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A NOVEL FRAGMENTATION REACTION OF AN α,β-EPOXYCYCLOPENTANONE. STEREOSELECTIVE FORMATION OF TRISUBSTITUTED E-DOUBLE BOND

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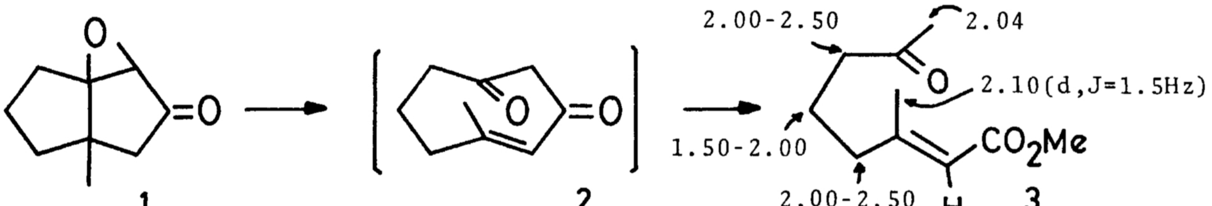
cis-1,6a-Epoxy-3a-methyloctahydropentalen-2-one readily undergoes fragmentation to give stereoselectively methyl (E)-3-methyl-7-oxo-2-octenoate in 75% yield, on treatment with a catalytic amount of sodium carbonate in methanol. A pericyclic mechanism is suggested for the new ring opening reaction.

In the course of studies on the synthesis of a certain sesquiterpene,1) we treated cis-1,6a-epoxy-3a-methyloctahydropentalen-2-one **1**2,3,4) (2g) with dil. methanolic Na_2CO_3 (0.2g/30cm^3) at rt (5h) to obtain an α,β-unsaturated methyl ester [ν (neat) 1720, 1650cm^{-1}, δ (CCl_4) 3.59 (3H, s), 5.52 (1H, m)] in 75% yield. The product was analyzed for $C_{10}H_{16}O_3$ and close examination of its nmr data (CCl_4, indicated in formula **3**) suggested that it is methyl (E)-3-methyl-7-oxo-2-octenoate. The stereochemistry of the double bond was deduced by comparison of the δ values of the C-2 proton with known data of related compounds.5)



