Epoxides and *trans*-chlorohydrins of 3-methoxycyclopentene and their use in conformational studies in the cyclopentane system^{1,2}

E. J. LANGSTAFF AND R. Y. MOIR

Department of Chemistry, Queen's University, Kingston, Ontario

AND

R. A. B. BANNARD AND A. A. CASSELMAN Defence Chemical Biological and Radiation Laboratories, Ottawa, Canada Received August 16, 1967

The stereoisomeric oxides of 3-methoxycyclopentene (3 and 4) and the four *trans*-chlorohydrins of the same olefin (6-9) were prepared by methods resembling those used previously in the cyclohexane system. Structure proofs were more difficult than in the cyclohexanes, but served to illustrate some interesting chemistry. Product ratios in the cleavage of each of the epoxides with hydrogen chloride were used to deduce the probable conformations of the four transition states, by comparing the results with those from the cyclohexane system. An unexpected outcome of the work was the new convincing evidence obtained for the intervention of chloronium ions in the addition of "hypochlorous acid" to the olefin.

Canadian Journal of Chemistry, 46, 3649 (1968)

For the past several years we have been interested in forming a reasonably accurate picture of the transition states involved in the formation and scission of the oxirane ring in the stereoisomeric oxides of 3-methoxycyclohexene (1 and 2) (1-8). Our approach has been that the model chosen for the transition state must explain both the relative rates of formation of the oxides from various halohydrins and the product ratios obtained in the scission of the oxides. In the present paper we report the synthesis of the corresponding compounds in the cyclopentane series and a study of the scission products of the epoxides (3 and 4). Kinetic studies of the rates of formation of the oxides will be reported later. From the comparison of the results in the two series, a clear picture emerges of the conformation of the transition states in the cyclopentane series.



¹Most of this work was presented at the National Meeting of the Chemical Institute of Canada, in Toronto, June 6, 1967.

²Discussion of recent related work has been added after the first submission.

Synthesis

Treatment of 3-methoxycyclopentene (5a) (9) with chlorine and sodium carbonate in aqueous acetone (10) gave a mixture of chlorohydrins from which two (6 and 7) were readily separated in pure form by preparative gas-liquid chromatography (g.l.c.). The chlorohydrin 6 on treatment with aqueous alkali gave *cis*-3-methoxycyclopentene oxide (3), and the chlorohydrin 7 gave the isomeric *trans*-oxide (4). A mixture of the two



oxides (3 and 4) was also obtained directly by the reaction of *meta*-chloroperbenzoic acid with the olefin, the *trans*-oxide predominating. Larger quantities of the oxides were prepared by the action of aqueous alkali either upon the crude chlorohydrin mixture obtained as above, or upon the mixture of bromohydrins resulting from the action of aqueous N-bromosuccinimide upon the olefin (5a), just as in the cyclohexane series (1, 4). The resulting oxide mixtures were separated by preparative g.l.c., the *trans*-oxide being obtained in much larger yields, as in the other series.

Treatment of the cis-oxide (3) with a cold solution of hydrogen chloride in ether gave a

20 -

CANADIAN JOURNAL OF CHEMISTRY. VOL. 46, 1968

mixture from which the chlorohydrin 8 was obtained in good yield by preparative g.l.c. Its stereoisomer 9 was formed in very high yield as the only detectable product from the similar reaction of the *trans*-oxide (4). Thus all four *trans*chlorohydrins of 3-methoxycyclopentene (6-9) had been obtained pure in amounts large enough for the kinetic studies.



Proofs of Structure

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The structures given above have been thoroughly verified in four different ways. One of these, the last to be accomplished, has already been published in another connection (19).³ The other, earlier proofs remain separately valid, add independent support to that already given (19), and are interesting in respect to the chemistry of cyclopentane.

To begin with, analogies with the corresponding cyclohexane compounds (and the underlying theory) were used to predict the structures of the oxides and chlorohydrins of the present series. These predictions proved to be entirely correct. In both series, the *cis*-oxide has the higher boiling point and higher index of refraction, as could be expected for the more internally hindered, more compact, structure (12, 13). In both series, the order of elution (gas-liquid chromatography) of the four isomeric chlorohydrins was the same, in terms of the steric orientation of the substituents. In both series, the stereoisomeric oxides were opened with hydrogen chloride to give mainly the 1-chloro-2-hydroxy-3-methoxycyclanes (e.g. 8 and 9), while the olefins reacted with "hypochlorous acid" to give mainly the 2-chloro-1-hydroxy-3-methoxycyclanes(e.g. 6 and 7). This was to be expected if, as always observed previously, the polar effect of methoxy predominates over steric effects in the opening either of the oxirane ring or the chloronium ion ring (1, 2, 5-8, 14-16).

The next proof obtained relied upon contrasting the products obtained from 3-methoxycyclopentene (5a), "active chlorine", and water with those from the olefin 5b, "active chlorine", and methanol. One would expect, by analogy with the reaction of aqueous N-chlorosuccinimide with olefins (7) and by the accepted theory of addition of halogens in methanol (17, 18) that methanolic N-chlorosuccinimide would attack an olefin to give methoxyl and chlorine adjacent and trans to each other. It therefore follows⁴ that of the four chlorohydrins (6-9) only 6 could be produced by the action of methanolic N-chlorosuccinimide upon 3-hydroxycyclopentene (5b), provided that no group wandering occurred due to neighbor participation. Careful consideration seemed to show that the only rearrangement to be expected was that involving the intermediate ion 10; conceivably it might have reacted via the epoxide 11 (or its conjugate acid) to give 9, a transchlorohydrin different from 6, the only possibility in the absence of rearrangement. Fortunately 6 and 9 could easily be distinguished by nuclear magnetic resonance (n.m.r.) spectroscopy.



