by Schlack and Kumpf[3] and shown its applicability to peptides and proteins in the identification of their C-terminal residues on a micro scale.[4] The work of other investigators[5,6] as well as our studies has shown that some amino acids, notably aspartic acid, glutamic acid, serine, arginine and proline are not revealed by the thiohydantoin method. In a search for an alternative or complementary method we have found that the reaction of amino acids discovered by Dakin and West[7] can be used to identify the C-terminal residues in peptides. If a peptide is heated with acetic anhydride and pyridine, and the reaction product is then hydrolyzed, the hydrolyzate does not contain the C-terminal amino acid. If such a hydrolyzate is spotted on paper and chromatographed, the C-terminal residue of the original peptide is found to be absent, as shown for several peptides in Fig. 1. In each case the comparison of the hydrolyzate of the untreated peptide with that of the reaction product permits an identification of the C-terminal amino acid.

$$-\mathrm{NHCHR'CONHCHRCOOH} \xrightarrow[C_5H_5N]{(CH_3CO)_2O} CO_2 + -\mathrm{NHCHR'CONHCHRCOCH_3}$$

$$\xrightarrow{H_2O} \mathrm{NH_2CHR'COOH} + \mathrm{NH_2CHRCOCH_3}$$

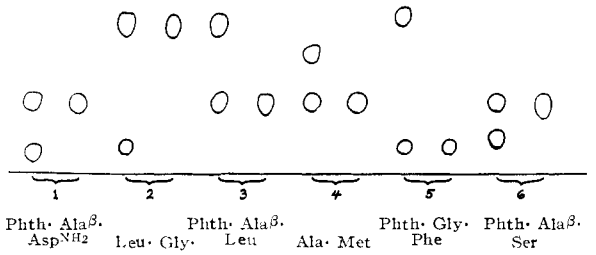

Fig. 1.—Drawing of paper chromatograms from six peptides: 1, phthaloyl-β-alanyl-DL-asparagine; 2, L-leucylglycine; 3, phthaloyl-β-alanyl-L-leucine; 4, DL-alanyl-DL-methionine; 5, phthaloylglycyl-DL-phenylalanine; 6, phthaloyl-β-alanyl-DL-serine. Of each pair of chromatograms the one on the left represents that obtained from a hydrolyzate of the peptide, while the one on the right represents that obtained from the hydrolyzate of the reaction product resulting from treatment of the peptide with acetic anhydride and pyridine.

It is noteworthy that phthaloyl-β-alanylserine gives a result that identifies serine as the C-terminal residue, while the thiohydantoin method failed to reveal a C-terminal residue in this peptide.[4]

The only previous example, in our knowledge, of an investigation of the reaction between a peptide and acetic anhydride in the presence of pyridine is that of Cleland and Niemann,[8] who showed that DL-alanylalanine evolved approximately the stoichiometric quantity of carbon dioxide.

(3) P. Schlack and W. Kumpf, *Z. physiol. Chem.*, **154**, 125 (1926).
(4) R. A. Turner and G. Schmerzler, *Biochem. Biophys. Acta*, in press.
(5) J. M. Swan, *Australian J. Sci. Research*, **A5**, 711, 721, 728 (1952).
(6) V. H. Baptist and H. B. Bull, THIS JOURNAL, **75**, 1727 (1953).
(7) H. D. Dakin and R. West, *J. Biol. Chem.*, **78**, 91, 745, 757 (1928).
(8) G. H. Cleland and C. Niemann, THIS JOURNAL, **71**, 841 (1949).

In our general procedure 5 to 10 mg. of peptide, 0.75 ml. of acetic anhydride and 0.50 ml. of pyridine were heated in a sealed tube at 150° for two to three hours. The contents of the tube were rinsed out with water and evaporated to dryness. After solution in water and evaporation to dryness a second time, the residue was dissolved in 3 ml. of 6 *N* hydrochloric acid and heated at 110° overnight. The hydrolyzate was evaporated to dryness *in vacuo*, then alternately dissolved in water and evaporated three times more in order to diminish the quantity of hydrochloric acid. The final residue was dissolved in 0.2 ml. of water, of which 5 to 10 μ l. was chromatographed on paper.

