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Regioselective synthesis of substituted isoxazolo[5,4-*d*]pyrimidines

Sergey B. Alyabiev,* Dmitri V. Kravchenko and Alexandre V. Ivachtchenko

Department of Organic Chemistry, Chemical Diversity Research Institute, 114401 Khimki, Moscow Region, Russian Federation. Fax: +7 495 626 9780; e-mail: alyabjev@iihr.ru

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A convenient regioselective synthesis of new N- and O-substituted isoxazolo[5,4-*d*]pyrimidine derivatives is described.

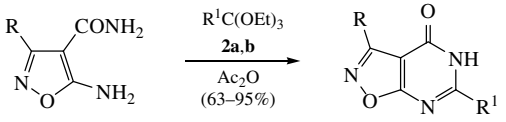
Pyrimidine and fused heterocyclic pyrimidine derivatives have a broad spectrum of biological activity.[1–12] Isoxazolo[5,4-*d*]-pyrimidines and their bioisosteric analogues are promising antiviral, antitumor and antimicrobial agents.[13] Isoxazolo[5,4-*d*]-pyrimidin-4-one derivatives were found to exhibit activity against human type V phosphodiesterase PDE V with IC_{50} = 100 nM.[14] Isoxazolo[4,5-*d*]pyrimidines were described as pesticides[15,16] and CRF antagonists.[17] Thus, isoxazolo[5,4-*d*]pyrimidine derivatives represent an important class of compounds with promising chemical and biological potentials.

Although the syntheses of these compounds are well known,[18,19] the regioselective alkylation of isoxazolo[5,4-*d*]pyrimidines is not well described. Only few synthetic approaches were developed to prepare 5N-substituted isoxazolo[5,4-*d*]pyrimidines.[20,21] For example, the cyclization of N,3-substituted 5-aminoisoxazole-4-carboxamides with (diethoxymethoxy)ethane in the presence of acetic anhydride led to 5N-substituted isoxazolo[5,4-*d*]-pyrimidines.[21]

Here, we report the synthesis of new 5N-substituted isoxazolo-[5,4-*d*]pirimidines and 4O-substituted isoxazolo[5,4-*d*]pirimidines.

First, we synthesised 3,6-disubstituted isoxazolo[5,4-*d*]pyrimidin-4(5*H*)-ones **3a–k** using a modified approach proposed by Taylor *et al.*[15] (Scheme 1).†

Initial 3-substituted 5-aminoisoxazole-4-carboxamides **1a–h**, obtained by a well-known synthetic method,[22] were easily converted into corresponding isoxazolo[5,4-*d*]pyrimidin-4(5*H*)-ones **3a–k** by reaction with esters **2a**,**b**. The cyclization proceeded smoothly in acetic anhydride at 120 °C to give the desired products in 61–95% yields.



1a–h **3a–k**

1a R = Me
1b R = Et
1c R = Ph
1d R = 4-FC_6H_4
1e R = 4-MeC_6H_4
1f R = 4-$MeOC_6H_4$
1g R = 3-FC_6H_4
1h R = 3-ClC_6H_4

2a R^1 = H
2b R^1 = Me

3a R = Me, R^1 = H
3b R = Et, R^1 = H
3c R = R^1 = Me
3d R = Et, R^1 = Me
3e R = Ph, R^1 = H
3f R = Ph, R^1 = Me
3g R = 4-FC_6H_4, R^1 = H
3h R = 4-MeC_6H_4, R^1 = H
3i R = 4-$MeOC_6H_4$, R^1 = H
3j R = 3-FC_6H_4, R^1 = H
3k R = 2-FC_6H_4, R^1 = H

Scheme 1

In contrast to the results described by Adhikari *et al.*,[23] we found that the reaction of isoxazolo[5,4-*d*]pyrimidines **3a–k** with α-chloroester **4a** or **4b** in the presence of K_2CO_3 directly led to corresponding N-alkylated products **5a–j** (Scheme 2).‡ The reaction smoothly proceeded in DMF at 70 °C to give the desired products in 76–98% yields. Previously,[23] it was postulated that an O-alkylated product was formed using isoxazolo[5,4-*d*]-pyrimidine **3e** and ester **4b** as initial reactants under similar reaction conditions. However, it seems unlikely that the regio-selective outcome of this reaction was interpreted correctly.

