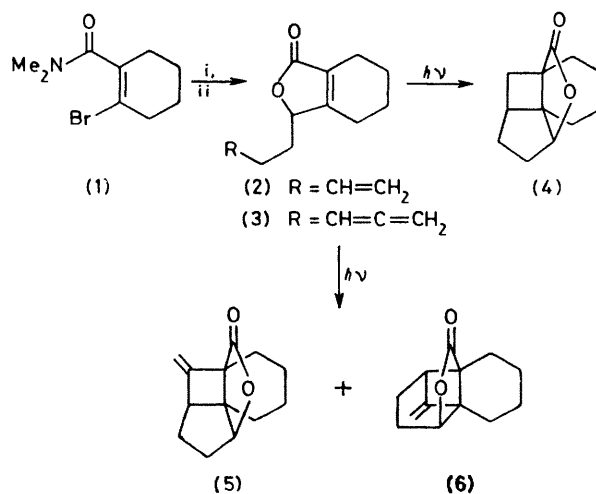


## Synthesis of Decahydrocyclopentacyclo-octene Derivatives *via* Intramolecular Photocycloaddition of $\Delta^{\alpha,\beta}$ -Butenolides and Reductive Cleavage

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**Summary** Irradiation of  $\Delta^{\alpha,\beta}$ -butenolides bearing but-3-enyl and penta-3,4-dienyl side-chains in the  $\gamma$ -position, (2) and (3), effected intramolecular [2 + 2] cycloaddition to form fused tricyclic lactones (4) and (5), respectively, as major products; reductive ring opening of the derived keto-acid (7a) and keto-ester (9) gave the octa- and deca-hydrocyclopentacyclo-octene derivatives (8) and (10) respectively.



SCHEME 1. Reagents: i, Bu<sup>t</sup>Li, ii, R[CH<sub>2</sub>]<sub>2</sub>CHO.

THE combination of intramolecular photochemical [2 + 2] cycloaddition of  $\alpha,\beta$ -unsaturated ketones with subsequent ring opening *via* retro-aldol or reductive cleavage reactions has provided a useful synthetic approach to a variety of carbocyclic ring systems.<sup>1</sup> We report herein a novel variant of this general strategy involving intramolecular [2 + 2] photoaddition of fused  $\alpha,\beta$ -unsaturated  $\gamma$ -lactones (2) and (3) which gave rise to octa- and deca-hydrocyclopentacyclo-octene derivatives (8) and (10) respectively following reductive scission of the cyclobutane ring.

The  $\Delta^{\alpha,\beta}$ -butenolides (2) and (3) bearing unsaturated side-chains were prepared by lithiation of the bromo-amide [(1) t-C<sub>4</sub>H<sub>9</sub>Li, THF, -75 to -80 °C, 45–60 min],<sup>2</sup> and reaction of the resulting vinyl-lithium reagent with pent-4-enal and hexa-4,5-dienal,<sup>†</sup> respectively [yields: (2), 68%; (3), 96%].<sup>‡§</sup>

Irradiation of the butenolide (2) in acetone solution (450 W Hanovia lamp, Vycor filter, N<sub>2</sub> purge) afforded the liquid tricyclic lactone (4) (77%): i.r. (film),  $\nu_{\max}$  1750 cm<sup>-1</sup>; <sup>1</sup>H n.m.r. (CDCl<sub>3</sub>),  $\delta$  4.50 (apparent d of d, *J* 2 Hz, 1H, CH-O).<sup>5</sup> In contrast, irradiation of the allenylbutenolide (3) in *p*-xylene gave both the fused and bridged photo-adducts, (5)

(low-melting solid) and (6) (m.p. 63–64 °C), in a 2–3:1 ratio (62%) as well as a small amount of a third photo-product presumed to arise from cycloaddition to the terminal double bond of the allene. The isomers were separated by medium pressure liquid chromatography<sup>2</sup> on silica gel with ether–hexane (1:9) as eluant, and characterized by the following spectral properties. Compound (5):

<sup>†</sup> Hexa-4,5-dienal was prepared from the trimethylsilyl ether of pent-4-en-1-ol by dibromocyclopropanation (0.2 equiv. PhHgCBr<sub>2</sub>, C<sub>6</sub>H<sub>6</sub>, reflux; 52%), ring opening (2 equiv. MeLi, Et<sub>2</sub>O, -50 °C to +20 °C; 85%), hydrolysis of the known hexa-4,5-dien-1-ol<sup>3</sup> (5% HCl, 20 °C; 81%), and oxidation [Me<sub>2</sub>S/*N*-chlorosuccinimide, pentane, -25 °C; Et<sub>3</sub>N, -25 °C to +20 °C; 32%].<sup>4</sup>

<sup>‡</sup> All new compounds reported in this paper gave i.r. and <sup>1</sup>H n.m.r. spectra, and in some cases, mass spectra in accord with the structures shown. Only key spectral data are cited. Satisfactory combustion analyses were obtained for all compounds except (10). In this case, the elemental composition was determined by high resolution g.c./m.s.

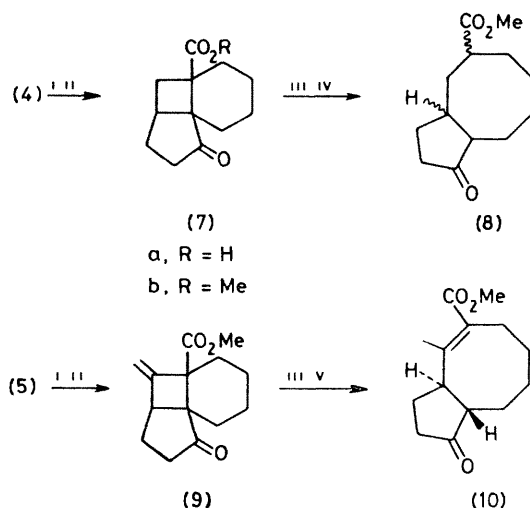
<sup>§</sup> The preparation of (3) was performed with a 1:2 molar ratio of hexa-4,5-dienal and (1).

