HETEROCYCLES, Vol. 78, No. 6, 2009, pp. 1445 - 1452. © The Japan Institute of Heterocyclic Chemistry
Received, 4th October, 2008, Accepted, 9th February, 2009, Published online, 12th February, 2009
DOI: 10.3987/COM-08-11569

CONVENIENT SYNTHESIS OF NOVEL NITRONES: (*Z*)-4-AMINO-5-(HYDROXYIMINO)-2,5-DIHYDRO-1*H*-IMIDAZOLE 3-OXIDES

Xue-Qin Cao,[a] Zhan-Xiong Li,[b] Wen-Xing Zhong,[a] Li-Hua Qiu,[a] and Guo-Qiang Chen[b]*

[a] College of Chemistry, Chemical Engineering and Materials Science, Soochow University, Suzhou 215123, P. R. China

[b] College of Textile and Clothing Engineering, Soochow University, Suzhou 215021, P. R. China

*Corresponding author. Tel: +86-512-67162166; fax: +86-512-67246786

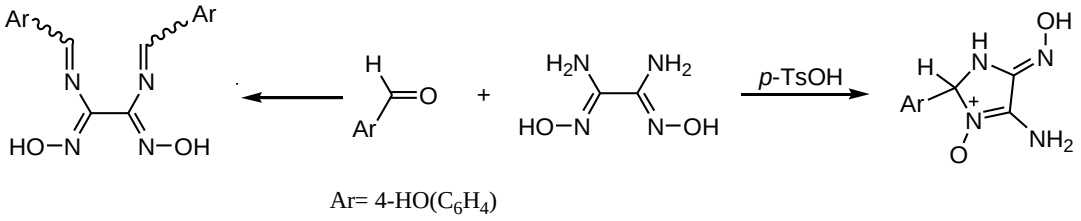
E-mail address: chenguojiang@suda.edu.cn

Abstract – Highly functionalized derivatives of (*Z*)-4-amino-5-(hydroxyimino)-2,5-dihydro-1*H*-imidazole 3-oxide were first and conveniently synthesized by the reactions of 3,4-diaminoglyoxime with benzaldehyde derivatives in the presence of *p*-toluenesulfonic acid. The procedure represents an effective method to obtain a new kind of nitrones.

INTRODUCTION

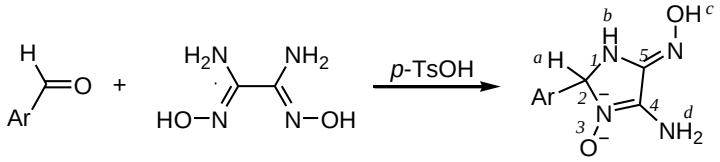
It is well known that nitrones are highly valuable intermediates in organic synthesis.[1] They are usually typical examples of 1,3-dipoles easily participating in cycloaddition reactions to provide various heterocyclic five-membered ring systems,[2] and chiral cyclic nitrones are recognized attractive synthons, especially for optically active alkaloids and amino sugars.[3] Furthermore, due to their stability of resulting nitroxide radicals and ease of chemical modification,[4] nitrones have a wide range of biological activity,[5] and specific nitrones not only be helpful to understand age-related disease processes but serendipitously have proven to be candidates for therapeutics in some cases.[6] At the same time, the derivatives of 2,5-dihydro-1*H*-imidazole 3-oxide and corresponding nitroxyl radicals possess magnetism.[7] On the other hand, the derivatives of oximes of five-membered heterocyclic compounds with two heteroatoms play an important role in antiviral property, for example, the oxime derivatives of imidazole have high fungicidal and protozoacidal activity.[8]