Isoxazolo[5,4-*d*]pyrimidines **3a**,**b**,**e**,**f** were converted into corresponding 4-chloroisoxazolo[5,4-*d*]pyrimidines **6a**,**b**,**e**,**f** by treatment with phosphorus oxychloride in *N*,*N*-dimethyl-*N*-phenylamine (yield 85–96%) (Scheme 3).§

† Melting points were measured with a Buchi B-520 apparatus and were not corrected. The NMR spectra were recorded on a Bruker AMX-400 or Varian spectrometer in [$^2H_6$]DMSO using TMS as an internal standard. Commercial reagents (Acros Organics, Aldrich and ChemDiv) were used without purification.

*General procedure for the preparation of 3,6-disubstituted isoxazolo-[5,4-*d*]pyrimidin-4(5*H*)-ones* **3a–k**. 5-Aminoisoxazole-4-carboxamide **1a–h** (0.2 mol) was suspended in ester **2a**,**b** (1.6 mol); then acetic anhydride (260 ml) was added to the solution. The reaction mixture was stirred at 120 °C for 3–5 h, and ethyl acetate was evaporated. The reaction was followed by TLC (5% MeOH in CH_2Cl_2). On completion, the reaction mixture was cooled to room temperature, the formed precipitate was filtered off, washed with methanol and dried in air to yield corresponding isoxazolo[5,4-*d*]pyrimidin-4(5*H*)-ones (yields 63–95%). Compounds **3a–k** were used at the next step without further purification.

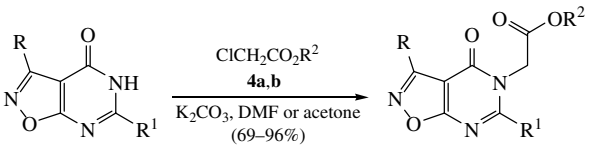
*3-Ethylisoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one* **3b**: yield 66%, mp 183–184 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 1.2 (t, 3H, Me, *J* 7.5 Hz), 2.8 (q, 2H, CH_2, *J* 7.5 Hz), 8.3 (s, 1H, 6-H), 13.1 (br. s, 1H, NH). Found (%): C, 51.06; H, 4.65; N, 25.12. Calc. for $C_7H_7N_3O_2$ (%): C, 50.91; H, 4.27; N, 25.44.

*3-Phenylisoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one* **3e**: yield 78%, mp 278–280 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 7.5–7.6 (m, 3H, H_{Ar}), 8.25 (d, 1H, H_{Ar}, *J* 7.2 Hz), 8.3 (d, 1H, H_{Ar}, *J* 7.2 Hz), 8.45 (s, 1H, 6-H), 13.2 (br. s, 1H, NH). Found (%): C, 62.03; H, 3.11; N, 19.92. Calc. for $C_{11}H_7N_3O_2$ (%): C, 61.97; H, 3.31; N, 19.71.

*6-Methyl-3-phenylisoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one* **3f**: yield 80%; mp 310–312 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 2.11 (s, 3H, Me), 7.44–7.49 (m, 3H, H_{Ar}), 8.15–8.19 (m, 2H, H_{Ar}), 13.09 (br. s, 1H, NH). Found (%): C, 63.47; H, 4.03; N, 18.55. Calc. for $C_{12}H_9N_3O_2$ (%): C, 63.43; H, 3.99; N, 18.49.

*3-(4-Methylphenyl)isoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one* **3h**: 83%; mp 245–247 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 2.21 (s, 3H, Ar*Me*), 7.3 (d, 2H, H_{Ar}, *J* 8.1 Hz), 8.15 (d, 2H, H_{Ar}, *J* 8.1 Hz), 8.41 (s, 1H, 6-H), 12.93 (br. s, 1H, NH). Found (%): C, 63.12; H, 3.90; N, 18.12. Calc. for $C_{12}H_9N_3O_2$ (%): C, 63.43; H, 3.99; N, 18.49.