1 r (film),  $\nu_{\max}$  1770 (C=O) and 1667 (C=C)  $\text{cm}^{-1}$ ,  $^1\text{H n m r}$  ( $\text{CDCl}_3$ )  $\delta$  5.10 (m,  $W_{\frac{1}{2}}$  3 Hz, 1H, vinyl H), 4.83 (m,  $W_{\frac{1}{2}}$  3 Hz, 1H, vinyl H), and 4.56 (t,  $J$  4 Hz, 1H, CH-O), compound (6), 1 r (film),  $\nu_{\max}$  1764 (C=O) and 1681 (C=C)  $\text{cm}^{-1}$ ,  $^1\text{H n m r}$  (220 MHz,  $\text{CDCl}_3$ )  $\delta$  5.04 (s, 1H, vinyl H), 4.95 (s, 1H, vinyl H), and 4.56 (s, 1H, CH-O)

Hydrolysis of the saturated lactone (4) to the sodium salt with 1M sodium hydroxide, followed by oxidation with 1.1 equiv of 0.05M sodium ruthenate (room temperature, 1 h)<sup>6</sup> afforded the keto-acid (7a) (58% after recrystallization from ethanol-water), m p 154–155 °C, 1 r ( $\text{CHCl}_3$ ),  $\nu_{\max}$  1736 (C=O) and 1701 (C=O)  $\text{cm}^{-1}$ . Treatment of crude (7a) with diazomethane furnished the corresponding methyl ester (7b) (81% from 4), m p 60–61 °C, 1 r ( $\text{CHCl}_3$ ),  $\nu_{\max}$  1724 (C=O)  $\text{cm}^{-1}$ . The major lactone (5) from irradiation of (3) was oxidized and esterified in a similar manner, providing the keto-ester (9) (65%), m p 51–52 °C, 1 r (film),  $\nu_{\max}$  1724 (C=O)  $\text{cm}^{-1}$ . The keto-acid (structure not shown) derived from the minor lactone (6) had the following physical properties: m p 192–194 °C, 1 r ( $\text{CHCl}_3$ ),  $\nu_{\max}$  1709 (C=O)  $\text{cm}^{-1}$ . The 1 r data cited indicated the presence of cyclopentanone rings in (7a), (7b), and (9), and a cyclohexanone ring in the keto-acid from (6).

The reductive cleavage of strained ring compounds bearing carbonyl groups in a 1,4-relationship has considerable precedent<sup>1d–e,7</sup>. The reduction of the saturated tricyclic keto-acid (7a) with lithium in liquid ammonia (THF, –33 °C with or without  $\text{Bu}^t\text{OH}$ ) was complicated by competing reduction of the carbonyl group of (7a). Consequently, the product mixtures were oxidized with chromic acid and esterified with diazomethane prior to chromatographic purification to separate recovered (7b) (20%). The product (44%) proved to be a mixture of at least three isomeric keto-esters to which structure (8) is assigned on the basis of spectral data and g c / m s analyses  $M^+$  224 1399, 224 1417, and 224 1420 (calc for  $\text{C}_{13}\text{H}_{20}\text{O}_3$  224 1407).

Similar reduction of the unsaturated keto-ester (9) with lithium in ammonia afforded a five-component mixture of  $\alpha,\beta$ - and  $\beta,\gamma$ -unsaturated esters according to g c analysis and n m r spectra. No reduction of the carbonyl groups was observed in this case. Equilibration with 0.1M sodium methoxide in methanol (reflux, 19 h) converted the mixture of isomers into a single  $\alpha,\beta$ -unsaturated ester (10) (68%), m p 72–73 °C, 1 r ( $\text{CDCl}_3$ ),  $\nu_{\max}$  1730 (C=O) and 1709 (C=O)  $\text{cm}^{-1}$ , u v (hexane),  $\lambda_{\max}$  230 nm ( $\epsilon$  7380),  $^1\text{H n m r}$



SCHEME 2 Reagents i, NaOH,  $\text{H}_2\text{O}$ , then  $\text{Na}_2\text{RuO}_4$ , ii,  $\text{CH}_2\text{N}_2$ , iii, Li,  $\text{NH}_3$ ,  $\text{THF}$ , iv,  $\text{H}_2\text{CrO}_4$ ,  $\text{Me}_2\text{CO}$  then  $\text{CH}_2\text{N}_2$  v NaOMe, MeOH

( $\text{CDCl}_3$ )  $\delta$  3.74 (s, 3H,  $\text{CO}_2\text{CH}_3$ ) and 2.03 (s, 3H,  $\text{C}=\text{CCH}_3$ ), m s,  $m/e$  ( $M^+$ ) 236.1412 (calc for  $\text{C}_{14}\text{H}_{20}\text{O}_3$ : 236.1407). The *trans*-ring fusion is assumed to be the more stable in analogy to related decahydrocyclopentacyclo-octanones<sup>1b,8</sup>.

The overall transformation of the cyclohexene derivative (1) to keto-esters (8) and (10) having the cyclopentacyclo-octene ring system may be viewed in general terms as an annulative two-carbon ring expansion. The four-stage reaction sequence described offers a relatively direct route for the construction of bicyclic and polycyclic compounds containing cyclo-octane rings, and may find application in the synthesis of ophiobolin and ceroplastol sesterterpenes.<sup>9</sup>

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