

Base-Promoted Reactions of Epoxides. I. Isomerization of Some Cyclic and Acyclic Epoxides by Lithium Diethylamide

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Several representative epoxides have been rearranged under the influence of lithium diethylamide. In general, three types of products are obtained: allylic alcohols, ketones, and saturated alcohols. The latter compounds probably arise by carbenoid insertion processes. It is proposed that the products of a given epoxide depend on the conformational features of the reactant, which in turn determine the choice of reaction mechanisms between α - and β -elimination possibilities. Suggestions are also made regarding the detailed mechanism of the α -elimination reaction.

The present paper is the first in a series devoted to examining the reactions of epoxides with poorly nucleophilic, strongly basic reagents. This is an aspect of epoxide chemistry which has not shared in the extensive exploitation¹ that this small-ring heterocycle has, in general, enjoyed. Nonetheless, there are several provocative observations in the literature which suggest that such reactions may be of considerable interest from both synthetic and mechanistic viewpoints.² Most of the prior work on the rearrangements of epoxides induced by strong bases derives from the studies of Cope and co-workers. These researchers have examined the reactions of some acyclic,³ medium-ring,⁴ and aryl-substituted⁵ epoxides.

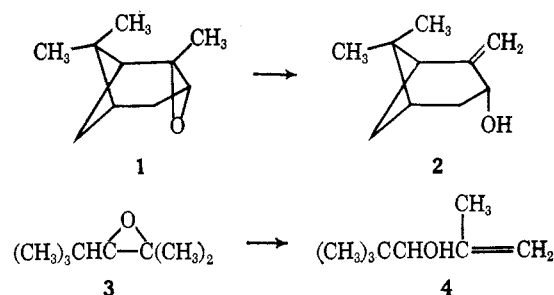
The results obtained with the medium-ring compounds are particularly interesting; for example, the action of lithium diethylamide on either *cis*- or *trans*-cyclooctene oxide yields a *cis*-2-bicyclo[3.3.0]octanol as the major product.⁶ Convincing evidence has been presented to support the notion that these bicyclic alcohols arise by α elimination and carbenoid insertion into a transannular C-H bond.⁷ However, these reactions are highly stereospecific since *cis*-cyclooctene oxide produces *endo,cis*-2-bicyclo[3.3.0]octanol exclusively and the *trans* epoxide gives only the epimeric *exo* alcohol. This observation requires either that α elimination and transannular insertion be compressed into one concerted step or, alternatively, that the transannular insertion of any free carbene intermediate be much faster than its conformational relaxation. Otherwise the stereospecific aspects of these reactions are inexplicable. Parallel results were observed with *cis*- and *trans*-cyclododecene oxides.⁸

Other workers have found that acyclic aliphatic oxides⁹ and the *cis*- and *trans*-cyclododecene oxides,^{10,11}

in contrast to the medium-ring compounds, give allylic alcohols as the major rearrangement products. These reactions probably all occur by β elimination, as has been demonstrated by deuterium-labeling studies in the instances of the 4-octene oxides.³ Finally, we have noted previously¹² that norbornene oxide, a molecule which cannot undergo β elimination, rearranges smoothly to the typical carbene insertion product, nortricyclanol. Subsequent work indicates that an α elimination is almost certainly involved here.¹³

Our research has been concerned with developing a general understanding of base-promoted reactions of epoxides and, in particular, determining the features of a substrate which cause conversion into carbene-like products. Accordingly we initiated our studies by examining some readily available epoxides which might be expected to lead to signal products should carbenoid intermediates intervene.

Treatment of α -pinene oxide (1) with lithium diethylamide gave allylic alcohol 2 exclusively. β -Diisobutylene oxide (3) was also converted into a single allylic alcohol, 4. These are clean, high-yield reactions of some preparative value. However, they undeniably proceed by β elimination. These observations serve to emphasize the importance of this very reasonable reaction mode.



