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Phosphorothioate-mercaptophosphonate rearrangement: synthesis of new *o*-mercaptoaryl- and *o*-mercaptoheteroaryl phosphonates and their derivatives

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Summary — New *o*-mercaptoaryl and *o*-mercaptoheteroaryl phosphonates and their derivatives were prepared via an *ortho*-lithiation of *O*,*O*-diisopropyl *S*-aryl, *S*-(2-pyridyl), *S*-(2-thienyl) and *S*-(3-thienyl) phosphorothioates followed by a phosphonyl group S → C migration.

phosphorothioate / *o*-mercaptoarylphosphonate / *o*-mercaptoheteroarylphosphonate / *ortho*-lithiation / [1,3]-sigmatropic rearrangement

Résumé — Réarrangement phosphorothioate-mercaptophosphonate : synthèse de nouveaux *o*-mercaptoaryl et *o*-mercaptohétéroaryl phosphonates et dérivés. *De nouveaux o-mercaptoaryl et o-mercaptohétéroaryl phosphonates et dérivés ont été préparés via une* ortho-*lithiation de S-aryl, S-(2-pyridyl), S-(2-thiényl) et S-(3-thiényl) phosphorothioates de O,O-diisopropyle suivie d'une migration S → C du groupe phosphonyle.*

phosphorothioate / *o*-mercaptoarylphosphonate / *o*-mercaptohétéroarylphosphonate / *ortho*-lithiation / sigmatropie-[1.3]

Introduction

Owing to their biological activity due to their structural analogy with phosphates [1], functionalized phosphonates are widely used in agriculture and medicine [2–6]. Moreover, chelating phosphorus-based extractants have considerable potentiality and they have attracted the interest of many scientists over the past decade. In particular, monoesters of alkylphosphonic acids such as mono(2-ethylhexyl)(2-ethylhexyl)phosphonic acid (EHEHPA) or dibutylbutylphosphonate (DBBP) have a widespread use. The former is a selective extractant, which is used commercially to separate cobalt from nickel and to carry out some of the more difficult rare earth separations such as neodymium and praeseodymium [7]. DBBP is finding increasing uses in the recovery of uranium [8], titanium, gold and silver [9].

Metal complexes of thiolates have also received considerable attention [10], in particular because of their involvement in enzymatic [11] and nonbiological catalytic processes [12].

The chemistry of mixed phosphorus-sulfur complexes, and especially that of phosphorus-arylthiol ligands has however been the subject of limited study. It has been reported that 2-phosphino and 2-phosphinyl benzenethiols, prepared from benzenethiol by dilithiation-electrophilic substitution procedures [13], formed interesting new classes of polydentate ligands in particular with molybdenum, rhodium and iridium [14].

Consequently, aryl and heteroaryl phosphonates that are *ortho*-substituted by a thiol group are expected to be good complexing agents. However, at the beginning of our work, we could find only one example of an *o*-mercaptoarylphosphonate: diethyl (2-mercaptophenyl)phosphonate. This mixed phosphorus-sulfur analogue of salicylate ester, which was mentioned without any physical or spectroscopic data, was obtained by radical phosphorylation of 2-iodobenzenethiol and used as an intermediate for the preparation of the corresponding phosphine [15].

In a previous paper, we described the synthesis of this phosphonate and its diisopropyl-substituted analogue by two different methods and its hydrolysis into the unknown (2-mercaptophenyl)phosphonic acid [16]. One method involves the dilithiation of the benzenethiol based on a recently developed procedure [17] followed by the addition of dialkyl phosphorochloridate. The other implies the phosphonyl group S → C migration ([1,3]-anionic sigmatropic rearrangement) of an *ortho*-lithiated *O*,*O*-diisopropyl *S*-phenyl phosphorothioate. Previously, the same reaction (well known with arylphosphates [18]) was not observed from a

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O,O-diethyl *S*-phenyl phosphorothioate and was considered to be impossible due to a nucleophilic attack of the lithium diisopropylamide (LDA) on the phosphinyl group which induces the S-P bond cleavage [19]. Then, starting from pyridyl and thienyl phosphorothioates, we also observed the rearrangement [20].

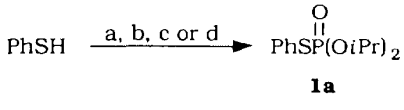
This full paper describes the synthetic potential of this phosphorothioate-mercaptophosphonate rearrangement and also the scope and limitations of this method which allows the preparation of various derivatives of mercaptoaryl and mercaptoheteroaryl phosphonates.

Results and discussion

Synthesis of the aryl and heteroaryl phosphorothioates and bis(phosphorothioates)

Due to the potential of *O,O*-dialkyl *S*-aryl phosphorothioates as effective pesticides [21], a variety of synthetic procedures have been investigated [22–28].

Phosphorothioate **1a** was prepared from benzenethiol by four different methods in order to compare their efficiency (fig 1): a) reaction between triethylamine and a carbon tetrachloride solution of benzenethiol and diisopropyl phosphite according to the method described [29] for the preparation of diethyl aryl phosphates; b) halophilic substitution involving triisopropyl phosphite, benzenethiol and bromotrichloromethane [26]; c) reaction between diisopropyl phosphorochloridate and benzenethiol in the presence of triethylamine; and d) reaction between sodium benzenethiolate (prepared from benzenethiol and sodium hydride) and diisopropyl phosphorochloridate [16]. The latter, which gave us the best yield, was selected for the synthesis of most of the other phosphorothioates.



1a

a) $HP(O)(OiPr)_2$ / CCl_4 / NEt_3, 74%
b) $P(OiPr)_3$ / $BrCCl_3$, 66%
c) $ClP(O)(OiPr)_2$ / THF / NEt_3, 47%
d) NaH / THF / $ClP(O)(OiPr)_2$, 92%

Fig 1

It is interesting to note that we could obtain phosphorothioate **1a** from phenylmagnesium bromide by equimolar insertion of sulfur followed by the condensation of the intermediate magnesium mercaptide **A** onto diisopropyl phosphorochloridate (fig 2). However, the yields were only 17% in ether, and 50% when THF was used at the phosphorylation step. In both cases, we could not avoid the formation of isopropyl phenyl sulfide resulting from an alkylation of the benzenethiolate **A** by the phosphorochloridate or by **1a**.

Fortunately, this secondary reaction did not occur with sodium benzenethiolate and method d (fig 1) was used for the preparation of *S*-aryl phosphorothioates

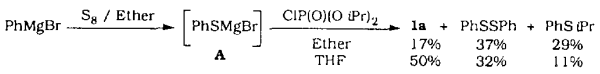
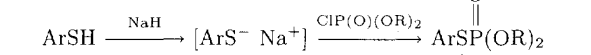


Fig 2

2a–8a, which are listed in table I together with their respective yields and ^{31}P NMR shifts.

According to the same method, bis(phosphorothioates) **9a–12a** and *S*-heteroaryl phosphorothioates **13a** and **14a** (table II) were prepared from the corresponding dithiols, pyridine-2-thione and thiophene-2-thiol. *S*-(3-Thienyl) phosphorothioate **15a** was obtained by phosphorylation of the lithium thiophene-3-thiolate [30].

Table I. Synthesis of *S*-aryl phosphorothioates **2a–8a**.



2a–8a

Phosphorothioate	*Ar*	*R*	^{31}P *NMR (CDCl₃) (ppm)*	*Yield (%)*
2a	Ph	Et	+22.7	63
3a	Ph	Ph	+14.9	85
4a	*p*-ClC_6H_4	*i*Pr	+19.6	73
5a	*p*-MeC_6H_4	*i*Pr	+20.2	83
6a	*p*-$tBuC_6H_4$	*i*Pr	+20.6	88
7a	*p*-EtC_6H_4	*i*Pr	+20.7	60
8a	2-Naphthyl	*i*Pr	+20.0	75

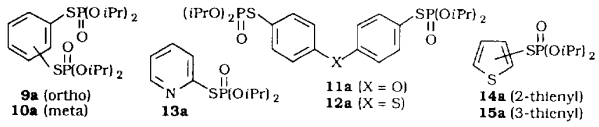
Reactivity of S-phenyl phosphorothioates with base

- *With lithium or sodium amide (table III)*

As mentioned in our earlier paper [16], the reaction of LDA with *O,O*-diisopropyl *S*-phenyl phosphorothioate **1a** induced an *ortho*-lithiation followed by the S → C migration of the phosphoryl group. The rearrangement is nearly quantitative according to ^{31}P NMR. However, due to the easy oxidation of the resulting thiol **1b** into disulfide **1c** during the work-up, several experiments gave yields in a range 60 to 91% after purification. As expected [19], with *O,O*-diethyl *S*-phenyl phosphorothioate **2a** the S_N2 (P) substitution by LDA was the main reaction leading to diethyl *N,N*-diisopropylphosphoramidate and benzenethiol. Nevertheless, we could isolate the rearranged diethyl (2-mercaptophenyl)phosphonate **2b** in 16% yield. These results demonstrate the importance of the substituent effect of the phosphoryl group on the course of the reaction. Such an effect was also observed in the reaction of diphenyl and diethyl arylphosphinates with LDA. The former undergo the O → C migration of the $P(O)Ph_2$ group [31], and the latter the nucleophilic addition of the LDA on the phosphinyl group [32].

Moreover, with the *O,O*-diethyl phosphorothioate **2a**, by using lithium tetramethylpiperidide (LTMP), a bulkier and therefore less nucleophilic amide anion, we could raise the yield to 42% in rearranged products (21% for **2b** and 21% for the corresponding disulfide

Table II. Synthesis of bis(phosphorothioates) **9a–12a** and *S*-heteroaryl phosphorothioates **13a–15a**.

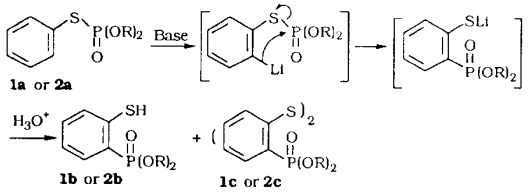


Phosphorothioate	*^{31}P NMR ($CDCl_3$) (ppm)*	*Yield (%)*
9a	+19.2	85
10a	+19.3	86
11a	+20.4	60
12a	+19.6	71
13a	+17.8	73
14a	+18.2	70
15a	+19.8	38

2c). The replacement of LDA by LTMP also allowed a yield of 79% of the phosphonate **1b** to be obtained. On the other hand, with silylated amide, lithium or sodium bis(trimethylsilyl)amide (XBTMSA), unchanged phosphorothioate **1a** was recovered indicating that no deprotonation occurred (table III).

In order to compare the reactivity of *S*-phenyl and *O*-phenyl phosphorothioate substituents, we examined the behavior of *O,O,S*-triphenyl phosphorothioate **3a** in the presence of one equivalent of LDA (fig 3). Phosphonothioate **3b** (50%) was the main product formed, which resulted from a first phosphate-hydroxyphosphonate rearrangement. Phosphinothioate **3c** (14%) was the consequence of the same rearrangement involving the second *O*-phenyl group. No phosphorothioate-mercaptophosphonate rearrangement was observed and the use of an excess of LDA gave a complex mixture of products. This is consistent with a less easy *ortho*-lithiation of the *S*-phenyl group. This result can be compared with the study of Modro et al [33]

Table III. Reactivity of *S*-phenyl phosphorothioates **1a** and **2a** with lithium or sodium amide.



R	*Phosphorothioate*	*Rearranged phosphonate*	*Base*	*Yield (%)*
			LDA	91
*i*Pr	**1a**	**1b**	LTMP[a]	79
			XBTMSA[b]	0
Et	**2a**	**2b** (+**2c**)	LDA	16 (+0)
			LTMP	21 (+21)

[a] LTMP = lithium tetramethylpiperidide; [b] XBTMSA = lithium (or sodium) bis(trimethylsilyl)amide.

concerning the behavior of *O,O*-diphenyl-*N*-methyl-*N*-phenylphosphoramidate in the presence of LDA. From this compound, the N → C migration occurs only after the O → C migrations are completed. In ^{31}P NMR spectroscopy of compounds **3a–c**, as observed before by Modro et al [33], the phosphorus atom becomes progressively more deshielded with each P-C bond introduced by the successive migration steps.

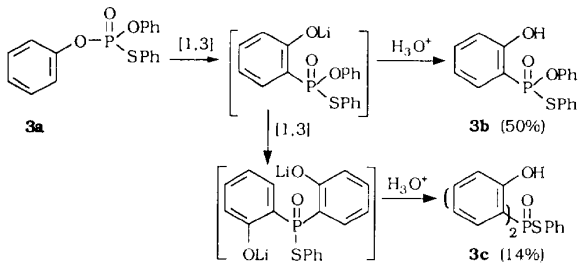


Fig 3

• *With alkyllithium*

We also examined the reaction of phosphorothioate **1a** with *n*-butyllithium or methyllithium. As we could expect, the use of alkyllithium, which is a more nucleophilic reagent than LDA, did not favor the rearrangement. Alkyllithium behaves both as nucleophilic and basic reagents. Therefore, we obtained a mixture of products, the main one being alkylphosphonate **1d** or **1e** but we also observed the formation of diphosphonate **1f** or **1g** resulting from the nucleophilic attack of phosphorothioate **1a** by the lithiated derivative of alkylphosphonate **1d** or **1e** (fig 4).

