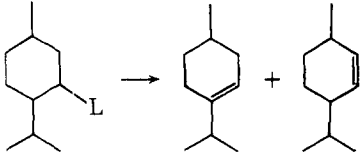


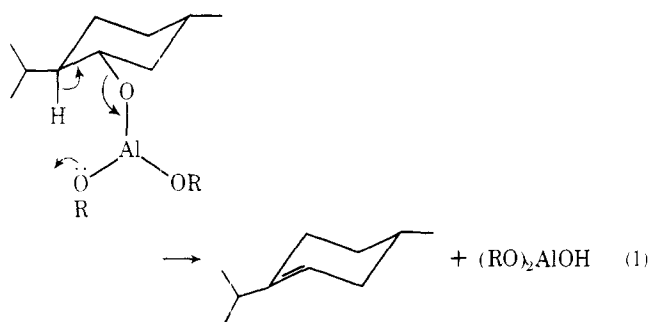
Table III. Elimination Reactions of Menthol and Its Derivatives


L	over-all yield, %	rel yields of products		ref
-OB(OR) ₂	92	90	10	11
-OH (H ₃ BO ₃)	82	87	13	11
-OCSSCH ₃	51	75	25	12
-OAc	65	65	35	13
-N(→O)(CH ₃) ₂	85	36	64	14
-OH (Al ₂ O ₃ , acidic)	94	53	47	15
		(31 actual)	(27 actual)	
			(36% Δ ¹)	
-OH (Al ₂ O ₃ , neutral)	98	20	80	15
		(19 actual)	(75 actual)	
			(<3% Δ ¹)	
-OH (Al ₂ O ₃ , basic)	95	18	78	15
- ⁺ N(CH ₃) ₃ OH ⁻	80		100	16
-OAl(OR) ₂	92	74	26	this work

(R = 2-propyl)

ferred product. It should be noted that our results with aluminate esters are clearly different from those using alumina as catalyst, suggesting either a different mode of elimination when using solid alumina as catalyst or isomerization of the initially formed product under the reaction conditions used with alumina.

The xanthate and acetate eliminations are generally considered as cyclic cis eliminations. The high proportion of Δ³-*p*-menthene formed by the thermal decomposition of the alkoxide suggests that a similar mechanism is operative. Presumably a nucleophilic oxygen removes the proton with concurrent cleavage of the C-O bond as pictured in eq 1.



Conclusion

The thermal decomposition of aluminum alkoxides represents a facile means for dehydration, especially for primary alcohols. The temperature threshold is well below that for comparable xanthate or acetate pyrolyses. Yields are better, although some isomerization occurs; even relatively sensitive alcohols such as the allylic terpenoid alcohols can be successfully dehydrated. The mechanism appears to be a standard concerted *cis*-1,2-elimination.

Experimental Section

Materials. Both freshly prepared and commercial aluminum triisopropoxide were, used with no significant difference. Analyses were performed using either a 5 ft × 1/8 in. × 10% SE-30 or a 10 ft × 1/8 in. × 10% TCEPE GLC column.

Preparation and Thermolysis of Aluminum Alkoxides. Aluminum isopropoxide (20.4 g, 0.1 mol) was combined with 0.1 mol of

the appropriate alcohol, and the mixture was heated. The theoretical amount of 2-propanol was removed by simple distillation in the case of high-boiling alcohols, or by fractional distillation in case of the lower boiling alcohols. After removal of the 2-propanol, the temperature was gradually increased. Depending on the structure of the alcohol, decomposition commences in the range 200–270 °C. The distillate is washed with water, dried, and distilled.

In case of nondistillable olefins, the mixture is heated to 270 °C for 0.5 h, and the mixture is then cooled and extracted with ether. The ether layer is washed with water, dried, and evaporated. The residue is further purified by recrystallization or chromatography. Yields are given in Table II.

Product identification was made in the usual manner using infrared and NMR spectroscopy.

Analysis of Octenes. Since 1-octene and *trans*-2-octene could not be satisfactorily separated by GLC, analysis of the product mixture was made by quantitative IR using the bands at 11.0 and 10.3 μm, respectively.