Attention was next turned to the alicyclic epoxide series where conformational effects might be expected to be important. Under the usual conditions cyclopentene oxide gave small amounts of neutral material consisting mainly of 2-cyclopentenol and cyclopentanone (7:2 ratio) along with substantial quantities of the nucleophilic addition product, *trans*-2-(diethylamino)cyclopentanol. Use of the more hindered base, lithium diisopropylamide, gave the same neutral products in higher yield with essentially no amine formation. Cyclohexene oxide provided 2-cyclohexenol in addition to a small amount of *trans*-2-(diethylamino)-

(1) An extensive review of epoxide chemistry is found in A. Rosowsky's chapter in "Heterocyclic Compounds with Three- and Four-Membered Rings," Part 1, A. Weissberger, Ed., Interscience Publishers, Inc., New York, N. Y., 1964, pp 1-523.

(2) For the purposes of the following discussion, we consider only epoxides without adjacent or neighboring functional groups which tend to control the chemistry of the system. This does not necessarily imply that the latter systems do not behave analogously but merely focuses attention on the capabilities of the epoxide ring.

(3) A. C. Cope and J. K. Heeren, *J. Am. Chem. Soc.*, **87**, 3125 (1965).

(4) A recent review of these studies is included in A. C. Cope, M. M. Martin, and M. A. McKervey, *Quart. Rev. (London)*, **20**, 119 (1966).

(5) A. C. Cope, P. A. Trumbull, and E. R. Trumbull, *J. Am. Chem. Soc.*, **80**, 2844 (1958).

(6) A. C. Cope, H. H. Lee, and H. E. Petree, *ibid.*, **80**, 2849 (1958).

(7) A. C. Cope, G. A. Berchtold, P. E. Peterson, and S. H. Sharman, *ibid.*, **82**, 6370 (1960).

(8) A. C. Cope, M. Brown, and H. H. Lee, *ibid.*, **80**, 2855 (1958).

(9) C. C. Price and D. D. Carmelite, *ibid.*, **88**, 4039 (1966).

(10) H. Nozaki, T. Mori, and R. Noyori, *Tetrahedron*, **22**, 1207 (1966).

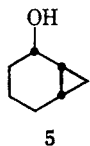
(11) L. I. Zakharkin, *Bull. Acad. Sci. USSR, Div. Chem. Sci. (Eng. Transl.)*, 2103 (1961).

(12) J. K. Crandall, *J. Org. Chem.*, **29**, 2830 (1964).

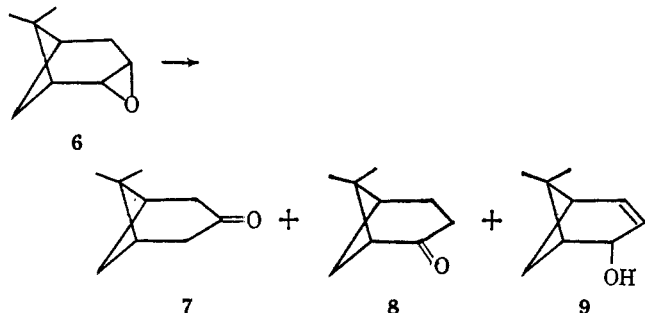
(13) L. H. Chang and J. K. Crandall, to be published.

cyclohexanol. Again this is a high-yield reaction which is synthetically useful for the production of the allylic alcohol. A similar result was observed some time ago for the reaction of *n*-propyl- and *n*-butyllithium¹⁴ with cyclohexene oxide. The possible intermediacy of the aminoalcohol in the formation of 2-cyclohexanol was excluded by the finding that the former was not affected by the reaction conditions.

Cycloheptene oxide did not undergo appreciable change when exposed to the usual conditions of lithium diethylamide in refluxing ether for 2 days. However, when refluxing benzene was used as the solvent, reaction was complete in this time. Under these conditions the products observed were cycloheptadiene, cycloheptanone, 2-cycloheptenol, and *endo,cis*-2-bicyclo[4.1.0]heptanol (**5**) in roughly equivalent amounts. Of the reactions examined in this paper only the bicyclic alcohol is readily recognized as a carbenoid product. As with the medium-ring epoxides which have been studied previously, **5** is formed to the complete exclusion of the epimeric alcohol in a highly stereospecific process. This point was verified by gas chromatographic comparison of the crude product with an authentic sample of the epimeric alcohol. The observation of appreciable amounts of cycloheptadiene was somewhat surprising. Resubjecting 2-cycloheptanol and its bicyclic isomer to the reaction conditions established that the former was converted into cycloheptadiene, whereas **5** was not. A control experiment ruled out the possibility of dehydration during work-up. At the present time the nature and generality of this remarkable transformation remains uncertain.



