References and Notes

(1) Photoinduced Reactions. 110

(2) For reviews, see (a) C. S. Foote, *Acc. Chem. Res.*, **1**, 104 (1968); (b) D. R. Kearns, *Chem. Rev.*, 71, 395 (1971); (c) R. W. Denny and A. Nickon, *Org. React.*, **20**, 133 (1973); (d) T. Matsuura and I. Saito, "Photochemistry of Heterocyclic Compounds", O. Buchardt, Ed., Wiley, New York, 1976, p 456; (e) A. P. Schaap and K. A. Zaklika, "Singlet Oxygen", H. H. Wasserman and R. W. Murray, Eds., Academic Press, New York, 1979, p 173.

(3) D. R. Kearns, *J. Am. Chem. Soc.*, **91**, 6554 (1969).

(4) K. Yamaguchi, T. Fueno, and H. Fukutome, *Chem. Phys. Lett.*, **22**, 466 (1973).

(5) P. D. Bartlett and A. P. Schaap, *J. Am. Chem. Soc.*, **92**, 3223 (1970).

(6) S. Inagaki, S. Yamabe, H. Fujimoto, and K. Fukui, *Bull. Chem. Soc. Jpn.*, **45**, 3510 (1972).

(7) M. J. S. Dewar and W. Thiel, *J. Am. Chem. Soc.*, **97**, 3978 (1975).

(8) P. D. Barlett, *Chem. Soc. Rev.*, **5**, 149 (1976); (b) A. A. Frimer, P. D. Bartlett, A. F. Boshung, and J. G. Jewett, *J. Am. Chem. Soc.*, **99**, 7977 (1977), and references cited therein; (c) L. A. Paquette, L. W. Hertel, R. Gleiter, and M. Böhm, *ibid.*, **100**, 6510 (1978).

(9) (a) L. B. Harding and W. A. Goddard, III, *J. Am. Chem. Soc.*, **99**, 4520 (1977); (b) L. B. Harding and W. A. Goddard, III, *Tetrahedron Lett.*, 747 (1978).

(10) C. S. Foote, "Singlet Oxygen—Reactions with Organic Compounds and Polymers", B. Rånby and J. F. Rabek, Eds., Wiley, New York, 1978, p 135.

(11) (a) T. Matsuura and I. Saito, *Tetrahedron Lett.*, 3273 (1968); (b) *Tetrahedron*, **25**, 549 (1969).

(12) (a) H. H. Wasserman, *Ann. N.Y. Acad. Sci.*, **171**, 108 (1970); (b) I. Saito, M. Imuta, and T. Matsuura, *Chem. Lett.*, 1173, 1197 (1972); (c) K. Orito, R. H. Manske, and R. Rodrigo, *J. Am. Chem. Soc.*, **96**, 1944 (1974); (d) F. McCapra and I. Beheshti, *J. Chem. Soc., Chem. Commun.*, 517 (1977); (e) C. W. Jefford and C. G. Rimbault, *Tetrahedron Lett.*, 2375 (1977).

(13) G. Rousseau, A. Lechevallier, F. Huet, and T. M. Conia, *Tetrahedron Lett.*, 3287 (1978).

(14) C. W. Jefford, *Tetrahedron Lett.*, 985 (1979).

(15) N. J. Turro, M-F. Chow, and Y. Ito, *J. Am. Chem. Soc.*, **100**, 5580 (1978).

(16) N. J. Turro, V. Ramamurthy, K. C. Krebs, and R. Kemper, *J. Am. Chem. Soc.*, **98**, 6758 (1976).

(17) (a) I. Saito, M. Imuta, and T. Matsuura, *J. Am. Chem. Soc.*, **97**, 7191 (1975); (b) I. Saito, M. Imuta, Y. Takahashi, S. Matsugo, and T. Matsuura, *ibid.*, **99**, 2005 (1977); (c) I. Saito, T. Matsuura, M. Nakagawa, and T. Hino, *Acc. Chem. Res.*, **10**, 346 (1977).

(18) C. W. Jefford and C. G. Rimbault, *J. Am. Chem. Soc.*, **100**, 6437 (1978).

(19) C. W. Jefford and C. G. Rimbault, *J. Am. Chem. Soc.*, **100**, 6515 (1978).

(20) N. J. Turro, Y. Ito, M-F. Chow, W. Adam, O. Rodriquez, and F. Yang, *J. Am. Chem. Soc.*, **99**, 5836 (1977).

(21) H. Takeshita and T. Hatsui, *J. Org. Chem.*, **43**, 3080 (1978).

(22) I. Saito, M. Imuta, S. Matsugo, H. Yamamoto, and T. Matsuura, *Synthesis*, 255 (1976).

(23) K. Inoue, I. Saito, and T. Matsuura, manuscript in preparation.

(24) I. Saito and T. Matsuura in ref 10, p 186.

(25) R. Huisgen, *Acc. Chem. Res.*, **10**, 199 (1977).

(26) W. Adam, *Adv. Heterocycl. Chem.*, **21**, 437 (1977).

(27) C. S. Foote, A. A. Dzakpasu, and J. W.-P. Lin, *Tetrahedron Lett.*, 1247 (1975).

(28) H. H. Wasserman and S. Terao, *Tetrahedron Lett.*, 1735 (1975).

(29) I. Saito, S. Matsugo, and T. Matsuura, *J. Am. Chem. Soc.*, **101**, 4757 (1979).

(30) K. Pfortner and K. Bernauer, *Helv. Chim. Acta*, **51**, 1787 (1968).

(31) N. M. Hasty and D. R. Kearns, *J. Am. Chem. Soc.*, **95**, 3380 (1973).

(32) W. Ando, K. Watanabe, J. Suzuki, and T. Migita, *J. Am. Chem. Soc.*, **96**, 6766 (1974).

(33) K. Yamaguchi, T. Fueno, I. Saito, and T. Matsuura, *Tetrahedron Lett.*, 3433 (1979). See also ref 4 and I. Saito, *Prepr., Div. Pet. Chem., Am. Chem. Soc.*, **24**, 95 (1979).

(34) A similar mechanism has recently been proposed for the explanation of high regioselectivity in singlet oxygenations of trisubstituted olefins.[14]

(35) J. G. Calvert and J. N. Pitts, Jr., "Photochemistry", Wiley, New York, 1966, p 740.

(36) T. H. Gradner and J. R. Stevens, *J. Am. Chem. Soc.*, **69**, 3086 (1947).

(37) W. E. Noland, L. R. Smith, and K. R. Rush, *J. Org. Chem.*, **30**, 3457 (1965).

(38) D. W. Dckenden and K. Schofield, *J. Chem. Soc.*, 612 (1953).

(39) E. C. Horming, *J. Am. Chem. Soc.*, **70**, 3935 (1948).

(40) L. J. Dolby and D. L. Booth, *J. Am. Chem. Soc.*, **88**, 1049 (1966).

(41) M. Nakazaki, *Bull. Chem. Soc. Jpn.*, **32**, 588 (1959).

Mechanistic Study of Anodic Intramolecular Coupling Reactions

John B. Kerr, Thomas C. Jempty, and Larry Miller*

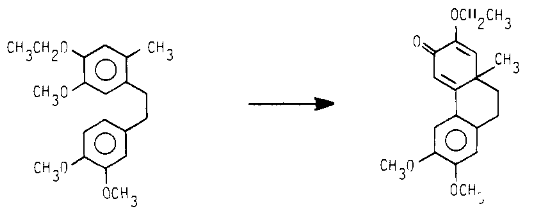
Contribution from the Department of Chemistry, University of Minnesota, Minneapolis, Minnesota 55455.

