Carbamoyl and Thiocarbamoyl Derivatives of 3-Aminopropyl-dimethyl-phosphine Oxide

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Dedicated to Professor Marko Kirilov on the occasion of his 80th birthday

A series of fourteen new 3-[N-substituted carbamoyl (or thiocarbamoyl)]-aminopropyl-dimethyl-phosphine oxides have been synthesized and characterized. The compounds were prepared *via* reaction of the 3-aminopropyl-dimethyl-phosphine oxide with the corresponding isocyanates or isothiocyanates. The composition of the compounds was proved by elemental analysis and the structures were confirmed by IR, ^{1}H, ^{31}P, ^{31}P{^{1}H} NMR spectroscopy and by mass spectrometry. The structures of 3[(N-phenyl-thiocarbamoyl)amino]propyl-dimethyl-phosphine oxide (**5**), 3[(N-4-chlorophenyl-thiocarbamoyl)amino]propyl-dimethyl-phosphine oxide (**6**), and 3[(N-benzyl-thiocarbamoyl)amino]propyl-dimethyl-phosphine oxide (**9**) have been confirmed by X-ray diffraction.

Key words: 3-[N-Substituted Carbamoyl (or Thiocarbamoyl)]-aminopropyl-dimethyl-phosphine Oxides, Phosphorus-Containing Ureas and Thioureas, Tertiary Phosphine Oxide

Introduction

Aminophosphonates and tertiary phosphine oxides, containing an amino group, are distinguished by their high reactivity as nucleophilic reagents in the preparation of various polyfunctional nitrogen-containing organophosphorus compounds [1 – 4].

The interaction between esters of aminophosphonic acids with iso- and isothiocyanates [5] and the reaction kinetics [6], as well as the reaction of aminomethyl-dimethyl-phosphine oxide (AMPO) and bis(dimethylphosphinyl-methylene)amine (BDMPO) with iso- and isothiocyanates [7, 8] have been studied. The basicity of AMPO and BDMPO [9, 10] is lower than that of primary and secondary aliphatic monoamines [11], due to the electron withdrawing effect of the phosphoryl group in the molecules. In spite of the relatively low basicity of the amino groups in these compounds their nucleophilicity is very high. The primary amine AMPO interacts very easily with aldehydes [3], oxiranes and bis-oxiranes [12, 13] and forms coordination compounds with metal salts very easily [14, 15].

It was shown that some of the compounds prepared from AMPO exhibit biological activity. Its platinum complexes and nitrosourea derivative possess antitumor activity and are of low toxicity [16, 17].

The introduction of carbamoyl and thiocarbamoyl groups in the structure of polyfunctional organophosphorus compounds improves their physiological activity [18] along with their complexation ability.

The present work is a continuation of previous investigations of some of us on the preparation of new carbamoyl and thiocarbamoyl derivatives of tertiary phosphine oxides functinalised with primary and secondary amino groups [7, 8]. We report here the synthesis and characterization of 3-[N-substituted carbamoyl (and thiocarbamoyl)] – aminopropyl-dimethyl-phosphine oxides **1 – 14**, which are expected to exhibit biological activity and complex-formation properties with metal ions.

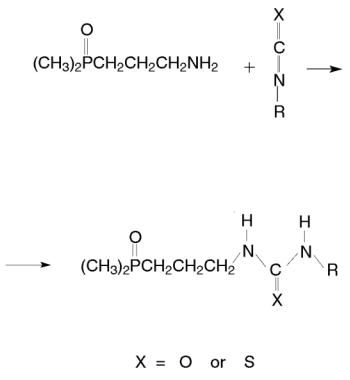
Table 1. Preparative and analytical data of compounds with general formula $(CH_3)_2P(O)CH_2CH_2CH_2NH\text{-}C(X)\text{-}NH\text{-}R$ **1 – 14**.

