Synthesis of *S*-thioacyl dithiophosphates, efficient and chemoselective thioacylating agents †

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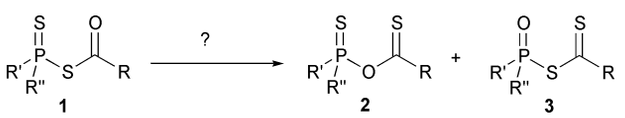
Easily available acyl dithiophosphates are not stable and isomerise reversibly to *O*-thioacyl monothiophosphates, especially when subjected to heating. Much slower but probably irreversible isomerisation to *S*-thioacyl monothiophosphates occurs. Since equilibrium states are established and *S*-thioacyl (mono)thiophosphates form slowly, reaction mixtures contain generally both thioacylating and acylating agents, and consequently cannot be used for efficient thioacylation. On the other hand, treatment of a mixture of isomeric anhydrides with an excess of a dithiophosphoric acid leads to exclusive formation of *S*-thioacyl dithiophosphates. They appear to be excellent thioacylating agents: relatively stable, inert towards water and oxygen and therefore easy to handle. Reactions with nitrogen or sulfur nucleophiles proceed very rapidly under ambient conditions, yielding respective thioacyl derivatives. Isolation of the products is very simple. Due to the low reactivity of *S*-thioacyl dithiophosphates towards oxygen nucleophiles they can be used for direct thioacylation of multifunctional nucleophiles with unprotected hydroxy groups. Respective thioacyl derivatives cannot readily be obtained using other methods.

Introduction

Thioacyl derivatives can be obtained using two main approaches. The first one consists of subsequent stages of activation of carboxylic acid, acylation of a nucleophile, and treatment of the formed acyl derivative with a so-called thionating agent. The most popular thionating agents are phosphorus pentasulfide and Lawesson's reagent.[1,2] Numerous other reagents have been described [*e.g.*, R_3OBF_4–NaHS,[3] R_2PSX,[4] $POCl_3$–$(Me_3Si)_2S$,[5] $(Et_2Al)_2S$,[1] B_2S_3 [1] or SiS_2 [1]]. However, they have not found as wide an application as the first two. The other, more chemoselective strategy leading to thioacyl derivatives consists of thioacylation of nucleophiles with an active derivative of thiocarboxylic acid. Unfortunately, thioacylating agents described in the chemical literature [*e.g.*, thioacyloxybenzotriazoles,[6] phenylmercury dithiocarboxylates,[7] bis(thioacyl) sulfides,[8] thioacyl trifluorosulfonyl sulfides,[9] *N*-methyl-*S*-thioacyl-2-sulfanylpyridinium iodides,[10] thioacyl halides,[1] succinimides,[1] phthalides,[11] benzimidazolones,[12] fluorobenzimidazolones,[13] imidazoles, triazoles or tetrazoles,[1] *etc.*] show many disadvantages. Most of these thioacylating agents are unstable (especially the aliphatic derivatives), and their synthesis is complicated or expensive. Less reactive reagents (like thioesters) react with nucleophiles very slowly or, in case of larger steric hindrance, do not react at all.[1] Moreover, most of the reagents described can only be prepared from dithiocarboxylic acids, which are scarce as commercial reagents and are not easy to synthesise in high yield or to handle in pure form. Furthermore, dithiocarboxylic acids generally have obnoxious odors.

Therefore, we aimed to establish whether mixed anhydrides of dithiophosphoric (dithiophosphonic or dithiophosphinic) and carboxylic acids of type **1** could be isomerised (Scheme 1) to *O*-thioacyl or *S*-thioacyl monothiophosphates (phosphonates, phosphinites) **2**, **3**, which are active derivatives of thiocarboxylic acids.



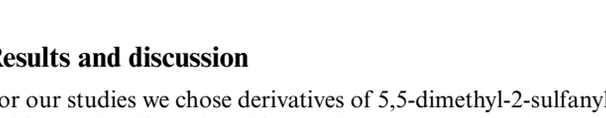
Scheme 1 Isomerisation of mixed anhydrides of type **1**.

If it were possible then it would be a comfortable method of synthesis of thioacylating agents, benefiting from easily available starting materials (carboxylic acids).

We have recently communicated [14] our results in this field and here we present the details of our research.

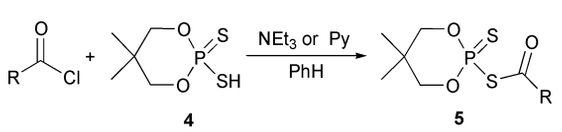
Results and discussion

For our studies we chose derivatives of 5,5-dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphinan **4** due to numerous advantages of this model [an easy-to-prepare (Scheme 2), crystalline, almost odorless dithiophosphoric acid; derivatives should have clear NMR spectra].



Scheme 2 Synthesis of 5,5-dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphinan **4**.

Reaction of the dithiophosphoric acid **4** with acyl chlorides in the presence of triethylamine or pyridine immediately yields the expected acyl dithiophosphates **5** (Scheme 3). In order to



Scheme 3 Synthesis of acyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfides **5**.

† Proofs for the reversibility of isomerisation of anhydrides **1** to **2**, melting points of amides and thioamides obtained from anhydrides **5**–**7** and ^{1}H, ^{13}C NMR and IR data of isolated anhydrides **5**–**7**, **17** are available as supplementary data. For direct access, see http://www.rsc.org/suppdata/p1/b2/b201233b/

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Table 1 Yields and chemical shifts of acyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfides **5**

Entry	R	^{31}P NMR, δ/ppm	Yield (%)
5a	Ph	69.1	98
5b	C_6H_4OMe-*p*	70.3	85
5c	$C_6H_4NO_2$-*p*	65.9	85
5d	1-Naphthyl	69.6	100
5e	CH=CHPh (*E*)	69.7	93
5f	Me	69.1	89
5g	Pr	70.1	92
5h	Pr^i	70.6	98
5i	Bu^t	70.8	96
5j	$CH(CH_2)_5$	71.0	93
5k	CH_2OPh	67.9	90
5l	CH_2Ph	68.9	90
5m	$CHPh_2$	69.4	94
5n	$(CH_2)_4COOMe$	69.2	100

Table 2 Yields of amides† obtained by acylation of amines with acyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfides **5**

Entry	R	Amine	Yield of amide (%)
5a	Ph	H_2NPh	99
5b	C_6H_4OMe-*p*	$HNEt_2$	94
5c	$C_6H_4NO_2$-*p*	H_2NPh	96
5d	1-Naphthyl	H_2NPr^i	97
5e	CH=CHPh (*E*)	$HNEt_2$	90
5f	Me	H_2NPh	95
5g	Pr	H_2NPh	97
5h	Pr^i	H_2NPh	99
5i	Bu^t	H_2NPh	99
5j	$CH(CH_2)_5$	H_2NPh	95
5k	CH_2OPh	$HN(CH_2)_2O(CH_2)_2$	95

obtain pure anhydrides **5**, the reaction mixture should be cooled with ice–water and work-up should be as fast as possible. Evaporation of the solvent should be carried out at room temperature, especially in the case of acyl chlorides with electron-donating groups. Then very good yields can be obtained, as can be seen from the data collected in Table 1.

