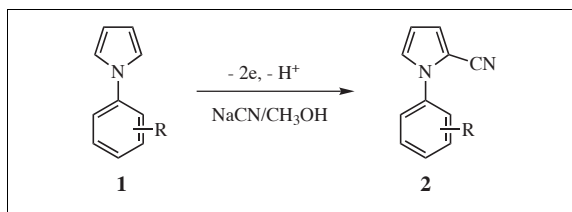


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Received August 29, 2005

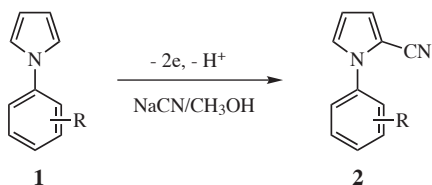


The electrooxidation of several 1-arylpyrroles has been carried out in methanol containing sodium cyanide at a platinum anode in a divided cell. In all instances, replacement of a heteroaromatic hydrogen by a cyano group occurred. On the basis of electroanalytical results, the anodic cyanation of the title compounds could be designed an EC process. As a result of two-electron oxidation, the corresponding pyrrole cyanides were obtained in yields ranging from 76-85%. The advantages of electrochemistry synthesis of pyrrole cyanides are simple reaction condition, low cost and high purity products.

J. Heterocyclic Chem., **43**, 681 (2006).

Introduction.

In recent years there has been increasing interest on pyrrole derivatives in pharmaceutical and material science due to their ubiquity in natural products [1] and important physical properties in polymer forms [2-6]. On the base of these considerations, cyanation of pyrrole has attracted considerable attention in recent years, because nitriles are valuable intermediates in organic synthesis for yielding a broad spectrum of compounds [7]. To date, the direct introduction of cyanide into pyrrole has also been reported by using chemical agents (such as hypervalent iodine(III) reagents [8], isocyanatophosphoric acid dichloride [9] and triphenylphosphine-thiocyanogen [10]).



Electrochemical method is expected to provide a promising method for synthesis of nitriles by reason of its positional reactivity, clean reaction products, and mild conditions. Previously the regioselective anodic cyanation of N-alkylpyrrole derivatives has been extensively investigated by Yoshida K. [11-13]. However, anodic cyanation of 1-arylpyrroles with varied substituents hadn't been reported in their study. On this base, we report here controlled potential electrochemical oxidations of 1-arylpyrroles in methanol containing sodium cyanide.

The corresponding pyrrole cyanides were obtained in good yields.

Results and Discussion.

The studies have been carried out with 1-arylpyrroles and cyanide anions by using cyclic voltammetry and preparative electrolysis. Prior to macroscale electrolysis, analytical investigations were performed at a platinum electrode and peak potentials, expressed in V. vs. SCE, were collected in Table 1.

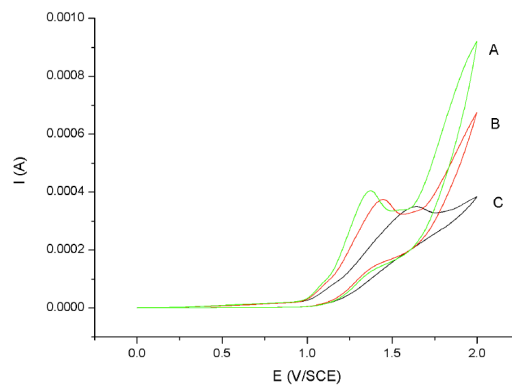


Figure 1. Voltammetric investigations in MeOH. **1d** (0.02 M), scan rate=100 mV/s; 8(A), 4(B), 2(C) equiv. of NaCN.

All the cyclic voltammograms of starting compounds were similar and these title compounds exhibited irreversible oxidation waves. The effect of the aryl-substituents on peak potentials was observed. The 1-arylpyrroles bearing an electron-withdrawing group on the aromatic ring were oxidized at more positive than

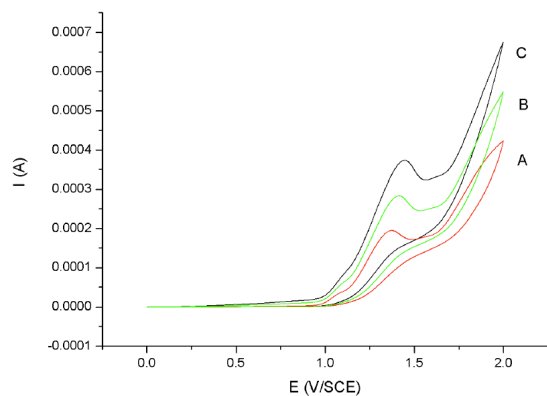


Figure 2. Voltammetric investigations in MeOH. **1d** (0.02 M) + 4 equiv. of NaCN, scan rate=20 mV/s (A), 50 mV/s (B), 100 mV/s (C).

