

## Photosynthetic Routes to Prostanoids. Ring Expansions of Some Substituted Cyclobutanones to Form Cyclic Acetals or $\gamma$ -Lactols

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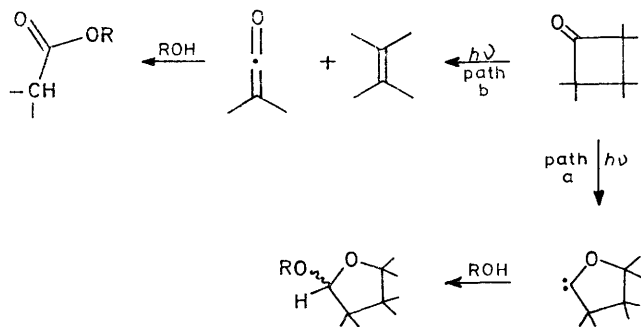
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**Summary** Photolysis of the cyclobutanones (5) and (6) in methanol gave the cyclic acetals (10) and (11) and the alkenes (18) and (19); irradiation of (5) and (6) in an aqueous solution gave the lactols (14) and (15), respectively, with only small quantities of the corresponding alkenes.

It is known that photolysis of simple cyclobutanones in alcoholic media furnishes cyclic acetals often in very high yield<sup>1</sup> through the intermediacy of an oxacarbene<sup>2</sup> (Scheme, path a). The major side-reaction that can occur is the formation of an ester and an alkene *via* a cycloelimination process (Scheme, path b). The latter reaction is particularly prevalent when the incipient double bond of the alkene forms part of a conjugated system.<sup>3</sup>



SCHEME

Previously, we demonstrated that photolysis of the epoxybicycloheptanone (1) in methanol gave the prostaglandin synthons (2) in 52% yield;<sup>4</sup> in subsequent large scale runs the ester (3) (6%) was isolated also.<sup>5</sup> We now illustrate that similar photolysis procedures can be applied to complex cyclobutanones to give ring-expanded products which are easily converted into prostaglandins.

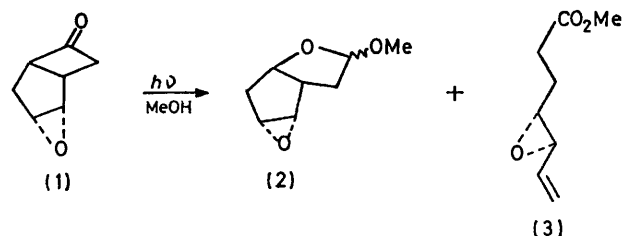
TABLE. Photolysis of some bicyclo[3.2.0]heptan-6-ones<sup>a</sup>

Substrate	Solvent(s) <sup>b</sup>	Irradiation time/h	Products (yield %) <sup>c</sup>	
			Ring-expanded product	Alkene
(4)	MeOH	16 <sup>d</sup>	(9) (33)	(17) (18)
(5)	MeOH	2	(10) (31)	(18) (37)
(6)	MeOH	2	(11) (35)	(19) (28)
(7)	Me <sub>2</sub> CO-H <sub>2</sub> O	2.5	(12) (75)	— <sup>e</sup>
(8)	THF-H <sub>2</sub> O	3.5	(13) (77)	— <sup>e</sup>
(5)	THF-H <sub>2</sub> O	4	(14) (40) <sup>f</sup>	(18) (15)
(6)	THF-H <sub>2</sub> O	1.5	(15) (50) <sup>f</sup>	(19) (15)
(7)	MeCO <sub>2</sub> H-Me <sub>2</sub> CO	2.5	(16) (100) <sup>g</sup>	—

<sup>a</sup> Ca.  $2 \times 10^{-2}$  M solution of the substrate irradiated using a medium-pressure Hanovia Lamp and a quartz filter unless stated otherwise. <sup>b</sup> THF = tetrahydrofuran. <sup>c</sup> Refers to isolated yields (after chromatography if necessary). <sup>d</sup> Pyrex filter employed. <sup>e</sup> Non-polar material observed on t.l.c. of reaction mixtures. <sup>f</sup> Compounds unstable to chromatography. <sup>g</sup> Yield of crude product.

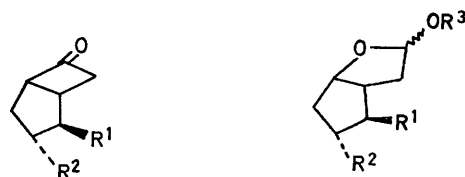
The cyclobutanones (4)<sup>6</sup> and (5)<sup>7</sup> gave the known prostaglandin intermediates (9)<sup>8</sup> and (10),<sup>8,9</sup> respectively, on photolysis in methanol; similarly the ketoester (6) gave the

acetal (11) (Table). The concurrent production of substantial amounts of the non-polar alkenes (17)—(19) reduced the viability of producing prostaglandin intermediates in this way. Variation of the wavelength of the incident light, the power of the light source, and the temperature of the reaction, and the use of quenchers and/or co-solvents made little difference to the ratio of acetal to alkene suggesting that the two compounds were formed from the same high energy state.



