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The Electron-Impact Promoted Fragmentation
of 1,2-Cyclohexene Oxide[†]

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Abstract. The mass spectrum of 1,2-cyclohexene oxide and important data from the spectra of three deuterium labeled analogs have been recorded and mechanistic rationalizations are given for the most important fragmentation processes observed. Multiple mechanisms are required to explain the indicated peak shifts in the labeled analogs for many of the ions discussed, thus demonstrating again the care that needs to be exercised in the interpretation of the mass peaks of relatively simple molecules.

Until recent years the mass spectral fragmentation patterns of epoxides have not been extensively studied. Detailed analyses of a series of aliphatic epoxides,¹ α,β -epoxyketones,² and aromatic alkene oxides³ have been reported. Discussions of the mass spectra of β -phenylglycidic esters and amides⁴ and long chain aliphatic epoxy esters⁵ have also appeared. In addition, isolated spectra, partial analyses, and high resolution data for various other epoxides have been published.⁶ No detailed analysis of the mass spectra of alicyclic epoxides has appeared to date, although a postulated fragmentation scheme for 1,2-epoxy-1-methylcyclohexane has been proposed,¹ and the spectra of this compound, 3,4-epoxymenthane, and 1,2-epoxymenthane have been presented and discussed with respect to the formation of m/e 69.^{7b} Therefore, we decided to examine in detail the mass spectral fragmentation of the parent cyclohexene oxide (I, Fig. 1 and 2) by means of deuterium labeled analogs (II-IV), medium resolution data,⁸ and metastable findings for both the labeled and unlabeled

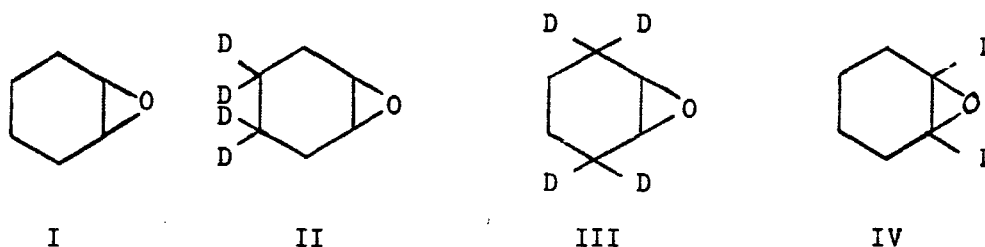
* For part CLXXVII see G. Eadon, J. Diekman, and C. Djerassi, submitted for publication.

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cyclohexene oxides.



The estimated deuterium content of each analog is listed in Table 1. Upon consideration of Figure 1, it became apparent that the deuterium incorporation in the three labeled analogs could not be calculated from the molecular ion region of the mass spectra of the epoxides. The very large $M-1$ peak (m/e 97), which apparently arises from random loss of a proton from all six carbons of the ring, necessitated a circumvention. A bracketing of isotopic purity was possible for epoxides III and IV, since the isotopic content of the precursor olefin and the acid hydrolysis product diol had been determined. The deuterium content of epoxide II, however, could be ascertained only from the precursor diol because the labeled cyclohexene was not isolated in pure form prior to epoxidation.

Table 1. Isotopic content of the labeled 1,2-cyclohexene oxide.

Compound	%d ₀	%d ₁	%d ₂	%d ₃	%d ₄	%d ₅
II	-	-	4 [†]	8 [†]	88 [†]	-
III	-	-	-	-	97 [†] -100 [*]	0 [*] -3 [†]
IV	0 [*] -1 [†]	8 [*] -11 [†]	88 [†] -92 [*]	-	-	-

[†] Data calculated from the spectra of the corresponding diols.

^{*} Data calculated from the spectra of the precursor olefins.

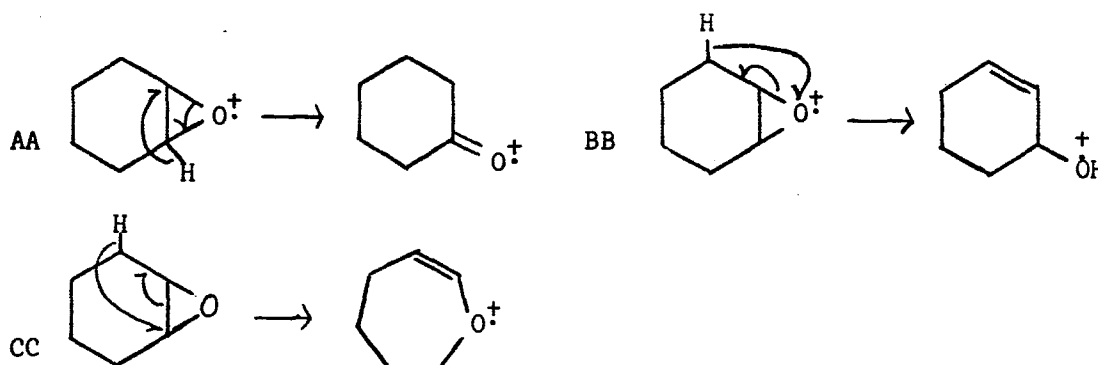
Three tautomeric shifts,^{*} shown below, can be postulated to occur prior to frag-

* It is recognized that ions produced by the rearrangements suggested here may differ in energy from the corresponding ions produced by direct ionization of a molecule (for example, cyclohexanone). It is also recognized that these two energetically different ions may produce fragmentation patterns differing slightly in peak intensities. Nevertheless, the arguments presented here seem sufficiently valid to warrant consideration.

mentation. The first of these, labeled AA, has been postulated to occur in cleavages observed in aliphatic epoxides¹ and aromatic alkene epoxides.³ In the present situation, this shift would give rise to the molecular ion of cyclohexanone, which has been studied in great detail.⁹ It has principal fragmentation peaks at m/e 42, m/e 55 (C_3H_3O), m/e 69, and m/e 70. The latter two peaks are present in 30% and 20% relative abundance with respect to the base peak of m/e 55. In the spectrum of I, 41% of the m/e 55 peak is C_3H_3O and this portion could only partly arise from the indicated tautomeric shift and subsequent fragmentation, since the spectra of the deuterated analogs II-IV demonstrate shifts in addition to those explained by this process. Therefore, this rearrangement cannot explain the entire C_3H_3O portion of m/e 55, if indeed any fragmentation occurs by this method. The intensity of the m/e 69 and m/e 70 peaks in the spectrum of cyclohexene oxide cannot be explained by this tautomeric shift AA, since the relative contribution to either peak through such an intermediate would be minimal. Therefore, it would seem that cyclohexene oxide, a simple cyclic epoxide, does not fragment to any great degree via this route.

