

limit; while the other phase (β) is present alone wherever this limit is exceeded. They also make plain the migration of the phase boundary with continued diffusion. Finally they show that the higher order diffraction lines from the β phase are much less intense than those of the α phase, a

fact probably due to the severe cold working which occurs as β is formed from α by a sudden expansion of over 3% (linear) at the advancing phase boundary.

METALS RESEARCH LABORATORY
CARNEGIE INSTITUTE OF TECHNOLOGY
PITTSBURGH, PENNSYLVANIA

RECEIVED JUNE 8, 1940

COMMUNICATIONS TO THE EDITOR

STRUCTURE OF CANNABIDIOL. VIII. POSITION OF THE DOUBLE BONDS IN CANNABIDIOL. MARIHUANA ACTIVITY OF TETRAHYDRO-CANNABINOLS

Sir:

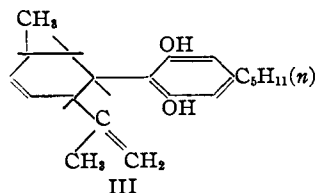
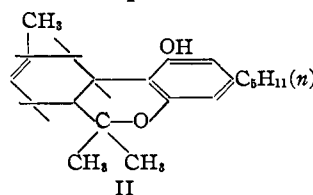
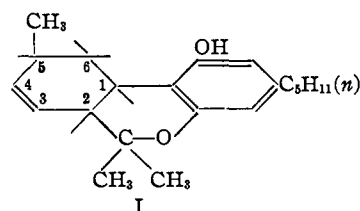
Certain mild reagents (previous papers V, VI) convert cannabidiol into a tetrahydrocannabinol $[\alpha]^{32D} -165 \pm 7^\circ$; more vigorous reagents to one with $[\alpha]^{32D} -240 \pm 10^\circ$. It is obvious from the rotations that these forms are not absolutely pure and each is probably contaminated with the other.

The lower-rotating tetrahydrocannabinol can be converted to the higher-rotating by the same reagents and under the same conditions which convert cannabidiol to the higher-rotating form; thus the lower-rotating form is presumably the initial reaction product in the isomerization of cannabidiol and the higher-rotating form a secondary product. Therefore, the lower-rotating form probably has the double bond in the same position as the corresponding double bond in cannabidiol.

Cannabidiol has been shown to have no double bond conjugated to the benzene ring; that its two double bonds are not conjugated to each other is indicated by the very close values of the absorption spectrum of cannabidiol (maximum $\log \epsilon$, 3.18), and that of tetrahydrocannabidiol (3.05) and confirmed experimentally by failure of repeated attempts to condense cannabidiol dimethyl ether with maleic anhydride. The double bond in each of the tetrahydrocannabinols has been shown not to be conjugated to the aromatic nucleus by comparison of their physical constants with that of a synthetic tetrahydrocannabinol of unequivocal constitution with the double bond conjugated (see paper VII). Positions 1,2 or 1,6

or 2,3 for the ring double bond in cannabidiol or in the tetrahydrocannabinols are thus excluded.

The migration of the double bond in the tetrahydrocannabinol, if 2,3 or 5,6, should proceed to the most favored position, in conjugation with the benzene ring. As this does not occur, positions 3,4 and 4,5 remain and are considered the most probable. The 3,4 is assigned to the lower-rotating tetrahydrocannabinol (I) and the 4,5 to the higher-rotating (II), for migration from the 3,4 to the 4,5 position (which has the methyl substitution) is more likely than *vice versa*. Through its relationship to the lower-rotating tetrahydrocannabinol, cannabidiol may be postulated as having structure III.



The tetrahydrocannabinols have a very potent marihuana activity which is markedly greater

than that of the synthetic optically inactive form with the double bond conjugated to the benzene ring. The hexahydrocannabinols have less marihuana activity. Comparative pharmacological values with that of a highly potent product obtained by Dr. J. C. Matchett through fractionation of purified red oil in a molecular still and used as a standard by Dr. S. Loewe at the Cornell Medical School in tests according to his procedure of "Bioassay by Approximation" (*J. Am. Pharm. Assoc.*, **28**, 427 (1939); *J. Pharm. Exptl. Therap.*, **66**, 23 (1939)) are shown in Table I.

