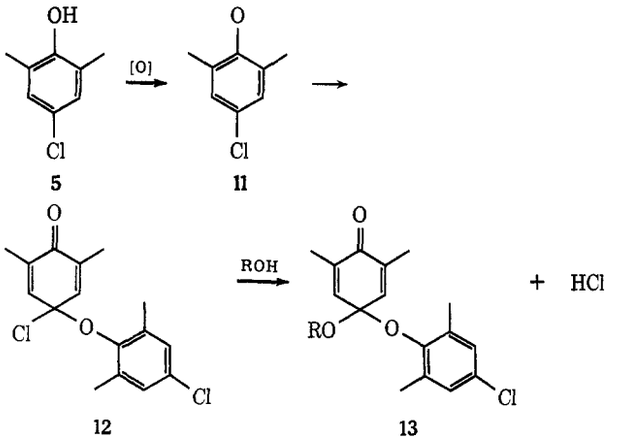
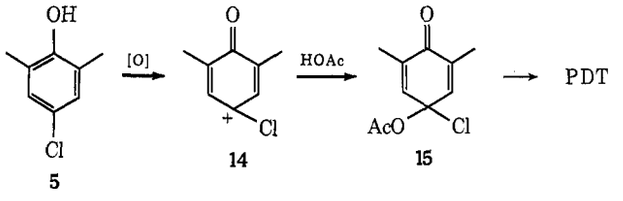


the phenol **5** could be oxidized directly to **14** and subsequently yield the products by a solvolysis mechanism.



In all of the reactions a polymeric material forms which is probably a polyphenylene oxide polymer but which was not characterized.

This reaction offers a method of making some substituted phenols which would be difficult to make by other means. The conditions are mild and the reaction easy to run.

The reaction is general in the sense that a wide variety of oxidants yield identical results. Lead dioxide, silver oxide, and potassium permanganate all give the same distribution of products. Phenols that fulfill the conditions of blocked ortho positions also will work. Alcohols do not give a similar product distribution and an investigation of this reaction is under way.

Experimental Section

4-Chloro-2,6-xylenol and 2,4,6-Trichlorophenol.—These materails were used as obtained from Aldrich Chemical Co.

4-*tert*-Butyl-2,6-xylenol.—This material was prepared by butylation of 2,6-xylenol.[7]

Oxidation of 4-Chloro-2,6-xylenol (5) in Acetic Acid.—The slow addition of powdered potassium permanganate (1.58 g, 0.05 equiv) to 4-chloro-2,6-xylenol (2.34 g, 0.015 mol) in glacial acetic acid (75 ml) produced a bright yellow solution which was poured into water and the organics were extracted with ether. The ether was washed with sodium bicarbonate solution and water and dried, and the ether was distilled, which left a yellow gum. Upon treatment with bis(trimethylsilyl)acetamide[9] the sample became sufficiently volatile so that it could be analyzed by vapor phase chromatography (vpc) and the major product was collected. This material is 4-acetoxy-2,6-xylenol trimethylsilyl ether, as shown by mass spectra (molecular weight and fragmentation pattern), infrared spectrum, and vpc retention time when compared with those of an authentic material.[12]

The residual oil gave pale yellow crystals (0.4 g, 8%) when dissolved in hexane and cooled to −20°. These crystals, mp 65–67°, are 2,6-xyloquinone, as shown by the mixture melting point and a comparison of infrared spectra with those of an authentic material.[6]

Oxidation of 4-Chloro-2,6-xylenol and Benzoic Acid.—Silver oxide (6.96 g, 0.03 mol) was stirred with a mixture of 4-chloro-2,6-xylenol (4.68 g, 0.03 mol), benzoic acid (3.66 g, 0.03 mol), magnesium sulfate, and dimethylformamide over an 18-hr period. The solid silver salts were filtered and the filtrate was placed in water. Ether extraction removed the organic materials, after which sodium bicarbonate and water washes removed contaminants. The dried ether was distilled, leaving a red, gummy residue. The gum was dissolved in hexane and cooled to −20°. Tan crystals formed in a yield of 12%. Recrystallization of these crystals gave a yellow solid which was 4-benzoyloxy-2,6-xylenol, mp 139–141°. The infrared spectrum shows a hydroxyl at 3430, carbonyl at 1725, and phenyl absorbtions at 710 and 735 cm^{-1} which support the assigned structure **6** (OAc = OBz).

Anal. Calcd for $C_5H_{14}O_3$: C, 74.4; H, 5.8; mol wt, 242. Found: C, 74.5; H, 5.7; mol wt, 245.

Oxidation of 4-*tert*-Butyl-2,6-xylenol and 2,4,6-Trichlorophenol.—4-*tert*-Butyl-2,6-xylenol (1.78 g, 0.01 mol) and 2,4,6-trichlorophenol (1.97 g, 0.01 mol) in benzene were stirred with silver oxide (2.3 g, 0.01 mol) for 0.5 hr and then filtered. A vpc of the silylated reaction mixture showed that the products were 80% phenoxy phenol **10** and 20% mixed monomers. A sample of silylated **10** was collected from the vpc and gave the correct mass spectrum for the trimethylsilyl derivative of **10**; major peaks at *m/e* 412, 410, and 177 (phenoxy) were found along with no evidence for three chlorines on the molecule.

