Chimica Techno Acta
published by Ural Federal University
eISSN 2411-1414
chimicatechnoacta.ru

ARTICLE
2023, vol. 10(4), No. 202310418
DOI: 10.15826/chimtech.2023.10.4.18

The transformations of thiols and their dimers in the redox-mediated thiol-disulfide exchange reaction

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This paper belongs to a Regular Issue.

Abstract

A search for new approaches to sulfurous waste utilization is one of the urgent tasks of chemical technology. Thiol-disulfide exchange reaction (TDE) is one of the possible ways to involve technogenic wastes in organic synthesis. Electricity can promote such type of interactions. In this paper, we have studied TDE reactions involving low molecular weight thiols or their dimers under electrochemical conditions. The exchange processes were examined using the model reaction between 1-propanethiol and phenyl disulfide. Electrolysis was performed in the presence of redox mediators such as arylphosphines, substituted amines, *o*-, *p*-aminophenols or catechol. These compounds can initiate a TDE process with a formation of unsymmetrical disulfides. 4-Amino-2,6-diphenylphenol was chosen as the most effective redox mediator, which reduces the anodic overvoltage of a thiol oxidation by 1.20 V. The advantage of electrolysis in an undivided cell is the increased yield of target unsymmetrical disulfides due to the possibility of reduction of homodimers at the cathode. The involvement of refining waste, such as C_3–C_4 disulfide oil, in the reaction with substituted thiophenols made it possible to obtain a number of unsymmetrical arylalkyl disulfides with biologically active fragments in a high yield (up to 97%) under indirect electrolysis conditions.

Keywords

industrial waste
thiols
thiol-disulfide exchange
unsymmetrical disulfides
redox-mediator
electrochemistry

Received: 09.12.23
Revised: 19.12.23
Accepted: 20.12.23
Available online: 29.12.23

Key findings

- The utilization of *n*-alkanethiols and their dimers (C_3, C_4) during the promoted thiol-disulfide exchange under electrochemical conditions is considered.
- A number of redox-mediators were studied as promoters of the thiol-disulfide exchange reaction.
- Thiol-disulfide exchange reactions lead to the formation of unsymmetrical disulfides.
- Unsymmetrical arylalkyl disulfides with anisole or veratrol fragments were obtained with a high yield (up to 97%).

Supplementary materials

1. Introduction

1.1. Sulfur-containing industrial waste

Low molecular weight C_1–C_4 thiols (RSH) are undesirable components of oil and gas condensate feedstocks. Known desulfurization processes are based on the oxidation of thiols to disulfide oil, which remains mixed with hydrocarbon feedstock, while the total sulfur content in the oil is not reduced. The extraction of disulfides allows to bring the concentration of sulfur compounds to standard values. The extracted disulfides (RSSR) can be used as substrates for the synthesis of valuable organosulfur compounds. From this standpoint, the use of low molecular weight thiols and disulfide oil in the synthesis of organic sulfur compounds, in particular unsymmetrical disulfides, via the interaction with (hetero-)aromatic thiols is very relevant challenge.

1.2. Synthesis and practical value of disulfides

Organic disulfides have found wide application in the pharmaceutical [1, 2] and food industry [3, 4] as well as in the production of synthetic rubbers [5] and new electrode materials [6] due to their unique physicochemical properties. There is a high biochemical significance of disulfide bonds

