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INTERACTION OF *N*-ALKOXY-*N*-CHLORO-*N'*-ARYLUREAS WITH TRIALKYL PHOSPHITES AS A ROUTE TO DIALKYL *N*-ALKOXY-*N*-(*N'*-ARYLCARBAMOYL)PHOSPHORAMIDATES. PRODUCTS STRUCTURE

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It is shown that the interaction of N-alkoxy-N-chloro-N'-arylureas with trialkyl phosphites in diethyl ether at room temperature yields dialkyl N-alkoxy-N-(N'-arylcarbamoyl)phosphoramidates. The structures of the dialkyl N-alkoxy-N-(N'-arylcarbamoyl)phosphoramidates were finally confirmed by a single-crystal X-ray diffraction study. The structural peculiarities of dialkyl N-alkoxy-N-(N'-arylcarbamoyl)phosphoramidates are discussed. The single-crystal X-ray diffraction study of dimethyl N-methoxy-N-(N'-4-nitrophenylcarbamoyl)phosphoramidate, dimethyl N-benzyloxy-N-(N'-4-nitrophenylcarbamoyl)phosphoramidate, and diethyl N-methoxy-N-(N'-4-chlorophenylcarbamoyl)phosphoramidate revealed the planar configuration of the N(OR) nitrogen atom. The strong conjugation of the lone pair on the N(OR) nitrogen atom with the π-systems of the P=O and C=O double bonds leads to a planar configuration of the N(OR) nitrogen. Differences in the N−C(=O) carbamoyl bond are observed in dialkyl N-alkoxy-N-(N'-arylcarbamoyl)phosphoramidates. The N(Ar)−C(O) bond is shorter than the N(OR)−C(O) bond; a significant length difference of the N−C(=O) carbamoyl bonds is observed. This phenomenon may be caused by the fact that the conjugation of the lone pair on the N(OR) nitrogen atom with the carbamoyl C=O group is weaker than the conjugation of the lone pair on the N(Ar) nitrogen atom with the same carbamoyl C=O group. In all cases, the N-aryl substituent is almost coplanar with the carbamoyl group.

Keywords: N-alkoxy-N-chloro-N'-arylureas, trialkyl phosphites, dialkyl N-alkoxy-N-(N'-arylcarbamoyl)phosphoramidates, structure, single-crystal X-ray diffraction study.

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Introduction

Urea derivatives are widely used in medicine and drug design [1]. Phosphoramidates have found widespread use in medicinal chemistry and agriculture [2]. Recently, we have synthesized dialkyl *N*-alkoxy-*N*-(carbamoyl)phosphoramidates (*N*-alkoxy-*N*-dialkoxyphosphorylureas) **1** [3], and dialkyl *N*-alkoxy-*N*-(*N'*-arylcarbamoyl)phosphoramidates **2** (*N*-alkoxy-

N'-aryl-*N*-dialkoxyphosphorylureas) [4] (Scheme 1) which possess structural features of both ureas and phosporamidates. The *N*-(carbamoyl)phosphoramidates **1** and **2** are potential biological active substances. The proposed method of P—N bond creation is based on the interaction of *N*-alkoxy-*N*-chloroureas **3** or *N*-alkoxy-*N*-chloro-*N'*-arylureas **4** with trialkyl phosphites. This reaction is a new kind of Michaelis-Arbuzov reaction.

N-Alkoxy-*N*-chloro-R-sulfonamides **5** i nteract with trialkyl phosphites in the same manner with formation of dialkyl *N*-alkoxy-*N*-R-sulfonylphosphoramidates **6** [5] (Scheme 2).

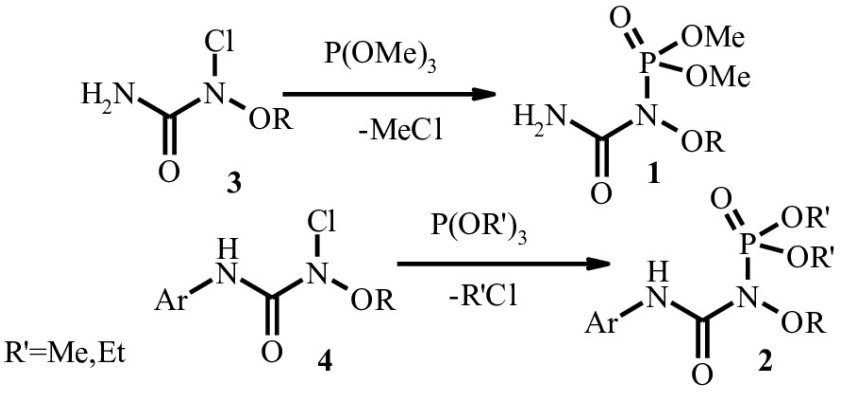
The formation of compounds **1**, **2**, and **6** is based on the possibility of the nucleophilic substitution of the chlotine atom in *N*-alkoxy-*N*-chloroamides, established in works by Glover [6—8].

The structure of *N*-alkoxy-*N*-dialkoxyphosphorylureas **1** [3] and dialkyl *N*-alkoxy-*N*-R-sulfonylphosphoramidates **6** [5] was clearly proven by XRD study. The structure of dialkyl *N*-alkoxy-*N*-(*N'*-arylcarbamoyl)phosphoramidates **2** was determined based ^{1}H, ^{31}P, and ^{13}C NMR spectra and mass spectra.

