"Trans" 1,4-Chloro-Bromocyclohexane

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Crystallographic equivalency of chlorine and bromine atoms in organic compounds was first described by Hendricks [1] in the case of *p*-chloro-bromobenzene. Recently the same phenomenon was observed by Wang Lund and the present authors [2] who prepared and studied 1*x*, 2*x* dichloro-4*x*, 5*x*-dibromocyclohexane. This compound is dimorphous and for both modifications the crystallographic examination indicated the presence of a molecular center of symmetry. However, the cyclohexane derivative which would correspond most closely to the *p*-chloro-bromobenzene is the "trans" 1,4-chloro-bromocompound which has not, it appears, so far been prepared.

We first prepared a mixture of the two stereoisomeric 4-chlorocyclohexanols from pure chinitol (100 g) and 35% hydrochloric acid (100 ml) by slowly heating the reaction mixture to 100° C and keeping it at that temperature for 3—4 hours. After cooling, the oil formed during the reaction was separated from the acid solution and the latter, after dilution with water, neutralized with solid sodium bicarbonate. The solution was saturated with sodium chloride and extracted with ethyl ether. The ether solution was washed with bicarbonate solution, then with water and finally dried over sodium sulphate. After evaporation of the ether the chlorocyclohexanol mixture was distilled *in vacuo*. (Cl found 26.28, calc. 26.35).

100 g of phosphorous tribromide was added drop by drop to 45 g of the 4-chlorocyclohexanol mixture. When the greater part of the phosphorous tribromide had been added the cooling bath was removed and the temperature allowed to rise. Subsequently the reaction mixture was heated to 70° C for about an hour and then cooled. After addition of water the reaction product was extracted with ethyl ether. The ether solution was washed with bicarbonate solution, then with water and finally dried over calcium chloride. After evaporation of the ether the remaining liquid was fractionated *in vacuo*. A fraction boiling between 62 and 64° C (0.5 mm) and kept at about 5° C for some time gave a good yield of crystals. After recrystallization from ligroin or ethyl alcohol needle-shaped monoclinic crystals of m.p. 102° C were obtained ($a = 11.81$; $b = 5.52$; $c = 5.95$; $\beta = 103°$):

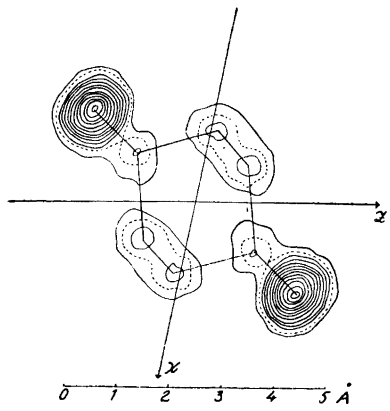

Fig. 1.

$C_6H_{10}ClBr$	Calc.	Br 40.48	Cl 17.93
	Found	» 40.37	» 18.12

X-ray analysis showed that the crystals are isomorphous with those of "trans" (*x*, *x*) 1,4-dibromocyclohexane m. p. 112° C and the corresponding diiodocyclohexane (m.p. 142° C)/. We may add that according to our observations the corresponding dichlorocyclohexane (m.p. 102° C) has a transition point at 12—13° C and that the modification stable *below* this temperature has a crystal structure corre-

sponding to that of the three trans 1,4-dihalogenocyclohexanes. A detailed X-ray study of the whole series of isomorphous compounds (including N,N′-dichloropiperazine [4]) is in progress. Part of a Fourier projection along the *b* axis of the bromine compound worked out by Bergskoug is reproduced in Fig. 1.[5]

In the case of the chloro-bromocompound the conclusion had to be drawn that the chlorine and bromine atoms are indeed crystallographically equivalent. No sign of a transition into a second modification could be observed in this case. It is therefore very probable that dichloro- and chloro-bromocyclohexane have different crystal structures at their melting points.

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Preparation of Carboxylabelled Oleic Acid *

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The above-mentioned labelled acid, which was required for metabolic studies, was prepared from erythro-9,10-dihydroxystearic acid.

The acid (m.p. 129°) was acetylated and subjected to the silver salt bromine degradation. The diacetoxybromide was deacetylated to erythro-8,9-dihydroxy-1-bromo-heptadecane m.p. 102—103°. A nitrile synthesis using labelled potassium cyanide, followed by alkaline hydrolysis, yielded carboxylabelled erythro-9,10-dihydroxystearic acid.

This labeled acid was then transformed into the dibromo acid with hydrogen bromide in acetic acid-sulphuric acid according to Ames and Bowman [1]. By following their procedure of debrominating the esterified dibromo acid, sterically pure oleic acid was obtained.

If the low melting threo-9,10-dihydroxystearic acid is used as starting material elaidic acid should be obtained by the same method [2].

EXPERIMENTAL. Dihydroxystearic acid (m.p. 129°) was prepared from oleic acid by oxidation with permanganate [3].

Silver salt of erythro-9,10-diacetoxy octadecanoic acid. 4.5 g of 9,10-dihydroxystearic acid was dissolved in a mixture of acetic anhydride (5 ml) and pyridine (10 ml) and heated on the steam bath for one hour. After concentration *in vacuo* to a syrup, ice and ether were added. The ether solution was washed with *N* hydrochloric acid and water, dried over sodium sulfate and evaporated to dryness. The crude product was dissolved in 50 ml ethanol and neutralized with sodium hydroxide (phenolphthalein). A solution of 2 g silver nitrate in 30 ml 60 per cent ethanol was added with rapid stirring. The resulting sticky mass of the precipitated silver salt was filtered off, washed with a little water and dried overnight in a vacuum oven at 60°. The silver salt forms a brown gum which is soluble in hot carbon tetrachloride.

1-Bromo-8,9-dihydroxyheptadecane. 65.5 g of crude oven-dried silver salt was dissolved in a mixture of 1 l of carbon tetrachloride and 200 ml of methylene chloride and the solvents distilled until the b.p. was 76.5° and water no longer appeared in the condenser. The residual solution was mixed with dry silver acetate (10 g) according to a procedure described earlier [4] and treated with bromine (11 ml).

* Part 7 on the Metabolism of lipids.