Synthesis of new bis-heteroaryl thiohydrazonates and their \textit{in situ} rearrangement

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Reaction of 3, 3'-bis(4-phenyl-1, 2, 4-triazole-5-thione) 1 with hydrazonoyl halides 2 in ethanol in the presence of sodium ethoxide affords directly the thiohydrazides 4, \textit{via in situ} rearrangement of the initially formed thiohydrazonate esters 3. The involvement of the latter was evidenced by an alternate synthesis of 4.

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Although 3, 3'-bis(4-phenyl-1, 2, 4-triazole-5-thione) 1 has been reported more than twenty years ago\(^1\), its reactions have been rarely studied hitherto. In the course of our continuing interest in the chemistry of hydrazonoyl halides\(^2\), now we wish to report the reactions of 1 with a series of hydrazonoyl halides 2 and with active chloromethylene compounds 5.

Results and Discussion

Treatment of 1 with two molar equivalents of each of the hydrazonoyl halides 2a-d in ethanol in the presence of sodium ethoxide at room temperature afforded products that can be assigned either the presence of sodium ethoxide at room temperature or the thiohydrazonoyl halides 2, \textit{via in situ} rearrangement of the initially formed thiohydrazonate esters 3. The involvement of the latter was evidenced by an alternate synthesis of 4.

Consistent with structure 4, it excludes structure 3. This is because heteroaryl thiohydrazonates have been reported\(^3-5\) to show peaks in their mass spectra corresponding to the loss of the elements of the heterocyclic thiol. Such peaks were not observed, however, in the spectra of the series prepared. The \(^13\)C NMR spectra of 4a and 4b, taken as representative examples of the series prepared, revealed in each case two characteristic signals at \(\delta\) 150-153 and 144-148 assignable to the thiohydrazide (-NHCS-) and C-3 of the 1, 2, 4-triazole ring residue, respectively.

To account for the formation of 4, it is suggested that reaction of 1 with 2 starts with the formation of thiohydrazonate esters 3 which undergo \textit{in situ} Smiles type rearrangement\(^4\) to give the respective thiohydrazides 4 as end-products as depicted in Scheme I. To shed some light on the involvement of 3, an attempt was made to prepare it by an alternate method. For this purpose, we prepared 6b by the reaction of 1 with 2-chloro-3-oxobutanilide 5b in ethanol in the presence of sodium ethoxide. The structure of 6b, which has not yet been reported, was consistent with its microanalyses and spectral data (IR and \(^1\)H NMR) and was further evidenced by its chemical transformations (Scheme I).

When 6b was treated with benzenediazonium chloride in ethanol in the presence of sodium acetate, it yielded unexpectedly the azo derivative 7b. The structure of the latter was based on its mass, IR and \(^1\)H NMR spectra together with its elemental analyses (see Experimental). When 7b was treated with sodium ethoxide in ethanol in an attempt to effect Japp-Klingemann cleavage of the acetyl group\(^6\) to get 3, we got instead a product identical in all respects with 4b. This interesting result suggests that the expected thiohydrazonate ester 3b rearranged \textit{in situ} to give 4b as the end-product.

In conclusion, the foregoing results indicate that reaction of hydrazonoyl halides 2 with 1 and the base catalyzed cleavage of 7 follow the same pathway that involves 3 as intermediate. The latter undergo \textit{in situ} Smiles type rearrangement\(^4\) to give 4 as end-products.

Experimental Section

All melting points were taken on a Gallenkamp apparatus and are uncorrected. Infrared spectra of all
new compounds were recorded in KBr using Fourier transform infrared spectrophotometer and Pye Unicam SP-300. $^1$H and $^{13}$C NMR spectra were recorded in CDCl$_3$ on a Varian Gemini 200 spectrometer using TMS as internal reference; and mass spectra on a GCMS-QP 100 EX spectrometer. Elemental analyses were carried out at the Microanalytical Laboratory at Cairo University, Giza, Egypt. The starting 3,3$'$-bis(4-phenyl-1,2,4-triazole-5-thione)$^1$ 1, the hydrazonoyl halides 7-10$^2$a-d and 2-chloro-3-oxobutanilide$^5$b were prepared as previously described.

