3-ALKOXY-1,5-DIARYL-4,5-DIHYDROXYIMIDAZOLIDIN-2-ONES AND 3-ALKOXY-1-ALKYL-5-ARYL-4,5-DIHYDROXYIMIDAZOLIDIN-2-ONES: SYNTHESIS AND STRUCTURE

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It has been found that 4-nitrophenylglyoxal reacts with *N*-alkoxy-*N'*-arylureas and *N*-alkoxy-*N'*-alkylureas in acetic acid medium with the selective formation of the diastereomers of the 3-alkoxy-1,5-diaryl-4,5-dihydroxyimidazolidin-2-ones and 3-alkoxy-1-alkyl-5-aryl-4,5-dihydroxyimidazolidin-2-ones with c*is*-orientation of OH-groups. The X-ray structural analysis of 3-propyloxy-4S,5S-4,5-dihydroxy-1-methyl-5-(4-nitrophenyl)imidazolidin-2-one and of 3-*n*-butyloxy-4S,5S-4,5-dihydroxy-1-(4-methylphenyl)-5-(4-nitrophenyl)imidazolidin-2-one has demonstrated this structural feature of these compounds.

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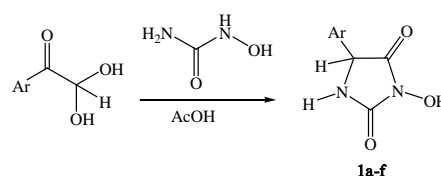   Phone: +380-97-651-61-72
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INTRODUCTION

Arylglyoxals are widely used in syntheses of heterocycles as syntones.[1-6] But the study of the arylglyoxals interaction with *N*-hydroxyurea[7-9] and its derivatives[8,10] has started recently and needs to be continued.

Arylglyoxals such as phenyl-, 4-bromophenyl-, 4-chlorophenyl-, 4-fluorophenyl-, 4-methoxyphenyl- and 4-methylglyoxal easily react with *N*-hydroxyurea in acetic acid medium (Scheme 1) at the room temperature yielding the proper 5-aryl-3-hydroxyimidazolidine-2,4-diones (5-aryl-3-hydroxyhydantoins) **1a-f**.[8] However, 4-nitrophenylglyoxal in acetic acid medium at room temperature reacts with *N*-hydroxyurea giving only a mixture of 5-aryl-3,4,5-trihydroxyimidazolidin-2-ones, **2a** and **3a,** in molar ratio near 3:1 (room temp., 25 h).[9] 3-Hydroxy-5-(4-nitrophenyl)hydantoin (**1g**) is not formed. This example has demonstrated, that the presence of a strong electron-withdrawing substituent on the benzene ring of arylglyoxals prevents a further conversion of 5-aryl-3,4,5-trihydroxyimidazolidin-2-ones into 5-aryl-3-hydroxy-imidazolidin-2,4-diones.[9]

We have obtained similar results in aqueous medium. 4-Nitrophenylglyoxal[9] and 4-chlorophenylglyoxal[7] form only the mixtures of 5-aryl-3,4,5-trihydroxyimidazolidin-2-ones (**2a**,**b** and **3a**,**b**) at 14-20 °C (Scheme 2).

Ar = p-XC₆H₄, X = H (a), Cl(b), Me(c), OMe(d), Br(e), F(f)

Scheme 1. Arylglyoxal's interaction with *N*-hydroxyurea in acetic acid (Ref. 8).


Af = p-O₂NC₆H₄ (a); p-ClC₆H₄(b)
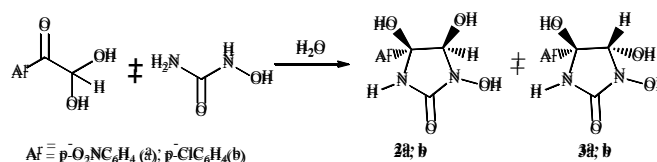
Scheme 2. Interaction of 4-nitrophenylgyoxal hydrate and 4-chlorophenylglyoxal hydrate with *N*-hydroxyurea in aqueous medium.

In these mixtures, the diastereomers of 5-aryl-3,4,5-trihydroxyimidazolidin-2-ones (**2a, 2b**) with *cis* orientation of hydroxyl groups at C-4,5 carbon atoms are the main products.[7-9] The structure of compounds **2a,b** has been proved by XRD study.[7,9]
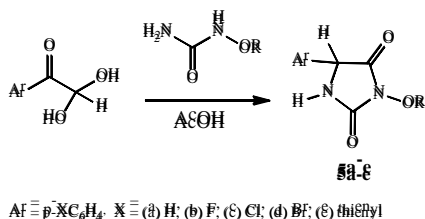
Phenylglyoxal reacts with *N*-hydroxyurea in aqueous solution at the room temperature, forming the mixture of unstable 3,4,5-trihydroxy-5-phenylimidazolidin-2-ones (**2c,3c**) and 3-hydroxy-5-phenylhydantoin (**1a**).[7,8] The compounds **2c** and **3c** are easily transformed to hydantoin **1a** by heating.[7,8]

4-Methoxyphenylglyoxal and 4-methylphenylglyoxal form with *N*-hydroxyurea a mixture of 5-aryl-3-hydroxyhydantoins (**1c,1d**) and acyclic ureas (**4c,4d**)[7] (Scheme 3).
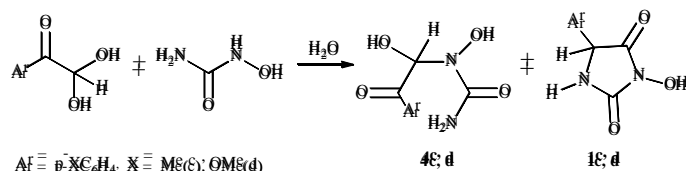
Scheme 3. Interaction of 4-methylphenylgyoxal hydrate and 4-methoxyphenylglyoxal hydrate with *N*-hydroxyurea in aqueous solution.

In acetic acid medium, the majority of arylglyoxals reacts with *N*-alkoxyureas forming only 3-alkoxy-5-arylhydantoins (**5a-e**) (Scheme 4).


Scheme 4. Interaction of arylglyoxals with *N*-alkoxyureas in acetic acid medium.

The arylgyoxal's interaction with *N*-alkoxy-*N'*-arylureas (**6**) has been particularly studied.[10] It has been shown that anhydrous phenylglyoxal reacts with *N*-ethoxy-*N'*-phenylurea (**6a**) in CH₂Cl₂ at 20 ºC yielding 3-ethoxy-1,5-bis(phenyl)imidazolidine-2,4-dione **7** in moderate (46 %) yield[10] (Scheme 5). Using *N*-benzyloxy-*N'*-(4-nitrophenyl)urea (**6b**), anhydrous phenylglyoxal produces (CH₂Cl₂, 20 ºC) 3-benzyloxy-4,5-dihydroxy-1-(4-nitrophenyl)-5-phenylimidazolidine-2-one **8** (56 %) and 3-benzyloxy-1-(4-nitrophenyl)-5-phenylhydantoin **9** (6 %).[10]
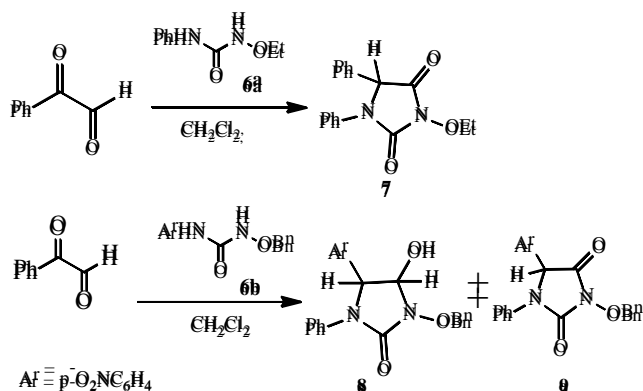
Scheme 5. Interaction of phenylglyoxal with *N*-alkoxy-*N'*-arylureas.
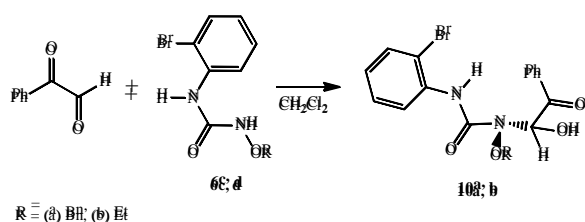
Scheme 6. Synthesis acyclic substituted *N*-alkoxyureas **10**.

