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

Vasiliy G. Shtamburg¹, Evgeniy A. Klots¹, Victor V. Shtamburg¹, Andrey A. Anishchenko²,
Svitlana V. Shiskina^{3,4}, Alexander V. Mazepa⁵, Svetlana V. Kravchenko⁶

¹Ukrainian State University of Science and Technologies, Nauky str., 8, Dnipro, 49005, Ukraine

²Oles Honchar Dnipro National University, Nauky str., 72, Dnipro, 49050, Ukraine,

³SSI Institute for Single Crystals, National Academy of Sciences of Ukraine, 60 Naukave, Kharkiv, 61001, Ukraine

⁴Institute of Organic Chemistry of National Academy of Sciences of Ukraine, Academician Kukhar str., 5, Kyiv-94, 02660, Ukraine

⁵A.V. Bogatsky Physico-Chemical Institute of National Academy of Sciences of Ukraine, Luystdorfskaya Doroga str., 86, Odessa, 65080, Ukraine

⁶Dnipro State Agrarian and Economic University, Efremova str., 25, Dnipro, 49600, Ukraine

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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, ¹H, ³¹P and ¹³C 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 ¹H, ³¹P and ¹³C 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)БЕНЗИМІДАТІВ З *N*-АЛКОКСИ-*N*-ХЛОРОБЕНЗАМІДІВ

Василь Г. Штамбург¹, Євген О. Клоц¹, Віктор В. Штамбург¹, Андрій О. Аніщенко²,
Світлана В. Шишкіна^{3,4}, Олександр В. Мазепа⁵, Світлана В. Кравченко⁶

¹Український державний університет науки і технологій, пр. Науки, 8, м. Дніпро, 49005, Україна

²Дніпровський національний університет імені Олеся Гончара, пр. Науки, 72, м. Дніпро, 49050, Україна

³Державна наукова установа «Інститут монокристалів» НАН України, вул. Наукова, 60, м. Харків, 61001, Україна

⁴Інститут органічної хімії НАН України, вул. Академіка Кухаря, 5, м. Київ, 02660, Україна

⁵Фізико-хімічний інститут імені О.В. Богатського НАН України, вул. Люстдорфська дорога, 86, м. Одеса, 65080, Україна

⁶Дніпровський державний аграрно-економічний університет, вул. Єфремова, 25, м. Дніпро, 49600, Україна

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, ¹H, ³¹P та ¹³C 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-

*Corresponding author: e-mail: koloxai@gmail.com

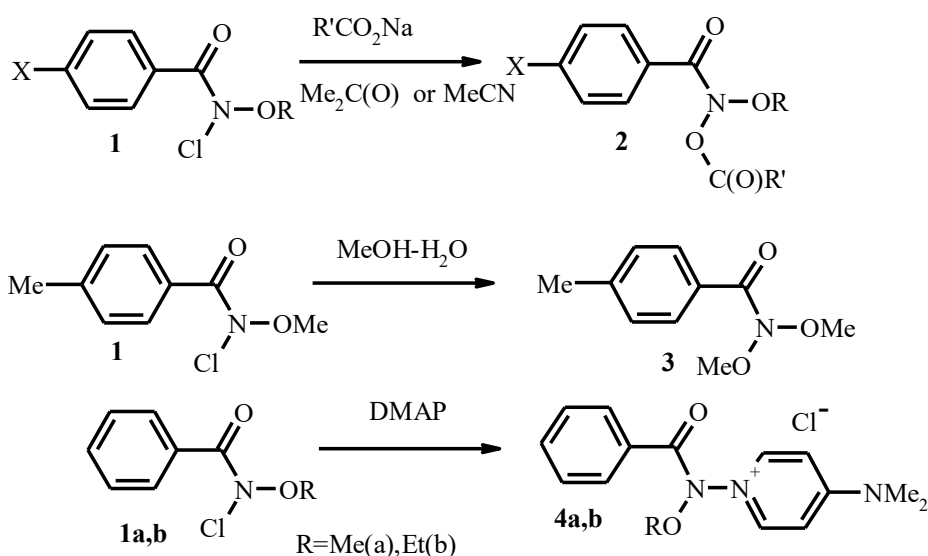
фосфорилоксиімідатів. У цьому дослідженні доведено можливість взаємодії *N*-алкокси-*N*-хлоробензамідів з *P*-нуклеофілами. Структуру *N*-алкокси-1-(диметоксифосфорилокси)бензімідатів підтверджено спектрами ^1H , ^{31}P і ^{13}C ЯМР, мас-спектрами та рентгеноструктурним дослідженням. XRD дослідження *N*-метокси-1-(диметоксифосфорилокси)-4-нітробензімідату показало, що ця сполука є *Z*-ізомером, а 4-нітрофенільний фрагмент і *N*-метокси група знаходяться в транс-положенні до подвійного зв'язку $\text{C}=\text{N}$. Копланарність ароматичного кільця та π -системи подвійного зв'язку $\text{C}=\text{N}$ 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