The tautomeric shift BB results in a species corresponding to the molecular ion of 2-cyclohexene-1-ol, whose mass spectrum is reproduced¹⁰ in Figure 3. The composition of the base peak of mass 70 is 100% C_4H_6O and is postulated to arise from the molecular ion by a retro-Diels-Alder fragmentation¹¹ (see scheme D). Medium resolution data (see Table 3) for the m/e 70 peak of cyclohexene oxide (27% relative abundance) show it to be 93% C_4H_6O . Therefore, it is conceivable that part of the peak in the epoxide could arise through the ionized cyclohexenol intermediate. The entire peak cannot be attributed to this process, however, since the deuterated analogs display mass shifts in addition to those explained by the fragmentation of the tautomeric species BB. Assuming that the fragmentation pattern of 2-cyclohexene-1-ol remains constant, the only other fragmentation peaks of I to which the tautomeric alcohol might contribute substantially would be m/e 55 and m/e 93. The ion of mass 55 in the spectrum

of cyclohexenol is principally oxygen-containing, while that in the spectrum of cyclohexene oxide is 41% C_3H_3O (see Table 3). A metastable peak at m/e 43.2 in the unlabeled spectrum (see Table 2) and appropriate metastable peaks in the spectra of the deuterium analogs II-IV substantiate a possible transition from the m/e 70 ion arising from the tautomeric cyclohexenol to the oxygen-containing ion of mass 55. The m/e 83 peak of cyclohexene oxide could result in part from the loss of methyl from the molecular ion of 2-cyclohexene-1-ol (see process B'), since the predicted fragmentation is supported by the mass shifts observed in the labeled analogs. However,



this type of fragmentation is not the principal mode of formation of m/e 83, since the contribution of the tautomeric species to this peak would have as a maximum approximately one-third of the relative abundance of m/e 70 (27 units), clearly a minor (10%) contribution to the base peak of cyclohexene oxide.

The third possible tautomeric shift CC would give rise to the molecular ion of tetrahydro-oxepin. The mass spectrum of this compound is unknown, and therefore, this rearrangement cannot be discounted or confirmed.

The base peak of both the 70 eV spectrum (Fig. 1) and the low voltage spectrum (nominal voltage 12 eV, Fig. 2) is m/e 83. With the exception of the region around m/e 42, the spectra are quite similar. The only substantial difference is the intensity of the remaining peaks, which, as expected, decrease at low voltage. This decrease is fairly uniform, except for m/e 68 and m/e 56, which seem to increase with respect to their neighboring ions, indicating that these ions are probably formed by a primary

fragmentation process, or by a rearrangement in the molecular ion prior to cleavage.¹² Metastable peaks are observed in the high voltage spectrum of I for the transitions given in Table 2. The spectra of II-IV demonstrate metastable peaks corresponding to the loss of the species and/or deuterium labeled analogs of the species listed in Table 2. The composition of the important fragment ions, obtained on a dual-focusing MS-9 mass spectrometer, are given in Table 3.

Table 2. Metastable peaks and possible transitions for 1,2-cyclohexene oxide.

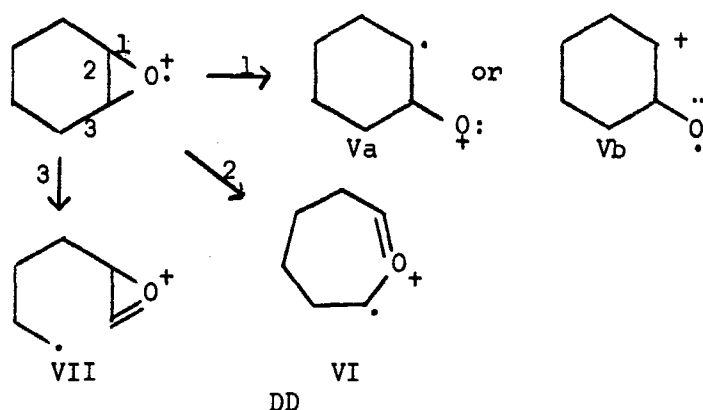
Metastable peak observe	Transition	Species lost
96.0	98 $\longrightarrow$ 97	H [•]
70.3	98 $\longrightarrow$ 83	CH ₃ [•]
48.6	98 $\longrightarrow$ 69	C ₂ H ₅ [•]
47.2	98 $\longrightarrow$ 68	CH ₂ O
43.2	70 $\longrightarrow$ 55	CH ₃ [•]
36.5	83 $\longrightarrow$ 55	CO

Table 3. Exact composition of important fragment ions of 1,2-cyclohexene oxide.

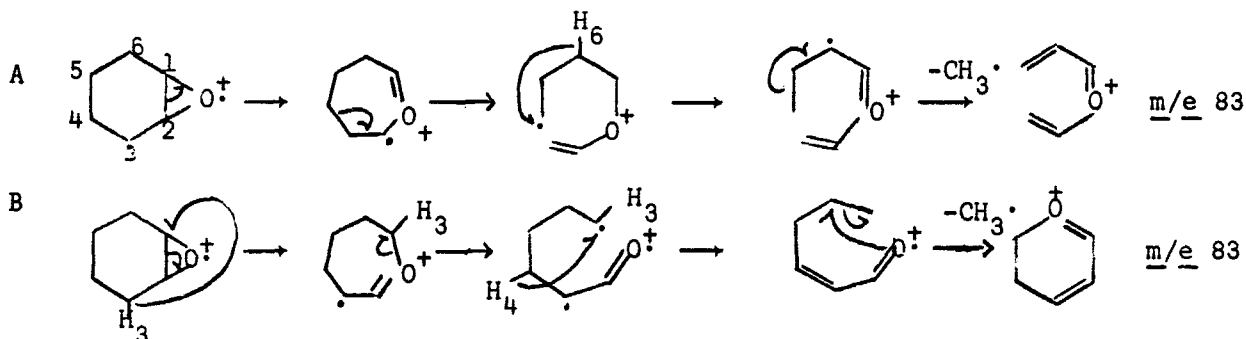
Fragment ion	Composition
<u>m/e</u> 70	C ₄ H ₆ O, 93%; C ₅ H ₁₀ , 7%
69	C ₄ H ₅ O, 56%; C ₅ H ₉ , 44%
68	C ₄ H ₄ O, 18%; C ₅ H ₈ , 82%
57	C ₃ H ₅ O
56	C ₃ H ₄ O, 81%; C ₄ H ₈ , 19%
55	C ₃ H ₃ O, 41%; C ₄ H ₇ , 59%
54	C ₄ H ₆

