

# Synthesis, reactivity, electrochemical and crystallographic studies of diferrocenoyl diselenide and ferrocenoyl selenides

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## Abstract

Diacyl diselenide (**8**), diacyl selenide (**9**) and acyl selenol esters (**10–12**) incorporating the ferrocenoyl substituent have been synthesized from ferrocene carboxylic acid (**13**). The new compounds (**8–10**) have been characterized by multinuclear NMR (<sup>1</sup>H, <sup>13</sup>C, <sup>77</sup>Se), IR spectroscopy and electrospray mass spectrometry. All compounds (**8–13**) undergo a one electron reversible oxidation at significantly more positive potential than ferrocene. The structures of the diselenide and selenide (**8** and **10**) have been confirmed by single crystal X-ray diffraction. The absolute structure parameter of **8** indicates that it crystallizes in an enantiomerically pure form. The peroxidase-like activities of the diselenide (**8**) and selenides (**9–12**) have been determined by the thiol assay.

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**Keywords:** Selenol esters; Ferrocene; Thiol peroxidase; X-ray crystal structures

## 1. Introduction

The acyl selenides are useful synthetic intermediates and are employed as building blocks for the synthesis of heterocyclic compounds (oxazole,  $\beta$ -lactone) [1], asymmetric aldol reactions [2] and precursors for acyl radical chemistry [3,4]. Acyl selenides and selenol esters can produce acyl radicals under mild conditions, which can be used in a large variety of inter- and intramolecular reactions [5]. Acyl selenides are also well known for their liquid crystalline properties [6]. In recent years, selenol esters and their analogues have attracted much attention from chemists interested in aspects of their structures [7]. Due to their potential applications, sev-

eral procedures have been developed to prepare these esters [8,9].

Besides that, selenol esters have also been used as glutathione peroxidase (GPx) mimics for the decomposition of hydrogen peroxides [10]. Compounds with a Se–C bond exhibit significant GPx activity, if the Se–C bond is easily cleaved by GSH. For example, some selenol esters and  $\alpha$ -(arylselenenyl) ketones (**1–7**) exhibit glutathione peroxidase-like (GPx) activity by reacting with GSH to produce catalytically active species (vide infra). Our group has reported that diselenides having a ferrocene-like redox active group show much better activity in the thiol assay than the diselenides based on benzene [11]. In this paper, we report the synthesis, characterization and the thiol peroxidase-like activity of diferrocenoyl diselenide (**8**), diferrocenoyl selenide (**9**) and ferrocenoyl selenol esters (**10–12**) where the selenium is not directly attached to a cyclopentadienyl (Cp) ring (Chart 1).

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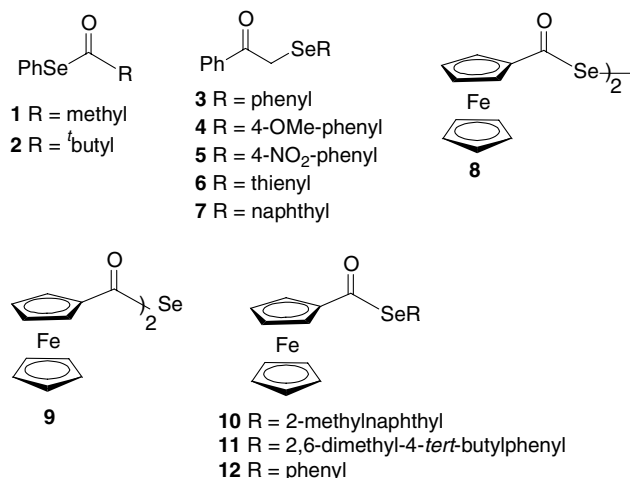


Chart 1. Selenol esters having GPx-like activity.

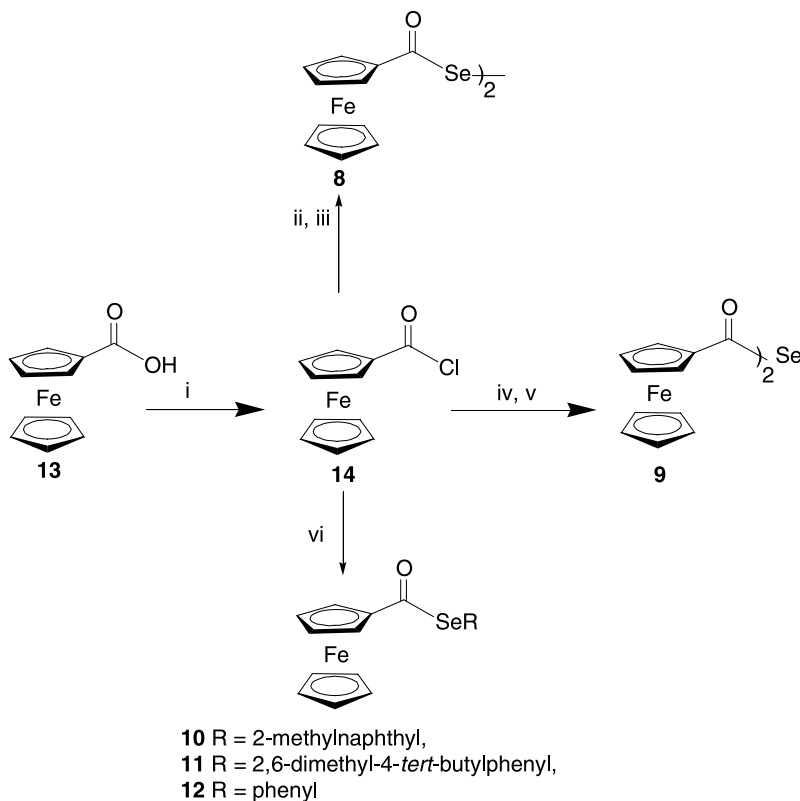
## 2. Results and discussion

### 2.1. Synthesis

The equimolar reaction of ferrocenoyl chloride [12] with LiAlHSeH [9] and subsequent quenching with 1

equiv. of I<sub>2</sub>/KI gave the orange coloured diferrocenoyl diselenide (**8**) in 20% yield. Alternatively diferrocenoyl diselenide (**8**) was synthesized in good yield (96%) by the reaction of Li<sub>2</sub>Se<sub>2</sub> [13] and ferrocenoyl chloride. 2:1 Molar reaction of ferrocenoyl chloride with LiAlHSeH gave the diferrocenoyl selenide (**9**) in 90% yield (Scheme 1).