those bearing an electron-donating group (Table 1). 1-(4-Methylphenyl)pyrrole (**1d**) was selected as the model compound. The progressive addition of sodium cyanide (from two to eight equiv of sodium cyanide relative to the substrate) caused a significant shift of the oxidation peak towards less positive values (Figure 1). Moreover, the oxidation potential is proportional to scan rate (Figure 2). These voltammetric characteristics indicated that oxidation was initiated by electron transfer from the substrate molecule, followed by a fast chemical reaction (EC process). By analogy with anodic aromatic substitution reactions [14-16], the plausible mechanism is shown in Scheme 1.

Preparative electrolysis was performed under the conditions described in Table 1. The anodic cyanation of pyrroles occurred preferentially at the carbon atom α to the nitrogen atom. In all cases, monocyanation products were formed (Table 1). In contrast with anodic cyanation of the 1-arylpiperidines[17], concomitant solvolysis of the nitriles **2a-i** were not observed in this electrolysis. Pyrrole cyanides **2a-i** were obtained in yields ranging from 76-85%. Methoxylation, which is often observed as a side reaction in the anodic oxidation in methanolic cyanide solution, was suppressed completely.

Conclusion.

In summary, the present study extended previous study on the electrochemical cyanation of pyrrole derivatives. It was found that various substituents on the aromatic ring had little effect on the product yields. The addition of the cyanide

Table 1
Anodic Cyanation of 1-Arylpyrroles.
Voltammetric Data and Products

Entry	Substrate R	E_p [a], V	E [b], V	Product
1	H	1.48	1.3	2a
2	<i>o</i> -CH ₃	1.46	1.3	2b
3	<i>m</i> -CH ₃	1.51	1.3	2c
4	<i>p</i> -CH ₃	1.45	1.2	2d
5	<i>p</i> -OCH ₃	1.36, 1.87	1.2	2e
6	<i>o</i> -Cl	1.51	1.4	2f
7	<i>m</i> -Cl	1.50	1.4	2g
8	<i>p</i> -Cl	1.53	1.4	2h
9	<i>p</i> -F	1.50	1.3	2i

[a] Peak potential from cyclic voltammetry. Pt anode, CH₃OH, 0.08 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 0.02 M. All voltammograms showed no cathodic peak corresponding to reversible reduction of a cation radical. [b] Potential for preparative electrolysis. The reaction was terminated at the stage when 3 F/mol of electricity was passed.

group proved to be highly efficient in the case of 1-arylpyrrole derivatives. Further studies of the chemical transformations of the cyano group are currently in progress.

EXPERIMENTAL

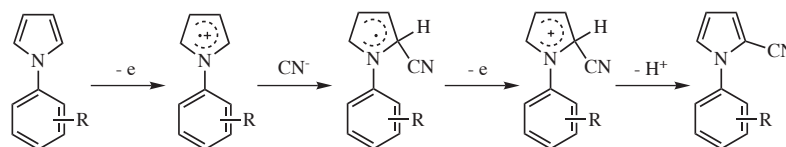
General.

The 1-arylpyrroles **1a-i** were synthesized according to the literature [18].

Melting points were determined on a X-4 melting point apparatus and were not corrected. Infrared spectra were recorded on AVATAR 360 FT-IR E.S.R.. ¹H NMR and ¹³C NMR spectra were recorded on a JEOL JNM-A300 spectrometer. Chemical shift (δ) are given in ppm relative to TMS and coupling constants (J) are given in Hz. Elemental analyses were carried out at the Elementar Vario EL(Germany). The ESI-HRMS was measured on a Bruker APEX sepectrometer in positive ion mode. The cyclic voltammetric experiments were performed by a CHI 660B analyzer.

Cyclic voltammetry was performed in a three-compartment cell. The working electrode was a platinum disk electrode, 2 mm in diameter, and the counter electrode was a platinum sheet. All potentials were referenced to a saturated calomel electrode (SCE) and ohmic drop was not corrected. The E_p values are shown in Table 1. Controlled potential electrolysis was carried out by means of a potentiostatic method.

Scheme 1



General Electrolysis Procedure.