Such behavior of phosphorothioate **1a** with alkyllithium is similar to those previously observed with diethyl phosphorochloridate [34].

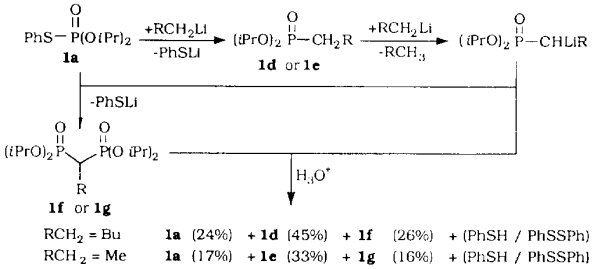
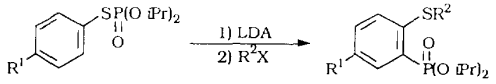


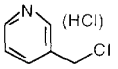
Fig 4

Synthesis of new mercaptoarylphosphonates and derivatives (table IV)

Using LDA and the convenient isopropyl substituents, we showed that the phosphorothioate-mercaptophosphonate rearrangement could be extended to various *para*-substituted *S*-phenyl phosphorothioates (table IV, entries 1–4) and also to an *S*-naphthyl phosphorothioate (entry 5). New *o*-mercaptoarylphosphonates **4b–8b** were isolated in the yields listed

Table IV. Synthesis of *o*-mercaptoarylphosphonates **4b**–**8b** and *S*-substituted derivatives **1h**–**l** of **1b**.



Entry	*Phosphorothioate*	R^1	R^2X	*Rearranged phosphonate*	^{31}P *NMR* ($CDCl_3$) *(ppm)*	*Yield (%)*
1	**4a**	Cl	HCl	**4b**	+14.9	68
2	**5a**	Me	HCl	**5b**	+15.9	56
3	**6a**	*t*Bu	HCl	**6b**	+16.3	61
4	**7a**	Et	HCl	**7b**	+16.0	72
5	**8a**[a]	–	HCl	**8b**[b]	+15.3	58
6	**1a**	H	MeI	**1h**	+14.5	82
7	**1a**	H	CH_2=$CHCH_2Br$	**1i**	+14.3	78
8	**1a**	H	$CH_3C(O)Cl$	**1j**	+13.1	67
9	**1a**	H	$CH_3(CH_2)_{10}Br$	**1k**	+14.7	43
10	**1a**	H		**1l**	+13.8	72

[a] **8a**: 2-naphthyl phosphorothioate; [b] **8b**: (2-mercapto-3-naphthyl)phosphonate.

in table IV. It is interesting to note out that the formation of the (2-mercapto-3-naphthyl)phosphonate **8b** results from an *ortho*-lithiation on the C_3 aromatic atom, a regioselectivity previously observed for the dimetallation of 2-naphthol [35]. Its structure was confirmed by the NMR data, in particular by the presence in ^1H NMR of a doublet at +8.53 ppm corresponding to the H_4 aromatic proton showing a coupling of 16.2 Hz with the phosphorus atom in position 3. Moreover, a partial cleavage of the S-P bond by LDA leading to naphthalenethiol and phosphoramidate was observed with the *S*-naphthyl phosphorothioate **8a**, whereas this cleavage was the main reaction with the phosphate analogue [32].

It was of course possible, after the transposition of the phosphoryl group of the lithiated phosphorothioate **1a**, to add an electrophilic reagent to the lithium thiolate obtained (entries 6–10). Thiosubstituted phenylphosphonates **1h**–**l** were thus isolated in satisfactory yields. However, with undecyl bromide (entry 9), a less reactive alkylating agent than methyl iodide, the alkylation (non-optimized) was incomplete (43%).

The conversion of thiols (usually unstable in air and readily oxidized to disulfides) in thiolcarbamates is one of the methods for their protection. We therefore prepared the phosphonylated thiolcarbamate **1m** (fig 5) by treating the thiol **1b** with *n*-propyl isocyanate in presence of traces of pyridine according to [36]. However, the reaction was very slow compared to those of benzenethiol or 1,3-benzenedithiol [36], and required several days refluxing in ether (73% yield). Further, we extended our investigation to the approach of unknown diphosphonylated polyethylene glycols **1n** and **1o** (fig 5), with potential chelating properties. Previous studies [37] have reported the beneficial effects of cesium ions coupled with a dipolar aprotic solvent like DMF in the formation of macrocyclic compounds by a thiolate alkylation [38]. Thus, when the caesium salt of **1b** was treated in DMF (60 °C, 16 h) with 1,8-dichloro-3,6-dioxaoctane (n = 2) and 1,11-dichloro-3,6,9-trioxaundecane (n = 3), the expected diphosphonylated compounds **1n** and **1o** were obtained in 83 and 87% yields, respectively. From oxy- and thiodiphenyl bis(phosphorothioates) **11a** and **12a** we could synthesize the rearranged dimercapto oxy- and thiodi(phenylphosphonates) **11b** (60%) and **12b** (78%) (fig 5), which are potentially suitable monomers for polymerization.

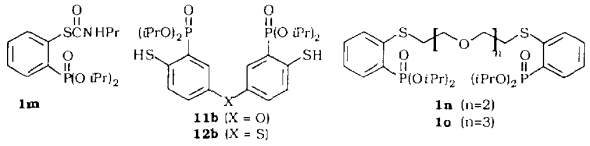
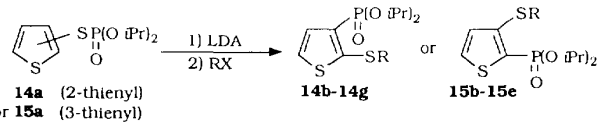


Fig 5

From the *o*-mercaptophenylphosphonate **1b**, we prepared the *S*-(2-phosphonophenyl) phosphorothioate **1p** by treatment of the sodium salt of **1b** with diisopropyl phosphorochloridate (fig 6) in order to create a second *ortho* C-P bond leading to diphosphonate **1q**. The ^{31}P NMR spectrum ($CDCl_3$) of **1p** exhibits two phosphorus doublets as expected, the phosphonate ester at +13.4 ppm and the phosphorothioate ester at +19.5 ppm. The two-bond P-P coupling constant is 3.5 Hz. When compound **1p** was treated with LDA in THF followed by a protonation, the ^{31}P NMR spectrum ($CDCl_3$) of the crude product showed a major signal at +14.4 ppm presumably corresponding to the mercaptodiphosphonate **1q** resulting from the phosphonyl group S → C migration of the lithiated phosphonate-phosphorothioate **1p**. However, due to some difficulties encountered for the purification of this thiol **1q**, the protonation was replaced by a methylation leading to the more stable diphosphonate **1r** (fig 6).

Treatment of *ortho*-phenylene bis(phosphorothioate) **9a** with two equivalents of LDA followed by a protonation led to the phosphonate-phosphorothioate **9b**

Table V. Synthesis of *o*-mercaptothienylphosphonates and derivatives **14b–14g** and **15b–15e**.



Entry	*Phosphorothioate*	*RX*	*Rearranged phosphonate*	*Yield (%)*	*^{31}P NMR ($CDCl_3$) (ppm)*
1	**14a**	HCl	**14b**	11	+7.6
			14c[a]	10	+7.0
2	**14a**	MeI	**14d**	36	+8.3
3	**14a**	$CH_3C(O)Cl$	**14e**	19	+7.3
4	**14a**	$PhC(O)Cl$	**14f**	45	+7.3
5	**14a**	$CH_3(CH_2)_{10}Br$	**14g**	45	+8.1
6	**15a**	HCl	**15b**	47	+9.3
7	**15a**	MeI	**15c**	63	+8.2
8	**15a**	$CH_3C(O)Cl$	**15d**	42	+6.0
9	**15a**	$CH_3(CH_2)_{10}Br$	**15e**	52	+7.9

[a] **14c** is the corresponding disulfide of **14b**.

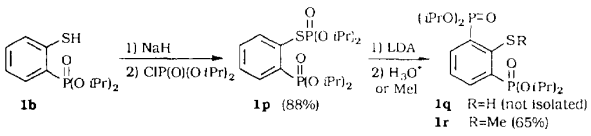


Fig 6

(the thiol corresponding to **9c**; fig 7) in 43% yield resulting from the rearrangement of only one phosphorothioate group. The same reaction followed by a methylation led to **9c** together with the bis(methylthio) derivative **9d** resulting from cleavage of the S-P bond of the second phosphorothioate substituent. When the amount of base was increased, we obtained a complex mixture of products and the double rearrangement was in no way observed. Furthermore, *meta*-phenylene bis(phosphorothioate) **10a** gave a complex mixture when treated with two equivalents of LDA. It is interesting to note that in the oxygen series, the double rearrangement was observed with 1,2- and 1,4-phenylene bis(phosphates) but not with the 1,3-analogue [39].

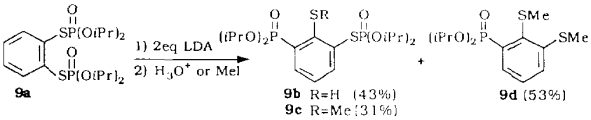


Fig 7

Synthesis of new mercaptoheteroarylphosphonates and derivatives

We then decided to examine whether this *ortho*-lithiation rearrangement could be applied in heterocyclic series. Substituted pyridine-2-thiones are known as complexing agents for transition metals [40] and some pyridylphosphonates present antibacterial, herbicidal, chelating or anticorrosion properties [41]. Some thienylphosphonates also have insecticidal properties [42] and others antidepressant activities [43]. However, to our knowledge, in the pyridine or thiophene series, no compound functionalized with both the thiol and phosphonate groups have been described.

In the pyridine series, starting from *S*-pyridyl phosphorothioate **13a**, the rearrangement was nearly quantitative and phosphonylated pyridine was isolated in the pyridinethione form **13b** (71–75% yield), which is a phosphonyl analogue of mercaptonicotinic esters; the disulfide **13c** (~10%) was also obtained (fig 8). Two methods were used to prepare the *S*-alkylated derivatives of **13b**. Method **A** implies the alkylation of the intermediate lithium thiolate of **13b**. Method **B** is an *S*-alkylation of the phosphonylated pyridinethione **13b** leading to the pyridinium salt which was converted, after the addition of sodium hydrogen carbonate, to the corresponding functionalized pyridines **13d** and **13e** (fig 8). For both methods, with undecyl bromide, prolonged refluxing in THF was necessary in order to get the corresponding compound **13e** in satisfactory yields.

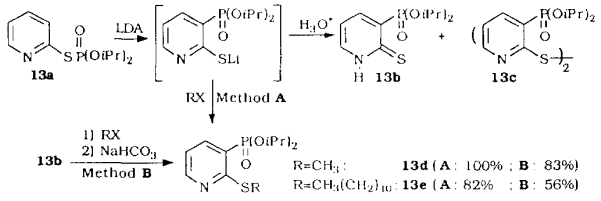


Fig 8

In the thiophene series, the reaction of the *S*-thienyl phosphorothioate **14a** with LDA followed by a protonation led to the formation of a mixture of byproducts [44] together with the expected rearranged thiol **14b** and disulfide **14c** in modest yield (table V, entry 1). However, relatively better yields could be obtained by alkylation (entry 2) or benzoylation (entry 4) of the intermediate rearranged lithium thiolate. Starting from the *S*-thienyl phosphorothioate **15a**, we isolated the expected phosphonates **15b–15e** (entries 6–9) in more

satisfactory yields (the formation of byproducts, observed in the ^1H NMR spectra of the crude products, was clearly lower).

Although the yields obtained from thiophenes are not as good as that from pyridine derivatives, these examples display the possibility of achieving the phosphonyl group S → C transposition via an *ortho*-lithiation reaction in heterocyclic series.

Conclusion

This work demonstrates that the *ortho*-lithiation of *S*-aryl and *S*-heteroaryl phosphorothioates followed by a phosphorothioate-mercaptophosphonate rearrangement is an efficient method for the preparation of the corresponding *o*-mercaptophosphonates. However, it is necessary to use diisopropyl instead of diethyl groups as substituents of phosphinyl moiety. This rearrangement was observed in benzene, naphthalene, pyridine and thiophene series. Quite a large number of new functionalized phosphonates with potential complexing properties have been prepared. Moreover, some of them, in particular phosphonic analogues of thiosalicylic and mercaptonicotinic acids, may have some biological applications.

