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The unusual influence of hetaryl groups on the direct conversion of some secondary alcohols into thiols with Lawesson's reagent: elucidation of the reaction mechanism

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ABSTRACT

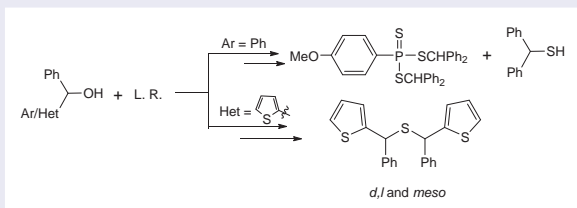
A series of hetaryl-substituted methanols were used for direct conversion into the corresponding thiols by treatment with Lawesson's reagent in boiling toluene. Unexpectedly, the respective sulfides were formed exclusively. In the case of chiral alcohols, the sulfides were obtained as 1:1-mixtures of *meso*- and *dl*-diastereoisomers. In contrast to hetaryl-substituted alcohols, the analogous protocol applied for benzhydryl alcohol led to a mixture of the expected secondary thiol and a bis(diphenylmethyl) trithiophosphonate. Finally, the analogous reactions with ferrocenyl(phenyl)methanol and diferrocenylmethanol, respectively, led to the corresponding thiols in good yield.

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1. Introduction

Thiols are an important class of organic compounds with great significance for organic syntheses. Diverse methods are known for their preparation [1], and in recent years, asymmetric syntheses of thiols have been studied extensively [2,3]. It is well known that many thiols are biologically active substances [4] and some of them are of special interest as odorous compounds [5].

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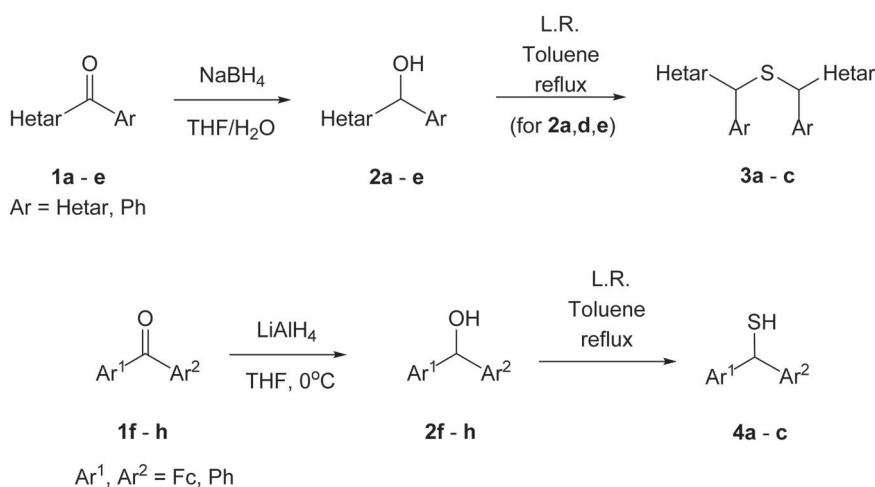
*Part of the planned Ph.D. Thesis of R. H.-F. (University of Łódź).

It is generally known that the treatment of primary, secondary or tertiary alcohols with Lawesson's reagent (LR) is a straightforward method for their conversion into the corresponding thiols [6,7]. In some recent publications, we described the synthesis of hetaryl and ferrocenyl ketones and their conversions into the sulfur analogues, *i.e.* thioketones [8,9]. The latter were tested as precursors of thiols by treatment with diverse reducing agents, and in the cases of aromatic and cycloaliphatic thioketones, only LDA gave satisfactory results [10]. In order to get an alternative, straightforward access to hetarylmethanethiols, the direct conversion of the corresponding secondary alcohols into the required thiols using Lawesson's reagent should be examined.

2. Results and discussion

The study started with the preparation of a series of hetaryl- and ferrocenyl-substituted ketones **1** via lithiated hetarenes [8] or via the *in situ*-generated mixed anhydrides [9].

The obtained ketones **1a–1e** were converted into the corresponding secondary alcohols **2a–2e** via reduction with NaBH₄ in THF solution (Scheme 1, Table 1) or alternatively, in the case of phenyl/ferrocenyl ketones **1f–1h**, with lithium aluminum hydride. In the first thiolation experiment, di(thiophen-2-yl)methanol (**2a**) was treated with ca. equimolar amounts of LR in boiling dry toluene. The progress of the reaction was monitored by TLC, and after 15 min, the starting material **2a** was completely consumed. The crude reaction mixture, after removal of toluene, was analyzed by ¹H NMR spectroscopy, which evidenced the formation of only one product. Along with two doublets and a triplet for the thiophene ring, the spectrum showed a singlet at 5.43 ppm. Surprisingly, the expected IR absorption band for the SH group at ca. 2500–2600 cm⁻¹ was missing. The elemental analysis of the purified sample showed a significantly reduced value for sulfur in comparison with that calculated for the desired thiol (40.99 instead of 47.09%). This value corresponded, however, to the molecular formula C₁₈H₁₄S₅ of the sulfide **3a**.



Scheme 1. Preparation of disubstituted methanols **2** and their transformations into sulfides **3** or thiols **4**.

1	Hetar or Ar ¹	Ar or Ar ²	2	Yield (%) ^a	3	4	Yield (%) ^a
a	Thiophen-2-yl	Thiophen-2-yl	a [11,12]	79	a	–	75
b	Thiophen-2-yl	Selenophen-2-yl	b [12]	94	–	–	– ^b
c	Furan-2-yl	Selenophen-2-yl	c	65	–	–	– ^b
d	Phenyl	Thiophen-2-yl	d [11,12]	93	b	–	92
e	Phenyl	Selenophen-2-yl	e [13]	68	c	–	75
f	Phenyl	Phenyl	f [14]	99	–	a [6]	90
g	Ferrocenyl	Phenyl	g [15]	84	–	b	58
h	Ferrocenyl	Ferrocenyl	h [16]	89	–	c	56

^bOnly non-identified decomposition products were obtained.

