REACTION OF THIOPHOSPHORYL TRICHLORIDE WITH *N,N′*-DIPHENYLTHIOUREA

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New heterocyclic thiophosphoric compounds containing the N–C–N sequence in the ring were prepared by the reaction of thiophosphoryl trichloride ($PSCl_3$) with *N,N′*-diphenylthiourea. Depending on the reaction conditions, two types of heterocyclic compounds were obtained, namely 2-chloro-1,3-diphenyl-1,3,2λ^5-diazaphosphetidine-2,4-dithione (**1**) and 2-chloro-1,3,5-triphenyl-1,3,5,2λ^5-triazaphosphinane-2,4,6-trithione (**2**). *N,N′,N″*-Triphenylguanidinium chloride (**3**) was identified in the reaction mixture as a by-product in all cases. The course of reactions was followed by ^{31}P NMR spectroscopy and compound **3** was characterized by single-crystal X-ray diffraction.

Keywords: Thiophosphoric compounds; Triphenylguanidinium chloride; Diazaphosphetidine; Triazaphosphinane; Phosphaheterocycles; Phosphorus.

Thiophosphoric acid chlorides are often used for syntheses of many thiophosphoric compounds including heterocycles where the phosphorus atom is a member of the ring[1–4]. The main reaction type is nucleophilic substitution of a halogen atom. It is supposed that the phosphorus atom in $PSCl_3$ is attacked, e.g., by nitrogen atoms of a nucleophilic reagent, and chlorine atoms are replaced.

The size and composition of heterocycles are usually strongly influenced by reaction conditions. The reaction between pyridinium phosphorochloridodithioate ($pyPS_2Cl$) and urea, e.g., leads to the formation of the cyclic ammonium 4,6-dioxo-2-thioxo-1,3,5,2λ^5-triazaphosphinane-2-thiolate. This compound can react first with aqueous solution of NH_4HCO_3 (ref.[5]) and then either with H_2O_2 yielding ammonium 2,4,6-trioxo-1,3,5,2λ^5-triazaphosphinane-2-olate or methyl chloroacetate yielding ammonium 4,6-dioxo-2-thioxo-1,3,5,2λ^5-triazaphosphinane-2-olate. The reaction of $pyPS_2Cl$ with *N,N′*-diphenylthiourea yields, depending on reaction conditions, two different heterocyclic compounds, pyridinium 1,3-diphenyl-2,4-dithioxo-1,3,2λ^5-

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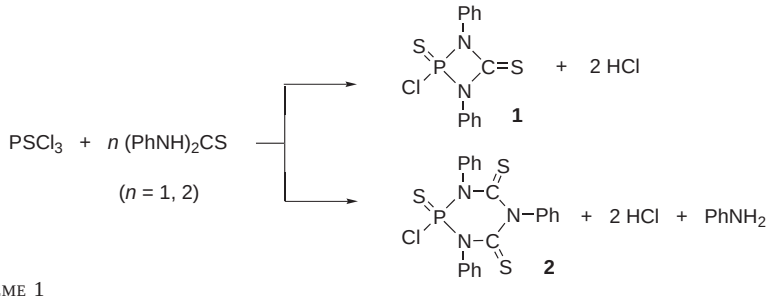
diazaphosphetidine-2-thiolate and pyridinium 1,3-diphenyl-2,4-dithioxo-1,3,2λ^5,4λ^5-diazadiphosphetidine-2,4-dithiolate. The latter substance is formed in the presence of triethylamine as an HCl acceptor[6].

The investigation of reactions between $PSCl_3$ and *N*-nucleophiles leads to many compounds that can be used in pharmaceutical industry, e.g. *N*,*N*′,*N*″-triethylenethiophosphoramide (thioTEPA)[7] serves as a polyfunctional alkylating agent in the treatment of cancer[8]. This article describes the reaction between $PSCl_3$ and *N*,*N*′-diphenylthiourea, $(PhNH)_2CS$. The course of the reaction is markedly different from previously studied reaction, in which $pyPS_2Cl$ was used as a substrate[6], when heterocyclic compounds containig exocyclic PS_2 group were formed together with pyridinium chloride as a by-product. In the case of the reaction $PSCl_3$ with $(PhNH)_2CS$, we obtained compounds **1** and **2** together with unexpectedly formed *N*,*N*′,*N*″-triphenylguanidinium chloride (**3**; Scheme 1).



