the ester,[4,5] dimethoxymethylborane, $CH_3B(OCH_3)_2$, (II), but is instead dimethylborylmethylperoxide, $(CH_3)_2BOOCH_3$, (I).

(I) was prepared by reaction of oxygen and trimethylborane in a flow system at room temperature and 10–15 mm. pressure and a 2–3 minute contact time. At molar flow ratios of oxygen to trimethylborane of 2:1, the reaction is quantitative (Table I). The peroxide, which appears to be the only product of this reaction, is a colorless liquid of negligible vapor pressure at −118°. Its vapor pressure curve lies between those of the esters methoxydimethylborane and dimethoxymethylborane. The peroxide liberates iodine quantitatively from a degassed sodium iodide-isopropyl alcohol solution acidified with glacial acetic acid, by the suggested equation

$$(CH_3)_2BOOCH_3 + 2I^- + 2H^+ \longrightarrow (CH_3)_2BOCH_3 + H_2O + I_2 \quad (I)$$

Supporting evidence for equation (I) is obtained from the reaction of the peroxide with two equivalents of anhydrous hydrogen iodide at −78°. Methoxydimethylborane, identified by its vapor pressure curve[6] and mass spectrum, was isolated from the reaction mixture in 80% yield together with substantial amounts of water and iodine. However, there is some indication that the primary products of this reaction are methanol and hydroxydimethylborane, and that the products isolated result from an esterification reaction during fractionation of the reaction mixture.

The peroxide (I) rearranges in a sealed tube in the liquid phase and in the gas phase (air absent) at room temperature to give approximately 90% of a compound of identical molecular weight. Preliminary results show that the rearrangement in the gas phase and in benzene solution follows first order kinetics; the half-life in the gas phase is approximately 60 days at room temperature. The rearranged product is dimethoxymethylborane (II), and shows the same mass spectrum, vapor pressure curve, and molecular weight as samples of II (b.p. 52.5°, 747 mm.) prepared by the reaction of trimethylborate and methyl Grignard reagent.

The peroxide (I) forms crystalline addition compounds when allowed to react with an equivalent amount of ammonia or pyridine. This reaction produces no substances not condensed at liquid nitrogen temperature, and preliminary results indicate no appreciable destruction of the peroxide bond by adduct formation. The ester (II) forms no adduct with pyridine.

The mass spectrum of the peroxide (I) is in agreement with the proposed structure and is inconsistent with the alternative hydroperoxide $(CH_3)_2BCH_2OOH$. Similarly, the hydroperoxide is excluded by consideration of the high vapor pressure of I as compared to that of hydroperoxides, the ease of rearrangement to the ester (II) and the nature of the reduction products.

Three explosions have been encountered thus far in the course of this investigation: two occurred during transfers of the peroxide in vacuo and a third during a peroxide preparation. The compound should be handled cautiously.

**Acknowledgment.**—We wish to express our appreciation to John W. Kraus for the determinations of the mass spectra and to Dr. Earl W. Malmberg for his counsel.

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(4) J. R. Johnson and M. G. Van Campen, Jr., THIS JOURNAL, **60**, 121 (1938).

(5) E. Frankland, *J. Chem. Soc.*, **15**, 363 (1862).

(6) A. B. Burg and R. I. Wagner, THIS JOURNAL, **75**, 3872 (1953).

## THE C-3 CONFIGURATION OF CERTAIN INDOLE ALKALOIDS[1]

*Sir:*

In connection with studies on the stereochemistry of indole alkaloids containing the ring system of yohimbine, ajmalicine, or corynantheine, we have had occasion to inspect the infrared spectra of chloroform solutions of various pairs of C-3 epimers. It became apparent that the 3.4–3.7 $\mu$ region of the C–H stretching vibration can be used to identify unmistakably the stereoconfiguration of the hydrogen atom at C-3 of the alkaloids or their derivatives. Thus, all compounds possessing an $\alpha$-hydrogen at C-3, *i.e.*, *normal* and *allo* products such as yohimbine[2] (IA), *d,l*-alloyohimbane[2] (IIA), and ajmalicine[2,3] (IIIA) (illustrated in the Figure below), exhibit two or more distinct and characteristic peaks of medium intensity on the high-wave length side of the major 3.46 $\mu$ band. However, those compounds containing a $C_3$-H $\beta$-orientation, *i.e.*, *pseudo* or *epiallo* products such as $\psi$-yohimbine[2] (IB), d,l-epialloyohimbane[2] (IIB), and 3-iso-ajmalicine (IIIB), m.p. 193–194° (found: C, 71.39; H, 6.96; N, 7.79), prepared by a zinc–acetic acid reduction[4] of 3-dehydroajmalicine,[3] show merely shoulders on the high-wave length side of the main peak.[5]

