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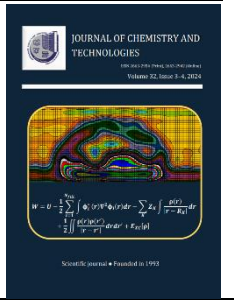

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SYNTHESIS *N*-ALKOXY-1-(DIMETHOXYPHOSPHORYLOXY)BENZIMIDATES FROM *N*-ALKOXY-*N*-CHLOROBENZAMIDES

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Abstract

Aim. To synthesize of *N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates from the interaction of *N*-alkoxy-*N*-chlorobenzamides with trimethylphosphite. To investigate *N*-alkoxy-1-(dimethoxyphosphoryloxy)-benzimidates structure using the XRD study. Methods. Mass spectrometry, ^{1}H, ^{31}P and ^{13}C NMR spectroscopy, XRD study. Results. This study explores the reaction of *N*-alkoxy-*N*-chlorobenzamides with trimethylphosphite in ether resulting in the formation *N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates. The obtained benzimidates are identified as the products of the nucleophilic substitution at nitrogen followed by an unusual N–O-migration of dimethoxyphosphoryl group. This reaction presents an original synthetic pathway to the *N*-alkoxy-1-phosphoryloxy imidates. In this research the possibility of the *N*-alkoxy-*N*-chlorobenzamides interaction with *P*-nucleophiles has been proved. The structure of *N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates has been confirmed by the ^{1}H, ^{31}P and ^{13}C NMR spectra, mass spectra and XRD study. The XRD study of *N*-methoxy-1-(dimethoxyphosphoryloxy)-4-nitrobenzimidate has demonstrated that this compound is Z-isomer, and 4-nitrophenyl moiety and *N*-methoxy group are in a *trans* position towards to the C=N double bond. The coplanarity of the aromatic ring and the π-system of the C=N double bond is evident from the XRD data. Conclusions. As the result of our study the feasibility of *N*-alkoxy-1-(phosphoryloxy)benzimidates formation through the interaction of *N*-alkoxy-*N*-chlorobenzamides with trialkylphosphites has been elucidated. This outcome holds significant value for a better understanding of the synthetic importance of *N*-alkoxy-*N*-chlorobenzamides. The structural elucidation of Z-*N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates has been done. A novel kind of the intramolecular N–O-migration of the phosphoryl group has established.

Keywords:*N*-alkoxy-*N*-chlorobenzamides; trimethylphosphite; *N*-alkoxy-1-(dimethoxyphosphoryloxy) benzimidates; synthesis; structure; XRD study; N–O-migration of dimethoxyphosphoryl group.

СИНТЕЗ *N*-АЛКОКСИ-1-(ДИМЕТОКСИФОСФОРИЛОКСИ)БЕНЗІМІДАТІВ З *N*-АЛКОКСИ-*N*-ХЛОРОБЕНЗАМІДІВ

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Анотація

Мета. Синтез *N*-алкокси-1-(диметоксифосфорилокси) бензімідатів взаємодією *N*-алкокси-*N*-хлоробензамідів з триметилфосфітом. Рентгеноструктурне дослідження будови *N*-алкокси-1-(диметоксифосфорилокси) бензімідатів. Методи. Мас-спектрометрія, ^{1}H, ^{31}P та ^{13}C ЯМР спектроскопія, рентгеноструктурний аналіз. Результати. Ця робота досліджує перебіг взаємодії *N*-алкокси-*N*-хлоробензамідів з триметилфосфітом в етері, яка призводить до утворення *N*-алкокси-1-(диметоксифосфорилокси)бензімідатів. Отримані бензімідати ідентифіковані як продукти нуклеофільного заміщення за атомом азоту з подальшою незвичайною N–O міграцією диметоксифосфорильної групи. Ця реакція є оригінальним шляхом синтезу *N*-алкокси-1-

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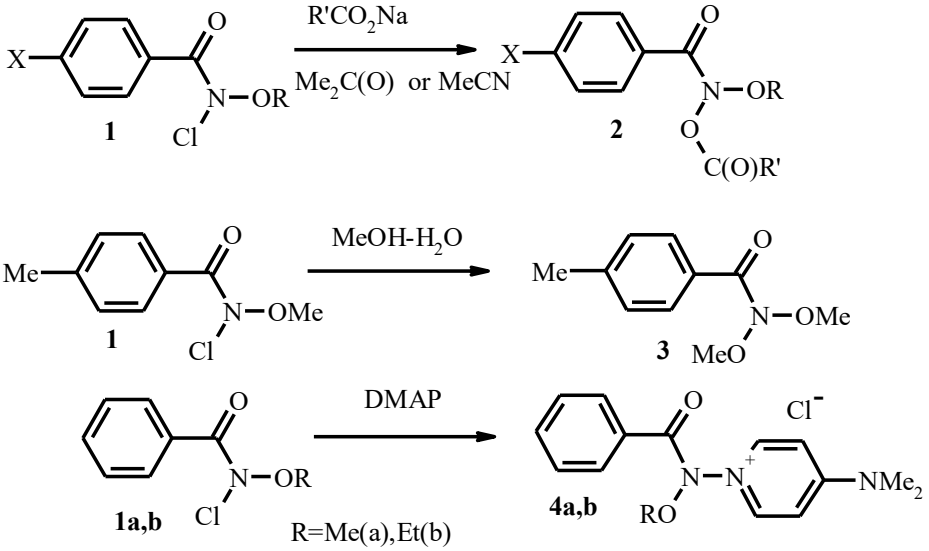
Journal of Chemistry and Technologies, 2024, *32*(3), 528-537

фосфорилоксиімідатів. У цьому дослідженні доведено можливість взаємодії *N*-алкокси-*N*-хлоробензамідів з *P*-нуклеофілами. Структуру *N*-алкокси-1-(диметоксифосфорилокси)бензімідатів підтверджено спектрами ^{1}H, ^{31}P і ^{13}СЯМР, мас-спектрами та рентгеноструктурним дослідженням. XRD дослідження *N*-метокси-1-(диметоксифосфорилокси)-4-нітробензімідату показало, що ця сполука є Z-ізомером, а 4-нітрофенільний фрагмент і *N*-метоксигрупа знаходяться в транс-положенні до подвійного зв'язку C=N. Копланарність ароматичного кільця та π-системи подвійного зв'язку C=N очевидна з даних XRD. Висновки. В результаті нашого дослідження з'ясована можливість утворення *N*-алкокси-1-(диметоксифосфорилокси) бензімідатів шляхом взаємодії *N*-алкокси-*N*-хлоробензамідів з триалкілфосфітами. Цей результат має важливе значення для кращого розуміння синтетичної важливості *N*-алкокси-*N*-хлоробензамідів. Зроблено з'ясування структури Z-*N*-алкокси-1-(диметоксифосфорилокси)бензімідатів. Встановлено новий спосіб внутрішньо-молекулярної N–O міграції фосфорильної групи.