But the reaction between phenylglyoxal and *N*-benzyloxy-*N'*-(2-bromophenyl)urea (**6c**) and *N*-ethoxy-*N'*-(2-bromophenyl)urea (**6d**) in dichloromethane solution (Scheme 6) at room temperature gives only acyclic ureas (**10a,b**).[10,11] It is probable that the bulky ortho-bromo substituent prevents the further cyclization. The structure of ureas **10a,b** has been confirmed by XRD study. In the crystalline state, compound **10a** exists in two forms (**10aA** and **10aB**), which are distinguished by the pyramidality degree of the acyclic amide nitrogen atom. The sum of bond angles centered of this atom (Σß) is 336.0(3)º and 341.2(3)º in the molecules **10aA** and **10aB**[10]**,** respectively. The urea **10b** exists in the single form, the sum of bond angles centered on the nitrogen atom is 340.0(3)º.[11]

So, the goal of our current research was to investigate the interaction of 4-nitrophenylglyoxal with *N*-alkoxy-*N'*-arylureas **6** in acetic acid medium.

EXPERIMENTAL

^{1}H NMR spectra were recorded on a Varian VXP-300 spectrometer and Varian Jemini 400 spectrometer (300 and 400 MHz, respectively). ^{13}C NMR spectra were recorded on a Varian VXP-300 spectrometer (75 MHz) and Varian Jemini 400 spectrometer (100 MHz). The solvents were DMSO-*d₆* (for the compounds **6**, **11a**-**g**, **13b** and **14a**, **b**) and CDCl₃ (for the compounds **6a,** **13a** and **14a**) ^{1}H NMR chemical shifts were reported relative to the residual solvent protons as an internal standard ((CD₃)₂SO: 2.500 ppm) or with TMS as an internal standard (in CDCl₃). Solvent carbon atoms served as an internal standard for ^{13}C NMR spectra ((CD₃)₂SO: 39.52 ppm). 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.4-Nitrophenylglyoxal hydrate was obtained according to published procedures.[9]

N-Ethoxy-*N'*-phenylurea (6a)

This compound was obtained according to published procedures,[10] yield was 60 %, colorless crystals, m.p. 101-104 ºC. ^{1}H NMR (400 MHz, DMSO-*d₆*): δ = 1.213 (3H, t, *J* = 7.2 Hz, NOCH₂Me), 3.823 (2H, q, *J* = 7.2 Hz, NOCH₂Me), 6.985 (1H, t, *J* = 7.6 Hz, C(4)H Ph), 7.257 (2H, t, *J* = 7.6, Hz C(3)H, C(5)H Ph), 7.567 (2H, d, *J* = 7.6 Hz, C(2)H, C(6)H Ph), 8.702 (1H, s, NH), 9.410 (1H, s, NHO). ^{1}H NMR (300 MHz, CDCl₃): δ = 1.337 (3H, t, *J* = 7.0 Hz, NOCH₂Me), 3.987 (2H, q, *J* = 7.0 Hz, NOCH₂Me), 7.105 (1H, t, *J* = 7.8 Hz, C(4)H Ph), 7.336 (2H, t, *J* = 7.8 Hz, C(3)H, C(5)H Ph), 7.488 (2H, d, *J* = 7.8 Hz, C(2)H, C(6)H Ph), 7.608 (1H, s, NH), 7.708 (1H, s, NHO). MS (FAB) m/z 361 [2M+H]⁺ (4), 181 [M+H]⁺(100). Anal. Calc. for C₉H₁₂N₂O₂: C 59.99, H 6.71, N 15.55. Found: C 59.81, H 6.83, N 15.44.

N-Methoxy-*N'*-phenylurea (6e)

A solution of phenyl isocyanate (918 mg, 7.706 mmol) in dry benzene (8 mL) was added to the solution of methoxyamine (444 mg, 9.434 mmol) in dry benzene (4

mL). The reaction mixture was maintained in a closed bulb at 20 ºC for 6 days, the obtained precipitate was then filtered off, washed with dry benzene (1mL) and dried under vacuum (2 mm Hg) to yield **6e** as colorless crystals, m.p. 112–113 ºC. [1]H (400 MHz, DMSO-d_6): δ = 3.615 (3H, s, NOMe), 6.984 (1H, t, *J* = 7.6 Hz, C(4)H Ph), 7.255 (2H, t, *J* = 7.6 Hz, C(3)H, C(5)H Ph), 7.575 (2H, d, , *J* = 7.6 Hz, C(2)H, C(6)H Ph), 8.840 (1H, s, NH), 9.482 (1H, s, NHO). MS (FAB) m/z 333 [2M+H]$^+$ (10), 167 [M+H]$^+$(100). Anal. Calc. for $C_8H_{10}N_2O_2$: C 57.82, H 6.07, N 16.86. Found: C 57.65, H 6.26, N 16.73.

In a similar manner, *N*-alkoxy-*N'*-arylureas (**6f-j**) and *N*-alkoxy-*N'*-alkylureas (**13a**, **b**) were obtained:

N-Benzyloxy-*N'*-phenylurea (6f)

This compound was obtained as colourless crystals, yield 78 %, m.p. 104-105ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 4.824 (2H, s, NOCH$_2$), 6.981 (1H, t, *J* = 7.6 Hz, C(4)H PhN), 7.252 (2H, t, *J* = 7.6 Hz, C(3)H, C(5)H PhN), 7.331 (1H, t, *J* = 6.8 Hz, C(4)H PhCH$_2$), 7.384 (2H, t, *J* = 6.8 Hz, C(3)H, C(5)H PhCH$_2$), 7.463 (2H, d, *J* = 6.8 Hz, C(2)H, C(6)H PhCH$_2$), 7.514 (2H, d, *J* = 7.6 Hz, C(2)H, C(6)H PhN), 8.704 (1H, s, NH), 9.465 (1H, s, NHO). MS (FAB) m/z 243 [M+H]$^+$(86), 91 Bn$^+$ (100). Anal. Calc. for $C_{14}H_{14}N_2O_2$: C 69.41, H 5.82, N 11.56. Found: C 69.57, H 5.75, N 11.50.

N-Methoxy-*N'*-(4-methylphenyl)urea (6g)

Obtained as colourless crystals, yield 95 %, m.p. 152-154 ºC. ^{1}H NMR (400 MHz, DMSO-d_6) :δ = 2.233 (3H, s, Me), 3.605 (3H, s, NOMe), 7.059 (2H, d, *J* = 8.4 Hz, C(3)H, C(5)H Ar), 7.446 (2H, d, *J* = 8.4 Hz, C(2)H, C(6)H Ar), 8.745 (1H, s, NH), 9.411 (1H, s, NHO). MS (FAB) m/z 181 [M+H]$^+$ (100). Anal. Calc. for $C_9H_{12}N_2O_2$: C 59.99, H 6.71, N 15.55. Found: C 59.68, H 6.56, N 15.39.

N-n-Butyloxy-*N'*-(4-methylphenyl)urea (6h)

Obtained as colourless crystals, yield 72 %, m.p. 78-79 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 0.900 (3H, t, *J* = 7.2 Hz, NO(CH$_2$)$_3$Me), 1.355 (2H, sex, *J* = 7.2 Hz, NO(CH$_2$)$_2$CH$_2$Me), 1.602 (2H, quint, *J* = 7.2 Hz, NOCH$_2$CH$_2$CH$_2$Me), 2.223 (3H, s, Me), 3.756 (2H, t, *J* = 7.2 Hz, NOCH$_2$CH$_2$CH$_2$Me), 7.061 (2H, d, *J* = 8.4 Hz, C(3)H, C(5)H Ar), 7.426 (2H, d, *J* = 8.4 Hz, C(2)H, C(6)H Ar), 8.551 (1H, s, NH), 9.348 (1H, s, NHO). MS (FAB) m/z 223 [M+H]$^+$ (100), 133 (10), 106 (22). Anal. Calc. for $C_{12}H_{18}N_2O_2$: C 64.84, H 8.16, N 12.60. Found: C 64.79, H 8.21, N 12.43.

N-Ethoxy-*N'*-(4-bromophenyl)urea (6i)

Obtained as colourless crystals, yield 92 %, m.p. 109-110 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.204 (3H, t, *J* = 7.2 Hz, NOCH$_2$Me), 3.812 (2H, q, *J* = 7.2 Hz, NOCH$_2$Me), 7.432 (2H, d, *J* = 9.2 Hz, C(2)H, C(6)H C$_6$H$_4$Br), 7.569 (2H, d, *J* = 9.2 Hz, C(3)H, C(5)H C$_6$H$_4$Br), 8.874 (1H, s, NH), 9.515 (1H, s, NHO). MS (FAB) m/z 261 [M+H]$^+$ (16), 259 [M+H]$^+$ (15), 102 (100). Anal. Calc. for $C_9H_{11}BrN_2O_2$: C 41.72, H 4.28, N 10.81. Found: C 41.59, H 4.21, N 10.56.