The initial step in many of the postulated mechanisms may be conceived as the cleavage of one of the three bonds shown below in DD. The resultant structures V-VII then undergo further fragmentation. The cleavage shown as 3 is actually the simple

α -cleavage which was shown to occur in aliphatic epoxides,^{1,5} but not as a principal process in the spectra of the lower molecular weight compounds.¹



An extremely large metastable peak ($[m^*]/[\text{daughter}] = 1\%$ according to the convention of McLafferty and Fairweather¹³) is observed for the transition from the molecular ion to the base peak at m/e 83, indicating that this process is an important one and probably occurs via a rearrangement in the molecular ion prior to cleavage.¹³ The following three mechanisms (A, B, and C) are proposed to explain the major mass shifts* observed in the labeled epoxides and recorded in Table 4. The fragmentation scheme B' is included at this point so that the peaks produced by the loss of a methyl radical from the molecular ion of the tautomeric 2-cyclohexene-1-ol could be easily compared with those predicted by the other three pathways.



* The percentages of mass shift for the various ions reported here and in later tables were calculated from the 70 ev spectra of the labeled epoxides and include a correction for natural isotopic C^{13} content and the fragmentation pattern found in the unlabeled epoxide.

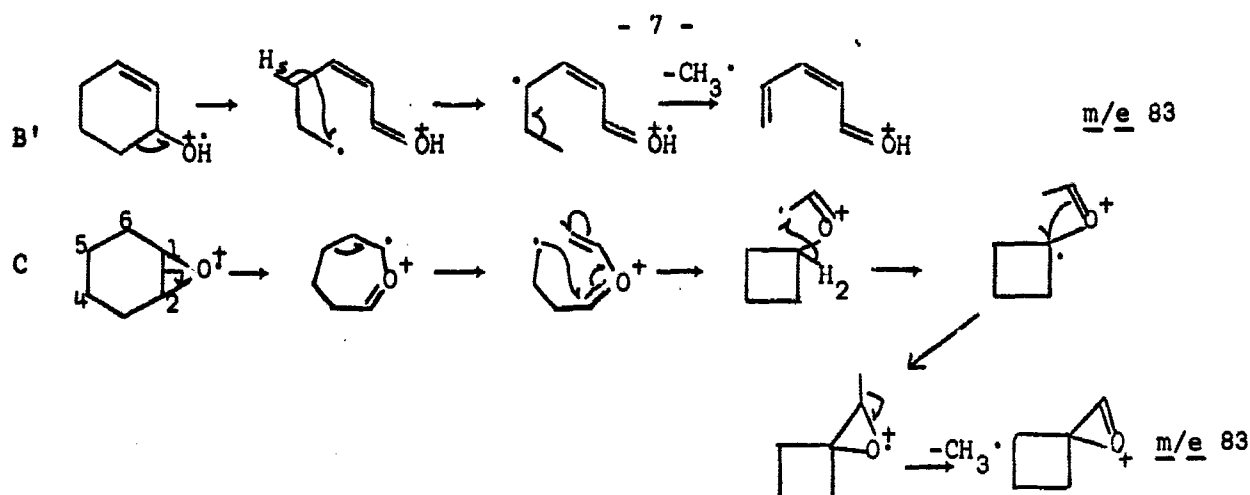


Table 4. Comparison of mass shifts of $\underline{m/e}$ 83 in the spectra of the labeled cyclohexene oxides and peaks resulting from the proposed processes.

Compound	Peak formed by process				% of $\underline{m/e}$ 83 which shifts to				
	A	E	B'	C	83	84	85	86	87
II	85	86	86	87	-	7	45	33	15
III	86	86	85	85	-	-	16	77	7
IV	85	84	85	84	2	42	56	-	-

The next group of peaks in the spectrum of cyclohexene oxide occur at $\underline{m/e}$ 70, 69, and 68. Metastable evidence for decomposition of the molecular ion to $\underline{m/e}$ 68 and $\underline{m/e}$ 69 indicates that these peaks are formed at least partially by distinct processes and not merely by hydrogen atom losses from a higher molecular weight ion. Although no metastable peak was observed for the formation of $\underline{m/e}$ 70, a stepwise process is highly unlikely. Therefore, this ion must also arise from the molecular ion. As shown in Table 3, the peak of mass 70 is principally oxygen-containing and may be visualized as being formed by the three processes (D, E, and F) given below. The mass shifts observed for the deuterium labeled epoxides and predicted by the three schemes are given in Table 5.

It will become apparent from consideration of Table 5 that the mass shift of compound III to $\underline{m/e}$ 73 is not explained by any of the proposed mechanisms. It was recognized early in our analysis of cyclohexene oxide that the results were complex and

multiple mechanisms would be required to explain most peaks in the spectrum. An attempt was made to present reaction schemes that satisfied the major portion of the labeling data, but not necessarily all the mass shifts indicated. Therefore, as in Table 5, the other tables also contain discrepancies of this type. The presence of these unexplained mass shifts may indicate that one or all of the postulated schemes are in error or merely that additional schemes would be necessary to describe the genesis of these shifts. One other explanation is possible; that some or all of the unexplained shifts are actually nonexistent i.e. the errors inherent in the calculation procedure are reflected in these figures.

