loid(s) and subjected to cation exchange chromatography (Carboxymethyl cellulose eluted with H_2O, 0.5 and 1% acetic acid). the labeled alkaloids were then recrystallized to constant specific activity.[9] As seen in experiments 1 and 2 (Table I) doubly labeled dopamine (I) was incorporated into norlaudanosoline (V) and norlaudanosolinecarboxylic acid (III) with no change in $^{3}H/^{14}C$ ratios. [Carboxy-^{14}C]D,L-dopa was efficiently utilized by *P. orientale* for the synthesis of amino acid III, but expectedly no label was found in norlaudanosoline (V) (experiments 3-5). [2-^{14}C]D,L-Dopa was incorporated into both 1,2-dehydronorlaudanosoline (IV) and amino acid (III). Experiments 1-6 establish direct conversion of dopamine and dopa into the tetrahydroisoquinoline alkaloids, *i.e.,* with minimal reutilization of their degradation products by CO_2 fixation.

These results suggest that dopa may be metabolized by *P. orientale* in at least two ways, decarboxylation and transamination. In experiments 7 and 8, [1,2-^{14}C]D,L-dopa was fed to *Papaver* seedlings and the norlaudanosolinecarboxylic acid (III) was isolated, purified, and subjected to decarboxylation. The CO_2 trapped possessed an average of 11% of the total specific activity in III. Since equal amounts of label were introduced into the 1 and 2 carbons of precursor dopa, the ratio of 78/11 represents the extent of decarboxylation over transamination.[10] This conclusion is valid if metabolism of dopa occurs solely within a putative vacuolar site of alkaloid synthesis as has been proposed for at least the latex system of *Papaver somniferum* by Fairbairn[12] and Roberts.[13,14]

Finally to establish the intermediacy of norlaudanosolinecarboxylic acid (III), we have synthesized a doubly labeled form and incubated it with latex of poppy capsules. As seen in Table I (experiment 9) III is readily converted to norlaudanosoline (V) with no change in the $^{3}H/^{14}C$ ratio. These results suggest that norlaudanosolinecarboxylic acid (III), as the first tetrahydroisoquinoline alkaloid of the series, is converted to norlaudanosoline which in turn has been shown to be a precursor of thebaine and isothebaine in this plant and related alkaloids in the Papaveraceae and other plant families.[2]

Biogenetic-type chemical synthesis of amino acid (III) from dopamine (I) and 3,4-dihydroxyphenylpyruvic acid (II) were affected under physiological conditions[6] in yields up to 80%. Chemical decarboxylation of III to afford at least 20% of 1,2-dehydronorlaudanosoline (IV) under physiological conditions[16] was also observed. In fact facile chemical Pictet-Spengler condensation has thwarted attempts to identify an enzymatic process using cell-free extracts from seedlings.

The above experiments support the putative intermediacy of imine (IV) in this pathway. Since dopa incorporation into IV was observed to occur at a relatively low rate, in experiment 6 the possibility of chemical decarboxylation of amino acid to afford IV during the isolation procedure cannot be excluded. However, a mechanism for decarboxylation of amino acid (III) to afford norlaudanosoline (V) directly has to our knowledge no precedent in nature.

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References and Notes

(1) Presented at the 9th International Symposium on the Chemistry of Natural Products, IUPAC, Ottawa, Canada, June 24–28, 1974.

(2) For an excellent review of alkaloid biosynthesis in general see I. D. Spenser in "Comprehensive Biochemistry," Vol. 20, M. Florkin and E. H. Stotz, Ed., Elsevier, Amsterdam, 1968.

(3) A. R. Battersby, A. R. Burnett, and P. G. Parsons, *J. Chem. Soc. C*, 1187, 1193 (1969).

(4) G. J. Kapadia, G. S. Rao, E. Leete, M. B. E. Fayez, Y. S. Vaishnar, and H. M. Fales, *J. Amer. Chem. Soc.*, **92**, 6943 (1970); I. J. McFarlane and M. J. Slaytor, *Phytochemistry*, **11**, 229, 235 (1972).