Comp. No	R	X	M. p. (°C)	Formula mol. mass	Yield %	Nitrogen (%) found	Nitrogen (%) calcd.
1	C_6H_5–	O	168 – 169	$C_{12}H_{19}N_2O_2P_2$ 254.27	96	10.86	11.02
2	3–ClC_6H_4–	O	151 – 152.5	$C_{12}H_{18}ClN_2O_2P$ 288.72	99	9.78	9.70
3	1–Naphthyl	O	183 – 184	$C_{16}H_{21}N_2O_2P$ 304.33	97	9.12	9.20
4	Cyclohexyl	O	127 – 128	$C_{12}H_{25}N_2OP$ 260.32	98	10.60	10.76
5	C_6H_5–	S	169 – 170	$C_{12}H_{19}N_2OPS$ 270.34	97	10.12	10.36
6	4–ClC_6H_4–	S	201.5 – 202.5	$C_{12}H_{18}ClN_2OPS$ 304.78	98	9.08	9.19
7	4–$CH_3OC_6H_4$–	S	172 – 173	$C_{13}H_{21}N_2O_2PS$ 300.36	96	9.56	9.33
8	4–$CH_3C_6H_4$–	S	186 – 187	$C_{13}H_{21}N_2OPS$ 284.37	94	9.70	9.85
9	$C_6H_5CH_2$–	S	159.5 – 160.5	$C_{13}H_{21}N_2OPS$ 284.37	95	9.85	9.72
10	$C_6H_5CH_2CH_2$–	S	143 – 144	$C_{14}H_{23}N_2OPS$ 298.39	99	9.43	9.39
11	Cyclohexyl	S	175 – 176	$C_{12}H_{25}N_2OPS$ 276.39	95	10.02	10.14
12	C_2H_5–	S	135 – 136	$C_8H_{19}N_2OPS$ 222.29	97	12.52	12.60
13	n–C_4H_9–	S	86 – 86.5	$C_{10}H_{23}N_2OPS$ 250.35	93	11.05	11.19
14	CH_3–	S	145 – 146	$C_7H_{17}N_2OPS$ 208.26	93	13.36	13.45

Results and Discussion

Carbamoyl and thiocarbamoyl derivatives of 3-aminopropyl-dimethyl-phosphine oxide **1 – 14** (Table 1) were synthesized by nucleophilic addition of 3-aminopropyl-dimethyl-phosphine oxide to the corresponding isocyanates or isothiocyanates according to Scheme 1.

The interaction between the reagents was realized in dichloromethane solution at room temperature and with an 1:1 molar ratio of the reagents. The products, after crystallization from the reaction mixture, were purified by washing with dry diethyl ether and recrystallisation from polar solvents such as ethanol.



Scheme 1.

3-Aminopropyl-dimethyl-phosphine oxide is a stronger nucleophilic agent in comparison with aminomethyl-dimethyl-phosphine oxide and bis(dimethyl-phosphinoylmethyl)-amine because of the effect of the electron accepting phosphoryl group (P=O). The position of the electron withdrawing phosphoryl group (P=O) is not near enough to the amino group in 3-aminopropyl-dimethyl-phosphine oxide to reduce its basicity and nucleophility. This is the reason why it interacts very easily with the highly reactive isocyanates and isothiocyanates at room temperature to form the corresponding 3-[N-substituted carbamoyl (or thiocarbamoyl)]-aminopropyl-dimethyl-phosphine oxides **1 – 14** in almost quantitative yields. The interaction proceeds with considerable (high) exothermal effect. This effect is significantly higher in the case of the arylisocyanates: phenyl-, 3-chlorophenyl-, 4-methoxy-phenyl- and 4-chloro-phenyl-, as well as phenyl- and 4-methyl-phenylisothiocyanate. Some preparative and analytical data for compounds **1 – 14** are given in Table 1. The compounds are colorless

Table 2. Characteristic infrared frequencies (ν, cm^{-1}) of carbamoyl derivatives of 3-aminopropyl-dimethyl-phosphine oxide **1 – 4**.

[a] The bands for CH_2 groups of this compound are at: 875(s), 2849(m) and 2937(s) cm^{-1}.

