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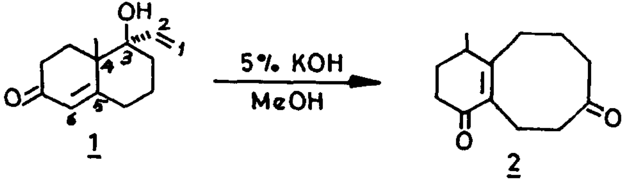
BASE CATALYZED REARRANGEMENT OF OXY-COPE SYSTEMS.

Miss R.Uma, S.Swaminathan and K.Rajagopalan*

Department of Organic Chemistry
University Of Madras, Guindy Campus
Madras - 600 025, INDIA.

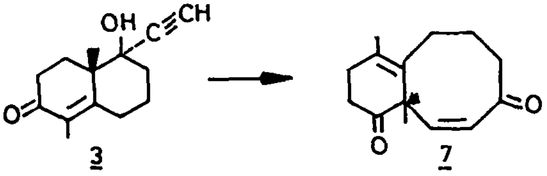
Abstract. The synthesis and rearrangement of the optically active ethynyl and vinyl carbinols 3 and 4 are reported. The rearrangements are found to be concerted when carried out with KH-THF and non-concerted with KOH-methanol.

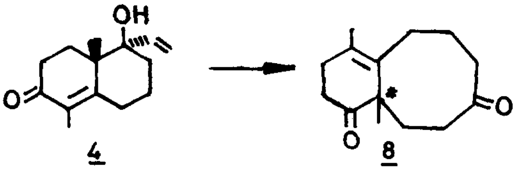
The earliest example of a base catalyzed rearrangement of an Oxy-Cope system was reported from our laboratory[1] for the bicyclic system 1 to the ring enlarged dione 2. Several δ- hydroxy α,β - enones have been found to rearrange smoothly on treatment with hydroxide base[2,3].



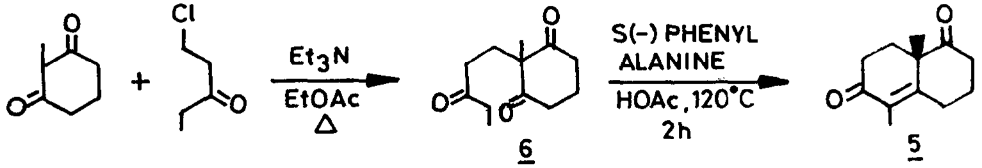
Two mechanistic pathways may be considered to account for these rearrangements : i) a stepwise Retro-Aldol mechanism and ii) a concerted (3,3) sigmatropic rearrangement of the Oxy-Cope moiety in the compound 1 (see numbering).

Evans et al[4] have established the concerted nature of the base catalyzed Oxy-Cope rearrangement with regard to other types of substrates by rearranging optically active diastereomers. For the rearrangement of bicyclic systems like 1, critical mechanistic evidence has been sought in the present work using the optically active substrates 3 and 4. The logistics behind the choice of these substrates is that on rearrangement a chiral centre is created at the ring junction and thus the product should show optical activity if the rearrangement were to proceed in a concerted manner.

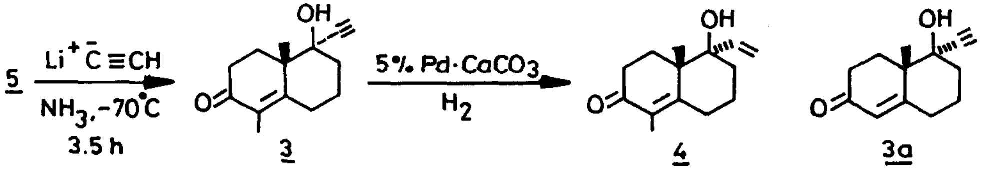




The optically active diketone 5, the necessary starting material for preparing the carbinols 3 and 4 was synthesized by the asymmetric cyclization[5,6] of the trione 6 obtained in turn in 75% yield by the alkylation of 2-methyl - 1,3 - cyclohexane dione with 1 - chloro - 3 - pentanone. The above asymmetric cyclization we have found, is best carried out by treating the triketone 6 with an equimolar amount of S (-) - phenylalanine in acetic acid at 120°C for 2 hr, when the diketone 5 is obtained in 80% chemical and 87.3% optical yield. $[\alpha]_D^{25}$ + 69° (MeOH, C = 0.017); Reported[7] ; $[\alpha]_D^{25}$ + 79° for 100% pure enantiomer. The diketone 5 has been assigned 8a S configuration in line with literature report[7] and comparison of CD curves[5].



