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Pyramidal nitrogen in the crystal of *N*-[(benzoyl)(hydroxy)methyl]-*N*-benzyloxy-*N′*-(2-bromophenyl)urea[†]

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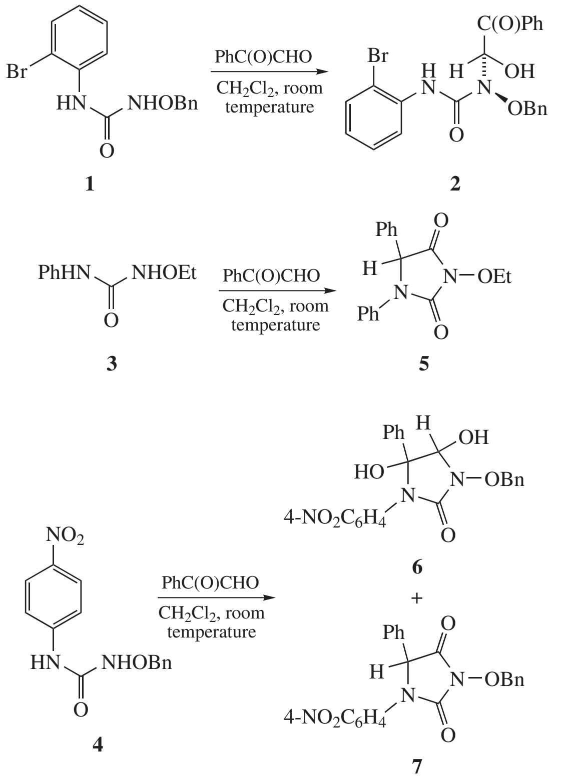
Phenylglyoxal reacts with *N*-benzyloxy-*N′*-(2-bromophenyl)urea forming *N*-[(benzoyl)(hydroxy)methyl]-*N*-benzyloxy-*N′*-(2-bromophenyl)urea. As it was found by XRD study, the molecules of the latter in crystal exist in two forms which vary in a different degree of pyramidality of the same nitrogen atom. Reactions of *N*-ethoxy-*N′*-phenylurea and *N*-benzyloxy-*N′*-(4-nitrophenyl)urea with phenylglyoxal lead to cyclic products.

Arylglyoxals react with *N*-hydroxyurea in neutral aqueous media to produce 5-aryl-3-hydroxyimidazolidine-2,4-diones[2] at the final stage. The reaction proceeds *via* intermediate acyclic substituted *N*-hydroxyureas and then 5-aryl-3,4,5-trihydroxyimidazolidin-2-ones. Some of these intermediates have been isolated and their structures have been established. XRD study revealed the *cis*-orientation of 4-OH and 5-OH groups in monocrystal of 5-(4-chlorophenyl)-3,4,5-trihydroxyimidazolidin-2-one.[2] Meanwhile, phenylglyoxal reacts with *N*-alkoxyureas in organic solvents to afford 3-alkoxy-5-phenylimidazolidine-2,4-diones.[3] In continuation of these investigations, we have studied reaction of phenylglyoxal with *N*-alkoxy-*N′*-arylureas.

Reaction between phenylglyoxal and *N*-benzyloxy-*N′*-(2-bromophenyl)urea **1** in dichloromethane solution at room temperature gives only acyclic *N*-[(benzoyl)(hydroxy)methyl]-*N*-benzyloxy-*N′*-(2-bromophenyl)urea **2** (Scheme 1). Probably, the bulky *ortho*-bromo substitutent retards the further cyclization into expected 3-benzyloxy-1-(2-bromophenyl)-4,5-dihydroxy-5-phenylimidazolidin-2-one.



Scheme 1

In contrast, analogous ureas **3**, **4** bearing aryl moieties depriving of *ortho* substituent react with phenylglyoxal to yield cyclic products (Scheme 1).[‡] *N*-Ethoxy-*N′*-phenylurea **3** is transformed into hidantoin **5**, while *N*-benzyloxy-*N′*-(4-nitrophenyl)urea **4** along with the similar hidantoin **7** gives also dihydroxyimidazolidinone **6**.

Compound **6** was isolated as a single diastereomer probably having *cis*-orientation of OH groups, by analogy with 5-(4-chlorophenyl)-3,4,5-trihydroxyimidazolidin-2-one.[2]

XRD study of urea **2**[§] (Figures 1, 2) finally evidenced its acyclic structure. Asymmetric part of the unit cell contains two molecules labeled as **2A** and **2B**, possessing the same relative

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[†] Asymmetric Nitrogen. Part 105; previous communication, see ref. 1.