Acylation of dithiophosphates is efficient even in the case of sterically hindered pivaloyl chloride (Table 1, entry **5i**), as well as of acyl chlorides with electron-withdrawing groups (Table 1, **5c**,**k**–**m**) and electron-donating groups (Table 1, **5b**,**h**–**j**). Unsaturated derivatives can also be prepared (Table 1, **5e**). The acyl dithiophosphates **5** are colorless crystalline solids. Their ^{31}P chemical shifts lay in a narrow range of δ_P 69–71 (only anhydrides with electron-withdrawing groups have slightly lower shifts). ^{1}H, ^{13}C NMR, IR and MS data also confirm their structure. Additional chemical proof comes from the treatment of anhydrides **5** with amines (in the presence of triethylamine) to yield amides (Table 2). ‡

Although synthesis of acyl dithiophosphates from acyl chlorides is very efficient, we searched for a method of acyl dithiophosphate synthesis directly from carboxylic acids. Many of the condensing agents we tested were unsuccessful; however, we found that carbonyldiimidazole (CDI) can be used for efficient synthesis of anhydrides **5**. Due to the high nucleophilicity of imidazole formed in the course of the reaction, three equivalents of dithiophosphoric acid **4** should be used (Scheme 4), which allows the preparation of acyl dithiophosphates with high yield (Table 3).

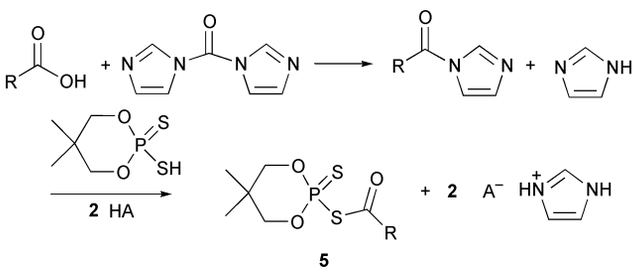
Due to the necessity of an excess of the reagent certain preparative issues, such as cost, solubility, isolation of products, *etc.*, make it advisable to modify the procedure. Thus, we decided to replace 2 eq. of dithiophosphoric acid with an acid which would be inexpensive, stronger than the

‡ Detailed structural studies were necessary because we found the literature concerning mixed anhydrides confusing.

Table 3 Direct synthesis of acyl dithiophosphates **5** from carboxylic acids

Entry	R	^{31}P NMR, δ (ppm)	Yield (%)
5a	Ph	69.1	94[a]
5d	1-Naphthyl	69.6	81[a]
5f	Me	69.1	95[b]
5g	Pr	70.1	98[b]
5i	Bu^t	70.8	84[a]; 99[b]
5n	$(CH_2)_4COOMe$	69.2	99[b]
5o	CH_2NPhth	65.7	81[a]
5p	CH_2CH_2NPhth	67.7	93[a]

[a] Method A: RCOOH + CDI + 3 $(RO)_2PSSH$. [b] Method B: RCOOH + CDI + $(RO)_2PSSH$ + 2CF_3COOH.



Scheme 4 Synthesis of acyl dithiophosphates **5** from carboxylic acids with CDI as condensing agent.

dioxaphosphinan **4**, poorly nucleophilic, and well soluble in the reaction medium. These conditions are fulfilled by trifluoroacetic acid. The method based on addition of carboxylic acid to CDI, followed by addition of dithiophosphoric acid and 2 eq. of trifluoroacetic acid, allows the obtention of acyl dithiophosphates **5** with high yields (the results are shown in Table 3).

Studying the synthesis of acyl dithiophosphates **5** we noticed that solutions of these anhydrides turn yellow to orange and, after a longer time, become pink to violet (especially on heating). Monitoring of reaction mixtures with ^{31}P NMR and TLC (see Fig. 1 and the results collected in Table 4 indicated that

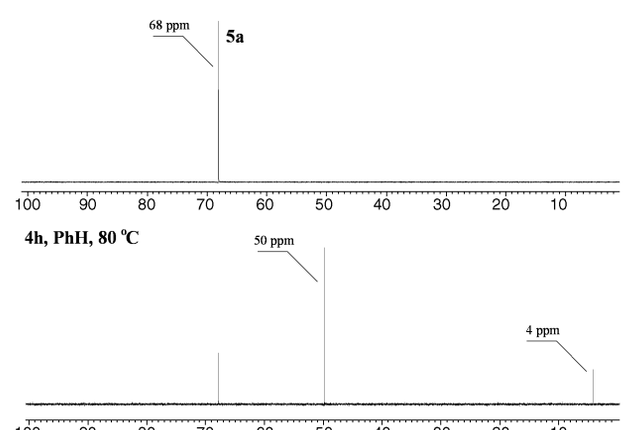


Fig. 1 Example of ^{31}P NMR spectrum of the reaction mixture formed by heating a solution of an acyl dithiophosphate **5** (R = Ph, 80 °C, 4 h).

these changes in color were due to two types of compounds being formed. One type, of lower polarity than the starting materials, has a ^{31}P NMR chemical shift of δ_P 48.5–51 whereas the other, being more polar, has δ_P 4–7. We managed to isolate some of these products (see Table 5). Based on analytical data, such as ^{31}P, ^{13}C, ^{1}H NMR, IR, MS, and reactions with amines yielding thioamides (see Tables 4 and 5) we assigned the expected structures of *O*-thioacyl **6** and *S*-thioacyl monothiophosphates **7**, respectively, to these products (Scheme 5). Our study is the first one where isomerisation of mixed anhydrides

Table 4 Chemical shifts and proportions (based on relative ^{31}P NMR signal intensities) of products, observed after heating acyl dithiophosphates **5** for 2 hours; yields of derived amides and thioamides †

Entry	R	^{31}P NMR, δ (ppm)			Proportions of **5** : **6** : **7**	Yield (%) of	
		5	**6**	**7**		amide	thioamide
a	Ph	67.7	49.8	4.1	33 : 62 : 5	27[b]	60
b	C_6H_4OMe-*p*	68.9	50.2	4.8	24 : 54 : 22[a]	15[c]	70
c	$C_6H_4NO_2$-*p*	65.6	49.6	4.0	22 : 78 : tr	25[b]	59
d	1-Naphthyl	68.7	49.4	3.7	51 : 6 : 43[a]	45[d]	42
f	Me	69.0	49.5	6.0	49 : 50 : 1	45[b]	45
g	Pr	69.7	50.0	5.6	74 : 12 : 14	65[b]	20
h	Pr^i	70.1	49.5	4.9	85 : 10 : 5	78[b]	7
i	Bu^t	71.1	50.1	5.1	75 : 15 : 10	74[b]	22
j	$CH(CH_2)_5$	70.6	50.8	5.5	33 : 35 : 32	30[b]	53
k	CH_2OPh	67.6	48.5		92 : 8 : 0	85[e]	5

[a] 1 h of heating; [b] Reaction with aniline; [c] Reaction with diethylamine; [d] Reaction with isopropylamine; [e] Reaction with morpholine.

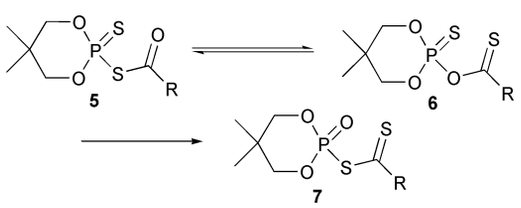
Table 5 Yields of isolated thioacyl thiophosphates **6**, **7**

Entry	R	Reaction time (*t*/h)	Yield (%)
6a	Ph	2	34
7a	Ph	20	47
7b	C_6H_4OMe-*p*	8	79
7d	1-Naphthyl	15[a]	100
7i	Bu^t	28	70

[a] Or 1 week at room temperature.

Table 6 Yields of thioamides obtained from *S*-thioacyl thiophosphates **7**

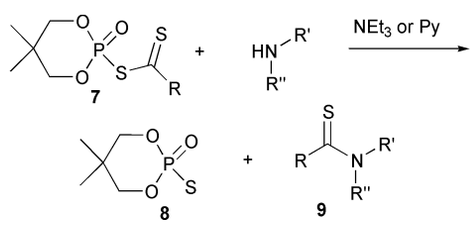
Entry	R	R′	R″	Yield (%)
9a	Ph	Ph	H	81
9b	C_6H_4OMe-*p*	Et	Et	93
9c	1-Naphthyl	Pr^i	H	96
9d	Bu^t	Ph	H	94



Scheme 5 Isomerisation of acyl dithiophosphates **5**.

of type **1** has been confirmed by isolation of respective isomers.

