N-Amination of 3-Amino-1,2,4-triazole with Hydroxylamine-*O*-sulfonic Acid: Synthesis of 1,5-Diamino-1,2,4-triazole

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N-Amination of the 3(5)-amino-1,2,4-triazolide anion with hydroxylamine-*O*-sulfonic acid is studied. This method provided an access to the previously unknown 1,5-diamino-1,2,4-triazole.

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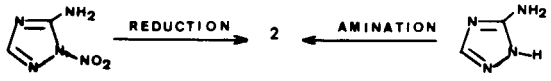
Ortho-*C*,*N*-diamino-1,2,4-triazoles are convenient reagents for the synthesis of a variety of fused *s*-triazolo-heterocycles, but only the 3,4-diamino-1,2,4-triazole **1** has been used for this purpose [1,2].

While this compound can be prepared in good yield by condensation of diaminoguanidine with formic acid [3], a similar method cannot be used in the case of 1,5-diamino-1,2,4-triazole **2**. In order to prepare this compound, we have investigated the two routes depicted in Scheme 1.

Scheme 1

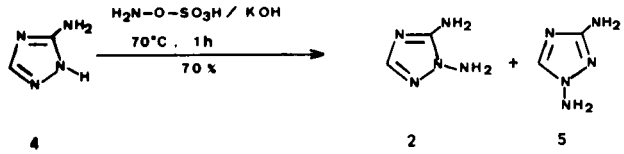


3 **4**

Attempts to prepare **2** from 1-nitro-5-amino-1,2,4-triazole **3**, obtained following literature references [4], were unsuccessful. Cleavage of the *N*-NO_2 bond took place instead as it is known to occur in *N*-nitroazoles [5]. It was thus decided to study the *N*-amination reaction. Aminations of unsubstituted or dialkylsubstituted 1,2,4-triazolide anions with hydroxylamine-*O*-sulfonic acid [6] or *O*-(2,4-dinitrophenyl) hydroxylamine [7] have been described but to the best of our knowledge, amination of 3(5)-amino-1,2,4-triazolide anion has not been studied so far.

When 3-amino-1,2,4-triazole was treated with hydroxylamine-*O*-sulfonic acid in basic media the *N*-aminated products **2** and **5** were obtained in 33% and 22% yield respectively.

Scheme 2



4 **2** **5**

The observed isomeric ratio of diaminated products was similar to that reported for the corresponding *N*-methyl derivatives of **4** when the methylation reaction was performed in basic media [8]. The absence of 3,4-diamino-1,2,4-triazole is in accordance to the low yield reported for the N_4-aminated derivative of 1,2,4-triazole in the same amination procedure [6].

A regioselectivity up to 3:1 (**2**:**5**) can be achieved at low temperatures and with short reaction times, but with a decrease in the overall yield. If we compare the ^{1}H nmr data of the new compounds **2** and **5** with those of reference compounds 3,4-diamino-1,2,4-triazole **1** [9], and the *C*-amino-*N*-methyl-1,2,4-triazoles **6**-**8** [8] (Table I), we can see that the C-H chemical shifts of **1** and its methyl analogue **8** are identical and that said values in the *N*-aminated products **2** and **5** are slightly shifted to upper fields in accordance to which is known to occur for the methyl analogues **6** and **7** [8].

Table I

^{1}H NMR δ Values (DMSO-d_6)

Compound	δ C-H	δ NH_2	
1	7.82	5.59	
2	7.20	5.82	5.89
5	7.75	5.13	6.05
6 [a]	7.36	6.18	
7 [a]	7.92	5.24	
8 [a]	7.82	5.70	

[a] **6** = 5-Amino-1-methyl-1,2,4-triazole, **7** = 3-amino-1-methyl-1,2,4-triazole, **8** = 3-amino-4-methyl-1,2,4-triazole.

^{13}C nmr data of compounds **1**-**3** and **5** together with those reported for compounds **4**, **6**-**8** [10] are collected in Table II.

When the 3:2 mixture of *C*,*N*-diamino-*s*-triazoles **2** and **5** was treated with acetic anhydride, a mixture of acetyl derivatives was obtained. The main isolated product was 1-diacetylamino-5-acetylamino-1,2,4-triazole (**9**) which reverted to **2** by alkaline hydrolysis. Similar triacylation products have been described for 1,5-diamino-tetrazole by Gaponik *et al.* [11].