[‡] N-*Benzyloxy*-N′-*(2-bromophenyl)urea* **1**. The solution of *o*-bromophenylisocyanate (1.230 g, 6.215 mmol) in benzene (8 ml) was added to the solution of benzyloxyamine (0.985 g, 0.800 mmol) in benzene (8 ml), reaction mixture was kept at 23 °C for 70 h, then the precipitate was filtered off and washed with hexane, giving 1.661 g (83%) of urea **1**, colourless crystals, mp 113–114 °C. ^{1}H NMR (300 MHz, [^{2}H$_6$]DMSO) δ: 4.89 (s, 2H, NOCH$_2$), 7.03 [td, 1H, C(4)H, ^3J 7.8 Hz, ^4J 1.2 Hz], 7.36 [td, 1H, C(5)H, ^3J 7.8 Hz, ^4J 1.2 Hz], 7.38–7.44 (m, 3H, Ph), 7.48–7.51 (m, 2H, Ph), 7.64 [dd, 1H, C(6)H, ^3J 7.8 Hz, ^4J 1.2 Hz], 8.01 [dd, 1H, C(3)H, ^3J 7.8 Hz, ^4J 1.2 Hz], 8.23 (br. s, 1H, NH), 10.00 (br. s, 1H, NHO). Found (%): N, 8.78; Br, 24.71. Calc. for $C_{14}H_{13}BrN_2O_2$ (%): N, 8.72; Br, 24.88.

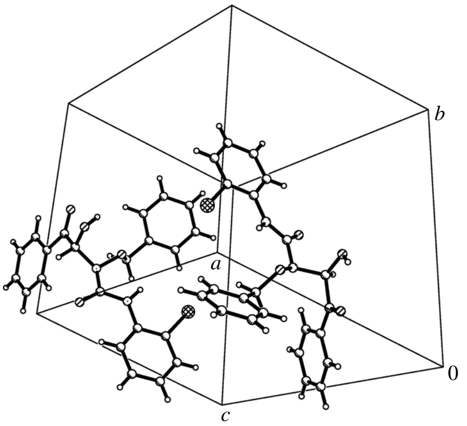

Figure 1 Symmetry of the unique part of the unit cell in the crystal of **2** containing two molecules. Hydrogen atoms were omitted for clarity.

configuration of their chiral centres, namely the saturated carbon atom C(8) and pyramidal nitrogen N(1). The N(1) atom in the molecule **2A** has slightly higher pyramidality degree as compared to the molecule **2B**. The sum of bond angles centered on this atom is 336.0(3)° in the molecule **2A** and 341.2(3)° in the molecule **2B**.

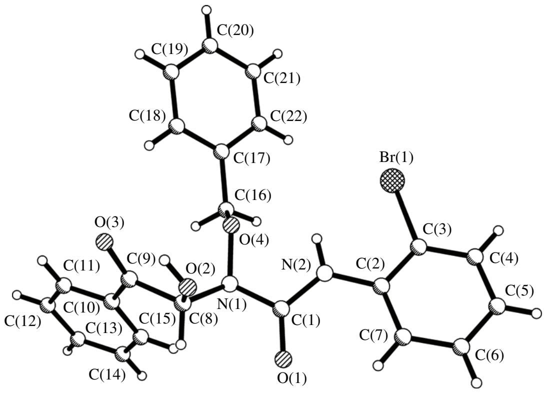

Figure 2 Structure of molecule **2A**.

The former value is close to that in *N*-methoxy-*N*-(pyridinium-1-yl)urea perchlorate (333.9°)[4] containing strongly pyramidal nitrogen atom. The deviation of the N(1) atom from the plane of bonded atom is 0.416(3) Å in the molecule **2A** [*cf.* 0.429 Å in *N*-methoxy-*N*-(pyridinium-1-yl)urea perchlorate[4]] and 0.366(3) Å in the molecule **2B**.