For characteristics of compounds **3a**,**c**,**d**,**g**,**i–k** see Online Supplementary Materials.



3a–k **5a–j**

4a R^2 = Me
4b R^2 = Et

5a R = R^2 = Me, R^1 = H
5b R = Me, R^1 = H, R^2 = Et
5c R = R^1 = R^2 = Me
5d R = Ph, R^1 = H, R^2 = Me
5e R = Ph, R^1 = H, R^2 = Et
5f R = 4-MeC_6H_4, R^1 = H, R^2 = Me
5g R = 4-MeC_6H_4, R^1 = H, R^2 = Et
5h R = 4-$MeOC_6H_4$, R^1 = H, R^2 = Me
5i R = 2-FC_6H_4, R^1 = H, R^2 = Me
5j R = 2-FC_6H_4, R^1 = H, R^2 = Et

Scheme 2

The reactions of equimolar amounts of 4-chloroisoxazolo[5,4-*d*]-pyrimidines **6a**,**b**,**e**,**f** and ethyl hydroxyacetate in the presence of K_2CO_3 (1.1 equiv.) afforded ethyl [(isoxazolo[5,4-*d*]pyrimidin-4-yl)oxy]acetates **7a**,**b**,**d**–**f** (Scheme 3).¶ The reaction proceeded in DMF at 80 °C to give pure products, which were precipitated from the reaction mixture in good yields (62–68%).

The structures of compounds **5e** and **7d** were assigned using NMR spectroscopy and firmly established by an X-ray crystallographic study (Figure 1).†† Based on these results, we accurately indicate the stereochemical outcome of this reaction. The stereoselective alkylation of isoxazolo[5,4-*d*]pyrimidine **3e** by ethyl

‡ *General procedure for the preparation of (4-oxoisoxazolo[5,4-*d*]-pyrimidin-5(4*H*)-yl)acetates* **5a**–**j**. α-Chloroester **4a**,**b** (0.12 mol) and anhydrous K_2CO_3 (0.13 mol) were added to a solution of isoxazolo[5,4-*d*]-pyrimidin-4(5*H*)-one **3a**,**c**,**e**,**h**,**i**,**k** in dry DMF (125 ml). The reaction mixture was stirred at 70 °C for 3–4 h. The reaction was followed by TLC (5% MeOH in CH_2Cl_2). The solution was cooled to room temperature and then poured into cold water (500 ml). The precipitate was filtered off and washed with water and hexane. The desired esters **5a**–**j** were obtained in good yields (76–98%).

*Ethyl (3-methyl-4-oxoisoxazolo[5,4-*d*]pyrimidin-5(4*H*)-yl)acetate* **5b**: yield 83%, mp 143–145 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 1.27 (t, 3H, Me, *J* 7.0 Hz), 2.52 (s, 3H, Me), 4.26 (q, 2H, OCH_2, *J* 7.0 Hz), 4.79 (s, 2H, NCH_2), 8.58 (s, 1H, 6-H). Found (%): C, 50.69; H, 4.61; N, 17.68. Calc. for $C_{10}H_{11}N_3O_4$ (%): C, 50.63; H, 4.67; N, 17.71.

*Methyl (3,6-dimethyl-4-oxoisoxazolo[5,4-*d*]pyrimidin-5(4*H*)-yl)acetate* **5c**: yield 76%, mp 50–52 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 2.44 (s, 3H, Me), 2.54 (s, 3H, Me), 3.76 (s, 3H, OMe), 4.60 (s, 2H, NCH_2). Found (%): C, 50.67; H, 4.71; N, 17.75. Calc. for $C_{10}H_{11}N_3O_4$ (%): C, 50.63; H, 4.67; N, 17.71.

