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Efficient Synthesis of New Phosphono-Substituted Dihydrothiopyrans via Hetero Diels–Alder Reaction, under Thermal and High Pressure Conditions

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Abstract—New α-phosphono-β-aryl- or β-heteroaryl-substituted α,β-unsaturated dithioesters **2** were easily prepared from diethyl phosphonodithioacetate **1** and used as thiadienes in thermal or high pressure hetero Diels–Alder cycloadditions with enol and thioenol ethers. The resulting new phosphono 3,4-dihydro 2*H*-thiopyrans **3** were isolated in excellent yields and with a *cis*- or *trans*-diastereoselectivity depending on the conditions of the reaction as well as the structure of the reagents. Some of the thiopyrans **3** were also favourably synthesized via a domino Knoevenagel–hetero Diels–Alder sequence.

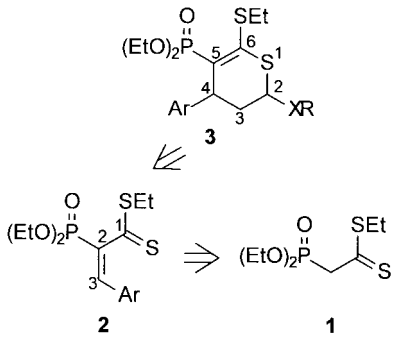
Introduction

In contrast to their carboxylic analogues, which rarely react as dienes in hetero Diels–Alder reactions,[1] α,β-unsaturated carbodithioic acid esters generally show good reactivity as heterodienes in cycloadditions with various dienophiles, under thermal and Lewis acid conditions.[2–5] Moreover, and as previously described by us, the first members of the series readily dimerize at low temperature through a head-to-tail [4+2] cyclocondensation, leading to the corresponding dihydrothiopyrans with high stereoselectivity.[6]

Its efficiency and versatility combined with its regio and stereochemical control render the thia Diels–Alder route an extremely attractive approach to dihydrothiopyrans,[7,8] which are potential precursors of a wide range of thioheterocycles exhibiting a variety of interesting biological properties.[9–14]

To the best of our knowledge, no example of phosphono-substituted dihydrothiopyrans has been reported to date. As an extension to our recent work on the hetero Diels–Alder reaction of α-carbonylated styrylphosphonates,[15] we decided to study a similar synthetic way to new 5-diethylphosphono-6-ethylthio-3,4-dihydro-2*H*-thiopyrans **3** variously substituted at the 2 and 4 positions, as shown in the retrosynthetic Scheme 1. Following this strategy, compounds **3** were obtained by [4+2] cycloadditions of vinyl ethers or thioethers with α,β-unsaturated carbodithioic acid esters **2**, prepared—or in situ generated—by Knoevenagel-type reactions of the readily available triethyl phosphonodithioacetate **1**.[16]

As observed for the phosphono oxadienes,[15] the presence of the electron-withdrawing phosphono group at the carbon 2 of the thiadienes **2** should favour their reactivity with electron-rich dienophiles (inverse-electron-demand)[17] such as enol or thioenol ethers (X=O or S), by lowering the energy



Scheme 1.

Keywords: diastereoselection; hetero Diels–Alder reactions; phosphonates; thiopyrans; domino reactions.

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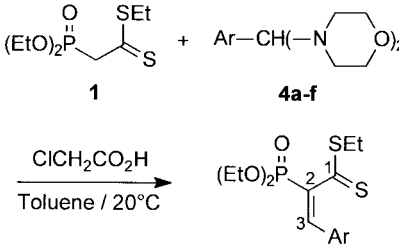


4, 2	Ar
a	Ph
b	4-NO_2-C_6H_4
c	4-CF_3-C_6H_4
d	4-MeO-C_6H_4
e	3-pyridyl
f	4-pyridyl

Scheme 2.

of the LUMO of the diene, which facilitates its overlap with the HOMO of the dienophile.[18]

Results and Discussion

Synthesis of α-phosphono-α,β-unsaturated dithioesters 2

First, we wish to report here the (*E*)-stereoselective synthesis of several new α-diethylphosphonyl-β-aryl- or β-heteroaryl-substituted α,β-unsaturated dithioesters **2** by reacting triethyl phosphonodithioacetate **1**[†] with aromatic or heteroaromatic bis-morpholino aminal derivatives **4**, following the conditions described by Sakoda et al.[21] (Scheme 2 and Table 1). The reaction can be conveniently monitored by ^{31}P NMR spectroscopy.

It is worthy of note that phosphonates **2** could be obtained directly from **1** and the corresponding aldehydes by using the conventional Knoevenagel reaction conditions,[22] but the yield of purified product was often lowered by the presence of impurities such as the corresponding Horner–Wadsworth–Emmons olefination derivatives. Moreover, the aminal method was totally (*E*)-stereoselective, whereas the formation of a few percentage of the (*Z*)-isomer of **2** was occasionally observed using the conventional conditions.

Having a representative range of the new phosphono-substituted α,β-unsaturated carbodithioic acid esters **2** of homogeneous (*E*)-configuration available, we studied their cycloaddition with some electron-rich dienophiles.

[†] Ethyl *O*,*O*-diethylphosphonodithioacetate **1** was synthesized in multigram scale from the commercially available *O*,*O*-diethylcyanomethylphosphonate, by addition of EtSH and dry HCl, followed by sulfhydrolysis of the intermediate thioimidoester hydrochloride, using the procedure developed by Marvel et al.,[19] for the synthesis of aliphatic dithioesters. The physical and analytical data of the prepared compound **1** were in full agreement with an earlier report.[20]

Table 1. Synthesis and ^{31}P NMR data of phosphonates **2**

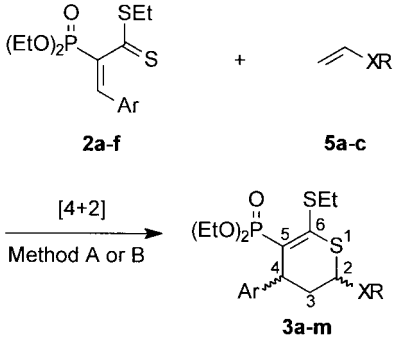
Product[a]	^{31}P ($CDCl_3$) δ (ppm)	Yield (%)[b]
(*E*)-**2a**	13.1	86
(*E*)-**2b**	11.5	88
(*E*)-**2c**	12.1	85
(*E*)-**2d**	13.8	73
(*E*)-**2e**	11.9	89
(*E*)-**2f**	11.4	81

[a] The (*E*)-geometry of the C_2=C_3 double bond in **2** was assigned by $^3J_{PH3}$ (~24 Hz) coupling constant measurements in ^1H NMR spectra[23,24] (see Experimental).

[b] Yield in pure product, isolated in an oily form. Purification by column chromatography over silica gel [eluent: Et_2O/CH_2Cl_2 (95:5), for **2a**, **2b**, **2d**; Et_2O, for **2c**; Et_2O/CH_2Cl_2 (90:10), for **2e**, **2f**]. Purity controlled and structures confirmed by ^1H and ^{13}C NMR spectroscopy. Satisfactory microanalyses were obtained.

Hetero Diels–Alder reaction of phosphonates 2 with enol and thioenol ethers

We have considered the cycloaddition of phosphonates **2a**–**f** with the two vinyl ethers **5a** and **5b**, and that of phosphonate **2b** with the vinyl thioether **5c**. The reactions were performed under different conditions of temperature and pressure, leading to new 5-diethylphosphonyl-3,4-dihydro-2*H*-thiopyrans **3a**–**m** (Scheme 3), isolated as a mixture of *trans*- and *cis*-diastereomers (*t*-**3a**–**m** and *c*-**3a**–**m** in Table 2). The progress of the reaction was monitored by ^{31}P NMR spectroscopy. Generally, the commercially available dienophiles were used in large excess (10 mol equiv.) and thus served as the reaction solvent.



5a X = O, R = Et
b X = O, R = Bu^t
c X = S, R = Et

3a Ar = Ph, X = O, R = Et
b Ar = 4-NO_2-C_6H_4, X = O, R = Et
c Ar = 4-CF_3-C_6H_4, X = O, R = Et
d Ar = 4-MeO-C_6H_4, X = O, R = Et
e Ar = 3-pyridyl, X = O, R = Et
f Ar = 4-pyridyl, X = O, R = Et
g Ar = Ph, X = O, R = Bu^t
h Ar = 4-NO_2-C_6H_4, X = O, R = Bu^t
i Ar = 4-CF_3-C_6H_4, X = O, R = Bu^t
j Ar = 4-MeO-C_6H_4, X = O, R = Bu^t
k Ar = 3-pyridyl, X = O, R = Bu^t
l Ar = 4-pyridyl, X = O, R = Bu^t
m Ar = 4-NO_2-C_6H_4, X = S, R = Et

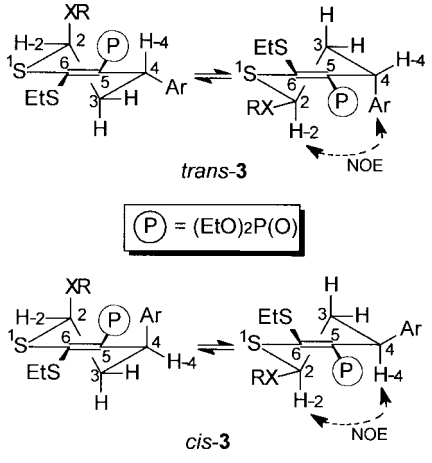
Scheme 3.