SCHEME 1

RESULTS AND DISCUSSION

Synthesis

The reactions between $PSCl_3$ and $(PhNH)_2CS$ were carried out in acetonitrile solution at various reaction conditions with the aim to prepare the desired compounds **1** and **2**. The reaction conditions are described in Table I. The molar ratio of starting compounds $PSCl_3$ and $(PhNH)_2CS$ was kept at 1:2 in the absence of pyridine (reaction mixture A) or at 1:1 in the presence of pyridine (reaction mixture B) that played the role of HCl acceptor. The course of reactions was followed by ^{31}P NMR spectroscopy over the period of several weeks. Chemical shifts are shown in Table I.

It follows from ^{31}P NMR measurements that a mixture of reaction products is mostly formed in the course of the reaction. This situation is documented by the NMR spectrum which corresponds to the reaction mixture A

at 20 °C after 18-h reaction (Table I). However, the composition of the reaction mixture is time dependent and that is why it was not possible to identify all intermediates (δ 85.4, 93.9 ppm). Within 14 days, these intermediates were gradually converted to only one reaction product with chemical shift δ 83.7 ppm. This resonance signal (Table I) was assigned to compound **1**. The same product can be prepared also by refluxing the reaction mixture A at 82 °C for 2 h.

When starting compounds were allowed to react in the presence of pyridine at ambient temperature for 14 days (reaction mixture B), compound **2** (with chemical shift 108.7 ppm, see Table I) was formed besides compound **1**. Single reaction product **2** can be obtained after refluxing the reaction mixture B for 3 h (Table I). After solvent evaporation, both substances form yellow oily liquids. Attempts to grow crystals were even after cooling solutions of **1** or **2** to –90 °C unsuccessful. The procedure yielded only amorphous, glassy substances. As follows from Table I, it is necessary to use different approaches for preparation of compounds **1** and **2**.

*Formation of Compound **3***

A white crystalline substance precipitated in the course of reaction in both cases. IR spectra of these solids were identical and therefore this compound was further denoted as **3**. In the presence of pyridine, compound **3** precipitated together with pyridinium chloride, which was proved by IR spectroscopy. The precipitation of **3** was accelerated when acetonitrile was partially evaporated.

TABLE I
Reaction of $PSCl_3$ and $(PhNH)_2CS$

Reaction mixture	Molar ratio $PSCl_3$:$(PhNH)_2CS$:(py[a])	Reaction temperature ° C	Reaction time	$\delta(^{31}P)$, ppm
A	1:2	20	18 h	83.7; 85.4; 93.9; 108.7
			14 d	83.7
	1:2	82	2 h	83.7
B	1:1:2	20	14 d	83.7; 108.7
		82	3 h	108.7

[a] py = pyridine.

*Identification of Compounds **1** and **2***

Both reaction products were investigated by mass spectrometry. The mass of compound **1** was found at *m/z* = 324 (exact mass is 323.971150), the molecular peak of **2** at *m/z* = 460 (exact mass is 458.985419). The found masses of fragments also support the formation of compounds **1** and **2**.

We also tried to substitute chlorine atom of compounds **1** and **2** by their reaction with ethylamine, *tert*-butylamine or aniline with the aim to prepare crystalline compounds that could be better identified, e.g., by X-ray diffraction. Unfortunately, these reactions led to decomposition of **1** or **2** (in the case of ethylamine or *tert*-butylamine) or no reaction was observed (aniline).

*Identification of Compound **3***

Mass spectrometry measurement determined *m/z* = 287 for compound **3**. The masses of fragments and their comparison with the library of mass spectra[9] led to the conclusion that this substance can be *N*,*N*′,*N*″-triphenylguanidine (exact mass 287.142249). However, X-ray diffraction studies of **3** (see below) proved that compound **3** is in fact *N*,*N*′,*N*″-triphenylguanidinium chloride.