No	ν P=O	ν CH_3P	ν C=O (Amide I)	δ C(O)-NH (Amide II)	ν N-H	ν C_6H_5
1	1150(vs)	1296(vs)	1693(vs)	1548(s)	3184(m)	1500(s)
	1158(vs)	1301(vs)			3260(m)	1598(s)
					3345(s)	
2	1133(vs)	1294(m)	1687(vs)	1544(m)	3250(m)	1504(m)
	1147(vs)	1305(m)	1711(vs)		3315(vs)	1600(m)
3	1137(vs)	1303(m)	1705(vs)	1525(vs)	3244(m)	—
					3305(s)	
4[a]	1155(vs)	1296(m)	1668(vs)	1516(vs)	3295(m)	1499(m)
	1174(m)	1306(m)			3338(m)	1601(m)

Table 3. Characteristic infrared frequencies (ν, cm^{-1}) of thiocarbamoyl derivatives of 3-aminopropyl-dimethyl-phosphine oxide **5 – 14**.

[a] The bands for CH_2 groups of this compound are at: 870(vs), 2849(s) and 2931(s) cm^{-1}.

No	ν P=O	ν CH_3P	ν C=S (Amide I)	δ C(O)-NH (Amide II)	ν N-H	ν C_6H_5
5	1139(vs)	1301(s)	946(m)	1555(vs)	3070(m)	1499(m)
			1256(m)		3165(w)	1601(m)
					3270(s)	
6	1137(vs)	1296(m)	943(m)	1551(vs)	3128(m)	1498(s)
		1303(s)	1250(m)		3186(w)	1606(m)
					3276(s)	
7	1150(vs)	1296(m)	871(m)	1557(vs)	3071(m)	1509(vs)
		1305(m)	1253(s)		3201(w)	1654(m)
					3268(m)	
8	1139(vs)	1295(m)	870(m)	1553(s)	3064(w)	1515(m)
		1300(m)	1257(m)		3275(m)	1605(m)
9	1149(vs)	1293(s)	868(m)	1539(vs)	3057(m)	1495(m)
		1302(m)	1278(m)		3236(m)	1593(m)
					3336(m)	
10	1157(vs)	1293(s)	870(m)	1559(vs)	3255(m)	1482(m)
		1302(m)	1278(m)		3315(m)	1600(m)
11[a]	1150(vs)	1297(s)	871(m)	1560(vs)	3087(s)	—
	1172(s)		1276(m)		3280(vs)	
12	1133(vs)	1295(s)	876(s)	1557(vs)	3302(s)	—
	1151(vs)		1271(s)			
13	1150(vs)	1295(m)	872(m)	1565(vs)	3300(s)	—
	1160(vs)		1250(m)			
14	1140(vs)	1290(s)	868(s)	1550(vs)	3313(s)	—
			1250(m)			

crystalline substances. They are easily dissolved in DMSO and DMFA and less soluble in methanol, ethanol, chloroform, dichloromethane and acetone. They are sparingly soluble in diethyl ether, tetrahydrofuran, dioxane and insoluble in aliphatic and aromatic hydrocarbons. The composition of **1 – 14** was established by elemental analysis for nitrogen (Table 1). The structures were confirmed by IR, ^1H, ^{31}P and $^{31}P\{^1H\}$ NMR spectroscopy and mass spectrometry, and those of compounds **5, 6** and **9** have been established by single crystal X-ray diffraction.

The infrared spectra of **1 – 14** (Table 2 and Table 3) show characteristic bands assigned to the phosphoryl group (P=O) at 1135 – 1174 cm^{-1}, methyl group bonded to a phosphorus atom (CH_3-P) at 1293 – 1310 cm^{-1}, bands for the carbonyl group (C=O) involved in hydrogen bonding at 1668 – 1711 cm^{-1} (Amide I), and thiocarbonyl groups (C=S) at 868 – 971 and 1250 – 1278 cm^{-1} (corresponding to Amide I), bands for HN-C(O) at 1516 – 1560 cm^{-1} (Amide II) and several bands at 3127 – 3336 cm^{-1} for NH. There are bands for aromatic rings at about 1500 and 1600 cm^{-1}, respectively, the first ones being more intense than the second in all cases. The bands of the phosphoryl groups (P=O) of **1 – 14** are shifted by 30 – 50 cm^{-1} to lower frequencies as compared to non-substituted tertiary phosphine oxides, due to their association with N-H amide and thioamide protons *via* hydrogen bonds [19]. Some of the compounds **1 – 14** show two bands for the phosphoryl group. This phenomenon could be ascribed to different spatial isomers and to two kinds of phosphoryl groups: the first one is

Table 4. ^{1}H and ^{31}P{^{1}H} NMR data of carbamoyl and thiocarbamoyl derivatives of 3-aminopropyl-dimethyl-phosphine oxide[a] **1 – 14**.

