

# A novel N—N bond cleavage reaction of 4-amino-1,2,4-triazole derivatives

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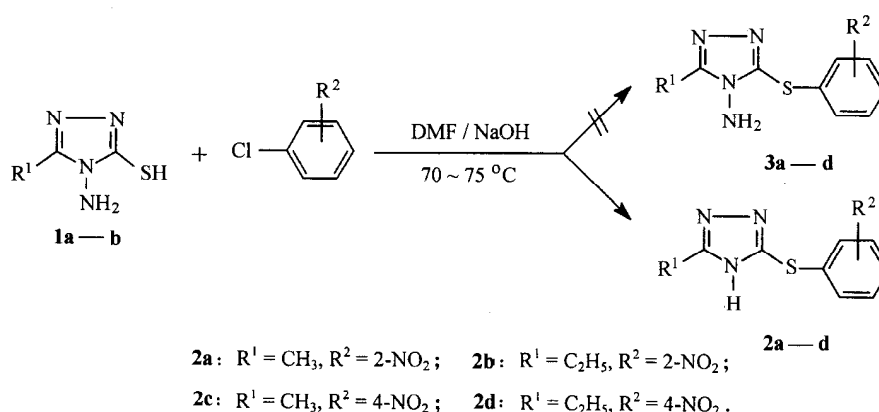
5-Substituted-4-amino-3-thiol-1,2,4-triazoles (**1a—b**) react with *ortho*-nitrochloro-benzene or *para*-nitrochlorobenzene to give N—N bond cleavage products **2a—d**, one structure of which (**2b**) has been unambiguously confirmed by an X-ray structural analysis.

**Keywords** N—N Bond cleavage reaction, 4-amino-3-thiol-1,2,4-triazole, X-ray diffraction

5-Substituted-4-amino-3-thiol-1,2,4-triazole derivatives **1a—b** are important intermediates for the synthesis of various fused heterocycles with great biological potential, such as 1,2,4-triazolo[3,4-b][1,3,4]-

thiadiazoles and 1,2,4-triazolo[3,4-b][1,3,4]thiadiazines.<sup>1-6</sup> In the course of our synthetic and bioassay projects of novel heterocyclic triazolo systems,<sup>7-10</sup> we have to need a number of intermediates 5-substituted-4-amino-3-(substituted) arylthio-1,2,4-triazoles (**3a—d**). However, when we applied the nucleophilic substitution reaction between 5-substituted-4-amino-3-thiol-1,2,4-triazoles (**1a—b**) and nitro-chlorobenzene to synthesize **3a—d** (Scheme 1), a novel N—N bond cleavage reaction was observed, which, to our knowledge, has not been reported in the literatures. Herein, we will report the experimental results.

Scheme 1



The required 5-substituted-4-amino-3-thiol-1,2,4-triazole derivatives **1a—b** were prepared in excellent

yields following the method of Invidiate *et al.*<sup>11</sup> At the presence of sodium hydroxide, when the DMF solution

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of **1a—b** and *ortho*-nitrochlorobenzene or *para*-nitrochlorobenzene was heated at 70—75°C, a yellow crystal product was obtained after pouring the whole reaction mixture into water. The structures of all products were characterized by <sup>1</sup>H NMR, MS and elemental analysis. Unfortunately, these data seemed consistent with the structures of **2a—d** rather than those of **3a—d**

(Scheme 1). In order to confirm the structures of the products unambiguously, we carried out an X-ray diffraction analysis of one of the products. Fig. 1 depicts the molecular structure of compound **2b**, which indicates that a novel N—N bond cleavage reaction has indeed taken place.

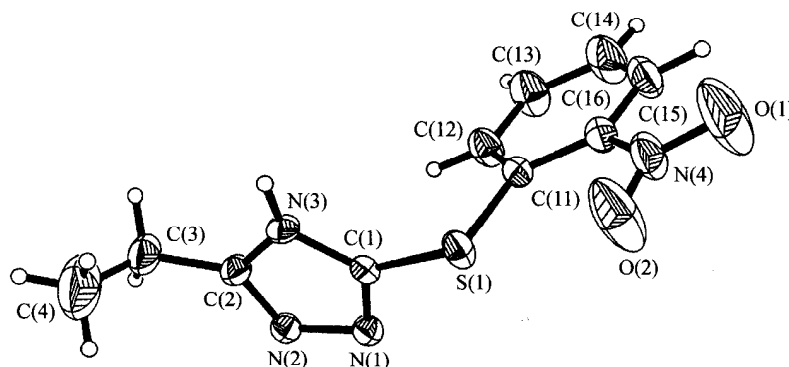


Fig. 1 Molecular structure of **2b** as obtained from X-ray diffractions.

In summary, we discovered a novel N—N bond cleavage reaction. To our knowledge, it is the first report of N—N bond cleavage reaction in 4-amino-1,2,4-triazole system. The further study on the cleavage mechanism is on the way.

