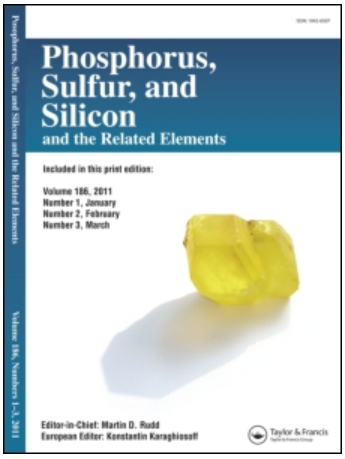


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# (CARBAMOYLAMINOPHENOXYMETHYL)-DIMETHYLPHOSPHINE OXIDES AND CORRESPONDING THIOCARBAMOYL DERIVATIVES

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# (CARBAMOYLAMINOPHENOXYMETHYL)-DIMETHYLPHOSPHINE OXIDES AND CORRESPONDING THIOCARBAMOYL DERIVATIVES

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A group of (carbamoylaminophenoxymethyl)-dimethylphosphine oxides **1–13** and corresponding thiocarbamoyl derivatives **14–26** were prepared via reaction of **2-, 3-**and **4-**(dimethylphosphinylmethoxy)-phenylamines with isocyanates and isothiocyanates resp., The composition of the new compounds was confirmed by elemental analysis, IR, $^{1}H$ and $^{31}P\{^{1}H\}$ MNR spectroscopy.

*Keywords:* (Carbamoylaminophenoxymethyl)-dimethyl-phosphine oxide; (thiocarbamoylaminophenoxymethyl)-dimethyl-phosphine oxides; synthesis; (dimethylphosphinylmethoxy)-phenylamines; phosphine oxides; isocyanates; isothiocyanates; urea and thiourea derivatives



## INTRODUCTION

The tertiary phosphine oxides are a large group of organophosphorus-compounds[1,2] with widespread practical applications[3,4]. During the last 10 to 15 years a great number of tertiary phosphine oxide derivatives has been synthesized, based on chloromethyl-dimethyl-phosphine oxide, bis(chloromethyl)-methyl-phosphine oxide[5–11] and corresponding phosphorus-containing primary mono- and diamines[12–18]. Some compounds and/or corresponding derivatives exhibit biological activity, E.g. platinum

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complexes and nitrosourea derivatives of the aminomethyl-dimethylphosphine oxide and bis-(aminomethyl)-methyl-phosphine oxide possess an antitumor activity being of low toxicity[15,16]. A series of 1-dimethyl-phosphinylmethyl-4-aryl-piperazines, synthesized by Glamkowski et al., exert an antihipertensive effect[6], while the phenoxyphenylaminoalkylphosphine oxides, prepared by L. Maier, are proved to be active herbicides[17,18].

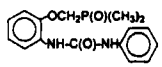
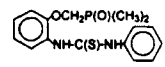
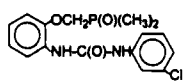
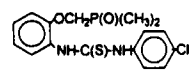
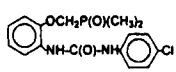
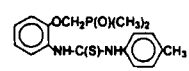
The present work is a continuation of our investigations on functionalized tertiary phosphine oxides[8–16] and reports the preparation of (carbamoyl-aminophenoxymethyl)-dimethyl-phosphine oxides **1–13** and the corresponding thiocarbamoyl derivatives **14–26**. They are expected to show complex-forming properties with metal ions and biological activities as well, similarly to that of known substituted urea and thiourea derivatives[19,20].

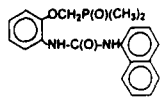
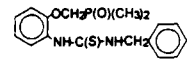
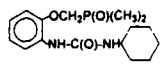
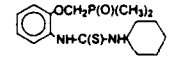
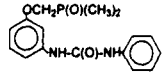
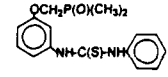
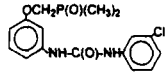
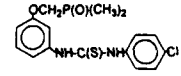
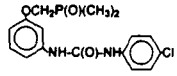
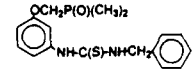
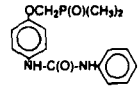
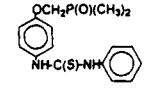
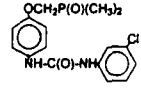
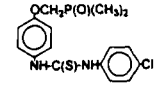
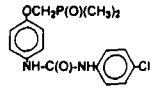
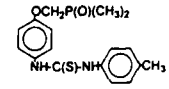
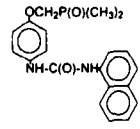
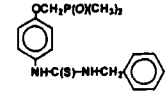
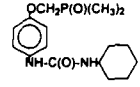
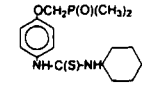


