

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-amino-methylindoline (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*]indole⁹ [IX, m.p. 91–92°; $\lambda_{\text{max}}^{\text{C}_2\text{H}_5\text{OH}}$ 253 (ϵ 10,800) and 218 $m\mu$ (16,000); $\lambda_{\text{max}}^{\text{N}_2\text{NaOH}-\text{C}_2\text{H}_5\text{OH}}$ 285 (ϵ 11,700) and 245 $m\mu$ (16,000)]. Acid decarboxylation of IX gave the ketone X in 60% yield [m.p. 82–83°; $\lambda_{\text{max}}^{\text{CH}_3\text{OH}}$ 257 (ϵ 6400) and 300 (sh) $m\mu$ (1500); $\nu_{\text{max}}^{\text{CHCl}_3}$ 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°; $\lambda_{\text{max}}^{\text{CH}_3\text{OH}}$ 402 (ϵ 5500), 290 (9000), and 255 $m\mu$ (16,300); $\nu_{\text{max}}^{\text{KBr}}$ 1750 cm^{-1}], presumably arising *via* methanol attack on the ketone carbonyl of XIa followed by butoxide displacement. Substitution of *t*-butyl glyoxylate¹² 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*]indole¹³ (XIb) in 59% yield [$\lambda_{\text{max}}^{\text{C}_2\text{H}_5\text{OH}}$ 378 (ϵ 5200) and 251 $m\mu$ (15,200); $\nu_{\text{max}}^{\text{CCl}_4}$ 1720 and 1710 cm^{-1}].

Reaction of XIb with dimethylxosulfonium methylide¹⁴ 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 [$\lambda_{\text{max}}^{\text{C}_2\text{H}_5\text{OH}}$ 428 (ϵ 5000), 300 (11,000), and 260 $m\mu$ (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–BaSO₄ 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 samples¹⁵ by melting point, infrared and ultra-

violet spectra, and thin layer chromatography; apo- β -erythroidine, m.p. 128–129° (lit.¹⁶ 132–132.5°); $\nu_{\text{max}}^{\text{CHCl}_3}$ 1737 cm^{-1} ; $\lambda_{\text{max}}^{\text{C}_2\text{H}_5\text{OH}}$ 345 (ϵ 3500) and 240 $m\mu$ (24,500); isoapo- β -erythroidine, m.p. 146–148° (lit.¹⁶ 146–147°); $\nu_{\text{max}}^{\text{CHCl}_3}$ 1705 cm^{-1} ; $\lambda_{\text{max}}^{\text{C}_2\text{H}_5\text{OH}}$ 379 (ϵ 6500), 288 (10,800), and 253 $m\mu$ (16,800).

(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 Fragmentation²

Sir:

Hydrogen rearrangements in mass spectrometric fragmentation reactions are frequently of great mechanistic significance³ and much attention has been paid recently to this subject in our laboratory.⁴ However, rearrangements of alkyl groups (initially encountered in hydrocarbons⁵) have not been studied extensively⁶ 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 spectrum⁷ 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 C₄H₅O⁺ rather than the C₅H₉⁺ ion. In the spectrum of the 4-*d*₁-labeled derivative IIB⁸ 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. Stållberg-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. Karlner, H. Budzikiewicz, and C. Djerassi, *J. Am. Chem. Soc.*, **87**, 580 (1965).

(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).

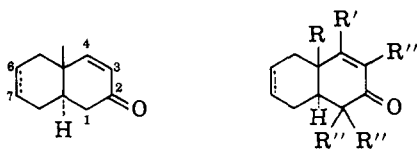
(12) This previously unknown compound was synthesized from di-*t*-butyl fumarate (m.p. 69–70°, prepared from fumaric acid and isobutylene) which was oxidized with permanganate to the tartrate (m.p. 84–85°), and the latter was converted to *t*-butyl glyoxylate by the action of lead tetraacetate. Recently, 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) Prepared¹⁶ from a sample of β -erythroidine hydrochloride, kindly supplied by Dr. Karl Folkers.