The preparative-scale electrolysis was performed in an H-type cell with a glass frit separating two compartments fitted with Pt sheet electrodes having an area of 3 cm². The anolyte was made up of pyrroles **1** (0.02 M) in methanolic sodium cyanide solution (0.08 M) and was stirred magnetically. The catholyte was a methanolic solution of sodium cyanide. The reaction was carried out at controlled anode potentials as indicated in Table 1 at 25 °C. The oxidation was terminated after passage of 3 F/mol of added pyrrole. The final anolyte was concentrated under reduced pressure. Then, a saturated aqueous NaCl solution was added and the mixture was extracted with ether. The organic layer was dried over Na₂SO₄ and concentrated. The crude products were purified by column chromatography on silica gel using ethyl acetate/petroleum ether (1:5) as the eluent.

1-Phenylpyrrole-2-carbonitrile (**2a**).

This compound was obtained as a light yellow solid in 77% yield. mp 57-59°; ir (potassium bromide): 2215 cm⁻¹ (CN); ¹H nmr (CDCl₃): δ 6.34 (t, 1H, J = 3.0 Hz PyH), 6.99 (dd, 1H, J = 1.6, 3.8 Hz PyH), 7.08 (m, 1H, PyH), 7.38-7.51 (m, 5H, ArH); ¹³C nmr (CDCl₃): δ 103.69, 110.44, 114.44, 121.99, 123.86, 126.77, 128.07, 129.42, 137.93; hrms (ESI): m/z Calcd for C₁₁H₈N₂ [M+H]⁺: 169.0766, Found: 169.0771.

1-(2-Methylphenyl)pyrrole-2-carbonitrile (**2b**).

This compound was obtained as a light yellow oil in 83% yield. ir (potassium bromide): 2220 cm⁻¹ (CN); ¹H nmr (CDCl₃): δ 2.13 (s, 3H, CH₃), 6.33 (t, 1H, J = 3.0 Hz PyH), 6.88 (m, 1H, PyH), 6.94 (d, 1H, J = 3.9 Hz PyH), 7.20-7.37 (m, 4H, ArH); ¹³C nmr (CDCl₃): δ 17.06, 105.38, 109.91, 113.43, 120.46, 126.73, 127.33, 127.74, 129.41, 131.10, 135.04, 137.11; hrms (ESI): m/z Calcd for C₁₂H₁₀N₂ [M+H]⁺: 183.0922, Found: 183.0920.

1-(3-Methylphenyl)pyrrole-2-carbonitrile (**2c**).

This compound was obtained as a light yellow solid in 83% yield. mp 56-58°; ir (potassium bromide): 2218 cm⁻¹ (CN); ¹H nmr (CDCl₃): δ 2.40 (s, 3H, CH₃), 6.31 (t, 1H, J = 3.0 Hz PyH), 6.96 (s, 1H, PyH), 7.04 (m, 1H, PyH), 7.22 (m, 3H, ArH), 7.34 (t, 1H, J = 3.8 Hz ArH); ¹³C nmr (CDCl₃): δ 21.20, 103.83, 110.37, 113.76, 121.08, 121.95, 124.63, 126.84, 128.97, 129.29, 138.02, 139.69; hrms (ESI): m/z Calcd for C₁₂H₁₀N₂ [M+H]⁺: 183.0922, Found: 183.0928.

Anal. Calcd. for C₁₂H₁₀N₂: C, 79.10; H, 5.53; N, 15.37. Found: C, 79.34; H, 5.77; N, 15.10.

1-(4-Methylphenyl)pyrrole-2-carbonitrile (**2d**).

This compound was obtained as a yellow solid in 80% yield. mp 55-56°; ir (potassium bromide): 2217 cm⁻¹ (CN); ¹H nmr (CDCl₃): δ 2.39 (s, 3H, CH₃), 6.31 (t, 1H, J = 3.1 Hz PyH), 6.95 (d, 1H, J = 3.8 Hz PyH), 7.03 (m, 1H, PyH), 7.29 (dd, 4H, J = 1.8, 14.8 Hz ArH); ¹³C nmr (CDCl₃): δ 20.93, 103.96, 110.32, 113.82, 121.78, 123.90, 126.88, 130.07, 135.67, 138.29; hrms (ESI): m/z Calcd for C₁₂H₁₀N₂ [M+H]⁺: 183.0922, Found: 183.0924.

1-(4-Methoxyphenyl)pyrrole-2-carbonitrile (**2e**).

