

## Ring Enlargement–Cyclopentane Annulation via Thermal Oxy-Cope Rearrangement

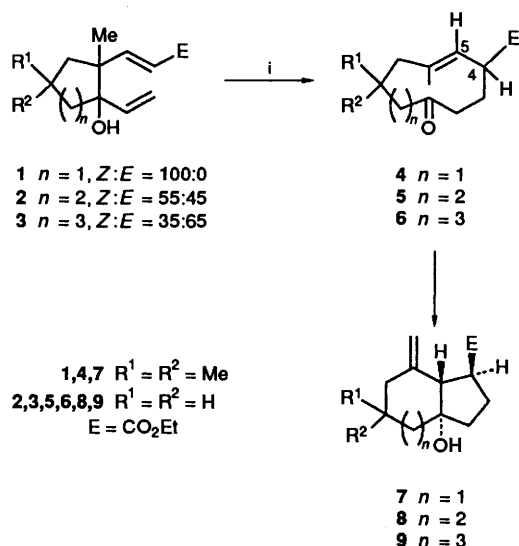
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Thermal oxy-Cope rearrangement of 1,2-divinylcycloalkanols led to ring expansion–cyclopentane annulation; the effect of ring size on the reaction has been studied.

The bicyclic systems hydrazulene and hydrindane, particularly those bearing a hydroxy group at the ring junction, have attracted considerable attention; many natural products of biological interest<sup>1</sup> contain these ring systems as an integral part of their structure, thus setting them apart as important synthetic targets. The synthesis of crucial intermediates<sup>2</sup> capable of transformation into these bicyclic ring systems and the recent reports in this area<sup>3</sup> prompted the communication of our findings; an expedient synthesis of the bicyclic systems 7–9 by a thermal oxy-Cope rearrangement of the vinyl alcohols 1–3 was envisaged.

Thermal and anionic oxy-Cope rearrangement of 1,2-divinylcycloalkanols is well documented and leads to cycloalkenones.<sup>4</sup> Earlier, the synthesis of angularly substituted bicyclic systems were reported from our laboratory<sup>5</sup> via anionic oxy-Cope rearrangement of 1–3. As a consequence of thermal oxy-Cope rearrangement, ring-enlarged compounds 4, 5 and 6 are likely to be generated which are capable of undergoing a transannular ene reaction<sup>6</sup> leading to the bicyclo[4.3.0]nonan-1-ol 7, bicyclo[5.3.0]decan-1-ol 8 and bicyclo[6.3.0]undecan-1-ol 9 respectively (Scheme 1).



**Scheme 1** Reagents and conditions: i, *o*-DCB, heat;  $n = 1$ , 12 h, 100%;  $n = 2$ , 14 h, 90%;  $n = 3$ , 14 h, 90%

The 1,2-divinylcycloalkanols 1–3 were prepared according to the literature procedure.<sup>5</sup> Thus, compound 1 was obtained as a single diastereoisomer, but compounds 2 and 3 were obtained as a mixture of diastereoisomers† as evidenced by <sup>1</sup>H NMR and HPLC analysis (Scheme 1). Compound 1 when heated in

*o*-dichlorobenzene (ODCB) at reflux temperature for 12 h was quantitatively converted into compound 7 which exhibited satisfactory spectral data.<sup>8</sup> The *trans* stereochemistry of the ring fusion was ascertained by comparison of the <sup>1</sup>H NMR spectra taken in CDCl<sub>3</sub> and in [<sup>2</sup>H<sub>5</sub>]pyridine (which revealed no shift for the bridgehead allylic hydrogen) and NOE studies.‡ The base-promoted rearrangement results in the formation of a C–C bond between the termini of the  $\pi$ -systems, with no skeletal change.<sup>5</sup> The thermal rearrangement initially leads to a ring enlargement with the formation of the dienol intermediate followed by tautomerisation of the dienol and an intramolecular ene reaction, due to the proximity of the methyl and carbonyl groups. The net result is the insertion of the extra carbon into the existing ring system.

The success encountered with compound 1 prompted us to study the behaviour of vinyl alcohols 2 and 3. The vinyl alcohol mixture 2 when heated in *o*-DCB at reflux temp. for 14 h afforded 8 in 90% yield along with the ring-enlarged compound 5 as a minor component. A noteworthy aspect of the rearrangement is that the mixture of vinyl alcohols leads to a single hydroazulene 8 implying the intervention of a common intermediate 5. Each diastereoisomeric divinylcyclohexanol 2 rearranges via a chair-like transition state to a distinct dienol differing from the other dienol only in the geometry of the enol double bond; this stereochemical difference is lost upon tautomerisation of the enol. The structure was confirmed by spectral data and the stereochemical assignment was made as for compound 7. Compound 3 when heated in *o*-DCB at reflux temp. for 14 h afforded cycloundec-5-enone 6 in 90% yield in which the alkene has the *E* configuration. NOE at the olefinic methyl causes 14.2% enhancement of 4-H. The ability of the ring-enlarged compounds 4 and 5 to undergo an intramolecular ene reaction and the failure encountered with 6 can be successfully explained in terms of the interatomic distance between C-1 and C-5.§ Thus, for compound 6, a distance of 3.33 Å separates the reactive centres C-1 and C-5. As a consequence, a transannular ene reaction does not operate.

