

Synthesis and characterization of *N*-phosphorylated thioureas RNHC(S)NHP(O)(*OiPr*)₂ (R = 2-MeC₆H₄, 2,6-Me₂C₆H₃, 2,4,6-Me₃C₆H₂)

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Abstract. Reaction of *O,O'*-diisopropylphosphoric acid isothiocyanate (*iPrO*)₂P(O)NCS with 2-methylaniline 2-MeC₆H₄NH₂, 2,6-dimethylaniline 2,6-Me₂C₆H₃NH₂ or 2,4,6-trimethylaniline 2,4,6-Me₃C₆H₂NH₂ leads to the *N*-phosphorylated thioureas RNHC(S)NHP(O)(*OiPr*)₂ (R = 2-MeC₆H₄-, **HL**^I; 2,6-Me₂C₆H₃-, **HL**^{II}; 2,4,6-Me₃C₆H₂-, **HL**^{III}). The new compounds were investigated by ¹H and ³¹P{¹H} NMR spectroscopy, and microanalysis. The molecular structure of the thiourea **HL**^{III} was elucidated by single crystal X-ray diffraction analysis. Single crystal X-ray diffraction studies showed **HL**^{III} forms both intra- and intermolecular hydrogen bonds, which in turn leads to the formation of polymeric chains. One of the intermolecular hydrogen bonds is of the type N–H···S. Moreover, the formation of intermolecular C–H···η⁶-phenyl interactions was established.

Keywords. Phosphorylthiourea; crystal structure; NMR spectroscopy; hydrogen bond.

1. Introduction

Amidophosphates RC(S)NHP(X)R'₂ and the related *N*-(thio)phosphorylated thioureas RNHC(S)NHP(X)R'₂ (R = various alkyl or aryl groups; X = O or S; R' = OR) have attracted the attention of researchers in the last three decades mainly due to their ability to form stable chelate complexes with IB, IIB, and VIIIIB group transition metal cations. These compounds offer a number of very interesting applications. Some of them exhibit remarkable antiviral activity,¹ they can be used as stationary phases for GLC,² as well as components of ion-selective electrodes,^{3–6} extractants,^{7–9} and masking reagents in analytical chemistry.¹⁰

Furthermore, RC(S)NHP(X)R'₂ can form various intra- and intermolecular bonds. Formation of hydrogen bonds of the type N–H···S is also possible. A detailed study on such compounds might be useful to provide information on such a type of interaction because the N–H···S hydrogen bond is not abundant.¹¹ However, this type of hydrogen bonding interactions is rather typical for RC(S)NHP(X)R'₂.¹²

This contribution is a continuation of our previously started investigations on the synthesis and characterization of *N*-(thio)phosphorylated (thio) amides and (thio)ureas.¹² Here, we report the synthesis and characterization of the three *N*-phosphorylated thioureas RNHC(S)NHP(O)(*OiPr*)₂ (R = 2-MeC₆H₄-, **HL**^I; 2,6-Me₂C₆H₃-, **HL**^{II}; 2,4,6-Me₃C₆H₂-, **HL**^{III}).

2. Experimental

2.1 Synthesis of **HL**^{I–III}

A solution of 2-methylaniline, 2,6-dimethylaniline or 2,4,6-trimethylaniline (5 mmol, 0.54, 0.61 or 0.68 g) in anhydrous CH₂Cl₂ (15 mL) was treated under vigorous stirring with a solution of (*iPrO*)₂P(O)NCS (6 mmol, 1.34 g) in the same solvent. The mixture was stirred for 1 h. The solvent was then removed under vacuum, and the product was purified by recrystallization from a 1:5 (v/v) mixture of dichloromethane and *n*-hexane.