The presented results differ significantly from the reported formation of diphenylmethanethiol (**4a**) from benzhydryl alcohol (**2f**) under similar conditions [6]. For that reason, the experiment with **2f** was repeated in boiling dry toluene, and the TLC analysis showed that already after 15 min the starting material was completely consumed, and two new spots evidenced the formation of two new products. After chromatographic separation, the less polar fraction was identified as the known diphenylmethanethiol (**4a**) [6] as the major product. The more polar fraction, obtained as the minor product, was isolated as a colorless solid, and the ^{31}P NMR spectrum indicated the presence of a P-atom by a signal at 78.2 ppm, *i.e.* in the region of aryltrithiophosphonates [17–20]. In the ^1H NMR spectrum, signals of a MeO group (3.78 ppm) and of a 4-MeOC₆H₄ residue (6.66–6.68 and 7.60–7.65 ppm) suggested the presence of a monomeric unit of Lawesson's reagent. In addition, comparison of the intensities of the MeO and the CHPh₂ groups (doublet at 5.79 ppm) proved the ratio 3:2 for the respective H-atoms. Based on these data, structure **5** (Scheme 2) was attributed to this product (*cf.* [19]). The elemental analysis supported the molecular formula C₃₃H₂₉OPS₃. Finally, the proposed structure was unambiguously confirmed by X-ray crystallography (Figure 1). The corresponding bis(diphenylmethyl) phenyltrithiophosphonate of type **5** has been obtained in a two-step reaction from phenylphosphine and thiobenzophenone [19].

$\text{Ph-CH(OH)-Ph} \xrightarrow[\text{Toluene reflux}]{\text{L.R.}} \text{Ph-CH(SH)-Ph} + \text{MeO-C}_6\text{H}_4\text{-P(S)(Ph}_2\text{)}_2$

2f **4a** **5**

Scheme 2. Reaction of benzhydryl alcohol (**2f**) with Lawesson's reagent (LR) in abs. toluene.

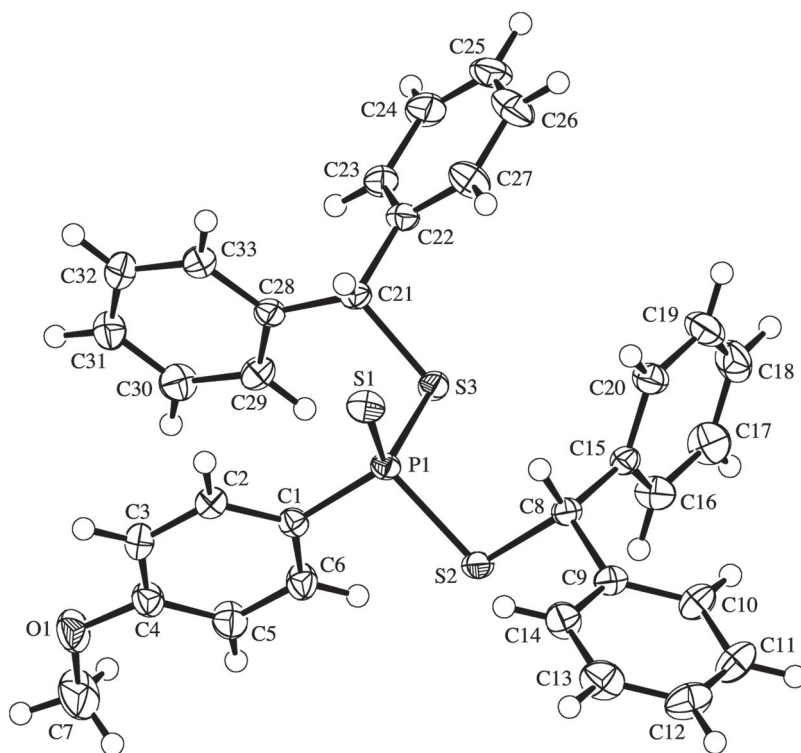
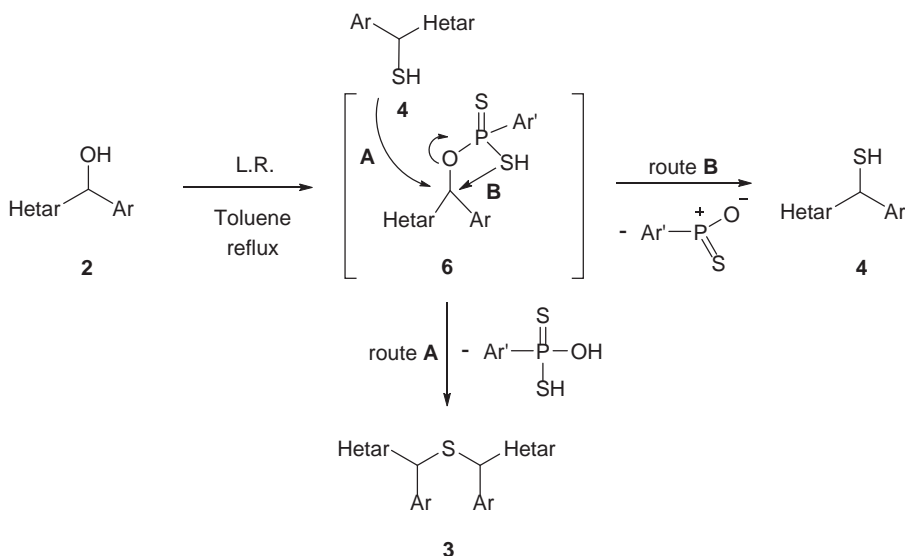


Figure 1. ORTEP plot [21] of the molecular structure of **5** (with 50% probability ellipsoids; arbitrary numbering of atoms).

thiols. As a matter of fact, in supplementary experiments performed with **2f** in wet toluene, the formation of **5** has not been observed, and thiol **4a** was isolated as the only product in good yield (90%), in agreement with the reported results. In a test experiment, the isolated compound **5** was heated in wet toluene over 0.5 h, but in this case the starting compound was recovered. Thus, thiol **4a** is not a product of hydrolysis of the initially formed **5**. In order to check whether the latter can be formed from thiol **4a** and monomeric LR, both reagents, used in a molar ratio of 2:1 were heated in boiling toluene until **4a** completely disappeared from the reaction mixture (TLC monitoring). In fact, the formation of **5** was evidenced by TLC, however, many other spots revealed a rather complicated outcome of the reaction. Based on this observation we conclude that the formation of **5** occurs via an intermediate formed in the initial step of the reaction from alcohol **2f** (and not from the *in situ*-formed thiol **4a**), and Lawesson's reagent. The detailed mechanism of this conversion is not yet clear.

Finally, the experiment with ferrocenyl(phenyl)methanol (**2g**) led to the corresponding thiol **4b**, which was isolated in 58% yield (Scheme 1, Table 1). In the reaction mixture, non-identified decomposition products were also present, but neither a sulfide of type **3** nor an analogue of **5** could be identified. An analogous result was obtained with diferrocenylmethanol (**2h**), and in this case diferrocenylmethanethiol (**4c**) was isolated in a comparable yield (Table 1).