Finally apopinene oxide (**6**), the demethylated derivative of **1**, was prepared and subjected to rearrangement conditions. It was thought that this bridged cyclohexene oxide derivative might, because of its slightly distorted geometry, undergo different reactions from the parent compound. This might lead to insertion products as is observed for the boat conformation variant of cyclohexene oxide present in norbornene oxide. In the actual event, no insertion products were found, although ketones **7** and **8** predominated over allylic alcohol **9**¹⁵ in the product mixture. The steric effect of the *gem*-dimethyl bridge undoubtedly is also influential in determining the course of this transformation.



(14) R. Letsinger, J. G. Traynham, and E. Bobko, *J. Am. Chem. Soc.*, **74**, 399 (1952).

Consideration of the present results in conjunction with those of previous workers does allow the formulation of a rational explanation for the course of base-promoted rearrangements. Thus, while the following proposals cannot be considered as proven, we believe that they provide a reasonable and self-consistent picture which not only accommodates the experimental data but provides a testable mechanistic framework.

The first question is that of the competition between α - and β -elimination mechanisms. It appears that the decisive feature which controls the balance between these two modes of reaction is the stereoelectronic requirement for β elimination. Thus, molecules existing mainly or exclusively in conformations capable of undergoing β elimination by way of the preferred transition state (*i.e.*, a *trans*, coplanar arrangement of one of the carbon-oxygen bonds of the epoxide ring and a proton on an adjacent carbon atom)^{17,18} apparently do so readily. Examples of this behavior include the 4-octene oxides, the five-, six-, and twelve-membered alicyclic derivatives, and α -pinene oxide.

The acyclic and normal-ring alicyclic cases are certainly overwhelmingly populated in conformations with the desired elimination geometry or something reasonably close to this. The clean transformation of α -pinene oxide to **2** by attack of base at the ring methyl reflects the unique capability of this methyl group to provide the required atomic arrangement for β elimination without being unduly subjected to the steric shielding effect of the *gem*-dimethyl bridge. This is not true of the single other proton which has the proper elimination orientation, namely the proton on the adjacent methylene group which is *trans* to the epoxide ring and therefore *syn* to the substituted bridge. In addition, ring strain in the internal olefin and distortion of the cyclohexene oxide moiety slightly from its usual conformation in the nonbridged molecule probably also mitigate against the other mode of elimination. When the methyl group is replaced by a hydrogen as in **6**, elimination to give the allylic alcohol **9** is still not the major reaction process but instead ketonic products result. Again steric hindrance, product strain, and/or bond-angle changes presumably dictate this deviation from the straightforward behavior of cyclohexene oxide.

Turning now to the medium-ring epoxides which display a propensity for generating insertion products, it is quite reasonable to attribute this deviant behavior

(15) The stereochemistry of this alcohol is assigned on mechanistic grounds assuming the indicated stereochemistry of **6**. A single, crystalline epoxide,¹⁶ mp 60–62°, which is homogeneous by gas chromatography, results from per acid oxidation of the corresponding olefin. This observation is in accord with exclusive attack of per acid from the less hindered side of the double bond.

(16) R. Dulou, Y. Chretien-Bessiere, and J. P. Montheard, *Compt. Rend.*, **264**, 3374 (1962).

(17) D. Banthorpe, "Elimination Reactions," Elsevier Publishing Co., New York, N. Y., 1963; J. Hine, "Physical Organic Chemistry," 2nd ed, McGraw-Hill Book Co., Inc., New York, N. Y., 1962, Chapter VIII; J. F. Bunnett, *Angew. Chem. Intern. Ed. Engl.*, **1**, 225 (1962).

