

Substituent Control of Stereochemistry in the Divinylketene–Cyclohexadienenone Cyclisation

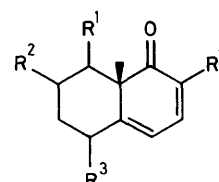
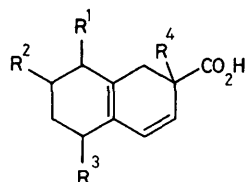
Ahmad Khodabocus, T. K. M. Shing, James K. Sutherland,* and Johnathan G. Williams

Chemistry Department, Victoria University of Manchester, Manchester M13 9PL, U.K.

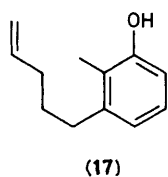
Stereochemical control is observed in the divinylketene–cyclohexadienone cyclisation only when a substituent is positioned vicinal to the atom at which bond formation occurs.

In previous work¹ we have shown that cyclisation of the acid (**1**) to the cyclohexadienone (**9**) gives a 1:1 mixture of epimers, despite formation of the *anti*-dimethyl isomer requiring a transition state with a chair conformation and axial methyl groups or a twist-boat conformation. In order to examine the stereochemical effects of substituents at other positions, the acids (**2**), (**3**), (**4**), and (**5**) were prepared and cyclised to give their respective dienones (**10**), (**11**), (**12**), and (**13**). Cyclisation of (**2**) with Ac₂O–pyridine gave a mixture in which the isomer with the AcO group in the axial position predominated; in the minor isomer the CHOAc proton resonated at δ_{H} 5.30 (*J* 11, 11, 4, and 4 Hz) and showed a substantial nuclear Overhauser effect (n.O.e.) with the angular methyl group. After thermolysis in dichlorobenzene

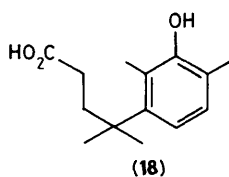
the minor isomer became the major product (75:25). The cyclisation of the methyl compound (**3**) formed only one isomer; the n.O.e.s between the two methyl groups were weak (1–2%) but a double quantum filtered 2-D COSY experiment revealed a strong axial–axial coupling between the methine proton and its ring neighbour consistent with the methyl groups being *cis*. Attempts to equilibrate the isomers thermally led to formation of the phenol (**17**). The silyl ether (**4**) cyclised to a single isomer (**1**) judged to be the β on the basis of δ_{H} 4.1 (*J* 13.5 and 4.5 Hz), suggesting an equatorial disposition of the ether group. Similar results were obtained with the acetate (**5**) which gave the dienone (**13**), δ_{H} 5.15 (*J* 11 and 6 Hz). From these and previous results it is apparent that neither the conformation of the product nor substituents other



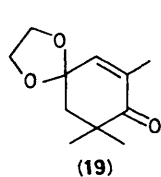
	R ¹	R ²	R ³	R ⁴	Isomer ratio
(1)	H	H	Me	H	(9) α:β
(2)	H	OAc	Me ₂	H	(10) 50:50
(3)	Me	H	H	H	(11) 30:70
(4)	OSiBu ^t Me ₂	H	Me ₂	Me	(12) <5:95
(5)	OAc	H	Me ₂	Me	(13) <15:85
(6)	=O	H	Me ₂	Me	(14) <5:95
(7)	H	H	Me ₂	Me	(15)
(8)	H	=O	Me ₂	H	(16)



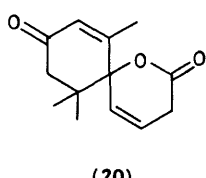
(17)



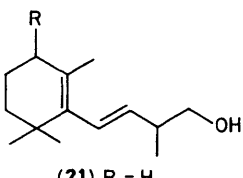
(18)



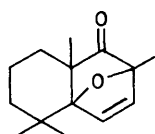
(19)



(20)



(21) R = H

(22) R = OSiBu^tMe₂

(23)

than in the vicinity of the bond being formed have a significant influence on product stereochemistry; perhaps this is due to an early 'reactant-like' transition state. The acids (7) and (8) were also exposed to cyclising conditions giving (15) and (16), however (6) was converted to the acid (18); evidently the dione (14) undergoes a 1,3-dione cleavage under the reaction conditions.

The acid (1) was prepared from 2,3-dimethylcyclohexanone by the sequence: alkylation with LiC≡CCH₂CH₂OSi-

Bu^tMe₂, dehydration, removal of the silyl group, acetylation, Lindlar reduction, removal of acetate, and Jones oxidation. The acids (2) and (8) were synthesised from the monoacetal (19) by alkylation with LiC≡CCH₂CH₂OTHP (THP = tetrahydropyran-2-yl), removal of the acetal groups, Lindlar reduction, and pyridinium chlorochromate (PCC) oxidation to the lactone (20), which formed (8) on SmI₂ reduction.² Reduction with NaBH₄ gave the alcohol. To prepare the acid (7) β-ionone was converted to the epoxide with Me₃S⁺I⁻/KOH and reduced with NaBH₄/CeCl₃ to form the alcohol (21); photoisomerisation and Jones oxidation gave (7). The t-butyltrimethylsilyl (TBDMS) ether of hydroxy-β-ionone was converted in a similar way to alcohol (22). After photoisomerisation and Jones oxidation, the ketone gave the ketone (6) while a two-stage oxidation (PCC then NaClO₂/NaH₂PO₄) formed the ether (4). Reduction of (6) followed by acetylation yielded the acetate (5). Since one of the objectives of this work was to explore new routes to highly oxygenated terpenoids the oxidation of the dienone (15) with some simple reagents was examined. With *m*-ClC₆H₄CO₃H the γ,δ-epoxide was obtained, which unexpectedly rearranged with BF₃ to the ether (23), ν_{max} 1755 cm⁻¹, δ_H 6.66 (1H, d, *J* 6 Hz), 6.14 (1H, d, *J* 6 Hz). Oxidation with Triton B-Bu^tOOH yielded the α,β-epoxide.

We thank Dr. G. A. Morris for the n.m.r. experiments.

Received, 23rd February 1989, Com. 9/00836E

References

- 1 C. A. Barron, N. Khan, and J. K. Sutherland, *J. Chem. Soc., Chem. Commun.*, 1987, 1728.
- 2 G. A. Molander and G. Hahn, *J. Org. Chem.*, 1986, **51**, 1135.