The reaction was actually found to give one, and only one, of the *trans*-chlorohydrins of 3methoxycyclopentene, and from its spectrum it was clearly 6 rather than 9. Similarly, when the olefin 5b was treated with methanolic N-bromosuccinimide, and the product allowed to react with aqueous base, some *cis*-oxide (3) but no *trans*-oxide (4) was formed. From these observations the structures of both oxides and all four chlorohydrins followed (see below).

The third proof was simpler and more direct. The chlorohydrin thought to be 9 was dehalogenated by the method described previously (19) to give a methoxycyclopentanol (12) which proved to be identical with authentic *trans*-2-methoxycyclopentanol (20) made by the alkali-catalyzed methanolysis of cyclopentene oxide. This settled

³Note added in proof: The chlorohydrins (6–9) were each separately related to the 1,2- and 1,3-cyclopentanediols. We take this occasion to acknowledge the important work of Sable and Posternak (11) in establishing the configurations of some of the latter.

⁴Space does not permit a full outline of the argument. Analogy with the products obtained by an identical mode of addition of the elements of hypochlorous or hypobromous acids with 3-methoxycyclenes (6-8) would predict a low yield of 6, because of the concurrent formation of *cis*-1,2-chlorohydrins or of 1,3-chlorohydrins. This does not spoil the proof since the formation of 7-8 is not possible. Fortunately also, none of the possible impurities in the 3-hydroxycyclopentene could lead to 6.

the relative position and configuration of methoxyl and hydroxyl. The position and orientation of the chlorine (in 9) followed from the conversion of the chlorohydrin by alkali to an epoxide (from which 9 could be regenerated with hydrogen chloride). The epoxide concerned could only have been the trans-isomer (4). (Its alternative formation from a peracid and olefin confirmed the presence of the epoxy-group, as did the presence in the infrared spectrum (21) of a band near 3040 cm^{-1} , absent in the chlorohydrin.) This same epoxide (4) could also be formed from another chlorohydrin, whose structure was therefore 7. The structure 3 clearly belonged to the stereoisomeric epoxide, and the two remaining chlorohydrins, both of which gave 3 with aqueous alkali, must have been 6 and 8. These two were finally distinguished by the n.m.r. spectra of their p-nitrobenzoates.⁵

In the *p*-nitrobenzoates of the chlorohydrins (13–16), the signal from H_x (geminal to the *p*-nitrobenzoxy group) was recognizable as the one farthest downfield (2, 7). Furthermore 15 and 16

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could be distinguished from 13 and 14 because the signal from H_x showed a much simpler coupling pattern for 15 and 16 than for the other pair. Similarly the signal from H_y showed a simpler pattern in 13 and 14 than in 15 and 16, as expected from the number of adjacent hydrogens. Thus 6 and 8 could be distinguished through the spectra of their *p*-nitrobenzoates (13 and 15, respectively), and the proof was complete. However, unlike the situation for the analogous cyclohexane compounds (7), the coupling patterns of H_y in 13 and 14, and of H_x in 15 and 16, could not be used for a completely independent determination of all four structures.⁵ The spectra are illustrated in Fig. 1.

Product Distribution in the Oxide Scissions with Hydrogen Chloride

In previous papers (1, 2, 5-8) we have set forth qualitatively the factors believed to influence the direction of oxide scission in the cyclohexane derivatives 1 and 2. Briefly, if Y is the ratio of product yield from attack at position-1 to that from attack at position-2, and k_1 and k_2 the respective rate constants, then by the usual approximations of transition state theory:⁶

$$\ln Y = \ln \frac{k_1}{k_2} = \frac{\Delta^2 F^{\ddagger}}{RT}.$$

Here, however:

$$\Delta^2 F^{\ddagger} = F_2^{\ddagger} - F_1^{\ddagger}$$

where F_2^{\ddagger} is the standard free energy of the transition state leading to scission at position-2, and F_1^{\ddagger} that of the transition state leading to scission at position-1. (The energies of the common ground state and of the other participants cancel.) Presumably the transition states for oxide scission and formation are essentially identical,⁷ and as will be shown in later papers, the kinetics

⁶The equations describe a particular case of the Curtin-Hammett Hypothesis (24). It is assumed that the conformational changes are relatively very fast, and that the product ratio is rate-controlled. The second assumption seems firmly based on the rather well-known chemistry of oxides (25) and is also supported by considerable evidence in the two series described here. In the cyclohexane series, the thermodynamically *less* stable product predominates in the scission of the *trans*-oxide. Furthermore, the product ratio does not vary appreciably when the nucleophile is changed from one giving a possibly reversible reaction (e.g. bromide or chloride) to one where reversibility is impossible (e.g. methoxide) (8). As will be shown later, yields and rates can be combined in a coherent system on this assumption. Less evidence is as yet available in the cyclopentane system, but aside from analogy, the fact that the kinetics of oxide closure show the same anomaly as the product ratio in oxide scission or chloronium ion scission seems to leave no doubt that rate control still applies in the new system.

⁷This seems a reasonable hypothesis for base-catalyzed scissions, strengthened in the cyclohexane work (8) by the observation that variations in the nucleophile caused little difference in the product ratios. It is of course not obvious that acid-catalyzed scissions have transition states similar geometrically to those for base-catalyzed scission, but the previously recorded observations (8) seem to make it clear that in the cyclohexane series, they do. The point has not yet been thoroughly verified in the cyclopentane series, but the regularities mentioned in footnote 6 seem to allow no other interpretation.

⁵Problems in the nuclear magnetic resonance spectroscopy of cyclopentane derivatives have been discussed by Professor Sable and his colleagues (16, 22, 23).



