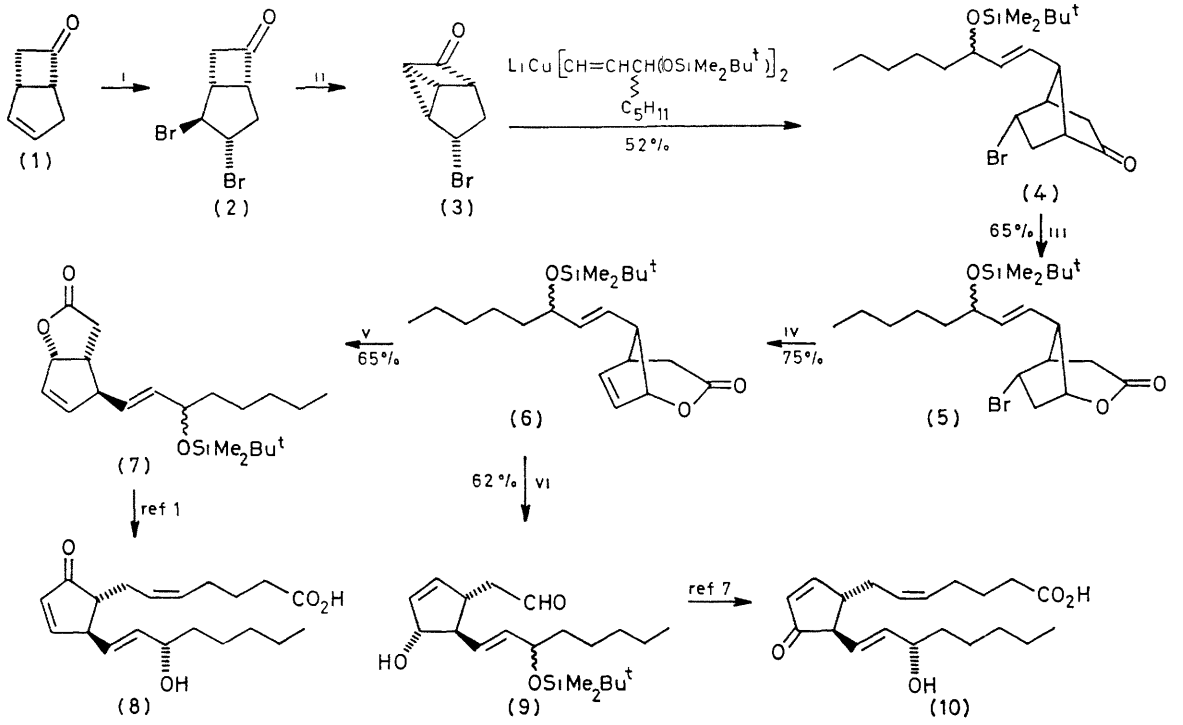
Summary Prostaglandin A_2 (**8**) has been synthesised in nine steps from the known tricyclic ketone (**3**).

PROSTAGLANDIN A_2 is an important, biologically active natural product and is amenable to simple modification to provide other primary prostaglandins. We recently described a synthesis of prostaglandin A_2 which involved an S_N' reaction on a cyclopentenyl epoxide.[1] Now we have found that the same compound can be prepared by adaption of our earlier routes to primary prostaglandins involving the intermediacy of a 3-substituted bicyclo[3.2.0.$0^{2,7}$]heptan-6-one.[2]

The bicycloheptenone (**1**) was converted into the dibromo-derivative (**2**) as described previously.[3] Treatment of the ketone (**2**) with sodium hexamethyldisilazide gave the stable, crystalline tricyclic ketone (**3**).[4] Reaction with the appropriate cuprate reagent[5] gave the norbornanone (**4**). As expected,[6] the oxidation of (**4**) to the δ-lactone (**5**) using peracid proceeded with high selectivity. Dehydrobromination was achieved using diazabicycloundecene to afford the δ-lactone (**6**) [ν_{max} 1750 cm^{-1}, δ ($CDCl_3$) 6·50 (1H, m, H-7 or H-6), 6·30 (1H, m, H-6 or H-7), 5·60—5·30 (2H, m, H-1′ and H-2′), 4·80 (1H, m, H-1), 4·00 (1H, m, H-3′), 3·00—2·50 (4H, m, H-5, H-8 and 2 × H-4), 1·45—1·15 (8H, m,



SCHEME Reagents i, Br_2, $NaHCO_3$, CCl_4, ii, $NaN(SiMe_3)_2$ iii, *m*-$ClC_6H_4CO_3H$, iv, 1,5-diazabicyclo[5 4 0]undec-5-ene, v, DMF, heat, vi, $HAlBu^i_2$

4 × CH_2), 1 10—0·70 (12H, s, 4 × Me), and 0 10 (6H, s, Si–Me_2), M^+, *m/e* 364·2431] which rearranged on boiling in *NN*-dimethylformamide (DMF) to give the known γ-lactone (**7**) This γ-lactone was converted into (±)-prostaglandin-A_2 (**8**) as described previously [1] Reduction of the δ-lactone (**6**) with di-isobutylaluminium hydride furnished the hydroxy-aldehyde (**9**) which was converted into the biologically active prostanoid (**10**) by known methods [7]

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