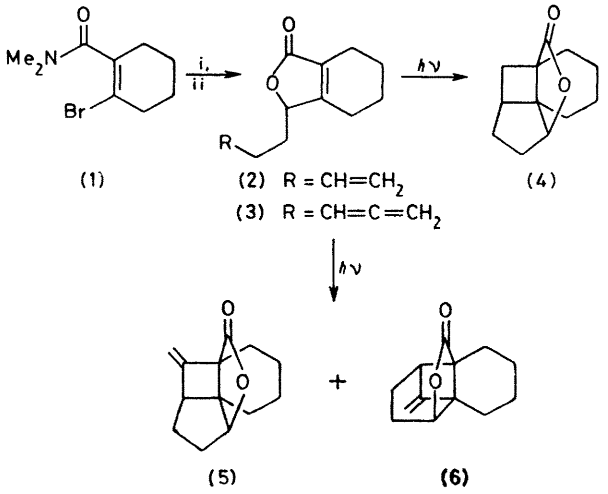
Synthesis of Decahydrocyclopentacyclo-octene Derivatives *via* Intramolecular Photocycloaddition of $\Delta^{\alpha,\beta}$-Butenolides and Reductive Cleavage

By William R. Baker, Peter D. Senter, and Robert M. Coates*
(*Department of Chemistry, University of Illinois, Urbana, Illinois* 61801)

Summary Irradiation of $\Delta^{\alpha,\beta}$-butenolides bearing but-3-enyl and penta-3,4-dienyl side-chains in the γ-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.

The combination of intramolecular photochemical [2 + 2] cycloaddition of α,β-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.[1] We report herein a novel variant of this general strategy involving intramolecular [2 + 2] photoaddition of fused α,β-unsaturated γ-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_4H_9Li, THF, −75 to −80 °C, 45—60 min],[2] and reaction of the resulting vinyl-lithium reagent with pent-4-enal and hexa-4,5-dienal,† respectively [yields: (**2**), 68%; (**3**), 96%].‡§



Scheme 1. Reagents: i, Bu^{t}Li, ii, R[CH$_2$]$_2$CHO.

Irradiation of the butenolide (**2**) in acetone solution (450 W Hanovia lamp, Vycor filter, N_2 purge) afforded the liquid tricyclic lactone (**4**) (77%): i.r. (film), ν_{max} 1750 cm^{-1}; ^1H n.m.r. ($CDCl_3$), δ 4·50 (apparent d of d, J 2 Hz, 1H, CH–O).[5] 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 photoproduct presumed to arise from cycloaddition to the terminal double bond of the allene. The isomers were separated by medium pressure liquid chromatography[2] on silica gel with ether–hexane (1 : 9) as eluant, and characterized by the following spectral properties. Compound (**5**):

---

† Hexa-4,5-dienal was prepared from the trimethylsilyl ether of pent-4-en-1-ol by dibromocyclopropanation (0·2 equiv. $PhHgCBr_3$, C_6H_6, reflux; 52%), ring opening (2 equiv. MeLi, Et_2O, −50 °C to +20 °C; 85%), hydrolysis of the known hexa-4,5-dien-1-ol[3] (5% HCl, 20 °C; 81%), and oxidation [Me_2S/*N*-chlorosuccinimide, pentane, −25 °C; Et_3N, −25 °C to +20 °C; 32%].[4]

‡ All new compounds reported in this paper gave i.r. and ^1H 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.

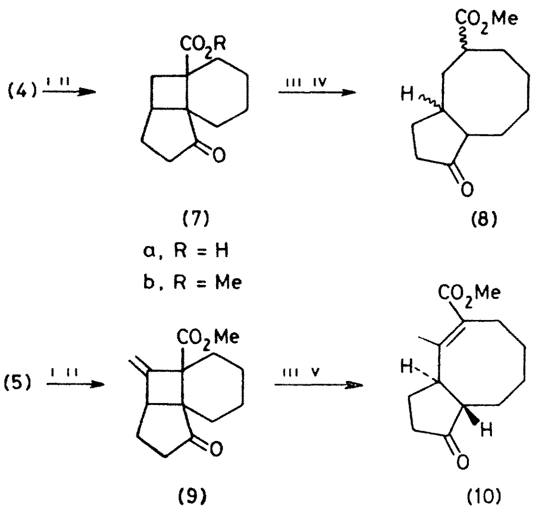
§ The preparation of (**3**) was performed with a 1 : 2 molar ratio of hexa-4,5-dienal and (**1**).