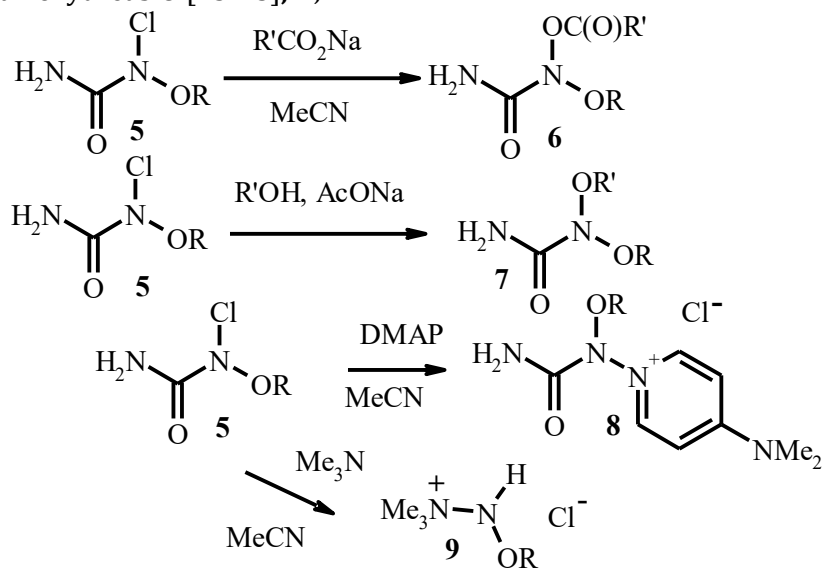
forming the products of the nucleophilic substitution at the nitrogen atom [1–12] (Scheme 1). These reactions are route to *N*-acyloxy-*N*-alkoxybenzamides **2**, *N,N*-dialkoxybenzamides **3** and unstable compounds **4**.



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-pyridinium)ureas **8** [14;17;18] (Scheme 2).

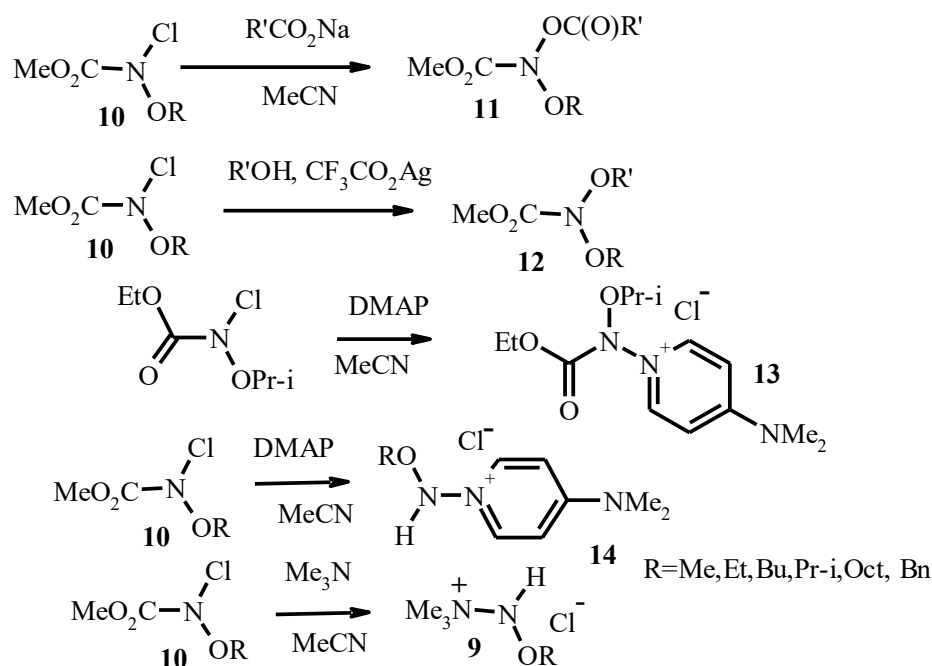


Scheme 2. The interaction of *N*-alkoxy-*N*-chloroureas **5** with *O*- and *N*-nucleophiles [13–19]