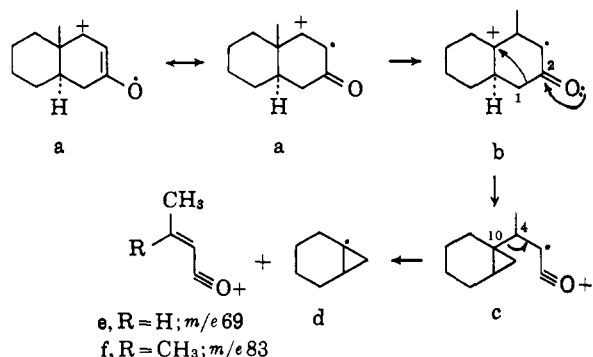
IIIb,⁹ from which we conclude that C-3, but not C-1, is implicated in the ion under question. Carbon atoms 2, 3, and 4 and their attached oxygen and hydrogen atoms correspond to C₃H₂O, leaving the elements of CH₃ unaccounted for. That these are derived from the angular methyl group could be demonstrated unambiguously by the synthesis¹⁰ of *trans*-Δ^{3,8}-10-trideuteriomethyl-2-octalone (IV), whose mass spectrum displayed an intense *m/e* 72 rather than *m/e* 69 peak.



Ia, without 6-7 double bond
b, with 6-7 double bond

II, R = CH₃, R' = D, R'' = H
III, R = CH₃, R' = H, R'' = D
IV, R = CD₃, R' = R'' = H
V, R = R' = CH₃, R'' = H
VI, R = CH₃, R' = CD₃, R'' = D

A plausible path for the abundant formation of the ion of mass 69 may be visualized through intermediacy of a molecular ion¹¹ a, in which one of the π-electrons of the double bond had been removed to furnish an "ionized double bond." Migration of the angular methyl group to b, followed by heterolysis of the 1-2 bond (c) and homolysis of the 4-10 linkage, would then yield the highly stabilized conjugated oxonium ion e (*m/e* 69) and a neutral radical, which may be represented by structure d. The major driving force for this process is probably not the conversion of a secondary (a) to a tertiary (b) carbonium ion but rather the formation of the energetically favored ion by what may well be a concerted process. The justification for this statement is that the base peak in the mass spectrum of the higher homolog, *trans*-Δ^{3,8}-4,10-dimethyl-2-hexalene (V),¹² is found at *m/e* 83 and can be attributed to structure f, since a shift to *m/e* 87 is encountered in the



(9) Prepared by heating under reflux for 20 hr. the appropriate ketone with sodium in methanol-O-*d* and heavy water. See R. H. Shapiro, J. M. Wilson, and C. Djerassi, *Steroids*, **1**, 1 (1963).

(10) The magnesium salt of cyclohexanone cyclohexylimine was alkylated (see G. Stork and S. R. Dowd, *J. Am. Chem. Soc.*, **85**, 2178 (1963)) with trideuteriomethyl iodide (F. A. Cotton, J. H. Fassnacht, W. D. Harrocks, and N. A. Nelson, *J. Chem. Soc.*, 4138 (1959)), and the resulting 2-trideuteriomethylcyclohexanone was converted (J. A. Marshall and W. I. Fanta, *J. Org. Chem.*, **29**, 2501 (1964)) to Δ¹⁽⁹⁾-10-trideuteriomethyl-2-octalone. Reduction with lithium in liquid ammonia, bromination at C-3, and dehydrobromination (for unlabeled analog see C. Djerassi and D. Marshall, *J. Am. Chem. Soc.*, **80**, 3986 (1958)) provided the desired labeled octalene IV.

(11) For details of this approach and description of symbolism (fish-hook = one-electron shift; arrow = two-electron movement) see H. Budzikiewicz, C. Djerassi, and D. H. Williams, "Structure Elucidation of Natural Products by Mass Spectrometry," Vol. II, Holden-Day, Inc., San Francisco, Calif., 1964, pp. 1-3.

