In a number of instances,[3] ready halogenation of chlorins has been observed, but it has been assumed that the reactions involve substitution at the 7 or 8 positions. Although these cases deserve reinvestigation in detail, there can now be little doubt that the views previously advanced are erroneous, and that the products of these reactions are γ or δ halogenated derivatives.

This work was generously supported by the National Institutes of Health.

(3) (a) H. Fischer and K. Herrle, *Ann.*, **530**, 236 (1937); (b) H. Fischer and E. A. Dietl, *ibid.*, **547**, 234 (1941); (c) H. Fischer, H. Kellermann and F. Baláž, *Ber.*, **75**, 1778 (1942); (d) H. Fischer and F. Baláž, *Ann.*, **555**, 81 (1943); (e) H. Fischer and F. Gerner, *ibid.*, **559**, 77 (1948).

CONVERSE MEMORIAL LABORATORY
HARVARD UNIVERSITY R. B. WOODWARD
CAMBRIDGE 38, MASSACHUSETTS VINKO ŠKARIĆ

INTRAMOLECULAR CYCLIZATION OF UNSATURATED DIAZOKETONES

Sir:

The intermolecular reaction of diazoketones with olefins has been described by Sorm and his collaborators.[1]

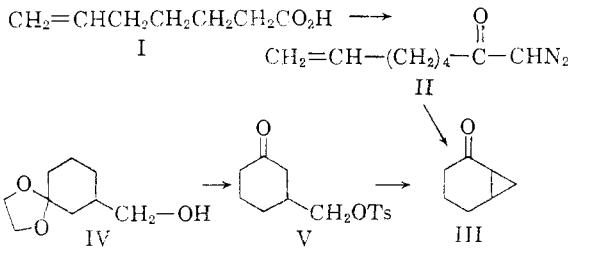
So far as we are aware the *intramolecular* counterpart of this reaction has not yet been reported. We were interested in exploring the feasibility of such a reaction for the synthesis of [0,1,4]bicycloheptane derivatives and have succeeded in synthesizing [0,1,4]bicycloheptanone-2 (III), one of the simplest substances that might be prepared by the "Δ^5 diazoketone" route.

Pure 5-hexenoic acid (I) was prepared from 4-penten-1-ol[2] *via* the corresponding bromide and nitrile.[3] The unsaturated acid was transformed into its acid chloride by reaction with oxalyl chloride in benzene at room temperature, and the acid chloride was converted, without distillation, into its diazoketone (II).

The diazoketone (5 g.) was refluxed for eleven hours in 250 ml. of cyclohexane in the presence of 0.5 g. of copper bronze. Shorter time led to incomplete reaction as evidenced by the presence of diazoketone in the mixture (infrared). Distillation gave 2.5 g. of a fraction boiling at 74–76° (8 mm.). This consisted mainly (see below) of the desired [0,1,4]bicycloheptanone-2 but was not completely homogeneous, as shown by the presence of two absorption bands in the carbonyl region of the infrared and by gas chromatography. The latter (5 ft. silicone column, 150°) showed the product to be contaminated with about 20% of a substance with absorption at 5.85 μ in the infrared. The pure III from the chromatogram had its carbonyl absorption at 5.96 μ, λ_{max}^{EtOH} 220 mμ and 275 mμ (ϵ 34),[4] and gave its 2,4-dinitrophenylhydrazone, m.p. 158° (calcd. for $C_{13}H_{14}N_4O_4$: C, 53.79; H, 4.86; N, 19.30. Found: C, 53.96; H, 4.90; N, 19.47). The same 2,4-dinitrophenylhydrazone was obtained before gas chromatography in 75% yield. The ultraviolet absorption spectrum of this derivative had $\lambda_{max}^{CHCl_3}$ 370 mμ as anticipated (*cf.* 2,4-dinitrophenylhydrazone of acetylcyclopropane: $\lambda_{max}^{CHCl_3}$ 371 mμ[5]). The n.m.r. spectrum of III showed absorption due to two non-equivalent hydrogens of the cyclopropane methylene at τ *ca.* 8.9 (lowered by conjugation with the carbonyl).