The formation of compound **3** in the reaction mixture can be explained by two routes:

a) It is known that *N*,*N*′-diphenylthiourea decomposes in acid media into aniline and phenyl isothiocyanate[10]. The decomposition products, aniline and phenylisothiocyanate, then react with HCl to form *N*,*N*′,*N*″-triphenylguanidinium chloride and CS_2.

b) Aniline, which is formed during the formation of the six-membered cycle (see Scheme 1), reacts in acid media with *N*,*N*′-diphenylthiourea forming *N*,*N*′,*N*“-triphenylguanidinium chloride.

*Crystal Structure of N,N′,N“-Triphenylguanidinium Chloride (**3**)*

The crystal structure of **3** has not been published so far. Compound **3** crystallizes in the monoclinic space group $P2_1/c$. All details of crystallographic determinations are given in Tables II and III and the molecular structure of **3** is drawn in Fig. 1. The asymmetric unit of compound **3** contains one formula unit the cation and anion of which are in general positions. Crystallographic data for *N*,*N*′,*N*″-triphenylguanidinium nitrate[11] or pure *N*,*N*′,*N*″-

triphenylguanidine (as monomer or trimer)[12,13] were reported (see the comparison in Table III).

The angles around the central carbon atom of the *N*,*N*′,*N*″-triphenylguanidinium cation (almost 360°) indicate planarity of the CN_3 unit whereas the mean deviation of the C(19) carbon atom from the plane N(1)–N(2)–N(3) is only 0.0019 Å. The lengths of C(19)–N bonds are between 1.333 and 1.340 Å which is comparable with the lengths of analo-

TABLE II
Basic crystallographic data and structure refinement for compound **3**

Empirical formula	$C_{19}H_{18}Cl_1N_3$
Formula weight	323.8
Temperature, K	183(2)
Crystal system	monoclinic
Space group	$P2_1/c$
Unit cell dimensions	
a, b, c, Å	14.0019(4), 15.8702(5), 7.7796(2)
α, β, γ, °	90, 101.5160(10), 90
Cell volume, $Å^3$	1693.93(8)
Calculated density, Mg/m^3	1.270
Formula units per unit cell	4
X-ray	MoKα
Wavelength, Å	0.71069
Absorption coefficient, mm^{-1}	0.228
Crystal size, mm^{-1}	0.40 × 0.30 × 0.20
θ range for data collection, °	1.96 to 27.01
Reflections collected/unique	15894/3670 [*R*(int) = 0.0211]
Completeness to θ = 25.00, %	99.9
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8620 and 0.7555
Refinement method	Full-matrix least-squares on F2
Goodness-of-fit on F^2	1.070
Final *R* indices [$I > 2\sigma(I)$]	R_1 = 0.0299, wR_2 = 0.0757
R indices (all data)	R_1 = 0.0432, wR_2 = 0.0791
Largest diff. peak and hole, eA^{-3}	0.159 and –0.217

TABLE III
Comparison of selected geometric parameters of compound **3** with structure data of similar compounds. Space groups in parentheses

Bond, Å Angle, °	3 ($P2_1/c$)	$TPGH^+NO_3^-$ [11] ($P\text{-}42_1/c$)	TPG [12] ($Pna2_1$)	TPG_3 [13] ($P2_1/c$)
N(1)–C(18)	1.425	1.427	1.430	1.453
N(1)–C(19)	1.340	1.355	1.362	1.390
N(2)–C(15)	1.426	1.440	1.429	1.415
N(2)–C(19)	1.334	1.335	1.335	1.264
N(3)–C(16)	1.429	1.442	1.414	1.452
N(3)–C(19)	1.333	1.354	1.321	1.409
N(1)–C(19)–N(2)	120.9	115.1	113.8	128.8
N(3)–C(19)–N(1)	117.2	118.7	117.9	113.8
N(3)–C(19)–N(2)	121.9	126.2	128.4	117.3
C(18)–N(1)–C(19)	127.9	124.5	126.0	117.6
C(15)–N(2)–C(19)	124.8	124.5	125.7	125.3
C(16)–N(3)–C(19)	124.7	124.1	120.2	116.9

[a] TPG = *N*,*N*′,*N*″-triphenylguanidine.

