Skell and Woodworth.[4,6] More accurate analyses were possible when using *trans*-2-butene and in the liquid phase at −70° the amounts of the compounds mentioned were respectively 51.0, 39.7 and 9.2%. Very similar values were obtained in the gas phase at 25° and moderate pressures (>1200 mm.). At lower pressures the ratio *trans*-1,2-dimethylcyclopropane to *trans*-2-pentene decreased and the formation of some *cis*-2-pentene, 2-methylbutene-1 and *cis*-1,2-dimethylcyclopropane was observed. It appears probable that at the lower pressures some of the initially formed "hot" cyclo compound isomerizes before it is stabilized by collision. The pressure at which half the initially formed cyclo compound isomerizes indicates that its lifetime is considerably longer than that of cyclopropane formed from methylene and ethylene,[7] which is to be expected for the more complex molecule.

Other differences between the gas and liquid phase reactions were seen in the secondary products formed in the former case, which were suppressed by the "cage effect" in the latter case. These differences together with the effects of inert gases will be fully discussed in a later paper.

The author wishes to thank The Royal Society for a grant toward the purchase of apparatus in connection with this work.

(6) P. S. Skell, private communication.
(7) H. M. Frey, THIS JOURNAL, **79**, 1259 (1957).

DEPARTMENT OF CHEMISTRY
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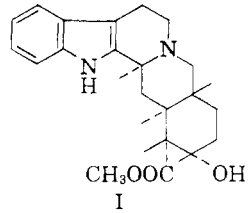
RECEIVED AUGUST 21, 1958

THE TOTAL SYNTHESIS OF YOHIMBINE

Sir:

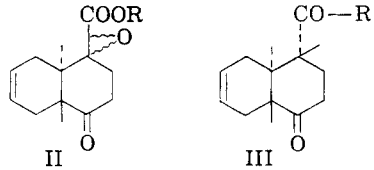
We wish to announce the total synthesis of the classical aphrodisiac alkaloid yohimbine (I), accomplished through a series of steps which repre-



I

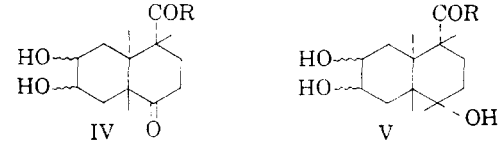
sents an entry into the D-E *trans* group of naturally occurring pentacyclic indole bases.[1]

cis-Δ^6-Octalin-1,4-dione, prepared by zinc–acetic acid reduction of the quinone–butadiene adduct,[2] was converted by the Darzens reaction, using ethyl chloroacetate and potassium *t*-butoxide, to the glycidic ester (II, R = C_2H_5), b.p. 135–155° (0.1 mm.). Saponification afforded a diastereoisomeric mixture of glycidic acids (II, R = H) (m.p.'s 138–140° and 210–211°) which, on heating, decarboxylated to give the unsaturated ketoaldehyde (III, R = H), b.p. 107–109° (0.01 mm.). Alkaline silver oxide converted the aldehyde to the acid (III, R = OH),[3] m.p. 145–146°.



II III

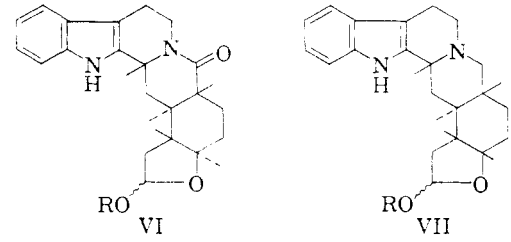
Treatment of the keto acid (III, R = OH) with oxalyl chloride yielded the corresponding acid chloride, which, without isolation, was used to acylate tryptamine, giving the amide (III, R = *β-ind*-CH_2CH_2NH), m.p. 161–162°. Hydroxylation with osmium tetroxide provided the keto diol (IV, R = *β-ind*-CH_2CH_2NH), m.p. 213–214°, which, on platinum-catalyzed hydrogenation,



IV V

yielded the triol (V, R = *β-ind*-CH_2CH_2NH),[3] m.p. 227–228°.

