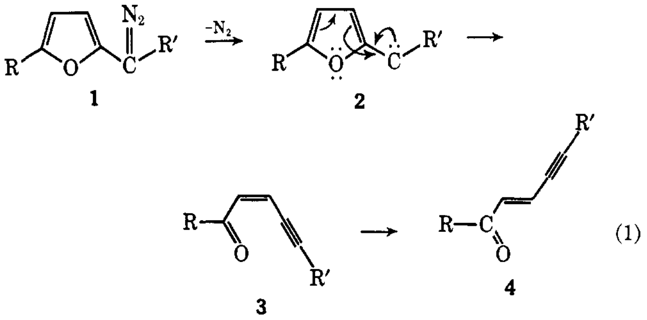
Ring-Opening Reactions of Furfurylidenes

Sir:

We wish to report that furfurylidenes (**2**) as generated by thermolysis of 1-diazo-1-(2-furyl)alkanes (**1**) undergo reorganization (eq 1) to *cis*- and *trans*-γ,δ-acetylenic α,β-olefinic aldehydes and ketones (**3** and **4**). This novel carbenic process is of interest in that collapse rather than rearrangement of the furan ring occurs and advantageous synthesis of **3** and **4** may be effected.[1]



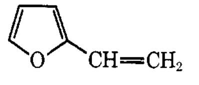
(1)

a, R = H; R' = H
b, R = CH_3; R' = H
c, R = H; R' = C_6H_5
d, R = H; R' = CH_3
e, R = H; R' = CH_2CH_3

Thus, short-path pyrolysis of diazo(2-furyl)methane (**1a**), as generated *in situ* from the sodium salt of furfural tosylhydrazone[2,3] at 250° (0.5 mm), and condensation and storage of the product at −78° gives *cis*- (**3a**, 81%) and *trans*- (**4a**, 19%) 2-penten-4-ynals[1a,4] in 66% yield along with furonitrile (4%). Since **3a** isomerizes readily to **4a** at elevated temperatures, it is likely that carbenic decomposition of **1a** occurs stereospecifically by a singlet electrocyclic process (eq 1) to give initially the cis ring-opened product **3a**. Similarly, diazo(5-methyl-2-furyl)methane (**1b**) and diazo(2-furyl)phenylmethane (**1c**), as derived from sodium salts of their precursor tosylhydrazones, decompose to *cis*- (**3b**, 87%) and *trans*- (**4b**, 13%) 3-hexen-5-yn-2-ones (43%)[1a] and to *cis*- (**3c**, 52.5%) and *trans*- (**4c**, 47.5%) 5-phenyl-2-penten-4-ynals (43%), respectively.

Aldehydes **3a**, **4a**, **3c**, and **4c** and ketones **3b** and **4b**, highly reactive monomers that degrade rapidly upon storage at room temperature and during preparative gas chromatography, were identified by their ir, nmr, and mass spectra. The aldehyde and/or the acetylene protons of the ring-opened products have distinctly different chemical shifts and thus their total yields and cis/trans ratios were determined conveniently by integration of their nmr spectra as determined in known weights of methylene chloride. Products **3a**, **3b**, and **4c** were isolated gas chromatographically in preparative quantities and converted to 2,4-dinitrophenylhydrazones of proper analysis, parent mass spectral ions, and ir and nmr spectra.[5]

Decomposition of 1-diazo-1-(2-furyl)ethane (**1d**) and 1-diazo-1-(2-furyl)propane (**1e**) was studied to determine if migration of the α hydrogen of the alkyl groups to yield conjugated alkenyl furans is competitive with carbenic collapse of the furan ring (eq 1).[6] Pyrolysis of **1d**[7a] at 275° results in *cis*- (**3d**, 73%) and *trans*- (**4d**, 27%) 2-hexen-4-ynals (36%, eq 1) along with 2-vinylfuran (**5**, 3.6%); **1e**[7b] thermolyzes similarly to *cis*- (**3e**, 68%) and *trans*- (**4e**, 32%) 2-hepten-4-ynals (47%, eq 1) and relatively small amounts (3.2%) of *cis*- and *trans*-2-(1-propenyl)furans (**6**). Reorganization of **2d** and **2e** resulting in ring opening thus occurs considerably more rapidly ((10–15)/1) than does isomerization involving hydrogen migration.