Proton magnetic resonance spectra of the paranitrobenzoates of the trans-chlorohydrins of 3-methoxy-FIG. 1. cyclopentene, taken at 60 MHz. Values on the scale are in Hz downfield from tetramethylsilane. (a) Compound 16, in pyridine- d_5 at 47 °C. Inset: at slightly different conditions, and offset. The spectrum in chloroform-d at 40° is similar. b) Compound 13, in pyridine- d_s at 47°C. Inset: at signify different conditions, and offset. The spectrum in chloroform-d at 40° is similar. (b) Compound 13, in pyridine- d_s at 47°. Inset is from an otherwise similar spectrum in chloroform-d solution at 40°. Peaks within 10 Hz to the left of methoxyl are spurious. (c) Compound 15, in pyridine- d_s at 74°. The inset was taken at slightly lower radio frequency field strength and spectrum amplitude, and is offset. The spectrum of a chloroform-dsolution at 40° was similar. (d) Compound 14, in pyridine- d_s at 74°. At 47° in pyridine- d_s , and in chloroform-d at 40°, the signal from H_x was a long, rounded hump with many scarcely discernable, small peaks, and the signal from H_y, less clearly resolved than in Fig. 1, had the appearance of a triplet, but on a pedestal.

of oxide formation show that the transition state is much more like the chlorohydrins than the oxides. Thus ordinary conformational analysis may be brought to bear to explain both the rates of oxide formation and the product ratios from oxide scission. This has now been done in several series of cyclohexane compounds (8).

In the present cyclopentane series, as in the cyclohexane series, scission of either stereoisomeric oxide (1 and 2, or 3 and 4) with hydrogen chloride gave mainly the 1-chloro compounds. This is attributed to an overriding inductive⁸ effect of methoxyl. However, a striking difference appears in the minor products of scission of the two series. In the cyclohexane series, the transoxide (2) gave appreciable amounts of scission at position-2, while the cis-oxide (1) gave no detectable amounts of minor product. The cyclopentane derivatives were just the opposite in this respect, the cis-oxide (3), but not the trans-oxide (4), giving appreciable amounts of scission at position-2.

An explanation of this difference in conformational terms proved surprisingly demanding, and clearly led to one particular set of conformations, among the many available in the cyclopentane series (24), as most probable for the transition states. Preferred conformations in the cyclopentanes and in the presumably related furanoses have been discussed by Hall (26) by Bishop and Cooper (27), and by Tolbert et al. (16), and the probable conformations, as well as the ambiguities in deciding which are in fact occupied, have been well described. Our work differs some-

3652

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⁸The term is used in the widest sense, as before (8). Polar effects in the scission of cyclopentene oxides have been discussed by Sable and his colleagues (14-16), and in particular Tolbert et al. (16) observed a major and a minor product in the scission with aqueous acid of (3/4)-3,4-dihydroxycyclopentene oxide in a ratio much like those observed in the present series.

what from that reported previously. Nearly all the former discussions have been concerned with ground state conformations. In the present work, the conformations of transition states alone are at issue, as shown above, involving molecular geometries much more strained than would be allowable in the ground states. In the present work, ambiguity has been largely removed by the insistence that the explanation be consistent for the *complete set* of stereoisomers, and for the cyclohexane and cyclopentane series at the same time. It turned out that our set of compounds was just large enough for removal of the ambiguities. The following discussion has been based on a very thorough study of the models.

It appears that only the particular set of slightly distorted twist conformations 17-20 (charges and the state of protonation being omitted) provide an adequate basis for the explanation. Space does not permit a full explanation of how the many other possibilities were eliminated, but this will be obvious from the experimental results and from a study of the models, remembering that the carbon bearing the chlorine will approach sp^2 geometry, that the chlorine and oxirane oxygen need to be close to trans-diaxial geometry, and that torsional and close-approach interactions need to be minimized. Structures 17 and 18 represent transition states for the scissions of the cis-oxide (3); 19 and 20 for the trans-oxide (4). Structures 17 and 19 are for the "normal" scissions at position-1, structures 18 and 20 for the "abnormal" scission at position-2. Abnormal scission of the cis-oxide of the cyclohexane series (1) is relatively unfavorable because of the 1,3-diaxial methoxyl and oxygen; this effect⁹ is absent in 18, so that more abnormal scission would be expected in the cyclopentane series (as observed). A 1,3-diaxial-like interaction interferes with normal scission at position-1 of the *trans*-oxide in both series (e.g., in 19); however, in the cyclopentane series (but not in the cyclohexanes) a still more serious interference occurs with abnormal scission. In 20 there is marked interference of a semieclipsing type between methoxyl and chlorine; the methoxyl cannot readily escape from this by distortion of the geometry, since it is trapped

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between the neighboring hydrogens. Escape into alternative conformations can only be had at the expense of almost eclipsing the four hydrogens on the unsubstituted carbons. Thus abnormal scission should be less favored in the *trans*-cyclopentane compound than in the cyclohexane, again as observed. This simple and elegant explanation, which arose entirely out of the present work, was also found to account for the relative rates of reaction of all four chlorohydrins with alkali, and their differences from the cyclohexane series. As will be shown in a later paper, all the factors mentioned above also appear clearly in the kinetics. Thus the suggested model has passed a very severe set of experimental tests.

One of the most interesting consequences of this analysis is the provision of strong evidence in favor of the chloronium ion as an intermediate in the formation of chlorohydrins from olefins. It is true that this is the currently accepted hypothesis, but as has been previously pointed out (17) the actual evidence is very slender.¹⁰ In an earlier paper (7) we expressed our misgivings in that a free carbonium ion, electrostatically but not covalently held by a neighboring group, could at least as well explain our experimental results. Later (8) we showed that a comparison of

⁹Tolbert *et al.* (16) have drawn attention to this vital difference between the cyclohexanes and cyclopentanes in supporting a diaxial-dihydroxy conformation for an isopropylidene derivative in the latter series.

¹⁰Poutsma's review (28) appeared after the first submission of this paper. Fahey and Schubert (29) offered evidence for chloronium ion intervention in the structure of *olefinic* products. Poutsma (30) showed that in nonpolar solvents the rate of chlorination shows a lack of positional effects for alkyl groups. The evidence for bromonium ion participation is of course stronger (17). For series related to the present one, Hasegawa and Sable (31) have called attention to the analogy between oxide and bromonium ion scission in neighbor-participation reactions. Another analogy between oxides and bromonium ions had been previously pointed out by Bannard *et al.* (6).