Table 2. Conditions, selectivities and yields of the synthesis of cycloadducts **3a–m**

Entry	XR	Ar	Products[a]	Method[b]	Time[c] (*t*/h)	Selectivity[d] *trans*/*cis*	Yield[e] (%)
1	OEt	Ph	*t*-**3a**/*c*-**3a**	A	10	15:85	85
2				B	48	68:32	88
3		4-NO_2-C_6H_4	*t*-**3b**/*c*-**3b**	A	2	15:85	86
4				B	24	64:36	90
5		4-CF_3-C_6H_4	*t*-**3c**/*c*-**3c**	A	3	16:84	87
6				B	60	75:25	87
7		4-MeO-C_6H_4	*t*-**3d**/*c*-**3d**	A	12	16:84	79
8				B	96	60:40	85
9		3-Pyr	*t*-**3e**/*c*-**3e**	A	6	19:81	87
10				B	18	15:85	89
11		4-Pyr	*t*-**3f**/*c*-**3f**	A	2.5	81:19	82
12				B	52	15:85[f]	84
13	OBu^t	Ph	*t*-**3g**/*c*-**3g**	A	24	22:78	79
14				B	72	25:75	84
15		4-NO_2-$C_6H_{ub\ 4}$	*t*-**3h**/*c*-**3h**	A	11	21:79	85
16				B	48	24:76	88
17		4-CF_3-C_6H_4	*t*-**3i**/*c*-**3i**	A	12	32:68	82
18				B	72	39:61	85
19		4-MeO-C_6H_4	*t*-**3j**/*c*-**3j**	A	–[g]	–	–
20				B	192	22:78	76
21		3-Pyr	*t*-**3k**/*c*-**3k**	A	6	31:69	90
22				B	48	16:84	82
23		4-Pyr	*t*-**3l**/*c*-**3l**	A	4	80:20	88
24				B	24	15:85[g]	88
25	SEt	4-NO_2-C_6H_4	*t*-**3m**/*c*-**3m**	A	6	7:93	89
26				B	48	86:14	83

[a] Products isolated as a mixture of *trans*- and *cis*-diastereomers.
[b] A: reaction is sealed tube, at 125°C; B: reaction under 11 kbar, at 20°C.
[c] Time for the complete consumption of phosphonate **2**, monitored by ^{31}P NMR spectroscopy.
[d] Determined on the crude mixture, by ^{31}P and/or ^1H NMR integration measurements.
[e] Yield of purified oily products. Purification by flash chromatography over silica gel [eluent: Et_2O/MeOH (95:5) for **3a–l**; Et_2O/CH_2Cl_2 (70:30) for **3m**]. Purity checked and structures established by ^1H and ^{13}C NMR spectroscopy. Satisfactory microanalyses or HRMS were obtained.
[f] During the work-up, the excess of reagents has to be removed at room temperature in order to avoid the thermal alteration of the diastereomeric ratio of the product.
[g] Incomplete reaction, after 10 days.

In the first set of experiments, we examined the ability of phosphonates **2** to react with ethyl vinyl ether **5a** (entries 1–12, Table 2), either under thermal conditions in a sealed tube at 125°C (method A), or at high pressure (11 kbar) at 20°C (method B). For example, the reaction between the *p*-nitrophenyl-substituted phosphonothiadiene **2b** and an excess of dienophile **5a** reached completion after 2 h following method A, giving quantitatively the crude cycloadduct **3b**, as a mixture of diastereomers *t*-**3b**/*c*-**3b** in the ratio 15:85 (entry 3); this ratio was not altered after purification by flash chromatography over silica gel (eluent: ether/methanol, 95:5), yielding 86% of the purified product.

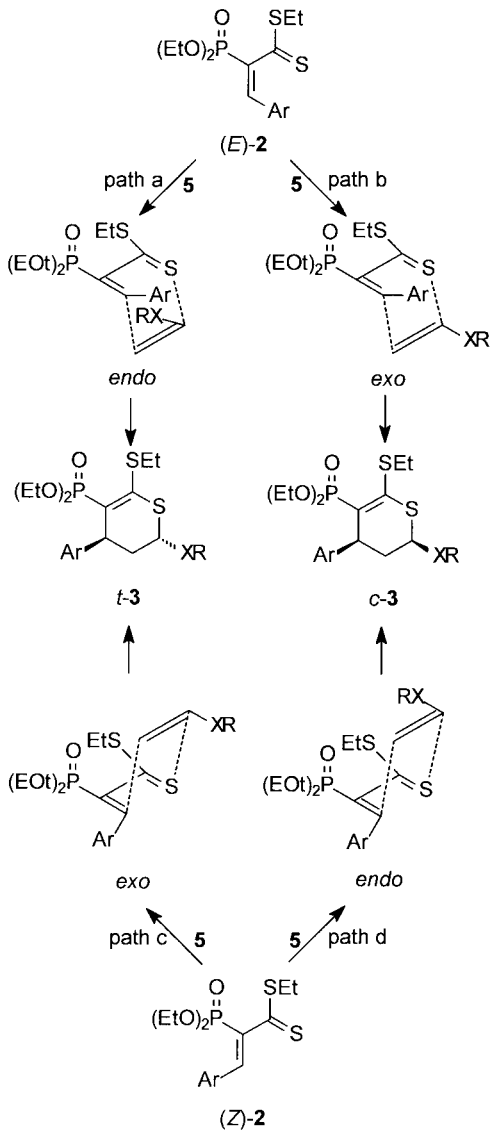


Scheme 4.

The dihydrothiopyran structure of the cycloadduct was unambiguously assigned by ^1H and ^{13}C NMR spectroscopy (see Experimental), and the relative configuration of each diastereomer was deduced from ^1H–^1H NOESY experiments. Thus, in the above example, an NOE effect was observed between the anomeric proton H-2 and proton H-4 for the major component, establishing its *cis*-configuration; conversely, the NOE effect between the proton H-2 and the *ortho*-aromatic protons for the minor component confirmed its relative *trans*-configuration. Moreover, as commonly accepted,[25–27] we assume that each diastereomer adopts a half-chair form in a rapid and equilibrated interconversion (Scheme 4).‡

Then, in order to evaluate the effect of reaction conditions, we exposed the same starting reagent mixture (**2b**+**5a**) to high pressure (method B): the reaction was complete after 24 h at room temperature; more interestingly, the diastereoselectivity was reversed in favour of the *trans*-diastereomer (entry 4).

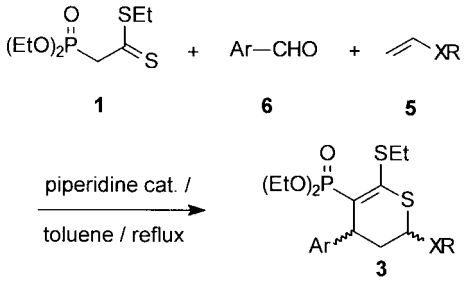
‡ As we observed in the case of phosphonodihydropyrans,[15] we verified here too that the ^{13}C NMR chemical shift of the C-2 anomeric carbon can be used as a criterion for the relative configurational assignment of the phosphonodihydrothiopyrans of type **3**, by using the previously established relationship $\delta_{C\text{-}2}{}^{trans} < \delta_{C\text{-}2}{}^{cis}$ (see Experimental).



Scheme 5.

In order to check the thermal stability of the cycloadducts **3b**, we heated the diastereomeric mixture resulting from the above experiment (entry 4); the corresponding 64:36 *trans*/*cis* ratio remained unchanged after several hours at 125°C. Moreover, having verified beforehand the configurational stability of the starting phosphonates (*E*)**-2** under the same thermal conditions, we could assume that the studied cycloadditions of **2b** with **5a** were kinetically controlled, and that the *trans*-cycloadduct was formed via an *endo*-transition state (path a), whereas the *cis*-isomer resulted from an *exo*-transition state (path b), as represented in Scheme 5.

The preferred *exo*-approach observed for the pair of reagents **2b**/**5a** under thermal conditions is worth underlying. Actually, with the same dienophile and under the same reaction conditions, α-keto-(*E*)-styrylphosphonates generally reacted via a preferred *endo*-transition structure, but with a poor diastereoselectivity;[15] in the system studied here, the weakness of the secondary orbital interactions between the oxygen atom of the dienophile and the weakly polarized C=S double bond[28] of the thiadiene **2a**, possibly



Scheme 6.

renders the congested *endo*-approach less favourable than the *exo*-one. However, as expected and as observed in the case of phosphonooxadienes, the *endo*-approach was preferred anew for the phosphonothiadiene, under high pressure (entry 4), which usually favours the more compact transition state.[29–32]

The other thiabutadienes of the aromatic series (**2a**, **2c** and **2d**) reacted with **5a** to give the expected adducts **3a**, **3c** and **3d** in excellent yields and with a selectivity very similar to that characterizing the pair **2b/5a**, i.e. a *cis*-diastereoselectivity under thermal conditions, and a *trans* one at high pressure. Only the reaction time varied significantly with the nature of the substituent on the aromatic ring. As expected for such an inverse-electron-demand cycloaddition reaction, an electron-withdrawing substituent as NO_2 or CF_3 increases the rate of the reaction (compare entry 1 with entry 3 or 5), whereas an electron-donating group as MeO slowed the reaction down (entries 7 and 8). We verified here too the thermal stability of the related cycloadducts.

More contrasted results were obtained with the pyridyl-substituted dienes **2e–f**, which showed a good reactivity with **5a** (entries 9–12), leading to the corresponding adducts **3e–f**, but with an unexpected selectivity. Thus, under thermal conditions, whereas the *cis*-isomer of the 3-pyridyl-substituted adduct **3e** (entry 9) predominated as for the above aromatic series, the 4-pyridyl-substituted **3f** was formed with a *trans*-diastereoselectivity (entry 11); just as surprising, under high pressure, the predominance of the *cis*-isomers was observed for these two adducts, which were obtained in an identical 15:85 *trans*/*cis* ratio (entries 10 and 12). However, we found that the *trans*/*cis* ratio of the 4-pyridyl adduct obtained at high pressure (entry 12) changed from 15:85 to 80:20, when heated for 3 h at 125°C. This result proves the thermal lability of the cycloadduct **3f** and suggests that the 81:19 *trans*/*cis* ratio observed using method A (entry 11) represents the ratio of the thermodynamical mixture, in which the *trans*-isomer allows the anomeric effect[33] to take place with a minimum of steric hindrance, as shown in the left-side conformation of *trans*-**3** (Scheme 4). The easy isomerization of *c*-**3f** into the more stable *t*-**3f** adduct under thermal conditions seems to be due to a retro Diels–Alder reaction, rather than a base-promoted deprotonation process.[§] Moreover, in order to

[§] The 15:85 *t*-**3f**/*c*-**3f** diastereomeric mixture proved to be unchanged, at room temperature, in the presence of bases as pyridine, 4-picoline, or piperidine. We gratefully acknowledge one of the referees, who suggested to us such an experiment.

explain the unexpected predominance of the *cis*-isomers in the mixtures resulting from the synthesis of cycloadducts **3e** and **3f** at high pressure, we considered a possible isomerization of the corresponding dienes, under the reaction conditions. Actually, whereas the dienes (*E*)-**2a**–**d** of the aromatic series were configurationally stable at 11 kbar and 20°C after 48 h, the pure dienes (*E*)-**2e** and (*E*)-**2f** were transformed, under the same conditions, into a mixture of (*E*)-**2e**/(*Z*)-**2e**[‖] and (*E*)-**2f**/(*Z*)-**2f**,[¶] respectively, in a ratio of ~98:2, measured after pressure release. If we assume that the (*Z*)-isomers of these mixtures, taken to be equilibrated at 11 kbar,[**] reacted more readily, for steric reasons, than their (*E*)-partners, and that the related addition occured via the *endo*-approach (path d, Scheme 5) as usually proposed at high pressure, we could thus explain the *cis*-stereoselectivity of the reactions.