Ключові слова:*N*-алкокси-*N*-хлоробензаміди; триметилфосфіт;*N*-алкокси-1-(диметоксифосфорилокси) бензімідати; синтез; структура; XRD-дослідження; N–O міграція диметоксифосфорильної групи.

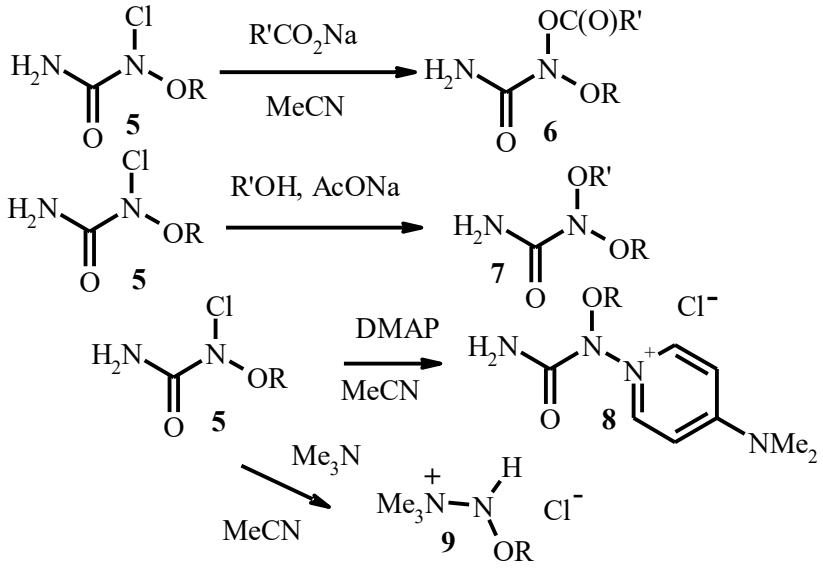
Introduction

As it was proved by Professor S.A. Glover's investigations, *N*-alkoxy-*N*-chlorobenzamides **1** interact with several *O*- and *N*-nucleophiles forming the products of the nucleophilic substitution at the nitrogen atom [1–12] (Scheme 1). These reactions are route to *N*-acyloxy-*N*-alkoxybenzamides **2**, *N,N*-dialkoxybenzamides **3** and unstable compounds **4**.



Scheme 1.The interaction of *N*-alkoxy-*N*-chlorobenzamides 1 with the *O*- and *N*-nucleophiles [1–12]

In the similar way the *N*-alkoxy-*N*-chloroureas **5** react with different nucleophiles properly yielding *N*-acyloxy-*N*-alkoxyureas **6** [13-15], *N,N*-dialkoxyureas **7** [14,16] and chlorides of *N*-alkoxy-*N*-(1-piridinium)ureas **8** [14;17;18] (Scheme 2).

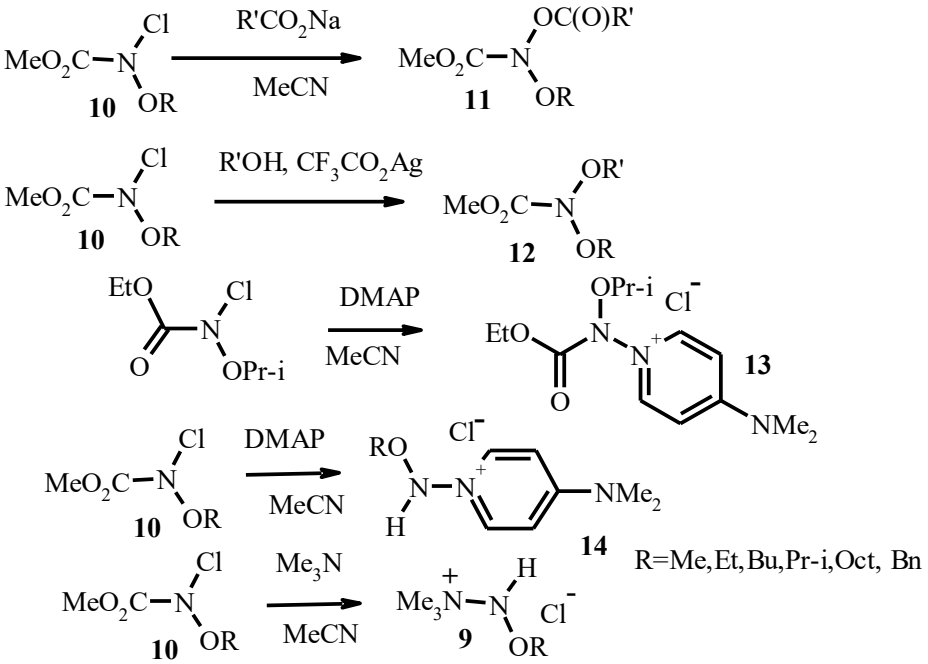


Scheme 2. The interaction of *N*-alkoxy-*N*-chloroureas 5 with *O*- and *N*-nucleophiles [13–19]

Journal of Chemistry and Technologies, 2024, *32*(3), 528-537

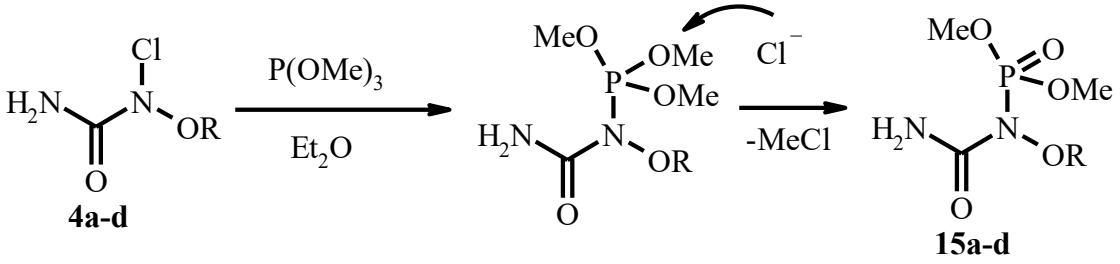
N-Alkoxy-*N*-chloroureas **5** react with trimethylamine yielding *N*-alkoxy-*N*,*N*,*N*-trialkylhydraziniumchlorides **9** [19] (Scheme 2).