Received May 31, 1979

Abstract: Anodic cyclization reactions of several methoxybibenzyls were studied. The reactions were: 2-methyl-3′,4′,5-trimethoxy-4-ethoxybibenzyl (**1**) to 9,10-dihydro-10a-methyl-2-ethoxy-6,7-dimethoxy-3(10a*H*)phenanthrone; laudanosine (**2**) to *O*-methylflavinatine (**5**) and 4,4′-dimethoxy[2,2]metacyclophane (**3**) to 2,7-dimethoxy-4,5,9,10-tetrahydropyrene (**6**). The solvent was acetonitrile and the anode was platinum. When using cyclic voltammetry, each of these compounds shows a $2e^-$ oxidation peak at + 0.5–1.1 V vs. Ag|0.1 M $AgNO_3$ which is irreversible at all sweep rates due to the rapid chemical reactions following electron transfer. At slightly more positive potentials, there is a reversible couple due to the products. Preparative electrolysis gave $n = 2$ and high isolated yields of the products. The reaction kinetics were studied by using the shift in the first peak potential (E_p) in linear sweep voltammetry as a function of sweep rate, concentration of substrate, and the acidity of the medium. The rate law was also elucidated by using the convolution potential sweep voltammetry method. The two techniques led to similar conclusions. For compound **1** the mechanism involves reversible electron transfer (e) and disproportionation (d) steps followed by a rate-limiting step which is most probably cyclization (c) of the dication. Compound **2** was studied in acidic media so that the amine group was initially protonated. The mechanism under these conditions involves reversible electron transfer from $\mathbf{2}H^+$, cyclization, and deprotonation of the amine followed by a rate-limiting solution phase electron transfer from a cyclized cation radical to a dication radical $\mathbf{2}H^{+\cdot}$. The importance of the amine/ammonium function in controlling the reaction pathway is discussed. Compound **3** reacts via an ec-type process in which the initial electron transfer and follow-up chemical reaction have a similar rate.

The oxidative, intramolecular coupling reactions of alkoxy aromatic compounds have received considerable attention in the past few years.[1-28] Although the reaction pathways and product structures differ in detail, many of the reactants which cyclize can be considered bibenzyls and, as shown in the following examples,[1,2,7] coupling involves two electrons/molecule and usually takes place para to an alkoxy group. Reactions of this type have been performed chemically with VOF_3,[17-21,25] thallium trifluoroacetate,[22,23] and manganic tris(acetylacetonate)[11] and electrochemically. The latter approach has proven to be particularly successful in providing useful routes to complex natural products such as morphinandienones.[2-6,14-16,24-26] In spite of this synthetic utility, there is considerable mechanistic ambiguity. A major question of interest is whether cation radicals or dications cyclize. The former corresponds to an ece (electrochemical-chemical-elec-

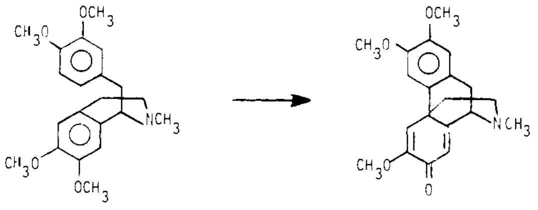
0002-7863/79/1501-7338$01.00/0



1

4

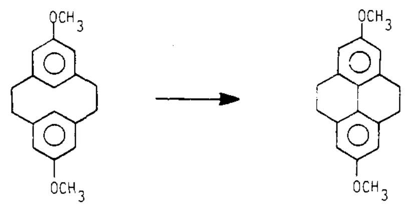
(ref. 1)



2

5

(ref. 2)



3

6

(ref. 7)

trochemical) type mechanism and the latter to an eec type mechanism. Although there have been a number of mechanistic suggestions, only a little evidence has been provided. Some of this comes from Parker and Ronlan and co-workers who studied the cyclizations of symmetrically and unsymmetrically substituted methoxybibenzyls by means of cyclic voltammetry (CV) and preparative electrolysis with product isolation.[9] In the case of an unsymmetrically substituted trimethoxy compound, it was shown that the cyclization reaction required high current densities. If low current densities were employed, dimers were formed. It was, therefore, proposed that the intramolecular coupling involved a dication and chemical arguments were put forward to support the involvement of an intermediate dication in the case of the symmetrically substituted bibenzyls. This work has been extended[10] to other methoxy-substituted compounds which contained a variable length of alkane chain between the aryl rings involved in the coupling reaction. Both dicationic and cation radical couplings were proposed as reaction pathways.

These authors have also given attention to the various coupled products possible from cyclization of analogues to **2** where O or CH_2 replaced NCH_3.[8] Second harmonic ac voltammograms for these analogues were those expected for a reversible one-electron transfer. It was, therefore, suggested that an ece type mechanism was involved, i.e., formation and chemical reaction of a cation radical. Neither of these studies have, however, presented kinetic evidence to elucidate the mechanism and it is abundantly clear that without such evidence it is not possible to distinguish important mechanistic details or understand other aspects of these reactions, e.g., the rearranged products like **4**, which are sometimes formed.

A similar difficulty arises in the case of the anodic cyclization of metacyclophanes.[27,28] The authors used CV and found that metacyclophanes oxidized at unexpectedly low potentials. They provided logical rationales for these shifts, but some of the oxidation potentials reflect kinetics, and an elucidation of the reaction mechanism is important for proper understanding.

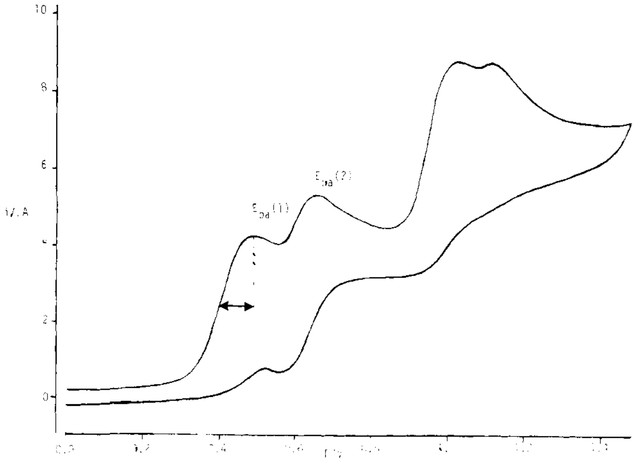


Figure 1. Cyclic voltammogram of 5,13-dimethoxy[2.2]metacyclophane (1 mM) in 0.1 M $LiClO_4-CH_3CN$ at Pt. $\nu = 0.1\ V\ s^{-1}$.

Finally, some information on the special mechanistic possibilities for coupling of laudanosine **2**[6] and methoxybibenzyl **1**[1] is available and will be used here, but no data pertinent to the early stages of the mechanism or to the timing of the various electron transfer and chemical steps have been presented.

The present investigation has probed the reactions of compounds **1–3** by using linear sweep voltammetry (lsv)[29,30] and convolution potential sweep voltammetry (cpsv).[31] Criteria by which the rate law and, therefore, mechanistic proposals can be obtained from lsv and cpsv data, have been provided for a large number of reaction types. Of utility here are the diagnostic criteria calculated for and successfully applied to cathodic cyclization reactions.[32-34] By using this approach, the cathodic cyclization of 1,3-dibenzoylpropane was found to involve intramolecular coupling of a diradical dianion previously formed by electronic disproportionation of two anion radicals in solution. Other cathodic cyclization reactions have been found to proceed via cyclization at the anion radical stage.[35] Transposition of the reasoning already employed for cathodic cyclizations to anodic cyclization processes is a simple matter, merely requiring a recognition of which steps in the anodic process correspond to those in the cathodic process. We have carried out this transposition and applied it to the anodic coupling of compounds **1–3.** This allows some general insight into the mechanisms of these reactions and allows us to evaluate some of the available hypotheses. Alternative approaches to mechanism elucidation involve the electrochemical or spectroscopic detection of short-lived intermediates. The reactions of interest here involve complex mechanisms (see Schemes I and II below) and very unstable intermediates not detectable by cyclic voltammetry. These aspects make the lsv, cpsv approach especially appropriate.

Results

Of initial interest are the CVs and coulometric n values for the three reactions. The experiments were performed by using acetonitrile solvent, a platinum working electrode, various electrolytes, a Ag/0.1 M $AgNO_3$ in CH_3CN reference electrode at 22 ± 2 °C. CVs have previously been published for the methoxybibenzyl **1**[1] and for laudanosine **2**[6] in acetonitrile. A CV of **3** is shown in Figure 1 and the voltammetric data for compounds **1–3** are listed in Table I. Compounds **1** and **3** and, under acidic conditions, compound **2** exhibited similar voltammetric patterns, exemplified by Figure 1. An initial, irreversible peak $E_p(1)$ roughly corresponding to two electrons by comparison with the reversible, one-electron ferrocene couple,

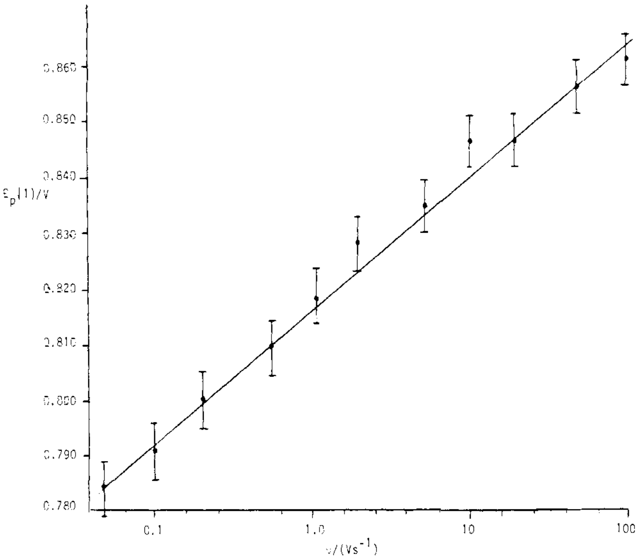


Figure 2. Variation of peak potential [$E_p(1)$] with sweep rate (ν) for 2-methyl-3′,4′,5-trimethoxy-4-ethoxybibenzyl (**1**); 1 mM at Pt in 0.4 M $LiClO_4$-CH_3CN.

