

Oxidative Transformation of Pyrazole into Triazole. Novel Synthesis of 4-Cyano-2H-1,2,3-triazole Derivatives

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Oxidation of 3,5-diamino-4-arylhydrazonopyrazoles with lead(IV) tetra-acetate provided 2-aryl-4-cyano-2H-1,2,3-triazoles in moderate yield. Tentative mechanisms *via* pyrazolotriazole and/or nitrene intermediates are proposed for this novel ring transformation.

The increasing interest in the chemistry of 2H-1,2,3-triazole derivatives¹ arose from their application as intermediates in the preparation of light stabilizers² and fluorescent whiteners for synthetic fibres and plastics,^{3,4} and from their pronounced biological activity, *e.g.* their application as precursors of derivatives having antileukaemic and anticarcinogenic activities,⁵ and herbicidal, defoliant, insecticidal, fungicidal, and nematocidal activities.⁶

In spite of the enormous literature dealing with the synthesis of 1H-1,2,3-triazoles, little attention has been paid to the synthesis of 2H-1,2,3-triazoles.

Aminopyrazoles are very useful compounds which have been extensively utilized as intermediates for the synthesis of fused heterocyclic compounds.^{7,8} In previous work, one of us (Z. E. K.) reported that 3,5-diaminopyrazoles could be easily prepared *via* arylazo group decoupling from 3,5-diamino-4-arylazopyrazole (1),⁷ and since then compounds (1) have been extensively used as starting materials for the synthesis of fused azole compounds of potential biological activity.^{9,10}

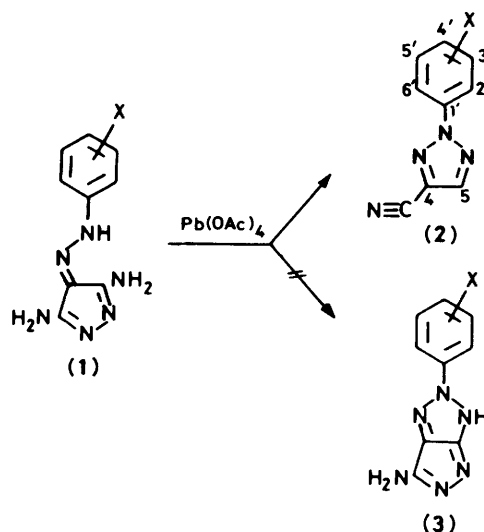
Although there are very many papers dealing with redox reactions of heterocyclic compounds, few papers^{11,12} have dealt with the reduction of pyrazoles of (1) and no oxidation of these compounds (1) has been reported so far.

Lead(IV) tetra-acetate (LTA) is a versatile oxidizing reagent with a wide range of applications;¹³ however, to our knowledge, there is only one report of its use for the preparation of triazoles in the literature.¹⁴

These facts, and our continuing interest in the chemistry of electron-deficient reactive nitrogen species,¹⁵ prompted us to investigate the oxidation of pyrazoles (1) with LTA.

Results and Discussion

Since oxidative cyclization of *o*-aminoarylazobenzenes¹⁶ and 4-amino-5-arylazopyrimidines¹⁴ to give fused triazole compounds is known, we first investigated the oxidation of pyrazoles (1) with 1 equiv. of LTA in dimethylformamide (DMF) solution. During the reaction, vigorous elimination of nitrogen gas was observed. Surprisingly, the respective 2-aryl-4-cyano-2H-1,2,3-triazole (2) was obtained as the sole product and the expected fused compound, *i.e.* the pyrazolo[3,4-*d*]-1,2,3-triazole (3), could not be isolated at all under a variety of experimental conditions (Scheme 1). We also found that the best way to obtain high yields of triazoles of (2) was to carry out the reaction in a mixed solvent [DMF-MeCN (1:1)] with 2 equiv. of LTA. In this case, the yield was *ca.* three times that with 1 equiv.



Scheme 1.

Table 1. Synthetic results of 2-aryl-4-cyano-2H-1,2,3-triazoles (2)

Compd.	X	Yield ^a (%)	M.p.
			(°C)
(2a)	H	46	88 (lit., ¹⁹ 88)
(2b)	4'-Me	58	102
(2c)	4'-Br	42	119
(2d)	4'-NO ₂	41	132
(2e)	3'-NO ₂	45	87—88
(2f)	4'-OMe	48	111
(2g)	3'-OMe	52	60

^a After purification.

The identification of triazoles (2) was first based on the presence of a strong absorption band, due to a cyano group, in the i.r. spectrum at 2 240—2 250 cm⁻¹, besides other bands characteristic for 2-aryl-1,2,3-triazoles.¹⁷ The structure of products (2) was further established by elemental analysis, mass, and ¹H, and ¹³C n.m.r. spectra.

The synthetic results and various spectral data are summarized in Tables 1—3.

