

# Synthesis of Pyrazole-Derived Dithioethers Using in situ Generation of Dithiolate-Ions

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## Abstract

A number of pyrazole-derived dithioethers were prepared by the reaction of diisothiuronium salts and 2-(3,5-dimethylpyrazol-1-yl)ethanol tosylate in a basic aqueous solution. Diisothiuronium salts were prepared by the reaction of thiourea with alpha,omega-dibromoalkanes containing from three to twelve methylene groups. The use of these salts allowed in situ generation of dithiolate ions, thus eliminating the need to use hazardous dimercaptanes.

**Keywords:** pyrazole, thioether ligands, thiourea, thiuronium salts

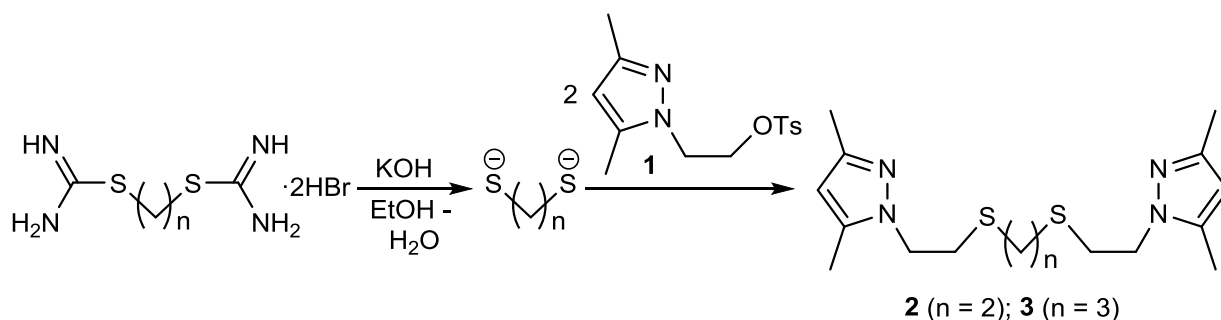
## Introduction

Compounds with two pyrazole moieties linked by an aliphatic spacer act as bidentate chelating ligands forming complexes with most transition metals and some main-group elements [1]. Coordinating ability of these ligands can be diversified by introducing additional donor atoms into the spacer between the heterocycles. Ligands with spacers bearing nitrogen, oxygen, and sulfur atoms have been reported, some of them were found to be effective steel corrosion inhibitors [2], while their chromium(III) and palladium(II) complexes demonstrated catalytic activity in ethylene oligomerization [3] and Heck cross-coupling reactions [4]. Recently we and others have reported high superoxide dismutase-like activity of copper(II) complexes with bis(pyrazole) ligands [5, 6]. Copper(II) complexes with azole-derived thioether ligands were proposed as models for type I copper proteins [7].

Here we present a facile method for the preparation of pyrazole-derived dithioethers by the reaction of diisothiuronium salts with 1-(2-tosyloxyethyl)-3,5-dimethylpyrazole.

