H, m), 5.8–6.2 (2 H, m), 6.3–6.5 (1 H, m); *m/e* 326 (M^+), 311, 236, 221, 208, 118, 105, 104, 103.
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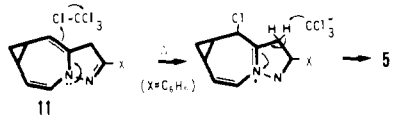
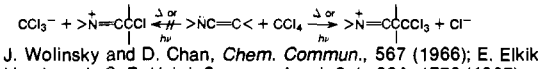
(11) A referee suggested the possibility of chlorination at the β position of the enamine function of **11** to give **5** by an ionic pathway as shown in Scheme III. It has been reported, however, that the thermal and photochemical re-

Scheme III



11

actions[12] of carbon tetrachloride with enamines do not afford chlorination products, but instead give rise to alkylation products.



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Regiospecific Anodic Cyanation of Pyrroles and Indoles

Sir:

I wish to report here that pyrrole cyanides are directly generated in high yield from pyrroles by an anodic process. The results obtained reveal a unique and potentially useful reaction which should be general for nitrogen heterocycles. Pyrrole cyanides are in general obtained from Mannich bases or aldoximes, but most of the reported routes are tedious to carry out and of poor yield in some cases.[1]

It was at first anticipated that, if the anodic oxidation of pyrroles is conducted in methanolic cyanide solution, a 1,4 addition of cyano and/or methoxy group to pyrrole ring would be observed to produce 3-pyrrolines, by analogy with our previous results of anodic cyanomethoxylation of 2,5-dimethylfuran and thiophene.[2] However, substitution products were exclusively formed.

The procedure is described for the conversion of 1-methylpyrrole to 1-methylpyrrole-2-carbonitrile. The reaction was performed at a controlled anode potential of 1.0 V vs. SCE, in a divided cell with platinum plate electrodes having an area of 8 cm^2 and a magnetic stirrer bar in the anode compartment, at room temperature, in methanolic sodium cyanide solution (organic substrate, 0.4 M; cyanide, 0.8 M). The oxidation was terminated after passage of 2 F/mol of added pyrrole. The anolyte was worked up by distillation of the methanol. Then, saturated aqueous NaCl was added and the mixture extracted in ether. The ethereal solution was dried over anhydrous magnesium sulfate, filtered, and evaporated, and the residual oil was distilled under reduced pressure (bp 101–103 °C (27 mmHg)). The distillate consisted of a single component. The product was identified by IR, mass, and NMR spectroscopy to be 1-methylpyrrole-2-carbonitrile, 64% yield. Anal. Calcd for $C_6H_6N_2$: C, 67.90; H, 5.70; N, 26.40. Found: C, 67.94; H, 5.68; N, 26.40.

Table I summarizes the results of electrochemical reactions using other compounds. All products were identified by the elemental and spectroscopic analyses and by comparison with the authentic samples prepared by other routes. One major advantage of the present reaction lies in its high selectivity with regard to the position of attack. VPC of the reaction product generally showed a single peak. The product yields from 1-phenylpyrroles are superior to those from 1-methylpyrroles. Cyanation of indoles occurs exclusively on the pyrrole part of the indole molecule. The reaction point of 1-methylindole in the present nucleophilic substitution is intriguing: electrophilic substitution usually occurs at position 3,[3] while the present anodic cyanation predominantly takes place on position 2. The alkyl or aryl group at the 1 position is not attacked. The current efficiency for the formation of pyrrole cyanides increases with decreasing amounts of passed electricity. Methoxylation, which is often observed as side reaction in the anodic oxidation in methanolic cyanide solution, was suppressed completely. Isocyanation was not observed.