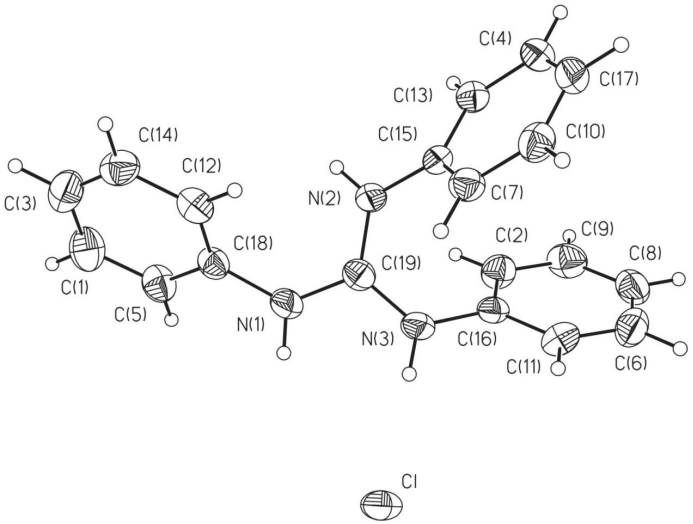


FIG. 1
The molecular structure of **3** (thermal ellipsoids are drawn at the 50% probability level)

gous bonds in *N*,*N*′,*N*″-triphenylguanidine, its trimer, nitrate[11–13], and other guanidine derivatives[14,15]. It follows from the data in Table III that the greatest differences in C(arom)–N bond lengths are in the trimer.

Two types of hydrogen bonds are present in the crystal structure of compound **3**. The chlorine atom is surrounded with two NH groups which belong to two different cations (Table IV). The angle around the chlorine atom is 127.1° and indicates linear bent orientation of the Cl-H_2 unit. The crystal packing overview of the compound **3** is shown in Fig. 2.

TABLE IV
Hydrogen bond parameters (in Å and °) for compound **3**

D–H···A	d(D–H)	d(H···A)	d(D···A)	<(DHA)
N(3)–H(3N)···Cl^{i}	0.843(16)	2.257(17)	3.0963(11)	173.8(14)
N(2)–H(2N)···Cl^{i}	0.843(16)	2.257(17	3.0963(11)	173.8(14)

Symmetry transformations used to generate equivalent atoms: (i) $-x + 1$, $y - 1/2$, $-z + 1/2$.

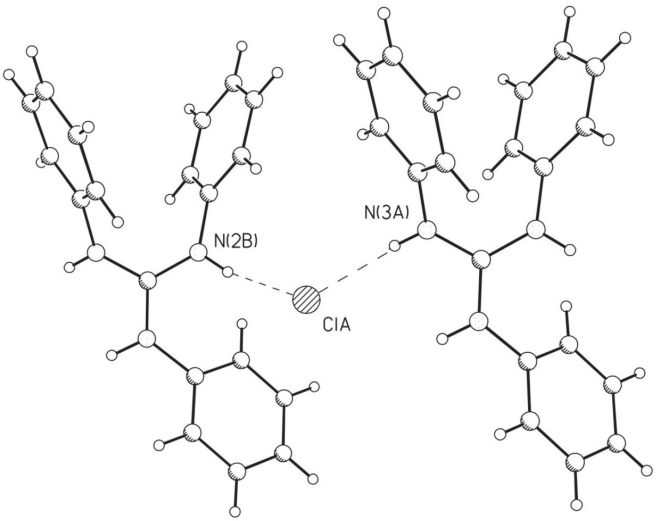


FIG. 2
Weak bonding interactions in compound **3** (thermal ellipsoids are drawn at the 50% probability level)

EXPERIMENTAL

Materials

$(PhNH)_2CS$ (Fluka) was dissolved in boiling ethanol and precipitated by adding hot water[16]. $PSCl_3$ was prepared from PCl_3 and sulfur in the presence of $AlCl_3$ (ref.[17]). Purification of acetonitrile and pyridine was carried out according to the known procedures[16].

