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The Zinc Bromide-catalyzed Rearrangement of Pulegone Oxide and Piperitone Oxide

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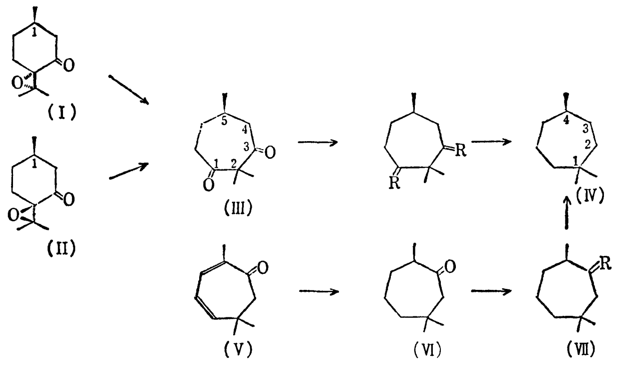
The rearrangement of (+)-*cis*- (I) and (—)-*trans*-pulegone oxide (II) was effected by the catalysis of zinc bromide in boiling benzene to give the same (—)-2,2,5-trimethylcyclohepta-1,3-dione (III), with a retention of the optical activity. The structure of (—)-III with the expanded 7-membered ring was confirmed by the chemical transformation into 1,1,4-trimethyl-cycloheptane(IV), which was identical with that derived from eucarvone(V). Piperitone oxide(VIII) was also converted into diosphenol(X) in the same manner as in pulegone oxides.

Reusch[1] has recently reported that both (+)-*cis*- (I) and (—)-*trans*-pulegone oxide (II), upon gas-phase pyrolysis at 200°C, yielded the same crystalline solid melting at 50—51°C; its structure was suggested to be 2,2,5-trimethylcycloheptane-1,3-dione on the basis of the IR and NMR spectra alone.

We also have obtained a colorless crystal (III), mp 55—56°C, by treating I or II with zinc bromide in boiling benzene according to the Settine procedure.[2] A comparison of the elemental analysis and the NMR, IR, and mass spectra of III with those of the Reusch compound described in the literature[1] has shown the identity of these two compounds, although there is a slight difference in their melting points. No description has been reported for the optical activity of the Reusch compound; however, levo-rotation is found for III in the present work.

We now wish to describe the confirmation of the structure proposed by Reusch and the stereochemistry of this compound, as determined by means of unambiguous chemical transformation.

Eucarvone (V) (semicarbazone, mp 184°C) was hydrogenated over palladium charcoal to give the corresponding tetrahydro-compound (VI), which was converted into the tosylhydrazone (VII) and then reduced with lithium aluminum hydride to yield 1,1,4-trimethylcycloheptane (IV).



Scheme 1

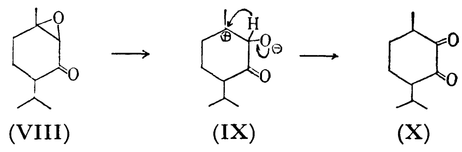
On the other hand, (—)-III was converted, *via* its ditosylhydrazone, into IV. The identity of these two oily products (IV), obtained by different transformations, was shown by a comparison of their physical properties and IR and NMR spectra. This conversion provides further convincing evidence for the 2,2,5-trimethylcycloheptane-1,3-dione structure of the Reusch dione as well as for that of the (—)-III obtained by the present authors. Since the configuration at C-5 of the rearrangement product, (—)-III, must be the same as that (R-) at the C-1 of the parent compounds, (+)-*cis*-I and (—)-*trans*-II, the R-configuration can safely be assigned to the C-5 of (—)-III.

Piperitone oxide (VIII), upon treatment with zinc bromide in boiling benzene, gave diosphenol (X).

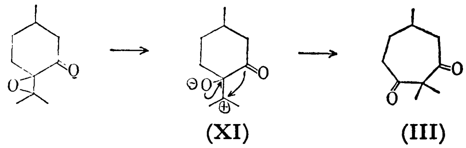
The zinc bromide-catalyzed rearrangements of I, II, and VIII in the present work seem to proceed *via* ionic intermediates; this is contrast to the thermal and photochemical rearrangements,[1,3–5] which have been looked upon as proceeding through radical pathways and which may be reasonably interpreted in terms of anionotropy.[6]

By Lewis-acid catalysis, the oxirane ring of piperitone oxide (VIII) undergoes heterolytic fission so as to form the most stable inoic intermediate (IX), in which the positive charge resides on the tertiary carbon, 1; there follows the 1,2-hydride shift (anionotropy), which fulfils the electron deficiency of the carbonium center, as is shown in Scheme 2. The same mechanism can be given for the formation of III (Scheme 3).

Under the same circumstances, the epimeric pule-



Scheme 2



Scheme 3

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1) W. Reusch, D. F. Anderson, and C. K. Johnson, *J. Amer. Chem. Soc.*, **90**, 4988 (1968).

2) R. L. Settine, G. L. Parks, and G. L. K. Hunter, *J. Org. Chem.*, **29**, 616 (1964).