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 alcoholysis of *N*-alkoxy-*N*-chlorocarbamates **10** in the presence of silver trifluoroacetate is represents a pathway leading to the formation to

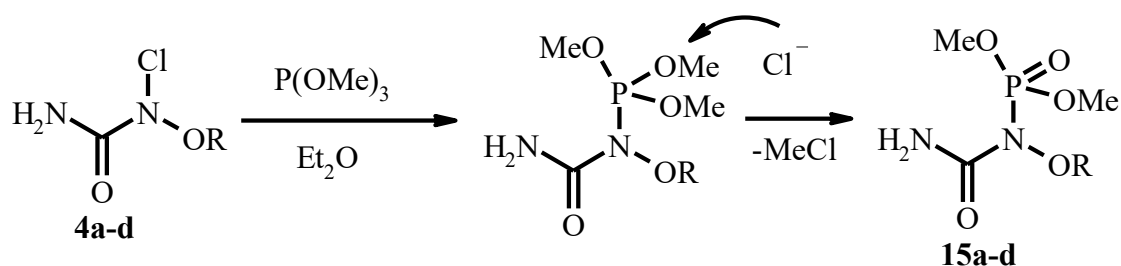
N,N-dialkoxycarbamates **12** [16] (Scheme 3). The *N*-alkoxy-*N*-chlorocarbamates **10** interaction with DMAP leads to *N*-alkoxy-*N*-(1-pyridinium)carbamate **13** [20] as well as 1-alkoxyamino-4-dimethylaminopyridinium chlorides **14** [21] (Scheme 3). The *N*-alkoxy-*N*-chlorocarbamates **10** interaction 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).



R=Me(**a**), Et(**b**), n-Bu(**c**), i-Pr (**d**)

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

^1H 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. ^1H 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 $73\text{--}74^\circ\text{C}$ (boiling hexane) (with decomp.). ^1H NMR (400 MHz, CDCl_3 , ppm): $\delta = 3.921$ (6H, d, $^{\text{HPJ}} = 12.0$ Hz, $\text{P}(\text{O})(\text{OMe})_2$); 4.073 (3H, s, NOME); 7.961 (2H, d, $^3J = 8.8$ Hz, C(2)H, C(6)H $\text{C}_6\text{H}_4\text{NO}_2$); 8.246 (2H, d, $^3J = 8.8$ Hz, C(3)H, C(5)H $\text{C}_6\text{H}_4\text{NO}_2$). ^{13}C NMR (100 MHz, CDCl_3 , ppm): $\delta = 55.68$ d, $^{\text{CPJ}} = 6.04$ Hz, $\text{P}(\text{O})(\text{OMe})_2$; 63.59 s NOME; 123.85 s C(3)H, C(5)H $\text{C}_6\text{H}_4\text{NO}_2$; 127.26 s C(2)H, C(6)H $\text{C}_6\text{H}_4\text{NO}_2$; 135.76 d, $^{\text{CPJ}} = 2.01$ Hz, C(1) $\text{C}_6\text{H}_4\text{NO}_2$; 143.995 d, $^{\text{CPJ}} = 9.06$ Hz, C=N); 149.04 s C(4)- NO_2 , $\text{C}_6\text{H}_4\text{NO}_2$. ^{31}P NMR (161.95 MHz, CDCl_3 , ppm): -9.53. Mass spectrum (FAB), $m/z(I_{\text{rel}}, \%)$: 305[M+H] $^+$ (44); 227 (9); 179 [M+HOP(O)(OMe) $_2$] $^+$ (100). Found, %: C 39.32; H 4.49; N 9.07. $\text{C}_{10}\text{H}_{13}\text{N}_2\text{O}_7\text{P}$. Calculated, %: C 39.48; H 4.31; N 9.21.

