Electrooxidation of *N*-Aminopyrazoles

Takashi ITOH, Kazuhiro NAGATA, Mamiko OKADA, and Akio OHSAWA*

School of Pharmaceutical Sciences, Showa University, Hatanodai, Shinagawa-ku, Tokyo 142, Japan. *Received December 5, 1989*

***N*-Aminopyrazoles were oxidized by electrolysis in CH_3CN to give 1,2,3-triazines and pyrazoles. The ratio of triazine formation increased when pyridine or H_2O was added to the solvent. Reaction mechanisms were investigated by the application of electrochemical methods.**

Keywords *N*-aminopyrazole; 1,2,3-triazine; electrolysis; oxidation; redox potential

N-Aminoazoles **1** are oxidized by various oxidizing reagents to cause ring expansion, dimerization, or deamination, depending on the reaction conditions.[1] *N*-Nitrenes were assumed to be their common intermediates,[2] but the reaction mechanisms were not clarified in detail. We have studied the oxidation of *N*-aminopyrazoles with some metal oxides under acidic conditions to give 1,2,3-triazines.[3] This time we adopted electrochemical oxidation, which is available for most reaction solvents and is able to be controlled through the redox potential.[4] In this paper we report the effects of the reaction media on the reaction of *N*-aminopyrazoles and the application of the results to the synthesis of 1,2,3-triazines.

First the oxidation potentials of *N*-aminopyrazoles **1** in CH_3CN were measured by means of cyclic voltammetry (Table I, columns 3,4). In the cases of **1c** and **1d**, second oxidation potentials were observed. Moreover the cyclic voltammograms showed that the redox cycles were irreversible, that is, a chemical process occurred immediately after one-electron oxidation. Electrolytic oxidation of **1** in CH_3CN was carried out with a platinum electrode and the results are summarized in Table I. Deaminated pyrazoles **3** were obtained in 10 to 27% yields and considerable polymer formation on the electrode was noted. Thus we examined the influence of the reaction conditions. Addition of an acid such as HCl or acetic acid had no effect on the reaction. However, a small amount of pyridine changed the ratio of **2c**/**3c**, and when 10eq of pyridine with respect to **1c** was added, **2c** was obtained almost exclusively (Fig. 1). Cyclic voltammograms of **1c** indicated that the electric current was increased by addition of pyridine (Fig. 2). This result suggests that a radical cation which was derived from one-electron oxidation of **1** was rapidly deprotonated by pyridine on the surface of the electrode.

Next the effect of a protic solvent was examined. The addition of water decreased the value of the second redox potential of **1b** (Table II). The oxidation of **1b—d** was run in CH_3CN–H_2O, and **2b—d** were obtained in good yield (Table III).

The oxidation of the parent *N*-aminopyrazole **1a** in CH_3CN resulted in the degradation of the starting material

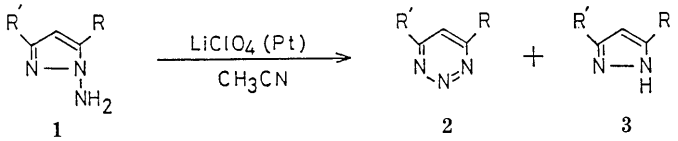


Chart 1

TABLE I. Oxidation Potentials of **1** and Reaction Yields of **2** and **3**

1	R	R′	$E^{1/2}$ (V *vs.* SCE)		Applied potential (V *vs.* SCE)	Yield (%) 2	3
a	H	H	+1.25		+1.28	0	0
b	Me	Me	+1.00		+1.22	25	10
c	Me	Ph	+0.93	+1.77	+1.23	31	26
d	Ph	Ph	+0.95	+1.27	+1.24	31	27

SCE: saturated calomel electrode.

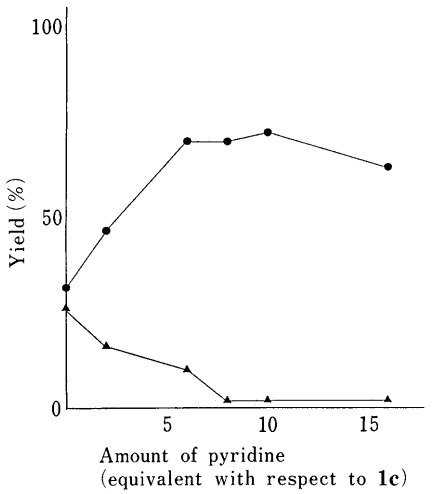


Fig. 1. Effect of Pyridine on the Reaction Yields of **2c** and **3c**
—●—, **2c**; —▲—, **3c**.

