mon, it has been shown[3] that ϕ_t can be represented as a linear function of the solution composition, or

$$\phi_t = \phi_b + (\phi_a - \phi_b)N_a = \phi_a + (\phi_b - \phi_a)N_b \quad (4)$$

If ϕ_t is a linear function of a or b, then log $(\gamma_\pm)_t$ would also be expected to be, such that

$$\log (\gamma_\pm)_t = \log (\gamma_\pm)_a + [\log (\gamma_\pm)_b - \log (\gamma_\pm)_a]N_b \quad (5)$$

Substitution of eq. 4 and 5 into eq. 3 yields, after rearrangement

$$(\Delta E_{1/2})_{obsd} = \{29.5[(1 - N_b) \log (\gamma_\pm)_a + N_b \log (\gamma_\pm)_b] + 4.62m[(1 - N_b)\phi_a + N_b\phi_b]\} \quad (6)$$

Now, $1 - N_b$ is equal to N_a, and eq. 6 becomes

$$(\Delta E_{1/2})_{obsd} = \{N_a[29.5 \log (\gamma_\pm)_a + 4.62m\phi_a] + N_b[29.5 \log (\gamma_\pm)_b + 4.62m\phi_b]\} \quad (7)$$

and since

$$[(\Delta E_{1/2})_{obsd}]_b = \{29.5 \log (\gamma_\pm)_b + 4.62\ m\phi_b\} \quad (8)$$

then eq. 7 becomes identical with eq. 1 when one considers that $(\Delta E_{1/2})_{obsd} = (E_{1/2})_{obsd} - (E_{1/2})_{\mu=0}$.

(3) R. A. Robinson and R. H. Stokes, "Electrolyte Solutions," 2nd Ed., Butterworths, London, 1959, p. 437.

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The Synthesis of Apo-β-erythroidine

Sir:

In their work directed toward the elucidation of the structure of β-erythroidine, a physiologically active alkaloid isolated from several species of *Erythrina*, Boekelheide and co-workers obtained a rearranged demethoxy derivative which they called apo-β-erythroidine.[1] The latter compound, to which structure XV was assigned,[1a] was of interest for its unusual tetracyclic structure, its relationship to the parent alkaloid, and its own physiological activity. Several attempts at synthesizing apo-β-erythroidine or its analogs were unsuccessful[2-4]; most noteworthy with respect to the results reported in this communication was the observed[4] inactivity of the carbonyl of 1-methyl-2,3,4,5-tetrahydro-5-oxo-1-benzazepine toward normal addition reactions (presumably due to nitrogen–carbonyl resonance interaction) and the well-known[3] difficulty in preparing 7-substituted indolines.

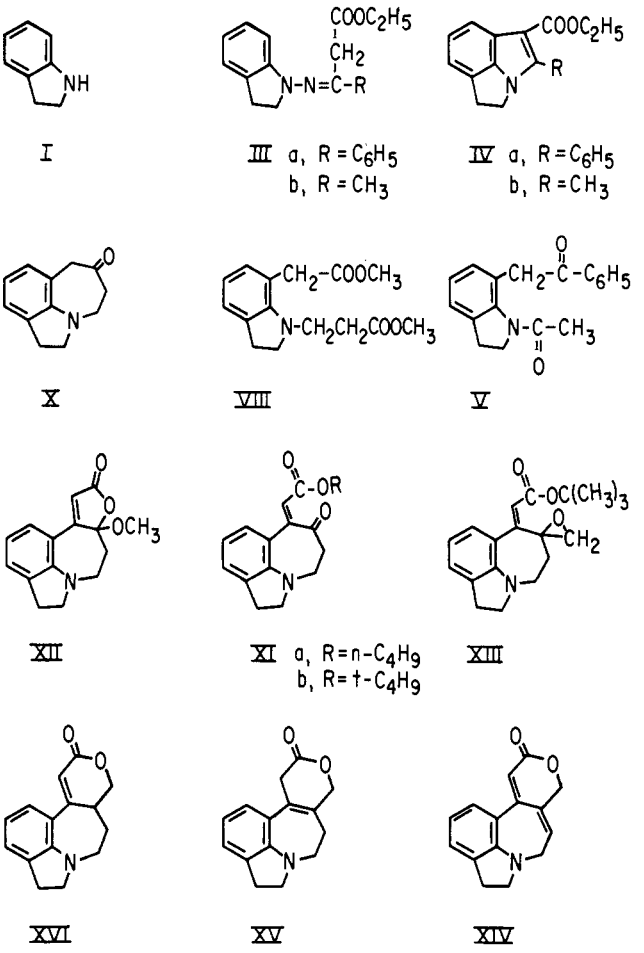
We now wish to report the synthesis of apo-β-erythroidine (XV) and isoapo-β-erythroidine (XVI).[5]