Unambiguous confirmation of the structure of our [0,1,4]bicycloheptanone-2 was obtained by an independent synthesis. Catalytic hydrogenation (rhodium-charcoal) of *m*-hydroxybenzoic acid, then esterification and oxidation with chromic acid–acetone–sulfuric acid, gave the known[6] ethyl-3-oxocyclohexanecarboxylate. Ketalization with ethylene glycol and reduction with lithium aluminum hydride gave the ketal of 3-oxo-cyclohexanemethanol (IV) b.p. 116–124° (0.2 mm.) (found: C, 62.32; H, 9.43). Reaction of IV with *p*-toluenesulfonyl chloride in pyridine and deketalization with aqueous methanolic hydrochloric acid produced the tosylate of 3-oxocyclohexanemethanol (V); 2,4-dinitrophenylhydrazone, m.p. 118° (found: C, 52.21; H, 4.99).

Cyclization of the keto tosylate V with sodium hydride[7] in tetrahydrofuran gave, in low yield, the bicyclic ketone III; 2,4-dinitrophenylhydrazone, m.p. 162–163°, undepressed by the sample from the diazoketone decomposition. The infrared spectra of the ketones made by the two routes were essentially identical, and so were the characteristic n.m.r spectra.



(5) D. H. R. Barton, T. Bruun and A. S. Lindsey, *J. Chem. Soc.*, 2210 (1952).

(6) G. K. Komppa, T. Hirn, W. Rohrmann and S. Beckmann, *Ann.*, **521**, 242 (1936).

(7) *Cf.* N. A. Nelson and G. A. Mortimer, *J. Org. Chem.*, **22**, 1146 (1957).

THE CHANDLER LABORATORY
COLUMBIA UNIVERSITY GILBERT STORK
NEW YORK 27, NEW YORK JACQUELINE FICINI

RECEIVED OCTOBER 20, 1961

THE STRUCTURE OF INDOLMYCIN

Sir:

We wish to propose structure **1** for indolmycin, previously designated PA-155A.[1,2] This antibiotic is the first example of a new structural type.

Indolmycin was isolated from a culture of *Streptomyces albus*[1] and some of its properties have been described.[2,3] The compound has the molecular formula $C_{14}H_{15}N_3O_2$ and an ultraviolet absorption spectrum closely resembling that of tryptophan.

(1) W. S. Marsh, A. L. Garretson and E. M. Wesel, *Antibiotics and Chemotherapy*, **10**, 316 (1960).

(2) K. V. Rao, *ibid.*, **10**, 312 (1960).

(3) A. R. English, T. J. McBride, *ibid.*, in press.

(1) F. Sorm and J. Novak, *Collection Czechoslov. Chem. Communs.*, **22**, 1836 (1957); F. Sorm and J. Ratusky, *ibid.*, **23**, 467 (1958); F. Sorm and J. Novak, *ibid.*, **23**, 1126 (1958).

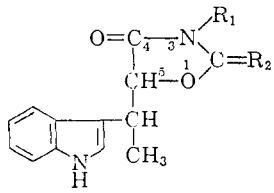
(2) R. Paul and H. Normant, *Bull. soc. chim.*, 484 (1943).

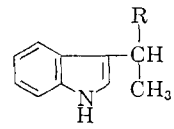
(3) F. B. LaForge, N. Green and W. Gersdorff, *J. Am. Chem. Soc.*, **70**, 3709 (1948).

(4) *Cf.* A. Sandoval, G. Rosenkranz and C. Djerassi, *ibid.*, **73**, 2383 (1951).

With Ehrlich reagent, it gives the color characteristic of α-unsubstituted indoles.