in the formation of cross-links in the tertiary structure of proteins in the processes of thiol-disulfide exchange (TDE) with the participation of glutathione [7, 8]. Reactions involving thiols in the presence of various oxidizing agents or catalysts are most often used for the synthesis of disulfides [9–11]. Preparative methods that are effective to obtain symmetrical disulfides (homodimers) are often not suitable for the synthesis of unsymmetrical analogues (heterodimers) due to the rapid TDE reaction. This process leads to the formation of symmetrical by products that are difficult to separate from the target unsymmetrical disulfides (R_1SSR_2). In this regard, synthesis of R_1SSR_2 requires a special methodological approach to increase the selectivity of heterodimer formation. Diethyl azodicarboxylate derivatives [12–14], trichloroisocyanuric acid [15], *tert*-butyl hydroperoxide with *N*-iodosuccinimide [16], *o*-benzo(imino)quinones [17, 18] can act as promoters of the reaction of oxidative coupling of thiols to unsymmetrical disulfides. The interaction of thiophenols with arylsulfonyl chlorides in the presence of PPh_3 [19], as well as the use of potassium *tert*-butoxide, potassium or cesium carbonates [20, 21] lead to the formation of unsymmetrical aryl disulfides. One of the direct ways to obtain R_1SSR_2 is the TDE reaction, which can either occur spontaneously [22, 23] or require more severe conditions and the presence of additional activators [24–27] depending on the nature of the starting sulfur compounds. Besides, an exchange process between two disulfides (disproportionation) is possible to form a heterodimer, which is catalyzed by nitrogen monoxide under aerobic conditions [28].

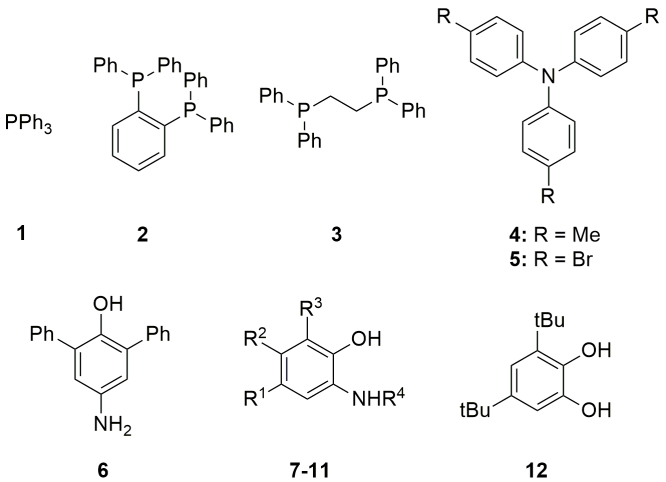
1.2.1. Sources of energy for the synthesis of disulfides

The reactions of thiol oxidative coupling, TDE and disproportionation of disulfides can be initiated by various physical means, such as electric current [29, 30], photo- and microwave irradiation [31–33]. In recent years, electrochemical approaches to the formation of carbon-heteroatom bonds have been widely used in organic synthesis due to such advantages as atom-efficiency, mild conditions (room temperature, atmospheric pressure, absence of metal-containing catalysts), and ease of varying reaction parameters [34, 35]. Electrosynthesis of organosulfur compounds is one of the promising areas of organic chemistry [36–39]. Unsymmetrical disulfides can be obtained by electrochemical oxidation of RSSR in aprotic solvents in the presence of a thiol or its dimer [40]. The electroactivation of organic trisulfides in the presence of (cyclo-)alkenes leads to the formation of unsymmetrical mono- and disulfides, also through the formation of sulfur-centered intermediates RS^+ and RSS^+ [41]. The electrooxidation of a thiol mixture [29] or a thiol and a sulfide [42] in galvanostatic mode leads to R_1SSR_2. The process of oxidation of RSH to RSSR occurs effectively under conditions of indirect electrolysis with the participation of various mediators (**Med**) [43, 44]. The advantage of this approach is the possibility of the redox mediator regeneration, as well as a decrease in the anodic overvoltage. We have previously showed that thiol oxidative coupling can occur in the presence of sterically hindered *o*-aminophenol as a redox mediator and lead to R^1SSR^2 [45]. Besides, undesirable reaction products (homodimers) participate in the TDE side process promoted by the *o*-aminophenol/*o*-iminobenzoquinone under electrochemical conditions [46].

The aim of the present work is to study TDE reactions in the presence of redox mediators **1–12** (Scheme 1) to promote exchange interaction. Indirect electrolysis is considered as an environmentally friendly and energy-efficient tool for the utilization of low molecular weight thiols and their dimers (disulfide oil), which are wastes from oil and gas processing. These compounds, formed during the desulfurization process, can be used as raw materials for the electrochemical synthesis of valuable unsymmetrical disulfides.