Many methods for the synthesis of imidazole-*N*-oxides have been reported, most of them are based on condensation of aldehydes with *N*-monosubstituted hydroxylamines, or oxidation of secondary amines or *N,N*-disubstituted hydroxylamines,[9] but there is no examples of 3,4-diaminoglyoxime acted as amine to synthesize imidazole-*N*-oxides. However, during the study of having attempted to synthesize bis-Schiff bases from 3,4-diaminoglyoxime and 2 equivalents of 4-hydroxybenzaldehyde in the presence of *p*-toluenesulfonic acid, we found that a novel imidazole-*N*-oxide was formed (Scheme 1), and the new structure was reported recently.[10] In order to study the novel method, we investigated the reactions of 3,4-diaminoglyoxime **2** with other benzaldehydes containing different substitutent than 4-hydroxybenzaldehyde (Scheme 2). Herein, we report the synthesis of the title compounds named as (*Z*)-4-amino-5-(hydroxyimino)-2,5-dihydro-1*H*-imidazole 3-oxides from these new reactions, and the reaction mechanism is also proposed.



Ar= 4-HO(C_6H_4)

Scheme 1. Reaction of 3,4-diaminoglyoxime and 4-hydroxybenzaldehyde



1 **2** **3a-h**

3a: Ar= Ph; **3b**: Ar= 2-HOC_6H_4;
3c: Ar= 4-MeC_6H_4; **3d**: Ar= 2-MeOC_6H_4;
3e: Ar= 2-$O_2NC_6H_4$; **3f**: Ar= 3-$O_2NC_6H_4$;
3g: Ar= 4-$O_2NC_6H_4$; **3h**: Ar= 2-Cl-5-$O_2NC_6H_3$.

Scheme 2. Synthesis of (*Z*)-4-amino-5-(hydroxyimino)-2,5-dihydro-1*H*-imidazole 3-oxide

RESULTS AND DISCUSSION

3,4-Diaminoglyoxime **2** was prepared according to a literature method.[11] During the study of the next reactions of 3,4-diaminoglyoxime **2** with benzaldehyde derivatives in the presence of *p*-toluenesulfonic acid, we found that if the aromatic aldehydes **1** have electron-donating group, for example, a hydroxyl or methyl group, the yield was higher; if the aromatic aldehydes **1** have electron-withdrawing group, for example, a nitro-group, even though the nitro-group was at the para-place to the carbonyl group which makes the steric hindrance smallest, the reaction time was extended about seven times, and the quantities

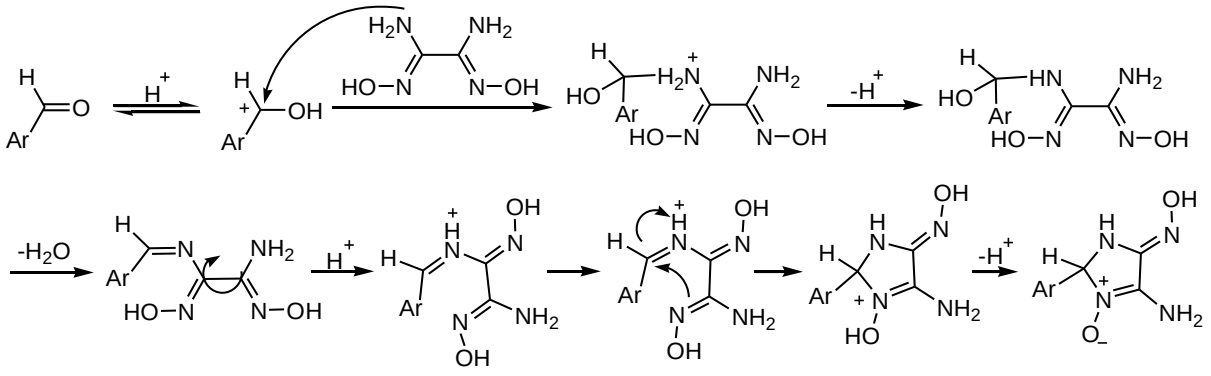
of aromatic aldehyde and *p*-toluenesulphonic acid were more, the yield was still lower than those having electron-donating group. Selected results from the above reactions are presented in Table 1. It is visible that the yields of **3b-d** are higher than that of **3e-h**.