Scheme 3. Proposed reaction mechanisms for the competitive formation of sulfides **3** and thiols **4**.

The results of the present study show that the presence of a hetaryl residue in the secondary alcohols **2** changes the reactivity of the system, and instead of methanethiols of type **4**, sulfides **3** are formed as unexpected products. It seems likely that the intermediate aryl dithiophosphonate **6** is attacked by the *in situ*-formed secondary thiol of type **4** to give the sulfide **3** (route **A**). Its formation suggests that intermediate **6** acts as a trapping agent for the nucleophilic thiol **4** (Scheme 3). This interpretation leads to the conclusion that the intermolecular S-attack is a competitive pathway to the intramolecular one, which leads to the formation of the thiol **4** (route **B**).

In the reaction with benzhydryl alcohol (**2f**) in dry toluene, the initially formed diphenylmethanethiol (**4a**) behaves differently and reacts with the monomer of Lawesson's reagent to give, after elimination of H₂S, dibenzhydryl (4-methoxyphenyl)trithiophosphonate (**5**, Scheme 2). However, in the presence of water **4a** is the exclusive product. A similar example of the formation of a trithiophosphonate from Lawesson's reagent and an *in situ*-generated pyrazole-3-thiol has already been described [23].

3. Conclusions

In continuation of our recent studies on hetaryl-substituted organic systems, the presented results demonstrate that hetaryl groups, in comparison with aryl groups, strongly modify the reactivity of such systems. The known protocol for the direct conversion of secondary diphenyl alcohols (benzhydryl alcohols) into the corresponding thiols by treatment with Lawesson's reagent leads, in the case of hetaryl analogues, to the corresponding sulfides as final products. The initially formed thiols are trapped by an activated intermediate generated from the starting alcohol and Lawesson's reagent. The importance of a hetaryl group is emphasized by the fact that both benzhydryl alcohol and ferrocenyl(phenyl)methanol behaved similarly, and in both cases only the respective thiols were

formed. These results point out that the presence of the hetaryl groups strongly modifies the reactivity of the SH moiety, very likely by the enhancement of its nucleophilicity. It should be emphasized that in a similar study performed with ferrocenyl/hetarylmethanols of type 2 and LR, another mechanism governs the reaction course and the formation of tetra-substituted ethane derivatives was observed [24]. All these results point out that the type of products obtained from secondary alcohols, derived from methanol, strongly depends on the substitution pattern and both hetaryl and ferrocenyl groups are of special importance.

4. Experimental

4.1. General

All solvents were dried over appropriate drying agents and distilled before use. Melting points were determined in a capillary using a Stewart[®] SMP 30 and they are uncorrected. The IR spectra were recorded on a Nexus FT-IR spectrophotometer. The ¹H, ¹³C and ³¹P NMR spectra were measured on a Bruker Avance III instrument (600, 150 and 243 MHz, respectively), using the solvent signal and H₃PO₄, respectively, as reference. The elemental analyses were recorded on a Vario Micro Cube. ESI-MS were recorded on a Varian 500-MS IT mass spectrometer. Column chromatography (CC) was carried out using Silica gel 60 (Sigma-Aldrich, 230–400 mesh). The notation Fc in this study represents the ferrocenyl residue. The applied ferrocenyl- and hetaryl-substituted ketones were obtained by known methods according to the literature protocols [8,9]. Other reagents used in the present study were commercially available.

4.2. Synthesis of secondary alcohols 2a–2f

To a solution of the corresponding ketone **1** (1 mmol) in THF (2 mL), water (0.06 mL) and NaBH₄ (1.25 mmol, 0.047 g) were added. The mixture was heated at reflux for 2 h. Then, the solution was diluted with water (10 mL) and THF was evaporated. The residue was extracted with ethyl acetate. The combined organic layers were dried over MgSO₄. The solvent was evaporated and crude products were purified by CC (SiO₂, petroleum ether/ethyl acetate 8:2).

4.2.1. Di(thiophen-2-yl)methanol (2a)

Colorless solid; yield: 147 mg (79%); m.p. 50.0–52.0°C (petroleum ether/CH₂Cl₂) ([12]: m.p. 53°C). ¹H NMR (600 MHz, CDCl₃): δ 2.76 (*d*, ³J_{H,H} = 4.2 Hz, OH), 6.30 (*d*, ³J_{H,H} = 4.2 Hz, CH–O), 6.99 (*dd*, ³J_{H,H} = 3.6 Hz, ³J_{H,H} = 4.8 Hz, 2CH_{arom}), 7.02–7.05 (*m*, 2CH_{arom}), 7.30 (*d*, ³J_{H,H} = 4.8 Hz, 2CH_{arom}) ppm. ¹³C{¹H} NMR (150 MHz, CDCl₃): δ 68.5 (CH–O), 125.0, 125.4, 126.6 (6CH_{arom}), 147.1 (2C_{arom}) ppm. IR (KBr): ν 3243s (OH), 3101*m*, 2923*m*, 2854*m*, 2357*m*, 2027*w*, 1945*w*, 1792*w*, 1733*w*, 1673*w*, 1606*w*, 1537*w*, 1439*m*, 1363*m*, 1347*m*, 1271*m*, 1230*m*, 1163*m*, 1135*m*, 1075*m*, 1006*s*, 850*m*, 796*m*, 752*m*, 701*vs* cm^{–1}. Anal. calcd for C₉H₈OS₂ (196.29): C 55.07, H 4.11, S 32.67; found: C 55.25, H 4.18, S 32.51.

4.2.2. (Selenophen-2-yl)(thiophen-2-yl)methanol (2b)

Pale yellow solid; yield: 228 mg (94%); m.p. 58.0–60.0°C (petroleum ether/CH₂Cl₂) ([12]: m.p. 62.5°C). ¹H NMR (600 MHz, CDCl₃): δ 2.74 (*d*, ³J_{H,H} = 3.6 Hz, OH), 6.30 (*d*, ³J_{H,H} = 3.6 Hz, CH–O), 6.97–7.01 (*m*, 1CH_{arom}), 7.04–7.07 (*m*, 1CH_{arom}), 7.17–7.19 (*m*, 1CH_{arom}), 7.20–7.23 (*m*, 1CH_{arom}), 7.30 (*dd*, ⁴J_{H,H} = 1.2 Hz, ³J_{H,H} = 5.4 Hz, 1CH_{arom}), 7.99 (*dd*, ⁴J_{H,H} = 1.2 Hz, ³J_{H,H} = 5.4 Hz, 1CH_{arom}) ppm. ¹³C{¹H} NMR (150 MHz, CDCl₃): δ 70.3 (CH–O), 124.9, 125.5, 126.6, 126.9, 129.1, 130.9 (6CH_{arom}), 147.5, 154.6 (2C_{arom}) ppm. IR (KBr): ν 3500s (OH), 3414s, 3098m, 3069m, 2955w, 2920w, 2854w, 1815w, 1736w, 1673w, 1606w, 1543m, 1447m, 1372m, 1347m, 1292m, 1261s, 1217s, 1173m, 1125s, 1066m, 1014m, 986s, 856m, 834s, 807m, 755m, 698vs cm^{−1}.