The synthesis of diacyl selenides has been a subject of several recent reports [14]. Jensen et al. [8d] have reported the existence of unstable dibenzoyl selenide, which was obtained by the elimination of hydrogen selenide from selenobenzoic acid at room temperature. Kato et al. [14] have reported the synthesis of diacyl selenides by the reaction of *O*-silyl selenocarboxylates with acyl chlorides. Here preparation of diferrocenoyl selenide (**9**) could be easily achieved in one pot and good yields. Ferrocenoyl(2-methylnaphthyl) selenide (**10**) was synthesized by the reaction of the lithium selenolate with ferrocenoyl chloride. Bis(2-methylnaphthyl) diselenide [15] was reduced by using 2 equiv. of lithium superhydride, [Li(C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>BH] to afford the selenolate. Similarly ferrocenoyl selenol esters **11** and **12** were synthesized by the reduction of the corresponding diselenides, bis(2,6-dimethyl-4-*tert*-butylphenyl) diselenide [11a] and diphenyl diselenide. Ferrocenoyl selenol esters



Reagents and conditions: i) (COCl)<sub>2</sub>, CH<sub>2</sub>Cl<sub>2</sub>; ii) LiAlH<sub>4</sub>, Se, KI, I<sub>2</sub>, THF; iii) LiHBEt<sub>3</sub>, Se; iv) LiAlH<sub>4</sub>, Se, THF; v) LiHBEt<sub>3</sub>, 2 SeTHF; vi) bis (2-methylnaphthyl) diselenide, diphenyl diselenide, bis(2,6-dimethyl-4-*tert*-butylphenyl) diselenide, Li(C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>BH, THF

Scheme 1. Synthesis routes to diferrocenoyl diselenide (**8**) and ferrocenoyl selenides (**9**–**12**).

(10–12) were purified by column chromatography and obtained in good yields (55–94%).

## 2.2. NMR and IR spectroscopic studies

The  $^1\text{H}$  NMR spectra show one singlet (4.28–4.43 ppm) due to the unsubstituted Cp ring and two pseudo-triplets (4.58–5.01 ppm) due to the mono-substituted Cp ring in compounds (8–12). In the  $^{77}\text{Se}$  NMR spectra, diferrocenoyl selenide (9) shows a signal at 763 ppm whereas diferrocenoyl diselenide (8) shows a signal at 581 ppm. A downfield shift for the selenide (9) as compared to the diselenide (8) is in contrast with the diaryl selenides where generally the reverse trends in  $^{77}\text{Se}$  NMR chemical shifts were found [11c,16]. The downfield shift of diferrocenoyl selenide (9) may be due to the presence of two electron withdrawing  $>\text{C}=\text{O}$  groups (both groups are bonded to a single selenium). However, the chemical shift of 9 is in close agreement with those of the reported diacyl selenides ( $765 \pm 38$  ppm) [8a]. The  $^{77}\text{Se}$  chemical shift for diferrocenoyl diselenide (581 ppm) is significantly upfield shifted compared to the corresponding value reported for dibenzoyl diselenide (615 ppm), bis(4-chlorobenzoyl) diselenide (621 ppm), bis(2-methoxybenzoyl) diselenide (615 ppm), bis(phenylacetyl) diselenide (644 ppm) and bis(2-methoxybenzoyl) diselenide (599 ppm) [7c]. The upfield shift of 8 may be due to the more electron donating nature of the ferrocenoyl group as compared to the phenyl substituents. Ferrocenoyl selenol esters (10–12) show  $^{77}\text{Se}$  NMR chemical shifts at 502, 405 and 628 ppm, respectively. These values are upfield shifted as compared to diferrocenoyl selenide (9).

In the IR spectra, the  $\nu_{\text{C}=\text{O}}$  vibration for diferrocenoyl diselenide (8), diferrocenoyl selenide (9) and ferrocenoyl selenol esters (10–12) are found in the range of 1670–1716  $\text{cm}^{-1}$  and are shifted to higher frequency range 17–63  $\text{cm}^{-1}$  as compared to the parent compound 13 ( $\nu_{\text{C}=\text{O}} = 1653 \text{ cm}^{-1}$ ).

## 2.3. Electrospray mass (ES-MS) spectrometry study

The electrospray mass of 8, 9 and 11 show the corresponding molecular ion peaks centered at  $m/z = 585.8$ , 505.9 and 454.0, respectively. In ES-MS of 8, 9 and 11 a peak at  $m/z = 213$  with 100% intensity was observed; this corresponds to the ferrocenoyl fragment  $[\text{Fe}(\eta^5\text{-C}_5\text{H}_5)(\eta^5\text{-C}_5\text{H}_4\text{C}=\text{O})]^+$  and suggests that its formation is easily possible under electrospray mass spectrometry conditions.

## 2.4. Electrochemical studies

The redox properties of diferrocenoyl diselenide (8), diferrocenoyl selenide (9), ferrocenoyl selenol esters

(10–12) and ferrocene carboxylic acid (13) were investigated by cyclic voltammetry in  $\text{CH}_3\text{CN}$  solution.

The electrochemical behavior of ferrocene derivatives (8–13) is in accordance with the monometallic nature of the compound. The cyclic voltammogram of diferrocenoyl diselenide (8) is shown as an example in Fig. 1 and the half wave potentials ( $E_{1/2}$ ) of compounds (8–13) are listed in Table 1. Each of the cyclic voltammograms of the ferrocenoyl compounds (8–13) showed a well-defined single electron wave that was reversible in nature, although peak separations were generally somewhat greater than the 59 mV expected theoretically [17,18]. The  $E_{1/2}$  values for these compounds are considerably more positive than the corresponding value for ferrocene. This may be due to the strong electron withdrawing nature of the carboxylic and selenol ester groups, which are bonded directly to the Cp ring, making the oxidation more difficult than that of unsubstituted ferrocene. It is interesting to note here that  $E_{1/2}$  values of diferrocenoyl selenide (9) and ferrocenoyl selenol esters (10–12) are significantly lower than the  $E_{1/2}$  values of 8. The difference in  $E_{1/2}$  between  $[\text{FcC}(\text{O})\text{Se}]_2$  (8) and  $[\text{FcC}(\text{O})]_2\text{Se}$  (9) was 39 mV. Morley et al. [17] have reported that the  $E_{1/2}$  difference between  $(\text{FcSe})_2$  and  $\text{FcSe}^n\text{Bu}$  was 80 mV and Shu et al. [18] have reported 125 mV  $E_{1/2}$  difference for the same compounds. The smaller difference in  $E_{1/2}$  between 8 and 9 as

