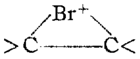
reaction mixture was cooled and poured onto ice. The dibromide was separated with the aid of some carbon tetrachloride and the extract was washed with potassium carbonate. Distillation at reduced pressure through a Weston-type[6] column yielded 39 and 42% yields of dibromides, from *threo-* and *erythro*-bromohydrins, respectively.

Analysis of Dibromides.—Comparison of the boiling points and refractive indices of the dibromides with the known[2,7] properties of the 2,3-dibromobutanes indicates that the dibromide samples are largely either *meso-* or *dl*-2,3-dibromobutane. Also, the samples are contaminated with a trace of some low-refractive index impurity, possibly bromohydrin. For samples not absolutely free of foreign materials, the best method of analyzing a mixture of *meso-* and *dl*-2,3-dibromobutanes is by way of the rate constant K_2 for the reaction of the sample with potassium iodide in methanol.[2] Mr. Harold Pokras kindly determined these rates and they are included in Table I along with the calculated compositions for the dibromide samples. The values of K_2 are slightly in doubt because of an uncertainty about the solvent correction of the solvent used in the rate measurements. The uncertainty in the compositions is about 4%.

Summary

The *erythro-* and *threo*-3-bromo-2-butanols are converted to dibromides by the action of phosphorus tribromide with a steric result of predominant retention of configuration.

It is considered probable that the steric result is due to the participation of the neighboring bromine atom in the replacement process with the formation of the bromonium ion



as an intermediate.

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[6] Weston, *Ind. Eng. Chem., Anal. Ed.*, **5**, 179 (1933).

[7] Wilson and Lucas, THIS JOURNAL, **58**, 2396 (1936).

[CONTRIBUTION FROM THE GATES AND CRELLIN LABORATORIES OF CHEMISTRY, CALIFORNIA INSTITUTE OF TECHNOLOGY, AND THE CHEMISTRY DEPARTMENT OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

The Role of Neighboring Groups in Replacement Reactions. IV. The Identity of Various Preparations of 1,2-Dibromocyclohexane

BY S. WINSTEIN

A number of reactions leading to 1,2-dibromocyclohexane have been investigated as to the steric result because of the interest in effects[1,2] of neighboring groups on replacement processes.

All of the preparations of 1,2-dibromocyclohexane, summarized in Table I, have been compared with the dibromide from cyclohexene. The latter dibromide has been assigned the *trans*-configuration for the following reasons. First, the predominance of *trans*-addition of halogen to olefins[3] leads one to this configuration. Further, the second-order rate constant at 74.90° for the reaction of cyclohexene dibromide with potassium iodide in methanol is 0.0204.[4] This value compares favorably with 0.0301 for *dl*-2,3-dibromobutane[5] and 0.0562 for *meso*-2,3-dibromobutane.[5] Since the favored mechanism[6] of the reaction is a *trans*-elimination of bromine by potassium iodide, the *trans*-configuration for cyclohexene dibromide is strongly indicated.

TABLE I

PROPERTIES OF DIFFERENT PREPARATIONS OF 1,2-DIBROMOCYCLOHEXANE

Prepn. no.	Source	$n^{25}D$	M. p., °C.
1[a]	Cyclohexene + Br_2	1.5507	−4.5
2[b]	*trans*-Diacetate + HBr − AcOH	1.5498	−6
3	*cis*-Diacetate + HBr − H_2O	1.5506	−4
4	*cis*-Diacetate + HBr − AcOH	1.5504	−4
5[c]	Oxide + HBr − H_2O	1.5504	−5
6	Bromohydrin from olefin + HBr − H_2O	1.5506	−4
7	Bromohydrin from ketone + HBr − H_2O	1.5490	−6
8	Bromohydrin from oxide + PBr_3	1.5497	−8
9	Bromohydrin *p*-toluenesulfonate + HBr − H_2O	1.5504	−4

[a] d^{25}_4 1.7826, MR_D 43.28. [b] K_2 at 74.90° for reaction with KI is 0.0203. [c] K_2 at 74.90°, 0.0205.