*Methyl (4-oxo-3-phenylisoxazolo[5,4-*d*]pyrimidin-5(4*H*)-yl)acetate* **5d**: yield 90%, mp 144–145 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 3.83 (s, 3H, OMe), 4.79 (s, 2H, NCH_2), 7.65–7.69 (m, 3H, Ar*H*), 8.12–8.16 (m, 2H, Ar*H*), 8.68 (s, 1H, 6-H). ^{13}C NMR (DMSO + CCl_4, 400 MHz) δ: 47.37 (NCH_2), 53.15 (OMe), 100.51 (C-3a), 126.97(C_{Ar}-4), 128.67 (C_{Ar}-3,5), 128.79 (C_{Ar}-2,6), 131.03 (C_{Ar}-1), 152.41 (C-3), 156.51 (C-4), 159.95 (C-6), 167.06 (*C*OOMe), 175.43 (C-7a). Found (%): C, 58.99; H, 3.82; N, 14.68. Calc. for $C_{14}H_{11}N_3O_4$ (%): C, 58.95; H, 3.89; N, 14.73.

*Ethyl (4-oxo-3-phenylisoxazolo[5,4-*d*]pyrimidin-5(4*H*)-yl)acetate* **5e**: yield 77%, mp 159–161 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 1.25 (t, 3H, Me, *J* 7.0 Hz), 4.18 (q, 2H, OCH_2, *J* 7.0 Hz), 4.87 (s, 2H, NCH_2), 7.45–7.49 (m, 3H, H_{Ar}), 8.20–8.25 (m, 2H, H_{Ar}), 8.69 (s, 1H, 6-H). ^{13}C NMR (DMSO + CCl_4, 400 MHz) δ: 12.44 (Me), 45.82 (NCH_2), 60.03 (OCH_2), 98.10 (C-3a), 125.47 (C_{Ar}-4), 126.97 (C_{Ar}-3,5), 127.11 (C_{Ar}-2,6), 129.29 (C_{Ar}-1), 152.99 (C-3), 154.81 (C-4), 157.77 (C-6), 165.59 (*C*OOEt), 173.90 (C-7a). Found (%): C, 60.24; H, 4.32; N, 13.98. Calc. for $C_{15}H_{13}N_3O_4$ (%): C, 60.20; H, 4.38; N, 14.04.

*Methyl [3-(4-methylphenyl)-4-oxoisoxazolo[5,4-*d*]pyrimidin-5(4*H*)-yl]-acetate* **5f**: yield 94%, mp 190–192 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 2.39 (s, 3H, Me), 3.72 (s, 3H, OMe), 4.90 (s, 2H, NCH_2), 7.37 (d, 2H, H_{Ar}, *J* 8.0 Hz), 8.13 (d, 2H, H_{Ar}, *J* 8.0 Hz), 8.78 (s, 1H, 6-H). Found (%): C, 60.16; H, 4.31; N, 14.11. Calc. for $C_{15}H_{13}N_3O_4$ (%): C, 60.20; H, 4.38; N, 14.04.

For characteristics of compounds **5a**,**g**,**h**,**j** see Online Supplementary Materials.

§ *General procedure for preparation of 4-chloroisoxazolo[5,4-*d*]-pyrimidines* **6a**,**b**,**e**,**f**. Phosphorus oxychloride (1 mol) and dimethylaniline (0.2 mol) were added to a solution of isoxazolo[5,4-*d*]pyrimidin-4(5*H*)-one **3a**,**b**,**e**,**f** (0.2 mol) in dry toluene. The resulting suspension was stirred at reflux for 3–4 h. The reaction was followed by TLC (5% MeOH in CH_2Cl_2). The solution was cooled to room temperature, poured onto crushed ice and neutralised with an aqueous solution of NaOH (10%). The organic layer was separated; the aqueous layer was extracted with benzene (3×200 ml). Combined extracts were washed with HCl (6%), water, $NaHCO_3$ and water again. The extracts were purified by flash chromatography on a silica gel/aluminium oxide column (eluent, benzene). The solvent was evaporated *in vacuo* and the resulting residue was poured into cold hexane. The formed precipitate was filtered off, washed with hexane and dried *in vacuo* over P_2O_5. Chlorides **6a**,**b**,**e**,**f** were obtained in 85–96% yield.