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 hypochlorite (230 mg, 2.115 mmol) in dichloromethane (2 mL) was added to the solution of *N*-methoxybenzamide (107 mg, 0.705 mmol) in dichloromethane (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 kept at 20°C under vacuum (2 mm Hg) yielding 131 mg (100%) of unstable *N*-chloro-*N*-methoxybenzamide **1a**, yellow oil. ^1H NMR (400 MHz, CDCl_3 , ppm): $\delta = 3.889$ (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): $\delta = 52.26$ 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, $n_D^{18} 1.4942$. ^1H NMR (400 MHz, CDCl_3 , ppm): $\delta = 3.891$ (6H, d, $^{\text{HPJ}} = 11.6$ Hz, $\text{P}(\text{O})(\text{OMe})_2$); 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, $^{\text{CPJ}}$ = 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, $^{\text{CPJ}}$ = 3.02 Hz, C(1)Ph; 130.72 s C(4)H, Ph; 145.66, d, $^{\text{CPJ}}$ = 10.06 Hz, C=N. ^{31}P NMR (161.95 MHz, CDCl_3 , ppm): -9.60. Mass spectrum (FAB), $m/z(I_{\text{rel}},\%)$: 260 [M+H] $^+$ (25); 134 [M+H-HOP(O)(OMe) $_2$] $^+$ (100); 127 (20). Found, %: C 46.48; H 5.56; N 5.17. $\text{C}_{10}\text{H}_{14}\text{NO}_5\text{P}$. Calculated, %: C 46.34; H 5.44; N 5.40.

B. The solution of trimethylphosphite (142 mg, 1.846 mmol) 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 $_2$ O-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. ^1H NMR (400 MHz, CDCl_3 , ppm): δ = 1.365 (3H, t, 3J = 7.0 Hz, NOCH_2Me); 3.894 (6H, d, $^{\text{HPJ}}$ = 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_2Me ; 55.40 d, $^{\text{CPJ}}$ = 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, $^{\text{CPJ}}$ = 2.01 Hz, C(1)Ph; 130.57 s C(4)H, Ph; 145.30, d, $^{\text{CPJ}}$ = 10.06 Hz, C=N. ^{31}P NMR (161.95 MHz, CDCl_3 , ppm): -9.65. Mass spectrum (FAB), $m/z(I_{\text{rel}},\%)$: 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. $\text{C}_{11}\text{H}_{16}\text{NO}_5\text{P}$. 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

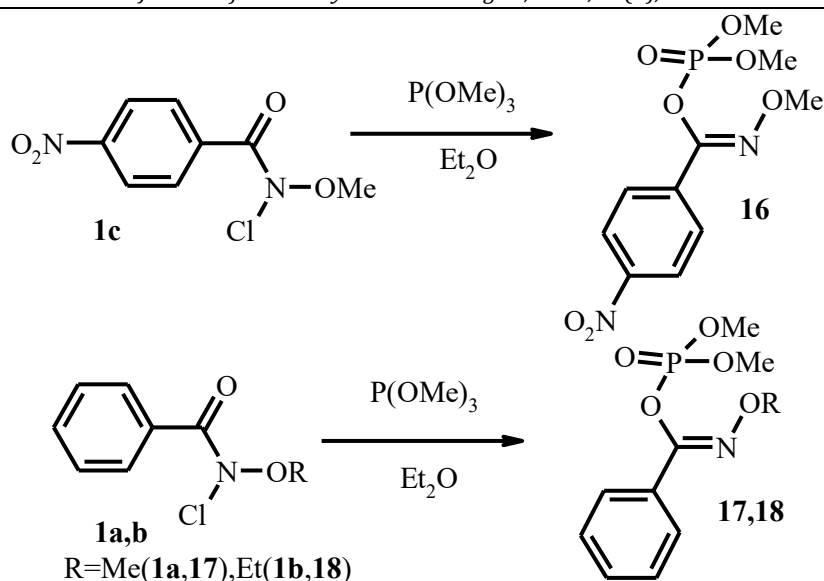
solution of *N*-chloro-*N*-ethoxybenzamide **1b** (119 mg, 0.596 mmol) [1] in ether (2 mL) at 6 °C. The reaction mixture was maintained at 6 °C during 23 h, the negligible precipitate was filtered off, washed by ether (2 mL), the combined Et $_2$ O-filtrate was evaporated under vacuum, the residue was 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** ($\text{C}_{10}\text{H}_{13}\text{N}_2\text{O}_7\text{P}$) 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 $\text{P}2_1/c$, d_{calc} = 1.506 g/cm 3 , $\mu(\text{MoK}\alpha)$ = 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 monochromated $\text{MoK}\alpha$ radiation, CCD detector, φ and ω -scanning, $2\theta_{\text{max}}$ = 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 $U_{\text{iso}} = nU_{\text{eq}}$ (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 $F > 4\sigma(F)$, S = 1.110).