(18) It should be noted that *cis* elimination cannot be ruled out *a priori*, especially for medium-ring compounds. *cis* eliminations apparently also show a strong preference for a planar array in the transition state. Consequently much of the following argument regarding conformational inhibition of β elimination will apply to *cis* elimination as well as the more common *trans* process. Further information on this subject can be found in the following references: C. H. DePuy, G. F. Morris, J. S. Smith, and R. J. Smat, *J. Am. Chem. Soc.*, **87**, 2421 (1965); N. A. LeBel, P. D. Beirne, E. R. Karger, J. C. Powers, and P. M. Subramanian, *ibid.*, **85**, 3199 (1963); J. Zavada, M. Svoboda, and J. Sicher, *Tetrahedron Letters*, 1627 (1966).

to the inherent torsional strain and transannular non-bonded interactions which strongly influence the stabilities of the various conformations available to medium-ring molecules. We suggest that the prevalence of transannular insertion reactions in the medium-ring examples is due primarily to the inhibition of the normal β -elimination process imposed by the scarcity of the required local reaction-site conformations for this occurrence. Retardation of the usual reaction mode allows a generally less favorable mechanism to operate, namely α elimination. This hypothesis receives qualitative experimental support from the observation that relatively more drastic conditions are, in general, required to cause medium-ring epoxides to suffer rearrangement.

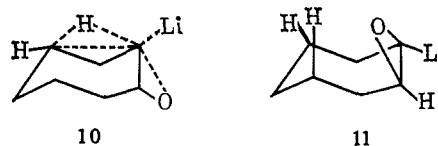
Examination of the Dreiding model of cycloheptene oxide suggests that, while conformations conducive to β elimination are probably present, a large proportion of the conformers present in the conformational equilibrium do not fulfill this requirement. Judging from the product distribution, the two eliminative modes are on reasonably equal footing for this epoxide. Similar considerations applied to the cyclooctane examples indicate that the conformational situation is even more aggravated in these molecules. In fact only a single, rather rigid model of *trans*-cyclooctene oxide can be made. It is almost inconceivable that a concerted, *trans* elimination to the allylic alcohol could occur for this compound and it is tempting to suggest that the small amount of 2-cyclooctenol observed as a product arises by another process in this case, probably *cis* elimination¹⁹ or α elimination. *cis*-Cyclooctene oxide can achieve the desired reaction-site stereochemistry but only at the expense of a very severe transannular 3,7-hydrogen-hydrogen interaction. Consequently mainly insertion products derived by α elimination are formed from both of the cyclooctene oxides. Increasing the ring size to ten⁸ imparts additional flexibility to the system and this is reflected by an increase in the amount of allylic alcohol which is now generated in amounts comparable to the transannular insertion product. Finally, the 12 carbon compounds achieve sufficient conformational mobility that their behavior is indistinguishable from that of acyclic epoxides^{10,11} and only β elimination is found. The alicyclic compounds thus present a self-consistent pattern in good accord with the proposed control of β elimination by conformational features. Norbornene oxide provides a striking example of the occurrence of transannular insertion where β elimination is rigorously precluded.¹²

Another possible requirement for the insertion reaction to take place is that there be a neighboring hydrogen within about 3 Å of the potential "carbenoid"²⁰ center in the reactive conformation. This is probably the situation in all examples thus far examined which give insertion products. The formation of the metallated epoxide as a first discrete step appears to be assured by the reported observation that *cis*-cyclodecene oxide exchanges its epoxide ring protons under the reaction conditions.⁷ The organometallic must be capable of maintaining its configurational integrity throughout its

lifetime,²¹ however, since there is no crossover in products from epimeric epoxides.