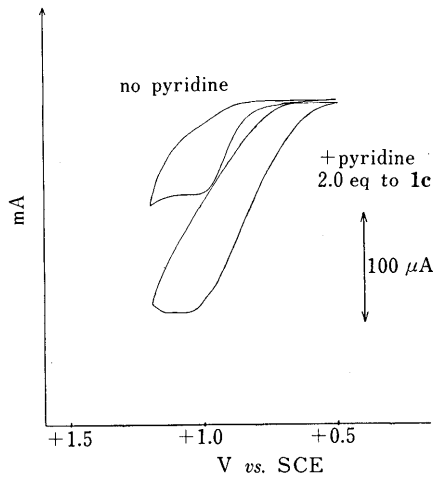
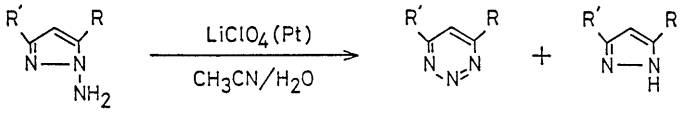


Fig. 2. Effect of Pyridine on the Cyclic Voltammogram
A 10 mM solution of **1c** in acetonitrile; scan rate 20 mV/s; temperature 25 °C.

Table II. Effect of H_2O on the Second Redox Potential of **1b**

H_2O/CH_3CN (v/v%)	$E^{1/2}$ (V *vs.* SCE)	
0	+1.00	—
0.5	+1.00	+1.86
2.4	+1.00	+1.40
4.3	+1.00	+1.34
7.0	+1.00	+1.23
11.1	+1.00	+1.15
23.0	+1.00	+1.10



1 2 3

Chart 2

Table III. Oxidation Yields of **2** and **3** in CH_3CN–H_2O Solvent

1	R	R′	Applied potential (V *vs.* SCE)	Yield (%) 2	3
b	Me	Me	+1.10	94	0
c	Me	Ph	+1.05	62	4
d	Ph	Ph	+1.18	81	1

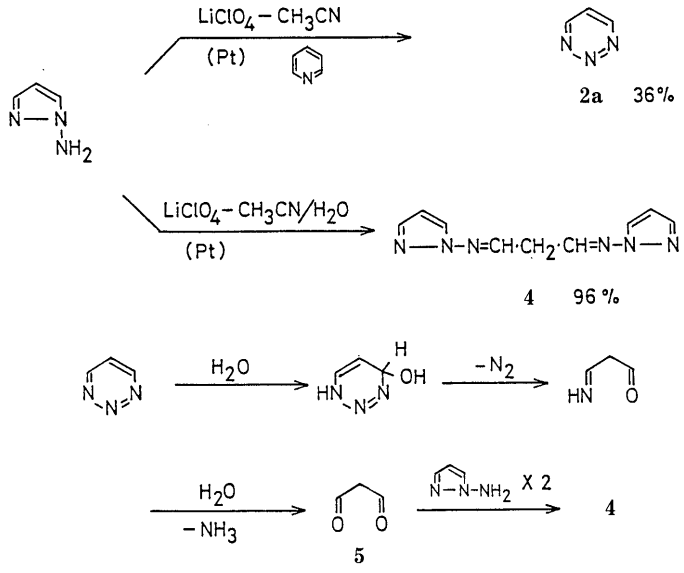


Chart 3

(Table I, entry a) and the above-mentioned solvent effects were examined with **1a** (Chart 3). The addition of pyridine (8 eq to **1a**) gave the parent 1,2,3-triazine (**2a**) in 36% yield, which was a better result than in the oxidation using metal oxides.[5] In the case of CH_3CN–H_2O as a solvent, *N*,*N*′-dipyrazolyl-1,3-propanediimine (**4**) was obtained in 96% yield. A possible mechanism for the formation of **4** is shown in Chart 3. The produced triazine was attacked by H_2O at its 4-position, leading to the ring opening, followed by the hydrolysis of imine to malonaldehyde (**5**), which was supposed to trap two moles of the starting material to form **4**.

The reaction mechanisms are summarized in Chart 4. The one-electron oxidation of **1** gave the ammoniumyl radical

