Synthesis and Characterization of *cis*- and *trans*-1,4-Dimethylenecyclohexane Diepoxide

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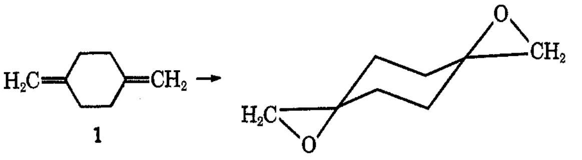
Convenient procedures for the synthesis of *cis*- and *trans*-1,4-dimethylenecyclohexane diepoxide are described. Reaction of 1,4-dimethylenecyclohexane (**1**) with *m*-chloroperbenzoic acid in benzene or tetrahydrofuran yields *trans*-1,4-dimethylenecyclohexane diepoxide (**2**), mp 106–108°, in 97–100% purity and in high yield. Reaction of **1** with aqueous *N*-bromoacetamide or *N*-bromosuccinimide yields *cis*-1,4-dihydroxy-1,4-bis(bromomethyl)cyclohexane (**3**), mp 163–164°, in 30% yield as a water-insoluble solid. The trans dibromohydrin **4**, mp 139–141°, can be recovered from the aqueous portion of the reaction mixture. Reaction of **3** with aqueous KOH yields *cis*-1,4-dimethylenecyclohexane diepoxide (**5**), mp 79–81°, in nearly quantitative yield. The structures of **2** and **5** were established by dipole moment and nmr measurements. Reduction of **2** or **5** with $NaAlH_2(OCH_2CH_2OCH_3)_2$ in THF yields the corresponding cis and trans isomers of 1,4-dihydroxy-1,4-dimethylcyclohexane.

During the course of studies on the polymerization of difunctional cyclohexane derivatives, we had occasion to develop convenient syntheses of *cis*- and *trans*-1,4-dimethylenecyclohexane diepoxide.[1] We report these procedures in this paper because the diepoxides are useful intermediaes for the synthesis of a variety of cis and trans 1,1,4,4-tetrasubstituted cyclohexane derivatives.

The reaction of 1,4-dimethylenecyclohexane[4,5] (**1**) with *m*-chloroperbenzoic acid[6] was found to be stereospecific when conducted in benzene or tetrahydrofuran, yielding *trans*-1,4-dimethylenecyclohexane diepoxide (**2**), mp 106–107°, in 97–100% purity. When conducted in $CHCl_3$ at 0°, the reaction yields product that is at least 90% trans. A single recrystallization from hexane affords the pure trans isomer. Mixtures of cis and trans isomers are obtained when other solvents or peracids are used. The results of an extensive study on the influence of reaction conditions in the course of the reaction are summarized in Table I.



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Although formation of the trans diepoxide is favored when conventional peracids are used, it is stereospecific only when the reactions are conducted in solvents with low dielectric constants. This suggests that polar contributions[7–9] to the transition state leading to the cis diepoxide cause cis diepoxidation to be less favorable than trans diepoxidation, particularly in nonpolar solvents. As has been observed in other olefin–peracid reactions,[6,10] longer reactions times were required when solvents capable of disrupting the intramolecular hydrogen bonding of the peracid were used.

TABLE I
STUDIES ON THE REACTIONS OF 1,4-DIMETHYLENECYCLOHEXANE WITH PERACIDS

Solvent	ε (solvent)	Temp, °C	Time, hr	Yield of diepoxide, %	Trans[a] content (±2%), %
	m-Chloroperbenzoic Acid				
Benzene	2.28	22	4	66	97
Chloroform	4.81	0	2	76	90
Chloroform	4.81	22	2	75	85
Tetrahydrofuran	7.6	22	34	44	100
Methylene chloride	9.1	40	48	79	70
Ethylene chloride	10.7	22	3	68	70
tert-Butyl alcohol	11.7	22	48	68	73
Acetonitrile	37.5	22	10	52	70
	Monoperphthalic Acid				
Diethyl ether	4.34	22	40	20	93
	Peroxybenzimidic Acid[b]				
Methanol	33.6	22	22	32	55
	Peracetic Acid				
Ethyl acetate	6.02	0	>48	25	85

[a] Determined by nmr. [b] Formed *in situ* from the reaction of hydrogen peroxide with benzonitrile.