Acid hydrolysis of **1** furnished, *inter alia*, methylamine and the oxazolidinedione **2**,[4] m.p. 179° $\lambda_{max}^{dioxane}$ 5.47, 5.67 μ (45%). Alkaline hydrolysis of **2** yielded ammonia, some amide, **3**, m.p. 188°, and two diastereoisomeric hydroxy acids, **4** (α-indolmycinic acid) m.p. 182°, and **4'** (β-indolmycinic acid) m.p. 143°, epimeric at the site of the hydroxyl group. Reduction of **4** with lithium aluminum hydride to the glycol **5**, m.p. 90°, and subsequent oxidation with sodium periodate gave the aldehyde **6** [semicarbazone, m.p. 182°, $[\alpha]^{24}D$ −23° (methanol). Found: C-CH_3, 5.99]. Analogous degradation of **4'** also gave **6**.





1, R_1 = H; R_2 = N'-CH_3
1', C-5 epimer of 1
2, R_1 = H; R_2 = O
2', C-5 epimer of 2
8, R_1 = CH_3; R_2 = O
12, R_1 = H; R_2 = $\overset{+}{N}$'HCH_3

3, R = CHOH-$CONH_2$
4, R = CHOH-COOH
4', epimeric to 4 at site of hydroxyl group
5, R = CHOH-CH_2OH
6, R = CHO
7, R = CHOH-$COOCH_3$

Permanganate oxidation of **4** furnished anthranilic acid, showing the benzene ring of the indole moiety to be unsubstituted.

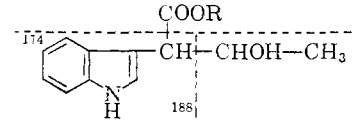
Confirmation of structure **1** for indolmycin was obtained by its partial synthesis from treatment of the α-hydroxy acid methyl ester, **7**, m.p. 83° (from α-indolmycinic acid) with N,N'-dimethylguanidine. This reaction also yielded the C-5 epimer, iso-indolmycin (**1'**), m.p. 245°.

The two C-5 epimers of **1** show differences in acid degradation behavior which suggest configurational assignments. Analogous to indolmycin (**1**), its epimer, **1'**, yielded as the main products methylamine and an oxazolidinedione (**2'**), m.p. 140° (65%), which was hydrolyzed by alkali to ammonia and the two epimeric acids **4** and **4'**. Iso-indolmycin (**1'**) also gave a second product, **8**, m.p. 170°, $\lambda_{max}^{CHCl_3}$ 5.52, 5.8 μ, (18%). This was degraded to methylamine and the epimeric acids **4** and **4'** by alkali. However, indolmycin (**1**) gave, besides compound **2**, two products with a rearranged carbon skeleton resulting from a 1–2 migration of the indole moiety.

These compounds were identified as the β-hydroxy acid **9**, m.p. 158°, $[\alpha]^{25}D$ +63° (methanol) and the oxazine derivative **10**, m.p. 233° dec., λ_{max}^{KBr} 3.1, 5.68, 5.78, 8.15, 8.28, 9.24 μ,[5] $[\alpha]^{24}D$ −10° (dioxane). The n.m.r. spectrum of the methyl ester of **9** showed a doublet (τ = 8.89, 9.04) indicating the CH_3–CH< moiety. The mass spectrum of **11** (parent peak *m/e* 233) showed strong peaks at *m/e* 189, 188, 174 and 130. Breakage of either benzylic type carbon–carbon bond results in fragments of mass 174 or 188. The peak at *m/e* 189 indicates retro-aldol cleavage to methyl-β-indolyl acetate and loss of the carbomethoxyl group from this molecule gives a fragment with mass 130.

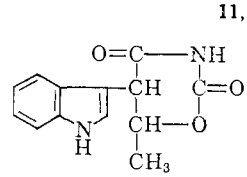
Treatment of **10** with refluxing 2 *N* sodium hydroxide gave β-indolylacetic acid by hydrolysis and retro-aldol cleavage. Alkaline hydrolysis of **10** at room temperature or heating **10** to its point of decomposition yielded α-(β-indolyl)-crotonamide, m.p. 157°. On alkaline hydrolysis at elevated temperature, this also furnished β-indolyl acetic acid. The α - (β - indolyl) - crotonamide, which showed an n.m.r. spectrum with a doublet (τ = 8.90, 9.02) for the CH_3–CH< moiety, was reduced catalytically to α-(β-indolyl)-butyramide. Its mass spectrum (parent peak *m/e* 202) had a very strong peak at *m/e* 158 resulting from fragmentation of the benzylic type bond.