Registry No.—Bis(isopropoxy)(1-octyloxy)aluminum, 69027-59-4; bis(isopropoxy)(1-decyloxy)aluminum, 69027-60-7; bis(isopropoxy)(1-octadecyloxy)aluminum, 69027-61-8; bis(isopropoxy)(geranyloxy)aluminum, 69027-62-9; bis(isopropoxy)(farnesyloxy)aluminum, 69027-63-0; bis(isopropoxy)(2-octyloxy)aluminum, 69027-64-1; bis(isopropoxy)(cyclohexyloxy)aluminum, 69027-65-2; bis(isopropoxy)(isopulegyloxy)aluminum, 69027-66-3; bis(isopropoxy)(menthyloxy)aluminum, 69027-67-4; bis(isopropoxy)(cholesteryloxy)aluminum, 69027-68-5; bis(isopropoxy)(linalyloxy)aluminum, 69027-69-6; bis(isopropoxy)(citronellyloxy)aluminum, 69027-70-9; aluminum triisopropoxide, 555-31-7.

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Ring-Size Effects in the Reaction of Benzocycloalkadiene Epoxides with Lithium Diisopropylamide

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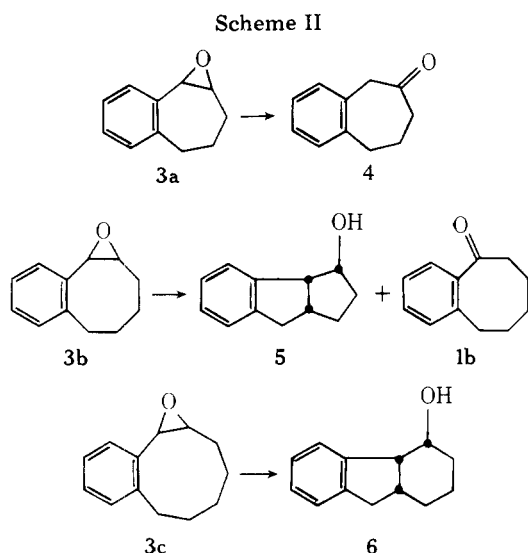
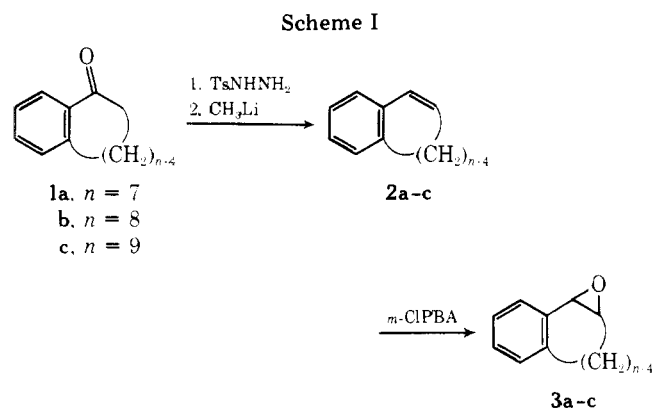
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As part of a study of ring enlargement reactions, we wished to know the behavior of benzocycloalkadiene oxides with strong base. Only indene oxide, which gives largely polymer, has been reported.¹ Studies of other epoxide systems^{1–5} show that a variety of products are possible, e.g., allylic alcohols, alcohols resulting from transannular insertion, carbonyl compounds with or without rearranged carbon skeletons, and amino alcohols. The seven- and eight-membered benzo epoxides were known^{6,7} but had not been reacted with strong base. The nine-membered case had not been reported previously.

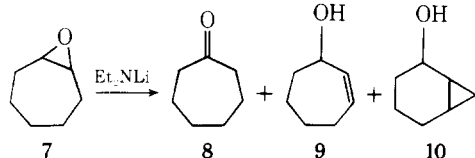
Results and Discussion

The desired epoxides were prepared by the sequence shown in Scheme I. The seven-membered ketone **1a** is available

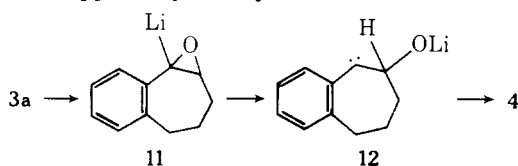


whereas the eight- and nine-membered cases, **1b** and **1c**, were prepared as described earlier.^{8,9} Compounds **2a-c** were prepared either by the sequence shown¹⁰ or by the earlier method;⁸ in all cases the coupling constant of the vinyl protons in the NMR spectra indicated that the *cis* isomer was produced. The epoxidation was straightforward, except that buffered conditions¹¹ were preferable in the seven-membered case.