4.2.3. (Furan-2-yl)(selenophen-2-yl)methanol (2c)

Isolated as a viscous oil turning brownish when stored at ambient conditions; yield: 148 mg (65%). ¹H NMR (600 MHz, CDCl₃): δ 2.72 (*d*, ³J_{H,H} = 4.8 Hz, OH), 6.07 (*d*, ³J_{H,H} = 4.8 Hz, CH–O), 6.31–6.33 (*m*, 1CH_{arom}), 6.35–6.38 (*m*, 1CH_{arom}), 7.17–7.19 (*m*, 1CH_{arom}), 7.20–7.24 (*m*, 1CH_{arom}), 7.41–7.42 (*m*, 1CH_{arom}), 8.00 (*dd*, ⁴J_{H,H} = 0.6 Hz, ³J_{H,H} = 6.0 Hz, 1CH_{arom}) ppm. ¹³C{¹H} NMR (150 MHz, CDCl₃): δ 68.1 (CH–O), 107.2, 110.3, 127.1, 129.1, 131.0, 142.5 (6CH_{arom}), 151.7, 155.1 (2C_{arom}) ppm. IR (KBr): ν 3430s (OH), 3107w, 3050w, 2930w, 1720s, 1701s, 1502m, 1448m, 1369m, 1233m, 1144m, 1071m, 1011m, 986m, 922m, 805m, 739s, 691vs cm^{−1}. All attempts to prepare this product as an analytically pure sample were unsuccessful.

4.2.4. Phenyl(thiophen-2-yl)methanol (2d)

Pale yellow solid; yield: 177 mg (93%); m.p. 58.0–60.0°C (petroleum ether/CH₂Cl₂) ([12]: m.p. 62.5°C). ¹H NMR (600 MHz, CDCl₃): δ 2.53–2.56 (*m*, OH), 6.03–6.07 (*m*, CH–O), 6.88–6.91 (*m*, 1CH_{arom}), 6.94–6.98 (*m*, 1CH_{arom}), 7.24–7.29 (*m*, 1CH_{arom}), 7.31–7.35 (*m*, 1CH_{arom}), 7.36–7.41 (*m*, 2CH_{arom}), 7.43–7.49 (*m*, 2CH_{arom}) ppm. ¹³C{¹H} NMR (150 MHz, CDCl₃): δ 72.4 (CH–O), 124.8, 125.3, 126.3, 126.6, 127.9, 128.5 (8CH_{arom}), 143.1, 148.1 (2C_{arom}) ppm. IR (KBr): ν 3256s (OH), 2664w, 2357m, 2338m, 2145w, 1958w, 1894w, 1796w, 1768w, 1600w, 1486m, 1458m, 1435m, 1353m, 1280m, 1258m, 1201m, 1144m, 1033m, 1008vs, 916m, 853m, 824m, 786m, 726m, 694vs, 590m, 527m cm^{−1}. Anal. calcd for C₁₁H₁₀OS (190.26): C 69.44, H 5.30, S 16.85; found: C 69.45, H 5.31, S 16.95.

4.2.5. Phenyl(selenophen-2-yl)methanol (2e)

Pale yellow solid; yield: 161 mg (68%); m.p. 64.0–66.0°C ([13]: m.p. 60–61°C). ¹H NMR (600 MHz, CDCl₃): δ 2.58 (*brs*, OH), 6.04 (*brs*, CH–O), 7.04–7.08 (*m*, 1CH_{arom}), 7.19 (*dd*, ³J_{H,H} = 3.6 Hz, ³J_{H,H} = 6.0 Hz, 1CH_{arom}), 7.31–7.35 (*m*, 1CH_{arom}), 7.37–7.41 (*m*, 2CH_{arom}), 7.46–7.49 (*m*, 2CH_{arom}), 7.97 (*dd*, ⁴J_{H,H} = 1.2 Hz, ³J_{H,H} = 6.0 Hz, 1CH_{arom}) ppm. ¹³C{¹H} NMR (150 MHz, CDCl₃): δ 74.2 (CH–O), 126.2, 126.6, 128.0, 128.5, 129.1, 130.6 (8CH_{arom}), 143.5, 155.8 (2C_{arom}) ppm. IR (KBr): ν 3215s (OH), 2866m, 2664w, 1958w, 1888w, 1784w, 1600w, 1587w, 1546w, 1496m, 1448s, 1328m, 1293m, 1258m, 1204m, 1195m, 1147m, 1081m, 1033m, 1021s, 922w, 821s, 758m, 707vs, 691vs, 637m, 580m cm^{−1}. Anal. calcd for C₁₁H₁₀OSe (237.16): C 55.71, H 4.25; found: C 55.87, H 4.25.

4.2.6. Diphenylmethanol (benzhydryl alcohol) (2f)

Colorless solid; yield: 182 mg (99%); m.p. 62.0–63.0°C ([14]: m.p. 65–66°C). ^1H NMR (600 MHz, CDCl_3): δ 2.37 (*d*, $^3J_{\text{H,H}} = 3.0$ Hz, OH), 5.85 (*brs*, CH–O), 7.27–7.31 (*m*, 2 CH_{arom}), 7.33–7.38 (*m*, 4 CH_{arom}), 7.39–7.42 (*m*, 4 CH_{arom}) ppm.

4.3. Synthesis of ferrocenyl(phenyl)methanol (2g) and diferrocenylmethanol (2h)

A solution of a ferrocenyl-substituted ketone (1 mmol) in dry THF (4 mL) was placed in an ice bath, and the reducing agent LiAlH_4 (1.2 mmol, 0.6 mL of a 2 M solution in THF) was added under an argon atmosphere. A color change from red to yellow was observed. The reaction was monitored by TLC, and after complete reaction, a saturated aqueous solution of MgSO_4 (4 mL) was added. The crude mixture was filtered through Celite, the solvent was evaporated, and alcohols **2g–2h** were obtained as analytically pure samples.

