

tween the other two possibilities (Fig. 6-B, D), but there are good reasons to believe that the arrangement shown in Fig. 6-B is the normal configuration of the ethyl ether molecule.²⁴

The addition of boron fluoride to an ethyl ether molecule with this configuration must be markedly hindered as a result of the position of the end methyl groups and the size of the boron fluoride molecule (Fig. 6-B). In all probability, the addition of the boron fluoride group to the oxygen atom is accompanied by a rearrangement of the ethyl ether molecule into a configuration of somewhat higher energy, such as is shown in Fig. 6-D. As a result, the stability of the ethyl ether complex with respect to dissociation into its components is lowered relative to the corresponding methyl ether complex (Fig. 6-A).

The argument may be extended to the isopropyl ether-boron fluoride complex (a possible configuration for which is shown in Fig. 6-C), leading to the conclusion that the dissociation of this complex is also favored by the steric effects. Of the three ethers, isopropyl ether is the weakest base (Table IX), although from the inductive effect of the alkyl groups, it would have been predicted to be the strongest.

In order to test the hypothesis, the study of the dissociation of tetrahydrofuran-boron fluoride was undertaken. On the basis of the factors com-

(24) Stuart, *op. cit.*, pp. 101-102, 236; *Phys. Rev.*, **38**, 1372 (1931); *Z. Physik*, **63**, 533 (1930). Stuart bases his conclusion upon evidence from dipole moment studies, upon his investigations of the Kerr constant, and upon considerations of atomic dimensions and bond angles.

monly believed to control base strength, it would be predicted that this cyclic ether would be approximately equal in strength to ethyl ether. If steric strains play the important role ascribed to them in this publication in altering the stability of addition compounds, it follows that the base strength of this cyclic ether should be markedly greater than that of ethyl ether, since the rigidity of the five-membered ring greatly reduces the possibility of steric strains (Fig. 6-E). The fact that tetrahydrofuran-boron fluoride is by far the most stable of the etherates studied (Table IX) lends considerable support to the hypothesis of steric strain.

Summary

1. The boron fluoride addition compounds with methyl ether, ethyl ether, isopropyl ether and tetrahydrofuran have been prepared and characterized.

2. The dissociation of these compounds ($R_2O:BF_3 \rightleftharpoons R_2O + BF_3$) was studied over a range of temperatures; and ΔH , ΔF and ΔS for the reaction were obtained.

3. The basic strength of the ethers decreases in the order: tetrahydrofuran, methyl ether, ethyl ether, isopropyl ether. This order is inexplicable on the basis of the factors generally believed to control base strength. The anomalies may be accounted for by taking into consideration the probable steric strains resulting from spatial limitations within the respective molecules.

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[CONTRIBUTION FROM THE GEORGE HERBERT JONES LABORATORY OF THE UNIVERSITY OF CHICAGO]

Studies in Stereochemistry. III. The Preparation of *d*-1-Deutero-2-methylbutane and the Study of Its Optical Rotation

BY HERBERT C. BROWN AND CORNELIUS GROOT¹

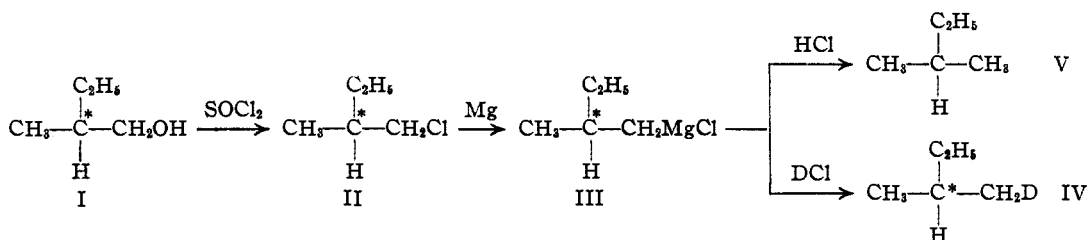
The discovery of isotopes has brought about far-reaching changes in the prevalent concepts and has opened up a wide variety of problems for investigation. One of these which is of considerable importance to stereochemistry has not yet been conclusively solved, in spite of numerous attempts. The point at issue is whether a substance

such as $R' \begin{array}{c} R_1 \\ | \\ C \\ | \\ R_2 \end{array} R''$, in which the two atoms or groups R' and R'' differ only in their isotopic composition, exhibits optical activity. At the present time, all attacks upon the problem have been restricted to the use of hydrogen and deuterium as the isotopic substituents. These two isotopes differ much more than others in their chemical and physical properties; moreover, until

