

Electron-transfer initiated nucleophilic substitution of thiophenolate anion by 1-chloro-substituted 4-(thiazol-2-ylazo)naphthalenes

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ABSTRACT

In this work, the electrochemical transformation of 5-chloro-2-[[4-chloronaphthalen-1-yl]azo]thiazoles (**A**) into the corresponding radical anion $A^{\cdot-}$ and its subsequent reaction with diphenyldisulfide (**PhSSPh**) was studied. It was found that the primarily generated azo anion radical $A^{\cdot-}$ is able to initiate an electron transfer process which converts the disulfide into its thiolate anion PhS^- . This anion was subsequently able to substitute the *Cl*- and *H*-groups by phenylmercapto moieties in the starting azo compound **A**. The structures of the phenylmercapto-substituted azo compounds thus generated were confirmed by thin-layer chromatography and mass spectrometry using independently prepared compounds as references.

1. Introduction

Although the reductive splitting of disulfides into thiols has been known for a long time and can be achieved by means of a large variety of methods, e.g. electrochemically [1–4], by using alkali hydroxides [5–7], alkali alkoxides [8–11], or silver salts [12–14], serious studies on the mechanism of this reduction have been published only recently [15]. The electrochemical reduction of disulfides $RS-SR$ into thiols takes place via intermediate radical anions $RS-SR^{\cdot-}$ which dissociate subsequently into a thiolate anion RS^- and a thiol radical RS^{\cdot} . This thiol radical can immediately accept a further electron from the electrode, giving rise to the formation of a second thiolate anion RS^- . Hence, the reductive transformation of disulfides into two thiolate anions is a two-electron transfer process, each of which can be accompanied by a protonation step as long as proton donors are present in the reaction mixture. In this case, two thiols RSH are formed as reduction products (Scheme 1).

The electrochemical reduction of disulfides mediated by radical anions $A^{\cdot-}$ generated from certain organic electron-accepting compounds **A**, such as quinones or azo compounds, has recently been reported [16] (Scheme 2). In addition, under these conditions, the disulfides were transformed into the corresponding thiolates at a rate that depends on the electronic nature of the radical anion mediators $A^{\cdot-}$ used. For example, the rate of disulfide splitting is relatively high when using, e.g. tetrazene or 4-dimethylaminoazobenzene as a mediator, and lower when certain quinones, such as anthra- or benzoquinone are used.

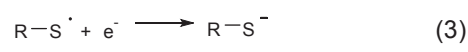
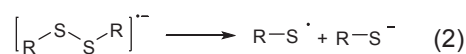
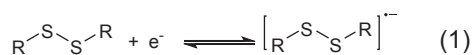
Although under the reported conditions a reaction of the thiolates RS^- with the starting mediator **A** seems possible, there is currently no information on this type of reaction. Therefore, to obtain such information, we have studied the reaction of diphenyldisulfide (**PhSSPh**) as a model organic disulfide with 1-chloro-4-(thiazol-2-ylazo)naphthalenes **1** under reductive conditions produced electrochemically. The use of these azo compounds in this study follows from our recent studies on the reaction of certain organic thiols with the above-mentioned azo compounds [17]. This reaction surprisingly gave rise to the formation of a large variety of products **2**, generated by replacing both the *Cl*- and *H*-substituents of the thiazole, as well as the naphthalene moieties in the starting azo compounds **1**, by the thiols used, e.g. by thiophenol (Scheme 3).

2. Experimental

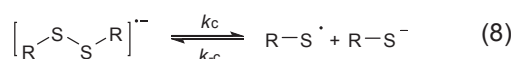
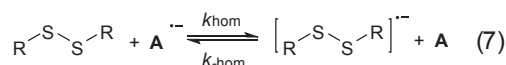
Cyclic voltammograms were carried out in acetonitrile containing 0.1 M tetra-*n*-butylammonium hexafluorophosphate ($n\text{-Bu}_4\text{NPF}_6$) as the supporting electrolyte, using a standard electrochemical cell with a platinum wire as the working electrode, a platinum foil as the counter electrode and a non-aqueous reference electrode (0.01 M Ag/Ag^+ in 0.1 M $n\text{-Bu}_4\text{NPF}_6$). All electrochemical measurements were performed under an inert (nitrogen) atmosphere. All potentials were measured against the ferrocenium/ferrocene (Fc^+/Fc) redox couple in the same solvent. The half-wave potential of Fc^+/Fc in acetonitrile solution was + 0.38 V versus the standard calomel electrode (SCE).