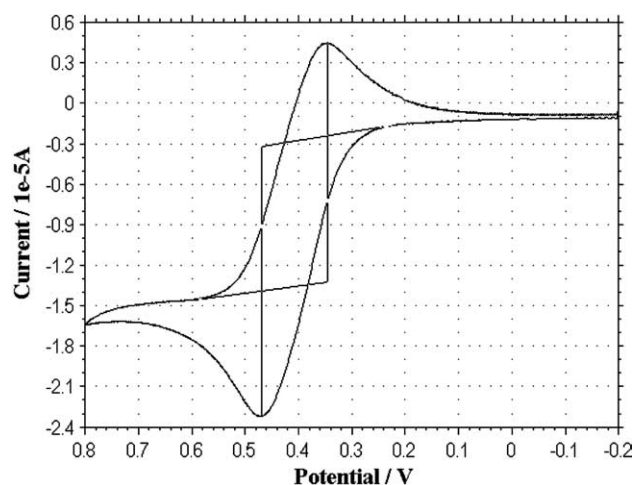


Fig. 1. Cyclic voltammogram of diferrocenoyl diselenide (8).

Table 1  
 $E_{1/2}$  and  $^{77}\text{Se}$  NMR chemical shifts of ferrocenoyl selenides

Compounds	$E_{1/2}$ (mV)	$^{77}\text{Se}$ NMR (ppm)
8	413	581
9	374	763
10	367	502
11	359	405
12	380	628
13	284	—

compared to  $(\text{FcSe})_2$  and  $\text{FcSe}^n\text{Bu}$  may be due to the presence of a  $>\text{C}=\text{O}$  group between selenium and the Cp ring.

Establishing the correlation between  $^{77}\text{Se}$  NMR chemical shifts and  $E_{1/2}$  is difficult, although it is noticeable that the diferrocenoyl diselenide (**8**), which shows a significantly upfield  $^{77}\text{Se}$  chemical shift (581 ppm), has the highest  $E_{1/2}$  value in this series. Furthermore, the  $^{77}\text{Se}$  chemical shifts (ppm) and  $E_{1/2}$  are in the same order for **10**, **11** and **12**. This relationship indicates that ferrocenoyl derivatives with upfield chemical shifts are difficult to oxidize on the electrochemical scale and this is in accordance with the report of Morley et al. [17]. A second wave was not observed initially in the case of all the compounds (**8–12**). To find the second wave, the cyclic voltammograms of these compounds were recorded over a much wider range. The results from additional experiments suggest that there is a second feature in the cyclic voltammograms of these compounds. However, this feature was not well defined and occurred at 1.60–1.90 V; it was electrochemically irreversible, since there was no corresponding reduction found. The additional feature may be due to the selenium acting as redox centre.

### 2.5. Initial reduction rates ( $v_0$ )

The catalytic activity of **8–12** was studied according to the method reported by Tomoda et al. [19] using benzene thiol (PhSH) as a glutathione alternative. The initial rates ( $v_0$ ) for the reduction of  $\text{H}_2\text{O}_2$  (3.75 mM) by benzene thiol (1 mM) in the presence of various catalysts (0.1 mM) (Eq. (1)) were determined in methanol medium by monitoring the UV absorption at 305 nm due to the formation of diphenyl disulfide (Fig. 2).

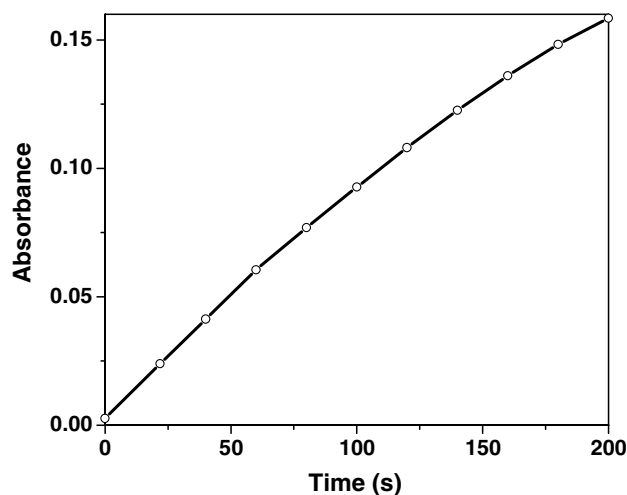
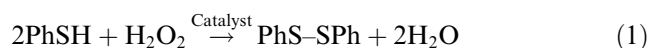


Fig. 2. A plot of absorbance at 305 nm vs. time due to formation of diphenyl disulfide.

