Russian Journal of Organic Chemistry, Vol. 41, No. 4, 2005, pp. 546–550. Translated from Zhurnal Organicheskoi Khimii, Vol. 41, No. 4, 2005, pp. 557–561.

Synthesis of Nitrogen-Containing Phenoxyacetic Acid Derivatives

E. T. Yamansarova, O. S. Kukovinets, R. A. Zainullin, F. Z. Galin, and M. I. Abdullin

[1] *Institute of Organic Chemistry, Ufa Research Center, Russian Academy of Sciences, pr. Oktyabrya 71, Ufa, 450054 Bashkortostan, Russia*
e-mail: chemorg@fnrb.ru

[2] *Bashkir State University, Ufa, Bashkortostan, Russia*

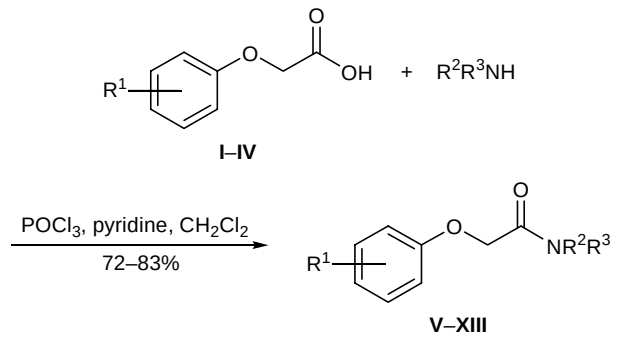
Received March 9, 2004

Abstract—Nitrogen-containing phenoxyacetic acid derivatives were synthesized by reactions of substituted phenoxyacetic acids with amines, urea, and ethyl carbamate.

Analysis of published data on pharmacological and pesticide activity of compounds possessing a phenoxyacetate moiety revealed a number of substances exhibiting phytohormone and herbicide properties. Moreover, derivatives of phenoxyacetic acid are characterized by a broad spectrum of physiological activity whose kind and strength depends on the substituents in both the aromatic ring and the acid fragment [1–4]. Introduction of nitrogen-containing groups was shown to improve the activity [2–4]. Taking the above stated into account, we converted aroxyacetic acids **I**–**IV** into *N*,*N*-diisopropyl and *N*-benzyl amides **V**–**XII** by reaction with the corresponding amines in the presence of $POCl_3$ (Scheme 1). The synthesis of acids **I**–**IV** was described previously [5]. From *p*-nitrophenoxyacetic acid (**II**) we also obtained *N*-methyl amide **XIII**.

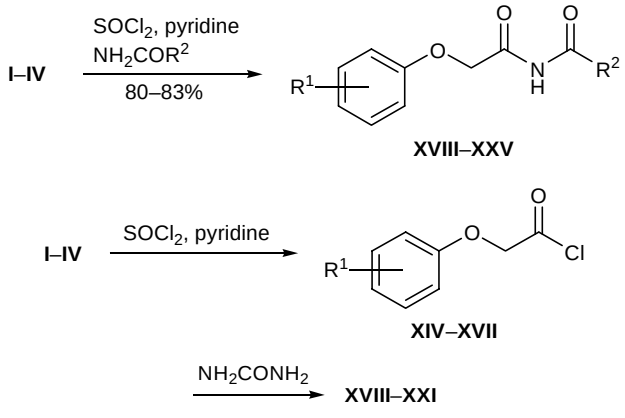
Substituted phenoxyacetic acids **I**–**IV** were also used to obtain the corresponding ureides **XVIII**–**XXI**. These compounds can be synthesized in two steps through intermediate aroxyacetyl chlorides **XIV**–**XVII** and in one step, by heating a mixture of the corresponding acid, urea, and thionyl chloride in an appropriate solvent. The latter procedure ensures a higher yield of the target products. We succeeded in avoiding formation of diacylated ureas by carrying out the reaction with 2–2.5 equiv of urea (Scheme 2). The reactions of phenoxyacetic acids **I**–**IV** with ethyl carbamate in the presence of thionyl chloride and pyridine afforded compounds **XXII**–**XXV** which attract interest as potential insect growth regulators. It was found that the product obtained by reaction of carbamic acid with 2,4-decadienol exhibits a strong juvenilizing effect toward large mealworm (*Tenebrio molitor*) [6–9] and that the presence of a phenoxy fragment improves the juvenoid activity [10].

Scheme 1.