4.3.1. Ferrocenyl(phenyl)methanol (2g)

Yellow solid; yield: 245 mg (84%); m.p. 74.2–75.9°C ([15]: m.p. 78–80°C). ^1H NMR (600 MHz, CDCl_3): δ 2.45 (*d*, $^3J_{\text{H,H}} = 3.0$ Hz, OH), 4.18–4.19 (*m*, 1 CH_{Fc}), 4.20–4.21 (*m*, 2 CH_{Fc}), 4.22–4.23 (*m*, 1 CH_{Fc}), 4.24 (*s*, 5 CH_{Fc}), 5.49 (*d*, $^3J_{\text{H,H}} = 3.0$ Hz, CH–O), 7.26–7.28 (*m*, CH_{arom}), 7.32–7.36 (*m*, 2 CH_{arom}), 7.39–7.41 (*m*, 2 CH_{arom}) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): δ 66.0, 67.4, 68.1, 68.2, 72.0 (4 CH_{Fc} , CH–O), 68.5 (*s*, 5 CH_{Fc}), 94.3 (C_{Fc}), 126.2, 127.4, 128.2 (5 CH_{arom}), 143.3 (C_{arom}) ppm. IR (KBr): ν 3392*m* (OH), 3082*w*, 3053*w*, 3025*w*, 2920*w*, 2851*w*, 1492*m*, 1454*m*, 1407*m*, 1382*m*, 1363*m*, 1318*m*, 1182*m*, 1100*m*, 1043*m*, 1005*s*, 926*m*, 821*s*, 723*s*, 701*vs*, 501*s*, 479*vs* cm^{-1} . Anal. calcd for $\text{C}_{17}\text{H}_{16}\text{OFe}$ (292.15): C 69.89, H 5.52; found: C 70.01, H 5.57.

4.3.2. Diferrocenylmethanol (2h)

Yellow solid; yield: 356 mg (89%); m.p. 171–173°C (decomp.) ([16]: m.p. 174–176°C). ^1H NMR (600 MHz, CDCl_3): 2.38 (*d*, $^3J_{\text{H,H}} = 3.0$ Hz, OH), 4.15–4.17 (*m*, 6 CH_{Fc}), 4.20 (*s*, 10 CH_{Fc}), 4.25–4.26 (*m*, 2 CH_{Fc}), 5.22 (*d*, $^3J_{\text{H,H}} = 3.0$ Hz, CH–O) ppm. $^{13}\text{C}\{^1\text{H}\}$ NMR (150 MHz, CDCl_3): δ 66.1, 67.2, 67.6, 67.8 (8 CH_{Fc}), 68.1 (CH–O), 68.5 (*s*, 10 CH_{Fc}), 93.0 (2 C_{Fc}) ppm. IR (KBr): ν 3458*s* (OH), 3104*m*, 3089*m*, 2925*m*, 2853*m*, 1640*m*, 1407*s*, 1319*m*, 1282*m*, 1199*m*, 1162*m*, 1103*vs*, 1046*s*, 1037*s*, 1024*s*, 1000*vs*, 910*m*, 818*vs*, 749*m*, 738*m*, 525*s*, 453*vs* cm^{-1} . Anal. calcd for $\text{C}_{21}\text{H}_{20}\text{OFe}_2$ (400.07): C 63.04, H 5.04, found: C 63.23, H 5.14.

4.4. Synthesis of sulfides 3a–3c

To a solution of the corresponding alcohol (1 mmol) in dry toluene (5 mL), under an argon atmosphere, Lawesson's reagent (0.6 mmol, 0.24 g) was added. The mixture was heated at reflux and the reaction monitored by TLC. When the alcohol was completely consumed, the solvent was evaporated and the crude products were purified by CC (SiO_2 , petroleum ether/ethyl acetate 8:2).

4.4.1. Bis[di(thiophen-2-yl)methyl]sulfide (3a)

Colorless oil; yield: 146 mg (75%). ^1H NMR (600 MHz, CDCl_3): δ 5.19 (*brs*, 1CH–S), 5.44 (*brs*, 1CH–S), 6.78–6.87 (*m*, 2 CH_{arom}), 6.96 (*dd*, $^3J_{\text{H,H}} = 3.6$ Hz, $^3J_{\text{H,H}} = 4.8$ Hz,

2CH_{arom}), 6.97–7.05 (*m*, 3CH_{arom}), 7.07–7.10 (*m*, 1CH_{arom}), 7.12 (*dd*, ⁴J_{H,H} = 1.2 Hz, ³J_{H,H} = 4.8 Hz, 1CH_{arom}), 7.28 (*dd*, ⁴J_{H,H} = 1.2 Hz, ³J_{H,H} = 4.8 Hz, 2CH_{arom}), 7.30 (*dd*, ⁴J_{H,H} = 1.2 Hz, ³J_{H,H} = 4.8 Hz, 1CH_{arom}) ppm. ¹³C{¹H} NMR (150 MHz, CDCl₃): δ 45.1 (2CH–S), 125.5, 126.2, 126.6 (12CH_{arom}), 144.5 (4C_{arom}) ppm. IR (film): ν 3104*m*, 3066*m*, 2927*w*, 2854*w*, 2464*w*, 2429*w*, 2287*w*, 2151*w*, 2075*w*, 1894*w*, 1793*m*, 1730*w*, 1676*w*, 1597*m*, 1527*m*, 1432*s*, 1363*m*, 1350*m*, 1277*m*, 1236*s*, 1102*m*, 1081*m*, 1043*s*, 853*s*, 755*m*, 698*s* cm^{−1}. Anal. calcd for C₁₈H₁₄S₅ (390.63): C 55.34, H 3.61, S 41.04; found: C 55.07, H 3.88, S 40.99.