N-n-Butyloxy-*N'*-(4-bromophenyl)urea (6j)

Obtained as colourless crystals, yield 61 %, m.p. 104-105 ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 0.89 (3H, t, *J* = 7.4 Hz, NO(CH$_2$)$_3$Me), 1.35 (2H, sex, *J* = 7.4 Hz, NOCH$_2$CH$_2$CH$_2$Me), 1.60 (2H, quint, *J* = 7.4, NOCH$_2$CH$_2$CH$_2$Me), 3.76 (2H, t, *J* = 6.6 Hz, NOCH$_2$), 7.43 (2H, d, *J* = 8.8 Hz, C(2)H,C(6)H, C$_6$H$_4$Br), 7.56 (2H, d, *J* = 8.8 Hz, C(3)H,C(5)H, C$_6$H$_4$Br), 8.85 (1H, s, NH), 9.54 (1H, s, NHO). MS (FAB) m/z 289 [M+H]$^+$ (95), 287 [M+H]$^+$ (100), 273 (17), 271 (17), 209 (40). Anal. Calc. for $C_{11}H_{15}BrN_2O_2$: C 46.01, H 5.26, N 9.76. Found: C 46.13, H 5.34, N 9.58.

N-Propyloxy-*N'*-methylurea (13a)

Obtained as colourless oil, yield 90 %, n_D^{20} 1.4550. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.95 (3H, t, *J* = 7.0 Hz, NOCH$_2$CH$_2$Me), 1.67 (3H, sex, *J* = 7.0 Hz, NOCH$_2$CH$_2$Me), 2.86 (3H, br. s, NMe), 3.77 (2H, t, *J* = 7.0 Hz, NOCH$_2$), 5.73 (1H, s, NH), 7.61 (1H, s, NHO). Anal. Calc. for $C_5H_{12}N_2O_2$: C 45.44, H 9.15, N 21.20. Found: C 45.37, H 9.24, N 21.46.

N-Ethoxy-*N'*-(1-naphthyl)methylurea (13b)

Obtained as colourless crystals, yield 74 %, m.p. 145-146ºC. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.157 (3H, t, *J* = 7.0 Hz, NOCH$_2$Me), 3.752 (2H, q, *J* = 7.0 Hz, NOCH$_2$Me), 4.740 (2H, d, *J* = 6.0 Hz, NCH$_2$), 7.353–7.386 (1H, m, H C$_{10}$H$_7$), 7.414–7.430 (1H, m, H C$_{10}$H$_7$), 7.495 (1H, t, *J* = 6.8 Hz, H C$_{10}$H$_7$), 7.535–7.572 (2H, m, NH and H C$_{10}$H$_7$), 7.827 (1H, d, *J* = 8.0 Hz, H C$_{10}$H$_7$), 7.942 (1H, d, *J* = 8.0 Hz, H C$_{10}$H$_7$), 8.173 (1H, d, *J* = 6.8 Hz, H C$_{10}$H$_7$), 9.138 (1H, s, NHO). MS (FAB) m/z 245 [M+H]$^+$ (52), 243 [M–H]$^+$ (7), 198 (6), 156 (13), 141 NafCH$_2^+$ (100), 117(14). Anal. Cal. for $C_{14}H_{16}N_2O_2$: C 68.83, H 6.60, N 11.47. Found: C 68.73, H 6.51, N 11.38.

Preparation of *cis*-diastereomer, 4*S*,5*S*-dihydroxy-3-methoxy-5-(4-nitrophenyl)-1-phenylimidazolidin-2-one (11a)

4-Nitrophenylglyoxal hydrate (102 mg, 0.518 mmol) was added to the solution of **6e** (86 mg, 0.518 mmol) in acetic acid (5 mL). The reaction mixture was stirred at 19 ºC for 19 h, then it was frozen and acetic acid was evaporated at 15ºC under vacuum (2 mmHg), the residue was washed by cold water (5 mL), dried under vacuum (2 mm Hg) to yield 154 mg (86 %, purity 95 %) *cis*-diastereomer, 4*S*,5*S*-4,5-dihydroxy-3-methoxy-5-(4-nitrophenyl)-1-phenylimidazolidin-2-one (**11a**) as colourless crystals, m.p. 158-159 (with decomp., CH$_2$Cl$_2$–hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.828 (3H, s, NOMe), 4.931 (1H, d, *J* = 6.5 Hz, CHOH), 7.066 (1H, t, *J* = 8.0 Hz, C(4)H Ph), 7.136 (1H, d, *J* = 6.5 Hz, CHOH), 7.207 (2H, t, *J* = 8.0 Hz, C(3)H, C(5)H Ph), 7.288 (1H, s, OH), 7.384 (2H, d, *J* = 8.0 Hz, C(2)H, C(6)H Ph), 7.763 (2H, d, *J* = 8.5 Hz, C(2)H, C(6)H C$_6$H$_4$NO$_2$), 8.150 (2H, d, *J* = 8.5 Hz, C(3)H, C(5)H C$_6$H$_4$NO$_2$). ^{13}C NMR (100 MHz, DMSO-d$_6$): δ = 64.0 (OMe), 87.1, 87.6 (CHOH, COH), 123.2, 124.8, 125.4, 128.26, 128.29 (C-2,C-6 C$_6$H$_4$NO$_2$,C-3,C-5 Ph, C-4 Ph, C-3,C-5 C$_6$H$_4$NO$_2$, C-2,C-6 Ph), 135.9 (C-1, C$_6$H$_4$NO$_2$), 147.0, 147.2 (C-1 Ph, C-4 C$_6$H$_4$NO$_2$), 156.7 (C=O). MS (FAB) m/z 346 [M+H]$^+$(100).

MS (FAB, KI) m/z 384 [M+K]$^+$(20), 346 [M+H]$^+$ (82), 192(100). Anal. Calc. for $C_{16}H_{15}N_3O_6$: C 55.65, H 4.38, N 12.17. Found: C 55.63, H 4.39, N 12.10.

3-Ethoxy-4*S*,5*S*-4,5-dihydroxy-5-(4-nitrophenyl)-1-phenylimidazolidin-2-one (11b)

4-Nitrophenylglyoxal hydrate (176 mg, 0.893 mmol) was added to the solution of **6a** (161 mg, 0.893 mmol) in acetic acid (6 mL). The reaction mixture was stirred at 17 ºC for 23 h, then it was frozen and acetic acid was evaporated at 15ºC under vacuum (2 mmHg), the residue was washed with water (6 mL), dried under vacuum (2 mmHg) to yield 286 mg (89 %, purity 96 %) *cis*-diastereomer, 3-ethoxy-4*S*,5*S*-4,5-dihydroxy-5-(4-nitrophenyl)-1-phenylimidazolidin-2-one (**11b**) as colourless crystals, m.p. 145-146ºC (with decomp., THF–CH_2Cl_2–C_6H_{14}). ^{1}H NMR (300 MHz, DMSO-d_6):δ = 1.24 (3H, t, *J* = 6.9 Hz, NOCH$_2$Me), 4.06 (2H, q, *J* = 6.9 Hz, NOC$\underline{H_2}$Me), 4.91 (1H, d, *J* = 6.6 Hz, C$\underline{H}$OH), 7.06 (1H, t, *J* = 7.5 Hz, C(4)H, Ph), 7.11 (1H, d, *J* = 6.6 Hz, CHO$\underline{H}$), 7.21 (2H, t, *J* = 7.5 Hz, C(3)H, C(5)H Ph), 7.25 (1H, s, OH), 7.40 (2H, d, *J* = 7.5 Hz, C(2)H, C(6)H Ph), 7.77 (2H, d, *J* = 8.7 Hz, C(2)H, C(6)H $C_6H_4NO_2$), 8.15 (2H, d, *J* = 8.7 Hz, C(3)H, C(5)H $C_6H_4NO_2$). ^{13}C NMR (75 MHz, DMSO-d$_6$): δ = 13.97 (Me), 71.36 (NOCH$_2$), 87.14, 87.74 (CHOH, COH), 123.29, 124.72, 125.33, 128.27, 128.31, 136.03 (C Ph, C $C_6H_4NO_2$), 147.25, 147.26 (C-1 Ph, C-4 $C_6H_4NO_2$), 156.93 (C=O). MS (FAB) m/z 360 [M+H]$^+$(100), 342 [M+H-H$_2$O]$^+$(8), 223 (74), 181 (99), 150 (26), 91 (30). Anal. Calc. for $C_{17}H_{17}N_3O_6$: C 56.82, H 4.77, N 11.69. Found: C 56.55, H 4.70, N 11.79.