CANADIAN JOURNAL OF CHEMISTRY. VOL. 46, 1968

the product ratios of chlorohydrin formation from olefin with those from oxide scissions showed parallels that suggested that threemembered rings were involved in both reactions. This parallel is now very much strengthened by the observation that the chlorohydrin yields from olefins show the same sort of differences between the cyclopentanes and cyclohexanes as do the oxide scissions. Thus in both series the predominant isomers are those (e.g., 6 and 7) resulting from scission at position-1 of the chloronium ion, as expected from the large inductive effect of methoxyl. However, whereas some 9 is formed in the reaction of "hypochlorous acid" with 5a, i.e. corresponding to "abnormal" scission at position-2 of the cis-chloronium ion (21), none of the corresponding "abnormal" isomer could be detected in the cyclohexane series (7). Similarly, although no 8, corresponding to "abnormal" scission of the trans-chloronium ion (22), could be detected in the present reaction, in the cyclohexane series the isomer representing



scission of the *trans*-chloronium ion at position-2 was formed in considerable amounts (7). It will be obvious that an analysis of the chloronium ion scissions similar to that done above for 17-20 of the epoxides (but with oxygen and chlorine exchanging roles as required) would lead to these observations as expected results, and that it would be difficult or impossible to explain them on the basis of any other currently favored mechanism.

Experimental

Infrared (i.r.) spectra were taken on a Perkin-Elmer model 21 spectrometer, repeatedly calibrated with polystyrene. Quoted comparisons are for spectra of chloroform solutions. The refractometer was calibrated with water at each use, and temperatures reported in its use are accurate to about $\pm 0.1^{\circ}$. Proton resonance spectra (p.m.r.) were determined on a Varian A-60 instrument at 60 mHz, tetramethylsilane being used as the internal standard with each sample. All preparative gas-liquid chromatographic (g.l.c.) separations were performed with a Fisher Preparative Partitioner, using 6 ft × 1 in. glass columns filled with 10% Versamid 900 on Chromosorb. Analytical g.l.c. was performed on a Jarrell-Ash model 700, using an electron-affinity detector. Quantitative g.l.c. analyses are from uncorrected peak areas, All analytical samples of liquids were shown (with two exceptions as noted) to be homogeneous by g.l.c. on columns shown able to distinguish the corresponding isomers. Melting points were determined on a precision apparatus (32), with calibrated short stem thermometers totally immersed in the bath. Boiling points are uncorrected.

DL-O-Methyl-2-cyclopenten-1-ol (3-Methoxycyclopentene) (5a)

The method is that of Alder and Flock (9). Freshly prepared, undistilled 3-chlorocyclopentene (350 g, n_D^{25} 1.4740 uncorrected) (37) was added slowly over a period of about 80 min to a slurry of sodium bicarbonate (400 g) in methanol (1100 ml) which was kept at -10° and vigorously stirred during the addition. Stirring was continued an additional 2 h. Enough water was then added to bring about the formation of two layers. The lower layer was extracted with ether, the ether extract united with the upper layer, dried, and fractionally distilled. The fraction of b.p. 55-106° was washed twice with water, dried, and redistilled to give product, b.p. 106-108°, n_D^{25} 1.4362, in a yield of 183 g (53 %), (lit. (9), 108°, n_D^{20} 1.4393). Analysis by g.l.c. showed the presence of about 1% of impurity.

Anal. Calcd. for $C_6H_{10}O$: C, 73.41; H, 10.28. Found: C, 73.51; H, 10.15.

In addition there was produced a rubber (8.6 g) and a high-boiling, evil-smelling liquid (15.9 g). At a reaction temperature of 20°, the rubber was the main product.

Reaction of 3-Methoxycyclopentene with

"Hypochlorous Acid"

(a) The reaction with water and N-chlorosuccinimide, which gave excellent results with 3-methoxycyclohexene (7), and moderate yields with cyclopentene, gave only intractable tars with 3-methoxycyclopentene.

(b) The source of hypochlorous acid is that of Sumrell et al. (10). Water (100 ml), acetone (450 ml), sodium carbonate (25 g), and 3-methoxycyclopentene (42 g, n_D^{25} 1.4370) were rapidly stirred while chlorine was slowly bubbled into the solution for about 1 h, until a distinct second layer formed and further chlorine tended to lighten the dark color. (During a similar, larger preparation, the temperature rose from 23 to 42°, then fell.) The resulting bottom layer was extracted twice with 50 ml portions of ether. The ether extracts were united with the upper layer, dried, and distilled, three fractions being collected: (1) b.p. $30-48^{\circ}/15 \text{ mm}$, n_{D}^{25} 1.4630, 3.4 g; (2) b.p. $48-105^{\circ}/15 \text{ mm}, n_{D}^{25} 1.4789, 23.2 \text{ g; and (3) b.p.}$ $60-85^{\circ}/0.03 \text{ mm}, n_{D}^{25} 1.4842, 19.8 \text{ g. Analytical g.l.c.}$ (10 ft column, neopentylglycol sebacate, 70°, 20 p.s.i.) showed for fraction (1), five peaks with retention times less than 10 min, for fraction (2) the same five peaks plus two new ones of much longer retention times, and for fraction (3), five initial peaks of much lower amplitude plus the same two peaks of fraction (2).