The crucial question of whether the next two processes of carbon-oxygen bond cleavage and insertion of the carbenoid carbon into the appropriate carbon-hydrogen bond are stepwise or concerted events is an important one. Initially it appeared to us that the concerted interaction of the number of atomic centers required for a one-step process (see structure 10) was an unattractive possibility. However it is difficult to ignore the fact that every transannular insertion reaction observed to date proceeds with complete stereospecificity to the accuracy of the analytical method used (usually gas chromatography). This does not unequivocally rule out an exceedingly rapid insertion of a carbene intermediate, but it does appear to place the burden of proof on the free carbene hypothesis. Consequently the concerted mechanism appears to be the logical choice as a working hypothesis. Some precedence for the proposed concerted α -elimination-insertion mechanism is provided by the accumulation of evidence in the recent literature which demonstrates that many typical "carbene" reactions do not proceed by way of free divalent carbon intermediates. The evidence is particularly compelling for additions to double bonds²² and there is, furthermore, an indication that insertion into C-H bonds also occurs without the intervention of a free carbene for at least one intramolecular example.²³ Decisive information concerning concerted *vs.* rapid, stepwise reaction mechanisms should be provided by determination of the deuterium isotope effect caused by replacing the reacting transannular hydrogen with its heavy isotope and we plan to carry out such experiments.

Another point of interest concerning the highly stereospecific insertions which have been uncovered to date is that the transannular carbon-hydrogen bond always approaches the "carbenoid" center from the side opposite the departing oxygen atom (assuming essentially sp^3 hybridization at the important carbon atom in the precursor organometallic and a concerted reaction). Two possible explanations can be advanced to account for this result. The first of these is that the particular stereoelectronic requirements of the insertion process make "backside attack" mandatory. A second possibility is that both "backside" and "frontside" attack of the carbon-hydrogen bond at the carbenoid site are possible in general, but that the conformational situation rules out the "frontside" process in the medium-ring compounds. Structure 10 depicts the correct cycloheptene oxide geometry for "backside" insertion. In 11, the "frontside" insertion conformation, the oxygen atom is subjected to considerable 1,3-



(19) Models of *trans*-cyclooctene oxide show that a *cis* elimination to give 2-cyclooctenol is probably feasible in terms of the molecular geometry.

(20) The term "carbenoid" is used here to indicate behavior of the type expected for carbenes but does not necessarily mean that a free carbene is involved.

(21) A discussion of the configurational stability of cyclopropyllithium compounds, the carbon analogs of this organometallic system, is found in D. J. Cram, "Fundamentals of Carbanion Chemistry," Academic Press Inc., New York, N. Y., 1965, pp 123-130.

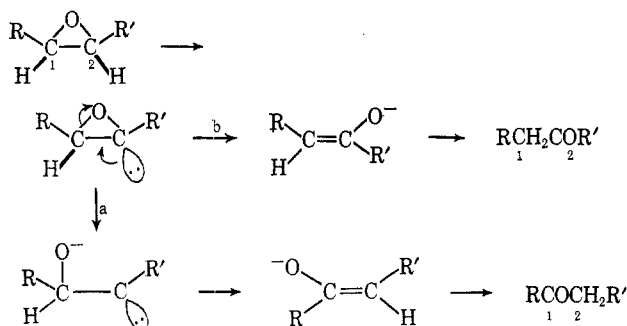
(22) A discussion including leading references is provided by G. L. Closs and J. J. Coyle, *J. Am. Chem. Soc.*, **87**, 4270 (1965); see also D. F. Hoeg, D. I. Lusk, and A. L. Crumbliss, *ibid.*, **87**, 4147 (1965).

(23) M. J. Goldstein and W. R. Dolbier, *ibid.*, **87**, 2293 (1965).

diaxial repulsive interaction. This may serve to destabilize conformation **11** enough to preclude product formation from it. For the present a decision between these two explanations cannot be made.

Finally, in several instances ketones were observed as products from the base-induced transformation of epoxides. These products appear to arise under circumstances where β elimination is retarded, but where there is not a readily available transannular hydrogen. It is tempting to speculate that ketones also come about by an α -elimination mechanism involving a 1,2-hydrogen shift from a "carbenoid" intermediate as depicted in Chart I (pathway a). Although such a

CHART I



process is distinguishable from the alternate and equally likely β -elimination route also shown (pathway b), there is at present no conclusive experimental evidence bearing on this point. (Note that the position of the carbonyl group with respect to the initial site of metalation in the starting material depends on which mechanism obtains.) Arylated epoxides rearrange to carbonyl compounds apparently by pathway b,⁵ but it is not clear whether the aryl groups are having an undue influence in this instance because of their stabilizing effect on carbanionic centers. Further consideration of the mode of ketone formation consequently must be deferred until a later date when more representative experimental evidence is in hand.