2. Experimental Part

Commercially available reagents from Sigma-Aldrich, Alfa Aesar were used as supplied. 4,6-Di-*tert*-butyl-2-(adamantyl amino)phenol [47] (**7**) and 4,6-di-*tert*-butyl-2-(2,6-diisopropylphenylamino)phenol [48] (**8**) were provided by the Laboratory of Metal Complexes with Redox-Active Ligands of Razuvaev Institute of Organometallic Chemistry RAS (Russia, Nizhny Novgorod). The solvents were purified and dried following the standard procedures [49]. The redox potentials of the compounds (5 mM) were measured by cyclic voltammetry (CV) in a three-electrode undivided cell under argon using a VersaSTAT 3 potentiostat (United States).



7: $R^1 = R^3 = tBu$, $R^2 = H$, $R^4 = Adamantyl$
8: $R^1 = R^3 = tBu$, $R^2 = H$, $R^4 = 2,6\text{-di-isopropylphenyl}$
9: $R^1 = Cl$, $R^2 = H$, $R^3 = NO_2$, $R^4 = H$
10: $R^1 = R^3 = Cl$, $R^2 = Me$, $R^4 = H$
11: $R^1 = tBu$, $R^2 = R^3 = R^4 = H$

Scheme 1 The studied redox mediators.

 DOI: 10.15826/chimtech.2023.10.4.18

The working electrode was a stationary platinum (Pt) electrode with a diameter of 3 mm; an auxiliary electrode was a platinum plate (S = 32 mm²). The reference electrode (Ag/AgCl/KCl(sat.)) has a waterproof diaphragm. The potential scan rate was 0.2 V·s^{-1}. The supporting electrolyte was 0.15 M $NaClO_4$ or $(n\text{-}Bu)_4NClO_4$ (99%, Acros) twice recrystallized from aqueous EtOH and dried in vacuum (48 h) at 50 °C. The oxidation (reduction) peaks of studied compounds are related to diffusion, which is determined by the linear dependence of the peak current I_{pa} on $v^{1/2}$ in the potential scan range from 0.05 to 1.00 V·s^{-1}.

The microelectrolysis of the mixture of *n*-PrSH and $(PhS)_2$ in the presence of **1–12** was performed at 25 °C in a diaphragmless three-electrode undivided cell (V = 2 mL) on Pt-electrode (S = 32 mm²) in a potentiostatic mode (τ = 2 h). Redox-mediator (5 mM), *n*-PrSH (0.05 M) and $(PhS)_2$ (0.025 M) were added to a pre-deaerated electrochemical cell containing a solution of supporting electrolyte (0.15 M $NaClO_4$) in CH_3CN or CH_2Cl_2. The microelectrolysis of the mixture of $(n\text{-}PrS)_2$ and different thiophenols in the presence of **6** was performed at 25 °C in a diaphragmless three-electrode undivided cell (V = 4 mL) on Pt-electrode (S = 32 mm²) in a potentiostatic mode (τ = 4 h). Med **6** (0.01 M), $(n\text{-}PrS)_2$ (0.03 M) and substituted thiophenols (0.02 M) were added to a pre-deaerated electrochemical cell containing a solution of supporting electrolyte (0.15 M $NaClO_4$) in acetonitrile and N-methylpyrrolidone mixture (1/1 vol.)

After electrolysis, the solution was concentrated under the reduced pressure, and the supporting electrolyte was precipitated by hexane. The solution was also concentrated under vacuum. The GC-MS was performed on Shimadzu GCMS-QP2010 Ultra instrument equipped with mass spectrometric (EI, 70 eV) and flame photometric detectors. Column temperature was programmed as follows: T_0 = 50 °C (isotherm 1 min), T_1 = 200 °C (isotherm 10 min), T_2 = 280 °C (isotherm 60 min), total analysis time τ = 82 min. Mass spectrometry data (m/z, the intensity I and the retention time τ_{ret}) for synthesized compounds are given in Table 1. Mass spectra are presented in Supplementary Data (Figures S1–S12).