As shown in Table 1, substituent groups on the benzene ring did not greatly affect the yield of the triazole (2). It should be noted that the observed δ -values of the benzene-ring atoms in the ¹³C n.m.r. spectra agreed well with those calculated on the basis of the substituent effect on a benzene ring.¹⁸

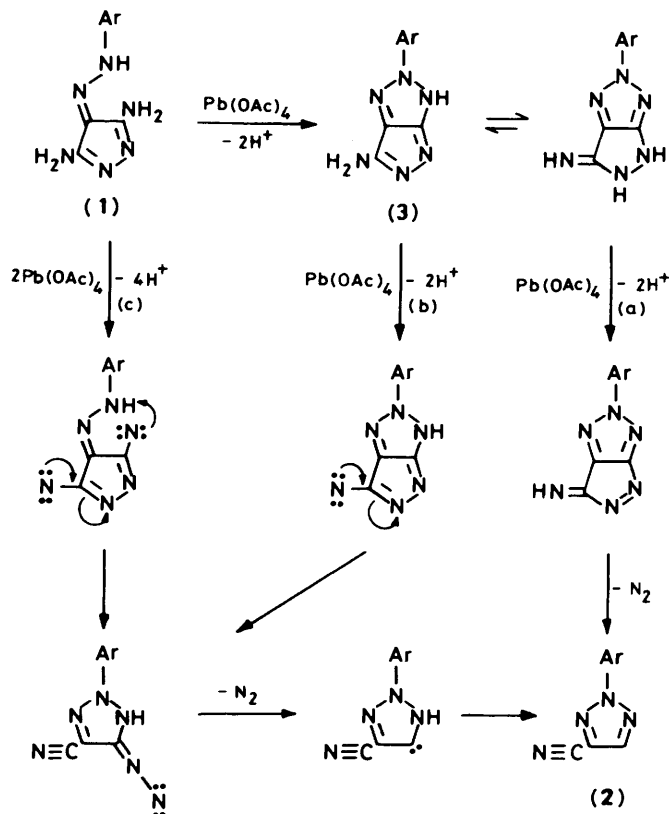
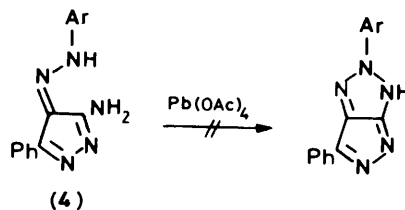
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Table 2. Analytical and spectral data for 2-aryl-4-cyano-2*H*-1,2,3-triazoles (**2**)

Compd. (formula)	ν_{\max} . (KBr; cm^{-1})		m/z	Found (%) (Required)		
	CH	C \equiv N		C	H	N
(2a) ($\text{C}_9\text{H}_6\text{N}_4$)	3 150	2 250	170 (M^+ , 55%), 92 (38), 77 (15), 28 (100)	63.8 (63.52)	3.3 (3.55)	32.8 (32.92)
(2b) ($\text{C}_{10}\text{H}_8\text{N}_4$)	3 145	2 250	184 (M^+ , 100%), 105 (56), 91 (13), 78 (19)	63.35 (65.21)	4.4 (4.38)	30.3 (30.42)
(2c) ($\text{C}_9\text{H}_5\text{BrN}_4$)	3 150	2 240	250 ($M^+ + 2$, 97%), 248 (M^+ , 100), 171 (39), 169 (40)	M^+	249.9677 (249.9677)	
(2d) ($\text{C}_9\text{H}_5\text{N}_5\text{O}_2$)	3 150, 3 090	2 250	215 (M^+ , 100%), 185 (57), 169 (10), 91 (51)	50.0 (50.24)	2.4 (2.34)	32.7 (32.55)
(2e) ($\text{C}_9\text{H}_5\text{N}_5\text{O}_2$)	3 160, 3 070	2 245	215 (M^+ , 100%), 169 (52), 157 (14), 91 (63)	50.3 (50.24)	2.5 (2.34)	32.3 (32.55)
(2f) ($\text{C}_{10}\text{H}_8\text{N}_4\text{O}$)	3 150, 3 030	2 240	200 (M^+ , 100%), 185 (23), 121 (54), 100 (15)	M^+	200.0687 (200.0696)	
(2g) ($\text{C}_{10}\text{H}_8\text{N}_4\text{O}$)	3 155, 3 020	2 250	200 (M^+ , 100%), 121 (11), 106 (28), 93 (18)	60.3 (60.00)	4.0 (4.03)	27.8 (27.99)

Among the triazoles prepared, only (**2a**) is known,^{19,20} and its ^{13}C n.m.r. spectrum was reported by Terui *et al.*²¹ According to their report, the two signals at δ_c 139.2 and 129.3 were assigned to C-4' and C-5 respectively. However, their assignment seems to be incorrect, and we have reversed the assignment since the observed chemical shifts are in fair agreement with the calculated ones without exception, according to our method, taking account of substituent effects.

Since it has been shown that oxidation of *ortho*-aminoaryloxy compounds with LTA provides fused triazole derivatives,^{14,16} oxidative ring closure of pyrazoles (**1**) to give the corresponding expected pyrazolotriazole (**3**) could be followed by an oxidative

**Scheme 2.****Scheme 3.**

fragmentation to give nitriles (**2**) as in shown in Scheme 2 (route a).