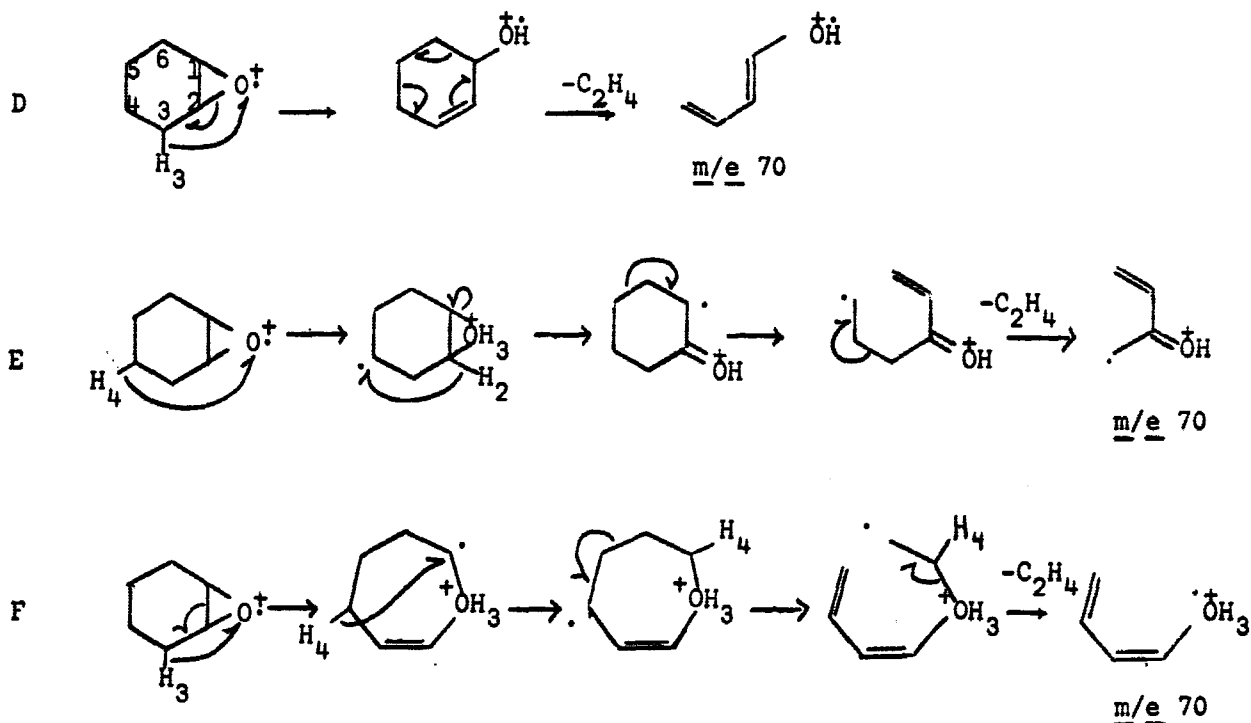


Table 5. Comparison of mass shifts of $\underline{m/e}$ 70 in the spectra of the labeled cyclohexene oxides and peaks resulting from the proposed processes.

Compound	Peak formed by process			% of $\underline{m/e}$ 70 which shifts to			
	D	E	F	71	72	73	74
II	72	71	73	14	48	32	6
III	72	74	72	-	21	26	53
IV	72	71	71	37	63	-	-

The ion of mass 69 is approximately a fifty-fifty mixture of the two possible isobaric species $C_5H_9^+$ and $C_4H_5O^+$. The formation of the hydrocarbon portion occurs primarily along a single pathway (G) and appears to have precedents in earlier work,^{1,7} while the oxygen fragment has a more complex origin; at least three schemes (H, I, and J) are needed to explain the principal fragmentations noted. The spectra of all four compounds (I-IV) display metastable peaks supporting the fragmentation scheme I. Both types of m/e 69 fragment ions, and the respective mass shifts of the deuterium labeled analogs are given in Table 6.

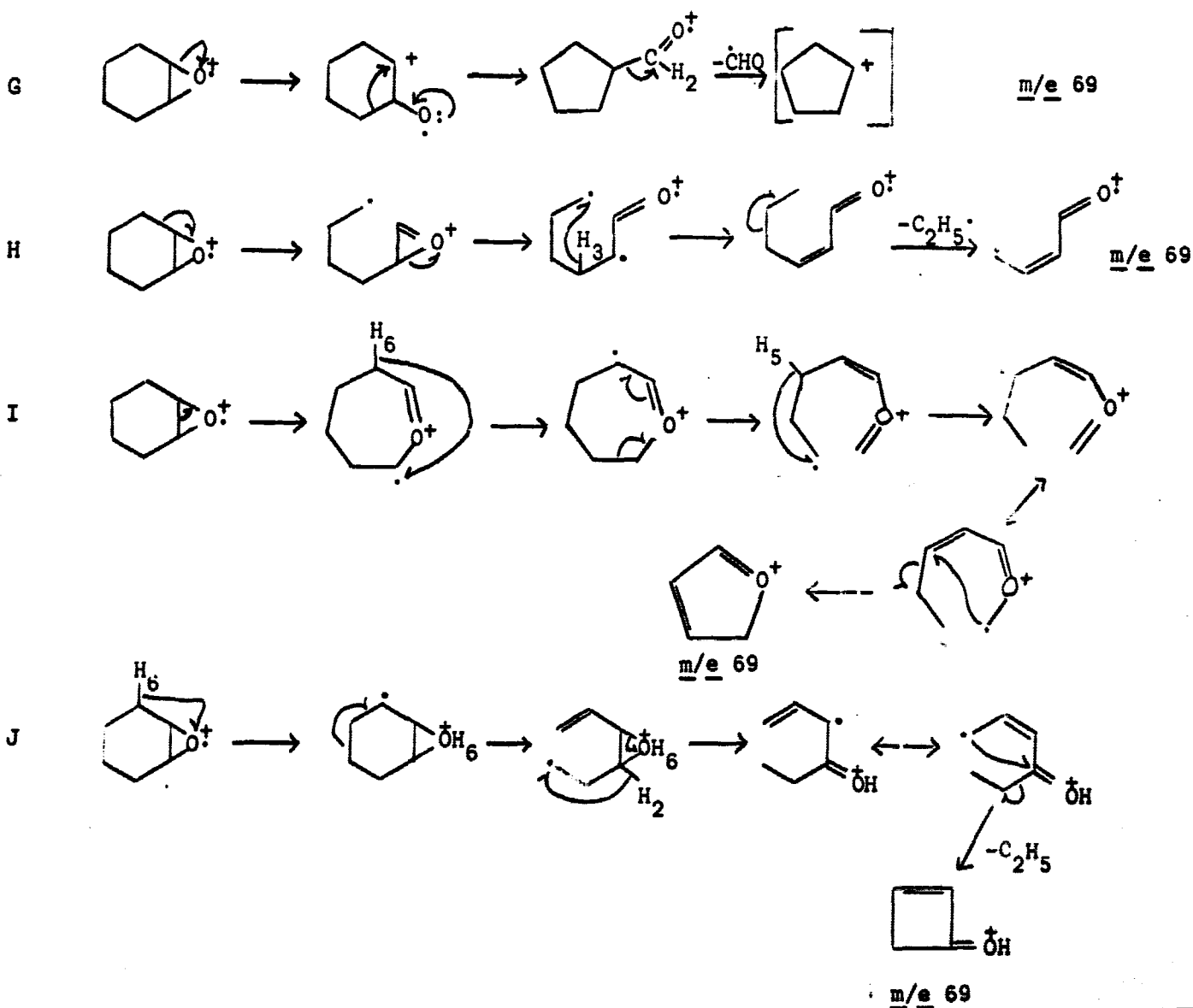
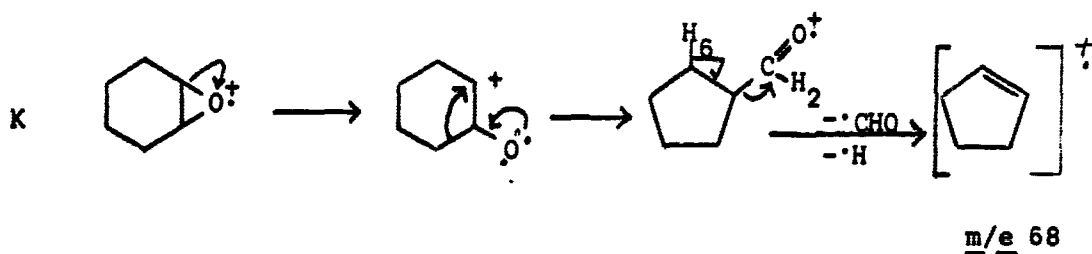