Experimental section

Flash liquid chromatography was carried out on Merck 60 (63–200 microns) silica gel. The ^1H NMR spectra were recorded on a Varian EM 360 spectrometer at 60 MHz in CCl_4, or a Bruker AC 250 spectrometer at 250.13 MHz in $CDCl_3$, using TMS as internal standard. The ^{13}C NMR spectra were recorded on a Bruker WP 80 SY spectrometer at 20.15 MHz or a Bruker AC 250 spectrometer at 62.89 MHz, in $CDCl_3$, with TMS as internal standard (proton decoupled, J_{CP} given). The ^{31}P NMR spectra were recorded on a Bruker WP 80 SY spectrometer at 32.44 MHz with H_3PO_4 as external standard. Chemical shifts are reported in δ units, parts per million (ppm). The mass spectra were recorded on a Varian Mat CH 5 or a Nermag Riber R10 spectrometer by electron impact at 70 eV. The IR spectra were recorded on a Perkin-Elmer 684 or a Perkin-Elmer 16 PC spectrometer (significant υ are given in cm^{-1}). For all the compounds bearing a diisopropylphosphonyl group, the ^1H and ^{13}C NMR spectra exhibit characteristic signals at 1.2–1.3 and 1.3–1.4 (2d, $^3J_{HH} \sim 6$ Hz, $(CH_3)_2CHO$), 4.7–4.8 (dsept, $^3J_{HH} \sim 6$ Hz, $^3J_{HP} \sim 8$–9 Hz, $(CH_3)_2CHO$), ~ 23 and ~ 24 (2d, $^3J_{CP} \sim 5$–7 Hz and ~ 4–5 Hz, $(CH_3)_2CHO$) and ~ 71–73 (d, $^2J_{CP} \sim 5$–7 Hz, $(CH_3)_2CHO$). Likewise, in IR spectra, characteristic absorptions at ~ 1 250 ($\upsilon_{P=O}$) and ~ 1 000 ($\upsilon_{P\text{-}OiPr}$) are observed. These data are not repeated for each compound described below. Melting points are uncorrected.

Preparation of O,O-*diisopropyl* S-*phenyl phosphorothioate* **1a** *(previously described [16])*

- *From benzenethiol*

■ *Method A*

Compound **1a** was prepared according to [29] from benzenethiol (1 mL, 9.7 mmol), diisopropyl phosphite (1.7 g, 10.2 mmol), carbon tetrachloride (5 mL) and triethylamine (1.4 mL, 10 mmol). The mixture was stirred for 72 h at room temperature. The solution was then diluted with water and extracted with methylene chloride. The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. Flash chromatography on silica gel [eluent: petroleum ether/ether 70:30] gave **1a** (1.98 g, 74%) as a colorless oil.

■ *Method B*

Compound **1a** was prepared according to [26] from benzenethiol (12.3 mL, 120 mmol), triisopropyl phosphite (7.4 mL, 30 mmol) and bromotrichloromethane (5.9 mL, 60 mmol). The mixture was stirred for 72 h at room temperature. The solution was then concentrated and the crude product was distilled (118–120 °C under 0.15 hPa). The main fraction (6.6 g) still containing benzenethiol was purified by flash chromatography on silica gel to give **1a** (5.4 g, 66%).

■ *Method C*

To a solution of benzenethiol (0.2 mL, 1.95 mmol) and diisopropyl phosphorochloridate (383 mg, 1.91 mmol) [45] in dry THF (5 mL) was slowly added, at room temperature, under N_2, triethylamine (0.28 mL, 2.01 mmol). The mixture was stirred for 72 h at room temperature. The solution was then diluted with water and extracted with ether. The organic phase was dried (Na_2SO_4) and concentrated under reduced pressure. Flash chromatography on silica gel gave **1a** (246 mg, 47%).

■ *Method D*

Compound **1a** was prepared according to [16] from benzenethiol (1 mL, 9.7 mmol), NaH (500 mg, 60% in mineral oil, 12.5 mmol) and diisopropyl phosphorochloridate (1.9 g, 9.5 mmol) in THF (30 mL). Flash chromatography on silica gel of the crude product (2.6 g) gave **1a** (2.4 g, 92%).

- *From phenylmagnesium bromide*

To a solution of phenylmagnesium bromide (5 mL, 1.69 M solution in ether, 8.45 mmol) in dry ether (5 mL) was portionwise added, at 0 °C, under N_2, sulfur (0.33 g, 10.3 mmol). The mixture was warmed to room temperature and stirred for 30 min. Ether was carefully removed under N_2 and replaced by dry THF (5 mL). Diisopropyl phosphorochloridate (2 g, 10 mmol) was slowly added and the mixture was stirred again for 16 h at room temperature. The solution was then poured into a saturated aqueous solution of NH_4Cl/HCl, extracted with ether, dried (Na_2SO_4) and concentrated under reduced pressure. Flash chromatography on silica gel gave **1a** (1.15 g, 50%). The first fraction contained a mixture of diphenyl disulfide (~ 32%) and isopropyl phenyl sulfide (~ 11%).

Synthesis of phosphorothioates **2a**–**14a** *and* **1p**

Thiol or dithiol (1 mmol) was slowly added, under N_2, to a stirred solution of NaH (1.3 equiv/HS) in dry THF (5 mL) at room temperature. After H_2 evolution had ceased, phosphorochloridate (2 equiv/HS) dissolved in dry THF (0.5 mL) was added dropwise. The mixture was stirred at room temperature for 16 h. The solution was then diluted with water, extracted with methylene chloride (or ether), dried (Na_2SO_4) and concentrated under reduced pressure to give the crude product.

- O,O-*Diethyl* S-*phenyl phosphorothioate* **2a**

Flash chromatography on silica gel (eluent: pentane/ether 60:40) gave **2a** (63%) as a colorless oil.

The ^1H NMR data agree with literature data [24b].

^{13}C NMR ($CDCl_3$): 16.0 (d, $^3J_{CP} = 7.1$ Hz, CH_3CH_2O), 64.1 (d, $^2J_{CP} = 6.5$ Hz, CH_3CH_2O), 126.8 (d, $^2J_{CP} = 7.2$ Hz, C_1), 129.0 (d, $^5J_{CP} = 2.8$ Hz, C_4), 129.3 (d, $^4J_{CP} = 1.5$ Hz, C_3, C_5), 134.6 (d, $^3J_{CP} = 5.2$ Hz, C_2, C_6).

MS m/z (%): 247 (M + 1/25), 246 ($M^{\cdot+}$/100), 218, 190, 137, 110, 109, 105, 94, 91, 81, 65, 51, 47, 45, 43.

• O,O,S-*Triphenyl phosphorothioate* **3a**

Flash chromatography on silica gel (eluent: petroleum ether/ether 90:10) gave **3a** (85%) as a colorless oil.

The ^{1}H NMR data agree with literature data [28].

MS m/z (%): 343 (M + 1/6), 342 ($M^{\cdot+}$/21), 155, 109, 77, 65, 51, 50, 49 (100), 47.

• O,O-*Diisopropyl* S-*(4-chlorophenyl) phosphorothioate* **4a**

Flash chromatography on silica gel (eluent: petroleum ether/ether 70:30) gave **4a** (73%) as a colorless oil.

The ^{1}H NMR data agree with literature data [24b].

^{13}C NMR ($CDCl_3$): 126.2 (d, $^2J_{CP}$ = 7.3 Hz, C_1), 129.4–129.5 (m, C_3, C_4, C_5), 135.6 (d, $^3J_{CP}$ = 5.5 Hz, C_2, C_6).

MS m/z (%): 309 (M + 1/7), 308 ($M^{\cdot+}$/31), 266, 251, 226, 225, 224 (100), 223, 146, 145, 144, 143, 128, 123, 108, 43.

• O,O-*Diisopropyl* S-*(4-methylphenyl)phosphorothioate* **5a**

Flash chromatography on silica gel (eluent: petroleum ether/ether 70:30) gave **5a** (83%) as a colorless oil.

The ^{1}H NMR data agree with literature data [24b].

^{13}C NMR ($CDCl_3$): 21.1 (s, ArCH_3), 123.7 (d, $^2J_{CP}$ = 6.9 Hz, C_1), 130.0 (d, $^4J_{CP}$ = 2.1 Hz, C_3, C_5), 134.4 (d, $^3J_{CP}$ = 5.3 Hz, C_2, C_6), 138.8 (d, $^5J_{CP}$ = 2.9 Hz, C_4).

MS m/z (%): 289 (M + 1/8), 288 ($M^{\cdot+}$/35), 246, 205, 204 (100), 124, 123, 108, 91, 77, 43.

• O,O-*Diisopropyl* S-*(4*-tert-*butylphenyl) phosphorothioate* **6a**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 90:10) gave **6a** (88%) as a colorless oil.

^{1}H NMR ($CDCl_3$): 1.29 (s, 9H, C(CH_3)$_3$), 7.35 (d, 2H, $^3J_{HH}$ = 8.3 Hz, C_3H, C_5H), 7.51 (dd, 2H, $^3J_{HH}$ = 8.3 Hz, $^4J_{HP}$ = 2.0 Hz, C_2H, C_6H).

^{13}C NMR ($CDCl_3$): 31.3 (s, C(CH_3)$_3$), 34.7 (s, C(CH_3)$_3$), 123.6 (d, $^2J_{CP}$ = 7.0 Hz, C_1), 126.4 (d, $^4J_{CP}$ = 2.2 Hz, C_3, C_5), 134.2 (d, $^3J_{CP}$ = 5.3 Hz, C_2, C_6), 152.1 (d, $^5J_{CP}$ = 3.0 Hz, C_4).

MS m/z (%): 331 (M + 1/10), 330 ($M^{\cdot+}$/ 43), 288, 246, 231, 86, 84, 49, 43 (100).

• O,O-*Diisopropyl* S-*(4-ethylphenyl)phosphorothioate* **7a**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 90:10) gave **7a** (60%) as a colorless oil.

^{1}H NMR ($CDCl_3$): 1.22 (t, 3H, $^3J_{HH}$ = 7.6 Hz, CH_3CH_2), 2.63 (q, 2H, $^3J_{HH}$ = 7.6 Hz, CH_3CH_2), 7.16 (d, 2H, $^3J_{HH}$ = 8.1 Hz, C_3H, C_5H), 7.49 (dd, 2H, $^3J_{HH}$ = 8.1 Hz, $^4J_{HP}$ = 2.0 Hz, C_2H, C_6H).

^{13}C NMR ($CDCl_3$): 15.4 (s, CH_3CH_2), 28.6 (s, CH_3CH_2), 123.8 (d, $^2J_{CP}$ = 6.9 Hz, C_1), 128.9 (d, $^4J_{CP}$ = 2.2 Hz, C_3, C_5), 134.5 (d, $^3J_{CP}$ = 5.3 Hz, C_2, C_6), 145.3 (d, $^5J_{CP}$ = 3.0 Hz, C_4).

MS m/z (%): 303 (M + 1/4), 302 ($M^{\cdot+}$/18), 219, 218 (100), 138, 123, 105, 86, 84, 49, 43.

• O,O-*Diisopropyl* S-*(2-naphthyl)phosphorothioate* **8a**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 80:20) gave **8a** (75%) as a pale yellow oil.

^{1}H NMR ($CDCl_3$): 7.47–7.54 and 7.79–7.84 (2m, 5H, C_4H, C_5H, C_6H, C_7H, C_8H), 7.65 (~ d, 1H, $^3J_{HH}$ ~ 8.6 Hz, C_3H), 8.11 (~ s, 1H, C_1H).

^{13}C NMR ($CDCl_3$): 124.7 (d, $^2J_{CP}$ = 7.6 Hz, C_2), 126.8, 127.0, 127.8, 127.8 (4d, J_{CP} ~ 1 Hz, C_5, C_6, C_7, C_8), 128.9 (d, $^4J_{CP}$ = 1.6 Hz, C_4), 130.9 (d, $^3J_{CP}$ = 4.4 Hz, C_3), 133.0 (d, J_{CP} = 2.5 Hz), 133.7 (s), 134.0 (d, $^3J_{CP}$ = 6.9 Hz, C_1).

MS m/z (%): 324 ($M^{\cdot+}$/3), 241, 240, 160, 159, 144, 115, 43 (100), 41.

• O,O,O′,O′-*Tetraisopropyl* S,S′-*(1,2-phenylene) bis(phosphorothioate)* **9a**

Flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate 80:20) gave **9a** (85%) as a pale yellow oil.

^{1}H NMR ($CDCl_3$): 7.28–7.35 (m, 2H, Ar), 7.83–7.87 (m, 2H, Ar).

^{13}C NMR ($CDCl_3$): 129.1 (~ t, $^4J_{CP}$ ~ $^5J_{CP}$ ~ 3.5 Hz, C_4, C_5), 132.2 (~ t, $^2J_{CP}$ ~ $^3J_{CP}$ ~ 7.6 Hz, C_1, C_2), 135.3 (~ t, $^3J_{CP}$ ~ $^4J_{CP}$ ~ 4.1 Hz, C_3, C_6).

• O,O,O′,O′-*Tetraisopropyl* S,S′-*(1,3-phenylene) bis(phosphorothioate)* **10a**

Flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate 80:20) gave **10a** (86%) as a pale yellow oil.

^{1}H NMR ($CDCl_3$): 7.32 (t, 1H, $^3J_{HH}$ = 7.8 Hz, C_5H), 7.61 (dd, 2H, $^3J_{HH}$ = 7.8 Hz, $^4J_{HP}$ = 1.7 Hz, C_4H, C_6H), 7.80 (t, 1H, $^4J_{HP}$ = 1.7 Hz, C_2H).