In summary we propose, as a working hypothesis, that the conformational features of a given epoxide define the products of its base-promoted rearrangement by determining which of the several competitive pathways predominates. Further experimental work designed to test the predictions generated by this model is currently underway.

Experimental Section

General.—All nmr spectra were recorded on a Varian A-60 spectrometer. Data are given in parts per million (ppm) relative to tetramethylsilane as an internal standard. Unless specified otherwise the solvent was carbon tetrachloride. Gas chromatography (glpc) was performed on Aerograph A600 (analytical) and A700 (preparative) instruments. Percentage composition data were estimated by peak areas and are uncorrected. All melting points were determined in capillary tubes and are uncorrected. The microanalyses were performed by Midwestern Microanalytical Laboratories and Huffman Laboratories, Inc.

Preparation of Epoxides.—The various epoxides were prepared by a modification of the procedure of Korach, *et al.*²⁴ To an ice-cold, mechanically stirred mixture of 1 molar equiv of olefin and 3 molar equiv of powdered, anhydrous sodium carbonate in

methylene chloride was added dropwise 1.1 equiv of 40% peracetic acid which had been treated with a small amount of sodium acetate. The mixture was stirred at room temperature until the methylene chloride solution gave a negative test with starch-iodide paper. The solid salts were removed by suction filtration and washed well with additional methylene chloride. The solvent was removed from the filtrate by distillation through a Vigreux column and the residue was purified by distillation on a spinning-band column.

Typical Procedure for Base-Promoted Rearrangements.—To an ice-cold solution of 2.5 equiv of diethylamine in anhydrous ether was added 2.5 equiv of commercial 15% butyllithium in hexane under a nitrogen atmosphere. After 10 min a solution of 1 equiv of the appropriate epoxide in anhydrous ether was added and the mixture was heated to reflux for 2 days or until the starting material was consumed. The reaction mixture was cooled and poured into water, and the organic layer separated. The aqueous layer was extracted with ether and the combined organic layers were washed with 1 N hydrochloric acid, saturated sodium bicarbonate solution, and water. After drying over anhydrous magnesium sulfate, the solvent was removed from the product by distillation through a column and the residue was purified by distillation. If the product was a mixture, further purification was effected by preparative glpc. Product identification was by comparison of spectral data with those of authentic samples obtained from commercial sources or by literature methods unless otherwise stated.

Rearrangement of 2,4,4-Trimethyl-2,3-epoxypentane.—The rearrangement was carried out on 10.3 g of **3** in 600 ml of ether. Distillation of the crude product gave 9.2 g (87%) of a colorless oil, bp 139–145°. Examination of this material by glpc indicated that a single product had been formed. This was identified as 2,4,4-trimethylpent-1-en-3-ol²⁵ (**4**) by spectral data and preparation of the 3,5-dinitrobenzoate derivative, mp 122–124° (lit.²⁵ mp 120–121°). The infrared spectrum (neat) has bands at 2.9, 3.22, 6.08, and 11.1 μ ; the nmr spectrum shows a nine-proton singlet at δ 0.90 [C(CH₃)₃], a three-proton triplet at 1.73 (C=CCH₃), a one-proton singlet at 2.05 (OH), a one-proton singlet at 3.70 (CHOH), and a two-proton multiplet at 4.86 (C=CH₂).

Oxidation of **4** with activated manganese dioxide gave the corresponding conjugated ketone, 2,4,4-trimethylpent-1-en-3-one: infrared spectrum (neat), 5.96, 10.95 μ ; ultraviolet spectrum (95% ethanol) λ_{\max} 221, 312 m μ (ϵ 4300, 44); the nmr spectrum showed a nine-proton singlet at δ 1.21 [C(CH₃)₃], a three-proton triplet at 1.85 (C=CCH₃), and a two-proton multiplet at 5.39 (C=CH₂). An analytical sample was prepared by glpc.

Anal. Calcd for C₈H₁₄O: C, 76.14; H, 11.18. Found: C, 76.03; H, 11.07.