However, oxidation of the 3-amino-4-arylhydrazono-5-phenylpyrazole (**4**) with LTA did not provide either a pyrazolotriazole or a triazole derivative (Scheme 3).

Since oxidation of aminoaryl compounds with LTA is well known to generate nitrenes^{13,22,23} [e.g., *o*-phenylenediamine provides *cis,cis*-1,4-dicyanobutadiene via *o*-dinitrenobenzene (*o*-phenylene dinitrene)²³], other plausible mechanisms via nitrene intermediates (routes b and c) can be proposed as shown in Scheme 2.

Although a few ring systems such as isoxazole,²⁴ oxadiazole,²⁵ and sydnone²⁶ are known to rearrange to 2*H*-1,2,3-triazole, our reaction shown here is of an entirely new type. Moreover, the product (**2**) has a cyano group, and therefore seems to have potential utility for the preparation of various triazole derivatives.

Begtrup first prepared nitrile (**2a**) by cyanation of 1-methoxy-2-phenyl-1,2,3-triazolium tetrafluoroborate.¹⁹ However, his method seems to be inefficient because the starting triazolium salt requires several steps for its synthesis. Since the starting compounds (**1**) are readily available,²⁷ and since the work-up after the reaction is quite simple, this novel reaction may be generally useful for the preparation of 4-cyano-2*H*-1,2,3-triazoles.

Experimental

M.p.s were measured on a Yamato MP-Z1 melting point apparatus and are uncorrected. ^1H and ^{13}C n.m.r. spectra were recorded at 500 MHz and 125 MHz respectively on JEOL-GX-500 MHz n.m.r. spectrometer using CDCl_3 and CCl_4 as solvent, respectively; Me_4Si was employed as an internal standard. I.r. spectra were obtained on a Hitachi 295 i.r. spectrophotometer. Electron-impact mass spectra were obtained at 70 eV on a JEOL JMS-D100 mass spectrometer by direct introduction *via*

Table 3. ^1H and ^{13}C N.m.r. spectral data (δ -values) of 2-aryl-4-cyano-2H-1,2,3-triazoles (**2**)

Compd.	$^{13}\text{C}^a$										^1H						
	Me	CN	C-4	C-5	C-1'	C-2'	C-3'	C-4'	C-5'	C-6'	Me	5-H	2'-H	3'-H	4'-H	5'-H	6'-H
(2a)		111.29	122.50	139.34	138.88	119.57	129.61	129.38	129.61	119.57	8.10	8.10	7.51	7.49	7.51	8.10	(d)
(2b)	21.15	111.40	122.21	139.67	136.83 (135.98)	119.52 (119.47)	130.14 (130.31)	139.16 (138.28)	130.14 (130.31)	119.52 (119.47)	2.44	8.06	7.96	7.28	(t)	7.28	7.96
(2c)		111.05	122.87	139.53	137.83 (137.28)	121.06 (120.27)	132.80 (133.01)	123.33 (123.88)	132.80 (133.01)	121.06 (120.27)	(s)	(s)	(d)	(d)	(d)	(d)	(d)
(2d)											8.23	8.33	8.43	(d)	8.43	8.33	
(2e)		110.67	132.82	139.30	140.07 (139.78)	114.96 (114.77)	149.04 (149.61)	124.97 (124.58)	130.92 (130.51)	124.97 (125.37)	8.21	8.97			8.47	7.77	8.33
(2f)											3.87	8.10	7.99	7.00	(d)	7.00	7.99
(2g)	55.65	111.27	122.47	139.27	139.86 (139.88)	105.20 (105.17)	160.53 (161.01)	115.50 (114.98)	130.44 (130.61)	111.75 (111.87)	3.89	8.09	7.60	(s)	6.94	7.37	7.66

^a Figures in parentheses show calc. values.

a probe. High-resolution mass spectral analyses were performed on a Hitachi M-80 mass spectrometer at the Mitsubishi Chemical Industries Research Center.

General Procedure for the Preparation of 2-Aryl-4-cyano-2H-1,2,3-triazoles (2).—A 3,5-diamino-4-(2-arylhydrazono)pyrazole (**1**) (5 mmol) was dissolved in DMF–MeCN (1:1) (50 ml) and the solution was cooled in an ice-bath. Dry nitrogen gas was bubbled through the solution for 10 min and then LTA (10 mmol) was added in small portions during 5–10 min. The mixture was stirred under nitrogen for 1.5–2 h at 0–5 °C (t.l.c. monitor) and then the reaction mixture was poured into water and extracted with ether (200 ml \times 3). The combined extracts were dried (anhydrous Na_2SO_4) and then chromatographed over alumina (70–230 mesh) with hexane–ether (1:1) as eluant.* The pure triazoles (**2**) were obtained in moderate yield as shown in Table 1. Analytical and spectral data are shown in Tables 2 and 3.

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* A different solvent, hexane–ethyl acetate (3:1), was used in the case of nitro derivatives (**2d** and **e**).

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