Comp. No	^{1}H NMR									^{31}P{^{1}H}
	$CH_3P(O)$		$CH_2P(O)$	P(O)C-CH_2-C	C-C-CH_2N	C-C-C-NH-C(X)		R-NH-C(X)	Ar-H	
	δ	$^2J_{HP}$	δ	δ	δ	δ	$^3J_{HH}$	δ	δ	
1[b]	1.46(d)	12.60	–[b]	–[b]	3.28(m)	6.36(t)	5.1	8.10(s)	6.80 – 7.40(m)	+ 46.53
2[b]	1.48(d)	12.60	–[b]	–[b]	3.28(m)	6.44(t)	5.0	8.39(s)	6.80 – 7.50(m)	+ 47.01
3	1.39(d)	12.65	1.68(m)	1.75(m)	3.28(m)	6.53(t)	5.0	8.10(s)	7.30 – 8.05(m)	+ 46.27
4[c]	1.42(d)	12.65	–[c]	–[c]	3.21(m)	5.64(t)	5.0	4.97(d)	–	+ 45.46
5	1.41(d)	12.60	1.71(m)	1.89(m)	3.69(m)	7.05(bs)	–	8.15(s)	7.15 – 7.40(m)	+ 44.96
6	1.43(d)	12.60	1.73(m)	1.92(m)	3.70(m)	7.26(t)	9.8	7.99(bs)	7.20 – 7.30(m)	+ 45.90
7[d]	1.41(d)	12.60	1.67(m)	1.86(m)	3.67(m)	6.45(bs)	–	7.64(bs)	6.80 – 7.15(m)	+ 44.25
8[e]	1.41(d)	12.60	1.68(m)	1.88(m)	3.68(m)	6.36(bs)	–	7.80(bs)	7.00 – 7.16(m)	+ 44.42
9[f]	1.22(d)	12.60	1.63(m)	1.79(m)	3.63(m)	–	–	7.62(bs)	7.15 – 7.30(m)	+ 46.69
10[g]	1.35(d)	12.60	1.68(m)	1.82(m)	3.69(bs)	6.72(bs)	–	7.54(bs)	7.12 – 7.24(m)	+ 46.52
11[h]	1.44(d)	12.60	1.86(m)	1.91(m)	3.61(bs)	6.78(bs)	–	7.23(bs)	–	+46.37
12[i]	1.45(d)	12.65	1.75(m)	1.89(m)	3.63(bs)	6.43(bs)	–	7.45(bs)	–	+46.61
13[j]	1.44(d)	12.60	1.75(m)	1.88(m)	3.63(bs)	6.71(bs)	–	7.40(bs)	–	+46.46
14[k]	1.45(d)	12.60	1.75(m)	1.90(m)	3.62(bs)	6.64(bs)	–	7.47(bs)	–	+46.78

