Synthesis of a *sym*-Oxepin Oxide with Restricted Conformational Mobility and Altered Reactivity. X-Ray Crystal and Molecular Structure of 4,7-Dibromo-3a,7a:5,6-diepoxyperhydroindene
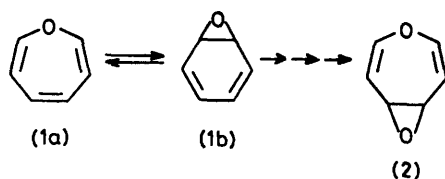
By William H. Rastetter,* Thomas J. Richard, Noel D. Jones,[a] and Michael O. Chaney[a]

(*Department of Chemistry, Massachusetts Institute of Technology, Cambridge, Massachusetts 02139; and, [a]The Lilly Research Laboratories, Eli Lilly and Co., Indiananpolis, Indiana 46206*)
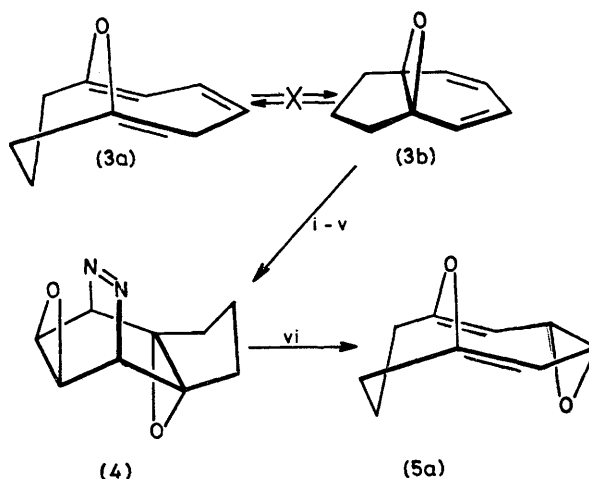
Summary Nitrogen extrusion from the azo diepoxide (4) generates the *sym*-oxepin oxide (5a), the altered reactivity of which is attributed to the conformational rigidity of (5a) as compared to the parent molecule (2); bromination of the bridgehead diene (5a) gives the dibromo-diepoxide (8) whose structure has been verified by X-ray crystal structure analysis.

We have reported the conversion of oxepin (1a)–benzene oxide (1b) into *sym*-oxepin oxide[1] (2) (4,8-dioxabicyclo-[5.1.0]octa-2,5-diene) (Scheme 1) and have studied the

Scheme 1

conformation and degenerate Cope rearrangement of (2) by [1]H n.m.r. spectroscopy.[2] Our route to (2) involves a protection–oxidation–deprotection sequence which in effect achieves a chemospecific[3] epoxidation of the oxepin valence tautomer (1a). We report here the application of our route

to the synthesis of the bridgehead diene (5a) (*transoid*-4,11-dioxatricyclo[5.1.0]undeca-1,6-diene†) from the indane oxide (3b) (Scheme 2).

Scheme 2 Reagents: i, $CCl_3CH_2O_2C-N=N-CO_2CH_2CCl_3$, $CHCl_3$; ii, 3,5-dinitroperoxybenzoic acid, 4,4′-thiobis(6-t-butyl-3-methyl-phenol) (1 wt. % *vs.* peracid), $ClCH_2CH_2Cl$, 75 °C; iii, Zn, HOAc, tetrahydrofuran, 0° C; iv, $CuCl_2$ (aq.); v, NH_3 (aq), $CHCl_3$, −35 °C; vi, $CHCl_3$, 20 °C.
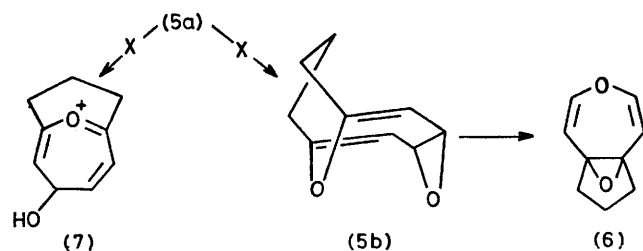
† Here *transoid* refers to the relative orientation of the two oxygen atoms; compare *transoid* (5a) (Scheme 2) with *cisoid* (5b) (Scheme 3).