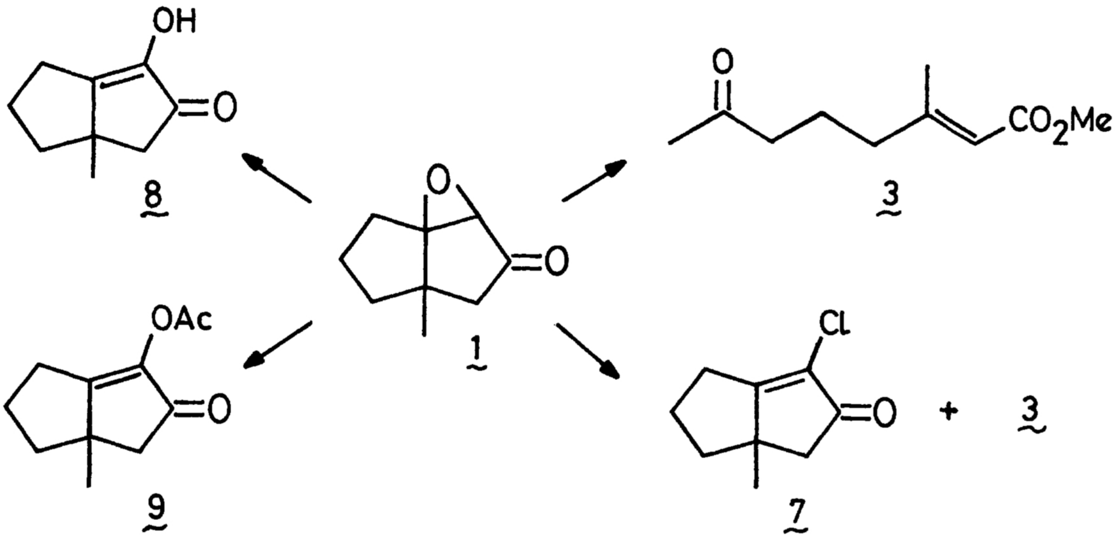
1 **2** **3**

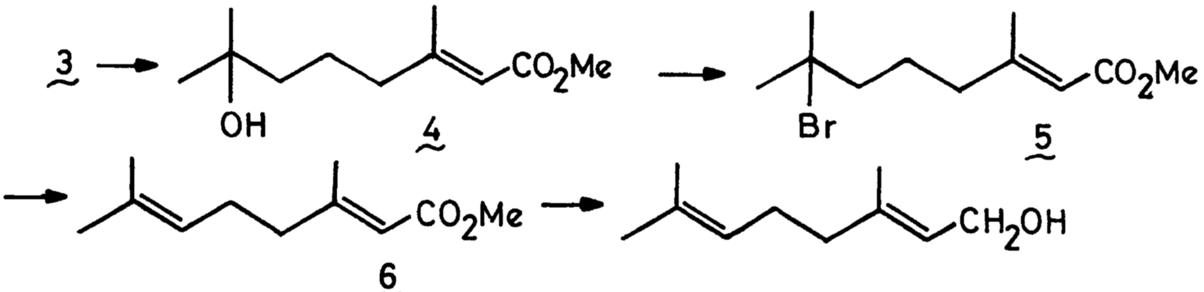
To confirm the structure, the product was transformed to geraniol as follows. Reaction of **3** with 1.5 eq. of MeMgI (Et_2O, 0°) gave alcohol **4**3,4) [δ (CCl_4) 1.15 (6H, s), 2.10 (3H, d, J=1.5 Hz), 3.59 (3H, s), 5.52 (1H, m), 90%] which on treatment with HBr in acetone at reflux gave bromide 5[3,4] [δ (CCl_4) 1.71 (6H, s), 85%]. Reaction of 5 with excess Bu_4NBr[6] (acetone, reflux, 4h) gave regioselectively methyl geranate 6[7] (85%). Reduction of 6 ($LiAlH_4$, Et_2O, reflux) afforded geraniol (90%), which was in all respects identical with an authentic sample.

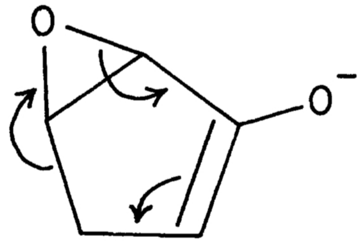
The product 3 is presumably formed through a two step fragmentation process 1→2→3, of which the first step is unprecedented. Since the fragmentation 1 → 3 under such mild conditions seemed quite unusual, some related reactions were next examined. Reaction of 1 with HCl in MeOH at rt gave α-chlorovinyl ketone 7[3,4,8] [ν (neat) 1730, 1645cm^{-1}, δ (CCl_4) 1.17 (3H, s), 2.30 (2H, s), 70%] accompanying a small amount (10%) of 3. With BF_3-etherate in benzene (rt, 1h) and with Ac_2O-pyridine (reflux, 2h) 1 afforded respectively diosphenol 8 [ν (neat) 1715, 1660 cm^{-1}, δ (CCl_4) 1.16 (3H, s), 2.28 (2H, s), 80%] and its acetate 9[3,4] [ν (neat) 1780, 1730, 1675cm^{-1}, δ (CCl_4) 1.17 (3H, s), 2.13 (3H, s), 2.25 (2H, s), 65%] without giving ring fission products.

The reason for the high reactivity of 1 is not clear at present. However, since *cis* and *trans*-1,7a-epoxy-3a-methyloctahydroinden-2-one[4,9] are both quite stable under the above described conditions (MeOH, Na_2CO_3), steric strain inherent to 3a,6a-disubstituted cis-octahydropentalene (for example see formula B in footnote 2) probably plays an important role. The high stereoselectivity is another remarkable point of the fragmentation reaction and suggests a retro Diels-Alder type reaction mechanism, depicted by formula 10. The three-system interaction theory[11] predicts the conrotatory ring opening of 3a,6a-bond (fomula 11), which leads to the formation of the observed *E*-ester.

We wish to thank Professor Ken'ichi Fukui, Kyoto University, for valuable discussions.