[a] Abrevations: bs – broad singlet, d – doublet, m – multiplet, q – quartet, s – singlet; [b] the signals for P(O)CH_2-C-C and P(O)C-CH_2-C-N protons overlapped and were on 1.68 – 1.82 ppm; [c] the resonance signal for CH_2 cyclohexane protons were at 0.98 – 1.84 ppm and overlapped with the signals for P(O)CH_2-C-C and P(O)C-CH_2-C-N protons. The signal for cyclohexane CH-N-C(O) was a multiplet at 3.42 – 3.50 ppm. The $^3J_{HH}$ for the amide proton R-NH-C(O) is 7.5 Hz; [d] the signal of methyl CH_3OAr protons was at 3.75(s) ppm; [e] the signal of methyl CH_3Ar proton was at 2.29(s) ppm; [f] the signal of PhCH_2N-C(X) proton was at 4.63(s) ppm. The signal of thioamide proton P(O)C-C-C-NH-C(S) overlapped with the signal for aromatic protons; [g] the signal for Ph-CH_2-C protons was at 2.83(t) with $^3J_{HH} = 6.96$ Hz. The signal for Ph-C-CH_2-N-C(S) protons was on 3.59(bs) ppm; [h] the cyclohexane CH_2 protons give five multiplets at 1.00 – 1.80 ppm. The signal for cyclohexane -CH-N-C(S) proton was at 3.92(bs) ppm; [i] the signal of ethyl CH_3 protons was at 1.28(t) pm with $^3J_{HH} = 7.50$ Hz. Th signal of ethyl CH_2 protons was at 3.40(bs) ppm; [j] the signals for butyl protons were respectively at: CH_3-C-C-C at 0.88(t) ppm with $^3J_{HH} = 7.55$ Hz, C-CH_2-C-C-N-C(S) at 1.31(m) ppm, C-C-CH_2-C-N-C(S) at 1.48(q) with $^3J_{HH} = 7.60$ Hz and for C-C-C-CH_2N-C(S) at 3.38(bs) ppm; [k] the signal for CH_3-N-C(S) protons was at 2.94(bs) ppm.

engaged in hydrogen bonding while the second one is not [19].

The NMR data confirm the structure of the compounds (Table 4). The ^{1}H NMR spectra of **1 – 14** show resonances as doublets for the methyl protons **H_3C**P=O at 1.22 – 1.48 ppm with $^2J_{HH}$ of 12.6 Hz. The signals of the methylene protons P(O)**CH_2** and P(O)C-**CH_2**–C were registered as multiplets at 1.78 – 1.86 and 1.75 – 1.92 ppm, respectively. The signals for P(O)C-C-C**H_2**-N protons were registered as quartets for **1 – 9** and as broad singlets for **10 – 14**. After deuterium exchange the shape of these signals changes to triplets for **1 – 9**, but not for **10 – 14**. The signals for amide and thioamide protons P(O)-C-C-C-N**H**-C(X) and R-N**H**-C(X) have been recorded as singlets and broad singlets or triplets at 6.36 – 7.26 and 7.23 – 8.15 ppm, respectively. Only the signals for the amide protons in **4** were at higher field – at 5.64(t) and 4.97(d) ppm, respectively. The resonances for both kinds of amide and thioamide protons disappear after deuterium exchange, which is a relatively slow process even in homogeneous solution in $CDCl_3$ or CD_3OD at room temperature. In most cases these signals do not disappear even for 10 h, but their intensity is significantly reduced.

The ^{31}P{^{1}H} and ^{31}P NMR spectra of **1 – 14** show singlet and multiplet signals, respectively, in the range of 44.25 – 47.01 ppm relative to 85% H_3PO_4, typical for tertiary phosphine oxides with alkyl groups at the phosphorus atom [2, 10, 20].

All compounds gave excellent electron impact (EI) mass spectra. These data are presented in Table 5. As expected, in all spectra signals due to the molecular ions can be found in high intensities. The intensities of $[M]^{+\cdot}$ of the thiocarbamoyl compounds (**5 – 14**) are significantly higher than those of the carbamoyl compounds **1 – 4**. $[M]^{+\cdot}$ undergoes fragmentation preferably *via* α-cleavage relative to the C=X group (X=O or S) and loss of $RNH^{\cdot}$ with formation of $[(CH_3)_2P(O)(CH_2)_3NHCX]^+$ (X=O *m/z* 162; X=S *m/z* 178). A further fragmentation pathway for the ionized thiocarbamoyl compounds only is the loss of $(CH_3)_2PO$ that leads to ions $[(CH_2)_3NHC(X)NHR]^{+\cdot}$. The latter fragmentation is characteristic of **5 – 14** and does not occur in the case of the carbamoyl compounds.

In the lower mass range the spectra exhibit the characteristic ions $[(CH_3)_2PO(CH_2)_3]^+$ (*m/z* 119), $[(CH_3)_2PO(CH_2)_2]^+$ (*m/z* 105), $[(CH_3)_2POH(CH_2)]^{+\cdot}$

Table 5. Selected mass spectrometric data (EI) for the carbamoyl (**1 – 4**) and thiocarbamoyl (**5 – 14**) derivatives of 3-aminopropyl-dimethyl-phosphine oxide [rel. Int. % (m/z)].