On the basis of the above results, we put forward the reaction mechanism as follows: Firstly, the protonated carbonyl carbon in benzaldehyde derivatives was attacked by the nitrogen atom in one of the amino groups of 3,4-diaminoglyoxime **2,** and the C=N bond was formed by deprotonation and dehydrating one molecule of water. Subsequently, the nitrogen of the newly formed C=N bond was protonated, then the carbon of the C=N bond was bonded with the nitrogen atom in the oxime group which is linked to the other amino group of 3,4-diaminoglyoxime **2**, and the five-membered heterocyclic ring was formed. By deprotonation, the final products **3** were obtained. The whole process is shown in Scheme 3. According to the mechanism, benzaldehydes having electron-withdrawing group will make the carbonium ion less stable, so benzaldehydes having electron-donating group are more suitable for the reaction, and the corresponding yields are higher.

Table 1. Synthesis of (*Z*)-4-amino-5-(hydroxyimino)-2,5-dihydro-1*H*-imidazole 3-oxides **3a-h**

Comp.	Ar	Time (h)	Yield[a] (%)
3a	Ph	6	67
3b	2-HOC_6H_4	3	85
3c	4-MeC_6H_4	3	72
3d	2-$MeOC_6H_4$	4	70
3e	2-$O_2NC_6H_4$	22	63
3f	3-$O_2NC_6H_4$	22	66
3g	4-$O_2NC_6H_4$	28	65
3h	2-Cl-5-$O_2NC_6H_3$	28	67

[a] Isolated yield.



Scheme 3. The plausible mechanism for the formation of (*Z*)-4-amino-5-(hydroxylimino)-2,5-dihydro-1*H*-imidazole 3-oxide **3a-h**

The structures of products **3** are entirely different from bis-Schiff bases which we assumed at first by 3,4-Diaminoglyoxime reacted with 2 equivalents of benzaldehyde derivatives, but a heterocyclic five-membered ring which is so-called 2,5-dihydro-1*H*-imidazole is formed. At the same time, the nitrogen atom of the double bond is also bonded to an oxygen atom which is outside of the ring of imidazole, so the products also belong to nitrones. Especially, in the structures of products **3**, a hydroxyimino group is directly linked to the ring of imidazole, which is the first example of this type of compounds to our knowledge. The novel structures are highly functionalized besides a chiral carbon C^2 by containing a hydroxyimino group, an amino group, a nitrogen-oxygen dipole and so on.

Formation of the (*Z*)-4-amino-5-(hydroxyimino)-2,5-dihydro-1*H*-imidazole 3-oxides structure was unambiguously supported by spectroscopic and analytical data. A singlet at about δ 6 ppm in the ^{1}H NMR spectra was assigned to H^a bonded to the chiral carbon C^2, δ 6.39-7.95 ppm to H^b of the imino group, around δ 10 ppm to H^c of the hydroxyimino group, δ 5.58-7.02 ppm to H^d of the amino group, but the two of former were occasionally observed as doublets. In the ^{13}C NMR spectra, C^2 appeared between 74.2 and 98.8 ppm, C^4 and C^5 resonated at 147.2 -163.7 ppm and 143.1-153.5 ppm, respectively**.** In addition, the structure of **3e** was also confirmed by X-ray crystallographic analysis as shown in Figure 1.

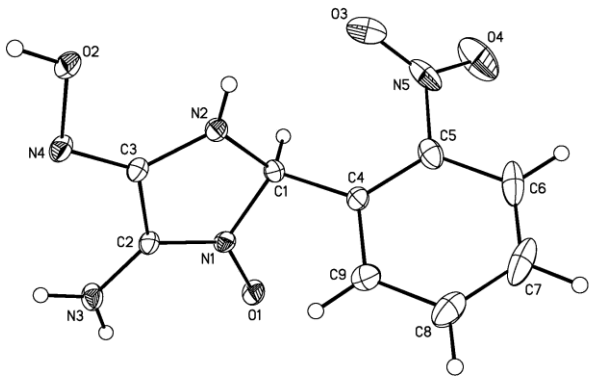
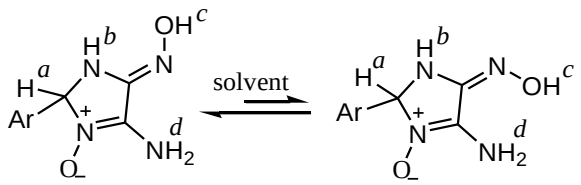