## RESULTS AND DISCUSSION

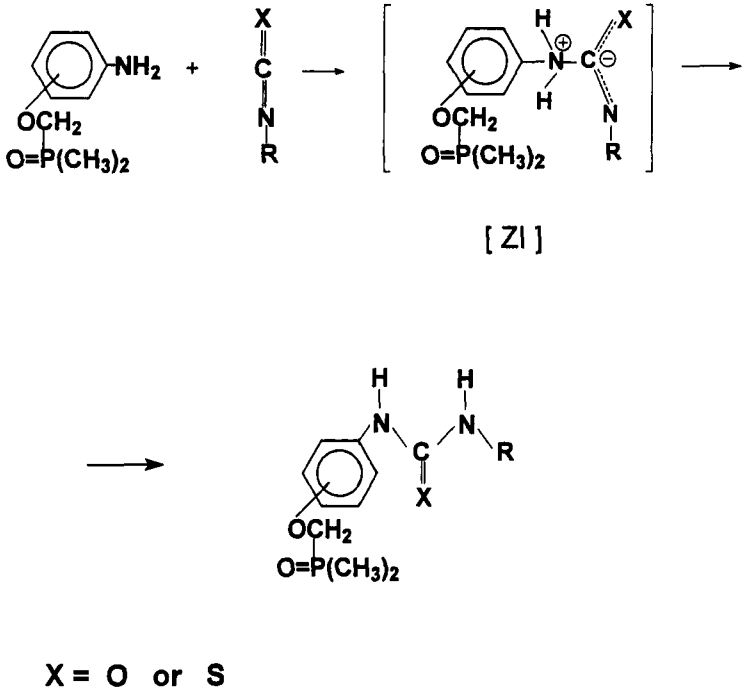
The compounds **1–26** (Table I) were prepared by interaction of **2-**, **3-** and **4**-(dimethylphosphinylmethoxy)-phenylamines and the corresponding isocyanates or isothiocyanates in dichloromethane at room temperature. This method was chosen because it is known to be a general route for preparation of asymmetric N-substituted urea and thiourea derivatives[19,20].

TABLE I Molecular structures of (carbamoylaminophenoxymethyl)-dimethylphosphine oxides and corresponding thiocarbamoyl derivatives

| *No* | *Compound* | *No* | *Compound* |
|---|---|---|---|
| **1** |  | **14** |  |
| **2** |  | **15** |  |
| **3** |  | **16** |  |

| No | Compound | No | Compound |
|---|---|---|---|
| 4 |  | 17 |  |
| 5 |  | 18 |  |
| 6 |  | 19 |  |
| 7 |  | 20 |  |
| 8 |  | 21 |  |
| 9 |  | 22 |  |
| 10 |  | 23 |  |
| 11 |  | 24 |  |
| 12 |  | 25 |  |
| 13 |  | 26 |  |

The reaction between the reagents proceeds as a nucleophilic addition of the **2-**, **3-** and **4**-(dimethylphosphinylmethoxy)-phenylamines to the isocyanates or isothiocyanates respectively according to Scheme **1**.




SCHEME 1

Williams and Jewncks[21] had shown that isocyanates react with amines via a stepwise mechanism forming an intermediate zwitterion [ZI]. All the compounds **1–26** (Tables II and III) were produced with very high yields (about or exceeding 90%) without application of catalyst as in the case of non-phosphinylated **2-, 3-** and **4**-methoxyphenylamines[22]. The high yields observed suggest that the electronegative dimethylphosphinyl group $(CH_3)_2P(O)$- does not decrease significantly the **p**,π-delocalization of the oxygen in the $-CH_2O-$ group, the latter compensating to a great extent the +**M**-effect of the $NH_2$-group in the substituted phenylamines. Obviously the $NH_2$ group of the phosphorylated methoxyphenylamines used keep the high nucleophilicity against isocyanate and isothiocyanates.[22] This suggestion is confirmed by the very close $pK_a$ values of **2-, 3-** and **4**-(dimethylphosphinylmethoxy)-phenylamines[9] to that of **2-, 3-** and **4**-methoxyphenylamines[23,24].