Table I. Peak Potentials Measured by Cyclic Voltammetry[a]

compd	$E_{pa}(1)$, V[b]	$E_{pa}(2)$, V[b]	$\delta(1)$, mV[c]
1	+0.80[d]	+1.14[e]	45 ± 5
2 $HClO_4$	+1.07[d]	+1.13[e]	48 ± 5
3	+0.48[d]	+0.69[e]	85 ± 10
4	+1.10[e]		60 ± 5
5	+1.13[e]		70 ± 5
6	+0.69[e]		65 ± 5

[a] Using 0.1 M $LiClO_4$-CH_3CN at Pt, concn = 1 mM, sweep rate = 100 mV s^{-1}. Reference is Ag/0.1 M $AgNO_3$. [b] See Figure 1 for definition. [c] Peak width, that is the difference in potential between the peak and the point where the current is half that of the peak current. [d] Irreversible couple at all sweep rates up to 100 V s^{-1}. [e] Reversible couple at 0.1 V s^{-1}.

was followed by a reversible or partially reversible couple. The anodic peak of this couple is designated $E_p(2)$. The first peak showed no signs of reversibility even at sweep rates of 50 V s^{-1}.

The CVs of **4**, the hydroperchlorate salt of **5**, and **6** showed reversible or partially reversible one-electron couples (Table I). The separation between the anodic and cathodic peaks was 60 mV for **4**, 70 mV for **5** hydroperchlorate and 65 mV for **6** at a sweep rate, $\nu = 0.1$ V s^{-1}. It can be seen from Table I that the peak potentials, $E_p(2)$, for compounds **1–3** are very similar to the $E_p(1)$ values for compounds **4–6**, respectively. In one case where very dry acetonitrile[36] was used as the solvent for the hydroperchlorate salt of **2** the second couple was entirely absent. Upon addition of water (2%), the second peak immediately returned.

Problems with electrode filming or adsorption phenomena were experienced with all of the compounds **1–6** under certain conditions. This was especially true if the potential excursion was extended to high values where further oxidations could take place (see Figure 1). Electrode filming was a particularly severe problem in the case of compound **3.** Indeed, the intital two-electron peak was often obscured giving rise to an apparently quasireversible couple at ca. 0.65–0.7 V. This appears to be what was reported in a previous communication on compound **3.**[7] The voltammetric pattern observed in the present study (Figure 1) is very similar to that reported by Sato and co-workers for related metacyclophanes.[27,28]

Coulometry performed by exhaustive electrolysis at a potential value greater than that of $E_p(1)$ but less than that of $E_p(2)$ was carried out for compounds **1** and **3** (1–5 mM in 0.1 M $LiClO_4$-CH_3CN) and the results (Table II) confirmed the previous conclusions from CV that the first peak corresponded to two electrons. The coulometry of **2** varied greatly depending upon the solvent/electrolyte system and n values calculated by (i) exhaustive electrolysis and (ii) analysis of the current/charge behavior with time according to the method of Avaca and Utley[37] are listed for various conditions in Table II. Cyclic voltammograms performed with the exhaustively electrolyzed solutions of **1** and **3** showed only the peaks attributable to **4** and **6**, respectively. In only a few experiments with **2** was **5** the only product peak visible in CV, and, indeed, the yield of **5** under most conditions is less than 50%.

Linear sweep voltammetry (lsv) was carried out on compounds **1–3.** Kinetic analysis utilized the variation of $E_p(1)$ with ν, the bulk concentration of reactant ($C°$), and the acidity of the solution. The initial potential of the voltage sweep was at least 200 mV less positive than $E_p(1)$ and the final potential was at least 100 mV positive of this peak. The variation of $E_p(1)$ with sweep rate (ν) in lsv is shown in Figure 2 for compound **1** after correction for uncompensated resistance effects. The slope of the line in this case was 24 mV/decade with a correlation coefficient, $r = 0.995$, SD of slope = ± 1 mV/decade. The error bars in the figure represent the estimated uncertainty in measuring peak potentials on the oscilloscope screen. Independent experiments gave slopes of 20 ± 2 and 23 ± 2 mV/decade ($r = 0.996$ for both). The residual uncompensated resistance for these experiments was of the order of 300–400 Ω and its effect is to shift E_p to more anodic values. Since the size of the shift increases with sweep rate, an erroneously high variation of E_p with ν results. Compensation for this error was accomplished by comparing the shift of $E_p(1)$ with the shift of E_p of the reversible couple of ferrocene present in the same solution at a concentration sufficient to give a peak current equal to that of **1.** Variation of the reactant concentration ($C°$) from 0.2 to 1 mM produced no change in the peak potential at $\nu = 0.1$ V s^{-1} where the effects of uncompensated resistance are negligible. Similarly, no change in this potential was observed upon adding pyridine (10–50 mM) to increase the basicity of the solution.

Further information concerning the mechanism could be obtained from the voltammograms by the application of convolution potential sweep voltammetry (cpsv). Since evaluation of the convolution current, I, was carried out with a calculator rather than by means of computer, we first checked the method for the oxidation of ferrocene. The i–E curve for ferrocene (1 mM) at $\nu = 0.1$ V s^{-1} was convoluted by using the equation given by VandenBorn and Evans[38] to calculate the convolution current I[31] (or $m(\tau)$).[38-40] As anticipated a wave having the same form as a classical polarogram was obtained. From the height of the plateau, I_L, the value of I at $E = \infty$, could be obtained in the same manner as the diffusion current i_d is obtained from a polarogram. The value of I_L was then used to make a logarithmic analysis of the I–E wave using a plot of log $[(I_L - I)I^{-1}]$ vs. $E - iR_u$, where iR_u represents a correction for the effect of uncompensated resistance in the cell.[31] The slope of the line obtained from this procedure was found to be 62 ± 2 mV, in good agreement with the theoretical value of 59 mV.[31] It was also verified that I was independent of ν.[31,37,40] When this procedure was applied to **1** (1 mM), $\nu = 0.1$ V s^{-1}, the resulting I–E curve was considerably more complex than that for ferrocene. In this case the curve resembled a polarogram (see, for example, Figure 3 for **2**) where the successive electron transfers are very closely spaced, and consequently estimation of I_L for the first wave was difficult. To reduce the error in this estimation, the i–E curves were convoluted to potential values greater than $E_p(2)$ and the I_L value for $E_p(2)$

Table II. Coulometry, lsv, and cpsv of **1**–**3**[a]

compd	electrolyte	*n* value i[b]	*n* value ii[c]	lsv $\partial E_p/\partial \log \nu$, mV	lsv $-\partial E_p/\partial \log C°$, mV	cpsv logarithmic anal. no.[d]	cpsv logarithmic anal. −slope, mV (±2mV)[e]
1	0.4 M $LiClO_4$	2.2	1.7	20 ± 3	0	1	40
				23 ± 3	0	2	42
				24 ± 3	0	3	68
2	0.4 M Et_4NBF_4	>4	>6	20 ± 3	0	1	50
	TFA (9:1)	2.7[f]	2.4[f]			2	81
		>4.5[g,f]	4.5[g,f,g]			3	59
2	0.2 M HBF_4 (50%)[h]	2.1	2.1	18 ± 6	0	1	56 (51,[i] 62[j])
						2	80 (70,[i] 90[j])
						3	59 (55,[i] 60[j])
2	0.1 M $LiClO_4$	>4	2.6			1	44
	$NaHCO_3$					2	70
	H_2O (2%)					3	47
2·$HClO_4$[k]	0.4 M $LiClO_4$[g]	>4	4.1	21 ± 3	0	1	40
						2	65
						3	40
2	0.4 M $LiBF_4$	>4	3.7	21 ± 3	0	1	59
						2	87
						3	59
3	0.4 M $LiClO_4$[h]	2.0	2.1	34 ± 6		1	78 70
				33 ± 6		2	129 135
						3	78 89

[a] Concentration, 1 mM, 23 °C, Pt electrode. [b] Coulometric *n* value by exhaustive electrolysis. [c] *n* value from current/charge vs. time behavior.[37] [d] $1 = \log [(I_L - I)i^{-1}]$; $2 = \log [(I_L - I)i^{-2/3}]$; $3 = \log [I_L - I)i^{-2/3}I^{-1/3}]$. [e] $\nu = 0.1$ V s^{-1}, unless otherwise stated. [f] H_2O (5%) added. [g] 10 mM in **2**. [h] Electrode filming observed. [i] $\nu = 0.5$ V s^{-1}. [j] $\nu = 5$ V s^{-1}. [k] Hydroperchlorate salt of **2**.