## Experimental

Melting points were obtained with a Yanaco MT-500 apparatus without correction. <sup>1</sup>H NMR spectra were measured with a Bruker AC-P200 spectrometer using TMS as internal standard and elemental analyses were performed on a Perkin-Elmer 240-C instrument. Starting materials **1a—b** were prepared according to the literature.<sup>11</sup>

### General procedure for the preparation of **2a—d**

The 5-substituted-4-amino-3-thiol-1, 2, 4-triazole derivatives **1a—b** (0.01 mol) and 0.40 g of sodium hydroxide were dissolved in 15 mL of DMF. To this mixture, *ortho*-nitrochlorobenzene or *para*-nitrochlorobenzene (0.01 mol) was added and the whole mixture was heated at 70—75°C for about 7 h. The reaction mixture was poured into 40 mL of water and the solid was filtered and recrystallized from acetone to give the

pure products as yellow crystals.

**2a** Yield 60.0%, yellow crystal, mp 223—225°C.  $\delta_{\text{H}}$  (DMSO): 2.41 (s, 3H, CH<sub>3</sub>), 7.07—8.26 (m, 4H, C<sub>6</sub>H<sub>4</sub>), 14.27 (s, 1H, NH).  $m/z$  (%) 236 (M<sup>+</sup>, 38.2), 190 (M<sup>+</sup> - NO<sub>2</sub>, 100). Anal. C<sub>9</sub>H<sub>8</sub>N<sub>4</sub>O<sub>2</sub>S. Calcd: C, 45.76; H, 3.38; N, 23.72. Found: C, 45.63; H, 3.28; N, 23.52.

**2b** Yield 81.2%, yellow crystal, mp 195—197°C.  $\delta_{\text{H}}$  (DMSO): 1.24 (t,  $J = 7.54$  Hz, 3H, CH<sub>3</sub>), 2.75 (d,  $J = 7.62$  Hz, 2H, CH<sub>2</sub>), 7.07—8.26 (m, 4H, C<sub>6</sub>H<sub>4</sub>), 14.27 (s, 1H, NH).  $m/z$  (%): 250 (M<sup>+</sup>, 36.8), 204 (M<sup>+</sup> - NO<sub>2</sub>, 100). Anal. C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S. Calcd: C, 48.00; H, 4.00; N, 22.40. Found: C, 48.16; H, 4.26; N, 22.82.

**2c** Yield 67.2%, yellow crystal, mp 227—228°C.  $\delta_{\text{H}}$  (DMSO): 2.39 (s, 3H, CH<sub>3</sub>), 7.45—8.16 (m, 4H, C<sub>6</sub>H<sub>4</sub>), 14.26 (s, 1H, NH). Anal. C<sub>9</sub>H<sub>8</sub>N<sub>4</sub>O<sub>2</sub>S. Calcd: C, 45.76; H, 3.38; N, 23.72. Found: C, 45.90; H, 3.58; N, 23.53.

**2d** Yield 78.5%, yellow crystal, mp 178—179°C.  $\delta_{\text{H}}$  (DMSO): 1.23 (t,  $J = 7.61$  Hz, 3H, CH<sub>3</sub>), 2.76 (d,  $J = 7.67$  Hz, 2H, CH<sub>2</sub>), 7.44—8.17 (m, 4H, C<sub>6</sub>H<sub>4</sub>), 14.28 (s, 1H, NH). Anal. C<sub>10</sub>H<sub>10</sub>N<sub>4</sub>O<sub>2</sub>S. Calcd: C, 48.00; H, 4.00; N, 22.40. Found: C, 48.32; H, 4.30; N, 22.64.

*Single-crystal X-ray structure determination of 2b*

A yellow crystal of **2b** having approximate dimensions 0.3 mm × 0.2 mm × 0.5 mm was mounted on a glass fiber in a random orientation. The determination of unit cell and the data collection were performed with Mo K $\alpha$  radiation ( $\lambda = 0.71073$  nm) on an Enraf-Nonius CAD4 diffractometer equipped with a graphite crystal monochromator situated in the incident beam. A total of 1932 independent reflections were collected in the range of  $2^\circ \leq \theta \leq 23^\circ$  by  $\omega$ - $2\theta$  scan technique at room temperature, in which 1496 reflections with  $I \geq 3\sigma(I)$  were considered to be observed and used in the succeeding refinements. The correction for Lp factors was applied. The structure was solved by the direct methods (MULTAN 82). The non-hydrogen atoms were located from an E-map. The hydrogen atoms were located theoretically and refined with riding position parameters and fixed isotropic thermal parameter. Then, the structure was refined by full matrix least-squares method with anisotropic thermal parameters for all non-hydrogen atoms. Final  $R$  and  $R_w$  (unit weight) are 0.057 and 0.062 ( $w = 1$ ) respectively and  $(\Delta/\sigma)_{\max} = 0.025$ ,  $S = 0.99$ . The highest peak on the final difference Fourier map had a height of  $0.65$  e/nm $^3$ . All calculations were performed on a PDP 11/44 computer using SDP PLUS program system.

*Crystal data for 2b*: C $_{10}$ H $_{10}$ N $_4$ O $_2$ S,  $M_r = 250$ , space group  $P2_1/n$ , monoclinic,  $a = 1.0966(2)$ ,  $b =$

$0.9618(2)$ ,  $c = 1.1325(2)$  nm,  $\beta = 95.10(3)^\circ$ ,  $V = 1.189(1)$  nm $^3$ ,  $Z = 4$ ,  $D_x = 1.397$  g/cm $^3$ ,  $F(000) = 520$ ,  $\mu = 0.2555$  mm $^{-1}$ .

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