(1) This paper is taken from a dissertation submitted by Cornelius Groot to the Faculty of the Division of the Physical Sciences of the University of Chicago, in partial fulfillment of the requirements for the degree of Master of Science.

recently they have been the only isotopes available in large quantities.

The question whether the difference between hydrogen and deuterium may give rise to optical activity has been investigated mainly by three general methods: (1) resolution of a suitable hydrogen-deuterium compound by classical means; (2) introduction of deuterium into a compound containing one asymmetric center so as to induce a new asymmetric center (partial asymmetric synthesis); and (3) introduction of deuterium into a suitable active compound in such a



way that two groups attached to the asymmetric center become structurally identical but isotopically distinct.

In spite of repeated investigations² involving each of the three general procedures, no definite decision to the question of isotopes as a source of optical activity can yet be made. It is evident that the first two methods (resolution and partial asymmetric synthesis) are less satisfactory than the third method mentioned. Failure to resolve a compound or failure to induce a new asymmetric center does not permit valid conclusions to be drawn with regard to the cause of the failure. This failure may be due to the experimental techniques, or to the insensitivity of the instruments used, or perhaps to the inherent nature of the substance. On the other hand, more definite information should be obtainable by suitable application of the third method. The compound formed will either be observed to be optically active or an upper limit will be put on the optical activity resulting in this instance from the hydrogen-deuterium asymmetry. To obtain such definite results, it is however essential that the starting material be optically active, easily obtained in moderately large quantities and easily purified; that it be readily transformed into the desired product by reactions which are very unlikely to affect the active center; and that the reaction product be one which can be rigorously purified.

(2) Previous work on the subject is reviewed by Buchanan, *J. Soc. Chem. Ind.*, **57**, 748 (1938).

These stringent conditions for the starting product are satisfactorily filled by *d*-2-methylbutanol-1 (I). Large quantities of this material can be isolated readily in a high state of purity from fusel oil³; moreover, the substance can be transformed by simple reactions (II, III) into the desired product, *d*-1-deutero-2-methylbutane (IV), which may be rigorously purified by distillation through an efficient column. The boiling point of isopentane (27.7°) or of its deuterium derivative is much lower than that of any probable optically active impurity.⁴

Accordingly, the preparation of *d*-1-deutero-2-methylbutane by these reactions was undertaken. A total of five preparations were carried out. In three of the preparations the Grignard reagent (III) was treated with deuterium chloride; in the other two, with hydrogen chloride. The product (IV or V) of each run was carefully fractionated in a column (rated efficiency: 100 theoretical plates) and 10 approximately equal fractions (10–12 cc.) collected. This material was then examined for possible activity in a sensitive polarimeter at the University of Illinois.⁵

The instrument, a Schmidt and Haensch (Berlin) product, was constructed to read rotations to a thousandth of a degree. Since for a colorless substance the magnitude of the rotation of plane polarized light is approximately inversely proportional to the square of the wave length, the mercury green line at 5461 Å. was utilized for the observations. After a number of preliminary experiments, the zero reading (the average of five consecutive determinations) could be reproduced with an average deviation of 0.001°.

(3) Brauns, *J. Research Natl. Bur. Stand.*, **18**, 315 (1937); Whitmore and Olewine, *THIS JOURNAL*, **60**, 2569 (1938).

