and 3,7-cyclooctadiene-1,2-dione (5 pages). Ordering information is given on any current masthead page.

References and Notes

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Regiocontrolled Anodic Cyanation of Nitrogen Heterocycles. Pyrroles and Indoles

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Abstract: A series of 1-substituted pyrroles and indoles was potentiostatically oxidized at platinum sheet. The anolyte was methanol–sodium cyanide and the reference electrode an SCE. In all instances substitution with cyanide ion was achieved. Annular replacement at a free 2 (or 5) position was favored for pyrroles lacking the substituent on either 2 or 5 (or both) position(s), whereas lateral substitution was favored for compounds with the methyl group on both 2 and 5 positions. Methyl displacement by the cyano group occurred slightly in some cases. The methyl or phenyl group at the 1 position was not attacked. Cyanation of indoles occurred exclusively on the pyrrole moiety of the molecule. In this case side-chain substitution was not observed. A scheme involving initial electron loss from the organic substrates, followed by a fast chemical reaction, can well elucidate products, coulometric data, and voltammetric results. A comparison with the photosensitized electron transfer cyanation in the same solvent system indicates that the above anodic system involves initial cation radical formation. Pyrrolecarbonitriles, annular substitution products, come from direct nucleophilic attack by cyanide ion on methylpyrrole cation radicals prior to competitive deprotonation from a methyl substituent. An MO calculation for the cation radicals by the ω technique supports the observed positional reactivity.

Introduction

The oxidation potential of cyanide ion is considerably low compared with common organic compounds,[1] so cyanide ion in homogeneous solution will not survive the potential necessary to oxidize the reactant. Indeed, there are apparently no reports in the literature describing chemical cyanations that are analogous to the electrochemical reaction.[2]

The discharge of cyanide ion in aqueous solution at a platinum electrode proceeds through an initial irreversible one-electron oxidation with $E_{1/2} \simeq 0.6$ V vs. SCE,[4] while chronopotentiometry in acetonitrile reveals a poorly defined, elongated oxidation transition with $E_{1/4} \simeq 0.9$ V vs. Ag^+/Ag.[5] Potentiostatic steady-state measurements[6,7] and cyclic voltammetry for the $NaCN/CH_3OH$ system indicate no substantial oxidation up to 1.6 V vs. SCE. It is the large positive shift in the anodic limit for this solvent system which permits the electrochemical method to work successfully.

In the last few years[8] we made attempts to avoid a concurrent methoxylation and eventually found this method to be quite useful for the cyanation of compounds containing nitrogen atom(s) or extended π-electron systems.

The present paper describes an anodic cyanation of nitrogen heterocycles.[9] 1-Methylpyrrole (**1**) can, for example, be converted to 1-methylpyrrole-2-carbonitrile (**11**), which can subsequently undergo anodic oxidation to afford 1-methylpyrrole-2,5-dicarbonitrile. Equations 1 and 2 are illustrative.

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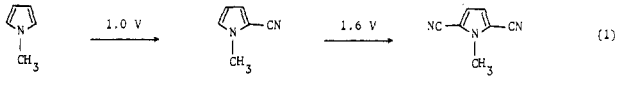
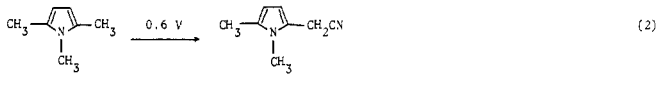
Table I. Preparative Anodic Cyanation Conditions and Products