The following explanation for the acid degradation of indolmycin (**1**) and its epimer, **1'**, is offered: Protonation occurs at the exocyclic nitrogen, N' (**12**). Hydrolysis of the methylimino group gives the oxazolidinedione **2**. Rupture of the (4–3) C–N bond in **12**, formation of a bond between C-4 and N' and hydrolysis of the imino group leads to **8**. Cleavage of the (5–1) C–O bond leads to the intermediate **13**. This, by internal ring closure, can either go back to **12**, or give a six-membered ring which loses methylamine to yield **10**. Hydrolytic cleavage of the cyclopropane ring in **13** ultimately yields **9**.

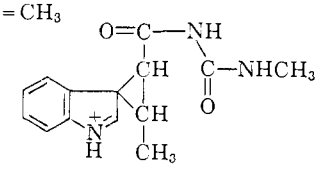


(R = CH_3)

9, R = H
11, R = CH_3

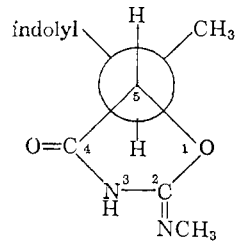


10

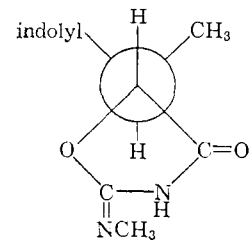


13

The difference in behavior of indolmycin and its epimer to acid treatment suggests that the β-indolyl group is *trans* to the (5–1) C–O bond in indolmycin in the least hindered conformation, corresponding to **14**. Iso-indolmycin, which does not rearrange



14



15

(4) Satisfactory analyses have been obtained for all degradation products.

(5) This spectrum is consistent with a 1,3-oxazine-2,4-dione derivative; E. Testa, L. Fontanella, G. Christiani and G. Gallo, *J. Org. Chem.*, **24**, 1928 (1959).

with migration of the indole moiety to any appreciable extent, then should be represented by **15**.

Acknowledgments.—We are greatly indebted to Professor K. Biemann for the determination and interpretation of the mass spectra. We also wish to acknowledge stimulating discussions with Professor G. Buchi and Dr. F. A. Hochstein.

MEDICAL RESEARCH LABORATORIES
CHAS. PFIZER AND CO., INC. M. SCHACH VON WITTENAU
GROTON, CONNECTICUT HANS ELS

RECEIVED SEPTEMBER 18, 1961

BOOK REVIEWS

Pyridine and its Derivatives. Part Two. Edited by ERWIN KLINGSBERG, American Cyanamid Company, Bound Brook, New Jersey. Interscience Publishers, Inc., 250 Fifth Avenue, New York 1, N. Y. 1961. x + 576 pp. 16.5 × 23.5 cm. Price, $37.50; subscription price, $32.50.

This is the second of a four volume series on pyridine in the over-all series on the "Chemistry of Heterocyclic Compounds" edited by Arnold Weissberger. The pyridine volumes are edited by Erwin Klingsberg and the present volume contains chapters on Quaternary Pyridinium Compounds and Pyridine N-Oxides by Elliot Shaw, Alkylpyridines and Arylpyridines by Leon Tenenbaum, Halopyridines by Holly Mertel, Organometallic Compounds of Pyridine by Harry Yale, and Nitropyridines and Their Reduction Products by Renat Mizzoni. The literature appears to have been reviewed carefully through about 1957 with occasional references to work as recent as 1960.

As indicated in Professor Lauer's review of the first volume, recently published in this Journal, the literature covering heterocyclic chemistry is expanding at such a rate that exhaustive reviews of this nature are especially valuable and are gratefully received by the practicing organic chemist, even though gratitude is tempered by the high price tags attached to the volumes.