As expected, the isolated thioacyl monothiophosphates **6**, **7** can be effectively applied to thioacylation of amines (Scheme 6,

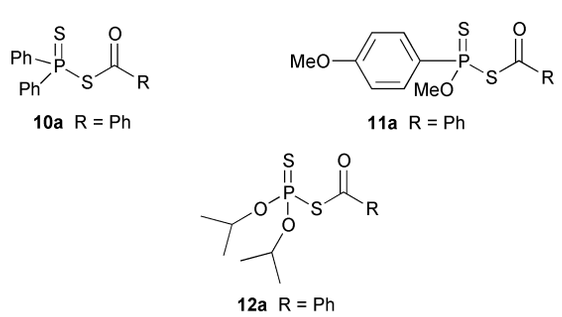


Scheme 6 Thioacylation of amines with *S*-thioacyl thiophosphates **7**.

Table 6). Reaction proceeds at room temperature, immediately yielding thioamides. Since ammonium monothiophosphates formed in this reaction are water-soluble, isolation of the product is exceptionally simple and yields are very good.

In an attempt to investigate the kinetics of thioacyl monothiophosphate formation, we applied ^{31}P NMR to monitor reaction mixtures formed during heating of benzene solutions of selected anhydrides **5** for 8 h. The results are shown in Table 7. Results of the experiments described above allow us to state that in most cases heating of acyl dithiophosphates leads to *O*-thioacyl monothiophosphates **6** comparatively rapidly and equilibrium mixtures † generally contain high amounts of starting material. Longer heating leads to formation of *S*-thioacyl monothiophosphates **7** but the process is very sluggish and only two models used (**5b**,**d**; R = 4-$MeOC_6H_4$, 1-naphthyl) were completely converted to these thioacylating agents. This suggests that electron-donating groups, especially those exercising an *M* + effect, promote the formation of both types of thioacyl monothiophosphate. Consequently, heating of acyl dithiophosphates **5** cannot be used as a general, efficient synthetic method for thioacylating agents of this type.

Therefore, we searched for a dithiophosphoric acid whose acyl derivatives could isomerise quickly and completely to acyl monothiophosphates. To investigate the influence of phosphorus atom substituents we prepared benzoyl dithiophosphinites, -phosphonates and -phosphates (Table 8) and heated them in benzene for 8 hours, monitoring the reaction mixtures with ^{31}P NMR and TLC.



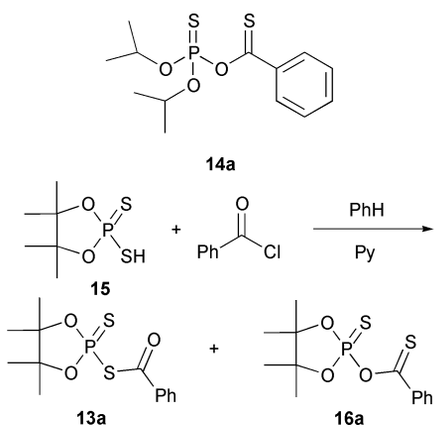
As shown by our experiments, dithio-phosphinites **10** and -phosphonates **11** do not isomerise (at least in boiling benzene) and two alkoxy groups are necessary for the isomerisation. Acyl *O,O*-diisopropyl dithiophosphates **12** isomerise much more slowly than do anhydrides **5** but due to their superior resistance to hydrolysis they are easier to handle. These properties allowed us to isolate pure *O*-thiobenzoyl *O,O*-diisopropyl monothiophosphate **14a**. However, during the synthesis of benzoyl (4,4,5,5-tetramethyl-2-thioxo-1,3,2-dioxaphospholan-2-yl) sulfide **13a**, immediately after triethylamine was added to a solution of 4,4,5,5-tetramethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphospholan **15** and benzoyl chloride, a mixture of benzoyl (4,4,5,5-tetramethyl-2-thioxo-1,3,2-dioxaphospholan-2-yl) sulfide **13a** (δ_P 85.87) and *O*-thiobenzoyl (4,4,5,5-tetramethyl-2-thioxo-1,3,2-dioxaphospholan-2-yl) ether **16a** (δ_P 68.52) was formed (Scheme 7, Fig. 2). However, in that case the equilibrium mixture also contained the acyl derivative. Consequently,

Table 7 Proportions (based on relative ^{31}P NMR signal intensities) of anhydrides **5** : **6** : **7** in mixtures formed while refluxing benzene solutions of anhydrides **5**

		Time/Proportions of **5** : **6** : **7**			
Entry	R	1 h	2 h	4 h	8 h
a	Ph	36 : 64 : 0	33 : 62 : 5	29 : 55 : 16	25 : 56 : 19
b	C_6H_4OMe-*p*	24 : 54 : 22	6 : 15 : 79	4 : 8 : 88	tr : 1 : 99
c	$C_6H_4NO_2$-*p*	23 : 77 : 0	22 : 78 : tr	12 : 83 : 5	10 : 85 : 5
d	1-Naphthyl	51 : 6 : 43	4 : 0 : 96	3 : 0 : 97	1 : 0 : 99
h	Pr^i	93 : 5 : 2	85 : 10 : 5	73 : 11 : 16	48 : 6 : 46
i	Bu^t	91 : 9 : 0	75 : 15 : 10	68 : 7 : 25	52 : 5 : 43
k	CH_2OPh	97 : 3 : 0	92 : 8 : 0	86 : 14 : 0	85 : 15 : 0

Table 8 ^{31}P NMR δ and proportions (based on relative ^{31}P NMR signal intensities) of anhydrides **1** : **2** : **3** in mixtures formed while refluxing benzene solutions of benzoyl dithiophosphinites, dithiophosphonates and dithiophosphates of type **1** (R = Ph)

		δ_P (ppm)/Anhydride type			proportions of **1** : **2** : **3**/Time	
No.	R′, R″	**1**	**2**	**3**	2 h	8 h
10a	Ph, Ph	60.8			100 : 0 : 0	100 : 0 : 0
11a	*p*-$MeOC_6H_4$, MeO	89.1			100 : 0 : 0	100 : 0 : 0
12a	Pr^iO, Pr^iO	76.9	57.7	14.5	82 : 18 : 0	69 : 31 : tr
13a	$OC(Me)_2C(Me)_2O$	84.9	68.8	17.0	9 : 75 : 16	10 : 64 : 26
5a	$OCH_2C(Me)_2CH_2O$	67.7	49.8	4.1	33 : 62 : 5	25 : 56 : 19



Scheme 7 Reaction of 4,4,5,5-tetramethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphospholan **15** with benzoyl chloride.