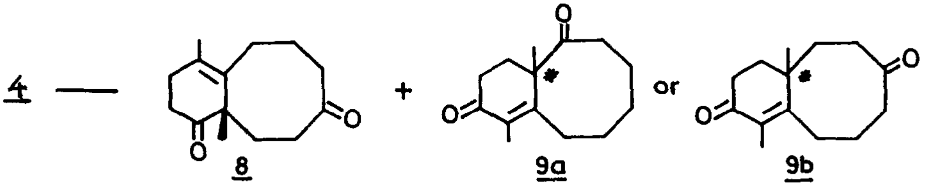
Reacting the diketone 5 with lithium acetylide in liquid ammonia at -70°C for 3.5 hr furnished the optically active ethynyl carbinol 3 in 40% yield as a crystalline solid ; m.p. 174-176°C ; $[\alpha]_D^{25}$ + 79.9° ($CHCl_3$, C= 0.017). Partial reduction of this carbinol 3 with 5% Pd-$CaCO_3$ in pyridine gave the vinyl carbinol 4 in 80% yield ; m.p. 89-91°C ; $[\alpha]_D^{25}$ + 178° ($CHCl_3$, C = 0.017). The carbinols 3 and 4 have been assigned the 1R, 8aS configuration in accord with literature report[8] for the compound 3a.



Carbinol 3 on treatment with one equivalent of KH in dry THF at 0-5°C 4 hr followed by workup furnished the ring enlarged dione 7 as a crystalline solid, m.p. 61-63°C (80% yield based on recovered starting material). After two crystallizations from hexane-chloroform, this compound melted at 64.5-65.5°. $[\alpha]_D^{25}$ + 335° ($CHCl_3$, C = 0.05). IR ($CHCl_3$) : 1720,1680 and 1620 cm^{-1} ; PMR ($CDCl_3$/TMS)δ values : 1.3 (s, 3H, CH_3), 1.65 (s, 3H, vinyl CH_3), 1.8-2.7 (m, 10H, methylene protons) and 5.5 (s, 2H, vinyl protons) ; Mass spectrum : m/e-218. Values Calcd.for $C_{14}H_{18}O_2$: C = 77.06 ; H = 8.2 : Found : C = 77.31; H = 8.1%

However, the carbinol 3 when treated with 0.2% NaOMe in methanol at room temperature for 12 hr, furnished a pale yellow viscous liquid which had almost the same spectral properties as the compound 7, but with zero rotation.

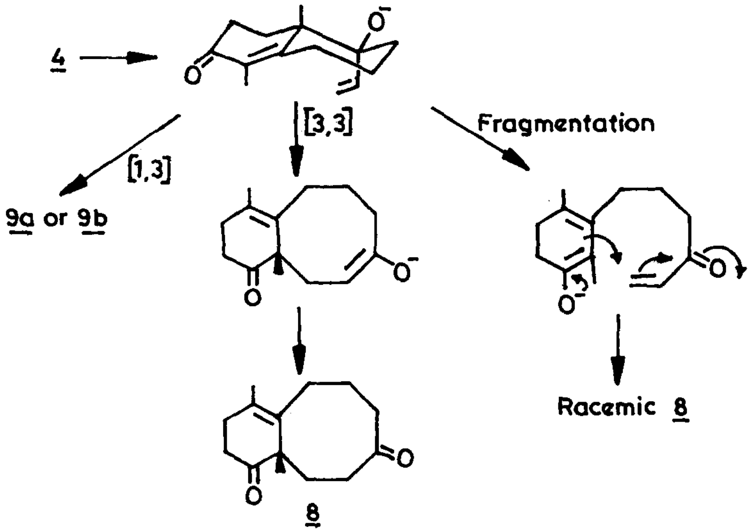
Treatment of the vinyl carbinol 4 with 5% methanolic KOH gave the ring enlarged dione 8 with zero rotation. However, the same compound on treatment with one equivalent of KH in dry THF at 0-5°C for 3 hr furnished a mixture of products. Separation by silica gel column chromatography, gave the optically active compounds 8 (m.p. 55-57°C) and 9a or 9b (viscous liquid) each in 30% chemical yield. These compounds had satisfactory spectral properties and elemental analysis. 8 ; $[\alpha]_D^{25}$ + 20.2° ; 9a or 9b : $[\alpha]_D^{25}$ + 24°



The rather low rotation of compound 8 cast some doubt as to whether the rearrangement was leading to some racemization. However, careful hydrogenation of the optically active compound 7 with PtO_2 at 50 psi hydrogen pressure gave a product identical with compound 8 in all respects including the rotation. With the available data at present, it has not been possible to decide between the structures 9a or 9b.

The retention of optical activity in these rearrangements effected with KH in THF undoubtedly supports a concerted Oxy-Cope mechanism operating in these substrates, while the racemization observed with KOH or NaOMe in MeOH is indicative of a fragmentation - recombination mechanism. Further, in view of the normal mode of (3,3) sigmatropic rearrangements viz., suprafacial with respect to both the pi-systems, it is reasonable to speculate that the resulting chiral centre at the ring junction in compounds 7 and 8 may have a 'R' configuration. The mode of rearrangement of the vinyl carbinol 4 to the racemic and optically active ring enlarged dione 8 is depicted in the Chart.

CHART



A similar mechanism may be proposed for the rearrangement of the ethynyl carbinol. Work is in progress to ascertain the optical purity of several of the compounds reported herein, configurational assignments and finer mechanistic details.

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