(1) (a) See V. Boekelheide, J. Weinstock, M. F. Grundon, G. L. Sauvage, and E. J. Agnello, *J. Am. Chem. Soc.*, **75**, 2550 (1953), for a summary of the structural work on β-erythroidine. (b) Also see V. Boekelheide in "The Alkaloids," Vol. VII, R. H. F. Manske, Ed., Academic Press Inc., New York, N. Y., 1960, pp. 201–227, for a recent summary of the structural work on the *Erythrina* alkaloids. (c) F. Koniuszy and K. Folkers, *J. Am. Chem. Soc.*, **73**, 333 (1951), isolated a derivative of β-erythroidine. The latter differed in melting point and particularly in optical rotation from the apo-β-erythroidine isolated by Boekelheide, *et al.*,[1a] and thus was apparently impure or not the same compound.

(2) V. Boekelheide and W. G. Gall, *J. Org. Chem.*, **19**, 504 (1954).

(3) W. G. Gall, B. D. Astill, and V. Boekelheide, *ibid.*, **20**, 1538 (1955).

(4) B. D. Astill and V. Boekelheide, *J. Am. Chem. Soc.* 77, 4079 (1955).



This synthesis was made possible by an interesting, partial reversal of the Fischer indole ring closure in the 1,2-dihydropyrrolo[3,2,1-*hi*]indole series and constitutes a practical synthesis of 7-substituted indolines.

Indoline[6] (I) was nitrosated and then reduced with lithium aluminum hydride to give 1-aminoindoline[7] (II) in 70% yield. Treatment of the substituted hydrazine II with either ethyl benzoylacetate or ethyl acetoacetate gave the hydrazones IIIa,b, which were unstable and could not be readily characterized but were converted, by sulfuric acid in absolute ethanol at reflux, to 4-phenyl-5-ethoxycarbonyl-1,2-dihydropyrrolo-[3,2,1-*hi*]indole (IVa) in 83% yield [m.p. 137–138°; $\lambda_{max}^{CH_3OH}$ 309 (ε 9500) and 251 mμ (18,000)], and to the methyl analog IVb in 54% yield [m.p. 89–90°; $\lambda_{max}^{CH_3OH}$ 297 (ε 14,000), 240 (22,600), and 220 mμ (38,000)]. This ring system was previously synthesized for the first time by a Fischer reaction on the hydrazone of 1-aminoindoline and ethyl pyruvate to give the 1,2-dihydro-4-ethoxycarbonyl derivative.[8]

When IVa was treated with sulfuric acid in aqueous ethanol at reflux, we obtained 7-phenacylindoline, which was acetylated to facilitate isolation and give 1-acetyl-7-phenacylindoline (V) in 90% yield (m.p. 136–137°). This hydrolytic opening is unknown in simpler systems and presumably is the result of considerable steric strain in the 6,5,5-fused ring system of IV.

(5) Isoapo-β-erythroidine is an isomer of apo-β-erythroidine obtained when the latter is chromatographed on alumina; see ref. 1a.

(6) H. Rapoport and J. R. Tretter, *J. Org. Chem.*, **23**, 248 (1958).

(7) Satisfactory elemental analyses were obtained for all compounds reported herein.

(8) H. Rapoport and J. R. Tretter, *J. Am. Chem. Soc.*, **80**, 5574 (1958).