^{13}C NMR ($CDCl_3$): 128.7 (~ t, $^2J_{CP}$ ~ $^4J_{CP}$ ~ 4.4 Hz, C_1, C_3), 129.8 (t, $^4J_{CP}$ = 1.6 Hz, C_5), 134.2 (~ t, $^3J_{CP}$ ~ $^5J_{CP}$ ~ 4.1 Hz, C_4, C_6), 139.1 (t, $^3J_{CP}$ = 6.1 Hz, C_2).

• O,O,O′,O′-*Tetraisopropyl* S,S′-*(oxydi-4,1-phenylene) bis(phosphorothioate)* **11a**

Flash chromatography on silica gel (eluent: ether) gave **11a** (60%) as a pale yellow oil.

^{1}H NMR ($CDCl_3$): 6.94–7.00 (m, 4H, Ar), 7.54–7.60 (m, 4H, Ar).

^{13}C NMR ($CDCl_3$): 119.7 (d, $^4J_{CP}$ = 1.8 Hz, C_3, C_5, $C_{3'}$, $C_{5'}$), 121.5 (d, $^2J_{CP}$ = 7.2 Hz, C_1, $C_{1'}$), 136.3 (d, $^3J_{CP}$ = 5.2 Hz, C_2, C_6, $C_{2'}$, $C_{6'}$), 157.4 (d, $^5J_{CP}$ = 3.0 Hz, C_4, $C_{4'}$).

• O,O,O′,O′-*Tetraisopropyl* S,S′-*(thiodi-4,1-phenylene) bis(phosphorothioate)* **12a**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 60:40) gave **12a** (71%) as a pale yellow oil.

^{1}H NMR ($CDCl_3$): 7.27 (d, 4H, $^3J_{HH}$ = 8.1 Hz, C_3H, C_5H, $C_{3'}$H, $C_{5'}$H), 7.53 (dd, 4H, $^3J_{HH}$ = 8.1 Hz, $^4J_{HP}$ = 1.9 Hz, C_2H, C_6H, $C_{2'}$H, $C_{6'}$H).

^{13}C NMR ($CDCl_3$): 126.9 (d, $^2J_{CP}$ = 7.2 Hz, C_1, $C_{1'}$), 131.8 (d, $^4J_{CP}$ = 1.8 Hz, C_3, C_5, $C_{3'}$, $C_{5'}$), 135.2 (d, $^3J_{CP}$ = 5.5 Hz, C_2, C_6, $C_{2'}$, $C_{6'}$), 136.6 (d, $^5J_{CP}$ = 3.2 Hz, C_4, $C_{4'}$).

MS m/z (%): 578 ($M^{\cdot+}$/1), 166, 123, 109, 96, 86, 84, 67, 51, 49 (100), 47, 43, 41.

• O,O-*Diisopropyl* S-*(2-pyridyl)phosphorothioate* **13a**

Flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate 80:20) gave **13a** (73%) as a yellow oil.

^{1}H NMR ($CDCl_3$): 7.18–7.24 and 7.61–7.73 (2m, 3H, C_3H, C_4H, C_5H), 8.52 (~ d, 1H, $^3J_{HH}$ ~ 4.7 Hz, C_6H).

^{13}C NMR ($CDCl_3$): 127.8 (d, $^2J_{CP}$ = 3.8 Hz, C_2), 122.5, 137.2 and 150.1 (3s, C_3, C_4, C_5, C_6).

MS *m/z* (%): 276 (M + 1/3), 275 ($M^{\cdot+}$/6), 217, 192, 191, 174, 111 (100), 97, 67, 43.

• O,O-*Diisopropyl* S-*(2-thienyl)phosphorothioate* **14a**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 90:10) gave **14a** (70%) as a yellow oil.

^{1}H NMR ($CDCl_3$): 7.02 (ddd, 1H, $^3J_{34}$ = 5.4 Hz, $^3J_{45}$ = 3.6 Hz, $^5J_{HP}$ = 0.4 Hz, C_4H), 7.26 (ddd ~ dt, 1H, $^3J_{45}$ ~ 3.5 Hz, $^4J_{35}$ = 1.3 Hz, $^6J_{HP}$ = 1.2 Hz, C_5H), 7.41 (ddd, 1H, $^3J_{34}$ = 5.4 Hz, $^4J_{35}$ = 1.3 Hz, $^4J_{HP}$ = 2.5 Hz, C_3H).

^{13}C NMR ($CDCl_3$): 124.0 (d, $^2J_{CP}$ = 9.0 Hz, C_2), 127.7 (d, $^4J_{CP}$ = 3.4 Hz, C_5), 130.7 (d, $^4J_{CP}$ = 4.3 Hz, C_4), 135.9 (d, $^3J_{CP}$ = 6.5 Hz, C_3).

MS *m/z* (%): 281 (M + 1/2), 280 ($M^{\cdot+}$/19), 239, 238, 197, 196, 116, 115, 114 (100), 113, 100, 99, 98, 71, 70, 43, 41.

• O,O-*Diisopropyl* S-*[2-(diisopropoxyphosphinyl)-phenyl] phosphorothioate* **1p**

Flash chromatography on silica gel (eluent: ethyl acetate) gave **1p** (88%) as a pale yellow oil.

^{1}H NMR ($CDCl_3$): 7.31–7.40 (m, 1H, Ar), 7.44–7.52 (m, 1H, Ar), 7.96–8.09 (m, 2H, Ar).

^{13}C NMR ($CDCl_3$): 127.2 (dd, $^3J_{CP}$ = 14.1 Hz, $^5J_{CSP}$ = 1.3 Hz, C_4), 131.7 (dd, $^1J_{CP}$ = 190.7 Hz, $^3J_{CSP}$ = 7.7 Hz, C_2), 132.4–132.8 (m, C_1, C_5), 133.5 (dd, $^3J_{CP}$ = 11.9 Hz, $^3J_{CSP}$ = 4.7 Hz, C_6), 135.1 (d, $^2J_{CP}$ = 9.2 Hz, C_3).

MS *m/z* (%): 439 (M + 1/3), 438 ($M^{\cdot+}$/8), 354, 312, 270, 253, 232, 191, 190 (100), 173, 172, 155, 109, 108, 86, 84, 65, 63, 58, 51, 49, 47, 43, 41.

Preparation of O,O-*diisopropyl* S-*(3-thienyl) phosphorothioate* **15a**

To a solution of 3-bromothiophene (1.47 g, 9 mmol) in dry ether (10 mL) was slowly added, at −70 °C under N_2, *n*-butyllithium (1 mL, 9 M in hexane, 9 mmol). The mixture was stirred for 1 h at −70 °C and sulfur (290 mg, 9 mmol) was added portionwise. Stirring was maintained for 1 h at −70 °C and diisopropyl phosphorochloridate (1.8 g, 9 mmol) was added. The mixture was progressively warmed to room temperature during 16 h, and then poured into a saturated aqueous of NH_4Cl, extracted with methylene chloride, washed with water, dried (Na_2SO_4) and concentrated under reduced pressure. Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 90:10) gave **15a** (950 mg, 38%) as a yellow oil.

^{1}H NMR ($CDCl_3$): 7.18 (d, 1H, $^3J_{HH}$ = 5.0 Hz, C_5H), 7.34 (dd, 1H, $^3J_{HH}$ = 5.0 Hz, $^4J_{HP}$ = 3.1 Hz, C_4H), 7.48–7.50 (m, 1H, C_2H).

^{13}C NMR ($CDCl_3$): 121.6 (d, $^2J_{CP}$ = 7.6 Hz, C_3), 126.2 (s, C_5), 129.2 (d, $^3J_{CP}$ = 7.6 Hz, C_2), 131.7 (d, $^3J_{CP}$ = 3.8 Hz, C_4).

MS *m/z* (%): 281 (M + 1/21), 280 ($M^{\cdot+}$/40), 238, 221, 198, 197, 196 (100), 43.

Synthesis of compounds **1b–9b**, **9c,d**, **1c–3c**, **1h–l**, **1r**, **11b**, **12b**, **13b–e**, **14b–g** *and* **15b–e**

A solution of phosphorothioate (1 mmol) or bisphosphorothioate (0.5 mmol) in dry THF (1 mL) was slowly added, under N_2, at −78 °C, to a solution of LDA (1.2 mmol) prepared from diisopropylamine (180 μL, 1.3 mmol), THF (15 mL) and *n*-butyllithium (800 μL, 1.5 M in hexane, 1.2 mmol). The mixture was allowed to warm to 0 °C for 30 min and stirred again for 30 min at 0 °C. Either the mixture was then added under N_2 to a stirred ice-cold solution of NH_4Cl/HCl in ether, extracted twice with ether, dried (Na_2SO_4) and concentrated under reduced pressure to give the crude thiol, or the halide was slowly added and the mixture was allowed to warm to room temperature for 16 h. The mixture was then poured into a saturated aqueous solution of NH_4Cl, extracted with methylene chloride, washed with water, dried (Na_2SO_4) and concentrated under reduced pressure to give the crude *S*-derivative.

• *Diisopropyl (2-mercaptophenyl)phosphonate* **1b** *(previously described [16])*

Flash chromatography on silica gel (eluent: petroleum ether/ether 60:40) gave **1b** (60–91%) as a green oil.

• *Tetraisopropyl 2,2'-dithiodi(phenylphosphonate)* **1c**

In some cases, we isolated the disulfide **1c** of **1b** as an off-white solid (mp: 128–129 °C).

^{1}H NMR ($CDCl_3$): 7.22–7.29 (m, 2H, C_5H, $C_{5'}$H), 7.38–7.44 (m, 2H, C_4H, $C_{4'}$H), 7.78–7.83 (m, 2H, C_3H, $C_{3'}$H), 7.95 (~ ddd, 2H, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.4 Hz, $^3J_{HP}$ = 14.3 Hz, C_6H, $C_{6'}$H).

^{31}P NMR ($CDCl_3$): +13.8 (s).

^{13}C NMR ($CDCl_3$): 125.8 (d, $^3J_{CP}$ = 14.0 Hz, C_5, $C_{5'}$), 126.5 (d, $^3J_{CP}$ = 12.5 Hz, C_3, $C_{3'}$), 127.8 (d, $^1J_{CP}$ = 189.3 Hz, C_1, $C_{1'}$), 132.7 (d, $^4J_{CP}$ = 2.4 Hz, C_4, $C_{4'}$), 134.6 (d, $^2J_{CP}$ = 8.9 Hz, C_6, $C_{6'}$), 140.7 (d, $^2J_{CP}$ = 7.7 Hz, C_2, $C_{2'}$).

MS *m/z* (%): 548 (M + 2/5), 547 (M + 1/12), 546 ($M^{\cdot+}$/17), 275, 274, 273, 233, 232, 231, 191, 190, 189 (100), 188, 173, 172, 171, 155, 97, 65, 63, 43, 42, 41.

Anal calc for $C_{24}H_{36}O_6P_2S_2$: S, 11.73. Found: S, 11.56.

• *Diisopropyl [(2-methylthio)phenyl]phosphonate* **1h**

Flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate 80:20) gave **1h** (82%) as a yellow oil.

^{1}H NMR ($CDCl_3$): 2.50 (s, 3H, SCH_3), 7.18 (~ td, 1H, $^3J_{HH}$ = 7.6 Hz, $^4J_{HP}$ = 3.3 Hz , C_5H), 7.26–7.49 (m, 2H, C_3H, C_4H) , 7.96 (ddd, 1H, $^3J_{HH}$ = 7.6 Hz, $^4J_{HH}$ = 1.5 Hz, $^3J_{HP}$ = 14.5 Hz, C_6H).

^{13}C NMR ($CDCl_3$): 16.2 (s, SCH_3), 123.9 (d, $^3J_{CP}$ = 14.3 Hz, C_5), 125.7 (d, $^3J_{CP}$ = 12.6 Hz, C_3), 127.5 (d, $^1J_{CP}$ = 188.0 Hz, C_1), 132.3 (d, $^4J_{CP}$ = 2.7 Hz, C_4), 134.9 (d, $^2J_{CP}$ = 9.4 Hz, C_6), 143.3 (d, $^2J_{CP}$ = 8.0 Hz, C_2).

MS *m/z* (%): 289 (M + 1/21), 288 ($M^{\cdot+}$/24), 246, 205, 204, 203, 171, 155, 125, 124, 123, 99 (100), 77, 43, 41.

Anal calc for $C_{13}H_{21}O_3PS$: S, 11.12. Found: S, 10.78.

• *Diisopropyl [(2-allylthio)phenyl]phosphonate* **1i**

Flash chromatography on silica gel (eluent: ether) gave **1i** (78%) as a pale yellow oil.

^{1}H NMR ($CDCl_3$): 3.65 (dd, 2H, $^3J_{HH}$ = 6.7 Hz, $^4J_{HH}$ = 1.0 Hz, SCH_2), 5.11 (~ d, 1H, $^3J_{HH}$ (*cis*) = 10.0 Hz, CH_2=CH), 5.23 (~ d, 1H, $^3J_{HH}$ (*trans*) = 17.0 Hz, CH_2=CH), 5.82–5.98 (m, 1H, CH_2=CH), 7.18–7.25 (m, 1H, C_5H), 7.35–7.46 (m, 2H, C_3H, C_4H), 7.98 (dd, 1H, $^3J_{HH}$ = 7.6 Hz, $^3J_{HP}$ = 14.4 Hz, C_6H).