Figure 1. Crystal structure of **3e**

It is worth to note that the peak number in the ^{13}C NMR spectra is almost double as the number of carbon atoms which might be due to a tautomerism of the hydroxyimino group (Scheme 4), but not all the same in the ^{1}H NMR spectra in all cases. Meanwhile, the peaks of active H are not always visible or only be seen as small parts. Fortunately, we calculated the proportion of two isomers is about 10:5.5 from the integral area in the ^{1}H NMR spectra of **3a**: the integral areas of the peaks at δ 5.77 and 5.61 ppm (H^a) are 1.29 and 0.73 respectively, at δ 7.82 and 6.39 ppm (H^b) are 1.08 and 0.59 respectively. Owing to the sterical hindrance, the left isomer in Scheme 4 is predominant.



Scheme 4. Tautomerism of the hydroxyimino group in products **3**

In summary, we have used 3,4-diaminoglyoxime for the first time to react with benzaldehyde derivatives to obtain nitrones. The synthesis complements other recognized methods and offers a novel kind of highly functionalized nitrones named as (*Z*)-4-amino-5-(hydroxyimino)-2,5-dihydro-1*H*-imidazole 3-oxide in good to excellent yields. Remarkably, this convenient and practical procedure does not require any special handling, unusual reagents, and proceeds without the exclusion of air or water.

EXPERIMENTAL

Melting points were determined on a WRR apparatus and are uncorrected. Elemental analyses (C, H, N) were performed on a EA1110 analyser. IR spectra were carried out on a Nicolet 5700 FTIR, using KBr pellets. ^{1}H NMR spectra were recorded on a Unity Inova 400 or Unity Inova 300 MHz spectrometer, deuterated dimethylsulfoxide was used as the solvent, and tetramethylsilane (TMS) as the internal standard. Chemical shift values are expressed as ppm downfield from TMS and *J* values are in Hz. Splitting patterns are indicated as s: singlet, d: doublet, t: triplet, m: multiplet. ^{13}C NMR spectra were also recorded on a Unity Inova (300 MHz) spectrometer in deuterated dimethylsulfoxide using TMS as the internal standard. Crystal data were collected on Rigaku Mercury CCD. All materials were obtained from commercial suppliers and used without further purification.

General procedure for the synthesis and analytical data of **3a-h:** A solution of 3,4-diaminoglyoxime (1.475 g, 12.5 mmol) in anhydrous ethanol (150 mL) was heated to 55-65 ^{o}C. Aromatic aldehyde (12.5-15 mmol) and *p*-toluenesulphonic acid (0.625-1.125 mmol) were added and the resulting mixture was stirred at this temperature. The progress of the reaction was monitored by TLC (MeOH/$CHCl_3$ 2:5). After completion of the reaction, the solid product was collected by filtration and washed with anhydrous ethanol or methanol several times. For further purification (if necessary), the above products were recrystallized from a water-EtOH (1:2) or water-MeOH (1:4) mixture.

(*Z*)-4-Amino-5-(hydroxyimino)-2-phenyl-2,5-dihydro-1*H*-imidazole 3-oxide (3a): White solid, mp 179-180 ^{o}C (decomp.); IR (KBr, cm^{-1}): 3360, 3251 (NH_2), 3190, 3097 (OH), 2890 (the ring of imidazole), 1720, 1686 (C=N), 1600, 1460 (the ring of benzene), 1360 (N=O), 1230 (C-N), 959, 922 (N-O); ^{1}H-NMR (300 MHz, DMSO-d_6): δ 5.61 (s, 1H, H^d), 5.77 (s, 1H, H^d), 6.39 (s, 1H, H^c), 6.50 (s,2H, H^a), 7.32-7.56 (m,

10H, H-Ar), 7.82 (s, 1H, H^c), 10.05 (s, 1H, H^b); ^{13}C-NMR (300 MHz, DMSO-d_6): δ 85.3, 98.8, 132.2, 133.1, 133.6, 133.8, 134.5, 134.7, 142.5, 145.1, 146.9, 150.5, 153.5, 157.0; Anal. Calcd for $C_9H_{10}N_4O_2$: C, 52.42; H, 4.89; N, 27.17. Found: C, 52.25; H, 4.90; N, 27.21.