2.1a **HL**^I *Yield*: 1.42 g (86%); m.p.: 72°C; Anal. Calcd. for C₁₄H₂₃N₂O₃PS (330.38): C, 50.90; H, 7.02; N, 8.48; Found: C, 50.96; H, 6.95; N, 8.52;

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^1H NMR δ (ppm): 1.39 (*d*, $^3J_{\text{H,H}} = 6.1$ Hz, 12H, CH_3 , *iPr*), 2.31 (*s*, 3H, CH_3 , Me), 4.83 (*d*, sept, $^3J_{\text{POCH}} = 7.1$ Hz, $^3J_{\text{H,H}} = 6.0$ Hz, 2H, OCH), 6.94–7.61 (*m*, overlapping with the solvent signal, $\text{C}_6\text{H}_4 + \text{PNH}$), 9.42 (*s*, 1H, NH); $^{31}\text{P}\{^1\text{H}\}$ NMR δ (ppm): –6.4.

2.1b **HL^{II}** Yield: 1.62 g (94%); m.p.: 89°C; Anal. Calcd. for $\text{C}_{15}\text{H}_{25}\text{N}_2\text{O}_3\text{PS}$ (344.41): C, 52.31; H, 7.32; N, 8.13; Found: C, 52.20; H, 7.37; N, 8.05; ^1H NMR δ (ppm): 1.43 (*d*, $^3J_{\text{H,H}} = 6.1$ Hz, 6H, CH_3 , *iPr*), 1.46 (*d*, $^3J_{\text{H,H}} = 6.2$ Hz, 6H, CH_3 , *iPr*), 2.32 (*s*, 6H, CH_3 , Me), 4.87 (*d*, sept, $^3J_{\text{POCH}} = 7.2$ Hz, $^3J_{\text{H,H}} = 6.1$ Hz, 2H, OCH), 7.09–7.36 (*m*, overlapped with the solvent signal, $\text{C}_6\text{H}_3 + \text{PNH}$), 9.59 (*s*, 1H, NH) ppm. $^{31}\text{P}\{^1\text{H}\}$ NMR δ (ppm): –6.3.

2.1c **HL^{III}** Yield: 1.29 g (72%); m.p.: 97°C; Anal. Calcd. for $\text{C}_{16}\text{H}_{27}\text{N}_2\text{O}_3\text{PS}$ (358.44): C, 53.62; H, 7.59; N, 7.82; Found: C, 53.71; H, 7.68; N, 7.89; ^1H NMR δ (ppm): 1.42 (*d*, $^3J_{\text{H,H}} = 6.2$ Hz, 12H, CH_3 , *iPr*), 2.24 (*s*, 6H, CH_3 , Me), 2.29 (*s*, 3H, CH_3 , Me), 4.77 (*d*, sept, $^3J_{\text{POCH}} = 6.8$ Hz, $^3J_{\text{H,H}} = 6.2$ Hz, 2H, OCH), 6.91 (*s*, 2H, C_6H_2), 7.02 (*br, s*, 1H, PNH), 10.07 (*s*, 1H, NH); $^{31}\text{P}\{^1\text{H}\}$ NMR δ (ppm): –5.9.

2.2 Physical measurements

NMR spectra in CDCl_3 were obtained on a Bruker Avance 300 MHz spectrometer at 25°C. ^1H and $^{31}\text{P}\{^1\text{H}\}$ NMR spectra were recorded at 299.948 and 121.420 MHz, respectively. Chemical shifts are reported with reference to SiMe_4 (^1H) and 85% H_3PO_4 ($^{31}\text{P}\{^1\text{H}\}$). Elemental analyses were performed on a CHNS HEKAtech EuroEA 3000 analyser.

2.3 Crystal structure determination and refinement

The X-ray data for **HL^{III}** were collected on STOE IPDS-II diffractometer with graphite-monochromatized Mo- K_α radiation generated by fine-focus X-ray tube operated at 50 kV and 40 mA. The images were indexed, integrated and scaled using the X-ray data reduction package.¹³ Data were corrected for absorption using the PLATON program.¹⁴ The structures were solved by direct methods using the SHELXS-97 program¹⁵ and refined first isotropically and then anisotropically using SHELXL-97.¹⁵ Hydrogen atoms were revealed from $\Delta\rho$ maps and those bound to C were refined using appropriate

riding models. H atoms bound to N were freely refined.