^{13}C NMR ($CDCl_3$): 36.8 (s, SCH_2), 118.1 (s, CH_2=CH), 124.9 (d, $^3J_{CP}$ = 14.2 Hz, C_5), 129.0 (d, $^3J_{CP}$ = 12.8 Hz, C_3), 129.4 (d, $^1J_{CP}$ = 188.6 Hz, C_1), 132.1 (d, $^4J_{CP}$ = 2.7 Hz, C_4), 133.1 (s, CH_2=CH), 134.9 (d, $^2J_{CP}$ = 9.2 Hz, C_6), 140.8 (d, $^2J_{CP}$ = 8.2 Hz, C_2).

MS m/z (%): 315 (M + 1/16), 314 ($M^{\cdot+}$/34), 273, 272, 230, 229, 197, 190, 189, 173, 172, 171, 156, 155, 97, 65, 63, 43, 42, 41 (100).

• *Diisopropyl[(2-acetylthio)phenyl]phosphonate* **1j**

Flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate 80:20) gave **1j** (67%) as a pale yellow oil.

^{1}H NMR ($CDCl_3$): 2.44 (s, 3H, C(O)CH_3), 7.46–7.61 (m, 3H, C_3H, C_4H, C_5H), 8.11 (dd, 1H, $^3J_{HH}$ ~ 7.1 Hz, $^3J_{HP}$ = 14.6 Hz, C_6H).

^{13}C NMR ($CDCl_3$): 30.4 (s, C(O)CH_3), 129.1 (d, $^3J_{CP}$ = 14.3 Hz, C_5), 130.7 (d, $^1J_{CP}$ = 190.1 Hz, C_1), 131.2 (d, $^2J_{CP}$ = 6.4 Hz, C_2), 132.5 (d, $^4J_{CP}$ = 2.7 Hz, C_4), 135.2 (d, $^2J_{CP}$ = 9.1 Hz, C_6), 138.1 (d, $^3J_{CP}$ = 12.3 Hz, C_3), 193.1 (s, C(O)).

MS m/z (%): 317 (M + 1/1), 316 ($M^{\cdot+}$/8), 274, 273, 232, 231, 190, 189, 172, 171, 109, 108, 86, 84, 65, 63, 43 (100), 41.

Anal calc for $C_{14}H_{21}O_4PS$: S, 10.14, Found: S, 10.16.

• *Diisopropyl[(2-undecylthio)phenyl]phosphonate* **1k**

Flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate 80:20) gave **1k** (43%) as a yellow oil.

^{1}H NMR ($CDCl_3$): 0.88 (~ t, 3H, $^3J_{HH}$ ~ 6.4 Hz, CH_2CH_3), 1.26 (~ s, 16H, CH_2), 1.70 (~ quintet, 2H, $^3J_{HH}$ ~ 7.4 Hz, SCH_2CH_2), 2.97 (t, 2H, $^3J_{HH}$ = 7.4 Hz, SCH_2), 7.15–7.22 (m, 1H, C_5H), 7.32–7.45 (m, 2H, C_3H, C_4H) 7.97 (dd, 1H, $^3J_{HH}$ = 7.6 Hz, $^3J_{HP}$ = 14.4 Hz, C_6H).

^{13}C NMR ($CDCl_3$): 14.1 (s, CH_2CH_3), 22.7 (s, CH_2CH_3), 28.7–29.6 (m, CH_2), 31.9 (s, SCH_2CH_2), 33.3 (s, SCH_2), 124.2 (d, $^3J_{CP}$ = 14.3 Hz, C_5), 127.5 (d, $^3J_{CP}$ = 13.3 Hz, C_3), 128.5 (d, $^1J_{CP}$ = 188.4 Hz, C_1), 132.2 (d, $^4J_{CP}$ = 2.8 Hz, C_4), 135.0 (d, $^2J_{CP}$ = 9.4 Hz, C_6), 142.3 (d, $^2J_{CP}$ = 8.1 Hz, C_2).

MS m/z (%): 429 (M + 1/2), 428 ($M^{\cdot+}$/6), 274, 250, 240, 232, 191, 190, 172, 166, 124, 114 (100), 43.

• *Diisopropyl [2-(3-picolylthio)phenyl]phosphonate* **1l**

The 3-(chloromethyl)pyridinium chloride was neutralized by one equivalent of triethylamine.

Flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate 50:50) gave **1l** (72%) as an orange oil.

^{1}H NMR ($CDCl_3$): 4.20 (s, 2H, SCH_2), 7.20–7.41 (m, 4H, C_3H, C_4H, C_5H, $C_{5'}$H), 7.69 (~ *d*, 1H, $^3J_{HH}$ = 7.8 Hz, $C_{4'}$H), 7.96 (dd, 1H, $^3J_{HH}$ = 7.6 Hz, $^3J_{HP}$ = 14.2 Hz, C_6H), 8.48 (~ d, 1H, $^3J_{HH}$ = 3.7 Hz, $C_{6'}$H), 8.54 (s, 1H, $C_{2'}$H).

^{13}C NMR ($CDCl_3$): 36.4 (s, SCH_2), 126.1 (d, $^3J_{CP}$ = 14.2 Hz, C_5), 130.7 (d, $^3J_{CP}$ = 13.1 Hz, C_3), 132.0 (d, $^1J_{CP}$ ~ 188 Hz, C_1), 132.3 (d, $^4J_{CP}$ = 2.8 Hz, C_4), 135.0 (d, $^2J_{CP}$ = 9.0 Hz, C_6), 139.5 (d, $^2J_{CP}$ ~ 8 Hz, C_2), 123.5, 136.6, 148.7, 150.3 (4s, Cpyr).

MS m/z (%) : 366 (M + 1/21), 365 ($M^{\cdot+}$/65), 323, 281, 280, 200, 189, 173, 172, 155, 109, 108, 92, 86, 84, 65, 63, 51, 49 (100), 47, 43, 41.

• *Tetraisopropyl (2-methylthio-1,3-phenylene)-diphosphonate* **1r**

Flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate 50:50) gave **1r** (65%) as a pale yellow oil.

^{1}H NMR ($CDCl_3$): 2.60 (s, 3H, SCH_3), 7.49 (tt, 1H, $^3J_{HH}$ = 7.7 Hz, $^4J_{HP}$ = 3.6 Hz, C_5H), 8.18 (~ dd, 2H, $^3J_{HH}$ = 7.7 Hz, $^3J_{HP}$ = 14.7 Hz, C_4H, C_6H).

^{31}P NMR ($CDCl_3$): +12.8 (s).

^{13}C NMR ($CDCl_3$): 24.3 (s, SCH_3), 128.0 (t, $^3J_{CP}$ = 14.0 Hz, C_5), 137.9–138.2 (m, C_4, C_6), 139.1 (dd, $^1J_{CP}$ = 195.2 Hz, $^3J_{CP}$ = 12.0 Hz, C_1, C_3), 143.4 (t, $^2J_{CP}$ = 9.6 Hz, C_2).

Anal calc for $C_{19}H_{34}O_6P_2S$: S, 7.09. Found: S, 7.21.

• *Diethyl (2-mercaptophenyl)phosphonate* **2b** *(previously described [16])*

This compound was prepared following the same conditions except that LTMP (1.2 mmol) prepared from 2,2,6,6-tetramethylpiperidine (250 µL, 1.5 mmol), THF (15 mL) and *n*-butyllithium (800 µL, 1.5 M in hexane, 1.2 mmol) was used instead of LDA. Flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate 80:20) gave **2b** (21%) as a blue oil.

• *Tetraethyl 2,2'-dithiodi(phenylphosphonate)* **2c**

Compound **2c** (21%) was isolated as an off-white solid (mp: 73–74 °C) during the purification of **2b**.

^{1}H NMR ($CDCl_3$): 7.24–7.31 (m, 2H, C_5H, $C_{5'}$H), 7.41–7.48 (m, 2H, C_4H, $C_{4'}$H), 7.80–7.86 (m, 2H, C_3H, $C_{3'}$H), 7.92 (~ ddd, 2H, $^3J_{HH}$ = 7.5 Hz, $^4J_{HH}$ = 1.4 Hz, $^3J_{HP}$ = 14.2 Hz, C_6H, $C_{6'}$H).

^{31}P NMR ($CDCl_3$): +16.2 (s).

^{13}C NMR ($CDCl_3$): 126.0 (d, $^3J_{CP}$ = 14.0 Hz, C_5, $C_{5'}$), 126.4 (d, $^1J_{CP}$ = 188.2 Hz, C_1, $C_{1'}$), 126.9 (d, $^3J_{CP}$ = 12.0 Hz, C_3, $C_{3'}$), 133.0 (d, $^4J_{CP}$ = 2.5 Hz, C_4, $C_{4'}$), 134.6 (d, $^2J_{CP}$ = 8.9 Hz, C_6, $C_{6'}$). 140.9 (d, $^2J_{CP}$ = 7.7 Hz, C_2, $C_{2'}$).

MS m/z (%): 492 (M + 2/10), 491 (M + 1/25), 490 ($M^{\cdot+}$/37), 247, 246, 245 (100), 219, 218, 217, 216, 191, 190, 189, 188, 173, 172, 171, 155, 97, 81, 79, 65, 63.

Anal calc for $C_{20}H_{28}O_6P_2S_2$: S, 13.07. Found: S, 13.26.

• O,S-*Diphenyl (2-hydroxyphenyl)phosphonothioate* **3b**

Flash chromatography on silica gel (eluent: petroleum/ether 80:20) gave **3b** (50%) as a pale yellow oil.

^{1}H NMR ($CDCl_3$): 6.78–7.45 (m, 13H, Ar), 7.55 (ddd, 1H, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.6 Hz, $^3J_{HP}$ = 16.1 Hz, C_6H).

^{31}P NMR ($CDCl_3$): +48.3 (s).

• S-*Phenyl di(2-hydroxyphenyl)phosphinothioate* **3c**

Compound **3c** (14%) was isolated as a pale yellow oil during the purification of **3b**.

^{1}H NMR ($CDCl_3$): 6.81–7.00 (m, 4H, Ar), 7.20–7.46 (m, 7H, Ar), 7.58 (ddd, 2H, $^3J_{HH}$ = 7.8 Hz, $^4J_{HH}$ = 1.6 Hz, $^3J_{HP}$ = 14.7 Hz, C_6H, $C_{6'}$H).

^{31}P NMR ($CDCl_3$): +62.6 (s).

MS m/z (%): 343 (M + 1/26), 342 ($M^{\cdot+}$/98), 233, 187, 169, 168 (100), 139, 65.

• *Diisopropyl (5-chloro-2-mercaptophenyl)-phosphonate* **4b**

Flash chromatography on silica gel (eluent: petroleum ether/ether 80:20) gave **4b** (68%) as a green oil.

^{1}H NMR (CCl_4): 6.28 (s, 1H, SH), 7.07–7.34 (m, 2H, C_3H, C_4H), 7.60 (~ *d*, 1H, $^3J_{HP}$ ~ 14 Hz, C_6H).

^{13}C NMR ($CDCl_3$): 128.8 (d, $^1J_{CP}$ = 187.3 Hz, C_1), 130.2–132.1 (m, C_3, C_5), 131.2 (d, $^4J_{CP}$ = 3.7 Hz, C_4), 134.1 (d, $^2J_{CP}$ = 9.1 Hz, C_6), 136.4 (d, $^2J_{CP}$ = 7.3 Hz, C_2).

MS m/z (%): 309 (M + 1/2), 308 ($M^{\cdot+}$/5), 267, 266, 226, 225, 224, 208, 207, 206, 189, 97, 81, 79, 65, 63, 43 (100).

Anal calc for $C_{12}H_{18}ClO_3PS$: S, 10.38, Found: S, 10.45.

• *Diisopropyl (2-mercapto-5-methylphenyl)-phosphonate* **5b**

Flash chromatography on silica gel (eluent: petroleum ether/ether 80:20) gave **5b** (56%) as a green oil.

IR (film NaCl): 2 595, 2 440 υSH.

^{1}H NMR ($CDCl_3$): 2.32 (s, 3H, $ArCH_3$), 5.20 (s, 1H, SH), 7.13–7.27 (m, 2H, C_3H, C_4H), 7.70 (d, 1H, $^3J_{HP}$ = 14.5 Hz, C_6H).

^{13}C NMR ($CDCl_3$): 20.8 (s, $ArCH_3$), 126.4 (d, $^1J_{CP}$ = 188.1 Hz, C_1), 130.5 (d, $^3J_{CP}$ = 14.0 Hz, C_3), 133.2 (d, $^4J_{CP}$ = 3.6 Hz, C_4), 133.9 (d, $^2J_{CP}$ = 8.9 Hz, C_2), 134.4 (d, $^3J_{CP}$ = 13.1 Hz, C_5), 135.4 (d, $^2J_{CP}$ = 8.9 Hz, C_6).

MS *m/z* (%): 289 (M + 1/4), 288 ($M^{\cdot+}$/14), 247, 246, 205, 204, 187, 186, 185 (100), 122, 121, 78, 77, 63, 43, 41.

