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OPTICAL ROTATION AND ATOMIC DIMENSION: THE FOUR OPTICALLY ACTIVE 2-HALOGENOPENTANES

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ABSTRACT

In previous articles by the author it is suggested that certain optically active halogen derivatives may be divided into two classes. The first class has the halogen directly attached to an asymmetric carbon atom. For these substances the writer has formulated the rule that the differences of their specific rotations, (Cl-F), (Br-Cl) and (I-Br), have the same numerical relation as the respective differences of the radii of the covalent-bonded atoms (41:17:21). The second class of optically active halogen derivatives has the halogen attached indirectly (by a chain of atoms) to an asymmetric carbon atom. For these latter substances the rule was formulated that the differences of their molecular rotations have a numerical relation, which likewise agrees with that for the respective differences of the radii of the neutral halogen atoms.

As these rules were established for halogen derivatives of carbohydrates, which contain several asymmetric carbon atoms, it was found desirable to investigate halogen derivatives, which contain only one asymmetric carbon. The results of the last investigation (see footnote 1) showed that the derivatives of the amyl alcohol, 2-methylbutanol-1, checked the above rule for the second class very well. The present communication reports the results obtained in checking the above rule for the first class, with the halogen derivatives of the other active amyl alcohol, pentanol-2. Pure optically active *D*- and *L*-pentanol-2 were prepared and halogenated by different methods in order to obtain the 2-fluoro-, 2-chloro-, 2-bromo- and 2-iodopentanes of highest rotation.

In spite of the difficulty that a partial inversion takes place in the halogenation, resulting in a mixture of *D* and *L* halogen derivative, the conclusion can be drawn that rule I is not contradicted by the values found, since the deviations can be plausibly explained by the incompleteness of the Walden inversion. Rule II should not be applicable to this type of compound, and the results confirm this.

It is further shown that all halogen derivatives of pentanol-2 of like configuration have the same sign of optical rotation. The specific gravity, refractive index, and boiling points at various pressures were also determined.

CONTENTS

I. INTRODUCTION

It is suggested in the writer's previous articles on this subject [1],[2] that certain halogen derivatives may be divided into two classes. The compounds which compose the first class have the halogen directly attached to an asymmetric carbon atom and differ only in having one halogen replaced by another. For these *D* (or *L*)[3] substances the differences of their specific rotations (Cl-F), (Br-Cl), and (I-Br) have the numerical relation 41:17:21, which agrees with the numerical relation 41:17:21[4] for the differences in atomic radii of the respective neutral or nonionized or covalent halogen atoms (rule I). Those in the second class have the halogen atom attached indirectly (by a chain of atoms) to an asymmetric carbon atom. For these latter *D* or *L* substances the differences of their molecular rotations have a numerical relation, which likewise agrees with that for the differences in atomic radii of the respective covalent-bonded halogen atoms (rule II).

These two rules for the two classes of compounds were formulated by the investigation of halogen derivatives of the carbohydrates. Inasmuch as these halogen derivatives contain several asymmetric carbons, it was found desirable to prepare and test the halogen derivatives of the two active amyl alcohols, 2-methylbutanol-1 and pentanol-2, since these compounds are simple in structure and contain only one asymmetric carbon atom.

The results of an investigation (see footnote 1) of the pure active halogen derivatives of 2-methylbutanol-1, in which the halogens are indirectly attached to the asymmetric carbon, showed that the differences of the molecular rotations have a numerical relation which agrees with that for the differences in atomic radii of the respective neutral halogen atoms as required by rule II.

The present paper reports the results obtained with the active halogen derivatives of pentanol-2, for which compounds rule I should be applicable, since the halogen is directly attached to the asymmetric carbon atom.

II. EXPERIMENTAL PART OF INVESTIGATION

1. PREPARATION OF THE COMPOUNDS

(a) DEXTRO- AND LEVOROTATORY PENTANOL-2 (METHYLPROPYLCARBINOL)

Four and a half kilograms of inactive pentanol-2 (methylpropylcarbinol) was prepared from propyl bromide and acetaldehyde according to the Grignard method [5] in batches that could be worked in 2-liter flasks. The preparation was kept for a few months over

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[1] J. Research NBS **18**, 315 (1937) RP978.

[2] J. Am. Chem. Soc. **47**, 1285 (1925); BS J. Research **7**, 573 (1931) RP358.

[3] *D* and *L* refer to configuration.

[4] For a discussion of the values used, see section III, p. 98.

[5] R. H. Pickard and J. Kenyon, J. Chem. Soc. **99**, 55 (1911).

dry potassium carbonate, for resinifying small amounts of aldehyde, which is hard to separate by fractionation. The preparation then gave directly on distillation a product having the correct boiling point. The yield was about 40 percent of the theoretical amount. In the course of the investigation there were prepared from the inactive alcohol 1,200 g of pure dextrorotatory and 600 g of pure levorotatory alcohol in batches of about 200 to 300 g. This large amount of active alcohol. requiring more than 2 years of fractional recrystallization of the brucine salt of the acid phthalate of methylpropylcarbinol, was needed because it was necessary to determine which method of halogenation causes the least racemization.

The remaining part of the inactive alcohol was used for certain preliminary experiments. The pure active alcohol is stable, although some of the preparations, even when stored in the refrigerator, diminished slightly in rotation (less than 0.4% in 1 year), but this change may be due to the presence of small amounts of water, which are difficult to remove.

The resolution to the active dextro- and levorotatory alcohols was performed according to the method of Pickard and Kenyon (see footnote 5), which consists of the fractional crystallization of the isomeric brucine amyl phthalates. Although the directions given by the authors were found to be reliable, the writer has made the two improvements mentioned below.

1. It is advantageous for increasing the yield and decreasing the time of reaction to use for the esterification of the alcohol pure, freshly distilled phthalic anhydride free from phthalic acid.
2. The following procedure has been found useful for evaluating the numerous fractions of the brucine amyl phthalate used for separating the *D* and *L* forms of the alcohol.

As soon as the crystals of a fraction are separated from the mother liquor, a sample of about 1 g is crushed in a dish with a small glass pestle and allowed to dry for 30 minutes in air, with occasional stirring. A solution containing exactly 0.6 g of this sample is made up to 25 ml at 20° C with chloroform, placed in a water-jacketed 4-dm tube at 20° C, and read with a polariscope. The reading varies for the fractions from —1.38 circular degrees for the pure compound of the *D* alcohol to —2.41 circular degrees for the pure compound of the *L* alcohol. This relatively small difference in rotation is nevertheless a great help in estimating the extent of separation of the fractions. For obtaining these results it is necessary to maintain uniform conditions not only as to concentration and temperature (since the rotation of the brucine salts is greatly influenced by these factors) but also as to the time used for powdering and drying the sample. The method of drying is of importance because it was found that the brucine salts crystallize with varying amounts of acetone of crystallization, and part of this is readily volatilized.

An investigation of the brucine amyl phthalates has revealed that the pure brucine salt of the acid phthalic ester of dextrorotatory methylpropylcarbinol crystallyzes with 2 molecules of acetone when a warm acetone solution is cooled. By longer standing of the mother liquor at room temperature, crystals with 1 molecule of acetone to 2 molecules of brucine salt may separate, whereas the mother liquor in the refrigerator may again yield the compound with 2 molecules of acetone. When 0.6 g of the freshly prepared compound with 2 molecules of acetone, $C_{36}H_{42}O_8N_2+2(C_3H_6O)$, is freed from acetone by drying to constant weight in a vacuum oven at 75° C and made up to 25 ml at 20° C with chloroform, it has a specific rotation of —17.5°, expressed on the acetone-free basis. The compound with 2 molecules of acetone loses 1 molecule of acetone easily in air; the other molecule is lost by standing in vacuum at room temperature for several weeks, or more quickly in a vacuum oven at 75° C.

Usually, the pure brucine salt of the acid phthalic ester of the levorotatory methylpropylcarbinol crystallizes from a warm acetone solution by cooling, with less than 2 molecules of acetone. The results of the quantitative determinations for different samples vary, and hence no definite conclusion as to the composition can be drawn. It was also found for the compound of the levorotatory alcohol that 1 molecule of acetone is strongly bound, but is lost by drying in a vacuum oven at 75° C. When 0.6 g of the pure brucine salt containing the levorotatory alcohol is freed from acetone by drying in a vacuum oven at 75° C, and made up to 25 ml at 20° C with chloroform, it has a specific rotation of —25.9°, expressed on the acetone-free basis. These results were obtained as an average of many determinations. The existence of these acetone compounds explains why the uniform procedure is necessary for the polariscopic evaluation of the acetone-containing brucine salts. Only 1 molecule of acetone of crystallization is left after powdering and drying the substance in air for 30 minutes. The method described is sufficiently accurate for the evaluations of the fractions.