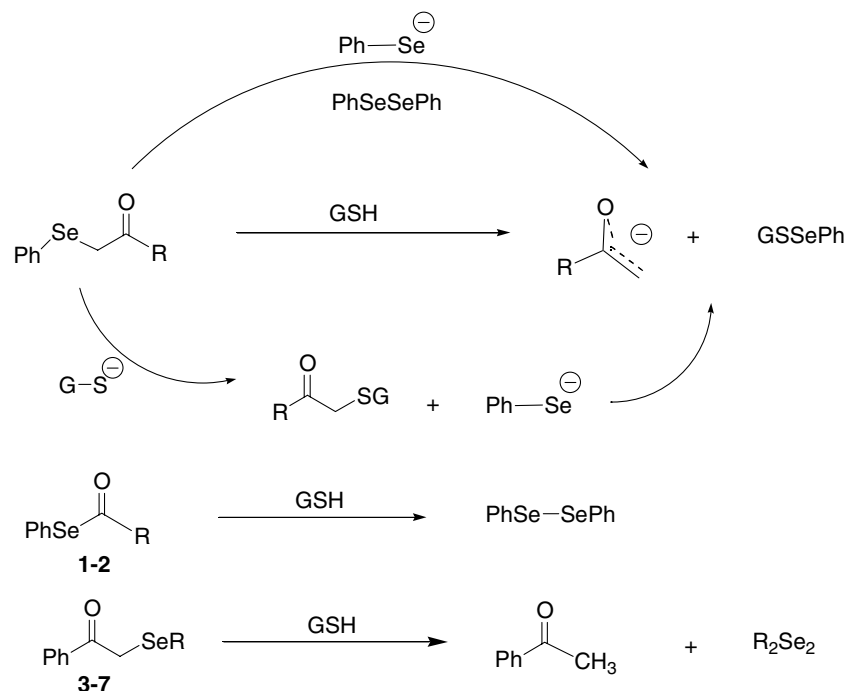
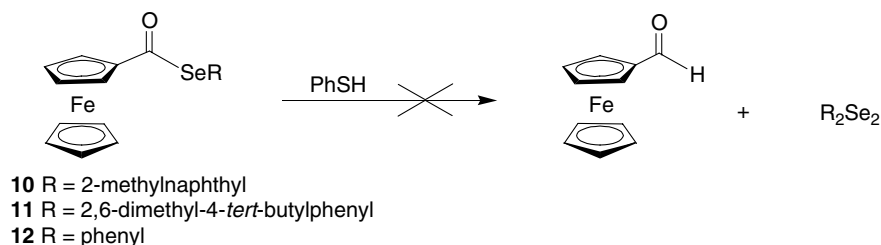
The initial reduction rates for previously reported diphenyl-, diferrocenyl- and dinaphthyl diselenides were also measured out under similar conditions to compare their catalytic activities with diferrocenoyl diselenide (**8**), diferrocenoyl selenide (**9**) and ferrocenoyl selenol esters (**10–12**). It is interesting to note that diselenide (**8**) [ $65.53 \pm 4.45 \mu\text{M min}^{-1}$ ] was found to be a  $\sim 2.5$  and  $\sim 2$  times more efficient catalyst than diphenyl diselenide [ $23.87 \pm 1.08 \mu\text{M min}^{-1}$ ] and diferrocenyl diselenide [ $34.01 \pm 0.39 \mu\text{M min}^{-1}$ ], respectively, and also better than dinaphthyl diselenide [ $53.07 \pm 5.39 \mu\text{M min}^{-1}$ ] in the reduction of  $\text{H}_2\text{O}_2$  with PhSH as a co-substrate [15]. The peroxidase-like activity of **8** indicates that diaryl diselenides can act as catalysts in the thiol assay to decompose the hydrogen peroxide in the same way as more commonly studied diaryl and dialkyl diselenides. Surprisingly diferrocenoyl selenide (**9**) and ferrocenoyl selenol esters (**10–12**) did not show any activity in the thiol assay even after 2- to 4-fold increase in the concentration of the catalyst. Engman et al. [10] have demonstrated that selenol esters and  $\alpha$ -(arylselenenyl) ketones (**1–7**) convert the  $\text{H}_2\text{O}_2$  into  $\text{H}_2\text{O}$  at the expense of glutathione and thus can act as mimics of the GPx enzyme. The rapid cleavage of the carbon–selenium bond of selenol esters (**1–2**) and  $\alpha$ -(arylselenenyl) ketones (**3–7**) takes place by glutathione and give the catalytic reactive intermediates [benzene selenolate, benzene selenenic acid and *S*-(phenylselenenyl) glutathione] (Scheme 2). Thus facile cleavage of the carbon–selenium [ $\text{C}(\text{O})\text{--SeR}$ ] bond is responsible for the GPx-like activity of selenol esters (**1–2**) [10]. To understand the poor activity of the ferrocenoyl selenol esters (**10–12**), the reaction of **12** with benzene thiol was carried out in methanol and 0.1 M phosphate buffer solution. No formation of the expected benzene selenolate (based on the formation of its oxidized product; diphenyl diselenide) and ferrocenecarboxaldehyde was observed even after 1 h as monitored by TLC (Scheme 3), and thus indicating no cleavage of  $\text{C}(\text{O})\text{--SeR}$  in ferrocenoyl selenol ester (**12**).

Concerning the reactions of ferrocenoyl selenol esters (**10–12**) and  $\alpha$ -(arylselenenyl) ketones (**1–2**) a note must be added that in the two systems different thiols (benzenethiol and glutathione) and different selenol esters were used.

### 2.6. Crystallographic studies

#### 2.6.1. Crystal structure of **8**

A perspective view of diferrocenoyl diselenide (**8**) is shown in Fig. 2, and the corresponding bond lengths and angles are listed in Table 2. The coordination geometry around the selenium atom is T-shaped where each selenium is bonded to a selenium, a carbon and an oxygen atom. The Se–Se distance of 2.282(7) Å relates well to the corresponding values reported for diaryl diselenides, which range from 2.29 to 2.39 Å [11a]. This value

Scheme 2. GPx activity of  $\alpha$ -(arylselenol) ketones (**1–7**).Scheme 3. Reaction of selenol esters (**10–12**) with benzene thiol.Table 2  
Significant bond lengths (Å) and angles (°) for **8** and **10**

Compound ( <b>8</b> )			
Se(1)–Se(2)	2.282(7)	C(11A)–C(10A)	1.455(6)
C(11)–Se(1)	1.970(5)	Se(2)···O(2)	2.780(4)
C(11)–O(1)	1.182(6)	Se(2)···O(1)	3.199(4)
C(11)–C(10)	1.465(6)	O(1)···Se(2)–C(11A)	93.6(16)
Se(1)···O(1)	2.789(9)	Se(2)···O(2)–C(11A)	36.6(3)
Se(1)···O(2)	3.198(4)	C(11)–Se(1)–Se(2)	98.4(13)
O(1)···Se(1)–C(11)	37.7(2)	C(11)–Se–Se–C(11A)	–89.1(18)
O(2)···Se(1)–C(11A)	94.9(13)		
Compound ( <b>10</b> )			
Se(1)–C(11)	1.919(2)	C(10)–C(11)	1.462(3)
Se(1)–C(12)	1.945(3)	C(11)–Se–C(12)	99.2(11)
C(11)–O	1.203(3)	Se(1)–C(11)–C(10)	113.3(18)

is also close to the mean value reported for the diacyl diselenide, bis(2-methoxybenzoyl) diselenide (2.311(9) Å) [7c] (see Fig. 3).