Volume one in the pyridine series was especially impressive by the imaginative way in which the over-all chemistry of pyridine and pyridine N-oxide was handled. Although the reviews in Volume two appear to have been prepared in a thorough and competent fashion, the originality of approach present in volume one is missing. Nevertheless volume two is a valuable addition to the reference library of anyone interested in pyridine chemistry.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF OREGON V. BOEKELHEIDE
EUGENE, OREGON

Radiation Damage in Solids. By DOUGLAS S. BILLINGTON and JAMES H. CRAWFORD, JR. Princeton University Press, Princeton, New Jersey. 1961. xi + 450 pp. 16 × 24 cm. Price, $12.50.

This book is a desirable addition to any general library which contains much material on radiation effects. The suitability of its inclusion in a more limited, personal library is a matter of some question. The favorable features, as well as many of the unfavorable, are summed up in the authors' own preface. However, the unfavorable features do not appear to be recognized as such by the authors.

After an introductory chapter, a theoretical survey presents in very condensed form the content and conclusions of several review articles. In its present position the theoretical presentation is insufficiently detailed for value (although it is a good guide to the literature) and so terse as to prove a stumbling block for the reader possessed of the notion that it is desirable to understanding of the remainder of the text.

The balance of the book is rather spotty. Good, short essays of variable length are interspersed with material remindful of a class of annual review which attempts coverage of the subject matter without undue commitment by its author. The chapter on relation between structure and properties is very readable; that on semi-conductors is superior to other parts of the book, doubtless because of the personal early involvement of one of the authors; the practical problems associated with uranium are interestingly discussed. However, in general, one gathers the impression (heightened by such juxtapositions as the treatment of radiation-affected silica gel catalyst at the end of a chapter on alloys) that the authors have unselectively presented all they know.

In cases where this reviewer has some personal acquaintance with details of the subject matter, he is impressed by the errors, by the manner of their presentation and by strange omissions. Some startling statements include an *obiter dictum* on radiation effects in organic solids (p. 82), a curious presentation of the mechanism of the Fricke dosimeter (p. 91), an extensive misconception of the early history of radiation damage studies (pp. 5, 395, 396), an erroneous discussion of the application of heavy-charged-particle accelerators "in the early days of the Manhattan Project" (p. 85), and the expressed notion (p. 5) that the terms "Wigner effect" and "discomposition," both originally suggested by this reviewer, are wholly synonymous. In view of the fact that the book is concerned about technological matters and does mention radiation-induced energy storage, omission of all reference to a possible thermal catastrophe, predicted by Szilard and unhappily demonstrated at Windscale, is rather notable.

The typography is exceptionally good, with only minor examples of bad usage (*cf.* p. 225) and but very few errors of spelling. It is unfortunate that the name of Van de Graaff is misspelled in its only three appearances in two different ways. Doubtless a second edition of this book will ultimately appear. When it does, it will be improved by many second thoughts of the authors.

RADIATION LABORATORY
UNIVERSITY OF NOTRE DAME MILTON BURTON
NOTRE DAME, INDIANA

Technique of Organic Chemistry. Volume I. Physical Methods of Organic Chemistry. Part III. Third Completely Revised and Augmented Edition. ARNOLD WEISSBERGER, EDITOR. Interscience Publishers, Inc., 250 Fifth Avenue, New York 1, N. Y. 1960. xii + 849 pp. 16 × 23 cm. Price, $24.50.

It is a striking indication of the growing dependence of organic chemistry upon more and more exotic physical techniques that a new and completely re-organized edition of this work should follow so soon the earlier edition. The volume at hand is Part III of a new Volume I; it deals with some topics covered in the earlier Volume I, Parts II and III, published in 1949 and 1954, respectively, together with some topics that have come into prominence, with respect to organic applications, in the intervening time.

The various branches of optical spectroscopy are now given expanded treatment in four chapters entitled, Spectroscopy and Spectrophotometry in the Visible and Ultraviolet (West), Infrared Spectroscopy (Anderson, Woodall and West), Colorimetry and Photometric Analysis (West), and Determination of Fluorescence and Phosphorescence (Wotherspoon and Oster). It is a question as to whether in these chapters the authors have not effected compromises