Chromatography of the residue after filtration and benzene removal, and elution by hexane followed by 20% benzene–hexane, gave several fractions. One consisted of 0.16 g of solids which a vpc analysis showed was 90% **10**. This fraction, when separated by preparative thin layer chromatography, gave 0.102 g of a gum which crystallized at −30°, giving white plates, mp 105–106°.

Anal. Calcd as $C_{18}H_{20}O_2Cl_2$: C, 63.7; H, 5.9. Found: C, 63.7; H, 6.2.

The nmr spectrum of this material (Figure 1) clearly shows that the structure of **10** is the assigned 4 isomer.

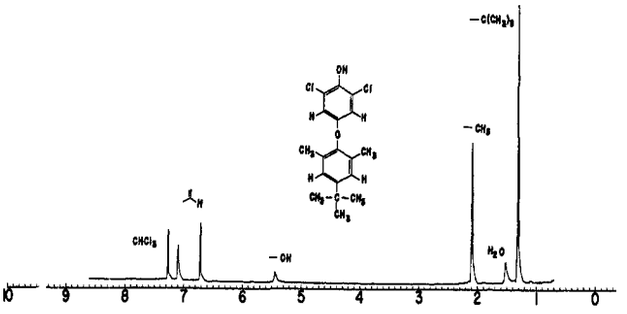


Figure 1.

Registry No.—**5**, 1123-63-3; **6** trimethylsilyl ether, 38645-01-1; **8**, 879-97-0; **9**, 88-06-2; **10**, 38645-02-2; 4-benzoyloxy-2,6-xylenol, 38645-03-3.

(12) H. Finkbeiner and A. Toothaker, *J. Org. Chem.*, **33**, 4347 (1968).

The Mechanism of the Cope Elimination

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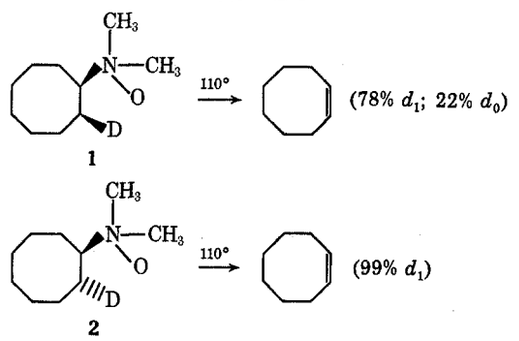
The Cope elimination[1] involves the thermal decomposition of an amine oxide by a five-membered cyclic transition state. This reaction has been extensively used as a "reference reaction" for syn elimination, since its mechanism has been considered to be essentially

(1) A. C. Cope and E. R. Trumbull, *Org. React.*, **11**, 317 (1960).

beyond doubt.[2] Although there is good evidence[1,3] that the pyrolysis of an amine oxide involves syn-elimination, this mechanism has never been rigorously tested by deuterium-labeling experiments. Since considerable emphasis has been placed on this reaction we now report unequivocal deuterium-labeling evidence that establishes the mechanism of the Cope elimination as a 100% syn elimination.

The specifically labeled *N,N*-dimethylcyclooctylamines were prepared according to the method of Coke.[4] The amine oxides were prepared by oxidation of the labeled tertiary amines with 36% hydrogen peroxide affording *cis*- and *trans*-*N,N*-dimethylcyclooctyl oxide-2-d_1. Pyrolysis of the cis-2-d_1 oxide **1** at 110° (11 mm) afforded *cis*-cyclooctene that had retained 78% of its initial deuterium content (Scheme I).

SCHEME I



From these data a syn k_H/k_D of 3.5 may be calculated. The deuterium content was analyzed by mass spectrometry on a sample purified by gas chromatography. Pyrolysis of the trans-2-d_1 oxide **2** afforded *cis*-cyclooctene that had retained 100% (within experimental error) of the deuterium initially present in the amine oxide, providing unequivical evidence for an exclusive syn elimination.

The complete absence of *trans*-cyclooctene (gc analysis) in the pyrolyses of **1** and **2** is worthy of comment. The stereoselective formation of cis olefin has been taken[3a,5] as evidence for the intramolecular cyclic mechanism, because the atoms eliminated would be in a preferred planar transition state. This reaction may be considered an analog of the ylide mechanism in which an α' oxy anion rather than the carbanion basic center is involved. We recently reported[6] that *trans*-cyclooctene can be readily formed by an α',β elimination in liquid ammonia using KNH_2 as the base (syn k_H/k_D = 5.89). Thus, a cyclic intramolecular transition state to form the more strained (~9 kcal/mol relative to the cis isomer) trans olefin is not precluded in the cyclooctyl system. Therefore the cis/trans ratio observed in these reactions should not be used as an indication of the mechanism involved.[7] As an alternate explanation we suggest that the exclusive formation of *cis*-cyclooctene is a manifestation of the weakly basic oxy anion. In the Cope elimination both C–H and C–N bond cleavage may be well advanced at the transition state with considerable development of double-bond character. However, with the strongly basic nitrogen ylide[6] there might be more C–H cleavage than C–N cleavage in the transition state. In support of this suggestion, stabilized benzyl ylides[7] and sulfonium ylides[8] also afford the thermodynamically favored cis olefin. Thus, in the present case product development control results in exclusive formation of the cis stereoisomer.