TABLE II Preparative and analytical data on (carbamoylaminophenoxymethyl)-dimethylphosphine oxides

| *No* | *Yield %* | *M.p.,°C* | *General formula Mol.mass* | *Nitrogen content,%* | |
|---|---|---|---|---|---|
| | | | | *Found* | *Calcd.* |
| **1** | 91 | 207–209 | $C_{16}H_{19}N_2O_3P$ 318.31 | 8.70 | 8.80 |
| **2** | 95 | 194–195 | $C_{16}H_{18}ClN_2O_3P$ 352.77 | 8.16 | 7.94 |
| **3** | 90 | 227–228 | $C_{16}H_{18}ClN_2O_3P$ 352.77 | 8.32 | 7.94 |
| **4** | 93 | 208–209 | $C_{20}H_{21}N_2O_3P$ 368.37 | 7.68 | 7.60 |
| **5** | 88 | 199–201 | $C_{16}H_{25}N_2O_3P$ 324.36 | 8.36 | 8.64 |
| **6** | 87 | 206–207 | $C_{16}H_{19}N_2O_3P$ 318.31 | 8.92 | 8.80 |
| **7** | 90 | 161–162 | $C_{16}H_{18}ClN_2O_3P$ 352.76 | 7.69 | 7.94 |
| **8** | 89 | 215–216 | $C_{16}H_{18}ClN_2O_3P$ 352.76 | 8.10 | 7.94 |
| **9** | 94 | 237–238 | $C_{16}H_{19}N_2O_3P$ 318.31 | 8.86 | 8.80 |
| **10** | 93 | 227.5–228.5 | $C_{16}H_{18}ClN_2O_3P$ 352.77 | 8.04 | 7.94 |
| **11** | 92 | 254–255 | $C_{16}H_{18}ClN_2O_3P$ 352.77 | 8.10 | 7.94 |
| **12** | 88 | 245–246 | $C_{20}H_{21}N_2O_3P$ 368.37 | 7.75 | 7.60 |
| **13** | 90 | 214–215 | $C_{16}H_{25}N_2O_3P$ 324.36 | 8.57 | 8.64 |

TABLE III Preparative and analytical data on (thiocarbamoylaminophenoxymethyl)-dimethylphosphine oxides

| *No* | *Yield %* | *M.p., °C* | *General formula Mol.mass* | *Nitrogen content,%* | |
|---|---|---|---|---|---|
| | | | | *Found* | *Calcd.* |
| **14** | 92 | 152–153 | $C_{16}H_{19}N_2O_2PS$ 334.37 | 8.41 | 8.38 |
| **15** | 79 | 147–148 | $C_{16}H_{18}ClN_2O_2PS$ 368.82 | 7.52 | 7.60 |
| **16** | 87 | 160–160.5 | $C_{17}H_{21}N_2O_2PS$ 348.40 | 8.12 | 8.04 |
| **17** | 93 | 175–176 | $C_{17}H_{21}N_2O_2PS$ 348.40 | 8.20 | 8.04 |
| **18** | 94 | 148–149 | $C_{16}H_{25}N_2O_2PS$ 340.37 | 7.89 | 8.23 |
| **19** | 86 | 161–161.5 | $C_{16}H_{19}N_2O_2PS$ 334.37 | 8.21 | 8.37 |
| **20** | 91 | 158–159 | $C_{16}H_{18}ClN_2O_2PS$ 368.82 | 7.75 | 7.60 |

| *No* | *Yield %* | *M.p., °C* | *General formula Mol.mass* | *Nitrogen content,%* | |
|---|---|---|---|---|---|
| | | | | *Found* | *Calcd.* |
| **21** | 93 | 156–157 | $C_{17}H_{21}N_2O_2PS$ 348.40 | 7.90 | 8.04 |
| **22** | 96 | 191–192 | $C_{16}H_{19}N_2O_2PS$ 334.37 | 8.28 | 8.38 |
| **23** | 90 | 197–198 | $C_{16}H_{18}ClN_2O_2PS$ 368.82 | 7.80 | 7.60 |
| **24** | 88 | 206–207 | $C_{17}H_{21}N_2O_2PS$ 348.40 | 7.94 | 8.04 |
| **25** | 89 | 172–173 | $C_{17}H_{21}N_2O_2PS$ 348.40 | 8.00 | 8.04 |
| **26** | 91 | 223–223.5 | $C_{16}H_{25}N_2O_2PS$ 324.36 | 8.38 | 8.23 |



The interaction between the initial substituted phenylamines and the isocyanates runs with an exothermal effect while with the isothiocyanates this effect was negligible. The latter agrees well with the lower reactivity of the isothiocyanates. It should be noted that all prepared compounds **1–26** were of high purity: the crude products melted at temperatures only 1–2°C below that of the corresponding purified substances, which was an indication that no side reactions occurred during their preparation.