N-*[(Benzoyl)(hydroxy)methyl]*-N-*benzyloxy*-N′-*(2-bromophenyl)urea* **2**. The solution of phenylglyoxal (0.127 g, 0.944 mmol) in CH_2Cl_2 (5 ml) was added to the solution of *N*-benzyloxy-*N*′-(2-bromophenyl)urea **1** (0.303 g, 0.944 mmol) in CH_2Cl_2 (7 ml). The reaction mixture was kept at 20–23 °C for 46 h, then the solvent was evaporated *in vacuo*, the residue was crystallized from benzene–hexane to give 0.345 g (80%) of the product **2**, colourless crystals, mp 86–88 °C (THF–hexane). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.65 (d, 1H, NOC*H*$_2$Ph, ^3J 10.5 Hz), 4.85 (d, 1H, NOC*H*$_2$Ph, ^3J 10.5 Hz), 4.97 (d, 1H, C*H*OH, ^3J 8.1 Hz), 6.76 (d, 1H, CHO*H*, ^3J 8.1 Hz), 6.97 [td, 1H, C(4)H, ^3J 7.5 Hz, ^4J 1.2 Hz], 7.30 [dd, 1H, C(6)H, ^3J 7.5 Hz, ^4J 1.2 Hz], 7.30–7.37 (m, 5H, *Ph*CH$_2$O), 7.52 [t and td, 3H, C(3′)H, C(5′)H and C(5)H, ^3J 7.5 Hz], 7.65 [t, 1H, C(4′)H, ^3J 7.5 Hz], 8.16 [d, 2H, C(2′)H, C(6′)H, ^3J 7.5 Hz], 8.29 [dd, 1H, C(3)H, ^3J 7.5 Hz, ^4J 1.2 Hz], 8.47 (s, 1H, NH). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 79.47 (CH_2), 80.50 (CHOH), 113.52 [C(2) in C_6H_4Br], 121.06 [C(3) in C_6H_4Br], 124.96 [C(6) in C_6H_4Br], 128.40 [C(4) in C_6H_4Br], 138.73 [C(5) in C_6H_4Br], 129.02 [C(2), C(6) in *Ph*CH$_2$], 129.26 [C(3), C(5) in *Ph*CO, *Ph*CH$_2$], 129.54 [C(4) in *Ph*CH$_2$], 132.27 [C(2), C(6) in *Ph*CO], 133.20 [C(1) in C_6H_4Br], 133.87 [C(1) in *Ph*CH$_2$], 134.52 [C(4) in *Ph*CO], 135.47 [C(1) in *Ph*CO], 155.52 (NHCO), 193.58 (Ph*C*O). IR (ν/cm^{-1}): 3470 (OH), 3361 (NH), 1705 (C=O), 1690 (C=O). MS (FAB, H$^+$): 455 [M + H]$^+$ (5.0), 240 [M – H_2O – BrC_6H_4N=C=O]$^+$ (100), 91 [Bn]$^+$ (97). Found (%): C, 58.07; H, 4.15; N, 6.08. Calc. for $C_{22}H_{19}BrN_2O_4$ (%): C, 58.04; H, 4.21; N 6.15.

N-*Ethoxy*-N-*phenylurea* **3** was obtained from phenylisocyanate and ethoxyamine in the similar manner as compound **1**, colourless crystals, yield 60%, mp 101–104 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.34 (t, 3H, NOCH$_2$*Me*, ^3J 7.0 Hz), 3.99 (q, 2H, NOC*H*$_2$Me, ^3J 7.0 Hz), 7.11 [t, 1H, C(4)H, ^3J 7.8 Hz], 7.34 [t, 2H, C(3)H, C(5)H, ^3J 7.8 Hz], 7.49 [d, 2H, C(2)H, C(6)H, ^3J 7.8 Hz], 7.61 (br. s, 1H, NH), 7.71 (br. s, 1H, NHO). IR (ν/cm^{-1}): 3330 (NH), 3195 (NH), 1668 (C=O). MS (FAB, H$^+$): 181 [M + H]$^+$ (100). Found (%): C, 60.11; H, 6.65; N, 15.61. Calc. for $C_9H_{12}N_2O_2$ (%): C, 59.99; H, 6.71; N, 15.55.

N-*Benzyloxy*-N′-*(4-nitrophenyl)urea* **4** was synthesized from benzyloxyamine and 4-nitrophenylisocyanate in the same manner as ureas **1** and **3**, pale yellow crystals, mp 136–138 °C. ^{1}H NMR (300 MHz, [^{2}H$_6$]DMSO) δ: 4.86 (s, 2H, OCH_2), 7.34–7.42 (m, 3H, Ph), 7.47–7.49 (m, 2H, Ph), 7.83 [d, 2H, C(2)H, C(6)H, ^3J 9.3 Hz], 8.19 [d, 2H, C(3)H, C(5)H, ^3J 9.3 Hz], 9.48 (s, 1H, NH), 9.93 (s, 1H, NHO). Found (%): N, 14.72. Calc. for $C_{14}H_{13}N_3O_4$ (%): N, 14.63.