Next, we studied the cycloaddition of dienes **2** with *tert*-butyl vinyl ether **5b** (entries 13–24, Table 2). As expected, the bulky dienophile **5b** reacted generally more slowly than its ethyl analogue **5a** under thermal, as well as high pressure conditions. Moreover, for the aromatic series (entries 13–20) the *cis*-adducts predominated under thermal conditions, probably owing to the steric hindrance of the Bu^t group, which favours the *exo*-approach (path b, Scheme 5).[34] This same argument probably accounts for the *exo*-approach preference under 11 kbar, and the *trans*/*cis* ratios very similar to the ones recorded under thermal conditions. In the heteroaromatic series at last (entries 21–24), the *cis*-isomer of the 3-pyridyl-substituted adduct **3k** predominated under conditions A or B (entries 21 and 22), as in the above aromatic series, but for the entry 22, the *cis*-isomer could result also from the *endo*-cycloaddition (path d, Scheme 5) of the (*Z*)-**2e** diene formed in situ under high pressure, as established above. The 4-pyridyl-substituted diene **2f** reacted rapidly and completely with **5b** to give the expected cycloadduct **3l**, but with a *trans*-diastereoselectivity under thermal conditions and with a *cis*-one at 11 kbar. Moreover, when the *t*-**3l**/*c*-**3l** mixture obtained under high pressure (entry 24) was heated for 4 h at 125°C, its diastereomeric ratio changed from 15:85 into 80:20, which likely represents the thermodynamical *trans*/*cis* ratio for this adduct, as it was discussed above for **3f**. Consequently, we assume that the preferred transition state for the cycloaddition of (*E*)-**2f** with the bulky dienophile **5b** was still the *exo*-one, using method A or B. However, the predominant *cis*-isomer formed in the first case likely isomerized under the thermal conditions into the more stable *t*-**3l** isomer. Such an isomerization did not occur at high pressure and 20°C, but in this case, the *c*-**3l** isomer might result too from the *endo*-addition of the diene (*Z*)-**2f** formed in situ.

Finally, we tested the behaviour of the dienophile **5c** in its reaction with the diene **2b**. A very good reactivity and an excellent *cis*-diastereoselectivity were observed for this pair of reagents under thermal conditions (entry 25), giving access to a new interesting 3,4-dihydro-2*H*-thiopyran **3m** bearing the ethylthio substituent at the position 2.[††] As expected, under 11 kbar, the selectivity was reversed in favour of the *trans*-isomer (entry 26). Having verified the stability of the 86:14 *t*-**3m**/*c*-**3m** mixture obtained at high pressure, when heated for 6 h at 125°C, we concluded that the remarkable *cis*-diastereoselectivity observed under thermal conditions resulted from an *exo*-approach of the two reagents, which preferred an *endo*-one at high pressure, as usually accepted.

One-pot synthesis of phosphonodihydrothiopyrans 3 from 1, through a domino Knoevenagel–hetero Diels–Alder sequence

As firstly introduced by Tietze et al.,[36] the synthesis of some dihydropyrans can be performed by a three-component reaction protocol, leading to the expected cycloadduct through the so called domino Knoevenagel–hetero Diels–Alder reaction, by using an activated methylene compound, an aldehyde and an electron-rich alkene as reagents.[37] Recently, this procedure allowed us to improve significantly the yield of the synthesis of phosphonodihydropyrans.[15] To the best of our knowledge, such a sequence has not been previously employed in thia Diels–Alder syntheses,[7] and therefore we decided to use it for a one-pot synthesis of phosphonodihydrothiopyrans **3** from phosphonodithioacetate **1**, as represented in Scheme 6.

A toluene solution of the phosphonate **1**, of the suitable aldehyde **6** and dienophile **5** was introduced into a reactor equipped with a Dean–Stark separator, then a few drops of piperidine were added and the mixture was refluxed, while the progress of the reaction was monitored by ^{31}P NMR spectroscopy. The procedure has been exploited for the synthesis of the cycloadducts **3b**, **3c**, **3e**, **3f** and **3m** and the results are reported in the Table 3.

The yields of isolated cycloadducts **3** synthesized by the domino-sequences were excellent and higher than the overall yields calculated for the corresponding sequences in two separated reactions. As expected, the selectivities observed by using this one-pot protocol were very similar to that reported for the corresponding separate cycloadditions, carried out under thermal conditions (method A, Table 2). Moreover, the excellent *cis*-diastereoselectivity (de=88%) obtained for the synthesis of the cycloadduct **3m** deserves to be underlined (entry 5).

Conclusion

In this work, we studied a thia-hetero Diels–Alder approach to new 5-diethylphosphono-6-ethylthio-3,4-dihydro-2*H*-thiopyrans **3**, variously substituted at 2 and 4 positions. Efficient and diastereoselective syntheses of the cycloadducts **3** were achieved starting from the readily available

‖ In ^{31}P NMR spectroscopy, the signal of the (*Z*)-isomer of **2e** was observed at 10 ppm.

¶ In ^{31}P NMR spectroscopy, the signal of the (*Z*)-isomer of **2f** was observed at 9.4 ppm.

** The (*Z*)-isomers of the pyridyl-substituted dienes **2e** and **2f** might be formed by the decomposition of a transient ionic dimer resulting from the Michael self-condensation of the corresponding (*E*)-isomers, the overall process being equilibrated under 11 kbar. Such unusual high-pressure-promoted Michael/retro-Michael isomerizations are currently being studied in our laboratory; results will be published in due course.

†† In carbohydrate chemistry, such alkylthio substituent have been favourably used in glycosylation reactions.[35]

Table 3. Synthesis of cycloadducts **3b**, **3c**, **3e**, **3f** and **3m** by domino Knoevenagel–hetero Diels–Alder reaction

Entry	Products[a]	Time[b] (*t*/h)	Selectivity[c] *trans*/*cis*	Yield (%)[d] (Calcd Yield)[e]
1	***t*-3b**/***c*-3b**	48	14:86	89 (74.8)
2	***t*-3c**/***c*-3c**	120	15:85	81 (73.9)
3	***t*-3e**/***c*-3e**	48	17:83	89 (77.4)
4	***t*-3f**/***c*-3f**	48	81:19	86 (66.4)
5	***t*-3m**/***c*-3m**	120	6:94	87 (78.3)

[a] Products isolated as a mixture of *trans*- and *cis*-diastereomers.
[b] Time for the complete consumption of phosphonate **1**, monitored by ^{31}P NMR spectroscopy.
[c] Determined on the crude mixture, by ^{31}P and/or ^{1}H NMR integration measurements.
[d] Yield of purified oily products. Purification by flash chromatography over silica gel [eluent: Et_2O/MeOH (95:5) for **3b**, **3c**, **3e**, **3f**; Et_2O/CH_2Cl_2 (70:30) for **3m**]. Purity checked and structures established by ^{1}H and ^{13}C NMR spectroscopy. Satisfactory microanalyses or HRMS were obtained.
[e] Calculated overall yield for the sequence in two separate reactions.

diethyl phosphonodithioacetate **1**, either in two separate reactions via the new α-phosphono-α,β-unsaturated carbodithioesters **2**, or in a sole reactor, by a domino Knoevenagel–hetero Diels–Alder reaction sequence.

Experimental

General

Solvents and reagents were purchased from common commercial suppliers and purified by conventional methods prior to use. High-pressure cycloaddition reactions were performed in a Unipress piston-cylinder apparatus for pressures up to 14 kbar. TLC was performed on Merck 60F-254 silica gel plates and column chromatography over silica gel SI 60 (230–400 mesh). Gas-liquid chromatography (GLC) was performed on a Varian 3300 chromatograph with a 15 m Megabore OV 101 column. Elemental microanalyses were carried out on a Carlo Erba EA 1110 analyser. HRMS measurements were performed under electronic impact at 70 eV on a JEOL AX 500 spectrometer. NMR spectra were recorded on a Bruker DPX-300 spectrometer operating at 300 MHz for proton, 75.4 MHz for carbon, and 121.5 MHz for phosphorus; chemical shift (δ) are expressed in ppm relative to TMS for ^{1}H and ^{13}C nuclei and to H_3PO_4 for ^{31}P nucleus; coupling constants (J) are given in Hz; coupling multiplicities are reported using conventional abbreviations.

General procedure for the synthesis of phosphonodithioesters 2

To a solution of phosphonate **1** (10 mmol) and chloroacetic acid (1.85 g, 20 mmol) in toluene (15 cm^3) was added the appropriate bis(morpholino) aminal **4**[‡‡] (10 mmol). The mixture was stirred under nitrogen atmosphere at 20°C for 48 h, the reaction being monitored by ^{31}P NMR spectroscopy. The reaction mixture was then hydrolysed by water (20 cm^3) and the residue obtained after the usual work-up was purified as indicated in Table 1, leading to pure thiadiene **2**, isolated as a deep orange liquid.

Ethyl (*E*)-2-diethoxyphosphoryl-3-phenylpropendithioate (*E*)-2a. δ_P 13.10; δ_H 1.17–1.34 (9H, m, CH_3CH_2S and CH_3CH_2OP), 3.23 (2H, q, J=7.4 Hz, CH_3CH_2S), 4.10 (4H, qui, J=7.2 Hz, CH_3CH_2OP), 7.42 (1H, d, J=23.8 Hz, *H*-C3), 7.18–7.30 and 7.44–7.51 (5H, 2m, $H_{arom.}$); δ_C 11.52 (s, CH_3CH_2S), 15.95 (d, J=7.1 Hz, CH_3CH_2OP), 30.60 (s, CH_3CH_2S), 62.79 (d, J=5.1 Hz, CH_3CH_2OP), 128.20, 129.80 and 130.10 (3s, *o*-, *m*-, *p*-$C_{arom.}$), 133.10 (d, J=20.1 Hz, *i*-$C_{arom.}$), 137.30 (d, J=177.3 Hz, C_2), 142.45 (d, J=8.7 Hz, C_3), 227.50 (d, J=9.4 Hz, C=S); Anal. Calcd for $C_{15}H_{21}O_3PS_2$: C, 52.31; H, 6.15; S 18.62. Found: C, 51.92; H, 5.98; S 18.42.