Some preparative and analytical data of the compounds **1–26** are given in Tables II and III. The compounds are colorless crystal like substances with comparatively high melting points, which are higher than the melting points of known similar carbamoyl and thiocarbamoyl derivatives of 2-aminophosphonic acid dialkyl esters[25,26]. This fact could be explained by the stronger hydrogen bonds formed in **1–26** since they include tertiary phosphine oxide group, which is more polar than the phosphonate group, present in the 2-aminophosphonic acid derivatives.

The compounds **1–26** are easily dissolved in DMSO and DMFA and are less soluble in methanol, ethanol, dichloromethane and chloroform. They are sparingly soluble in acetone, diethyl ether, tetrahydrofurane, dioxane, aliphatic and aromatic hydrocarbons and are insoluble in water.

The expected composition of **1–26** was established by elemental analysis for nitrogen (Tables II and III). Their structure was confirmed by IR, $^1H$ and $^{31}P\{^1H\}$ NMR spectroscopy.

The infrared spectra (Tables IV and V) showed characteristic bands assigned to the phosphoryl group (P=O) at 1140–1199 $cm^{-1}$, methyl ($CH_3P$) and methylene ($CH_2P$) groups bonded to a phosphorus atom respectively at 1292–1317 $cm^{-1}$ and 720–796 $cm^{-1}$, bands of carbonyl group (C=O) nonbonded with hydrogen bonds at 1680–1709 $cm^{-1}$ (Amide I) and thiocarbonyl groups (C=S) at 933 –944 $cm^{-1}$ and 1046–1089 $cm^{-1}$ (corresponding to Amide I)[27,28], bands of NH groups associated via hydrogen bonds at 1534–1562 $cm^{-1}$ (Amide II) and several bands at 3068–3379 $cm^{-1}$, characteristic bands of C-N bonds at 1403–1403 $cm^{-1}$ (Amide III). There are bands of aromatic rings at 1484–1500 $cm^{-1}$ and 1592–1605 $cm^{-1}$, respectively. The bands of the phosphoryl group (P=O) of **1–26** are shifted with 30–50 $cm^{-1}$ to lower frequencies as compared to the nonsubstituted tertiary phosphine oxides, which is due to its association with N-H amide and thioamide protons via hydrogen bonds[29]. Additional bands of the phosphoryl group (P=O) have been observed in some of the compounds (**1–4, 7–14, 17–19**). This phenomenon could be ascribed to different spatial isomers and two kinds of phosphoryl groups: first one bonded and the second one nonbonded with hydrogen bonds or bonded with more weak hydrogen bonds[29].

$^1H$ NMR spectra of **1–26** (Tables VI and VII) showed resonance signals as doublets for the methyl group protons $C\underline{H}_3$-P=O at 1.29–1.69 ppm and $^2J_{PH}$ = 11.6–13.9 Hz for the methylene group protons $C\underline{H}_2P$=O at 4.05–4.35 ppm and $^2J_{PH}$ = 2.5–8.0 Hz. The resonance signals of the N-**H**amide and thioamide group protons of the O-Ar-N**H**-**C(X)** group were registered as singlets in more weaker fields than the resonance signals of the second N**H**protons of the C(X)-N**H**-Ar(R) group, because of the active deshielding of the electronegative phosphoryl group and its mesomeric effect along the benzene ring. The resonance signals of both kinds of N**H** protons in **7, 14, 15, 19, 20** and **23** overlapped and were registered as singlets. The signal of **NH** proton of the C(S)N**H**$CH_2$Ph group in **21** was registered as a triplet because of the coupling with $CH_2$Ph protons, while in **17** and **25** as a broad singlet because of the larger halfwidth. The resonance signals of the N-$C\underline{H}_2$Ph protons were doublets, which after deuterium exchange change to a singlet, since the coupling with NH proton disappeared. The resonance signals of both kinds of N**H** amide and thioamide protons disappeared after deuterium exchange with $D_2O$ or $CD_3OD$.