reactant	E_p, V[a]	E, V[b]	product	bp, °C (mmHg), or mp, °C	yield,[c] %
1-methylpyrrole (**1**)	1.20, 1.74	1.0	1-methylpyrrole-2-carbonitrile	101–103 (27)	64
1,2-dimethylpyrrole (**2**)	0.98, 1.53	1.1	1,5-dimethylpyrrole-2-carbonitrile	53.5–55	60
			1-methylpyrrole-2-acetonitrile	oil	tr
1,3-dimethylpyrrole (**3**)	1.08	1.0	1,3-dimethylpyrrole-2-carbonitrile	53.5–54.5	74
			1,4-dimethylpyrrole-2-carbonitrile	oil	13
1,2,3-trimethylpyrrole (**4**)	0.86, 1.31	0.9	1,4,5-trimethylpyrrole-2-carbonitrile	68–68.5	83
1,2,4-trimethylpyrrole (**5**)	0.90, 1.46	0.9	1,3,5-trimethylpyrrole-2-carbonitrile	44.5–45	69
1,3,4-trimethylpyrrole (**6**)	0.96, 1.47	0.9	1,3,4-trimethylpyrrole-2-carbonitrile	50–50.5	79
1,2,5-trimethylpyrrole (**7**)	0.81, 1.01	0.55	1,5-dimethylpyrrole-2-carbonitrile		1
			1,5-dimethylpyrrole-2-acetonitrile	90–91	29
			1,2,5-trimethylpyrrole-3-carbonitrile	76–85	1
1,2,3,4-tetramethylpyrrole (**8**)	0.76, 1.28	0.7	1,3,4,5-tetramethylpyrrole-2-carbonitrile	74.5–75.5	87
			1,3,4-trimethylpyrrole-2-acetonitrile	198–203	2
1,2,3,5-tetramethylpyrrole (**9**)	0.67, 0.91, 1.34	0.35	1,4,5-trimethylpyrrole-2-carbonitrile		2
			1,3,5-trimethylpyrrole-2-acetonitrile	94–94.5	17
			1,4,5-trimethylpyrrole-2-acetonitrile	95–97	25
1,2,3,4,5-pentamethylpyrrole (**10**)	0.59, 0.80, 1.31	0.25	1,3,4,5-tetramethylpyrrole-2-acetonitrile	70–72	60
1-methylpyrrole-2-carbonitrile (**11**)	1.73	1.6	1-methylpyrrole-2,5-dicarbonitrile	101–102.5	34
1-methylpyrrole-2-acetonitrile (**12**)	1.23	1.2–1.4	5-cyano-1-methylpyrrole-2-acetonitrile	126.5–127.5	17
ethyl 1-methylpyrrole-2-acetate (**13**)	1.14, ~1.7	1.2	methyl 5-cyano-1-methylpyrrole-2-acetate[d]	oil	28
1-phenylpyrrole (**14**)	1.34	1.2	1-phenylpyrrole-2-carbonitrile	65–66	82
2,5-dimethyl-1-phenylpyrrole (**15**)	0.92, 1.30, 1.56	0.65	5-methyl-1-phenylpyrrole-2-acetonitrile	37.5–40	53
			2,5-dimethyl-1-phenylpyrrole-3-carbonitrile	61–67	5
2,3,5-trimethyl-1-phenylpyrrole (**16**)	0.82, 1.27, 1.56	0.5	3,5-dimethyl-1-phenylpyrrole-2-acetonitrile	oil	16
			4,5-dimethyl-1-phenylpyrrole-2-acetonitrile	oil	34
2,3,4,5-tetramethyl-1-phenylpyrrole (**17**)	0.71, 1.23 1.50	0.4	3,4,5-trimethyl-1-phenylpyrrole-2-aceto-nitrile	oil	67
1-methylindole (**18**)	1.09, 1.58	1.3	1-methylindole-2-carbonitrile	68–69	50
			1-methylindole-3-carbonitrile	oil	9
3-methylindole (**19**)	0.88, 0.97	1.6	3-methylindole-2-carbonitrile	102–103.5	16
1,2-dimethylindole (**20**)	0.98, 1.48	0.8	1,2-dimethylindole-3-carbonitrile	104–105	45
1,3-dimethylindole (**21**)	0.93, 1.48	0.6	1,3-dimethylindole-2-carbonitrile	70–71	77
1,2,3-trimethylindole (**22**)	0.82, 1.06 1.35, 1.50	0.8	no cyanation		
1-methylcarbazole (**23**)	1.20				

[a] Peak potential from cyclic voltammetry. Pt anode, CH_3OH, 0.4 M NaCN. SCE reference. Scan rate is 0.1 V/s. Values are obtained on first scan from 0.00 to 2.00 V. Substrate concentration is 2×10^{-2} M. All voltammograms showed no cathodic peak corresponding to reversible reduction of a cation radical. [b] Potential for preparative electrolysis. [c] Based on pyrrole used. This yield corresponds to the current efficiency since the reaction was terminated at the stage when 2 F/mol of electricity was passed. [d] A base-catalyzed ester interchange. [e] Electrode filming.