(4) To illustrate this point, calculation reveals that the distillation of a 50:50 mixture of *d*-1-deutero-2-methylbutane and *d*-1-chloro-2-methylbutane through a column operating at an efficiency of 50 theoretical plates yields a product which, per mole, contains less than 10^{-30} mole of the active chloride.

(5) The authors wish to express their appreciation of the kindness of Professors Roger Adams and Duane T. Englis in placing this instrument at their disposal. They also wish to acknowledge the assistance given them by Professor Englis and numerous students in the Department of Chemistry of the University of Illinois during this phase of the investigation.

In each run, fractions 2 through 9 were examined in the polarimeter in a tube of 1 dm. in length (the end fractions 1 and 10 were not studied, since such impurities as may have been present in the crude product would have concentrated in these fractions). Five consecutive readings of each fraction were taken. The results for all eight fractions in a run were then averaged to obtain the value for the run. These values, with the average deviations, are listed in Table I.

TABLE I
SUMMARY OF OPTICAL ROTATION DATA (1-DM. TUBE) FOR
d-1-DEUTERO-2-METHYL BUTANE AND ISOPENTANE

Run	Substituent	Rotation	Average deviation
A	Deuterium	0.002	0.003
B	Hydrogen	.003	.005
C	Deuterium	.000	.003
D	Hydrogen	-.001	.002
E	Deuterium	.001	.001
Average for deuterium runs		.001	.001
Average for hydrogen runs		.001	.002

In Table II the data for run E are expanded to illustrate the accuracy which was attained. It is concluded that the optical rotation (1-dm. tube) of *d*-1-deutero-2-methylbutane is definitely less than 0.005° and is probably less than 0.002°.⁶

butanol-1 from fusel oil was packed with single-turn metal helices.⁷ The dimensions of the packed section were 108 inches by 7/8 inch. For convenience in assembling and handling, the column was constructed in three sections of equal lengths which fitted together by means of standard ground glass joints. Each section was vacuum-jacketed and equipped with an individual heating jacket. Since these heating jackets offer some advantages over the more conventional designs, they will be described in some detail. Each jacket consists of a 36-inch length of 2-inch glass tubing, the ends of which fit into grooves cut into Transite plates. These plates are held against the glass tube by four 0.25 inch steel rods, threaded at the ends and fitted with nuts. (In later designs of this heating jacket used for other fractionating columns, the end plates are constructed of Bakelite and the supporting rods are included within the glass tube, making a very compact unit.) The heating element consists of 12 lengths of 24 gage (B. and S.) nichrome wire. These wires, encased in lengths of 4-mm. glass tubing, extend longitudinally through the jacket, and are joined in series by means of connections on the Transite ends. A thermometer is suspended in each jacket. Since the heat loss from the column is greatly reduced by the vacuum jacket, it is unnecessary to control the temperature of the heating jackets very closely. Usually the temperature was maintained at 2-5° below the boiling point of the material being distilled, but considerably greater variations (such as sometime occurred at night during continuous operation) did not noticeably affect the efficiency of the column.

The construction of the column in three individual sec-

TABLE II
EXPANDED DATA OF DISTILLATION AND OPTICAL ROTATION (1-DM. TUBE) OF *d*-1-DEUTERO-2-METHYL BUTANE (RUN E)

Fraction	Volume, cc.	Boiling point, °C.	Barometric pressure, mm.	Polarimeter readings	Average	Rotation ^a
1	11	19.2-26.8	746
2	10	26.8-27.0	746	2.323, 2.324, 2.322, 2.325, 2.327	2.324	0.001
		Zero readings		2.331, 2.325, 2.326, 2.324, 2.327	2.327	
3	10	27.0	746	2.325, 2.325, 2.324, 2.324, 2.323	2.324	.001
4	10	27.0	746	2.327, 2.327, 2.329, 2.325, 2.321	2.326	.003
		Zero readings		2.316, 2.326, 2.319, 2.323, 2.313	2.320	
5	10	27.0	746	2.328, 2.329, 2.351, 2.354, 2.334	2.339	.016 ^b
6	12	26.9	744	2.326, 2.321, 2.321, 2.323, 2.322	2.323	.000
7	10	26.9	744	2.330, 2.329, 2.329, 2.330, 2.329	2.329	.006
		Zero readings		2.326, 2.328, 2.317, 2.322, 2.314	2.321	
8	10	26.9	744	2.327, 2.325, 2.326, 2.326, 2.326	2.326	.003
9	10	27.0	744	2.312, 2.322, 2.323, 2.311, 2.325	2.318	-.005
10	9	Holdup