TABLE IV Characteristic IR frequences (ν $cm^{-1}$) of (carbamoylaminophenoxymethyl)-dimethylphosphine oxides

| *No* | *P=O* | $CH_3P$ | $CH_2P$ | *C=O Amide I* | *C-O-Ar* | *N-H* | | | *C-N Amide III* | $C_6H_5$ |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | *Amide II* | $\nu_{NH}$ | | | |
| **1** | 1157(vs) | 1317(s) | 747(m) | 1701(s) | 1243(m) | 1535(vs) | 3199(m) | 3336(s) | 1425(m) | 1499(m) |
| | 1199(vs) | | | | 1056(w) | | 3276(m) | | | 1600(s) |
| **2** | 1159(vs) | 1304(s) | 749(m) | 1709(s) | 1245(s) | 1534(vs) | 3187(w) | 3336(s) | 1426(m) | 1484(s) |
| | 1197(vs) | | | | 1054(w) | | | | | 1597(s) |
| **3** | 1161(vs) | 1315(m) | 731(m) | 1701(vs) | 1243(s) | 1542(vs) | 3185(w) | 3330(vs) | 1432(m) | 1488(vs) |
| | 1198(s) | | | | 1051(m) | | 3299(s) | | | 1605(s) |
| **4** | 1159(vs) | 1297(w) | 763(m) | 1699(s) | 1252(s) | 1536(vs) | 3183(m) | 3311(s) | 1424(m) | 1490(s) |
| | 1193(s) | | | | 1031(w) | | 3275(m) | | | 1599(s) |
| **5**[a] | 1156(s) | 1294(m) | 739(m) | 1680(s) | 1250(s) | 1553(vs) | 3191(s) | 3379(s) | 1437(m) | 1489(m) |
| | | | | | 1037(w) | | 3262(s) | | | 1603(s) |
| **6** | 1158(vs) | 1313(m) | 746(m) | 1698(s) | 1250(s) | 1557(vs) | 3195(m) | 3328(s) | 1419(m) | 1494(s) |
| | | | | | 1040(w) | | 3292(m) | | | 1597(vs) |
| **7** | 1158(vs) | 1297(m) | 761(m) | 1700(w) | 1259(s) | 1544(s) | 3170(m) | 3321(s) | 1433(w) | 1488(s) |
| | 1168(m) | | | | 1053(w) | | 3216(m) | | | 1596(vs) |
| **8** | 1161(vs) | 1303(s) | 743(m) | 1706(vs) | 1250(w) | 1543(vs) | 3199(w) | 3328(s) | 1430(w) | 1491(vs) |
| | 1168(m) | | | | 1041(w) | | 3285(s) | | | 1597(vs) |
| **9** | 1155(vs) | 1292(s) | 744(s) | 1700(vs) | 1225(s) | 1557(m) | 3201(m) | 3317(m) | 1412(m) | 1500(w) |
| | 1175(s) | | | | 1038(m) | | 3281(s) | | | 1602(m) |

| *No* | *P=O* | *$CH_3P$* | *$CH_2P$* | *C=O Amide I* | *C-O-Ar* | *N-H* | | | *C-N Amide III* | *$C_6H_5$* |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | *Amide II* | *$\nu_{NH}$* | | | |
| **10** | 1151(vs) | 1291(s) | 740(m) | 1701(vs) | 1228(s) | 1560(s) | 3228(w) | 3313(s) | 1406(m) | 1513(vs) |
| | 1169(s) | | | | 1041(m) | | 3278(s) | | | 1593(vs) |
| **11** | 1148(vs) | 1290(m) | 738(s) | 1701(vs) | 1245(s) | 1565(w) | 3229(s) | 3320(s) | 1400(m) | 1491(m) |
| | 1173(m) | | | | 1037(w) | | 3279(vs) | | | 1596(w) |
| **12** | 1161(vs) | 1302(m) | 730(s) | 1708(vs) | 1250(s) | 1558(s) | 3243(m) | 3342(s) | 1415(s) | 1514(s) |
| | 1179(w) | | | | 1041(m) | | 3305(s) | | | 1618(s) |
| **13**[a] | 1165(vs) | 1297(w) | 743(m) | 1683(vs) | 1250(s) | 1557(vs) | 3206(w) | 3314(vs) | 1409(m) | 1508(vs) |
| | 1178(s) | | | | 1047(m) | | 3256(m) | | | 1598(s) |

a. The bands of $CH_2$ groups in the cyclohexane ring are at: compound No **5**: 891(w), 2853(s), 2930(vs); compound No 13: 891(w), 2851(s) and 2931(vs).

