

fractions were taken after drying the samples for a day in a vacuum desiccator over sulfuric acid. After this treatment, all of the crops melted over the range, 130–160°. The rotations were first read at 0°, then at 20°, and finally again at 0° in order to observe any possible mutarotation. All fractions exhibited, within the limits of experimental error, the following identical rotations: $[\alpha]_D^{20} + 158 \pm 1$ ($c = 1.000, l = 1 \text{ dec.}, \alpha_D^{20} + 1.58$); $[\alpha]_D^{20} + 152 \pm 1$ ($c = 1.000, l = 1 \text{ dec.}, \alpha_D^{20} + 1.52$). There was no indication of mutarotation in any of the fractions.

Anal. (micro-Dumas). Calcd. for $C_4H_4D_2O_4 \cdot 2C_{12}H_{22}ON_2$: N, 7.90. Found: N, 7.80.

Cinchonine Salt of Succinic Acid.—This salt, used as a comparison standard, was prepared in the manner described above for the deuterium analog. The dried sample melted over a range of 130–160°. As in the above instance all rotations were taken on solutions of the same concentration and at temperatures controlled to within 0.1°. The latter precautions were taken to prevent ionization. The following rotations were observed for this hydrogen analog: $[\alpha]_D^{20} + 159 \pm 1$ ($c = 1.008, l = 1 \text{ dec.}, \alpha_D^{20} + 1.60$); $[\alpha]_D^{20} + 153 \pm 1$ ($c = 1.008, l = 1 \text{ dec.}, \alpha_D^{20} + 1.54$).

Summary

1. Diethyl succinate- α -*d*, α' -*d* was prepared

from both diethyl maleate and diethyl fumarate by reduction with deuterium. The presence of more than one compound was not indicated.

2. Succinic- α -*d*, α' -*d* acid from diethyl succinate- α -*d*, α' -*d* from either diethyl maleate or fumarate appeared to be a homogeneous substance. It melted 0.5° lower than succinic acid. Its alkaloidal salts exhibited the same rotation as the corresponding salts of succinic acid. No separation of diastereoisomeric salts was possible.

3. Succinic- α -*d*, α' -*d* anhydride melted at the same point as succinic anhydride.

4. The densities of diethyl succinate- α -*d*, α' -*d* and of succinic- α -*d*, α' -*d* anhydride indicated no appreciable replacement of deuterium by hydrogen during the various reactions. The values were slightly lower than those calculated from the densities of the hydrogen analogs on the basis of the assumption that the molecular volume of hydrogen and deuterium is identical.

URBANA, ILLINOIS

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY OF THE UNIVERSITY OF ILLINOIS]

Stereochemistry of Deuterium Compounds of the Type RR'CHD: Camphane-2,3-*d*₂

BY MARLIN T. LEFFLER¹ AND ROGER ADAMS

A recent article by Biilmann, Jensen and Knuth² described the preparation and subsequent study of the optical properties of camphane-2-*d*. Although camphane, due to its symmetry, is optically inactive, camphane-2-*d* was found to have an observed rotation of $\alpha_D + 0.08^\circ$ ($c = 10.00$ of ether, $l = 2 \text{ dec.}$). This was presented as direct evidence in favor of the asymmetry of the molecule RR'CHD. As pointed out by the above authors, the preparation of the hydrogen and deuterium analogs of camphane by the hydrolysis of bornylmagnesium chloride with water and deuterium oxide, respectively, is accompanied by the formation of several other optically active products. The latter must necessarily be removed completely by repeated crystallizations before any comparison can be drawn between the optical properties of camphane and camphane-2-*d*.

(1) For the previous article in this field see Leffler and Adams, *THIS JOURNAL*, **58**, 1551 (1936).

A description of this investigation herewith reported was included in an address in connection with the Willard Gibbs Medal award to the senior author, May 23, 1936.

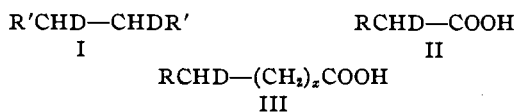
(2) Biilmann, Jensen and Knuth, *Ber.*, **69**, 1031 (1936).

The difficulty with which camphane derivatives are purified renders any process of purification questionable as to its thoroughness. No attempt was made by Biilmann to characterize the camphane or camphane-*d* used for comparative rotation studies either by analysis, density or other physical constants with the exception of melting points, which are not significant. Since the results of these investigators are not in complete accord with the present and previous^{1,3} researches concerning this problem of asymmetry, it seems advisable to make the herein described report at this time before the investigation is satisfactorily finished. In addition, it is worth mentioning that the first mentioned authors found that the sample of active camphane-2-*d* was converted into an inactive product, presumably camphane, by treatment with hydrogen in the presence of platinum and carbon at room temperature. It is rather odd that cleavage by hydrogen of an ordinary carbon-deuterium bond would occur with

(3) Erlenmeyer and Gärtner, *Helv. Chim. Acta*, **19**, 145, 331 (1936).