This compound was obtained as a light yellow solid in 84% yield. mp 72-74°; ir (potassium bromide): 2214 cm⁻¹ (CN); ¹H

nmr (CDCl₃): δ 3.84 (s, 3H, CH₃), 6.31 (t, 1H, J = 3.0 Hz PyH), 6.95-7.01 (m, 4H), 7.35 (m, 2H); ¹³C nmr (CDCl₃): δ 55.52, 104.30, 110.20, 113.87, 114.63, 121.50, 125.57, 127.13, 131.24, 159.41; hrms (ESI): m/z Calcd for C₁₂H₁₀N₂O [M+H]⁺: 199.0871, Found: 199.0870.

1-(2-Chlorophenyl)pyrrole-2-carbonitrile (**2f**).

This compound was obtained as a yellow solid in 85% yield. mp 54-55°; ir (potassium bromide): 2220 cm⁻¹ (CN); ¹H nmr (CDCl₃): δ 6.36 (t, 1H, J = 3.5 Hz PyH), 6.97 (m, 2H, PyH), 7.37-7.48 (m, 3H, ArH), 7.55 (m, 1H, ArH); ¹³C nmr (CDCl₃): δ 105.52, 110.20, 113.12, 121.05, 127.71, 128.10, 128.92, 130.53, 130.64, 131.46, 135.52; hrms (ESI): m/z Calcd for C₁₁H₇ClN₂ [M+H]⁺: 203.0376, Found: 203.0380.

Anal. Calcd. for C₁₁H₇ClN₂: C, 65.20; H, 3.48; N, 13.82. Found: C, 65.52; H, 3.62; N, 13.60.

1-(3-Chlorophenyl)pyrrole-2-carbonitrile (**2g**).

This compound was obtained as a light yellow solid in 81% yield. mp 48-49°; ir (potassium bromide): 2220 cm⁻¹ (CN); ¹H nmr (CDCl₃): δ 6.37 (t, 1H, J = 3.1 Hz PyH), 7.02 (d, 1H, J = 3.8 Hz PyH), 7.08 (m, 1H, PyH), 7.37-7.48 (m, 4H, ArH); ¹³C nmr (CDCl₃): δ 104.06, 110.01, 113.45, 122.37, 122.67, 124.44, 126.85, 128.55, 130.70, 135.32, 139.96; hrms (ESI): m/z Calcd for C₁₁H₇ClN₂ [M+H]⁺: 203.0376, Found: 203.0379.

Anal. Calcd. for C₁₁H₇ClN₂: C, 65.20; H, 3.48; N, 13.82. Found: C, 65.47; H, 3.66; N, 14.20.

1-(4-Chlorophenyl)pyrrole-2-carbonitrile (**2h**).

This compound was obtained as a light yellow solid in 76% yield. mp 85-86°; ir (potassium bromide): 2218 (CN); ¹H nmr (CDCl₃): δ 6.36 (t, 1H, J = 2.9 Hz PyH), 7.01 (d, 1H, J = 4.2 Hz PyH), 7.05 (m, 1H, PyH), 7.40 (dd, 2H, J = 2.1, 6.1 Hz ArH), 7.48 (dd, 2H, J = 2.1, 6.0 Hz ArH); ¹³C nmr (CDCl₃): δ 104.09, 110.95, 113.53, 122.43, 125.39, 126.85, 129.84, 134.25, 136.62; hrms (ESI): m/z Calcd for C₁₁H₇ClN₂ [M+H]⁺: 203.0376, Found: 203.0380.

1-(4-Fluorophenyl)pyrrole-2-carbonitrile (**2i**).

This compound was obtained as a light yellow solid in 81% yield. mp 54-55°; ir (potassium bromide): 2214 cm⁻¹ (CN); ¹H nmr (CDCl₃): δ 6.34 (t, 1H, J = 3.0 Hz PyH), 7.03 (m, 2H, PyH), 7.18 (t, 2H, J = 8.6 Hz ArH), 7.42 (m, 2H, ArH); ¹³C nmr (CDCl₃): δ 104.28, 110.64, 113.52, 116.35, 116.66, 122.0, 126.01, 126.12, 127.07, 134.24, 160.44, 163.73; hrms (ESI): m/z Calcd for C₁₁H₇FN₂ [M+H]⁺: 187.0672, Found: 187.0670.

Anal. Calcd. for C₁₁H₇FN₂: C, 70.96; H, 3.79; N, 15.05. Found: C, 71.12; H, 3.62; N, 14.79.

Acknowledgment.

The authors thank the financial supports of Beijing TH-UNIS-Insight Co. Ltd. and the Chinese National Science Foundation (No.20572061), the Ministry of Science and Technology, the Chinese Ministry of Education and Tsinghua University.

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