The intramolecular distances of Se(1)···O(2) and Se(2)···O(1) are 3.198(4) and 3.199(4) Å, respectively,

which are significantly shorter than the sum of their van der Waals radii (3.40 Å) [20]. These values are slightly longer than the corresponding mean value reported for bis(2-methoxybenzoyl) diselenide (3.138(5) Å) [7c]. These distances are also longer than the 1,4 intramolecular distance between selenium and the oxygen of a methoxy group in (*R,R*)-bis{2-[1-(hydroxyl)ethyl]-6-methoxyphenyl}diselenide (2.977 Å) [21] and the distance between Se and O in selenazafurin (3.012 Å) [22] but smaller than that in 5-amino-selenazafurin (3.314(4) Å) [23]. Intramolecular short distances between Se(1)···O(1) and Se(2)···O(2) are also found and these distances (2.789(9) and 2.780(4) Å) are significantly shorter than the distances between Se(1)···O(2) and Se(2)···O(1). The short distances between Se(1)···O(1) and Se(2)···O(2) may be due to the geometrical arrangement of the –C(O)Se– group. The most interesting feature of this structure is that compound **8** crystallizes in a chiral space group *Pna*2<sub>1</sub> with an orthorhombic crystal system. Refinement of the Flack enantiopole parameter [24] shows that



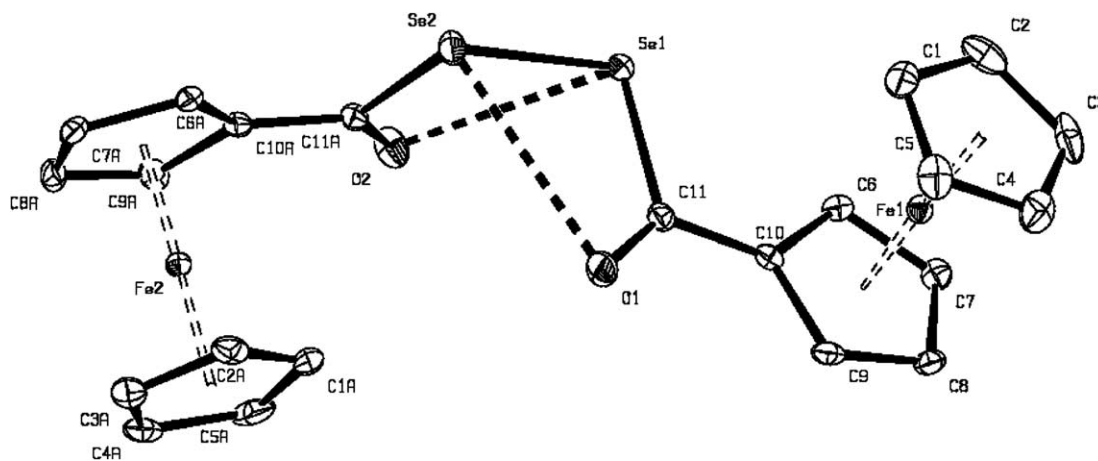


Fig. 3. Molecular structure of **8** (hydrogen atoms are removed for clarity).

compound (**8**) has crystallized in an enantiomerically pure form. Diferrocenoyl diselenide (**8**) also shows optical activity in solution. The torsion angle  $[\text{C}(11)\text{--Se}(1)\text{--Se}(2)\text{--C}(11\text{A}) = -89.1(18)^\circ]$  is significantly less than the corresponding value reported for bis(2-methoxybenzoyl) diselenide  $[104.8(2)^\circ]$ . However, this value is well within the range of those reported for diaryl diselenides  $(87.5(0)\text{--}95.6(3)^\circ)$  [11a]. The torsion angle in **8**,  $\text{C}(11)\text{--Se}(1)\text{--Se}(2)\text{--C}(11\text{A})$  indicates the skew conformation. This is in accordance with theoretical *ab initio* MO and NBO (natural bond orbital) calculations on diacyl dichalcogenides. Kato et al. [7c] have reported that the skew conformation is more stable than the planar in the case of the diselenide based on the 2-methoxybenzoyl group.

Another feature in the structure is the existence of  $\text{H}\cdots\text{O}=\text{C}$  intermolecular hydrogen bonding (Fig. 4). The intermolecular distance between carbonyl oxygen and hydrogen  $[\text{O}(2)\cdots\text{H}\text{--C}(9\text{b}) = 2.552(8) \text{ \AA}]$  relates well to the disulfide analogue of **8**  $(2.542 \text{ \AA})$  [25]. Intermolecular hydrogen bonding between the Cp hydrogens and O/N atoms has been reported in the ferrocene carboxaldehyde derivative, 4'-formyl-4-biphenylferrocene [26].

#### 2.6.2. Crystal structure of **10**

The perspective view of **10** is shown in Fig. 5. The significant bond lengths and angles are listed in Table 3. The compound crystallizes in the monoclinic crystal system with 4 molecules per unit cell. The Se–C bond distances  $[\text{Se}\text{--C}(11), 1.919(2); \text{Se}\text{--C}(12), 1.945(3) \text{ \AA}]$  are within the range of reported oxazolinylferrocenyl phenyl selenide and oxazolinylphenyl benzyl selenide  $(1.906(4)$  and  $1.928(4) \text{ \AA})$  [16,27]. The  $\text{C}(11)\text{--O}(1)$  distance  $(1.203(3) \text{ \AA})$  is shorter than the corresponding distance of diferrocenoyl diselenide (**10**). The  $\text{C}(11)\text{--Se}\text{--C}(12)$  bond angle  $[99.2(11)^\circ]$  is comparable with reported diaryl and ferrocenyl aryl selenides  $[100.2(12)$  and  $96.2(2)^\circ]$ .

In this molecule no intermolecular  $\text{O}\cdots\text{H}$  hydrogen bonding was observed.

### 3. Experimental

#### 3.1. General comments

All reactions were carried out under nitrogen or argon using standard vacuum-line techniques. Solvents were purified by standard procedures [28] and were freshly distilled prior to use. Ferrocene carboxylic acid [12], bis(2-methylnaphthyl) diselenide [15], bis(2,6-dimethyl-4-*tert*-butylphenyl) diselenide [11a] were prepared by following the literature methods. Melting points were recorded in capillary tubes and are uncorrected. The IR spectra were recorded as KBr pellets on a Nicolet Impact 400 FTIR spectrometer. The  $^1\text{H}$  NMR and  $^{13}\text{C}$  NMR spectra were obtained at 300 MHz in  $\text{CDCl}_3$  on a Varian VXR 300S spectrometer. The  $^1\text{H}$  and  $^{13}\text{C}$  NMR chemical shifts are cited with respect to  $\text{SiMe}_4$  as internal standard. The  $^{77}\text{Se}$  NMR spectra were obtained at 95.35 MHz, respectively, in  $\text{CDCl}_3$  on a Bruker AMX500 spectrometer using diphenyl diselenide as external standard. The chemical shifts are reported relative to dimethyl selenide ( $^{77}\text{Se}$ ) by assuming that the resonance of the standard is at 461 ppm. Elemental analyses were performed on a Carlo-Erba model 1106 elemental analyzer. Optical rotations were measured by a JASCO Model DIP 370 digital polarimeter. Electrospray mass spectra (ES-MS) were performed at room temperature on a Q-ToF micro (YA-105) mass spectrometer. The  $m/z$  values are quoted with reference to isotopomers containing  $^{80}\text{Se}$ ; calculated and observed isotope distribution patterns were in good agreement. Cyclic voltammetry: CHI660 scanning potentiostat; Pt working and auxiliary electrodes;  $\text{Ag}/\text{Ag}^+$  (0.1M  $\text{AgNO}_3$  in  $\text{CH}_3\text{CN}$ ) as reference elec-