Treatment of the epoxides with lithium diisopropylamide in THF led to a different product mixture in each case as shown in Scheme II. The rearrangement of **3a** to the β -ketone **4** is surprisingly clean in comparison to cycloheptene oxide **7** which gives three primary products in comparable amounts.⁴ The difference can be attributed to the benzene ring next to the epoxide in **3a** which favors removal of a proton α to the aromatic ring. This then leads to intermediate **11** which can rearrange to **4** via the carbenoid **12**. The formation of products like **9** and **10** from **12** is blocked by the benzene ring. A product



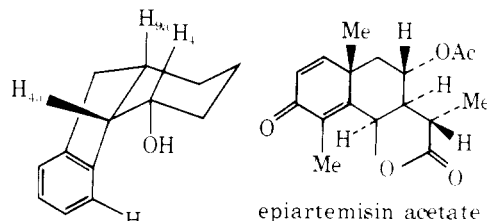
like **9** could also be formed by base attack on a proton next to the epoxide (γ to the aromatic ring), but the removal of the α proton is apparently heavily favored. It is interesting that



the reaction of *cis*- β -methylstyrene oxide with lithium diethylamide gives 7% of 1-phenylprop-2-en-1-ol, 85% of the α -ketone (phenyl ethyl ketone), and only 1.5% of the β -ketone (benzyl methyl ketone).¹ The change of product ratio with time in that system suggested that most if not all of the α -ketone was formed by rearrangement of 1-phenylprop-2-en-1-ol, a product that is presumed to arise by base attack at a proton next to the epoxide. Such attack is less favorable both sterically and stereoelectronically for ring systems⁴ such as **3a-c**, which would explain the considerable difference in products formed in the open chain system relative to epoxide **3a**.

The reaction of **3c** to give highly selective formation of the transannular insertion product, **6**, is strikingly different from **3a** but has precedent in earlier studies.^{2,12-14} The structure of **6** was assigned from decoupling experiments with added $\text{Eu}(\text{fod})_3$ which demonstrated that the proton on the carbon bearing the hydroxyl was coupled to a benzylic proton, and this benzylic proton is coupled to one other proton which in turn is coupled to the other two benzylic protons.

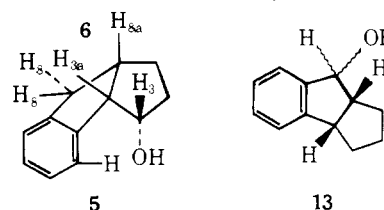
The *cis,syn* stereochemistry of **6** was assigned from the clean



triplet pattern ($J = 5.5$ Hz) for H_{4a} which is consistent with the structure shown, viz., $J_{4,4a} = J_{4a,9a} = J_{ax,eq}$. The coupling constant for the *cis* ring juncture agrees with that for epiarthemisin acetate ($J_{cis} = 5.7$ Hz) rather than artemisin acetate ($J_{trans} = 11.6$ Hz).¹⁵ Shift reagent studies are consistent with the assignment in that the relative order of movement downfield with added $\text{Eu}(\text{fod})_3$ is $\text{H}_4 > \text{H}_5 > \text{H}_{4a} > \text{H}_{9a}$. Comparing the four possible stereoisomers in conformations with $J_{4,4a} \approx J_{4a,9a} \approx 5.5$ Hz indicates that only the *cis,syn* stereochemistry will give that order. Additional support was obtained by spectral and melting point comparisons with material that was tentatively assigned the *cis,syn* stereochemistry based on the reduction steps used in its synthesis.¹⁶

In previous studies of cyclodecene,¹² cyclooctene,¹³ and cyclooctadiene oxides,¹⁴ the *cis,syn* alcohol products were postulated to arise by highly stereoselective insertion of the carbenoid into a carbon-hydrogen bond across the ring from the carbenoid.² Presumably **3c** forms a nine-membered-ring carbenoid in the same way that **3a** forms **12**, but the carbenoid reacts differently because the transannular pathway to **6** is much more favorable than a comparable route for **12**.

