# Anodic Cyanation of 1-Methylpyrazole



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The electrooxidation of 1-methylpyrazole in methanol containing sodium cyanide produced 1-methylpyrazole-4-carbonitrile **2** and -5-carbonitrile **3** in yields of 23 and 8%, respectively (2e-oxidation products), together with 4-methoxy-1-methylpyrazole-5-carbonitrile **4** (4e-oxidation product, 4%).

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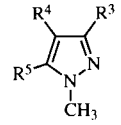
A wide variety of heterocyclic aromatic compounds are subject to electrochemical reactions [1]. The reactions are frequently similar to those of carbocyclic compounds. As part of our program of electrochemical functionalization of five-membered heterocyclic aromatic compounds, the present paper describes the anodic cyanation of 1-methylpyrazole [2].



**1** $R^3$ = CN, $R^4$ = H, $R^5$ = H
**2** $R^3$ = H, $R^4$ = CN, $R^5$ = H
**3** $R^3$ = H, $R^4$ = H, $R^5$ = CN
**4** $R^3$ = H, $R^4$ = OMe, $R^5$ = CN

## Results.

Cyclic voltammograms were recorded using a solution of 0.4 *M* sodium cyanide in methanol. The reference electrode was a saturated calomel electrode (sce). The background current with this system began to increase at potentials more anodic than 1.60 V. Addition of 1-methylpyrazole did not produce usable voltammetry curves.

The reaction was carried out at a controlled anode potential in a divided cell with a platinum anode at room temperature. Initially the potential was set at 1.80 V. The oxidation was terminated after passage of 2 F $mole^{-1}$ of added substrate. Analysis (gc) of the product mixture showed the presence of unchanged starting material, together with small amounts of cyanated products.

Secondly, the electrooxidation was conducted at 2.0 V until 6.5 F $mole^{-1}$ of added substrate had passed through the solution, the anolyte was extracted with chloroform and isolated by preparative gc. They were identified by elemental and $^1H$ nmr, ir, and mass spectroscopic analyses as well as by comparison with literature data (Table 1). The gc analysis showed the presence of **2** and **3** in yields of 23 and 8%, respectively (based on unrecovered starting material), with **4** (4%). The 3-cyanation product was not detected. The conversion was 25%.

The structure assigned to **4** was based on its spectroscopic characteristics. The $C_6H_7N_3O$ molecular formula was indicated by mass spectroscopy and verified by elemental analysis. The ir spectrum indicated the presence of a cyano group. The $^1H$ nmr spectrum showed one methoxy resonance at 3.60 (3H, s), one methyl resonance at 4.26 (3H, s) and a singlet at 7.50 (1H, 3-protium

Table 1

Physical Characteristics of Cyanation Products

| Compound | Mp (°C) | $^1H$ NMR [e] δ (ppm), J (Hz) | IR [f] ν ($cm^{-1}$) | MS m/z ($M^+$) |
|---|---|---|---|---|
| **1** [a] | 44.5-45.0 | 3.99 (3H, s)<br>6.67 (1H, d, J = 2.3)<br>7.45 (1H, d, J = 2.3) | 2230 (CN) | |
| **2** [b] | 59.0-59.5 (cyclohexane) | 3.94 (3H, s)<br>7.76 (2H, s br) | 2230 (CN) | |
| **3** [c] | 27.0-29.0 | 4.07 (3H, s)<br>6.79 (1H, d, J = 2.1)<br>7.56 (1H, d, J = 2.1) | 2230 (CN) | |
| **4** [d] | 95.5-96.0 (cyclohexane) | 3.60 (3H, s)<br>4.26 (3H, s)<br>7.50 (1H, s br) | 2220 (CN)<br>1025 (C-O-C) | 137 |

