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GENERATION AND COPE REARRANGEMENT OF TWO METHYLATED OXEPIN OXIDES

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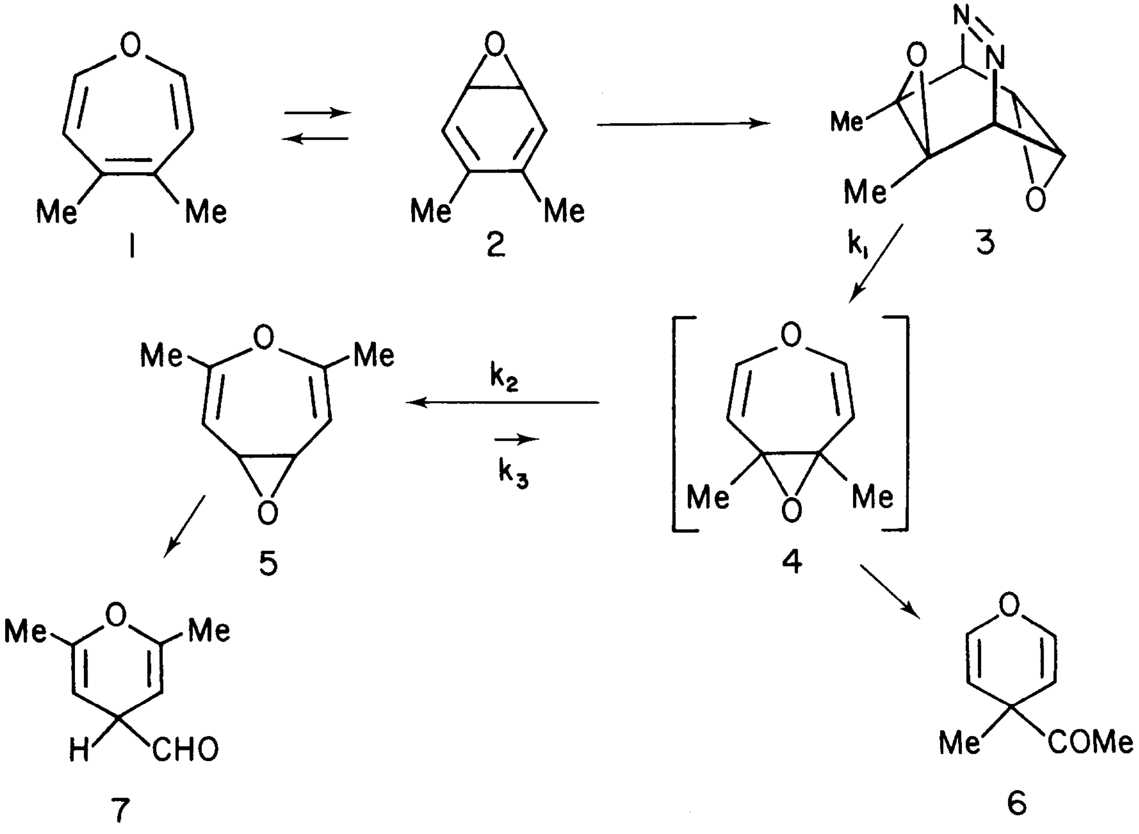
We have reported the synthesis of sym-oxepin oxide[1] and of two substituted derivatives.[2a,b] The generation of a specifically labelled dideuterated derivative[2a] has revealed an ambient temperature, degenerate Cope rearrangement of the parent compound, while a substituted derivative constrained to exist in a transoid conformation[2b] does not undergo facile rearrangement. Herein we report the generation of 4,5-dimethyl-sym-oxepin oxide (4) and its Cope rearrangement to 2,7-dimethyl-sym-oxepin oxide (5) (Scheme).

4,5-Dimethyl oxepin (1)[3] and its valence tautomer 2 serve as the starting point for the production of the sym-oxepin oxides 4 and 5. Benzene oxide 2 is converted via its Diels-Alder adduct[4,5] with bis(trichloroethyl)azodicarboxylate (yield, 79%) and an adduct diepoxide[4,6] (yield for epoxidation of adduct by p-nitroperoxybenzoic acid, 79%) to the azo diepoxide 3[7] (yield from adduct diepoxide, 81%). Ambient temperature nitrogen extrusion from 3 in $CDCl_3$ (Al_2O_3 treated) solution, monitored by ^1H nmr, shows the transient production of oxepin oxide 5 and the quantitative ring contraction of 5 to aldehyde 7[8] (rate of N_2 extrusion at 34.7 ± 0.5° in $CDCl_3$, $k = 2.21 \pm 0.05 \times 10^{-4}$ sec^{-1}).[9,10] In d_5 pyridine containing KOH the extrusion gives unrearranged 5.