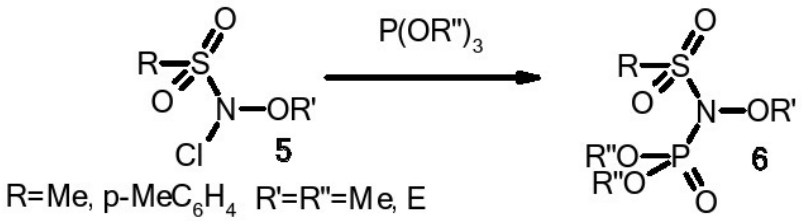
However, the interaction of *N*-alkoxy-*N*-chlorobenzamides **7** with trimethyl phosphite yields *Z*-*N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates **8** [9] (Scheme 3).

Probably, in this case in the primary substitution product **A,** the N—O migration of phosphoryl group occurs [9]. The structure of compounds **8** was clearly proven by XRD study [9].

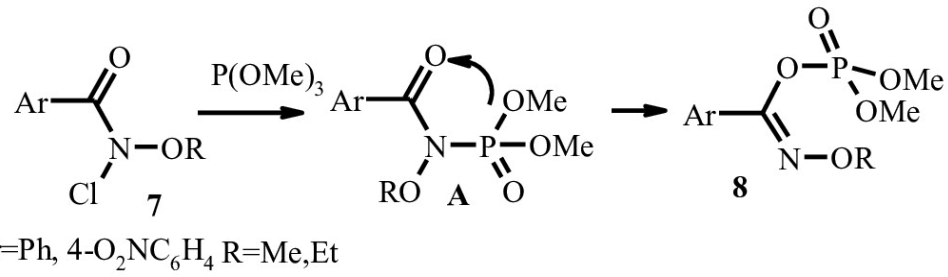
We believe that the peculiarities of the structure of dialkyl *N*-alkoxy-*N*-(*N'*-arylcarbamoyl)phosphoramidates **2** must be established by XRD study too.



Scheme 1. The interaction of *N*-alkoxy-*N*-chloroureas **3** and *N*-alkoxy-*N*-chloro-*N'*-arylureas **4** with trialkyl phosphites [3,4]



Scheme 2. The interaction of *N*-alkoxy-*N*-chloro-R-sulfonamides **5** with trialkyl phosphites [5]



Scheme 3. The interaction of *N*-alkoxy-*N*-chlorobenzamides **7** with trimethyl phosphite [9]

Experimental

Materials and equipment

^{1}H NMR spectra were recorded on a VARIAN VNMRS 400 spectrometer (400 MHz). ^{13}C NMR spectra were recorded on a VARIAN VNMRS 400 spectrometer (100 MHz). $CDCl_3$ and $(CD_3)_2SO$ were used as the solvent. ^{1}H NMR chemical shifts relative to the residual solvent protons as an internal standard [$(CD_3)_2SO$: 2.500 ppm, $CDCl_3$: 7.260 ppm] were reported. The solvent carbon atoms served as an internal standard for ^{13}C NMR spectra [$CDCl_3$: 77.16 ppm]. ^{31}P NMR spectra were recorded on a VARIAN VNMRS 400 spectrometer (161.95 MHz), the solvent $CDCl_3$ was used, 98% H_3PO_4 was used as external standard. Mass spectra were recorded in fast atom bombardment mode (FAB) on a VG 70-70EQ mass spectrometer. The solvents were purified and dried according to standard procedures.

Synthesis

*Dimethyl N-methoxy-N-(N'-4-nitrophenylcarbamoyl)phosphoramidate (**2a**)*

A. The solution of trimethyl phosphite (153 mg, 1.233 mmol) in Et_2O (6 mL) was added to the solution of *N*-chloro-*N*-methoxy-*N'*-(4-nitrophenyl)urea **4a** (79 mg, 0.322 mmol) [10] in Et_2O (7 mL) at 26^{0}C. The reaction mixture was maintained at 26^{0}C during 71 h, then the negligible precipitate was filtered off, the ether filtrate was evaporated under vacuum, the obtained residue was maintained at 75–85^{0}C under vacuum (2 mm Hg), then it was dissolved in CH_2Cl_2 (2.5 mL), and hexane (4 mL) was added. This mixture was maintained at 10^{0}C during 71 h, the obtained precipitate was filtered off and identified by ^{1}H NMR as *N*-methoxy-*N'*-(4-nitrophenyl)urea (6 mg, 8.8%). Hexane (2 mL) was added to the obtained filtrate, the obtained solution was kept at 6^{0}C during 120 h, the obtained precipitate was filtered off and dried 60^{0}C under vacuum (2 mm Hg), yielding 54 mg (52.5%) of *N*-methoxy-*N*-(*N'*-4-nitrophenylcarbamoyl))phosphoramidate **2a** yellowish crystals, mp. 132–133^{0}C (Et_2O). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ=3.920 (3H, s, NOMe); 3.945 (6H, d, ^{HP}J=11.6 Hz, P(O)$(OMe)_2$); 7.657 (2H, d, ^3J=9.2 Hz, C(2)H,C(6)H $C_6H_4NO_2$); 8.202 (2H, d, ^3J=9.2 Hz, C(3)H,C(5)H $C_6H_4NO_2$); 9.719 (1H, br. s, NH). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ=55.50 d, ^{CP}J=6.036 Hz, P(O)$(OMe)_2$; 64.80 s NOMe; 118.98 s C(2)H, C(6)H $C_6H_4NO_2$; 125.24 s C(3)H, C(5)H $C_6H_4NO_2$; 143.47 s C(4)–NO_2 $C_6H_4NO_2$; 143.85 s $C(1)_q$ $C_6H_4NO_2$; 151.25 d, ^{CP}J=18.11 Hz, C=O. ^{31}P NMR (161.95 MHz, $CDCl_3$, ppm): 0.241. Mass spectrum (FAB), *m/z*(I_{rel}, %): 320 $[M+H]^+$ (100); 127 (45). Found, %: C 37.46; H 4.57; N 13.04. $C_{10}H_{14}N_3O_7P$. Calculated, %: C 37.63; H 4.42; N 13.16.