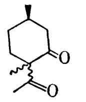
3) H. Wehrli, C. Lehmann, K. Schaffner, and O. Jeger, *Helv.*, **47**, 1336 (1964).

4) O. Jeger, K. Schaffner, and H. Wehrli, *Pure Appl. Chem.*, **9**, 555 (1964).

5) C. K. Johnson, B. Dominy, and W. Reusch, *J. Amer. Chem. Soc.*, **85**, 3894 (1963).

6) C. D. Gutsche, "Organic Reaction," Vol. **8**, John Wiley & Sons, Inc., N.Y. (1954).

gone oxides, (+)-I and (−)-II, are converted into the transient polar-state intermediate (XI in Scheme 3), which then spontaneously rearranges with the anionoid migration of the carbonyl group (C-3) bearing the more negative charge. This mode of rearrangement can reasonably be preferred to that involving the migration of the C-5 methylene residue with the less negative charge. The intermediate (XI) should also be preferred, on the same basis, to an alternative which would lead to XII, the product obtained by the photo-induced rearrangement.[3-5]



(XII)

It should be noted that the ground-state reaction under the acid catalysis of both epimeric epoxides (I) and (II) produced exclusively (−)-III, with an expanded carbocycle resulting from the anionotropy of the carbonyl group, while the photo-induced rearrangement (excited-state reaction) afforded the isomeric diketone (XII),[3-5] which resulted from the rather unusual methyl migration, and the pyrolysis gave a mixture of the two.[1]

Experimental

Zinc Bromide-catalyzed Rearrangement of Pulegone Oxide. (+)-*cis*-Pulegone oxide (mp 59°C, $[\alpha]_D^{20}$ +46.6° (*c* 0.3, methanol), 6.4 g: 0.038 mol) was boiled with zinc bromide (3.2 g: 0.014 mol) in dry benzene (200 m*l*) for 6 hr. After this period, water was added to the reaction mixture and it was extracted with ether. The combined extract was dried and the solvent was removed to give a crude crystalline product, III-a, (5.8 g, 90%), which melted at 55—56°C after several recrystallizations from petroleum ether.

Found: C, 71.23; H, 9.61%. Calcd for $C_{10}H_{16}O_2$: C, 71.37; H, 9.59%. $[\alpha]_D^{25}$ −81.6° (*c* 1.15, ethanol). IR spectrum: 1690 (cm^{-1}), 1730, 1370, 1355. NMR spectrum: τ 8.99 doublet 3H (-CH_3). τ 8.79 singlet 6H (-C(CH_3)$_2$). CD: mμ ([θ] in methanol) 342(0), 313.5(−8170), 240(0), 212 (+11100); mμ ([θ] in isooctane) 345(0), 325(−7830), 321(−7030), 315(−9790), 307(−7680), 304(−4900), 240—225(0), 210(+15500).

(−)-*trans*-Pulegone oxide (II: mp 54—55°C; $[\alpha]_D^{20}$ −18.8° (*c* 2.4, ethanol); 0.4 g; 0.0024 mol) was treated with zinc bromide (0.2 g, 0.0089 mol) in benzene (25 m*l*) in exactly the same manner as has been described above and then worked up to give III-b (mp 55—56°C 0.32 g, 80%). The melting point of this crop was not depressed by the admixture of III-a. The IR- and NMR spectroscopical comparisons, as well as the polarimetrical comparisons, corroborated the identity of these two crops, III-a and III-b, from different sources.

Reduction of 2,2,5-Trimethylcycloheptane-1,3-dione (III). According to the usual procedure in the literature,[7] (−)-III was converted into ditosylhydrazone (mp 262°C); a 2-g portion was then reduced with lithium aluminum hydride (1.2 g) to yield an oily product (IV) after purification by means of preparative vpc; yield, 0.1 g (14%). The optical activity of this compound was substantially null at the wavelength of sodium D-line, but it seemed to possess a feeble dextrorotation in the shorter-wavelength region.

Reduction of Eucarvone (V). Eucarvone (V; its semicarbazone, mp 184°C) was hydrogenated over palladium charcoal (150 mg) to yield tetrahydroeucarvone (VI; its semicarbazone, mp 190°C; yield, 1.8 g (90%). The tosylhydrazone of VI (mp 262°C; 0.3 g, 0.0009 mol) was reduced with lithium alminium hydride (0.46 g) and then worked up as usual[7] to yield a liquid, 1,1,4-trimethylcycloheptane (0.11 g, 84%). The IR and NMR spectra of this compound were identical in every respect with those of IV.

Zinc Bromide-catalyzed Rearrangement of Piperitone Oxide. In the same manner as with pulegone oxides (*vide supra*), (−)-piperitone oxide (3 g, 0.0178 mol) was treated with zinc bromide (1 g) in benzene (200 m*l*) and then worked up to give crude diosphenol (1.8 g, 60%), which, after washing with a 3% sodium bicarbonate solution and recrystallizations, melted at 82—83°C. The melting point was not depressed at all by the admixture of the authentic specimen prepared from menthone.

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[7] L. Caglioti and P. Grasselli, *Chem. Ind.*, **1964**, 153; L. Caglioti and M. Magi, *Tetrahedron*, **19**, 1127 (1963).