*4-Chloro-3-methylisoxazolo[5,4-*d*]pyrimidine* **6a**: yield 92%, mp 67–68 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 2.71 (s, 3H, Me), 9.01 (s, 1H, 6-H). Found (%): C, 42.61; H, 2.35; Cl, 20.93; N, 24.82. Calc. for $C_6H_4ClN_3O$ (%): C, 42.50; H, 2.38; Cl, 20.91; N, 24.78.

*4-Chloro-3-phenylisoxazolo[5,4-*d*]pyrimidine* **6e**: yield 96%, mp 100–102 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 7.59–7.67 (m, 3H, H_{Ar}), 7.80–7.86 (m, 2H, H_{Ar}), 9.10 (s, 1H, 6-H). Found (%): C, 57.11; H, 2.67; Cl, 15.41; N, 18.22. Calc. for $C_{11}H_6ClN_3O$ (%): C, 57.04; H, 2.61; Cl, 15.31; N, 18.14.

*4-Chloro-6-methyl-3-phenylisoxazolo[5,4-*d*]pyrimidine* **6f**: yield 94%, mp 112–114 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 2.80 (s, 3H, Me), 7.56–7.66 (m, 3H, H_{Ar}), 7.77–7.82 (m, 2H, H_{Ar}). Found (%): C, 58.73; H, 3.33; Cl, 14.45; N, 17.08. Calc. for $C_{12}H_8ClN_3O$ (%): C, 58.67; H, 3.28; Cl, 14.43; N, 17.10.

¶ *General procedure for the preparation of (isoxazolo[5,4-*d*]-pyrimidin-4-yl)oxyacetates* **7a**,**b**,**d**,**e**,**f**. Ethyl hydroxyacetate (0.11 mol) and anhydrous K_2CO_3 (0.11 mol) were added to a solution of chloride **6a**,**b**,**e**,**f** (0.1 mol) in dry DMF (115 ml). The reaction mixture was stirred at 80 °C for 4–5 h, then cooled to rt and poured into cold water. The precipitate was filtered off, washed with hexane and recrystallised from ethanol or acetonitrile to give desired esters **7a**,**b**,**d**,**e**,**f** in moderate yields (62–68%).

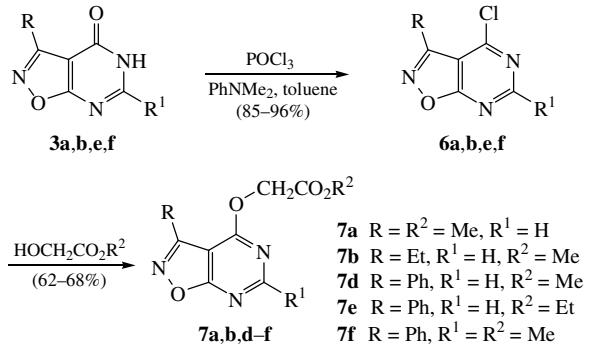
*Methyl [(3-methyl-4,5-dihydroisoxazolo[5,4-*d*]pyrimidin-4-yl)oxy]-acetate* **7a**: mp 96–98 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 2.64 (s, 3H, Me), 3.74 (s, 3H, OMe), 5.21 (s, 2H, OCH_2), 8.70 (s, 1H, 6-H). Found (%): C, 48.04; H, 4.88; N, 18.69. Calc. for $C_9H_{11}N_3O_4$ (%): C, 48.00; H, 4.92; N, 18.66.

*Methyl [(3-ethyl-4,5-dihydroisoxazolo[5,4-*d*]pyrimidin-4-yl)oxy]acetate* **7b**: mp 150–153 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 1.36 (t, 3H, Me, *J* 7.4 Hz), 2.99 (q, 2H, CH_2, *J* 7.4 Hz), 3.72 (s, 3H, OMe), 5.28 (s, 2H, OCH_2), 8.79 (s, H, 6-H). Found (%): C, 50.68; H, 4.75; N, 18.82. Calc. for $C_{10}H_{11}N_3O_4$ (%): C, 50.63; H, 4.67; N, 17.71.