Table 6. Comparison of mass shifts of $\underline{m/e}$ 68 and $\underline{m/e}$ 69 in the spectra of the labeled cyclohexene oxides and peaks resulting from the proposed processes.

Compound	Peak formed by process					% shift of $\underline{m/e}$ 69 (HC) to				
	G	H	I	J	K	69	70	$\underline{71}$	72	73
II	73	71	70	71	72	-	-	-	28	72
III	73	70	71	71	71	-	-	-	30	70
IV	70	71	71	70	70	3	69	28	-	-

Compound	% shift of $\underline{m/e}$ 69 (O) to				% shift of $\underline{m/e}$ 68 to			
	69	70	$\underline{71}$	72	69	70	$\underline{71}$	72
II	15	69	16	-	-	-	31	69
III	-	30	53	17	-	-	95	5
IV	22	58	20	-	100	-	-	-

The $\underline{m/e}$ 68 peak is primarily hydrocarbon in nature and is formed by the loss of the components of formaldehyde. The single reaction process K explains the major mass shifts observed for the three labeled compounds and recorded in Table 6. The spectra of all four epoxides display metastable peaks supporting this fragmentation scheme.

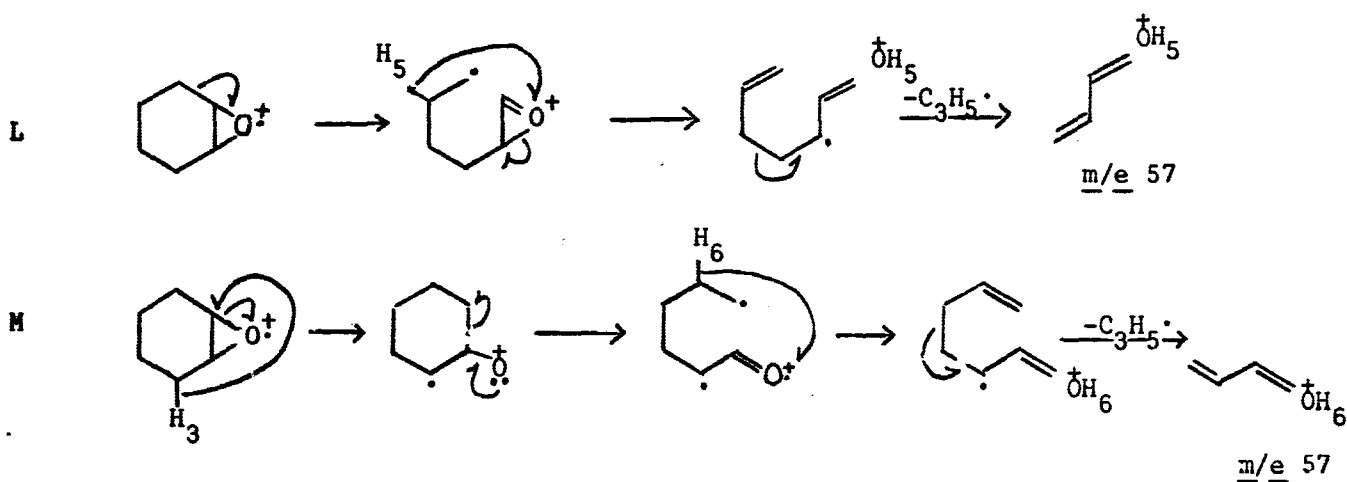


The four remaining important fragment ions in the spectrum of cyclohexene oxide occur at $\underline{m/e}$ 57, 56, 55, and 54. The ion of mass 57 has been shown to be entirely oxygen-containing. Only two hypothetical reaction schemes (L and M) are required to explain the majority of mass shifts observed in the deuterium labeled spectra and re-

corded in Table 7.

Table 7. Comparison of mass shifts of $\underline{m/e}$ 57 in the spectra of the labeled cyclohexene oxides and peaks resulting from the proposed processes.