The writer's results are in accord with those of Pickard and Kenyon,[6] with the exception of the rotation of the hydrogen phthalic ester of dextrorotatory methylpropylcarbinol, concerning which Pickard and Kenyon made the following remark:

> Determinations of the molecular rotatory powers of the hydrogen phthalic esters in chloroform solution gave results which run practically parallel with those of the alcohols in the pure state, although in the case of the esters the first member occupies apparently a normal place in the series and has not, as in the case of the alcohols (as also in so many series described by other investigators) an abnormal rotatory power.

If the values for the specific and the molecular rotations of the hydrogen phthalic ester of dextrorotatory methylpropylcarbinol: $[\alpha]_D=+36.94$ and $[M]_D=+87.2$ given by Pickard and Kenyon are replaced by $[\alpha]_D=+43.05$ and $[M]_D=+101.6$, which were found by the author for the concentration and in the same solvent as used by Pickard and Kenyon, and checked many times in the course of this investigation, it is readily seen (table 1) that now also for the hydrogen phthalic esters, the first member occupies an abnormal place in the series just as in the case of the alcohols.

Since the melting point of the ester agrees with that reported by Pickard and Kenyon, it seems that the difference in the optical rotations must be due to an error in the measurement of the optical rotation.

(b) DEXTROROTATORY 2-FLUOROPENTANE

In the preparation of 2-fluoropentane, the method previously used for preparing 1-fluoro-2-methylbutane (see footnote 1) by the action

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[6] R. H. Pickard and J. Kenyon, J. Chem. Soc. **99**, 52 (1911).

Table 1.—*Comparison of rotations of a homologous series of hydrogen phthalates of active alcohols*

Hydrogen phthalate of—	Rotation in chloroform (5%). Average values			
	$[\alpha]_D$		$[M]_D$	
	Pickard and Kenyon	Brauns	Pickard and Kenyon	Brauns
Methylethylcarbinol	33.53	----------	74.5	--------
Methylpropylcarbinol	36.94	[a] 43.05	87.2	101.7
Methyl *n*-butylcarbinol	43.39	----------	108.5	--------
Methyl *n*-amylcarbinol	43.92	----------	116.0	--------
Methyl *n*-hexylcarbinol	42.94	----------	119.3	--------
Methyl *n*-heptylcarbinol	41.11	----------	120.0	--------
Methyl *n*-octylcarbinol	39.06	----------	119.5	--------
Methyl *n*-nonylcarbinol	37.27	----------	119.2	--------
Methyl *n*-decylcarbinol	35.59	----------	[b] 121.0	119.0
Methyl *n*-undecylcarbinol	35.34	----------	123.1	--------

[a] The constants of optically active pentanol-2 and its halogen derivatives of highest purity prepared for this investigation are recorded in tables 2 and 3.

[b] Error in calculation, corrected in next column.

of silver fluoride on the corresponding bromine derivative was improved by following a modification by Bockemueller,[7] who employed finely divided silver fluoride mixed with pure calcium fluoride. A short description of the preparation of the reagent follows. Pure calcium fluoride free from silica was prepared by the addition of a hot solution of calcium chloride to pure hydrofluoric acid solution in a platinum dish; the precipitated calcium fluoride was separated by decantation, collected on a filter and washed with water until free from chloride. A concentrated silver fluoride solution was prepared by dissolving silver carbonate in pure aqueous hydrofluoric acid in a platinum dish. The calcium fluoride was added to the silver fluoride solution in the proportions of 3 to 2, and the mixture was dried in a shallow platinum dish suspended by platinum wires from the stopper of the cover of a large paraffined desiccator provided with potassium hydroxide pellets. The desiccator was evacuated at first with a water pump and after a few days with an efficient oil pump protected by a soda-lime tower.

From time to time the material was stirred and finally powdered with a platinum pestle. The preparation was made in subdued light and kept in the dark. This procedure differs from the one given by Bockemueller, in that no heat was applied for drying the material.

The following method was used for preparing the fluorine derivative: Thirty grams of 2-bromopentane having a specific rotation of -35.9 (which is 99% of that of the highest-rotating 2-bromopentane, with $[\alpha]^{20}_D = -36.2$) was mixed with 90 ml of pure dry acetonitrile. A 250-ml platinum bottle containing 75 g of the silver fluoride-calcium fluoride mixture was closed with a rubber stopper and cooled in ice water. The solution of 2-bromopentane in acetonitrile was quickly added, and the tightly closed bottle (inserted in a Thermos bottle containing cold water) was shaken for 22 days. The temperature of the water was kept at 5° to 15° C. Three portions, 3 g each, of the silver fluoride-calcium fluoride mixture were added at about equal

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[7] W. Bockemueller, Liebigs Ann. Chem. **506**, 20 (1933).

intervals during the period of the shaking. Also the rotation of a small filtered sample was determined in a 0.2-dm tube at these intervals in order to determine the end of the reaction. When the end was reached, the mixture was filtered on a fritted-glass disk and the flask cooled with ice water.

After removing the filtrate, a slight suction (600-mm pressure) was applied for washing with acetonitrile. About 80 ml of solution rotating +0.65 sugar degrees (°S) in a 0.2-dm tube was thus obtained. The filtrate was then distilled in a platinum distilling apparatus. The retort was heated gradually in an oil bath to 120° C, and the condenser and receiver were cooled with ice water. The distillate was kept overnight in contact with potassium carbonate in the icebox and then filtered. The filtrate was distilled and then fractionated at ordinary pressure from a Pyrex fractionating column, which has been formerly described. (See footnote 1.) The condenser and receiver were cooled with ice water. Finally, a microfractionating column with fine platinum-ruthenium spirals was used. For preventing bumping, a slow stream of dry nitrogen was introduced through a fine capillary. This procedure was applied for the fractionation of all halogen derivatives. 2-Fluoropentane can be distilled at ordinary pressure without decomposition. The yield was about 3 g. The constants are recorded in tables 2 and 3. The quantitative fluorine determination was performed according to a new procedure.[8] Weight of substance: 0.1104 g; loss by etching: 0.0221 g; calculated for $C_5H_{11}F$: F, 21.09 percent; found: 21.1 percent.

(c) LEVOROTATORY 2-CHLOROPENTANE

Miss Sherrill[9] applied a method of low-temperature chlorination for inactive secondary heptylalcohol, which is an adaptation of the method of Norris and Taylor[10] modified by Lucas.[11]

Following this procedure, 20 g of active methylpropylcarbinol ($[\alpha]^{20}_D = +13.8$) was added to an ice-cold solution of 62 g of zinc chloride in 46 g of 36-percent hydrochloric acid in a 300-ml Erlenmeyer flask. The flask was closed with a glass stopper and shaken for 7 hours at 0° C. The oily layer was separated after standing overnight in a separatory funnel, and shaken with a new solution of 62 g of zinc chloride in 46 g of 36-percent hydrochloric acid for 7 hours at 0° C. After separating the oily layer, the process was repeated for a third time. The oily layer was washed three times with concentrated hydrochloric acid, afterward four times with ice-cold water, once with ice-cold 10-percent sodium hydroxide solution, twice with cold 15-percent sodium chloride solution, and finally washed once with cold water. The product was dried over a mixture of calcium chloride and potassium carbonate, filtered, distilled, and finally fractionated at a pressure of 250 mm. About 17 g of a chlorine derivative was obtained.

A quantitative chlorine determination by the Carius method gave the following results: Substance, 0.2260 g; AgCl, 0.3034 g. Calculated for $C_5H_{11}Cl$: Cl, 33.28. Found: Cl, 33.21 percent. The rotation of the product in a 0.2 dm-tube at 20° C was −3.0° S, which is very low compared with the rotation of the product obtained by the follow-

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[8] D. H. Brauns, J. Research NBS **27**, 105 (1941) RP1406.
[9] Mary L. Sherrill, J. Am. Chem. Soc. **52**, 1985 (1930).
[10] J. F. Norris and H. B. Taylor, J. Am. Chem. Soc. **46**, 753 (1924).
[11] H. J. Lucas, J. Am. Chem. Soc. **51**, 249 (1929).

ing method of chlorination. Inasmuch as zinc chloride acts not only as a catalyst but as a dehydrating agent, it leads to the formation of amylenes, which in turn combine with hydrogen chloride with the formation of isomeric chlorine derivatives.