(2) J. Zavada, J. Krupicka, and J. Sicher, *Collect. Czech. Chem. Commun.*, **31**, 4273 (1966); J. Sicher, *Angew. Chem., Int. Ed. Engl.*, **11**, 200 (1972).

(3) (a) C. H. DePuy and R. W. King, *Chem. Rev.*, **60**, 431 (1960); (b) M. R. V. Sahyun and D. J. Cram, *J. Amer. Chem. Soc.*, **85**, 1263 (1963).

(4) J. L. Coke and M. C. Mourning, *J. Amer. Chem. Soc.*, **90**, 5561 (1968).

(5) A. C. Cope, R. A. Pike, and C. F. Spencer, *J. Amer. Chem. Soc.*, **75**, 3213 (1953).

(6) (a) R. D. Bach and D. Andrzejewski, *J. Amer. Chem. Soc.*, **93**, 7118 (1971); (b) R. D. Bach, K. W. Bair, and D. Andrzejewski, *ibid.*, **94**, 8608 (1972).

(7) G. Wittig and R. Polster, *Justus Liebigs Ann. Chem.*, **612**, 102 (1958); C. L. Bumgardner, *J. Org. Chem.*, **27**, 1035 (1962).

Experimental Section

Mass spectral analyses were performed on an MS-902 mass spectrometer. *cis*-Cyclooctene and *N,N*-dimethylcyclooctylamine were purified by preparative gas chromatography and analyzed at 11 eV. The deuterium analyses were corrected for 83.3% and the 86.7% isotopic purity of the starting compounds, *N,N*-dimethyl-*cis*- and *N,N*-dimethyl-*trans*-cyclooctylamine-2-d_1. The *cis*-cyclooctene and the labeled amines were collected on a 6-ft 10% SE-30 column at 150° prior to mass spectral analysis. Gas chromatographic analyses of the reaction mixtures were carried out with a 6-ft 10% NMPN column at 80°.

The *cis*-cyclooctene was obtained as a gift from Columbian Carbon Co. *trans*-Cyclooctene was prepared as reported previously.[9] *cis*- and *trans*-cyclooctene were converted to *cis*- and *trans*-cyclooctylamine-2-d_1, bp 80–81° (20 mm), according to the procedure of Coke and Mourning.[4] The Clark–Eschweiler procedure described by Icke[4,10] was used to prepare the specifically labeled *N,N*-dimethylcyclooctylamines.

***N,N*-Dimethyl-*cis*-cyclooctylamine-2-d_1 Oxide.**—To a stirring solution of 1 ml of reagent methanol was added 0.028 g (0.180 mmol) of *N,N*-dimethyl-*cis*-cyclooctylamine-2-d_1[4] and 30 μl (1.3 mmol) of 36% hydrogen peroxide. After 3 days at room temperature the solvent was removed by rotary evaporation, affording the crude amine oxide as a viscous oil.

***N,N*-Dimethyl-*trans*-cyclooctylamine-2-d_1 Oxide.**—The above procedure was repeated on 0.028 g of *N,N*-dimethyl-*trans*-cyclooctylamine-2-d_1 affording the trans labeled amine oxide as a viscous oil.

Cope Elimination.—The crude amine oxides were heated at 110° (11 mm) and the temperature was slowly raised to 120° over a 30-min period. The pyrolysis products were collected in a cold trap in a pentane solution and washed with 10% HCl. The *cis*-cyclooctene was isolated by preparative gas chromatography. The product composition was at least 99.9% *cis*-cyclooctene with none of the trans isomer being observed by gc analysis.

Registry No.—**1**, 38645-04-4; **2**, 38645-05-5.

Acknowledgment.—We wish to express our appreciation to donors of the Petroleum Research Fund, administered by the American Chemical Society, for the support of this research.

(8) V. Franzen and H. J. Schmidt, *Chem. Ber.*, **94**, 2937 (1961).

(9) A. C. Cope and R. D. Bach, *Org. Syn.*, **49**, 39 (1969).

(10) R. N. Icke, B. B. Wisegarver, and G. A. Alles, "Organic Syntheses," Collect. Vol. III, E. C. Hornung, Ed., Wiley, New York, N. Y., 1955, p 723.

The Synthesis of Hycanthone

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Hycanthone (**7**), a schistosomicidal agent, was first prepared by Rosi, *et al.*, by microbiological oxidation of the corresponding 4-methylthioxanthenone,