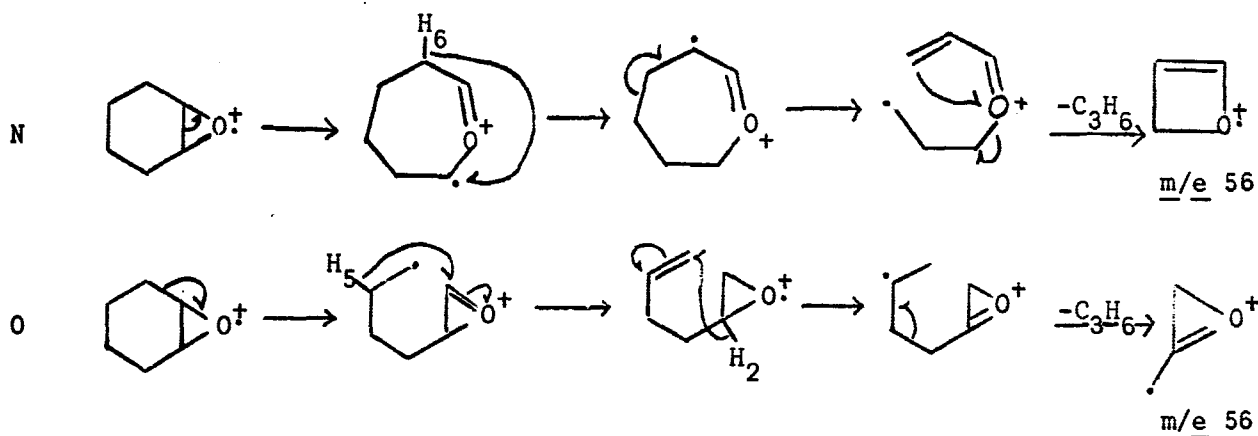
Compound	Peak formed by process		% of $\underline{m/e}$ 57 which shifts to		
	L	M	58	59	60
II	58	59	28	65	7
III	59	59	33	62	5
IV	59	58	63	37	-



The $\underline{m/e}$ 56 peak consists principally of the oxygen isobar (see Table 3) and appears to be formed by two main fragmentation schemes (N and C) originating from the molecular ion. The peaks resulting from the processes N and O operating on the labeled epoxides and the actual mass shifts calculated from the spectra are summarized in Table 8.

Table 8. Comparison of mass shifts of $\underline{m/e}$ 56 in the spectra of the labeled cyclohexene oxides and peaks resulting from the proposed processes.

Compound	Peak formed by process		% of $\underline{m/e}$ 56 which shifts to	
	N	O	57	58
II	58	57	61	39
III	57	58	87	13
IV	57	57	75	25

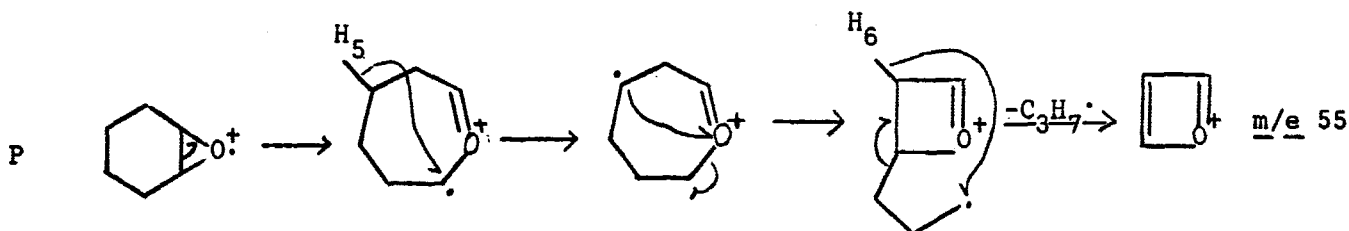


The $\underline{m/e}$ 55 peak is approximately a fifty-fifty mixture of the two possible isobaric ions. The hydrocarbon portion is again the simplest to interpret. This fragment arises from carbon monoxide expulsion from a $\underline{m/e}$ 83 precursor. In order to satisfy the labeling results (Table 9), the species resulting from mechanisms B and C must be implicated.

The oxygen portion of the ion of mass 55 appears to be formed at least partially from one of the $\underline{m/e}$ 70 ions, according to metastable evidence given in Table 2. However, no mechanism is postulated for this process. Approximately half of the mass shifts observed for the deuterium labeled analogs can be explained by the postulated scheme P, which originates with the molecular ion. The data for this scheme is found in Table 9.

Table 9. Comparison of mass shifts of $\underline{m/e}$ 55 in the spectra of the labeled cyclohexene oxides and peaks resulting from the proposed processes.

Compound	Peak formed by process P	% Shift of $\underline{m/e}$ 55 (O) to			% shift of $\underline{m/e}$ 55 (HC) to				
		55	$\underline{m/e}$ 56	57	55	56	$\underline{m/e}$ 57	58	59
II	56	25	47	28	-	-	7	46	47
III	56	12	70	18	-	-	65	35	-
IV	56	21	44	35	1	88	11	-	-



The origin of the $\underline{m/e}$ 54 peak in the spectrum of cyclohexene oxide (I) is not clear. The ion of mass 54 could arise from the molecular ion directly or via one of three intermediates, $\underline{m/e}$ 83 or the hydrocarbon portions of $\underline{m/e}$ 55 or 69. The loss of a formyl radical from $\underline{m/e}$ 83 would result in an ion of mass 54 containing only C_4H_6 . The loss of a methyl group from $\underline{m/e}$ 69 or the loss of a hydrogen atom from $\underline{m/e}$ 55 would also yield the ion in question. Since no metastable peaks were observed for any of these processes, no differentiation between them could be made, and no fragmentation schemes have been postulated.

It is apparent from the data presented in this paper that the fragmentation pattern of the unsubstituted cyclohexene oxide is complex. This conclusion, together with the results of our study of 1,2-cyclohexanediol,¹⁴ prompts a warning to those who are tempted to assume that simple molecules have mass spectra that are easily explained. Frequently, extensive deuterium labeling, high resolution (or medium resolution) data on the com-

position of the various ions, and metastable peak evidence are necessary in order to obtain meaningful interpretations of the peaks in the mass spectra of even a relatively simple compound.

The complicated interpretation of the mass spectrum of I prompted us to question the accuracy of extending to substituted cases the fragmentation patterns indicated to occur in the unsubstituted molecule. The high voltage mass spectra of the three possible mono-methylated cyclohexene oxides were investigated using as a basis the above cited fragmentation schemes and available high resolution data on the composition of peaks in the spectra. The peaks in the methylated spectra that were analogous to those analyzed above could be explained by the schemes postulated. Nonetheless, this result should be viewed with caution, for the agreement may be merely superficial, since no deuterium labeled compounds were considered.