At the potential adopted only organic substrates are oxidized to produce cation radical intermediates.[2a] If the reaction of the

Scheme I

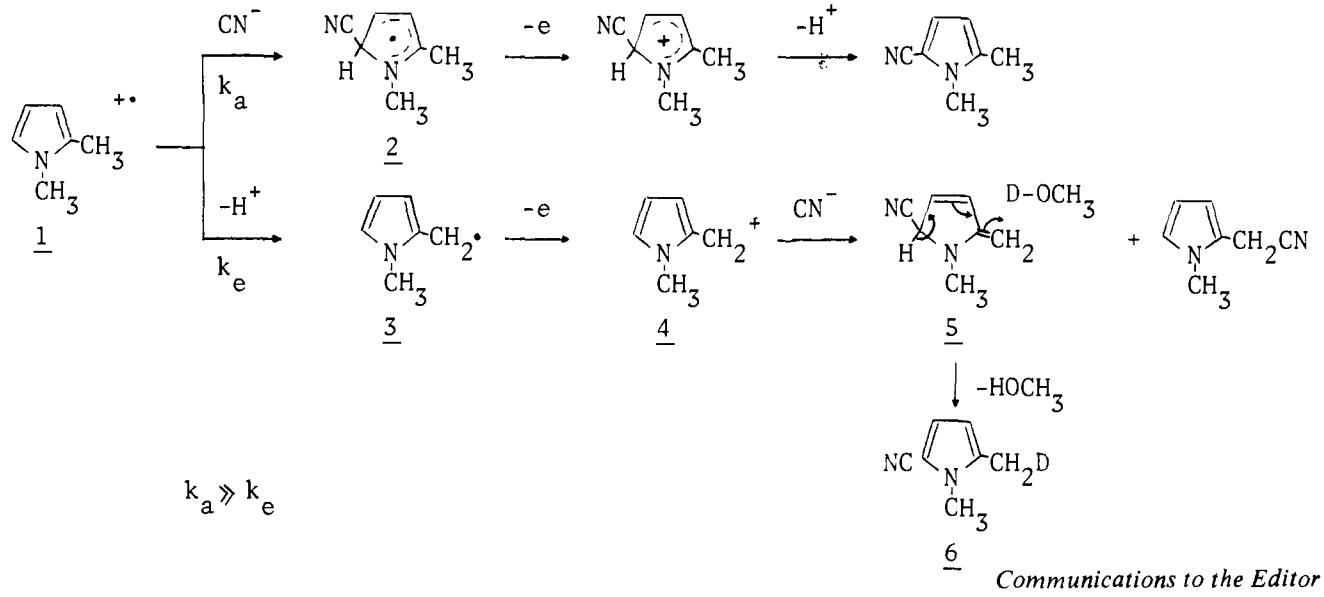
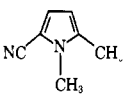
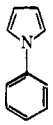
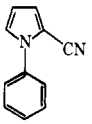
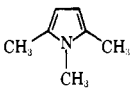
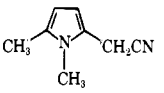
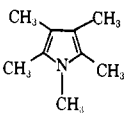
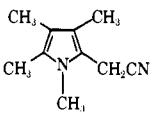
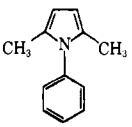
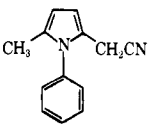
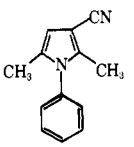
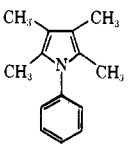
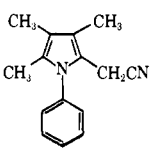
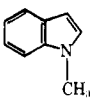
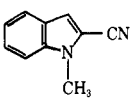
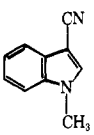
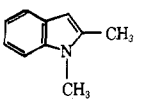
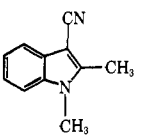
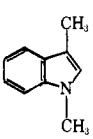
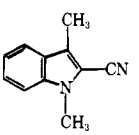
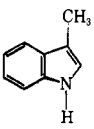
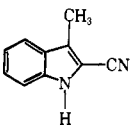