4.4.2. (1:1)-Mixture of meso- and d,l-bis[phenyl(thiophen-2-yl)methyl]sulfide (3b)

Pale yellow oil; yield: 174 mg (92%). ¹H NMR (600 MHz, CDCl₃): δ 5.10 (*brs*, 1CH–S), 5.11 (*brs*, 1CH–S), 6.93–7.00 (*m*, 4CH_{arom}), 7.26–7.28 (*m*, 2CH_{arom}), 7.29–7.33 (*m*, 2CH_{arom}), 7.34–7.39 (*m*, 4CH_{arom}), 7.40–7.46 (*m*, 4CH_{arom}) ppm. ¹³C{¹H} NMR (150 MHz, CDCl₃): δ 49.79, 49.82 (2CH–S), 125.2, 125.3, 125.9, 126.0, 126.6, 126.7, 127.6, 127.7, 128.2, 128.5, 128.6 (16CH_{arom}), 140.5, 140.6, 145.1, 145.2 (4C_{arom}) ppm. IR (KBr): ν 3104*m*, 3059*m*, 3025*m*, 2921*m*, 2851*m*, 1945*w*, 1879*w*, 1798*w*, 1635*w*, 1598*m*, 1493*s*, 1454*s*, 1432*m*, 1264*m*, 1230*m*, 1075*m*, 1029*m*, 853*m*, 821*m*, 698*vs*, 637*m*, 590*m*, 512*m* cm^{−1}. Anal. calcd for C₂₂H₁₈S₃ (378.57): C 69.80, H 4.79, S 25.41; found: C 69.69, H 4.87, S 25.40.

4.4.3. (1:1)-Mixture of meso- and d,l-bis[phenyl(selenophen-2-yl)methyl]sulfide (3c)

Colorless, viscous oil; yield: 177 mg (75%). ¹H NMR (600 MHz, CDCl₃): δ 5.18 (*brs*, 1CH–S), 5.19 (*brs*, 1CH–S), 7.03–7.08 (*m*, 2CH_{arom}), 7.14–7.21 (*m*, 2CH_{arom}), 7.29–7.38 (*m*, 6CH_{arom}), 7.40–7.46 (*m*, 4CH_{arom}), 7.92–7.97 (*m*, 2CH_{arom}) ppm. ¹³C{¹H} NMR (150 MHz, CDCl₃): δ 52.2, 52.3 (2CH–S), 127.6, 127.7, 128.0, 128.1, 128.2, 128.3, 128.6, 128.7, 129.1, 130.8, 130.9 (16CH_{arom}), 141.0, 152.8, 152.9 (4C_{arom}) ppm. IR (film): ν 3060*m*, 3028*m*, 2923*m*, 1951*w*, 1888*w*, 1806*w*, 1727*w*, 1600*m*, 1540*w*, 1492*m*, 1451*s*, 1333*w*, 1261*m*, 1230*m*, 1106*m*, 1074*m*, 1030*m*, 805*m*, 739*m*, 698*vs* cm^{−1}. Anal. calcd for C₂₂H₁₈SSe₂ (472.36): C 55.94, H 3.84, S 6.79; found: C 55.88, H 4.12, S 7.09.

4.5. Synthesis of diphenylmethanethiol (4a)

A solution of benzhydryl alcohol (**2f**) (1 mmol, 0.18 g) in a mixture of toluene (5 mL) and water (1.4 mmol, 0.025 g) with Lawesson's reagent (2.4 mmol, 0.97 g) was heated at reflux for 30 min. Next, the toluene was evaporated under reduced pressure. The crude product was purified by CC (SiO₂, petroleum ether/ethyl acetate 9:1). Colorless oil; yield of **4a** [**6**]: 180 mg (90%). ¹H NMR (600 MHz, CDCl₃): δ 2.29 (*d*, ³J_{H,H} = 4.8 Hz, SH), 5.47 (*d*, ³J_{H,H} = 4.8 Hz, CH–S), 7.24–7.28 (*m*, 2CH_{arom}), 7.31–7.36 (*m*, 4CH_{arom}), 7.42–7.46 (*m*, 4CH_{arom}) ppm.

4.6. Synthesis of ferrocenyl(phenyl)methanethiol (4b) and diferrocenylmethanethiol (4c)

Lawesson's reagent (0.6 mmol, 0.24 g) was added to a solution of ferrocenyl-substituted methanols **2g** or **2h** (1 mmol) in dry toluene (5 mL) under argon and heated at reflux for 10 min. Then, the solvent was evaporated and the crude product was purified by CC (SiO₂,

petroleum ether/CH₂Cl₂ 7:3). Both products undergo decomposition, even when stored at -78°C (dry ice) for a longer time.

4.6.1. Ferrocenyl(phenyl)methanethiol (**4b**)

Viscous yellow oil; yield: 179 mg (58%). ¹H NMR (600 MHz, CDCl₃): δ 2.38 (*d*, ³J_{H,H} = 4.2 Hz, SH), 4.09 (*brs*, 1CH_{FC}), 4.14 (*brs*, 1CH_{FC}), 4.18 (*s*, 5CH_{FC}), 4.20 (*brs*, 1CH_{FC}), 4.43 (*brs*, 1CH_{FC}), 5.17 (*d*, ³J_{H,H} = 4.2 Hz, CH–S), 7.20–7.24 (*m*, 1CH_{arom}), 7.28–7.32 (*m*, 2CH_{arom}), 7.33–7.38 (*m*, 2CH_{arom}) ppm. ¹³C{¹H} NMR (150 MHz, CDCl₃): δ 44.1 (CH–S), 67.7, 67.8, 67.9, 68.1 (4CH_{FC}), 69.0 (5CH_{FC}), 91.8 (C_{FC}), 127.1, 127.3, 128.4 (5 CH_{arom}), 144.6 (C_{arom}) ppm. IR (KBr): ν 3091*m*, 3028*m*, 2965*m*, 2923*m*, 2854*w*, 2566*w*, 1951*w*, 1875*w*, 1641*m*, 1600*m*, 1496*m*, 1451*s*, 1413*m*, 1268*m*, 1103*s*, 1027*s*, 995*m*, 821*vs*, 707*vs* cm^{−1}. Anal. calcd for C₁₇H₁₆FeS (308.22): C 66.25, H 5.23, S 10.40; found: C 66.08, H 5.24, S 10.27.

4.6.2. Diferrocenylmethanethiol (**4c**)

Viscous yellow oil; yield: 233 mg (56%). ¹H NMR (600 MHz, C₆D₆): δ 2.40 (*brs*, SH), 3.89–3.95 (*m*, 6CH_{FC}), 4.08 (*s*, 10CH_{FC}), 4.25 (*brs*, 2CH_{FC}), 4.73 (*brs*, CH–S) ppm. ¹³C{¹H} NMR (150 MHz, C₆D₆): δ 67.4, 67.5, 67.9, 68.2 (8CH_{FC}), 69.3 (10 CH_{FC}), 69.5 (CH–S), 93.7 (2C_{FC}) ppm. IR (KBr): ν 3085*m*, 2920*m*, 2847*m*, 2569*w*, 1613*m*, 1461*m*, 1410*m*, 1258*m*, 1103*s*, 1021*m*, 1002*m*, 818*s*, 479*vs* cm^{−1}. Anal. calcd for C₂₁H₂₀Fe₂S (416.14): C 60.61, H 4.84, S 7.71; found: C 60.48, H 4.74, S 7.52.