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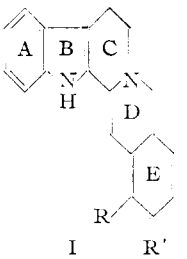
THE STEREOSPECIFIC SYNTHESIS OF *dl*-YOHIMBANE

Sir:

Yohimbane (I, R = R′ = H) has been obtained from the alkaloid *yohimbine* (I, R = COOCH$_3$; R′ = OH) by Oppenauer oxidation and



I

decarbomethoxylation to yohimbone[1] followed by Wolff–Kishner reduction,[2] a route which leaves unaltered the three remaining asymmetric centers in the derived molecule. The synthesis of *dl*-yohimbane described in this communication—apart from serving as a model for total synthesis—allows the unequivocal assignment of the relation between two of these centers, *viz.*, the carbon atoms common to rings D and E, as *trans*.[3,4]

dl-trans-Hydrindan-2-one,[5] on oxidation with perbenzoic acid, afforded the lactone of *dl-trans*-2-hydroxymethylhexahydrophenylacetic acid, m.p. 38–39° (Calcd.: C, 70.10; H, 9.15. Found: C, 70.35; H, 9.11); transformation of the lactone into ethyl *dl-trans*-2-bromomethylhexahydrophenylacetate, b.p. 129° at 1.4 mm. (Calcd.: Br, 30.3. Found: Br, 29.6) was accomplished by the action of alcoholic hydrogen bromide at room

(1) B. Witkop, *Ann.*, **554**, 105 (1943).
(2) J. Jost, *Helv. Chim. Acta*, **32**, 1301 (1949).
(3) B. Witkop (THIS JOURNAL, **71**, 2559 (1949)), basing his view on the results of certain drastic degradation experiments, has expressed a preference for the *trans* juncture of the D and E rings in yohimbine.
(4) A like conclusion has been reached by G. Stork and R. Hill (*ibid.*, **76**, 949 (1954)), who synthesized *dl*-alloyohimbane by a route similar to that outlined herein.
(5) R. S. Thakur, *J. Chem. Soc.*, 2147 (1932).

temperature. Alkylation of tryptamine with the bromoester in boiling ethanol in the presence of potassium carbonate led directly to the lactam of *dl-trans*-N-(β-3′-indolylethyl)-2-aminomethylhexahydrophenylacetic acid, m.p. 243–245° (Calcd.: C, 77.0; H, 8.16. Found: C, 77.19; H, 7.94). The latter substance was cyclized by means of phosphorus oxychloride in benzene to a yellow, crystalline solid (m.p. 196–198°), the analysis of which (Found: C, 55.16; H, 5.46) is consistent with its formulation as the dichlorophosphate[6] of *dl*-Δ^3-dehydroyohimbane (Calcd.: C, 55.23; H, 5.61). Hydrogenation of this salt over Adams catalyst gave, after treatment with aqueous alkali, a high yield of *dl-yohimbane*, m.p. 180° (Calcd.: C, 81.38; H, 8.63. Found: C, 81.71; H, 8.35), which was identified by comparison of its infrared spectrum with that of yohimbane derived from the natural source—tracings of both substances dissolved in chloroform were identical in every detail. The synthesis of an optically active form of yohimbane is now under way in this Laboratory.

(6) K. Gleu, S. Nitzsche and A. Schubert, *Ber.*, **72**, 1093 (1939).

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BOOK REVIEWS

Elsevier's Encyclopaedia of Organic Chemistry. Series III—Carboisocyclic Condensed Compounds. Volume 12B—Naphthalene. A. Compounds Containing One Naphthalene Nucleus. By F. RADT (Editor). Elsevier Publishing Company, 402 Lovett Boulevard, Houston, Texas. 1953. xlviii + pages 3261–3964. 19 × 26 cm. Price, Single Vol. $66.00; Series Sub. $58.00; Complete Sub. $50.00.

