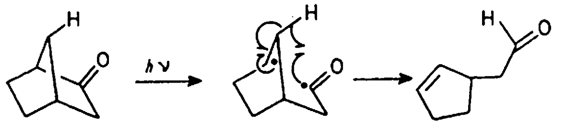
Photosynthetic Routes to Prostanoids. Synthesis of Alkyl and Trialkylsilyl Derivatives of 9α-Hydroxy-9-deoxyprostaglandin-C_2

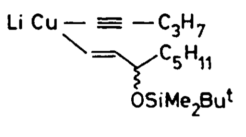
By NOELLE M. CROSSLAND and STANLEY M. ROBERTS*
(*The Ramage Laboratories, Department of Chemistry and Applied Chemistry, Salford University, Salford* M5 4WT)
and ROGER F. NEWTON*
(*External Projects Department, Allen and Hanburys Research Ltd., Ware, Hertfordshire* SG12 0DJ)

Summary Photolysis of 5-*endo*-,7-*anti*-disubstituted bicyclo[2.2.1]heptan-2-ones gave cyclopentene aldehydes in good yield: the substituents were selected so that conversions into prostaglandin-C_2 (PG-C_2) analogues were readily achieved.

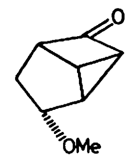
IT has been established that bicyclo[2.2.1]heptanones undergo Norrish Type 1 cleavage (α-cleavage) at the C(1)–C(2) bond to produce an acyl–alkyl diradical. The acyl radical abstracts the adjacent proton at C(7) (when available) to give an unsaturated aldehyde probably through the triplet manifold (Scheme 1).[1] We have applied this photon-induced isomerisation of norbornan-2-ones to give some novel derivatives of the interesting 9α-hydroxy-9-deoxyprostaglandin-C_2 system.[2]



SCHEME 1

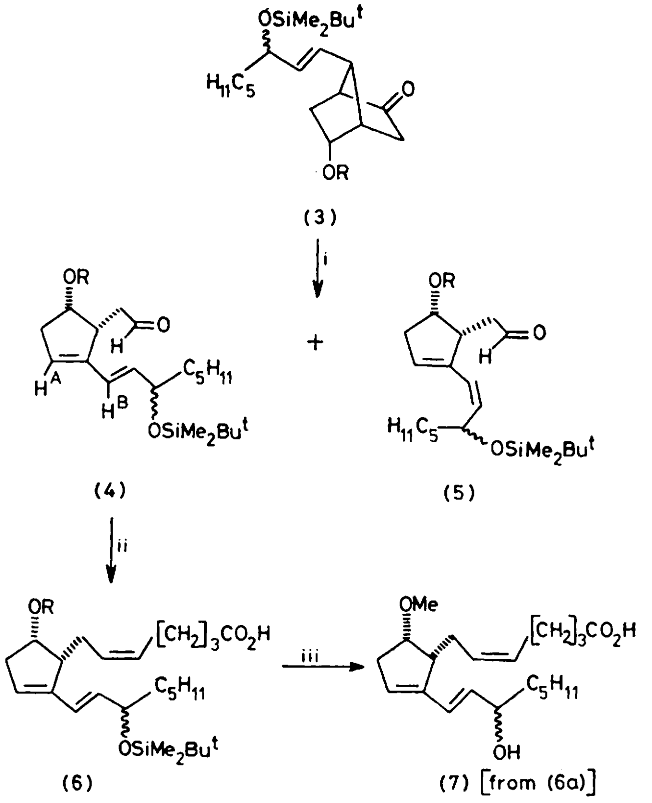


(1)



(2)

Thus photolysis of the ketone (**3a**), prepared by homoconjugate addition of the copper reagent (**1**) to 3-*endo*-methoxytricyclo[3.2.0.0^{2,7}]heptan-6-one (**2**),[3] gave the desired aldehyde (**4a**) cleanly in 70% yield (Scheme 2).



a; R = Me
b; R = $SiMe_2Bu^t$
c; R = CH_2Ph

SCHEME 2. i, hν. ii, $Ph_3P{=}CH[CH_2]_3CO_2^-$. iii, $MeCO_2H$, H_2O, tetrahydrofuran, 4 days, 40 °C.

Concurrently a secondary slower photo-reaction was observed in which, we believe, isomerisation of the exocyclic *trans*-double bond occurred to give the aldehyde (**5a**) as a minor impurity.

The optimum yield of the isomeric aldehydes was obtained by photolysis through a Pyrex filter of a 0·02 M solution of the ketone (**3a**) in deoxygenated methanol containing a trace of potassium carbonate. The products were purified by t.l.c. over silica, and the major component was characterised as the aldehyde (**4a**) by spectroscopic techniques; in particular, the presence in the n.m.r. spectrum of a low-field doublet (*J* 16 Hz) due to the coupling of H^A and H^B is typical of the diene unit.[4]

Chain extension of the aldehyde (**4a**) under Wittig–Horner conditions proceeded smoothly and in good yield to form the acid (**6a**); treatment of this acid with aqueous acetic acid for several days produced the hydroxy acid (**7**).

Similar photolysis of the ketones (**3b**) and (**3c**) gave the aldehydes (**4b**) and (**4c**), respectively. After separation of aldehydes from minor impurities [including the isomeric aldehydes (**5b**) and (**5c**)] chain extension furnished the bis-silyloxy acid (**6b**) (a potential precursor to the known 9α-hydroxy-9-deoxyprostaglandin-C_2[5]) and the benzyloxy acid (**6c**).

We thank the S.R.C. and Allen and Hanburys Research Ltd. [C.A.S.E. award (to N.M.C.)] for financial support.

(*Received*, 31*st August* 1977; *Com.* 906.)

---

[1] P. Yates and R. O. Loutfy, *Accounts Chem. Res.*, 1975, **8**, 209; J. Meinwald and R. A. Chapman, *J. Amer. Chem. Soc.*, 1968, **90**, 3218; P. Yates, *J. Photochemistry*, 1976, **5**, 91; P. Yates, *Pure Appl. Chem.*, 1968, **16**, 93.

[2] S. Kori, Japan P. 74 35,625 (*Chem. Abs.*, 1974, **82**, 124879 f); K. Irmscher and D. Orth, *Ger. Offen.*, 2,448,392 (*Chem. Abs.*, 1975, **83**, 58255s); P. Crabbé, *ibid.*, 2,429,354 (*Chem. Abs.*, 1975, **83**, 58245p).

[3] M. J. Dimsdale, R. F. Newton, D. K. Rainey, C. F. Webb, T. V. Lee, and S. M. Roberts, *J.C.S. Chem. Comm.*, 1977, 716.

[4] P. Crabbé, A. Guzman, and M. Vera, *Tetrahedron Letters*, 1973, 3021, 4730.

[5] R. L. Jones, *Biochem. J.*, 1974, **139**, 381.