Ethyl (*E*)-2-diethoxyphosphoryl-3-(4-nitrophenyl)propendithioate (*E*)-2b. δ_P 11.50; δ_H 1.22–1.38 (9H, m, CH_3CH_2S and CH_3CH_2OP), 3.20 (2H, q, J=7.4 Hz, CH_3CH_2S), 4.12 (4H, qui, J=7.2 Hz, CH_3CH_2OP), 7.50 (1H, d, J=23.5 Hz, *H*-C3), 7.60 and 8.10 (4H, 2d, J=8.8 Hz, $H_{arom.}$); δ_C 11.65 (s, CH_3CH_2S), 16.10 (d, J=6.9 Hz, CH_3CH_2OP), 30.87 (s, CH_3CH_2S), 63.30 (d, J=5.4 Hz, CH_3CH_2OP), 123.56 and 130.50 (2s, *o*-, *m*-$C_{arom.}$), 139.43 (d, J=8.9 Hz, C_3), 139.72 (d, J=20.4 Hz, *i*-$C_{arom.}$), 141.70 (d, J=175.2 Hz, C_2), 147.88 (s, *p*-$C_{arom.}$), 225.96 (d, J=9.5 Hz, C=S); Anal. Calcd for $C_{15}H_{20}NO_5PS_2$: C, 46.26; H, 5.18; N, 3.60; S 16.47. Found: C, 46.27; H, 5.11; N, 3.65; S 16.28.

Ethyl (*E*)-2-diethoxyphosphoryl-3-(4-trifluoromethylphenyl)propendithioate (*E*)-2c. δ_P 12.10; δ_H 1.18–1.35 (9H, m, CH_3CH_2S and CH_3CH_2OP), 3.25 (2H, q, J=7.7 Hz, CH_3CH_2S), 4.10 (4H, qui, J=7.1 Hz, CH_3CH_2OP), 7.44 (1H, d, J=24.5 Hz, *H*-C_3), 7.48 and 7.58 (4H, 2d, J=8.2 Hz, $H_{arom.}$); δ_C 11.62 (s, CH_3CH_2S), 16.00 (d, J=7.1 Hz, CH_3CH_2OP), 30.88 (s, CH_3CH_2S), 63.79 (d, J=5.4 Hz, CH_3CH_2OP), 123.38 (q, J=272.5 Hz, F_3CAr), 125.10 (q, J=3.6 Hz, *m*-$C_{arom.}$), 131.33 (s, *o*-$C_{arom.}$), 131.80 (q, J=32.7 Hz, CCF_3), 136.68 (d, J=20.3 Hz, *i*-$C_{arom.}$), 139.93 (d, J=177.3 Hz, C_2), 140.50 (d, J=9.4 Hz, C_3), 226.26 (d, J=9.4 Hz, C=S); Anal. Calcd for $C_{16}H_{20}F_3O_3PS_2$: C, 46.60; H, 4.89, S, 15.55. Found: C, 46.72; H, 5.02; S 15.14.

Ethyl (*E*)-2-diethoxyphosphoryl-3-(4-methyoxyphenyl)-propendithioate (*E*)-2d. δ_P 13.80; δ_H 1.22–1.30 (9H, m, CH_3CH_2S and CH_3CH_2OP), 3.25 (2H, q, J=7.4 Hz, CH_3CH_2S), 3.78 (s, CH_3O-Ar), 4.10 (4H, qui, J=7.1 Hz, CH_3CH_2OP), 6.76 (2H, d J=8.8 Hz, $H_{arom.}$), 7.32 (1H, d, J=24.1 Hz, *H*-C_3), 7.42 (2H, d, J=8.8 Hz, $H_{arom.}$); δ_C 11.66 (s, CH_3CH_2S), 16.07 (d, J=7.2 Hz, CH_3CH_2OP), 30.78 (s, CH_3CH_2S), 55.20 (s, CH_3O-Ar), 62.70 (d,

[‡‡] The required aminals were prepared from the corresponding aldehyde according to Ref. 21.

J=5.1 Hz, CH_3CH_2OP), 113.84 and 132.34 (2s, *o*-, *m*-$C_{arom.}$), 125.86 (d, J=20.5 Hz, *i*-$C_{arom.}$), 134.55 (d, J=178.9 Hz, C_2), 142.33 (d, J=8.9 Hz, C_3), 160.92 (s, *p*-$C_{arom.}$), 228.60 (d, J=9.8 Hz, C=S); Anal. Calcd for $C_{16}H_{23}O_4PS_2$: C, 51.32; H, 6.19; S, 17.12. Found: C, 51.03; H, 6.28; S, 17.18.

Ethyl (*E*)-2-diethoxyphosphoryl-3-(3-pyridyl)propendithioate (*E*)-2e. δ_P 11.90; δ_H 1.20–1.32 (9H, m, CH_3CH_2S and CH_3CH_2OP), 3.23 (2H, q, J=7.2 Hz, CH_3CH_2S), 4.03–4.20 (4H, m, CH_3CH_2OP), 7.17 (1H, dd, J=4.9, 8.3 Hz, $H_{arom.}$), 7.35 (1H, d, J=23.7 Hz, *H*-C_3), 7.75 (1H, d, J=8.3 Hz, $H_{arom.}$), 8.46 (1H, d, J=4.9 Hz, $H_{arom.}$), 8.64 (1H, bs, $H_{arom.}$); δ_C 11.59 (s, CH_3CH_2S), 16.02 (d, J=6.9 Hz, CH_3CH_2OP), 29.90 (s, CH_3CH_2S), 63.00 (d, J=5.2 Hz, CH_3CH_2OP), 123.03 135.68, 150.21 and 150.88 (4s, *o*-, *m*-, *p*-$C_{arom.}$), 129.39 (d, J=20.2 Hz, *i*-$C_{arom.}$), 138.61 (d, J=9.1 Hz, C_3), 140.27 (d, J=176.5 Hz, C_2), 226.25 (d, J=9.2 Hz, C=S); Anal. Calcd for $C_{14}H_{20}NO_3PS_2$: C, 48.68; H, 5.84; N, 4.06; S, 18.56. Found: C, 48.54; H, 5.98; N, 4.46; S, 18.06.

Ethyl (*E*)-2-diethoxyphosphoryl-3-(4-pyridyl)propendithioate (*E*)-2f. δ_P 11.40; δ_H 1.20–1.32 (9H, m, CH_3CH_2S and CH_3CH_2OP), 3.20 (2H, q, J=7.4 Hz, CH_3CH_2S), 4.15 (4H, qui, J=7.2 Hz, CH_3CH_2OP), 7.30 (2H, d, J=6.1 Hz, $H_{arom.}$), 7.34 (1H, d, J=23.1 Hz, *H*-C_3), 8.33 (2H, d, J=5.9 Hz, $H_{arom.}$); δ_C 11.45 (s, CH_3CH_2S), 15.96 (d, J=7.0 Hz, CH_3CH_2OP), 30.68 (s, CH_3CH_2S), 63.08 (d, J=6.2 Hz, CH_3CH_2OP), 123.36 and 149.82 (2s, *o*-, *m*-$C_{arom.}$), 139.02 (d, J=8.7 Hz, C_3), 140.70 (d, J=20.2 Hz, *i*-$C_{arom.}$), 142.54 (d, J=174.9 Hz, C_2), 225.38 (d, J=8.8 Hz, C=S); Anal. Calcd for $C_{14}H_{20}NO_3PS_2$: C, 48.68; H, 5.84; N, 4.06; S, 18.56. Found: C, 48.30; H, 5.87; N, 4.25; S, 18.19.

General procedure for the synthesis of phosphonothiopyrans 3 in a sealed tube (method A)

A solution of thiadiene **2** (2 mmol) in an excess of dienophile **5** (10 equiv.) was placed in a sealed tube and heated at 125°C for a time indicated in Table 2, the reaction being monitored by ^{31}P NMR spectroscopy. The excess of dienophile was then evaporated under reduced pressure and the residue was purified as indicated in Table 2 to give the pure cycloadduct **3**, isolated as a mixture of diastereomers, which were not separated.

General procedure for the synthesis of phosphonothiopyrans 3 by the pressure-promoted hetero Diels–Alder reaction (method B)

A solution of thiadiene **2** (2 mmol) in an excess of dienophile **5** (10 equiv.) was introduced in a pressure vessel, then put in the high-pressure apparatus, and left under 11 kbar at 20°C and for a time indicated in Table 2. Then, after release of pressure, further work-up and purification were carried out as above, leading to the pure product **3**, isolated as a viscous liquid.

5-Diethoxyphosphoryl-3,4-dihydro-2-ethoxy-6-ethylthio-4-phenyl-2*H*-thiopyran 3a. HRMS required for $C_{19}H_{29}O_4PS_2$ (M): 416.1244. Found: M^+: 416.1244.

***t*-3a**—δ_P 16.60; δ_H 1.00 (3H, t, J=7.1 Hz, CH_3CH_2S), 1.02–1.36 (9H, m, CH_3CH_2O and CH_3CH_2OP), 2.00–2.20 and 2.25–2.35 (2H, m, *H*-C_3), 2.95–3.10 (2H, m, CH_3CH_2S), 3.25–3.68 and 3.75–3.90 (6H, 2m, CH_3CH_2O and CH_3CH_2OP), 4.10–4.25 (1H, m, *H*-C_4), 4.64 (1H, dd, J=3.6, 10.1 Hz, *H*-C_2), 7.05–7.30 (5H, m, $H_{arom.}$); δ_C 14.60 (s, CH_3CH_2S), 14.97 (s, CH_3CH_2O), 16.00–16.17 (m, CH_3CH_2OP), 28.85 (s, CH_3CH_2S), 37.42 (d, J=8.1 Hz, C_3), 43.44 (d, J=10.4 Hz, C_4), 61.55 and 61.90 (2d, J=6.0, 5.8 Hz, CH_3CH_2OP), 65.35 (s, CH_3CH_2O), 80.33 (s, C_2), 124.00 (d, J=189.0 Hz, C_5), 126.60, 127.90 and 128.40 (3s, *o*-, *m*-, *p*-$C_{arom.}$), 142.10 (d, J=1.3 Hz, *i*-$C_{arom.}$), 147.09 (d, J=12.3 Hz, C_6).

