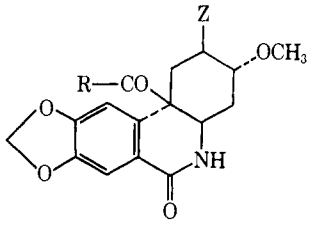
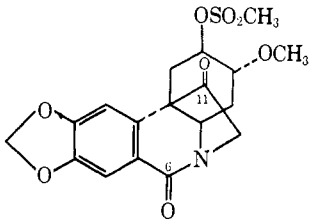
followed by heating with 0.1 *N* NaOH solution and cooling to crystallize the epoxy acid salt (82%). The methoxy lactone **3**, Z = OCH_3, mp 279° (70%), was then prepared by stirring in $BF_3 \cdot CH_3OH$ overnight.

Hydrolysis of **3**, Z = OCH_3, and normal esterification did not serve to free the C-2 hydroxyl for reaction owing to preferential relactonization, but saponification followed by displacement in phenacyl bromide by the carboxylate anion (in DMF) did afford an ester, **4** (Z = OH, R = $OCH_2COC_6H_5$), mp 157° (85%), which could be mesylated in cold pyridine to **4** (Z =



4

OSO_2CH_3, R = $OCH_2COC_5H_6$), mp 233° (66%), containing a leaving group appropriate for later trans elimination only to the desired $\Delta^{2,3}$-olefin.[5] The bridge to nitrogen was now prepared by saponification to **4**, R = OH, acid chloride formation with thionyl chloride, and treatment with diazomethane to the diazo ketone **4** (Z = OSO_2CH_3, R = CHN_2), mp 180° (90%). The bridge was closed with dry HCl to yield **5**, mp 194° (55%). The carbonyl at C-6 in **5** is essentially un-



5

available for stablizing amide resonance with nitrogen owing to Bredt's rule (*cf.* ref 3 and 6) and hence is readily solvolyzed, or reduced by cold $NaBH_4$ to a carbinolamine still containing the C-11 ketone. This carbinolamine, like haemanthidine,[7] is self-equilibrated (*via* C-6 aldehyde) to an equilibrium configuration at C-6.

Since reduction at C-11 in natural 11-oxo derivatives yields predominantly the wrong 11-epimer,[8] our retention of the axial mesylate at C-2 was intended to reverse this trend by steric hindrance. Indeed, reduction of **5** with $NaBH_4$ (in boiling isopropyl alcohol) followed by hot alkaline elimination yielded exclusively nortazettine, identical with a sample obtained from haemanthidine in base;[9] no 11-epimer was formed. As methylation of nortazettine yields tazettine,[1] this constitutes a synthesis of the latter alkaloid.

The internal Cannizzaro hydride transfer that converts haemanthidine to nortazettine occurs in mild base and it was established that the same reaction had occurred here in the hot $NaBH_4$ reduction of **5**.[10] Accordingly, acid reduction with a hindered borane (refluxing disiamylborane–THF) was used to avoid this further conversion. The crude diol was acetylated to prevent the Cannizzaro transfer in the subsequent elimination of mesylate with base (hot 1,5-diazabicyclo[3.4.0]nonene-5), and the products were deacetylated with $LiAlH_4$ and chromatographed to yield *d,l*-haemanthidine, mp 195° (20%), and 5% of the 11-epimer. The alkaloids were identical with natural samples by spectral comparisons and thin layer chromatograms in five different solvent systems.[9,11] Although stereospecificity in the borane reduction is not as complete as with hot $NaBH_4$, nevertheless the stereochemical distinction between the C-11 epimers formed may be established independently of their identification with natural material since only haemanthidine can form the cyclic ether, apohaemanthidine, in acid.[1] Conversion of several of these synthetic materials to other alkaloids of the crinine family is being investigated.

Acknowledgment. We wish gratefully to acknowledge the support of the National Institutes of Health (Grant No. GM-10715) for the work reported here.

(5) Eliminations at this stage resulted in concomitant decarboxylation.

(6) S. Uyeo, H. M. Fales, R. J. Highet, and W. C. Wildman, *J. Amer. Chem. Soc.*, 80, 2590 (1958).

(7) R. W. King, C. F. Murphy, and W. C. Wildman, *ibid.*, 87, 1912 (1965).

(8) H. M. Fales and W. C. Wildman, *ibid.*, 82, 197 (1960); W. C. Wildman and D. T. Bailey, *ibid.*, 91, 150 (1969); and independent examinations in these laboratories.