CCDC 737532 (**HL^{III}**) contains the supplementary crystallographic data. These data can be obtained free of charge via <http://www.ccdc.cam.ac.uk/conts/retrieving.html>, or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or e-mail: deposit@ccdc.cam.ac.uk.

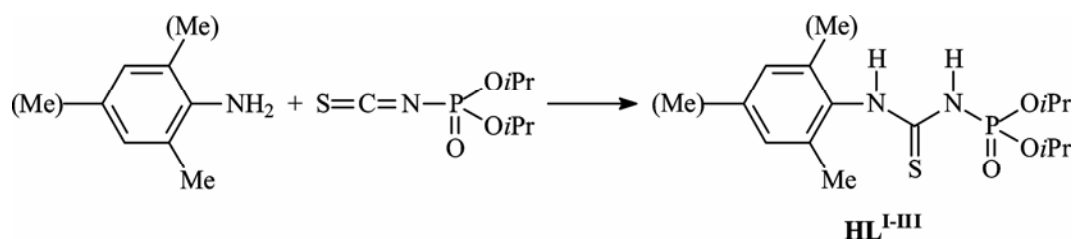
3. Results and discussion

The compounds **HL^{I-III}** were synthesized by treating 2-methylaniline, 2,6-dimethylaniline or 2,4,6-trimethylaniline with the isothiocyanate (*iPrO*)₂P(O)NCS (scheme 1) in good yields for **HL^I** and **HL^{II}** and reasonable yield for **HL^{III}**. Their compositions were proved by microanalysis data (see Experimental Section). The formation of **HL^{I-III}** by the addition reaction of the NH_2 group of the corresponding amine and (*iPrO*)₂P(O)NCS was proved by the NMR data.

The $^{31}\text{P}\{^1\text{H}\}$ NMR spectra of **HL^{I-III}** each contain a singlet signal at –6.4, –6.3 and –5.9 ppm, respectively, which is typical for *N*-phosphoryl thioureas.¹¹ The ^1H NMR spectra of the thioureas contain one set of signals for the *iPr* protons: one doublet (**HL^I** and **HL^{III}**) or two doublets (**HL^{II}**) for the CH_3 protons at 1.39–1.46 ppm and a doublet of septets for the CH protons in the range of 4.77–4.87 ppm. The Me proton signals of the aryl substituents were observed at 2.24–2.32 ppm. The aromatic ring and PNH proton signals are at 6.91–7.61 ppm. Signals for the arylNH protons in the spectra are at 9.42–10.07 ppm. These signals are low-field shifted probably due to the formation of hydrogen bonds of the type arylN–H...O=P, as has been observed for related thiophosphorylated thioureas.

Crystals of **HL^{III}** were obtained by recrystallization from dichloromethane–*n*-hexane solution. The crystal structure data is collected in table 1, while the molecular conformation and geometric parameters are shown in figure 1.

The compound **HL^{III}** crystallizes in the space group *P*–1. The asymmetric unit contains two independent molecules. The parameters of the C=S, C–N, P–N and P=O bonds observed for **HL^{III}** (figure 1) are in the typical range for *N*-phosphorylated thiourea derivatives.¹² The S–C–N–P backbone in the crystal phase has a *E*-conformation. The aryl fragment is almost orthogonal to the N–C(S)–N–P