Anal calc for $C_{13}H_{21}O_3PS$: C, 54.22; H, 7.45; O, 16.67; S, 11.12. Found : C, 53.88; H, 7.31; O, 16.78; S, 11.03.

• *Diisopropyl (2-mercapto-5-*tert*-butylphenyl)-phosphonate* **6b**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 90:10) gave **6b** (61%) as a green oil.

IR (film NaCl): 2 555, 2 420 υSH.

^{1}H NMR ($CDCl_3$): 1.30 (s, 9H, $C(CH_3)_3$), 5.35 (s, 1H, SH), 7.22–7.38 (m, 2H, C_3H, C_4H), 7.86 (dd, 1H, $^4J_{HH}$ = 2.3 Hz, $^3J_{HP}$ = 15.2 Hz, C_6H).

^{13}C NMR ($CDCl_3$): 31.2 (s, $C(CH_3)_3$), 34.5 (s, $C(CH_3)_3$), 126.2 (d, $^1J_{CP}$ = 188.4 Hz, C_1), 129.6 (d, $^4J_{CP}$ = 3.1 Hz, C_4), 130.4 (d, $^3J_{CP}$ = 14.5 Hz, C_3), 131.6 (d, $^2J_{CP}$ = 9.4 Hz, C_6), 134.2 (d, $^2J_{CP}$ = 8.4 Hz, C_2), 147.7 (d, $^3J_{CP}$ = 13.0 Hz, C_5).

MS *m/z* (%): 331 (M + 1/4), 330 ($M^{\cdot+}$/6), 288, 247, 246 (100), 231, 213, 185, 128, 86, 84, 49, 43, 41.

Anal calc for $C_{16}H_{27}O_3PS$: C, 58.24; H, 8.19; O, 14.55; S, 9.72. Found: C, 57.96; H, 8.23; O, 14.24; S, 9.67.

• *Diisopropyl (5-ethyl-2-mercaptophenyl)-phosphonate* **7b**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 95:5) gave **7b** (72%) as a green oil.

IR (film NaCl): 2 594, 2 486 υSH.

^{1}H NMR ($CDCl_3$): 1.21 (t, 3H, $^3J_{HH}$ = 7.6 Hz, CH_3CH_2), 2.61 (q, 2H, $^3J_{HH}$ = 7.6 Hz, CH_3CH_2), 5.23 (s, 1H, SH), 7.16–7.27 (m 2H, C_3H, C_4H), 7.71 (dd, 1H, $^4J_{HH}$ = 1.9 Hz, $^3J_{HP}$ = 14.6 Hz, C_6H).

^{13}C NMR ($CDCl_3$): 15.4 (s, CH_3CH_2), 28.2 (s, CH_3CH_2), 126.4 (d, $^1J_{CP}$ = 187.6 Hz, C_1), 130.5 (d, $^3J_{CP}$ = 14.0 Hz, C_3), 132.1 (d, $^4J_{CP}$ = 2.9 Hz, C_4), 134.1 (d, $^2J_{CP}$ = 7.6 Hz, C_2), 134.3 (d, $^2J_{CP}$ = 8.8 Hz, C_6), 140.8 (d, $^3J_{CP}$ = 13.5 Hz, C_5).

MS *m/z* (%): 303 (M + 1/1), 302 ($M^{\cdot+}$/3), 260, 219, 218 (100), 200, 185, 84, 83, 82, 67, 55, 49, 43.

• *Diisopropyl (2-mercapto-3-naphthyl)-phosphonate* **8b**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 90:10) gave **8b** (58%) as a green oil.

^{1}H NMR ($CDCl_3$): 5.08 (s, 1H, SH), 7.43–7.87 (m, 5H, C_1H, C_5H, C_6H, C_7H, C_8H), 8.53 (d, 1H, $^3J_{HP}$ = 16.2 Hz, C_4H).

^{13}C NMR ($CDCl_3$): 118.2 (d, $^1J_{CP}$ = 180.6 Hz, C_3), 126.9 (d, $^4J_{CP}$ = 3.8 Hz), 128.8 (d, $^3J_{CP}$ = 12.7 Hz, C_1), 131.3 (d, $^3J_{CP}$ = 11.4 Hz), 134.7 (d, $^2J_{CP}$ = 9.0 Hz, C_2), 144.2 (d, $^2J_{CP}$ = 9.2 Hz, C_4), 125.1, 127.2, 129.1, 132.6 (~ s, C_5, C_6, C_7, C_8).

MS *m/z* (%): 325 (M + 1/1), 324 ($M^{\cdot+}$/3), 250, 222, 166, 124, 86, 84 (100), 82, 67, 55, 49, 43, 41.

Anal calc for $C_{16}H_{21}O_3PS$: S, 9.88. Found: S, 9.89.

• O,O-*Diisopropyl* S-*[2-mercapto-3-(diisopropoxyphosphinyl)phenyl] phosphorothioate* **9b**

Flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate 80:20) gave **9b** (43%) as a yellow oil.

^{1}H NMR ($CDCl_3$): 6.44 (s, 1H, SH), 7.16 (td, 1H, $^3J_{HH}$ = 7.7 Hz, $^4J_{HP}$ = 3.6 Hz, C_5H), 7.83–7.92 (m, 2H, C_4H, C_6H).

^{31}P NMR ($CDCl_3$): +15.2 (s , P-C), +19.0 (s , P-S).

• O,O-*Diisopropyl* S-*[2-methylthio-3-(diisopropoxyphosphinyl)phenyl] phosphorothioate* **9c**

Flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate 80:20) gave **9c** (31%) as a yellow oil.

^{1}H NMR ($CDCl_3$): 2.47 (s, 3H, SCH_3), 7.39 (td, 1H, $^3J_{HH}$ = 7.8 Hz, $^4J_{HP}$ = 4.2 Hz, C_5H), 7.93 (dd, 1H, $^3J_{HH}$ ~ 7.8 Hz, $^3J_{HP}$ ~ 14.0 Hz, C_4H), 8.12 (~ *d*, 1H, $^3J_{HH}$ ~ 8.0 Hz, C_6H).

^{31}P NMR ($CDCl_3$): +13.0 (s, P-C), +19.5 (s , P-S).

• *Diisopropyl [2,3-(dimethylthio)phenyl]-phosphonate* **9d**

9d (53%) was isolated as a yellow oil during the purification of **9c**.

^{1}H NMR ($CDCl_3$): 2.4 (s, 6H, SCH_3), 7.27 (~ d, 1H, $^3J_{HH}$ ~ 8.0 Hz, C_4H), 7.39 (td, 1H, $^3J_{HH}$ = 7.8 Hz, $^4J_{HP}$ = 4.1 Hz, C_5H), 7.77 (ddd, 1H, $^3J_{HH}$ = 7.5 Hz, $^3J_{HP}$ = 13.7 Hz, $^4J_{HH}$ = 1.2 Hz, C_6H).

^{31}P NMR ($CDCl_3$): +13.8 (s).

^{13}C NMR ($CDCl_3$): 15.5 (s, SCH_3), 127.1 (d, $^4J_{CP}$ = 2.8 Hz, C_4), 128.8 (d, $^3J_{CP}$ = 15.3 Hz, C_5), 130.1 (d, $^2J_{CP}$ = 9.0 Hz, C_6), 135.0 (d, $^2J_{CP}$ = 9.1 Hz, C_2), 136.9 (d, $^1J_{CP}$ = 192.1 Hz, C_1), 148.3 (d, $^3J_{CP}$ = 14.3 Hz, C_3).

• *Tetraisopropyl 2,2′-dimercapto-5,5′-oxydi(phenylphosphonate)* **11b**

Flash chromatography on silica gel (eluent: ether) gave **11b** (60%) as a green oil.

IR (film NaCl): 2 480, 2 240 υSH.

^{1}H NMR ($CDCl_3$): 5.32 (s, 2H, SH), 6.93–7.00 and 7.30–7.35 (m, 4H, C_3H, $C_{3'}H$, C_4H, $C_{4'}H$), 7.49 (dd, 2H, $^4J_{HH}$ = 2.8 Hz, $^3J_{HP}$ = 15.1 Hz, C_6H, $C_{6'}H$).

^{31}P NMR ($CDCl_3$): +13.9 (s).

^{13}C NMR ($CDCl_3$): 123.0 (d, $^4J_{CP}$ = 3.0 Hz, C_4, $C_{4'}$), 124.8 (d, $^2J_{CP}$ = 9.4 Hz, C_6, $C_{6'}$), 128.8 (d, $^1J_{CP}$ = 188.9 Hz, C_1, $C_{1'}$), 131.8 (d, $^2J_{CP}$ = 8.0 Hz, C_2, $C_{2'}$), 132.3 (d, $^3J_{CP}$ = 15.7 Hz, C_3, $C_{3'}$), 154.1 (d, $^3J_{CP}$ = 17.8 Hz, C_5, $C_{5'}$).

Anal calc for $C_{24}H_{36}O_7P_2S_2$: C, 51.23; H, 6.45; S, 11.40. Found: C, 51.25; H, 6.51; S, 11.40.

• *Tetraisopropyl 2,2′-dimercapto-5,5′-thiodi(phenylphosphonate)* **12b**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 60:40) gave **12b** (78%) as a green oil.

IR (film NaCl): 2 592, 2 486 υSH.

^{1}H NMR ($CDCl_3$): 5.60 (s, 2H, SH), 7.23–7.25 (m, 4H, C_3H, $C_{3'}H$, C_4H, $C_{4'}H$), 7.79 (dd, 2H, $^4J_{HH}$ = 1.0 Hz, $^3J_{HP}$ = 14.3 Hz, C_6H, $C_{6'}H$).

^{31}P NMR ($CDCl_3$): +14.0 (s).

^{13}C NMR ($CDCl_3$): 127.8 (d, $^1J_{CP}$ = 188.1 Hz, C_1, $C_{1'}$), 131.2 (d, $^3J_{CP}$ = 14.0 Hz, C_3, $C_{3'}$), 131.7 (d, $^3J_{CP}$ = 15.3 Hz, C_5, $C_{5'}$), 134.6 (d, $^4J_{CP}$ = 2.8 Hz, C_4, $C_{4'}$), 136.8 (d, $^2J_{CP}$ = 9.2 Hz, C_6, $C_{6'}$), 137.6 (d, $^2J_{CP}$ = 8.9 Hz, C_2, $C_{2'}$).

MS m/z (%): 579 (M + 1/13), 578 ($M^{\cdot+}$/39), 536, 494, 452, 412, 411, 410 (100), 374, 330, 250, 205, 203, 43, 41.

• *Diisopropyl (1,2-dihydro-2-thioxo-3-pyridyl)-phosphonate* **13b**

Flash chromatography on silica gel (eluent: ethyl acetate) gave a mixture of **13b/13c**. The thione **13b** (71–75%) was separated as a yellow solid (mp: 164 °C) from the corresponding disulfide **13c** by diluting the mixture in water, filtration and concentration of the aqueous solution.

^{1}H NMR ($CDCl_3$): 6.77 (~ td, 1H, $^3J_{45} \sim {}^3J_{56} \sim 6.6$ Hz, $^4J_{HP} = 3.0$ Hz, C_5H), 7.72 (~ td, 1H, $^4J_{46} \sim {}^5J_{HP} \sim 1.5$ Hz, $^3J_{56} = 6.1$ Hz, C_6H), 8.22 (ddd, 1H, $^3J_{45} = 7.3$ Hz, $^4J_{46} = 1.5$ Hz, $^3J_{HP} = 15.3$ Hz, C_4H).

^{31}P NMR ($CDCl_3$): +10.6 (s).

^{13}C NMR ($CDCl_3$): 112.2 (d, $^3J_{CP} = 13.8$ Hz, C_5), 132.9 (d, $^1J_{CP} = 201.8$ Hz, C_3), 140.7 (s, C_6), 146.3 (d, $^2J_{CP} = 8.2$ Hz, C_4), 178.3 (d, $^2J_{CP} = 17.9$ Hz, C_2).

MS m/z (%): 276 (M + 1/1), 275 ($M^{\cdot+}$/2), 233, 218, 192, 191 (100), 190, 174, 173, 172, 111, 67, 51, 43, 41.

Anal calc for $C_{11}H_{18}NO_3PS$: S, 11.65. Found: S, 11.36.

• *Tetraisopropyl 2,2′-dithio-3,3′-di(pyridyl-phosphonate)* **13c**

Compound **13c** (~ 10%) was isolated as a yellow solid (mp: 124–125 °C) during the purification of **13b**.

^{1}H NMR ($CDCl_3$): 7.11 (ddd, 2H, $^3J_{45} = 7.6$ Hz, $^3J_{56} = 4.7$ Hz, $^4J_{HP} = 2.3$ Hz, C_5H, $C_{5'}H$), 8.17 (ddd, 2H, $^3J_{45} = 7.6$ Hz, $^4J_{46} = 1.8$ Hz, $^3J_{HP} = 14.3$ Hz, C_4H, $C_{4'}H$), 8.40 (~ td, $^4J_{46} \sim {}^5J_{HP} \sim 2.3$ Hz, $^3J_{56} = 4.7$ Hz, C_6H, $C_{6'}H$).

^{31}P NMR ($CDCl_3$): +11.9 (s).