Two other preparations were made; each was partially separated by distillation as above (to facilitate the subsequent separation by g.l.c.). Preparative separation was then performed on material from all the runs at $100^{\circ}/$ 20 p.s.i. Material corresponding to the first five peaks above was collected as fraction (a), material corresponding to the first peak of long retention time as fraction (b),

3654

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TABLE I Gas-liquid chromatography characteristics of the methoxychlorocyclopentanols

Compound	Retention time on column of:			
	10% NGS on Embacel*	10% Versamid-900 on Chromosorb P†	30% DEGS on Anakrom‡	10% S.E. on Fluoropak
8 6 9 7	8.5 12.5 21.8 29.5	5 9 16.5 23	6.5 11 17.5 24	7.5 7.5 9 13

*6 ft $\times \pm$ in. column, 70°, 20 p.s.i. †45/60 mesh,5 ft \times 3/8 in. aluminium column, helium flow rate 300 ml/min. ‡60/70 mesh, 10 ft \times 3/8 in. aluminium column, same flow rate. §5 ft \times 3/8 in. aluminium column, helium flow rate 150 ml/min.

and material corresponding to the second peak of long retention time as fraction (c). Approximately 15 g were collected in each of (b) and (c). Each fraction was distilled through a small column, kept 15 months, then redistilled successively from a Claisen flask and then in a Späth apparatus just before analysis and use in kinetic studies.

The total crude product from one of these later, larger preparations was vacuum distilled to give a complete "chlorohydrin" fraction, b.p. 50-80°/0.04 mm, yield 58.3%, and this unfractionated material was analyzed on a 6 ft $\times \frac{1}{4}$ in. column packed with 10% neopentylglycol sebacate polymer on Embacel at 80° and 20 p.s.i. The peak areas (normalized to a total yield of 48%) suggested the following yields:

3-chloro-1-O-methyl-(1,3/2)-1,2-cyclopentanediol (9), 1.9%;

3-chloro-1-O-methyl-(1,2/3)-1,2-cyclopentanediol (8), absent;

2-chloro-1-O-methyl-(1,3/2)-1,3-cyclopentanediol (6), 15%;

2-chloro-1-O-methyl-(1,2/3)-1,3-cyclopentanediol (7), 10%; and

two unknown products (probably dichlorides), 12% Partial fractionation and preparative v.p.c. then followed as above.

DL-2-Chloro-1-O-methyl-(1,3/2)-1,3-cyclopentanediol (6) Fraction (b) obtained just above was a clear colorless

oil, b.p. 65–75°/0.01–0.02 mm, n_D^{25} 1.4748. Anal. Calcd. for C₆H₁₁O₂Cl: C, 47.86; H, 7.36; Cl,

23.55. Found: C, 47.98; H, 7.33; Cl, 23.52. The p-nitrobenzoate was obtained in a yield of 64%

after three recrystallizations, m.p. 67.7-68.9°

Anal. Calcd. for C13H14O5NCl: C, 52.07; H, 4.71; N, 4.68; Cl, 11.84. Found: C, 52.11; H, 5.01; N, 4.71; Cl, 11.89.

The 2,4-dinitrobenzenesulfenate was obtained in a yield of 60%, m.p. 96.9–98.2°.

Anal. Calcd. for C12H13O6N2SCI: C, 41.30; H, 3.76; S, 9.20. Found: C, 41.42, 41.50; H, 3.57, 3.63; S, 9.36, 9.43.

DL-2-Chloro-1-O-methyl-(1,2/3)-1,3-cyclopentanediol (7) Fraction (c) was also obtained as a clear, colorless oil, b.p. 75–80°/0.01–0.02 mm, $n_{\rm D}^{25}$ 1.4815.

Anal. Calcd. for C₆H₁₁O₂Cl: C, 47.86; H, 7.36; Cl, 23.55. Found: C, 48.12; H, 7.27; Cl, 23.61.

The p-nitrobenzoate was obtained in a yield of 93% after one recrystallization, m.p. 63.5-64.6°.

Anal. Calcd. for C13H14O5NCI: C, 52.07; H, 4.71; N, 4.68; Cl, 11.84. Found: C, 52.28; H, 4.88; N, 4.60; Cl, 11.81.

Gas-liquid chromatographic characteristics of the four stereoisomers are given in Table I. It will be observed that excellent separations of all four isomers are possible, and that the order of elution is the same on all columns tried.

DL-2-Cyclopenten-1-ol (3-Hydroxycyclopentene) (5b)

In our hands the method of Alder and Flock (9) was superior to that used by Bergstahler and Nordin (33) for the corresponding cyclohexene derivative. By the former method, crude 3-chlorocyclopentene (37) (240 g) was converted to crude 3-hydroxycyclopentene, b.p. 40-80°/ 14 mm, judged by g.l.c. to contain about 75% of the desired compound (retention time 5.3 min) as well as two impurities (retention times 1.9 and 8.5 min, respectively), the first impurity peak having about twice the area of the second. The i.r. spectrum showed a large hydroxyl absorption. Further purification was not practicable owing to the rapid decomposition of the material. Other runs showed a more complex set of impurity peaks, suggesting that decomposition in the flash evaporator might have been the source of some of them.

The p-nitrobenzoate after two recrystallizations from ethanol had m.p. 79.5-80.5°.

Anal. Calcd. for C₁₂H₁₁O₄N: C, 61.77; H, 4.76; N, 6.01. Found: C, 61.60; H, 4.82; N, 6.07.

Another run gave crude 3-hydroxycyclopentene approximately 85% pure by g.l.c. It was used in the preparations reported below.

The Stereoisomeric Oxides of 3-Methoxycyclopentene (3 and 4)

(a) A mixture of stereoisomeric chlorohydrins prepared as above from 3-methoxycyclopentene and "hypochlorous acid" was partially separated by fractional distillation. Each fraction was allowed to react, with stirring, with a slight excess of aqueous sodium hydroxide at 65° for a few min, until the oily layer moved to the top. Ethereal extracts of the acidified lower layers were united

with the top layers, dried, and fractionally distilled; this partial separation facilitated the next step. Preparative gas chromatography was carried on with manual programming between 100 and 130° and 20-28 p.s.i.; the traps were kept in a bath of dry ice and acetone. The final yields were 12.9 g (41%) of the *trans*-oxide (4) and 2.8 g (9%) of the *cis*-oxide (3) based on the original *olefin* used.