B. The solution of trimethyl phosphite (120 mg, 0.967 mmol) in Et_2O (5 mL) was added to the solution of *N*-chloro-*N*-methoxy-*N'*-(4-nitrophenyl)urea **4a** (109 mg, 0.445 mmol) in Et_2O (8 mL) at 25^{0}C. The reaction mixture was maintained at 25^{0}C during 94 h, the obtained precipitate was filtered off, dried under vacuum yielding 50 mg (35.2%) of *N*-methoxy-*N*-(*N'*-4-nitrophenylcarbamoyl))phosphoramidate **2a** as yellowish crystals.

*Dimethyl N-benzyloxy-N-(N'-4-nitrophenylcarbamoyl))phosphoramidate (**2b**)*

The solution of trimethyl phosphite (90 mg, 0.729 mmol) in Et_2O (5 mL) was added to the solution of *N*-benzyloxy-*N*-chloro-*N'*-(4-nitrophenyl)urea **4b** (117 mg, 0.364 mmol) [10] in Et_2O (5 mL) at 27^{0}C. The reaction mixture was maintained at 27^{0}C for 70 h. The formed precipitate was filtered off, the Et_2O-filtrate was evaporated under vacuum, the obtained residue was maintained at 80–87^{0}C under vacuum (2 mm Hg) for 10 min. The residue was twice extracted by boiling hexane (2×10 mL), the combine hexane extract was maintained at –14^{0}C for 90 h, the formed precipitate was filtered off, giving 67 mg (46.5%) of dimethyl *N*-benzyloxy-*N*-(*N'*-4-nitrophenylcarbamoyl))phosphoramidate **2b**, yellowish crystals, m.p. 79–81^{0}C. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ=3.935 (6H, d, ^{HP}J=12.0 Hz, P(O)$(OMe)_2$); 5.067 (2H, s, $NOCH_2$); 7.386–7.454 (3H, m, C(3)H, C(4)H, C(5)H Ph); 7.483–7.527 (2H, m, C(2)H, C(6)H Ph); 7.640 (2H, d, ^3J=9.2 Hz, C(2)H, C(6)H $C_6H_4NO_2$); 8.203 (2H, d, ^3J=9.2 Hz, C(3)H,C(5)H $C_6H_4NO_2$); 9.600 (1H, br. s, NH). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ=55.04 d, ^{CP}J=6.037 Hz, P(O)$(OMe)_2$; 79.05 s $NOCH_2$; 119.51 s C(2)H, C(6)H $C_6H_4NO_2$; 124.62 s C(3)H, C(5)H $C_6H_4NO_2$; 128.27 s $2C_{Ph}$(H) Ph; 128.92 C(4)H Ph; 130.11 $2C_{Ph}$(H) Ph; 133.97 C_q(1) Ph; 142.43 s C(4)–NO_2 $C_6H_4NO_2$; 144.37 $C(1)_q$ $C_6H_4NO_2$; 152.28 d, ^{CP}J=14.09 Hz, C=O. ^{31}P NMR (161.95 MHz, $CDCl_3$, ppm): 0.470. Mass spectrum (FAB), *m/z*(I_{rel}, %): 396 $[M+H]^+$ (75); 127 (57); 91 Bn^+(100). Found, %: C 48.34; H 4.68; N 10.45. $C_{16}H_{18}N_3O_7P$. Calculated, %: C 48.61; H 4.59; N 10.63.

*Diethyl N-methoxy-N-(N'-4-chlorophenylcarbamoyl)phosphoramidate (**2c**)*

The solution of *t*-BuOCl (162 mg, 1.495 mmol) in CH_2Cl_2 (3) was added to the mixture of *N*-methoxy-*N'*-(4-chlorophenyl)urea (100 mg, 0.498 mmol) [11] and CH_2Cl_2 (2 mL) at 24^{0}C. The reaction mixture was maintained at 24^{0}C for 1 h, then it was evaporated under vacuum, the residue was dried under vacuum