(5) G. Billek and E. F. Herrmann, *Monatsh. Chem.*, **90**, 89 (1959); F. Weygand, W. Steglich, and H. Tanner, *Justus Liebigs Ann. Chem.*, **650**, 128 (1962).

(6) W. M. Whaley and T. R. Govindachari, *Org. React.*, **6** (1951).

(7) S. Teitel, J. O'Brien, and A. Brossi, *J. Med. Chem.*, **15**, 845 (1972).

(8) S. Kubota, T. Masui, E. Fujita, and S. M. Kupchan, *J. Org. Chem.*, **31**, 516 (1966).

(9) All final specific radioactivities were higher than 300 cpm/mg, and recrystallization was continued until three successive values varied by less than 5%.

(10) This is identical with the ratio of decarboxylation to transamination of dopa observed in rat liver *in vitro.*[11]

(11) G. H. Wada and J. H. Fellman, *Biochemistry*, **12**, 5212 (1973).

(12) J. W. Fairbairn, F. Hakim, and Y. E. Kheir, *Phytochemistry*, **13**, 1133 (1974).

(13) M. F. Roberts, *Phytochemistry*, **13**, 119 (1974).

(14) Although we used seedlings instead of latex in this experiment, the compartmentalization of alkaloid synthesis may occur in both. We have recently gained evidence[15] that an enzyme involved in the biosynthesis of indole alkaloids is located in vacuoles of 5-day old seedlings of *Vinca rosea*.

(15) K. M. Madyastha, J. Dwyer, T. Meehan, and C. J. Coscia, unpublished observations.

(16) M. L. Wilson and C. J. Coscia, manuscript in preparation.

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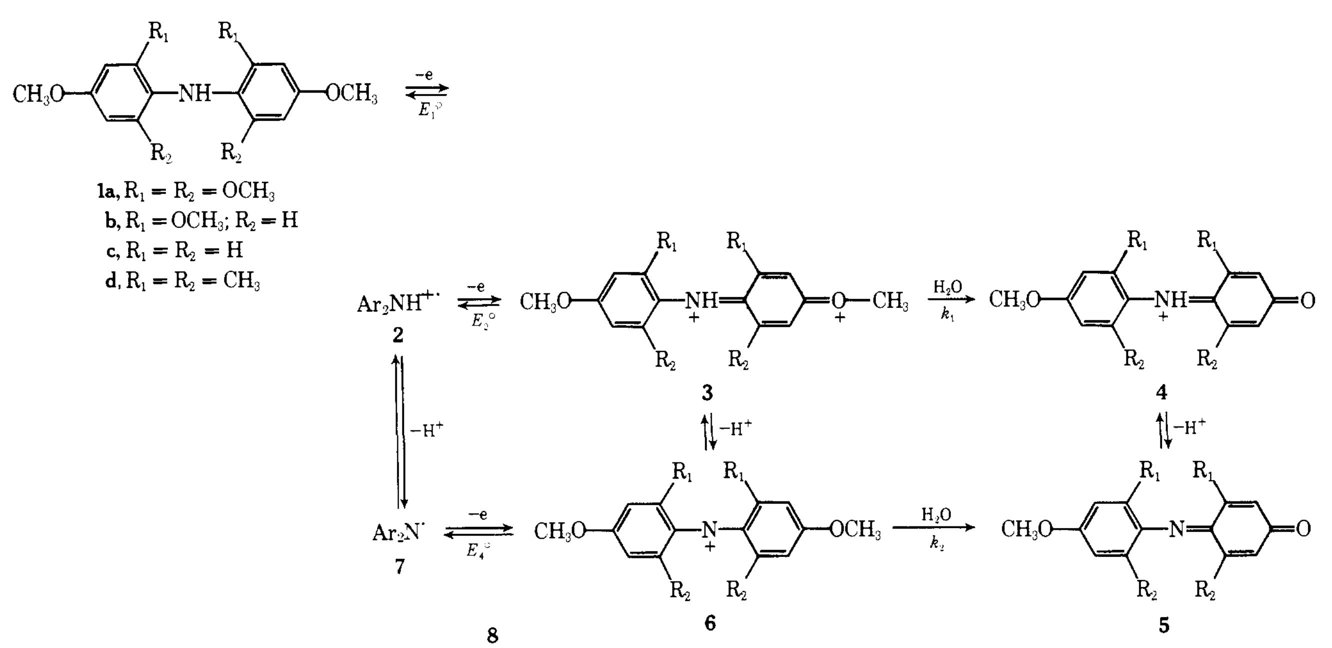
Chemistry of Electrogenerated Diarylnitrenium Ions. Absorption Spectra of Stable Protonated Nitrenium Ions