Table III. Effect of Various Additives to the Solution on the Peak Potentials of **2**·$HClO_4$ and Ferrocene

additive[a]	ΔE_p(**2**), mV[b]	ΔE_{pa}(Ferr)*E*, mV[c]
2% $HClO_4$ (70%)	−35 (−25[d])	−15
2% CF_3COOH	−23 (+5[d])	0
2% CH_3COOH	0	0
0.3 M $LiClO_4$	−22 (−11[e])	−15
0.1 M $BuNClO_4$[f]	−8 (−4[d])	0

[a] Original voltammogram carried out by using 0.1 M $LiClO_4$–CH_3CN; concentration = 1 mM and sweep rate = 100 mV s^{-1}. [b] Shift in peak potential of **2** after addition of additive. [c] Shift in peak potential of ferrocene after addition of additive. [d] Shift in peak potential of **1** for the same additive. [e] Shift in peak potential of veratraldehyde for the same additive. [f] Original voltammogram carried out by using 0.1 M Bu_4NClO_4 and a second at 0.2 M.

was estimated. As recommended[41] the logarithmic analyses described by Saveant and co-workers[34] were than applied over both waves by using this value of I_L, and the slopes resulting from the portion of the curve corresponding to $E_p(1)$ are given in Table II.

The CV of **2** in non-acidic acetonitrile shows the presence of a broad peak at +0.5 V which disappears upon addition of acid. Under conditions where this peak (due to amine oxidation) is absent, the ammonium ion **2**H^+ is present in solution. As shown in Table II for various solvent, electrolyte combinations, $E_p/\delta \log C° = 0$ and $E_p/\delta \log \nu \approx 21$ mV. Cpsv results are also shown there as well as in Figure 3. The addition of acids caused substantial changes in E_p, but interpretations of these changes were complicated because the liquid junction potential between working and reference electrodes changed. The data for **1**, **2**, and for ferrocene are displayed in Table III.

The CV for **3** was superficially similar to those from **1** and **2** showing an irreversible peak $E_p(1)$ followed by a reversible couple ($E_p^a(s) - E_p^c(2) = 65$ mV) due to the product **6**. It was noted, however, that the width of the peak of $E_p(1)$ was 80–90 mV (see Table I). This contrasts sharply with the data for **1** and **2**.

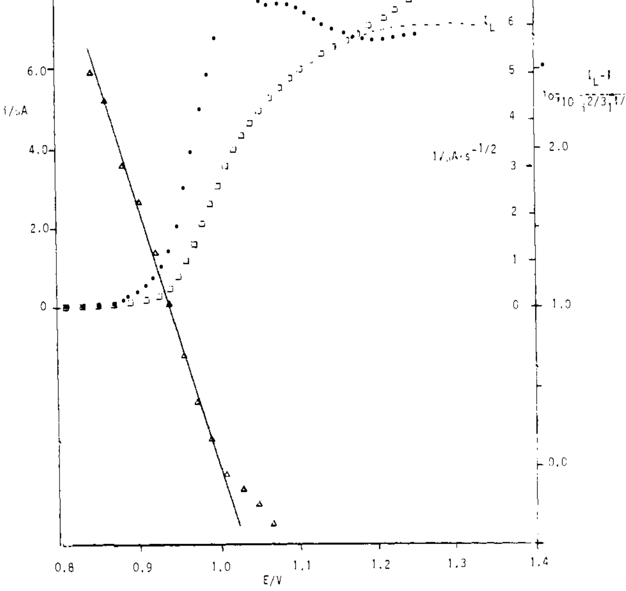
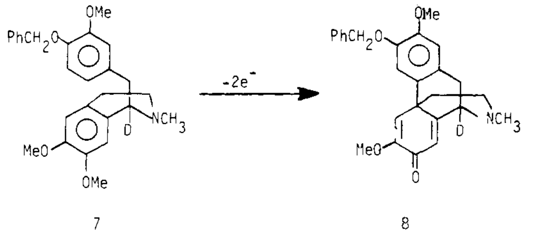


Figure 3. Convolution and logarithmic analysis of a voltammogram of laudanosine (**2**) in 0.2 M HBF_4 (50%)–CH_3CN. $C° = 1$ mM; $\nu = 0.5$ V s^{-1}; ● = *i*; □ = *I*; △ = log $(I_L - I)i^{-2/3}I^{-1/3}$.

A complete lsv study of compound **3** proved to be extremely difficult due to the filming/adsorption problems mentioned before. The variations of E_p with ν given in Table II were only measurable over the range 0.05–2 V s^{-1} so that the slope values are considerably less certain than for **1** and **2** where sweep rates from 0.1 to 100 V s^{-1} were employed. The filming problem also prevented any meaningful measurement of the variation of E_p with concentration or acidity.

Preparative oxidations of compounds **1** and **3** have been described elsewhere.[5,7,9,13] It has been proposed that the oxidation of **2** to the dienone, **5**, could involve loss of the benzylic hydrogen from the 1-position.[42] To check this possibility, we have synthesized an analogue of **2**, *O*-benzylpseudocodamine,

7, labeled with deuterium in the 1-position. Preparative oxidation of deuterated **7** was performed by using 2% aqueous acetonitrile containing sodium bicarbonate and lithium perchlorate at 1.1 V. After passage of 3.0 F/mol, the product **8** was isolated in 31% yield (a 24% yield was obtained from protiated **7**). Low resolution mass spectrometry demonstrated that the product retained >95% of the isotopic label. A similar result was obtained by using sodium carbonate in place of sodium bicarbonate.



7 **8**

It has been checked briefly that oxidation of **2** in the presence of TFA leads to **5** by TLC analysis of the anolyte. It was noted, however, that some cleavage products were present using an initial concentration in **2** of 1 mM and that these were the major products upon increasing the concentration to 10 mM in **2** while the measured *n* values were also increased (Table II). However, using concentrations of >30 mM in **2** in the presence of 0.2 M HBF_4 leads to **5** in excellent yields.[8]

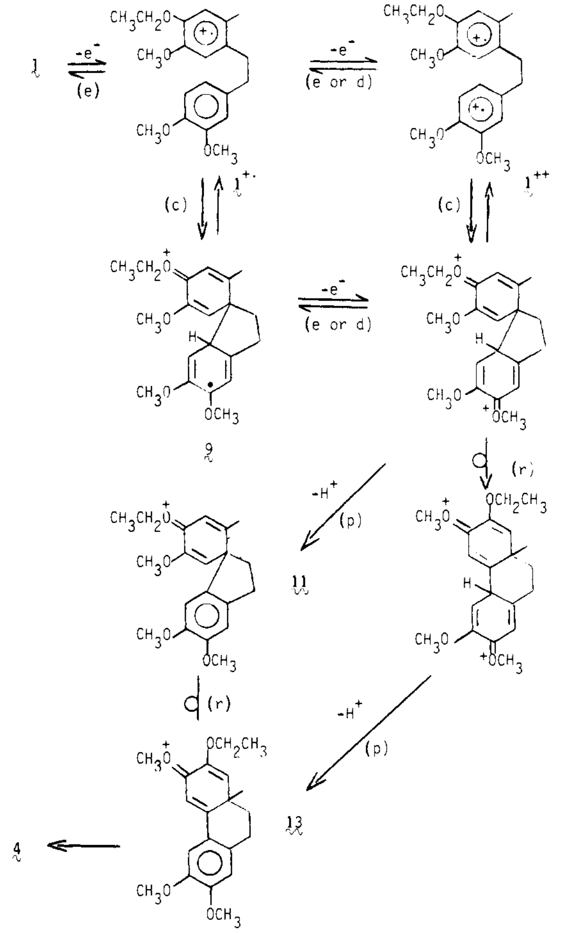
Alternative means of achieving the protonation of the amine function are given in the solvent/electrolyte conditions listed in Table II. These systems have been found to be less effective in this respect and a more detailed account is delayed until full product analyses have been carried out. We note in particular, however, that aqueous sodium bicarbonate in acetonitrile is not as good as aqueous fluoroboric acid in acetonitrile.