### Experimental

#### General Procedure for Thermal Oxy-Cope Rearrangement.—

A solution of vinyl alcohol (5 mmol) in *o*-DCB (20 cm<sup>3</sup>) was refluxed under nitrogen for 12 h. The solution was cooled, the *o*-DCB removed under reduced pressure (0.5 Torr¶), and the

† In ref. 5 it was suggested that the addition of the lithium acetylide to the ketone exclusively delivered a single diastereoisomeric alcohol.

‡ In cyclic systems, it is known that the <sup>1</sup>H NMR chemical shifts of a hydrogen that is vic and *syn* to the hydroxy group is deshielded and shifted downfield in [<sup>2</sup>H<sub>5</sub>]pyridine relative to the chemical shift of the same hydrogen in CDCl<sub>3</sub>.<sup>7</sup>

§ Evaluation by means of MMX calculations using a PC model for *trans*-cycloalk-5-enones gave transannular gaps between C-1 and C-5 for potential cyclisation: for compound 4 2.68 Å; 5 2.95 Å; and 6 3.33 Å.

¶ 1 Torr  $\approx$  133 Pa.

residue was chromatographed over silica gel [hexane-ethyl acetate (10:1)] to give the rearranged product.\*

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### References

- 1 (a) L. Porter, *Chem. Rev.*, 1967, **67**, 441; (b) N. H. Fischer, E. J. Olivier and H. D. Fischer, *Fortschr. Chem. Org. Naturst.*, 1979, **38**, 47, 270, 272; (c) E. Rodriguez, G. H. N. Towers and J. C. Mitchell, *Phytochemistry*, 1976, **15**, 1573; (d) C. H. Heathcock, in *Total Synthesis of Natural Products*, ed. T. Apsimon, Wiley, New York,

- 1973, vol. 2; (e) P. A. Wender, H. Lee, R. S. Wilhelm and P. D. Williams, *J. Am. Chem. Soc.*, 1989, **111**, 8954; (f) P. W. Coddling, *J. Am. Chem. Soc.*, 1984, **106**, 7905.
- 2 S. Janardhanam, P. Shanmugam and K. Rajagopalan, *Synth. Commun.*, in the press.
- 3 (a) M. Sworin and K. C. Lin, *J. Am. Chem. Soc.*, 1989, **111**, 1815; (b) L. A. Paquette, J. Reagan, S. L. Schreiber and L. A. Teleha, *J. Am. Chem. Soc.*, 1989, **111**, 2331; (c) L. A. Paquette and Y. J. Shi, *J. Org. Chem.*, 1989, **54**, 5205; (d) L. Jisheng, J. Gallardo and J. B. White, *J. Org. Chem.*, 1990, **55**, 5426; (e) L. A. Paquette and Y. J. Shi, *J. Am. Chem. Soc.*, 1990, **112**, 8478.
- 4 (a) W. C. Still, *J. Am. Chem. Soc.*, 1977, **99**, 4186; (b) 1979, **101**, 2493; (c) D. L. J. Clive, C. G. Russell and S. C. Suri, *J. Org. Chem.*, 1982, **47**, 1632; (d) T. Kato, H. Kondo, M. Nishino, M. Tanaka, G. Hata and A. Miyake, *Bull. Chem. Soc. Jpn.*, 1980, **53**, 2958; (e) J. W. Herdon, L. A. McMullen and C. E. Daitch, *Tetrahedron Lett.*, 1990, **31**, 4547.
- 5 G. Sathyamoorthi, K. Thangaraj, P. C. Srinivasan and S. Swaminathan, *Tetrahedron*, 1990, **46**, 3359.
- 6 L. Lorenc, M. Rajkovic, A. Milovanovic and M. Lj. Mihailovic, *J. Chem. Soc., Perkin Trans. 1*, 1988, 1495.
- 7 P. V. Demarco, E. Farkas, D. Doddrell, B. L. Myalri and E. Wenkert, *J. Am. Chem. Soc.*, 1968, **90**, 5480.
- 8 H. C. Mez, G. Rist, O. Ermer, L. Lorenc, J. Kalvoda and M. Lj. Mihailovic, *Helv. Chim. Acta*, 1976, **59** (4), 1273.

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