Rearrangement of α -Pinene Oxide.—The reaction was carried out on 10.7 g of **1** in 600 ml of ether according to the general procedure. Distillation of the product gave 9.9 g (92%) of a colorless oil: bp 109–111 (34 mm); infrared spectrum (neat), 2.9, 3.22, 6.09, and 11.2 μ . Examination by glpc showed that essentially a single compound had been formed. The nmr spectrum of this material displays three-proton singlets at δ 0.63 and 1.27 attributable to the *syn*- and *anti*-methyl groups, a one-proton doublet ($J = 7$ cps) centered at 4.33 (CHOH), and one-proton multiplets at 4.73 and 4.96 (C=CH₂). The spectral evidence and melting point of the *p*-nitrobenzoate derivative (mp 96.5–98°, lit.²⁶ mp 96.5–97°) serve to establish the structure of this material as pinocarveol (**2**).

Manganese dioxide oxidation of this alcohol gave the corresponding conjugated ketone: infrared spectrum (neat), 5.85, 6.13, and 10.7 μ ; the nmr spectrum displays three-proton methyl singlets at δ 0.80 and 1.37 and an AB pattern ($J = 2.5$ cps) centered at 5.40 (C=CH₂).

Rearrangement of Cyclopentene Oxide.—A solution of 8.4 g of cyclopentene oxide in 600 ml of ether was treated with lithium diethylamide in the usual fashion to produce 1.0 g (12%) of volatile neutral product. This material consisted of cyclopentanone (21%) and 2-cyclopentenol²⁷ (70%) in addition to three minor components. The aqueous layer from the work-up procedure was made basic and extracted five times with ether. The combined extracts were dried, the solvent was removed, and the residue was distilled *in vacuo* to give 5.6 g (36%) of a yellow liquid. Examination by glpc showed a single major constituent

(24) M. Korach, D. R. Nielsen, and W. H. Rideout, *J. Am. Chem. Soc.*, **82**, 4328 (1960).

(25) E. L. Eliel and M. N. Rerick, *ibid.*, **82**, 1362 (1960).

(26) R. N. Moore, C. Golumbic, and G. S. Fisher, *ibid.*, **78**, 1173 (1956).

(27) K. Alder and F. H. Flock, *Chem. Ber.*, **89**, 1732 (1956).

which was assigned the *trans*-2-(diethylamino)cyclopentanol²⁸ structure on the basis of its characteristic nmr spectrum.

Rearrangement of Cyclopentene Oxide with Lithium Diisopropylamide.—To a solution of 27 g of commercial lithium diisopropylamide in 300 ml of anhydrous ether was added 4.2 g of cyclopentene oxide in 25 ml of ether under a nitrogen atmosphere. After heating to reflux for 7 hr the mixture was poured into water and the resulting mixture was saturated with sodium chloride. The organic layer was separated and the aqueous layer was extracted with ether four times. The combined ether solutions were washed with 1 *N* hydrochloric acid and saturated sodium bicarbonate solution and dried over magnesium sulfate. The solvent was removed through a Vigreux column and the residue was distilled to give 1.27 g of a colorless liquid, bp 85–100° (98 mm). Glpc examination showed the presence of 2-cyclopentenol (17% yield) and cyclopentanone (3.4%) which were collected and compared spectrally with authentic samples.

The aqueous portion from the work-up was made basic with sodium hydroxide and extracted five times with ether; the extracts were dried over magnesium sulfate. Removal of the solvent and distillation of the residue gave an additional 0.8 g of 2-cyclopentenol-cyclopentanone mixture.

Rearrangement of Cyclohexene Oxide.—The rearrangement of 6.0 g of cyclohexene oxide in 600 ml of ether was carried out as described in the general procedure. Distillation of the residue under vacuum gave 4.0 g (67%) of 2-cyclohexenol.²⁹ The aqueous washes from the work-up were made basic and extracted with ether to give additional 2-cyclohexenol and a small amount of *trans*-2-(diethylamino)cyclohexanol.³⁰

Reaction of *trans*-2-(Diethylamino)cyclohexanol with Lithium Diethylamide.—The reaction was carried out with 1.7 g of *trans*-2-(diethylamino)cyclohexanol in 100 ml ether at reflux for 2 days. The reaction mixture was cooled, poured into water, and saturated with sodium chloride, and the layers were separated. The aqueous layer was extracted with ether twice. The combined ether extracts were washed with 1 *N* hydrochloric acid, sodium bicarbonate solution, and water and dried over magnesium sulfate. The solvent was removed by distillation through a spinning-band column leaving only a small amount of starting material.