N-Alkoxy-*N*-chlorocarbamates **10** react with sodium salts of carboxylic acids in acetonitrile resulting in the formation of *N*-acyloxy-*N*-alkoxycarbamates**11** [13] (Scheme 3). The alkoholysis of *N*-alkoxy-*N*-chlorocarbamates **10** in the presence of silver trifluoroacetate is represents a pathway leading to the formation to *N*,*N*-dialkoxycarbamates **12** [16] (Scheme 3). The *N*-alkoxy-*N*-chlorocarbamates **10** interaction with DMAP leads to *N*-alkoxy-*N*-(1-pyridinium)carbamate **13** [20] as well as1-alkoxyamino-4-dimethylaminopyridinium chlorides **14** [21] (Scheme 3). The *N*-alkoxy-*N*-chlorocarbamates **10** interaction with trimethylamine is a way to obtain *N*-alkoxy-*N*,*N*,*N*-trialkylhydrazinium salts **9** [22] (Scheme 3).



Scheme 3. The interaction of *N*-alkoxy-*N*-chlorocarbamates 10 with *O*- and *N*-nucleophiles [13; 16; 20-22]

However, there have been no previous reports on the interaction of *N*-alkoxy-*N*-chlorobenzamides, *N*-alkoxy-*N*-chloroureas, and *N*-alkoxy-*N*-carbamates with *P*-nucleophiles. In our earlier studies, we observed the selective reaction of *N*-alkoxy-*N*-chloroureas **5a–d** with trimethylphosphite, resulting in the formation of *N*-alkoxy-*N*-phosphorylureas **15a–d** [23] (Scheme 4).



Scheme 4. The interaction of *N*-alkoxy-*N*-chloroureas 5a–d with trimethylphosphite [23].

The generation of *N*-phosphorylureas **15** through the interaction of *N*-alkoxy-*N*-chloroureas **5** with trimethylphosphite can be considered as a new way to obtain to the *N*-phosphorylureas and a convenient method of the N–P bond formation.

However, the potential interaction of *N*-alkoxy-*N*-chlorobenzamides with trimethylphosphite has not been investigated. Nevertheless *N*-alkoxy-*N*-chlorobenzamides **1** readily react with different *O*- and *N*-nucleophiles [1–12].

Thus, the objective of our current study was to explore the potential interaction of *N*-alkoxy-*N*-chlorobenzamides **1** with such *P*-nucleophile, as trimethylphosphite, and characterize the structure of the resulting products.

Experimental

^{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). The solvent $CDCl_3$ was used. ^{1}H NMR chemical shifts relative to the residual solvent protons as an internal standard [$CDCl_3$: 7.260 ppm,] were reported. 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 on a VG 70–70EQ mass spectrometer in fast atom bombardment mode (FAB). The solvents were purified and dried according to the standard procedures.

N-Methoxy-1-(dimethoxyphosphoryloxy)-4-nitrobenzimidate **(16)**. **A.** The solution of trimethylphosphite (86 mg, 0.693 mmol) in ether (5 mL) was added to the mixture of *N*-methoxy-*N*-chloro-4-nitrobenzamide **1c** (82 mg, 0.356 mmol) [12] and ether (5 mL) at –28 °C. The reaction mixture was maintained at –28 °C during 20 min, then at 10 °C during 71 h. The negligible precipitate was filtered off, washed by ether (5 mL), the combined Et_2O-filtrate was evaporated under vacuum, dried under vacuum (2 mmHg), giving 99 mg (91 %) of *N*-methoxy-1-(dimethoxyphosphoryloxy)-4-nitrobenzimidate **16**, colorless crystals, mp 73–74 °C (boiling hexane) (with decomp.).^{1}H NMR(400 MHz, $CDCl_3$, ppm): δ = 3.921 (6H, d,^{HP}J = 12.0 Hz, P(O)$(OMe)_2$); 4.073 (3H, s, NOMe); 7.961 (2H, d, ^3J = 8.8 Hz, C(2)H,C(6)H $C_6H_4NO_2$); 8.246 (2H, d, ^3J = 8.8 Hz, C(3)H,C(5)H $C_6H_4NO_2$). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 55.68 d, ^{CP}J = 6.04 Hz, P(O)$(OMe)_2$; 63.59 s NOMe; 123.85 s C(3)H, C(5)H $C_6H_4NO_2$; 127.26 s C(2)H, C(6)H $C_6H_4NO_2$; 135.76 d, ^{CP}J = 2.01 Hz, C(1) $C_6H_4NO_2$; 143.995 d, ^{CP}J=9.06 Hz, C=N); 149.04 s C(4)-NO_2, $C_6H_4NO_2$. ^{31}P NMR (161.95 MHz, $CDCl_3$, ppm): -9.53. Mass spectrum (FAB), m/z(I_{rel},%): 305$[M+H]^+$ (44); 227 (9);179 $[M+H-HOP(O)(OMe)_2]^+$ (100). Found, %: C39.32; H4.49; N9.07. $C_{10}H_{13}N_2O_7P$. Calculated, %: C 39.48; H 4.31; N9.21.

B. The solution of trimethylphosphite (105 mg, 0.846 mmol) in ether (5 mL) was added to the mixture of *N*-methoxy-*N*-chloro-4-nitrobenzamide **1c** (114 mg, 0.493 mmol) [12] and ether (6 mL) at –25 °C. The reaction mixture was maintained at –25 °C during 25 min, then at 10 °C during 22 h. The negligible precipitate was filtered off, washed by ether (5 mL), the combined Et_2O-filtrate was evaporated under vacuum, the residue was maintained at 50 °C during 30 min under vacuum (2 mmHg), giving 145 mg (96 %) of *N*-methoxy-1-(dimethoxyphosphoryloxy)-4-nitrobenzimidate **16**.

C. The solution of trimethylphosphite (94 mg, 0.758 mmol) in ether (5 mL) was added to the mixture of *N*-methoxy-*N*-chloro-4-nitrobenzamide **1c** (99 mg, 0.428 mmol) [12] and ether (5 mL) at –25 °C. The reaction mixture was maintained at –26 °C during 20 min, then at 10 °C during 119 h. The negligible precipitate was filtered off, washed by ether (5 mL), the combined Et_2O-filtrate was evaporated under vacuum, the residue was maintained at 50 °C during 30 min under vacuum (2 mmHg), the residue was extracted by boiling hexane (3·10 mL). The hexane extract was cooled to 10 °C, the obtained precipitated was filtered off, dried under vacuum (2 mmHg), giving 113 mg (86 %) of *N*-methoxy-1-(dimethoxyphosphoryloxy)-4-nitrobenzimidate **16**, colorless crystals.