Treatment of the eight-membered case, **3b**, with lithium diisopropylamide gives predominantly **5** with a minor amount of ketone **1b**. The structure of **5** was assigned in a similar way to **6**. Decoupling experiments demonstrated coupling between H_3 , H_{3a} , and H_{8a} . The H_8 and H_{8a} protons were too close together in chemical shift, even with added shift reagent, to demonstrate decoupling. The clearly defined coupling pat-



terns for the H_8 protons show geminal coupling and indicate that each H_8 proton is coupled to only one other proton which

must be H_{8a} . The magnitudes of the couplings (9 and 4 Hz) are quite similar to those observed previously¹⁷ for **13** ($J_{\text{syn}} = 8.4$ Hz, $J_{\text{anti}} = 2.0$ Hz). The ring juncture coupling constant for **5** ($J_{3a,8a} = 8$ Hz) is somewhat larger than for **6** which is expected since the cis protons of **5** must be closer to a 0° dihedral angle. The syn coupling constant ($J_{3a,3} = 7$ Hz) agrees reasonably well with that observed for **13** (see above). The transannular product **5** is presumably formed in the same way as **6**.

The minor product (**1b** in Scheme II) is analogous to the formation of phenyl ethyl ketone from *cis*- β -methylstyrene. The earlier work indicated that removal of a proton γ to the aromatic ring leads first to 1-phenylprop-2-en-1-ol which subsequently undergoes isomerization of the double bond to form phenyl ethyl ketone. Such a mechanism is possible for **3b** also; however, **1b** could also arise by removal of the benzylic proton followed by isomerism of the anion¹⁸ or by removal of a proton β to the aromatic ring followed by rearrangement via a carbenoid.

Several recent studies of the reaction of cyclooctene oxide indicate a dramatic change in product ratio with changing conditions, e.g., lithium diisopropylamide gave 98% of the transannular insertion product whereas butyllithium or potassium *tert*-butoxide/ Me_2SO gave 100% cyclooct-2-en-1-ol, and lithium diethylamide gave different ratios depending on solvent and temperature.¹⁹⁻²¹ Since the allylic alcohol from **3c** was potentially useful for another study, the base systems listed above were examined. In all cases **3c** only rearranged to **6**. The allylic alcohol is presumably not formed from **3c** because proton removal is greatly favored at the benzylic position, which cannot lead to allylic alcohol product. The increased acidity of that proton is also evident in the rate of reaction, viz., **3a-c** react in hours rather than days required for the nonbenzo systems.

Experimental Section

General. Spectral measurements utilized Beckman IR8, Perkin-Elmer 727B, Varian EM360, Varian HA100, and CEC 110B instruments.²² Gas-liquid chromatography (GLC) analyses were carried out on Varian 920 or Varian 1200 instruments using OV101, AN600, or DEGS columns.

6,7-Dihydro-5H-benzocycloheptene (2a). A solution of 10 g (0.0625 mol) of benzosuberone (Aldrich), 50 mL of absolute ethanol, 10.86 g (0.0685 mol) of tosylhydrazine, and 5 drops of concentrated HCl was refluxed for 1 h. Removal of the ethanol under reduced pressure gave an oily yellow solid that was crystallized from 95% ethanol. A solution of 10 g (0.033 mol) of the tosylhydrazone in 250 mL of anhydrous ether was stirred at room temperature as 51.8 mL (0.0932 mol) of 1.8 M methylolithium was slowly injected into it. After 1 h (the larger rings required overnight), 50 mL of water was added. The ether layer was washed with saturated $NaHCO_3$, dried over magnesium sulfate, and concentrated. Kugelrohr transfer gave 6.8 g (76%) of the known⁶ compound **2a**: NMR (CCl_4) δ 7.1 (m, 4 H), 6.33 (d of t, $J = 12$, 2 Hz, 1 H), 5.75 (d of t, $J = 12$, 4 Hz, 1 H), 2.6-2.9 (m, 2 H), 2.05-2.4 (m, 2 H), 1.6-2.05 (m, 2 H).

5,6-Epoxy-6,7,8,9-tetrahydro-5H-benzocycloheptene (3a). The buffered *m*-chloroperbenzoic acid method¹¹ gave after Kugelrohr vacuum transfer a 73% yield of the known epoxide⁶ **3a**: NMR (CCl_4) δ 6.8-7.5 (m, 4 H), 3.9 (d, $J = 4$ Hz, 1 H), 3.2 (d, $J = 4$ Hz, 1 H), 2.4-2.8 (m, 2 H), 1.2-2.1 (m, 4 H).