It is interesting that approximatly equal amounts of cis and trans diepoxides are obtained when "peroxybenzimidic acid,[11,12] formed *in situ* from benzonitrile in methanol at pH 8, is the oxidant. Carlson and Behn[13] have also noted that "peroxybenzimidic acid" acts differently from conventional peracids in olefin epoxidation reactions, and their results show that the presence of methanol is not responsible for the results obtained. It would seem that a species other than a peracid is the active reagent in "peroxybenzimidic acid" oxidations.

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[1] We are pleased to acknowledge preliminary work in our laboratories by Dr. F. D. Shannon.[2] Dr. F. Lautenschlaeger, of the Dunlop Research Center, Toronto, Canada, has informed us privately that he has also prepared a mixture of the diepoxides and has separated them by fractional crystallization. The trans isomer seems to have been obtained previously[3] from the reaction of diazomethane with 1,4-cyclohexanedione.

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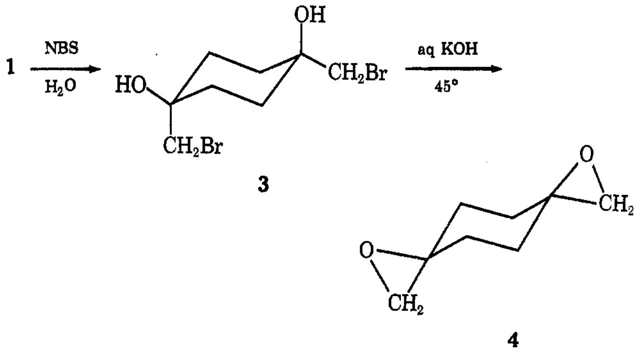
trans-1,4-Dimethylenecyclohexane diepoxide was characterized by its low dipole moment (0.1 ± 0.1 D), by the fact that it could be reduced to *trans*-1,4-dihydroxy-1,4-dimethylcyclohexane[14] with $NaAlH_2(OCH_2CH_2OCH_3)_2$, and by its nmr spectrum, details of which will be discussed later. It should be noted that *trans*-1,4-dihydroxy-1,4-dimethylcyclohexane has been difficult to obtain in pure form in reasonable yield hitherto, but that it can now be prepared easily in two steps from dimethylenecyclohexane.

Although *cis*- and *trans*-1,4-dimethylenecyclohexane diepoxide can be separated by fractional crystallization from hexane, the separation is tedious and an efficient route to the cis diepoxide was sought. Work by Schultz[15] and Morales[16] has shown that the reaction of 1,4-dimethylenecylcohexane with aqueous *N*-bromoacetamide or *N*-bromosuccinimide yields *cis*-1,4-dihydroxy-1,4-bis(bromomethyl)cyclohexane (**3**) in 20–30% yield. This material is the only easily isolated product formed in the reaction. It separates from the reaction mixture as an oily solid and can be purified by recrystallization from benzene–ethanol or benzene–methanol. Reaction of **3** with aqueous KOH afforded *cis*-1,4-dimethylenecyclohexane diepoxide (**4**), mp 79–81°, in 90% yield. Although the formation of **3** is a low-yield process, the material is easy to isolate and the sequence **1** → **3** → **4** provides a convenient route to the cis diepoxide.



The cis diepoxide was characterized by its high dipole moment (4.2 ± 0.5 D), by the fact that it is lower melting than the trans isomer, by the fact that it can be reduced to *cis*-1,4-dihydroxy-1,4-dimethylcyclohexane,[14] and by its nmr spectrum, details of which will be considered next. In addition, its infrared spectrum was more complex than that of the trans isomer, in keeping with the lower symmetry of the cis isomer.

The nmr spectra of the cis and trans diepoxides provided evidence supporting their configurational assignments. The nmr spectrum of the trans isomer at room temperature consisted of a singlet at 2.57 ppm (oxirane CH_2) and an AA'BB' pattern (cyclohexane CH_2), the strongest signals of which occurred at 2.18, 2.02, 1.40, and 1.26 ppm. The resonance of the oxirane methylene protons was observed as a singlet at −100°, the half-width of which was comparable to that of TMS resonance. At elevated temperatures, the AA'BB' multiplet peaks shifted only slightly toward the center of the pattern. These results suggest that the trans isomer has a preferred conformation at room temperature.