3-Benzyloxy-4*S*,5*S*-4,5-dihydroxy-5-(4-nitrophenyl)-1-phenylimidazolidin-2-one (11c)

4-Nitrophenylglyoxal hydrate (80 mg, 0.406 mmol) was added to the solution of **6f** (98 mg, 0.405 mmol) in acetic acid (5 mL), the reaction mixture was stirred at 18 ºC for 21 h, then it was frozen and acetic acid was evaporated at 16ºC under vacuum (2 mm Hg), the residue was twice washed with cold water (3 mL), dried under vacuum (2 mm Hg) giving 147 mg (86 %, purity 96 %) 3-benzyloxy-4S,5S-4,5-4,5-dihydroxy-5-(4-nitrophenyl)-1-phenylimidazolidin-2-one (**11c**) as colourless solid, m.p. 62-65ºC (with decomp., CH_2Cl_2–hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 4.813 (1H, d, *J* = 6.0 Hz, C$\underline{H}$OH), 5.053 (2H, s, NOCH$_2$), 7.068 (1H, t, *J* = 7.6 Hz, C(4)H PhN), 7.212 (2H, t, *J* = 7.6 Hz, C(3)H, C(5)H PhN), 7.272 (1H, d, *J* = 6.0 Hz, CHO$\underline{H}$), 2.277 (1H, s, OH), 7.313–7.414 (5H, m, CH$_2$Ph), 7.481 (2H, d, *J* = 6.8 Hz, C(2)H, C(6)H PhN), 7.704 (2H, d, *J* = 8.8 Hz, C(2)H, C(6)H $C_6H_4NO_2$), 8.136 (2H, d, *J* = 8.8 Hz, C(3)H, C(5)H $C_6H_4NO_2$). ^{13}C NMR (75 MHz, DMSO-d$_6$): δ = 77.86 (NOCH$_2$), 87.28, 87.44 (CHOH, COH), 123.30, 124.71, 125.37, 128.12, 128.20, 128.28, 128.35, 129.06, (C PhN, C P$\underline{h}$CH$_2$, C $C_6H_4NO_2$), 135.93, 136.08 (C-1 Bn, C-1 $C_6H_4NO_2$), 147.18, 147.29 (C-1 PhN, C-4 $C_6H_4NO_2$), 156.77 (C=O). MS (FAB) m/z 422 [M+H]$^+$(16), 243 (34), 194 (7), 150 (15), 91 Bn$^+$ (100). Anal. Calc. for $C_{22}H_{19}N_3O_6$ C 62.70, H 4.54, N 9.97. Found: C 62.39, H 4.65, N 9.81.

4*S*,5*S*-4,5-Dihydroxy-3-methoxy-1-(4-methylphenyl)-5-(4-nitrophenyl)imidazolidin-2-one (11d)

4-Nitrophenylglyoxal hydrate (151 mg, 0.765 mmol) was added to the solution of **6g** (138 mg, 0.765 mmol) in acetic acid (5 mL). The reaction mixture was stirred at 17 ºC for 21 h, then it was frozen and acetic acid was evaporated at 16 ºC under vacuum (2 mm Hg), the residue was twice washed with cold water (5 mL), dried under vacuum (2 mm Hg) giving 245 mg (89 %, purity 95 %) **11d** as colourless crystals, m.p. 157-159ºC (with decomp., CH_2Cl_2–hexane). ^{1}H NMR (400 MHz, DMSO-d_6): δ = 2.168 (3H, s, Me), 3.825 (3H, s, NOMe), 4.924 (2H, d, *J* = 6.4 Hz, C$\underline{H}$OH), 7.005 (2H, d, *J* = 7.6 Hz, C(3)H, C(5)H $C_6\underline{H}_4$Me), 7.099 (1H, d, *J* = 6.4 Hz, CHO$\underline{H}$), 7.237 (1H, s, COH), 7.248 (2H, d, *J* = 7.6 Hz, C(2)H, C(6)H $C_6\underline{H}_4$Me), 7.753 (2H, d, *J* = 8.4 Hz, C(3)H, C(5)H $C_6H_4NO_2$), 8.142 (2H, d, *J* = 8.4 Hz, C(2)H, C(6)H $C_6H_4NO_2$). ^{13}C NMR (75 MHz, DMSO-d$_6$): δ = 20.43 (Me), 64.05 (NOMe), 87.13, 87.74 (CHOH, COH), 123.25, 125.23, 128.39, 128.86, 133.24, 134.90 (C Ar), 147.18, 147.28 (C-1 C_6H_4Me, C-4 $C_6H_4NO_2$), 156.92 (C=O). MS (FAB) m/z 360 [M+H]$^+$(86), 342 [M+H-H$_2$O]$^+$(8), 299 (28), 257 (10), 209 (100), 181 (85), 150 (40), 133 (44), 106 (25), 90 (39). Anal. Calc. for $C_{17}H_{17}N_3O_6$: C 56.82, H 4.77, N 11.69. Found: C 56.85, H 4.77, N 11.46.

3-*n*-Butyloxy-4*S*,5*S*-4,5-dihydroxy-1-(4-methylphenyl)-5-(4-nitrophenyl)imidazolidin-2-one (11e)

4-Nitrophenylglyoxal hydrate (105 mg, 0.533 mmol) was added to the solution of **6h** (119 mg, 0.533 mmol) in acetic acid (4 mL). The reaction mixture was stirred at 17 ºC for 19 h, then it was frozen and acetic acid was evaporated under vacuum (2 mm Hg), the residue was twice washed with cold water (4 mL) at 4 ºC for 20 h, dried under vacuum (2 mmHg) giving 193 mg (90 %, purity 94 %) **11e** as colourless crystals, m.p. 139-141 (with decomposition, CH_2Cl_2-hexane).

^{1}H NMR (400 MHz, DMSO-d_6) δ = 0.902 (3H, t, *J* = 7.2 Hz, NOCH$_2$CH$_2$CH$_2$Me), 1.385 (2H, sex, *J* = 7.2 Hz, NOCH$_2$CH$_2$C$\underline{H_2}$Me), 1.617 (2H, quint, *J* = 7.2 Hz, NOCH$_2$C$\underline{H_2}$CH$_2$Me), 2.166 (3H, s, Me), 3.948–4.046 (2H, m, NOCH$_2$), 4.893 (1H, d, *J* = 6.0 Hz, C$\underline{H}$OH), 7.000 (2H, d, *J* = 8.4 Hz, C(3)H, C(5)H C_6H_4Me), 7.029 (1H, d, *J* = 6.0 Hz, CHO$\underline{H}$), 7.191 (1H, s, OH), 7.255 (2H, d, *J* = 8.4 Hz, C(2)H, C(6)H C_6H_4Me), 7.755 (2H, d, *J* = 8.1 Hz, C(2)H, C(6)H $C_6H_4NO_2$), 8.141 (2H, d, *J* = 8.1 Hz, C(3)H, C(5)H $C_6H_4NO_2$). ^{13}C NMR (75 MHz, DMSO-d$_6$): δ = 13.78 [(CH$_2$)$_3$M$\underline{e}$], 18.60 (CH$_2$), 20.39 (C_6H_4M$\underline{e}$), 30.08 (CH$_2$), 75.66 (NOCH$_2$), 87.08, 87.94 (CHOH, COH), 123.21, 125.06, 128.33, 128.80 (C-3, C-5 $C_6H_4NO_2$, C-3,C-5 C_6H_4Me, C-2,C-6 C_6H_4Me, C-2, C-6 $C_6H_4NO_2$), 133.33, 134.71 (C-4 C_6H_4Me, C-1 $C_6H_4NO_2$), 147.24, 147.30 (C-1 C_6H_4Me, C-4 $C_6H_4NO_2$), 157.00 (C=O). MS (FAB) m/z 402 [M+H]$^+$(12), 384 [M+H-H$_2$O]$^+$(4), 257 (7), 251 (26), 241 (17), 235 (7), 223 (100), 195 (15), 150 (38), 133 (34), 106 (46). Anal. Calc. for $C_{20}H_{23}N_3O_6$: C 59.84, H 5.78, N 10.47. Found: C 59.73, H 5.86, N 10.39.

