OPTIMIRANJE REAKCIJE KONDENZACIJE CINKOVIH BIS(2-AMINOTIOFENOLATA)

OPTIMISING CONDENSATION REACTIONS OF ZINC BIS(2-AMINOTHIOPHENOLATES)

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INTRODUCTION

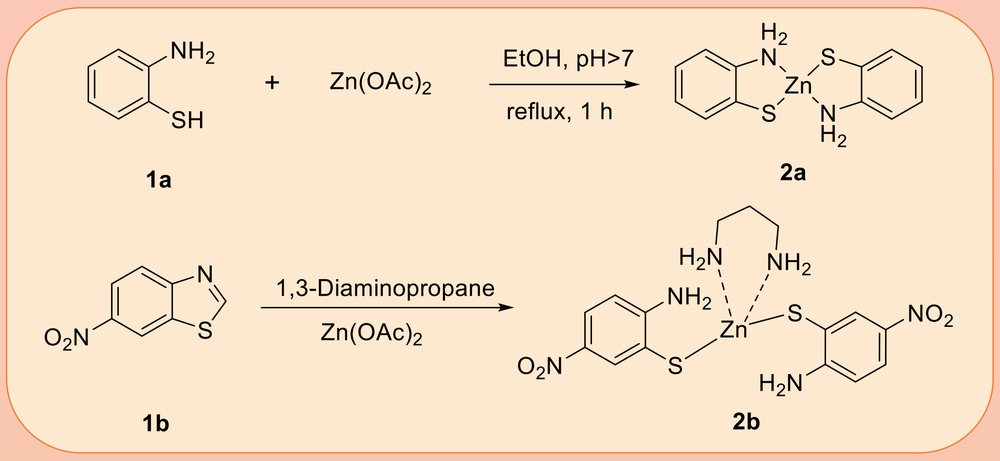
Benzothiazole derivatives see widespread use, particularly in medicine and molecular biology due to their biological activity. One of the most common methods for preparing 2-substituted benzothiazole derivatives are condensation reactions of 2-aminothiophenol with aldehydes, carboxylic acids and their derivatives. One drawback of this method is the instability of 2-aminothiophenol derivatives, which like most thiols easily oxidize into the corresponding disulfide form when exposed to air. While 2-aminophenyl disulfide derivatives may still be used for condensation reactions with aldehydes they tend to require more intense reaction conditions compared to thiols which can result in the formation of byproducts and lower yield of desired products [1]. The aim of this work is the preparation of zinc 2-aminothiophenolate complexes and assessing their suitability for condensation reactions with aromatic aldehydes.

RESULTS AND DISCUSSION

The unsubstituted zinc bis(2-aminothiophenolate) complex (**2a**) was prepared from 2-aminothiophenol (**1a**) according to a literature procedure [2] depicted in scheme 1 in a yield of 82%.

A new nitro substituted zinc bis(5-nitro-2-aminothiophenolate) complex was prepared starting from 6-nitrobenzothiazole in a one-pot reaction. First, the thiazole ring is opened with 1,3-diaminopropane in glycerol, followed by addition of zinc acetate solution. The product precipitates in the form of an orange powder in a yield of 93% with purity greater than 95%.

X-ray diffraction confirmed the ratio of ligands to the zinc metal centre and the presence of a 1,3-diaminopropane ligand in the structure (fig. 1)