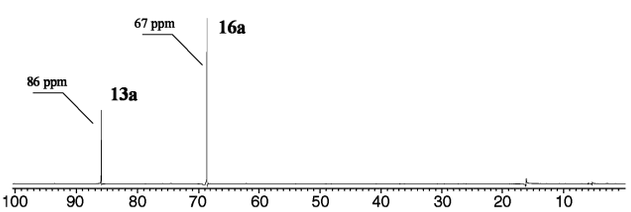
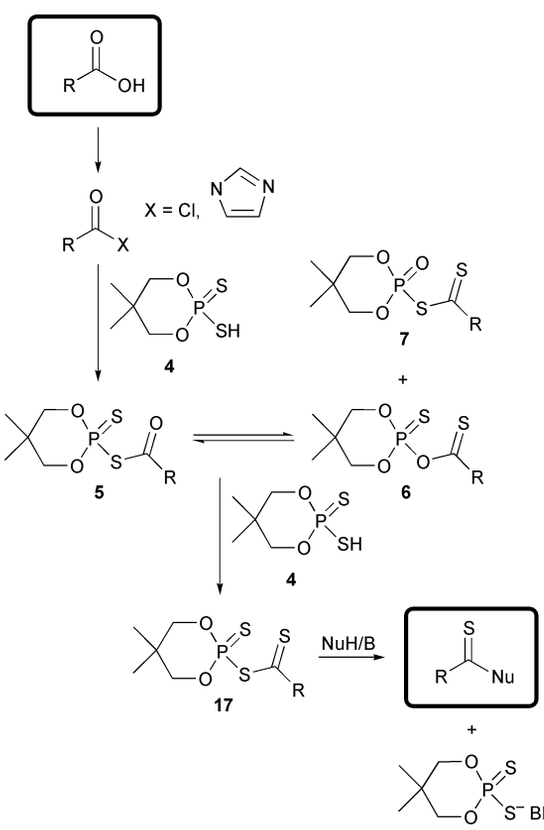


Fig. 2 ^{31}P NMR spectrum of products formed by benzoylation of 4,4,5,5-tetramethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphospholan **15**.

addition of aniline and triethylamine to this mixture yielded benzanilide (37%) and thiobenzanilide (59%).

Results of the experiments carried out in our laboratory show that isomerisation of *S*-acyl dithiophosphates leads to the formation of active derivatives of thiocarboxylic acids, namely thioacyl monothiophosphates. Despite that, the reaction cannot be used for efficient thioacylation as the mixtures formed by heating acyl dithiophosphates generally contain high amounts of acylating agents **5** (starting materials). Nonetheless, we have discovered that addition of the dithiophosphoric acid to the mixture of isomeric anhydrides **5**, **6** and **7** leads to the formation of *S*-thioacyl dithiophosphates **17**. Therefore, we were able to develop an efficient method of synthesis of new thioacylating agents (Scheme 8). *S*-Thioacyl dithiophosphates



Scheme 8 Thioacylation of nucleophiles with *S*-thioacyl dithiophosphates **17** obtained from carboxylic acids.

are formed exclusively when a benzene solution of an *S*-acyl dithiophosphate **5** (or mixture of isomeric anhydrides **5**, **6** and **7**) and two equivalents of the dithiophosphoric acid **4** is refluxed for 1.5–6 h (until the complete disappearance of starting material). As indicated by the data collected in Table 9, aromatic (**17a**,**b**,**d**) and aliphatic (**17f**,**g**,**i**,**n**) derivatives can be obtained. Reagents with electron-donating (Table 9, **17i**) and electron-withdrawing groups (Table 9, **17b**) as well as sterically hindered reagents (Table 9, **17i**) and those possessing additional ester functionality (Table 9, **17n**) have been shown to give high yields.

Table 9 *S*-Thioacyl dithiophosphates **17**

Entry	R	^{31}P NMR δ (ppm)	Time (t/h)	Yield (%)
17a	Ph	68.6	2	94
17b	$C_6H_4NO_2$-*p*		6	86[a]
17d	1-Naphthyl	67.8	1.5	90
17f	Me	68.4	3	88[a]
17g	Pr	68.5	3	92[a]
17i	Bu^t	70.7	4	91
17n	$(CH_2)_4COOMe$	67.2	4	88[a]

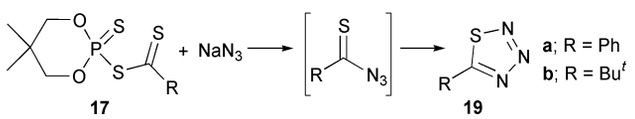
[a] Yield based on the isolated derivative.

Table 10 Thioacylations with *S*-thioacyl dithiophosphates **17**

Entry	R	Nucleophile	Product	Yield (%)
9e	Ph	$NH_{3\ (aq)}$	$PhCSNH_2$	95
9a	Ph	$PhNH_2$, NEt_3	PhCSNHPh	99
9f	Ph	$(CH_2)_5NH$, NEt_3	$PhCSN(CH_2)_5$	98
9g	Ph	$HOCH_2CH_2NH_2$, NEt_3	$PhCSNHCH_2CH_2OH$	94
18a	Ph	MeNHOH·HCl, NEt_3	PhCSN(OH)Me	68
18b	Ph	Pr^{i}NHOH·$(COOH)_2$, NEt_3	PhCSN(OH)Pr^i	73
19a	Ph	$NaN_{3\ (aq)}$	$PhCSN_3$[b]	89
9h	$C_6H_4NO_2$-*p*	$PhNH_2$, NEt_3	*p*-$O_2NC_6H_4CSNHPh$	85[a]
9c	1-Naphthyl	Pr^iNH_2, NEt_3	1-NaphthylCSNHPr^i	96
9i	Me	$PhNH_2$, NEt_3	MeCSNHPh	88[a]
9j	Pr	$PhNH_2$, NEt_3	PrCSNHPh	92[a]
9d	Bu^t	$PhNH_2$, NEt_3	Bu^{t}CSNHPh	97
9k	Bu^t	CH_2=HCH_2NH_2, NEt_3	Bu^t$CSNHCH_2CH$=CH_2	100
9l	Bu^t	*o*-$HOC_6H_4NH_2$, NEt_3	*o*-Bu^t$CSNHC_6H_4OH$	99
18c	Bu^t	MeNHOH·HCl, NEt_3	Bu^{t}CSN(OH)Me	71
19b	Bu^t	$NaN_{3\ (aq)}$	Bu^tCSN_3[b]	92
20a	Bu^t	$HOCH_2CH_2SH$, NEt_3	Bu^t$CSSCH_2CH_2OH$	97
9m	$(CH_2)_4COOMe$	$(CH_2)_5NH$, NEt_3	$MeOCO(CH_2)_4CSN(CH_2)_5$	88[a]

[a] Procedure B; [b] Thioacyl azides are an unstable species and isomerise *in situ* to thiatriazoles.

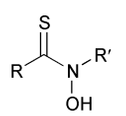
Compounds **17** show relative stability and resistance towards air and water (they can even be washed with 10% aq. NaOH). They can be isolated, as well as handled without special precautions, or used *in situ* for thioacylation reaction. Thioacyl dithiophosphates **17** in the presence of triethylamine (pyridine) react with nitrogen and sulfur nucleophiles at room temperature very rapidly, producing the respective thioacyl derivatives in very good yields. Reaction proceeds with ammonia (Table 10, **9e**), primary (Table 10, **9a**,**c**,**d**,**g**–**l**) and secondary amines (Table 10, **9f**,**m**). Unsaturated amines are efficiently thioacylated as well (Table 10, **9k**). Thioacyl derivative can be easily separated from water-soluble salts of thiophosphoric acids. As anhydrides **17** do not react with alcohols or water (under our given reaction conditions), they can chemoselectively thioacylate nitrogen and sulfur nucleophiles in the presence of oxygen ones. This property allowed us to obtain hydroxy thioamides (Table 10, **9g**,**l**), thiohydroxamic acids (**18a**–**c**), and hydroxy dithioesters (**20a**) directly from substrates not protected on the hydroxy group. It is worth mentioning that these kinds of compounds are only difficulty available *via* thionation of non-protected hydroxy amides, hydroxy-*S*-thioesters, or hydroxamic acids with Lawesson's reagent.[15,16] Thioacylation of azide anion is also an interesting reaction because thioacyl azides thus formed are unstable and isomerise in the reaction mixture to 5-substituted 1,2,3,4-thiatriazoles[17] (Scheme 9, Table 10, **19a**,**b**),



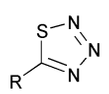
17 **19**

Scheme 9 Synthesis of 1,2,3,4-thiatriazoles **19** by reaction of *S*-thioacyl dithiophosphates **17** with sodium azide.

which are hard to obtain using other methods (to our best knowledge, sulfuration of acyl azides has not been reported).