The possible products are currently subjects of great interest and are also useful as the important precursors in manufacturing antiinflammatory agents such as aminoquinazolines, phenothiazines, or triazines.[10] Pyrroleacetonitriles and carbonitriles, the expected products of cyanation, are usually obtained from Mannich bases and aldoximes, respectively, but most of the reported routes are tedious to carry out and of poor yield in some cases.[10f,11]

Results

Preparative electrolyses were performed potentiostatically in a three-compartment cell at 25 °C. The anodic, cathodic, and reference electrode solutions were separated by glass frits which allowed enough diffusion for conductivity but prevented gross mixing of these three solutions. This simplifies the chemistry. The anode was a platinum sheet and the reference electrode was an SCE. Methanol–0.4 M sodium cyanide was used in both anode and cathode compartments. The anode and cathode compartments were crudely purged with nitrogen in most experiments to prevent the oxidation of the starting material by air. The background current with this system was negligible up to 1.4 V. During the run the current dropped with time and was discontinued when the background level was reached. The reaction time for pyrrole oxidation was about 12 h. Coulometry was accomplished with an electronic counter.

The products reported in Table I were isolated by using a usual technique such as distillation, recrystallization, or preparative VPC, following extraction with ether and water. They were identified by the elemental and ^1H NMR, IR, and mass spectroscopic analyses and by comparison with the authentic samples prepared by other routes. *Caution:* A methanolic sodium cyanide solution must be handled in a well-ventilated room as it contains hydrogen cyanide as a results of the equilibrium between CN^- and the solvent methanol!

The anodic substitution of pyrroles occurs preferentially at the 2 (and 5) position. In all instances monocyanation products were formed. When the substituent is attached to the 2 position, further substitution of the pyrrole ring occurs at a free 5 position without distinction of the nature of the substituent already present. The 2,5-dialkyl compounds lead to the for-

mation of side chain substitution products, viz., pyrroleacetonitrile. The introduction of a methyl group in the 3 position has significant control over the orientation of the substituted products to give both the 2- and the 5-substituted products, whereas symmetric polymethylpyrroles afford a single product. Methyl displacement by the cyano group occurs slightly in some cases. The product yields from 1-phenylpyrroles are superior to those from 1-methylpyrroles. The alkyl or aryl group at the 1 position is not attacked. Cyanation of indoles occurs exclusively on the pyrrole moiety of the molecule. Furthermore, the reaction point of 1-methylindole in the present anodic reaction is intriguing: electrophilic substitution usually occurs at the 3 position,[12] while the present anodic reaction predominantly takes place on the 2 position. Side-chain displacement of methylindoles was not observed. The current efficiency for the formation of these cyanides increases with decreasing amounts of passed electricity. Methoxylation, which is often observed as a side reaction in the anodic oxidation in methanolic cyanide solution, was suppressed completely. Isocyanation[13] was not observed. The technique is synthetically attractive because of this positional selectivity, the mild conditions, and clean reaction products. It should be applicable to many types of nitrogen heterocycles.

The yield of side chain substitution products is not always high. This would be ascribable to the close oxidation potentials of the starting material and the primarily generated monosubstitution product. At the controlled potential used in preparative electrolysis, the primary product would be consumed as well by further oxidations ($(EC)_n$ process). In fact, the current efficiency for the formation of 1-methylpyrroleacetonitriles decreases with increasing amounts of passed electricity. In addition, the anodic oxidation of 1,5-dimethylpyrrole-2-acetonitrile does not give the simple products: VPC of the reaction mixture showed many peaks and the expected product, 1-methyl-2,5-bis(cyanomethyl)pyrrole,[14] could not be identified.