3. Results and Discussion

Arylphosphines (**1–3**), substituted amines (**4**, **5**), substituted *o*-, *p*-aminophenols (**6–11**), and 3,5-di-*tert*-butylcatechol (**12**) were studied as redox mediators. These compounds can promote the thiol-disulfide exchange reaction under electrochemical conditions. The studied compounds can be classified into two types depending on the mechanism of the action: electron transfer (ET) mediators and dehydrogenating (hydrogen atom transfer, HAT) agents. The first type includes substituted amines and phosphines (**1–5**), and the second type is represented by sterically hindered catechol and substituted *o*-, *p*-aminophenols (**7–12**).

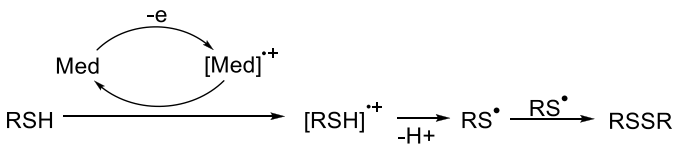
The active form of ET mediators is generated at the anode during one-electron transfer, which leads to the formation of the radical cation [**Med**]$^{\bullet+}$. Subsequently, the thiol is activated to a radical cation, and then a reactive organylthiyl radical (RS$^{\bullet}$) dimerizes to RSSR in a solution (Scheme 2).

The oxidized form (**Med$_{ox}$**) of HAT mediators is the corresponding *o*-benzoquinone or *o*-iminobenzoquinone. These compounds act as dehydrogenating agents towards the thiol. Activation of thiols leads to the formation of disulfides (Scheme 3).

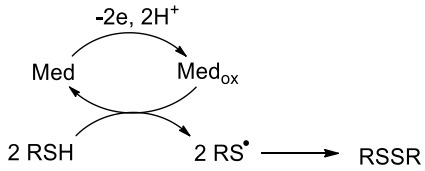
The effectiveness of Med **1–12** in the formation of the target 1-propyl-2-phenyl disulfide (**15**) through the interaction of phenyl disulfide and 1-propanethiol under electrochemical conditions was estimated (Scheme 4, Table 2). In the electrochemical cell, 1-propanethiol is indirectly oxidized to propyl disulfide **17**, but it was detected in insignificant amounts (4–7%).

Table 1 Mass spectrometry data for obtained compounds.

Compound	m/z (I (%))	τ_{ret}, min
15	$[M]^+$ 184 (51), 142 (44), 109 (42), 78 (100), 65 (43), 43 (42)	15.039
16	$[M]^+$ 110 (100), 109 (25), 84 (25), 77 (17), 66 (44), 51 (21)	8.881
17	$[M]^+$ 150 (22), 108 (18), 73 (6), 43 (100)	10.876
19a	$[M]^+$ 214 (10), 138 (19), 108 (100), 77 (25), 58 (10), 43 (61)	17.650
19b	$[M]^+$ 228 (26), 172 (10), 138 (22), 108 (100), 77 (21), 57 (25), 41 (50)	18.853
19c	$[M]^+$ 214 (31), 172 (111), 139 (91), 108 (100), 96 (45), 77 (20), 43 (52), 41 (78)	17.850
19d	$[M]^+$ 228 (15), 172 (10), 139 (57), 124 (14), 108 (61), 57 (28), 41 (80)	19.044
19e	$[M]^+$ 244 (88), 229 (4), 201 (19), 187 (7), 169 (89), 202 (11), 154 (17), 138 (100), 125 (26), 111 (15), 95 (27), 43 (34), 41 (42)	19.775
19f	$[M]^+$ 258 (67), 202 (14), 187 (8), 169 (61), 154 (11), 138 (100), 125 (17), 111 (17), 57 (16), 41 (32)	21.128
20a	$[M]^+$ 278 (13), 138 (17), 111 (95), 96 (42), 77 (52), 65 (100), 45 (87)	28.780
20b	$[M]^+$ 278 (26), 139 (100), 124 (10), 96 (18)	29.231
20c	$[M]^+$ 338 (27), 169 (100), 154 (11), 139 (3), 125 (17), 96 (14)	43.367