One group of dibromocyclohexane samples was prepared from 2-bromocyclohexanol. The 2-bromocyclohexanol, which is prepared from cyclohexene and which is presumably[2,7] of the *trans*-configuration, reacts smoothly with fuming hydrobromic acid to yield dibromide. In preparing

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[1] (a) Winstein and Lucas, THIS JOURNAL, **61**, 1576 (1939); (b) Winstein and Lucas, *ibid.*, **61**, 2845 (1939).

[2] Winstein and Buckles, *ibid.*, **64**, 2780 (1942).

[3] (a) Michael, *J. prakt. Chem.*, **52**, 344 (1893); (b) Terry and Eichelberger, THIS JOURNAL, **47**, 1067 (1925).

[4] Kindly determined by Dr. D. Pressman.

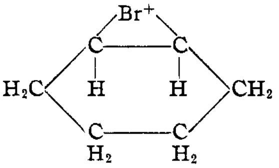
[5] Dillon, THIS JOURNAL, **54**, 952 (1932).

[6] Winstein, Pressman and Young, *ibid.*, **61**, 1645 (1939).

[7] Bartlett, *ibid.*, **57**, 224 (1935).

cyclohexene dibromide in this manner, one can treat cyclohexene oxide directly with fuming hydrobromic acid without first converting it to bromohydrin.[8] Phosphorus tribromide reacts with *trans*-bromohydrin[2,7] from cyclohexene oxide to yield, along with what is probably some elimination product, considerable 1,2-dibromocyclohexane. Cyclohexene bromohydrin can be converted to dibromide by way of the *p*-toluenesulfonate. The *p*-toluenesulfonate was non-crystalline but its behavior on treatment with fuming hydrobromic acid was reasonable for the *p*-toluenesulfonate of the bromohydrin. Smooth conversion to dibromide occurred.

The products of these three reactions are almost indistinguishable, on the basis of physical properties and mixed melting points, from the dibromide prepared directly from cyclohexene. Thus complete retention of configuration obtains in these reactions. It would seem that all three reactions proceed by way of the cyclohexene bromonium[1,2] ion I.



I

The reaction[2] of I with bromide ion with inversion gives a net apparent retention of configuration as the steric result.

The bromohydrin from the reduction of 2-bromocyclohexanone with aluminum isopropoxide[9] was also converted to dibromide with fuming hydrobromic acid. Whether the bromocyclohexanol, a somewhat impure product which did not keep well, contained any *cis*-compound[7] is uncertain. The dibromide was almost identical with the dibromides from the other reactions.

The *cis*- and *trans*-1,2-diacetoxycyclohexanes yielded the other preparations of cyclohexene dibromide by some reactions which merit further investigation.[8] Both esters yield dibromide smoothly on treatment with hydrogen bromide in acetic acid. The *cis*-diacetate yields dibromide on treatment with fuming hydrobromic acid. All three of these dibromides are almost indistinguishable from the dibromide from cyclohexene.

On treatment with fuming hydrobromic acid, *trans*-1,2-diacetoxycyclohexane behaves differently from the *cis*-isomer. The reaction mixture turns very dark and yields no dibromide. Possibly the diacetate yields the glycol, which undergoes rearrangement.

The various preparations of 1,2-dibromocyclohexane all appeared to be quite pure *trans*-isomer. A similar tendency for the production of only one dihalide of a cyclic olefin by replacement reactions is seen in the results of other workers. Thus, Mousseron and Granger[10] report that 2-bromocyclohexanol and phosphorus pentabromide and 2-chlorocyclohexanol and phosphorus pentachloride give rise to the same dihalides obtained from the fixation of halogen to cyclohexene. Also, Suter and Lutz[11] have reported that the treatment of *trans*-indene chlorohydrin with phosphorus pentachloride and both *cis*- and *trans*-indene chlorohydrins with thionyl chloride gives one and the same dichloride. This dihalide is apparently the same as indene gives with chlorine. Suter and Lutz[11] have drawn attention to the fact that apparently the only report of a pair of isomeric dihalides of a simple cyclic olefin is that of the cyclohexene dichlorides.[12]

The factors operating to make one dihalide, the *trans*-isomer, the favored product in nucleophilic replacement reactions have been partly discussed already.[2] Thus it has been pointed out that S_N1 type replacement reactions with *cis*- and *trans*-derivatives of cyclic olefins will tend to give *trans*-product if a neighboring group such as a halogen atom is available for participation in the replacement process.