I, **V**, **IX**, R^1 = H; **II**, **VI**, **X**, **XIII**, R^1 = 4-O_2N; **III**, **VII**, **XI**, R^1 = 3-PhO; **IV**, **VIII**, **XII**, R^1 = 2,4-Cl_2; **V**–**VIII**, R^2 = R^3 = *i*-Pr; **IX**–**XII**, R^2 = H, R^3 = $PhCH_2$; **XIII**, R^2 = H, R^3 = Me.

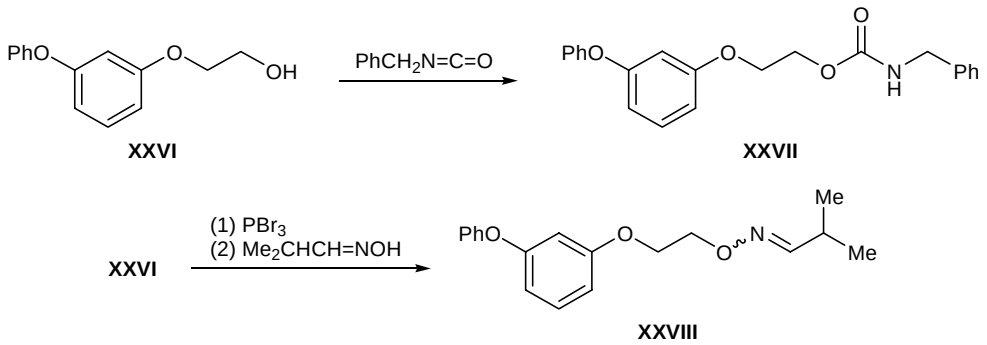
Scheme 2.



I, **XIV**, **XVIII**, **XXII**, R^1 = H; **II**, **XV**, **XIX**, **XXIII**, R^1 = 4-O_2N; **III**, **XVI**, **XX**, **XXIV**, R^1 = 3-PhO; **IV**, **XVII**, **XXI**, **XXV**, R^1 = 2,4-Cl_2; **XVIII**–**XXI**, R^2 = NH_2; **XXII**–**XXV**, R^2 = EtO.

1070-4280/05/4104-0546

Scheme 3.



By reaction of 2-phenoxyethanol **XXVI** with benzyl isocyanate we obtained carbamate **XXVII**. As starting material we selected a compound containing a phenoxy group, for an analogous fragment is present in the molecule of one of the most active juvenile hormone analog, Phenoxycarb (3-phenoxyphenyl ethylcarbamate) [11]. The presence of an oxime moiety is also known to enhance biological activity of juvenoids [12]. We synthesized such a juvenile hormone analog by treatment of 2-(*m*-phenoxyphenoxy)ethanol (**XXVI**) with 2-methylpropanal oxime (Scheme 3). The structure of product **XXVIII** thus obtained was confirmed by the spectral data.

Preliminary tests showed that the prepared compounds exhibit herbicide and growth-regulating activity with respect to dicotyledons at a level comparable with the activity of 2,4-dichlorophenoxyacetic acid.

EXPERIMENTAL

The IR spectra were recorded on UR-20 and Specord M-80 spectrometers from samples prepared as thin films or dispersed in mineral oil. The ^{1}H and ^{13}C NMR spectra were measured on a Bruker AM-300 instrument (300 and 75.46 MHz, respectively) from solutions in $CDCl_3$ and acetone-d_6 using tetramethylsilane as internal reference. GLC analysis was performed on a Chrom-5 chromatograph equipped with a 1.2-m column; stationary phase SE-30 on Chromaton N-FW-DMCS (0.16–0.20 mm); carrier gas helium; oven temperature programming from 50 to 300°C at 12 deg/min. TLC analysis was performed on Silufol UV-366 plates.

Amides V–XIII (*general procedure***).** Acid **I–IV** [5], 2.5 mmol, was dissolved in 5 ml of methylene chloride, and 2.5 mmol of anhydrous pyridine and 3 mmol of the corresponding amine were added at 0°C. A solution of 2.5 mmol of $POCl_3$ in methylene chloride was then added dropwise at 0°C, and the mixture was stirred for 1 h at 0°C and for 1 h at 20°C and poured into 5.2 ml of water. The organic phase was separated, and the aqueous phase was extracted with diethyl ether. The extracts were combined with the organic phase, washed with a 10% solution of $NaHCO_3$ and a saturated solution of NaCl, and dried over $MgSO_4$. The solvent was removed, and the residue was subjected to chromatography on silica gel using petroleum ether–ethyl acetate (6:1) as eluent.