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Scheme 1. Mechanism of disulfide reduction.



Scheme 2. Electrochemical reduction of disulfides mediated by radical anions.

In situ ESR/UV-Vis-NIR spectroelectrochemical experiments were performed in the optical ESR cavity (ER 4104OR, Bruker, Germany). ESR spectra were recorded with an EMXmicro X-band CW spectrometer (Bruker, Germany) at 100 kHz modulation. UV-Vis-NIR spectra were measured with an Avantes spectrometer AvaSpec-2048x14-USB2 with a CCD detector and AvaSpec-NIR256-2.2 with an InGaAs detector using the AvaSpec software. Both the ESR spectrometer and the UV-Vis-NIR spectrometer were linked to a HEKA potentiostat PG 390 (HEKA Elektronik, Germany), which triggered both spectrometers. Triggering was performed by the software package PotMaster v2x80. A flat cell was used for the spectroelectrochemical experiments, with a laminated gold- μ -mesh (Goodfellow) as the working electrode, a silver-chloride-coated silver wire as the pseudo reference electrode, and a platinum wire as the counter electrode. The ESR and UV-Vis-NIR spectra were collected at a continuous potential scan rate. Each UV-Vis-NIR spectrum was collected relative to that of the uncharged compound at the initial potential.

3. Results and discussion

3.1. (Spectro)-Electrochemical experiments

Fig. 1a demonstrates the cyclic voltammograms (CV) of compound **1b** and PhSSPh (**3**) as single components measured in a standard

electrochemical cell. The CV of **1b** exhibits a reversible one-electron reduction process at a half-wave potential of -1.06 V (vs. Fc^+/Fc). PhSSPh is reduced at a much lower potential compared to the azo compound **1b** (increase in the current is observed at ca. -2.0 V).

For the spectroelectrochemical experiments, a solution with an equimolar concentration of the azo compound **1b** and **3** was used. The ESR and optical spectra were recorded *in situ* during the cyclic voltammetry measurements. The potential was switched to -1.4 V only to generate exclusively radical anions of **1b**. In the course of these measurements, an irreversible reduction peak was obtained in the CV and the intensity of the ESR signal of the radical anions $\text{1b}^{\cdot-}$ was strongly reduced (Fig. 1b,c). Moreover, the UV-Vis absorption bands of $\text{1b}^{\cdot-}$, seen in the spectroelectrochemical experiments without PhSSPh [18], changed dramatically (Fig. 1d). With an excess of **3** in the solution of **1b** in acetonitrile, neither absorption bands nor the ESR signal of $\text{1b}^{\cdot-}$ were detected (see Fig. S1 in the Supporting Information).

3.2. Analytical experiments

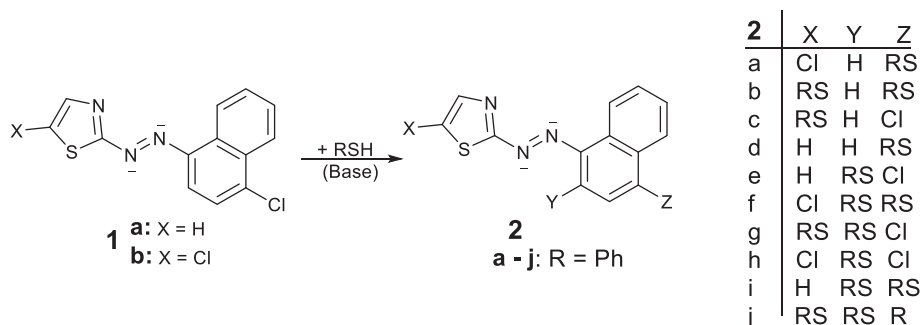
10 mL of an acetonitrile solution containing 6.16 mg of the azo compound **1b** and 4.36 mg of the diphenyldisulfide **3** was used for the analytical experiments. After the electrolysis had been performed under the conditions described above by applying a potential of -1.2 V (Fig. S2), the reaction mixture was concentrated *in vacuo* and the oleic residue was filtered over silica and washed with toluene to remove the ionic components used as electrolyte. The toluene in the solution was then removed by evaporation and the residue (ca. 8 mg) was analyzed by thin-layer chromatography (TLC) using silica as the stationary phase and toluene as the mobile phase. The compounds **2b** and **2c** were found to be the main products in a ratio of about 1:1, while the compounds **2a** and **2d** were obtained as by-products in a relative amount of less than 10%, together with traces of **1a** and **1b**. The compounds **2a-2d** used as reference materials in the TLC analysis were synthesized via a base-mediated reaction of the azo compound **1b** with thiophenol, as reported in [17].