General Procedure

All reactions and subsequent manipulations were carried out in the atmosphere of dry nitrogen.

Apparatus and Methods

^1H, ^{13}C and ^{31}P NMR spectra were recorded on a 500 MHz NMR spectrometer Bruker DRX Avance. Chemical shifts are given in ppm (δ-scale) relative to 85% H_3PO_4 as an external standard. Mass spectrometric analyses were performed on a multifunctional quadrupole spectrometer TRIO 1000 Series II, Finnigan MAT, Fisons Instruments. The ionization energy was 35 eV (for compounds **1** and **2**) and 70 eV (for compound **3**). The samples were inserted into the spectrometer by the Direct Insert Probe. FT-IR spectra were measured on an Equinox 55/S/NIR FTIR Bruker spectrometer. Compound **3** was analyzed in Nujol. Crystal structure determination was performed with a three-circle diffractometer Siemens Smart-CCD by the ω-scan method using a graphite monochromatized MoKα radiation (λ = 0.71069 Å). The structure was solved by direct methods. Non-hydrogen atoms were refined anisotropically while hydrogen atoms were inserted in calculated positions and isotropically refined assuming a "ride-on" model. The SHELX97 [18] program package was used for the structure determination; drawings were made with XP program of Bruker SHELXTL NT, Version 5.1 [19]. CCDC 284389 (for compoond **3**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via 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 336033; or deposit@ccdc.cam.ac.uk).

2-Chloro-1,3-diphenyl-1,3,2λ^5-diazaphosphetidine-2,4-dithione (**1**)

A solution of 1 g $PSCl_3$ (5.90 mmol) in 15 cm^3 CH_3CN was added to a suspension of 2.7 g (11.83 mmol) $(PhNH)_2CS$ in 30 cm^3 CH_3CN and the reaction mixture was refluxed at 82 °C for 2 h. The reaction mixture turned pale yellow and first portion of a white solid **3** precipitated. The solution was then concentrated under vacuum and further portion of precipitated compound **3** was filtered off. The solvent was then completely evaporated. Compound **1** was isolated as a viscous yellow liquid always slightly contaminated with **3**. Yield 1.67 g (87% based on $PSCl_3$). ^1H NMR (CH_3CN): 7.25–7.40 m, 10 H (ArH). ^{13}C NMR (CH_3CN): 126.46 s (Ar); 128.44 s (Ar); 130.58 s (Ar); 131.33 s (Ar); 150.9 s (CS). ^{31}P NMR (CH_3CN): 83.7 s. EI MS, *m/z* (%): 324 (1) $C_{13}H_{10}ClN_2PS_2$, 180 (3) $C_7H_5N_2PS$, 167 (3) C_7H_6NPS, 154 (2) C_6H_5NPS, 151 (3) $C_7H_7N_2S$, 135 (44) C_7H_5NS, 118 (19) $C_7H_6N_2$, 103 (3) CN_2PS, 93 (100) C_6H_7N, 77 (44) C_6H_5, 63 (8) PS. IR: 3399 (sh), 3313 (sh), 3174 (sh), 3079 (sh) ν_{CH}, 3051 (sh) ν_{CH}, 3035 (sh) ν_{CH}, 3005 (sh) ν_{CH}, 2944 (sh), 2888 (sh), 2768 (sh), 2702 (sh), 2556 (vw), 2457 (vw), 2162 (s), 2089 (vs), 1666 (s) δ_{CH}, 1629 (s) ν_{CC}, 1585 (sh) ν_{CC}, 1582 (vs) ν_{CC}, 1492

(s) δ_{CH}, 1441 (w) δ_{CH}, 1352 (w) δ_{CH}, 1071 (w) δ_{CH}, 752 (vs) PS, 704 (sh), 691 (s) PS, 577 (m) PS, 504 (w) ν_{PCl}, 489 (w) ν_{PCl}, 443 (w).