TABLE V Characteristic IR frequences ($\nu$ $cm^{-1}$) of (thiocarbamoylaminophenoxymethyl)-dimethylphosphine oxides

| *No* | *P=O* | *$CH_3P$* | *$CH_2P$* | *C=S* | *C-O-Ar* | *N-H* | | | *C-N Amide III* | *$C_6H_5$* |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | *Amide II* | *$\nu_{NH}$* | | | |
| **14** | 1146(vs) | 1310(s) | 742(m) | 937(s) | 1248(s) | 1543(vs) | 3166(s) | 3287(vs) | 1418(m) | 1491(m) |
| | 1168(w) | | | 1069(w) | 1047(m) | | 3217(s) | | | 1592(s) |
| **15** | 1155(vs) | 1294(m) | 752(m) | 938(m) | 1252(s) | 1540(vs) | 3169(m) | 3291(m) | 1406(m) | 1490(s) |
| | | | | 1081(m) | 1038(m) | | 3229(m) | | | 1595(s) |
| **16** | 1158(s) | 1309(m) | 754(m) | 936(m) | 1254(s) | 1541(vs) | 3176(m) | 3301(m) | 1406(m) | 1490(m) |
| | | | | 1047(w) | 1034(w) | | 3235(m) | | | 1597(m) |
| **17** | 1161(vs) | 1309(m) | 767(m) | 944(m) | 1239(s) | 1562(vs) | 3099(s) | 3323(s) | 1425(s) | 1493(m) |
| | 1183(s) | | | 1075(m) | 1041(m) | | 3203(s) | | | 1596(w) |
| **18**[a] | 1149(vs) | 1302(m) | 747(vs) | 944(s) | 1252(vs) | 1543(vs) | 3068(w) | 3345(m) | 1422(m) | 1494(s) |
| | 1158(vs) | | | 1046(m) | 1036(m) | | 3262(m) | | | 1601(w) |
| **19** | 1151(vs) | 1315(s) | 751(m) | 942(s) | 1258(s) | 1547(vs) | 3129(m) | 3314(s) | 1403(w) | 1489(vs) |
| | 1174(s) | | | 1081(w) | 1054(s) | | 3216(w) | | | 1596(vs) |
| **20** | 1159(vs) | 1298(s) | 759(m) | 941(s) | 1246(s) | 1547(vs) | 3120(m) | 3310(m) | 1418(w) | 1488(vs) |
| | | | | 1089(m) | 1057(m) | | 3233(m) | | | 1594(vs) |
| **21** | 1156(vs) | 1309(w) | 748(w) | 933(s) | 1243(s) | 1547(s) | 3102(m) | 3318(m) | 1412(w) | 1496(s) |
| | | | | 1078(w) | 1031(m) | | 3268(m) | | | 1604(s) |
| **22** | 1154(vs) | 1295(s) | 757(m) | 940(m) | 1259(s) | 1555(m) | 3176(m) | 3286(m) | 1418(w) | 1498(m) |
| | | | | 1081(m) | 1053(m) | | 3222(m) | | | 1597(m) |

| *No* | *P=O* | *$CH_3P$* | *$CH_2P$* | *C=S* | *C-O-Ar* | *N-H* | | | *C-N Amide III* | *$C_6H_5$* |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | *Amide II* | *$\nu_{NH}$* | | | |
| **23** | 1151(vs) | 1293(s) | 732(s) | 937(w) | 1247(w) | 1557(w) | 3143(m) | 3261(s) | 1403(w) | 1491(w) |
| | 1171(s) | | | 1096(w) | 1037(m) | | 3193(m) | | | 1596(w) |
| **24** | 1158(vs) | 1294(s) | 720(m) | 936(m) | 1256(w) | 1544(s) | 3183(s) | 3314(s) | 1409(w) | 1507(vs) |
| | 1169(s) | | | 1106(m) | 1046(m) | | 3240(s) | | | 1597(w) |
| **25** | 1162(vs) | 1295(s) | 796(m) | 943(s) | 1234(s) | 1557(s) | 3135(s) | 3323(s) | 1412(w) | 1510(vs) |
| | 1182(s) | | | 1076(m) | 1037(w) | | 3279(s) | | | 1587(w) |
| **26**[a] | 1136(vs) | 1289(s) | 753(m) | 939(s) | 1228(s) | 1556(m) | 3195(w) | 3315(w) | 1428(w) | 1506(vs) |
| | 1158(s) | | | 1073(s) | 1043(w) | | 3256(w) | | | 1597(w) |

a. Explanations: The bands of cycloxexane ring $CH_2$groups are at: compound No **18**: 898(s), 2850(s) and 2924(vs); compound No **26**: 898(s), 2848(s), 2922(vs).

The $^{31}P\{^{1}H\}$ NMR spectra of **1–26** were singlet resonance signals in the range of +39.37 to +43.08 ppm, which is typical of tertiary phosphine oxides containing two methyl groups and a methylene group at the phosphorus atom[5].