i r (film), ν_{max} 1770 (C=O) and 1667 (C=C) cm^{-1}, ^{1}H n m r (CDCl$_3$) δ 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, C*H*–O), compound (**6**), i r (film), ν_{max} 1764 (C=O) and 1681 (C=C) cm^{-1}, ^{1}H n m r (220 MHz, CDCl$_3$) δ 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)[6] afforded the keto-acid (**7a**) (58% after recrystallization from ethanol–water), m p 154—155 °C, i r (CHCl$_3$), ν_{max} 1736 (C=O) and 1701 (C=O) cm^{-1} Treatment of crude (**7a**) with diazomethane furnished the corresponding methyl ester (**7b**) (81% from **4**), m p 60–61 °C, i r (CHCl$_3$), ν_{max} 1724 (C=O) 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, i r (film), ν_{max} 1724 (C=O) cm^{-1} The keto-acid (structure not shown) derived from the minor lactone (**6**) had the following physical properties m p 192—194 °C, i r (CHCl$_3$), ν_{max} 1709 (C=O) cm^{-1} The i 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 [1d–e,7] The reduction of the saturated tricyclic keto-acid (**7a**) with lithium in liquid ammonia (THF, −33 °C with or without Bu^{t}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 $C_{13}H_{20}O_3$ 224 1407)

Similar reduction of the unsaturated keto-ester (**9**) with lithium in ammonia afforded a five-component mixture of α,β- and β,γ-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 α,β-unsaturated ester (**10**) (68%), m p 72—73 °C, i r (CDCl$_3$), ν_{max} 1730 (C=O) and 1709 (C=O) cm^{-1}, u v (hexane), λ_{max} 230 nm (ϵ 7380), ^{1}H n m r (CDCl$_3$) δ 3·74 (s, 3H, CO$_2$CH$_3$) and 2 03 (s, 3H, C=CCH$_3$), m s , m/e (M^+) 236·1412 (calc for $C_{14}H_{20}O_3$: 236·1407) The *trans*-ring fusion is assumed to be the more stable in analogy to related decahydrocyclopentacyclo-octanones [1b,8]



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

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 annelative 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 [9]

This research was supported in part by grants from the National Science Foundation Gas chromatographic mass spectra were funded in part by a grant from the National Institutes of General Medical Sciences

(*Received*, 6*th June* 1980, *Com* 614)

---

[1] (a) W Oppolzer and T Godel *J Am Chem Soc* 1978 **100** 2583 (b) M J Begley, M Mellor, and G Pattenden *J Chem Soc* , *Chem Commun* , 1979 235, (c) W Oppolzer and T G C Bird, *Helv Chim Acta*, 1979, **62**, 1199 (d) E Wenkert and J E Yoder, *J Org Chem* , 1970 **35**, 2986, P E Eaton, R A Hudson and C Giordano, *J Chem Soc* , *Chem Commun* , 1974, 978, (e) P E Eaton, *Tetrahedron*, 1979 **35**, 2189

[2] W R Baker and R M Coates, *J Org Chem* , 1979, **44**, 1022

[3] B Ragonnet, M Santelli and M Bertrand, *Bull Soc Chim Fr* , 1973 3119

[4] E J Corey, C U Kim, and P F Misco, *Org Synth* , 1978, **58**, 122

[5] The intermolecular photochemical cycloaddition of $\Delta^{\alpha,\beta}$-butenolides to olefins has been reported M Tada, T Kokubo and T Sato, *Tetrahedron*, 1972 **28**, 2121 H Kosugi S Sekigughi, R Sekita, and H Uda *Bull Chem Soc Jpn* , 1976, **49**, 520 Subsequent to the completion of this work, intramolecular photochemical cycloadditions of $\Delta^{\alpha,\beta}$-butenolides have been reported B A Pearlman *J Am Chem Soc* , 1979, **101**, 6398, 6404

[6] D G Lee D T Hall, and J H Cleland, *Can J Chem* 1972 **50**, 3741, see also E J Corey, R L Danheiser, S Chandrasekaran, G E Keck, B Gopalan, S D Larsen P Siret, and J -L Gras *J Am Chem Soc* 1978 **100** 8034

[7] P G Gassman and X Creary, *J Chem Soc* , *Chem Commun* 1972 1214, J J Bloomfield, R G Todd and L T Takahasi, *J Org Chem* , 1963, **28**, 1474, J J Bloomfield, R A Martin, and J M Nelke, *J Chem Soc* , *Chem Commun* , 1972, 96, J Dekker, F J C Martins, and J A Kruger, *Tetrahedron Lett* , 1975, 2489

[8] M Umehara, H Takayanagi, H Ogura, and S Hishida, *Bull Chem Soc Jpn* , 1978, **51**, 3277

[9] G A Cordell, *Phytochemistry*, 1974, **13**, 2343