*Methyl [(3-phenyl-4,5-dihydroisoxazolo[5,4-*d*]pyrimidin-4-yl)oxy]acetate* **7d**: mp 122–123 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 3.73 (s, 3H, OMe), 5.29 (s, 2H, OCH_2), 7.62 (m, 3H, H_{Ar}), 8.09 (m, 2H, H_{Ar}), 8.87 (s, 1H, 6-H). ^{13}C NMR (DMSO + CCl_4, 400 MHz) δ: 52.34 (OMe), 64.17 (OCH_2), 104.19 (C-3a), 129.54 (C_{Ar}-4), 131.45 (C_{Ar}-2,6), 134.01 (C_{Ar}-3,5), 143.41 (C_{Ar}-1), 156.51(C_{Ar}-6), 162.28 (C-3), 166.23 (C-7a), 168.08 (C-4), 168.43 (*C*OOMe). Found (%): C, 58.57; H, 4.51; N, 14.66. Calc. for $C_{14}H_{13}N_3O_4$ (%): C, 58.53; H, 4.56; N, 14.63.

*Ethyl [(3-phenyl-4,5-dihydroisoxazolo[5,4-*d*]pyrimidin-4-yl)oxy]acetate* **7e**: mp 96–98 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 1.22 (t, 3H, Me, *J* 7.1 Hz), 4.19 (q, 2H, OCH_2, *J* 7.1 Hz), 5.27 (s, 2H, OCH_2), 7.59–7.63 (m, 3H, Ar), 8.07–8.11 (m, 2H, Ar), 8.88 (s, 1H, 6-H). ^{13}C NMR (DMSO + CCl_4, 400 MHz) δ: 13.84 (Me), 61.05 (OCH_2), 64.43 (OCH_2), 105.51 (C-3a), 130.17 (C_{Ar}-4), 131.92 (C_{Ar}-2,6), 134.99 (C_{Ar}-3,5), 143.19 (C_{Ar}-1), 157.38 (C-6), 162.18 (C-3), 166.13 (C-7a), 167.98 (C-4), 168.88 (*C*OOEt). Found (%): C, 59.83; H, 4.97; N, 14.01. Calc. for $C_{15}H_{15}N_3O_4$ (%): C, 59.79; H, 5.02; N, 13.95.

*Methyl [(6-methyl-3-phenyl-4,5-dihydroisoxazolo[5,4-*d*]pyrimidin-4-yl)-oxy]acetate* **7f**: mp 131–133 °C. ^{1}H NMR (DMSO + CCl_4, 400 MHz) δ: 2.65 (s, 3H, Me), 3.73 (s, 3H, OMe), 5.25 (s, 2H, OCH_2), 7.61 (m, 3H, -H_{Ar}), 8.09 (m, 2H, H_{Ar}). Found (%): C, 59.83; H, 4.98; N, 13.99. Calc. for $C_{15}H_{15}N_3O_4$ (%): C, 59.79; H, 5.02; N, 13.95.



Scheme 3

chloroacetate **4b** led to corresponding N-substituted isoxazolo-[5,4-*d*]pyrimidine **5e** as distinct from O-alkylated product.