[a] Reference [10], mp 42-44° (cyclohexane); $^1H$ nmr (deuteriochloroform): δ (ppm) 3.99, 6.67, 7.44. [b] Reference [11], mp 60° (cyclohexane); $^1H$ nmr (deuteriochloroform): δ (ppm) 3.93, 7.71. [c] Reference [10], mp 23-26° (hexane); $^1H$ nmr (deuteriochloroform): δ (ppm) 4.07, 6.80, 7.56. [d] *Anal.* Calcd. for $C_6H_7N_3O$: C, 52.54; H, 5.15; N, 30.64. Found: C, 52.44; H, 5.12; N, 30.70. [e] Deuteriochloroform solution, 100 MHz, standard, TMS. [f] Mull for solid sample.

group). The chemical-shift difference between the substituent methyl group of compound **4** and that of the parent 1-methylpyrazole was 0.36 ppm. Such a large difference will be obtained for the 5-cyanation product.

Discussion.

Substitution on the pyrazole ring is formally a 2-equivalent change. The first step is the oxidation of the substrate to the cation radical. 1-Methylpyrazole oxidizes above the onset of background processes and does not show a cyclic voltammetric peak ($E_p$). The ionization potential of 1-methylpyrazole is higher compared with that of 1-methylimidazole [3]. Gas-phase ionization potentials commonly correlate to solution-phase oxidation potentials [4,5]. In these reactions the current efficiency for the nitriles formation is not always high. Even when 6.5 F mole$^{-1}$ of electricity was passed, conversion was only about 25%. Most of the current would be consumed in parallel oxidation of the cyanide ion, an inorganic electrode process not producing isolable cyanated products.

The present cyanation takes place preferencely at the 4 (and 5) position. A similar high reactivity of the 4 position in 1-methylpyrazole has been observed in conventional electrophilic substitutions [6,7], whereas a radical reaction occurs predominantly at the 5 position [8]. A similar product distribution has been reported for the electroreaction in aqueous cyanide (presumably as a potassium salt, experimental details were not furnished) [9]. It contains no mention of compound **4**.

## EXPERIMENTAL

General.

Spectrometers and electrochemical equipment have been described previously [2a].

Materials.

Methanol and reagent-grade sodium cyanide are used without purification. 1-Methylpyrazole was obtained commercially and was purified by distillation, bp 127-128°; $^1$H nmr (deuteriochloroform): δ 3.90 (3H, s), 6.22 (1H, s), 7.33 (1H, s [12]), 7.46 (1H, s [12]). Nitriles **1** and **3** were prepared by the dehydration of the amides, which were obtained by the ammonolysis of the corresponding esters [10].

Cyclic Voltammetry.

Voltammograms were recorded as described previously (Pt electrodes) [2a,2c]. The reference electrode was an sce. In 1-methylpyrazole the oxidation wave was not observed due to the large background current from the concurrent electrooxidation of the solvent-electrolyte system.

Electroreaction of 1-Methylpyrazole.

The cell and general procedure have been described [2a,2c]. The electrooxidation was carried out at 2.0 V *vs.* sce in a three-compartment cell with a glass frit separating the compartment fitted with Pt sheet electrode (2 x 2 cm). The anolyte was made up of 1-methylpyrazole (0.82 g, 0.01 mole), sodium cyanide (2.0 g, 0.04 mole) and methanol (50 ml). The catholyte was the same medium in the absence of the substrate. The anode and cathode compartments were kept under nitrogen and the solution was stirred magnetically. The reaction was discontinued when 6.5 F mole$^{-1}$ of added substrate had passed through the solution, which generally took 30 hours. An internal standard for gc analysis was added to the product mixture, which was then treated with brine and extracted with chloroform. The chloroform solution was concentrated under aspirator vacuum and analyzed by gc using a Silicone OV-17 column at 100°. Each product was separated in pure form by preparative gc. Identification was made on the basis of elemental and $^1$H nmr, ir and mass spectroscopic analyses (Table 1). **CAUTION**: a cyanide salt in methanol must be handled in a fume hood since it contains hydrogen cyanide as a result of the equilibrium between cyanide anion and the solvent methanol.

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