^{13}C NMR ($CDCl_3$): 120.0 (d, $^3J_{CP} = 10.3$ Hz, C_5, $C_{5'}$), 123.9 (d, $^1J_{CP} = 188.4$ Hz, C_3, $C_{3'}$), 142.6 (d, $^2J_{CP} = 8.3$ Hz, C_4, $C_{4'}$), 152.0 (s, C_6, $C_{6'}$), 159.9 (d, $^2J_{CP} = 11.1$ Hz, C_2, $C_{2'}$).

Anal calc for $C_{22}H_{34}N_2O_6P_2S_2$: S, 11.69. Found: S, 11.51.

• *Diisopropyl (2-methylthio-3-pyridyl)-phosphonate* **13d**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 50:50) gave **13d** (100%) as a yellow oil.

^{1}H NMR ($CDCl_3$): 2.58 (s, 3H, SCH_3), 7.05 (ddd, 1H, $^3J_{45} = 7.5$ Hz, $^3J_{56} = 4.9$ Hz, $^4J_{HP} = 2.5$ Hz, C_5H), 8.13 (ddd, 1H, $^3J_{45} = 7.5$ Hz, $^4J_{46} = 1.8$ Hz, $^3J_{HP} = 14.6$ Hz, C_4H), 8.54 (~ td, 1H, $^4J_{46} \sim {}^5J_{HP} \sim 2.4$ Hz, $^3J_{56} = 4.9$ Hz, C_6H).

^{31}P NMR ($CDCl_3$): +12.7 (s).

^{13}C NMR ($CDCl_3$): 13.8 (s, SCH_3), 118.1 (d, $^3J_{CP} = 10.3$ Hz, C_5), 123.4 (d, $^1J_{CP} = 189.4$ Hz, C_3), 142.4 (d, $^2J_{CP} = 7.7$ Hz, C_4), 151.6 (d, $^4J_{CP} = 1.4$ Hz, C_6), 163.0 (d, $^2J_{CP} = 11.4$ Hz, C_2).

MS m/z (%): 289 ($M^{\cdot+}$/1), 246, 205, 204, 188, 187, 186, 174, 173, 170, 124, 65, 63, 43 (100), 41.

• *Diisopropyl (2-undecylthio-3-pyridyl)-phosphonate* **13e**

After the addition of undecyl bromide, the mixture was refluxed in THF for 16 h.

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 80:20) gave **13e** (82%) as a yellow oil.

^{1}H NMR ($CDCl_3$): 0.88 (~ t, 3H, $^3J_{HH} \sim 6.6$ Hz, CH_2CH_3), 1.27 (~ s, 16H, CH_2), 1.70 (~ quint, 2H, $^3J_{HH} \sim 7.3$ Hz, SCH_2CH_2), 3.22 (t, 2H, $^3J_{HH} = 7.3$ Hz, SCH_2), 7.01 (ddd, 1H, $^3J_{45} = 7.4$ Hz, $^3J_{56} = 4.9$ Hz, $^4J_{HP} = 2.5$ Hz, C_5H), 8.12 (ddd, 1H, $^3J_{45} = 7.4$ Hz, $^4J_{46} = 1.9$ Hz, $^3J_{HP} = 14.6$ Hz, C_4H), 8.50 (~ td, 1H, $^4J_{46} \sim {}^5J_{HP} \sim 2.4$ Hz, $^3J_{56} = 4.9$ Hz, C_6H).

^{31}P NMR ($CDCl_3$): +12.6 (s).

^{13}C NMR ($CDCl_3$): 14.2 (s, CH_2CH_3), 22.8 (s, CH_2CH_3), 29.1–29.7 (m, CH_2), 30.5 (s, SCH_2CH_2), 32.0 (s, SCH_2), 118.1 (d, $^3J_{CP} = 10.3$ Hz, C_5), 123.4 (d, $^1J_{CP} = 189.1$ Hz, C_3), 142.7 (d, $^2J_{CP} = 8.0$ Hz, C_4), 151.6 (s, C_6), 163.0 (d, $^2J_{CP} = 10.3$ Hz, C_2).

MS m/z (%): 430 (M + 1/4), 429 ($M^{\cdot+}$/6), 290, 289, 275, 265, 264, 246, 233, 192, 191, 174, 173, 111, 99, 97, 81, 67, 43 (100), 41.

• *Diisopropyl (2-mercapto-3-thienyl)phosphonate* **14b**

Flash chromatography on silica gel (eluent: pentane/ethyl acetate 70:30) gave **14b** (11%) as a green oil.

^{1}H NMR ($CDCl_3$): 3.72 (broad s, 1H, SH), 7.07 (dd ~ t, 1H, $^3J_{HH} \sim {}^4J_{HP} \sim 3.4$ Hz, C_5H), 7.45 (dd, 1H, $^3J_{HH} = 3.5$ Hz, $^3J_{HP} = 8.8$ Hz, C_4H).

Anal calc for $C_{10}H_{17}O_3PS_2$: S, 22.87. Found: S, 22.45.

• *Tetraisopropyl 2,2′-dithio-3,3′-di(thienyl-phosphonate)* **14c**

Compound **14c** (10%) was isolated as an orange oil during the purification of **14b**.

^{1}H NMR ($CDCl_3$): 7.17 (dd ~ t, 2H, $^3J_{HH} \sim {}^4J_{HP} \sim 3.5$ Hz, C_5H, $C_{5'}H$), 7.50 (dd, 2H, $^3J_{HH} = 3.7$ Hz, $^3J_{HP} = 8.6$ Hz, C_4H, $C_{4'}H$).

^{13}C NMR ($CDCl_3$) : 134.9 (d, $^3J_{CP} = 15.5$ Hz, C_5, $C_{5'}$), 136.3 (d, $^2J_{CP} = 10.8$ Hz, C_4, $C_{4'}$), 136.4 (d, $^1J_{CP} = 204.8$ Hz, C_3, $C_{3'}$), 143.8 (d, $^2J_{CP} = 7.0$ Hz, C_2, $C_{2'}$).

• *Diisopropyl (2-methylthio-3-thienyl)-phosphonate* **14d**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 90:10) gave **14d** (36%) as an orange oil.

^{1}H NMR ($CDCl_3$): 2.56 (s, 3H, SCH_3), 6.99 (dd ~ t, 1H, $^3J_{HH} \sim {}^4J_{HP} \sim 3.6$ Hz, C_5H), 7.48 (dd, 1H, $^3J_{HH} = 3.7$ Hz, $^3J_{HP} = 8.6$ Hz, C_4H).

^{13}C NMR ($CDCl_3$): 20.6 (s, SCH_3), 128.7 (d, $^3J_{CP} = 16.4$ Hz, C_5), 130.0 (d, $^1J_{CP} = 209.9$ Hz, C_3), 136.8 (d, $^2J_{CP} = 10.7$ Hz, C_4), 147.4 (d, $^2J_{CP} = 7.6$ Hz, C_2).

MS m/z (%): 295 (M + 1/3), 294 ($M^{\cdot+}$/16), 252, 211, 210 (100), 193, 192, 97, 43, 41.

• *Diisopropyl (2-acetylthio-3-thienyl)-phosphonate* **14e**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 90:10) gave **14e** (19%) as an orange oil.

IR (film NaCl): 1 732 υC=O.

^{1}H NMR ($CDCl_3$): 2.17 (s, 3H, $C(O)CH_3$), 7.16 (dd ~ t, 1H, $^3J_{HH} \sim {}^4J_{HP} \sim 3.5$ Hz, C_5H), 7.59 (dd, 1H, $^3J_{HH} = 3.7$ Hz, $^3J_{HP} = 8.6$ Hz, C_4H).

^{13}C NMR ($CDCl_3$): 27.0 (s, $C(O)CH_3$), 133.6 (d, $^2J_{CP} = 8.7$ Hz, C_2), 135.1 (d, $^3J_{CP} = 16.5$ Hz, C_5), 135.9 (d, $^1J_{CP} = 206.2$ Hz, C_3), 136.2 (d, $^2J_{CP} = 10.3$ Hz, C_4), 192.2 (s, $C(O)CH_3$).

MS m/z (%): 323 (M + 1/1), 322 ($M^{\cdot+}$/2), 280, 238, 197, 196, 195, 114, 97, 84, 83, 82, 67, 43 (100), 41.

• *Diisopropyl (2-benzoylthio-3-thienyl)-phosphonate* **14f**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 50:50) gave **14f** (45%) as an orange oil.

IR (film NaCl): 1 690 υC=O.

^{1}H NMR ($CDCl_3$): 7.27 (dd ~ t, 1H, $^3J_{HH} \sim {}^4J_{HP} \sim 3.5$ Hz, C_5H), 7.48–7.54 (m, 2H, $C_{3'}H$, $C_{5'}H$), 7.61–7.68 (m, 2H, C_4H, $C_{4'}H$), 8.00 (~ d, 2H, $^3J_{HH} \sim 8.2$ Hz, $C_{2'}H$, $C_{6'}H$).

^{13}C NMR ($CDCl_3$): 127.8, 129.1 (2s, $C_{2'}$, $C_{3'}$, $C_{5'}$, $C_{6'}$), 133.1 (d, $^2J_{CP} = 7.6$ Hz, C_2), 134.4 (s, $C_{4'}$), 135.7 (d, $^3J_{CP} = 16.0$ Hz, C_5), 135.7 (s, $C_{1'}$), 135.9 (d, $^1J_{CP} = 206.0$ Hz, C_3), 136.3 (d, $^2J_{CP} = 11.4$ Hz, C_4), 188.3 (s, C(O)Ph).

MS m/z (%): 385 (M + 1/1), 384 ($M^{\cdot+}$/1), 342, 300, 195, 178, 105 (100), 77, 51, 43, 41.

• *Diisopropyl (2-undecylthio-3-thienyl)-phosphonate* **14g**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 80:20) gave **14g** (45%) as an orange oil.

^{1}H NMR ($CDCl_3$): 0.88 (t, 3H, $^3J_{HH} = 6.6$ Hz, CH_2CH_3), 1.26 (~ s, 16H, CH_2), 1.64 (~ quint, 2H, $^3J_{HH} = 7.3$ Hz, SCH_2CH_2), 2.89 (t, 2H, $^3J_{HH} = 7.3$ Hz, SCH_2), 7.04 (dd ~ t, 1H, $^3J_{HH} \sim {}^4J_{HP} \sim 3.6$ Hz, C_5H), 7.47 (dd, 1H, $^3J_{HH} = 3.7$ Hz, $^3J_{HP} = 8.8$ Hz, C_4H).

^{13}C NMR ($CDCl_3$): 14.2 (s, CH_2CH_3), 22.7 (s, CH_2CH_3), 28.6–29.6 (m, CH_2), 32.0 (s, SCH_2CH_2), 38.3 (s, SCH_2), 131.4 (d, $^3J_{CP} = 15.5$ Hz, C_5), 131.4 (d, $^1J_{CP} = 208.5$ Hz, C_3), 136.6 (d, $^2J_{CP} = 11.4$ Hz, C_4), 145.2 (d, $^2J_{CP} = 7.7$ Hz, C_2).

MS m/z (%): 435 (M + 1/11), 434 ($M^{\cdot+}$/44), 350, 270, 197, 196, 195, 149, 141, 116, 115, 99 (100).

Anal calc for $C_{21}H_{39}O_3PS_2$: S, 14.75. Found: S, 14.54.

• *Diisopropyl (3-mercapto-2-thienyl)phosphonate* **15b**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 90:10) gave **15b** (47%) as a green oil.

IR (film NaCl): 2 536, 2 485 υSH.

^{1}H NMR ($CDCl_3$): 5.63 (broad s, 1H, SH), 6.96 (dd, 1H, $^3J_{HH} = 5.0$ Hz, $^4J_{HP} = 3.5$ Hz, C_5H), 7.56 (dd ~ t, 1H, $^3J_{HH} \sim {}^4J_{HP} \sim 5.0$ Hz, C_4H).

^{13}C NMR ($CDCl_3$): 119.1 (d, $^1J_{CP} = 210.9$ Hz, C_2), 130.2 (d, $^3J_{CP} = 16.8$ Hz, C_5), 132.2 (d, $^3J_{CP} = 6.7$ Hz, C_4), 137.8 (d, $^2J_{CP} = 11.5$ Hz, C_3).

MS m/z (%): 281 (M + 1/3), 280 ($M^{\cdot+}$/20), 238, 237, 223, 221, 178, 177, 115, 114, 43, 41.

Anal calc for $C_{10}H_{17}O_3PS_2$: S, 22.87. Found: S, 22.98.

• *Diisopropyl (3-methylthio-2-thienyl)-phosphonate* **15c**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 90:10) gave **15c** (63%) as a yellow oil.

^{1}H NMR ($CDCl_3$): 2.53 (s, 3H, SCH_3), 7.08 (dd, 1H, $^3J_{HH} = 5.0$ Hz, $^4J_{HP} = 3.7$ Hz, C_5H), 7.61 (dd, 1H, $^3J_{HH} = 5.0$ Hz, $^4J_{HP} = 5.5$ Hz, C_4H).