The second procedure for converting active pentanol-2 to its chlorine derivative by the use of dry hydrogen chloride without zinc chloride gives better results. It was found that hydrogen chloride reacts with the alcohol at a temperature of 75° to 80° C, and thus it is necessary to seal the reaction tube to prevent loss. These preliminary experiments were made with inactive methylpropylcarbinol. Subsequently, experiments with the active alcohol were made for finding the conditions under which the highest-rotating chlorine derivative is formed. The following procedure was finally adopted:

Twenty grams of active methylpropylcarbinol ($[\alpha]_D^{20}=+13.8$) was cooled in a Pyrex pressure tube with ice and salt, and saturated with a slow stream of dry hydrogen chloride. The tube was sealed and heated gradually to 80° C in a shaking machine and kept at this temperature with shaking for 2.5 hours. The tube was then cooled, opened, and the upper layer separated from the aqueous layer in a separatory funnel. The upper layer was extracted twice with 8 ml of cold 10-percent sodium hydroxide solution, and then repeatedly with ice water. The product was separated from adhering drops of water, by pouring into a dry Erlenmeyer flask and decanting therefrom, after which it was dried over potassium carbonate for several hours and then filtered. The filtrate was first distilled and then fractionated at 250-mm pressure. The rotation of the product was not changed by additional fractionation. The preparation was repeated with another 20 g of active alcohol for obtaining a sufficient amount of chlorine derivatives. The total yield was 7 g. A quantitative chlorine determination by the Carius method gave the following results: Substance, 0.2071 g; AgCl, 0.2771 g. Calculated for $C_5H_{11}Cl$: Cl, 33.28. Found: Cl, 33.10 percent. The rotation of the product in a 0.2-dm tube at 20° C was −15.2° S, which is about five times that found for the product obtained by the zinc chloride-hydrogen chloride method of chlorination.

Chlorination with thionyl chloride and with phosphorus pentachloride did not give satisfactory results, whereas the chlorination with phosphorus trichloride gave the highest-rotating product. The last method was studied as before, first with inactive methylpropylcarbinol, and finally with the active alcohol. Thus it was found that heating the alcohol with phosphorus trichloride at 95° C is necessary for obtaining a sufficient rate of reaction. The following method was finally adopted.

Twenty grams of active methylpropylcarbinol ($[\alpha]_D^{20}=+13.6$) was cooled in a Pyrex pressure tube with ice water, and 18.9 g (12 ml) of phosphorus trichloride was added drop by drop from a small burette; calcium chloride tubes were used for excluding moisture. The pressure tube was closed with a calcium chloride tube and allowed to attain room temperature. It was sealed, shaken for 2.5 hours at 95° C, then cooled in ice and salt, and opened. The chlorinated product was poured from the sirupy phosphorous acid into a beaker of cracked ice and some water, under stirring. The product was repeatedly shaken with small portions of ice water in a separatory funnel until the water was neutral to litmus paper. The product was separated from adhering drops of water, and dried over potassium carbonate. The ice water used for the purification was extracted with ether. The ether solution was dried and fractionated, and the yield of the alcohol was thus increased to about 17 g.

Since the chlorine derivative thus obtained had a higher specific rotation than the product of any other method of chlorination, 170 g of active alcohol in 30-g batches was converted by this method to the chlorine derivative. The crude product after distillation rotated in a 0.2-dm tube at 20° C about −13.6° S. The fractionations were carried out in a fractionating column similar to the one previously described (see footnote 1). The column, 10 mm in diameter and 900 mm in length, containing glass helices 0.65 mm thick and 4.5 mm in diameter, is equivalent to a column of 22 theoretical plates.[12] The fractionations were carried out at 250-mm pressure. The capillary was supplied with dry nitrogen, and the condenser and receiver were cooled with ice water. Fractions were taken regularly from the slow fractionations, and the optical rotations were read in a 0.2-dm tube. The final product, which had a constant rotation on fractionation (−17.5° S. in a 0.2-dm tube at 20° C) was obtained after 4 months of fractionation. A quantitative chlorine determination by the Carius method gave the following results: Substance, 0.1915 g: AgCl, 0.2581 g. Calculated for $C_5H_{11}Cl$: Cl, 33.28. Found: Cl, 33.24 percent. The constants for the highest-rotating 2-chloropentane are recorded in tables 2 and 3.

(d) LEVOROTATORY 2-BROMOPENTANE

Two methods of bromination (with hydrobromic acid and with phosphorus tribromide) were studied. The bromination with hydrobromic acid was performed according to the procedure described for the preparation of the bromide derivative of the primary amyl alcohol (see footnote 1).

Forty grams of active methylpropylcarbinol ($[\alpha]^{20}_D = +13.8$) was saturated at 0° C with hydrogen bromide in a double flask. The solution was heated under reflux for 2 hours. The temperature was maintained at 70° C except for the last quarter hour, when it was allowed to rise to 85° C. The reaction product was worked up and dried as described for the bromination of the primary alcohol. The preparation was repeated for two other 40-g batches of active methylpropylcarbinol. The combined preparations were dried with potassium carbonate and distilled at 150-mm pressure to remove small amounts of the dissolved drying agent. The yield was 180 g, or 88 percent of the theoretical amount. The product was then carefully fractionated at 150-mm pressure in the column of 22 theoretical plates. A quantitative bromine determination by the Carius method on the highest-rotating fraction gave the following results: Substance, 0.2282 g: AgBr, 0.2848 g. Calculated for $C_5H_{11}Br$: Br, 52.95. Found: Br, 53.16 percent. The rotation of the product in a 0.2-dm tube at 20° C was −22.7° S.

The bromination with phosphorus tribromide was studied under various conditions with 10-g batches of active alcohol. The following method was adopted: Forty grams of active methylpropyl-

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[12] F. C. Whitmore, et al., J. Am. Chem. Soc. **62**, 797 (1940).

carbinol ($[\alpha]^{20}_{D}=+13.6$) was cooled in ice in a flask provided with a calcium chloride tube. The flask was also connected with a burette containing 60.8 g of redistilled phosphorus tribromide, which was protected by a calcium chloride tube. The phosphorus tribromide was added slowly drop by drop to the cooled methylpropylcarbinol, and the flask was occasionally rotated. The mixture was allowed to stand at room temperature overnight, and the next morning it was heated for three quarters of an hour on the steam bath. The preparation was then cooled in an ice and salt mixture. The supernatant liquid was decanted from the sirupy phosphorus derivatives into a mixture of ice and water, under stirring. The oily bromine derivative, which separated from the ice water, was shaken repeatedly in a separatory funnel with small amounts of ice water until the wash water was neutral to litmus paper. A centrifuge was helpful for separating the product from the wash water. The preparation was separated from the adhering water and then dried over potassium carbonate. The dry preparation on distillation gave 63 g of product, or 92 percent of the theoretical amount.

The preparation was repeated several times, to yield 300 g of impure bromine derivative ranging from −22.3 to −23.0° S in a 0.2-dm tube at 20° C. This product was purified by fractional distillation at 110-mm pressure until it exhibited no increase in rotation on further fractionation. The rotation of the pure product in a 0.2-dm tube at 20° C was −25.3° S, which is appreciably higher than the rotation of the bromine derivative made with hydrobromic acid. A quantitative bromine determination by the Carius method gave the following results: Substance, 0.2607g: AgBr, 0.3251g. Calculated for $C_5H_{11}Br$: Br, 52.92. Found: Br, 53.07 percent. The constants found for the highest-rotating 2-bromopentane are recorded in tables 2 and 3.

(c) LEVOROTATORY 2-IODOPENTANE

The preparation of this compound was studied by two methods: The first method was by the action of hydriodic acid, and the second was by action of phosphorus triiodide on the alcohol.

The first method was performed according to the procedure described for the preparation of the iodine derivative of the primary amyl alcohol (see footnote 1) with 40 g of active methylpropylcarbinol ($[\alpha^{20}_{D}=+13.8$). The yield of the product distilled at 50-mm pressure was 80 g or 89 percent of the theoretical amount. The yield of three 40-g batches was combined and carefully fractionated at 50-mm pressure. The rotation of the fraction, which did not change on further fractionation, was −34.4° S in a 0.2-dm tube at 20° C. A quantitative iodine determination on this fraction by the Carius method gave the following results: Substance, 0.1647g: AgI, 0.1956g. Calculated for $C_5H_{11}I$: I, 64.09. Found: I, 64.19 percent.