Fragments	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**
$[M]^{+\cdot}$	12	10	7	12	31	27	12	29	43	27	81	88	22	82
	(254)	(288)	(304)	(260)	(270)	(304)	(300)	(284)	(284)	(298)	(276)	(222)	(250)	(208)
$[M\text{-}NHR]^{+}$	40	100	11	100	22	25	6	13	68	39	26	8	9	4
	(162)	(162)	(162)	(162)	(178)	(178)	(178)	(178)	(178)	(178)	(178)	(178)	(178)	(178)
$[M\text{-}(CH_3)_2PO]^{+}$	—	—	—	—	20	12	2	14	25	16	83	71	27	69
					(193)	(227)	(223)	(207)	(207)	(221)	(199)	(145)	(173)	(131)
$[CS]^{+\cdot}$ m/z 44	—	—	—	—	33	27	7	14	41	32	50	47	1	33
$[C_3H_6N]^{+}$ m/z 56	4	12	4	70	21	14	11	8	34	22	46	29	100	33
$[CH_3POH]^{+}$ m/z 63	6	15	6	11	12	12	21	9	15	11	12	17	31	19
$[(CH_3)_2PO]^{+}$ m/z 77	28	55	21	49	100	83	74	73	85	88	100	68	57	65
$[(CH_3)_2POH]^{+\cdot}$ m/z 78	16	35	18	51	24	28	35	39	34	29	30	32	18	36
$[(CH_3)_2P(CH_2)OH]^{+\cdot}$ m/z 92	20	38	25	72	78	100	100	100	100	100	99	100	43	100
$[(CH_3)_2PO(CH_2)_2]^{+}$ m/z 105	3	6	3	9	12	9	3	11	13	38	21	20	8	19
$[(CH_3)_2PO(CH_2)_3]^{+}$ m/z 119	11	18	4	15	51	43	20	43	53	53	94	51	27	32

Table 6. Crystal data and details of the structure determination for compounds **5**, **6** and **9**.

Parameter	Compound		
	5	**6**	**9**
Chemical formula	$C_{12}H_{19}N_2OPS$	$C_{12}H_{18}ClN_2OPS$	$C_{13}H_{21}N_2OP$
Formula weight	270.32	304.76	284.35
Crystal system	monoclinic	monoclinic	triclinic
Space group	$C2/c$	$C2/c$	$P\bar{1}$
a (Å)	18.457(2)	18.720(2)	8.6859(9)
b (Å)	9.0588(8)	8.9129(11)	10.1464(13)
c (Å)	18.2983(15)	18.8255(19)	10.5839(17)
α (°)	90	90	62.177(12)
β (°)	110.932(14)	111.140(17)	88.321(14)
γ (°)	90	90	67.771(11)
Volume (Å^3)	2857.5(5)	2929.6(6)	751.16(17)
Z	8	8	2
D_{calc} (g cm^{-3})	1.257	1.382	1.257
$F(000)$	1152	1280	304
μ (mm^{-1})	0.326	0.503	0.313
Temp (K)	140	140	140
Wavelength (Å)	0.71073	0.71073	0.71073
Measured reflections	8172	8528	4460
Unique reflections	2299	2461	2347
Unique reflections $[I > 2(I)]$	2137	2052	2063
Data / parameters	2299 / 154	2461 / 164	2347 / 164
R^a $[I > 2\delta(I)]$	0.0394	0.0329	0.0338
$wR2^a$ (all data)	0.1033	0.0770	0.1098
GoF^b	1.120	1.030	1.157

[a] $R = \Sigma||F_o| - |F_c||/\Sigma|F_o|$, $wR2 = \{\Sigma[w(F_o^2 - F_c^2)^2] / \Sigma[w(F_o^2)^2]\}^{1/2}$; [b] GoF = $\{\Sigma[w(F_o^2 - F_c^2)^2]/(n-p)\}^{1/2}$, where n is the number of data and p is the number of parameters refined.