***N*,*N*-Diisopropylphenoxyacetamide (V).** Yield 0.46 g (79%), yellow–brown amorphous substance, mp 89–93°C. IR spectrum, ν, cm^{-1}: 1500 m, 1520 s, 1540 s, 1600 w, 1650 s, 1680 s. ^{1}H NMR spectrum, δ, ppm: 1.25 d (12H, Me, J = 6.0 Hz), 3.78 m (2H, CH), 4.64 s (2H, CH_2O), 7.28 m (5H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 13.82 q and 14.94 q (Me), 44.31 d (CH), 65.42 t (CH_2O), 114.64 d (C^p), 121.83 d (C^o), 129.18 d (C^m), 158.61 q (C^i), 178.54 s (C=O). Found, %: C 70.98; H 8.62; N 5.64. $C_{14}H_{21}NO_2$. Calculated, %: C 71.48; H 8.96; N 5.96.

***N*,*N*-Diisopropyl(4-nitrophenoxy)acetamide (VI).** Yield 0.56 g (80%), yellow oily liquid. IR spectrum, ν, cm^{-1}: 1495 m, 1510 s, 1540 s, 1600 w, 1645 s, 1675 s. ^{1}H NMR spectrum, δ, ppm: 1.26 d (12H, Me, J = 6.0 Hz), 3.72 m (2H, CH), 4.68 s (2H, CH_2O), 7.12 d (*o*-H, J = 8.0 Hz), 8.21 d (*m*-H, J = 8.0 Hz). ^{13}C NMR spectrum, δ_C, ppm: 13.86 q and 14.76 q (Me), 44.59 d (CH), 64.87 t (CH_2O), 114.88 d (C^o), 158.63 s (C^i), 163.17 s (C^p), 168.51 s (C=O). Found, %: C 60.06; H 7.24; N 10.41. $C_{14}H_{20}N_2O_4$. Calculated, %: C 60.00; H 7.14; N 10.00.

***N*,*N*-Diisopropyl(3-phenoxyphenoxy)acetamide (VII).** Yield 0.59 g (72%), yellow–brown oily liquid. IR spectrum, ν, cm^{-1}: 1500 m, 1520 s, 1540 s, 1605 w, 1650 s, 1680 s. ^{1}H NMR spectrum, δ, ppm: 1.25 d (12H, Me, J = 6.0 Hz), 3.68 m (2H, CH), 4.64 s (2H, CH_2O), 6.48 s (1H, *o*-H), 6.53–6.59 m (3H, *o*-H, *m*-H, *p*-H), 6.93–7.34 m (5H, H'_{arom}). ^{13}C NMR spectrum, δ_C,

ppm: 13.73 q and 14.82 q (Me), 44.52 d (CH), 65.04 t (CH_2O), 101.97 d (C^2), 107.38 d (C^6), 112.08 d (C^4), 117.90 d ($C^{2'}$, $C^{6'}$), 120.32 d (C^4), 129.60 d and 129.64 d (C^5, $C^{3'}$, $C^{5'}$), 156.29 d (C^3), 158.73 s ($C^{1'}$), 159.18 s (C^1), 168.81 s (C=O). Found, %: C 73.41; H 7.84; N 4.18. $C_{20}H_{25}NO_3$. Calculated, %: C 73.39; H 7.65; N 4.28.

***N*,*N*-Diisopropyl(2,4-dichlorophenoxy)acetamide (VIII).** Yield 0.63 g (83%), yellow–brown oily liquid. IR spectrum, ν, cm^{-1}: 1500 m, 1510 s, 1555 s, 1600 w, 1640 s, 1675 s. ^1H NMR spectrum, δ, ppm: 1.25 d (12H, Me, J = 6.0 Hz), 3.54 m (2H, CH), 4.58 s (2H, CH_2O), 6.75 d (1H, 6-H, J = 8.8 Hz), 7.01 d (1H, 5-H, J = 8.8 Hz), 7.36 s (1H, 3-H). ^{13}C NMR spectrum, δ_C, ppm: 13.84 q and 14.65 q (Me), 44.58 d (CH), 64.92 t (CH_2O), 114.65 d (C^6), 124.10 s (C^2), 126.92 s (C^4), 127.53 d (C^5), 130.24 d (C^3), 152.37 s (C^1), 163.18 s (C=O). Found, %: C 55.34; H 6.21; Cl 23.48; N 4.82. $C_{14}H_{19}Cl_2NO_2$. Calculated, %: C 55.26; H 6.25; Cl 23.36; N 4.61.