TABLE I

Substance	Min.	Max.	Mean value potency max. deviation
	Potency above	Potency below	
Standard red oil	1.00
Cannabidiol	0.00
Tetrahydrocannabinol, -165°	1.50	2.80	2.15 ± 0.66
Tetrahydrocannabinol, -240°	1.50	2.00	1.75 ± .25
Hexahydrocannabinol, -70°	0.60	0.80	0.70 ± .10
Tetrahydrocannabinol (syn.)	.13	.27	.20 ± .07
Hexahydrocannabinol (syn.)	.10	.20	.15 ± .05

The acetates and methyl ethers of the two tetrahydrocannabinols were colorless, highly viscous oils. Tetrahydrocannabinol $[\alpha]^{34D} -164^\circ$ gave an acetate $[\alpha]^{34D} -167^\circ$ and methyl ether $[\alpha]^{32D} -166^\circ$; tetrahydrocannabinol $[\alpha]^{30D} -240^\circ$ gave an acetate $[\alpha]^{34D} -229^\circ$ and methyl ether $[\alpha]^{32D} -226^\circ$.

NOYES CHEMICAL LABORATORY
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IN COLLABORATION WITH THE
TREASURY DEPARTMENT
NARCOTICS LABORATORY
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RECEIVED AUGUST 13, 1940

HINDERED INTERNAL ROTATION OF METHYL GROUPS: THE ENTROPY OF SILICON TETRAMETHYL

Sir:

We have recently completed an investigation which indicates that the potential hindering internal rotation of methyl groups is probably due to hydrogen repulsions.

A study of the entropy of gaseous silicon tetramethyl yields a potential of 1280 calories, compared to 4800 calories for tetramethylmethane. If the potential were mainly due to lack of cylindrical symmetry in the bond orbitals caused by electron interactions, a higher potential than 4800 calories might be predicted for silicon tetra-

methyl, due to the large number of electrons. Conclusion of complete calorimetric measurements in this Laboratory down to 12°K. on silicon tetramethyl permits an accurate estimate of the hindering potential. The entropy has been calculated using the following frequencies and distances¹:

Carbon skeleton: ${}^1\omega_1 = 598$, ${}^2\omega_2 = 202$, ${}^3\omega_{4,5,6} = 239$, ${}^3\omega_{7,8,9} = 800$ cm.⁻¹.

CH₃ internal: ${}^4\delta(\pi) = 1264$, ${}^5\delta(\sigma) = 1427$, ${}^4\nu(\pi) = 2905$, ${}^5\nu(\sigma) = 2963$ cm.⁻¹.

CH₃ rocking: ${}^6\delta = 950$ cm.⁻¹.

Distances: Si-C = 1.93 Å., C-H = 1.09 Å.

The frequency ${}^3\omega_{7,8,9}$ is estimated from the frequencies 696 and 831 cm.⁻¹ which are apparently a result of resonance degeneracy. The rocking frequencies are estimated by analogy with ethane. The calculation of the entropy at 227.0°K. and at 299.8°K. (the normal boiling point) is summarized in Table I along with the corresponding calorimetric values.

TABLE I

THE ENTROPY OF SILICON TETRAMETHYL IN THE IDEAL GAS STATE FROM MOLECULAR AND SPECTROSCOPIC DATA

	227.0°K., e. u.	299.8°K., e. u.
Translational and rotational (free)	72.40	75.73
Vibrational (${}^3\omega_{7,8,9}$)	0.23 ± 0.08	0.64 ± 0.1
Vibrational (${}^6\delta = 950$)	.28 ± .08	.85 ± .2
Vibrational (other modes)	7.59	10.59
Total	80.50 ± 0.16	87.81 ± 0.3
Calorimetric	77.94 ± .30	86.33 ± .6
$(S_f - S) \times 4$ (experimental)	2.56 ± 0.46	1.48 ± 0.9
$(S - S) \times 4$ ($V = 1280$, $I = 5.3 \times 10^{-40}$)	2.56	1.73

The heat of vaporization was obtained temporarily from the measured vapor pressure equation and approximate state data. Hence the larger error at the higher temperature where the correction to the gas volume is larger. The potential of 1280 ± 160 calories was obtained from Pitzer's tables² to fit the experimental discrepancy, $(S_f - S) \times 4$. At the lower temperature if the 950 frequency were in error by 200 cm.⁻¹, and if $\omega_{7,8,9}$ should really be at 696 cm.⁻¹, the entropy would only be raised by 0.7 e. u. and the potential would then be 1600 calories.

THE SCHOOL OF CHEMISTRY AND PHYSICS
THE PENNSYLVANIA STATE COLLEGE
STATE COLLEGE, PA.