(2 mm Hg) for 10 min. The obtained *N*-chloro-*N*-methoxy-*N'*-(4-chlorophenyl)urea **4c** (as a white solid) was immediately dissolved in Et_2O (7 mL), and the solution of triethyl phosphite (166 mg, 0.997 mmol) in Et_2O (5 mL) was added. The reaction mixture was maintained at 24^{0}C for 100 h, then reaction solution was evaporated under vacuum, the residue was dried at 93–95^{0}C under vacuum (2 mm Hg) for 15 min. The obtained residue was extracted by hexane (6 mL) at 24^{0}C for 24 h, then the hexane extract **A** was separated off. The remaining solid residue was dried under vacuum (2 mm Hg), giving 58 mg (34.5%) of diethyl *N*-methoxy-*N*-(*N'*-4-chlorophenylcarbamoyl)phosphoramidate **2c**, colorless crystals, m.p. 65–68^{0}C (Et_2O–hexane). ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ=1.417 (6H, td, 3*J*=7.1 Hz, ^{HP}J=1.2 Hz, P(O)($OCH_2Me)_2$); 3.898 (3H, s, NOMe); 4.182–4.351 (4H, m Hz, P(O)($OCH_2Me)_2$); 7.265 (2H, d, ^3J=8.8 Hz, C(2)H,C(6)H $C_6H_4NO_2$); 7.439 (2H, d, 3*J*=8.8 Hz, C(3)H,C(5)H $C_6H_4NO_2$); 9.284 (1H, br. s, NH). ^{13}C NMR (100.6093 MHz, $CDCl_3$, ppm): δ=16.19 d, ^{CP}J=7.04 Hz, P(O)(OCH_2Me)2; 64.70 s NOMe; 65.35 d, ^{CP}J=6.04 Hz, P(O)($OCH_2Me)_2$; 120.89 s C(2)H, C(6)H C_6H_4Cl; 128.80 s C(4)–Cl C_6H_4Cl; 129.11 s C(3)H, C(5)H C_6H_4Cl; 136.48 s $C(1)_q$ C_6H_4Cl; 151.62 d, ^{CP}J=18.11 Hz, C=O. ^{31}P NMR (161.9439 MHz, $CDCl_3$, ppm): −2.023. Mass spectrum (FAB), *m/z*(I_{rel}, %): 339 $[M+H]^+$ (27); 337 $[M+H]^+$ (100); 323 (24); 321(71); 153 (30); 156 (87). Found, %: C 42.69; H 5.65; N 8.16. $C_{12}H_{18}ClN_2O_5P$. Calculated, %: C 42.81; H 5.39; N 8.32. The hexane extract **A** was evaporated under vacuum, the residue was dried under vacuum (2 mm Hg) at 95^{0}C, additionally giving 47 mg (28.0%) of compound **2c**.

X-ray diffraction study

Dimethyl N-methoxy-N-(N'-4-nitrophenylcarbamoyl)phosphoramidate **2a**

The crystals of compound **2a** ($C_{10}H_{14}N_3O_7P$) are monoclinic, from CH_2Cl_2–hexane, at −100.5^{0}C, **a**=10.7153(3) Å , **b**=7.5625(2) Å , **c**=17.3997(5) Å , β=105.391(2)^0, V=1359.41(7) Å^3, M_r=319.21, *Z*=4, space group $P2_1/n$, d_{calc}=1.560 g/cm^3, μ(MoK_α)=0.241 mm^{-1}, F(000)=664. Unit cell parameters and intensities of 19248 reflections (3968 independent, R_{int}= 0.0376) were measured on the «Bruker APEX-II CCD» diffractometer (graphite monochromated MoK_a radiation, CCD detector, φ- and ω-scaning, $2\Theta_{max}$=60^0). The structure was solved by direct method using SHELXTL package [12]. Positions of the hydrogen atoms were located from electron density difference maps and refined by «riding» model with U_{iso}=nU_{eq} (n=1.5 for methyl groups and n=1.2 for other hydrogen atoms) of the carrier atom. The NH group hydrogen atoms are refined in an isotropic approximation. The structure was refined by F^2 full-matrix least-squares in anisotropic approximation for non-hydrogen atoms to wR_2=0.1278 for 3968 reflections (R_1=0.0448 for 3247 reflections with F>4σ(F), S=1.028).

Dimethyl N-benzyloxy-N-(N'-4-nitrophenylcarbamoyl)phosphoramidate **2b**

The crystals of compound **2b** ($C_{16}H_{18}N_3O_7P$) are triclinic, from Et_2O–hexane, at −100.5^{0}C, **a**=7.8181(3) Å, **b**=8.6751(3) Å, **c**=14.3002(6) Å , α=105.995(2)^0, β=98.698(3)^0, γ=93.862(2)^0, V=915.52(6) Å^3, M_r=395.30, Z=2, space group $P\bar{1}$, d_{calc}=1.434 g/cm^3, d_{calc}=1.434 g/cm^3, μ(MoK_α)=0.195 mm^{-1}, F(000)=412. Unit cell parameters and intensities of 12722 reflections (3216 independent, R_{int}=0.0338) were measured on the «Bruker APEX-II CCD» diffractometer (graphite monochromated MoK_a radiation, CCD detector, ω-scaning, $2\Theta_{max}$=50^0). The structure was solved by direct method using SHELXTL package [12]. Positions of the hydrogen atoms were located from electron density difference maps and refined by «riding» model with U_{iso}=nU_{eq} (n=1.5 for methyl groups and n=1.2 for other hydrogen atoms) of the carrier atom. The NH group hydrogen atoms are refined in an isotropic approximation. The structure was refined by F^2 full-matrix least-squares in anisotropic approximation for non-hydrogen atoms to wR_2=0.1097 for 3216 reflections (R_1=0.0411 for 2641 reflections with F>4σ(F), S=1.041).