(b) A crude mixture of isomeric bromohydrins (157 g, approximately 70% yield) was obtained by the reaction of 3-methoxycyclopentene with N-bromosuccinimide and water in the same way described for the cyclohexene analogue (6). The mixture was allowed to react with a solution of sodium hydroxide (30 g) in water (250 ml) at room temperature, with vigorous stirring, until an upper layer appeared. This was removed, and the water layer allowed to react a further 15 min. After acidification, the water layer was extracted with five 50 ml portions of ether. Separation and isolation were achieved in the same way as described above. The final yield was 32.4 g of the *trans*-oxide (4) and 12.5 g of the *cis*-oxide (3), a total yield of 47.5%, based on the *olefin* used.

(c) A solution of meta-chloroperbenzoic acid (80 g) in anhydrous ether (350 ml) at -20° was treated with 3-methoxycyclopentene (43 g, 95-99% pure by g.l.c., the impurity being methanol). After being kept 3 days at -20° , the solution still showed (g.l.c.) much unreacted olefin. It was therefore allowed to warm up slowly. A vigorous reaction ensued with the evolution of heat. When this subsided, olefin was still present (g.l.c.), but after the mixture had been heated 1.5 h under reflux, only a trace of olefin remained. The excess peracid was destroyed by washing the solution with three 30 ml portions of 10% aqueous ferrous sulfate, then with three 30 ml portions of 10% aqueous sodium hydroxide, and finally with two portions of water. The ethereal layer was then dried and distilled in vacuo. Mixed oxides were obtained in a yield of 17.4 g (35%), the cis- and transoxides being present in the ratio 1:6, respectively, as judged by the peak areas in g.l.c. (The oxides were identified by peak enhancement using authentic samples.) All g.l.c. analyses were performed in a 4 ft $\times \frac{1}{4}$ in. stainless steel column packed with 10% neopentylglycol sebacate on Embacel at 65-75° and 15-25 p.s.i.

(d) A mixture of N-bromosuccinimide (267 g) and methanol (600 ml) was brought to reflux temperature, and then freshly prepared 3-hydroxycyclopentene (crude, 85% pure by g.l.c., approximately 134 g judged by volume and g.l.c. analysis) (see above) was slowly added at such a rate that the mixture continued to boil. When the reaction had subsided, the solution was cooled, most of the methanol removed on the rotary evaporator, and the resulting oil filtered from the precipitated succinimide, and distilled. The distillate (b.p. 30-100°/0.3 mm) was dissolved in water. Aqueous sodium hydroxide was slowly added with vigorous stirring over about 20 min, until the mixture remained basic for 5 min. The mixture was then neutralized, the aqueous layer twice extracted with 50 ml portions of ether, the ether extract united with the upper layer, dried, and distilled to yield two fractions: (1) b.p. $60-72^{\circ}/0.1$ mm, 18.3 g; and (2) b.p. $72-100^{\circ}/$ 0.1 mm, 201.9 g. Analysis on a 6 ft $\times \frac{1}{4}$ in. column filled with 10% neopentylglycol sebacate on Chromosorb, at 60° and 23 p.s.i., fraction (1) showed the following peaks: (a) a large peak, retention time 5.25 min (from cyclopentenone, see below), (b) a minor peak, retention time 9.00 min (unknown) and (c) a large peak, retention time 10.50 min, reinforced by the addition of authentic cis-oxide (3), whose retention time was the same. The retention time of authentic trans-oxide on the same column was 5.00 min. When authentic trans-oxide (4) was added to the sample, peak (a) was enlarged but the shape of the peak was changed, indicating two incompletely separated substances. Fraction (1) was separated on the Fisher Prep Partitioner, two major fractions being obtained: (i), corresponding to peak (a), was shown by the i.r. spectrum to be an unsaturated ketone. Some of the material (1.12 g, 99.5% pure by g.l.c.) was converted to its 2,4-dinitrophenylhydrazone, m.p. 167.2-168.4°. A twice crystallized sample was used for analysis. Its i.r. spectrum was identical to that of an authentic sample (34) of the 2,4-dinitrophenylhydrazone of Δ^2 -cyclopentenone kindly given us by Dr. S. Wolfe and W. R. Pilgrim, and the mixture m.p. showed no depression.

Anal. Calcd. for C₁₁H₁₀N₄O₄: *C*, 50.36; H, 3.89; N, 21.38. Found: C, 50.67; H, 4.47; N, 21.07.

Fraction (*ii*), corresponding to peak (*c*) above, from the preparative v.p.c. was shown by retention time and peak enhancement on an analytical column, by refractive index, and by its i.r. spectrum to be identical to *cis*-3-methoxycyclopentene oxide (**3**) obtained from methods (*a*) and (*b*).

The large fraction (2) from the initial distillation showed on the same analytical column only one major peak with a retention time of 75 min. It gave no oxide on further treatment with base, and has not been further investigated.

(e) Pure 3-chloro-1-O-methyl-(1,3/2)-1,2-cyclopentanediol (3.00 g, n_D^{25} 1.4747) was stirred with a solution of sodium hydroxide (0.9 g) in water (10 ml) until all the oil had disappeared (about 10 min). The mixture was carefully neutralized with hydrochloric acid, and extracted with four 30 ml portions of ether. The dried ether extracts were distilled in the Späth apparatus to give 1.85 g (90%) of a clear colorless oil, whose i.r. spectrum was identica to that of pure *trans*-3-methoxycyclopentene oxide (4).

(f) Pure 2-chloro-1-O-methyl-(1,2/3)-1,3-cyclopentanediol (n_D^{25} 1.4815) was similarly treated and the product, isolated in the same way in 93% yield, also gave an i.r. spectrum identical to that of pure *trans*-3-methoxycyclopentene oxide (4).

(g) Pure 2-chloro-1-O-methyl-(1,3/2)-1,3-cyclopentanediol (n_D^{25} 1.4748), treated in the same way, gave an 88% yield of an oil whose i.r. spectrum was identical to that of the *cis*-3-methoxycyclopentene oxide (3) of the united sample below.

Corresponding purified fractions of the oxides from methods (a) and (b) were united.