Cyclic voltammograms were recorded for each compound using a solution of 0.4 M sodium cyanide in methanol. A two-compartment cell was employed in which the SCE reference electrode with an agar bridge was separated from the platinum anode and the cathode by a glass frit. The background current with this system began to increase at potentials more anodic than 1.60 V. The E_p values are collected in Table I. 1-Methylpyrrole gave two anodic peaks. The electrochemical data revealed that the height of the first peak varied linearly with concentration, and there was no evidence of a reversible cathodic peak for any of the pyrroles even at sweep rates of 100 V/s. The current function, $i_p/v^{1/2}C^*$, where i_p is the peak current, v is the scan rate, and C^* is the concentration of the pyrrole, decreased, and E_p shifted more positive with increasing scan rate. The second oxidation peak was attributed to the oxidation of the product since cyclic voltammograms of the nitrile alone had identical oxidation potential. Also, after completion of the electrolysis, the first oxidation peak was not observed, but the second with increased height was. Similar voltammetric data were noted for other substituted pyrroles. Controlled-potential electrolysis indicated that $n = 2$. All of the preceding data are consistent with a fast chemical reaction following the electron transfer.

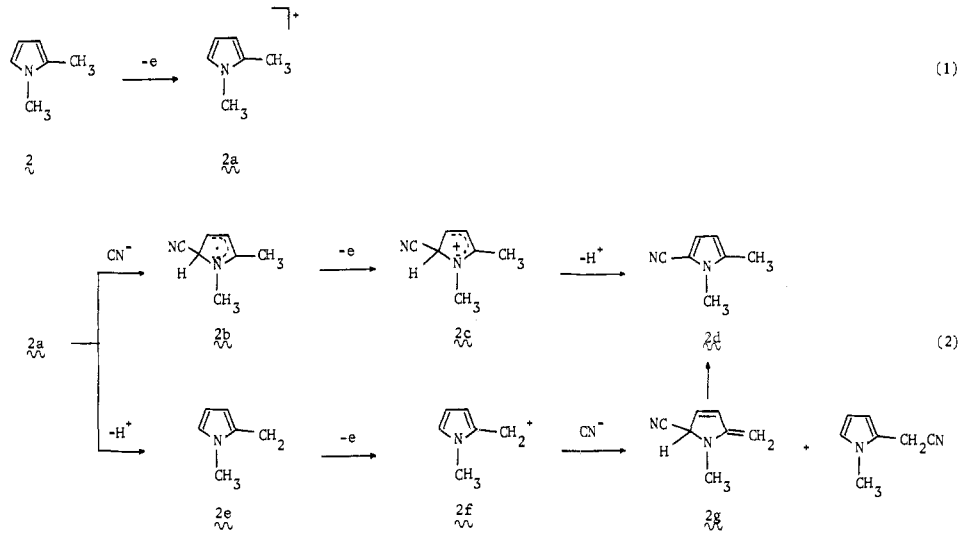
Discussion

The cyanation products for a variety of substituted pyrroles have been characterized. Two general reaction types are observed: side-chain substitutions are favored for pyrroles having an alkyl substitutent on both 2 and 5 positions and ring substitutions for compounds lacking the substituent on either 2 or 5 (or both) position(s). These reactions have some synthetic interest as a route to pyrroleacetonitriles and pyrrolecarbonitriles. Most importantly, this study begins to reveal the anodic reactivity of a variety of nitrogen heterocycles. The following discussion correlates the results, suggests mechanistic explanations, and explores the analogy between photosensitized electron transfer and anodic reactions.

Mechanism. Both annular and lateral oxidation of alkylpyrroles are formally a 2-equiv change. Consideration of the voltammetric characteristics, coulometry, and products leads to mechanistic Scheme I, illustrated for 1,2-dimethylpyrrole. The first step is the electron-transfer step which involves the direct discharge of the substrate. Most of these pyrroles oxidize well below the onset of background processes and show well-defined cyclic voltammetry peaks (Table I). Reactions were performed at potentials near the first voltammetric wave. At the potential region adopted only organic substrates are oxidized to produce a cation radical intermediate. The ionization potential of methylpyrrole and indole is relatively low and their cation radicals have clearly been recognized in the gas phase.[15] The propriety of the proposed mechanism that anodic cyanation involves initial cation radical formation is proved as well by comparison with the photosensitized electron transfer reaction, as discussed below.