The result of the TLC analysis is depicted in Fig. 2.

To confirm the results of this TLC analysis, mass spectra of the separated compounds were recorded. The corresponding m/z values are included in Fig. 2.

3.3. Discussion

The results described above demonstrate unambiguously the formation of phenylmercapto-substituted azo compounds in the course of the electrolysis of the chloro-substituted azo compound in presence of PhSSPh. From these results, the mechanism depicted in Scheme 4 can be deduced. In the first step, the starting azo compound **1b** is reductively transformed, due to its lower reduction potential compared with PhSSPh (**3**), into the corresponding radical anion $\text{1b}^{\cdot-}$. This species is able to transfer its unpaired electron onto **3**, giving rise to the formation of a thiophenolate anion PhS^- (**4**⁻) and a thiophenyl radical

Scheme 3. Products obtained by reaction of 1-chloro-4-(thiazol-2-ylazo)naphthalenes **1** with thiophenol.

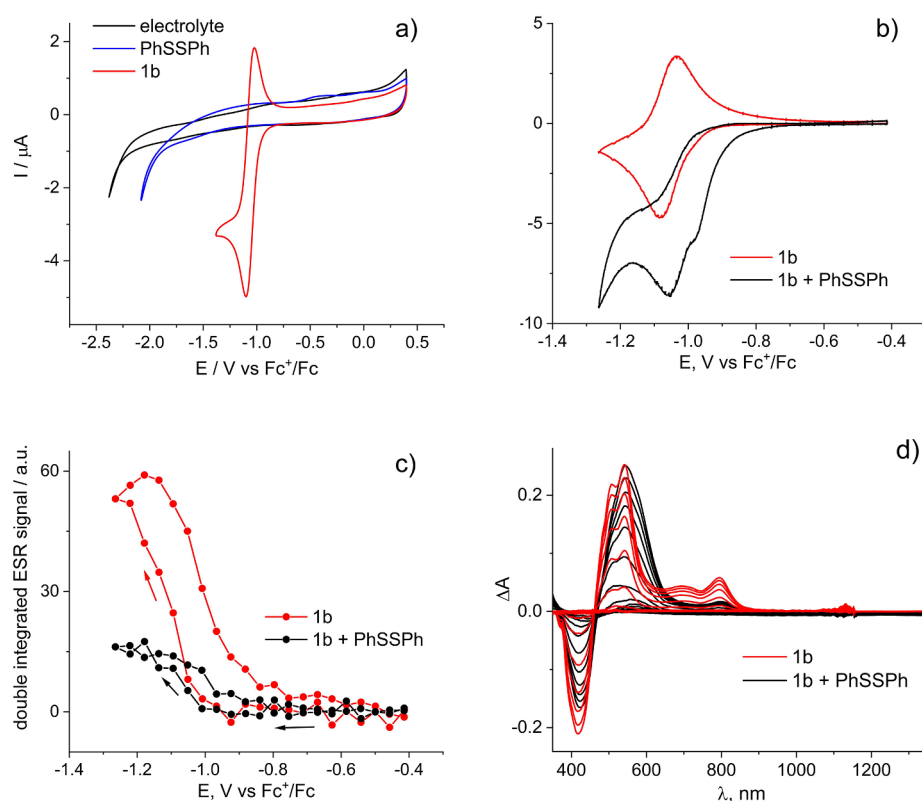


Fig. 1. (a) Cyclic voltammograms of compound **1b** and **PhSSPh** measured on a Pt electrode in acetonitrile containing 0.1 M *n*-Bu₄NPF₆ at a scan rate 0.1 V/s. (b) Cyclic voltammogram of compound **1b** in the absence (red line) and in the presence (black line) of **PhSSPh**, measured in a spectroelectrochemical cell. (c) Dependence of the intensity of the ESR signal on the applied potential; (d) in situ UV-Vis-NIR spectra measured during the reduction.