This volume is part VI of Volume 12B, and covers the naphthalenecarboxylic acids with the carboxyl group in the side chain. Previously issued bound parts of various volumes of the different series of this encyclopedia have received glowing praise by reviewers. "We have had full opportunity to convince ourselves of its reliability, completeness and usefulness." "High character with respect to organization, scholarship, scope, accuracy and quality of composition and printing." "A splendid encyclopedia, which should be part of every good chemical library." "A fresh breeze blowing through the tedious field of organic chemical documentation." The present volume lives up to these superlatives in every respect.

This part of Volume 12B is divided into four major sections, monocarboxylic acids, dicarboxylic acids, tricarboxylic acids and tetracarboxylic acids. Each of the first two sections is divided into simple acids, halogen-acids, nitro-acids, hydroxylamino-acids, amino-acids, hydrazino-acids, hydroxy-acids, and oxo-acids. The available information on the tri- and tetracarboxylic acids is very limited. The literature has been completely covered through 1944, but there are many later references, a few as recent as 1952. The data presented are generally more nearly complete than found in "Beilstein." For example, the treatise on Santoninic acid, santonin, and its derivatives covers eighty-one pages, and is very complete. It includes not only the usual brief concise accounts of physical properties, methods of formation, and reactions, but also several reaction scheme charts showing the relationship of various derivatives, and accounts of the physiological properties and therapeutic uses, and analytical methods.

The volume is well indexed. A complete table of contents is followed by a special index of all hydronaphthalene acids recorded in the book, which is very useful, since these compounds are classed as derivatives of the parent aromatic, and would otherwise have to be searched out individually. Each section is prefaced by a unique and quite useful summary table, whereby one may locate quickly any specific isomer. Finally, there are complete subject and formula indices at the end of the book.

The typography should receive special mention. It stands in strong contrast to most catalogs of this kind, in that it is very readable, and has no sections which require a reading glass to decipher. It is to be hoped that the publisher will be able to maintain the excellent format and editing and at the same time issue the remaining volumes of the set at a more rapid rate in the future.

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Tratado de Química Orgánica Segunda Edición. By DR. ENRIQUE ZAPPI, Profesor Titular de Química Orgánica en la Universidad de Buenos Aires. Librería "El Ateneo" Editorial, Florida 340, Cordoba 2099, Buenos Aires, Argentina. 1952. 17 × 24 cm. *Serie Acíclica:* 2189 pp. Price, 3 Ts. Enc. m$n 480.00, equivalente u$s 35.55. *Serie Cíclica:* 1804 pp. Price, 3 Ts. Enc. m$n 480.00, equivalente u$s 35.55.

Dr. Enrique Zappi, widely known by his teaching in the Buenos Aires and Plata Universities, is the author of an extensive work on organic chemistry, the first edition of which appeared in 1941.

His work is a very important contribution to the chemical bibliography in the Spanish language, and the publication of a second edition shows the interest that the book has aroused. The new edition maintains the general plan of the original one, but every part of it has been rewritten, a few mistakes have been corrected and a number of new facts or conceptions have been included. In this way, an increase of 300 pages has been obtained over the first edition. Thus, in the Cyclic Series (three volumes) four new chapters have been added under the titles: Carbohydrates with condensed nuclei, Acidic derivatives of amines, Dyeing materials and Biological catalysts.

The work is divided into 6 volumes, the three first dealing with Acyclic Organic Chemistry; the fourth and fifth with aromatic compounds and the last one with heterocycles.

The general distribution of Dr. Zappi's work follows the orientation marked by the classic treatises on organic chemistry: that is to say, it starts with the description of the common characteristics of each homogeneous group of substances, their methods of production and general properties, both physical and chemical. It then describes the main terms, thus avoiding the mistake found in many recently published books in which the author starts with the study of the first term of an homologous series, trying to deduce from this one, the properties that are common to the other terms.