Reaction of the phenacylindoline V with hydrazoic acid in chloroform followed by alkaline hydrolysis of the resulting mixture of amides gave a 52% yield of 7-indolinacetic acid (VI, m.p. 157–158°) plus 7-aminomethylindoline (VII), as a colorless oil, in 10 to 15% yield. Esterification of VI and alkylation with methyl β-bromopropionate gave VIII, which on cyclization with potassium *t*-butoxide in benzene resulted in a 55% yield of 6-oxo-7-methoxycarbonyl-1,2,4,5,6,7-hexahydroazepino[3,2,1-*hi*]indole[9] [IX, m.p. 91–92°; $\lambda_{max}^{C_2H_5OH}$ 253 (ε 10,800) and 218 mμ (16,000); $\lambda_{max}^{N\ NaOH-C_2H_5OH}$ 285 (ε 11,700) and 245 mμ (16,000)]. Acid decarboxylation of IX gave the ketone X in 60% yield [m.p. 82–83°; $\lambda_{max}^{CH_3OH}$ 257 (ε 6400) and 300 (sh) mμ (1500); $\nu_{max}^{CHCl_3}$ 1713 cm.$^{-1}$].

When the ketone X was treated with the readily available *n*-butyl glyoxylate[10,11] in methanol, using a piperidine–acetic acid catalyst, we obtained not the desired ester XIa but instead the lactol ether XII [m.p. 176°; $\lambda_{max}^{CH_3OH}$ 402 (ε 5500), 290 (9000), and 255 mμ (16,300); ν_{max}^{KBr} 1750 cm.$^{-1}$], presumably arising *via* methanol attack on the ketone carbonyl of XIa followed by butoxide displacement. Substitution of *t*-butyl glyoxylate[12] as reagent and *t*-butyl alcohol as solvent gave 6-oxo-7-*t*-butoxycarbonylmethylene-1,2,4,5,6,7-hexahydroazepino[3,2,1-*hi*]indole[13] (XIb) in 59% yield [$\lambda_{max}^{C_2H_5OH}$ 378 (ε 5200) and 251 mμ (15,200); $\nu_{max}^{CCl_4}$ 1720 and 1710 cm.$^{-1}$].

Reaction of XIb with dimethyloxosulfonium methylide[14] in dimethyl sulfoxide gave 6-hydroxymethyl-7-carboxymethylene-1,2,4,7-tetrahydroazepino[3,2,1-*hi*]-indole δ-lactone (XIV), presumably arising from rearrangement of the expected intermediate epoxide XIII. The assignment of structure XIV is supported by the following data: (1) extended conjugation as seen in the electronic spectrum [$\lambda_{max}^{C_2H_5OH}$ 428 (ε 5000), 300 (11,000), and 260 mμ (10,000)]; (2) infrared spectrum (single carbonyl band at 1723 cm.$^{-1}$); (3) elemental analysis; (4) mass spectrum (mass peak at 239); (5) nuclear magnetic resonance absorption (deuterioacetone) which showed six protons in the region δ 2.5–3.5 (TMS, external standard), a two-proton singlet at δ 4.4 corresponding to the methylene on the lactone oxygen, two vinyl protons at δ 6 corresponding to a singlet superimposed on a triplet, and three aromatic protons.

Hydrogenation of the diene lactone XIV with 5% Pd–$BaSO_4$ in ethyl acetate gave apo-β-erythroidine (XV) and isoapo-β-erythroidine (XVI) in 14 and 20% yields, respectively, which were shown to be identical with authentic samples[15] by melting point, infrared and ultraviolet spectra, and thin layer chromatography; apo-β-erythroidine, m.p. 128–129° (lit.[16] 132–132.5°); $\nu_{max}^{CHCl_3}$ 1737 cm.$^{-1}$; $\lambda_{max}^{C_2H_5OH}$ 345 (ε 3500) and 240 mμ (24,500); isoapo-β-erythroidine, m.p. 146–148° (lit.[16] 146–147°); $\nu_{max}^{CHCl_3}$ 1705 cm.$^{-1}$; $\lambda_{max}^{C_2H_5OH}$ 379 (ε 6500), 288 (10,800), and 253 mμ (16,800).

(9) Nomenclature is based on the parent aromatic compound, azepino[3,2,1-*hi*]indole, as used in *Chemical Abstracts*.

(10) See M. S. Newman, W. C. Sagar, and C. C. Cochran, *J. Org. Chem.*, **23**, 1832 (1958), for the use of glyoxylate condensations to add a two-carbon acid side chain to ketones.

(11) F. J. Wolff and J. Weijlard, *Org. Syn.*, **35**, 18 (1955).

