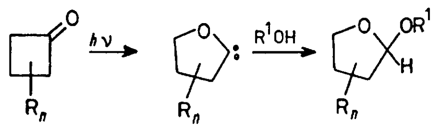
Photosynthetic Routes to Prostaglandins: Conversion of 2,3-*endo*-Epoxybicyclo-[3.2.0]heptan-6-one into 6,7-*endo*-Epoxy-3-alkoxy-2-oxabicyclo[3.3.0]octanes

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, Herts* SG12 0DJ)

Summary Photolysis of the epoxide (**2**) in methanol gives the acetal (**3**), a known prostaglandin precursor; the intermediate oxacarbene is trapped less effectively by homologous alcohols.

The mechanism involved in the conversion of cyclobutanones into cyclic acetals by photolysis in alcoholic solutions has been studied in detail, particularly by Turro and Yates.[1] From this work it seems that the reaction proceeds from a singlet or unquenchable triplet excited state to give an oxacarbene intermediate which is efficiently trapped under the reaction conditions (Scheme). Now we have developed



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a novel application of this photo-ring expansion as part of a synthetic route to a naturally occurring compound.

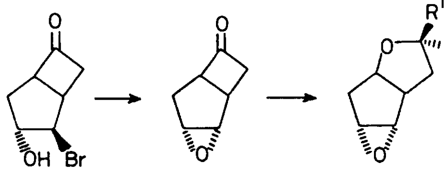
The known bromohydrin (**1**)[2] gave the epoxybicycloheptanone (**2**) in quantitative yield upon treatment with methoxide ion. Photolysis of the epoxide (**2**) in methanol containing small amounts of sodium hydrogen carbonate and 2,5-dimethylhexa-2,4-diene, using a medium pressure mercury lamp and quartz apparatus resulted in the swift formation of the isomeric acetals (**3**) (42%)† and (**4**) (11%).† Separation of the acetals from each other and from starting material (6%)† was effected by chromatography over alumina. Irradiation of the ketone (**2**) in the absence of the triplet quencher led to the formation of unidentified polar material and lower yields of the ring-expanded products (Table).

TABLE. Photolysis of 2,3-*endo*-epoxybicyclo[3.2.0]heptan-6-one (**2**)

Apparatus	Solvent	Time/h	% Acetals *exo*	% Acetals *endo*	% Recovered epoxide (**2**)
Pyrex	MeOH	52	(**3**) 25	(**4**) 4	7
Quartz	MeOH	0·5	(**3**) 20	(**4**) 3	10
Quartz	MeOH[a]	2·5	(**3**) 33	(**4**) 10	15
Quartz	MeOH[b]	0·5	(**3**) 33	(**4**) 10	30
Quartz	MeOH[b]	3·5	(**3**) 42	(**4**) 11	6
Quartz	EtOH[b]	2·5	(**5**) 21		20
Quartz	Pr^iOH[b]	2·5	(**6**) 16		<5
Quartz	Bu^tOH[b]	2·5	(**7**) 11		<5

[a] 2,5-Dimethylhexa-2,4-diene added. [b] 2,5-Dimethylhexa-2,4-diene and $NaHCO_3$ added.

Corey had previously used the acetal (**3**) to synthesise prostaglandin-$F_{2\alpha}$;[3] moreover the acetal (**4**) may be readily isomerised to (**3**).[4] Using the above approach the acetal (**3**) is produced under mild conditions at ambient temperature thus circumventing the need for low-temperature work and the use of the hazardous di-isobutylaluminium hydride as required by Corey's route.



(1) (2)

(3) R¹ = OMe; R² = H
(4) R¹ = H; R² = OMe
(5) R¹ = OEt; R² = H
(6) R¹ = OPrⁱ; R² = H
(7) R¹ = OBuᵗ; R² = H

Other alcohols proved to be less effective in trapping the intermediate carbene. Photolysis of the epoxyketone (**3**) in ethyl, isopropyl, and t-butyl alcohol gave, after chromatography, the 3-*exo*-alkoxy-2-oxabicyclo-octanones (**5**) (21%),† (**6**) (16%),[3] and (**7**) (11%),† respectively, together with minor amounts of starting material (Table).

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† Yield of pure material isolated after chromatography.

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[3] E. J. Corey and R. Noyori, *Tetrahedron Letters*, 1970, 311.

[4] E. J. Corey, K. C. Nicolaou, and D. J. Beames, *Tetrahedron Letters*, 1974, 2439.