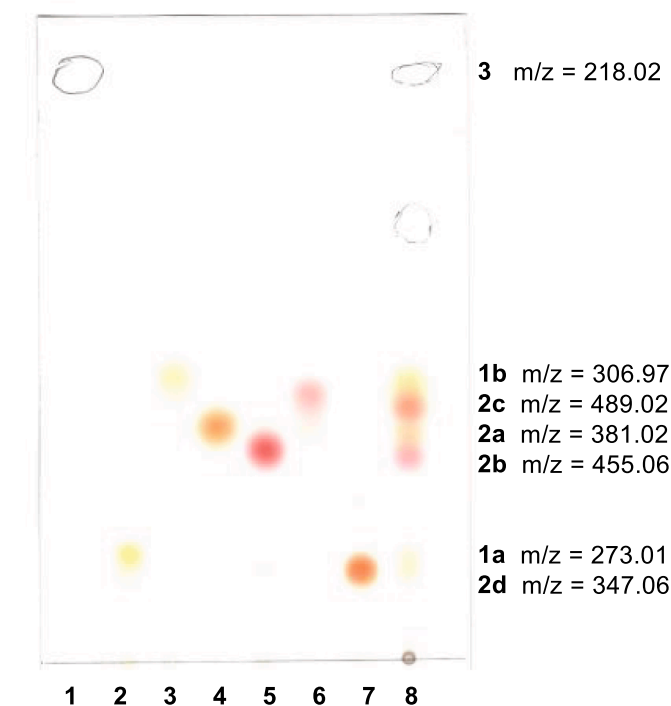


Fig. 2. TLC analysis of the electrolysis solution with independently prepared compounds **2a–2d** and their starting compounds **1a**, **1b** and **3**.

PhS[−] (**4**) (route A). While the thiophenyl radical **4'** can dimerise (with a second thiophenyl radical) to form a **PhSSPh** species, the thiophenolate anion **4[−]** attacks the azo compound **1b** and transforms this into the corresponding Meisenheimer complex **5[−]** from which a chloride elimination occurs, yielding the substitution product **2a**. This compound can react with a further thiophenolate anion **4[−]** yielding either the compound