N-Methoxy-1-(dimethoxyphosphoryloxy)benzimidate **(17). A.** The solution of *tert*-butyl hypoclorite (230 mg, 2.115 mmol) in dicloromethane (2 mL) was added to the solution of *N*-methoxybenzamide (107 mg, 0.705 mmol) in dicloromethane (6 mL), the reaction mixture was maintained at 15 °C during 45 min, then it was evaporated under vacuum (20 mm Hg), the residue was keptat 20 °C under vacuum (2 mm Hg) yielding 131 mg (100%) of unstable *N*-chloro-*N*-methoxybenzamide**1a**, yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ 3.889 (3H, s, NOMe); 7.459 (2H, t, ^3J = 7.6 Hz, C(3)H,C(5)H Ph); 7.579 (1H, t, ^3J = 7.6 Hz, C(4)H Ph); 7.784 (2H, dd, ^3J = 8.4 Hz, ^4J = 1.2 Hz, C(2)H, C(6) Ph). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ =52.26 NOMe; 128.50, 129.71 C(3,5)H and C(2,6)H Ph; 133.05 C(4)H Ph; 135.46 $C(1)_q$Ph; 167.27 C=O. The solution of trimethylphosphite (105 mg, 0.846 mmol) in ether (2 mL) was added to the solution of *N*-chloro-*N*-methoxybenzamide (131 mg, 0.705 mmol) in ether (2 mL) at –33 °C. The reaction mixture was maintained at –33 °C during 1 h, then at 4 °C during 94 h. The reaction solution was evaporated under vacuum (20 mm Hg), the obtained residue was maintained at 50 °C during 30 min under vacuum (2 mmHg) yielding 180 mg (98 %) of *N*-methoxy-1-(dimethoxyphosphoryloxy)benzimidate**17**, colorless oil, n_D^{18} 1.4942. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 3.891 (6H, d, ^{HP}J = 11.6 Hz, P(O)$(OMe)_2$); 4.013 (3H, s, NOMe); 7.360–7.432 (3H, m, C(3)H, C(4)H, C(5)H Ph); 7.775 (2H, dd, ^3J = 8.4 Hz, J = 1.6 Hz, C(2)H, C(6)H Ph).^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 55.49 d, ^{CP}J = 6.04 Hz,P(O)$(OMe)_2$;

63.01 s NOMe; 126.47 s C(3)H, C(5)H Ph; 128.61 s C(2)H, C(6)H Ph; 129.665 d, ^{CP}J = 3.02 Hz, C(1)Ph; 130.72 s C(4)H, Ph; 145.66, d, ^{CP}J=10.06 Hz, C=N. ^{31}P NMR (161.95 MHz, $CDCl_3$, ppm): –9.60. Mass spectrum (FAB), *m/z*(I_{rel},%): 260 $[M+H]^+$ (25); 134 $[M+H-HOP(O)(OMe)_2]^+$ (100); 127 (20). Found, %: C 46.48; H 5.56; N 5.17. $C_{10}H_{14}NO_5P$. Calculated, %: C 46.34; H 5.44; N 5.40.

B. The solution of trimethylphosphite (142 mg, 1.846mmol) in ether (5 mL) was added to the solution of *N*-chloro-*N*-methoxybenzamide**1a** (190 mg, 1.026 mmol) in ether (5 mL) at –25 °C. The reaction mixture was maintained at –25 °C during 1 h, then at 10 °C during 69 h. The obtained reaction solution was evaporated under vacuum (20 mm Hg), the obtained residue was maintained at 50 °C during 40 min under vacuum (2 mmHg) yielding 260 mg (97 %) of *N*-methoxy-1-(dimethoxyphosphoryloxy)benzimidate **17**.

N-Ethoxy-1-(dimethoxyphosphoryloxy)benzimidate **(18). A.** The solution of trimethylphosphite (85 mg, 0.685 mmol) in ether (4 mL) was added to the solution of *N*-chloro-*N*-ethoxybenzamide**1b** (125 mg, 0.625 mmol) [1] in ether (5 mL) at –29 °C. The reaction mixture was maintained at –25 °C during 1h, then at 4 °C during 24h, the negligible precipitate was filtered off, washed by ether (5 mL), the combined Et_2O-filtrate was evaporated under vacuum, the residue was maintained at 50 °C during 30 min under vacuum (2 mmHg), giving 151 mg (88 %) of *N*-ethoxy-1-(dimethoxyphosphoryloxy)benzimidate **18**, colorless oil, n_D^{18} 1.4960. ^{1}H NMR (400 MHz, $CDCl_3$, ppm): δ = 1.365 (3H, t, ^3J = 7.0 Hz, $NOCH_2\underline{Me}$); 3.894 (6H, d, ^{HP}J = 11.6 Hz, $P(O)(OMe)_2$); 4.261 (2H, q,^3J = 7.0 Hz, $NOCH_2$); 7.353–7.428 (3H, m, C(3)H, C(4)H, C(5)H Ph); 7.780 (2H, dd, ^3J = 7.8 Hz, J = 1.6 Hz, C(2)H, C(6)H Ph). ^{13}C NMR (100 MHz, $CDCl_3$, ppm): δ = 14.57 s $NOCH_2\underline{Me}$; 55.40 d, ^{CP}J = 7.04 Hz, $P(O)(OMe)_2$; 70.99 s $NOCH_2$; 126.44 s C(3)H, C(5)H Ph; 128.58 s C(2)H, C(6)H Ph; 129.96 d, ^{CP}J = 2.01 Hz, C(1)Ph; 130.57 s C(4)H, Ph; 145.30, d, ^{CP}J= 10.06 Hz, C=N. ^{31}P NMR (161.95 MHz, $CDCl_3$, ppm): -9.65. Mass spectrum (FAB), *m/z*(I_{rel},%): 274 $[M+H]^+$ (48); 213 (6); 148 $[M+H-HOP(O)(OMe)_2]^+$ (100); 127 (11). Found, %: C 48.13; H 5.96; N 5.09. $C_{11}H_{16}NO_5P$. Calculated, %: C 48.36; H 5.90; N 5.13.

B. The solution of trimethylphosphite (104 mg, 0.838 mmol) in ether (4 mL) was added to the solution of *N*-chloro-*N*-ethoxybenzamide**1b** (119 mg, 0.596 mmol) [1] in ether (2 mL) at 6 °C. The reaction mixture was maintained at 6 °C during 23 h, the negligible precipitate was filtered off, washed by ether (2 mL), the combined Et_2O-filtrate was evaporated under vacuum, the residue was maintained at 55 °C during 30 min under vacuum (2 mmHg), giving 148 mg (91 %) of *N*-ethoxy-1-(dimethoxyphosphoryloxy)benzimidate **18**.