3-Ethoxy-1,5-diphenylimidazolidine-2,4-dione **5**. The solution of phenylglyoxal (0.087 g, 0.646 mmol) in CH_2Cl_2 (8 ml) was added to the solution of *N*-ethoxy-*N*-phenylurea **1** (0.116 g, 0.646 mmol) in CH_2Cl_2 (4 ml). The reaction mixture was kept at 20 °C for 70 h, then the solvent was evaporated *in vacuo*, the residue was crystallized from Et_2O–hexane to give 0.084 g (46%) of the product **5**, colourless crystals, mp 125–126 °C. ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.41 (t, 3H, NOCH$_2$*Me*, ^3J 6.9 Hz), 4.30 (qd, 2H, NOC*H*$_2$Me, ^3J 6.9 Hz, ^2J 2.4 Hz), 5.45 (s, 1H, PhC*H*), 7.12 [t, 1H, C(4′)H, ^3J 7.5 Hz], 7.31–7.38 (m, 7H, Ph and Ph′), 7.47 [d, 2H, C(2′)H, C(6′)H, ^3J 7.5 Hz]. IR (ν/cm^{-1}): 1772 (C=O), 1730 (C=O). MS (FAB, H$^+$): 297 [M + H]$^+$ (100), 296 [M]$^+$ (44.6). Found (%): C, 69.17; H, 5.62; N, 9.24. Calc. for $C_{17}H_{16}N_2O_3$ (%): C, 68.91; H, 5.44; N, 9.45.

3-Benzyloxy-4,5-dihydroxy-1-(4-nitrophenyl)-5-phenylimidazolidin-2-one **6** *and 3-benzyloxy-1-(4-nitrophenyl)-5-phenylimidazolidine-2,4-dione* **7**. *N*-Benzyloxy-*N*′-(4-nitrophenyl)urea **4** (0.516 g, 1.798 mmol) was added to the solution of phenylglyoxal (0.307 g, 2.289 mmol) in CH_2Cl_2 (24 ml), the reaction mixture was stirred at 20–23 °C for 25 h, the solid was filtered off, the filtrate was evaporated *in vacuo*, the residue was dissolved in benzene (6 ml) and hexane (10 ml) was added. The precipitate was filtered off, dissolved in THF (6 ml) and Et_2O (6 ml) was added. The precipitate was filtered off, washed by the mixture of Et_2O (2 ml) and hexane (2 ml), yielding 0.040 g (6%) of compound **7**, colourless crystals, mp 220–221 °C (decomp.). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 5.24 (s, 2H, PhC*H*$_2$O), 5.38 (s, 1H, CH), 7.12–7.18 (m, 2H, Ph), 7.33–7.42 (m, 6H, Ph and CH$_2$*Ph*), 7.47–7.50 (m, 2H, Ph), 7.62 [d, 2H, C(2)H, C(6)H in $C_6H_4NO_2$, ^3J 9.3 Hz], 8.14 [d, 2H, C(3)H, C(5)H in $C_6H_4NO_2$, ^3J 9.3 Hz]. IR (ν/cm^{-1}): 1784 (C=O), 1730 (C=O), 1510 (NO_2), 1335 (NO_2). MS (EI), *m*/*z*: 403 [M]$^+$ (7.8), 297 [M – PhC(O)H]$^+$ (59.5), 226 (14.6), 91 [Bn]$^+$ (100). Found (%): C, 65.66; H, 4.53; N, 10.22. Calc. for $C_{22}H_{17}N_3O_5$ (%): C, 65.50; H, 4.25; N, 10.42. The filtrate was concentrated *in vacuo* and hexane was added. The precipitate was filtered off, crystallized from CH_2Cl_2–hexane mixture, yielding 0.422 g (56%) of the product **6**, yellow crystals, mp 139–140 °C (decomp.). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 4.05 (s, 1H, OH), 4.64 (s, 1H, CH), 4.74 (br. s, 1H, OH), 5.02 (d, 1H, PhC*H*$_2$O, ^2J 11.1 Hz), 5.09 (d, 1H, PhC*H*$_2$O, ^2J 11.1 Hz), 7.28–7.32 (m, 3H, Ph), 7.33–7.40 (m, 7H, Ph and CH$_2$*Ph*), 7.78 [d, 2H, C(2)H, C(6)H in $C_6H_4NO_2$, ^3J 9.3 Hz], 8.05 [d, 2H, C(3)H, C(5)H in $C_6H_4NO_2$, ^3J 9.3 Hz]. IR (ν/cm^{-1}): 3420 (OH), 1725 (C=O), 1510 (NO_2), 1330 (NO_2). MS (FAB, H$^+$), *m*/*z*: 422 [M + H]$^+$ (32.9), 404 [M – OH]$^+$ (4.8), 91 [Bn]$^+$ (100). Found (%): C, 62.55; H, 4.67; N, 9.82. Calc. for $C_{22}H_{19}N_3O_6$ (%): C, 62.70; H, 4.54; N, 9.97.