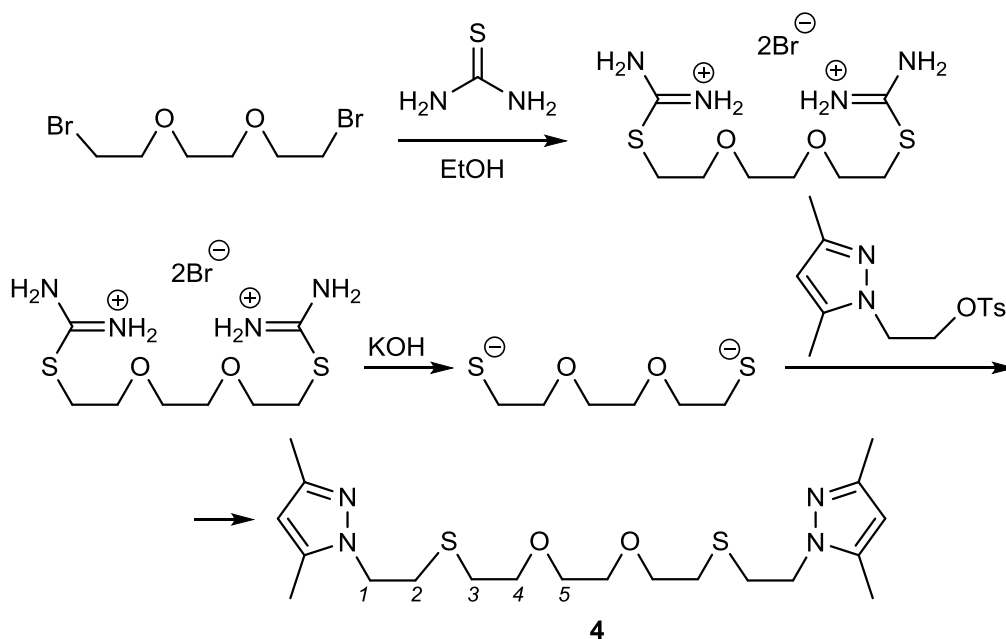
## Results and discussion

Alkaline hydrolysis of thiuronium salts is known to lead to thiolate ions [8], which in our syntheses then acted as nucleophiles in the reaction with tosylate **1** (scheme 1). The proposed method allows to generate dithiolate-ions *in situ* and avoid the use of toxic and malodorous dithiols, which gives it an advantage to known methods for preparation of similar products [9].



Scheme 1

Using the proposed method we have prepared dithioethers with polymethylene linkers between sulfur atoms (compounds **2**, **3**) and hybrid ligand **4** with hard oxygen and soft sulfur donor atoms in the linker between pyrazole rings (scheme 2).



Scheme 2

NMR  $^1\text{H}$  spectrum of compound **4** shows three triplets ( $\text{CH}_2$  groups 1, 2 and 3) at 4.09, 2.89 and 2.59 ppm correspondingly and a triplet overlapping with a singlet ( $\text{CH}_2$  groups 4 and 5) at 3.55 ppm.

Typical experimental procedure is given in the experimental part.

## Experimental

NMR spectra were recorded on Bruker AV300 instrument operating at 300 MHz for  $^1\text{H}$  and 75 MHz for  $^{13}\text{C}$ .

### 1,8-Bis(3,5-dimethylpyrazol-1-yl)-3,6-dithiaoctane (typical procedure)

(**2**). A solution of 1,2-dibromoethane diisothiuronium salt (3.46 g, 10 mmol), KOH (5.6 g, 100 mmol) in water (15 ml) were refluxed for 5 hours. Then, tosylate **1** (5.88 g, 20 mmol) was added, refluxing and vigorous stirring were continued for 8 hours. After cooling to room temperature, precipitate formed, which was filtered and washed with water. Yield 73 %, colorless crystals, m.p. 85-87 °C (*i*-PrOH), lit. m.p. 78 °C [2]. IR bands,  $\text{cm}^{-1}$ : 1549; 1461; 1315 (Pz), 787 (C-S). NMR  $^1\text{H}$  ( $\text{CDCl}_3$ ),  $\delta$ , ppm: 2.18, 2.24 (s, 12H,  $\text{CH}_3$ ), 2.52 (s, 4H,  $\text{SCH}_2\text{CH}_2\text{S}$ ), 2.91 (t, 4H,  $\text{PzCH}_2\text{CH}_2\text{S}$ ,  $J$  6.6 Hz), 4.10 (t, 4H,  $\text{PzCH}_2\text{CH}_2\text{S}$ ,  $J$  6.6 Hz), 5.76 (s, 2H,  $\text{H}^4$  (Pz)). NMR  $^{13}\text{C}$  ( $\text{CDCl}_3$ ),

$\delta$ , ppm: 11.0 (5-CH<sub>3</sub>), 13.3 (3-CH<sub>3</sub>), 32.0 (SCH<sub>2</sub>CH<sub>2</sub>S and PzCH<sub>2</sub>CH<sub>2</sub>S), 48.5 (PzCH<sub>2</sub>CH<sub>2</sub>S), 104.9 (C<sup>4</sup> (Pz)), 139.1 (C<sup>5</sup> (Pz)), 147.7 (C<sup>3</sup> (Pz)). Found, %: C 56.31; H 7.65; N 16.56; S 18.48. Calculated for C<sub>16</sub>H<sub>26</sub>N<sub>4</sub>S<sub>2</sub>, %: C 56.77; H 7.74; N 16.55; S 18.94.

### Acknowledgements

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