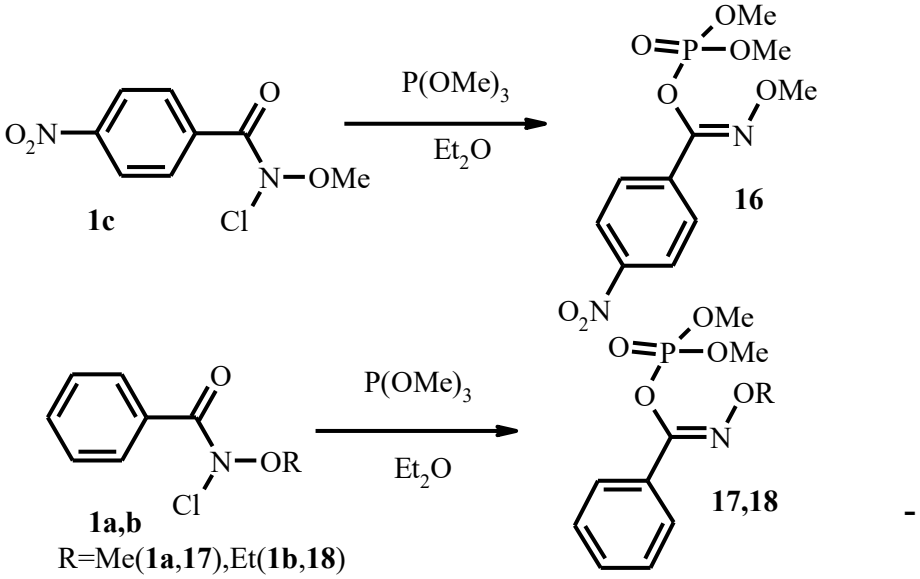
XRD structural study of the N-methoxy-1-(dimethoxyphosphoryloxy)-4-nitrobenzimidate **(16).** The colorless crystals of compound **16** ($C_{10}H_{13}N_2O_7P$) are monoclinic, from hexane. At -100.5°C, ***a*** = 7.7641(7), ***b*** = 27.878(2), ***c*** = 6.8819(6) Å, β =115.775(5), V = 1341.4(2) Å^3, M_r = 304.19, Z = 4, space group $P2_1/c$, d_{calc}= 1.506 g/cm^3, μ(MoK_α) = 0.239 mm^{-1}, F(000) = 632. Intensities of 14515 reflections (2353 independent, R_{int}=0.074) were measured on the«Bruker APEX-II CCD» diffractometer (graphite monochromatedMoK_α radiation, CCD detector,φ and ω-scaning, $2\Theta_{max}$ = 50°). The structure was solved by direct method using SHELXTL package [24]. 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. Full-matrix least-squares refinement against F^2 in anisotropic approximation for non-hydrogen atoms using 1590 reflections was converged to wR_2 = 0.174 (R_1 = 0.064 for 1729 reflections with F>4σ(F), S = 1.110).

The atomic coordinates, molecular geometry parameters, and crystallographic data of compound **16** are preserved atthe 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 number CCDC 2312716.

Results and discussion

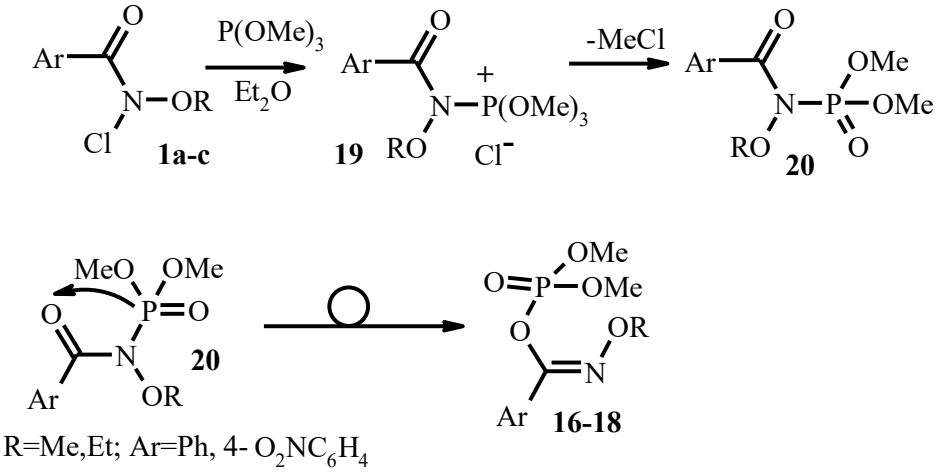
We investigated the interaction between *N*-alkoxy-*N*-chlorobenzamides **1a-c** and trimethylphosphite in ether. *N*-Alkoxy-*N*-chlorobenzamides **1a-c** selectively react with trimethylphosphite, leading to the selective formation of *N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates **16–18** (Scheme 3).

Journal of Chemistry and Technologies, 2024, *32*(3), 528-537



Scheme 5. **The synthesis of *N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates 16–18**

This is supposed to be another possible mechanism of *N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates **16–18** formation. At the first stage the labile *N*-alkoxy-*N*-(trimethoxy-phosphonium)benzamide chlorides **19** formed by the nucleophilic substitution at the nitrogen in the *N*-alkoxy-*N*-chlorobenzamides **1a-c** (Scheme 6). At the second stage the *O*-demethylation of the intermediate **19** by the chloride anion takes place (this is the new kind of Arbuzov reaction). It releases the waiting *N*-alkoxy-*N*-(dimethoxyphosphoryl)benzamides **20**. At the third stage unusual N–O-migration of dimethoxyphosphoryl group occurs yielding *N*-alkoxy-1-(dimethoxyphos-phoryloxy)benzimidates **16–18**. The driving force behind this migration could be the creation of a robust P–O bond. Various other types of N–O-migration involving the phosphoryl group are known [25,26].



Scheme 6. A possible mechanism of *N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates 16–18 formation.

N-Methoxy-1-phosphoryloxyimidates may be synthesized by copper-catalyzed cross-dehydrogenative coupling of *N*-methoxyamides with various phosphites [27]. *N*-Propyloxy-1-phosphoryloxyimidates were obtained by the *N*-propyloxy-1-(chloro)benzimidate (PhC(Cl)=NOPr) interaction with $HOP(O)(OR)_2$ (R=Me,Et,Pr,Bu) in the presence of trietylamine [28]. Thus, the proposed synthesis of *N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates **16–18** may be regarded as a new original synthesis of these compounds.