The apparent generation of 5 directly from azo diepoxide 3[11] is in contradiction to the preferred geometry for small ring participation in the retro homo-Diels-Alder reaction. Precedent[2a] indicates that nitrogen extrusion from 3 should occur with participation of the epoxide anti-fused to the azo bridge, i.e., with direct generation of 4. Fortunately, the rapid, acid catalyzed rearrangement of sym-oxepin oxides to 4-substituted pyrans[1] offers an ideal method for the trapping of an oxepin oxide as it is generated. Thus, the extrusion of nitrogen from 3 in the presence of 0.2 mole % $MeSO_3H$ gives 4-methyl 4-acetylpyran (6)[12] as the only observable product (^1H nmr; rate for nitrogen extrusion at 34.7 ± 0.5° in $CDCl_3$ containing $MeSO_3H$, $k = 2.06 \pm 0.05 \times 10^{-4}$ sec^{-1}).[13] The rates for nitrogen extrusion from 3, in the presence and in the absence of trace acid, are the same,[14] strongly suggesting that 6 and 5 are produced via the same rate determining step, i.e., k_1 (Scheme). The apparent production of 5 directly from 3 is attributed to two factors: (1) k_2 is larger than rate determining k_1, and (2) the equilibrium $4 \rightleftarrows 5$ ($K_{eq} = k_2/k_3$) favors (>95%) 5.[11] The equilibrium $4 \rightleftarrows 5$ favors the product with more substituted double bonds and shifts away from the tetrasubstituted epoxide. The same factors drive 1,2-dimethylbenzene oxide toward the predominant valence tautomer, 2,7-dimethyloxepin.[3,15]

Scheme



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References and Footnotes

1. W.H. Rastetter, J. Amer. Chem. Soc., 98, 6350 (1976).
2. a) D.D. Haas and W.H. Rastetter, ibid, 98, 6353 (1976).
   b) W.H. Rastetter, T.J. Richard, N.D. Jones, and M.O. Chaney, J. Chem. Soc., Chem. Commun., 377 (1978).
3. E. Vogel and H. Günther, Angew. Chem., Int. Ed. Engl., 6, 385 (1967).
4. Satisfactory combustion analysis was obtained for this compound.
5. Data for adduct: m.p. 112.5-113°; ^{1}H nmr ($CDCl_3$) δ (Me_4Si) 1.84(s, 6H); 3.60(br m, 2H); 4.82(br s, 4H); 5.11(br d, 2H); ir (KBr) 1760, 1710 cm^{-1}.
6. Data for adduct diepoxide: m.p. 200-201°; ^{1}H nmr ($CDCl_3$) δ (Me_4Si) 1.38 (d, 6H); 3.70(m, 2H); 4.80(m, 6H); ir (KBr) 1768, 1750 cm^{-1}.
7. Data for 3: ^{1}H nmr ($CDCl_3$) δ (Me_4Si) 1.29(s, 6H); 3.34(m, 2H); 5.65(m, 2H); ir (KBr) 2995, 2970, 1529, 1200 cm^{-1}; exact mass for parent minus N_2, calculated, 138.068; found, 138.070.
8. Data for 7: ^{1}H nmr ($CDCl_3$) δ (Me_4Si) 1.87(d, $J \leq$ 1 Hz, 6H); 3.50(m, 2H); 4.58(d, 2H); 9.47(d, 1H); ir ($CDCl_3$) 1726 cm^{-1}; exact mass of p-nitrophenylhydrazone, calculated, 273.111; found, 273.113.
9. Measured by decrease of azo diepoxide (3) ^{1}H nmr absorptions at δ (Me_4Si) 5.65 and 1.29; rate calculated from 30 spectral observations over ~$3t_{1/2}$; error is at the 95% confidence limit.

10. Azo diepoxide 3 extrudes N_2 at a rate slower than the parent azo compound,[2a] $k^{34.7°}_{calc.} = 2.01 \pm 0.04 \times 10^{-3}$ sec^{-1}.
11. ^1H nmr absorptions attributable to a small concentration of 4 are seen early in the N_2 extrusion in d_5 pyridine; these absorptions are absent from the final spectrum of 5.
12. Data for 6: ^1H nmr ($CDCl_3$) δ (Me_4Si) 1.25(s, 3H); 2.27(s, 3H); 4.75 (AA'XX' half spectrum, 2H); 6.42(AA'XX' half spectrum, 2H); ir ($CDCl_3$) 1706 cm^{-1}; exact mass of *p*-nitrophenylhydrazone, calculated, 273.111; found, 273.110.
13. Measured as in footnote 9 from 29 spectral observations.
14. The small difference in rates is within the experimental error imposed by temperature variation between kinetic runs.
15. See also our accompanying paper (following pages).

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