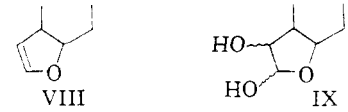
Glycol cleavage of the triol to the dialdehyde (not isolated), followed by cyclization to the hexacyclic lactol lactam (VI, R = H), m.p. 218–220° (dec.),[3] was achieved by periodate oxidation followed by brief heating with dilute phosphoric acid.



VI VII

Acid-catalyzed methanolysis to the lactol ether lactam (VI, R = CH_3), m.p. 268–270°, preceded lithium aluminum hydride reduction, which gave the lactol ether base (VII, R = CH_3), m.p. 133–137°.

The remainder of the synthesis was carried through without deliberate purification of intermediates. The acetic acid salt of the O-acetate (VII, R = CH_3CO), on brief heating at 280–290° (*in vacuo*), afforded a sublimate, the acetate salt of the enol ether (VIII). Osmium tetroxide



VIII IX

hydroxylation gave the expected diol (IX), which was cleaved, on treatment with metaperiodate, to the O-formate of *dl*-pseudoyohimbaldehyde produce. Chromic acid oxidation of the aldehyde, carried out in methanol–acetone in the presence of sulfuric acid, gave rise to *dl*-pseudoyohimbine m.p. 252–256°. Resolution of the synthetic base was accomplished by means of *l*-camphorsulfonic acid, which gave a salt (m.p. 274–278°) identical with the *l*-camphorsulfonate (m.p. 276–278°) of natural *d*-pseudoyohimbine (mixed m.p. undepressed and infrared spectra

(1) For synthesis of the D-E *cis* type, exemplified by reserpine, see R. B. Woodward, F. E. Bader, H. Bickel, A. J. Frey and R. W. Kierstead, THIS JOURNAL, **78**, 2023, 2657 (1956); *Tetrahedron*, **2**, 1 (1958).
(2) K. Alder and G. Stein, *Ann.*, **501**, 247 (1933).
(3) Direct evidence for the stereochemistry of this and related intermediates will be presented in a subsequent publication.

identical). The regenerated synthetic base was identical with natural *d*-pseudoyohimbine, on the basis of m.p., optical rotation and infrared spectral comparison. Since pseudoyohimbine already has been epimerized to yohimbine,[4] the steps outlined constitute the total synthesis of the latter alkaloid.[5]

Acknowledgments.—The authors wish to express their appreciation to the National Institutes of Health (G3892) and the National Science Foundation (G1240 and G3506) for financial support; to Merck and Company for generous coöperation in supplying osmium tetroxide; and to Gordon Knapp and Frank Lornitzo for invaluable experimental assistance.

(4) W. O. Godfredsen and S. Vandegal, *Acta Chim. Scand.*, **10**, 1414 (1956).

(5) Except where specified, satisfactory analytical and spectral data were obtained for each of the intermediates described.

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RECEIVED AUGUST 18, 1958

BOOK REVIEWS

Chemistry of the Steroids. By CHARLES W. SHOPPEE, D. Phil. (Basle), D.Sc. (Lond.), F.R.S., Professor of Organic Chemistry, University of Sydney, Formerly Professor of Chemistry, University of Wales. Organic Chemistry Monographs. Academic Press, Inc., 111 Fifth Avenue, New York 3, N. Y. 1958. vii + 314 pp. 15 × 22 cm. Price, $9.00.

Anyone brave enough to write a text dealing with steroids must expect to have it compared with Fieser and Fieser's "Natural Products Related to Phenanthrene," one of the most superbly written books in the field of organic chemistry. The comparison is not too favorable and consequently any advantage must be limited to coverage beyond the 1949 publication date of the Fieser book. The bulk of the research work between 1949–1958 has been in the field of adrenal hormones and there are a series of adequate review articles (two of them by Shoppee) which cover a good part of that period. Considering that even though the Shoppee book was published in 1958 it covers the literature only to 1955, there seems to be little justification for its existence except that it manages to condense an amazing amount of information in a rather small space. This is done at the expense of detail of exposition and there is no question that this book cannot be used as a text in graduate school or as an introduction to steroid chemistry. The expert will find it useful in order to locate leading references, but these must be checked because on cursory inspection quite a number of errors were noted such as the following:

Page 72: Ref. 365 consists of 2 parts. The *Experientia* reference (1951 not 1957) is not by Ruzicka and does not favor the 4,4-dibromo but rather the now commonly accepted 2,4-dibromo-3-keto formulation. Page 119: The interconversion of equilin and estrone is ascribed to ref. 80 or 83 while in fact it should refer to 81. Page 173: In the discussion on Reichstein's substances C, D, and V, it is stated that only D has been synthesized (ref. 9); V has been synthesized in 1952 (*J. Biol. Chem.*, **195**, 751 (1952)) and ref. 9 has nothing to do with the synthesis of D which is described in ref. 284 and 286. Page 192: Ref. 153 concerns the bromination at C-11 of a 12-ketone and not the replacement of a 12-hydroxyl group by bromine and ref. 156 has nothing to do with hecogenin. Page 207: Ref. 286, which reports the first synthesis of cortisone from diosgenin is not quoted in that connection but rather in relation to the first synthesis of that hormone from hecogenin, which is actually recorded in ref. 159. Page 211: The biological activity of 19-norcortisol was not recorded in ref. 290 and certainly does not exceed that of cortisone as mentioned on that page. Shoppee's annoying habit—of rearranging the order of author's names in the references and especially of skipping those of junior authors—still persists although it is improved over what was done in the Rodd book. Nevertheless, authors of future papers cannot at all rely on the accuracy of the citations and must consult the original literature.

The coverage follows the standard scheme and the book consists of six chapters concerned with introductory material, sterols and bile acids, sex hormones, adrenal hormones, cardiac glycosides and aglycones, and finally saponins and sapogenins. At one stage of the reviewer's perusal, he thought that he would have some contributions to make to the *New Yorker's* "Funny Coincidence Department" since the last paragraph on p. 128 and the first on p. 129 are verbatim copies from pp. 901 and 902 of "Chemistry of Carbon Compounds" Vol. IIB, edited by Rodd. But then it was noticed that p. 137 corresponds to 912, 150 and 151 to 925 and 926, 172–178 (except for one page on aldosterone) to 931, *et seq.*, and it finally became clear that a very appreciable portion of this book is nothing but a verbatim copy of the Rodd book (published by Elsevier rather than Academic Press). In all fairness to Shoppee, one must point out that the chapters in the Rodd book (1953) were also written by Shoppee but nowhere in the present book is there any indication that this is only a slightly up-to-date version (literature coverage to 1955 rather than 1952) of an earlier and more comprehensive volume which prospective customers of the present volume may already have purchased.

The best chapter is probably the one on adrenal hormones and this is the only one which offers any advantage (by being more up-to-date) over the Fieser book. The section on estrogens is very poor, while the chapters on cardiac aglycones and sapogenins contain only a few additional comments (*e.g.*, ouabagenin—which incidentally is misspelled and consequently misplaced in the index). The sapogenin chapter contains a desirable table (quite up-to-date including the Petrow formulation (1957) of ruscogenin), but many rotations are missing in spite of the fact that these have been published. In fact, all that would have been necessary is to look them up in Mathieu and Petit's "Pouvoir Rotatoire Naturel I. Steroïdes," which though published in 1956 still represents the single, most useful collection of steroid references available at the present time. Only one paragraph on p. 291 is devoted to the synthesis of steroid hormones from sapogenins and the references pertain to 1940–1942 papers. It is doubtful whether the use of the methods given in those references could have caused the revolution in steroid industry whereby the major portion of steroid hormones is now derived from sapogenins. It is true that the expert is familiar with this fact, but it is otherwise so well hidden that the novice in the steroid field would never realize this.

The index is fair (a search for "equilin" and "Oppenauer oxidation" was fruitless) and the structural formula reproductions excellent. There remains only one question: "When is the next edition of Fieser and Fieser's steroid book coming out?"

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