J. G. ASTON
R. M. KENNEDY

RECEIVED AUGUST 23, 1940

(1) Rank and Bordner, *J. Chem. Phys.*, **3**, 248 (1935).

(2) Pitzer, *ibid.*, **5**, 469 (1937).

THE SYNTHESIS OF 1-*BETA*-GLUCOSIDOFRUCTOSE. A CORRECTION

Sir:

In a recent publication by Pacsu, Wilson and Graf [THIS JOURNAL, 61, 2675 (1939)] 1- β -glucosidofructose was described as a new disaccharide. The authors regret that in carrying out and publishing their work they have overlooked the fact that the same sugar had previously been prepared by Brigl and Widmaier [*Ber.*, 69, 1219 (1936)] by a different method. The latter investigators used dibenzal-fructopyranose as starting material and obtained the disaccharide in a 18.8% over-all yield, whereas Pacsu, Wilson and Graf prepared the sugar from 2,3-4,5-diacetone- β -fructopyranose in a 50% yield. The physical constants of the disaccharide as reported from the two sources are practically identical. It should be added that no reference to the work of Brigl and Widmaier can be found either in the latest book on the carbohydrates (Micheel, "Chemie der Zucker und Polysaccharide," Akademische Verlagsgesellschaft m. b. H., Leipzig, 1939), or in the latest comprehensive report on the synthesis of the oligosaccharides (Zemplén, "Neuere Richtungen der Oligosaccharid-Synthese" in "Fortschritte der Chemie organischer Naturstoffe" edited by Zechmeister, Julius Springer, Wien, 1939).

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PRINCETON UNIVERSITY
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EUGENE PACSU

RECEIVED FEBRUARY 3, 1940

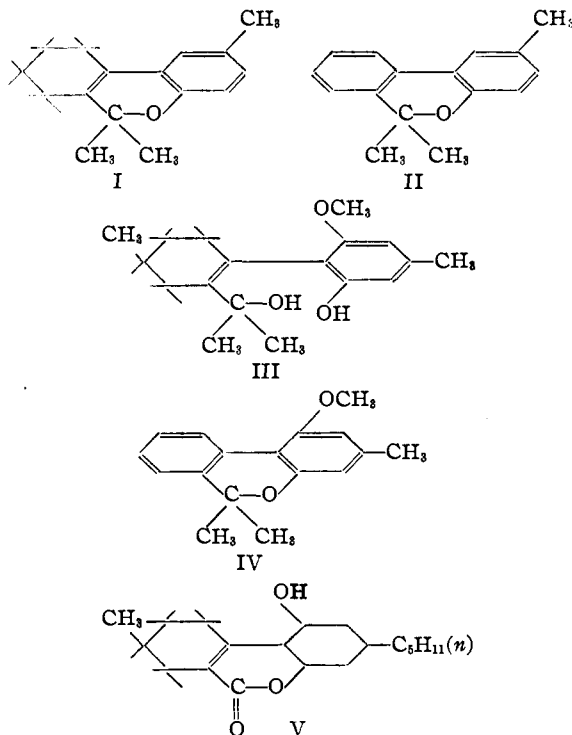
SYNTHESIS OF CANNABINOL

Sir:

We note in a recent communication (THIS JOURNAL, 62, 2245 (1940)) that Adams and his co-workers have reported a method for the preparation of compounds analogous to cannabinol which involves the condensation of 5-methylcyclohexanone-2-carboxylate with orcinol in the presence of phosphorous oxychloride, followed by treatment with methylmagnesium iodide. One instance of the use of this method was reported to give a tetrahydropyran.

We wish to report that we have been using this method for some time in the synthesis of compounds analogous to cannabinol with the view to the synthesis of cannabinol itself. The condensation of cyclohexanone-2-carboxylate as well as 5-methylcyclohexanone-2-carboxylate with *p*-cresol,

orcinol and olivetol in the presence of sulfuric acid have been carried out with subsequent treatment with methylmagnesium iodide to give the tetrahydropyran I (plates from alcohol, m. p. 69°, found: C, 84.24; H, 8.98; calcd.: C, 84.2; H, 8.77) and the glycol III (white crystals, m. p. 105–106°, found: C, 74.47; H, 8.98; calcd.: C, 74.5; H, 8.98).



Some of these tetrahydropyrans have been dehydrogenated (II, white plates, m. p. 58°, found: C, 85.9; H, 7.35; calcd.: C, 85.7; H, 7.2) to establish the feasibility of passing from these to the pyrans of the cannabinol type. The condensation with orcinol has been carried out and the mono-methyl ether of the condensation product treated with methylmagnesium iodide to give the glycol III, which was dehydrogenated, after the loss of the elements of water to close the pyran ring, to give a cannabinol type of compound, IV.