The structures of compounds synthesised in this work were determined using elemental analysis and ^{1}H NMR spectroscopy. In particular, the ^{1}H NMR spectra of **5e** and **7e** were clean and showed characteristic signals from five protons of a phenyl ring and corresponding substituents at the oxygen and nitrogen atoms, respectively. These results were compared to the data obtained by Adhikari (Table 1). As shown in Table 1, the ^{1}H NMR spectra of compound **5e** contain the characteristic signals of five aromatic protons, which can be seen as multipletes in the ranges δ 7.45–7.49 and 8.20–8.25 ppm. On the contrary, in the ^{1}H NMR spectra of compound **7e** suggested by Adhikari[23], the same signals are compactly grouped in the range δ 7.0–7.3 ppm. It is even more important that the chemical shifts of two aliphatic protons of methylene group of the compound **5e** (a singlet at δ 4.87 ppm) obtained in this work and the one postulated by Adhikari were not significantly different from each other. In contrast, the ^{1}H NMR spectra of compound **7e**, which was unambiguously established as ethyl [(3-phenylisoxazolo[5,4-*d*]-pyrimidin-4-yl)oxy]acetate by X-ray crystallography, contain two aliphatic protons of the methylene group, which can be seen as a singlet at δ 5.27 ppm. This effect is strongly correlated with the influence of the oxygen atom of OCH_2 (the signal was shifted downfield by 0.4 ppm). Moreover, the signal of two phenyl *o*-protons of compound **5e** can also be seen in the lower field region (δ 8.22 ppm) as against to compound **7d**. These experimental data are consistent with the role of carbonyl oxygen in a similar molecular environment.[24] Based on these arguments, we can confidently assert that the reaction of isoxazolo[5,4-*d*]-pyrimidines **3a–k** with α-chloroesters **4a** and **4b** directly leads to corresponding N-alkylated products.

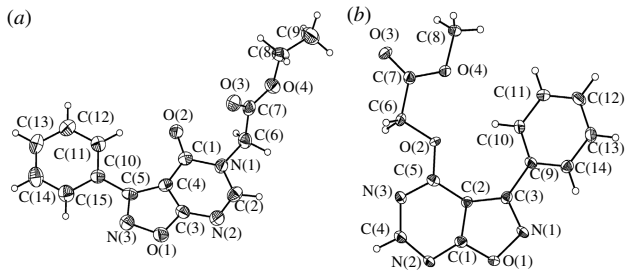


Figure 1 Crystal structure of compounds (*a*) **5e** and (*b*) **7d**.

Table 1 ^{1}H NMR spectral data for compounds **5e** and **7e**.

Compound **5e**	Compound **7e** (lit.[13])	Compound **7e**
8.69 (s, 1H, H_{Ar})	8.35 (s, 1H, 6-H)	8.88 (s, 1H, 6-H)
8.20–8.25 (m, 2H, H_{Ar})	7.0–7.3 (m, 5H, H_{Ar})	8.07–8.11 (m, 2H, H_{Ar})
7.45–7.49 (m, 3H, H_{Ar})		7.59–7.63 (m, 3H, H_{Ar})
4.87 (s, 2H, NCH_2)	**4.65** (s, 2H, NCH_2)	**5.27** (s, 2H, OCH_2)
4.20 (q, 2H, $COOCH_2$)	4.00 (q, 2H, $COOCH_2$)	4.19 (q, 2H, $COOCH_2$)
1.25 (t, 3H, Me)	1.20 (t, 3H, Me)	1.22 (t, 3H, Me)

Online Supplementary Materials

Supplementary data associated with this article can be found in the electronic version at doi:10.1016/j.mencom.2008.05.011.

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†† *X-ray diffraction data.*

For **5e**: at 120(2) K crystals of $C_{15}H_{13}N_3O_4$ (M = 299.28) are monoclinic, space group $P2_1/n$, a = 14.602(6), b = 4.9659(19) and c = 19.499(8) Å, β = 106.299(10)°, V = 1357.0(9) Å^3, Z = 4; μ = 0.109 mm^{-1}; number of independent reflections, 2618 [R_{int} = 0.0866]. Final R indices [$I > 2\sigma(I)$] R_1 = 0.0523, wR_2 = 0.1011; R indices (all data) R_1 = 0.1452, wR_2 = 0.1279.

For **7d**: at 100(2) K crystals of $C_{14}H_{11}N_3O_4$ (M = 285.26) are orthorhombic, space group *Pbca*, a = 17.298(6), b = 7.271(3) and c = 20.007(9) Å, V = 2516.3(17) Å^3, Z = 8, μ = 0.113 mm^{-1}; number of independent reflections, 2709 [R_{int} = 0.0863]. Final R indices [$I > 2\sigma(I)$] R_1 = 0.0631, wR_2 = 0.0919; R indices (all data) R_1 = 0.1743, wR_2 = 0.1211.

CCDC 686673 and 686674 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2008.