1-(4-Bromophenyl)-3-ethoxy-4*S*,5*S*-4,5-dihydroxy-5-(4-nitrophenyl)imidazolidin-2-one (11f)

4-Nitrophenylglyoxal hydrate (56 mg, 0.281 mmol) was added to the solution of **6i** (73 mg, 0.281 mmol) in acetic acid (4 mL). The reaction mixture was stirred at 17 °C for 22 h, then it was frozen and acetic acid was evaporated at 15°C under vacuum (2 mm Hg), the residue was twice washed with cold water (5 mL) and dried under vacuum (2 mm Hg) to yield 110 mg (89 %, purity 93 %) of **11f** as colourless crystals, m.p. 165-166°C (with decomp.)(CH$_2$Cl$_2$-hexane). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 1.23 (3H, t, *J* = 6.8 Hz, NOCH$_2$Me), 4.05 (2H, q, *J* = 6.8 Hz, NOCH$_2$Me), 4.90 (1H, d, *J* = 6.6 Hz, CHOH), 7.16 (1H, d, *J* = 6.6 Hz, CHOH), 7.35 (1H, s, OH), 7.35–7.43 (4H, m, C$_6$H$_4$Br), 7.76 (2H, d, *J* = 8.7 Hz, C(2)H, C(6)H C$_6$H$_4$NO$_2$), 8.16 (2H, d, *J* = 8.7 Hz, C(3)H, C(5)H C$_6$H$_4$NO$_2$). ^{13}C NMR (75 MHz, DMSO-d$_6$): δ = 13.94 (Me), 71.40 (NOCH$_2$), 87.13, 87.51 (CHOH, COH), 117.65, 123.39, 126.12, 128.20, 131.25, 135.49 (C Ar), 146.88, 147.35 (C-1 C$_6$H$_4$Br, C-4 C$_6$H$_4$NO$_2$), 156.55 (C=O). MS (FAB) m/z 440 [M+H]$^+$(39), 438 [M+H]$^+$(39), 261(100): 259 (94), 223 (81), 214 (48), 150 (45). Anal. Calc. for C$_{17}$H$_{16}$BrN$_3$O$_6$: C 46.59, H 3.68, N 9.59. Found: C 46.32, H 3.74, N 9.35.

1-(4-Bromophenyl)-3-*n*-butyloxy-4*S*,5*S*-4,5-dihydroxy-5-(4-nitrophenyl)imidazolidin-2-one (11g)

4-Nitrophenylglyoxal hydrate (50 mg, 0.254 mmol) was added to the solution of **6j** (73 mg, 0.254 mmol) in acetic acid (5 mL). The reaction mixture was stirred at 18 °C for 18 h, then it was frozen and acetic acid was evaporated at 16°C under vacuum (2 mm Hg), the residue was twice washed with cold water (5 mL) and dried under vacuum (2 mm Hg) to yield 110 mg (93 %, purity 93 %) of **11g** as colourless solid, m.p. 114-117 °C (with decomp., CH$_2$Cl$_2$-hexane). ^{1}H NMR (300 MHz, DMSO-d_6): δ = 0.90 (3H, t, *J* = 7.0 Hz, NO(CH$_2$)Me), 1.40 (2H, sex, *J* = 7.0 Hz, NOCH$_2$CH$_2$CH$_2$Me), 1.61 (2H, quint, *J* = 7.0 Hz, NOCH$_2$CH$_2$CH$_2$Me), 3.97–4.02 (2H, m, NOCH$_2$), 4.90 (1H, d, *J* = 6.3 Hz, CHOH), 7.16 (1H, d, *J* = 6.3 Hz, CHOH), 7.33–7.47 (5H, m, C$_6$H$_4$Br and COH), 7.76 (2H, d, *J* = 8.4 Hz, C(2)H, C(6)H C$_6$H$_4$NO$_2$), 8.17 (2H, d, *J* = 8.4 Hz, C(3)H, C(5)H C$_6$H$_4$NO$_2$). ^{13}C NMR (75 MHz, DMSO-d$_6$): δ = 13.78 [(CH$_2$)$_3$Me], 18.58 (CH$_2$), 30.04 (CH$_2$), 75.72 (NOCH$_2$), 87.12, 87.59 (CHOH, COH), 117.69 (C-4 C$_6$H$_4$Br), 123.40 (C-3, C-5 C$_6$H$_4$NO$_2$), 126.18, 128.24 (C-2,C-6 C$_6$H$_4$NO$_2$, C-2,C-6 C$_6$H$_4$Br), 131.26 (C-3,C-5 C$_6$H$_4$Br), 135.50 (C-1 C$_6$H$_4$NO$_2$), 146.89, 147.38 (C-1 C$_6$H$_4$Br, C-4 C$_6$H$_4$NO$_2$), 156.59 (C=O). MS (FAB) m/z 468 [M+H]$^+$ (19), 466 [M+H]$^+$ (18), 450 [M+H-H$_2$O]$^+$ (10), 289 (100), 287 (84), 251 (88), 195 (68), 150 (94). Anal. Calc. for C$_{19}$H$_{20}$BrN$_3$O$_6$: C 48.94, H 4.32, N 9.01. Found: C 48.75, H 4.46, N 8.96.

4*S*,5*S*-4,5-Dihydroxy-1-methyl-5-(4-nitrophenyl)-3-propyloxyimidazolidin-2-one (14a)

A solution of **13a** (177 mg, 1.336 mmol) in acetic acid (4 mL) was added to the mixture of nitrophenylglyoxal hydrate (263 mg, 1.336 mmol) and acetic acid (2 mL). The reaction mixture was stirred at 11 °C for 4 h, then it was frozen and acetic acid was evaporated at 11°C under vacuum (2 mm Hg), the residue was dissolved in water (3 mL) at 4°C and

the aqueous solution was frozen and acetic acid was evaporated at 10°C under vacuum (2 mm Hg) to give 400 mg (96 %, purity 99 %) of **14a** as colourless crystals, m.p. 151-152°C (with decomp., CH$_2$Cl$_2$-hexane). ^{1}H NMR (300 MHz, DMSO-d_6), δ = 0.92 (3H, t, *J* = 7.2 Hz, NOCH$_2$CH$_2$Me), 1.62 (2H, sex, *J* = 7.2 Hz, NOCH$_2$CH$_2$Me), 2.52–2.74 (3H, m, NMe), 3.84–3.96 (2H, m, NOCH$_2$), 4.71 (1H, d, *J* = 7.8 Hz, CHOH), 6.73 (1H, d, *J* = 7.8 Hz, CHOH), 6.78 (1H, s, OH), 7.72 (2H, d, *J* = 8.7 Hz, C(2)H, C(6)H C$_6$H$_4$NO$_2$), 8.28 (2H, d, *J* = 8.7 Hz, C(3)H, C(5)H C$_6$H$_4$NO$_2$). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.95 (3H, t, *J* = 7.2 Hz, NOCH$_2$CH$_2$Me), 1.69 (2H, sex, *J* = 7.2 Hz, NOCH$_2$CH$_2$Me), 3.97 (2H, td, ^3J = 6.9 Hz, ^2J = 1.8 Hz, NOCH$_2$), 4.50 (1H, br. s, CHOH), 4.61 (1H, br. s, CHOH), 4.92 (1H, s, OH), 7.66 (2H, d, *J* = 9.0 Hz, C(2)H, C(6)H C$_6$H$_4$NO$_2$), 8.27 (2H, d, *J* = 9.0 Hz, C(3)H, C(5)H C$_6$H$_4$NO$_2$). ^{13}C NMR (75 MHz, DMSO-d$_6$): δ = 10.30 (Me), 21.23 (OCH$_2$CH$_2$Me), 25.15 (NMe), 77.44 (NOCH$_2$), 85.85, 88.25 (CHOH, COH), 123.39 (C-3,C-5 C$_6$H$_4$NO$_2$), 128.07 123.39 (C-2,C-6 C$_6$H$_4$NO$_2$), 147.12, 147.47 (C-1, C-4 C$_6$H$_4$NO$_2$), 158.79 (C=O). MS (FAB) m/z 312 [M+H]$^+$(69), 294 [M+H–H$_2$O]$^+$(20), 278 (5), 237 (100), 221 (15), 195 (32), 150 (62), 133 (58). Anal. Calc. for C$_{13}$H$_{17}$N$_3$O$_6$: C 50.16, H 5.50, N 13.50. Found: C 50.08, H 5.67, N 13.46.