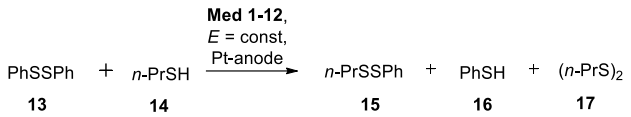


Scheme 2 The mechanism of disulfide formation in the presence of ET redox mediator.



Scheme 3 The mechanism of a disulfide formation in the presence of HAT redox mediator.

 DOI: 10.15826/chimtech.2023.10.4.18



Scheme 4 The TDE reaction between $(C_6H_5S)_2$ and n-C_3H_7SH under electrochemical conditions.

Table 2 The yield[a] of reaction products, the conversion of $(PhS)_2$ during the microelectrolysis of n-PrSH (0.05 M) and $(PhS)_2$ (0.025 M) mixture in the presence of Med **1–12** (5 mM) (Pt-anode, Ag/AgCl, CH_3CN_2, 0.15 M $NaClO_4$, τ_{el} = 2 h).[b]

Med	The yield of *n*-PrSSPh, %	The yield of PhSH, %	The conversion of $(PhS)_2$, %
1	69	10	80
2	53	5	60
3	64	29	94
4	74	15	89
5	86	6	93
6	77	4	81
7	20	2	23
8	31	0	31
9	82	<1	85
10	42	2	48
11	52	1	55
12	82	2	85

[a] The yield of reaction products is calculated based on GC-MS data.
[b] The reaction with Med **1–5** were performed using 0.15 M $(n\text{-Bu})_4NClO_4$ in CH_2Cl_2.

In the case of arylphosphines (triphenylphosphine (**1**), 1,2-bis(diphenylphosphino)benzene (**2**), 1,2-bis(diphenylphosphino)ethane (3)), the major product is the target n-PrSSPh (53–69%). The maximum conversion of $(PhS)_2$ (94%) and the yield of PhSH (29%) are observed in the reaction with the oxidized form of 1,2-bis(diphenylphosphino)benzene (**3**). In the presence of **1–2**, thiophenol is formed in moderate amounts (5–10%). The total charge varied from 2.5–3.6 F/mol in electrolysis with substituted phosphines (Table 3).

It was noted that among the studied redox mediators, only arylphosphines have a promoting effect on the TDE reaction in the absence of electric current. However, the electrogenerated oxidized forms of arylphosphines **1–3** increase the rate of formation of the target unsymmetrical disulfide by 25–200 times compared to blank experiments without an electric current. Mediator electrosynthesis involving arylphosphines makes it possible to reduce the anodic overvoltage by 0.60–0.80 V compared to direct anodic activation of 1-propanethiol.

The electrochemically promoted TDE reaction in the presence of substituted amines (tri-*p*-tolylamine (**4**), tri-*p*-bromophenylamine (**5**)) is characterized by high conversion of phenyl disulfide (89–93%), a good yield of the target disulfide (74–86%) and an insignificant concentration of thiophenol. In the presence of tri-*p*-tolylamine, electrolysis occurs at a more energetically favorable value of the anodic potential (0.80 V) compared to tri-*p*-bromophenylamine (1.15 V). The total charge also significantly varies: in the case of the reaction with **4**, Q is 2.3 F/mol, and for **5** this parameter is 6.0 F/mol.

