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AN EXAMPLE OF THE BASE INDUCED ISOMERISATION OF THE EPOXIDE RING IN ENOLIZABLE EPOXYKETONES: ISOMERISATION OF 8,9-EPOXY-6,7,8,9-TETRAHYDRO-5H-BENZOCYCLOHEPTEN-5-ONE AND SOME OF ITS DERIVATIVES

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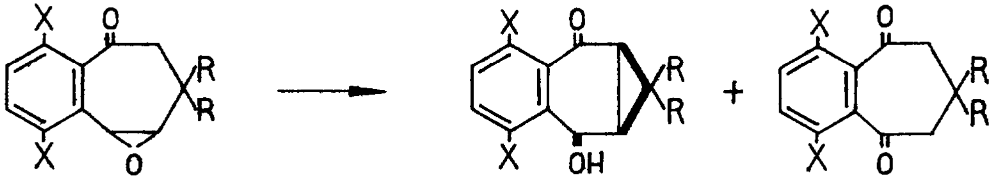
Summary: The title compounds in the basic medium (RO^-/ROH) afford an unique example of competition between isomerisation via the enolate anion and epoxide-ketone isomerisation.

In strong basic media (eg.LDA, tert-BuLi,etc.) epoxides isomerise to carbonyl compounds or allylic alcohols[1]. In epoxides with enolizable keto groups the addition of the enolate anion to the oxirane ring takes place, instead of the "normal" isomerisation. This reaction occurs under milder condition (eg.RO^-, R_3N, etc.)[1a,2].

We have found that some 8,9-epoxy-6,7,8,9-tetrahydro-5H-benzocyclohepten-5-ones (1 - 4), synthesised for the first time in our laboratory[3] afford a unique example of competition between isomerisation via the enolate anion and "normal" epoxide isomerisation.



1	X = H	R = H	5	88%	-	
2	X = OCH_3	R = H	6	89%	-	
3	X = H	R = CH_3	7	38%	9	55%
4	X = OCH_3	R = CH_3	8	32%	10	64%

Compounds 1 and 2, refluxed for 15 min in a solution of sodium isopropoxide in isopropanol[4], quickly isomerise to the hydroxyketones 5 and 6[5] in high yield. We were unable to confirm by ^{1}H NMR the exact stereochemistry of products obtained[6]. The most probable reaction mechanism involves backside displacement of the epoxide oxygen at C-8 by the enolate anion created at C-6 with inversion at C-8[2a,c]. The cyclopropane ring is therefore presumably cis relative to the OH group in the products obtained.

The epoxyketones 3 and 4 gave as main products the diones 9 and 10 respectively under the same reaction conditions. The hydroxyketones 7 and 8 were minor components of the reaction mixture [5,7].

Rearrangement of 7 and 8 into 9 and 10 does not occur under the reaction conditions. The diketones 9 and 10 are therefore formed by a "normal" isomerisation of oxirane ring, even in the presence of an enolizable keto group.

The reduced reactivity of the hydrogen atoms in the α position to carbonyl group caused by the presence of two methyl groups at C-7 in compounds 3 and 4 is probably the most important reason for this "normal" isomerisation [8].

The fact that the diones 9 and 10 are formed easily in relatively mild basic medium shows the markedly increased reactivity of hydrogen atom at C-9 caused by the presence of the carbonyl function.

References and Notes

1. (a) V.N. Yandovskii and B.A. Ershov, *Uspekhi Khimii* 41, 785 (1972) and references therein; (b) M. Hassan, A.R.O. Abdel Nour and A.M. Satti, *Rev. Roum. Chim.*, 23, 747 (1978); (c) R.W. Thies and R.H. Chiarello, *J. Org. Chem.*, 44, 1342 (1979).
2. (a) Y. Gaoni, *Tetrahedron* 28, 5533 (1972) and references therein; (b) P.B.D. de la Mare and R.D. Wilson, *J.C.S. Perkin II*, 1977, 975; (c) E.W. Warnhoff and V. Srinivasan, *Can. J. Chem.*, 55, 1629 (1977).
3. The epoxyketones 1 - 4 were obtained by epoxidation of the corresponding unsaturated ketones by m-chloroperbenzoic acid in CH_2Cl_2 at 0°C. Yields were 74-98%. Satisfactory spectral and elemental analyses were obtained for these compounds.
4. These reaction conditions gave the best yields. In our first experiments we used sodium methoxide in methanol. In no case have we observed products from the solvolytic opening of the oxirane ring.
5. 5:IR(neat):3420 cm^{-1},1665cm^{-1}, ^{1}H NMR($CDCl_3$):δ 7.1-8(m,4H,ArH); 5.30(m,1H, CH-OH); 3.08(s,1H,OH); 2.0-2.4 and 0.8-1.5(m,4H, cyclopropane ring protons). MS: m/e 174(M^+). The structure of this compound was confirmed by oxidation ($BaMnO_4$, 94% yield) to 2,3-dihydro-2,3-methano-1,4-naphthoquinone. 6:IR(KBr): 3500cm^{-1},1670cm^{-1}, ^{1}H NMR($CDCl_3$):δ 7.05 and 6.88(d,d,J=10Hz,2H,ArH); 5.44 (d,J=4Hz,1H,CH-OH); 4.94(s,1H,OH) 3.88 and 3.86(s,s,6H,OCH_3); 2.0-2.4 and 1.1-1.4(m,4H, cyclopropane ring protons). MS: m/e 234 (M^+). 7:IR(neat): 3460 cm^{-1},1665cm^{-1}. ^{1}H NMR($CDCl_3$):δ 7.1-8.1(m,4H,ArH):5.41 (d,J=6Hz,1H,CH-OH); (2.65 s,1H,OH); 1.7-2.1(m,2H,cyclopropane ring protons); 1.29 and 1.00(s,s, 6H,CH_3). MS: m/e 202(M^+).
6. Compare: J. Carnduff and D.G. Leppard, *J.C.S.Perkin I*, 1977, 1325.
7. The reaction mixtures were separated by preparative TLC. Their compositions were determined by ^{1}H NMR. 9: IR(KBr): 1685cm^{-1}. ^{1}H NMR($CDCl_3$):δ 7.5-8.0(m, 4H,ArH), 2.71(s,4H,CH_2); 1.24(s,6H,CH_3). MS: m/e 202(M^+). The dione 10 was indentified by comparing its m.p. and spectra with those of an authentic sample(W.E.Hahn and Z.Madeja-Kotkowska, *Roczniki Chem.*, 37, 1447 (1963)).
8. Compare: H.O. House, Modern Synthetic Reactions, W.A.Benjamin, Inc., Menlo Park, California 1972 p.500 and references therein.

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