

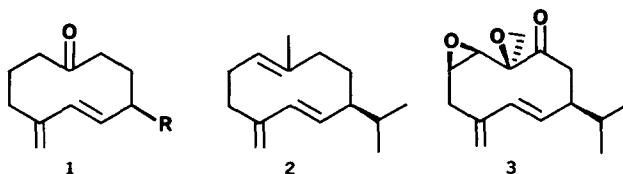
A CYCLOBUTENE BRIDGEHEAD OLEFIN APPROACH
TO THE GERMACRANES

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Summary: A model study for the synthesis of the germacranes is described which utilizes a consecutive oxy-Cope/cyclobutene ring opening rearrangement sequence. The β,γ -unsaturated enone necessary for the rearrangement is obtained directly from the photocycloaddition of allene and cyclohexenone.

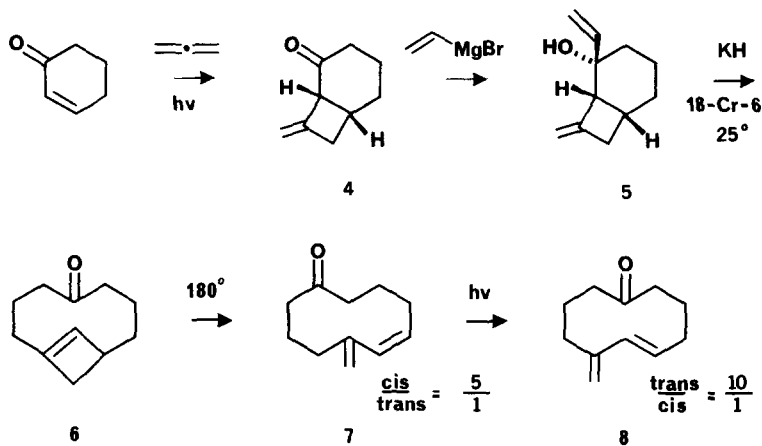
We are interested in developing a strategy for the synthesis of germacranes that involves the construction of a ten-membered carbocyclic ring containing the butadiene unit as in 1. This type of structural unit is found to occur in such members of the



germacrane class as germacrene D¹, 2, and periplanone-B^{2,3}, 3. It could also serve as a useful precursor to the functionality found at these carbon centers in the other members of this structural class.⁴ Our approach to the cyclic diene involves the use of a consecutive oxy-Cope/cyclobutene ring opening rearrangement sequence and utilizes the regioselectivity observed in the photocycloaddition of allene to cyclohexenones.

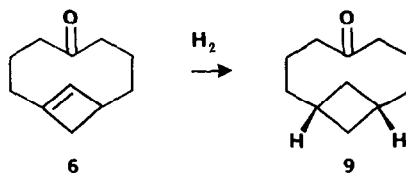
Photocycloaddition of allene to cyclohexenone regioselectively generated the β,γ -enone 4, as reported previously.⁵ Addition of vinyl magnesium bromide (THF, -70°) to 4 gave a 79% yield of the tertiary alcohol, 5. The assignment of the endo alcohol stereochemistry

is based on the expected attack of the Grignard reagent from the convex face of 4.



Divinyl cyclohexanols have been shown to be extremely useful in the synthesis of cyclodecanoids,^{3,6} by way of the oxy-Cope rearrangement, and this divinylcyclohexanol proved to be no exception. When 5 was treated with KH and 18-crown-6⁸ in THF at room⁹ temperature for two hours and quenched with NH_4Cl , the cyclobutene bridgehead olefin 6¹⁰ was obtained in 71% isolated yield.

The structure of the bridgehead cyclobutene was concluded on the basis of its spectral data¹¹ and chemical behavior. Thus hydrogenation of 6 (1 atm. H_2 , 10% Pd/C, hexane, 2 min., 99% yield) gave a single product, the symmetrical bridged cyclobutane 9. As expected from consideration of the symmetry of 9, the fully decoupled¹³ ^{13}C spectrum displayed



only six carbon signals,¹² whereas the cyclobutene 6 displayed the expected eleven.