Diethyl N-methoxy-N-(N'-4-chlorophenylcarbamoyl)phosphoramidate **2c**

The crystals of compound **2c** ($C_{12}H_{18}ClN_2O_5P$,) are monoclinic, from hexane, at −100.5^{0}C, ***a***=13.4851(7) Å, ***b***=7.6231(3) Å, ***c***=15.4609(6) Å, β=92.154(3)^0, V=1588.23(12) Å^3, M_r=336.70, *Z*=4, space group $P2_1/n$, d_{calc}=1.408 g/cm^3, μ(MoK_α)=0.362 mm^{-1}, F(000)=704. Unit cell parameters and intensities of 10551 reflections (2796 independent, R_{int}=0.0337) were measured on the «Bruker APEX-II CCD» diffractometer (graphite monochromated MoK_a radiation, CCD detector, ω-scaning, $2\Theta_{max}$=50^0). The structure was solved by direct method using SHELXTL package [12]. Positions of the hydrogen atoms were located from electron density difference maps and refined by «riding» model with U_{iso}=nU_{eq} (n=1.5 for methyl groups and n=1.2 for other hydrogen atoms) of the carrier atom. The NH group hydrogen atoms are refined in an isotropic approximation. The structure was refined by F^2 full-

matrix least-squares in anisotropic approximation for non-hydrogen atoms to wR_2=0.1204 for 2796 reflections (R_1=0.0443 for 2267 reflections with F>4σ(F), S=1.034).

The atomic coordinates, molecular geometry parameters, and crystallographic data of compounds **2a–c** are preserved at the Cambridge Crystallographic Data Center, 12 Union Road, CB2, 1EZ UK [fax:+44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk and are available on request quoting the deposit numbers CCDC 2421346 (**2a**), 2421345 (**2b**), 2421347 (**2c**).

Results and discussion

Synthesis

Dialkyl *N*-alkoxy-*N*-(*N'*-arylcarbamoyl)phosphoramidates **2a–c** were obtained by the interaction of *N*-alkoxy-*N*-chloro-*N'*-arylureas **4a–c** with trialkyl phosphites in ether at room temperature [4] (Scheme 4).

Structural features

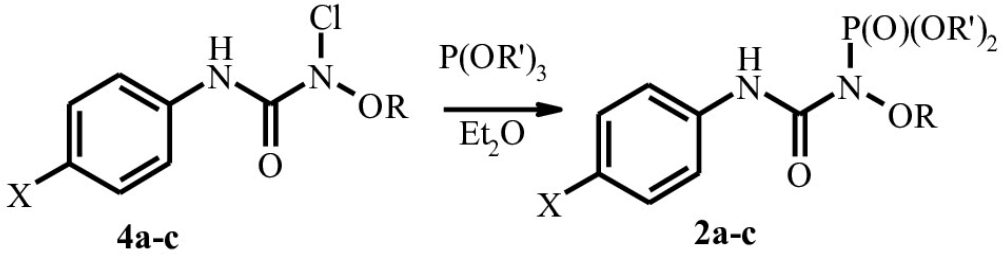
The structure of compounds **2a–c** has been proved by the single-crystal X-ray diffraction (XRD) study. The structure of dimethyl *N*-methoxy-*N*-*(N'*-4-nitrophenylcarbamoyl)phosphoramidate **2a** has many interesting peculiarities and is shown in Figs. 1 and 2.

In the molecule **2a**, the N(1) atom has planar configuration, the sum of bond angles (Sb) is 358.8°. The difference of the N–C carbamoyl bonds is observed. The N(2)–C(1) bond (its length is 1.363(2) Å) is shorter than the N(1)–C(1) bond (its length is 1.409(2) Å). This may suppose that the conjugation of electron lone pair (Lp) of N(1) atom with the C(1)=O(1) group is weaker than the conjugation of Lp of N(2) atom with the same C(1)=O(1) group. This phenomenon may be caused by the strong conjugation of π-systems of the O(1)=C(1)–N(2) moiety and the aromatic cycle, which are coplanar (the C(1)–N(2)–C(2)–C(3) torsion angle is 2.9(2)°). This mutual position of the two fragments results from the two following opposite factors: the intramolecular hydrogen bond C(3)–H···O(1) (the H···O distance is 2.25 Å, the C–H···O angle is 121.8°) and steric repulsion, as evidenced by shortened intramolecular contact H(2)···H(7) 2.27 Å with the sum of van der Waals radii of 2.34 Å [13].

The N(1)–O(2) bond length (1.4060(16) Å) is similar to the length of N–O(Me) bond (1.401(2) Å) in $(MeO_2C)_2NOMe$ [14]. The N(1)–P(1) bond (its length is 1.6860(14) Å) is elongated relative to the average N–P bond (1.652 Å) [15]).

The intramolecular hydrogen bond N(2)–H···O2 takes place (the H···O distance is 2.17(2) Å and the N–H···O angle is 111(2)°).

The dimethoxyphosphoryl substituent is rotated



Scheme 4. The synthesis of dialkyl *N*-alkoxy-*N*-(*N'*-arylcarbamoyl)phosphoramidates **2a–c**: X=NO_2, R=R'=Me (**2a**); R=CH_2Ph, R'=Me (**2b**); X=Cl, R=Me, R'=Et (**2c**)

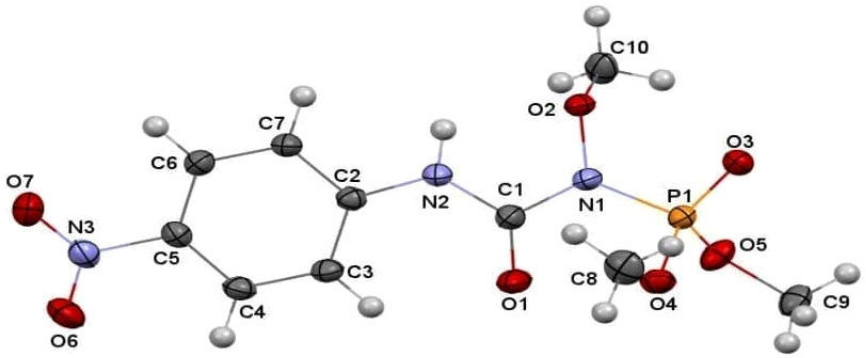


Fig. 1. Molecular structure of dimethyl *N*-methoxy-*N*-*(N'*-4-nitrophenylcarbamoyl)phosphoramidate **2a** according to X-ray diffraction data. Thermal ellipsoids are shown at 50% probability level

in such a way that the P(1)=O(3) bond is coplanar to N(1)−O(2) bond (the O(3)−P(1)−N(1)−O(2) torsion angle is 2.0(1)^0) and is oriented anti-periplanar C(1)=O(1) bond (the O(3)−P(1)···C(1)−O(1) pseudo-torsion angle is −172.3(1)^0).