(12) This previously unknown compound was synthesized from di-*t*-butyl fumarate (m.p. 69–70°, prepared from fumaric acid and isobutylene) which was oxidized with permanganate to the tartrate (m.p. 84–85°), and the latter was converted to *t*-butyl glyoxylate by the action of lead tetraacetate. Recently, L. A. Carpino [*J. Org. Chem.*, **29**, 2820 (1964)] has isolated *t*-butyl glyoxylate as the hydrate from hydrolysis of the α-bromo-α-alkoxyacetate.

(13) The stereochemistry of XIb is presumed to be *cis*-*t*-butoxycarbonyl with respect to the ketone group on the basis of the observed cyclization of XIa and the subsequent cyclization of the epoxide XIII.

(14) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **84**, 867 (1962).

(15) Prepared[16] from a sample of β-erythroidine hydrochloride, kindly supplied by Dr. Karl Folkers.

(16) G. L. Sauvage and V. Boekelheide, *J. Am. Chem. Soc.*, 72, 2062 (1950).

(17) National Institutes of Health Predoctoral Fellow.

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Mass Spectrometry in Structural and Stereochemical Problems. LXIX.[1] Methyl Migration in an Electron Impact Induced Fragmentation[2]

Sir:

Hydrogen rearrangements in mass spectrometric fragmentation reactions are frequently of great mechanistic significance[3] and much attention has been paid recently to this subject in our laboratory.[4] However, rearrangements of alkyl groups (initially encountered in hydrocarbons[5]) have not been studied extensively[6] and have largely escaped mechanistic scrutiny. We now wish to record an interesting example of methyl migration for which a plausible rationale can be proposed.

The second most intense peak in the mass spectrum[7] of *trans*-Δ^3-10-methyl-2-octalone (Ia) and its 6,7-dehydro analog Ib occurs at *m/e* 69 and has been shown by high-resolution mass measurements to correspond to the $C_4H_5O^+$ rather than the $C_5H_9^+$ ion. In the spectrum of the 4-d_1-labeled derivative IIb[8] the peak is moved to *m/e* 70 and, since migration of a deuterium (respectively hydrogen) atom attached to a double bond is an unlikely process,[3] this result implies that carbon atom 4 is retained in the ion of mass 69 in Ia and Ib. Furthermore, since the high-resolution mass measurements demonstrated the presence of the oxygen atom, carbon atoms 2 and 3 must also be included in the ion. Only a one mass unit shift to *m/e* 70 was observed in the mass spectra of the 1,1,3-d_3-labeled analogs IIIa and

(1) Paper LXVIII: H. Budzikiewicz, R. T. Aplin, D. A. Lightner, C. Djerassi, R. Mechoulam, and Y. Gaoni, *Tetrahedron*, in press.

(2) Financial support provided by the National Institutes of Health of the U. S. Public Health Service (Grants No. CA-07195 and AM-04257) is gratefully acknowledged.

(3) See, for instance, H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Interpretation of Mass Spectra of Organic Compounds," Holden-Day, Inc., San Francisco, Calif., 1964.

(4) C. Djerassi, *Pure Appl. Chem.*, **9**, 159 (1964), and references cited therein.

(5) F. H. Field and J. L. Franklin, "Electron Impact Phenomena," Academic Press Inc., New York, N. Y., 1957, pp. 185–194; N. Dinh-Nguyen, R. Ryhage, S. Ställberg-Stenhagen, and E. Stenhagen, *Arkiv Kemi*, **18**, 393 (1961).

(6) Some examples are the ion (ionized methyl ethyl ketone?) resulting from loss of carbon monoxide (confirmed in our laboratory by high-resolution measurements) from isopropenyl acetate (A. S. Newton and P. O. Strom, *J. Phys. Chem.*, **62**, 24 (1958)), the elimination of a propyl radical from positions 2, 3, and 4 of long-chain methyl esters (see E. Stenhagen, *Z. anal. Chem.*, **205**, 109 (1964)), the expulsion of ethylene from the straight-chain portion of isohexyl cyanide (R. Beugelmans, D. H. Williams, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **86**, 1386 (1964)), and reactions associated with the loss of carbon dioxide in ethyl carbamates (C. P. Lewis, *Anal. Chem.*, **36**, 176 (1964)).

(7) See Figures 8 and 9 in ref. 3, p. 157.

(8) J. Karliner, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 580 (1965).