^{13}C NMR ($CDCl_3$): 17.4 (s, SCH_3), 122.0 (d, $^1J_{CP} = 211.3$ Hz, C_2), 128.4 (d, $^3J_{CP} = 16.7$ Hz, C_5), 132.2 (d, $^3J_{CP} = 7.6$ Hz, C_4), 143.3 (d, $^2J_{CP} = 10.2$ Hz, C_3).

MS m/z (%): 295 (M + 1/1), 294 ($M^{\cdot+}$/6), 216, 210, 177, 129, 97, 96, 91, 88, 86, 85, 84, 51, 49 (100), 47, 45, 43, 41.

• *Diisopropyl (3-acetylthio-2-thienyl)-phosphonate* **15d**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 80:20) gave **15d** (42%) as a yellow oil.

IR (film NaCl): 1 703 υC=O.

^{1}H NMR ($CDCl_3$): 2.43 (s, 3H, C(O)CH_3), 7.27 (dd, 1H, $^3J_{HH} = 4.9$ Hz, $^4J_{HP} = 3.4$ Hz, C_5H), 7.68 (dd ~ t, 1H, $^3J_{HH} \sim {}^4J_{HP} \sim 5.2$ Hz, C_4H).

^{13}C NMR ($CDCl_3$): 30.3 (s, C(O)CH_3), 131.2 (d, $^2J_{CP} = 8.9$ Hz, C_3), 132.1 (d, $^3J_{CP} = 7.6$ Hz, C_4), 122.4 (d, $^1J_{CP} = 208.5$ Hz, C_2), 134.7 (d, $^3J_{CP} = 15.3$ Hz, C_5).

MS m/z (%): 323 (M + 1/1), 322 ($M^{\cdot+}$/1), 281, 280, 238, 198, 197, 196 (100), 195, 179, 178, 43, 41.

• *Diisopropyl (3-undecylthio-2-thienyl)-phosphonate* **15e**

Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 80:20) gave **15e** (52%) as a yellow oil.

^{1}H NMR ($CDCl_3$): 0.88 (~ t, 3H, $^3J_{HH} \sim 6.5$ Hz, CH_2CH_3), 1.26 (~ s, 16H, CH_2), 1.61–1.72 (m, 2H, SCH_2CH_2), 2.97 (t, 2H, $^3J_{HH} = 7.4$ Hz, SCH_2), 7.09 (dd ~ t, 1H, $^3J_{HH} \sim {}^4J_{HP} \sim 4.2$ Hz, C_5H), 7.58 (dd ~ t, 1H, $^3J_{HH} \sim {}^4J_{HP} \sim 5.3$ Hz, C_4H).

^{13}C NMR ($CDCl_3$): 14.2 (s, CH_2CH_3), 22.8 (s, CH_2CH_3), 29.1–29.7 (m, CH_2), 32.0 (s, SCH_2CH_2), 34.5 (s, SCH_2), 123.2 (d, $^1J_{CP} = 211.2$ Hz, C_2), 129.3 (d, $^3J_{CP} = 17.0$ Hz, C_5), 132.1 (d, $^3J_{CP} = 8.0$ Hz, C_4), 142.2 (d, $^2J_{CP} = 10.1$ Hz, C_3).

Masse m/z (%): 435 (M + 1/6), 434 ($M^{\cdot+}$/16), 349, 269, 268, 198, 197, 196, 187, 178, 157, 124, 115, 99, 67, 55, 43 (100), 41.

Anal calc for $C_{21}H_{39}O_3PS_2$: S, 14.75. Found: S, 14.85.

Reaction of the phosphorothioate **1a** *with alkyllithium*

To a solution of *n*-butyllithium (450 μL, 2.25 M solution in hexane, 1 mmol) at −78 °C, or methyllithium (720 μL, 1.4 M solution in ether, 1 mmol) at −90 °C in dry THF (10 mL), was added, under N_2, the phosphorothioate **1a** (274 mg, 1 mmol). The mixture was stirred at the same temperature for 10 min, and was allowed to warm to 0 °C for 15 min. The mixture was then poured into a stirred ice-cold solution NH_4Cl, extracted with methylene chloride, washed with water, dried (Na_2SO_4) and concentrated under reduced pressure to give the crude material. Flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate 80:20) gave **1a** (65 mg, 24%), **1d** (100 mg, 45%) and **1f** (50 mg, 26%) as pale yellow oils for the reaction with *n*-butyllithium and **1a** (46 mg, 17%), **1e** (59 mg, 33%) and **1g** (27 mg, 16%) as pale yellow oils for the reaction with methyllithium.

• *Diisopropyl butylphosphonate* **1d**

Previously described [34].

• *Diisopropyl methylphosphonate* **1e**

Previously described [34].

• *Tetraisopropyl 1,1-butylidenediphosphonate* **1f**

^{1}H NMR ($CDCl_3$): 0.92 (t, 3H, $^3J_{HH} = 7.1$ Hz, CH_3CH_2), 1.12–1.96 (m, 5H, $(CH_2)_2CH$).

^{31}P NMR ($CDCl_3$): +22.1 (s).

MS m/z (%): 387 (M + 1/4), 386 ($M^{\cdot+}$/6), 371, 357, 345, 303, 261, 221, 219 (100), 201, 177, 137, 43.

• *Tetraisopropyl methylenediphosphonate* **1g**

Previously described [34].

Preparation of the diisopropyl 2-[(propylcarbamoyl)-thio]phenylphosphonate **1m**

To a solution of the phosphonate **1b** (137 mg, 0.5 mmol) and *n*-propylisocyanate (60 μL, 0.65 mmol) in dry ether (5 mL) at 0 °C was added under N_2, one drop of pyridine. The mixture was refluxed for one week, and was then concentrated under reduced pressure. Compound **1m** (131 mg, 73%) was obtained as a white solid (mp: 103 °C) by crystallization from pentane.

^{1}H NMR ($CDCl_3$): 0.87 (~ t, 3H, $^3J_{HH}$ = 7.4 Hz, CH_3CH_2), 1.42–1.55 (m, 2H , CH_2), 3.23 (~ q, 2H, $^3J_{HH}$ ~ 6.7 Hz, CH_2N), 5.67 (s, 1H, NH), 7.45–7.59 (m, 2H, C_3H, C_4H), 7.70–7.75 (m, 1H, C_5H), 8.08 (dd, 1H, $^3J_{HH}$ = 7.5 Hz, $^3J_{HP}$ = 14.0 Hz, C_6H).

^{31}P NMR ($CDCl_3$): +13.3 (s).

MS m/z (%): 360 ($M^{\cdot+}$ + 1/1), 359 ($M^{\cdot+}$/3), 273, 231, 190, 189, 188, 172, 171, 109, 108, 97, 81, 65, 63, 43 (100), 41.

Anal calc for $C_{16}H_{26}NO_4PS$: C, 53.47; H, 7.29; N, 3.90; O, 17.81; S, 8.92. Found: C, 53.28; H, 7.24; N, 3.90; O, 17.09; S, 9.13.

Synthesis of diphosphonylated polyethylene glycols **1n–o**

To a solution of cesium carbonate (360 mg, 1.1 mmol) in DMF (25 mL) at room temperature was added under N_2, the phosphonate **1b** (549 mg, 2 mmol) and the dichlorinated polyethylene glycol (1 mmol). The mixture was heated at 60 °C for 16 h, concentrated under reduced pressure, diluted with methylene chloride, washed with water, dried (Na_2SO_4) and again concentrated. Flash chromatography on silica gel (eluent: petroleum ether/ethyl acetate 25:75) gave **1n** (551 mg, 83%) or **1o** (616 mg, 87%) as pale yellow oils.

• *Tetraisopropyl 2,2′-(4,7-dioxa-1,10-dithiadecane-1,10-diyl)-di(phenylphosphonate)* **1n**

^{1}H NMR ($CDCl_3$): 3.20 (t, 4H, $^3J_{HH}$ = 7.2 Hz, CH_2S), 3.62 (~ s, 4H, OCH_2CH_2O), 3.71 (t, 4H, $^3J_{HH}$ = 7.1 Hz, SCH_2CH_2), 7.18–7.28 (m, 2H, C_5H, $C_{5'}H$), 7.39–7.47 (m, 4H, C_3H, C_4H, $C_{3'}H$, $C_{4'}H$), 7.96 (~ dd, 2H, $^3J_{HH}$ = 7.4 Hz, $^3J_{HP}$ = 14.6 Hz, C_6H, $C_{6'}H$).

^{31}P NMR ($CDCl_3$): +14.2 (s).

^{13}C NMR ($CDCl_3$): 32.8 (s, CH_2S), 69.8, 70.3 (2s, CH_2O), 125.0 (d, $^3J_{CP}$ = 14.2 Hz, C_5, $C_{5'}$), 128.4 (d, $^3J_{CP}$ = 12.8 Hz, C_3, $C_{3'}$), 129.4 (d, $^1J_{CP}$ = 188.9 Hz, C_1, $C_{1'}$), 132.3 (d, $^4J_{CP}$ = 2.8 Hz, C_4, $C_{4'}$), 134.9 (d, $^2J_{CP}$ = 9.2 Hz, C_6, $C_{6'}$), 140.8 (d, $^2J_{CP}$ = 8.1 Hz, C_2, $C_{2'}$).

MS m/z (%): 664 (M + 2/9), 663 (M + 1/25), 623, 622, 621, 601, 600, 579, 477, 86, 84, 61, 60, 51, 49 (100), 48, 47, 45, 43, 41.

Anal calc for $C_{30}H_{48}O_8P_2S_2$: C, 54.37; H, 7.30; O, 19.31; S, 9.68. Found: C, 54.13; H, 7.70; O, 19.09; S, 9.47.

• *Tetraisopropyl 2,2′-(4,7,10-trioxa-1,13-dithiatridecane-1,13-diyl)-di(phenylphosphonate)* **1o**

^{1}H NMR ($CDCl_3$): 3.20 (t, 4H, $^3J_{HH}$ = 7.2 Hz, CH_2S), 3.63 (~ s, 8H, OCH_2), 3.70 (t, 4H, $^3J_{HH}$ = 7.2 Hz, SCH_2CH_2), 7.18–7.28 (m, 2H, C_5H, $C_{5'}H$), 7.42–7.47 (m, 4H, C_3H, C_4H, $C_{3'}H$, $C_{4'}H$), 7.96 (~ dd, 2H, $^3J_{HH}$ = 7.4 Hz, $^3J_{HP}$ = 14.6 Hz, C_6H, $C_{6'}H$).

^{31}P NMR ($CDCl_3$): +14.1 (s).

^{13}C NMR ($CDCl_3$): 32.8 (s, CH_2S), 69.5, 70.2, 71.0 (3s, CH_2O), 124.7 (d, $^3J_{CP}$ = 14.0 Hz, C_5, $C_{5'}$), 128.3 (d, $^3J_{CP}$ = 12.8 Hz, C_3, $C_{3'}$), 129.2 (d, $^1J_{CP}$ = 188.4 Hz, C_1, $C_{1'}$), 132.1 (d, $^4J_{CP}$ = 2.2 Hz, C_4, $C_{4'}$), 134.6 (d, $^2J_{CP}$ = 9.0 Hz, C_6, $C_{6'}$), 140.8 (d, $^2J_{CP}$ = 8.2 Hz, C_2, $C_{2'}$).

Anal calc for $C_{32}H_{52}O_9P_2S_2$: C, 54.38; H, 7.42; O, 20.37; P, 8.76. Found: C, 54.17; H, 7.43; O, 19.36; S, 8.44.

Synthesis of (alkylthio)pyridylphosphonates **13d–e** *from the thione* **13b**

To a solution of the pyridinethione **13b** (138 mg, 0.5 mmol) in dry THF (10 mL) was added at room temperature the alkyl halide (1 mmol). The mixture was stirred at room temperature for 30 min (with methyl iodide) or was refluxed for 60 h (with undecyl bromide). The solvent was then removed, and methylene chloride and an aqueous solution of sodium bicarbonate were added to the residue. The solution was vigorously stirred, the organic phase was separated, dried (Na_2SO_4) and concentrated under reduced pressure. Flash chromatography on silica gel (eluent: cyclohexane/ethyl acetate 64:40) gave **13d** (120 mg, 83%) or **13e** (119 mg, 56%).

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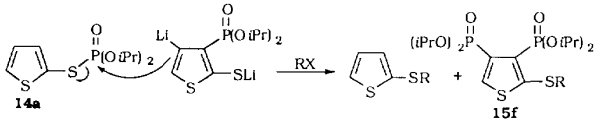
44 For the reaction in which undecyl bromide was used, we could isolate one of the main byproducts. Its ^{1}H and ^{31}P NMR spectra suggest the structure of (2-undecylthio-3,4-thienylene) diphosphonate **15f** (^{31}P NMR ($CDCl_3$): 7.22, 8.42 (2d, $^{3}J_{PP}$ = 4.6 Hz); ^{1}H NMR ($CDCl_3$): 7.71 (dd, H_5, $^{3}J_{HP}$ = 8.6 Hz, $^{4}J_{HP}$ = 4.4 Hz)). The formation of this product can be explained by a second *ortho*-lithiation on the thienyl ring after the rearrangement followed by a nucleophilic attack on the starting *S*-thienylphosphorothioate **14a**.



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