It is possible that a neighboring halogen atom contrives in another way to make the *trans*-dihalide the favored product of replacement reactions. Evidence from studies on restricted rotation[13] of dihalides leads to a considerable barrier for passage through a configuration with two bromine atoms *cis* to each other. With this kind of energy effect to modify the activation energy of an S_Ni or S_N2 reaction leading to *cis*-dihalide, it is possible for the S_Ni or the S_N2 mechanism to disappear to the exclusive operation of mechanisms leading to *trans*-product.

This latter kind of effect of a β-halogen atom we hope to demonstrate independently. This is desirable first, because it is not clear to what

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(8) Winstein and Lucas, THIS JOURNAL, **61**, 1581 (1939).

(9) Winstein, *ibid.*, **61**, 1610 (1939).

(10) Mousseron and Granger, *Compt. rend.*, **205**, 327 (1937).

(11) Suter and Lutz, THIS JOURNAL, **60**, 1360 (1938).

(12) Komatsu and Kawamoto, *C. A.*, **26**, 5080 (1932).

(13) (a) Beach and Palmer, *J. Chem. Phys.*, **6**, 639 (1938); (b) Beach and Turkevich, THIS JOURNAL, **61**, 303 (1939).

extent S_N2[14] and S_Ni mechanisms operate in cyclic systems such as those being discussed. Secondly, except for the above-postulated effect, a β-halogen atom would be expected to increase[15] the rate of an S_N2 process.

Experimental

Cyclohexene Oxide.—Cyclohexene was converted to chlorohydrin, which, without being isolated as a pure product, was converted to oxide. 123 g. (1.5 moles) of cyclohexene was treated with hypochlorous acid solution.[16] The chlorohydrin layer was separated, the aqueous layer was extracted with a 300-ml. portion of isopropyl ether and the chlorohydrin and ether extracts were stirred for one and one-quarter hours with a solution of 80 g. of sodium hydroxide in 400 ml. of water. The ether layer was then separated, usually dried over potassium carbonate and distilled through a Vigreux column. There was obtained 53–66 g. of oxide, b. p. 127–130°, 69.5–71.0° (100 mm.), yield 36–45%.

***trans*-1,2-Cyclohexanediol.**—Cyclohexene oxide, 114.5 g., was shaken with 330 ml. of water to which 8 drops of 60% perchloric acid had been added. The mixture became warm and was homogeneous after about a half hour. The solution was neutralized with sodium hydroxide, the water was distilled off at reduced pressure, and the residue was recrystallized from 300 ml. of benzene. 108 g., 80%, of glycol, m. p. 103–104°, was obtained without working up the mother liquor.

***trans*-1,2-Diacetoxycyclohexane.**—This substance was prepared from glycol as described previously.[2]

***cis*-1,2-Diacetoxycyclohexane.**—This substance was some prepared previously.[2] Most of the work with *cis*-diacetate was performed on the product of the reaction of 1,2-dibromocyclohexane with silver acetate in acetic acid on the basis of Rothstein's report.[17] We have since[2,18] investigated this reaction and now know that the product must have been a mixture of mono- and diacetates of the *cis*-glycol, the mole per cent. of monoacetate being about 65.

2-Bromocyclohexanol from Oxide.—This was carried out in the same manner in which butene oxide was converted to bromohydrin.[1] Forty-nine grams of oxide and 100 ml. of 48% hydrobromic acid yielded 65 g., 73%, of bromohydrin, b. p. (10 mm.) 86°, $n^{25}\mathrm{D}$ 1.5178.

2-Bromocyclohexanol from Cyclohexene.—Cyclohexene was converted to bromohydrin by treatment with acetbromamide as directed by Schmidt, Knilling and Ascherl.[19] The product was obtained in 60% yield, b. p. (10 mm.) 86°, $n^{25}\mathrm{D}$ 1.5165. Later,[2] the use of acid as a catalyst in this reaction was found advantageous, but it is possible that these conditions give rise to a little dibromide with the bromohydrin.

