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A NOVEL FRAGMENTATION REACTION

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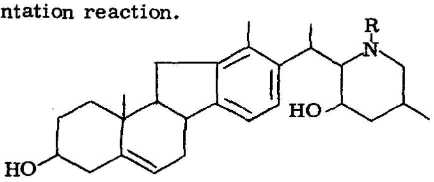
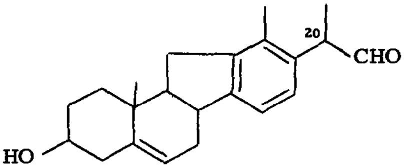
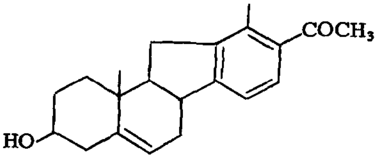
IN connection with a study aimed at the total synthesis of veratramine (I, R = H), we have been in search of a facile method for degrading the heterocyclic ring E to give a product with a simple functional group at C-17 which would be potentially useful as a relay substance for comparison with totally synthetic material as well as for the reelaboration of ring E. This communication discloses the realization of this objective *via* a novel fragmentation reaction.



I

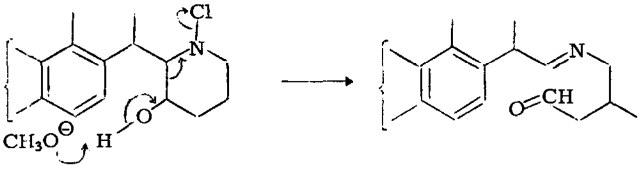


II



III

Veratramine (I, R = H) was converted, by the action of N-chlorosuccinimide, into N-chloroveratramine (I, R = Cl)[1] which, on treatment with sodium methoxide in methanol, evidently underwent the fragmentation depicted in the accompanying formulas. The resulting imino compound was



not isolated but was instead hydrolyzed directly by treatment with dilute hydrochloric acid at room temperature. In this way the aldehyde II was isolated as a crystalline mixture of C-20 epimers, m.p. 144-148°, in 94% over-all yield (Found after evaporative distillation at 130°/0.05 mm.: C, 81.85; H, 8.5), $\lambda_{max}^{CCl_4}$ 3.74 μ (aldehyde C-H), 5.81 (aldehyde C=O). The NMR spectrum[2] exhibited absorption for 3 protons as a singlet at δ = 1.12 p.p.m. (C-19 CH_3); 3 protons as a doublet centered at 1.37 (J = 7 c.p.s.) (C-21 CH_3); 3 protons as a singlet at 2.23 (C-18 CH_3); 1 proton as an unresolved multiplet at 5.43 (vinyl H at C-6); 2 protons as an unresolved multiplet at 6.97 (aromatic H); 1 proton as a doublet (J = 1.1 c.p.s.) centered at 9.57 (aldehyde H). The aldehyde II was easily degraded further, by treatment with butyl nitrite and sodium n-butoxide

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[1] H. Ruschig and J. Schmidt-Thome, U. S. Patent No. 2,697,107 (Dec. 14, 1954). [Chem. Abst. 49, 15,986i (1955)].

[2] NMR spectra were determined at 60 megacycles. Tetramethylsilane was used as an internal standard and deuterochloroform as solvent.

in n-butyl alcohol which effected nitrosation at C-20 and cleavage of the formyl group to give the oxime of III,[3] m.p. 253-255° (Found: C, 77.2; H, 8.45; N, 4.2). Hydrolysis of the oxime with dilute hydrochloric acid yielded the ketone III, m.p. 148-150° (Found: C, 81.5; H, 8.6), $\lambda_{max}^{95\%\ EtOH}$ 259 mμ (ε 13,000); $\lambda_{max}^{CHCl_3}$ 5.95 μ (aromatic ketone C=O). The NMR spectrum exhibited absorption for 3 protons as a singlet at δ = 1.10 p.p.m. (C-19 CH_3); 3 protons as a singlet at 2.38 and 3 protons as a singlet at 2.50 (acetyl and C-18 CH_3); 1 proton as an unresolved multiplet at 5.37 (vinyl H at C-6); 1 proton as a doublet centered at 6.90 (J = 8 c.p.s.) (aromatic H); and 1 proton as a doublet centered at 7.40 (J = 8 c.p.s.) (aromatic H). The ketone was also obtained by chromic acid oxidation of the morpholine enamine of the aldehyde II.[4]

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[3] Cf. R. B. Woodward and W. E. Doering, *J. Amer. Chem. Soc.* **67**, 860 (1945).

[4] Cf. D. A. Shepherd, R. A. Dania, J. A. Campbell, B. A. Johnson, R. P. Holysz, G. Slomp, Jr., J. E. Stafford, R. L. Pederson and A. C. Ott, *J. Amer. Chem. Soc.* **77**, 1212 (1955).