The second method was applied in the following way: Ten grams of active methylpropylcarbinol ($[\alpha]^{20}_{D}=+13.6$) was introduced in a flask provided with a calcium chloride tube and condenser, and the flask was cooled in ice water. Forty-five grams of phosphorus triiodide of pea size, weighed off in a weighing bottle, was added to the alcohol and another 10 g of active methylpropylcarbinol was added for rinsing down the phosphorus triiodide adhering to the neck of the flask. The ice-cold mixture was gradually heated to room temperature and then heated slowly on the steam bath until all phosphorus triiodide was dissolved to form a colored solution, which required about half an hour.

The warm solution was poured on a mixture of water and cracked ice under stirring, and purified and dried as described for the first method. The yield of the distilled product was about 89 percent of the theoretical amount. Three months of careful fractional distillation at 50-mm. pressure gave a sufficient amount of the final product. The rotation of this fraction, which did not change on further fractionation, was −34.5° S in a 0.2-dm tube at 20° C. This rotation is somewhat higher than that of the final product from the first method, even though a higher-rotating alcohol was used in the preparation by the first method. Thus the second method seems to be preferable. A quantative iodine determination by the Carius method gave the following results: Substance, 0.1739g: AgI, 0.2067g. Calculated for $C_5H_{11}I$: I, 64.09. Found I, 64.25 percent. The constants found for the highest-rotating 2-iodopentane are recorded in tables 2 and 3.

2. PROPERTIES OF COMPOUNDS

(a) OPTICAL ROTATION

The optical rotation was determined with a polariscope with a circular scale and double-field Lippich polarizer. Jacketed glass polariscope tubes were used. These were checked for the recorded length. For each compound investigated the rotation was determined for the two wave lengths 5892.5 and 5461 A on the circular-scale polariscope, using spectrally purified light from a sodium-vapor lamp and a mercury-vapor lamp, respectively. A third determination was made with the same sample and tube in the Bates saccharimeter, using white light and a bichromate filter, which give an effective wavelength of about 5850 A. These data are given in table 2, together with values reported by Pickard and Kenyon.

(b) SPECIFIC GRAVITY

Picnometers similar to those previously described (see footnote 1) were used for determining the specific gravity of the substances at 20° C. and a formula was applied for obtaining the specific gravity at 20°/4° in vacuum.

(c) REFRACTIVE INDEX

The values of the refractive index of the substances were determined at 20° C. with an Abbe refractometer. These data, together with calculated values of the molecular refraction, are given in table 2. A comparison of the refractivities of pentanol-2 and its halogen derivatives with the refractivities of 2-methylbutanol-1 and its halogen derivatives is given in table 6.

TABLE 2.—*Optical rotation, specific gravity, and refraction of dextrorotatory pentanol-2 and its halides of highest rotation*

Substance	Optical rotation							Specific gravity		Refractivity	
	Observed rotation, α, for—			$\frac{\alpha}{ld}$, Specific rotation at 20.0° C for—			Specific rotation by other investigators	d_4^{20} vac.	*d* by other investigators	Refractive index, n_D^{20}	Molecular refraction, $M=\frac{(n^2-1)}{(n^2+2)d}$
	λ 5892.5 A	λ 5461 A	White light and filter	λ 5892.5 A	λ 5461 A	White light and filter					
Dextrorotatory pentanol-2	+11.261 [a] (1 dm)	+13.238 (1 dm)	+11.290 (1 dm)	+13.901	+16.341	+13.930	[b] $[\alpha]_D^{20}=+13.70$	0.8101	[b] 0.8116	1.4056	26.704
Dextrorotatory 2-fluoropentane	+2.589 (0.2 dm)	+3.041 (0.2 dm)	+2.595 (0.2 dm)	+16.621	+19.521	+16.659		.7788		1.3520	25.032
Dextrorotatory 2-chloropentane	+5.930 (0.2 dm)	+7.026 (0.2 dm)	+5.94 (0.2 dm)	+34.072	+40.373	+34.10		.8702		1.4065	30.121
Dextrorotatory 2-bromopentane	+8.719 (0.2 dm)	+10.398 (0.2 dm)	+8.75 (0.2 dm)	+36.190	+43.161	+36.34		1.2046		1.4409	33.107
Dextrorotatory 2-iodopentane	+11.989 (0.2 dm)	+14.417 (0.2 dm)	+11.96 (0.2 dm)	+39.921	+48.015	+39.82	[b] $[\alpha]_D^{20}=+37.15$	1.5013	[b] 1.5067 for d_4^{17}	1.4951	38.478

[a] Length of tube *l* in decimeters.
[b] Pickard and Kenyon.

(d) BOILING POINTS AT VARIOUS PRESSURES

A Cottrell-Washburn boiling-point apparatus was used with some modifications, as described in the former publication (see footnote 1). Calibration corrections were applied to the thermometer readings. The values of the boiling points correspond to the given pressures in millimeters of mercury at 0° C and standard gravity. The results are shown in tables 3 and 7, and are shown graphically in figure 1 in comparison with the boiling-point curves for 2-methylbutanol-1 and its halides.

TABLE 3.—*Boiling points of pentanol-2 and its halides*

Pressure	Pentanol-2	2-Fluoropentane	2-Chloropentane	2-Bromopentane	2-Iodopentane
mm of Hg	° *C*	° *C*	° *C*	° *C*	° *C*
50	57.2	------	24.7	42.5	63.4
100	71.0	------	39.4	58.3	80.1
150	79.2	14.4	49.5	68.2	90.7
200	85.4	20.8	56.6	75.9	98.4
300	94.5	30.6	67.9	87.7	110.9
400	101.6	37.8	76.2	96.2	120.3
500	107.6	43.1	82.8	103.6	128.6
736.5 [a]	------	------	------	116.9	------
745.9 [a]	------	------	95.6	------	------
753.4 [a]	------	------	95.9	------	------
756 [a]	119.2	------	------	------	------
750 [a]	------	54.9	------	------	------
760 [b]	119.4	55.3	96.2	118.0	(c)

[a] Atmospheric pressure observed.
[b] Values calculated to normal boiling point according to Int. Crit. Tables **3**, 246 (1928).
[c] Decomposed.

3. EXPERIMENTS FOR THE CLASSIFICATION OF THE FOUR ACTIVE HALOGENOPENTANES

Before rule I could be tested it was necessary that the four active halogen derivatives be classified according to their configuration, since only derivatives of like configuration are comparable. It has been found by many investigators that starting from active secondary alcohols some reactions yield active derivatives with an inverted configuration. The subject of inversion is treated in more detail in section III.

It seemed highly probable that reaction of an optically active alcohol with analogous halogenating agents, as with HCl, HBr, and HI, or with PCl_3, PBr_3, and PI_3, should yield three active halogen derivatives of predominantly *D* configuration or three derivatives of predominantly *L* configuration. Efforts to obtain the fluorine derivative by methods analogous to those used for obtaining the other halogen derivatives were not successful, and many experiments with hydrofluoric acid under different conditions did not yield an active fluorine compound. As already described, the active 2-fluoropentane was obtained from the active bromo- or idopentane by the action of silver fluoride. Hence the above scheme could not be applied for the classification of all halogen derivatives.

It was finally realized that an analogous saponification method might be useful for deciding the question. Indeed, the following experiments led to the solution of the problem. (It is necessary to describe these experiments in detail to arrive at an interpretation.)

Twelve grams of levorotatory 2-chloropentane originally prepared by the hydrogen chloride method and rotating −14.3° S in a 0.2-dm tube (about 83% of the rotatory power of the highest-rotating 2-chloropentane) was shaken with 200 ml of aqueous normal sodium hydroxide solution in a sealed tube at 135° C for 24 hours. After cooling the tube it was opened and the upper layer separated. The aqueous solution was neutralized with 3-normal nitric acid, filtered, and extracted with ether. The ether extract was added to the separated layer and the mixture dried and fractionated, first at ordinary pressure for separating the ether and then at 200-mm pressure. After three fractionations, in which the highest-rotating fractions were combined, a 3-g fraction was collected. This had a rotation of +4.2° S, in a 0.2-dm tube. This fraction could be identified by its positive rotation, boiling point, refractive index, and odor, and the melting point of its acid phthalate as dextrorotatory methylpropylcarbinol.