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

Results and discussion

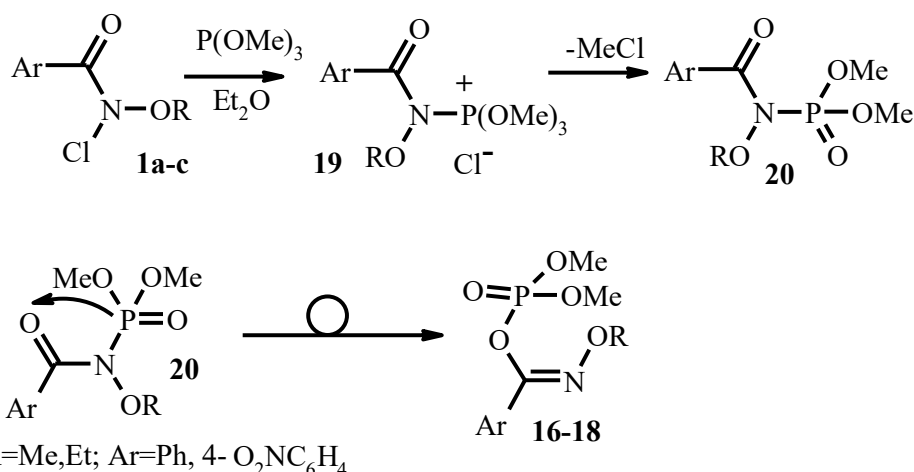
We investigated the interaction between *N*-alkoxy-*N*-chlorobenzamides **1a-c** and trimethylphosphite in ether. *N*-Alkoxy-*N*-chlorobenzamides **1a-c** selectively react with trimethylphosphite, leading to the selective formation of *N*-alkoxy-1-(dimethoxyphosphoryloxy)benzimidates **16-18** (Scheme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



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)benzamidates **20**. At the third stage unusual *N*-*O*-migration of dimethoxyphosphoryl group occurs yielding *N*-alkoxy-1-(dimethoxyphosphoryloxy)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-phosphoryloxyimides may be synthesized by copper-catalyzed cross-dehydrogenative coupling of *N*-methoxyamides with various phosphites [27]. *N*-Propyloxy-1-phosphoryloxyimides 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 triethylamine [28–36]. 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 ¹H, ¹³C, ¹³P 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 ¹H NMR spectra of compounds **16–18** show such a common characteristic as doublet of dimethoxyphosphoryl moiety and singlet of MeON-group (Table 1).

Table 1

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

compound	^1H 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.

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 (NOCH₂ for compound **18**), the carbon atoms of dimethoxyphosphoryl group and the carbon atom of C=N bond (Table 2).

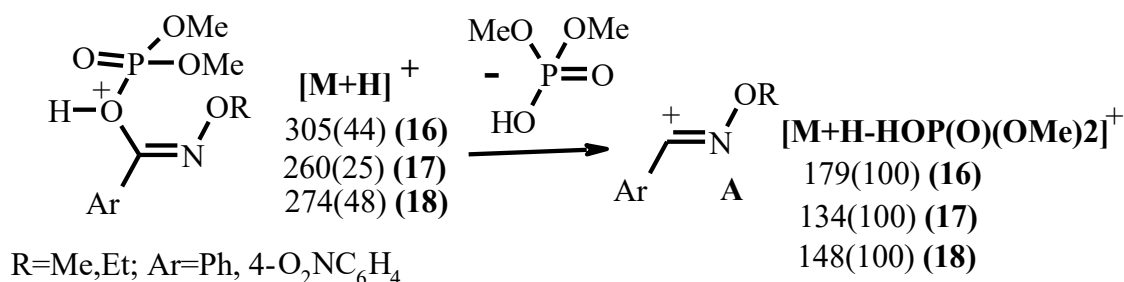
Table 2

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 $[\text{M}+\text{H}]^+$ peaks at the appropriate m/z values. But the main peak is

$[\text{M}+\text{H}-\text{HOP}(\text{O})(\text{OMe})_2]^+$ with the intensity 100%. The phosphoryloxy moiety elimination gives the stable ion **A** in all cases (Scheme 7).