The structure of compounds **16–18** has been proved by the ^{1}H, ^{13}C, ^{13}P NMR spectra and mass spectra. Also, the structure of compound **16** has been confirmed by the single crystal X-ray diffraction (XRD) study (Figures 1, 2).

The ^{1}H NMR spectra of compounds **16–18** show such a common characteristic as doublet of dimethoxyphosphoryl moiety and singlet of MeON-group (Table 1).

Journal of Chemistry and Technologies, 2024, *32*(3), 528-537

Table 1

The typical ^{1}H NMR and ^{31}P chemical shifts of *N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates 16–18 (in $CDCl_3$).

compound	^{1}H NMR shifts, ppm		^{31}P NMR shifts, ppm
	NOMe s	P(O)(OMe)$_2$ d	
16	4.073	3.921	–9.53
17	4.013	3.891	–9.60
18	4.259 q ($NOCH_2$)	3.891	–9.65

In the ^{31}P NMR spectra of compounds **16–18** the chemical shifts of the phosphorus atom lie in the range –9.53 – –9.65 ppm.

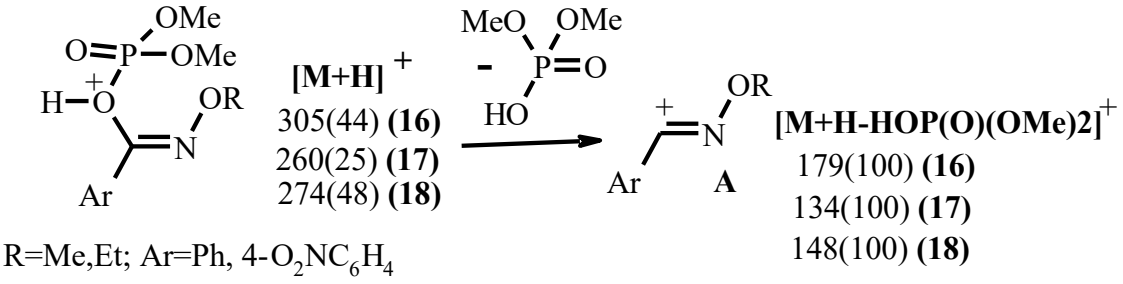
The ^{13}C NMR spectra of compounds **16–18** demonstrate numerous shared features and common characteristics. They include the chemical shifts of the NOMe carbon atoms ($NOCH_2$ for compound **18**), the carbon atoms of dimethoxyphosphoryl group and the carbon atom of C=N bond (Table 2).

Table 2

The typical ^{13}C NMR chemical shifts of carbon atoms of *N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates 16–18 (in $CDCl_3$).

compound	shifts, ppm		
	NOMe, s	C=N, d	P(O)(OMe)$_2$, d
16	63.59	143.995	55.68
17	63.01	145.66	55.49
18	70.99 ($NOCH_2$)	145.30	55.40

The mass spectra of compounds **16–18** display protonated molecular ion $[M+H]^+$ peaks at the appropriate *m/z* values. But the main peak is $[M+H-HOP(O)(OMe)_2]^+$ with the intensivity 100 %. The phosphoryloxy moiety elimination gives the stable ion **A** in all cases (Scheme 7).



Scheme7. The mass spectrometric fragmentation of *N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates 16–18 (FAB mode)

The structure of the compounds **16** has many interesting peculiarities that merit inclusion in this article. The structure of *N*-methoxy-1-(dimethoxyphosphoryl)-4-nitrobenzimidate **16** is represented on Figure 1.

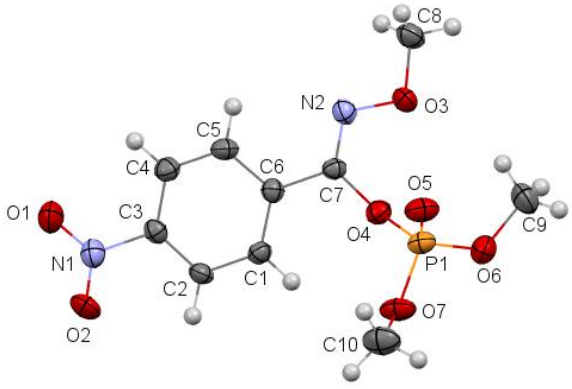


Fig. 1. Molecular structure of Z-*N*-methoxy-1-(dimethoxyphosphoryloxy)-4-nitrobenzimidate (16) according to X-ray diffraction data. Thermal ellipsoids are shown at 50 % probability level

The *para*-nitrophenyl substituent and the methoxy group are *trans*-orientated to the C(7)=N(2) double bond (the C(6)–C(7)–N(2)–O(3) torsion angle is -178.0(3)°). The phosphoryloxy

Journal of Chemistry and Technologies, 2024, *32*(3), 528-537

moiety and the methoxy group are *sic*-orientated to the C(7)=N(2) double bond (the O(3)–N(2)–C(7)–O(4) is -3.2(5) °). Thus, *N*-methoxy-1-(dimethoxyphosphoryloxy)-4-nitrobenzbenzimidate **16** is Z-isomer. It may be supposed that the compounds **17**, **18** are Z-isomer too. But, by the copper-catalyzed cross-dehydrogenative coupling of *N*-methoxyamides with phosphites release mainly E-isomers of *N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates [27]. It is evident that the proposed synthesis of *N*-alkoxy-1-(dimethoxyphosphoryloxy)benz-imidates **16**–**18** is diastereoselective mode of the formation of Z-isomers of their compounds.

The *para*-nitrophenyl substituent is coplanar to the C(7)=N(2) double bond (the C(5)–C(6)–C(7)–N(2) torsion angle is -2.8(6)°). The $C(8)H_3$ methyl group is located in anti-periplanar position in relation to the C(7)=N(2) double bond (the C(7)–N(2)–O(3)–C(8) torsion angle is 174.4(4)°).

The dimethoxyphosphoryloxy moiety at C(7) atom is orthogonal to the C(7)=N(2) double bond (the N(2)–C(7)–O(4)–P(1) torsion angle is 96.5(4)°). This substituent is deployed in such a way that the P(1) = O(5) bond is syn-peryplanar with the C(7)–O(4) bond (the C(7)–O(4)–P(1)–O(5) torsion angle is –15.6(4)°). The methyl groups of methoxy substituents at the phosphorus atom are in –ac and +sc positions relative to the O(4)–P(1) bond (the C(10)–O(7)–P(1)–O(4) torsion angle is -129.9(3)°, the C(9)–O(6)–P(1)–O(4) torsion angle is 81.1(4)°).