***c*-3a**—δ_P 16.30; δ_H 0.75 (3H, t, J=7.0 Hz, CH_3CH_2S), 1.06–1.36 (9H, m, CH_3CH_2O and CH_3CH_2OP), 2.10–2.20 and 2.47–2.57 (2H, m, *H*-C_3), 2.95–3.10 (2H, m, CH_3CH_2S), 3.25–3.68 and 3.75–3.90 (6H, 2m, CH_3CH_2O and CH_3CH_2OP), 4.10–4.25 (1H, m, *H*-C_4), 4.85 (1H, bs, *H*-C_2), 7.05–7.30 (5H, m, $H_{arom.}$); δ_C 14.34 (s, CH_3CH_2S), 14.54 (s, CH_3CH_2O), 16.00–16.17 (m, CH_3CH_2OP), 29.13 (s, CH_3CH_2S), 36.45 (d, J=8.4 Hz, C_3), 42.10 (d, J=9.6 Hz, C_4), 61.52 and 61.95 (2d, J=6.0, 5.7 Hz, CH_3CH_2OP), 64.62 (s, CH_3CH_2O), 81.46 (s, C_2), 126.46 (d, J=192.1 Hz, C_5), 125.80, 127.45 and 128.42 (3s, *o*-, *m*-, *p*-$C_{arom.}$), 142.73 (s, *i*-$C_{arom.}$), 145.07 (d, J=11.3 Hz, C_6).

5-Diethoxyphosphoryl-3,4-dihydro-2-ethoxy-6-ethylthio-4-(4-nitrophenyl)-2*H*-thiopyran 3b. Anal. Calcd for $C_{19}H_{28}NO_6PS_2$: C, 49.45; H, 6.11; N, 3.03; S, 13.89. Found: C, 49.21; H, 6.12; N, 3.01; S, 13.76.

***t*-3b**—δ_P 16.10; δ_H 1.00–1.40 (12H, m, CH_3CH_2S, CH_3CH_2O and CH_3CH_2OP), 2.21–2.30 (2H, m, *H*-C_3), 2.90–3.15 (2H, m, CH_3CH_2S), 3.20–4.00 (6H, 2m, CH_3CH_2O and CH_3CH_2OP), 4.20–4.35 (1H, m, *H*-C_4), 4.63 (1H, dd, J=4.6, 8.0 Hz, *H*-C_2), 7.25 and 8.10 (4H, 2d, J=8.2 Hz, $H_{arom.}$); δ_C 14.55 (s, CH_3CH_2S), 14.85 (s, CH_3CH_2O), 15.60–15.70 (m, CH_3CH_2OP), 28.62 (s, CH_3CH_2S), 37.81 (d, J=7.7 Hz, C_3), 43.02 (d, J=10.3 Hz, C_4), 61.50–62.00 (m, CH_3CH_2OP), 65.41 (s, CH_3CH_2O), 79.86 (s, C_2), 122.50 (d, J=189.3 Hz, C_5), 123.65 and 128.58 (2s, *o*-, *m*-$C_{arom.}$), 146.57 (s, *i*-$C_{arom.}$), 148.26 (d, J=11.8 Hz, C_6), 150.65 (s, *p*-$C_{arom.}$).

***c*-3b**—δ_P 15.70; δ_H 0.70 (3H, t, J=7.0 Hz, CH_3CH_2S), 1.00–1.40 (9H, m, CH_3CH_2O and CH_3CH_2OP), 2.16–2.20 and 2.50–2.63 (2H, 2m, *H*-C_3), 2.90–3.15 (2H, m, CH_3CH_2S), 3.20–4.00 (6H, 2m, CH_3CH_2O and CH_3CH_2OP), 4.20–4.35 (1H, m, *H*-C_4), 4.85 (1H, bs, *H*-C_2), 7.23 and 7.90 (4H, 2d, J=8.6 Hz, $H_{arom.}$); δ_C 14.25 (s, CH_3CH_2S), 14.55 (s, CH_3CH_2O), 15.60–15.7 (m, CH_3CH_2OP), 28.96 (s, CH_3CH_2S), 35.37 (d, J=7.9 Hz, C_3), 41.27 (d, J=9.5 Hz, C_4), 61.50–62.00 (m, CH_3CH_2OP), 64.65 (s, CH_3CH_2O), 80.86 (s, C_2), 122.57 and 129.22 (2s, *o*-, *m*-$C_{arom.}$), 124.36 (d, J=190.6 Hz, C_5), 146.00 (s, *i*-$C_{arom.}$), 146.50 (d, J=11.0 Hz, C_6), 151.29 (s, *p*-$C_{arom.}$).

5-Diethoxyphosphoryl-3,4-dihydro-2-ethoxy-6-ethylthio-4-(4-trifluoromethylphenyl)-2*H*-thiopyran 3c. Anal. Calcd for $C_{20}H_{28}F_3O_4PS_2$: C, 49.58; H, 5.82; S, 13.23. Found: C, 49.89; H, 5.84; S, 13.42.

***t*-3c**—δ_P 16.30; δ_H 0.75 (3H, t, J=7.0 Hz, CH_3CH$_2$S), 1.02–1.18 (6H, m, CH_3CH$_2$O and CH_3CH$_2$OP), 1.32 (3H, t, J=7.3 Hz, CH_3CH$_2$OP), 2.18–2.34 (2H, m, H-C$_3$), 2.90–3.10 (2H, m, CH$_3$CH_2S), 3.40–3.95 (6H, 2m, CH$_3$CH_2O and CH$_3$CH_2OP), 4.20–4.30 (1H, m, H-C$_4$), 4.65 (1H, dd, J=3.8, 9.4 Hz, H-C$_2$), 7.18 and 7.50 (4H, 2d, J=7.8 Hz, $H_{arom.}$); δ_C 14.60 (s, CH$_3$CH$_2$S), 15.10 (s, CH$_3$CH$_2$O), 16.01–16.21 (m, CH$_3$CH$_2$OP), 28.80 (s, CH$_3$$CH_2$S), 37.62 (d, J=8.0 Hz, C$_3$), 43.18 (d, J=10.3 Hz, C$_4$), 61.60–62.00 (m, CH$_3$$CH_2$OP), 65.48 (s, CH$_3$$CH_2$O), 80.13 (s, C$_2$), 123.10 (d, J=189.4 Hz, C$_5$), 124.10 (q, J=271.8 Hz, F$_3$$C$Ar), 125.50 (q, J=4.0 Hz, m-C$_{arom.}$), 127.80 (s, o-C$_{arom.}$), 128.80 (q, J=32.5 Hz, CCF$_3$), 146.70 (s, i-C$_{arom.}$), 147.92 (d, J=12.0 Hz, C$_6$).

***c*-3c**—δ_P 15.90; δ_H 0.70 (3H, t, J=7.0 Hz, CH_3CH$_2$S), 1.02–1.18 (6H, m, CH_3CH$_2$O and CH_3CH$_2$OP), 1.34 (3H, t, J=7.4 Hz, CH_3CH$_2$OP), 2.15–2.26 and 2.50–2.60 (2H, 2m, H-C$_3$), 2.90–3.10 (2H, m, CH$_3$CH_2S), 3.40–3.95 (6H, 2m, CH$_3$CH_2O and CH$_3$CH_2OP), 4.20–4.30 (1H, m, H-C$_4$), 4.84 (1H, t, J=2.5 Hz, H-C$_2$), 7.28 and 7.40 (4H, 2d, J=8.0 Hz, $H_{arom.}$); δ_C 14.20 (s, CH$_3$CH$_2$S), 14.58 (s, CH$_3$CH$_2$O), 16.01–16.21 (m, CH$_3$CH$_2$OP), 29.12 (s, CH$_3$$CH_2$S), 35.77 (d, J=7.5 Hz, C$_3$), 41.48 (d, J=9.8 Hz, C$_4$), 61.60–62.00 (m, CH$_3$$CH_2$OP), 64.66 (s, CH$_3$$CH_2$O), 81.17 (s, C$_2$), 123.05 (q, J=271.9 Hz, F$_3$$C$Ar), 124.40 (q, J=3.0 Hz, m-C$_{arom.}$), 125.40 (d, J=190.0 Hz, C$_5$), 128.10 (q, J=32.3 Hz, CCF$_3$), 128.30 (s, o-C$_{arom.}$), 146.10 (d, J=10.9 Hz, C$_6$), 147.20 (s, i-C$_{arom.}$).

5-Diethoxyphosphoryl-3,4-dihydro-2-ethoxy-6-ethylthio-4-(4-methoxyphenyl)-2*H*-thiopyran 3d. HRMS required for $C_{20}H_{31}O_5PS_2$ (M): 446.1350. Found: M^+: 446.1348.

***t*-3d**—δ_P 16.70; δ_H 1.00–1.38 (12H, m, CH_3CH$_2$S, CH_3CH$_2$O and CH_3CH$_2$OP), 2.05–2.25 (2H, m, H-C$_3$), 3.00 (2H, q, J=7.1 Hz, CH$_3$CH_2S), 3.05–3.60 (4H, m, CH$_3$CH_2O and CH$_3$CH_2OP), 3.70 (3H, s, CH_3O-Ar), 3.88–3.95 (2H, m, CH$_3$CH_2OP), 4.05–4.20 (1H, m, H-C$_4$), 4.65 (1H, dd, J=3.6, 10.3 Hz, H-C$_2$), 6.75 and 7.05 (4H, 2d, J=8.5 Hz, $H_{arom.}$); δ_C 14.64 (s, CH$_3$CH$_2$S), 15.05 (s, CH$_3$CH$_2$O), 16.10–16.26 (m, CH$_3$CH$_2$OP), 28.90 (s, CH$_3$$CH_2$S), 37.45 (d, J=8.6 Hz, C$_3$), 42.74 (d, J=10.2 Hz, C$_4$), 55.14 (s, CH$_3$O-Ar), 61.50 and 61.60 (2d, J=5.8, 5.6 Hz, CH$_3$$CH_2$OP), 65.41 (s, CH$_3$$CH_2$O), 80.48 (s, C$_2$), 113.80 and 128.71 (2s, o-, m-C$_{arom.}$), 124.54 (d, J=188.3 Hz, C$_5$), 134.06 (d, J=1.7 Hz, i-C$_{arom.}$), 146.53 (d, J=12.7 Hz, C$_6$), 158.26 (s, p-C$_{arom.}$).

***c*-3d**—δ_P 16.40; δ_H 0.80 (3H, t, J=7.0 Hz, CH_3CH$_2$S), 1.00–1.38 (9H, m, CH_3CH$_2$O and CH_3CH$_2$OP), 2.10–2.20 and 2.40–2.50 (2H, 2m, H-C$_3$), 3.00 (2H, q, J=7.1 Hz, CH$_3$CH_2S), 3.05–3.60 (4H, m, CH$_3$CH_2O and CH$_3$CH_2OP), 3.62 (3H, s, CH_3O-Ar), 3.88–3.95 (2H, m, CH$_3$CH_2OP), 4.05–4.20 (1H, m, H-C$_4$), 4.82 (1H, bs, H-C$_2$), 6.62 and 6.97 (4H, 2d, J=8.5 Hz, $H_{arom.}$); δ_C 14.45 (s, CH$_3$CH$_2$S), 14.60 (s, CH$_3$CH$_2$O), 16.10–16.26 (m, CH$_3$CH$_2$OP), 29.17 (s, CH$_3$$CH_2$S), 36.60 (d, J=8.2 Hz, C$_3$), 41.48 (d, J=9.8 Hz, C$_4$), 55.14 (s, CH$_3$O-Ar), 61.40 and 61.80 (2d, J=5.9, 5.8 Hz, CH$_3$$CH_2$OP), 64.70 (s, CH$_3$$CH_2$O), 81.58 (s, C$_2$), 112.89 and 129.51 (2s, o-, m-C$_{arom.}$), 127.04 (d, J=190.1 Hz, C$_5$), 134.88 (s, i-C$_{arom.}$), 144.40 (d, J=11.0 Hz, C$_6$), 157.81 (s, p-C$_{arom.}$).