The C(8)H_3 group is in −s*c*-conformation relative to the P(1)−N(1) bond (the C(8)−O(4)−P(1)−N(1) torsion angle is −73.0(1)^0). The C(9)H_3 group is anti-periplanar to the same bond (the C(9)−O(5)−P(1)−N(1) torsion angle is −173.7(1)^0). The nitro-group is somewhat non-coplanar with the plane of the benzene ring (the C(4)−C(5)−N(3)−O(6) torsion angle is −19.3(2)^0), despite the presence of attractive interactions H(4)···O(6) (2.48 Å) and H(6)···O(7) (2.48 Å).

In the crystal, molecules of compound **2a** form a zigzag chain (Fig. 2) along the crystallographic direction [010] due to the intermolecular N(2)−H···O(3') hydrogen bonds (symmetry operation 1.5−x, 0.5+y, 1.5−z; H···O distance is 2.19(2) Å, the N−H···O angle is 162(2)^0). The formation of a sufficiently strong intermolecular hydrogen bond also leads to an elongation of the P(1)−O(3) (length is 1.4603(11) Å) compared to its average value of 1.449 Å [15].

The structure of dimethyl *N*-benzyloxy-*N*-(*N'*-4-nitrophenylcarbamoyl)phosphoramidate **2b** is presented in Fig. 3.

In the molecule **2b**, the N(1) atom has planar configuration, Σβ is 358.9^0. This is probably due to the orientation of P=O group of the dimethoxyphosphoryl moiety (the C(7)−N(1)−P(1)−O(3) torsion angle is −6.1(2)^0) and its participation in the intramolecular hydrogen bond N(2)−H···O(3) (the H···O distance is 1.95(2) Å, the N−H···O angle is 149(2)^0). This conformation of this moiety promotes stronger conjugation of Lp of N(1) atom with the π-systems of P=O and C=O double bonds leading to the planar configuration of N(1) atom. The participation of the P=O group in the hydrogen bond causes its lengthening to 1.461(1) Å compared to the average value of 1.449 Å [15].

The difference of the N−C carbamoyl bonds takes place. The N(2)−C(7) bond (its length is 1.364(2) Å) is shorter than the N(1)−C(7) bond (its length is 1.416(2) Å). This may suppose that the conjugation of Lp of N(1) atom with the C(7)=O(1) group is weaker than the conjugation of Lp of N(2) atom with the same C(7)=O(1) group.

The *p*-nitrophenyl substituent is almost coplanar with carbamoyl moiety (the C(7)−N(2)−C(1)−C(6) torsion angle is 11.8(3)^0). This is further stabilized by the C(6)−H···O(1) intramolecular hydrogen bond (the H···O distance is 2.23 Å, the C−H···O angle is 120^0).

The benzyl moiety is in an orthogonal position relative to the C(7)−N(1) bond (the C(7)−N(2)−C(1)−C(6) torsion angle is 86.9(2)^0). Its phenyl group is in a conformation intermediate between −*ac* and *ap* with respect to the N(1)−O(2) bond and is significantly rotated with respect to the O(2)−C(8) bond (the N(1)−O(2)−C(8)−C(9) torsion angle is −158.7(1)^0, the O(2)−C(8)−C(9)−C(10) is 73.1(2)^0). Methyl groups C(15)H_3 and C(16)H_3 are in +*sc* and −*sc* conformations, respectively, with respect to N(1)−P(1) bond (the N(1)−P(1)−O(4)−C(15) torsion angle is 78.9(2)^0, the N(1)−P(1)−O(5)−C(16) torsion angle is −65.5(2)^0).

The structure of diethyl *N*-methoxy-*N*-(*N'*-4-chlorohenylcarbamoyl)phosphoramidate **2c** has many interesting peculiarities and is represented in Fig. 4.

The N(1) atom in the molecule **2c** has almost planar configuration, Σβ is 355.5^0. The *p*-chlorophenyl substituent is coplanar to the plane of carbamoyl moiety (the C(7)−C(2)−N(2)−C(1) torsion angle is −4.7(4)^0), which is additionally stabilized by the C(7)−H···O(1)

