stabilized[10] and their generation from **2** is directly analogous to isomerization of benzylidenes to cycloheptatrienylidenes.[11]

The applicability of carbenic fission and rearrangement of other heterocyclic systems is currently under investigation.

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(11) (a) G. G. Vander Stouw, *Diss. Abstr.*, **25** (12), 6974 (1965), in summary of a Ph.D. Dissertation, The Ohio State University, Columbus, Ohio, 1964; (b) R. C. Joines, A. B. Turner, and W. M. Jones, *J. Amer. Chem. Soc.*, **91**, 7754 (1969); (c) P. Schissel, M. E. Kent, D. J. McAdoo, and E. Hedaya, *ibid.*, **92**, 2197 (1970); (d) C. Wentrup and K. Wilczek, *Helv. Chim. Acta*, **53**, 1959 (1970); (e) W. J. Baron, M. Jones, Jr., and P. P. Gaspar, *J. Amer. Chem. Soc.*, **92**, 4739 (1970); and (f) J. A. Meyers, R. C. Joines, and W. M. Jones, *ibid.*, **92**, 4740 (1970).

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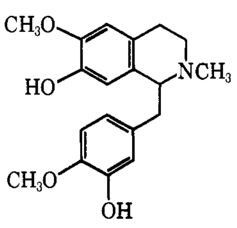
Electrooxidative Cyclization of Laudanosine. A Novel Nonphenolic Coupling Reaction

Sir:

The oxidative cyclization of phenolic 1-benzyltetrahydroisoquinolines, *e.g.*, reticuline (**1**), plays an important role in the biosynthesis of alkaloids and many laboratory syntheses have been designed analogously.[1] Although the yields of many of these reactions when performed with chemical oxidants are abysmal, the electrooxidative alternative has seldom been explored.[2] We have, therefore, been investigating the potentialities of this method and report here on the successful high-yield conversion of laudanosine (**2**) to a morphinandienone. This is an especially novel and intriguing reaction in that **2** is not a phenol. The result suggests that electrooxidation may provide a unique tool of wide applicability for alkaloid synthesis.



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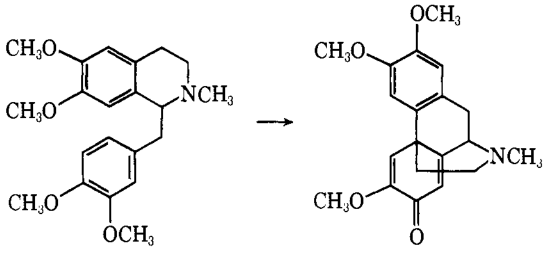

2 **3**

(±)-Laudanosine (200 mg) was oxidized at a platinum electrode in acetonitrile under several conditions. In all cases, a three-compartment cell and a Ag–$AgNO_3$ reference electrode were utilized. Product **3** was formed in several reactions, the most successful being carried out at 1.1 V in the presence of sodium carbonate at 0° and with tetramethylammonium tetrafluoroborate as the electrolyte. The current dropped smoothly from 110 to 8 mA in 70 min passing a total of 2.0 mfaradays. The uv spectrum of the anolyte matched that of the major component isolated by stripping the acetonitrile, adding chloroform and water, and separating the chloroform-soluble products by preparative tlc on silica gel. This compound (R_f = 0.37 with benzene–methanol (3:2) eluent) had uv, nmr, and ir spectra identical with those of *O*-methylflavinantine (**3**).[3] The mass spectrum of the hydrochloride was consistent with this assignment and the *N*-methiodide derivative melted at 222–223° uncorrected (lit.[4] 223–224°). The isolated yield of pure **3** was 52% which is a marked improvement over Kametani's overall yield of 1% of **3** starting from reticuline.[4,5] The yields in typical oxidative cyclizations of phenolic alkaloids have rarely exceeded 10%.