Sir:

Anodic oxidation of di-*p*-anisylamine in nitromethane or acetonitrile solutions has been used as a route to the cation radical.[1] We have studied the hydrolysis of the dication by residual water in the CH_3CN medium and we have observed this species in organic solutions of Lewis acids.[2] Recently, a note has been published about the isolation of a salt of the di-*p*-anisylamine dication generated by $SbCl_5$ oxidation of a CH_2Cl_2 solution of this amine.[3] We wish to report the strong effect of the number of methoxyl groups upon the stability of the dioxidized species formed from diphenylamines **1**. The hexasubstituted compound **1a** allows the generation of both the dication and its stable deprotonated form, the diarylnitrenium ion, in CH_3CN.

This study was performed with 10^{-3} *M* solutions of amines **1** in anhydrous CH_3CN and 10^{-1} *M* Et_4NClO_4 (water level near 3.10^{-3} *M*). At a platinum disk electrode, compounds **1a** and **1b** give a cyclic voltammogram with two reversible one-electron redox couples for a voltage sweep rate equal to 33 mV sec^{-1}. The mean of the oxidation and reduction peak potentials matches the half-wave potentials, $E_{1/2}$, recorded at a rotating disk electrode (Table I). The first one-electron transfer produces the cation radical **2** and further oxidation gives the dication **3.** The lifetime of this last species from **1a** and **1b** is larger than 1 sec in contrast with the low stability of the dication **3c.** Exhaustive oxidation at the level of the first wave requires 1.0 faraday/mol and gives the stable cation radicals **2** characterized by their uv-visible absorption spectra (Table I). Macroscale electrolysis for a fluoroborate solution allows the isolation[4] of the salts of **2a** and **2b.** During the one-electron oxidation of **2a** the green color of the radical changes into a deep blue (λ_{max} 590 nm) of the dication **3a.** However, this species disappears more or less quickly by reaction with residual water which leads to the monoprotonated quinone imine **4a.** The addition of a base such as acetate produces the neutral form



1a, $R_1 = R_2 = OCH_3$
b, $R_1 = OCH_3$; $R_2 = H$
c, $R_1 = R_2 = H$
d, $R_1 = R_2 = CH_3$

5a (λ_{max} 297 nm, log ϵ 4.31, and λ_{max} 544, log ϵ 3.68) identified by comparison with the corresponding spectrum of an authentic sample.

In basic medium, the diarylnitrenium ion Ar_2N^+ is the likely product from oxidation[5] of a diarylamine Ar_2NH. A solution of **1a** with 2 equiv of 2,6-lutidine gives a characteristic cyclic voltammogram for a quasi-reversible bielectronic transfer.[4] A controlled potential electrolysis at 0.30 V produces the nitrenium ion **6a** (λ_{max} in Table I) which is responsible for the two-electron cathodic wave with $E_{1/2}$ = −0.07 V. A reduction at −0.5 V results in nearly quantitative regeneration of **1a** as demonstrated by identical voltammograms and uv spectra before and after the oxidation reduction cycle. After addition of Na_2CO_3 to the solution of **6a** and stirring, the voltammetric curve shows two cathodic waves at −0.26 and −0.72 V. The first one corresponds to a reversible monoelectronic process as shown by cyclic voltammetry and the epr spectrum of the radical $Ar_2N\cdot$ can be recorded as soon as the reduction at −0.40 V is started.[6] From a 10^{-3} *M* solution of **1b** with 2,6-lutidine, in the same conditions as for **1a**, the yield for the corresponding ion Ar_2N^+ is about 70% after a complete oxidation; this requires 8 min. In this case **6b** disappears mainly by the hydrolysis reaction giving **5b** but for higher concentrations of the amine (or with lower current density) a 5,10-diaryl 5,10-dihydrophenazine compound is produced.[8] The very effective stabilizing power of the donor methoxy groups is illustrated by the decrease in stability[9] of the Ar_2N^+ ion in going from **6a** to **6b** and then to **6c**. The high reactivity of **6c** is illustrated by a transformation into the dihydrophenazine compound[1b] faster than the hydrolysis into **5c**.