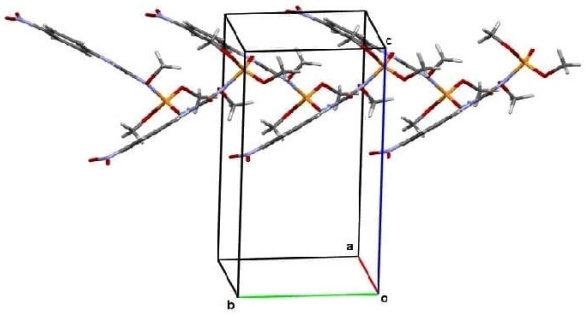


Fig. 2. Hydrogen bonded chain of the molecules **2a** in the crystal

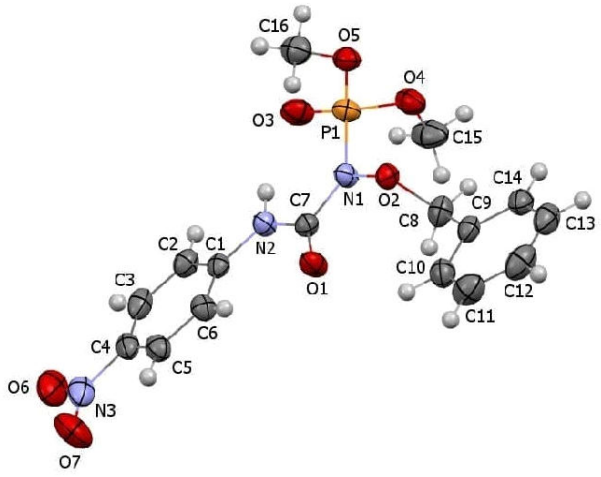


Fig. 3. Molecular structure of dimethyl *N*-benzyloxy-*N*-(*N'*-4-nitrophenylcarbamoyl)phosphoramidate **2b** according to X-ray diffraction data. Thermal ellipsoids are shown at 50% probability level

intramolecular hydrogen bond (the H···O distance is 2.25 Å, the C(7)−H···O angle is 122⁰).

In the molecule **2c**, the difference between the N−C carbamoyl bonds is observed. The N(2)−C(1) bond (its length is 1.350(3) Å) is shorter than the N(1)−C(1) bond (its length is 1.410(3) Å). This may suppose that the conjugation of Lp of N(1) atom with the C(1)=O(1) group is weaker than the conjugation of Lp of N(2) atom with the same C(1)=O(1) group.

The $C(12)H_3$ methyl group is located almost orthogonally to the C(1)−N(1) bond (the C(1)−N(1)−O(2)−C(12) torsion angle is 100.3(2)⁰).

The diethoxyphosphoryl group is in the *ap*-position relative to the C(1)=O(1) carbonyl bond (the O(1)−C(1)−N(1)−P(1) torsion angle is 23.6(3)⁰). The P(1)=O(3) bond is anti-periplanar to the C(1)−N(1) bond (the C(1)−N(1)−P(1)−O(3) torsion angle is 176.0(2)⁰). The ethyl group at the O(4) atom is in a position intermediate between −*ac* and *ap* relative to the N(1)−P(1) bond (the N(1)−P(1)−O(4)−C(8) torsion angle is −164.6(2)⁰). Its C(8)−C(9) bond is almost anticlinal to the P(1)−O(4) (the P(1)−O(4)−C(8)−C(9) torsion angle is −142.1(3)⁰). The ethyl group at the O(5) atom is located almost orthogonally to the P(1)−N(1) bond, and the C(10)−C(11) bond, in turn, is orthogonal to the P(1)−O(5) bond (the N(1)−P(1)−O(5)−C(10) torsion angle is −87.1(2)⁰, the P(1)−O(5)−C(10)−C(11) torsion angle is −93.7(2)⁰).

Thus, the single-crystal X-ray diffraction study of compound **2a−c** revealed the planar configuration of the (RO)N nitrogen atom and the significant length difference of the N−C carbamoyl bonds. The same structural peculiarities were established for *N*-(carbamoyl)phosphoramidates **1** [3]. The observed conformation of the P=O moiety promotes stronger conjugation of Lp of N(1) atom with the π-systems of P=O and C=O double bonds leading to the planar configuration of N(1) atom.

Conclusions

The structural elucidation of dialkyl *N*-alkoxy-*N*-(*N'*-arylcarbamoyl)phosphoramidates **2a−c** was confirmed by the single-crystal X-ray diffraction study of dimethyl *N*-methoxy-*N*-(*N'*-4-nitrophenylcarbamoyl)phosphoramidate **2a**, dimethyl *N*-benzyloxy-*N*-(*N'*-4-nitrophenylcarbamoyl))phosphoramidate **2b**, and diethyl *N*-methoxy-*N*-(*N'*-4-chlorophenylcarbamoyl)phosphoramidate **2c**. The planar configuration of (RO)N(1) atom and the length difference of the N−C bonds have been established.

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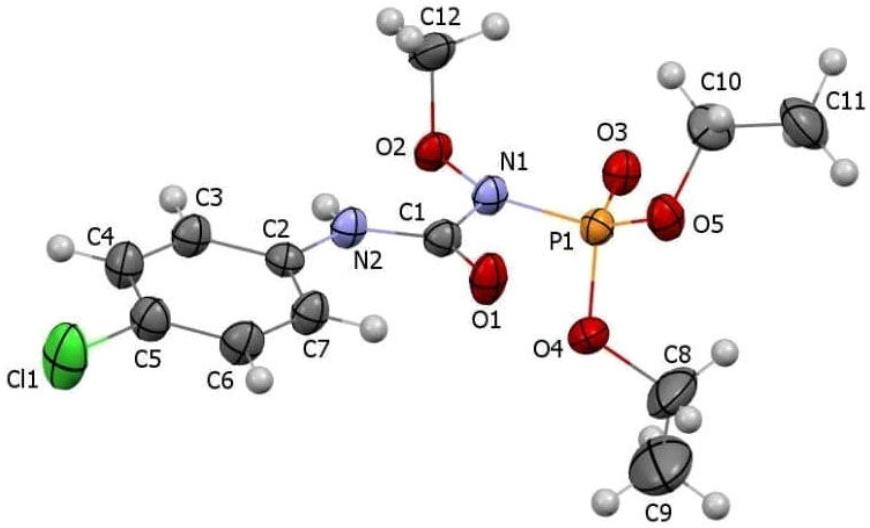