***N*-Benzyl(phenoxy)acetamide (IX).** Yield 0.49 g (81%), yellow–brown oily liquid. IR spectrum, ν, cm^{-1}: 1500 w, 1510 s, 1550 s, 1600 m, 1630 s, 1670 s, 3080 w, 3240 br.s. ^1H NMR spectrum, δ, ppm: 4.45 s (2H, CH_2O), 4.51 s (2H, CH_2N), 6.90 d (2H, *o*'-H, J = 8.0 Hz), 6.95 d (2H, *o*-H, J = 8.0 Hz), 7.05 m (1H, *p*-H), 7.30 m (5H, *m*-H, *m*'-H, *p*'-H). ^{13}C NMR spectrum, δ_C, ppm: 43.38 t (CH_2N), 67.13 t (CH_2OAr), 114.52 d (C^4), 121.54 d ($C^{p'}$), 122.18 d (C^o), 127.50 d ($C^{o'}$), 127.58 d ($C^{m'}$), 129.54 d (C^m), 137.63 s ($C^{i'}$), 156.98 s (C^i), 168.51 s (C=O). Found, %: C 74.56; H 6.34; N 5.91. $C_{15}H_{15}NO_2$. Calculated, %: C 74.69; H 6.22; N 5.81.

***N*-Benzyl(4-nitrophenoxy)acetamide (X).** Yield 0.58 g (82%), yellow oily substance. IR spectrum, ν, cm^{-1}: 1500 w, 1505 s, 1550 s, 1600 m, 1630 s, 1690 s, 3080 w, 3240 br.s. ^1H NMR spectrum, δ, ppm: 4.46 s (2H, CH_2O), 4.63 s (2H, CH_2N), 6.90 d (2H, *o*'-H, J = 8.0 Hz), 7.05 d (2H, *o*-H, J = 8.0 Hz), 7.30 m (3H, *m*'-H, *p*'-H), 7.68 d (2H, *m*-H), 7.44 s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 43.44 t (CH_2N), 66.92 t (CH_2O), 114.65 d (C^o), 121.25 d (C^m), 122.18 d ($C^{p'}$), 127.36 d ($C^{o'}$), 127.94 d ($C^{m'}$), 137.53 s ($C^{i'}$), 156.94 s (C^i), 168.10 s (C^p), 168.51 s (C=O). Found, %: C 63.04; H 4.85; N 9.68. $C_{15}H_{14}N_2O_4$. Calculated, %: C 62.94; H 4.90; N 9.79.

***N*-Benzyl(3-phenoxyphenoxy)acetamide (XI).** Yield 0.62 g (75%), yellow–brown oily liquid. IR spectrum, ν, cm^{-1}: 1500 m, 1510 s, 1550 s, 1605 m, 1630 s, 1690 s, 3080 w, 3250 br.s. ^1H NMR spectrum, δ, ppm: 4.34 s (2H, CH_2O), 4.57 s (2H, CH_2N), 6.70–7.4 m (14H, H_{arom}), 7.41 s (1H, NH). Found, %: C 75.51; H 5.84; N 4.33. $C_{21}H_{19}NO_3$. Calculated, %: C 75.68; H 5.71; N 4.20.

***N*-Benzyl(2,4-dichlorophenoxy)acetamide (XII).** Yield 0.61 g (80%), yellow–brown oily liquid. IR spectrum, ν, cm^{-1}: 1505 w, 1510 s, 1540 s, 1600 m, 1640 s, 1690 s, 3080 w, 3200–3300 br.s. ^1H NMR spectrum, δ, ppm: 4.42 s (2H, CH_2O), 4.63 s (2H, CH_2N), 6.75 d (1H, 6-H, J = 8.8 Hz), 6.90 d (2H, *o*'-H, J = 8.0 Hz), 7.01 d (2H, 5-H, J = 8.8 Hz), 7.32 m (3H, *m*'-H, *p*'-H), 7.39 d (1H, 3-H), 7.46 s (1H, NH). ^{13}C NMR spectrum, δ, ppm: 43.41 t (CH_2N), 65.98 t (CH_2O), 114.65 d (C^6), 122.18 d ($C^{p'}$), 124.10 s (C^2), 126.92 s (C^4), 127.36 d ($C^{o'}$), 127.63 d (C^5), 127.98 d ($C^{m'}$), 130.24 d (C^3), 137.44 s ($C^{i'}$), 155.87 s (C^1), 169.02 s (C=O). Found, %: C 58.17; H 4.01; Cl 22.76; N 4.73. $C_{15}H_{13}Cl_2NO_2$. Calculated, %: C 58.06; H 4.19; Cl 22.90; N 4.52.

