The Stereochemistry of the Reaction of Hydrogen Bromide with Cyclohexene and 1-Methylcyclohexene in the Presence of Oxygen

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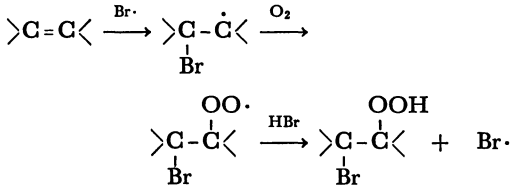
The reaction of hydrogen bromide with cyclohexene or 1-methylcyclohexene in the presence of oxygen, followed by reduction with lithium aluminium hydride afforded *trans*-2-bromocyclohexanol or *t*-2-bromo-1-methyl-*r*-1-cyclohexanol. These findings show that oxygen attacks intermediate bromocyclohexyl radicals formed by addition of a bromine atom to a double bond exclusively on the side opposite to the bromine substituent. Mechanistic implications are discussed.

The free radical addition of hydrogen bromide to olefins takes place preferentially in *anti* fashion.[1] If oxygen is present, it attacks an intermediate radical generated by addition of a bromine atom to an olefinic bond in competition with hydrogen bromide, giving rise to a bromine-containing hydroperoxide[2] or oxygenated bromine compounds,[3] probably through an intermediate hydroperoxide.

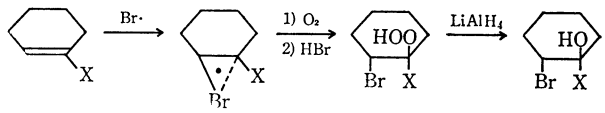


It seemed of interest to examine the stereochemistry of attack of oxygen on the cyclohexyl type of radicals generated by addition of a bromine atom to cyclohexenes, because in the autoxidation of methylcyclohexanes it has been shown that oxygen attacks intermediate radicals with nearly equal probability on both sides of the radical centre.[4] The present report deals with the stereochemistry of reaction of oxygen with the radicals generated by addition of a bromine atom to cyclohexene and 1-methylcyclohexene.

Results and Discussion

Anhydrous hydrogen bromide and oxygen were passed through cyclohexene or 1-methylcyclohexene containing a little benzoyl peroxide at about 60 °C, and reaction mixtures were treated with lithium aluminium hydride to reduce hydroperoxides produced to the corresponding alcohols. Gas-liquid partition chromatographic (glpc) analysis showed that *trans*-2-bromocyclohexanol or *t*-2-bromo-1-methyl-*r*-1-cyclohexanol was formed, but no *cis* isomers were detected. The results are summarized in Table 1.

It is evident that oxygen attacks the intermediate radicals formed by addition of a bromine atom to the cyclohexenes exclusively on the side opposite to the bromine atom, in striking contrast to the case of autoxidation of methylcyclohexanes, in which an almost random attack of oxygen occurs.[4] The completely stereoselective attack of oxygen may be explained in terms of a bromine bridged radical[5] (Fig. 1); thus, oxygen would attack intermediate radical **1** only from the opposite direction of the bromine bridge resulting in *anti* stereochemistry. An alternative explanation for the observed stereochemistry might involve intermediate radical **2**, in which the C-2 bromine occupies an axial position and would prevent an access of oxygen from the *cis* direction (Fig.



1 X=H, CH_3

Fig. 1.

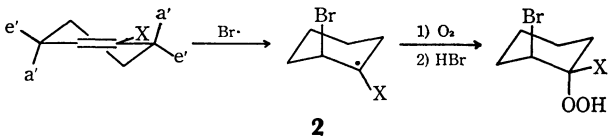


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Fig. 2.

TABLE 1. REACTIONS OF HYDROGEN BROMIDE WITH CYCLOHEXENE AND 1-METHYLCYCLOHEXENE IN THE PRESENCE OF OXYGEN

Olefin (mol)		BPO[a] (mmol)	Temp. (°C)	Reaction time (hr)	Peroxide[b] (mmol)	Bromohydrin[c] (mmol)	
						cis	*trans*
Cyclohexene	0.34	1.09	64±3	3.0	10.2	0	1.6[d]
1-Methylcyclohexene	0.25	0.96	61±3	3.5	22.8	0	1.3[e]

a) Benzoyl peroxide. b) Titrated iodometrically by Wagner's method.[11] c) After reduction with lithium aluminium hydride. d) *trans*-2-Bromocyclohexanol. e) *t*-2-Bromo-1-methyl-*r*-1-cyclohexanol.

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2). This explanation, however, does not seem convincing, because, although the 2-bromocyclohexyl radical will be produced in the form shown in Fig. 2 with the bromine substituent in an axial conformation, it will interconvert in quick equilibrium with the form in which the bromine is equatorial before it reacts with oxygen,[6] undoubtedly resulting in almost random attack of oxygen.