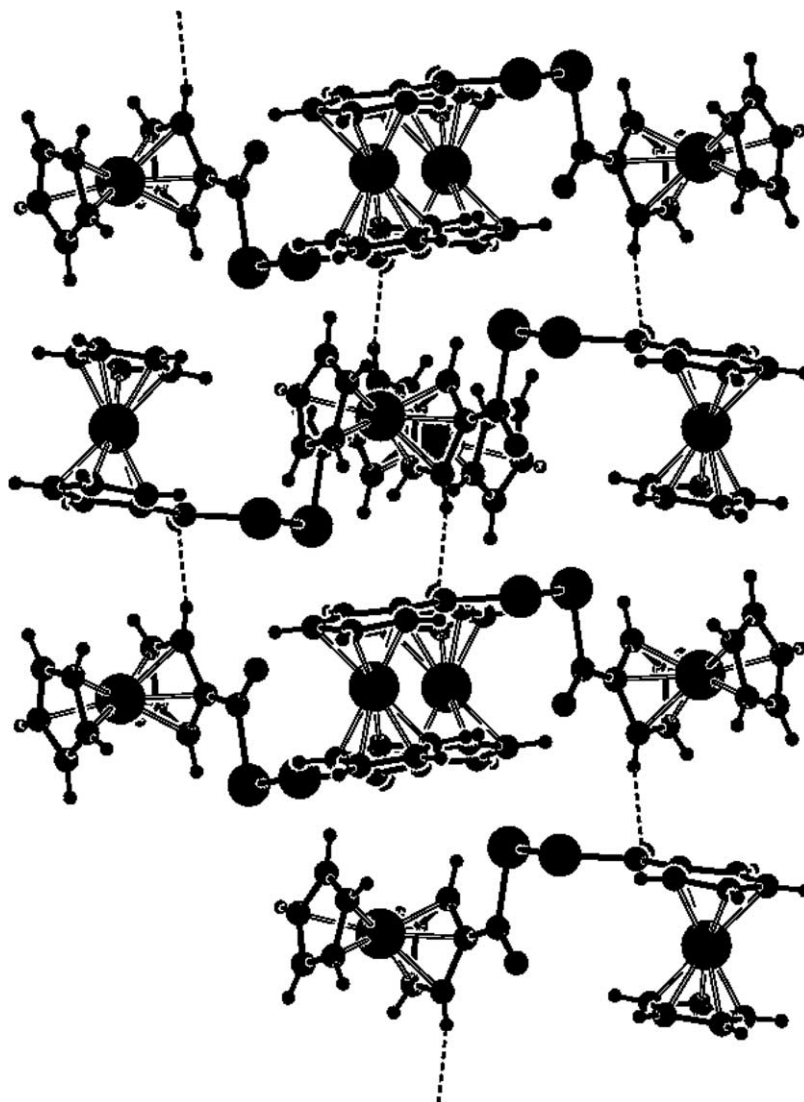


Fig. 4. Packing diagram of **8** showing C–H...O intermolecular hydrogen bonding.

trode; 0.1 M  $[\text{NBu}_4][\text{ClO}_4]$  in  $\text{CH}_3\text{CN}$  as a supporting electrolyte; scan rate  $200 \text{ mVs}^{-1}$ ; under these conditions  $[\text{Fe}(\text{C}_5\text{H}_5)_2]/[\text{Fe}(\text{C}_5\text{H}_5)_2]^+$  has  $E_{1/2} = +0.60 \text{ mV}$ .

### 3.2. Preparation of diferrocenoyl diselenide (**8**)

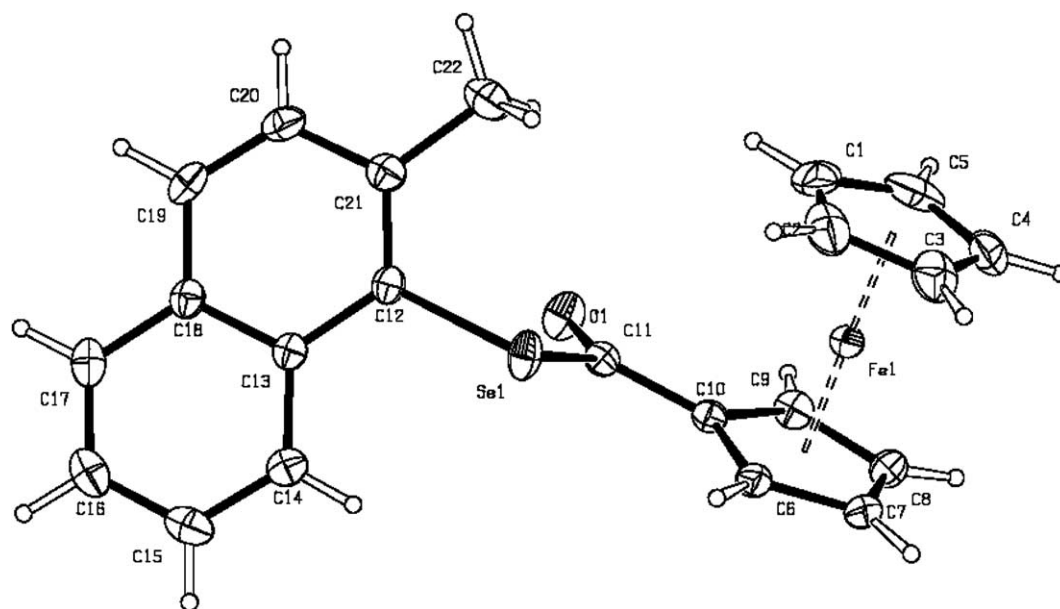
#### 3.2.1. Method (A)

Grey selenium (0.8 g, 1 mmol) was added portion wise to  $\text{LiAlH}_4$  (0.04 g, 1 mmol) in THF with stirring under an argon atmosphere. Gas evolution occurred, and the suspension turned dark brown-red. The  $\text{LiAlHSeH}$  thus formed was stirred for at least 30 min. Ferrocenoyl chloride (1 mmol), which was prepared by the reaction of ferrocene carboxylic acid (0.23 g, 1 mmol) and oxalyl chloride (0.9 mL, 1 mmol) in situ, was added to the solution of  $\text{LiAlHSeH}$  (1 mmol). The reaction mixture was stirred at  $0^\circ\text{C}$  for 1 h. Iodine (0.13 g, 1.0 mmol) and KI (0.04 g, 0.2 mmol) in THF (15 mL)

were added to the reaction mixture. The reaction mixture was stirred at  $0^\circ\text{C}$  for 2 h, then extracted with  $\text{CH}_2\text{Cl}_2$  and washed with 1%  $\text{NaHSO}_3$  and water. Standard work-up gave the crude solid of **8**. This was purified by flash chromatography on silica gel with hexane and ethyl acetate (2:1) to give **8** (0.18 g, 30%) as a red solid.