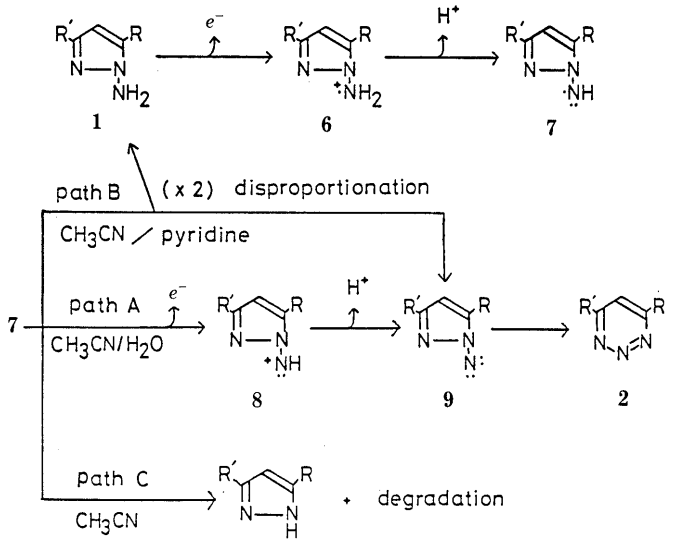


Chart 4

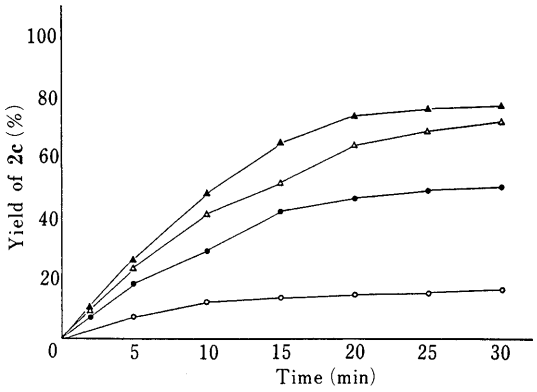


Fig. 3. Reaction Yield of **2c** in Various Solvents

(○), CH_3CN 100%; (●), CH_3CN + pyridine (10 eq to **1c**); (△), CH_3CN–H_2O (3 : 1); (▲), CH_3CN–H_2O + pyridine.

6, which was deprotonated to form the aminyl radical **7**. This deprotonation process was presumably very fast because the cyclic voltammogram was irreversible at the one-electron oxidation step. In the case of CH_3CN–H_2O as a solvent, the second oxidation potential was close to the first one (Table II), thus the second oxidation step (Chart 4 path A) was considered to proceed without difficulty. The aminyl radical[6] is a relatively electron-deficient species, so H_2O molecules were supposed to coordinate to **7**[7] and increase its electron density to facilitate the second oxidation step to form the cation **8**. This cation **8** was deprotonated to the nitrene intermediate **9**, which undergoes ring enlargement to the triazine **2**. On the other hand, addition of pyridine may accelerate the first oxidation step (Fig. 2), so **7** would be formed at high concentration near the anode. The aminyl radical is known to have a tendency to disproportionate,[8] so it is likely that **7** disproportionates to **1** and **9**, and the latter rearranges to **2** (Chart 4 path B). In the absence of H_2O or pyridine, the formation of **7** may be relatively slow, and **7** partly disproportionates to produce triazine, but is partly deaminated bacause of the low concentration of **7**.

The above results show that the first and second oxidation processes were promoted by pyridine and H_2O, re-

spectively. Figure 3 summarizes the solvent effects on the reaction. The effect of pyridine was less than that of H_2O because the formation of the nitrene **9** was the rate-determining step and **9** was supposed to be produced less effectively by the disproportionation of **7** in CH_3CN–pyridine than by the direct oxidation of **7** to **9** in CH_3CN–H_2O. The fact that the addition of pyridine to CH_3CN–H_2O caused little stimulation of the oxidation also suggested that the second oxidation step was rate-determining. Thus we were able to analyze the mechanism of oxidation by using electrochemistry. Application of this approach to the oxidation of other *N*-aminoazoles is in progress.

Experimental

***N*-Aminopyrazoles** **1a**, **1c** and **1d** were synthesized by *N*-amination of the corresponding pyrazoles with hydroxylamine *O*-sulfonic acid (HAS)[9] in C_2H_5OH–H_2O. *N*-Amination of **1b** with HAS gave a low yield. *N*-Amination with *O*-Mesitylene sulfonamide (MSH) in CH_2Cl_2 afforded **1b** in 88% yield.

Redox Potential *N*-Aminopyrazole (0.1 mmol) was dissolved 10 ml of 0.1 M tetraethylammonium perchlorate solution. The redox potential and cyclic voltammogram were measured with a Yanaco P-1100 polarographic analyzer.

General Procedure for the Oxidation of *N*-Aminopyrazoles (1a—d) The oxidation was performed with a Yanaco VE-9 potentio/galvanostatic electrolyzer. A 0.1 M lithium perchlorate solution in acetonitrile or acetonitrile–water (3 : 1, 40 ml) was placed in an H cell. The solution was degassed with nitrogen (10 min), and 0.15 mmol of *N*-aminopyrazole was added to the anode chamber. Electrode oxidation was carried out under nitrogen bubbling until the starting material was no longer detectable by thin-layer chromatography (TLC). After the reaction, the anolyte and catholyte were mixed and evaporated. Ether was added, and the combined organic solutions were washed with water and brine. After drying ($MgSO_4$) and removal of the solvents the residue was purified by preparative TLC. Electrolysis was run at +1.22 to +1.28 V (*vs.* SCE) in CH_3CN, +1.05 to +1.18 V in CH_3CN–H_2O, +1.09 to +1.21 V in CH_3CN–pyridine, and +0.95 to +1.15 V in CH_3CN–H_2O–pyridine.

References and Notes

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