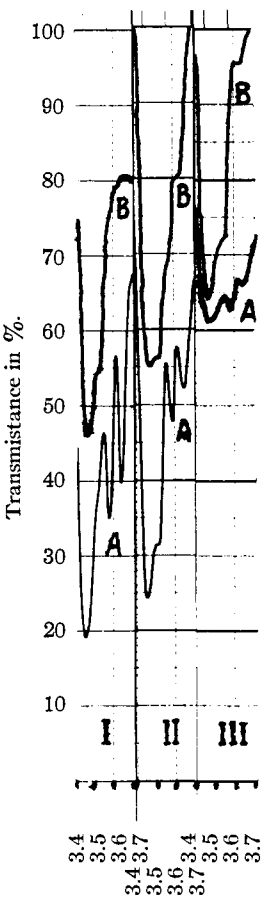


Fig. 1.

On the basis of the above spectrophotometric

(1) This work was supported in part by a research grant (M 1301) from the National Institutes of Health, Public Health Service, Department of Health, Education, and Welfare.

(2) For a recent review of the stereochemistry of this compound and related derivatives, *cf.* J. E. Saxton, *Quart. Revs.*, **10**, 108 (1956).

(3) E. Wenkert and D. K. Roychaudhuri, *J. Org. Chem.*, in press.

(4) F. L. Weisenborn and P. A. Diassi, THIS JOURNAL, **78**, 2022 (1956).

(5) *Epiallo* compounds containing 18-aroyloxy groups, *e.g.*, reserpine, show a fully developed extra peak instead of one of the shoulders.

method, the following compounds are *normal* or *allo* systems: yohimbine, yohimbone, yohimbane, β-yohimbine, corynanthine, alloyohimbine, rauwolscine, 11-methoxyalloyohimbane and its racemate, methyl isoreserpate, corynantheine, ajmalicine, and tetrahydroalstonine,[6] while the succeeding substances: reserpine, rescinnamine, deserpidine, methyl reserpate, 3-epi-α-yohimbine, ψ-yohimbine, and ψ-yohimbane,[7] m.p. 96–97° (found: C, 81.32; H, 8.57; N, 9.59), prepared by a zinc–acetic acid reduction[4] of 3-dehydroyohimbane,[3] belong to the *pseudo* or *epiallo* series. The configurational assignment of these twenty compounds is in complete accord with their previously designated stereochemistry.[2,8]

Infrared analysis suggests that the formerly proposed *pseudo* structure for serpine[9] and *epiallo* formula for methyl 18-desoxydeserpidate[10] require reassignment into the *normal* or *allo* series.

Finally, the new analytical method permits the classification of fifteen alkaloids of unknown configuration. Aricine,[11] tetraphylline,[11] reserpinine,[11] mayumbine,[2] isoreserpiline,[2] and corynantheidine[12] belong to the *normal* or *allo* series, while isorauhimbine,[2] raunescine,[13] isoraunescine,[13] raujemidine,[14] pseudoreserpine,[15] isoreserpinine,[11] raumitorine,[2,16] reserpiline,[2,16] and akuammigine[2] are part of the *pseudo* or *epiallo* series of alkaloids.[17]

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(6) Catalytic hydrogenation or sodium borohydride reduction of 3-dehydro or ring C tetradehydro compounds, *e.g.*, alstonine, yields only *normal* or *allo* products (as yet unpublished observations in this laboratory and *cf.* ref. 3 and references contained therein).

(7) The preparation of this compound not only makes available the fourth and last, till now unknown, isomer of yohimbane, but also constitutes a total synthesis of the same in view of its derivation from yohimbane and the formation of the latter from totally synthetic yohimbone [G. A. Swan, *J. Chem. Soc.*, 1534 (1950); J. Jost, *Helv. Chim. Acta*, **32**, 1301 (1949)].

(8) (a) C. F. Huebner, M. E. Kuehne, B. Korzun, and E. Schlittler, *Experientia*, **12**, 249 (1956) and preceding papers; (b) E. E. van Tamelen, P. E. Aldrich, and T. J. Katz, *Chemistry and Industry*, 793 (1956).

(9) A. Chatterjee and S. Bose, *Experientia*, **10**, 246 (1954). The authors are most grateful to Dr. Hochstein for informing them of the fact that serpine is a mixture of yohimbine and rauwolscine (F. A. Hochstein, *J. Org. Chem.*, in press).