5-Diethoxyphosphoryl-3,4-dihydro-2-ethoxy-6-ethylthio-4-(3-pyridyl)-2*H*-thiopyran 3e. Anal. Calcd for $C_{18}H_{28}NO_4PS_2$: C, 51.78; H, 6.76; N, 3.35; S, 15.36. Found: C, 51.72; H, 6.64; N, 3.42; S, 15.51.

***t*-3e**—δ_P 16.20; δ_H 0.74 (3H, t, J=6.9 Hz, CH_3CH$_2$S), 1.01–1.20 (6H, m, CH_3CH$_2$O and CH_3CH$_2$OP), 1.28 (3H, t, J=7.2 Hz, CH_3CH$_2$OP), 2.25–2.40 (2H, m, H-C$_3$), 2.90–3.15 (2H, m, CH$_3$CH_2S), 2.30–4.00 (6H, m, CH$_3$CH_2O and CH$_3$CH_2OP), 4.15–4.28 (1H, m, H-C$_4$), 4.65 (1H, dd, J=4.2, 9.4 Hz, H-C$_2$), 7.20 (1H, dd, J=3.0, 7.8 Hz, $H_{arom.}$), 7.42 (1H, d, J=7.2 Hz, $H_{arom.}$), 7.42 (1H, d, J=4.8 Hz, $H_{arom.}$), 8.40 (1H, bs, $H_{arom.}$); δ_C 14.03 (s, CH$_3$CH$_2$S), 14.77 (s, CH$_3$CH$_2$O), 15.90–16.00 (m, CH$_3$CH$_2$OP), 28.36 (s, CH$_3$$CH_2$S), 37.50 (d, J=7.2 Hz, C$_3$), 40.80 (d, J=10.1 Hz, C$_4$), 61.53 and 61.76 (2d, J=6.3, 6.0 Hz, CH$_3$$CH_2$OP), 65.30 (s, CH$_3$$CH_2$O), 79.86 (s, C$_2$), 123.17, 135.00, 147.10 and 149.28 (4s, o-, m-, p-C$_{arom.}$), 124.10 (d, J=190.0 Hz, C$_5$), 138.33 (s, i-C$_{arom.}$), 145.80 (d, J=11.2 Hz, C$_6$).

***c*-3e**—δ_P 15.80; δ_H 0.74 (3H, t, J=6.9 Hz, CH_3CH$_2$S), 1.01–1.20 (6H, m, CH_3CH$_2$O and CH_3CH$_2$OP), 1.28 (3H, t, J=7.2 Hz, CH_3CH$_2$OP), 1.31 (3H, t, J=7.2 Hz, CH_3CH$_2$OP), 2.21 (1H, ddd, J=2.6, 6.7, 14.3 Hz, H-C$_3$), 2.54 (1H, dq, J=2.6, 14.3 Hz, H-C$_3$), 2.90–3.15 (2H, m, CH$_3$CH_2S), 2.30–4.00 (6H, m, CH$_3$CH_2O and CH$_3$CH_2OP), 4.15–4.28 (1H, m, H-C$_4$), 4.86 (1H, bs, H-C$_2$), 7.05 (1H, dd, J=4.8, 7.5 Hz, $H_{arom.}$), 7.45 (1H, d, J=7.5 Hz, $H_{arom.}$), 8.25 (1H, d, J=4.8 Hz, $H_{arom.}$), 8.40 (1H, bs, $H_{arom.}$); δ_C 14.03 (s, CH$_3$CH$_2$S), 14.42 (s, CH$_3$CH$_2$O), 15.90–16.00 (m, CH$_3$CH$_2$OP), 29.02 (s, CH$_3$$CH_2$S), 35.30 (d, J=7.9 Hz, C$_3$), 39.16 (d, J=9.5 Hz, C$_4$), 61.4 and 61.76 (2d, J=6.3, 6.0 Hz, CH$_3$$CH_2$OP), 65.58 (s, CH$_3$$CH_2$O), 81.05 (s, C$_2$), 122.13, 135.10, 146.77 and 149.76 (4s, o-, m-, p-C$_{arom.}$), 124.83 (d, J=189.9 Hz, C$_5$), 138.33 (s, i-C$_{arom.}$), 145.80 (d, J=11.2 Hz, C$_6$).

5-Diethoxyphosphoryl-3,4-dihydro-2-ethoxy-6-ethylthio-4-(4-pyridyl)-2*H*-thiopyran 3f. Anal. Calcd for $C_{18}H_{28}NO_4PS_2$: C, 51.78; H, 6.76; N, 3.35; S, 15.36. Found: C, 52.02; H, 6.82; N, 3.14; S, 15.02.

***t*-3f**–δ_P 16.00; δ_H 0.72 (3H, t, J=7.2 Hz, CH_3CH$_2$S), 1.08 (3H, t, J=7.0 Hz, CH_3CH$_2$O), 1.15 and 1.32 (6H, 2t, J=7.4, 7.1 Hz, CH_3CH$_2$OP), 2.28–2.35 (2H, m, H-C$_3$), 2.90–3.10 and 3.30–3.97 (6H, m, CH$_3$CH_2S and CH$_3$CH_2OP), 4.12–4.26 (1H, m, H-C$_4$), 4.62 (1H, dd, J=3.9, 9.2 Hz, H-C$_2$), 7.12 and 8.36 (4H, 2d, J=6.0 Hz, $H_{arom.}$); δ_C 14.53 (s, CH$_3$CH$_2$S), 14.59 (s, CH$_3$CH$_2$O), 16.06–16.14 (m, CH$_3$CH$_2$OP), 28.73 (s, CH$_3$$CH_2$S), 37.20 (d, J=7.8 Hz, C$_3$), 42.70 (d, J=10.1 Hz, C$_4$), 61.67 and 61.75 (2d, J=5.8 Hz, CH$_3$$CH_2$OP), 65.46 (s, CH$_3$$CH_2$O), 80.01 (s, C$_2$), 122.32 (d, J=190.2 Hz, C$_5$), 123.00 and 149.82 (2s, o-, m-C$_{arom.}$), 146.54 (d, J=10.9 Hz, C$_6$), 151.80 (d, J=1.7 Hz, i-C$_{arom.}$).

***c*-3f**—δ_P 15.60; δ_H 0.72 (3H, t, J=7.2 Hz, CH_3CH$_2$S), 1.05 (3H, t, J=7.1 Hz, CH_3CH$_2$O), 1.14 and 1.34 (6H, 2t, J=7.2 Hz, CH_3CH$_2$OP), 2.20 (1H, ddd, J=3.0, 6.0, 14.2 Hz, H-C$_3$), 2.57 (1H, dq, J=3.0, 14.2 Hz, H-C$_3$), 2.90–3.10 and 3.30–3.97 (6H, m, CH$_3$CH_2S and CH$_3$CH_2OP), 4.12–4.26 (1H, m, H-C$_4$), 4.85 (1H, bs,

H-C_2), 7.08 and 8.48 (4H, 2d, J=5.8 Hz, $H_{arom.}$); δ_C 14.01 (s, CH_3CH_2S), 14.43 (s, CH_3CH_2O), 16.06–16.14 (m, CH_3CH_2OP), 29.58 (s, CH_3CH_2S), 35.03 (d, J=7.8 Hz, C_3), 40.85 (d, J=9.2 Hz, C_4), 61.65 and 61.98 (2d, J=6.9, 6.6 Hz, CH_3CH_2OP), 64.67 (s, CH_3CH_2O), 80.87 (s, C_2), 124.24 (d, J=190.8 Hz, C_5), 123.89 and 148.46 (2s, *o*-, *m*-$C_{arom.}$), 146.32 (d, J=10.8 Hz, C_6), 153.0 (bs, *i*-$C_{arom.}$).

2-*tert*-Butoxy-5-diethoxyphosphonyl-3,4-dihydro-6-ethylthio-4-phenyl-2*H*-thiopyran 3g. HRMS required for $C_{21}H_{33}O_4PS_2$ (M): 444.1557. Found: M^+: 444.1557.

***t*-3g**—δ_P 17.00; δ_H 1.00 [9H, s, $C(CH_3)_3$], 1.05–1.32 (9H, m, CH_3CH_2S and CH_3CH_2OP), 2.10–2.40 (2H, m, *H*-C_3), 2.95–3.10 (2H, m, CH_3CH_2S), 3.70–3.95 (4H, m, CH_3CH_2OP), 4.10–4.25 (1H, m, *H*-C_4), 4.74 (1H, dd, J=3.8, 10.8 Hz, *H*-C_2), 7.05–7.20 (5H, 2d, J=8.6 Hz, $H_{arom.}$); δ_C 14.97 (s, CH_3CH_2S), 16.00–16.18 (m, CH_3CH_2OP), 27.90 [s, $C(CH_3)_3$], 28.63 (s, CH_3CH_2S), 38.09 (d, J=7.8 Hz, C_3), 43.81 (d, J=10.5 Hz, C_4), 61.71–61.90 (m, CH_3CH_2OP), 73.30 (s, C_2), 75.61 [s, $C(CH_3)_3$], 120.35 (d, J=189.9 Hz, C_5), 126.70, 128.05 and 128.53 (3s, *o*-, *m*-, *p*-$C_{arom.}$), 142.20 (s, *i*-$C_{arom.}$), 148.40 (d, J=12.0 Hz, C_6).