2-Bromocyclohexanol from 2-Bromocyclohexanone.—The reduction of 2-bromocyclohexanone with aluminum isopropoxide has already been described.[9] The product from this method darkened rapidly and underwent some change for, on redistillation after ten days, it showed $n^{25}\mathrm{D}$ 1.5142 instead of $n^{25}\mathrm{D}$ 1.5165 first obtained. The density was now d^{25}_4 1.3990 compared to d^{25}_4 1.4542 for the product from cyclohexene. When samples of about 0.8 g. of this material were left in 20 ml. of 0.4 N sodium hydroxide diluted with 20 ml. of alcohol and the mixtures then back-titrated with standard acid, the sample was found to use up 88% of the theoretical amount of alkali in four minutes at room temperature, 90% in twenty-four minutes at room temperature, and 91% in six minutes at the boiling point. The bromohydrin from cyclohexene, similarly treated, consumed 98% of the theoretical amount of alkali in five minutes at room temperature.

1,2-Dibromocyclohexane from Cyclohexene.—Cyclohexene was converted to dibromide by the method of Greengard.[20] The dibromide turns dark rapidly on standing, as is reported, due to impurities. When the impure material is stored over potassium carbonate and fractionated twice through a Weston[21] column, the bulk of the material distils at 99.6–99.9° (13 mm.). This substance remains colorless indefinitely whether exposed to air or not.

Preparation of 1,2-Dibromocyclohexane from Diacetates and Hydrogen Bromide in Acetic Acid.—The method was the same as for the diacetoxybutanes.[8] A heating period of ten hours on a water-bath was used. The crude yield of product was approximately 85%, the bulk of material distilling at constant temperature at reduced pressure.

Preparation of 1,2-Dibromocyclohexane Using Fuming Hydrobromic Acid.—The procedure was the same as for the butene derivatives.[1,8] The reaction mixtures became cloudy in a half hour or less and were left at room temperature several days. Crude yields were about 90% for the products except the one from bromohydrin from bromoketone. These products distilled sharply through the Weston column. In the case of the experiment with bromohydrin from bromoketone the yield was lower and the reaction mixture was very dark. The product was separated with the aid of some carbon tetrachloride. On distillation, the yield of product, not as pure as some of the others, was 55%.

cis-1,2-Diacetoxycyclohexane, on treatment with fuming hydrobromic acid, behaved, from external appearances, just as the monoacetate–diacetate mixture.

When *trans*-1,2-diacetoxycyclohexane was dissolved in fuming hydrobromic acid and the mixture left at room temperature, no dibromide layer formed, but instead, the reaction mixture became somewhat colored in one day and extremely dark in a week. Heating a small portion of the reaction mixture after two days at room temperature at 75° in a sealed tube for one and one-quarter hours and steam-distilling afterwards yielded only traces of oil, $n^{22}\mathrm{D}$ 1.527.

Dibromocyclohexane from Bromohydrin and Phosphorus Tribromide.—26.8 g., 0.15 mole, of bromohydrin was dropped with stirring into 6 ml. of phosphorus tribromide in a three-necked 100-ml. flask equipped with a dropping funnel, a mercury-sealed stirrer, a drying tube and an ice-bath. The bromohydrin was added over a period of twenty minutes and a little hydrogen bromide

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[14] Bartlett and Rosen, THIS JOURNAL, **64**, 544 (1942).

[15] Hughes, *Trans. Faraday Soc.*, **37**, 625 (1941).

[16] Coleman and Johnstone, "Organic Syntheses," Coll. Vol. I, 1932, p. 151.

[17] Rothstein, *Ann. chim.*, **14**, 461 (1930).

[18] Winstein and Buckles, THIS JOURNAL, **64**, 2787 (1942).

[19] Schmidt, Knilling and Ascherl, *Ber.*, **59B**, 1280 (1926).

[20] Greengard, "Org. Syntheses," **12**, 26 (1932).