The aqueous layer from the work-up was made basic with sodium hydroxide, saturated with sodium chloride, and extracted with ether four times. After drying over magnesium sulfate the solvent was removed by distillation through a Vigreux column. Distillation of the residue gave 1.47 g (86%) of starting material.

Rearrangement of Cycloheptene Oxide.—Mainly recovered starting material was obtained when the epoxide was treated according to the general procedure using ether as solvent. However, when 10.0 g of cycloheptene oxide was treated with base in refluxing benzene, the reaction was complete. Two

fractions were obtained by careful distillation. The low-boiling material was a mixture of benzene and cycloheptadiene estimated to contain 1.1 g (13%) of the latter by glpc. The high-boiling material (4.4 g, 44%) consisted of three major products in the proportions 1.6:1.8:1 in order of glpc elution. These compounds were identified as cycloheptanone, *endo,cis*-2-bicyclo[4.1.0]heptanol³¹ (5), and 2-cycloheptenol.³² No attempt was made to recover any basic product that may have been formed. The epimer of 5 was shown to be absent by glpc.

Reaction of 2-Cycloheptenol with Lithium Diethylamide.—The reaction was carried out on 1.0 g of 2-cycloheptenol in the usual fashion for epoxides using 100 ml of benzene as solvent. After the usual work-up procedure, the solvent was removed by distillation through a Vigreux column. The residue gave 1.4 g of a mixture of benzene and cycloheptadiene in addition to 0.4 g of starting material. Examination of the lower boiling fraction by glpc and ultraviolet indicated the presence of a 10–14% yield of cycloheptadiene.

Reaction of *endo,cis*-2-Bicyclo[4.1.0]heptanol with Lithium Diethylamide.—The reaction was carried out as in the general procedure with 1.12 g of 5 in 100 ml of benzene. The solvent was removed by distillation through a Vigreux column and the residue was distilled to give 0.80 g (71%) of starting material. Glpc examination indicated that a very small amount of cycloheptadiene was formed at most.

Rearrangement of 6,6-Dimethyl-*anti*-2,3-epoxybicyclo[3.1.1]heptane.¹⁶—The rearrangement of 4.14 g of 6 was carried out in 150 ml of benzene at reflux temperature for 2 days. Distillation gave 3.14 g (76%) of a pale yellow liquid, bp 85–98° (22 mm). Three components were present in the ratio of 52:26:22 as determined by glpc.

The first compound was a crystalline solid, mp 40–41°, identified as 6,6-dimethyl-3-bicyclo[3.1.1]heptanone (7) on the basis of its spectral properties: infrared spectrum (neat) 5.80 μ ; nmr spectrum, a broad, four-proton singlet at δ 2.45 (CH_2CO), a two-proton multiplet at 2.14 (bridgehead protons), and methyl peaks at 1.33 and 0.90 obscuring two additional protons. The 2,4-dinitrophenylhydrazone was also prepared, mp 163–165° (lit.³³ mp 162). The second component was identified as nopinone.³⁴ The third substance is *anti*-6,6-dimethylbicyclo[3.1.1]hept-3-en-2-ol (9) based on its spectral properties; infrared (neat) 3.0, 3.27, 6.15, and 13.8 μ ; nmr, a one-proton multiplet at δ 6.25 and a broad one-proton doublet at 5.56 ($J = 8$ cps) ($CH=CH$), one-proton signals at 4.21 ($CHOH$) and 3.73 (OH), a three-proton multiplet at 2.1, and methyl resonances at 1.31 and 0.89 obscuring the signal from an additional proton.

Anal. Calcd for $C_{10}H_{14}O$: C, 78.21; H, 10.21. Found: C, 77.93; H, 10.20.

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