Experimental[7]

Materials. Cyclohexene was prepared by dehydration of cyclohexanol with potassium hydrogensulphate,[8] followed by fractional distillation with a packed column, bp 82—82.5 °C. 1-Methylcyclohexene was prepared according to the method of Bartlett and Rosenwald[9] by the Grignard reaction of cyclohexanone to give 1-methylcyclohexanol, followed by dehydration and fractionation with a concentric column, bp 110.2—110.4 °C. Hydrogen bromide was evolved by the action of bromine on tetralin.[10] The hydrogen bromide was freed from bromine by bubbling through tetralin and dried by passing through a trap cooled at —50 °C and then a tube packed with anhydrous calcium sulphate.

Reactions of Hydrogen Bromide with Cyclohexene and 1-Methylcyclohexene in the Presence of Oxygen. Cyclohexene (0.34 mol) or 1-methylcyclohexene (0.25 mol) containing benzoyl peroxide (1 mmol) was placed in a reaction flask equipped with two bubbler tubes and a reflux condenser protected from moisture by a drying tube filled with anhydrous calcium sulphate. The reaction flask was immersed in a water bath which was kept at about 60 °C. The cyclohexene was stirred by means of a magnetic stirrer, and dry hydrogen bromide and oxygen were passed through simultaneously. The reaction was allowed to proceed for 3—3.5 hr. The reaction mixture was washed with water and dried over anhydrous magnesium sulphate. A portion of this mixture was analysed for peroxides formed by the iodometric method of Wagner *et al.*[11] The remaining portion was dissolved in anhydrous ether and added to a suspension of excess of lithium aluminium hydride in anhydrous ether. After the mixture had been stirred for 1 hr at room temperature, excess of lithium aluminium hydride was destroyed with dilute sulphuric acid. The ether layer was separated, the aqueous layer extracted with ether, and the combined ether solutions were dried over anhydrous sodium sulphate. The ether was removed by distillation and the residue subjected to glpc analysis.

Gas-Liquid Partition Chromatography. A Perkin-Elmer model 154D instrument was utilized. The product mixture from cyclohexene was examined using a Carbowax column 1 m long (steel tube) at 111 °C. The products from 1-methylcyclohexene was analysed using a diisodecyl phthalate column 0.5 m long (glass tube) at 103 °C or a Carbowax column 0.5 m long (glass tube) at 99.5 °C.

Preparation and Characterization of Authentic Samples. cis-*2-Bromocyclohexanol*: To 35 g (0.20 mol) of 2-bromocyclohexanone[12] in 50 ml of methanol was added portionwise 6 g (0.16 mol) of sodium borohydride with stirring. Stirring was continued for an additional 20 min. Dilute aqueous solution of acetic acid was added, the organic layer separated, and the aqueous layer extracted with ether. The combined organic layer and extracts were dried over anhydrous sodium sulphate, and then distilled to give 11 g of colourless liquid, bp 50 °C/1 mmHg, which crystallized in a refrigerator. Glpc analysis showed that it consisted of 90% of *cis*-2-bromocyclohexanol and 10% of the *trans* isomer. Two recrystallizations from petroleum ether gave a pure specimen of the *cis*-isomer in needles, mp 28.5—29.0 °C (lit,[13] mp 29.0—29.5 °C), ν_{max} (liquid film) 3450 cm^{-1} (OH); *p*-toluenesulphonate, mp 77—78 °C (lit,[14] mp 79—80 °C) (Found: C, 47.13; H, 5.35%. Calcd for $C_{13}H_{17}BrO_3S$: C, 46.85; H, 5.14%). The Meerwein-Ponndorff reduction of 2-bromocyclohexanone[13] afforded a mixture of *cis*- and *trans*-2-bromocyclohexanol in a ratio of about 1 : 2.

trans-*2-Bromocyclohexanol*: This compound was obtained according to the procedure of Guss and Rosenthal[15] by the reaction of cyclohexene with *N*-bromosuccinimide in water, bp 87—87.5 °C/10 mmHg, mp 26.5—27 °C (lit, bp 90—91 °C/13 mmHg,[16] mp 27.5 °C[17]), ν_{max} (liquid film) 3400 cm^{-1} (OH); *p*-toluenesulphonate, mp 42—42.5 °C (lit,[14] mp 44—45 °C).

c-*2-Bromo-1-methyl*-r-*1-cyclohexanol*: This compound was prepared according to the method of Bartlett and Rosenwald[9] by the reaction of 2-bromocyclohexanone with methylmagnesium iodide, bp 51—52.5 °C/2 mmHg, n_D^{27} 1.5057 (lit,[9] bp 83 °C/7 mmHg, n_D^{27} 1.5032), ν_{max} (liquid film) 3500 cm^{-1} (OH) (Found: Br, 40.3%. Cald for $C_7H_{13}BrO$: Br, 41.4%). Glpc analysis showed that this material contained trace amount of the *trans* isomer.

t-*2-Bromo-1-methyl*-r-*1-cyclohexanol*: This compound was synthesized according to the directions of Filler *et al.*[18] by the reaction of 1-methylcyclohexene with *N*-bromosuccinimide in water, bp 70.8—72.9 °C/3 mmHg, n_D^{25} 1.5150 (lit,[18] bp 96—98 °C/8.5 mmHg, n_D^{25} 1.5150), ν_{max} (liquid film) 3450 cm^{-1} (OH) (Found: Br, 41.4. Calcd for $C_7H_{13}BrO$: Br, 41.4%).

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