The nmr spectrum of the cis isomer at room temperature consists of a sharp singlet at 2.54 ppm (oxirane CH_2) and a broad resonance centered at 1.72 ppm (cycohexane CH_2). At −100°, the oxirane methylene proton resonance is observed as a pair of resonances of equal intensity, separated by 4 Hz. In addition, the resonance of the cyclohexane protons at −100° becomes similar to that of the trans isomer. These results indicate that the cis isomer readily undergoes conformational interconversion at room temperature, but that the rate of this process becomes slow on the nmr time scale at −100°.

The relative chemical shifts of the oxirane methylene protons are also in accord with the configurational assignments. The trans isomer can be expected to favor the conformation having equatorial oxirane methylene groups,[17] whereas the oxirane methylene groups must be in both axial and equatorial positions in the cis isomer. Since the resonance of oxirane methylene protons in an equatorial position occurs at lower field than when they have an axial position,[13,17] it is reasonable that the oxirane proton resonance of the trans isomer occurs at lower field than that of the cis isomer.

Experimental Section[18]

***trans*-1,4-Dimethylenecyclohexane Diepoxide.**—A solution of *m*-chloroperbenzoic acid (8.90 g of 85.4% active material, 44 mmol) in chloroform (100 ml) was added slowly (20 min) to a solution of 1,4-dimethylenecyclohexane[4,5] (2.37 g, 22 mmol) in $CHCl_3$ (50 ml) at 0°. The reaction mixture was stirred until it showed a negative reaction to starch–iodide paper. The mixture was filtered and then washed with 10% $NaHCO_3$ solution and with distilled water. The $CHCl_3$ solution was then dried over Na_2SO_4 and evaporated to dryness in a stream of nitrogen. The solid residue, 2.34 g (76%), mp 90–101°, was shown by thin layer chromatography to consist of two species, presumably the cis and trans isomers. *Anal.* Calcd for $C_8H_{12}O_2$ (140): C, 68.54; H, 8.63. Found: C, 68.78; H, 8.80.

The product was recrystallized from *n*-hexane to obtain 1.8 g (60%) pure *trans*-1,4-dimethylenecyclohexane diepoxide: mp 106–108° (white needles); ir 3.29, 7.69, 10.1, 10.89, and 11.96 μ (single bands, oxirane ring[22,23]); near-ir 2.213 and 2.223 (terminal epoxide[24]) and 2.355 μ (cyclohexane CH_2); nmr (CCl_4) δ 2.18, 2.02, 1.40, and 1.26 (strongest lines in AA'BB' pattern, 8, cyclohexane CH_2), 2.57 (s, 4, oxirane CH_2). The material can be further purified by sublimation. *Anal.* Found: C, 68.49; H, 8.71.

When the reaction was conducted in other solvents, the procedure used was essentially the same as that described above, although the amount of solvent employed sometimes had to be adjusted to dissolve the peracid.

In those cases where *m*-chlorobenzoic acid was soluble in the reaction mixture, it was evaporated to dryness *in vacuo* and the

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(18) Nmr spectra of the materials were recorded using Varian A-60 and T-60 spectrometers. CCl_4 was used as a solvent for most nmr and ir studies. Tetramethylsilane was used as an internal standard.

Dipole moments were determined by the procedure of Hedestrand,[19,20] using apparatus assembled by Dr. G. Corsaro. Benzene was used as a solvent and measurements were made at room temperature. $P^0_{2\infty}$ values were estimated from molecular refractivities calculated[21] for the diepoxides.

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diepoxide was extracted from the residue with $CHCl_3$. The results obtained are summarized in Table I.

Reaction of 1,4-Dimethylenecyclohexane with Monoperphthalic Acid.—1,4-Dimethylenecyclohexane was added dropwise to an ethereal solution of monoperphthalic acid[25] (2 mol of peracid to 1 mol of diene) and the solution was allowed to stand for 40 hr at room temperature. Phthalic acid which precipitated was filtered and the filtrate was washed with 10% $NaHCO_3$ and with distilled water. The ether solution was then dried over anhydrous Na_2SO_4 and evaporated to dryness under nitrogen. The solid residue (20% yield) was shown by nmr analysis to contain 93% of the trans isomer.