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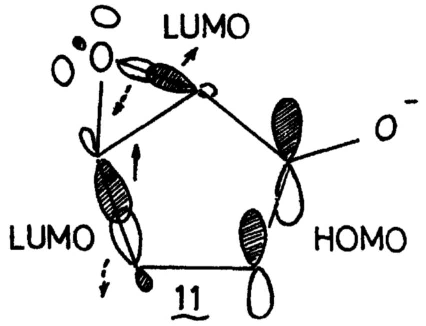
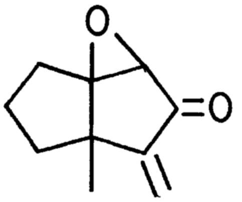


References and Notes

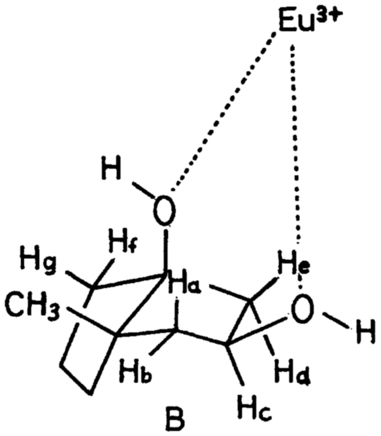
1) H. Hashimoto, K. Tsuzuki, F. Sakan, H. Shirahama, and T. Matsumoto, Tetrahedron Lett., 1974, 3745.

2) Prepared through epoxidation (H_2O_2-NaOH, MeOH, -25°, 1h) of 6a-methyl-1,2,4,5,6,6a-hexahydropentalen-2-one.[1] Assignment of the cis stereochemistry of 1 is based on the analogy of the formation of related cis-epoxide A from the corresponding α,β-unsaturated ketone under quite similar conditions and on the following evidence: reduction ($NaBH_4$, EtOH) of 1 yielded stereoselectively 2β-alcohol,[4] which in turn was reduced ($LiAlH_4$) to a diol B.[4] The cis relationship of the two hydroxyl group of the diol was shown by the ir band at 3580cm^{-1} (CCl_4, 2.7×10^{-3}mmol/cm^3). Nmr spectral data of B in the presence of Eu(fod)$_3$,

(B : Eu^{3+}=1 : 0.65, $CDCl_3$ solution) tabulated below, are satisfactorily accounted for in terms of conformation B and show the cis structure of 1.



A



B

Ha	$\delta(CDCl_3)$ 6.40 (dd, Jab = 15 Hz, Jae = 3 Hz)	*S = 7.5
Hb	4.82 (dd, Jab = 15 Hz, Jbc = 5 Hz)	S = 5.5
Hc	7.65 (m, Jbc = 5 Hz, Jcd = 4.5 Hz, Jce = 3 Hz)	S = 5
Hd	6.40 (dd, Jde = 15 Hz, Jcd = 4.5 Hz)	S = 5.5
He	8.80 (m, Jde = 15 Hz, Jce = 3 Hz, Jae = 3 Hz)	S = 10
Hf,g	4.60 (2H, t, J = 7 Hz)	S = 5
CH_3	3.72 (3H, s)	S = 4

*A. F. Cockerill and D. M. Rackham, Tetrahedron Lett., 1970, 5149.

3) Satisfactory analytical data were obtained for this compound.

4) Satisfactory ir, nmr, and mass spectral data were obtained for this compound.

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8) For similar ring opening of α,β-epoxy ketone to α-chlorovinyl ketone see, N. Neeman, J. S. O'Grodrick, and K. Morgan, J. Chem. Soc., Perkin Trans. I, 1972, 2302.

9) The cis compound was prepared through epoxidation (H_2O_2-NaOH, MeOH, rt, 1h) of 7a-methyl-1,4,5,6,7,7a-hexahydro-2H-inden-2-one.10) The trans isomer was yielded from the enone through the following reactions: (1) DIBAL, toluene, -78°, (2) m-CPBA, CH_2Cl_2, rt, (3) Jones Ox.

10) R. F. Jullien, C. Frejaville, and V. Toure, Bull. Soc. Chim. Fr., 1966, 3725.

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