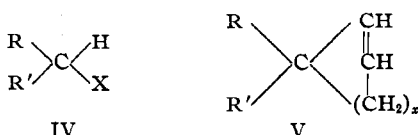
such ease and completeness. At least this does not seem in accord with our present knowledge of the hydrogen-deuterium interchange reactions.

The desirability of using a structure of the camphane type in studying this problem is worth emphasizing and may be most clearly brought out by mentioning briefly the difficulties involved in other modes of attack. A stereochemical study of a molecule of the type I, as described in the previous paper by the present authors,^{1,4} is complicated by at least two factors: namely, the production of this type by the reduction of either the



cis or *trans* unsaturated compound might lead to the formation of one and the same stereo form, thus making the search for a *meso* and a *racemic* modification of no consequence; in addition, if the *meso* modification was the one form so produced, obviously any attempts at resolution would be meaningless. The use of acids of the structure II in investigating the problem adds to the complication due to the possibility of racemization through the enolization of the alpha hydrogen or deuterium. The latter difficulty would be materially avoided by the use of the molecule shown in III. It is to be noted, however, that all of these three types involve either the isolation of diastereoisomers or the resolution into optically active forms. This evidence when obtained in the form of negative results is, at best, only indirect proof of the symmetry of the RR'CHD molecule.

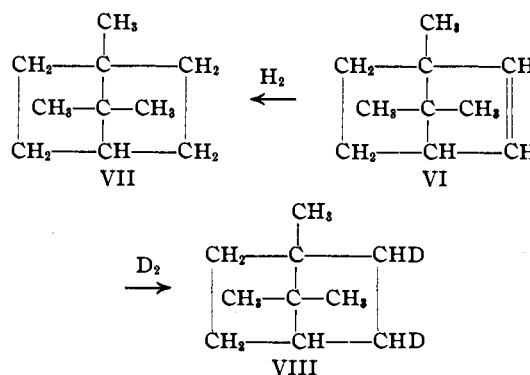
A more direct and definite proof is possible through the utilization of an optically active substance which loses its activity on reaction with hydrogen, such as the structures illustrated in IV and V. Since the substitution of X in IV by



deuterium involves the replacement of a group directly attached to the asymmetric center and thus the possibility of inversion and racemization, the structure V is the more desirable of the two. In addition, cyclic structures commonly have a higher rotation than open chain molecules. The

(4) McLean and Adams, *THIS JOURNAL*, **58**, 804 (1936).

latter is of distinct advantage in comparing the rotation of the products resulting from the action of hydrogen and deuterium on the original molecule. The terpene bornylene, VI, corresponds to the structure V and thus lends itself to the study of the problem at hand. On reduction of *l*-bornylene with hydrogen, camphane VII results, inactive due to the symmetry of the molecule; on the other hand, the reduction of *l*-bornylene with deuterium leads to the formation of camphane-2,3-*d*₂, VIII, which if deuterium differs properly from hydrogen should still be optically active.



Although *l*-bornylene represents, from a theoretical standpoint, a most ideal type of structure for the study of this problem, its use involves several experimental difficulties. Due to its extreme volatility, purification is by no means an easy task. Furthermore there seems to be no practical method of preparing the substance in a pure state. The decomposition of methyl bornylxanthate,⁵ although the most practical and convenient method of preparation, is accompanied by the formation of a rearrangement product, tricyclene,^{5,6} from which *l*-bornylene cannot be separated easily. Henderson and Caw⁷ described a method for the purification of bornylene containing this impurity by the preferential oxidation of the tricyclene by hydrogen peroxide. However, this was not found to be entirely satisfactory⁸ due to the poor yields and incompleteness of the purification. Fortunately, however, the presence of tricyclene as an impurity in the bornylene does not interfere with the results of the following experiments, since by its symmetry, it is optically inactive.