5,6-Epoxy-5,6,7,8,9,10-hexahydrobenzocyclooctene (3b) was prepared by the same sequence as described for **3a**. Preparations of **1b**, **2b**, and **3b** have also been carried out by alternative routes.^{7,8}

6,7,8,9-Tetrahydro-5H-benzocyclononene (2c) was prepared as above from **1c** which was prepared from cycloheptanone.⁹ NMR ($CDCl_3$) δ 7.1 (m, 4 H), 6.55 (d, $J = 10$ Hz, 1 H), 5.8 (m, 1 H), 2.4-2.8 (m, 2 H), 1.7-2.4 (m, 8); IR (neat) 3050, 3005, 2920, 2850, 1490, 1455, 1445, 1110, 1090, 850, 790, 745, 735 cm^{-1} ; exact mass m/e 172.124 (calcd for $C_{13}H_{16}$, 172.125).

Anal. Calcd for $C_{13}H_{16}$: C, 90.64; H, 9.26. Found: C, 90.91; H, 9.10.

5,6-Epoxy-6,7,8,9,10,11-hexahydro-5H-benzocyclononene (3c) was prepared as above from **2c**: NMR ($CDCl_3$) δ 6.9-7.3 (m, 4), 3.9 (d,

$J = 4$ Hz, 1 H), 3.05 (d of t, $J = 4$, 10 Hz, 1 H), 2.5-2.9 (m, 2 H), 1.0-2.3 (m, 8 H); IR (neat) 3005, 2920, 2850, 1450, 1365, 1315, 900, 850, 840 cm^{-1} ; exact mass m/e 188.119 (calcd for $C_{13}H_{16}O$, 188.120).

Rearrangement of 3a. A solution of 0.77 mL (0.0055 mol) of diisopropylamine in 15 mL of anhydrous ether was cooled to $-78^\circ C$ and slowly injected with 2.4 mL (0.0055 mol) of 2.3 M butyllithium. The reaction was stirred for 15 min and allowed to warm to room temperature. A solution of 0.3455 g (0.0022 mol) of **3a** in 5 mL of anhydrous ether was slowly injected. The reaction was stirred 1 h at room temperature and 5 mL of H_2O was added. The H_2O layer was extracted twice with 10 mL of ether. The ether layers were washed with 10% HCl, dried over $MgSO_4$, and concentrated. Kugelrohr transfer gave 0.2216 g (64%) of 5,7,8,9-tetrahydro-6H-benzocyclohepten-6-one (**4**):^{6,23} NMR ($CDCl_3$) δ 7.2 (s, 4 H), 3.7 (s, 2 H), 2.8-3.0 (m, 2 H), 2.3-2.8 (m, 2 H), 1.6-2.0 (m, 2 H).

Rearrangement of 3b. Treatment of compound **3b** in the manner described above gave a 65% yield of 7,8-benzobicyclo[3.3.0]octen-2-ol (**5**) and 7,8,9,10-tetrahydro-5(6H)-benzocyclooctenone (**1b**) in a 83:17 ratio. (**5**): NMR ($CDCl_3$) δ 7.1 (s, 4 H), 4.1-4.4 (m, 1 H), 3.5-3.8 (m, 1 H), 2.5-3.4 (m, 3 H), 1.3-2.1 (m, 5 H); IR (CCl_4) 3570, 3450, 3060, 3010, 2930, 1480, 1460, 1440, 1170, 1075, 1000 cm^{-1} ; exact mass m/e 174.104 (calcd for $C_{12}H_{14}O$, 174.104).

Rearrangement of 3c. Treatment of compound **3c** in the manner described above gave a 65% yield of 8,9-benzobicyclo[4.3.0]nonen-2-ol (**6**):¹⁶ NMR ($CDCl_3$) δ 7.0-7.6 (m, 4 H), 3.9-4.2 (m, 1 H), 3.2-3.4 (t, $J = 5$ Hz, 1 H), 2.6-2.9 (m, 2 H), 2.4-2.6 (m, 1 H), 1.2-1.9 (m, 7 H); IR (CCl_4) 3600, 3450, 3070, 3020, 2930, 2850, 1450, 1230, 1055 cm^{-1} ; exact mass m/e 188.120 (calcd for $C_{13}H_{16}$, 188.120).

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Registry No.—**1a**, 826-73-3; **1b**, 829-14-1; **1c**, 830-77-3; **2a**, 7125-62-4; **2b**, 60676-30-4; **2c**, 69028-31-5; **3a**, 4443-71-4; **3b**, 69028-32-6; **3c**, 69028-33-7; **4**, 34663-15-5; **5**, 69028-34-8; **6**, 28083-55-8; lithium diisopropylamide, 4111-54-0.

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- Exact masses were determined by peak matching on samples shown to be pure by GLC and NMR.
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