18 **a** R = Ph, R′ = Me
b R = Ph, R′ = Pr^i
c R = Bu^t, R′ = Me



19 **a** R = Ph
b R = Bu^t

Due to the low reactivity of thioacyl dithiophosphates towards oxygen nucleophiles, thioacylation reactions can be performed in two-phase systems with water as a solvent. Another advantage of our method is that the synthesis of thioacyl dithiophosphates and the thioacylation reaction can be monitored easily, because the thioacyl dithiophosphates are colorful. During the synthesis of anhydrides **17** the reaction mixture turns from pink to dark violet and during the reaction with a nucleophile the color changes to yellow or the reaction mixture becomes colorless.

Conclusions

Acyl dithiophosphates can be obtained in high yield by acylation of dithiophoshoric acids with acyl chlorides in the presence of a base or by acylation with acylimidazoles generated *in situ*. These compounds are not stable and isomerise to *O*-thioacyl monothiophosphates and an equilibrium mixture is formed. The reaction is accompanied by a much slower formation of *S*-thioacyl monothiophosphates. For some substituents on the acyl moiety the latter process seems to be irreversible. Acyl dithio-phosphinites and -phosphonates do not isomerise (at least in boiling benzene) and two alkoxy substituents on the phosphorus atom appear to be crucial for the isomerisation. The mixture of isomers contains acylating and thioacylating agents, and therefore can hardly be used for efficient thioacylation. Nonetheless, the reaction of this mixture

with an excess of a dithiophosphoric acid leads to exclusive formation of *S*-thioacyl dithiophosphates. These proved to be excellent thioacylating agents. They are relatively stable, and inert towards water and oxygen. Crystalline products can be stored for months without noticeable change. Even thioacyl dithiophosphates derived from aliphatic acids can be handled without special precautions. The reactions with nitrogen and sulfur nucleophiles proceed very rapidly at ambient conditions, yielding the respective thioacyl derivatives. Isolation of the product is very simple. Due to the low reactivity of thioacyl dithiophosphates towards oxygen nucleophiles, our method can be employed for direct thioacylation of multifunctional nucleophiles containing unprotected hydroxy groups. These types of thioacyl derivatives can be obtained only with diffculty using other methods. To recapitulate, we have developed a new strategy of thioacylation, starting from carboxylic acids. In this one-pot method the exchange of a C=O into a C=S group and activation of the thiocarboxylic function occur simultaneously.

Experimental

General

All reactions were carried out under argon atmosphere in dry solvents (benzene and THF dried over benzophenone ketyl, methylene dichloride and alcohols over CaH_2, chloroform over P_2O_5, hexane and cyclohexane over potassium). Chromatography was carried out on Silica Gel 60 (0.15–0.3 mm) Macherey Nagel®. NMR was performed on a Varian Gemini 500 MHz, with *J*-values in Hz; IR on a Bruker IFS66 (liquids: film; solids: KBr tablet); MS were acquired on a MASPEC II system [II32/99D9] in EI mode, and if necessary liquid SIMS technique was applied.

5,5-Dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphinan 4

This was prepared from P_2S_5 and 2,2-dimethylpropane-1,3-diol according to the method described by Chauhan *et al.*,[18] in 79.7% yield; mp 81–82 °C; $\delta_P(CDCl_3)$ 77.68.

4,4,5,5-Tetramethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphospholan 15

This was prepared from P_2S_5 and 1,1,2,2-tetramethylethane-1,2-diol according to the method described by Chauhan *et al.*,[18] in 61% yield; mp 68–69 °C; $\delta_P(CDCl_3)$ 93.18.

Diphenyldithiophosphinic acid

This was prepared from P_2S_5 and benzene in the presence of $AlCl_3$ according to the procedure of Higgins *et al.*,[19] in 75% yield; mp 54–56 °C; $\delta_P(CDCl_3)$ 56.5.

Triethylammonium O,O-diisopropyl dithiophosphate

This was prepared from P_2S_5, propan-2-ol and triethylamine according to Almasi *et al.*,[20] in 61% yield; mp 100–102 °C; $\delta_P(CDCl_3)$ 108.28.

S-Acyl dithio-phosphates and -phosphinites 5, 10, 13; general procedure

An acyl chloride (3 mmol) was added to a solution of the appropriate dithiophosphoric (dithiophosphinic) acid (3 mmol) in benzene (10 cm^3). Subsequently, triethylamine (0.303 g, 3 mmol) or pyridine (0.237g, 3 mmol) was added dropwise to the ice-cold solution. Immediately, triethylammonium chloride precipitated. After 15 min the reaction mixture was filtered through a short pad of silica gel. After the solvent had been evaporated, pure product was obtained.

In the case of 4-nitrobenzoyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfide **5c**, methylene dichloride was used instead of benzene to avoid problems with solubility.

Yields and ^{31}P NMR chemical shifts are collected in Table 1; HRMS measurements and melting points of anhydrides **5** are collected in Table 11; ^1H, ^{13}C NMR and IR data are available as supplementary data.†

Benzoyl diphenyldithiophosphinite 10a. Yield 100 %; mp 119–120 °C (lit.,[21] 120–121 °C); $\delta_P(CDCl_3)$ 60.82; *m/z* 354.03117 ($C_{19}H_{15}OPS_2$ requires *M*, 354.03019).

Mixture of benzoyl (4,4,5,5-tetramethyl-2-thioxo-1,3,2-dioxaphospholan-2-yl) sulfide 13a and O-thiobenzoyl (4,4,5,5-tetramethyl-2-thioxo-1,3,2-dioxaphospholan-2-yl) ether 16a. Yield 100%; mp 76–79 °C; ν_{max}/cm^{-1} 1748 (C=O), 1162 (C=S), 1592, 1453 ($C=C_{Ar}$), 1013, 945 (P–O–C); *m/z* 316.03497 ($C_{13}H_{17}O_3PS_2$ requires *M*, 316.03567); $\delta_P(CDCl_3)$ 85.87 (anhydride **13a**); δ_P 68.52 (anhydride **16a**).

Reaction of the mixture of benzoyl (4,4,5,5-tetramethyl-2-thioxo-1,3,2-dioxaphospholan-2-yl) sulfide 13a and *O*-thiobenzoyl (4,4,5,5-tetramethyl-2-thioxo-1,3,2-dioxaphospholan-2-yl) ether 16a with aniline

A mixture of anhydrides **13a** and **16a** (0.632, 2 mmol), obtained as described above, was dissolved in benzene (6 cm^3) and a mixture of aniline (2 mmol) and triethylamine (0.202 g, 2 mmol) was added dropwise while cooling with ice–cold water. The reaction mixture was washed with water, next dried with $MgSO_4$, and the solvent was evaporated. The obtained mixture was subjected to column chromatography on silica gel using chloroform as eluent. Thiobenzanilide (0.252 g, 59.2%), mp 97–98 °C[4] and benzanilide (0.146 g, 37.1%), mp 162–164 °C[22] were obtained.