***N*-Methyl(4-nitrophenoxy)acetamide (XIII).** Yield 0.39 g (81%), yellow–brown viscous oily substance. IR spectrum, ν, cm^{-1}: 1500 m, 1520 s, 1560 s, 1600 m, 1640 s, 1670 s, 3200–3300 br.s. ^1H NMR spectrum, δ, ppm: 2.80 br.s (3H, MeN), 4.64 s (2H, CH_2O), 7.05 d (2H, *o*-H, J = 8.5 Hz), 7.71 d (2H, *m*-H, J = 8.5 Hz). Found, %: C 51.18; H 4.89; N 13.01. $C_9H_{10}N_2O_4$. Calculated, %: C 51.43; H 4.76; N 13.30.

Phenoxyacetylureas XVIII–XXI (*general procedure*). *a*. Urea, 13 mmol, and pyridine, 7 mmol, were added to a solution of 5.9 mmol of phenoxyacetyl chloride **XIV**–**XVII** (prepared by standard procedure from the corresponding acid **I**–**IV**) in 3 ml of toluene. The mixture was heated for 2–2.5 h at 70–75°C until the initial acetyl chloride disappeared (TLC, petroleum ether–ethyl acetate, 6:1). The mixture was cooled to 50°C, 1.4 ml of water was added, the mixture was stirred for 0.5 h, and the organic phase was separated, washed with a 5% solution of $NaHCO_3$ and with water until neutral reaction, and dried over $MgSO_4$. The solvent was distilled off, and the residue was purified by column chromatography on silica gel using petroleum ether–ethyl acetate (6:1) as eluent.

b. Phenoxyacetic acid **I**–**IV**, 3.5 mmol, was dissolved in 10 ml of anhydrous benzene, and 7 mmol of urea, 4.2 mmol of freshly distilled thionyl chloride, and 4.2 mmol of anhydrous pyridine were added. The mixture was heated for 2–2.5 h under reflux until the initial acid disappeared (TLC, petroleum ether–ethyl acetate, 6:1). It was then cooled to 50°C, 1.4 ml of water was added, the mixture was stirred for 0.5 h at

that temperature, and the product was isolated as described above in *a*.

(Phenoxyacetyl)urea (XVIII). Yield 0.43 g (63%, *a*), 0.48 g (81%, *b*), light brown crystalline substance, mp 90–93°C [13].

(4-Nitrophenoxyacetyl)urea (XIX). Yield 0.48 g (65%, *a*), 0.69 g (83%, *b*), brown viscous oily liquid. IR spectrum, ν, cm^{-1}: 780 m, 870 s, 1110 s, 1510 m, 1520 m, 1600 m, 1690 s, 1705 s, 2600–3300 br.s. ^{1}H NMR spectrum, δ, ppm: 4.69 s (2H, CH_2O), 5.15 br.s (2H, NH_2), 6.95 d (2H, *o*-H, *J* = 8.8 Hz), 8.21 d (2H, *m*-H, *J* = 8.8 Hz), 12.10 br.s (1H, NH). Found, %: C 45.34; H 3.62; N 17.73. $C_9H_9N_3O_5$. Calculated, %: C 45.19; H 3.77; N 17.57.

(3-Phenoxyphenoxyacetyl)urea (XX). Yield 0.70 g (60%, *a*), 0.94 g (80%, *b*), light brown oily substance. IR spectrum, ν, cm^{-1}: 1490 m, 1510 s, 1600 m, 1615 s, 1690 s, 1715 s, 3150 m, 3300 br.s. ^{1}H NMR spectrum, δ, ppm: 4.55 s (2H, CH_2O), 5.15 br.s (2H, NH_2), 6.36 s (1H, 2-H), 6.61 d (1H, 6-H, *J* = 8.0 Hz), 6.76 m (1H, 4-H), 6.96 d (2H, *o*'-H, *J* = 8.0 Hz), 7.03 m (1H, *p*'-H, *J* = 8.0 Hz), 7.15 m (2H, *m*'-H), 7.40 s (1H, NH), 7.54 (1H, 5-H), 13.29 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 61.61 (OCH_2), 106.09 d (C^2), 110.25 d (C^6), 110.65 d (C^4), 119.20 d ($C^{o'}$), 123.39 d ($C^{p'}$), 129.68 d ($C^{m'}$), 130.28 d (C^5), 156.76 s (C^3), 158.73 s ($C^{i'}$), 159.00 s (C^1), 163.01 s and 163.16 s (C=O). Found, %: C 62.87; H 4.99; N 9.66. $C_{15}H_{14}N_2O_4$. Calculated, %: C 62.94; H 4.90; N 9.79.