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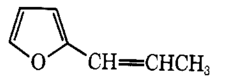
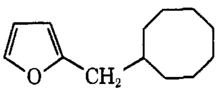


6 (cis and trans)

Thermolysis of **1a** in a trapping environment was studied in an effort to determine whether furfurylidene (**2a**) is possibly generated as a discrete intermediate under conditions in which **3a** and **4a** are formed. Decomposition of the sodium salt of furfural tosylhydrazone in cyclooctane at 140° results in furfurylcyclooctane[8] (**7**, 7%) along with **3a** and **4a**. Formation of **7** is indeed rationalizable on the basis of carbenic insertion of **2a** into a carbon–hydrogen bond of cyclooctane. The sodium salt of furfural tosylhydrazone also decomposes in neat styrene at 140° to give *trans*-1-(2-furyl)-2-phenylcyclopropane[8] (**8**, 15%), **3a**, and **4a**. Although it cannot yet be decisively concluded whether **8** is formed by addition of **2a** or **1a** to styrene at 140°, it is clear that 1-diazo-1-(2-furyl)alkanes offer promise, even at high temperatures, for effective addition to olefinic systems to yield the corresponding cyclopropanes.[9]



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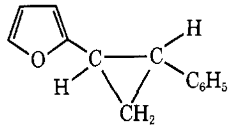

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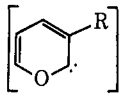
It is also of note that as yet there is no evidence (dimerization, insertion, capture, or fragmentation) for isomerization of furfurylidenes (**2**) to α-pyranylidenes (**9**). Carbenes such as **9** are predicted to be highly



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[1] Such carbonyl derivatives have been prepared previously by (a) F. Bohlmann and H. Viehe, *Chem. Ber.*, **88**, 1330 (1955), and (b) I. Bell, E. Jones, and M. Whiting, *J. Chem. Soc.*, 1313 (1958).

[2] The tosylhydrazones of this study were converted to their sodium salts by reaction with sodium hydride in methylene chloride until evolution of hydrogen ceased. The salts were filtered under nitrogen and vacuum desiccated before use.

[3] Decompositions of the salts of the sulfonylhydrazones were effected by procedures similar to that of C. M. Kaufman, J. A. Smith, G. G. Vander Stouw, and H. Shechter, *J. Amer. Chem. Soc.*, **87**, 935 (1965).

[4] A diisodecyl phthalate column (20%, 10 ft) operating at 140° with a helium flow of 120 ml/min was used for all separations except for **4c** which could be separated on an SE-30 column (20%, 6 ft) at 200° with a helium flow of 100 ml/min.

[5] Aldehydes **3d**, **4d**, **3e**, and **4e** were characterized similarly.

[6] Rearrangement of hydrogen to give olefins is one of the most facile intramolecular reactions of carbenes: L. Friedman and H. Shechter, *J. Amer. Chem. Soc.*, **81**, 5512 (1959).

[7] Generated *in situ* from sodium salts of tosylhydrazones of (a) methyl 2-furyl ketone and (b) ethyl 2-furyl ketone.

[8] Insertion products **7** and **8** were identified by their analyses and their ir, nmr, and mass spectra.

[9] T. Sasaki, S. Eguchi, and A. Kojima (*Bull. Soc. Chem. Jap.*, **41** 1658 (1968)) report that diazo(5-nitro-2-furyl)methane does not undergo thermal or photochemical reactions with styrene, cyclohexene, α-morpholinostyrene, or tetrahydrofuran.

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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(10) R. Gleiter and R. Hoffmann, *J. Amer. Chem. Soc.*, **90**, 5457 (1968).

(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).

Robert V. Hoffman, Harold Shechter*
Department of Chemistry, The Ohio State University
Columbus, Ohio 43210

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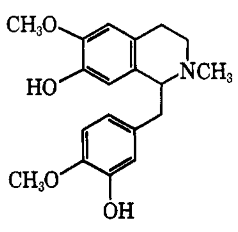
Electrooxidative Cyclization of Laudanosine. A Novel Nonphenolic Coupling Reaction

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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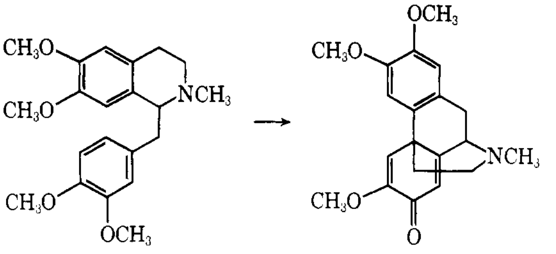

2 3

(±)-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).