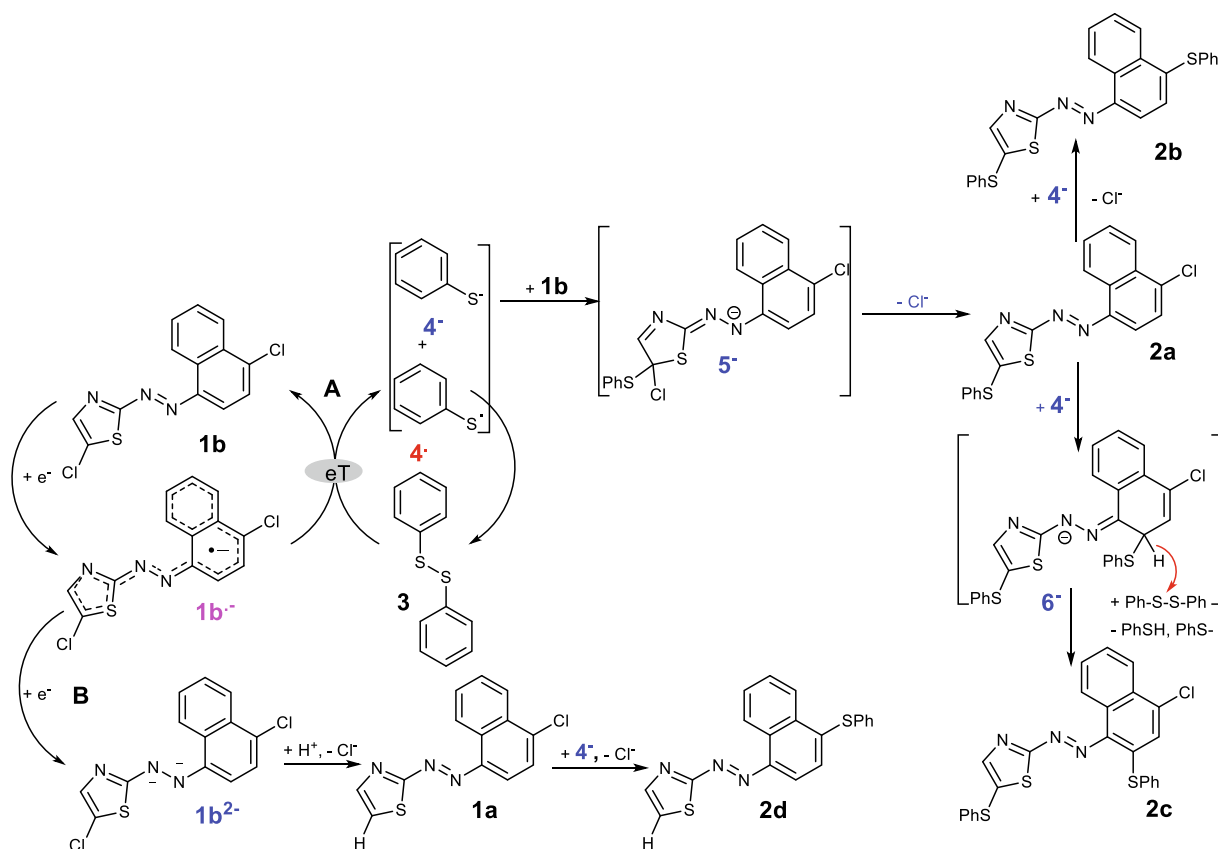
2b in the course of a normal nucleophilic substitution [19–25] or, alternatively, the compound **2c** in the course of a diphenyldisulfide-mediated hydride transfer from the Meisenheimer complex **6[−]** formed as an intermediate [23].

Because the compound **2d**, which contains no chloro-substituent at its thiazole moiety, is also formed (in low amounts) in the electrochemical experiments, there must have been second reaction route B. This involves the formation of dianion **1b^{2−}** by the acceptance of a second electron either from the electrode or, more probably, from a second radical anion **1b^{•−}** in the course of a radical disproportionation reaction [26–30]. After protonation, this dianion **1b^{2−}** eliminates a chloride ion with the formation of compound **1a** with a 5*H*-thiazol-2-yl moiety which can, as known [17], subsequently undergo a nucleophilic substitution with the thiophenolate anion **4[−]** [31], giving rise to the formation of the phenylmercapto-substituted compound **2d**.

4. Conclusions

As expected, the electrochemically generated radical anions **1b^{•−}** of 5-chloro-2-[(4-chloronaphthalen-1-yl)az]thiazole (**1b**) can act either as an electron shuttle, transforming **PhSSPh** into the corresponding thiophenolate anions PhS[−] which initiates a nucleophilic substitution of the *Cl*- and *H*-groups at the starting azo compound **1b**, giving rise to the formation of the phenylmercapto-substituted 1-(thiazol-2-yl)azo-naphthalenes **2a–2c** (route A) or, to a small extent, can disproportionate with the formation of the starting azo compound **1b** and its corresponding dianion **1b^{2−}** from which the compound **1a** results after protonation and subsequent chloride elimination (route B). Subsequently, this compound with a 5*H*-thiazol-2-yl moiety reacts with the thiophenolate anion PhS[−], yielding the compound **2d**.

All of the phenylmercapto-substituted azo compounds described have been independently prepared, accordingly to [17], by reaction of the azo compounds **1a** and **1b** with thiophenol in the presence of triethylamine and characterized by means of mass spectrometry, ¹H NMR and UV-Vis spectrometry.



Scheme 4. Mechanism of the reaction of 1-chloro-4-(thiazol-2-ylazo)naphthalenes **1** with thiophenol.

CRedit authorship contribution statement

Evgenia Dmitrieva: Conceptualization, Investigation, Visualization, Writing - original draft. **Xiuling Yu:** Validation, Investigation, Resources. **Horst Hartmann:** Conceptualization, Supervision, Writing - original draft.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.elecom.2020.106706>.

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