Two competitive pathways for reaction of this alkylpyrrole cation radical are considered. Firstly, the anodically generated cation radical **2a** is attacked by the cyanide ion to produce the radical **2b,** followed by further anodic oxidation and successive

Scheme I



proton release, thus leading to the annular cyanation product (**2d**). Alternatively, **2a** could undergo deprotonation to afford an analogue of a benzylic radical intermediate **2e,** which would subsequently undergo anodic oxidation to give a cation **2f,** followed by nucleophilic attack by cyanide ion to give 5-methylene-1-methyl-3-pyrroline-2-carbonitrile (**2g**), which should be eventually aromatized in protic solvents. Indeed, compounds of the type **2g** would be important as reaction intermediates. 5-Methylene-2,5-dihydro-2-furonitrile is a primary product of abnomal product formation in the reaction of 2-(chloromethyl)furan with aqueous cyanide solution.[16] Substitution with rearrangement (S_N') of chlorine (or trimethylamine) by cyanide is also observed with other chloromethyl (or trimethylammonium-methyl) heterocyclic compounds.[9,11i,17] The reaction of 2-dimethylaminomethyl-1-methylpyrrole methiodide with sodium cyanide in water gave rise to 1,2-dimethylpyrrole-5-carbonitrile (**2d**) as well as 1-methylpyrrole-2-acetonitrile (1:6). The reaction of 3-trimethylammonium methylindole with aqueous sodium cyanide produced not only 1-methylindole-3-acetonitrile but also 1,3-dimethylindole-2-carbonitrile. To distinguish these two possibilities, anodic oxidation of 1,2-dimethylpyrrole was examined in the methanol-*O-d* solution of sodium cyanide. Incorporation of deuterium in the 2-methyl group of compound **2d,** 1,2-dimethylpyrrole-5-carbonitrile-*2-d,* was not observed (mass and NMR spectroscopies). Trace amounts of 1-methylpyrrole-2-acetonitrile were detected. Therefore, the latter mechanism is not important for annular substitution. Analogous results were obtained in the case of anodic cyanation of 1,3-dimethylindole in methanol-*O-d.* In this case, 1-methylindole-3-acetonitrile could not be detected.

Photosensitized Electron Transfer Cyanation. It is of interest to compare these electrochemical results with the photosensitized electron transfer reaction using electron-accepting sensitizers in the same solvent system to estimate the reactivity of the solution-phase cation radicals. It is known that these heterocyclic compounds form fluorescent exciplexes with electron-accepting sensitizers such as 1-cyanonaphthalene, 1,4-dicyanobenzene, or methyl *p*-cyanobenzoate,[18] and in polar media exciplexes can dissociate before reaction into the solvent-separated ion radicals.[19]

Typical conditions for the photosensitized cyanations undertaken in this study involve irradiation[20] of a solution of heterocycle (0.04 M), sensitizer (0.04 M), and sodium cyanide (0.4 M) in methanol. A Pyrex filter, which absorbs radiation of wavelengths shorter than 280 nm, was used in all experiments to ensure that direct excitation of the substrate does not occur. Under these conditions light is absorbed only by the sensitizer. The sensitizer was partially recovered.[21] The involvement of the sensitizer was easily confirmed; upon irradiation under identical conditions, but in the absence of a sensitizer, no reaction occurred.

Table II summarizes the results of the photosensitized reaction, together with the corresponding data from the electrochemical reaction. Unsymmetric 1,3-dimethylpyrrole was chosen as a model compound in order to estimate orientation of the substitution products. The isomer distribution of the resulting products coincided in both cases (entry 4). Substitution of 1-methylindole occurred preferentially and again on position 2. The observation that the same product mixture is formed and that in the same ratio both electrochemically and via photosensitized electron transfer reaction is consistent with the hypothesis that the anodic cyanation involves initial cation radical formation. Scheme II accounts for these observations.