[21] Weston, *Ind. Eng. Chem., Anal. Ed.*, **5**, 179 (1933).

was evolved at the end of the addition. After a half-hour at the ice-bath temperature the material in the reaction flask was still one phase. The ice-bath was removed. After two hours' standing, there was still no change. Then, 5 ml. more of phosphorus tribromide was added and the reaction mixture was warmed. After one and one-half hours the temperature had been raised to 100°, with slight evolution of hydrogen bromide. A gummy viscous deposit had formed on the walls. Two hours further heating at 95–100° was allowed. The reaction mixture was then cooled and poured onto ice and sodium bicarbonate with which it was well stirred. The dibromide was separated with the aid of 25 ml. of carbon tetrachloride after hydrochloric acid was added to break an emulsion. The extract of the dibromide was washed with potassium carbonate solution, dried over potassium carbonate, filtered and distilled through the Weston column. There were obtained 15 g., 41%, of dibromide, b. p. 93.1–94.1° (10 mm.) as well as 7 g. of a low boiling fraction, b. p. 50.3–51.0 (13 mm.), n^{25}_D 1.4941, d^{24}_4 1.325 (in a 2-ml. pycnometer). The low boiling fraction gave an immediate precipitate with aqueous 1 *N* silver nitrate and it absorbed bromine in carbon tetrachloride, not instantaneously but at a moderate rate, without evolution of hydrogen bromide.

1,2-Dibromocyclohexane from Bromohydrin *p*-Toluenesulfonate.—Ten grams, 0.056 mole, of cyclohexene bromohydrin from the oxide, 10.9 g. of *p*-tosyl chloride and 4.4 ml. of pyridine were mixed, whereupon the mixture warmed up to 40 or 50° and cooled off after about an hour. Solid precipitated. After two days the mixture was poured into dilute hydrochloric acid and stirred well. An oil settled out which was not induced to crystallize. The oil was separated and added to 30 ml. of 48% hydrobromic acid. The oil remained as an upper layer after the mixture was saturated with hydrogen bromide gas at 0° and sealed off in an ampoule. After several hours at room temperature, a good deal of solid seemed to have formed, presumably *p*-toluenesulfonic acid. After several days of standing at room temperature, the ampoule was cooled and opened, and the contents were poured into water. The dibromide was washed with potassium carbonate and dried over potassium carbonate, 11.0 g. (81% yield) of crude product being obtained. The bulk of this material distilled at 110.8–111.0° at 16 mm.

Properties of Dibromide Preparations.—About 90 ml. combined preparations 1, 2, 3, 4, 5 and 6, Table I, in a large test-tube equipped with a thermometer, mercury-sealed stirrer and a drying tube was frozen out and allowed to melt while the test-tube was kept in a Dewar flask for insulation. The temperature was −5.0° when the mixture was too thick to stir even by hand and all the solid was gone at −4.0°, so the combined material melted substantially over a range of 1.0° and negligible amounts of isomeric impurities were indicated.

The melting points of individual preparations were taken by freezing about 10-ml. portions in test-tubes and warming the portions with stirring. The points of disappearance of solid are given in Table I. Mixed melting points were taken on various pairs of samples and no melting point lowerings were ever experienced.

Boiling ranges of the dibromides were very narrow and the spread in the values was from 98.6–99.9° at 13 mm., mostly because of difficulty in reproducing pressures.

It is a pleasure to acknowledge the many suggestions of Professor H. J. Lucas and Dr. E. R. Buchman of the California Institute of Technology.

Summary

Preparations of 1,2-dibromocyclohexane from the action of: fuming hydrobromic acid on cyclohexene oxide, 2-bromocyclohexanol derived from cyclohexene, and 2-bromocyclohexanol derived from 2-bromocyclohexanone; phosphorus tribromide on 2-bromocyclohexanol derived from oxide; fuming hydrobromic acid on 2-bromocyclohexyl *p*-toluenesulfonate; fuming hydrobromic acid on *cis*-1,2-diacetoxycyclohexane; and hydrogen bromide in acetic acid on *cis*- and *trans*-1,2-diacetoxycyclohexane all proved to be essentially pure and identical with the known dibromide derived from cyclohexene.

The known 1,2-dibromocyclohexane is assigned the *trans*-configuration. It is pointed out how a β-halogen atom contrives to make the *trans*-dihalide the favored product of nucleophilic replacement reactions.

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