#### 3.2.2. Method (B)

Grey selenium (0.8 g, 1 mmol) was added portionwise to 1.2 mL of  $\text{Li}(\text{C}_2\text{H}_5)_3\text{BH}$  (1.2 mmol, 1 M solution in THF) with stirring under an argon atmosphere. Gas evolution occurred, and the suspension turned dark brown-red. The  $\text{Li}_2\text{Se}_2$  thus formed was stirred for at least 30 min. Ferrocenoyl chloride (1 mmol) in 5 mL THF was added to the suspension of  $\text{Li}_2\text{Se}_2$  at  $0^\circ\text{C}$  and stirred for 1 h. The reaction mixture was stirred for a further 3 h at room temperature. The reaction

Fig. 5. Molecular structure of **10**.Table 3  
Crystal data and structure refinement for **8** and **10**

Compound	<b>8</b>	<b>10</b>
Empirical formula	C <sub>22</sub> H <sub>18</sub> Fe <sub>2</sub> O <sub>2</sub> Se <sub>2</sub>	C <sub>22</sub> H <sub>18</sub> FeOSe
Formula weight	583.98	433.17
Crystal system	Orthorhombic	Monoclinic
Space group	<i>Pna</i> 2 <sub>1</sub>	<i>P</i> 2 <sub>1</sub> / <i>c</i>
<i>a</i> (Å)	12.3711(8)	10.8664(8)
<i>b</i> (Å)	12.4168(10)	14.2021(8)
<i>c</i> (Å)	13.1517(11)	12.2651(8)
$\alpha$ (°)	90	90
$\beta$ (°)	90	108.972(8)
$\gamma$ (°)	90	90
<i>V</i> (Å <sup>3</sup> )	2020.2(3)	1790.0(2)
<i>Z</i>	4	4
<i>D</i> <sub>calc.</sub> (Mg/m <sup>3</sup> )	1.920	1.607
Abs. coeff. (mm <sup>-1</sup> )	5.055	2.882
Obs. refl. [ <i>I</i> > 2σ( <i>I</i> )]	29188	27378
Final <i>R</i> ( <i>F</i> ) [ <i>I</i> > 2σ( <i>I</i> )] <sup>a</sup>	0.0280	0.0325
<i>wR</i> ( <i>F</i> <sup>2</sup> ) [ <i>I</i> > 2σ( <i>I</i> )]	0.0537	0.0799
Absolute str. parameter	0.023(12)	–
Data/restraints/parameters	3946/1/253	3781/0/227
Goodness-of-fit on <i>F</i> <sup>2</sup>	0.895	1.018

<sup>a</sup> Definitions:  $R(F_o) = \sum |F_o| - |F_c| / \sum |F_o|$  and  $wR(F_o^2) = \{ \sum [w(F_o^2 - F_c^2)^2] / \sum [w(F_c^2)^2] \}^{1/2}$ .

mixture was poured in saturated aqueous solution of brine and left overnight. The solidified product was separated by filtration and dried under vacuum. The crude product was purified by flash chromatography on silica gel with hexane and ethyl acetate (2:1) to give **8** as a red solid. Compound **8** was recrystallized from hexane and CH<sub>2</sub>Cl<sub>2</sub> to afford red needles. Yield: 0.56 g (96%),  $[\alpha]_D^{25} = -4.88$  (0.037 c, CHCl<sub>3</sub>), m.p. 163–165 °C; Anal. Calc. for C<sub>22</sub>H<sub>18</sub>O<sub>2</sub>Fe<sub>2</sub>Se<sub>2</sub>: C, 45.26; H, 3.10. Found: C, 44.97; H, 2.92; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 4.39 (s, 10H), 4.60

(t, 4H), 4.95 (t, 4H); ES-MS *m/z* 585.1 (M<sup>+</sup>, 25), 231.2 (30), 213 (100), 185 (10); IR (KBr) ν 3112, 2940, 2848, 1683, 1440, 1242, 1045, 841, 775, 676, 499 cm<sup>-1</sup>.

### 3.3. Preparation of diferrocenoyl selenide (**9**)

Ferrocenoyl chloride (1 mmol) in 5 mL THF was added to the suspension of LiAlHSeH at 0 °C prepared as in Section 3.2.1 and stirred for 1 h. The reaction mixture was further stirred for 3 h at room temperature. The standard work-up gave a red coloured solid. The crude product was purified by column chromatography on silica gel by using hexane/ ethyl acetate (2:1) and gave the two fractions (i) diferrocenoyl diselenide (0.01 g), (ii) diferrocenoyl selenide (**9**), which was crystallized from hexane/CH<sub>2</sub>Cl<sub>2</sub> to afford dark red plates. Yield: 0.46 g, 90%, m.p. 174–176 °C; Anal. Calc. for C<sub>22</sub>H<sub>18</sub>O<sub>2</sub>Fe<sub>2</sub>Se: C, 52.33; H, 3.59. Found: C, 52.23; H, 3.47; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 4.34 (s, 10H), 4.58 (t, 4H), 4.86 (t, 4H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 69.74, 70.05, 70.83, 71.25, 72.90, 81.69, 187.98; ES-MS *m/z* 505.9 (M<sup>+</sup>, 10), 230.0 (30), 213 (100), 185 (10), 136 (20); IR (KBr) ν 2927, 2847, 1709, 1431, 1237, 1035, 831, 761, 487 cm<sup>-1</sup>.

### 3.4. Preparation of 1-(2-methylnaphthyl) ferrocenoyl selenide (**10**)

To a cold solution of bis(2-methylnaphthyl) diselenide [10d] (0.44 g, 1 mmol) in THF, Li(C<sub>2</sub>H<sub>5</sub>)<sub>3</sub>BH (2.2 mL, 2.2 mmol, 1 M solution in THF) was added portionwise under an argon atmosphere at 0 °C and stirred for 1 h at this temperature. Ferrocenoyl chloride (2 mmol) was added to the reaction mixture at 0 °C.