Discussion

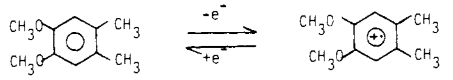
Each of the reactions studied has some mechanistic or experimental complication but the conversion of **1** to **4** is the most tractable and interesting. This reaction is therefore discussed first, followed by comparative reports on the reactions of **2** and **3**.

The shape of the lsv curves for **1** gives no indication that adsorption phenomena are important to the kinetics and, therefore, the chemical reactions which follow the initial heterogeneous electron transfer are considered to take place in solution. It is also implicit in the following discussion that the initial electron transfer step and the following chemical reactions are not concerted since otherwise different lsv shapes would be observed.[30] In essence, two electrons, a proton, and a methyl group must be lost from each molecule of **1**; one carbon-carbon bond must be formed and a rearrangement must occur. It was previously shown[1] that intermediate **13** was formed in the anolyte. It was stable at 0 °C in dry acetonitrile but could be hydrolyzed rapidly to **4**. This demonstrates that loss of the methyl group by hydrolysis is the last stage of the reaction. In order to explain the formation of only **4** by loss of methyl and no loss of ethyl, the rearrangement, e.g., **10** to **12** shown in Scheme I, was proposed. The final product clearly rules out an alternative methyl migration and we will initially assume that this is, indeed, the stage at which rearrangement takes place. Furthermore as discussed below, there is some reason to believe that deprotonation as well as loss of methyl and rearrangement comes after the coupling step. Scheme I then summarizes many of the pathways of interest. In this scheme and the following discussion: e = electron transfer at the electrode; d = a solution phase oxidation of a cation radical to a dication; p = deprotonation; and r = rearrangement.

Scheme I



Information which supports this general scheme comes from many studies of anodic oxidations which produce stable cation radicals. We cite as a model compound 3,4-dimethylveratrole, **14**. This is essentially one-half of **1** and its CV behavior can be used to help discriminate between some particular mechanisms. The CV of **14** in acetonitrile at platinum with ν = 0.5 V s^{-1} shows a reversible couple at +0.90 V.[1] This reversibility demonstrates that the electron transfer reactions interconverting **14** and $\mathbf{14^{+\cdot}}$ are rapid and that $\mathbf{14^{+\cdot}}$ is stable on this time scale. It is proposed that the more complex reaction of $\mathbf{1^{+\cdot}}$ is analogously initiated by a rapid, reversible formation of $\mathbf{1^{+\cdot}}$, but that $\mathbf{1^{+\cdot}}$ is unstable due to the cyclization reaction sequence. This, of course, explains the absence of a reverse peak due to the reduction of $\mathbf{1^{+\cdot}}$. The relative stability of $\mathbf{14^{+\cdot}}$ also argues strongly that deprotonation and demethylation occur after coupling. If these steps precede coupling, then $\mathbf{14^{+\cdot}}$ should be as unstable as $\mathbf{1^{+\cdot}}$.



14 $\mathbf{14^{+\cdot}}$

The Scheme I incorporates these proposals and indicates several other mechanistic ramifications which must be deciphered. In particular, one needs to consider the intermediacy of the dicationic species $\mathbf{1^{2+}}$.[43] Because there are two semi-independent and very similar, oxidizable moieties in **1**, such species are not energetically unreasonable. The species $\mathbf{1^{2+}}$ could be generated in two ways: by direct transfer of two electrons to the electrode or by electronic disproportionation of a pair of $\mathbf{1^{+\cdot}}$ in solution. The latter reaction, which is second order in $\mathbf{1^{+\cdot}}$, is especially probable near the electrode where there is a locally high concentration of $\mathbf{1^{+\cdot}}$.

For an irreversible process like this one, the $E_p(1)$ value is a kinetic parameter. If the reaction rate speeds up, $E_p(1)$ shifts

Table IV. Variation of Peak Characteristics of $E(1)$ in lsv and cpsv for Different Mechanisms[a]

	lsv			cpsv	
				logarithmic anal.	
reaction scheme[b]	$\partial E_p/\partial$ log v, mV	$-\partial E_p/\partial$ log $C°$, mV	$-\partial E_p/\partial$ log $Z°$[c] (or pH)	no.[d]	− slope, mV
e-**C**-e-p-p	29.6	0	0	1	58.6
e-c-d-**P**-p	19.5	0	19.5	1	39.0
e-c-p-**D**-p(B)[e]	19.5	19.5	19.5	2	58.6
e-c-p-**D**-p(U)[f]	19.5	0	19.5	3	58.6
e-e-**C**-p-p	14.6	0	0	1	29.3
e-**D**-c-p-p	19.5	19.5	0	2	58.6
e-d-**C**-p-p	19.5	0	0	1	39.0
e-d-c-**P**-p	19.5	0	19.5	1	39.0

[a] Values taken from Table IV, reference 17 and Table I, reference 19, using a temperature of 22 °C. [b] Extra p step can be deprotonation or loss of Me. [c] $Z°$ = concn of added base. [d] See Table II. [e] Buffered solution. [f] Unbuffered solution.

to less positive potentials. Thus, it is clear from the fact that the addition of a strong base like pyridine does not affect $E_p(1)$, deprotonation is not involved in the rate-limiting step. Since $E_p(1)$ also did not vary with an increase of substrate concentration ($C°$), the reaction must be first order in **1**.

The various possibilities are most easily considered by employing the nomenclature e, c, d, and p used by Andrieux and Saveant[32] for the different steps. One mechanism is then e-d-**C**-p:

$$\begin{array}{llll}
\mathbf{1} & \xrightleftharpoons{-e^-} & \mathbf{1}^{+\cdot} & \text{e} \\
2\,\mathbf{1}^{+\cdot} & \rightleftharpoons & \mathbf{1}^{++} + \mathbf{1} & \text{d} \\
\mathbf{1}^{++} & \longrightarrow & \mathbf{10} & \mathbf{C}\ \text{(rate limiting step)} \\
\mathbf{10} & \longrightarrow & \mathbf{12} \longrightarrow \mathbf{13} & \text{p}
\end{array}$$

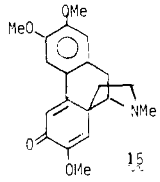
The capital letter represents the rate-limiting step. The lsv and cpsv properties for several relevant mechanisms are listed in Table IV. These values were obtained from references 32 and 34, where values for a further eight mechanistic possibilities may also be found.

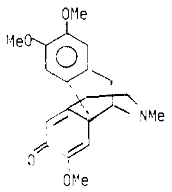
A comparison of the experimental lsv data for **1** in Table II with the theoretical values in Table IV rules out many mechanisms and indicates that the most likely mechanism is e-d-**C**-p. The difference between the measured and theoretical value for $\delta E_p/\delta$ log ν may result from inadequate compensation for *iR* drop effects. Comparison of the cpsv slope values in Tables II and IV shows that analysis number 1 with an experimental value of 40 mV is closest to any of the theoretical values. The mechanisms corresponding to this value include e-d-**C**-p. Thus, the conclusions from both methods are in agreement.

In the above analysis, the effect of the rearrangement (r), e.g., **10** to **12**, upon the kinetics has been ignored. If the rearrangement is not the rate-limiting step, it will indeed contribute nothing to the overall kinetics and one may then conclude that coupling proceeds via the dicationic species $\mathbf{1}^{2+}$. On the other hand, if rearrangement is rate limiting, it must be followed by deprotonation and the mechanistic possibilities are: e-d-c-**R**-p and e-c-d-**R**-p. These should display the same lsv and cpsv characteristics as e-d-**C**-r-p or e-d-**C**-p-r since they incorporate a first-order rate-limiting step ($\delta E_p/\delta$ log $C° = 0$), a preceding electronic disproportionation ($\delta E_p/\delta$ log $\nu = 19.5$ mV) and a following deprotonation ($\delta E_p/\delta$ log $Z° = 0$). The mechanisms involving rate-limiting rearrangement imply that deprotonation of **12** is fast, while deprotonation of **10** must be slow. A brief inspection of **10** and **12** (Scheme I) shows that this is unlikely since the species are so similar. It therefore appears that the mechanisms involving rate-limiting rearrangement are less likely.