Bobbitt and coworkers have investigated the electrooxidation of similar tetrahydroisoquinolines and have observed intermolecular coupling and cleavage reactions.[2,6] Although the causes for the differences in some of these reactions are not entirely explicable, control over the oxidation pathway by the most easily oxidized moiety in the molecule is a first consideration. In the molecules of interest there are three groups, two aromatic rings and the amine, to be considered. If there is a phenoxide present, this will usually provide the most easily oxidized center and the chemistry will involve that group. This is clearly indicated in Bobbitt's results where coupling to phenolic rings occurs.[2] Cyclic voltammetry indicates that in laudanosine the dimethoxydialkylbenzene moiety of the isoquinoline ring is most easily oxidized. Peak potentials in acetonitrile *vs.* Ag–0.1 *N* $AgNO_3$ at platinum are: **2**, 1.08 V; **3**, 1.12 V; **4**, 1.04 V; **5**, 1.10 V. The E_p for **2** is not affected by added acid. The similarities of the E_p for these compounds in which the two structural features other than the dimethoxydialkylbenzene are varied is consistent with the above hypothesis. The following scheme (Scheme I) is one which will then explain formation of **3**. The oxidative cleavage of alkyl groups from suitable alkyl phenyl ethers has an analogy[7] but the timing of cyclization and cleavage as well as the cleavage mechanism remain unelucidated.

It will be noted that the E_p for **2** and **3** are very similar. This indicated that **3** should not survive exhaustive electrolysis in high yield. Overoxidation is, in fact, often a problem in coupling reactions and may in part be circumvented in this case because of the insolubility of **3** in acetonitrile. The oxidation of **5** has also been undertaken in order to test the influence of the tertiary

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(1) A. R. Battersby in "Oxidative Coupling of Phenols," W. I. Taylor and A. R. Battersby Ed., Marcel Dekker, New York, N. Y., 1967, p 119.

(2) J. M. Bobbitt and R. C. Hallcher, *Chem. Commun.*, 543 (1971).

(3) We thank Professor T. Kametani for copies of the ir, nmr, and uv spectra of *O*-methylflavinantine.

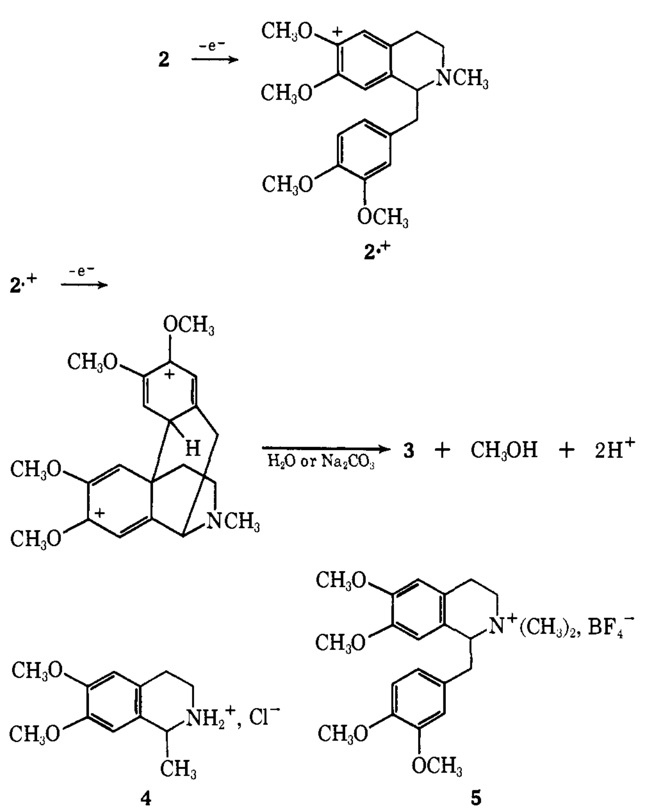
(4) T. Kametani, K. Fukumoto, F. Sato, and H. Yagi, *J. Chem. Soc. C*, 520 (1969).

(5) Not unexpectedly, **2** was unreactive toward potassium ferricyanide.

(6) J. M. Bobbitt, K. H. Weisgraber, A. S. Steinfeld, and S. G. Weiss, *J. Org. Chem.*, **35**, 2884 (1970).

(7) L. Papachoudo, J. Bacon, and R. N. Adams, *J. Electroanal. Chem.*, **24**, App. 1 (1970).

Scheme I



amine center on the pathway and the yield. Initial results indicate that cyclization to the morphinandienone took place in relatively high yield.

(8) National Science Foundation Trainee, 1970–1971.