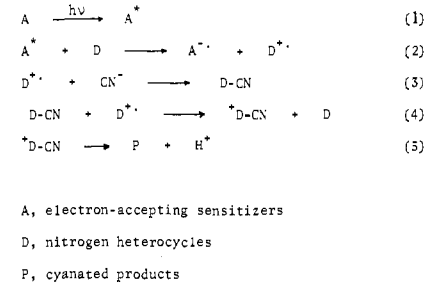
Step 1, excitation of the photosensitizer, is assured by the use of an appropriate filter. Furthermore, no reaction is observed upon irradiation of D under identical conditions except for the absence of a sensitizer. Step 2 may involve several intermediate stages (encounter complex, excited complex, solvated ion radical pair, etc.), but leads finally to the solvent-separated ion radicals.[19,24] The latter half of this mechanism (steps 3–5) is similar to those proposed for the anodic reaction. Step 3 involves reaction of the cation radical with the nucleophile. This reaction is closely related to, and in fact should complement, anodic reaction. In the anodic process the cation radical would be near the anode and the radical resulting from the anodically generated cation radical–cyanide anion combination reaction would further be oxidized to the corresponding carbonium ion, which subsequently should release a proton.

Table II. Photosensitized Electron Transfer[a] and Anodic Cyanation Products

entry	substrate (λ,[b] nm)	sensitizer[c]	position substituted	isomer distribution, % photosensitized	anodic
1	**1**(437)	A	2	100[d]	100
2	**1**	B	2	100[e]	
3	**2**	B	5	100[f]	100
4	**3**	B	2	85[g]	85
			5	15	15
5	**14**	A	2	100[h]	100
6	**14**	B	2	100[i]	100
7	**18**(440)	A	2	83[j]	85
			3	17	15
8	**18**	B	2	84[k]	
			3	16	

[a] [Substrate] = [sens] = 0.02 M. [b] Wavelengths of maximum emission for exciplexes with 1-cyanonaphthalene in benzene (data from ref 18). [c] A, 1-cyanonaphthalene (irradiation, 6 h); B, 1,4-dicyanobenzene (2.5 h). [d-k] % yield based on unrecovered substrate (fraction of unrecovered substrate, %). [d] 23 (31). [e] 49 (29). [f] 50 (17). [g] 30 (43). [h] 40 (16). [i] 51 (38). [j] 13 (29). [k] 25 (80).

Scheme II

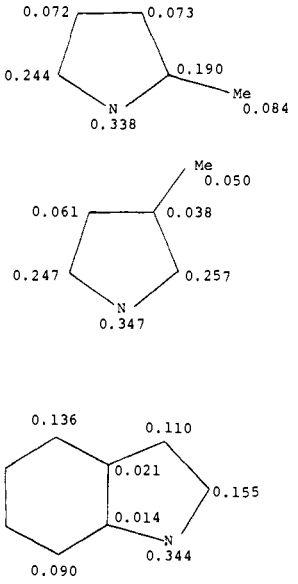


Regioreactivity. One major advantage of the present reaction lies in its high selectivity with regard to the position of attack. Cyanation occurs exclusively on the α-type position of the pyrrole ring. According to the proposed mechanism in Scheme I, it is to be expected that the carbon atoms of a higher positive charge in the cation radical would react more readily with a nucleophile. Net charge distributions calculated for these cation radicals by the ω technique are shown in Chart I. The following parameters were used: $h = 3.0$ and $k = 0.8$ for methyl group, $h = 1.5$ and $k = 1.0$ for pyrrole nitrogen (same for N–H, N–CH_3), $\delta = 0.1$, $\omega = 1.4$ (heteroatom model). It is clear that in all cases the greatest positive charges are imparted on the α positions, in accord with the products obtained. The calculated spin density distribution does not support the observed reactivity of 1-methylindole.

Conclusion

This study has revealed that the general reaction of alkylpyrroles is the positionally selective substitution with cyanide ion. Application to symmetric alkylpyrroles should prove especially profitable from a synthetic viewpoint. Consideration

Chart I. Net Charge Distributions of Cation Radicals of Methylpyrrole and Indole (ω Technique)



of the voltammetric characteristics and products leads to the initial oxidation of organic substrates. This reaction shows great similarities to photosensitized electron transfer reaction. The latter reaction proceeds via a free cation radical intermediate; it thus appears that the electrochemistry is controlled by formation and reaction of a similar species. The observed positional reactivity of the cation radicals is shown to be consistent with an MO reactivity index.