It may be calculated that by using the purest 2-chloropentane (prepared by the phosphorus trichloride method) which rotates 100/83 times higher than the 2-chloropentane used in the saponification method, a dextrorotatory methylpropylcarbinol of 4.2/0.83=5.05° S in a 0.2-dm tube could be obtained. As the alcohol originally used for the chlorination rotated +6.45° S in a 0.2-dm tube, the methylpropylcarbinol recovered from the saponification of the 2-chloropentane had the same sign of rotation as the original alcohol used for the chlorination, but the magnitude of its rotation was only 78 percent of that of the original alcohol.

The saponification of 2-bromopentane can be performed under milder conditions than those used in the saponification of 2-chloropentane. Ten grams of levorotatory 2-bromopentane of −25.2° S in a 0.2-dm tube (the purest 2-bromopentane obtained rotated −25.3° S in a 0.2-dm tube) was shaken with 140 ml of aqueous normal sodium hydroxide solution in a sealed tube at 90° C for 12 hours and worked up as described for the saponification of 2-chloropentane. A 2.5-g fraction was obtained, which exhibited an optical rotation of +4.5° S in a 0.2-dm tube. Hence the methylpropylcarbinol recovered from the saponification of 2-bromopentane had the same sign of rotation as the original alcohol used for the bromination, but the magnitude of the rotation was only 70 percent of that of the original alcohol.

The saponification of 2-iodopentane gave only a small yield of alcohol. Fifteen grams of 2-iodopentane of −33.8° S in a 0.2-dm tube (the purest 2-iodopentane rotated −34.5° S in a 0.2-dm tube) was shaken with 150 ml of aqueous normal sodium hydroxide solution in a sealed tube at 110° C for 42 hours and worked up as described for the saponification of 2-chloropentane. One and one-half grams of a fraction rotating +4.4° S in a 0.2-dm tube was obtained. The product was identified, as described for 2-chloropentane, as dextrorotatory methyl propylcarbinol. It may be calculated that by using the purest 2-iodopentane, a methylpropylcarbinol of $+4.4\times(34.5/33.8)=+4.5°$ S in a 0.2-dm tube could be obtained. Hence the methylpropylcarbinol recovered from the saponification of 2-iodopentane had the same sign of rotation as the original alcohol used for the iodination, but the magnitude of its rotation was 70 percent of that of the original alcohol.

For the saponification of dextrorotatory 2-fluoropentane, obtained by treatment of levorotatory 2-bromopentane with silver fluoride, the following procedure was used. In a preliminary experiment, 3.6 g of slightly inpure 2-fluoropentane of +6.2° S in a 0.2-dm tube was shaken with 100 ml of half-normal aqueous sodium hydroxide solution at 95° to 100° C in a sealed tube for 12 hours. For determining the progress of the reaction, the tube was cooled and opened.

The reaction mixture consisted of a supernatant liquid and an aqueous alkaline solution. The supernatant liquid, largely unchanged fluorine derivative, was separated and without further purification showed an optical rotation of +6.6° S in a 0.2-dm tube, or an increase of 6.5 percent. The aqueous alkaline solution gave a test for bromides and was destrorotatory. Since the fluorine derivative was prepared from levorotatory 2-bromopentane, it must have been contaminated with this substance, which, on treatment with sodium hydroxide, gives sodium bromide and dextrorotatory methylpropylcarbinol. The increase in the dextrorotation of the fluoropentane was caused by removal of the levorotatory impurity, whereas the dextrorotation of the aqueous solution was caused by the presence of the dextrorotatory alcohol. In fact, a sample of the fluorine derivative obtained by microfractionations, as described elsewhere, gave an optical rotation of +7.5° S in a 0.2-dm tube, a value considerably higher than that of the material used for hydrolysis.

Unfortunately, the writer did not have a sufficient quantity of this pure material to make saponification measurements.

To effect saponification of the fluorine derivative, more vigorous treatment is necessary. The material, after treatment with sodium hydroxide, as described above, was shaken with 8 g of barium hydroxide ($Ba(OH)_2+8H_2O$) and 100 ml of water in a sealed tube at 135° C. Following the progress of the reaction, the tube was intermittently cooled and opened; a portion of the barium hydroxide solution was neutralized and filtered, and its rotation was read to determine the amount of dissolved active alcohol. The rotation of the liquid after 7 days of shaking at 135° C remained constant. The reaction product was worked up as described, and about 1 g of a levorotatory fraction of −4.1° S in a 0.2-dm tube was obtained. The optical rotation of the fraction was 64 percent of that of the alcohol originally used for the preparation. The product was identified, as described before, as the levorotatory methylpropylcarbinol. Hence the enantiomorphic levorotatory 2-fluoropentane would yield by alkaline saponification a dextrorotatory alcohol. Thus the saponification experiments show that all halogen derivatives of pentanol-2 of the same sign of rotation have the same configuration.

Another important conclusion can be drawn from the saponification experiments in conjunction with the work of Ingold and Hughes, who established (for literature, see sec. III, p. 97), that alkaline alcoholic hydrolysis of chlorine and bromine derivatives of secondary alcohols yield active alcohols with about 90 percent retention of optical activity. Thus the separation of a 60- to 70-percent optically pure alcohol by the alkaline aqueous hydrolysis indicates that the parent chlorine and bromine derivatives were about 75 percent optically pure. The low yield of alcohol from the iodine derivative may be explained by cleavage of hydrogen iodide with the formation of amylenes, but nevertheless the alcohol obtained was about 70 percent optically pure. Assuming a 90 percent retention of optical activity, the parent iodine derivative was about 80 percent optically pure. For the fluorine compound, however, another interpretation is indicated. As already mentioned, treatment of the crude fluorine derivative with half-normal sodium hydroxide increased the dextrorotation by 6.5 percent. This increase was attributed to the hydrolysis of a small quantity of the levorotatory bromine compound present as an impurity. Of equal importance is the peculiarity that the time and temperature necessary for the saponification of the fluorine compound are considerably greater than those required for the other halogen compounds. Since the fluorine compound is exceptionally resistant to saponification, its ionization is undoubtedly low.

According to Ingold and Hughes, see footnote 13, reaction with retention of configuration usually requires ionization. Inasmuch as the fluorine compound exhibits an exceptionally low ionization, one might anticipate that replacement of the fluorine by alkaline saponification would occur almost exclusively with inversion and the optical purity of the alcohol (64%) obtained on saponification would be a measure of the optical purity of the fluorine compound. This value is questionable because the fluorine compound contained small amounts of optically inactive impurities that could be removed by fractionation and the drastic conditions of hydrolysis may have produced racemization of the alcohol formed. From these considerations the author estimates that the specific rotation of the fluorine compound obtained is approximately 65 percent (±10%) of that for the optically pure fluorine compound.

III. DISCUSSION OF RESULTS

1. GENERAL

As already noted, it has been established by many investigations that active secondary alcohols in which the OH group is directly attached to the asymmetric carbon atom yield with some reagents active derivatives of the same configuration and with other reagents, active derivatives with a predominantly inverted configuration. These investigations clearly showed that by displacing one of the elements directly attached to the asymmetric carbon of an optically active compound, in this case the oxygen atom of the OH group, the asymmetric grouping may be changed to its mirror image, with a more or less complete Walden inversion. But if only the hydrogen atom of the OH group is replaced and the oxygen is left undisturbed, the product of the reaction will have the same configuration as that of the original alcohol.

A part of these observations recorded in the literature which is of interest here can be condensed to the following generalizations.[13]

1. The change of an optically active secondary alcohol to a halogen derivative will involve a predominating Walden inversion of configuration.

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[13] The following references are not complete but indicate the development:
A. Werner, Liebigs Ann. Chem. **386,** 70 (1912).
J. Gadamer, J. prakt. Chem [2] **87,** 344 (1913).
J. Meisenheimer, Liebigs Ann. Chem. **456,** 121 (1927).
B. Holmberg, Ber. deut. chem. Ges. **59,** 125 (1926).
H. N. K. Rørdam, J. Chem Soc. **1930,** 2017.
H. Phillips, J. Chem. Soc. **123,** 44 (1923).
N. Meer and M. Polanyi, Z. physik. Chem [B] **19,** 164 (1932).
E. D. Hughes, C. K. Ingold, and S. Masterman, J. Chem. Soc. (**1937**) 1196, and subsequent publications. Discussion in "Physical Organic Chemistry" by L. P. Hammett, McGraw-Hill Book Co., New York, N. Y., 1940.