DL-2,3-Epoxy-1-O-methyl-(1/2,3)-1-cyclopentanol

(trans-3-Methoxycyclopentene Oxide) (4)

The united preparations mentioned above were obtained as a colorless liquid, b.p. $35-37^{\circ}/9$ mm, $n_{\rm D}^{25}$ 1.4400.

Anal. Calcd. for $C_6H_{10}O_2$: C, 63.11; H, 8.83. Found: C, 63.22, 63.20; H, 9.01, 9.10.

DL-2,3-Epoxy-1-O-methyl-(1,2,3/)-1-cyclopentanol

(cis-3-Methoxycyclopentene Oxide) (3)

The united preparations above formed a colorless

3656

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liquid, b.p. $48-50^{\circ}/9.0$ mm, n_D^{25} 1.4468. However, the analytical sample was from preparation (g) above. It contained about 0.3% of an unknown impurity, not the *trans*-oxide. This sample was also used as the standard for the i.r. spectrum.

Anal. Calcd. for $C_6H_{10}O_2$: C, 63.11; H, 8.83. Found: C, 62.86; H, 8.86.

On a 6 ft $\times \frac{1}{4}$ in. copper column packed with 10% butanediol succinate polymer on Embacel at 85° and 25 p.s.i., the *trans*-oxide (4) had a retention time of 6.0 min, and the *cis*-oxide (3) a retention time of 9.0 min.

DL-3-Chloro-1-O-methyl-(1,3/2)-1,2-cyclopentanediol (9) Scission of the trans-Oxide with Hydrogen Chloride

A solution of pure trans-3-methoxycyclopentene oxide $(27.5 \text{ g}, n_D^{25} 1.4395)$ in anhydrous ether (50 ml) was cooled to -50° , saturated with dry hydrogen chloride, kept for 1 h at -50° , and then allowed to warm slowly to room temperature. Some hydrogen chloride was removed in a stream of air drawn through the solution, and the rest by five washings with water (325 ml in all) (200 ml more ether being added). The ether layer was dried and fractionally distilled through a small column to give three fractions: (1) b.p. up to $55^{\circ}/0.02$, very small amount; (2) $55-65^{\circ}/0.02$, 19.2 g; and (3) $65-155^{\circ}/0.02$ mm, nearly all at 155° , 5.1 g. Fraction (1) did not warrant further attention. Fraction (2) showed a single, sharp peak in the g.l.c., and fraction (3) the same peak plus a larger new peak of longer retention time. The n.m.r. spectrum of fraction (3) was almost identical to that of fraction (2), although its b.p. was considerably higher, suggesting that the former was a condensation product of the latter. Fraction (2) was a clear, colorless oil n_D^{25} 1.4747, b.p. 55-65°/0.02 mm.

Anal. Calcd. for $C_6H_{11}O_2Cl$: C, 47.86; H, 7.36; Cl, 23.55. Found: C, 47.83; H, 7.40; Cl, 23.45.

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The *p-nitrobenzoate* was obtained in a yield of 72% after three recrystallizations, m.p. 68.0-69.2°.

Anal. Calcd. for $C_{13}H_{14}O_5NCl: C$, 52.07; H, 4.71; N, 4.68; Cl, 11.84. Found: C, 51.90, 52.10; H, 4.72, 4.87; N, 4.80, 4.63; Cl, 11.74, 11.67.

The presence of fraction (3) suggested trial of a more dilute reaction-mixture, and this succeeded. When the *trans*-oxide (4) (19.80 g) was allowed to react in ether (50 ml) and treated as before, only one compound was obtained, and in a yield of 24.93 g (95.9%). Careful analysis by g.l.c. under conditions known to be capable of separating all four chlorohydrins showed the presence only of the compound of the title.

DL-3-Chloro-1-O-methyl-(1,2/3)-1,2-cyclopentanediol (8) Scission of the cis-Oxide with Hydrogen Chloride

A sample of *cis*-3-methoxycyclopentene oxide (11.87 g, containing 1.7% *trans*-oxide and 1.0% of unknown impurity by g.l.c.) was treated with ethereal hydrogen chloride as above. The total product was collected in one fraction (b.p. $35-85^{\circ}/0.02 \text{ mm}$) in a yield of 14.10 g (90.5%). It was analyzed carefully by g.l.c. (6 ft × 1 in., neopentylglycol sebacate polymer 70°, 20 p.s.i.), giving the following peaks: (1) retention time 1.75 min, *trans*-oxide, trace; (2) retention time 3.50 min, *cis*-oxide, none; (3) retention times 5.40 and 6.80 min, impurities from oxide, traces; (4) retention time 8.5 min, 3-chloro-1-*O*-methyl-(1,2/3)-1,2-cyclopentanediol (8), relative area 4.8; (5) retention time 12.5 min, 2-chloro-1-*O*-methyl-(1,3/2)-

1,3-cyclopentanediol (6), relative area 1.0; (6) retention time 21.8 min, 3-chloro-1-O-methyl-(1,3/2)-1,2-cyclopentanediol (9), trace; and (7) retention time 29.5 min, 2chloro-1-O-methyl-(1,2/3)-1,3-cyclopentanediol (7), none. Authentic materials added for each of peaks (5), (6), and (7) gave exactly the retention times shown, and enhanced the corresponding product peaks for (5) and (6). Preparative g.l.c. was used to collect material corresponding to the two major peaks.

DL-3-Chloro-1-O-methyl-(1,2/3)-1,2-cyclopentanediol (8)

Material corresponding to peak (4) was twice distilled to give a clear, colorless oil, n_D^{25} 1.4720, b.p. 49-60°/ 0.02 mm.

Anal. Calcd. for $C_6H_{11}O_2Cl$: C, 47.86; H, 7.36; Cl, 23.55. Found: C, 47.91; H, 7.43; Cl, 23.58.

The *p*-nitrobenzoate, usually a gum, was obtained as a solid only with extraordinary difficulty, and was impossible to recrystallize. It was obtained in a yield of 12%, m.p. $37.5-39.5^{\circ}$.