(*Z*)-4-Amino-5-(hydroxyimino)-2-(2-hydroxyphenyl)-2,5-dihydro-1*H*-imidazole 3-oxide (3b): Yield (85%). White solid, mp 110-112 °C (decomp.); IR (KBr, cm^{-1}): 3414, 3330 (NH_2), 3268, 3182 (OH), 2760 (the ring of imidazole), 1729, 1700 (C=N), 1609, 1464 (the ring of benzene), 1369 (N=O), 1230 (C-N), 959, 930 (N-O); ^{1}H-NMR (300 MHz, DMSO-d_6): δ 1.06 (t, J = 6.99 Hz, 6H), 3.44 (m, 4H,), 4.36(s, 2H), 5.58 (s, 2H, 2OH), 6.25 (d, J = 1.62 Hz, 1H, H^a), 6.66 (d, J = 1.36 Hz, 1H, H^a), 6.81-6.85 (m, 4H, H-Ar), 7.02 (s, 2H, H^d), 7.12 (d, J=1.38 Hz, 1H, H^b), 7.15-7.35 (m, 4H, H-Ar), 7.95 (d, J = 1.89 Hz, 1H, H^b), 10.16 (s, 1H, H^c), 10.23 (s, 1H, H^c); ^{13}C-NMR (300 MHz, DMSO-d_6): δ 24.0, 61.5, 81.5, 93.7, 120.8, 123.0, 124.2, 129.1, 130.6, 130.9, 132.4, 132.5, 135.4, 135.7, 143.4, 147.1, 149.8, 156.9, 160.8, 162.7; Anal. Calcd for $C_{11}H_{16}N_4O_4$: C, 49.25; H, 6.01; N, 20.88. Found: C, 49.17; H, 5.96; N, 21.09.

(*Z*)-4-Amino-5-(hydroxyimino)-2-(4-methylphenyl)-2,5-dihydro-1*H*-imidazole 3-oxide (3c): Yield (72%). White solid, mp 182.5-184 °C (decomp.); IR (KBr, cm^{-1}): 3360, 3260 (NH_2), 3190, 3097 (OH), 2880 (the ring of imidazole), 1720, 1686 (C=N), 1600, 1523, 1450 (the ring of benzene), 1360 (N=O), 1230 (C-N), 959, 928 (N-O); ^{1}H-NMR (300 MHz, DMSO-d_6): δ 2.32 (s, 6H, $2CH_3$), 5.59 (s, 1H, H^a), 5.71(s, 1H, H^a), 6.35 (s, 1H, one of H^d), 6.43 (s, 2H, H^d), 7.20-7.35 (m, 8H, H-Ar), 7.49 (s, 1H, H^b), 7.75 (s, 1H, H^b), 9.98 (s, 1H, H^c), 10.21 (s, 1H, H^c); ^{13}C-NMR (300 MHz, DMSO-d_6): δ 26.3, 85.2, 98.8, 132.2, 133.0, 134.1, 134.3, 139.5, 142.1, 142.2, 143.9, 144.1, 147.0, 150.6, 157.0; Anal. Calcd for $C_{10}H_{12}N_4O_2$: C, 54.54; H, 5.49; N, 25.44. Found: C, 54.30; H, 5.63; N, 25.56.