The reaction mixture was stirred for 1 h at 0 °C and 3 h at room temperature. The mixture was extracted with diethyl ether and washed with saturated NaCl solution. The organic layer was dried over sodium sulfate and evaporated to dryness. The residue was purified by flash chromatography on silica gel with CH<sub>2</sub>Cl<sub>2</sub>/hexane (1:1). The compound (**10**) was recrystallized from CH<sub>2</sub>Cl<sub>2</sub>/hexane (1:2) to afford crystals of **10** as dark red plates. Yield: 0.82 g (94%), m.p. 156–157 °C; Anal. Calc. for C<sub>22</sub>H<sub>18</sub>OFeSe: C, 61.01; H, 4.18. Found: C, 60.89; H, 4.17; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 2.71 (s, 3H), 4.33 (s, 5H), 4.62 (t, 2H), 5.01 (t, 2H), 7.48–7.51 (m, 4H), 7.82 (t, 1H), 8.44 (d, 1H); IR (KBr) ν 3104, 3039, 2920, 2848, 1670, 1433, 1236, 1032, 946, 782, 449 cm<sup>-1</sup>.

### 3.5. Synthesis of 2-(2,6-Dimethyl-4-tert-butylphenyl)ferrocenoyl selenide (**11**)

Compound **11** was prepared by a similar method as described for **10** using bis(2,6-dimethyl-4-tert-butylphenyl) diselenide [10c]. The standard work-up gave a red oil. The crude product was purified by flash chromatography by using hexane/ethyl acetate (5:1) to afford a red oil, which solidified on standing and was recrystallized from hexane. Yield: 0.5 g (55%), m.p. 78–81 °C; Anal. Calc. for C<sub>23</sub>H<sub>26</sub>OFeSe: C, 60.96; H, 5.78. Found: C, 60.87; H, 5.66; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 1.32 (s, 12H), 2.48 (s, 6H), 4.30 (s, 5H), 4.52 (t, 2H), 4.89 (t, 2H), 7.20 (s, 1H), 7.25 (s, 1H); <sup>13</sup>C NMR (CDCl<sub>3</sub>) δ 24.82, 24.88, 29.78, 31.34, 34.52, 69.22, 70.18, 70.69, 72.00, 87.78, 81.78, 124.58, 125.16, 142.76, 152.35; ES-MS *m/z* 454.0 (M<sup>+</sup>, 20), 213 (100), 186 (90), 136 (10); IR (KBr) ν 3106, 3068, 2830, 1680, 1441, 1258, 949, 768, 499 cm<sup>-1</sup>.

### 3.6. Synthesis of phenyl ferrocenoyl selenide (**12**)

The compound was synthesized by the reduction of diphenyl diselenide following the method as described for **10**. The crude product was purified by flash column chromatography using hexane/CH<sub>2</sub>Cl<sub>2</sub> (1:2). The compound (**12**) was recrystallized from hexane/CH<sub>2</sub>Cl<sub>2</sub> to give red plates. Yield: 0.66 g (89%), m.p. 90–92 °C; Anal. Calc. for C<sub>17</sub>H<sub>14</sub>OFeSe: C, 55.33; H, 3.82. Found: C, 54.89; H, 3.65; <sup>1</sup>H NMR (CDCl<sub>3</sub>) δ 4.28 (5H, s), 4.53 (t, 2H), 4.86 (t, 2H), 7.38–7.40 (m, 3H), 7.58–7.60 (m, 2H); IR (KBr) ν 2933, 2848, 1716, 1440, 1236, 1045, 834, 769, 492 cm<sup>-1</sup>.

### 3.7. PhSH assay

The reactions of model compounds with benzenethiol (PhSH) and H<sub>2</sub>O<sub>2</sub> were studied by following the appearance of the disulfide absorption at 305 nm, at 25 °C. Each initial velocity was measured at least 6 times and calculated from the first 5–10% of the reaction. For

the peroxidase activity, the rates were corrected for the background reaction between H<sub>2</sub>O<sub>2</sub> and PhSH. The actual concentration of PhSH in the kinetic apparatus was measured from the 305 nm absorbance, and rates were corrected for any variation in the concentration of PhSH. The molar extinction coefficient of PhSSPh ( $\epsilon_1 = 1.24 \times 10^3 \text{ M}^{-1}\text{cm}^{-1}$ ) at the wavelength was much larger than that of PhSH ( $\epsilon_2 = 9 \text{ M}^{-1}\text{cm}^{-1}$ ). The concentration of diphenyl disulfide was, therefore, calculated from the absorbance (*A*) according to the following equation:  $C = A/(\epsilon_1 - 2\epsilon_2) \approx a/\epsilon_1$ . The concentration of the H<sub>2</sub>O<sub>2</sub> stock solution was determined by permanganate titration.

### 3.8. X-ray crystallography

The diffraction measurements were performed on a STOE (Darmstadt, Germany) IPDS imaging plate single crystal diffractometer at room temperature with graphite-monochromated Mo K  $\alpha$  radiation ( $\lambda = 0.7107 \text{ \AA}$ ). The structures were solved by direct methods and full-matrix least-squares refinement on *F*<sup>2</sup> (program SHELXL-97) [29]. Hydrogen atoms were localized by geometrical means. A riding model was chosen for refinement. The isotropic thermal parameters of the H atoms were fixed at 1.5 times (CH<sub>3</sub> groups) or 1.2 times *U*(eq) (Ar–H) of the corresponding C atom. Some details of the data collection and refinement are given in Table 3.

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### Appendix A. Supporting material

NMR and electrospray mass spectra of compounds **8**–**12** and thiol peroxidase activity data of compound (**8**) may be obtained from <http://www.sciencedirect.com>. Crystallographic data for the structural analyses have been deposited with the Cambridge Crystallographic Data Centre; CCDC Nos. 238713 and 238714 for compounds **8** and **10**, respectively. Copies of this information may be obtained free of the charge from The Director, CCDC, 12 Union Road, Cambridge, CB2 1 EZ, UK (fax: +44-1223-336033; email: [deposit@ccdc.cam.ac.uk](mailto:deposit@ccdc.cam.ac.uk) or <http://www.ccd.cam.ac.uk>). Supplementary data associated with this article can be found, in the online version at [doi:10.1016/j.jorgchem.2004.06.054](https://doi.org/10.1016/j.jorgchem.2004.06.054).

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