***c*-3g**—δ_P 16.80; δ_H 0.95 [9H, s, $C(CH_3)_3$], 1.05–1.32 (9H, m, CH_3CH_2S and CH_3CH_2OP), 2.10–2.40 (2H, m, *H*-C_3), 2.95–3.10 (2H, m, CH_3CH_2S), 3.70–3.95 (4H, m, CH_3CH_2OP), 4.10–4.25 (1H, m, *H*-C_4), 5.03 (1H, bs, *H*-C_2), 7.05–7.20 (5H, 2d, J=8.6 Hz, $H_{arom.}$); δ_C 14.88 (s, CH_3CH_2S), 16.00–16.18 (m, CH_3CH_2OP), 27.78 [s, $C(CH_3)_3$], 29.05 (s, CH_3CH_2S), 38.20 (d, J=7.9 Hz, C_3), 42.10 (d, J=9.6 Hz, C_4), 61.71–60.90 (m, CH_3CH_2OP), 74.41 (s, C_2), 75.40 [s, $C(CH_3)_3$], 123.14 (d, J=190.2 Hz, C_5), 125.93, 127.55 and 128.60 (3s, *o*-, *m*-, *p*-$C_{arom.}$), 142.80 (s, *i*-$C_{arom.}$), 146.50 (d, J=11.0 Hz, C_6).

2-*tert*-Butoxy-5-diethoxyphosphonyl-3,4-dihydro-6-ethylthio-4-(4-nitrophenyl)-2*H*-thiopyran 3h. Anal. Calcd for $C_{21}H_{32}NO_6PS_2$: C, 51.52; H, 6.59; N, 2.86; S, 13.10. Found: C, 51.82; H, 6.89; N, 3.11; S, 12.96.

***t*-3h**—δ_P 16.40; δ_H 1.05 [9H, s, $C(CH_3)_3$], 1.08–1.28 (9H, m, CH_3CH_2S and CH_3CH_2OP), 2.10–2.15 (2H, m, *H*-C_3), 3.00 (2H, q, J=7.6 Hz, CH_3CH_2S), 3.72–3.89 (4H, m, CH_3CH_2OP), 4.28–4.40 (1H, m, *H*-C_4), 4.70 (1H, dd, J=5.4, 9.3 Hz, *H*-C_2), 7.33 and 8.16 (4H, 2d, J=8.6 Hz, $H_{arom.}$); δ_C 14.56 (s, CH_3CH_2S), 16.06–16.19 (m, CH_3CH_2OP), 27.82 [s, $C(CH_3)_3$], 28.54 (s, CH_3CH_2S), 38.50 (d, J=7.9 Hz, C_3), 43.73 (d, J=10.4 Hz, C_4), 61.60–61.92 (m, CH_3CH_2OP), 72.81 (s, C_2), 75.59 [s, $C(CH_3)_3$], 120.55 (d, J=190.7 Hz, C_5), 123.70 and 128.46 (2s, *o*-, *m*-$C_{arom.}$), 146.66 (s, *i*-$C_{arom.}$), 150.19 (d, J=12.1 Hz, C_6), 150.39 (s, *p*-$C_{arom.}$).

***c*-3h**—δ_P 16.10; δ_H 0.90 [9H, s, $C(CH_3)_3$], 1.08–1.22 (9H, m, CH_3CH_2S and CH_3CH_2OP), 1.30 (3H, t, J=7.3 Hz, CH_3CH_2OP), 2.16–2.22 and 2.40–2.51 (2H, 2m, *H*-C_3), 3.00 (2H, q, J=7.6 Hz, CH_3CH_2S), 4.00–3.02 (4H, m, CH_3CH_2OP), 4.28–4.40 (1H, m, *H*-C_4), 5.05 (1H, bs, *H*-C_2), 7.34 and 8.01 (4H, 2d, J=8.6 Hz, $H_{arom.}$); δ_C 14.48 (s, CH_3CH_2S), 16.06–16.19 (m, CH_3CH_2OP), 27.52 [s, $C(CH_3)_3$], 28.95 (s, CH_3CH_2S), 38.50 (d, J=7.9 Hz, C_3), 42.03 (d, J=9.5 Hz, C_4), 61.60–61.92 (m, CH_3CH_2OP), 74.31 (s, C_2), 75.43 [s, $C(CH_3)_3$], 122.64, 129.21 (2s, *o*-, *m*-$C_{arom.}$), 123.40 (d, J=191.1 Hz, C_5), 145.97 (s, *i*-$C_{arom.}$), 147.86 (d, J=10.9 Hz, C_6), 151.67 (s, *p*-$C_{arom.}$).

2-*tert*-Butoxy-5-diethoxyphosphonyl-3,4-dihydro-6-ethylthio-4-(4-trifluoromethylphenyl)-2*H*-thiopyran 3i. HRMS required for $C_{22}H_{32}F_3O_4PS_2$ (M): 512.1431. Found: M^+: 512.1432.

***t*-3i**—δ_P 16.70; δ_H 1.00 [9H, s, $C(CH_3)_3$], 1.07 (3H, t, J=7.0 Hz, CH_3CH_2S), 1.16 and 1.33 (6H, 2t, J=7.0 Hz, CH_3CH_2OP), 2.05–2.20 (2H, m, *H*-C_3), 2.95–3.10 (2H, m, CH_3CH_2S), 3.88 (4H, qui, J=7.0 Hz, CH_3CH_2OP), 4.20–4.32 (1H, m, *H*-C_4), 4.68 (1H, dd, J=4.4, 10.3 Hz, *H*-C_2), 7.27 and 7.55 (4H, 2d, J=7.8 Hz, $H_{arom.}$); δ_C 15.20 (s, CH_3CH_2S), 16.06–16.37 (m, CH_3CH_2OP), 27.90 [s, $C(CH_3)_3$], 31.19 (s, CH_3CH_2S), 38.10 (d, J=7.8 Hz, C_3), 43.85 (d, J=10.6 Hz, C_4), 61.68–61.90 (m, CH_3CH_2OP), 73.06 (s, C_2), 75.70 [s, $C(CH_3)_3$], 121.30 (d, J=190.4 Hz, C_5), 123.56 (q, J=272.2 Hz, F_3CAr), 125.50 (q, J=3.7 Hz, *m*-$C_{arom.}$), 128.10 (s, *o*-$C_{arom.}$), 129.20 (q, J=32.9 Hz, CCF_3), 146.60 (s, *i*-$C_{arom.}$), 149.70 (d, J=12.2 Hz, C_6).

***c*-3i**—δ_P 16.40; δ_H 0.88 [9H, s, $C(CH_3)_3$], 1.05 (3H, t, J=7.0 Hz, CH_3CH_2S), 1.18 and 1.34 (6H, 2t, J=7.0 Hz, CH_3CH_2OP), 2.10–2.08 and 2.20–2.30 (2H, m, *H*-C_3), 2.95–3.10 (2H, m, CH_3CH_2S), 3.65–3.10 (4H, m, CH_3CH_2OP), 4.20–4.32 (1H, m, *H*-C_4), 5.05 (1H, bs, *H*-C_2), 7.40 and 7.48 (4H, 2d, J=8.0 Hz, $H_{arom.}$); δ_C 14.60 (s, CH_3CH_2S), 16.06–16.37 (m, CH_3CH_2OP), 28.91 [s, $C(CH_3)_3$], 30.55 (s, CH_3CH_2S), 39.00 (d, J=8.1 Hz, C_3), 44.00 (d, J=9.7 Hz, C_4), 61.68–61.90 (m, CH_3CH_2OP), 74.70 (s, C_2), 76.40 [s, $C(CH_3)_3$], 122.00 (q, J=272.1 Hz, F_3CAr), 123.40 (d, J=190.9 Hz, C_5), 125.80 (q, J=3.1 Hz, *m*-$C_{arom.}$), 128.80 (s, *o*-$C_{arom.}$), 129.01 (q, J=32.7 Hz, CCF_3), 147.70 (d, J=11.0 Hz, C_6), 147.90 (s, *i*-$C_{arom.}$).

2-*tert*-Butoxy-5-diethoxyphosphonyl-3,4-dihydro-6-ethylthio-4-(4-methoxyphenyl)-2*H*-thiopyran 3j. HRMS required for $C_{22}H_{35}O_5PS_2$ (M): 474.1663. Found: M^+: 474.1668.

***t*-3j**—δ_P 17.00; δ_H 1.00 [9H, s, $C(CH_3)_3$], 1.05–1.32 (9H, m, CH_3CH_2S and CH_3CH_2OP), 2.09–2.35 (2H, m, *H*-C_3), 2.90–3.10 (2H, m, CH_3CH_2S), 3.68 (3H, s, CH_3O-Ar), 3.75–3.90 (4H, m, CH_3CH_2OP), 4.08–4.20 (1H, m, *H*-C_4), 4.74 (1H, dd, J=4.1, 11.0 Hz, *H*-C_2), 6.78 and 7.05 (4H, 2d, J=8.7 Hz, $H_{arom.}$); δ_C 14.99 (s, CH_3CH_2S), 16.02–16.19 (m, CH_3CH_2OP), 27.95 [s, $C(CH_3)_3$], 28.68 (s, CH_3CH_2S), 38.12 (d, J=8.3 Hz, C_3), 43.13 (d, J=10.2 Hz, C_4), 55.28 (s, CH_3O-Ar), 61.56 and 61.70 (2d, J=5.8, 5.7 Hz, CH_3CH_2OP), 74.20 (s, C_2), 75.65 [s, $C(CH_3)_3$], 113.90 and 128.70 (2s, *o*-, *m*-$C_{arom.}$), 120.31 (d, J=189.1 Hz, C_5), 134.20 (s, *i*-$C_{arom.}$), 146.37 (d, J=12.5 Hz, C_6), 158.10 (s, *p*-$C_{arom.}$).

***c*-3j**—δ_P 16.90; δ_H 0.97 [9H, s, $C(CH_3)_3$], 1.05–1.32 (9H, m, CH_3CH_2S and CH_3CH_2OP), 2.09–2.35 (2H, m, *H*-C_3), 2.90–3.10 (2H, m, CH_3CH_2S), 3.68 (3H, s, CH_3O-Ar), 3.75–3.90 (4H, m, CH_3CH_2OP), 4.08–4.20 (1H, m, *H*-C_4), 5.01 (1H, bs, *H*-C_2), 6.70 and 7.10 (4H, 2d, J=8.6 Hz, $H_{arom.}$); δ_C 14.91 (s, CH_3CH_2S), 16.02–16.19 (m,

CH_3CH_2OP), 27.67 [s, $C(CH_3)_3$], 28.98 (s, CH_3CH_2S), 37.32 (d, J=7.8 Hz, C_3), 42.43 (d, J=9.9 Hz, C_4), 55.29 (s, CH_3O-Ar), 61.45 and 61.88 (2d, J=5.9, 5.8 Hz, CH_3CH_2OP), 75.40 (s, C_2), 75.43 [s, $C(CH_3)_3$], 113.00 and 129.50 (2s, *o*-, *m*-$C_{arom.}$), 123.10 (d, J=190.3 Hz, C_5), 135.00 (s, *i*-$C_{arom.}$), 145.40 (d, J=11.1 Hz, C_6), 158.71 (s, *p*-$C_{arom.}$).