This electrochemical study for the CH_3CN medium clearly shows that the nitrenium ion **6** is less reactive toward water than its protonated form, the dication **3**. (For the two hydrolysis reactions k_2 is well below k_1 by a factor larger than 50 for species produced from **1a**.) The absorption spectra of **3** are more easily recorded in CH_3NO_2 or CH_2Cl_2 solutions of $AlCl_3$ or $SbCl_5$. In CH_2Cl_2 solutions the dioxidized species from **1c** gives an intense band at 688 nm in agreement with previous observations.[3] The wavelength maxima recorded for **1a** and **1b** in these systems are also gathered in Table I with the results obtained for the 98% H_2SO_4 medium.

The spectra reported for **1a** solutions in these various acid media match well the spectrum of the corresponding electrogenerated dication **3a** in CH_3CN. This fact supports the formation of the dication from other diphenylamines **1b** and **1c**. Moreover, for **1a** and **1b**, a confusion between the dication **3** and the nitrenium ion spectra is excluded[10] since the higher wavelength maxima of **3** has a wavelength value smaller than the one for the corresponding band of the nitrenium ion **6** (Table I). The absorption spectra obtained in the present work can be considered as some reference model for the identification of the species produced from di-para-substituted diphenylamines dissolved in an oxidizing medium.[4]

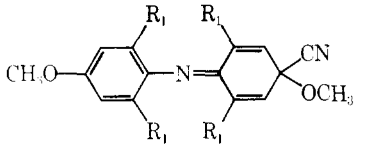
The voltammetric and spectroscopic observation of the cations **6a** and **6b** appear to be the first indication of stability of such diarylnitrenium ions which had only been postulated without direct evidence to be present in some chemical reactions.[11] The controlled electrochemical generation of these species in the presence of various nucleophilic re-

Table I. Half-Wave Potentials for Oxidation of Diphenylamines **1** in CH_3CN and Absorption Spectra of the Corresponding Oxidized Species ($E_{1/2}$ (V) *vs.* Ag|10^{-2} *M* Ag^+; λ_{max}, nm (log ϵ))

									λ_{max} **3**			
Amine	$E_{1/2}$		λ_{max} **2** neutral CH_3CN			λ_{max} **6** CH_3CN with 2,6-lutidine			98% H_2SO_4[c]			CH_2Cl_2–$SbCl_5$[d]
1a	0.035	0.57[a]	345(4.19)	373(4.02)	796(4.23)	364(4.36)	535(3.43)	723(4.39)	254	351	590	600(4.63)
1b	0.18	0.725	259(3.66)	377(4.34)	798(4.46)	378(4.27)		675(4.58)	242	278	620	633(4.60)
1c	0.295	0.85	294(3.98)	360(4.23)	762(4.50)			660[b]		272	638	668(4.74)

[a] With the rotating disk electrode, the morphology of the second wave of **1a** is abnormal as a consequence[4] of the deprotonation of the dication **3a**. A cyclic voltammogram for **1a** gives peaks potentials in agreement with $(E_{1/2})_2$ value for a solution of the cation radical **2a**. [b] Value obtained in neutral medium by specular reflectance spectroscopy.[10] [c] For **1c** the oxidizing power of the medium must be increased by addition of a small amount of lead dioxide. [d] The ϵ values may be minimum values since in some cases incomplete oxidation and/or partial hydrolysis can occur.