EXPERIMENTAL

All mass spectra reported were obtained by Mr. R. C. Ross on an AEI MS-9 instrument using the heated inlet system (150°) and an ion source temperature of 180°. Medium resolution measurements of the unlabeled cyclohexene oxide were also obtained on this instrument. The test medium resolution refers to the process of increasing the resolution of ^{the} instrument until the isobaric components of a single peak are sufficiently separated to allow accurate height measurements to be made. Nuclear magnetic resonance (NMR) spectra were obtained on a Varian A-60 machine.

Epoxides used in this work were prepared from the corresponding cyclohexenes by the standard method of mixing methylene chloride solutions of the olefin and *m*-chloroperbenzoic acid and allowing the mixture to stand at room temperature for 3-18 hours.* After washing with 5% sodium hydroxide solution and water, the solution was dried and the solvent removed. Samples were purified by preparative vapor phase chromatography (VPC) using a 10' x 1/4" column.

* The preparation of compound II is an exception. Please refer to the synthesis given below.

column of Apiezon L on Teflon before being submitted for mass spectral analysis.

Syntheses of 1,2-d₂-cyclohexene and 4,4,5,5-d₄-cyclohexene oxide are given below. The deuterium labeled olefin, 3,3,6,6-d₄-cyclohexene is commercially available from Merck, Sharp, and Dohme, Montreal, Canada.

4,4,5,5-d₄-Cyclohexene oxide (II)

(1) To a solution of acetylene dicarboxylate dimethyl ester (40.01 g, 0.27 mole) in anhydrous ethyl acetate (250 ml) was added 10% Pd/C (2.41 g). Deuterium gas was introduced using a Parr apparatus. The deuteration proceeded rapidly, requiring approximately half an hour to reach completion. The catalyst was removed by filtration and the solvent distilled under reduced pressure to yield 43.75 g of 2,2,3,3-d₄-dimethylsuccinate.

(2) Lithium aluminum hydride (10 g, 0.26 mole) was suspended in freshly distilled tetrahydrofuran (THF) (1 liter). While dry nitrogen passed through the flask, a solution of d₄-dimethylsuccinate (33.0 g, 0.22 mole) in freshly distilled THF was added slowly with stirring. After heating under reflux for 72 hours, the excess LiAlH₄ was decomposed by the slow addition of 5 ml water, 10 ml 15% sodium hydroxide solution, and 30 ml water in that order. After filtration and solvent removal, 18.7 g (99%) of a pale yellow 2,2,3,3-d₄-1,4-butanediol was obtained.

(3) A mixture of d₄-butanediol (18.2 g, 0.20 mole), 48% hydrogen bromide solution (182 ml) and concentrated sulfuric acid (46 ml) was heated at reflux temperature for 24 hours. The biphasic reaction mixture was poured in water (300 ml) and extracted several times with ether. The combined ether extracts were washed with saturated sodium bicarbonate, water, and dried (MgSO₄). Filtration and evaporation gave 38.26 g (87%) of a dark-red liquid, which was distilled to yield 33.48 g of pure 2,2,3,3-d₄-butane-1,4-dibromide, bp 57-9°/4 mm. (Found: C, 21.96; H(D), 5.37; Br, 72.89. Calc. for C₄H₄D₄Br₂: C, 21.84; H(D), 5.49; Br, 72.66%) The NMR spectrum showed a single peak at δ=3.41, indicating a deuterium purity of approximately 90%.

(4) A solution of the d_4 -dibromide (32.48 g, 0.15 mole) in ethanol (50 ml) was slowly added to a solution of sodium cyanide (17.90 g) in water (18 ml) that had been heated on a steam bath. The resulting mixture was heated at reflux temperature for four days. The solvent was evaporated and the residue was extracted several times with ethyl acetate, which was then removed under reduced pressure. The residual liquid was distilled to yield 10.52 g (64%) of 2,2,3,3- d_4 -adiponitrile, bp $88^\circ/0.2$ mm.

(5) A mixture of *p*-toluenesulfonic acid monohydrate (54.96 g), methanol (7.6 g), d_4 -adiponitrile (10.42 g, 0.093 mole) and benzene (4 ml) was heated under reflux for 24 hours. The reaction mixture was cooled and sufficient water was added to dissolve the salts present. The resulting biphasic system was stirred vigorously for 1 hour and then extracted several times with ether. The ether extract was washed with 20% sodium carbonate, water and saturated sodium chloride before being dried ($MgSO_4$). The original water layer was returned to the flask and stirred for an additional hour before the extraction procedure above was repeated, to insure that complete alcoholysis had occurred. The organic solvents were evaporated to yield 13.75 g (83%) of colorless 3,3,4,4- d_4 -1,2-dimethyladipate.

(6) Following the procedure described by Bloomfield,¹⁵ a solution of d_4 -dimethyladipate (13.5 g, 0.076 mole), chlorotrimethylsilane (38.6 g), and sodium-dried toluene (140 ml) was added dropwise with stirring to a freshly prepared dispersion of sodium (8.0 g) in toluene (300 ml). The reaction mixture was allowed to reflux under nitrogen for 17 hours while being vigorously stirred. The cooled mixture was filtered, the solvent removed, and the residual liquid distilled to yield 14.29 g (74%) of 4,4,5,5- d_4 -bis-trimethylsiloxycyclohexene, bp $79^\circ/2$ mm.

(7) Using the procedure of Schräpler and Rühlmann,¹⁶ a mixture of 1 N hydrochloric acid (3.05 g), d_4 -bis-trimethylsiloxycyclohexene (14.02 g, 0.054 mole), and THF (16.3 ml) was heated at reflux temperature over a water bath for 1 hour. Powdered calcium carbonate (1.96 g) was added to the cooled reaction mixture, which was then stirred for 1 hour. The suspended solids were removed by filtration and the solvent removed under

vacuum. The resulting liquid solidified upon standing for a short time. This solid was removed from the flask and washed free of dark-colored contaminants with cold THF, leaving 3.40 g (54%) of 4,4,5,5-d₄-adipoin (α-hydroxycyclohexanone). Recrystallization from acetone produced white needles, mp 109-111°.