(9) We wish to thank Professors W. C. Wildman (Iowa State) and F. L. Warren (Capetown) for generous gifts of natural alkaloids.

(10) This was shown by acetylation directly following reduction, which yielded an acetamide, reduced by $LiAlH_4$ to an *N*-ethyl derivative.

(11) Analyses and spectra of all the intermediates were consistent with the formulations given.

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Book Reviews

Separation Methods in Organic Chemistry and Biochemistry. By FRANK J. WOLF, Merck Sharp and Dohme Research Laboratories, Rahway, New Jersey. Academic Press, Inc., 111 Fifth Ave., New York, N. Y. 1969. vii + 237 pp. 23.5 × 16 cm. $11.50.

One of the most tedious chores facing the nonchemist working in biological–medical fields is the search through multitudes of publications dealing in a specialized way with the numerous techniques and procedures utilized by chemists, in order to select procedures which are suitable for his problem. Books which present a survey of methods are indeed rare and for this reason this volume will be welcomed not only by chemists but biologists and medical investigators as well. Not so comprehensive as to overwhelm the nonchem-

ist, it presents procedures and theory in a concise and adequate manner and provides an extensive bibliography for those wishing to pursue particular aspects further. Types of separations, distribution coefficients, and an evaluation of separation processes are considered in the introduction. Chapter I presents general principles concerning stability, group separations, and fractionation separations. Chapter II deals with the determination of molecular properties by means of chromatographic procedures and micro tests. The chief concern of Chapter III is solvent extraction. Included in this chapter are discussions of partition ratio, application of solvent extraction for group separation and fractionation separation, partition chromatography, and countercurrent distribution. Chapter IV is devoted to gel-filtration and gel-permeation chromatography, and chapter V presents a general discussion and applications of ion exchange. The sixth and final chapter deals with general principles and application of adsorption processes. The four appendices are particularly useful. I presents the dielectric constants of common solvents, II tabulates characteristics of ion-exchange resins as well as sources from which they may be purchased, III deals with general thin-layer and paper chromatography techniques, and IV is a conversion table for R_f and R_m. This book, then, provides an excellent starting point for investigators with separation problems. Its major objective as stated by the author, "to provide perspectives for the commonly used methods and indications for their use," has been achieved.

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Electrometric Methods. Edited by D. R. BROWNING. McGraw-Hill Book Co., 330 West 42nd St., New York, N. Y. 1969. viii + 131 pp. 14 × 22 cm. $7.50.

The contents of this concise little monograph embrace: conductivity (22 pp), high-frequency titrimetry (13 pp), potentiometry (31 pp), and coulometry (16 pp) by W. H. Lee; voltammetry (23 pp) and polarography (14 pp) by R. J. Hill and J. Broadhead; and electrogravimetry (8 pp) by D. R. Browning. The coverage of these topics is ambivalent, including both general or research aspects as well as analytical applications.

In discussing this number of topics in so few pages, the authors adopt the Boltzmann–Einstein concept that, "... matters of elegance should be left to the tailors and cobblers." The book attempts a clean-cut presentation of first principles, in first-order approximation, and draws reasonably clear correlations between visualizable physical concepts and the principal mathematical equations. The typography is good and lapses, such as *antidate* (p 90), are few. The use of *c/s* for *hertz*, and a table of oxidation potentials (3.1) which needs a footnote explanation that all signs should be reversed for use in the equations, will strike some users as being perverse. Most of the *objectionable* features comprise *nitpicking* in that they relate to the obvious limitations which are inherent in such a highly condensed treatment.

The token treatment (less than 8 pp) of electrogravimetry contrasts with 13 pp of high-frequency titrimetry. The inclusion, in the former place, of mercury cathode *separations* is misleading with respect to the extent of any actual exposition on their real utility. The description of a 1930-vintage Melaven cell is only relieved by the comment that "automatic equipment" is available. The sentence (p 125), "Normally, this (the current) is high enough to reduce all the components of the solution, but this is avoided because of efficient stirring and because of the heating effects of the current," conveys little that is clear or accurate. With respect to organic polarography (p 103) the caution, "... control of the pH ... essential for ... reproducibility ...," is cryptic and inadequate in emphasizing the need for a high buffer capacity.

On the whole, this concise exposition is relatively clear and does provide a useful starting point for chemical technicians and other nonspecialists in electrometric methods.

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