2-Chloro-1,3,5-triphenyl-1,3,5,2λ^5-triazaphosphinane-2,4,6-trithione (**2**)

A mixture of 0.7 g (4.13 mmol) $PSCl_3$, 0.95 g (4.13 mmol) $(PhNH)_2CS$, 2.0 g (8.26 mmol) pyridine, and 25 cm^3 CH_3CN was refluxed for 3 h. Then CH_3CN was partially evaporated and the precipitated solid, a mixture of compound **3** and pyHCl, was filtered off. The solvent was then completely removed. Compound **2** was isolated as a viscous yellow liquid. Yield 1.88 g (98% based on $PSCl_3$). ^{1}H NMR (CH_3CN): 7.2–7.5 m, 15 H (ArH). ^{13}C NMR (CH_3CN): 120.2 s (Ar); 124.3 s (Ar); 126.3 s (Ar); 128.3 s (Ar); 128.5 s (Ar); 129.1 s (Ar); 136.8 s (Ar); 139.5 s (Ar); 236.7 s (CS). ^{31}P NMR (CH_3CN): 108.7 s. EI MS, *m/z* (%): 460 (1) $C_{20}H_{15}ClN_3PS_3$, 383 (5) $C_{14}H_{10}ClN_3PS_3$, 324 (1) $C_{13}H_{10}ClN_2PS_2$, 271 (2) $C_8H_6N_3PS_3$, 167 (2) C_7H_6NPS, 154 (6) C_6H_5NPS, 135 (100) C_7H_5NS, 118 (31) $C_7H_6N_2$, 103 (6) CN_2PS, 93 (55) C_6H_7N, 77 (90) C_6H_5, 63 (27) PS. IR: 2377–2867 (s), 2347 (m), 2291 (m), 1992 (s) δ_{CH}, 1572 (m) ν_{CC}, 1560 (sh) ν_{CC}, 1486 (vs) ν_{CC}, 1197 (w) δ_{CH}, 1054 (m) δ_{CH}, 1002 (m), 964 (m) δ_{CH}, 682 (vs) PS, 608 (m) PS, 596 (m) PS, 507 (w) ν_{PCl}, 437 (w).

N,*N*′,*N*″-Triphenylguanidinium Chloride (**3**)

Compound **3** was formed in the case of both described reactions between $PSCl_3$ and $(PhNH)_2CS$ as a by-product. M.p. 252–255 °C (decomp.). ^{1}H NMR ($CDCl_3$): 7.05–7.19 m, 15 H (ArH); 10.08 bs, 3 H (NH). ^{13}C (APT) NMR ($CDCl_3$): 124.26 s (Ar); 127.42 s (Ar); 129.83 s (Ar); 134.84 s, 3 C (C_{arom}-N); 153.12 s, 1 C (CN_3). EI MS, *m/z* (%): 287 (47) $C_{19}H_{17}N_3$, 194 (100) $C_{13}H_{10}N_2$, 168 (4) $C_{12}H_{10}N$, 118 (7) $C_7H_6N_2$, 104 (8) C_7H_6N, 93 (95) C_6H_7N, 77 (46) C_6H_5. IR: 3277 (m), 3209 (m), 3156 (m), 3105 (m), 3047 (m), 3028 (m) ν_{NH}, 2987 (sh) ν_{NH}, 1644 (m) $\nu_{C=N}$, 1603 (w) ν_{CC}, 1598 (m) ν_{CC}, 1579 (m) ν_{CC}, 1540 (m) ν_{CN}, 1495 (m) ν_{CC}, 1445 (m) ν_{CC}, 1323 (m) ν_{CC}, 1313 (sh) ν_{CC}, 1292 (w) δ_{CH}, 1256 (m) δ_{CH}, 756 (m) γ_{CH}, 749 (sh) γ_{CH}, 731 (m) γ_r, 696 (w) δ_{CC} + ν_{CC}, 689 (m).

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