agents is an attractive route to new compounds. As an example, with tetraethylammonium cyanide the product of oxidation of **1a** is isolated with a yield near 90% and a similar compound is obtained from **1d**. These products result from the addition of one cyanide ion to the nitrenium ion **6** as indicated by satisfactory elemental analyses and mass molecular weights. Their spectroscopic and electrochemical properties[12] suggest the structure **8**. The reaction stops at the first stage without rearomatization but simple aromatic substitution has been observed for monosubstituted diphenylamines during anodic oxidation in methanolic sodium cyanide solutions.[13] A recent study proposed a route to aryl nitrenium ions *via* an electron reaction between aminyl radicals formed during the deoxygenation of aryl nitroxydes radicals by trialkyl phosphites in alcohol solutions.[14] It should be pointed out that anodic oxidation of arylamines can be used as an independent route to arylnitrenium species prepared from *N*-chloroarylamines following Gassman's work.[15]



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Moreover, **1a** allows, for the first time with an aromatic amine, the estimation of the formal potential $E_4° = -0.26$ V of the redox couple Ar_2N^+–$Ar_2N\cdot$ which lies lower than the value $E_1° = 0.035$ V for the couple $Ar_2NH^{+}\cdot$–Ar_2NH. This fact has some implications regarding the pathways involved in anodic coupling reactions of various diphenylamines.[4]

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References and Notes

(1) (a) G. Cauquis and D. Serve, *Tetrahedron Lett.*, 17 (1970); (b) G. Cauquis, H. Delhomme, and D. Serve, *ibid.*, 4645 (1971).
(2) (a) G. Cauquis and D. Serve, *C. R. Acad. Sci., Ser. C*, **273**, 1715 (1971); (b) D. Serve, Thesis, Grenoble, 1972; CNRS No. AO 7174.
(3) U. Svanholm and V. D. Parker, *J. Amer. Chem. Soc.*, **96**, 1234 (1974).
(4) Full details of the anodic processes of amines **1** will appear in the near future (G. Cauquis and D. Serve, in preparation).
(5) For a similar study with compounds bearing a NH group, see G. Cauquis, A. Deronzier, and D. Serve, *J. Electroanal. Chem.*, **47**, 193 (1973).
(6) The epr spectrum is a triplet 1:1:1 ($g = 2.0038$) with $a_N = 7.65$ G, in agreement with $a_N = 8.2$ or 8.08 G measured[7] for a spectrum of 7**a** chemically produced in a benzene solution of 1**a**.
(7) (a) B. G. Pobedimskii, A. L. Buchachenko, and M. B. Neiman, *Russ. J. Phys. Chem.*, **42**, 748 (1968); (b) F. A. Neugebauer and S. Bamberger, *Chem. Ber.*, 107, 2362 (1974).
(8) Its conditions of isolation and properties will be given later.[4] This compound gives a very stable cation radical with a epr spectrum erroneously attributed to a tetraarylhydrazinium radical cation.[7a]
(9) Steric hindrance around the nitrogen nucleus does not seem to be the main factor since there is a strong decrease in the stability of the Ar_2N^+ ion in going from 6*a* to 6d.
(10) Here only remains the problem of the absorption of the cation **6**c because its spectrum is not obtained by conventional spectroscopy in the presence of 2,6-lutidine. Nevertheless, a spectroelectrochemical study with specular reflectance suggests that the dication **3c** and the cation 6**c** have nearly the same band between 640 and 670 nm in the visible part of the absorption spectrum (A. Bewick and D. Serve, unpublished results, Southampton University, 1973).
(11) S. Hünig and F. Brühne, *Justus Liebigs Ann. Chem.*, **667**, 86 (1963). In ref 3, the information about **6c** is limited to the existence of a cathodic peak in the cyclic voltammogram of **1c** in neutral CH_3CN with suspended alumina.
(12) From **1d** only one product is isolated (mp 98°; ir (KBr) $\nu_{C\equiv N}$ 2225 cm^{-1} (w); uv_{max} (CH_3CN) 245, 425 nm) but **1a** gives a mixture of the para and ortho cyano derivatives as will be discussed elsewhere.[4] The structure **8** is supported by the results of a comparative study of the cyano derivatives and of 5**a**. Anodic oxidation of all these compounds produces a cation radical characterized by a large a_N value near 13 G in the epr spectrum.
(13) K. Yoshida and T. Fueno, *J. Org. Chem.*, **37**, 4145 (1972).
(14) J. I. G. Cadogan and A. G. Rowley, *J. Chem. Soc., Perkin Trans. 2*, 1030 (1974).
(15) P. G. Gassman, G. A. Campbell, and R. C. Frederick, *J. Amer. Chem. Soc.*, **94**, 3884 (1972); for a review on nitrenium ions see P. G. Gassman, *Accounts Chem. Res.*, **3**, 26 (1970).