The route to the *sym*-oxepin oxide (**5a**) began with the Diels–Alder reaction of bis(trichloroethyl) azodicarboxylate[4] with indane 3a,7a-oxide[5] (**3b**) [1·1 equiv. of (**3b**) used with respect to dienophile; crystalline adduct,‡ m.p. 104—105 °C, obtained in 81% yield]. Epoxidation of the double bond of the adduct by 3,5-dinitroperoxybenzoic acid stabilized with 4,4'-thiobis(6-t-butyl-3-methylphenol)[6] yielded a crystalline adduct diepoxide‡ (m.p. 137—139 °C, 59% yield). A deprotection sequence (Scheme 2) produced the thermally labile azodiepoxide (**4**) characterized by ¹H n.m.r. spectroscopy at −40 °C (CDCl₃): δ (Me₄Si) 1·48 (m, 6H), 3·40 (m, 2H), and 6·01 (m, 2H). Brief warming to ambient temperature led to nitrogen extrusion from (**4**) and the quantitative (¹H n.m.r.) generation of (**5a**).‡ The product readily sublimes (60 °C at 0·05 mmHg) giving white prisms, m.p. 67—69 °C; i.r. (CDCl₃) 1676, 1662, 1396, and 1101 cm⁻¹; ¹H n.m.r. (CDCl₃), δ (Me₄Si) 2·33 (m, 6H), 3·83 (AA'XX', 2H), and 5·00 (AA'XX', 2H); ¹³C n.m.r. (CDCl₃), δc (Me₄Si) 29·56 (t, *J ca.* 130 Hz), 30·21 (t, *J ca.* 130 Hz), 53·29 (d, *J* 175 Hz), 107·86 (d, *J* 164 Hz), and 169·11 (s); u.v. (MeCN) λ_{max} (shoulder) 230 nm (ε 850); M⁺, *m/e* 150·070 (calc. 150·068).

The ¹H n.m.r. spectrum of (**5a**) corroborates the conclusions reached previously[2] regarding the conformation of *sym*-oxepin oxide (**2**). Simulation (SIMEQ[7]) of the epoxide proton absorption of (**5a**) places an upper limit of 2·0 Hz on the coupling to the vicinal, vinyl protons.§ The corresponding coupling in (**2**) is 4·52 Hz[2] indicating an average or preferred conformation for (**2**) which is flatter than the fixed *transoid* geometry of (**5a**).

Some strain is expected for the bridgehead diene (**5a**). The strain associated with bridgehead double bonds curtails the benzene oxide–oxepin valence tautomerism of indane 3a,7a-oxide [(**3b**) ⇌ (**3a**), Scheme 2]. (The same effect is seen in the corresponding norcaradiene[5]). Thus, unlike the parent system (**1a**) ⇌ (**1b**) which is orange owing to the valence tautomer (**1a**), indane 3a,7a-oxide is colourless.

At ambient temperature (**2**) undergoes a degenerate Cope rearrangement,[2] yet (**5a**), despite its expected strain energy, does not rearrange. Compound (**5a**) is recovered as the sole volatile component after sublimation in a nitrogen stream (7 cm³ min⁻¹) through a hot tube at 220 and at 320 °C (estimated average residence time 40 s). Heating of (**5a**) at 142 °C in Cl₂CDCDCl₂ solution for 2 h causes no perceptible change of the ¹H n.m.r. spectrum; at 192 °C extensive decomposition to unidentified products is observed after 1 h. The high activation barrier to Cope rearrangement of (**5a**) is

presumably due to the inability of *transoid* (**5a**) to interconvert with the *cisoid* conformer (**5b**) (Scheme 3). The geometry for optimal orbital overlap in the Cope rearrangement transition state for (**2**)[2] and related compounds[8] is *cisoid*. Were the *cisoid* conformer (**5b**) accessible, Cope rearrangement would be likely to generate the *sym*-oxepin oxide (**6**). [We have generated (**6**) from an azo diepoxide derived from indane 5,6-oxide; details will be published elsewhere].