S-Benzoyl *O,O*-diisopropyl dithiophosphate 12a

Benzoyl chloride (0.422 g, 3 mmol) was added dropwise to a suspension of triethylammonium *O,O*-diisopropyl dithiophosphate (0.945, 3 mmol) in benzene (10 cm^3). After 15 min the reaction mixture was filtered through a short pad of silica gel. After the solvent had been evaporated, pure product was obtained (0.9 g, 94.3%), mp 46–47 °C; ν_{max}/cm^{-1} 1682 (C=O), 1594, 1580, 1468, 1450 ($C=C_{Ar}$), 1027, 982 (P–O–C), 687 (P=S); $\delta_P(CDCl_3)$ 76.87; $\delta_H(CDCl_3)$ 7.93 (2H, d, *J* 7.3), 7.61 (1H, t, *J* 7.8), 7.47 (2H, t, *J* 7.8), 5.06 (1H, spt, *J* 6.4), 5.04 (1H, spt, *J* 5.9), 1.42 (6H, d, *J* 6.3), 1.36 (6H, d, *J* 5.9); $\delta_C(CDCl_3)$ 186.54, 136.67, 134.59, 129.12, 128.35, 74.98 (d, J_{P-C} 6.6), 24,12 (d, J_{P-C} 4.4), 23.45 (d, J_{P-C} 5.3); *m/z* 318.05246 ($C_{13}H_{19}O_3PS_2$ requires *M*, 318.05132).

S-Benzoyl *O*-methyl 4-methoxyphenyldithiophosphonate 11a

This was prepared according to the method of Shabana,[23] in 30% yield; $\delta_P(CDCl_3)$ 89.06.

Reactions of acyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfides 5 with amines

A mixture of amine (aniline, isopropylamine, diethylamine) (1 mmol) and triethylamine (0.101 g, 1 mmol) was added dropwise to a solution of an acyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfide **5** (1 mmol) in benzene (3 cm^3) while cooling with ice-cold water. Triethylammonium (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl)thiolate precipitated immediately. After 15 min the reaction mixture was filtered through silica gel and the amide was eluted with methylene dichloride. All products were compared with authentic samples. Yields and melting points are collected in Table 2.

Synthesis of acyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfides 5 directly from carboxylic acids; general procedure

Method A. A solution of carbonyldiimidazole (0.324 g, 2 mmol) in methylene dichloride or chloroform (3 cm^3) was

Table 11 Melting points and HRMS measurements for anhydrides **5**–**7**, **17**

No.	R	Mp (θ/°C)	Formula	Calculated	Found
5a	Ph	114–115	$C_{12}H_{15}O_3PS_2$	302.02002	302.01975
5b	C_6H_4OMe-*p*	92–93	$C_{13}H_{17}O_4PS_2$	332.03059	332.02928
5c	$C_6H_4NO_2$-*p*	159–162	$C_{12}H_{14}NO_5PS_2$	347.00510	347.00457
5d	1-Naphthyl	106–108	$C_{16}H_{17}O_3PS_2$	352.03567	352.03241
5e	$CH{=}CH_2Ph$	105–107	(M + Na) $C_{14}H_{17}NaO_3PS_2$	351.02544	351.02681[a]
5f	Me	71–72	$C_7H_{13}O_3PS_2$	240.00437	239.99691
5g	Pr	98–99	$C_9H_{17}O_3PS_2$	268.03568	268.03562
5h	Pr^i	70–71	$C_9H_{17}O_3PS_2$	268.03568	268.03526
5i	Bu^t	112–113	$C_{10}H_{19}O_3PS_2$	282.05132	282.05046
5j	$CH(CH_2)_5$	96–97	(M + H) $C_{12}H_{22}O_3PS_2$	309.07480	309.07423[a]
5k	CH_2OPh	113–114	$C_{13}H_{17}O_4PS_2$	332.03059	332.03128[a]
5l	CH_2Ph	100–101	(M + H) $C_{13}H_{18}O_3PS_2$	317.04350	317.04472[a]
5m	$CHPh_2$	130–131	$C_{19}H_{21}O_3PS_2$	392.06697	392.06543
5n	$(CH_2)_4COOMe$	≈ 25	(M + H) $C_{12}H_{22}O_5PS_2$	341.06463	341.06308[a]
5o	CH_2NPhth	166–168	$C_{15}H_{16}NO_5PS_2$	385.02075	385.02138
5p	CH_2CH_2NPhth	120–122	$C_{16}H_{18}NO_5PS_2$	399.03640	399.03584
6a	Ph	102–103	$C_{12}H_{15}O_3PS_2$	302.02002	302.01921
7a	Ph	≈ 20	$C_{12}H_{15}O_3PS_2$	302.02002	302.01934
7b	C_6H_4OMe-*p*	83–85	$C_{13}H_{17}O_4PS_2$	332.03059	332.03009
7d	1-Naphthyl	144–145	$C_{16}H_{17}O_3PS_2$	352.03567	352.03243
7i	Bu^t	115–117	$C_{10}H_{19}O_3PS_2$	282.05132	282.05073
17a	Ph	95–97	$C_{12}H_{15}O_2PS_3$	317.99718	317.99997
17d	1-Naphthyl	139–140	$C_{16}H_{17}O_2PS_3$	368.01283	368.01032
17i	Bu^t	153–154	$C_{10}H_{19}O_2PS_3$	298.02848	298.02853

[a] LSIMS method.

added dropwise to a solution (or suspension) of the carboxylic acid (2 mmol) in methylene dichloride or chloroform (1 cm^3). Following complete evolution of CO_2 (15–30 min), a solution of 5,5-dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphinan **4** (1.188 g, 6 mmol) in methylene dichloride (chloroform) (3 cm^3) was added, while cooling with ice–water. After being stirred for 15 min under ambient conditions, the reaction mixture was washed with water, and the organic layer was dried over $MgSO_4$. Solvent evaporation yielded a crude product, which was purified by means of silica gel chromatography or crystallisation from a benzene–cyclohexane mixture. Results are collected in Table 3.

Method B. 2 mmol of an acylimidazole was generated as above and a solution of 5,5-dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphinan **4** (0.396 g, 2 mmol) in methylene dichloride (chloroform) (1 cm^3) was added, with cooling of the reaction mixture with ice–water. Then trifluoroacetic acid (0.456 g, 4 mmol) was added dropwise. After 15 min of stirring at ambient conditions, imidazolium trifluoroacetate precipitated. Then, the reaction mixture was filtered through a short pad of silica gel. Solvent evaporation yielded pure product. Yields and ^{31}P NMR chemical shifts are collected in Table 3; HRMS measurements and melting points are collected in Table 11; ^1H, ^{13}C NMR and IR data are available as supplementary data. †

Isomerisation of acyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfides 5; general procedure

A solution of anhydride **5** (3 mmol) in benzene (20 cm^3) was refluxed for 1–28 h. For analytical purposes, ≈0.5 cm^3 of the reaction mixture was taken to perform ^{31}P NMR measurement (≈0.2 cm^3 of C_6D_6 was added to set up the lock). When the experiment was finished, a mixture of an amine (aniline, isopropylamine, diethylamine, or piperidine) (3 mmol) and triethylamine (0.303 g, 3 mmol) was added dropwise while cooling. Such a reaction mixture was subjected to column chromatography. Thioamide was eluted with benzene and then the amide was eluted with methylene dichloride. Results are collected in Tables 4 and 6.

To isolate anhydrides **6** and **7**, after heating anhydrides **5**, the solvent was evaporated off and the residue was subjected to column chromatography. Yields and ^{31}P NMR chemical shifts are collected in Table 5; HRMS measurements and melting points are collected in Table 11; ^1H, ^{13}C NMR and IR data are available as supplementary data. †

Thiobenzoyl (5,5-dimethyl-2-thioxo-1,3,2,-dioxaphosphinan-2-yl) ether 6a. 2 h of heating; eluent $CHCl_3$–hexane 2 : 5.

Thiobenzoyl (5,5-dimethyl-2-oxo-1,3,2-dioxaphosphinan-2-yl) sulfide 7a. 20 h of heating; eluent CH_2Cl_2.

4-Methoxythiobenzoyl (5,5-dimethyl-2-oxo-1,3,2-dioxaphosphinan-2-yl) sulfide 7b. 8 h of heating; after cooling, the product precipitated. Filtration yielded pure product.