4.7. Synthesis of dibenzhydryl 4-methoxyphenyltrithiophosphonate (**5**)

To a solution of benzhydryl alcohol (**2f**) (1 mmol, 0.18 g) in absolute toluene (5 mL), Lawesson's reagent (2.4 mmol, 0.97 g) was added, and the mixture was heated at reflux. After 15 min, the solvent was evaporated and the crude products were separated by CC (SiO₂, petroleum ether/ethyl acetate 9:1). Yield of **4a**: 122 mg (61%). **5**: Colorless solid; yield: 104 mg (18%); m.p. 109.0–110.0°C. ¹H NMR (600 MHz, CDCl₃): δ 3.78 (*s*, CH₃O), 5.79 (*brs*, 1CH–S), 5.81 (*brs*, 1CH–S), 6.67–6.71 (*m*, 2CH_{arom}), 7.09–7.16 (*m*, 6CH_{arom}), 7.19–7.25 (*m*, 6CH_{arom}), 7.26–7.30 (*m*, 4CH_{arom}), 7.32–7.36 (*m*, 4CH_{arom}), 7.61–7.68 (*m*, 2CH_{arom}) ppm. ¹³C{¹H} NMR (150 MHz, CDCl₃): δ 55.4 (CH₃O), 56.8, 56.9 (2CH–S), 113.4, 113.5, 127.0, 127.2, 128.2, 128.3, 128.7, 128.9, 132.8, 132.9 (24CH_{arom}), 140.5, 140.6, 140.8, 140.9, 162.4, 162.5 (6C_{arom}) ppm. ³¹P NMR (243 MHz, CDCl₃): δ 78.22 ppm. IR (KBr): ν 3056*w*, 3022*w*, 2996*w*, 2873*w*, 1597*s*, 1499*m*, 1492*m*, 1451*m*, 1309*m*, 1264*s*, 1182*m*, 1100*s*, 1024*m*, 831*m*, 698*vs*, 530*s* cm^{−1}. Anal. calcd for C₃₃H₂₉OPS₃ (568.75): C 69.69, H 5.14, S 16.91; found: C 69.66, H 5.26, S 16.67.

4.8. Attempted reaction of diphenylmethanethiol (**4a**) with Lawesson's reagent

A sample of pure **4a** (190.0 mg, 1.0 mmol) and Lawesson's reagent (242.0 mg, 0.6 mmol) were dissolved in 6 mL of dry toluene and the mixture was heated at reflux. The disappearance of **4a** was monitored by TLC (SiO₂, petroleum ether/ethyl acetate 9:1), and after 15 min, no starting material (*R*_f = 0.70) could be detected. The formation of the expected trithiophosphonate **5** was evidenced by comparison with a pure sample (*R*_f = 0.40).

4.9. X-ray crystal structure determination of compound 5 [25]

All measurements were made on *Rigaku Oxford Diffraction SuperNova* area-detector diffractometer [26] using $\text{MoK}\alpha$ radiation ($\lambda = 0.71073 \text{ \AA}$) from a micro-focus X-ray source and an *Oxford Instruments Cryojet XL* cooler. The data collection and refinement parameters are given below [25] and a view of the molecule is shown in Figure 1. Data reduction was performed with *CrysAlisPro* [26]. The intensities were corrected for Lorentz and polarization effects, and an empirical absorption correction using spherical harmonics [26] was applied. Equivalent reflections were merged. The structure was solved by dual space methods using *SHELXT-2014* [27], which revealed the positions of all non-hydrogen atoms. The non-hydrogen atoms were refined anisotropically. All of the H-atoms were placed in geometrically calculated positions and refined by using a riding model where each H-atom was assigned a fixed isotropic displacement parameter with a value equal to $1.2U_{\text{eq}}$ of its parent atom ($1.5U_{\text{eq}}$ for the methyl group). The refinement of the structure was carried out on F^2 by using full-matrix least-squares procedures, which minimized the function $\sum w(F_o^2 - F_c^2)^2$. A correction for secondary extinction was not applied. Neutral atom scattering factors for non-H-atoms were taken from [28], and the scattering factors for H-atoms were taken from [29]. Anomalous dispersion effects were included in F_c [30]; the values for f' and f'' were those of [31]. The values of the mass attenuation coefficients are those of [32]. All calculations were performed using the *SHELXL-2014* program [33].

Crystal data for 5: $\text{C}_{33}\text{H}_{29}\text{OPS}_3$, $M = 568.71$, crystallized from petroleum ether/ CH_2Cl_2 , colorless, prism, crystal dimensions $0.15 \times 0.25 \times 0.26 \text{ mm}$, triclinic, space group $P\bar{1}$, $Z = 2$, reflections for cell determination 21105, 2θ range for cell determination $5\text{--}65^\circ$, $a = 10.2285(2) \text{ \AA}$, $b = 10.8866(2) \text{ \AA}$, $c = 14.7543(3) \text{ \AA}$, $\alpha = 80.4281(18)^\circ$, $\beta = 84.6407(17)^\circ$, $\gamma = 62.910(2)^\circ$, $V = 1442.04(6) \text{ \AA}^3$, $T = 160(1) \text{ K}$, $D_x = 1.310 \text{ g cm}^{-3}$, $\mu(\text{MoK}\alpha) = 0.338 \text{ mm}^{-1}$, scan type ω , $2\theta_{(\text{max})} = 64.9^\circ$, transmission factors (min; max) = 0.955; 1.000, total reflections measured 45,039, symmetry independent reflections 9732, reflections with $I > 2\sigma(I)$ 8001, reflections used in refinement 9732, parameters refined 344, $R(F)$ [$I > 2\sigma(I)$ reflections] = 0.0340, $wR(F^2)$ [all data] = 0.0886 ($w = [\sigma^2(F_o^2) + (0.0357P)^2 + 0.5162P]^{-1}$, where $P = (F_o^2 + 2F_c^2)/3$), goodness of fit 1.042, final $\Delta_{\text{max}}/\sigma$ 0.002, $\Delta\rho$ (max; min) = 0.36; -0.25 e \AA^{-3} .

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Disclosure statement

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References

- [1] Acton AQ, editor. Sulfur compounds – Advances in research and application. Atlanta, GA: Scholarly Edition; 2012.