The epoxide (**5a**) does not show the extreme acid sensitivity of the parent (**2**). The increased stability of (**5a**) towards acid is attributed to the inability of the divinyl ether oxygen to participate in carbonium ion stabilization *via* the resonance form (**7**) (Scheme 3; note the *trans* double bond in the six-membered ring).
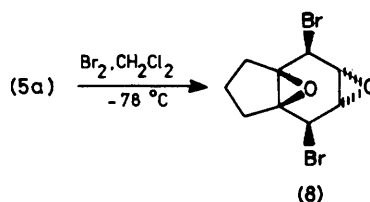
Scheme 4

Titration of (**5a**) with bromine at −78 °C (Scheme 4) gave the dibromo-diepoxide (**8**) (49% yield); m.p. 169—170 °C; ¹H n.m.r. (CDCl₃), δ (Me₄Si) 1·62 (m, 4H), 2·30 (m, 2H), 3·53 (s, 2H), and 4·43 (s, 2H); i.r. (KBr) 2968, 2938, 1385, 1170, 890, 786, and 710 cm⁻¹; M⁺, *m/e* 311·901 (calc. for
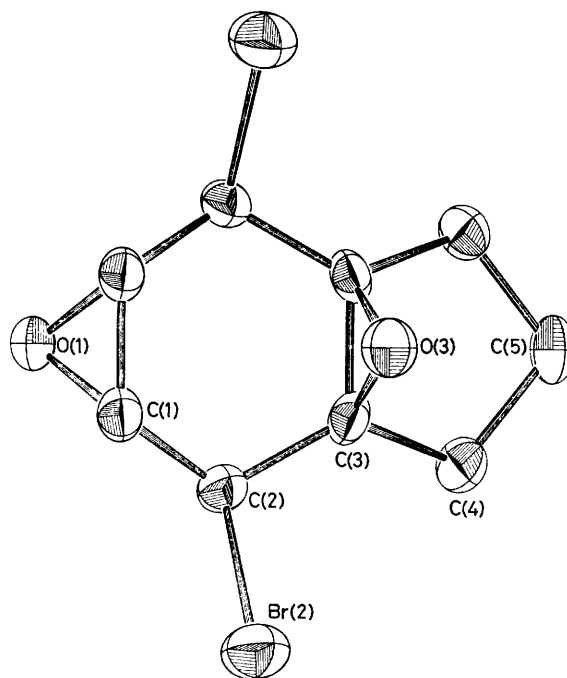

Scheme 3

Figure. ORTEP plot of the molecular structure of the dibromo-diepoxide (**8**) with thermal ellipsoids drawn at the 50% probability level; crystallographic numbering system is given.

‡ Satisfactory spectral and combustion analytical data were obtained for this compound.

§ A comparison of ¹³C–¹H coupling constants in (**2**) and (**5a**) indicates no major differences in hybridization of the relevant C–H bonds in the two molecules; hence, a change in the magnitude of the vicinal coupling most likely indicates different dihedral angles between vicinal C–H bonds in the two molecules.

$C_9H_{10}{}^{81}Br_2O_2$, 311·901). The structure of (**8**) has been determined by X-ray crystallography.

Crystal data: compound (**8**) crystallizes as prismatic needles from MeOH, space group *Pmcn*, $a = 12·524(3)$, $b = 4·516(1)$, $c = 17·116(5)$ Å; D_m (by flotation) $= 2·11$ g cm^{-3}; D_c ($M = 310·0$) $= 2·13$ g cm^{-3}. The four molecules in the unit cell are restricted by the space group to lie on mirror planes. The intensities of 827 unique reflections, to $2\theta = 116·0°$, were measured using monochromated Cu-K_α radiation on a four-angle automated diffractometer. The structure was refined by the least-squares method to an R value of 0·074. The final refinement included anisotropic temperature factors for all atoms except hydrogen, which were placed at assumed positions. The structure of (**8**) is shown in the Figure.¶

The transannular bromination producing (**8**) occurs by *anti*-periplanar addition to each bridgehead double bond of (**5a**). A similar divinyl ether bromination[9] exhibits the same stereochemical preference.[10] Vogel, *et al*. have reported[11] bromination of a related substrate, [10]annulene 1,6-oxide, but incomplete stereochemical information is available.**

¶ The atomic co-ordinates are available on request from the Director of the Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW. Any request should be accompanied by the full literature citation for this communication.

** The bromination of [10]annulene 1,6-oxide need not occur in a transannular fashion. Vogel's product could arise by a two-step process involving a 1,4-bromination and an oxepin → benzene oxide valence tautomerization.

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