Scheme 7. 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.

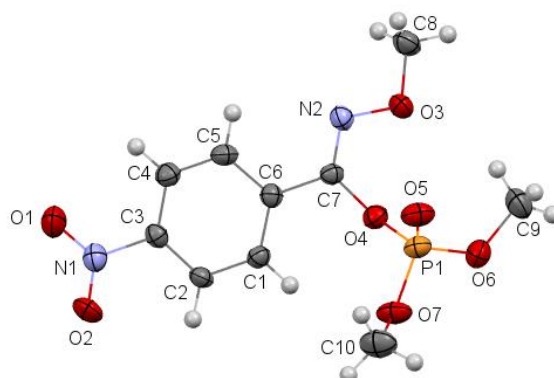


Fig. 1. Molecular structure of *Z*-*N*-methoxy-1-(dimethoxyphosphoryloxy)-4-nitrobenzimidate (**16**) according to X-ray diffraction data. Thermal ellipsoids are shown at 50% probability level

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 $-178.0(3)^\circ$). The phosphoryloxy 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 $-3.2(5)^\circ$). Thus, *N*-methoxy-1-(dimethoxyphosphoryloxy)-4-nitrobenzimidate **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)benzimidates **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 $-2.8(6)^\circ$). The C(8)H₃

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 $174.4(4)^\circ$).

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 $96.5(4)^\circ$). This substituent is deployed in such a way that the P(1) = O(5) bond is syn-periplanar with the C(7)–O(4) bond (the C(7)–O(4)–P(1)–O(5) torsion angle is $-15.6(4)^\circ$). 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 $-129.9(3)^\circ$, the C(9)–O(6)–P(1)–O(4) torsion angle is $81.1(4)^\circ$).

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°).

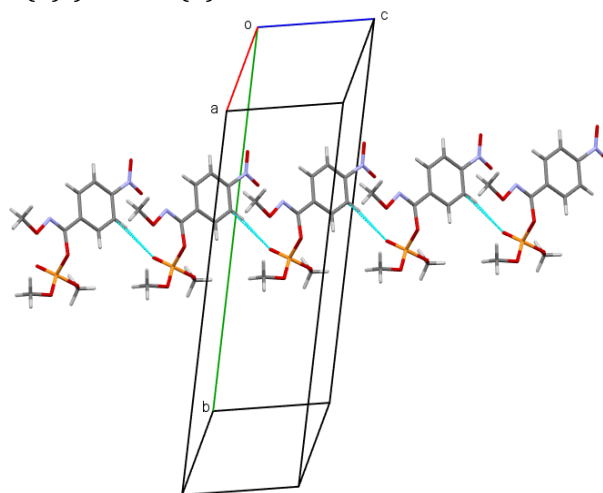


Figure 2. The chains of molecules of *Z*-*N*-methoxy-1-(dimethoxyphosphoryloxy)-4-nitrobenzimidate (**16**) formed by the weak hydrogen bonds (cyan dotted lines) in the crystal

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 ¹H, ¹³C, ³¹P 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](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](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 Functional 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/MC2006v016n04ABEH0021>
- [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., Prosyaniuk, A.V., Mazepa, A.V., Kostyanovsky, R.G. (2009). Chiral Ureas with Two Electronegative Substituents 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-dialkoxyureas. *Mendeleev Commun.*, 21(12), 50–52. <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](https://doi.org/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](https://doi.org/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.mencom.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-isopropoxy)amino-4-dimethylaminopyridinium Chloride. Synthesis and Structure. *Eur. Chem. Bull.*, 6 (10) (2017) 470–474. doi: [10.17628/ecb.2017.6.470-474](https://doi.org/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. <https://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.

- Acta Cryst., 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.