1-Thionaphthoyl (5,5-dimethyl-2-oxo-1,3,2-dioxaphosphinan-2-yl) sulfide 7d. 15 h of heating; after solvent evaporation pure enough product was obtained.

Thiopivaloyl (5,5-dimethyl-2-oxo-1,3,2-dioxaphosphinanyl) sulfide 7i. 28 h of heating; eluent CH_2Cl_2.

Thioacylation of amines with thioacyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) ethers 6 and thioacyl (5,5-dimethyl-2-oxo-1,3,2-dioxaphosphinan-2-yl) sulfides 7; general procedure. A mixture of triethylamine (0.101 g, 1 mmol) and an amine (isopropylamine, aniline or diethylamine) (1 mmol) was added to a solution of an anhydride **6** or **7** (1 mmol) in benzene (5 cm^3). The color of the reaction mixture changed and triethylammonium (5,5-dimethyl-2-oxo-1,3,2-dioxaphosphinan-2-thiolate **8a** precipitated. After 15 min the reaction mixture was filtered through a short pad of silica gel, and after evaporation of the solvent the corresponding pure thioamide **9** was obtained.

Reaction of thiobenzoyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) ether 6a with aniline. Thiobenzanilide **9a** was isolated; yield 93%; mp 98–99 °C.[4]

Reaction of thiobenzoyl (5,5-dimethyl-2-oxo-1,3,2-dioxaphosphinan-2-yl) sulfide 7a with aniline. Thiobenzanilide **9a** was isolated; yield 81.4%; mp 97–98 °C.[4]

Reaction of 4-methoxythiobenzoyl (5,5-dimethyl-2-oxo-1,3,2-dioxaphosphinan-2-yl) sulfide 7b with diethylamine. *N,N*-diethyl-4-methoxythiobenzamide **9b** was isolated; yield 93.2%; mp 43–45 °C,[24] $\delta_H(CDCl_3)$ 7.19 (2H, d, *J* 8.8), 6.84 (2H, d, *J* 8.5), 4.11 (2H, q, *J* 7), 3.79 (3H, s), 3.47 (2H, q, *J* 7), 1.14 (3H, t, *J* 7), 1.37 (3H, t, *J* 7), $\delta_C(CDCl_3)$ 200.68, 159.69, 136.78, 126.99, 113.86, 48.09, 46.54, 14.15, 11.53.

Reaction of 1-thionaphthoyl (5,5-dimethyl-2-oxo-1,3,2-dioxaphosphinan-2-yl) sulfide 7d with isopropylamine. *N*-(1-Thionaphthoyl)-isopropylamine **9c** was isolated; yield 96.1%; mp 99–100 °C.[25]

Reaction of thiopivaloyl (5,5-dimethyl-2-oxo-1,3,2-dioxaphosphinanyl) sulfide 7i with aniline. Two hours were necessary to complete the reaction; the product was eluted with chloroform; *N*-thiopivaloylaniline **9d** was isolated; yield 94.3%; mp 88–89 °C.[26]

Comparison of thermal stability of acyl dithiophosphinites 10, dithiophosphonates 11 and dithiophosphates 12, 13

A the solution of an acyl dithophosphate (dithiophosphonate, dithiophosphinite) (3 mmol) in benzene (20 cm^3) was refluxed for 8 h and the reaction mixture was monitored by ^{31}P NMR. The solvent was then evaporated off. In case of benzoyl diphenyldithiophosphinite **10a** and *S*-benzoyl *O*-methyl 4-methoxyphenyldithiophosphonate **11a** the starting material was recovered. In the case of *S*-benzoyl *O,O*-diisopropyl dithiophosphate **12a** the obtained orange solid was subjected to column chromatography (eluent benzene–cyclohexane 1 : 2) and *O*-thiobenzoyl *O,O*-diisopropyl thiophosphate **14a** was isolated (0.357 g, 37.4%) as an orange oil (solidifying in the fridge); $\delta_P(CDCl_3)$ 57.66; $\delta_H(CDCl_3)$ 8.15 (2H, dd, J_1 8.3, J_2 1.5), 7.58 (1H, t, *J* 7.3), 7.4 (2H, t, *J* 7.8), 5.04 (1H, sept, *J* 6.4), 5.03 (1H, sept, *J* 6.4), 1.43 (6H, d, *J* 6.4), 1.42 (6H, d, *J* 6.4); $\delta_C(CDCl_3)$ 202.71 (d, J_{P-C} 6.7), 138.59 (d, J_{P-C} 9.2), 133.86, 129.28, 128.59, 75.27 (d, J_{P-C} 6.6), 23.86 (d, J_{P-C} 4.4), 23.6 (d, J_{P-C} 5.3); *m/z* 318.04909 ($C_{13}H_{19}O_3PS_2$ requires *M*, 318.05132); ν_{max}/cm^{-1} 1593, 1465, 1450 ($C{=}C_{Ar}$), 1268 (C=S), 1041, 994 (P–O–C), 686 (P=S).

The reaction mixture obtained from benzoyl (4,4,5,5-tetramethyl-2-thioxo-1,3,2-dioxaphospholan-2-yl) sulfide **13a** and thiobenzoyl (4,4,5,5-tetramethyl-2-thioxo-1,3,2-dioxaphospholan-2-yl) ether **16a** contained ≈ 25% of thiobenzoyl (4,4,5,5-tetramethyl-2-oxo-1,3,2-dioxaphospholan-2-yl) sulfide (δ_P 16.99). However, the mixture was inseparable.

Thioacyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfides 17; general procedure

A solution of an acyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfide **5** (5 mmol) and 5,5-dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphinan **4** (1.98 g, 10 mmol) in 35 cm^3 of benzene was heated under reflux for 1.5–6 hours (until complete disappearance of the starting material). Then phosphoric thioacids were removed by washing successively with aqueous sodium carbonate and water. Subsequently, the organic layer was dried with magnesium sulfate and the solvent was evaporated off. The crude product was used for thioacylation without further purification or, where necessary, it was purified by means of silica gel chromatography or crystallisation. Yields and ^{31}P NMR chemical shifts are collected in Table 9; HRMS measurements and melting points are collected in Table 11; ^1H, ^{13}C NMR and IR data are available as supplementary data. †

Thiobenzoyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfide 17a. Reaction time 2 h; eluent benzene.

1-Thionaphthoyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfide 17d. Reaction time 1.5 h; eluent benzene.

Thiopivaloyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfide 17i. Reaction time 4 h. Before being washed with aq. $NaHCO_3$, the reaction mixture was diluted with chloroform because the product started to precipitate. Crystallisation was from benzene.

Thiobenzamide 9e. A solution of thiobenzoyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfide **17a** (0.636 g, 2 mmol) in benzene (10 cm^3) with 1 cm^3 of 30% aqueous ammonia was stirred vigorously overnight. The, organic layer was diluted with chloroform, separated, washed with water, and dried over $MgSO_4$. After the mixture had been evaporated, thiobenzamide **9e** was obtained (0.259 g, 94.5%); mp 115–118 °C.[27]

Thioacylation with thioacyl dithiophosphates 17; general procedure

Method A. A solution of an amine or thiol (5 mmol) and pyridine or triethylamine (5,5 mmol) in benzene (5 cm^3) was added dropwise to a solution of a thioacyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfide **17** (5 mmol) in benzene (15 cm^3). Pyridinium or triethylammonium dithiophosphate precipitated out and was removed by filtration or by successive washings with water and aqueous sodium carbonate. Evaporation of the solvent generally yielded pure-enough product. If necessary, the thioacyl derivative was purified by means of chromatography or crystallisation.