(2,4-Dichlorophenoxyacetyl)urea (XXI). Yield 0.59 g (64%, *a*), 0.74 g (81%, *b*), light brown oily substance. IR spectrum, ν, cm^{-1}: 1490 s, 1600 m, 1650 s, 1690 s, 3150 m, 3250 br.s. ^{1}H NMR spectrum, δ, ppm: 4.60 s (2H, CH_2O), 5.00 br.s (2H, NH_2), 6.75 d (1H, C^6, *J* = 8.8 Hz), 7.01 d (1H, 5-H, *J* = 8.8 Hz), 7.36 s (1H, 3-H), 12.10 br.s (1H, NH). Found, %: C 41.37; H 2.96; Cl 27.14; N 10.74. $C_9H_8Cl_2N_2O_3$. Calculated, %: C 41.06; H 3.04; Cl 27.00; N 10.65.

Reaction of phenoxyacetic acid derivatives with ethyl carbamate (*general procedure***).** Phenoxyacetic acid **I**–**IV**, 3.5 mmol, was dissolved in 10 ml of anhydrous toluene, and 4.2 mmol of ethyl carbamate, 4.2 mmol of freshly distilled thionyl chloride, and 4.2 mmol of anhydrous pyridine were added. The mixture was heated for 4–4.5 h under reflux until the initial acid disappeared (TLC, petroleum ether–ethyl acetate, 6:1), and the products were isolated and purified as described above for compounds **XVIII**–**XXI**.

Ethyl (phenoxyacetyl)carbamate (XXII). Yield 0.77 g (81%), brown oily liquid. IR spectrum, ν, cm^{-1}: 1230 s, 1498 m, 1588 s, 1690 s, 1730 s, 3380 br.s. ^{1}H NMR spectrum, δ, ppm: 1.25 t (3H, Me, *J* = 7.0 Hz), 4.21 q (2H, $CH_3C\mathbf{H}_2O$, *J* = 7.0 Hz), 4.69 s (2H, $C\mathbf{H}_2OPh$), 6.90–7.15 m (5H, H_{arom}), 7.30 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 14.06 q (CH_3), 51.24 t (OCH_2), 64.03 t ($\mathbf{C}H_2OPh$), 114.64 d (C^p), 121.18 d (C^o), 129.80 d (C^m), 158.34 s (C^i), 163.18 s (C=O), 171.98 s (C=O). Found, %: C 59.35; H 5.77; N 6.04. $C_{11}H_{13}NO_4$. Calculated, %: C 59.19; H 5.83; N 6.28.

Ethyl (4-nitrophenoxyacetyl)carbamate (XXIII). Yield 0.91 g (87%), light brown amorphous substance, mp 100–104°C. IR spectrum, ν, cm^{-1}: 1240 s, 1490 m, 1510 m, 1605 m, 1690 s, 1715 s. ^{1}H NMR spectrum, δ, ppm: 1.25 t (3H, Me, *J* = 7.0 Hz), 4.21 q (2H, $CH_3C\mathbf{H}_2O$, *J* = 7.0 Hz), 4.64 s (2H, $C\mathbf{H}_2OC_6H_4$), 7.15 d (2H, *o*-H, *J* = 8.8 Hz), 7.20 br.s (1H, NH), 8.16 d (2H, *m*-H, *J* = 8.8 Hz). ^{13}C NMR spectrum, δ_C, ppm: 14.13 q (Me), 52.03 t (OCH_2), 64.21 t ($\mathbf{C}H_2OC_6H_4$), 114.10 d (C^o), 124.82 d (C^m), 141.12 s (C^p), 161.64 s (C=O), 167.86 s (C=O), 162.34 s (C^i). Found, %: C 49.18; H 4.51; N 10.37. $C_{11}H_{12}N_2O_6$. Calculated, %: C 49.25; H 4.48; N 10.45.