Reaction of 1,4-Dimethylenecyclohexane with *in Situ* Peroxybenzimidic Acid.[11,12]—Thirty per cent hydrogen peroxide (10.6 g, 93 mmol) was slowly added to a stirred solution of 1,4-dimethylenecyclohexane (4.75 g, 44 mmol), benzonitrile (9.60 g, 93 mmol), and $KHCO_3$ (1.50 g) in methanol (50 ml). The mixture was stirred at room temperature for 18 hr and was then heated for 4 hr at 45–50°. The resulting solution was diluted with water (75 ml) and thoroughly extracted with 25-ml portions of $CHCl_3$. The combined $CHCl_3$ extracts were washed with water and dried over anhydrous Na_2SO_4. The $CHCl_3$ was allowed to evaporate and the solid obtained was extracted with boiling hexane and filtered to remove benzamide. Evaporation of the hexane filtrate yielded the diepoxide mixture (1.96 g, 32%, mp 72–95°), which was shown by nmr analysis to contain 55% of the trans isomer.

Reaction of 1,4-Dimethylenecyclohexane with Peracetic Acid.[26,27]—A calculated amount of a solution of peracetic acid in ethyl acetate (13.40 g of solution, 44 mmol of CH_3CO_3H) was added slowly at 0° to a solution of 1,4-dimethylenecyclohexane (2.375 g, 22 mmol) in ethyl acetate (50 ml) containing *ca.* 1 g of anhydrous Na_2CO_3. The mixture was vigorously stirred so that the Na_2CO_3 remained suspended.

After 48 hr, the mixture showed a positive reaction to starch–iodide paper. The unreacted peracid was decomposed with 10% Na_2SO_3 and the mixture was then washed thoroughly with water and dried over anhydrous Na_2SO_4. Evaporation of the ethyl acetate under reduced pressure yielded a mixed diepoxide (25% yield) that was shown by nmr analysis to contain 85% of the trans isomer.

***cis*-1,4-Dihydroxy-1,4-bis(bromomethyl)cyclohexane[15,16] (3).**—A mixture of 1,4-dimethylenecyclohexane (3.56 g, 33 mmol), *N*-bromosuccinimide (11.8 g, 66 mol), and water was vigorously shaken for about 35 min, and was then allowed to stand in the dark for 1 hr. The mixture was then filtered. The oily solid collected was washed with ether, dried, and recrystallized from benzene–ethanol mixtures to obtain *cis*-1,4-dihydroxy-1,4-bis(bromomethyl)cyclohexane, 2.0 g, as white needles: mp 163–164°; nmr (DMSO-d_6) δ 3.52 (s, 2, CH_2Br), ~4.6 (s, temperature and concentration dependent, 1, OH), 1.55 (m, 4, ring CH_2); mass spectrum *m/e* 221 and 223 (parent − CH_2Br). *Anal.* Calcd for $C_8H_{14}Br_2O_2$ (302.1): C, 31.80; H, 4.67; Br, 53.00. Found: C, 31.73; H, 4.51; Br, 53.18; mol wt (Rast), 341.

Saturation of the aqueous phase with NaCl caused an additional quantity of the cis bromohydrin to precipitate. The total yield obtainable is about 30%.

Ether-soluble products isolated from the reaction mixture by chromatography on alumina include a brominated dibromohydrin (7%), mp 110–112° (*Anal.* Calcd for $C_8H_{13}Br_3O_2$: C, 25.16; H, 3.41; Br, 62.99; O, 8.44. Found: C, 26.19; H, 3.62; Br, 60.55; O, 8.39); *p*-xylylene dibromide (2%), mp and mmp 144–145°, and a large amount of uncharacterized oil.

In addition, *trans*-1,4-dihydroxy-1,4-bis(bromomethyl)cyclohexane (5%) was obtained by allowing the aqueous phase to concentrate by evaporation: mp 139–141°; nmr (DMSO-d_6) δ 3.42 (s, 2, $-CH_2Br$), 1.32, 1.46, 1.56 (b), 1.65, 1.82 (part of AA′BB′ pattern, 4, ring CH_2).