Scheme 1: Synthesis of zinc bis(2-aminothiophenolate) complexes

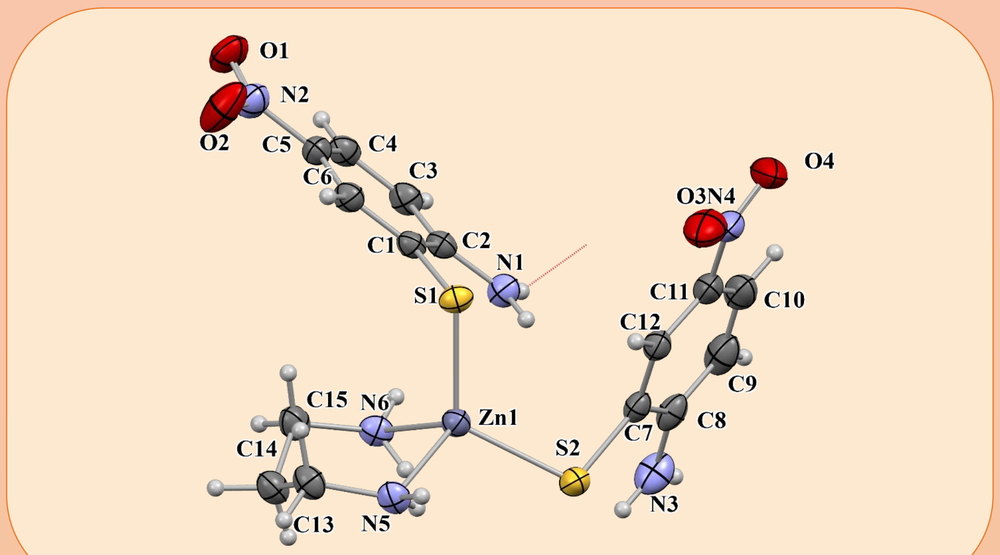
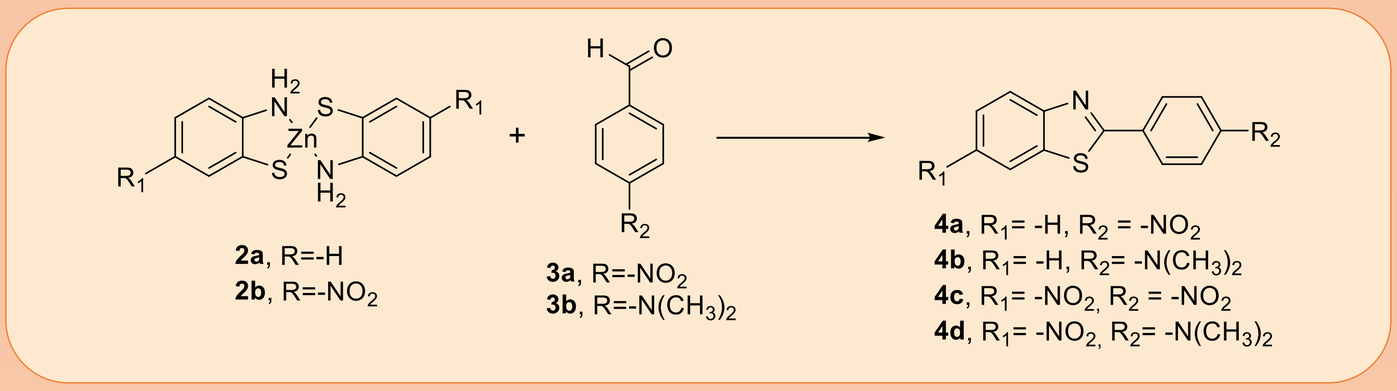


Figure 1: Mercury rendered ORTEP view of (propane-1,3-diamine)bis(5-nitro-2-aminothiophenolate)zinc(II) complex

Zinc complexes **2a** and **2b** were used for condensation reactions with benzaldehydes **3a** and **3b** according to scheme 2.



Scheme 2: Condensation reactions of zinc complexes with aromatic aldehydes

Table 1: Condensation reactions parameters and yield

Compound	Solvent	Temperature (°C)	Time(h)	Addition	Yield
4a	Acetic acid	r.t.	22	-	46%
4a	Acetic acid	120°C	4	Citric acid	76%
4a	Glycerol	140°C	2	Citric acid	46%
4a	NMP	80	24	-	25%
4a	NMP	120	3	-	42%
4a	NMP	140	4	-	69%
4a	NMP	140	4	Citric acid	100%
4b	NMP	140	3	Citric acid	94%
4c	NMP	100	24	-	90%
4d	NMP	140	3	Citric acid	86%

Optimization of reaction conditions was carried out on compound **4a** (Table 1). Using N-methyl-2-pyrrolidone as a solvent at a temperature of 140°C for 4 hours with citric acid as an addition gave the highest yield and didn't require further purification. Compounds **4b-d** similarly gave the best yield in NMP.

Generally, we found that the addition of a chelating compound such as citric acid increased the yield of the products. The presence of electron donating and withdrawing groups did not have a significant impact on product yield.

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