Method B. A solution of acyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfide **5** (5 mmol) and 5,5-dimethyl-2-sulfanyl-2-thioxo-1,3,2-dioxaphosphinan **4** (1.98 g, 10 mmol) in 35 cm^3 of benzene was heated under reflux for 2–6 hours. A solution of an amine or thiol (5 mmol) and pyridine or triethylamine (16.5 mmol) in benzene was added dropwise. The resulting mixture was worked up as above.

Thiobenzanilide 9a. Method A; yield 98.6%; mp 97–99 °C.[4]

***N*-(1-Thionaphthoyl)isopropylamine 9c.** Method A; filtration through a short pad of silica gel gave pure product; yield 95.6%; mp 99–100 °C.[25]

***N*-Thiopivaloylaniline 9d.** Method A; the reaction was performed in 100 cm^3 of benzene; reaction time 36 h; column chromatography; eluent benzene–hexane 1 : 1; yield 96.6%; mp 88–89 °C.[26]

***N*-Thiobenzoylpiperidine 9f.** Method A; column chromatography, eluent $CHCl_3$; yield 97.7%; mp 62–64 °C.[28]

***N*-Thiobenzoylethanolamine 9g.** Method A; the reaction was performed in chloroform; column chromatography, eluent $Bu^tOMe–CH_2Cl_2$ 1 : 6; yield 94.1%; mp 91–92 °C.[29]

4-Nitrothiobenzanilide 9h. Method B; 4 h of heating; column chromatography, eluent benzene; yield 85.3%; mp 154–155 °C.[30]

Thioacetanilide 9i. Method B; 3 h of heating; column chromatography; eluent $CHCl_3$; yield 87.8%; mp 74–76 °C.[31]

Thiobutyranilide 9j. Method B; 3 h of heating; column chromatography; eluent $CHCl_3$; yield 91.8%; mp 31–32 °C.[32]

***N*-Thiopivaloylallylamine 9k.** Method A; reaction mixture was filtered through a short pad of silica gel. Solvent evaporation yielded pure product; yield 100%; $\delta_H(CDCl_3)$ 7.39 (1H, bs), 5.93 (1H, m), 5.28 (1H, m), 5.21 (1H, m), 4.31 (2H, m), 1.36 (9H, s), $\delta_C(CDCl_3)$ 213.98, 132.55, 118.79, 49.15, 45.05, 30.65.[33]

2-(Thiopivaloylamino)phenol 9l. Method A; the reaction was performed in THF; reaction time was 3 h; before washing with water the reaction mixture was diluted with chloroform; column chromatography; eluent chloroform–methanol 30 : 1; yield 99%; mp 123–124 °C; $\delta_H(CDCl_3)$ 8.72 (1H, s), 7.24 (2H, d, *J* 8.3), 6.79 (2H, d, *J* 8.8), 5.9 (1H, bs), 1.47 (9H, s), $\delta_C(CDCl_3)$ 214.42, 155.17, 131.73, 127.06, 116.26, 45.45, 30.53; *m*/*z* 209.08827 ($C_{11}H_{15}NOS$ requires *M*, 209.08744).

***N*-[5-(Methoxycarbonyl)thiopentanoyl]piperidine 9m.** Method B; 4 h of heating; column chromatography; eluent methylene dichloride; yield 87.9%; $\delta_H(CDCl_3)$ 4.26 (2H, t, *J* 5.7), 3.68 (2H, t, *J* 5.5), 3.67 (3H, s), 2.88 (2H, t, *J* 7.7), 2.36 (2H, t, *J* 7), 1.71 (10H, m); $\delta_C(CDCl_3)$ 201.32, 173.63, 51.69, 51.66, 51.02, 43.67, 33.88, 28.69, 27.7, 25.58, 24.81, 24.36; *m*/*z* 243.12879 ($C_{12}H_{21}NO_2S$ requires *M*, 243.12930).

Synthesis of thiohydroxamic acids 18; general procedure

Triethylamine (respectively, 1 mmol, 2 mmol or 3 mmol) was added to a solution of hydroxylamine, a suspension of hydroxylamine hydrochloride, or a suspension of hydroxylamine oxalate (1 mmol) in chloroform (2 cm^3). Then a solution of a thioacyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfide **17** (1 mmol) in chloroform (4 cm^3) was added dropwise. After 15 min the reaction mixture was filtered through a short pad of silica gel and the solvent was evaporated off. The crude product was purified by means of column chromatography.

***N*-Hydroxy-*N*-methylthiobenzamide 18a.** *N*-Methylhydroxylamine hydrochloride was used; eluent Bu′OMe–hexane 10 : 3; yield 68.3%; $\delta_H(CDCl_3)$ 11 (1H, bs), 7 (5H, m), 3.4 (3H, s); positive Fe^{3+} test.[34]

***N*-Hydroxy-*N*-isopropylthiobenzamide 18b.** *N*-Isopropylhydroxylamine oxalate was used; eluent benzene; yield 73.3%; $\delta_H(CDCl_3)$ 9.75 (1H, s), 6.9 (5H, s), 4.15 (1H, m), 1.2 (6H, d, *J* 6); positive Fe^{3+} test.[15]

***N*-Hydroxy-*N*-methylthiopivalamide 18c.** *N*-Methylhydroxylamine hydrochloride was used; the reaction was performed in methylene dichloride; eluent chloroform; yield 71.1%; ν_{max}/cm^{-1} 3298 (O–H), 2963, 2874 (C–H), 1221 (C=S); $\delta_H(CDCl_3)$ 11.39 (1H, s), 3.72 (3H, s), 1.38 (9H, s), $\delta_C(CDCl_3)$ 192.72, 41.74, 40.22, 30.45; *m*/*z* 147.07199 ($C_6H_{13}NOS$ requires *M*, 147.07179); positive Fe^{3+} test.

1,2,3,4-Thiatriazoles 19; general procedure

A solution of sodium azide (0.098 g, 1.5 mmol) in 0.5 cm^3 of water was added to a solution of a thioacyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfide **17** (1 mmol) in metylene dichloride (5 cm^3). The reaction mixture was stirred vigorously overnight, and the organic layer was separated, washed with water, and dried over $MgSO_4$. After the solution had been evaporated, the crude product was subjected to column chromatography.

5-Phenyl-1,2,3,4-thiatriazole 19a. Eluent cyclohexane–THF 80 : 1; yield 88.9%; mp 94–95 °C.[17]

5-*tert*-Butyl-1,2,3,4-thiatriazole 19b. Eluent cyclohexane–THF 80 : 1; yield 92%; $\delta_H(CDCl_3)$ 1.57 (s); $\delta_C(CDCl_3)$ 192.3, 36.02, 31.87.[35]

2-(Thiopivaloylsulfanyl)ethanol 20a

2-Sulfanylethanol(mercaptoethanol) (0.078 g, 1 mmol) was added to a solution of thiopivaloyl (5,5-dimethyl-2-thioxo-1,3,2-dioxaphosphinan-2-yl) sulfide **17i** (0.298 g, 1 mmol) in chloroform (3 cm^3), and then triethylamine (0.111 g, 1.1 mmol) was added dropwise. The reaction mixture immediately changed color from red to dark yellow. After 15 min the reaction mixture was washed with water and dried over $MgSO_4$. After the solvent had been evaporated off, the reaction mixture was subjected to column chromatography (chloroform as eluent) to yield pure 2-(thiopivaloylsulfanyl)ethanol **20a** (0.173 g, 97.2%); $\delta_H(CDCl_3)$ 3.84 (2H, t, *J* 5.9), 3.44 (2H, t, *J* 5.9), 2.4 (1H, s), 1.45 (9H, s), $\delta_C(CDCl_3)$ 251.04, 60.29, 52.52, 39.12, 31.96; *m*/*z* 178.04944 ($C_7H_{14}OS_2$ requires *M*, 178.04861).

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