^a Calculated using the zero value 2.323 (average of 2.327, 2.320, 2.321). ^b Large part of fraction lost by evaporation in course of making measurements—unable to repeat observations to check result. Value is not included in average.

Experimental Part

Fractionation Column. Isolation of *d*-2-Methylbutanol-I.—The column used for the isolation of *d*-2-methyl-

(6) It had been hoped that a more definite answer to the problem under discussion could be obtained by the use of a meter-long tube for the measurements. However, a number of circumstances made this impossible. The present activities of the authors make it highly improbable that they will be able to carry this project out within the next few years. The preparations have been carefully preserved, and will be available to anyone with the time and means for making the measurements.

tions permits compensation for the difference between floor and ceiling temperatures (often as high as 20°). The glass construction of the column and the jackets permits instantaneous observation of flooding and constant examination of the condition of the packing. The efficiency of a single section of the column was examined in considerable detail with a *n*-heptane-methylcyclohexane test mixture, using the convenient graph of Lecky and

(7) Fenske, Tongberg and Quiggle, *Ind. Eng. Chem.*, **26**, 1169 (1934); Fenske, Tongberg, Quiggle and Cryden, *ibid.*, **28**, 644 (1936).

Ewell.⁸ This section reached equilibrium conditions in less than forty-five minutes. At this time the composition of the test mixture in the head indicated an efficiency of 17 theoretical plates; at the end of four hours, the indicated efficiency was but slightly higher, 18 theoretical plates. The efficiency is thus one theoretical plate for every two inches of column length—a result which corresponds fairly well with the value obtained by Fenske and his co-workers.⁷

The fusel oil, a product of the United States Industrial Alcohol Company, contained 15.6% of the active material. Roughly 17% of the material distilled below 126°; this portion consisted chiefly of isobutyl alcohol (ca. 60%) and *n*-butyl alcohol (ca. 20%). Two distillations of the 2-methylbutanol-1-isoamyl alcohol fraction raised the concentration of the active alcohol to 85–90%. This material was considered satisfactory for the purposes of the investigation.

Preparation of *d*-1-Chloro-2-methylbutane.—The active alcohol was transformed into the corresponding active chloride by treatment with thionyl chloride and pyridine, according to Darzens' procedure.⁹

Four moles each of the active amyl alcohol and pyridine were placed in a 2-liter flask cooled by an ice-salt mixture. An efficient reflux condenser was attached to the flask by a ground glass joint; to the top of the condenser was fixed a dropping funnel and a tube to carry away the evolved gases. Through the dropping funnel 6 moles of thionyl chloride was added, the first two moles slowly over a period of sixty minutes, the remainder rapidly. The mixture was allowed to stand overnight at room temperature, then heated on the steam-bath for twenty-four hours, and finally poured into a 2-liter separatory funnel. The lower layer was drained off. The upper layer was treated with ice (to decompose excess thionyl chloride) and then washed first with small portions of water, next with saturated sodium carbonate solution, and finally again with water. The crude product was dried with calcium chloride and distilled. The fraction taken boiled from 98–102°. The yield of this crude product was 87%. This product was carefully fractionated and the fraction boiling at 99.5° at 750 mm., with n_D^{20} 1.4126 and $\alpha_D^{25} +1.33^\circ$, was used in the subsequent experiments.