**Scheme 1.****Table 1.** Crystal structure and data refinement parameters for **HL^{III}**.

Empirical formula	C ₁₆ H ₂₇ N ₂ O ₃ PS
Formula weight (g mol ⁻¹)	358.43
Temperature (K)	173(2)
Crystal system	triclinic
Space group	<i>P</i> -1
<i>a</i> (Å)	10.6334(7)
<i>b</i> (Å)	13.4890(8)
<i>c</i> (Å)	15.7710(10)
α (°)	82.491(5)
β (°)	70.663(5)
γ (°)	67.113(5)
<i>V</i> (Å ³)	1966.4(2)
<i>Z</i>	4
<i>D</i> _{calc} (Mg m ⁻³)	1.211
Absorption coefficient, μ (mm ⁻¹)	0.260
<i>F</i> (000)	768
Crystal size (mm)	0.32 × 0.26 × 0.21
Recording range, θ (°)	3.55–25.59
Number of recorded reflections	21017
Number of recorded independent reflections	7336 [<i>R</i> (int) = 0.0465]
Final <i>R</i> indices [<i>I</i> > 2 sigma(<i>I</i>)]	<i>R</i> 1 = 0.0389, <i>wR</i> 2 = 0.0937
<i>R</i> indices (all data)	<i>R</i> 1 = 0.0568, <i>wR</i> 2 = 0.0989
<i>S</i>	0.951

Table 2. Hydrogen bond lengths (Å) and angles (°) for **HL^{III}**.

D–H...A	<i>d</i> (D–H)	<i>d</i> (H...A)	<i>d</i> (D...A)	\angle (DHA)
N(1)–H(1)...S(1A)#1	0.85(3)	2.51(3)	3.328(2)	164(2)
N(2)–H(2)...O(3)	0.82(3)	2.22(3)	2.920(2)	143(2)
N(2)–H(2)...O(3')	0.82(3)	2.18(3)	2.811(10)	133(2)
N(2)–H(2)...O(3A)	0.82(3)	2.27(3)	2.927(2)	136(2)
N(1A)–H(1A)...S(1)#2	0.83(3)	2.50(3)	3.317(2)	166(2)
N(2A)–H(2A)...O(3)	0.79(3)	2.30(3)	2.943(2)	139(2)
N(2A)–H(2A)...O(3')	0.79(3)	2.19(3)	2.761(8)	130(2)
N(2A)–H(2A)...O(3A)	0.79(3)	2.22(2)	2.874(2)	141(2)

Symmetry transformations used to generate equivalent atoms: #1 $x + 1, y, z$; #2 $x - 1, y, z$.

plane. The crystal structure is stabilized by intramolecular hydrogen bonds of the types N(2)–H(2)...O(3)[O(3')]–P(1) and N(2A)–H(2A)...O(3A)–P(1A) (figure 1, table 2). Two independent molecules form a dimer due to intermolecular hydrogen

bonds of the types N(2)–H(2)...O(3A)–P(1A) and N(2A)–H(2A)...O(3)[O(3')]–P(1) (figure 1, table 2). Yet another mode of aggregation is found for this dimer. Two independent molecules exhibit interactions between the OCH hydrogen atoms and the aryl