It has been shown previously by Henderson

- (5) Tschugaeff, *Ber.*, **32**, 3332 (1889); *Ann.*, **368**, 280 (1912).
 (6) Bredt and co-workers, *Ann.*, **366**, 1 (1909); *J. prakt. Chem.*, (ii) **131**, 137 (1931).
 (7) Henderson and Caw, *J. Chem. Soc.*, **101**, 1416 (1912).
 (8) Sutherland, private communication.

and Pollock⁹ that the catalytic nickel-hydrogen reduction of bornylene to camphane proceeds without rearrangements, even at temperatures of 170–190°. The *l*-bornylene obtained in the present investigation by the decomposition of methyl bornylxanthate was completely reduced catalytically by both hydrogen and deuterium at room temperature and practically atmospheric pressure, yielding camphane and camphane-2,3-*d*₂, respectively. Although pure camphane is optically inactive, the sample obtained by the reduction with hydrogen was found to have an observed rotation of $\alpha^{25}_D + 0.02^\circ$ ($\neq 0.01$) (Table I). This small degree of activity could not have been due to incomplete reduction, as the rotation of the original bornylene was negative and the final product was shown to be completely saturated. It is to be explained by the presence of some dextro-rotatory impurity. Camphane-2,3-*d*₂ resulting from the reduction of bornylene with deuterium gave an observed rotation of $\alpha^{25}_D + 0.02^\circ$ ($\neq 0.01$) (Table I) under identical conditions. Care was exercised to run control experiments with blank samples and the rotations of the hydrogen and deuterium analogs were each checked in triplicate. In every case there was an observable but identical rotation.

A density determination (Table I), using the method of McLean and Adams,⁴ on both camphane and camphane-2,3-*d*₂ definitely distinguished these two substances.

It is to be conceded that the above evidence, due to its qualitative nature, should not be accepted as definite proof of the inactivity of the RR'CHD structure. It is certain, however, that the effect of the deuterium atom on the optical activity of this structure is of an extremely small order of magnitude. Further studies along these lines are in progress; in particular a similar investigation is being conducted on menthene and a further attempt is being made to obtain pure bornylene in order to repeat the experiments reported here.

Experimental

***l*-Bornylene.**—*d*-Borneol was converted into *d*-methyl bornylxanthate as described by Tschugaeff.⁵ After two recrystallizations from alcohol, the xanthate melted at 57–58°; rotation in dioxane was $[\alpha]^{25}_D + 31.5^\circ$ ($c = 2.00$). The rotation and melting point checked those previously reported and were unchanged by further purification. ***l*-Bornylene** was obtained from methyl bornylxanthate

by dry distillation⁵ at 170–190° and freed from sulfur impurities by repeated sublimations from metallic sodium. The sample of *l*-bornylene prepared in this manner melted at 105–106.5°; rotation was $[\alpha]^{25}_D - 10.66^\circ$ ($c = 4.627$ in toluene), $[\alpha]^{25}_D - 9.57^\circ$ ($c = 16.00$ in ethyl acetate); density, d^{15}_4 , 0.7666. As the first two constants indicate and as was earlier pointed out by Bredt and co-workers,⁶ bornylene prepared in this manner is contaminated by a rearrangement product, tricyclene, from which it cannot be completely separated by ordinary methods of purification. Bredt and Sandkuhl¹⁰ obtained a sample of bornylene melting at 113° and having a rotation of $[\alpha]_D - 21.69^\circ$ which they believed to be essentially pure. The presence of tricyclene as an impurity should have no effect, however, on the optical inactivity of camphane formed by the reduction of the impure bornylene.

Camphane.—The apparatus employed for the reduction of bornylene by hydrogen (or deuterium) was the same as that previously described by McLean and Adams.⁴ Two reduction tubes were used, the charge in each tube being 1.36 g. of *l*-bornylene, 0.05 g. of platinum catalyst and 8 cc. of ethyl acetate (dry and acid and alcohol free). One-half of the theoretical amount of hydrogen was absorbed in one and one-half hours. There was no further absorption in an additional hour. That complete reduction had been obtained was substantiated by the settling of the catalyst in the reduction tubes.

The contents from the reduction tubes, after separation from the catalyst, were shaken with 1 liter of cold water in order to precipitate the crude camphane. The crude material was separated by filtration, dried for a short time over phosphorus pentoxide, and finally allowed to sublime at room temperature from metallic sodium. The camphane obtained in this manner gave no test for unsaturation as shown by bromine in glacial acetic acid and had the physical constants listed in Table I.

The rotations recorded in Table I were checked in triplicate, care being taken to maintain a constant temperature of $\pm 0.2^\circ$ during the observations and to use a blank control in each case. In every instance there was evidence of slight activity due to the presence of some dextro-rotatory impurity.

Camphane-2,3-*d*₂.—Practically 100% deuterium was prepared as earlier described⁴ by the electrolysis of deuterium oxide. This deuterium was employed for the reduction of *l*-bornylene, using conditions identical to those given above for the hydrogen analog. Complete reduction was attained in two hours as compared with one and

TABLE I
CONSTANTS ON CAMPHANE AND CAMPHANE-2,3-*d*₂

Compound	M. p., °C. ^a	Density ^b obs., d^{15}_4	$\alpha^{25}_D \neq 0.1^\circ$
Camphane	145	0.7458	+0.02 ($\neq 0.01$)
Camphane-2,3- <i>d</i> ₂	143	0.7552	+0.02 ($\neq 0.01$)

^a These low melting points for camphane indicate the presence of the impurity of tricyclene carried through from bornylene.