2. If the halogen of a derivative is displaced by another halogen, a predominating Walden inversion will take place.

3. The saponification of the halogen derivative by sodium or potassium hydroxide to the alcohol will likewise involve a Walden inversion.

In the present investigation it has been shown that dextrorotatory pentanol-2 yields, on halogenation, the levorotatory chloride, bromide or iodide; similarly, the levorotatory alcohol yields the corresponding dextrorotatory halides. Furthermore, levorotatory 2-bromopentane and 2-iodopentane on treatment with silver fluoride yield dextrorotatory 2-fluoropentane. Likewise, dextrorotatory 2-bromopentane yields levorotatory 2-fluoropentane. According to the generalizations outlined above, each of these reactions involves a Walden inversion, and it follows that dextrorotatory pentanol-2 and the four dextrorotatory halides all have the same configuration and that the levorotatory compounds are similarly related. The results of the saponification experiments reported in this paper are in harmony with this conclusion, since they show that 2-fluoro-, 2-chloro-, 2-bromo-, and 2-iodopentane of the same sign of rotation have the same configuration. The results, however, do not establish the relationship of the configuration of these compounds to that of pentanol-2.

It is appropriate to make a few remarks concerning the atomic diameter values used in this investigation.

At the beginning of this investigation only Bragg's values for the radii of ions of inorganic substances were available. Later it was found that radii of the ions of inorganic substances differ appreciably from the atomic radii of the same elements when in covalent combination. The latter radii are properly required for the author's comparisons of optical rotation and atomic dimension. However, the ratio of the differences (Cl-F):(Br-Cl):(I-Br) for the radii of the ions is nearly the same as the ratio of the corresponding differences of radii of the same elements in covalent combination. This was a rather fortunate circumstance in the development of this investigation. As soon as reliable data for the radii of the halogens in covalent combination were available, these data were used in the comparisons. Thus the ratio of the differences of Bragg's values for the ionized atoms (41:16:24) were replaced by the Goldschmidt values for the atoms in covalent combination, compiled by Wherry [14] (giving the ratio 41:14:20) or by those of de Boer and van Arkel [15] (giving the ratio 41:17:22.6) and finally by the data in Pauling's book [16] (giving the ratio 41.0:17.5:22.2). Additionally, the atomic radius data [17] derived from measurements of tetrafluoro-, tetrachloro-, tetrabromo-, and tetraiodomethane (compounds which, on account of their structure, seem to be especially suitable for arriving at reliable values) give the ratio 41.0:16.1:21.8.

Before considering the tabulated results of this investigation, attention should be given to the experimental optical-rotation values on which rules I and II, are based. The best experimental values for

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[14] E. Wherry, Am. Mineral. **14**, 54 (1920).

[15] J. H. deBoer and A. E. van Arkel, Z. Physik **41**, 27 (1927).

[16] Linus Pauling, The Nature of the Chemical Bond and the Structure of Molecules and Crystals, p. 164 (Cornell Univ. Press, 1940).

[17] L. O. Brockway, J. Phys. Chem. **41**, 191, 747 (1937).
L. O. Brockway and H. O. Jenkins, J. Am. Chem. Soc. **59**, 2042 (1936).
H. A. Levy and L. O. Brockway, J. Am. Chem. Soc. **59**, 1662 (1937).
C. Finbak and O. Hassel, Z. physik. Chem. **36**, [B], 301 (1937).

establishing the ratio of the specific rotations for compounds of the first class, in which the halogen is directly attached to the asymmetric carbon atom, are obtained from the α-halogenotetraacetylglucoses. The ratio of the differences corresponding to (Cl-F):(Br-Cl):(I-Br) is 41.0:17.1:21.4. These values agree with the ratio of the differences in atomic dimension quoted above, for which the ratio 41:17:21 may be taken as an average.

If we interchange the H atom and OH group of the optically active *D*-isomer of a secondary alcohol, the active *L*-isomer of this alcohol is obtained. The structures in space of these two compounds are similar, one being the mirror image of the other. Also their physical properties are alike, but the D compound rotates the plane of polarization of light as much to the right as the other to the left. When either isomer of the alcohol is halogenated, mixtures of *D* and *L* halogen derivatives are obtained, and because of the equality of behavior of the *D* and *L* isomers and their inability to form diastereomeric derivatives, without alteration of the asymmetric center, the mixtures of these halogenated secondary alcohols are not separable by any procedure known.

In marked contrast to the halogen derivatives of the secondary alcohols, the alpha and beta modifications of a halogenoacetyl sugar are relatively easy to separate and obtain in a pure state because they are not enantiomorphs and do not have like solubilities and other physical properties. When we compare the above-mentioned optically active secondary alcohols with the optically active modifications of glucose obtained by interchange of the groups attached to carbon I, several important distinctions are apparent. By interchange of the OH group and the H atom two isomers are formed; one isomer is called α-glucose, the other β-glucose.

It has been pointed out in a detailed stereochemical study by the author[18] that the alpha and beta valences of glucose, by which the H atom and OH group are attached to asymmetric carbon I, are not equivalent in direction with respect to the structure of the entire molecule, in spite of the fact that the directions of these valences are equivalent or normal in regard to the other two valences of the first carbon. In other words, it is the ring structure which is the cause of the peculiarity.

This peculiarity in behavior is illustrated by the large difference in specific rotation between the alpha and beta sugars and derivatives, and by the fact that one pure isomer of a sugar will separate by concentrating a solution, which contains an equilibrium mixture of the isomers. This shows the difference is solubility of the two isomers. Likewise, there is considerable difference in the properties of the alpha and beta halogen derivatives. The α-halogenotetraacetylglucoses can be obtained free from the β compounds in optically pure condition and are fairly stable, whereas the β halogen derivatives are much less stable. As the four α-halogenotetraacetylglucoses differ from each other only in that one halogen (which is directly attached to an asymetric carbon atom) is replaced by another, they were excellent materials, for establishing rule I. The halogen derivatives of secondary alcohols, which are considered in this paper are not so suitable for testing rule I, because the saponification recorded and discussed

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[18] D. H. Brauns, J. Am. Chem. Soc. **51,** 1821 (1929).

in this paper show the products contain *D* and *L* isomers which are not separable.

For the testing of rule II, compounds are required in which the halogen is indirectly attached (by a chain of atoms) to the asymmetric carbon. The carbohydrate derivatives are for the most part not suitable for the test because of the presence of many asymmetric centers, which, when interacting, may act partly according to rule I and partly according to rule II. However, the simple halogen derivatives containing only one asymmetric carbon atom give results in accordance with rule II, as shown for the 1-halogeno-2-methylbutanes. See footnote 1.

On account of the difficulty of obtaining the 2-halogenopentanes in the pure state, it was not possible to test the validity of rule I by the results of the present investigation. However, by assuming that chlorine, bromine, and iodine derivatives of like optical purity are obtained by treatment of pure active pentanol-2 with phosphorus trichloride, phosphorus tribromide, and phosphorus triiodide, respectively, comparisons can be made which favor the validity of rule I, and decidedly contradict the validity of rule II for this series of compounds. The preparation of 2-fluoropentane, however, required the action of silver fluoride on the active 2-bromopentane or 2-iodopentane, which reaction involves a second Walden inversion. Hence the active 2-fluoropentane might be expected to differ from the other halides in its optical purity.

On the basis of the above considerations, the following scheme was adopted for testing the relationship of the differences of specific rotations, and also the differences of the molecular rotations, to the respective differences of the atomic radii. In comparing the (Cl-F):(Br-Cl):(I-Br) ratio of the experimentally found values of the differences of specific rotations with the corresponding ratio of the differences of atomic radii (41:17:21), the (Br-Cl) rotational difference is reduced to the (Br-Cl) atomic radius difference, which is 17, and consequently the correspondingly reduced (I-Br) rotational value should not differ materially from 21. However, the correspondingly reduced (Cl-F) rotational value can be expected to differ appreciably from 41, since a second Walden inversion was involved in the preparation of the 2-fluoropentane and its optical purity may be quite different from that of the other halogen derivatives. The same scheme is also applied for testing rule II for the differences of the molecular rotations. In tables 4 and 5 the results of the investigation are recorded according to this scheme together with comments on these results.