Table I. Anodic Cyanation Products of Pyrroles and Spectroscopic Data

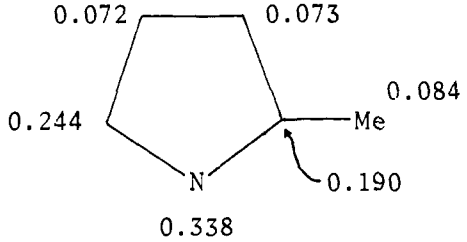
Reactant	E_p, V[a]	E, V[b]	Product	Bp, °C (mmHg) or mp, °C	IR, ν_{CN}, cm^{-1}	MS, m/e (M^+)	^1H NMR,[c] δ, ppm (J in Hz)	Yield, %[d]
	1.25	1.00		101–103 (27)	2240 (s)	106	3.72 (3 H, s) 6.10 (1 H, s) 6.0–6.2 (1 H, m) 6.6–6.85 (1 H, m)	64
	0.98	1.10		53.5–55	2240 (s)	120	2.23 (3 H, s) 3.59 (3 H, s) 5.88 (1 H, d, J = 3.8) 6.67 (1 H, d, J = 3.8)	60
	1.34	1.20		65–66	2240 (s)	168	6.31 (1 H, m) 6.2–6.38 (1 H, m) 6.85–7.1 (1 H, m) 7.40 (5 H, s)	82
	0.81	0.55		90–91	2240 (w)	134	2.18 (3 H, s) 3.41 (3 H, s) 3.61 (2 H, s) 3.78 (1 H, d, J = 3.8) 3.96 (1 H, d, J = 3.8)	29
	0.59	0.25		70–72	2250 (w)	162	1.90 (3 H, s) 1.95 (3 H, s) 2.10 (3 H, s) 3.45 (3 H, s) 3.62 (2 H, s)	60
	0.92	0.65		38–40	2280 (w)	196	2.00 (3 H, s) 3.41 (2 H, s) 5.95 (1 H, m) 6.17 (1 H, m) 7.1–7.6 (5 H, m)	53
				65–67	2250 (s)	196	1.96 (3 H, s) 2.13 (3 H, s) 6.02 (1 H, s) 7.0–7.7 (5, H, m)	5
	0.71	0.40			2270 (w)	224	1.92 (3 H, s) 1.97 (3 H, s) 2.03 (3 H, s) 3.38 (2 H, s) 7.1–7.6 (5 H, m)	67
	1.09	1.30		68–69	2250 (s)	156	3.85 (3 H, s) 7.1–7.8 (5 H, s)	50
				115 (5)	2250 (s)	156	3.80 (3 H, s) 7.2–7.95 (5 H, m)	9
	0.98	0.80		104–105	2240 (s)	170	2.53 (3 H, s) 3.65 (3 H, s) 7.1–7.8 (4 H, m)	45
	0.93	0.60		70–71	2240 (s)	170	2.44 (3 H, s) 3.77 (3 H, s) 6.9–7.7 (4 H, m)	77
	0.88	1.61		102–103.5	2240 (s)	156	2.48 (3 H, s) 7.1–7.7 (4 H, m) 8.0–8.5 (1 H, s, br)	16

[a] Peak potential from cyclic voltammetry. Pt anode, CH_3OH, 0.4 M NaCN. SCE reference. Scan rate is 100 mV/s. Values are obtained on first scan from 0.00 to 1.80 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] 60 MHz, $CDCl_3$ solution. [d] 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.