Preparation of *d*-1-Deutero-2-methylbutane.—The Grignard reagent was prepared from the active chloride in *n*-butyl ether and treated with deuterium chloride, conveniently generated by the action of benzoyl chloride on "heavy water."¹⁰

A 2-liter 3-necked flask was fitted with a 500-cc. dropping funnel, a mercury-sealed stirrer, and a reflux condenser protected by a calcium chloride tube. In this flask were placed 36 g. (1.5 moles) of magnesium, 100 cc. of *n*-butyl ether, and a few drops of methyl iodide to catalyze the formation of the reagent. Active 1-chloro-2-methylbutane, 143 g. (1.33 moles), was placed in the dropping funnel, and a few cc. were run into the reaction flask. The flask was heated on the steam-bath until cloudiness of the liquid indicated that reaction had begun. The dropping funnel was then nearly filled with *n*-butyl ether (approximately 350 cc.), its contents stirred, and the mixture

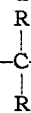
run into the flask, drop by drop. The reaction was kept under control by cooling the flask with a water-bath (20–25°). (A colder bath stopped the reaction completely, thus causing a dangerous accumulation of the active 1-chloro-2-methylbutane.) The mixture of *n*-butyl ether and 1-chloro-2-methylbutane was added over a period of two hours, after which the water-bath was removed and the reaction mixture allowed to stand. After another hour, heat was no longer evolved, and the reaction was assumed to be complete. The mixture was then diluted to a total volume of 1000 cc. with more *n*-butyl ether.

A 2-ml. sample was pipetted out, added to about 40 ml. of 0.1 *N* standard acid, heated to boiling, and back-titrated with standard base, using phenolphthalein as indicator. The yield of Grignard reagent was 1.16 moles, or 87% of the amount calculated.

The apparatus for generating deuterium chloride¹⁰ was connected to the reaction flask in place of the dropping funnel and deuterium oxide, 11.7 g. (1.17 equiv.), was converted to deuterium chloride, which was passed into the solution, cooled by means of an ice-bath, over a period of two to three hours. The solution was agitated vigorously in order to prevent caking of the magnesium salt. When the reaction appeared complete, the contents of the dry-ice trap were returned to the reaction flask, the deuterium chloride apparatus was replaced by a Vigreux stillhead and condenser, and the reflux condenser was replaced by a cork holding a thermometer. The receiving flask, immersed in an ice-bath, was connected to the condenser by an adapter. The only air outlet was through a side-arm on the adapter; this outlet led through a dry-ice trap. The reaction flask was heated in an oil-bath (at ca. 150°) until the inside temperature was 142°, the boiling point of pure *n*-butyl ether. The receiving flask was removed and weighed: the yield of crude product was 79 g. (1.08 moles), 92% of the calculated quantity based on either the Grignard reagent or the deuterium oxide. The material was then carefully fractionated in a Podbielniak "Heli-Grid" column.¹¹

Summary

The object of the investigation was to determine whether a compound of the type R_H-C-R_D



(where the groups R_H and R_D differ only in their hydrogen and deuterium composition), exhibits a measurable optical activity. *d*-1-Deutero-2-methylbutane was prepared from *d*-2-methylbutanol-1 and examined in a sensitive polarimeter. It is concluded that the optical activity of the pure hydrocarbon in a 1-dm. tube is definitely less than 0.005° and probably less than 0.002°.

CHICAGO, ILL.

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(8) Lecky and Ewell, *Ind. Eng. Chem., Anal. Ed.*, **12**, 544 (1940).

(9) Darzens, *Compt. rend.*, **152**, 1314 (1911); Gerrard, *J. Chem. Soc.*, 99 (1939).

(10) Brown and Groot, *This Journal*, **64**, 2223 (1942).

(11) The column, somewhat modified from the standard design of the Podbielniak Centrifugal Super-Contacter Company, was constructed for use with a total reflux-partial takeoff head. Solid carbon dioxide was used as the refrigerant in the head to minimize losses of the volatile product. The rated efficiency of the column is 100 theoretical plates. Its holdup, approximately 15 cc., is remarkably small for a column of such high efficiency, and made the column particularly useful for the purpose.