From all of the kinetic data presented and from the reasoning outlined above, the most likely mechanism for oxidation of **1** involves (i) loss of an electron at the electrode to form a cation radical $\mathbf{1}^{+}\cdot$; (ii) reversible, electronic disproportionation of two of these cation radicals to form the dicationic species $\mathbf{1}^{2+}$; (iii) rate-limiting cyclization of the dication; (iv) deprotonation and rearrangement to form the stable cation **13**, the exact order of these two steps being uncertain; (v) demethylation of **13** to form **4**.

Turning now to the oxidation of **2**, it is first noted that the formation of **5** involves no structural rearrangement corresponding to that involved in the oxidation of **1**. Furthermore, although rearrangements of morphinandienones are well known,[19,20] we find no evidence for other dienone products, e.g., **15**, which corresponds to structure **4**. Similarly, no trace of **16** has been found.

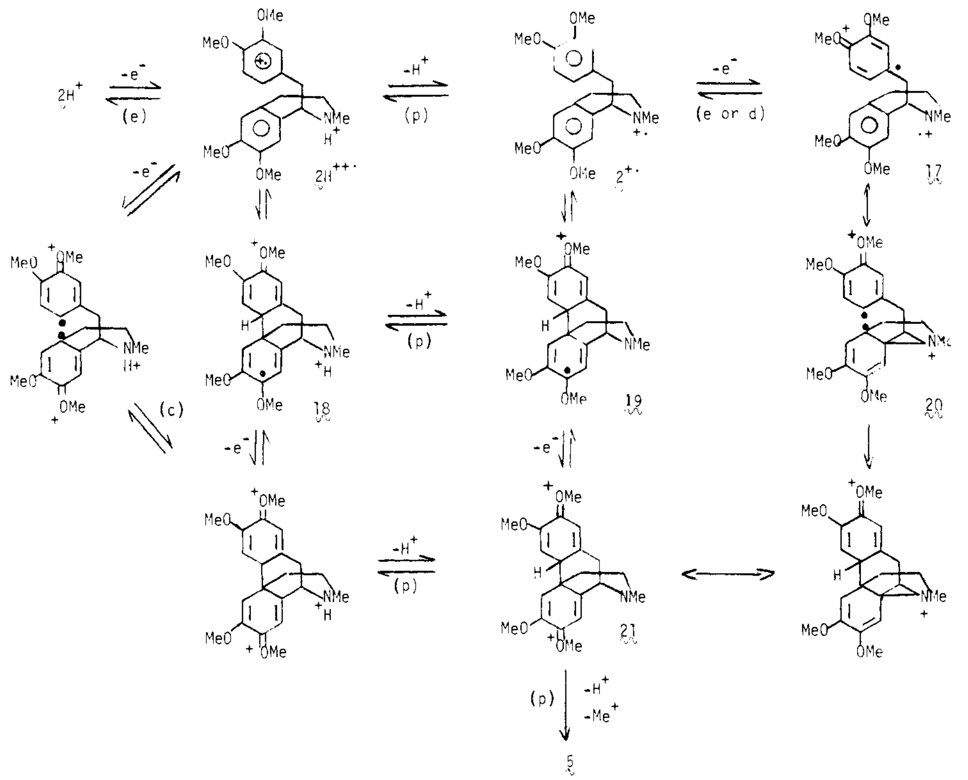




16

Ronlan and co-workers have recently found dienones corresponding to **5**, **15**, and **16** upon oxidation of laudanosine analogues. Obviously, the replacement of the NMe group in **2** by CH_2 or O has a significant effect upon the mechanism of coupling. It is clear from the deuterium-labeling experiment as well as experiments using optically active *O*-benzylpseudocodamine **7**[44] that deprotonation α to the nitrogen is not involved in the oxidation. In many previous experiments as well as the kinetic ones reported here, the solutions are acidic and the amine group of **2** is protonated giving $\mathbf{2}H^+$. As indicated earlier,[6] this reduces experimental and interpretational complications due to oxidation of the amine function. Such conditions may be produced by the addition of strong acid (HBF_4, TFA) to the solution and an overall picture of many of the mechanistic possibilities is provided in Scheme II. Again we will assume that loss of methyl is the last step, that loss of the aromatic proton must occur after cyclization, and that this is irreversible and not rate limiting. These assumptions are reasonable and supported by the findings for compound **1**. It is no longer valid to assume, as was done for **1**, that deprotonation of the initially formed cation radical is insignificant (the ammonium could deprotonate to the amine), and hence the diagnostic criteria presented by Saveant and co-workers[32,34] cover only some of the possible mechanisms. In spite of the mechanistic complexity and the difficulty presented by the ill-defined cpsv plateau (see above), an informative analysis can be performed. By comparison of the lsv and cpsv data listed in Table II for the oxidation of **2** in the presence of strong acid (HBF_4, TFA) with the theoretical values in Table IV, it can be seen that of the mechanisms listed (there are 39 possible using this set of intermediates) e-c-p-**D**-p(U) is the one consistent with the kinetic data.

Scheme II



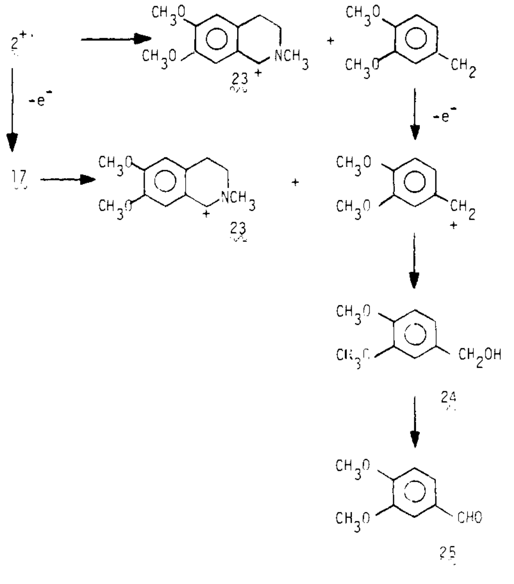
This mechanism is quite different from that found for **1** and as discussed below, it is useful for understanding the products formed from **2** or **2H**$^+$ under various conditions. At this point it is noted that the mechanism involves three reversible steps before a rate-limiting solution electron transfer. These steps include a deprotonation and, although the kinetics do not specify that the ammonium ion is deprotonated, the required reversibility of that step strongly indicates that this is the case.[45] Therefore, the steps up to and including the rate-limiting one are:

$$\begin{array}{lcl} 2H^{+} & \underset{}{\overset{e}{\rightleftharpoons}} & 2H^{++\cdot} \\ 2H^{++\cdot} & \overset{c}{\rightleftharpoons} & 18 \\ 18 & \overset{p}{\rightleftharpoons} & 19 + H^{+} \\ 19 + 2H^{+\cdot} & \overset{D}{\dashrightarrow} & \end{array}$$

It is interesting that the rate-limiting step is a solution electron transfer because such reactions might be expected to have rates approaching that of diffusion control. In this case, however, the concentration of the easily oxidized **19** is depressed by the acidity of the media. This lowers the rate and could account for this electron transfer being the rate-limiting step.

Another mechanism with the same rate law is e-p-c-**D**-p (via **2**$^{+\cdot}$) and this is, of course, also consistent with the experimental results since the same type of preequilibria and rate-limiting step are involved. A mechanism which has not been treated theoretically, but which should have the same rate law is e-p-**D**-c-p via **2**$^{+\cdot}$ and **17**. Each of these latter two mechanisms involve the intermediate **2**$^{+\cdot}$. This is also the intermediate formed by one-electron oxidation of **2** in nonacidic media. In such media the cyclized product is formed, but cleavage of the dimethoxybenzyl group is a major competitive route. Thus in $CH_3CN/LiClO_4$ the yield of **5** is only about 30% ($n \geqslant 3.5$) and **23**–**25** are formed. In an electrolyte 0.2 M in HBF_4 (as a 50% aqueous solution) the yield of **5** is >90%. Acids prevent cleavage by amine protonation. This is understandable since as shown in Scheme III, the isoquinolyl radical or cation

Scheme III



formed by cleavage will be stabilized by the amine but not by the corresponding ammonium ion. In terms of the mechanism, acid depresses the concentration of **2**$^{+\cdot}$ and **17** which are the intermediates responsible for cleavage.