Table 4.—*Comparison of the numerical relation* (Cl–F):(Br–Cl):(I–Br) *of the specific rotations of dextrorotatory 2-halogenopentanes for 5892.5 A and for 5461 A at 20° C. with the numerical relation of the differences in the radii for the respective covalent halogen bonds*

[The values given in column 5 have been obtained by multiplying the values of column 3 by a factor which will reduce the second value to 17. This value has been chosen in order to conform to the values given in column 4 for the numerical relation between the differences of neutral atomic radii, by equalizing the (Br–Cl) value.]

Halogen substituent in the 2-halogenopentane	Specific rotation	Differences between specific rotations	Relation of the differences between atomic radii	Reduced relations of differences between specific rotations
1	2	3	4	5
	For 5892.5 A			
F	+16. 621	17. 451	0. 41	1. 40
Cl	+34. 072	2. 118	. 17	0. 17
Br	+36. 190	3. 731	. 21	. 299
I	+39. 921			
	For 5461 A			
F	+19. 521	20. 852	. 41	1. 27
Cl	+40. 373	2. 788	. 17	0. 17
Br	+43. 161	4. 854	. 21	. 296
I	+48. 015			

Table 5.—*Comparison of the numerical relation* (Cl-F):(Br-Cl):(I-Br) *of the molecular rotations of dextrorotatory 2-halogenopentanes for 5892.5 A and for 5461 A at 20° C with the numerical relation of the atomic radii differences between the respective halogens.*

[The values given in column 6 have been obtained by multiplying the values of column 4 by a factor which will reduce the second value to 17. This value has been chosen in order to conform to the values given in column 5 for the numerical relation between the differences of neutral atomic radii by equalizing the (Br-Cl value.]

Halogen substituent in the 2-halogenopentane	Molecular weight	Molecular rotation in circular degrees	Differences between molecular rotations	Relation of the differences between atomic radii in angstroms	Reduced relations of differences between molecular rotations
1	2	3	4	5	6
		For 5892. 5*A*			
F	90. 138	+1498. 2	2133. 7	0. 41	0. 198
Cl	106. 595	+3631. 9	1834. 7	. 17	. 17
Br	151. 054	+5466. 6	2440. 1	. 21	. 226
I	198. 058	+7906. 7			
		For 5461 A			
F	90. 138	+1759. 6	2544. 0	. 41	. 195
Cl	106. 595	+4303. 6	2216. 0	. 17	. 17
Br	151. 054	+6519. 6	2990. 1	. 21	. 229
I	198. 058	+9509. 7			

2. COMMENTS ON TABLE 4

The reduced values for the (I-Br) difference of the specific rotations for the two wavelengths agree well but do not agree so well with the required ratio of 0.21. As the purification of the bromine derivative is the most laborious, and hence the compound is probably less pure than the chlorine and iodine derivatives, it was calculated how much the specific rotation of the bromine derivative has to be changed to yield the value 0.21 instead of 0.29 for the (I-Br) reduced value. This required change for these high rotating derivatives is small, as, instead of +36.190 and +43.161 for the two wavelengths, the specific rotation of the bromine derivative should be +36.69 and +43.79. These values are only 0.5 and 0.6 circular degree higher, respectively. In other words, the bromine derivative appears to contain about 1.4 percent of inactive impurities (or only 0.7 percent of the enantiomorph). Another possibility is that the amounts of inversion which took place during the preparation of the chlorine, bromine, and iodine derivatives were not the same.

The reduced values, for the two wavelengths, of the (Cl-F) differences of the specific rotations do not agree so well with themselves or with the required ratio of 0.41. The relatively small amount of the prepared fluorine derivative (about 3 g) did not allow repeated fractionations, and the presence of amylenes or other impurities may account for the discrepency.

The large difference between the (Cl-F) value, 1.40, and the required value, 0.41, may be due to the imcompleteness of the second Walden inversion (with silver fluoride) in the preparation of the fluoride from the pure active alcohol. The value for the specific rotation of the fluorine derivative calculated on the assumption that the atomic radius relationship of rule I should hold is +28.96 for 5892.5 A. Hence the experimentally found value (+16.621) is 57.4 percent of the required value. A discrepancy of this magnitude is not surprising, since Walden inversions with silver salts are known to give variable results.[19]

It is noteworthy that the calculation of the specific rotation of the fluorine derivative from the dextrorotatory chlorine, bromine, and iodine derivatives by application of rule I gives a positive value. This indicates that the dextrorotatory fluorine derivative has the same configuration as the dextrorotatory chlorine, bromine, and iodine derivatives. This deduction is in harmony with the results of the saponification experiments. Apparently the results in table 4 support the possibility that the specific rotational values for the pure optically active 2-halogenopentanes conform to rule I.

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[19] W. A. Cowdrey, E. D. Hughes, and C. K. Ingold, J. Chem. Soc. **(1937)** 1247. In this communication, replacements of one halogen by another are not included in the silver salt inversions, but the range of optical purity of 30 to 90 percent for the prepared compounds shows the possibility of a 57-percent value.

3. COMMENTS ON TABLE 5

The reduced values for the (I-Br) differences of the molecular rotations for the two wavelengths agree reasonably well with each other and with the value for the difference between the respective atomic radii. The (Cl-F) differences of the molecular rotations agree for both wavelengths, but they differ considerably from the value for the difference between the respective atomic radii. The calculated value for the molecular rotation of the fluorine derivative, based on the values for the molecular rotations of the other halogen derivatives and on the assumption that the relationship according to rule II should hold, is $[M]_D^{20}=-792.0$ $[\alpha]_D^{20}=-8.77$ for $\lambda=5892.5$ *A* and $[M]_{5461}^{20}=-1042.8$ $[\alpha]_{5461}^{20}=-11.57$ for $\lambda=5461$ *A*. This negative value for the rotation is in contradiction to the positive value established by the saponification experiments discussed before. Undoubtedly, the values for the molecular rotations of the pure optically active chlorine, bromine, and iodine derivatives are higher than those used in the calculation. However, if these values should be increased in approximately the same ratio the calculated optical rotation of the fluorine derivative would become even more levorotatory. Hence the experimental results for the 2-halogenopentanes in table 5 do not show a relationship between the differences in molecular rotation and the respective differences in the radii of the halogen atoms in covalent combination.

4. NUMERICAL RELATIONS FOR OTHER PHYSICAL PROPERTIES

A series of optically active halogen compounds containing a single asymmetric center was prepared primarily to furnish fundamental data for testing the relationship of the optical rotations to the atomic radii. Other physical constants were determined with the object of furnishing fundamental data, which should prove of theoretical importance. In this paper, attention will be paid to the values for the refractive indices and for the boiling points at various pressures.

Since the refractivity and boiling point of the pure *D* compound are the same as those of the pure *L* compound, these constants for mixtures containing the *D* and *L* isomers will not differ from the constants characteristic of the optically pure substances. The pentanol-2, the 2-methylbutanol-1, and the halogen derivatives of the latter were substantially pure isomers.

(a) REFRACTIVITY

In table 6 the refractive indices and the molecular refractions of the halogen derivatives of pentanol-2 are compared with similar constants for the corresponding derivatives of 2-methylbutanol-1. The results show that within the limits of error the ratios of the differences for the molecular refractions of the halogen derivatives of both amylalcohols are the same.

TABLE 6.—*Comparison of differences of the refractive indices and molecular refractions of halogen derivatives of pentanol-2 as well as those of halogen derivatives of 2-methylbutanol-1* (Cl-F):(Br-Cl):(I-Br) *with respective differences of atomic radii.*

[In the penultimate row of figures, the value 17 has been obtained by multiplying the (Br-Cl) difference by a factor which will reduce it to 17. This value has been chosen in order to conform to the (Br-Cl) value of the ratio of the difference of the neutral atomic radii (41:17:21).]

Substances	Refractivity			
	Refractive indices, n_D^{20}		Molecular refractions, $M=\frac{n^2-1}{(n^2+2)d}$	
	Pentanol-2 and halogen derivatives	2-Methylbutanol-1 and halogen derivatives	Pentanol-2 and halogen derivatives	2-Methybutanol-1 and halogen derivatives [a]
Alcohol	1.4056	1.4107	26.704	26.696
F derivative	1.3520	1.3576	25.032	25.011
Cl derivative	1.4065	1.4124	30.121	29.972
Br derivative	1.4409	1.4451	33.107	32.868
I derivative	1.4951	1.4977	38.478	38.041
Ratio of differences of above refractivities (Cl-F):(Br-Cl):(I-Br) and of respective atomic radii				
Ratio of differences of refractivity	0.0545:0.0344:0.0542	0.0548:0.0327:0.0526	5.089:2.986:5.371	4.961:2.896:5.173
Reducing the (Br-Cl) refractivity value to 17	27:17:27	28.5:17:29.3	29:17:30.6	29.1:17:30.4
Ratio of differences of atomic radii	41:17:21	41:17:21	41:17:21	41:17:21

[a] An error in calculating molecular refractions of 1-halogeno-2-methylbutanes was made in the preceding publication (p. 327, footnote 1). The correct values are recorded here.