(m/z 92), $[(CH_3)_2POH]^{+\cdot}$ (m/z 78), $[(CH_3)_2PO]^{+}$ (m/z 77), $[CH_3POH]^{+}$ (m/z 63), and $[C_3H_6N]^{+}$ m/z 56, and in case of the thiocarbamoyl compounds $[CS]^{+}$ (m/z 44). As mentioned earlier [7] the spectra of the compounds with aromatic substituents R show intense signals for $[RNH_2]^{+\cdot}$ as the base peaks in the spectra of **1** and **3**. Here, too, there is experimental evidence that the amine radical ions are formed by EI-fragmentation of the molecular ions but the origin of the hydrogen is unknown. A contamination of the substances by amine is unlikely.

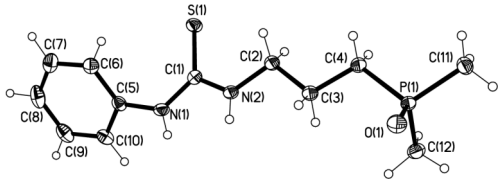


Fig. 1. Ortep representation of the crystal structure of **5**. Selected bond lengths [Å] and angles [°]: S1-C1, 1.691(2); P1-O1, 1.5091(15); N1-C1, 1.365(3); N1-C5, 1.417(3); N2-C1, 1.345(3); N2-C2, 1.460(3); C1-N1-C5, 127.79(18); C1-N2-C2, 123.79(17); N2-C1-N1, 113.48(19); N2-C1-S1, 121.94(16); N1-C1-S1, 124.52(17).

Very few crystal structures have been reported of thiocarbamoyl derivatives containing a P=O moiety [21], and to the best of our knowledge the structures presented here are the first crystal structures of thiocarbamoyl derivatives of 3-aminopropyl-dimethyl-phosphine oxide. Details on the crystal data and structure refinements are listed in Table 6 whereas relevant geometrical parameters (bond lengths, bond angles and hydrogen bonds), are included into the figure captions.The crystal structures of **5**, **6** and **9** (depicted in Fig. 1, 2 and 3) show some common features: *cis* arrangements of the NH moieties and intermolecular H-bond networks between two symmetry related molecules (showing a head-to-tail disposition). These two features are strictly related.

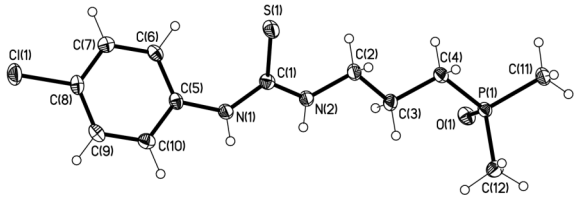


Fig. 2. Ortep representation of the crystal structure of **6**. Selected bond lengths [Å] and angles [°]: Cl1-C8, 1.750(2); S1-C1, 1.689(2); P1-O1, 1.5105(15); N1-C1, 1.369(3); N1-C5, 1.418(3); N2-C1, 1.334(3); N2-C2, 1.460(3); C1-N1-C5, 128.22(18); C1-N2-C2, 123.88(17); N2-C1-N1, 113.62(18); N2-C1-S1, 121.49(15); N1-C1-S1, 124.84(16).

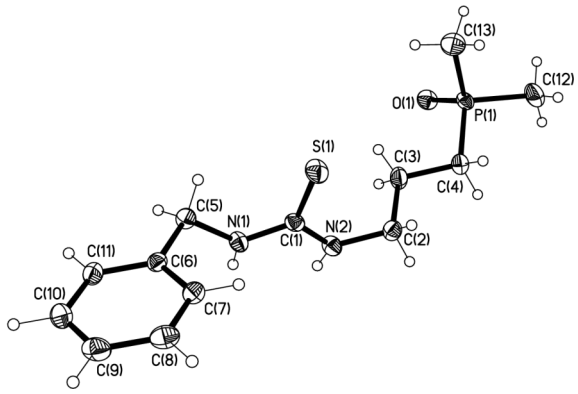


Fig. 3. Ortep representation of the crystal structure of **9**. Selected bond lengths [Å] and angles [°]: S1-C1, 1.688(2); P1-O1, 1.5050(15); N1-C1, 1.350(2); N1-C5, 1.449(3); N2-C1, 1.351(3); N2-C2, 1.456(2); C1-N1-C5, 124.92(17); C1-N2- C2, 124.50(16); N2-C1-N1, 113.80(17); N2-C1-S1, 122.57(15); N1-C1-S1, 123.63(16).