Another series of redox mediators that promote TDE reactions includes substituted *o*-, *p*-aminophenols (**6–11**), which are characterized by low oxidation potentials (0.56–0.66 V) with the exception of *o*-aminophenol **9** (1.14 V), containing an electron withdrawing nitro group. The highest yield of n-PrSSPh (77–82%) is observed for electrolysis in the presence of sterically hindered *p*-aminophenol **6** or 2-amino-4-chloro-6-nitrophenol (**9**) at high values of the $(PhS)_2$ conversion (81–85%). A moderate yield of the target heterodimer (31–52%) is observed in cases of **8**, **10** and **11** at comparable values of the aromatic disulfide conversion. The electrolysis with **7** containing an adamantyl substituent at the nitrogen atom is characterized by low conversion and yield of unsymmetrical disulfide (23% and 20%, respectively). Electrochemical reactions involving substituted *o*-aminophenols are accompanied by insignificant formation of thiophenol (<4%) during electropromoted TDE. It may be due to the effective mediator oxidation of PhSH to the starting disulfide and its re-involvement in the exchange reaction. In electrolysis with substituted aminophenols, the value of total charge is in the range of 0.5–6.3 F/mol depending on the substituents on the aromatic ring and on the nitrogen atom. The interaction of phenyl disulfide and 1-propanethiol in the presence of an electroactivated form of 3,5-di-*tert*-butylcatechol (**12**) leads to the formation of **15** in a good yield (82%). These data are comparable to the results obtained for electrolysis with substituted aminophenols.

It was established that the target disulfide **15** is formed with the highest yield (77–86%) in the presence of the following compounds: tri-*p*-bromophenylamine (**5**), 4-amino-2,6-diphenylphenol (**6**), 2-amino-4-chloro-6-nitrophenol (**9**) and 3,5-di-*tert*-butylcatechol (**12**). From the energy efficiency, the choice of *p*-aminophenol **6**, which is oxidized at 0.58 V, is preferable (Figure 1). An increase in the conversion and the yield of the target disulfide with the participation of the selected redox mediator can be achieved by increasing the electrolysis time.

Table 3 The electrochemical parameters of microelectrolyses with n-PrSH (0.05 M) and $(PhS)_2$ (0.025 M) mixture in the presence of Med **1–12** (5 mM) (Pt-anode, Ag/AgCl, τ_{el} = 2 h).

Med	E_{el}, V	ΔE, V	Q, F/mol
1	1.30	0.60	3.6
2	1.10	0.80	2.7
3	1.20	0.70	2.5
4	0.80	1.10	2.3
5	1.15	0.75	6.0
6	0.70	1.20	1.6
7	0.70	1.20	0.5
8	0.70	1.20	1.0
9	1.20	0.70	6.3
10	0.70	1.20	1.1
11	0.70	1.20	1.3
12	1.20	0.70	3.5

DOI: 10.15826/chimtech.2023.10.4.18

It is important to note that electrolysis in an undivided cell favors the transformation of aryl disulfides on the counter electrode due to a shift in their reduction potentials to wards the anodic region compared to alkyl disulfides. The use of HAT mediators leads to the formation of an alkylthiyl radical. Hydrogen is released at the counter electrode due to the reduction of protons formed as a result of the Med oxidation. The generation of PhSH upon protonation of the PhS-anion or hydrogenation of the disulfide will further increase the selectivity of the oxidative coupling reaction for the unsymmetrical product (Scheme 5).

In addition to processes of a radical nature, exchange reactions between a thiol and a disulfide can occur in an electrochemical cell via an ionic mechanism (Scheme 5), as was shown earlier in the study of thiol oxidative coupling [46]. The combination of these transformations leads to an effective accumulation of the target unsymmetrical disulfide.

To establish the possibility of an exchange reaction between aliphatic disulfides (disulfide oil) and aromatic thiols under indirect electrolysis conditions, the interactions of alkyl disulfides (C_3, C_4) and thiophenol derivatives **18a–c** were considered in the presence of **6** in CH_3CN/NMP (Scheme 6). The choice of NMP as a co-solvent is caused by its ability to selectively extract sulfur compounds and good efficiency in the redox-mediated oxidative coupling of thiols [18, 44].