It is readily seen from the last two rows of figures in table 6 that no correlation exists between differences of refractive indices or molecular refractivities on the one hand, and differences of respective atomic radii on the other. However, it is remarkable, that within the limits of error the reduced ratios of the differences of the molecular refractions for the two sets of halogen derivatives of the two amyl alcohols are the same, as discussed above.

(b) BOILING POINTS AT VARIOUS PRESSURES

It has been pointed out and discussed in former publications [20, 21] that the reduced differences in the boiling points at the same pressure of the (Br-Cl) and (I-Br) derivatives of 2-methylbutanol-1 have a numerical relation which agrees with that for the differences in atomic radii of the respective neutral atoms, whereas a deviation for the (Cl-F) difference exists. The measurements were made with the pure halogen derivatives uncontaminated with the enantiomorph. In this investigation we are dealing with mixtures of the *D* and *L* 2-halogenopentanes, and the data in table 7 show that also for these derivatives the (Br-Cl) and (I-Br) differences in the boiling points at the same pressure have a numerical relation which is similar to that for the differences in atomic radii of the respective neutral atoms. (The boiling points of the pure *D* compounds are the same as the boiling points of the pure *L* compounds). In figure 1, boiling point curves for 2-methylbutanol-1 and its halides (heavy lines) are compared with boiling-point curves for pentanol-2 and its halides.

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[20] J. Research NBS **18**, 315 (1937) RP978.

[21] D. H. Brauns, J. Research NBS **17**, 337 (1939) RP915.

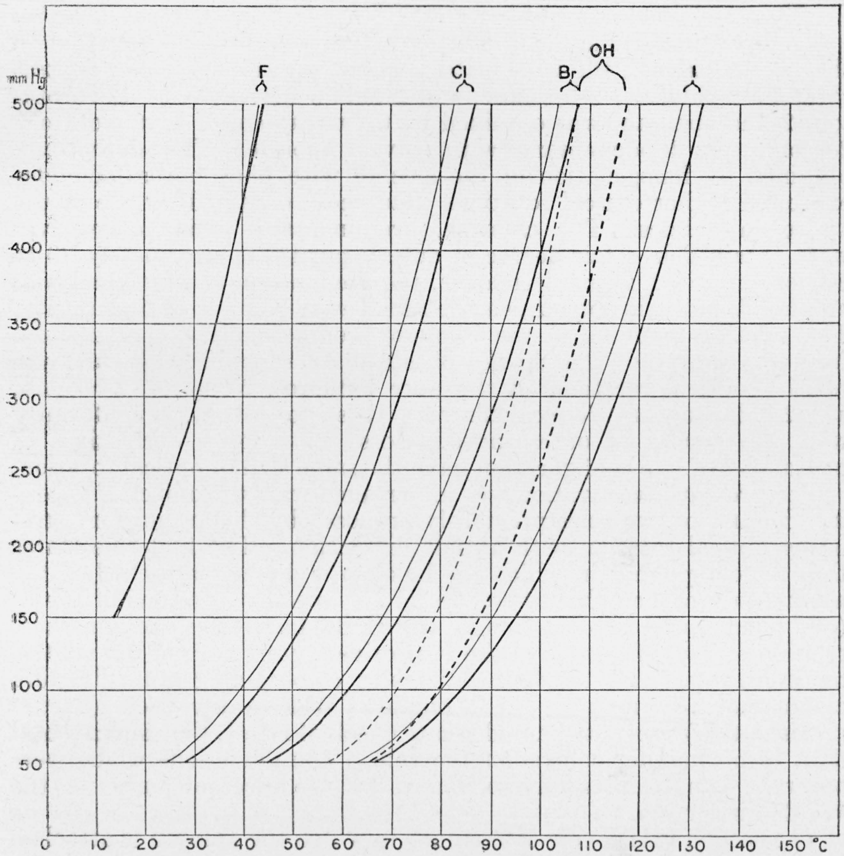

FIGURE 1.—*Boiling-point curves for 2-methylbutanol-1 and its halides (heavy lines) in comparison with boiling-point curves for pentanol-2 and its halides*

TABLE 7.—*Comparison of boiling points of 2-halogenopentanes and 1-halogeno-2-methylbutanes with the differences in the atomic radii of the hologens*

[The values given in column 3 were obtained by multiplying the values of column 2 (derived from table 3) by a factor. which will reduce the second value to 17. The value was chosen in order to conform to the (Br-Cl) value of the ratio of the differences of the neutral atomic radii (41:17:21).]

Pressure (mm of Hg)	Numerical relation between boiling point differences (Cl-F):(Br-Cl):(I-Br) for 2-halogenopentanes	Reduced numerical relation between boiling point diff (Cl-F):(Br-Cl):(I-Br) for 2-halogenopentanes	Numerical relation between differences in radii of neutral atoms (Cl-F):(Br-Cl)—(I-Br)	Reduced numerical relation between boiling point diff. (Cl-F):(Br-Cl):(I-Br) for 1-halogeno-2-methylbutanes
1	2	3	4	5
50	----:17.8:20.9	----:17:20	41:17:21	----:17:21.1
100	----:18.9:21.8	----:17:19.6		----:17:21.0
150	35.1:18.7:22.5	31.9:17:20.5		35.6:17:21.7
200	35.8:19.3:22.5	31.5:17:19.8		35.3:17:21.4
300	37.3:19.8:23.3	32.1:17:20.0		35.7:17:21.4
400	38.4:19.8:23.2	33.0:17:19.9		35.7:17:21.3
500	39.7:20.8:25.0	32.4:17:20.4		35.6:17:20.8

IV. CONCLUSIONS

The enantiomorphic modifications of pentanol-2 were prepared in the pure state, and the levorotatory isomer was converted to dextrorotatory 2-chlorine, 2-bromine, and 2-iodine derivatives. Levorotatory 2-fluoropentane was obtained by the treatment of dextrorotatory 2-bromo or 2-iodopentane with silver fluoride. The derivatives obtained by halogenation of the alcohol with phosphorus trihalides exhibited higher optical rotations than those obtained by use of the hydrogen halides. The chlorine, bromine, and iodine derivatives were obtained in a fair degree of optical purity, approximately 70 to 80 percent; the fluorine derivative, the preparation of which involved another Walden inversion, was obtained with a lower optical purity. The relative amounts of the isomeric modifications were estimated from the purity of the alcohol obtained by saponification, and the relative optical rotations of the pure 2-fluoro-, 2-chloro-, 2-bromo-, and 2-iodopentanes were calculated. It is shown that, in conformity with the results of other investigators, all halogen derivatives of pentanol-2 of like configuration have the same sign of optical rotation.

The present investigation was undertaken with the object of checking the first of two rules previously proposed by the author for correlating optical rotation with atomic dimension. The first rule states that for compounds in which the halogen is directly attached to the asymmetric carbon the differences of the specific rotations of the *D* (or *L*) compound (Cl-F), (Br-Cl), and (I-Br) have the same numerical relation as the differences of the respective atomic radii of the neutral halogen atoms. Although the difficulty of obtaining optically pure compounds, on account of incomplete Walden inversion (partial racemization) prevented an adequate check of rule I, the experimental data in no manner contradict the rule. The deviations which were observed can be plausibly explained by the incompleteness of the Walden inversion.

The second rule covers compounds in which the halogen is attached indirectly (by a chain of atoms) to the asymmetric carbon, and was applied in the comparison of the molecular rotational values of the 1-halogeno-2-methylbutanes. Rule II should not be applicable to the 2-halogenopentanes, and the results agree with this.

In contrast to this difference in optical rotation behavior between the halogen derivatives of the two active amyl alcohols (2-halogenopentanes and 1-halogeno-2-methylbutanes), it was found that these two sets of compounds are similar as to refractivity and boiling points at different pressures.

WASHINGTON, *March 26, 1943.*