Anal. Calcd for $C_8H_{14}BrO_2$: C, 31.78; H, 4.63; Br, 52.98; O, 10.59. Found: C, 31.82; H, 4.63; Br, 53.99; O, 9.56.

***cis*-1,4-Dimethylenecyclohexane Diepoxide.**—One gram of *cis*-1,4-dihydroxy-1,4-bis(bromomethyl)cyclohexane was added slowly, as a solid, to a stirred solution of KOH (450 mg of 85% material) in water (60 ml) at 40°. The mixture was maintained at this temperature for 1 hr after the dibromohydrin had completely dissolved. The reaction mixture was then saturated with NaCl and extracted with five portions of ether. The ether extracts were combined, dried over anhydrous $MgSO_4$, and evaporated under nitrogen to obtain 441 mg (95%) of *cis*-1,4-dimethylenecyclohexane diepoxide: mp 79–81°; nmr (CCl_4) δ 2.54 (s, 4, oxirane CH_2), 1.72 (b m, 8, cyclohexane CH_2); ir 3.29 (oxirane CH), 7.69 + 7.94, 9.13 + 9.82, 7.69 + 7.94, 10.87 + 11.11,[28] 11.84 + 12.43, no band at 10.1 μ; near ir 2.218 (terminal oxirane), 2.355, and 2.339 μ (cyclohexane CH_2).

The compound can be further purified by sublimation. *Anal.* Calcd for $C_8H_{12}O_2$: C, 68.54; H, 8.63. Found: C, 68.46; H, 8.62.

The trans diepoxide can also be prepared by dehydrohalogenation of *trans*-1,4-dihydroxy-1,4-bis(bromomethyl)cyclohexane with aqueous KOH.

Reduction of *cis*-1,4-Dimethylenecyclohexane Diepoxide with $NaAlH_2(OCH_2CH_2OCH_3)_2$.—VITRIDE reducing agent[29] (2.5 ml) was added to a solution of *cis*-1,4-dimethylenecyclohexane diepoxide (0.577 g) in THF (20 ml) during 15 min. The reaction mixture was allowed to stand for 1 hr and was then poured into a small volume of water. The mixture was then evaporated to dryness and the residue was extracted with dry acetone. Evaporation of the acetone extract yielded 0.41 g (72%) of crude diol, mp 135–158°. This was purified by sublimation to obtain *cis*-1,4-dihydroxy-1,4-dimethylcyclohexane, mp 164–165° (reported[14] mp 166–167°).

Reduction of *trans*-1,4-Dimethylenecyclohexane Diepoxide with $NaAlH_2(OCH_2CH_2OCH_3)_2$.—A solution of VITRIDE reducing agent[29] (2.8 ml) in 5 ml of THF was added to a solution of the trans diepoxide (0.68 g) in 25 ml of THF with stirring. After 2 hr, the reaction mixture was worked up as is described for the reduction of the cis isomer. The crude product (0.53 g) yielded 0.23 g (33%) of *trans*-1,4-dihydroxy-1,4-dimethylcyclohexane, mp 196–198°, after recrystallization from acetone. Courtot, *et al.*,[14] report a melting point of 199–200° for the trans diol.

Registry No.—**1**, 4982-20-1; **2**, 28250-09-1; *cis*-**3**, 38312-48-0; *trans*-**3**, 38312-49-1; **4**, 28250-28-4; *m*-chloroperbenzoic acid, 937-14-4; monoperphthalic acid, 2311-91-3; peroxybenzimidic acid, 20996-66-1; peroxyacetic acid, 79-21-0.

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[28] The band at 11.1 μ was used to determine the cis-isomer content of diepoxide mixtures. Nmr analyses were obtained by comparing the relative intensities of cyclohexane or oxirane methylene proton resonances due to the cis and trans isomers. The results of both techniques were in good agreement.

[29] VITRIDE reducing agent is a 70% solution of $NaAlH_2(OCH_2CH_2OCH_3)_2$ in benzene that is available from Eastman Kodak Company, Eastman Organic Chemicals, Rochester, N. Y. 14650.