Ethyl (3-phenoxyphenoxyacetyl)carbamate (XXIV). Yield 1.02 g (72%), light brown oily liquid. IR spectrum, ν, cm^{-1}: 1210 s, 1480 m, 1570 m, 1600 m, 1640 s, 1730 s, 3300 br.m. ^{1}H NMR spectrum, δ, ppm: 1.25 t (3H, Me, *J* = 7.0 Hz), 4.16 q (2H, $CH_3C\mathbf{H}_2O$, *J* = 7.0 Hz), 4.53 s (2H, $C\mathbf{H}_2OC_6H_4$), 6.47 s (1H, 2-H), 6.71 d (1H, 6-H, *J* = 8.0 Hz), 6.76 d (1H, 4-H, *J* = 8.0 Hz), 6.96 d (2H, *o*'-H, *J* = 8.0 Hz), 7.02 m (1H, *p*'-H), 7.14 m (2H, *m*'-H), 7.42 m (1H, 5-H), 11.55 br.s (1H, NH). Found, %: C 64.47; H 5.61; N 4.37. $C_{17}H_{17}NO_5$. Calculated, %: C 64.76; H 5.40; N 4.44.

Ethyl (2,4-dichlorophenoxyacetyl)carbamate (XXV). Yield 0.96 g (85%), brown amorphous substance, mp 93–95°C. IR spectrum, ν, cm^{-1}: 1240 s, 1490 s, 1500 m, 1600 w, 1705 s, 1740 s, 3200 br.m. ^{1}H NMR spectrum, δ, ppm: 1.25 t (3H, Me, *J* = 7.0 Hz), 4.23 q (2H, $CH_3C\mathbf{H}_2O$, *J* = 7.0 Hz), 4.58 s (2H, $C\mathbf{H}_2OC_6H_3$), 6.94 s (1H, 6-H, *J* = 8.5 Hz), 7.06 d (1H, 5-H, *J* = 8.5 Hz), 7.36 s (1H, 3-H), 8.60 br.s (1H, NH). ^{13}C NMR spectrum, δ_C, ppm: 13.96 q (Me), 51.18 t ($O\mathbf{C}H_2CH_3$), 64.37 t ($\mathbf{C}H_2OC_6H_3$), 114.66 d (C^6), 124.15 d (C^2), 126.68 s (C^4), 126.98 d and 127.53 d (C^3, C^5), 152.06 s (C^1), 157.18 s (C=O), 163.96 s (C=O). Found, %: C 45.39; H 3.26; Cl 24.76; N 4.83. $C_{11}H_{11}Cl_2NO_4$. Calculated, %: C 45.21; H 3.77; Cl 24.32; N 4.79.

2-(3-Phenoxyphenoxy)ethyl benzylcarbamate (XXVII). A solution of 46.7 mmol of benzylamine in

50 ml of ethyl acetate was added dropwise at room temperature to 50 ml of ethyl acetate, and phosgene, 15 ml, was simultaneously passed through the solution at such a rate that no disubstituted urea precipitated. When the addition of benzylamine was complete, an additional 5 ml of phosgene was bubbled through the solution. The mixture was then stirred for 1.5 h at 20°C and was carefully heated (to avoid overheating) to distill the solvent off. The residue was treated with 30 ml of carbon tetrachloride, the precipitate was filtered off, and the filtrate was evaporated to obtain 24 mmol of benzyl isocyanate. The product was dissolved in 20 ml of ethyl acetate, and 24 mmol of 2-(3-phenoxyphenoxy)ethanol (**XXVI**) [12] was added. The mixture was stirred for 8 h at room temperature, washed with a 10% solution of $NaHCO_3$ and with a saturated solution of NaCl, and dried over $MgSO_4$. The solvent was distilled off, and the residue was purified by column chromatography on silica gel using petroleum ether–ethyl acetate (8:1) as eluent. Yield of **XXVII** 6.60 g (76%), brown oily substance. IR spectrum, ν, cm^{-1}: 1550 m, 1600 s, 1710 s, 3080 w. ^1H NMR spectrum, δ, ppm: 3.94 s (2H, CH_2N), 4.41 t (2H, CH_2O, J = 5.5 Hz), 4.51 t (2H, C**H**$_2$OC$_6$H$_4$, J = 5.5 Hz), 6.60–6.72 m (5H, *o*-H, *m*-H, NH), 7.12–7.50 m (10H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 44.89 t (CH_2N), 62.90 t (OCH_2), 65.76 t (**C**$H_2OC_6H_4$), 101.97 d (C^2), 107.38 d (C^6), 112.08 d (C^4), 117.90 d ($C^{o'}$), 120.32 d ($C^{p'}$), 122.18 d ($C^{p''}$), 129.60 d and 129.64 d ($C^{m'}$, C^5), 127.36 d ($C^{o''}$), 127.96 d ($C^{m''}$), 137.44 s ($C^{i''}$), 156.78 (C^3), 158.18 s ($C^{i'}$), 159.18 s (C^1), 173.28 s (C=O). Found, %: C 72.86; H 5.48; N 3.94. $C_{22}H_{21}NO_4$. Calculated, %: C 72.73; H 5.79; N 3.86.