**Reaction of 3,3$'$-bis(4-phenyl-1,2,4-triazole-5-thione) 1 with hydrazonoyl halides 2a-g.** To a stirred ethanolic sodium ethoxide solution (0.46 g sodium in 20 mL absolute ethanol) was added 1 (10 mmoles). After 10 min the appropriate hydrazonoyl halide 2a-d (20 mmoles) was added to the resulting solution and the mixture was stirred at room temperature for 12 hr during which the hydrazonoyl chloride dissolved and the crude reaction product precipitated. The precipitate was filtered, washed with water, dried and crystallized from either ethanol or ethanol-acetic acid mixture as indicated below to give products 4.

**Compound 4a:** Yield 80%; m.p. 234$^o$C (EtOH-AcOH); IR (KBr): 3330 (NH), 1446 (C=S) cm$^{-1}$; $^1$H NMR: $\delta$ 6.8-7.5 (m, 20H), 7.6-7.9 (m, 10H), 9.7 (s, 2H); $^{13}$C NMR: $\delta$ 155.5, 153.2, 148.7, 141.7, 140.4, 131.4, 130.5, 129.9, 129.4, 129.1, 126.7, 125.0, 122.0, 119.9, 119.4; MS: m/z (%) 740 (M$^+$, 10), 663 (20), 619 (35). Found: C, 68.0; H, 4.4; N, 18.9; S, 8.6. C$_{42}$H$_{32}$N$_{10}$S$_2$ (740.5) requires C, 68.11; H, 4.32; N, 18.92; S, 8.65%.

**Compound 4b:** Yield 73%; m.p. 244$^o$C (EtOH-AcOH); IR (KBr): 3400, 3198 (NH), 1668 (C=O), 1442 (C=S) cm$^{-1}$; $^1$H NMR: $\delta$ 7.0-7.4 (m, 20H), 7.4-7.6 (m, 10H), 8.4 (s, 2H), 9.3 (s.2H); $^{13}$C NMR:
\[ \delta 160.1, 150.1, 144.2, 142.5, 139.1, 133.4, 130.6, 130.2, 129.4, 129.1, 127.7, 126.5, 124.4, 123.5, 121.3, 117.3; \text{MS: m/z (\%)} 826 (M^+, 10), 706 (20), 662 (30). \text{Found: C, 64.0; H, 4.2; N, 20.3; S, 7.7.} \]

\[ \text{C}_{34}\text{H}_{28}\text{N}_{10}\text{O}_{2}\text{S}_{2} (826.5) \text{requires C, 64.64; H, 4.45; N, 19.13; S, 7.7.} \]

\[ \text{C}_{36}\text{H}_{32}\text{N}_{10}\text{O}_{4}\text{S}_{2} (732.5) \text{requires C, 59.02; H, 4.37; N, 18.77; S, 7.15%.} \]

\[ \text{C}_{44}\text{H}_{32}\text{N}_{14}\text{O}_{6}\text{S}_{2} (916.5) \text{requires C, 57.64; H, 3.49; N, 18.77; S, 9.52%.} \]

\[ \text{C}_{46}\text{H}_{38}\text{N}_{12}\text{O}_{2}\text{S}_{2} (854.5) \text{requires C, 64.64; H, 4.45; N, 19.13; S, 7.7%.} \]

\[ \text{C}_{34}\text{H}_{28}\text{N}_{10}\text{O}_{2}\text{S}_{2} (672.5) \text{requires C, 60.71; H, 4.17; N, 57.1; S, 9.5.} \]

\[ \text{C}_{36}\text{H}_{32}\text{N}_{10}\text{O}_{4}\text{S}_{2} (687.5) \text{requires C, 58.9; H, 4.4; N, 19.1; S, 7.49%.} \]

\[ \text{C}_{36}\text{H}_{32}\text{N}_{10}\text{O}_{4}\text{S}_{2} (752.5) \text{requires C, 57.6; H, 3.5; N, 21.0; S, 6.7.} \]

\[ \text{C}_{46}\text{H}_{38}\text{N}_{12}\text{O}_{2}\text{S}_{2} (910.5) \text{requires C, 63.2; H, 4.1; N, 18.4; S, 7.0.} \]