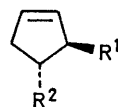
However, a most convenient solution to the problem of concurrent alkene production was found on conducting the photolyses in aqueous media. The simple bicycloheptanones (7) and (8) gave encouragingly high yields of the corresponding lactols (12) and (13) (Table): trace amounts of non-polar material (presumably the corresponding alkenes) were detected by t.l.c. The readily available ketone (5) gave the lactol (14) (40%) and the alkene (18) (15%) after chromatography over silica. However, the yield of crude lactol is considerably greater than that of the isolated material as shown by a further reaction performed on the crude photolysis mixture.<sup>10</sup> Photolysis of the ketone (6) in aqueous tetrahydrofuran gave the lactol (15) (50%) [a known prostaglandin- $D_2$  intermediate<sup>11</sup> which we further characterized by hydrolysis and oxidation to the more stable ketolactone (20)] and the alkene (19) (15%).

While the lactols (12)—(15) appeared to be reasonably stable under the photolysis conditions employed, substantial decomposition was observed after prolonged (48 h) irradiation. In hypothetical cases in which the required lactol was more photolabile, it might be preferable to irradiate in acetic acid to give the corresponding lactol acetate. In this connection we have found that irradiation of the ketone (7) gave the acetate (16) and this compound afforded the lactol (12) on filtration through a silica column.

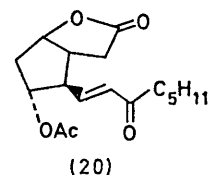


- (4)  $R^1 = a, R^2 = d$   
 (5)  $R^1 = b, R^2 = d$   
 (6)  $R^1 = c, R^2 = e$   
 (7)  $R^1 = R^2 = f$   
 (8)  $R^1 = g, R^2 = d$

- (9)  $R^1 = a, R^2 = d, R^3 = h$   
 (10)  $R^1 = b, R^2 = d, R^3 = h$   
 (11)  $R^1 = c, R^2 = e, R^3 = h$   
 (12)  $R^1 = R^2 = R^3 = f$   
 (13)  $R^1 = g, R^2 = d, R^3 = f$   
 (14)  $R^1 = b, R^2 = d, R^3 = f$   
 (15)  $R^1 = c, R^2 = e, R^3 = f$   
 (16)  $R^1 = R^2 = f, R^3 = e$



- (17)  $R^1 = a, R^2 = d$   
 (18)  $R^1 = b, R^2 = d$   
 (19)  $R^1 = c, R^2 = e$



- |   |                    |
|---|--------------------|
| $a = \text{CH}(\text{SMe})\text{CH}:\text{CHSMe}$               | $d = \text{OH}$    |
| $b = \text{CH}:\text{CHCHC}_5\text{H}_{11}$                     | $e = \text{OCOMe}$ |
| $\left. \begin{array}{c} \text{OH} \\   \end{array} \right\}$   | $f = \text{H}$     |
| $c = \text{CH}:\text{CHCHC}_5\text{H}_{11}$                     | $g = \text{Bu}^n$  |
| $\left. \begin{array}{c} \text{OTHP} \\   \end{array} \right\}$ | $h = \text{Me}$    |

THP = tetrahydropyran—2—yl

The only other photolytic conversion of a cyclobutanone to a  $\gamma$ -lactol reported in the literature occurred through the adventitious presence of water in the solvent,<sup>12</sup> while Brook had established previously that a siloxacarbene can be trapped by acetic acid.<sup>13</sup>

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<sup>5</sup> cf. R. D. Miller, D. L. Dolce, and V. Y. Merritt, *Tetrahedron Letters*, 1974, 3347.

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<sup>9</sup> R. B. Woodward, J. Gosteli, I. Ernest, R. J. Friary, G. Nestler, H. Raman, R. Sitrin, C. Suter, and J. K. Whitesell, *J. Amer. Chem. Soc.*, 1973, **95**, 6853.

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<sup>11</sup> E. F. Jenny, P. Schaublin, H. Fritz, and H. Fuhrer, *Tetrahedron Letters*, 1974, 2235.

<sup>12</sup> D. R. Morton, E. Lee-Ruff, R. M. Southam, and N. J. Turro, *J. Amer. Chem. Soc.*, 1970, **92**, 4349.

<sup>13</sup> J. M. Duff and A. G. Brook, *Canad. J. Chem.*, 1973, **51**, 2869.