The H-bond network is rather strong and occurs between the NH and the P=O moieties of paired molecules [**5**; N1…O1A, 2.864(2) Å, N1-H1…O1A, 154.5°, N2…O1A, 2.848(2), N2-H2…O1A, 154.9°, **6**; N1…O1A, 2.912(2) Å, N1-H1…O1A, 148.4°, N2…O1A, 2.832(2), N2-H2…O1A, 156.2°, Letter A represents the following symmetry transformation: $-x$, y, $-z+1/2$, **9**; N1…O1B, 2.778(2) Å, N1-H1…O1B, 155.7°, N2…O1B, 3.108(2), N2-H2…O1B, 143.4°, Letter B represents the following symmetry transformation: $-x$, $-y$, $-z$]. There are also some weak intermolecular interactions between a methyl group (C11) and O1 for **5** and **6**, which may be considered very similar compounds, whereas for **9** they are replaced by very weak C-H…S intra- and intermolecular contacts.

The dihedral angles, between the NC(S)N moiety and the aromatic ring give an idea of the steric hindrance and the effect of a -CH_2- group between the NH group and the ring [**5**, 48.3°; **6**, 43.9°; **9**, 77.8°].

Experimental Section

Starting materials: 3-Aminopropyl-dimethyl-phosphine oxide was a gift of Hoechst AG, Frankfurt M. Germany. The isocyanates and isothiocyanates were commercially available products from Fluka and Merck. The solvents were dried by standard procedures before use.

*Characterization of the prepared compounds **1 – 14**:* The elemental analysis for nitrogen content was performed according to the method of Dumas. The melting points were measured on a Boetzius microheating plate PHMK05 (Germany) and are uncorrected. Infrared spectra (400 – 4000 cm^{-1}) were recorded on a Bruker Vector-22 IR spectrometer as KBr pellets. The ^{1}H NMR spectra were taken on a Bruker Avance DRX 500 spectrometer at 500.13 MHz in $CDCl_3$. The chemical shifts are given relative to TMS. The ^{31}P and $^{31}P\{^1H\}$ NMR spectra were registered in the same solvent on the same instrument at 202.45 MHz. The chemical shifts are given relative to 85% aqueous H_3PO_4. EI-mass spectra [EI-MS] were measured at 70 eV, source temperature 200 °C, using the direct inlet system, FAB mass spectra on a Finnigan MAT 8200 mass spectrometer.

X-ray data

Data collections were performed with the aid of an Oxford Diffraction KM4 Sapphire CCD and a 4-circle kappa goniometer at 140 K. Cell refinements and data reductions were carried out with CrysAlis RED, release 1.6.9 [22]. Data sets were not corrected for absorption. Structure solutions, structure refinements, molecular graphics and geometrical calculations were performed with the SHELXTL software package [23]. The structures were refined using the full-matrix least-squares on F^2 with all non-H atoms anisotropically defined. Hydrogens were placed in calculated position using the riding model.

General procedure for the preparation of carbamoyl and thiocarbamoyl derivatives **1 – 14**

A solution of isocyanate or isothiocyanate (4.0 mmol) in dichloromethane (1.0 ml), was added

dropwise to a stirred solution of 3-aminopropyl-dimethyl-phosphine oxide (4.0 mmol) in dry dichloromethane (3.0 ml) at r. t. An exothermal reaction was observed and the reaction mixture was stirred at 30 – 40 °C for 10 min and kept at r. t. for about 3 h. The products crystallized in most of the cases. In the other cases approximately 1 ml of hexane or diethylether was added and the reaction mixture was cooled. The crude product was separated by filtration, washed with diethyl ether and recrystallized from ethanol or an ethanol / ethylacetate mixture untill a constant melting point was reached. The preparative and analytical data of **1 – 14** are presented in Table 1.

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