The thermal ring opening of the cyclobutene 6 proceeded smoothly in toluene in a sealed tube at 180° for twelve hours to produce a readily separable (preparative tlc) 5:1 mixture of the cis olefin, 7, and the trans olefin, 8, respectively,^{13,14} in 95% yield. Photolysis in cyclohexane (Hanovia medium pressure lamp, quartz filter) of either pure cis (7) or pure trans (8) butadiene, or of the mixture obtained from the thermolysis established a photostationary state containing a 10:1 mixture of trans and cis isomers, respectively,¹⁵ in 81% yield. In this fashion, an olefin/mixture enriched in either cis or trans isomer can be established. We are currently studying extensions and applications of this chemistry in bridgehead olefin and natural product synthesis.

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References and Footnotes

1. Structure: K. Yoshihari, Y. Ohta, T. Sakai, and Y. Hirose, Tetrahedron Lett., 2263, (1969).
2. Structure: C.J. Persoons, P.E.J. Verwiel, F.J. Ritter, E. Talman, P.J.F. Nooijen and W.J. Nooijen, Tetrahedron Lett., 2055 (1976).
3. Synthesis (and structure): W.C. Still, J. Am. Chem. Soc., 101, 2493 (1979).
4. For example, 1,4-oxidation of a similar diene has been reported via reaction with singlet oxygen: E. Demole, C. Demole and D. Berthet, Helv. Chim. Acta, 56, 265 (1973).
5. E.J. Corey, J.D. Bass, R. LeMahieu, and R.B. Mitra, J. Am. Chem. Soc., 86, 5570 (1964).
6. a) E.N. Marvell and W. Whalley, Tetrahedron Lett., 509 (1970); b) W.C. Still, J. Am. Chem. Soc., 99, 4186 (1977).
7. D.A. Evans and A.M. Golob, J. Am. Chem. Soc., 97, 4765 (1975).
8. No appreciable rearrangement was observed in the absence of the crown ether.
9. For a recent review on aspects of bridgehead olefin chemistry, see: K.J. Shea, Tetrahedron, 36, 1683 (1980).
10. The details of this transformation will be reported shortly.
11. Spectral Data of 6: ¹H NMR (CDCl₃, 90 MHz): 5.78 δ (bs, 1H); 2.90-1.60 δ (m, 15H);

^{13}C NMR (CDCl_3 , 67.9 MHz): 213.5(s), 148.6(s), 136.6(d), 43.9, 42.0, 38.3, 33.8, 30.4, 28.8, 26.2, 19.2; FT-IR (neat): 3019, 1699, 1630 cm^{-1} ; GC-MS: $m/e = 164$ (M+).

12. The stereochemistry assigned to 9 is based on peripheral attack³ of hydrogen on the cyclobutene. For a similar structural proof on an isomeric system, see: M. Kahn, Tetrahedron Lett., 4547 (1980); S.G. Levine, R.L. MacDaniel, J. Org. Chem., **46**, 2199, (1981).
13. Spectral Data of 7: ^1H NMR (CDCl_3 , 90 MHz): 5.84 δ (d, $J = 10.8$ Hz, 1H), 5.42 δ (dt, $J_d = 10.8$ Hz, $J_t = 7$ Hz, 1H), 4.96 δ (bs, 1H), 4.78 δ (bs, 1H); FT-IR (neat): 3078, 1708, 1630, 900, 775 cm^{-1} ; UV (hexane): $\lambda_{\text{max}} = 225$ nm.; GC-MS: $m/e = 164$ (M+).
Spectral Data of 8: ^1H NMR (CDCl_3 , 270 MHz): 6.11 δ (d, $J = 16.1$ Hz, 1H), 5.38 δ (dt, $J_d = 16.1$ Hz, $J_t = 7.4$ Hz, 1H), 4.90 δ (bs, 1H), 4.88 δ (bs, 1H); FT-IR (neat): 3075, 1702, 1649, 982, 889 cm^{-1} ; UV (hexane): $\lambda_{\text{max}} = 236$ nm.; GC-MS: $m/e = 164$ (M+).
14. When either pure cis (7) or pure trans (8) isomer was resubjected to the reaction conditions (180° , 12 hours) only a small degree of interconversion (<10%) took place, indicating the 5:1 cis:trans thermolysis ratio reflects a kinetic preference in the ring opening.
15. For a discussion of photoisomerization of dienes, see: R.O. Kan, "Organic Photochemistry", Ch. 2., section 2.1, McGraw Hill Book Co., N.Y., 1966.
16. Under these conditions, no electrocyclic ring closure of the dienes back to the cyclobutene 6 was detected.

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