In the crystal phase, molecules of **16** form the chains toward the [001] crystallographic direct (Figure 2) due to the weak intermolecular hydrogen bonds C2–H…O5’ (the symmetry operation is x, y, 1+z; H…O 2.34 Å, C–H…O 154°).

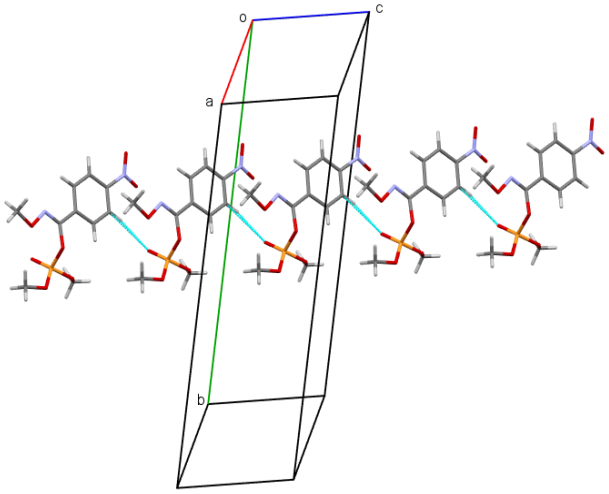


Figure 2. The chains of molecules of Z-*N*-methoxy-1-(dimethoxyphosphoryloxy)-4-nitrobenzimidate (16) formed by the weak hydrogen bonds (cyan dotted lines) in the crystal

Conclusions

The significance of this study lies in exploring a novel synthetic pathway to *N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates.

Through the reaction of *N*-alkoxy-*N*-chlorobenzamides **1a-c** with trimethylphosphite in ether we observed a nucleophilic substitution at the nitrogen atom accompanied by the N–O-migration of the dimethoxyphosphoryl group. *N*-Alkoxy-*N*-chlorobenzamides **1a–c** selectively interacts with trimethylphosphite, resulting in the formation of Z-*N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates **16–18**. This process represents a new synthesis of *N*-alkoxy-1-(phosphoryloxy)benzimidates from *N*-alkoxy-*N*-chlorobenzamides.

Consequently, the feasibility of *N*-alkoxy-1-(phosphoryloxy)benzimidates formation through the interaction of *N*-alkoxy-*N*-chlorobenzamides with trialkylphosphites has been elucidated. This outcome holds significant value for a better understanding of the synthetic importance of *N*-alkoxy-*N*-chlorobenzamides. The findings of this investigation may find practical applications in organic syntheses and the pharmaceutical industry.

The structural elucidation of Z-*N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates **16–18** was confirmed through ^{1}H, ^{13}C, ^{31}P NMR spectra, mass spectra, and by the single crystal X-ray diffraction study. This study revealed a novel intramolecular kind of N–O-migration of the phosphoryl group.

References

[1] Gerdes, R.G., Glover, S.A., ten Have, J.F., Rowbottom, C.A. (1989). N-Acetoxy-N-alkoxyamides – a New Class of Nitrenium Ion Precursors Which are Mutagenic. *Tetrahedron Lett., 30*(20), 2649–26521. https://doi.org/10.1016/S0040-4039(00)99089-0

[2] Glover, S.A. (1998). Anomeric Amides – Structure, Properties and Reactivity. Tetrahedron, 54(26), 7229–7271. https://doi.org/10.1016/S0040-4020(98)00197-5

[3] Gillson, A.-M., Glover, S.A., Tucker, D.J., Turner, P. (2003). Crystal structures and properties of mutagenic N-acyloxy-N-alkoxyamides – "most pyramidal" acyclic amides. *Org. Biomol. Chem., 1*(19), 3430–3437. https://doi.org/10.1039/B306098P

[4] Glover, S.A. (2009). *N-Heteroatom-substituted hydroxamic esters. in The Chemistry of Hydroxylamines, Oximes and Hydroxamic Acids*, EdsRappoport, Z., Liebman, J. F., John Wiley and Sons, New York. PATAI'S Chemistry of Funcional Groups. v.1. https://doi.org/10.1002/9780470682531.pat0470

[5] Glover, S.A., Rosser, A.A., (2018). Heteroatom Substitution at Amide Nitrogen – Resonance Reduction and HERON Reactions of Anomeric Amides. *Molecules, 23*(11), 2834. https://doi.org/10.3390/molecules23112834

[6] Glover, S.A., Rosser, A.A. (2022). *Modification of Amidic Resonance Through Heteroatom Substitution at Nitrogen: Anomeric Amides. Amide Bond Activation*. Ed. M. Szostak, John Wiley and Sons, New York. https://doi.org/10.1002/9783527830251.ch2

[7] Buccigross, J.M., Glover, S.A., Hammond, G.P. (1995). Decomposition of N,N'-Diacyl-N,N'-dialkoxyhydrazines Revisited. *Aust. J. Chem. 48*(2), 353–361. https://doi.org/10.1071/CH9950353

[8] Glover, S.A., Mo, G. (2002). Hindered ester formation by SN2 azidation of N-acetoxy-N-alkoxyamides and N-alkoxy-N-chloroamides – novel application of HERON rearrangement. *J. Chem. Soc., Perkin Trans, 2*(10), 1728–1739. https://doi.org/10.1039/B111250N

[9] Glover, S.A., Hammond, G.P., Bonin, A.M. (1998). A Comparison of the Reactivity and mutagenicity of N-(Benzoyloxy)-N-(benzyloxy)benzamides. *J. Org. Chem., 63*(26), 9684–9689. https://doi.org/10.1021/jo980863z

[10] Cavanagh, K.L., Glover, S.A., Price, H.L., Schumacher, R.R. (2009). SN2 Substitution reactions at the Amide Nitrogen in the Anomeric Mutagens, N-Acyloxy-N-alkoxyamides. *Aust. J. Chem., 62*(7), 700–710. https://doi.org/10.1071/CH09166

[11] Glover, S.A.; White, J.M.; Rosser, A.A.; Digianantonio, K.M. (2011). Structure of N,N-Dialkoxyamides: Pyramidal Anomeric Amides with Low Amidicity, *J. Org. Chem., 76,* 9757–9763. https://doi.org/10.1021/jo201856u

[12] Shtamburg, V.G., Tsygankov, A.V., Shishkin, O.V., Zubatyuk, R.I., Uspensky, B.V., Shtamburg, V.V., Mazepa, A.V., Kostyanovsky, R.G. (2012). The properties and structure of N-chloro-N-methoxy-4-nitrobenzamide. *Mendeleev Commun., 22*(3), 164–166. https://doi.org/10.1016/j.mencom.2012.05.019