§ *X-Ray diffraction data.* Single crystals of **2** ($C_{22}H_{19}N_2O_4Br$) were grown from THF–hexane at 5 °C. Diffraction data were collected on an Xcalibur 3 diffractometer (graphite-monochromated MoKα radiation, $2\theta/\theta$-scan, $2\theta_{max} = 52°$). At 298 K crystals are triclinic, space group $P\bar{1}$, $a = 9.7866(3)$, $b = 13.7761(8)$ and $c = 17.0022(11)$ Å, $\alpha = 67.117(6)°$, $\beta = 76.467(4)°$, $\gamma = 77.892(4)°$, $V = 2035.09(19)$ Å^3, $M = 455.30$, $F(000) = 928$, $d_{calc} = 1.526$ g cm^{-3}, $Z = 2$, $\mu = 2.05$ mm^{-1}. 25428 reflections were collected of which 7945 were unique. The structure was solved by direct method using the SHELX-97 program package.[6] Refinement against F^2 in an anisotropic approximation (the hydrogen atoms were isotropic in the riding model) by a full matrix least-squares method for 7495 reflections was carried out to $wR_2 = 0.064$ [$R_1 = 0.037$ for 3470 reflections with $F > 4\sigma(F)$, $S = 0.98$].

CCDC 749267 contains 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, 2010.

The first example of two types of pyramidality for the same nitrogen in the same crystal coexistence was recently reported for *N*-chloro-*N*-ethoxyurea.[1]

Molecules **2A** and **2B** possess rather similar conformation. Amide fragment is almost orthogonal to idealized position of the lone pair of the N(1) atom [the N(2)–C(1)–N(1)–Lp(N1) torsion angle is 106° in **2A** and 99° in **2B**]. The C(8)–C(9) bond has *sc*-orientation with respect to Lp(N1) [the C(9)–C(8)–N(1)–Lp(N1) torsion angle is –56° for **2A** and –38° for **2B**]. Such conformation of substituent is stabilized by attractive O(1)···H(8) interaction (the O···H distance is 2.48 Å for **2A**, 2.40 Å for **2B**). The C(2)···C(7) and C(10)···C(15) aromatic rings are almost coplanar to the planes of the N(2)–C(1)–O(1) amide fragment and the C(9)–O(3) carbonyl group, respectively [the C(1)–N(2)–C(2)–C(7) and O(3)–C(9)–C(10)–C(11) torsion angles are –17.7(5)° and –7.3(4)° for **2A**, and –12.6(5)° and –6.2(4)° for **2B**, respectively].

Molecules **2A** and **2B** are linked in the crystal by the O(2b)–H(2b)···O(1a) hydrogen bond [H···O 2.15 Å, O···O 2.911(3) Å, O–H···O 154°]. At the same time, hydroxy group in the molecule **2A** forms intramolecular hydrogen bond O(2a)–H(2a)···O(3a) [H···O 2.14 Å, O···O 2.614(3) Å, O–H···O 117°]. Bromine atoms form short intermolecular contacts Br(1)···C(9′) $(1+x, y, z)$ 3.41 Å (contact between two **2A** molecules) and 3.49 Å (contact between two **2B** molecules), van der Waals radii sum is 3.68 Å.[5] Those contacts are presumably attractive interactions between lone pairs of the Br atoms and partially positively charged carbon atoms. This results from the values of the C(3)–Br(1)···C(9′) $(1+x, y, z)$ 129° (**2A**···**2A**), 133° (**2B**···**2B**) angles. Note that NH group does not form any hydrogen bonds in crystal despite the presence of proton accepting groups.

In summary, the outcome of the reaction between phenylglyoxal and *N*-alkoxy-*N′*-arylureas depends on the substitution pattern of *N′*-aryl group. The unusual case of the existence of the same nitrogen atom in two forms having the different degrees of pyramidality was found.

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