Experimental Section

Equipment. A Jasco Model IR-E IR spectrophotometer, a JEOL Model JNM-C-60HL NMR spectrometer, and a Hitachi Model RMS-4 mass spectrometer were used for structure determination.

Cyclic voltammetry was performed in a two-compartment cell in which the calomel reference electrode with an agar bridge was separated from the platinum anode and the cathode by a glass frit. The working electrode was a 1-cm platinum wire sealed in glass, and the auxiliary electrode was a platinum sheet. A Hokuto Denko HB-107A voltage scanner, HA-104 potentiostat, and Yokogawa Type 3083 XY recorder were used. All measurements were carried out at 25 °C.

Controlled-potential electrolyses were performed by using a three-compartment cell (which separated the anode, cathode, and reference electrode solutions by glass frits). The anode compartment held 50 mL of anolyte, the cathode held 20 mL of catholyte, and the reference held 5 mL of an electrolyte solution. An 8-cm^2 platinum sheet was employed as the anode. A platinum wire was used as the cathode, and an SCE with an agar bridge as the reference. Anode potential was controlled by means of a Yanaco Model VE-3 controlled-potential electrolyzer.

Coulometry was carried out with a Hokuto Denko Model HF 108A current integrator.

Materials. Methanol was purified by fractional distillation from magnesium methoxide. Reagent grade sodium cyanide was used.

1-Methylpyrrole (**1**) and 3-methylindole (**19**) were obtained commercially and were purified by distillation and recrystallization, respectively.

Most 1-methylpyrroles (**2–6, 8, 10**) were prepared by N-methylation of potassium salts of the corresponding pyrrole according to the method of Hinman and Theodoropulos.[26] The parent pyrroles were obtained according to the literature: 2-methylpyrrole, 2,3-dimethylpyrrole, 3,4-dimethylpyrrole, 2,3,4-trimethylpyrrole,[26] 3-methylpyrrole,[27] 2,4-dimethylpyrrole,[28] and 2,3,4,5-tetramethylpyrrole.[29]

1,2,3,5-Tetramethylpyrrole (**9**) was prepared by the hydrazine reduction of 3-formyl-1,2,5-trimethylpyrrole[26] according to a modification of the procedure of Rips and Buu-Hoï.[30]

The following materials were prepared according to the literature: 1,2,5-trimethylpyrrole (**7**),[31] 1-methylpyrrole-2-carbonitrile (**11**),[11b] 1-methylpyrrole-2-acetonitrile (**12**),[32] ethyl 1-methylpyrrole-2-acetate (**13**),[33] 1-phenylpyrrole (**14**),[34] 2,5-dimethyl-1-phenylpyrrole (**15**),[35] 2,3,5-trimethyl-1-phenylpyrrole (**16**),[30] 2,3,4,5-tetramethyl-1-phenylpyrrole (**17**),[30] 1-methylindole (**18**),[36] 1,2-dimethylindole (**20**),[36a] 1,2,3-trimethylindole (**22**),[37] 1-methylcarbazole (**23**),[38] and 1-methylindole-3-acetonitrile.[10i,11a] 1,3-Dimethylindole (**21**) was obtained by methylation of skatole according to the procedure of Potts and Saxton.[36] 1,2-Dimethylpyrrole-5-carbonitrile and 1,3-dimethylindole-2-carbonitrile were obtained together with 1-methylpyrrole-2-acetonitrile and 1-methylindole-3-acetonitrile, respectively.

1-Methylindole-3-carbonitrile was prepared from 3-formyl-1-methylindole[39] by a modification of the method of Blatter, Lukaszewski, and de Stevens,[40] bp 115 °C (5 mm).

General Electrolysis Procedure. The anolyte (50 mL) was made up of the organic substrate (2 mmol) in methanolic sodium cyanide solution (0.4 M). The catholyte was a methanolic solution of sodium cyanide. The anode and cathode compartments were crudely purged with nitrogen in most experiments. The reaction was carried out at a controlled anode potential at 25 °C. During the electrolysis, the solution was stirred magnetically. Reaction was usually discontinued when the current dropped to ~5 mA, which generally took 10 h. To the electrolyzed mixture were added internal standards for VPC analyses, the mixture was treated with water, and the organic material was extracted with ether. The ethereal solution was analyzed by VPC using either an Apiezon-L column or a PEG 6000 column.