This route to cannabinol having been thus fairly well examined, we condensed 5-methylcyclohexanone-2-carboxylate with olivetol, giving a compound which we believe to be V (light brown crystals, m. p. 172–173°, found: C, 75.77; H, 8.2; calcd.: C, 76.0; H, 8.1). Work is now in progress in the treatment of pyrone V or its methyl ether with methylmagnesium iodide with the view of dehydrogenating it to cannabinol.

Isomerism is not excluded in these condensations with the dihydroxybenzenes, and we have refrained from reporting our results. The publication of the note by Adams and his co-workers makes it desirable to point out what has already

been done in this type of condensation in these Laboratories.

CHEMISTRY LABORATORIES
COLUMBIA UNIVERSITY
NEW YORK, N. Y.

GARFIELD POWELL
THOMAS H. BEMBRY

RECEIVED AUGUST 12, 1940

NEW BOOKS

The Systematic Identification of Organic Compounds.

By RALPH L. SHRINER, Professor of Chemistry in the University of Illinois, and REYNOLD C. FUSON, Professor of Chemistry in the University of Illinois. Second edition. John Wiley and Sons, 440 Fourth Avenue, New York, N. Y., 1940. xi + 312 pp. 15.5 × 24 cm. Price, \$2.75.

The first edition of this book, in contrast to the more lengthy works in this field, was outstanding in its adaptability to the teaching of organic chemistry through the excellent medium of "organic qualitative" courses. This feature is retained in the second edition. Here also, the basic principle of dividing organic compounds into large groups according to their solubilities, and further subdividing these groups by certain classification reactions, remains unchanged. No discussion of the utility of this system as compared with others will be undertaken. That this method of attack is practical and useful, not only for the identification of organic compounds but also for teaching organic chemistry and as an introduction to organic research, has been abundantly demonstrated.

The considerably increased length of the book cannot be ascribed to any particular section or chapter but rather to the addition of new material and the introduction of modern ideas throughout. In Chapter II, the relation of solubility to structure is discussed in more detail. To many of the classification experiments have been added discussions of the limits of usefulness of the reactions. This information is extremely helpful in aiding the student to interpret the results of the tests. Five new experiments have been added in this chapter.

The chapter dealing with special laboratory methods includes, with the methods of determining physical constants, a discussion of the relationship of these constants to the structures of the compounds. New methods of analysis for the elements and for determination of saponification equivalent have been presented in detail.

The most extensive change in the form of the book is the separation of the tables of derivatives from the description of the methods of preparing them. These have been placed in separate chapters and arranged in a more convenient order. Almost an innovation for textbooks in this field are the tables and the data on derivatives of sulfonic acids which appear in this edition. A new chapter dealing

with the interpretation of experimental data might prove to be particularly instructive to students.

The inclusion of most of the important recent advances in the field, both with regard to new derivatives and new experimental methods, should make the book as useful to the organic research man as to the teacher and the student.

WILLIAM P. CAMPBELL

Magnetism and Very Low Temperatures. By H. B. G. CASIMIR, Kamerlingh Onnes Laboratory, Leiden. Cambridge: at the University Press; New York: The Macmillan Company, 60 Fifth Avenue, New York, N. Y., 1940. 93 pp. 14 figs. 14 × 21.5 cm. Price, 6 s. net.

This short book deals primarily with investigations in the low temperature regions which have been made accessible by the adiabatic demagnetization method.

The author deals principally with methods of attacking both the experimental and theoretical side of the problems involved. Advantages and disadvantages of the several experimental procedures used in making magnetic and other measurements are presented in a brief and interesting manner.

No adequate quantum statistical methods of treating the magnetic data at very low temperatures have been devised but some progress has been made and the author's comments on the present status of this subject give a clear picture of such conclusions as may be drawn and some of the difficulties to be overcome.

The thermodynamic methods of treating magnetic data are presented. The equations by means of which thermodynamic temperature may be obtained from magnetic and calorimetric observations are given. The measurement of magnetic moment by the several static and induction methods and the importance of demagnetization corrections are treated.

Magnetic heat capacity, stark splitting, magnetic interaction including ferromagnetism are discussed.

Although the book does not attempt to summarize the experimental results so far obtained, a number of actual cases notably compounds of titanium, chromium, iron and gadolinium are discussed and some data are included.