In this light a choice can be made between the three mechanisms found to be consistent with the kinetic data for acidic media. The mechanisms e-p-c-**D**-p and e-p-**D**-c-p both involve **2**$^{+\cdot}$. If this intermediate were to play a significant role, similar product ratios should be observed upon oxidation of **2** in acidic or nonacidic media. This is contrary to observation and instead the e-c-p-**D**-p route is most probable.

It is also interesting to note that the kinetic data change with the acidity of the medium (Table II). This indicates that the branching of the routes does not occur after the rate-limiting step. Again, the e-p-**D**-c-p mechanism is indicated to be inconsistent with the data. The correct mechanism under nonacidic conditions cannot be deciphered since the yields of cyclized product are low and the number of reasonable mechanisms is very large.

The regiospecificity for coupling para to a methoxy group and the lack of rearranged products like **4** from **1** are of considerable synthetic significance. Analogues of **2** where NCH_3 is replaced by O or CH_2 do not give regiospecific coupling under very similar conditions. It is, therefore, apparent that the nitrogen is intimately involved in determining the coupling mode even in acidic solutions. The kinetic data make it clear that the mechanism for oxidation of $\mathbf{2H^+}$ is special and involves the amine/ammonium functionality. In particular, however, it may be noted that in acidic media the amine is "unmasked' during the mechanism and it seems likely that this is important in determining the regiospecificity.

Oxidation of compound **3** does not have the amine problem, but does present some unique features due to its rigid geometry. The cpsv and lsv data for **3** listed in Table II must be treated in the light of its observed "filming". The values of $\delta E_p(1)/\delta \log \nu = 33$ and 34 mV point to the occurrence of a first-order process, e.g., e-C-e-p, by comparison with the diagnostic criteria listed in Table IV. However, the peak width of $E(1)$ is rather large ($\delta = 85$ mV). This could in principle be due to filming, but this is contradicted by the observation that $E_{pa}(2) - E_{pc}(2) = 65$ mV which is close to the theoretical value of 60 mV expected for a clean electrode. Furthermore, the logarithmic analyses in cpsv do not give slopes which correspond to any of the 16 mechanisms considered, the slope values being much larger than any of the theoretical values given in Table IV. An explanation of these observations is that some degree of mixed charge transfer-chemical reaction kinetic control[30] is occurring. In other words, the rates of the chemical reaction following electron transfer are of similar magnitude to the rate of the electron transfer itself and, although the fast initial chemical step could be cyclization, the data cannot reveal that. Indeed, the voltammetric results do not define the structure of the cation radical formed from **3**. It has been suggested that there is some trans-annular delocalization in this species, based upon ionization potentials and $E_{1/2}$ values.[7,27,28] Thus, the ionization potential of [2,2]metacyclophane is less than that of *m*-xylene. Similar observations are made by using $E_{1/2}$ values, but here the interpretation is clouded by the kinetics. The oxidation in acetonitrile is not reversible and the peak potential is artificially low due to the fast follow-up reaction.

The mixed kinetic control explains the irreproducibility observed in the cyclic voltammograms. Any films formed upon the electrode surface would immediately alter the rate of heterogeneous electron transfer and upset the balance of reaction rates thus leading to an anodic shift in peak potential. This would cause the peak potential to eventually merge with the wave corresponding to **6** giving rise to a quasireversible wave. Such a perturbation of the delicate rate balance obviously produced the erroneous conclusion concerning the stability of the initially formed cation radical $\mathbf{3^{+\cdot}}$ in the previous study of **3**.[7]

Summary

Three coupling reactions have been studied. Although the reactants and conditions are all quite similar and the reactions are all clean, two-electron processes, the mechanisms are all different. The mechanistic sequence for **1** involves reversible electron transfer and disproportionation steps and a first-order rate-limiting step, which is probably cyclization. In **2** the amine/ammonium function distorts this scheme by its acid-base chemistry and probably directs the regiochemistry of coupling. The most likely mechanism is e-c-p-**D**, where the p step involves amine deprotonation. Finally, compound **3** shows an e-c type of mechanism where the follow-up step is so rapid that the initial electron transfer partially controls the rate. There is no direct evidence concerning the nature of this step, but it would appear that the rigid geometry of **3** has an important effect on the rates. The observed sensitivity of mechanism to structure is perhaps not so surprising when it is realized that all the kinetically important steps in any of these mechanisms are fast reactions. The relative rates of various steps tend to be similar and the exact kinetic scheme is, therefore, sensitive, to the details of structure.

Experimental Section

Cyclic and linear sweep voltammetry were carried out by using a Princeton Applied Research (PAP) potentiostat, Model 173, in conjunction with a PAR 175 universal programmer. Voltammograms were recorded on a Varian F-80A X-Y recorder or a Tektronix 5111 storage oscilloscope. Coulometry and preparative electrolyses were performed with the same potentiostat coupled with a PAR 179 digital coulometer. Cpsv was carried out by measuring the currents at regularly spaced intervals on the lsv *i–E* recorder (or photograph for high sweep rates). Intervals of 0.01 V were generally found to be convenient and the *I–E* curve was calculated by using the equation

$$I = 2\left[\frac{\delta}{\pi}\right]^{1/2}\left\{i(l)\sqrt{N} + \sum_{j=1}^{N-1}\sqrt{N-j}\,[k(j+1) - i(j))\right\}$$

where I is the convoluted current, $i(N)$ is the current data, δ is the time between data points, and N is the serial number of the data.[38] The values of I were computed by using a programmed Texas Instrument TI-57 calculator. In addition to being tedious this procedure has much scope for human error and digital acquisition procedures with computer evaluation of the data are to be preferred. However, for occasional use of cpsv procedures as a check on lsv and other kinetic techniques the use of inexpensive calculators has financial advantages which must, of course, be weighed against the decreased accuracy of the results.

Acetonitrile (Burdick and Jackson-UV) was used as received. Lithium perchlorate (G. F. Smith), tetraethylammonium fluoroborate (Southwestern Analytical Chemicals), and tetra-*n*-butylammonium perchlorate (G. F. Smith) were used without further purification.

The cell for cyclic voltammetry was a single compartment cell containing the reference electrode (Ag/0.1 M $AgNO_3$) which was separated from the main compartment by a cracked-glass tube. The counter electrode was a platinum wire or sheet and the working electrode was a polished disc of platinum (diameter = 0.7 mm) set in soft glass. The volume of solution was generally 25 mL. A Luggin capillary was used to reduce the uncompensated resistance of the cell.

Coulometry was performed in the same cell with about 20 mL of solution but the cathode was separated from the anode and reference electrode by a glass frit. The anode used in this case was a platinum gauze or sheet (12.5 cm^2).

Allowance for iR drop effects in linear sweep voltammetry was made by comparing the behavior of a known reversible couple such as ferrocene with that of the compound under study in the same conditions.[46] The residual uncompensated resistance was minimized by the use of high concentrations of supporting electrolyte (0.4 M) and iR compensation. This allowed values of peak potentials to be measured up to 100 V s^{-1} with a reasonable degree of certainty. Correction for iR drop in cpsv was carried out according to the literature.[31]

Procedures for the syntheses of compounds **1–6** have been previously described.[1,2,7]

[1-^{2}H]-(±)-*O*-Benzylpseudocodamine (7). 1-(3-Methoxy-4-benzyloxybenzyl)-3,4-dihydro-6,7-dimethoxyisoquinoline methiodide[2] (5.27 g) was dissolved in 250 mL of methanol and 10 g of $NaBD_4$ was added cautiously. A very exothermic reaction ensued. Removal of the solvent under reduced pressure, after stirring for 2 h at room temperature, gave a residue which was admixed with water and extracted with CH_2Cl_2. The combined organic extracts were dried over Na_2CO_3 and evaporated under reduced pressure to yield 5.05 g of **7** as a pale yellow syrup. The deuterium content was determined by MS to be 90%. The IR, NMR, and MS were consistent with expectations based upon the spectra of undeuterated *O*-benzylpseudocodamine.[2] Chemical ionization mass spectrometry using NH_3 as the reagent gas indicated the following: *m/e* 435 [(mH^+), 68], 434 [(m^+), 7], 344 [($mH^+ - CH_2Ph$], 91 [($C_7H_7^+$), 100].