- [2] Clayden J, MacLellan P. Asymmetric synthesis of tertiary thiols and thioethers. *J Org Chem.* **2011**;7:582–595.
- [3] Monaco MR, Prévost S, List B. Catalytic asymmetric synthesis of thiols. *J Am Chem Soc.* **2014**;136:16982–16985.
- [4] McMurry J. Organic chemistry with biological applications. Belmont: Brooks/Cole; **2011**. Chapter 13; p. 501–554.
- [5] Polster J, Schieberle P. Structure–odor correlations in homologous series of alkanethiols and attempts to predict odor thresholds by 3D-QSAR studies. *J Agric Food Chem.* **2015**;63:1419–1432.
- [6] Nishio T. Direct conversion of alcohols into thiols. *J Chem Soc Perkin Trans 1.* **1993**; 1113–1117.
- [7] Mlostoń G, Hamera-Fałdyga R, Celeda M, et al. Synthesis of ferrocenyl- and hetaryl-substituted 2,2,2-trifluoroethanols and their conversion into 2,2,2-trifluoroethanethiols using Lawesson's reagent. *J Fluorine Chem.* **2016**;188:147–152.
- [8] Mlostoń G, Urbaniak K, Gębicki K, et al. Hetaryl thioketones: synthesis and selected reactions. *Heteroatom Chem.* **2014**;25:548–555.
- [9] Mlostoń G, Hamera R, Heimgartner H. Synthesis of ferrocenyl thioketones and their reactions with diphenyldiazomethane. *Phosphorus Sulfur Silicon Relat Elem.* **2015**;190: 2125–2133.
- [10] Gebert A, Jasiński M, Mlostoń G, et al. Reduction of thiocarbonyl compounds with lithium diisopropylamide. *Helv Chim Acta.* **2014**;97:931–938.
- [11] Gupta I, Ravikanth M. One-flask synthesis of mono- and trifunctionalized 21-thia and 21-oxaporphyrin building blocks and their application in the synthesis of covalent and noncovalent unsymmetrical porphyrin arrays. *J Org Chem.* **2004**;69:6796–6811.
- [12] Struhárik M, Toma S. The diastereoselectivity of the addition of tricarbonyl-(η^6 -2-lithiothiophene) chromium(O) complexes on aldehydes. *J Organometal Chem.* **1994**;464: 59–63.
- [13] Yur'ev YK, Mezentsova NN, Vas'kovskii VE. Chemistry of selenophene. XV. 2-Vinylselenophene. *Zh Obsch Khim.* **1958**;28:3262–3265.
- [14] Matsuda T, Mizuno K, Watanuki S. Rhodium-catalyzed arylation of acylsilanes with sodium tetraarylborates. *J Organometal Chem.* **2014**;765:64–67.
- [15] Kovač S, Rapić V. Ferrocene compounds XVII. Synthesis of some ferrocenyl carbinols, ethers, and ureas. *J Organometal Chem.* **1990**;384:147–153.
- [16] Bickar D, Lukas B, Neshvad G, et al. Mössbauer studies on ferrocene complexes: XI. Stabilisation and electron transfer in diferrocenyl monocations and related species. *J Organometal Chem.* **1984**;263:225–234.
- [17] Burišov AR, Drozdova YA, Pudovik MA, et al. Interaction of phosphorus(III) thioesters with oxygen. *Izv Akad Nauk SSSR, Ser Khim.* **1991**;9127–9132.
- [18] Navech J, Revel M, Kraemer R, et al. Quelques propriétés chimiques du tris(tertiobutyl)-2,4,6-phenyldithiophosphorane. *Phosphorus Sulfur Relat Elem.* **1986**;26:83–89.
- [19] Romanov GV, Ryzhikova TY, Pudovik AN. Reactions of phenyl- and trimethylsilylphenylphosphines with thiobenzophenone. *Izv Akad Nauk SSSR, Ser Khim.* **1984**;2116–2117.
- [20] Murav'ev IV, Fedorovich IS. Arylation of the acid halides of di- and triphosphoric acid esters. *Zh Obsh Khim.* **1976**;46:789–791.
- [21] Johnson CK. ORTEP II, report ORNL-5138. Oak Ridge, TN: Oak Ridge National Laboratory; **1976**.
- [22] Ohno M, Miyamoto M, Itoshi K, et al. Development of dual-acting benzofurans for thromboxane A_2 receptor antagonist and prostacyclin receptor agonist: synthesis, structure–activity relationship, and evaluation of benzofuran derivatives. *J Med Chem.* **2005**;48:5279–5294.
- [23] Tagawa Y, Minami S, Yoshida T, et al. Preparation and antibacterial activity of 3-methyl-1-*p*-substituted phenylpyrazole-5-thiol. *Arch Pharm.* **2002**;335:99–103.
- [24] Mlostoń G, Hamera-Fałdyga R, Heimgartner H. Unexpected course of the attempted conversions of ferrocenyl(hetaryl)methanols into thiols using Lawesson's reagent. *Phosphorus Sulfur Silicon Relat Elem.* **2017**. doi:10.1080/10426507.2017.1286491.

- [25] CCDC-1531780 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the *Cambridge Crystallographic Data Centre* via www.ccdc.cam.ac.uk/structures
- [26] CrysAlisPro. Version 1.171.38.43. Abingdon: Rigaku Oxford Diffraction; 2015.
- [27] Sheldrick GM. SHELXT – integrated space-group and crystal-structure determination. *Acta Crystallogr Sect A*. 2015;71:3–8.
- [28] Maslen EN, Fox AG, O’Keefe MA. International tables for crystallography. In: Wilson AJC, editor. Vol. C. Dordrecht: Kluwer Academic; 1992. Table 6.1.1.1. p. 477–486.
- [29] Stewart RF, Davidson ER, Simpson WT. Coherent X-ray scattering for the hydrogen atom in the hydrogen molecule. *J Chem Phys*. 1965;42:3175–3187.
- [30] Ibers JA, Hamilton WC. Dispersion corrections and crystal structure refinements. *Acta Crystallogr*. 1964;17:781–782.
- [31] Creagh DC, McAuley WJ. In: International tables for crystallography. Wilson AJC, editor. Vol. C. Dordrecht: Kluwer Academic; 1992. Table 4.2.6.8. p. 219–222.
- [32] Creagh DC, Hubbell JH. In: International tables for crystallography. Wilson AJC, editor. Vol. C. Dordrecht: Kluwer Academic; 1992. Table 4.2.4.3. p. 200–206.
- [33] Sheldrick GM. Crystal structure refinement with SHELXL. *Acta Crystallogr Sect C*. 2015;71:3–8.