## EXPERIMENTAL

### Starting materials

Starting **2-, 3-** and **4**-(dimethylphosphinylmethoxy)-phenylamines were prepared according to ref.[9]. Isocyanates and isothiocyanates were commercial products from Fluka and Merck. Solvents were dried by standard procedures prior to use.



### Characterization of the prepared compounds 1–26

The elemental analysis for nitrogen content was performed according to the method of Duma. The melting points were measured on a Boetuis microheating plate PHMK 05 (Germany) and were uncorrected. The infrared spectra (400–4000 $cm^{-1}$) were recorded on a Bruker Vector-22 infrared spectrometer as KBr pellets. The $^{1}H$ NMR spectra were taken on a Bruker DRX 500 NMR spectrometer at 500.13 MHz in $CDCl_3$ or in DMSO-$d_6$ (see Tables VI and VII). The chemical shifts are given against TMS. The $^{31}P\{^{1}H\}$ NMR spectra were registered in the same solvents on the same instrument at 202.45 MHz. The chemical shifts are given against 85% $H_3PO_4$.

### General procedure for the preparation of (carbamoylaminophenoxy-methyl)-dimethylphosphine oxides and corresponding thiocarbamoyl derivatives 1–26

To a stirred solution of **2-, 3-** and **4**-(dimethylphosphinylmethoxy)-phenylamine (3.5 mmol) in dry methylenechloride (3.0 ml) at room temperature was added dropwise a solution of isocyanate or isothiocyanate (3.5 mmol) in dry methylenechloride (3.0 ml). After the slightly exothermal reaction was completed, the reaction mixture was allowed to stay at room temperature for about 3 hrs and cooled. The precipitate was isolated by filtration, washed with diethyl ether and dried. The prepared crude product was recrystallized from ethanol.

TABLE VI $^{1}H$ and $^{31}P\{^{1}H\}$ NMR data of (carbamoylaminophenoxymethyl)-dimethylphosphine oxides

| $^{1}H$ NMR data, protons | | | | | | | $^{31}P(^{1}H)$ | Solv |
|---|---|---|---|---|---|---|---|---|
| $CH_3P=O$ | | $CH_2P=O$ | | $O\text{-}Ar\text{-}NH\text{-}C(O)$ | $C(O)\text{-}NH\text{-}Ar(R)$ | $Ar\text{-}H$ | | |
| δ | $^{2}J_{PH}$ | δ | $^{2}J_{PH}$ | δ | δ | δ | δ | |
| 65(d) | 12.6 | 4.22(d) | 3.1 | 8.53(s) | 8.23(bs) | 6.88 – 8.33(m) | +42.41 | CD( |
| 69(d) | 13.2 | 4.23(d) | 2.5 | 8.69(s) | 8.49(bs) | 6.80 – 8.32(m) | +42.72 | CD( |
| 48(d) | 13.2 | 4.29(d) | 5.7 | 9.36(s) | 7.91(s)[a] | 6.80 – 7.95(m) | +38.95 | DMS( |
| 40(d) | 12.6 | 4.15(d) | 3.8 | –[a] | 8.02(bs) | 6.90 – 8.40(m) | +42.39 | CD( |
| 54(d) | 13.2 | 4.19(d) | 3.1 | 7.94(s) | 5.77(d) $^{3}J_{HH}$=7.5 | 6.80 – 8.30(m) | +41.61 | CD( |
| 53(d) | 13.2 | 4.28(d) | 6.9 | 8.65(bs) | 8.62(s) | 6.60 – 7.50 (m) | +39.61 | DMS( |
| 52(d) | 13.2 | 4.29(d) | 6.9 | 9.74(s) | | 6.80 – 7.55(m) | +39.54 | DMS( |
| 52(d) | 13.2 | 4.27(d) | 6.9 | 8.76(s) | 8.68(s) | 6.65 – 7.55(m) | +39.54 | DMS( |
| 32(d) | 11.9 | 4.07(d) | 6.9 | 8.34(s) | 8.27(s) | 6.75 – 7.26(m) | +39.62 | DMS( |
| 29(d) | 13.8 | 4.05(d) | 6.9 | 8.54(s) | 8.32(s) | 6.70 – 7.50 (m) | +.39.62 | DMS( |
| 30(d) | 13.2 | 4.05(d) | 6.9 | 8.48(s) | 8.29(s) | 7.05 – 7.30 (m) | +39.60 | DMS |
| 52(d) | 13.2 | 4.28(d) | 6.9 | 8.87(s) | 8.66(s) | 7.00 – 8.20 (m) | +39.63 | DMS |
| 48(d) | 13.4 | 4.21(d) | 6.7 | 8.13(s) | 5.96(d) $^{3}J_{HH}$=7.8 | 6.85 – 7.30 (m) | +39.74 | DMS |

ns: δ – in ppm, J – in Hz; bs – broad singlet, d – doublet, s – singlet, t – triplet.

nals of shown amide protons overlapped with the signals of Ar-H protons;

nals of methylene cyclohexane protons were at δ=1.0 – 2.0 ppm as five multiplets, while the signals of the cyclohexane C**H**-N-C(O
4(m) ppm in compound 5and at δ=3.44(m) ppm in compound 13;

nals of both kinds of N**H** protons overlapped and the resulting signal was at shown chemical shift.