3-Ethoxy-4*S*,5*S*-4,5-dihydroxy)-1-(1-naphthyl)methyl-5-(4-nitrophenyl)imidazolidin-2-one (14b)

A mixture of 4-nitrophenylglyoxal hydrate (134 mg, 0.680 mmol) and **13b** (157 mg, 0.641 mmol) was dissolved in acetic acid (4 mL) with stirring. The reaction mixture was maintained at 16 °C for 6 h, then acetic acid was evaporated at 16°C under vacuum (2 mm Hg), the residue was washed by cold water (5 mL), then it was filtered off and dried under vacuum (2 mm Hg) yielding 252 mg (93 %, purity 93 %) of **14b** as yellowish solid, m.p. 155-156°C (with decomp., CH$_2$Cl$_2$-hexane). ^{1}H NMR (400 MHz, DMSO-d$_6$): δ = 1.254 (3H, t, *J* = 6.8 Hz, NOCH$_2$Me), 3.98–4.13 (2H, m, NOCH$_2$Me), 4.531 (1H, d, ^2J = 15.0 Hz, NCH$_2$), 4.837 (1H, d, *J* = 6.9 Hz, CHOH), 4.918 (1H, d, ^2J = 15.0, NCH$_2$), 6.894–6.916 (2H, M, CHOH, COH), 7.09–7.17 (2H, m, C$_{10}$H$_7$), 7.321 (2H, d, *J* = 8.7 Hz, C(2)H, C(6)H C$_6$H$_4$NO$_2$), 7.43–7.52 (3H, m, C$_{10}$H$_7$), 7.672 (2H, d, *J* = 8.7 Hz, C(3)H, C(5)H C$_6$H$_4$NO$_2$), 7.75–7.85 (2H, m, C$_{10}$H$_7$),), 8.07–8.13 (1H, m, C$_{10}$H$_7$). ^{13}C NMR (75 MHz, DMSO-d$_6$): δ = 14.00 (NOCH$_2$Me), 41.29 (NCH$_2$), 71.38 (NOCH$_2$), 86.02, 87.82 (CHOH, COH), 122.05 (C-3, C-5 C$_6$H$_4$NO$_2$), 123.37, 124.80, 125.55, 126.10, 127.49, 127.50 (C$_{10}$H$_7$), 127.63 (C-2, C-6 C$_6$H$_4$NO$_2$), 128.26, 130.87, 132.53, 132.91 (C$_{10}$H$_7$), 146.63 (C-1 C$_6$H$_4$NO$_2$), 147.14 (C4 C$_6$H$_4$NO$_2$), 158.80 (C=O). MS (FAB) m/z 424 [M+H]$^+$ (15), 245(18), 223(29), 182(28), 156(20), 141 NafCH$_2$$^+$ (100). Anal. Calc. for C$_{22}$H$_{21}$N$_3$O$_6$: C 62.41, H 5.00, N 9.92. Found: C 62.28, H 4.86, N 9.83.

Crystals of the compound **11e** were grown from CH$_2$Cl$_2$-C$_6$H$_{14}$ at 10 °C. The studied crystal was monoclinic, C$_{20}$H$_{23}$N$_3$O$_6$, at 20° C, *a* = 15.261(3) Å, *b* = 19.409(2) Å, *c* = 15.676(3) Å, *β* = 117.31(2) °, *V* = 4125.6(14) Å^3, M_r = 401.41, Z = 8, space group P2$_1$/c, $d_{calc.}$= 1.293 g/cm^3, μ (MoK$_α$) = 0.097 mm^{-1}, F(000) = 1696. Crystals of the compound **14a** were grown from CH$_2$Cl$_2$-C$_6$H$_{14}$ at -14 °C. The studied crystal was monoclinic, C$_{13}$H$_{17}$N$_3$O$_6$, at 20 °C, *a* = 25.112(5) Å, *b* = 11.250(2) Å, *c* = 10.591(2) Å, *β* = 94.360(17)°, *V* = 2983.6(11) Å^3, M_r = 311.29, Z = 8, space group P2$_1$/c, $d_{calc.}$= 1.386 g/cm^3, μ(MoK$_α$) = 0.111 mm^{-1},

$F(000) = 1312$. X-ray structural study of compounds **11e** and **14a** was performed on a Xcalibur 3 automatic four-circle diffractometer (MoK$_\alpha$-radiation, graphite monochromator, Sapphire-3 CCD detector, ω-scanning, $2\theta_{max}=50°$).

The structures were solved by direct methods using the SHELX-2016[13] software. The positions of the hydrogen atoms were located from electron density difference maps and refined by the "riding" model with $U_{iso} = nU_{eq}$ of the carrier atoms (n=1.5 for methyl groups and hydroxyl groups and n=1.2 for other hydrogen atoms). Full-matrix least-squares refinement of the structures against F^2 in anisotropic approximation for non-hydrogen atoms was converged to $wR_2 = 0.230$ using 7224 reflections ($R_1 = 0.1037$ for 2769 reflections with F>4σ(F), S = 0.981) for structure **11e** and $wR_2 = 0.292$ using 1759 reflections ($R_1 = 0.1256$ for 635 reflections with F>4σ(F), S = 0.958) for structure **14a**. The atomic coordinates, molecular geometry parameters, and crystallographic data of compounds **11e** and **14a** were deposited at the Cambridge Crystallographic Data Center, 12 Union Road, CB2, 1EZ UK [fax:+44-1223-336033, e-mail: deposit@ccdc.cam.ac.uk and is available on request quoting the deposit number CCDC 1942124 (**11e**) and number CCDC 1942123 (**14a**)].

RESULTS AND DISCUSSION

We have found that 4-nitrophenylglyoxal with *N*-alkoxy-*N'*-arylureas (**6a,e-j**) in acetic acid medium at 17–20°C selectively forms 3-alkoxy-1-aryl-4,5-dihydroxy-5-(4-nitrophenyl)imidazolidin-2-ones (**11a-g**), mainly as diastereomers with *cis* orientation of 4-HO- and 5-HO-groups (93–96%) (Scheme 7). The diastereomers **12a-g** with *trans* orientation of 4-HO- and 5-HO-groups have been observed in the trace amounts in the reaction mixtures (¹H NMR).
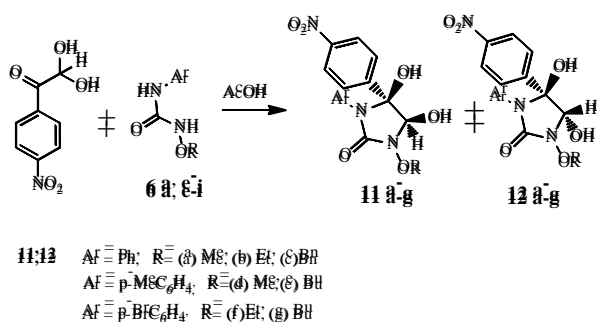
Scheme 7. Synthesis of 3-alkoxy-1-aryl-4,5-dihydroxy-5-(4-nitrophenyl)imidazolidin-2-ones (**11a-g, 12a-g**).

Under similar conditions, 4-nitrophenylglyoxal reacts with *N*-propyloxy-*N'*-methylurea (**13a**) and *N*-ethoxy-*N'*-(1-naphthyl)methylurea (**13b**) give 3-alkoxy-1-alkyl-4,5-dihydroxy-5-(4-nitrophenyl)imidazolidin-2-ones (**14a,b**) mainly as *cis* diastereomer (Scheme 8).

The *trans* diastereomers **15a,b** have been observed in reaction products in the trace amounts as well. The *cis* diastereomers **11** and **14** can be easily obtained in pure form by the crystallization.
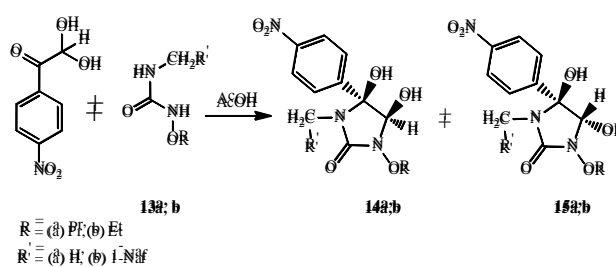

Scheme 8. Synthesis of 3-alkoxy-1-alkyl-4,5-dihydroxy-5-(4-nitrophenyl)imidazolidin-2-ones (**14a,b**, **15a,b**).