1,2-dimethylpyrrole cation radical with the nucleophile is considered, there are two initial possibilities. Firstly, the anodically generated cation radical **1** is attacked by the cyanide ion to produce the radical **2**, followed by further anodic oxidation and successive proton release, thus leading to the aromatic cyanation product. Alternatively, **1** could undergo deprotonation to afford an analogue of a benzylic radical intermediate **3**, which would subsequently undergo anodic oxidation to give a cation **4**, followed by nucleophilic attack by cyanide ion to give 5-methylene-1-methyl-3-pyrroline-2-carbonitrile (**5**, Scheme I) which should be eventually aromatized in protic solvents. Indeed, the compound of the type of **5** would be important as a reaction intermediate. 5-Methylene-2,5-dihydro-2-furonitrile is a primary product of abnormal product formation in the reaction of 2-(chloromethyl)furan with aqueous cyanide solution.[4] The reaction of 2-dimethylaminomethyl-1-methylpyrrole methiodide with sodium cyanide in water[5] gave rise to 1,2-dimethylpyrrole-5-carbonitrile (**6**) as well as 1-methylpyrrole-2-acetonitrile (1:6). To distinguish these two possibilities, anodic oxidation of 1,2-dimethylpyrrole was examined in the CH_3OD–NaCN system. Incorporation of deuterium in the 2-methyl group of compound **6**, 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 so important for this reaction ($k_a \gg k_e$).

The current efficiency for these reactions was 60% or so and the remainder of the current would consumed with side reactions. Anodically generated cationic species chemically oxidize cyanide ion to regenerate the parent neutral substrate or the radical **2** and produce cyano radical, which might attack the coexisting cyanide ion to form cyanogen anion radical or dimerize to cyanogen.

In order to evaluate qualitatively the distribution of the positive charge in the 1,2-dimethylpyrrole cation radical, a MO calculation by the ω technique was carried out.[6] These data showed a relatively high charge density at position 5, thus supporting the observed reactivity at this position.



Acknowledgment. This work was supported by a grant from the Ministry of Education.

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(5) W. Herz and J. L. Rogers, *J. Am. Chem. Soc.*, **73**, 4921 (1951).
(6) The parameters used were as follows: $h = 3.0$ 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).

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Novel Phosphonothioate Substrates for Phosphodiesterases

Sir:

Phosphodiesterases of the 5′-nucleotidase type[1] have been found to hydrolyze *O-p*-nitrophenyl phenylphosphonothioate (I). In addition they hydrolyze very rapidly 3-carboxy-4-nitrobenzene phenylphosphonyl disulfide (II), bis(phenylphosphonyl) disulfide (III), and probably 3-carboxy-4-nitrobenzene phenylphosphonyl trisulfide.

Compound I was made by hydrolysis of bis(*O-p*-nitrophenyl) phenylphosphonothioate[2] (10 g) in 1 M KOH (82.4 mL) with CH_3CN (150 mL) with vigorous shaking for 50 min at 25 °C. After removal of CH_3CN the aqueous residue was adjusted to pH 5 with Dowex 50W/H^+, extracted with ether (12 × 25 mL), and then evaporated. Addition of excess aqueous 1 M cyclohexylammonium chloride to a concentrated aqueous solution of I (K^+ salt) yielded the cyclohexylammonium salt of I as an oil which crystallized on cooling. Recrystallization from CH_3CN yielded white needles;[3] the ultraviolet spectrum of this salt had $\lambda_{max}^{H_2O}$ at 292 (ϵ 9560). ^{31}P NMR of the K^+ salt (D_2O) showed one peak (δ −68.4); ^1H NMR of the same solution showed the presence of one phenyl group (multiplet, δ 7.54) per nitrophenyl ester group (quartet, δ 7.0–8.1). Hydrolysis of I to phenylphosphonothioate and *p*-nitrophenolate was monitored either spectrophotometrically or by pH stat autotitration with KOH, at pH 8.8. Venom phosphodiesterase from *Crotalus adamanteus* (type II, Sigma Chemical Co.) catalyzed the hydrolysis of I until a measured 49.5% of the anticipated *p*-nitrophenol had been released, after which no further hydrolysis occurred, indicating the high stereospecificity of this enzyme toward the chiral phosphorus center. The 5′-nucleotide phosphodiesterase from bovine gut[1,4] behaved in the same way.

Attempts to oxidize dilute solutions of I and its hydrolysis product, phenylphosphonothioate,[5] with mild oxidants (iodate,

Scheme I