TABLE VII $^{1}H$ and $^{31}P\{^{1}H\}$ NMR data of (thiocarbamoylaminophenoxymethyl)-dimethylphosphine oxide[a]

| $^{1}H$ NMR data, protons | | | | | | | $^{31}P\{^{1}H\}$ | Solv |
|---|---|---|---|---|---|---|---|---|
| $CH_3P=O$ | | $CH_2P=O$ | | O-Ar-NH-C(S) | C(S)-NH-Ar(R) | Ar-H | | |
| δ | $^{2}J_{PH}$ | δ | $^{2}J_{PH}$ | δ | δ | δ | δ | |
| 45(d) | 13.1 | 4.17(d) | 6.9 | 8.05(s) | 7.96(s) | 6.90 – 8.03(m) | +42 37 | CDC |
| 59(d) | 13.2 | 4.26(d) | 5.0 | 8.49(bs) | | 7.00 – 8.20(m) | +42 03 | CDC |
| 56(d) | 13.2 | 4.33(d) | 6.9 | 9.77(s) | 8.90(s) | 6.95 – 7.70(m) | +40.52 | DMSO |
| 79(d) | 13.3 | 4.36(d) | 8.1 | 7.99(s) | 6.29(bs) | 7.00 – 7.60(m) | +42.73 | CDC |
| 77(d) | 13.2 | 4.28(d) | 7.0 | 7.66(s) | 7.56(d) $^{3}J_{HH}$=7.5 | 6.08 – 7.35(m) | +43 08 | CDC |
| 58(d) | 13.2 | 4.35(d) | 6.3 | 9.81(s) | | 6.85 – 7.60 (m) | +39.38 | DMSO |
| 80(d) | 13.9 | 4.08(d) | 6.9 | 9.69(s) | | 6.60 – 7.35(m) | +39.37 | DMSO |
| 59(d) | 13.8 | 4.16(d) | 6.3 | 9.47(s) | 8.06(t) $^{3}J_{HH}$=5.6 | 665 – 7.30(m) | +39.41 | DMSO |
| 83(d) | 13.2 | 4.11(d) | 6.9 | 9.40(s) | 9.38(s) | 6.80 – 7.35(m) | +39.54 | DMSO |
| 81(d) | 13.2 | 4.09(d) | 5.9 | 9.44(bs) | | 6.75 – 7.40 (m) | +.39.49 | DMSO |
| 48(d) | 13.2 | 4.26(d) | 6.6 | 9.46(s) | 9.43(s) | 6.95 – 7.40 (m) | +39.55 | DMSO |
| 62(d) | 13.2 | 4.28(d) | 8.1 | 7.95(s) | 6.15(bs) | 6.80 – 7.40 (m) | +42 38 | CDC |
| 66(d) | 13.2 | 4.25(d) | 7.6 | 7.46(s) | 5.68(d) $^{3}J_{HH}$=6.9 | 6.98 – 7.20 (m) | +42.18 | CDC |

s: δ – in ppm, J – in Hz; bs – broad singlet, d- doublet, m-multiplet, s – singlet, t- triplet; [a]The signals of both kinds of NH protons of **15**
apped and were singlets at shown chemical shifts; [b]The signal of $CH_3Ar$ protons were: compound 16 at δ=2.29(s) ppm, and compoun
pm; [c]The signals of N-$CH_2$-Ar protons of were; for compound No 16 at δ-5.03(d) ppm, $^{3}J_{HH}$=2.4 Hz, compound No **21** at δ=4
and for compound No **25** at δ-4.85(d) ppm and $^{3}J_{HH}$-5. 1 Hz. These signals became singlets after deuterium exchange with $CD_3OD$
ethylene cyclohexane protons were at δ=1.0- 2. 1 ppm as five multiplets. The signal of cyclohexan CH-N-C(S) proton was at δ=4.25 pp
with the signal of P-$CH_2$ protons.

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