Anal. Calcd. for $C_{13}H_{14}O_5NCl: C, 52.07; H, 4.71; N, 4.68; Cl, 11.84. Found: C, 52.31; H, 4.62; N, 4.87; Cl, 10.53.$

All the material corresponding to fraction (5) above was converted to its *p*-nitrobenzoate, yield (after two recrystallizations) 0.325 g or 55%, m.p. $68.9-69.7^\circ$. Mixture melting points with the *p*-nitrobenzoates of each of the four isomeric chlorohydrins gave a depression except with that of 2-chloro-1-O-methyl-(1,3/2)-1,3cyclopentanediol (6), thus establishing its identity. It is important to note that neither isolated chlorohydrin could have arisen from the small amount of *trans*-oxide impurity in the *cis*-oxide used to produce them.

Reaction of Methanol and N-Chlorosuccinimide with 3-Hydroxycyclopentene

A mixture of N-chlorosuccinimide (200 g) and methanol (600 ml) was brought to reflux. Freshly prepared 3-hydroxycyclopentene (crude, about 85% pure by g.l.c., judged by volume and g.l.c. to contain about 126 g) was slowly added at such a rate as to maintain refluxing. After all the olefin had been added, the mixture was cooled, the methanol removed by evaporation, and the resulting oil (45.6 g) separated from the precipitated succinimide. Careful g.l.c. analysis (6 ft $\times \frac{1}{4}$ in. stainless steel column, 10% neopentylglycol sebacate on Embacel, 60°, 20 p.s.i.) gave the following results (retention times in min, relative areas in %): (1) 17.0 min, 36.6%, unknown; (2) 25.5 min, 42.6%, unknown; (3) 32.5 min, none, 3-chloro-1-O-methyl-(1,2/3)-1,2-cyclopentanediol (8); (4) 39.0 min, 8.2%, unknown; (5) 58.75 min, 12.6%, 2-chloro-1-*O*-methyl-(1,3/2)-1,3-cyclopentanediol (6); (6) 68.5 min, none, 3-chloro-1-O-methyl-(1,3/2)-1,2-cyclopentanediol (9); and (7) more than 80 min, none, 2-chloro-1-Omethyl-(1,2/3)-1,3-cyclopentanediol (7). Peaks were identified by addition in succession of each of the four authentic trans-chlorohydrins of 3-methoxycyclopentene.

A preparative g.l.c. separation (100° , 20 p.s.i.) gave a very small amount of material corresponding to peak (5) just above. All of it was converted to the *p*-nitrobenzoate, m.p. 67.8–68.9° undepressed on admixture with the *p*-nitrobenzoate of authentic 2-chloro-1-O-methyl-(1,3/2)-1,3-cyclopentanediol (6) made from the reaction of 3-methoxycyclopentene with aqueous *N*-chlorosuccinimide.

CANADIAN JOURNAL OF CHEMISTRY, VOL. 46, 1968

DL-trans-2-Bromocyclopentanol

The compound was prepared by the action of aqueous N-bromosuccinimide upon cyclopentene following the general method of Guss and Rosenthal (35) as modified by Hawkins and Bannard (3) for the preparation of trans-2-bromocyclohexanol. The cyclopentene-N-bromosuccinimide reaction was much more exothermic than any of the olefin-N-bromosuccinimide reactions we have examined previously (3, 4) and efficient external cooling of the reaction vessel was necessary to prevent the loss of some of the cyclopentene. The product was obtained as a colorless oil, b.p. 83.5-85.0°/10 mm, np²⁵ 1.5144, in 79% yield, (lit. (36), b.p. $92^{\circ}/15 \text{ mm}$, n_{D}^{20} 1.5162).

1,2-Epoxycyclopentane (Cyclopentene Oxide)

This substance was prepared by the dropwise addition at 21-39° over a period of 15 min of aqueous sodium hydroxide (24.0 g in 60 ml of water) to a mechanically stirred mixture of trans-2-bromocyclopentanol (61.1 g) and water (20 ml). The oxide layer was decanted, and in view of the observations of Owen and Smith regarding the volatility of the oxide in ether (36), was dried over magnesium sulfate separately from the ether extract of the aqueous phase. (We did not experience the difficulty they encountered with emulsion formation in the preparation from the analogous chlorohydrin.) Separate distillations of the two fractions gave 25.6 g (81 %) of a colorless, fragrant oil, b.p. 101–102°, n_D^{25} 1.4328, (lit. (36), b.p. $102^{\circ}, n_{\rm D}^{16}$ 1.4370).

DL-1-O-Methyl-(1/2)-cyclopentanediol (12)

(a) Cyclopentene oxide (12.6 g) was added to a solution made from sodium (1.0 g) in methanol (75 ml). The mixture, protected from moisture, was heated under reflux for 90 h. About 35 ml of methanol were then removed by distillation. The residue was cooled and neutralized with glacial acetic acid (2.6 g), and the precipitate collected and washed with ether. Fractional distillation of the combined filtrates gave 12.1 g (70%) of a colorless, mobile oil, b.p. $77^{\circ}/10 \text{ mm}$, n_{D}^{25} 1.4518, (lit. (20), b.p. 175° , n_{D}^{20} 1.4534.

(b) DL-3-Chloro-1-O-methyl-(1,3/2)-1,2-cyclopentanediol (9) (950 mg) on dechlorination in the manner described previously (15) furnished 697 mg (96%) of a colorless oil, n_D^{25} 1.4504, on distillation at 10 mm pressure from an air bath at 80-90°. Its i.r. spectrum was identical with that of the material from part (a).

Acknowledgments

Partial support of the work, and the grant of a Scholarship to one of us (E.J.L.), by the National Research Council of Canada is gratefully acknowledged. We thank Mr. J. Helie for performing some of the analyses reported here. Some of the experimental work was performed by Messrs. A. D. McKinnon, H. Johnston, and M. Little,

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