[13] Shishkin, O.V., Zubatyuk, R.I., Shtamburg, V.G., Tsygankov, A.V., Klots, E.A., Mazepa, A.V., Kostyanovsky, R.G. (2006). Pyramidal Amide Nitrogen in N-Acyloxy-N-alkoxyureas and N-Acyloxy-N-alkoxycarbamates. Mendeleev Commun., 16 (4), 222–223. https://doi.org/10.1070/MC2006v016n04ABEH002195

[14] Shtamburg, V.G., Shishkin, O.V., Zubatyuk, R.I., Kravchenko, S.V., Shtamburg, V.V., Distanov, V.B., Tsygankov, A.V., Kostyanovsky, R.G. (2007). Synthesis, structure and properties of N-alkoxy-N-(1-pyridinium)urea salts, N-alkoxy-N-acyloxyureas and N,N-dialkoxyureas. *Mendeleev Commun., 17*(3), 178–180.https://doi.org/10.1016/j.mencom.2007.05.016

[15] Shishkin, O.V., Shtamburg, V.G., Zubatyuk, R.I., Olefir, D.A., Tsygankov, A.V., Prosyanik, A.V., Mazepa, A.V., Kostyanovsky, R.G. (2009). Chiral Ureas with Two Electronegative Substituens at 1-N and Unusual Case of Coexisting a Pyramidal and Almost Planar 1-N in The Same Crystal. *Chirality, 21*(7), 642–647. https://doi.org/10.1002/chir.20668

[16] Shtamburg, V.G., Tsygankov, A.V., Gerasimenko, M.V., Shishkin, O. V., Zubatyuk, R. I., Mazepa, A. V., Kostyanovsky, R.G. (2011). New approach to N,N-dialkoxy-N'-arylureas and N,N-dialkoxycarbamates. *Mendeleev Commun., 21*(12), 50–32. https://doi.org/10.1016/j.mencom.2011.01.021

[17] Shtamburg, V.G., Shtamburg, V.V.,Tsygankov, A.V., Anishchenko, A.A., Zubatyuk, R.I. Shishkina, S.V., Mazepa, A.V., Klots, E.A. (2016). Synthesis and Structure of New N-Alkoxy-N-(1-pyridinium)urea Chlorides. *Eur. Chem. Bull., 5*(4), 142–146. doi: 10.17628/ECB.2016.5.142

[18] Shtamburg, V.G., Shtamburg, V.V., Kravchenko, S.V., Mazepa, A.V., Anishchenko, A.A., Posokhov, E.A. (2017). A New Synthesis of N-Alkoxyaminopyridinium Salts. *Bulletin of National University "KhPI". Series: New solutions in modern technology*, (7), 211–218. doi:10.20998/2413-4295.2017.07.30

[19] Shtamburg, V.G., Shishkin, O.V., Zubatyuk, R.I., Shtamburg V.V., Tsygankov, A.V., Mazepa, A.V., Kadorkina, G.K., Kostyanovsky, R.G. (2013). Synthesis and structure of N-alkoxyhydrazines and N-alkoxy-N',N',N-trialkylhydrazinium salts. *Mendeleev Commun., 23*(5), 289–291.https://doi.org./10.1016/j.men.com.2013.09.018

[20] Shtamburg, V.G., Anishchenko, A.A., Shishkina, S.V., Konovalova, I.S., Shtamburg, V.V., Mazepa, A.V., Kravchenko, S.V. (2017). 1-(N-Ethoxycarbonyl-N-isopropyloxy)amino-4-dimethylaminopyridinium Chloride. Synthesis and Structure. *Eur. Chem. Bull., 6* (10) (2017) 470–474. doi: 10.17628/ecb.2017.6.470-474

[21] Shtamburg, V.G., Shishkina, S.V., Shtamburg, V.V., Mazepa, A.V., Kadorkina, G.K., Kostyanovsky, R.G. (2016). 1-Alkoxyamino-4-dimethylaminopyridinium salts: synthesis and structure. *Mendeleev Commun., 26*(2), 169–171. https://doi.org/10.1016/j.mencom.2016.03.030

[22] Shtamburg, V.G., Shtamburg, V.V., Klots, E.A., Anishchenko, A.A., Mazepa, A.V., Kravchenko, S.V. (2020). Nucleophilic Substitution in N-Alkoxy-N-chlorocarbamates as a Way to N-Alkoxy-N',N',N'-trimethylhydrazinium chlorides. *Eur. Chem. Bull., 9*(1), 28–32. http://dx.doi.org/10.17628/ecb.2020.9.28-32

[23] Shtamburg, V.G., Klots, E.A., Shtamburg, V.V., Anishchenko, A.A., Shishkina, S.V., Mazepa, A.V. (2023). Nucleophilic substitution at nitrogen atom. N-Alkoxy-N-(dimethoxyphosphoryl)ureas, synthesis and structure. *J. Mol. Structure, 1277*, 134865. https://doi.org/10.1016/j.molstruc.2022.134865

[24] Sheldrick, G.M. (2008). A short history of SHELX. *ActaCryst., Sect. A., A 64*, 112–122. https://doi.org/10.1107/S0108767307043930

[25] Plapinger, R.E., Wagner-Jauregg, T. (1953). A Nitrogen-to-Oxygen Phosphoryl Migration: Preparation of dl-Serinephosphoric and Threoninephosphoric Acid. *J. Am. Chem. Soc., 75*(22), 5757–5758. https://doi.org/10.1021/ja01118a524

[26] Gao, X., Deng, H., Tang, G., Liu, Y., Xu, P., Zhao, Y. (2011). Intermolecular Phosphoryl Transfer of N-Phosphoryl Amino Acids. *Eur. J. Org. Chem., 2011*(17), 3220−3228. https://doi.org/10.1002/ejoc.201100234

[27] Deng, X., Wang, Y., Liu, J.-B., Wan, C., Luo, N. (2022). Synthesis of N-methoxy-phosphoryloxyimidates through a copper-catalyzed cross-dehydrogenative coupling of N-methoxyamides with phosphites. *Tetrahedron Lett. 105*, 154049. https://ssrn.com/abstract=4150600

[28] Zimin, M.G., Fomakhin, E.V., Sadykov, A.R., Smirnov, V.N., Pudovik, A.N. (1985). Synthesis and rearrangements of phosphorylated derivatives of phenyl isohydroxamic acid. *Journal of General Chemistry of the USSR*– Zhurnal Obshchei Khimii, *55*(8), 1526−1531.