Firstly, the *cis* orientation of 4-HO- and 5-HO-groups has been proposed for the compounds **11a-j** and **14a,b** based on their ¹H NMR spectra. For compounds **11a-j** and **14a,b** the doublet of **CH**OH proton is situated in the higher field than doublet of **CH**OH proton of *trans* diastereomers **12a-j** and **15a,b**, as earlier it has been demonstrated for 5-aryl-3,4,5-trihydroxyimidazolidin-2-ones **2a,b**[7-9] (Table 1).

Table 1. The characteristic ¹H NMR chemical shifts of doublet of **CH**OH proton of **2a,b**, **3a,b**, **11a–g**, **12a-g** and **14a,b**, **15a,b**.

cis Diastereomers		*trans* Diastereomers	
	δ, ppm (J, Hz)		δ, ppm (J, Hz)
2a	4.55(7.5)[9]	**3a**	4.91(5.4)[9]
2b	4.52(7.2)[7]	**3b**	4.84(5.7)[8]
11a	4.93(6.5)	**12a**	5.20(5.5)
11b	4.91(6.6)	**12b**	5.18(6.0)
11c	4.81(6.0)	**12c**	5.23(6.0)
11d	4.92(6.4)	**12d**	5.19(4.8)
11e	4.90(6.0)	**12e**	5.17(3.9)
11f	4.90(6.8)	**12f**	5.17(5.7)
11g	4.90(6.3)	**12g**	5.16(5.1)
14a	4.71(7.8)	**15a**	5.04(6.0)
14b	4.81(7.2)	**15b**	5.16(6.0)
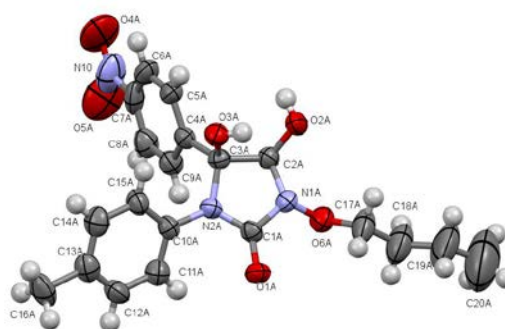
Figure 1. The molecular structure of 3-*n*-butyloxy-4*S*,5*S*-4,5-dihydroxy-1-(4-methylphenyl)-5-(4-nitrophenyl)-imidazolidin-2-one (**11eA**), showing the atom labelling. Displacement ellipsoids are drawn with the 50% probability level according to the data X-ray structural analysis.

There are two molecules of compound **11e** (**11eA** and **11eB**) in the asymmetric part of the unit cell. Molecules **11eA** and **11eB** have some different structural parameters. Earlier the similar existence of compound in the two geometrical forms in the crystal was found for the *N*-alkoxyurea **10a**[10] and in other cases.[13-15]

The five-membered ring has an envelope conformation in both molecules. The C(2) atom deviates on 0.37 Å (**11eA**) and 0.53 Å (**11eB**) off the plain of remaining ring atoms. The N(1) atom has a pyramidal configuration. The sum of bond angles centered at the N(1) atom (Σß) is 339.3° in molecule **11eA** and 336.8 in molecule **11eB**. The N(2) nitrogen atom has a planar configuration (Σß is 358.3° in molecule **11eA** and 359.5° in molecule **11eB**). The C(3)–OH group has axial orientation relative to five-membered ring(the torsion angle N(1)–C(2)–C(3)–O(3) is 97.0(5)° (molecule **11eA**), -87.9(6)° (molecule **11eB**). The C(2)–OH group has equatorial orientation to five-membered ring (the torsion angle C(1)–N(1)–C(2)–O(2) is 143.7(5)° (molecule **11eA**), 154.6(5)° (molecule **11eB**).

The 4-nitrophenyl substituent has equatorial orientation to five-membered ring [the torsion angle N(1)–C(2)–C(3)–C(4) is -142.0(5)°(molecule **11eA**), 152.3(5)°(molecule **11eB**)]. It is rotated relatively to the C(2)–C(3) endocyclic bond [the torsion angle C(2)–C(3)–C(4)–C(9) is 75.8°(molecule **11eA**), 104.4° (molecule **11eB**)]. The nitro group is slightly rotated towards the plane of the aromatic cycle [the torsion angle C(6)–C(7)–N(3)–O(4) is -7.2(2)° (molecule **11eA**), -15.4(2)° (molecule **11eB**), the torsion angle C(8)–C(7)–N(3)–O(5) is -0.3(1)° (molecule **11eA**), -18.6(9)° (molecule **11eB**)].

In the compound **11e** the ordinary bonds O(2)–C(2) and O(3)–C(3) are in some way different: the O(3)–C(3) bond [1.399(6) Å (**11eA**), 1.405(6) Å (**11eB**)] is little bit longer than the O(2)–C(2) bond [1.380(7) Å (**11eA**), 1.369(7) Å (**11eB**)]. The similar bond difference was found for 5-aryl-3,4,5-trihydroxyimidazolidin-2-ones **2a**[9], **2b**[7]. The lengths of O(6)–N(1) bond [1.410(6) Å (**11eA**), 1.401(6) Å (**11eB**)] is similar to the same bond's lengths in compounds **2a,b** [1.398(7) Å in compound **2a**,[9] 1.405(1) Å in compound **2b**[7]].

The butyloxy group has *+ac*-conformation to the endocyclic C(2)–N(1) bond in the molecule **11eA** and *–ac*-conformation in the molecule **11eB** [the torsion angle C(2)-N(1)–O(6)–C(17) is 121.3(6)° (molecule **11eA**), -107.6(6)° (molecule **11eB**)]. It has transoid conformation [the torsion angle N(1)–O(6)–C(17)–C(18) is -179.0(7)° (molecule **11eA**), 170.1(6)° (molecule **11eB**), the torsion angle O(6)–C(17)–C(18)–C(19) is 171.7(1)° (molecule **11eA**), -159.4(1)° (molecule **11eB**)].

In the crystal, the molecules **11eA** and **11eB** are linked into dimers by the intermolecular hydrogen bond O(3B)-H(3B)…O(1A)' (x, y, z) (H…O 1.87 Å, O-H…O 167°). These dimers form the chains toward crystallographic direction [0 0 1] due to intermolecular hydrogen bonds O(3A)–H(3A)…O(2A)' (1-x, 1-y, -z) (H…O 2.23 Å, O–H…O 148°) и O(3B)–H(3B)…O(1A)' (x, y, z) (H…O1.87 Å, O–H…O 167°).

The molecular structure 4*S*,5*S*-4,5-dihydroxy-1-methyl-5-(4-nitrophenyl)-3-propyloxyimidazolin-2-one (**14a**) is very similar to the molecular structure of compound **11e**.

There are two molecules of 4*S*,5*S*-4,5-dihydroxy-1-methyl-5-(4-nitrophenyl)-3-propyloxyimidazolidin-2-one (**14a**) (**14aA** and **14aB**) in the asymmetric part of the unit cell. These molecules have different structural parameters.
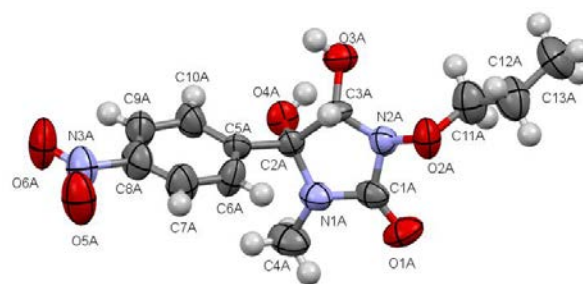

Figure 2. Molecular structure of 4*S*,5*S*-4,5-dihydroxy-1-methyl-5-(4-nitrophenyl)-3-propyloxyimidazolidin-2-one (**14aA**) with atoms represented by thermal vibration ellipsoids of 50% probability level according to the data of X-ray structural analysis.

The five-membered ring has an envelope conformation in both molecules. The C(3) atom deviation of the plane of the remaining ring atoms is 0.42 Å in the molecule 1**4aA** and 0.46 Å in the molecule **14aB**. The nitrogen atom N(1) has the planar configuration (Σβ=356° in the molecule **14aA** and Σβ=357° in the molecule **14aB**). The nitrogen atom N(2) has the pyramidal configuration (Σβ=337.4° in the molecule **14aA** and Σβ=336° in the molecule **14aB**). The hydroxyl group at the C(2) atom has an axial orientation relatively to the five-membered ring [the N(2)–C(3)–C(2)–O(4) torsion angle is -90.6(7)° in **14aA**, 92.3(7)° in **14aB**]. The hydroxyl group at the C3 atom has an equatorial orientation to the five-membered ring (the C(1)–N(2)–C(3)–O(3) torsion angle is -146.2(7)° (**14aA**), 152.1(7)° (**14aB**)).