Table II

^{13}C NMR δ Values of Compounds **1-8**

No.	Solvent	C-NH_2	C-H	$^{1}J_{C-H}$	$^{3}J_{C-H}$	$^{3}J_{CNNH}$
1	[a]	155.8	142.5	214.9		
2	[b]	153.4	144.9	202.8	7.0	
3	[b]	163.1	143.1	233.4	14.1	
4	[b]	158.4	148.0	202.7	7.1	
5	[b]	161.4	140.8	209.9	13.0	2.9
6	[b]	155.4	148.0	[c]	[c]	
7	[b]	164.2	143.0	[c]	[c]	
8	[b]	155.2	140.9	[c]	[c]	

[a] = DMSO-d_6/D_2O, [b] = DMSO-d_6. [c] No reported values.

EXPERIMENTAL

All melting points are uncorrected and were measured with a Reichert microscope melting point apparatus. Infrared spectra were recorded on a Perkin-Elmer 577 spectrometer. Nuclear magnetic resonance spectra were carried out on Bruker WM 200 SY spectrometer with TMS as internal standard.

The reaction mixtures were examinated by hplc on a C-18 reverse phase column μ-Bondapak 3.9 mm x 30 mm, 1 ml/minute, 95:5 water/methanol, using PIC B_7 and 214 nm detection.

Amination of 3-Amino-1,2,4-triazole.

Method A.

Hydroxylamine-*O*-sulfonic acid (9.2 g, 0.088 mole) was slowly added to a stirred hot solution (70°) of 4.7 g of 3-amino-1,2,4-triazole (**4**) (0.056 mole) and 10 g of potassium hydroxide (0.250 mole) in 400 ml of water, keeping the temperature constant throughout the addition and for one hour further. The solution was then continuously extracted with ethyl acetate and the organic phase was dried and evaporated giving 70% yield of a mixture, which was separated by column chromatography using chloroform/methanol (8/2) as the eluent.

Method B.

Hydroxylamine-*O*-sulfonic acid (3.8 g, 0.033 mole) was slowly added to a concentrated solution of 2.52 g of 3-amino-1,2,4-triazole (**4**) (0.030 mole) and 5.6 g of potassium hydroxide (0.140 mole), in an ice bath. The mixture was then kept at room temperature for 45 minutes and extracted with ethyl acetate. The organic phase was dried and evaporated giving 34% yield of mixture, which was separated as in A giving 27% of **2** and 9% of **5**.

1,5-Diamino-1,2,4-triazole (**2**).

This compound had mp 190-192° (acetonitrile); ir (potassium bromide): 3300, 3050, 1660, 1640 cm^{-1}; retention time 11.55 minutes.

Anal. Calcd. for $C_2H_5N_5$: C, 24.24; H, 5.08; N, 70.67. Found: C, 24.48; H, 5.40; N, 70.93.

1,3-Diamino-1,2,4-triazole (**5**).

This compound had mp 166-168° (acetonitrile); ir (potassium bromide): 3400, 3300, 3210, 3180, 3100, 1650 cm^{-1}; retention time 4.18 minutes.

Anal. Calcd. for $C_2H_5N_5$: C, 24.24; H, 5.08; N, 70.67. Found: C, 24.39; H, 5.27; N, 70.38.

1-Diacetylamino-5-acetylamino-1,2,4-triazole (**9**).

A 3:2 mixture of compounds **2** and **5** (2.65 g, 0.026 mole) was refluxed in 55 ml of acetic anhydride for 2 hours. The solution was concentrated under vacuum and 2.8 g of compound **9** was collected from the solid residue with dichloromethane (46% yield), mp 258-260° (dicloromethane); ir (potassium bromide): 3300, 3200, 3100, 3020, 1750, 1710 cm^{-1}; ^{1}H nmr (deuteriodimethyl sulfoxide): δ 2.15 (s, 3H, CH_3), 2.3 (s, 6H, $(CH_3)_2$), 8 (s, 1H, arom).

Anal. Calcd. for $C_8H_{11}N_5O_3$: C, 42.67; H, 4.92; N, 31.10. Found: C, 42.82; H, 5.01; N, 30.85.

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