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The Structure of Vakognavine. A Novel Diterpene Alkaloid Bearing a C(4) Aldehyde Group

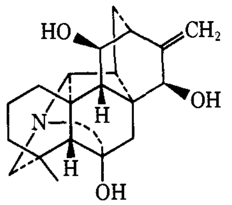
Sir:

Recent studies of diterpene alkaloids have disclosed several compounds of possible biogenetic significance. Denudatine,[1-3] for example, has a skeleton of the type postulated by Wiesner[4] for an intermediate in the biogenetic transformation of the atisine-type alkaloids to the *Aconitum*-type alkaloids; pseudokobusine[5,6] (I) is possibly a precursor of the N–C(6) bridge in the hetisine-type alkaloids.

We now wish to report the structure determination of the hydriodide salt of vakognavine[7,8] ($C_{34}H_{37}NO_{10}$), an alkaloid of *Aconitum palmatum*, and the first example of an N,C(19) secoditerpene alkaloid. An nmr spectrum ($CDCl_3$) indicated that the alkaloid possesses a tertiary methyl (δ 1.12, s, 3 H), a benzoate group (δ 7.62, 5 H), three acetate groups, and an *N*-methyl group (δ 2.07, s, 6 H; δ 2.18, s, 3 H; δ 2.33, s, 3 H). The infrared spectrum shows absorption for five carbonyl groups at 1754, 1740, 1710, 1695, and 1661 cm^{-1}.

In order to determine the substitution pattern of this highly oxygenated alkaloid, an X-ray crystallographic study was undertaken. Crystals of vakognavine hydriodide were prepared and crystallized from aqueous ethanol, mp 232–234° (cor). The crystals were tetragonal with cell dimensions $a = b = 14.31$ Å, $c = 33.31$ Å. The measured density of 1.468 g/cm^3 (flotation, CCl_4–hexane) compares favorably with that calculated, 1.456 g/cm^3, for $C_{34}H_{38}NO_{10}I$, $Z = 8$. The space group was chosen as $P4_12_12$ from systematic absences. Three-dimensional intensity data were collected about the *b* axis by the Weissenberg equiinclination method using the multiple film technique and Ni-filtered Cu Kα radiation. The intensities of the 1316 unique nonzero reflections used in the analysis were estimated visually with a standard intensity strip. Lorentz and polarization corrections were applied, but no absorption correction was made. The structure was solved by the heavy atom method[9] and refined in a full-matrix least squares with anisotropic temperature factors for the iodide and isotropic temperature factors for the remaining atoms. C–C single bond lengths average 1.54 Å (0.06) and aromatic C–C lengths average 1.37 Å (0.06). All bond lengths are within 3σ of accepted values. The conventional R is equal to 0.14 at this stage of refinement. Vakognavine hydriodide was thus shown to have structure III.[10]

That vakognavine base exists as II is shown by the presence of an aldehyde signal (($CDCl_3$) δ 9.43, s,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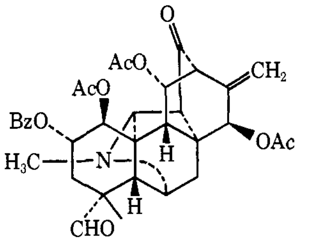
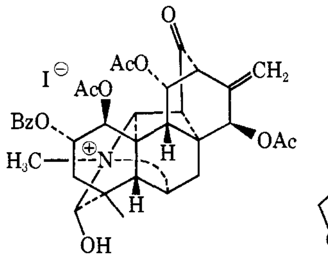
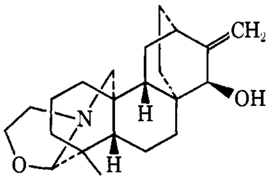

II


III


IV

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(2) F. Brisse, *ibid.*, 4373 (1969).

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(8) N. Singh and S.S. Jaswal, *Tetrahedron Lett.*, 2219 (1968).

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(10) The product of selenium dehydrogenation of vakognavine reported earlier[8] as 1,9-dimethyl-7-ethylphenanthrene is almost certainly incorrectly identified. Unless deep-seated rearrangements occur, the vakognavine structure would not be expected to lead to 1,9-dimethyl-7-ethylphenanthrene on dehydrogenation.