The 4-nitrophenyl substituent is equatorially oriented to the five-membered ring [the torsion angle N(2)–C(3)–C(2)–C(5) is 147.6(6)° (**14aA**), -150.6(7)° (**11eB**)]. It is rotated towards the C(2)–C(3) endocyclic bond (the torsion angle C(3)–C(2)–C(5)–C(6) is -68.6° (**14aA**), 74.4° (**14aB**)]. The nitro group is slightly rotated towards the plane of the aromatic cycle [the torsion angle C(7)–C(8)–N(3)–O(5) is -2.8(2)° (**14aA**), 10.5(2)° (**14aB**), the torsion angle C(9)–C(8)–N(3)–O(6) is -4.9(2)° (**14aA**), 5.4(1)° (**14aB**)].

In the compound **14a** the ordinary bonds O(4)–C(2) and O(3)–C(3) are in some way different: the O(4)–C(2) bond [1.427(8) Å (**14aA**), 1.431(9) Å(**14aB**)] is a longer than the O(3)–C(3) bond [1.381(9) Å (**14aA**), 1.387(9) Å(**14aB**)]. The similar bond difference takes place in the compounds **2a**,**2b**,**11e**.[7,9] The length of O(2)–N(2) bond [1.420 (8) Å (**14aA**), 1.418 (8) Å (**14aB**)] is similar to the same bond's length in the compound **11e**. The propyloxy group has *–ac*-conformation to the endocyclic C(3)–N(2) bond in the molecule **14aA** and *+ac*-conformation in the molecule **14aB** [the torsion angle C(3)–N(2)–O(2)–C(11) is - 106.8(8)° (**14aA**), 115.5(8) (**14aB**)]. It has transoid conformation [the torsion angle N(2)–O(2)–C(11)–C(12) is 175.8(8)° (**14aA**), 175.5(9)° (**14aB**), the torsion angle O(2)–C(11)–C(12)–C(13) is -174.2(9)° (**14aA**), -179.0(1)° (**14aB**)].

In the crystal molecules **14aA** and **14aB** are linked in the dimers by the intermolecular hydrogen bond O(3B)–H(3B)…O(1A)' (x, y, z) (H…O 1.98 Å, O–H…O 167°). These dimers form the chains toward crystallographic direction [0 1 0] due to intermolecular hydrogen bonds O(3A)–H(3A)…O(4B)' (x,1+y,z) (H…O 2.06 Å, O–H…O 178°) and O(4A)–H(4A)…O(2A)' (x, 1.5-y, -0.5+z) (H…O 2.12 Å, O–H…O 136°) (Figure 3).
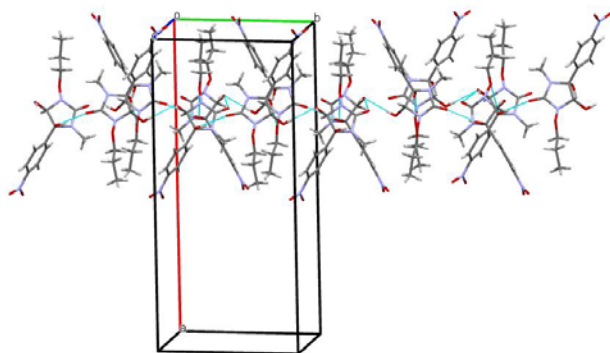
Figure 3. The rearrangement molecules **14aA** and **14aB** in the crystal according to the data of X-ray structural analysis.

For the studied reaction of arylglyoxals with *N*-hydroxyurea,[7-9] *N*-alkoxy-*N'*-arylureas[10] and *N*-alkoxy-*N'*-alkylureas a possible mechanism results dominating the formation of the diastereomers with *cis* orientation of 4-HO- and 5-HO-groups has been proposed (Scheme 9). At the first stage, the open-chain *N*-alkoxyurea **16A** is formed which has intramolecular hydrogen bond. The intermediate **16A** can isomerize into the enolic form **16B** possessing the same intramolecular hydrogen bond. In the further cyclization of intermediate **16A** (route **i** Scheme 9), or intermediate **16B** (rout **ii** Scheme 9) yields the diastereomer with *cis* orientation of 4-HO- and 5-HO-groups due to presence of this intramolecular hydrogen bond. The mild conditions of the reaction (no heating) preserve the further isomerization of the forming *cis* diastereomers **11**, **14** into *trans* diastereomers **12**, **15**.
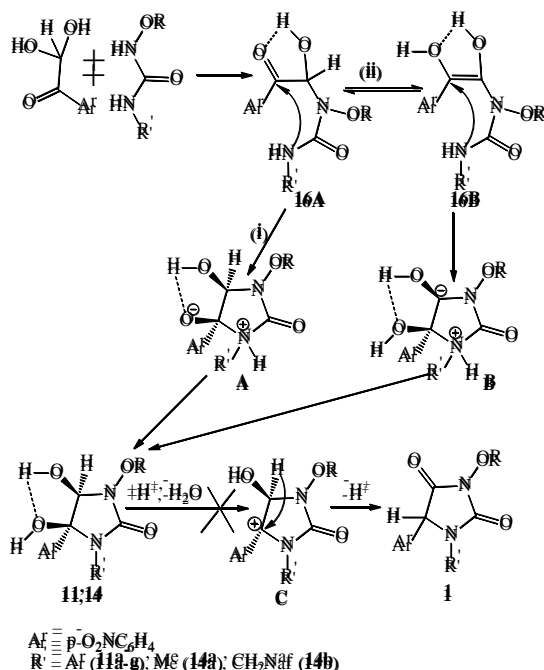
Scheme 9. The proposed mechanism of the interaction of 4-nitrophenylglyoxal with *N*-alkoxy-*N'*-arylureas and *N*-alkoxy-*N'*-alkylureas.

It is probable that the presence of such a strong electronegative substituent in 5-aryl's moiety, as nitro group, destabilizes "benzylic" cation **C** and makes impossible the further transformation of the compounds **11** and **14** into

hydantoins **1**.[9] Thus, as for the reaction of 4-nitrophenylglyoxal with *N*-alkoxy-*N'*-arylureas (**6a,e-i**) and *N*-alkoxy-*N'*-alkylureas (**13a,b**) it has been discovered that the process leads only to the mixture of diastereomers of 3-alkoxy-4,5-dihydroxy-5-(4-nitrophenyl)imidazolidin-2-ones (**11a-g**,**12a-g**) and 3-alkoxy-1-alkyl-4,5-dihydroxy-5-(4-nitrophenyl)imidazolidin-2-ones (**14a,b** and **15a,b**).

The diastereomer with *sic* orientation of HO-groups is the main product in both cases. The structure of 3-*n*-butyloxy-4*S*,5*S*-4,5-dihydroxy-1-(4-methylphenyl)-5-(4-nitrophenyl)-imidazolidin-2-one (**11e**) and 4*S*,5*S*-4,5-dihydroxy-1-methyl-5-(4-nitrophenyl)-3-propyloxyimidazo-lidin-2-one (**14a**) has been studied by X-ray structural analysis.

Conclusions

4-Nitrophenylglyoxal reacts with *N*-alkoxy-*N'*-arylureas (**6a,e-i**) and *N*-alkoxy-*N'*-alkylureas (**13a,b**) in acetic acid medium at the room temperature forming mainly 3-alkoxy-4,5-dihydroxy-5-(4-nitrophenyl)imidazolidin-2-one (**11a-g**) and 3-alkoxy-1-alkyl-4,5-dihydroxy-5-(4-nitrophenyl)-imidazolidin-2-ones (**14a,b**), respectively, which have *cis* oriented hydroxyl groups. X-Ray structural analysis of 3-*n*-butyloxy-4*S*,5*S*-4,5-dihydroxy-1-(4-methylphenyl)-5-(4-nit-rophenyl)imidazolidin-2-one (**11e**) and 4*S*,5*S*-4,5-dihydroxy-1-methyl-5-(4-nitrophenyl)-3-propyloxyimidazo-lidin-2-one (**14a**) has confirmed this special structural feature of these compounds.

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