(12) L. H. Zalkow, F. X. Markley, and C. Djerassi, *J. Am. Chem. Soc.*, **82**, 6354 (1960).

mass spectrum of the *d*₆-labeled analog VIb.⁹ No particularly favorable driving force can be ascribed to the methyl migration step (a → b) *per se* in a molecular ion of V analogous to a.

Work is currently under way in our laboratory to examine the scope and possible generality in mass spectrometry of the presently described methyl migration. We are indebted to Dr. D. A. Lightner and Mr. John Smith, respectively, for the high- and low-resolution mass spectra.

(13) National Institutes of Health Postdoctoral Fellow, 1964-1965.

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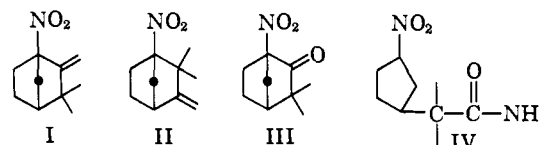
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Deamination of 1-Amino-3,3-dimethylbicyclo[2.2.1]heptan-2-ol

Sir:

Photochemical reactions¹⁻⁵ have provided the only route to bicyclo[2.1.1]hexane derivatives. The deamination of bicyclic amines⁶ has provided an abundance of molecular rearrangements, and we wish to report the rearrangement of the amino alcohol VI to 5,5-dimethylbicyclo[2.1.1]hexane-1-carboxaldehyde (VII). Syntheses of highly strained cyclic systems by the deamination of 2-aminocyclohexanols have not been reported, although the reaction has been observed in medium-ring compounds.⁷ Reactions of 1-nitrocamphene (I),⁸ an important intermediate in our work, have been described recently, which prompts our report.

The Wagner-Meerwein rearrangement of 2-bromo-2-nitrobornane with silver nitrate was discovered by Forster,⁹ and Asahina¹⁰ assumed the product to be 1-nitrocamphene. The product of the rearrangement⁹ is isolated in low yield (40%). In addition to the evidence presented by Lipp¹¹ for the structure of the product, which does not exclude the isomer II, the hitherto unknown nitro ketone III has been isolated



from the ozonization of 1-nitrocamphene in chloroform at 0°, 90% yield, m.p. 96-97.2°; [α]_D²⁴ + 89.0° (c 5.00,

(1) R. S. H. Liu and G. S. Hammond, *J. Am. Chem. Soc.*, **86**, 1892 (1964).

(2) R. C. Cookson, J. Hudec, S. A. Knight, and B. R. D. Whetear, *Tetrahedron*, **19**, 1995 (1963).

(3) K. B. Wiberg, B. R. Lowry, and T. H. Colby, *J. Am. Chem. Soc.*, **83**, 3998 (1961).

(4) J. Meinwald and P. G. Gassman, *ibid.*, **82**, 2857 (1960); **82**, 5445 (1960).

(5) L. Horner and E. Spietschka, *Ber.*, **88**, 934 (1955).

(6) J. A. Berson, "Molecular Rearrangements," Vol. I, P. de Mayo, Ed., John Wiley and Sons, Inc., New York, N. Y., 1963, p. 205.

(7) J. G. Traynham and M. T. Yang, Abstracts, 148th National Meeting of the American Chemical Society, Chicago, Ill., Sept. 1964, p. 57S.

(8) Y. Brunel, H. Lemaire, and A. Rassat, *Bull. soc. chim. France*, 1895 (1964).

(9) M. O. Forster, *J. Chem. Soc.*, **75**, 1141 (1899); **79**, 644 (1901); **81**, 264 (1902).

(10) Y. Asahina and K. Yamaguchi, *Ber.*, **71**, 318 (1938).

(11) P. Lipp and H. Knapp, *ibid.*, **73**, 915 (1940).