(10) H. B. MacPhillamy, C. F. Huebner, E. Schlittler, A. F. St. André, and P. R. Ulshafer, THIS JOURNAL, **77**, 4335 (1955). The authors are most thankful to Dr. Huebner for instructing them of the fact that he has succeeded in proving by chemical means that the above deserpidine derivative possesses the *allo* configuration.

(11) The authors are most grateful to Drs. Djerassi and Diassi for the information of the fact that mercuric acetate oxidation, followed by reduction, of the cited alkaloids has led to the same stereochemical assignment (C. Djerassi, J. Fishman, M. Gorman, and J. P. Kutney, *ibid.*, in press).

(12) When considered along with the chemical evidence (ref. 8b), the infrared data suggest the *allo* configuration for this alkaloid.

(13) N. Hosansky and E. Smith, *J. Am. Pharm. Assoc., Sci. Ed.*, **44**, 639 (1955).

(14) P. R. Ulshafer, M. L. Pandow, and R. H. Nugent, *J. Org. Chem.*, **21**, 923 (1956).

(15) Taken in conjunction with previous chemical evidence [M. W. Klohs, F. Keller, R. E. Williams, and G. W. Kusserow, *Chemistry and Industry*, 187 (1956)], the infrared spectrum reveals the alkaloid to be a trimethoxybenzoyl derivative of methyl 17-demethyl-reserpate.

(16) The stereochemical identification of these two substances can be considered only tentative at this time because of the uncertainty of their spectra. It would appear that available samples might be admixed with an impurity that absorbs also at 3.4–3.7 μ.

(17) The authors are greatly indebted to Professor Janot, Sir Robert Robinson and Drs. Aghoramurthy, Hofmann, Huebner, Klohs, Neuss, and Ulshafer for supplying them with samples and/or infrared spectra for this study and to the Institute of Atomic Research, Iowa State College, for the use of a Baird infrared spectrophotometer.

# BOOK REVIEW

**Annual Review of Biochemistry.** Volume 25. By J. MURRAY LUCK, Editor, Stanford University, FRANK W. ALLEN, Associate Editor, University of California, and GORDON MACKINNEY, Associate Editor, University of California. Annual Reviews, Inc., Palo Alto, California. 1956. ix + 794 pp. 16.5 × 23 cm. Price, $7.00.

The current volume of the Annual Review of Biochemistry represents the twenty-fifth anniversary of an undertaking which has proved of tremendous value to the busy scientist who wishes to keep abreast of the biochemical literature. As stated in 1932 by Dr. J. Murray Luck and his advisory committee, it was hoped that critical surveys of the literature would minimize the task of referring constantly to original works. This goal has been admirably achieved by the Reviews in spite of the increasingly difficult task of examining critically the burgeoning field of biochemistry. The present volume includes among its many discriminating surveys a chapter completed by the friends and colleagues of Seymour Korkes as a tribute to his memory. A prefatory chapter is devoted to the life and work of Sir Edward Mellanby.

The contents are as follows: Sir Edward Mellanby by B. S. Platt; Nonoxidative and Nonproteolytic Enzymes by A. Meister; Proteolytic Enzymes by J. S. Fruton and M. J. Mycek; Carbohydrate Chemistry by E. J. Bourne and R. Stephens; Chemistry of the Lipides by F. B. Shorland; Metabolism of Purines and Pyrimidines by C. E. Carter; Biochemistry of Viruses by F. W. Putnam; Metabolism of Lipides by S. Bergström and B. Borgström; Biochemistry of Cellular Particles by W. C. Schneider and G. Hogeboom; Chemistry of the Fungi by C. E. Stickings and H. Raistrick; Biological Oxidations by S. F. Velick; The Chemistry of Proteins and Peptides by H. Fraenkel-Conrat; The Hemoglobins by H. A. Itano; Metabolism of Amino Acids and Proteins by E. A. Adelberg and M. Rabinovitz; Water-Soluble Vitamins, Part I, by J. J. Pfiffner and O. D. Bird; Water-Soluble Vitamins, Part II, by E. E. Snell and D. E. Metzler; Water-Soluble Vitamins, Part III, by G. W. E. Plaut and J. J. Betheil; Fat-Soluble Vitamins by E. Kodicek; Nutrition by W. H. Griffith and M. E. Swendseid; The Biochemistry of Cancer by C. Heidelberger; Cholesterol Metabolism by M. Friedman, S. O. Byers, and S. St. George; Chemical Constitution and Immunological Specificity by M. Heidelberger; Metabolism of Drugs and Other Organic Substances by W. H. Fishman, and Carbohydrate Metabolism by S. Korkes.

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