2-Methylpropanal *O*-[2-(3-phenoxyphenoxy)-ethyl]oxime (XXVIII). Phosphorus(III) bromide, 3.15 mmol, was added dropwise to a solution of 2.63 mmol of 2-(3-phenoxyphenoxy)ethanol (**XXVI**) and 2.63 mmol of anhydrous pyridine in 15 ml of anhydrous THF, stirred at 5°C under argon. The mixture was stirred for 1 h at 5°C and for 12 h at room temperature, diluted with 20 ml of anhydrous THF, washed with a saturated solution of ammonium chloride, and dried over Na_2SO_4. The solvent was removed to obtain 0.58 g of 1-bromo-2-(3-phenoxyphenoxy)ethane, 15 ml of anhydrous 1,4-dioxane, 4.01 mmol of 2-propanal oxime, and 4.01 mmol of potassium *tert*-butoxide were added, and the mixture was heated for 1 h under reflux and poured into water. The organic phase was separated and dried over $MgSO_4$, the solvent was distilled off, and the residue was purified by column chromatography on silica gel using hexane–ethyl acetate (9:1) as eluent. Yield of **XXVIII** 0.48 g (58%), yellow–brown oily substance. IR spectrum, ν, cm^{-1}: 1100 s, 1115 s, 1505 m, 1600 s, 1630 w, 3100 w. ^1H NMR spectrum, δ, ppm: 0.92 d and 1.05 d (6H, Me, J = 6.0 Hz), 1.68 m (1H, CH), 1.87 m (2H, $CH_2C{=}C$),* 4.34 t (2H, CH_2O, J = 5.5 Hz), 4.51 t (2H, C**H**$_2$OC$_6$H$_4$, J = 5.5 Hz), 6.96 t (1H, CH=N, J = 6.7 Hz), 7.10–7.50 m (9H, H_{arom}). Found, %: C 72.67; H 7.01; N 4.63. $C_{19}H_{23}NO_3$. Calculated, %: C 72.84; H 7.35; N 4.47.

REFERENCES

1. Ovchinnikov, Yu.A., *Bioorganicheskaya khimiya* (Bioorganic Chemistry), Moscow: Prosveshchenie, 1987, p. 784.
2. JPN Patent Appl. no. 90-212460, 1990; *Chem. Abstr.*, 1991, vol. 114, no. P42281v.
3. Czech. Patent no. 105266, 1962; *Ref. Zh., Khim.*, 1964, no. 6N230P.
4. Okawara, Ikeda, N., Yamassaki, T., and Furukawa, M., *Chem. Pharm. Bull.*, 1988, vol. 36, p. 3628.
5. Yamansarova, E.T., Kukovinets, A.G., Kukovinets, O.S., Zainullin, R.A., Galin, F.Z., Kunakova, R.V., Zorin, V.V., and Tolstikov, G.A., *Russ. J. Org. Chem.*, 2001, vol. 37, p. 246.
6. US Patent no. 3904773, 1975; *Ref. Zh., Khim.*, 1976, no. 12O319P.
7. Hsing-Jang, L. and Iyer, S.S., *Can. J. Chem.*, 1980, vol. 58, p. 2645.
8. JPN Patent Appl. no. 55-38921, 1980; *Ref. Zh., Khim.*, 1981, no. 13O323P.
9. JPN Patent Appl. no. 60-180062, 1985; *Ref. Zh., Khim.*, 1986, no. 12O402P.
10. Hoffman, F., EP Patent no. 0004334-VI, 1981.
11. Wimmer, Z., Streinz, L., and Romanuk, M., *Collect. Czech. Chem. Commun.*, 1985, vol. 50, p. 2453.
12. Kukovinets, O.S., Zainullin, R.A., Kasradze, V.G., Burov, V.N., Mokrousova, E.P., Odinokov, V.N., and Tolstikov, G.A., *Agrokhimiya*, 1999, no. 9, p. 60.
13. Del'nik, V.P., Katsnel'son, M.G., and Ostrovskii, D.I., *Khim.-Farm. Zh.*, 1967, no. 6, p. 21.

* As in Russian original.—*Publisher.*