Fig. 4. Molecular structure of diethyl *N*-methoxy-*N*-(*N'*-4-chlorophenylcarbamoyl)phosphoramidate **2c** according to X-ray diffraction data. Thermal ellipsoids are shown at 50% probability level

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ВЗАЄМОДІЯ *N*-АЛКОКСИ-*N*-ХЛОРО-*N'*-АРИЛСЕЧОВИН З ТРИАЛКІЛФОСФІТАМИ ЯК ШЛЯХ ДО ДІАЛКІЛ-*N*-АЛКОКСИ-*N*-(*N'*-АРИЛКАРБАМОЇЛ)ФОСФОРАМІДАТІВ. СТРУКТУРА ПРОДУКТІВ

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Показано, що взаємодія *N*-алкокси-*N*-хлоро-*N'*-арилсечовин з триалкілфосфітами у діетиловому етері за кімнатної температури приводить до утворення діалкіл-*N*-алкокси-*N*-(*N'*-арилкарбамоїл)фосфорамідатів. Структури діалкіл-*N*-алкокси-*N*-(*N'*-арилкарбамоїл)фосфорамідатів остаточно підтверджено рентгенівським дослідженням монокристалів. Обговорено особливості структури діалкіл-*N*-алкокси-*N*-(*N'*-арилкарбамоїл)фосфорамідатів. Дослідження структури диметил-*N*-метокси-*N*-(*N'*-4-нітрофенілкарбамоїл)фосфорамідату, диметил-*N*-бензилокси-*N*-(*N'*-4-нітрофенілкарбамоїл)фосфорамідату та диетил-*N*-метокси-*N*-(*N'*-4-хлорофенілкарбамоїл)фосфорамідату виявило планарну конфігурація атома азоту, що пов'язаний з алкоксигрупою. Сильне спряження неподіленої електронної пари атома азоту N(OR) з π-системами подвійних зв'язків P=O та C=O приводить до плоскої конфігурації атома азоту N(OR). У діалкіл-*N*-алкокси-*N*-(*N'*-арилкарбамоїл)фосфорамідатах має місце різниця карбамоїльних зв'язків N–C(=O). Зв'язок N(Ar)–C(=O) коротший за зв'язок N(OR)–C(=O), спостерігається значна різниця довжин карбамоїльних зв'язків N–C(=O). Це явище може бути викликане тим, що спряження неподіленої електронної пари атома азоту N(OR) з карбамоїльною групою C=O слабше, ніж спряження неподіленої електронної пари атома азоту N(Ar) з тією ж карбамоїльною групою C=O. У всіх сполуках *N*-арильний замісник знаходиться майже в одній площині з карбамоїльною групою.

Ключові слова: *N*-алкокси-*N*-хлоро-*N'*-арилсечовини, триалкілфосфіти, діалкіл-*N*-алкокси-*N*-(*N'*-арилкарбамоїл)фосфорамідати, будова, рентгеноструктурний

INTERACTION OF *N*-ALKOXY-*N*-CHLORO-*N'*-ARYLUREAS WITH TRIALKYL PHOSPHITES AS A ROUTE TO DIALKYL *N*-ALKOXY-*N*-(*N'*-ARYLCARBAMOYL)PHOSPHORAMIDATES. PRODUCTS STRUCTURE

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It is shown that the interaction of N-alkoxy-N-chloro-N'-arylureas with trialkyl phosphites in diethyl ether at room temperature yields dialkyl N-alkoxy-N-(N'-arylcarbamoyl)phosphoramidates. The structures of the dialkyl N-alkoxy-N-(N'-arylcarbamoyl)phosphoramidates were finally confirmed by a single-crystal X-ray diffraction study. The structural peculiarities of dialkyl N-alkoxy-N-(N'-arylcarbamoyl)phosphoramidates are discussed. The single-crystal X-ray diffraction study of dimethyl N-methoxy-N-(N'-4-nitrophenylcarbamoyl)phosphoramidate, dimethyl N-benzyloxy-N-(N'-4-nitrophenylcarbamoyl)phosphoramidate, and diethyl N-methoxy-N-(N'-4-chlorophenylcarbamoyl)phosphoramidate revealed the planar configuration of the N(OR) nitrogen atom. The strong conjugation of the lone pair on the N(OR) nitrogen atom with the π-systems of the P=O and C=O double bonds leads to a planar configuration of the N(OR) nitrogen. Differences in the N−C(=O) carbamoyl bond are observed in dialkyl N-alkoxy-N-(N'-arylcarbamoyl)phosphoramidates. The N(Ar)−C(O) bond is shorter than the N(OR)−C(O) bond; a significant length difference of the N−C(=O) carbamoyl bonds is observed. This phenomenon may be caused by the fact that the conjugation of the lone pair on the N(OR) nitrogen atom with the carbamoyl C=O group is weaker than the conjugation of the lone pair on the N(Ar) nitrogen atom with the same carbamoyl C=O group. In all cases, the N-aryl substituent is almost coplanar with the carbamoyl group.

Keywords: N-alkoxy-N-chloro-N'-arylureas; trialkyl phosphites; dialkyl N-alkoxy-N-(N'-arylcarbamoyl)phosphoramidates; structure; single-crystal X-ray diffraction study.

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