[1-^{2}H]-(±)-*O*-Benzylflavinantine (8). The oxidation of **7** was performed as described previously[2] by using either sodium carbonate or sodium bicarbonate with 0.1 M lithium perchlorate in 2% aqueous acetonitrile. The solvent (Drake Bros.) was purified by distillation from P_2O_5. After all the starting material had reacted as determined by TLC (typically 3.0–3.4 F/mol), the solvent was removed from the anolyte under reduced pressure and the residue was taken up in water and extracted with methylene chloride. The combined organic layers were dried with anhydrous sodium sulfate, filtered, and concentrated under vacuum. This crude mixture was then extracted with a pH 2 buffer (HCl/NaCl). The aqueous phase was quickly basified with sodium bicarbonate and then extracted with methylene chloride. The combined organic layers were dried with anhydrous sodium carbonate, filtered, and concentrated under vacuum. This oil was dissolved in a minimum of absolute ethanol, and then 70% perchloric acid in absolute ethanol and absolute ether was added slowly until neutral on indicator paper. This perchlorate salt was then recrystallized from EtOH to yield pure dienone **8**. The IR, NMR, and MS were as expected. The yields of purified **8** varied from 24 to 36%. Mass spectra at 20 eV, 200 °C, were obtained. $[^1H]$**8:** *m/e* 417 [(m^+), 1557], 416 [($m^+ - 1$), 89], 326 [($m^+ - 91$), 4263], 325 [($m^+ - 92$), 320]. $[^2H]$**8:** from $NaHCO_3/CH_3CN$; *m/e* 418 [(m^+), 2145], 417 [($m^+ - 1$), 174], 327[($m^+ - 91$), 3941], 326 [($m^+ - 92$), 271]. $[^2H]$**8:** from Na_2CO_3/CH_3CN; *m/e* 418 [(m^+), 346], 417 [($m^+ - 1$), 59], 327 [($m^+ - 91$), 695], 326 [($m^+ - 92$), 104].

Acknowledgment. This work was supported by the National Institutes of Health and in part by the donors of the Petroleum Research Fund, administered by the American Chemical Society. Samples of compounds **1–3** were obtained from V. Boekelheide and T. Morgan and from J. R. Falck and F. R. Stermitz. Helpful comments from J. Evans and D. Evans concerning the manuscript are also acknowledged.

References and Notes

(1) J. R. Falck, L. L. Miller, and F. R. Stermitz, *J. Am. Chem. Soc.*, **96**, 2981 (1974).
(2) J. R. Falck, L. L. Miller, and F. R. Stermitz, *J. Am. Chem. Soc.*, **95**, 2651 (1973).
(3) J. R. Falck, L. L. Miller, and F. R. Stermitz, *Tetrahedron*, **30**, 931 (1974).
(4) L. L. Miller, R. F. Stewart, J. P. Gillespie, V. Ramachandran, Y. H. So, and F. R. Stermitz, *J. Org. Chem.*, **43**, 1580 (1978).
(5) L. L. Miller, F. R. Stermitz, J. Y. Becker, and V. Ramachandran, *J. Am. Chem. Soc.*, **97**, 2922 (1975).
(6) J. Y. Becker, L. L. Miller, and F. R. Stermitz, *J. Electroanal. Chem.*, **68**, 181 (1976).
(7) J. Y. Becker, L. L. Miller, V. Boekelheide, and T. Morgan, *Tetrahedron Lett.*, 2939 (1976).
(8) U. Palmquist, A. Nilsson, T. Pettersson, A. Ronlan, and V. D. Parker, *J. Org. Chem.*, **44**, 196 (1979).
(9) A. Ronlan, O. Hammerich, and V. D. Parker, *J. Am. Chem. Soc.*, **95**, 7132 (1973).
(10) V. D. Parker and A. Ronlan, *J. Am. Chem. Soc.*, **97**, 4714 (1975).
(11) A. Ronlan and V. D. Parker, *J. Org. Chem.*, **39**, 1014 (1974).
(12) M. Sainsbury and J. Wyatt, *J. Chem. Soc.*, Perkin *Trans. 1*, 661 (1976).
(13) M. Sainsbury and R. F. Schinazi, *J. Chem. Soc., Chem. Commun.*, 718 (1972).
(14) E. Kotani, N. Takeuchi, and S. Tobinaga, *Chem. Commun.*, 551 (1973).
(15) E. Kotani and S. Tobinaga, *Tetrahedron Lett.*, 4759 (1973).
(16) E. Kotani, F. Miyazaki, and S. Tobinaga, *Chem. Commun.*, 300 (1974).
(17) S. M. Kupchan, O. P. Dinghra, C.-K. Kim, and V. Kameswaran, *J. Org. Chem.*, **43**, 252 (1978).
(18) S. M. Kupchan, A. J. Liepa, V. Kameswaran, and R. F. Bryan, *J. Am. Chem. Soc.*, **95**, 6861 (1973).
(19) S. M. Kupchan, V. Kameswaran, J. T. Lynn, D. K. Williams, and A. J. Liepa, *J. Am. Chem. Soc.*, **97**, 5622 (1975).
(20) S. M. Kupchan and C.-K. Kim, *J. Am. Chem. Soc.*, **97**, 5623 (1975).
(21) S. M. Kupchan, O. P. Dinghra, V. Ramachandran, and C.-K. Kim, *J. Org. Chem.*, **43**, 105 (1978).
(22) A. E. McKillop, A. G. Turrell, and E. C. Taylor, *J. Org. Chem.*, **42**, 765 (1977).
(23) E. C. Taylor, J. G. Andrade, and A. E. McKillop, *J. Chem. Soc., Chem. Commun.*, 538 (1977).
(24) T. Kametani, K. Shishido, and S. Takano, *J. Heterocycl. Chem.*, **12**, 305 (1974).
(25) I. W. Elliott, *J. Org. Chem.*, **42**, 1090 (1977); I. W. Elliott, *ibid.*, **44**, 1162 (1979).
(26) U. Hess, K. Hiller, R. Schroeder, and E. Grundemann, *J. Prakt. Chem.*, **319**, 568 (1977).
(27) T. Sato and M. Kamada, *J. Chem. Soc., Perkin Trans. 2*, 384 (1977).
(28) T. Sato and K. Torizuka, *J. Chem. Soc., Perkin Trans. 2*, 1199 (1978).
(29) R. S. Nicholson and I. Shain, *Anal. Chem.*, **36**, 707 (1964).
(30) L. Nadjo and J. M. Saveant, *J. Electroanal. Chem.*, **48**, 113 (1973), and references therein.
(31) J. C. Imbeaux and J. M. Saveant, *J. Electroanal. Chem.*, **44**, 169 (1973).
(32) C. P. Andrieux and J. M. Saveant, *J. Electroanal. Chem.*, **53**, 165 (1974).
(33) F. Ammar, C. P. Andrieux, and J. M. Saveant, *J. Electroanal. Chem.*, **53**, 402 (1974).
(34) C. P. Andrieux, J. M. Saveant, and D. Tessier, *J. Electroanal. Chem.*, **63**, 429 (1975).
(35) C. P. Andrieux, D. J. Brown, and J. M. Saveant, *Nouv. J. Chim.*, **1**, 157 (1977).
(36) G. A. Forcier and J. W. Olver, *Anal. Chem.*, **37**, 1447 (1965).
(37) L. A. Avaca and J. H. P. Utley, *J. Chem. Soc., Perkin Trans. 1*, 971 (1975).
(38) H. W. VandenBorn and D. H. Evans, *Anal. Chem.*, **46**, 643 (1974).
(39) K. B. Oldham, *Anal. Chem.*, **44**, 196 (1972).
(40) M. Grenness and K. B. Oldham, *Anal. Chem.*, **44**, 1121 (1972).
(41) F. Ammar and J. M. Saveant, *J. Electroanal. Chem.*, **47**, 215 (1973).
(42) M. Sainsbury, University of Bath, England, suggested this possibility: "Abstracts of the Electrochemical Society Meeting", Seattle, Wash., May 1978.
(43) 1^{2+} may be a bis-cation radical in which one electron has been lost from each ring. Anionic analogues have been discussed: F. Ammar and J. M. Saveant, *J. Electroanal. Chem.*, **47**, 115 (1973).
(44) T. E. Rogers and L. L. Miller, unpublished results.
(45) Although there is excess acid present in the medium, the solution near the electrode cannot be considered to be buffered in a classical sense. More specifically, the acidity of the medium and the p*k* of the intermediates are unknown so that the effectiveness of any buffering is unknown. The kinetic and preparative results suggest that the medium is unbuffered in the sense defined by ref 32.
(46) For a more detailed description, see E. Lamy, L. Nadjo, and J. M. Saveant, *J. Electroanal. Chem.*, **42**, 189 (1973), and references therein.