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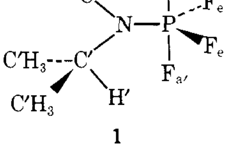
A Dynamic Nuclear Magnetic Resonance Study of Diisopropylaminotetrafluorophosphorane. Ground State Geometry and Barriers to Fluxional Processes

Sir:

Substituted derivatives of phosphorus pentafluoride are of interest because they can exhibit several stereochemical processes. For example, in the case of aminofluorophosphoranes of the type $R_1R_2NPF_4$ or $[R_1R_2N]_2PF_3$ these processes comprise: (a) fluorine positional interchange, (b) rotation around the nitrogen–phosphorus bond(s), (c) pyramidal inversion at nitrogen, and (d) rotation around the N–C bonds of the $-NR_1R_2$ moieties. At this point quantitative information regarding these stereochemical features is very sparse and, in fact, limited to one measurement[1] of the barrier to process *a* in $(CH_3)_2NPF_4$ and one measurement[2] of the barrier to process *b* in $(H_2N)_2PF_3$. The present paper describes the measurement of the barriers to processes *a* and *d* and an estimation of a lower limit for the barrier to process *b* in the title compound.

Diisopropylaminotetrafluorophosphorane (**1**) was prepared[3] by both the thermal decomposition[4] of the adduct $[(CH_3)_2CH]_2NH\cdot PF_5$ and by the liquid phase reaction[5] between $[(CH_3)_2CH]_2NSi(CH_3)_3$ and PF_5. For the dynamic nmr (dnmr) experiments, **1** was dissolved in various halomethane solvents ($HCCl_2F$, $HCClF_2$, F_2CCl_2, $DCCl_3$, and CCl_3F) at a substrate concentration of *ca.* 2 *M*.

Above −20° all the stereochemical processes (a, b, c, and d) are rapid on the nmr time scale since (i) the isopropyl methyl (doublet, τ 8.68, $J_{HCCH} = 6.75$ Hz) and methine protons (overlapping doublet of heptets, τ 6.11, J_{PNCH} (average) = 26.5 Hz, $J_{HCCH} = 6.68$ Hz) are equivalent in the ambient temperature ^1H spectrum (Figure 1a), (ii) the methyl (singlet, +103.6 ppm[6]) and methine (singlet, +75.5 ppm) carbon atoms are equivalent in the ambient temperature ^{13}C spectrum, (iii) the ambient temperature ^{19}F spectrum consists of a doublet (+60.3 ppm,[6] $J_{PF} = 868$ Hz) thereby indicating that the axial and equatorial fluorine environments are being averaged, and (iv) the −20° ^{31}P spectrum (Figure 1b) is a quintet of triplets centered at +65.8 ppm[6] with $J_{PF} \simeq 870$ and J_{PNCH} (average) $\simeq 26$ Hz.



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On cooling from ambient temperature to −110°, the ^{19}F spectrum of **1** changes from a doublet to a set of five triplets possessing an intensity ratio 1:1:1:3:2 (Figure 1c). If, as is usually found,[7] the equatorial ^{19}F resonances appear at higher field, this is consistent with the ground state struc-