The products were purified by either distillation or recrystallization and characterized spectroscopically as detailed in Table III. In the cases where isomeric nitriles were produced, isolation was made by preparative VPC. Satisfactory elemental analysis data were obtained for all compounds.

If methanol-*O-d* was employed as a solvent, the anolyte was concentrated, triturated with methylene chloride, filtered, reduced to 1–2 mL on a rotary evaporator, and analyzed by VPC.

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Supplementary Material Available: ^{1}H NMR, IR, and mass spectral data and elemental analyses (Table III) for the products (5 pages). Ordering information is given on any current masthead page.

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Syntheses, Properties, and Photoelectron Spectra of Substituted and Layered [2.2](2,6)Pyridinoparacyclophanes

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Abstract: Syntheses of methyl-substituted [2.2](2,6)pyridinoparacyclophanes **15**, **16**, and **17**, as well as their corresponding 1,9-dienes, **19**, **20**, and **21**, are reported. The triple-layered [2.2](2,6)pyridinoparacyclophanes **23**, **24**, and **30** have also been prepared. The temperature-dependent NMR behavior of the simple [2.2](2,6)pyridinoparacyclophanes is in accord with a geometry where the pyridine ring is more or less parallel to the benzene ring, but undergoing rapid conformational flipping with an energy barrier of about 12 kcal/mol. The triple-layered cyclophane **30** shows a similar behavior, but with a slightly smaller energy barrier (11 kcal/mol). However, the apparent geometry of the corresponding 1,9-dienes has the pyridine ring essentially perpendicular to the benzene ring. This is true also of the triple-layered cyclophane **23**, where both pyridine rings are almost perpendicular to the central benzene ring. The [2.2](2,6)pyridinoparacyclophanes show enhanced basicity compared to simple model pyridine derivatives, whereas their 1,9-diene analogues show greatly reduced basicity. Photoelectron spectra have been measured for a number of the [2.2](2,6)pyridinoparacyclophanes and their corresponding 1,9-dienes and orbital assignments have been proposed for their lower energy ionization potentials.

In a previous study,[2] syntheses of [2.2](2,6)pyridinoparacyclophane (**14**) and its corresponding 1,9-diene **18** were reported together with the interesting observation that the NMR spectrum of **14** is temperature dependent, indicating conformational mobility, whereas the NMR spectrum of **18** is temperature independent. Furthermore, an X-ray crystallographic analysis of [2.2](2,6)pyridinoparacyclophane-1,9-diene (**18**) showed the two aromatic rings in this molecule to be essentially perpendicular to each other.[3] To gain a better understanding of the physical and chemical properties of this type of structure, we have now prepared a series of methyl-substituted derivatives and three triple-layered analogues.

The syntheses of the methyl-substituted derivatives are summarized in Scheme I. In each case, the intermediate dithiacyclophane (**6–9**) was converted to the corresponding ring-contracted compound (**10–13**) by the benzyne–Stevens rearrangement procedure.[4] Benzyne was generated thermally from 1-(2′-carboxyphenyl)-3,3-dimethyltriazene,[5] and overall this proved to be a much more efficient and convenient procedure than the simple Stevens rearrangement reported earlier for the parent case (**6**).[2] Treatment of the phenylthiacyclophanes (**10–13**) with Raney nickel catalyst gave the [2.2](2,6)pyridinoparacyclophanes (**14–17**) in good yield, whereas oxidation of the phenylthiacyclophanes (**10–13**) to the corresponding bissulfoxides, followed by thermal elimination, gave the [2.2](2,6)pyridinoparacyclophane-1,9-dienes (**18–21**) in fair to good yields.

The first property examined for these methyl-substituted [2.2](2,6)pyridinoparacyclophanes was their nuclear magnetic resonance behavior. Each of the [2.2](2,6)pyridinoparacyclophane-1,9-dienes (**18–21**) showed a symmetrical pattern in its ^{1}H NMR spectrum, which was temperature independent. Thus, either the barrier to conformational flipping in these compounds is quite low or, as is more likely, these compounds

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