2-*tert*-Butoxy-5-diethoxyphosphonyl-3,4-dihydro-6-ethylthio-4-(3-pyridyl)-2*H*-thiopyran 3k. Anal. Calcd for $C_{20}H_{32}NO_4PS_2$: C, 53.91; H, 7.24; N, 3.14; S, 14.39. Found: C, 53.82; H, 7.32; N, 3.29; S, 13.98.

***t*-3k**—δ_P 16.50; δ_H 0.95 [9H, s, $C(CH_3)_3$], 1.05–1.30 (9H, m, CH_3CH_2S and CH_3CH_2OP), 2.05–2.20 and 2.30–2.38 (2H, 2m, *H*-C_3), 2.92–3.10 (2H, m, CH_3CH_2S), 3.69–4.00 (4H, m, CH_3CH_2OP), 4.18–4.30 (1H, m, *H*-C_4), 4.72 (1H, dd, J=5.7, 9.4 Hz, *H*-C_2), 7.20 (1H, dd, J=4.9, 7.2 Hz, $H_{arom.}$), 7.48 (1H, dm, J=7.2 Hz, $H_{arom.}$), 8.29 (1H, dd, J=1.9, 4.9 Hz, $H_{arom.}$), 8.43 (1H, bs, $H_{arom.}$); δ_C 14.6 (s, CH_3CH_2S), 16.01–16.17 (m, CH_3CH_2OP), 28.65 [s, $C(CH_3)_3$], 29.04 (s, CH_3CH_2S), 38.42 (d, J=7.6 Hz, C_3), 41.56 (d, J=10.6 Hz, C_4), 61.55 and 61.85 (2d, J=6.4 Hz, CH_3CH_2OP), 72.84 (s, C_2), 76.33 [s, $C(CH_3)_3$], 123.24, 135.18, 148.00 and 149.56 (4s, *o*-, *m*-, *p*-$C_{arom.}$), 123.81 (d, J=190.9 Hz, C_5), 137.92 (s, *i*-$C_{arom.}$), 147.34 (d, J=11.3 Hz, C_6).

***c*-3k**—δ_P 16.10; δ_H 0.93 [9H, s, $C(CH_3)_3$], 1.05–1.30 (9H, m, CH_3CH_2S and CH_3CH_2OP), 2.05–2.20 and 2.30–2.38 (2H, 2m, *H*-C_3), 2.92–3.10 (2H, m, CH_3CH_2S), 3.69–4.00 (4H, m, CH_3CH_2OP), 4.18–4.30 (1H, m, *H*-C_4), 5.06 (1H, bs, *H*-C_2), 7.06 (1H, dd, J=4.9, 7.9 Hz, $H_{arom.}$), 7.52 (1H, dm, J=7.9 Hz, $H_{arom.}$), 8.29 (1H, dd, J=1.9, 4.9 Hz, $H_{arom.}$), 8.40 (1H, d, J=2.3 Hz, $H_{arom.}$); δ_C 14.48 (s, CH_3CH_2S), 16.01–16.17 (m, CH_3CH_2OP), 27.81 [s, $C(CH_3)_3$], 29.22 (s, CH_3CH_2S), 38.55 (d, J=7.8 Hz, C_3), 39.97 (d, J=9.2 Hz, C_4), 61.55 and 61.85 (2d, J=6.4 Hz, CH_3CH_2OP), 74.50 (s, C_2), 75.46 [s, $C(CH_3)_3$], 122.43, 136.38, 146.49 and 149.50 (4s, *o*-, *m*-, *p*-$C_{arom.}$), 123.81 (d, J=190.9 Hz, C_5), 138.90 (s, *i*-$C_{arom.}$), 147.34 (d, J=11.3 Hz, C_6).

2-*tert*-Butoxy-5-diethoxyphosphonyl-3,4-dihydro-6-ethylthio-4-(4-pyridyl)-2*H*-thiopyran 3l. HRMS required for $C_{20}H_{32}NO_4PS_2$ (M): 445.1510. Found: M^+: 445.1500.

***t*-3l**—δ_P 16.40; δ_H 1.00 [9H, s, $C(CH_3)_3$], 1.12 (3H, t, J=7.1 Hz, CH_3CH_2S), 1.16 and 1.32 (6H, 2t, J=7.1 Hz, CH_3CH_2OP), 2.10–2.28 (2H, m, *H*-C_3), 2.95–3.10 (2H, m, CH_3CH_2S), 3.65–3.98 (4H, m, CH_3CH_2OP), 4.15–4.24 (1H, m, *H*-C_4), 4.66 (1H, dd, J=4.5, 10.3 Hz, *H*-C_2), 7.07 and 8.46 (4H, 2d, J=5.6 Hz, $H_{arom.}$); δ_C 14.66 (s, CH_3CH_2S), 16.11–16.30 (m, CH_3CH_2OP), 27.90 [s, $C(CH_3)_3$], 28.70 (s, CH_3CH_2S), 38.00 (d, J=7.6 Hz, C_3), 43.60 (d, J=10.4 Hz, C_4), 61.65–62.03 (m, CH_3CH_2OP), 73.00 (s, C_2), 76.50 [s, $C(CH_3)_3$], 120.30 (d, J=191.1 Hz, C_5), 122.87 and 150.03 (2s, *o*-, *m*-$C_{arom.}$), 150.25 (d, J=12.1 Hz, C_6), 151.70 (s, *i*-$C_{arom.}$).

***c*-3l**—δ_P 16.00; δ_H 0.85 [9H, s, $C(CH_3)_3$], 1.10 (3H, t, J=7.2 Hz, CH_3CH_2S), 1.18 and 1.34 (6H, 2t, J=7.0 Hz, CH_3CH_2OP), 2.12–2.25 and 2.29–2.40 (2H, 2m, *H*-C_3), 2.95–3.10 (2H, m, CH_3CH_2S), 3.65–3.98 (4H, m, CH_3CH_2OP), 4.15–4.24 (1H, m, *H*-C_4), 5.02 (1H, bs, *H*-C_2), 7.11 and 8.35 (4H, 2d, J=5.6 Hz, $H_{arom.}$); δ_C 14.58 (s, CH_3CH_2S), 16.11–16.30 (m, CH_3CH_2OP), 27.60 [s, $C(CH_3)_3$], 29.14 (s, CH_3CH_2S), 38.25 (d, J=7.9 Hz, C_3), 41.65 (d, J=9.6 Hz, C_4), 61.65–62.03 (m, CH_3CH_2OP), 74.44 (s, C_2), 75.66 [s, $C(CH_3)_3$], 123.52 (d, J=191.2 Hz, C_5), 147.00 (d, J=10.1 Hz, C_6), 123.88 and 148.84 (2s, *o*-, *m*-$C_{arom.}$), 152.83 (s, *i*-$C_{arom.}$).

5-Diethoxyphosphonyl-2,6-diethylthio-3,4-dihydro-4-(4-nitrophenyl)-2*H*-thiopyran 3m. Anal. Calcd for $C_{19}H_{28}NO_5PS_3$: C, 47.78; H, 5.91; N, 2.93; S, 20.14. Found: C, 47.82; H, 5.34; N, 2.83; S, 19.69.

***t*-3m**—δ_P 15.90; δ_H 1.00–1.40 (12H, m, CH_3CH_2S and CH_3CH_2OP), 2.05–2.18 and 2.25–2.38 (2H, 2m, *H*-C_3), 2.58 (2H, q, J=7.2 Hz, CH_3CH_2S), 2.95–3.15 (2H, m, CH_3CH_2S), 3.65–3.95 (4H, m, CH_3CH_2OP), 4.25 (1H, t, J=6.6 Hz, *H*-C_4), 4.38 (1H, dd, J=0.8, 11.0 Hz, *H*-C_2), 7.28 and 8.15 (4H, 2d, J=8.4 Hz, $H_{arom.}$); δ_C 14.74 and 14.79 (2s, CH_3CH_2S), 16.20 and 16.30 (2d, J=4.2 Hz, CH_3CH_2OP), 24.10 and 29.02 (2s, CH_3CH_2S), 36.70 (d, J=8.0 Hz, C_3), 43.03 (s, C_2), 44.50 (d, J=10.1 Hz, C_4), 61.70 and 62.05 (2d, J=6.2 Hz, CH_3CH_2OP), 121.50 (d, J=191.4 Hz, C_5), 123.90 and 128.80 (2s, *o*-, *m*-$C_{arom.}$), 146.95 (s, *i*-$C_{arom.}$), 149.79 (d, J=11.2 Hz, C_6), 150.45 (s, *p*-$C_{arom.}$).

***c*-3m**—δ_P 16.10; δ_H 1.00–1.40 (12H, m, CH_3CH_2S and CH_3CH_2OP), 2.01–2.15 (1H, m, *H*-C_3), 2.52–2.68 (3H, m, CH_3CH_2S and *H*-C_3), 2.87–2.90 and 3.03–3.17 (2H, 2m, CH_3CH_2S), 3.66–3.91 (4H, m, CH_3CH_2OP), 4.10 (1H, dd, J=2.6, 8.6 Hz, *H*-C_2), 4.18–4.29 (1H, m, *H*-C_4), 7.36 and 8.08 (4H, 2d, J=8.7 Hz, $H_{arom.}$); δ_C 14.60 (s, CH_3CH_2S), 16.19 (d, J=6.7 Hz, CH_3CH_2OP), 25.55 and 28.78 (2s, CH_3CH_2S), 42.65 (d, J=9.0 Hz, C_3), 46.61 (s, C_2), 46.68 (d, J=10.1 Hz, C_4), 61.62 and 61.85 (2d, J=6.3 Hz, CH_3CH_2OP), 123.20 (d, J=189.7 Hz, C_5), 123.50 and 128.80 (2s, *o*-, *m*-$C_{arom.}$), 146.50 (s, *i*-$C_{arom.}$), 150.40 (d, J=10.4 Hz, C_6), 151.80 (s, *p*-$C_{arom.}$).

General procedure for the one-pot synthesis of phosphonothiopyrans 3

To a 100 cm^3 flask equipped with a Dean–Stark trap and a reflux condenser were added a mixture of phosphonate **1** (1.28 g, 5 mmol), the appropriate aldehyde **6** (5 mmol) and the dienophile **5** (50 mmol) in toluene (50 cm^3). Then two drops of piperidine were introduced. The reaction mixture was refluxed for a time indicated in Table 3, then the toluene was removed by distillation under reduced pressure. Further work-up and purification were carried out as above, giving the pure product **3** (Table 3).

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