(8) A mixture of sodium borohydride (0.86 g) and d₄-adipoin (2.99 g, 0.025 mole) in absolute ethanol (300 ml) was stirred at room temperature for 18 hours. Saturated potassium carbonate solution (100 ml) was added and the biphasic mixture stirred vigorously for 3 hours. An additional 25 ml of the saturated solution was added, and after 45 minutes of further agitation, the ethanol phase was removed and dried over anhydrous potassium carbonate. The solvent was evaporated to yield 2.94 g of solid material, which upon recrystallization from toluene gave 2.33 g of 4,4,5,5-d₄-1,2-cyclohexanediol, mp 98-101°.

(9) A mixture of the d₄-diol (0.099 g, 0.8 mole), pyridine (1.1 ml), and methanesulfonyl chloride (0.7 ml) was kept in the refrigerator for 53 hours. The reaction mixture was dissolved in chloroform (20 ml) and washed with 10% hydrochloric acid solution (4 times with 10 ml), water (to neutrality), and saturated sodium chloride solution, and dried (MgSO₄). Removal of the solvent yielded 0.178 g (80%) of a brown solid. Recrystallization twice from ethanol gave fine white needles of 4,4,5,5-d₄-1,2-dimesylcyclohexane, mp 131.5-132.5°.

(10) Sodium iodide (5.07 g), d₄-dimesylcyclohexane (0.84 g, 3 mmole) and diglyme (15 ml, distilled from lithium aluminum hydride) were placed in a Carius tube which was then sealed, put in an oven, and heated at 160° for 46 hours. The contents of the cooled tube were quickly transferred to a 100 ml flask and crushed sodium thiosulfate (excess) was added. The tightly stoppered reaction mixture was stirred at room temperature for 3 hours before the entire liquid portion was distilled under reduced pressure (0.5 mm) and collected in a receiver cooled to -78°. This distillate was redistilled at atmospheric pressure and fractions were collected. The initial fractions were purified by preparative VPC using a

20M on 45/60 Chromosorb W,
20' x 1/2" column of 20% Carbowax Δ and the d_4 -cyclohexene peak was collected in a methylene chloride-filled receiver cooled to -78° . The solution was transferred to a small flask and *m*-chloroperbenzoic acid (0.43 g) was added. The cooled flask was swirled until the solid dissolved, stoppered, and left at room temperature for three hours. The reaction mixture was washed with 5% sodium hydroxide (8 ml), water (to neutrality), saturated sodium chloride (8 ml), and dried ($MgSO_4$). The solution was concentrated by cautious distillation of solvent from a warm (42.5°) water bath. This concentrated solution was chromatographed ^(VPC) Δ and several milligrams of 4,4,5,5- d_4 -cyclohexene oxide (II) was isolated.

1,2- d_2 -Cyclohexene

(1) Cyclohexene-1,2-dicarboxylic acid anhydride was heated with a ten-fold excess of water until a homogeneous solution was formed. The crude white solid which precipitated as the solution cooled was collected and recrystallized from water to yield 1,2-cyclohexane-dicarboxylic acid, mp $200-201^\circ$.

(2) The above product (2.5 g, 14 mmole) was dissolved in a mixture of methanol (4.0 g), benzene (10 ml) and concentrated sulfuric acid (1.7 g), and the solution was heated under reflux for seven hours, before being cooled and poured into water (25 ml). The layers were separated and the aqueous layer was washed with ether. The combined organic layers were washed to neutrality with saturated sodium bicarbonate and dried (Na_2SO_4). After removal of the organic solvents, the residual liquid was distilled to yield 1.8 g (65%) of dimethyl-1,2-cyclohexanedicarboxylate, bp $88-90^\circ/0.5$ mm.

(3) A mixture of the dimethyl ester (1.0 g, 5 mmole), methanol- $O-d$ (8.0 g), deuterium oxide (0.5 g), and anhydrous potassium carbonate (30 mg) was heated under reflux for 24 hours. The bulk of solvent was removed under reduced pressure (15-20 mm), and ether was added. The ether phase was washed to neutrality with water and dried (Na_2SO_4).

The solvent was removed under reduced pressure and the exchange was repeated twice. Following the third exchange, the crude product was distilled to yield 0.8 g (79%) of dimethyl-1,2-d₂-1,2-cyclohexanedicarboxylate, bp 88-90/0.5 mm. The NMR spectrum of this compound showed no resonance at $\delta = 2.72$ where the tertiary protons of the unlabeled compound appeared, indicating that the isotopic incorporation in the labeled compound was at least 90%.

(4) Sodium (4.6 g) was dissolved in portions in freshly prepared methanol-O-d (70 ml, > 95% d₁) over 1 1/2 to 2 hours. The temperature of the suspension was kept at 35-40° for 1 hour, while a continuous flow of nitrogen was passed through the apparatus. Dimethyl-1,2-d₂-cyclohexane-1,2-dicarboxylate (1.0 g, 5 mmole) and deuterium oxide (20 ml) were added cautiously to the warm reaction mixture, which caused precipitation of the d₂-diacid. The reaction mixture was heated to 50-60°, maintained at this temperature for 2 hours, allowed to cool, and poured into water (100 ml). The aqueous solution was neutralized and then made slightly acidic prior to extraction with ether. After removal of the ether solvent, the 1,2-d₂-cyclohexane-1,2-dicarboxylic acid was recrystallized from water yielding 0.62 g (71%) of white crystals, mp 199-201°.

(5) Lead tetraacetate (6.1 g) and the d₂-diacid (2.0 g, 12 mmole) were dissolved with stirring in dry DMSO under dry nitrogen. Dry γ -picoline (2.4 ml) was added and the suspension gently heated (40-45°) to attain homogeneity. The 1,2-d₂-cyclohexene formed was removed by the nitrogen flow and condensed at -78°. After 4 hours, the reaction was stopped and the condensate in the cold trap was analyzed by preparative VPC using a column of 20% Apiezon L on 60/80 Chromosorb W. The d₂-cyclohexene was easily separated from contaminating DMSO and γ -picoline on this column and 300 mg (30%) of pure product were obtained.

- 20 -

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LEGENDS TO FIGURES

Fig. 1 Mass spectrum (70 eV) of 1,2-cyclohexene oxide (MS-9 mass spectrometer, heated inlet system).

Fig. 2. Low voltage (nominal 12 eV) mass spectrum of 1,2-cyclohexene oxide (MS-9 mass spectrometer, heated inlet system).

Fig. 3. Mass spectrum (70 eV) of 2-cyclohexene-1-ol (MS-9 mass spectrometer, heated inlet system).