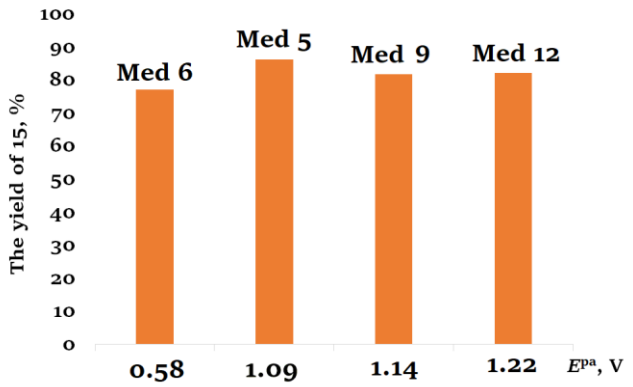
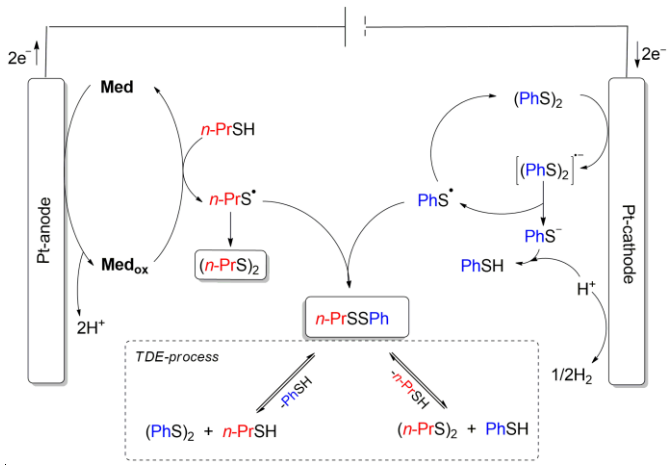


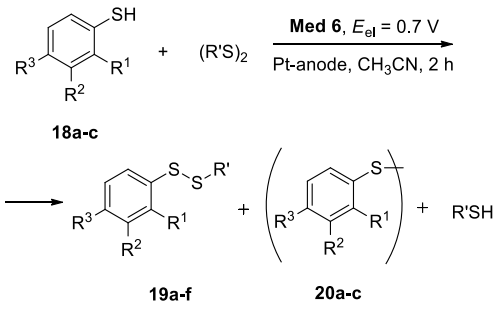
Figure 1 The anodic potentials (E^{pa}) of redox-mediators **5–6**, **9**, **12** in CH_3CN (Pt-anode, Ag/AgCl) and the yield of disulfide **15**.



Scheme 5 The proposed mechanism of radical and ionic processes in the undivided cell in the presence of HAT-mediator.

During electrolysis, the target unsymmetrical disulfides **19a–f** were obtained in yields of 20–97% (Table 4). In cases of reactions with 4-methoxy- or 3,4-dimethoxythiophenol, the formation of symmetrical aromatic disulfide **20b–20c** was not detected in the reaction products, which indicated a high selectivity for the formation of heterodimers. But 2-methoxythiophenol tended to form dimer **20a** (46–53%) under the conditions considered. The maximum conversion (97–98%) was achieved for 4-methoxythiophenol. The formation of R'SH was detected in trace amounts, which is due to their immediate oxidation into the started dimer under electrolysis conditions. The total charge varied from 0.32–0.61 F/mol.

It is noted that *o*-benzoiminoquinone (Med_{ox}) is indifferent to the disulfide, since it acts as a dehydrogenating agent and, therefore, participates only in the activation of the thiol. In this regard, RSSR transformations can occur either at the electrodes or through the direct interaction with a thiol (or another disulfide) in the solution. However, the applied anodic potential (0.7 V) is not sufficient for direct electroactivation of alkyl disulfide, since RSSR are oxidized in the potential range 1.4–1.6 V. The thiol formed during TDE is easily converted into the started disulfide under redox-mediated electrolysis conditions.