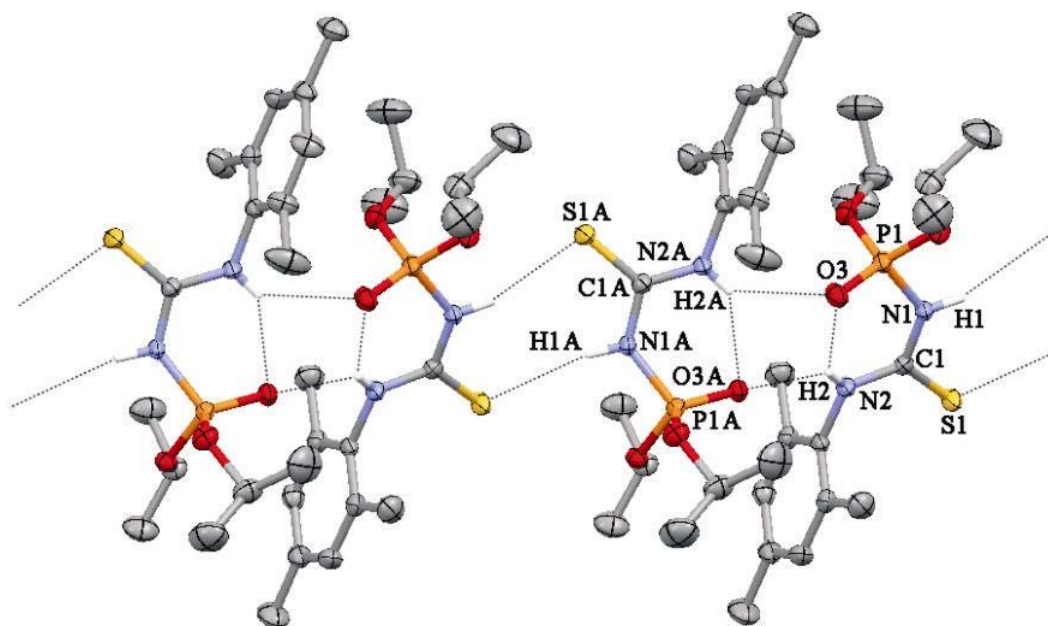


Figure 1. View on the crystal structure of **HL^{III}**. Ellipsoids are drawn at the 50% probability level. H-atoms, not involved in hydrogen bonding, are omitted for clarity. Selected bond distances (Å) and angles (°): P(1)–O(3) 1.482(2), P(1)–O(3′) 1.391(7), P(1)–N(1) 1.656(2), S(1)–C(1) 1.675(2), N(1)–C(1) 1.383(2), N(2)–C(1) 1.333(2), P(1A)–O(3A) 1.4656(14), P(1A)–N(1A) 1.658(2), S(1A)–C(1A) 1.673(2), N(1A)–C(1A) 1.378(2), N(2A)–C(1A) 1.334(2); O(3)–P(1)–N(1) 113.29(9), O(3′)–P(1)–N(1) 116.3(4), C(1)–N(1)–P(1) 128.61(14), N(2)–C(1)–N(1) 117.1(2), N(1)–C(1)–S(1) 119.45(14), N(2)–C(1)–S(1) 123.44(13), O(3A)–P(1A)–N(1A) 113.02(8), C(1A)–N(1A)–P(1A) 128.27(14), N(2A)–C(1A)–N(1A) 116.8(2), N(1A)–C(1A)–S(1A) 120.05(14), N(2A)–C(1A)–S(1A) 123.11(14).

Table 3. Selected C–H... η^6 -phenyl interactions for **HL^{III}**.

C–H	Cg(<i>J</i>) ^a	H...Cg (Å)	C...Cg (Å)	C–H...Cg (°)
C(5)–H(5)	Cg(2) ^{#1}	2.96	3.876(3)	153
C(5A)–H(5A)	Cg(1) ^{#1}	2.53	3.497(3)	163

^aCg refers to the ring center of gravity and the numbers represent the rings involved in the interactions.

^bSymmetry codes: #1 *x*, *y*, *z*. Cg(1): C(11)–C(12)–C(13)–C(14)–C(15)–C(16); Cg(2): C(11A)–C(12A)–C(13A)–C(14A)–C(15A)–C(16A).

rings of an adjacent molecule (table 3). Furthermore, dimers form polymeric chains due to the intermolecular hydrogen bonds of the types N(1)–H(1)···S(1A)#1–C(1A)#1 and N(1A)–H(1A)···S(1)#2–C(1)#2 (figure 1, table 2).

4. Conclusions

In summary, we have demonstrated the syntheses of three new *N*-phosphorylated thioureas **HL^{I–III}** by addition of phosphorylisothiocyanate to the corresponding amine.

Single crystal X-ray diffraction studies showed that the thiourea **HL^{III}** forms both intra- and intermolecular hydrogen bonds in the solid, which leads to the formation of polymeric chains. Moreover, intermolecular C–H... η^6 -phenyl interactions were established in **HL^{III}**.

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