**Coupling of 6b with benzenediazonium chloride.**

To a solution of compound 6b (10 mmoles) in ethanol (80 mL) sodium acetate trihydrate (6 g) was added and the mixture was cooled to 0-5°C and stirred. To the resulting cold solution, a cold solution of benzene-diazonium chloride [prepared by diazotizing aniline (20 mmoles)] in water (20 mL) was added portionwise. After all of diazonium salt solution was added, the mixture was stirred for further 30 min in ice-bath. The solid that precipitated was filtered, washed with water and crystallized from ethanol to give the corresponding phenylazo compound 7b (85%), m.p. 220-22°C; IR (KBr): 3393 (NH), 1685 (C=O) cm ^{-1}; 1H NMR: \( \delta 2.3 (s, 6H), 2.3 (s, 6H), 1.61 (s, 3H), 1.87 (s, 3H), 7.0-7.5 (m, 20H), 8.30 (s, 2H); \text{MS: m/z (\%)} 910 (M^+, 10), 834 (20), 796 (30). \text{Found: C, 63.2; H, 4.1; N, 18.4; S, 7.0.} \]

**Base-catalysed cleavage of bis-azo compound 7b.**

To a stirred ethanolic sodium ethoxide solution (0.46 g sodium metal in 40 mL absolute ethanol) the compound 7b was added and the mixture was stirred at room temperature for 12 hr, during which the starting reagent 7b dissolved and the crude reaction product precipitated. The precipitate was filtered, washed with water and then crystallized from EtOH-AcOH (1:1; v/v) mixture to afford the bis-azo compound 4b, which proved to be identical in all respects (m.p., mixed m.p., TLC and mass spectra) with that obtained from the reaction of 1 with 2b.

**References**


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**Reaction of 3,3′-bis(4-phenyl-1,2,4-triazole-5-thione) 1 with 2-chloro-3-oxobutanilide 5b.** To a stirred ethanolic sodium ethoxide solution (0.46 g sodium metal in 40 mL absolute ethanol) was added the compound 1. After 10 min stirring at room temperature, the compound 5b (20 mmoles) was added and the mixture was stirred at room temperature for 15 hr, then water (20 mL) was added. The solid formed was collected and crystallized from methanol to give compound 6b, yield 70%; m.p. 132-34°C; IR (KBr): 3377, 3311(NH), 1683, 1658 (C=O) cm ^{-1}; 1H NMR: \( \delta 1.61 (s, 3H), 1.87 (s, 3H), 2.38 (s, 1H), 3.38 (s, 1H), 7.0-7.5 (m, 20H), 8.66 (s, 1H), 8.72 (s, 1H); \text{MS: m/z 702 (M^+).} \text{Found: C, 61.5; H, 4.2; N, 15.9; S, 9.1.} \]

**Base-catalysed cleavage of bis-azo compound 7b.**

To a stirred ethanolic sodium ethoxide solution (0.46 g sodium metal in 40 mL absolute ethanol) the compound 7b was added and the mixture was stirred at room temperature for 12 hr, during which the starting reagent 7b dissolved and the crude reaction product precipitated. The precipitate was filtered, washed with water and then crystallized from EtOH-AcOH (1:1; v/v) mixture to afford the bis-azo compound 4b, which proved to be identical in all respects (m.p., mixed m.p., TLC and mass spectra) with that obtained from the reaction of 1 with 2b.

**References**