18a, **20a**: $R^1 = OCH_3$, $R^2 = R^3 = H$
18b, **20b**: $R^1 = R^2 = H$, $R^3 = OCH_3$
18c, **20c**: $R^1 = H$, $R^2 = R^3 = OCH_3$
19a: $R^1 = OCH_3$, $R^2 = R^3 = H$, R' = *n*-C_3H_7
19b: $R^1 = OCH_3$, $R^2 = R^3 = H$, R' = *n*-C_4H_9
19c: $R^1 = R^2 = H$, $R^3 = OCH_3$, R' = *n*-C_3H_7
19d: $R^1 = R^2 = H$, $R^3 = OCH_3$, R' = *n*-C_4H_9
19e: $R^1 = H$, $R^2 = R^3 = OCH_3$, R' = *n*-C_3H_7
19f: $R^1 = H$, $R^2 = R^3 = OCH_3$, R' = *n*-C_4H_9

Scheme 6 The mediated TDE reaction between thiophenols **18a–c** and alkyl disulfides under electrochemical conditions.

Table 4 The yield of reaction products, the conversion of thiols during the TDE between **18a–c** and alkyl disulfides in the presence of Med **6** (5 mM) (Pt-anode, Ag/AgCl, CH_3CN:NMP (1:1, v/v), 0.15 M $NaClO_4$, τ_{el} = 4 h).[a]

Entry	The yield of heterodimer, %	The yield of homodimer, %	The conversion of thiol, %
1	20 (**19a**)	53 (**20a**)	74 (**18a**)
2	42 (**19b**)	46 (**20a**)	89 (**18a**)
3	96 (**19c**)	traces (**20b**)	97 (**18b**)
4	97 (**19d**)	traces (**20b**)	98 (**18b**)
5	51 (**19e**)	traces (**20c**)	52 (**18c**)
6	70 (**19f**)	traces (**20c**)	72 (**18c**)

[a] The yield of reaction products is calculated based on GC-MS data.

DOI: 10.15826/chimtech.2023.10.4.18

4. Limitations

The thiol-disulfide exchange reaction between *n*-alkyl disulfides (C_3, C_4) and 2,6-di-*tert*-butyl-4-mercaptophenol did not lead to the formation of the unsymmetrical disulfide under the studied conditions. Besides, *tert*-butyl disulfide also was not involved in an interaction with studied thiophenols. These exchange processes are probably hindered due to steric factor in the thiol or disulfide structures.

5. Conclusions

Hereby, an electrochemical approach to obtaining unsymmetrical disulfides from alkanethiols C_3–C_4 and their dimers was investigated. The method is based on a thiol-disulfide exchange between an aliphatic thiol (or disulfide) and an aromatic substrate in the presence of an organic redox mediator. This reaction leads to the formation of unsymmetrical disulfides, which potentially have biological activity. The optimization of the redox mediator made it possible to select 4-amino-2,6-diphenylphenol (**6**) as the most effective and accessible reagent among twelve compounds of various nature. The use of redox-mediator **6** allows reducing the anodic overvoltage of 1-propanethiol oxidation by 1.20 V and obtaining the target disulfide with good yield. The interaction of *n*-alkyl disulfides and methoxy derivatives of thiophenol was carried out in the presence of this mediator. The highest yield of unsymmetrical disulfide (96–97%) was obtained in the reaction of 4-methoxythiophenol and *n*-propyl- or *n*-butyl disulfide. It is noteworthy that the structure and reactivity of the starting compounds influences the yield of target heterodimers in the thiol-disulfide exchange reaction. Besides, the advantage of this method is the use of an undivided cell, which leads to the accumulation of the target product due to the reduction of a homodimer at the counter electrode.

• Supplementary materials

This manuscript contains supplementary materials, which are available on the corresponding online page.

• Funding

This work was supported by the Grant for the young PhD scientists MK-2488.2022.1.3 (agreement No. 075-15-2022-526) https://grants.extech.ru/.

• Acknowledgments

None.

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• Conflict of interest

The authors declare no conflict of interest.

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 DOI: 10.15826/chimtech.2023.10.4.18