^b The method employed for the density determination was that described in a previous paper.⁴

^c Concentration = 0.85 g. in 5 cc. of ethyl acetate. $l = 1$.

(9) Henderson and Pollock, *J. Chem. Soc.*, **97**, 1620 (1910).

(10) Bredt and Sandkuhl, *Ann.*, **366**, 11 (1909).

one-half hours for the absorption of an equivalent amount of hydrogen. The product, camphane-2,3- d_2 (plus impurity from the bornylene) was isolated in the same manner used for camphane and gave no test for unsaturation. The physical constants are listed in Table I. In measuring the rotation and in making comparisons with the hydrogen analog, care was exercised to maintain identical conditions throughout. In no instance was there any observable difference between the optical activity of the samples of camphane and camphane-2,3- d_2 .

Summary

l-Bornylene upon reduction with hydrogen gives a camphane having a rotation of $+0.02$ (± 0.01) due to some impurity. Reduction with deuterium results in a molecule of identical rotation. The densities of camphane and camphane-2,3- d_2 were shown to be markedly different.

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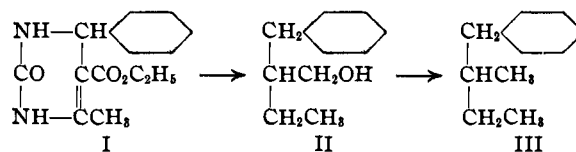
[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, YALE UNIVERSITY, AND THE RESEARCH LABORATORY OF MERCK AND CO., INC.]

Hydrogenation and Hydrogenolysis of a 2-Keto-1,2,3,4-tetrahydropyrimidine Derivative to 2-Benzyl- and 2-Hexahydrobenzylbutanol-1¹

BY KARL FOLKERS²

The action of hydrogen on 2-keto-1,2,3,4-tetrahydropyrimidines over nickel and copper-barium-chromium oxide catalysts at approximately 200 atmospheres pressure and at temperatures up to 200° was recently described.³ It was shown that 2-keto-4-phenyl-5-carbethoxy-6-methyl-1,2,3,4-tetrahydropyrimidine, I, was reduced to a mixture of at least two isomeric hexahydropyrimidine derivatives. The reduction of the pyrimidine 5,6-double bond took place at 200°, and the yield of the isolated hexahydropyrimidines was 77%. There was evidence for the presence of side products resulting from further reactions with hydrogen. It was to be expected that a higher temperature would increase the extent of these reactions, and this paper summarizes the results of allowing the 2-keto-1,2,3,4-tetrahydropyrimidine derivative, I, to react with hydrogen at 250° over a copper-barium-chromium oxide catalyst.

It could be predicted that, as the temperature of the reaction neared 250°, a rather complex combination of hydrogenation and hydrogenolysis reactions would occur. Thus, the pyrimidine 5,6-double bond and the carbethoxy group would be definitely susceptible to reduction. The formed carbinol group would be somewhat susceptible to reduction to a methyl group. The ring 3,4-bond



and the 1,6-bond would be susceptible to cleavage because of the neighboring activating influences. Theoretically, it could be said that the initial reaction of hydrogen might follow four courses leading to four different products. These four products, on further reaction with hydrogen, could lead to seven new products, and these, in their turn, could lead to seven more. These last seven molecules could lead to four products, and these four would lead to a single molecule, 2-benzylbutane, III. Thus, in this theoretical stepwise transformation of I to III, there are twenty-two intermediates to be considered, exclusive of stereoisomers, and exclusive of change in the -NH-CO-NH-grouping.

It was never possible, in this hydrogenation at 250°, to obtain full hydrogen absorption, and there was isolated a small amount of a low boiling fraction which appeared to be the product II, 2-benzylbutanol-1. After repeated purifications, only traces of impurities containing nitrogen remained, and the carbon and hydrogen analyses were not quite satisfactory for 2-benzylbutanol-1.

For further identification, the alcohol, II, was synthesized in order that comparable derivatives, etc., could be made. It was readily obtained by the following series of reactions

(1) Researches on Pyrimidines CLII.

(2) Post-doctorate Research Fellow, 1933-1934, Yale University. The greater part of this study was made at Yale University under the administration of Professor Treat B. Johnson. The courtesy of Dr. Randolph T. Major for permission to complete the investigation in the Merck Laboratory is gratefully acknowledged.

(3) Folkers and Johnson, *THIS JOURNAL*, **56**, 1180 (1934).