(*Z*)-4-Amino-5-(hydroxyimino)-2-(2-methoxyphenyl)-2,5-dihydro-1*H*-imidazole 3-oxide (3d): White solid, mp 181-182.5 °C (decomp.); IR (KBr, cm^{-1}): 3315, 3265 (NH_2), 3182 (OH), 2892 (CH_3), 1711, 1690 (C=N), 1604, 1494, 1469 (the ring of benzene), 1348 (N=O), 1273,1023 (Ar-O-C), 1223 (C-N), 930 (N-O); ^{1}H-NMR (300 MHz, DMSO-d_6): δ 3.80 (s, 3H, CH_3), 5.58 (s, 2H, H^a), 6.66 (d, J = 1.97 Hz, 1H, H^d), 7.04 (d, J = 8.10 Hz, 2H, H-Ar), 7.21(s, 1H, H^c), 7.40 (m, 2H, H-Ar), 10.16 (s, 1H, H^b); ^{13}C-NMR (300 MHz, DMSO-d_6): δ 61.0, 61.3, 80.8, 93.5, 116.6, 117.0, 125.7, 125.8, 130.3, 132.2, 132.6, 133.3, 135.7, 135.8, 143.1, 147.0, 150.9, 156.8, 162.5, 163.7; Anal. Calcd for $C_{10}H_{12}N_4O_3$: C, 50.84; H, 5.12; N, 23.72. Found: C, 50.41; H, 5.25; N, 23.45.

(*Z*)-4-Amino-5-(hydroxyimino)-2-(2-nitrophenyl)-2,5-dihydro-1*H*-imidazole 3-oxide (3e): Yellow solid, mp 191-193 °C (decomp.); IR (KBr, cm^{-1}): 3350, 3251 (NH_2), 3180, 3106 (OH), 2880 (the ring of imidazole), 1700, 1677 (C=N), 1600, 1530, 1471 (the ring of benzene), 1350 (N=O), 1335 (NO_2), 1240 (C-N), 976, 941 (N-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 6.51 (s, 1H, H^d), 7.52 (dd, J = 7.81, 1.30 Hz, 1H, H-Ar), 7.67 (dt, J = 8.09, 8.08, 1.40 Hz, 1H, H-Ar), 7.79 (dt, J = 7.58, 7.57, 0.93 Hz, 1H, H-Ar), 8.03 (dd, J = 8.11, 1.06 Hz, 1H, H-Ar); ^{13}C-NMR (300 MHz, DMSO-d_6): δ 80.5, 94.2, 129.3, 130.2,

133.2, 133.6, 135.7, 136.1, 139.1, 139.5, 140.2, 142.8, 143.4, 146.7, 150.4, 152.8, 155.1, 156.6; Anal. Calcd for $C_9H_9N_5O_4$: C, 43.03; H, 3.61; N, 27.88. Found: C, 43.04; H, 3.63; N, 27.92.

(*Z*)-4-Amino-5-(hydroxyimino)-2-(3-nitrophenyl)-2,5-dihydro-1*H*-imidazole 3-oxide (3f): Yield (66%), Yellow solid, mp 190-192 ^{o}C (decomp.); IR (KBr, cm^{-1}): 3422, 3350, 3243 (NH_2), 3180, 3097 (OH), 2880 (the ring of imidazole), 1720, 1686 (C=N), 1600, 1540, 1455 (the ring of benzene), 1350 (N=O), 1318 (NO_2), 1230 (C-N), 942, 916 (N-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 6.01 (s, 1H, H^a), 7.73 (t, J = 7.88, 1H, H-Ar), 7.85 (d, J = 7.58 Hz, 1H, H-Ar), 8.21 (s, 1H, H-Ar), 8.28 (d, J = 8.06 Hz, 1H, H-Ar); ^{13}C-NMR (300 MHz, DMSO-d_6): δ 92.3, 121.5, 121.8, 124.2, 124.7, 130.7, 131.0, 134.0, 136.4, 142.0, 142.9, 144.8, 145.5, 148.6, 148.8, 149.0, 152.2; Anal. Calcd for $C_9H_9N_5O_4$: C, 43.03; H, 3.61; N, 27.88. Found: C, 42.97; H, 3.62; N, 27.94.

(*Z*)-4-Amino-5-(hydroxyimino)-2-(4-nitrophenyl)-2,5-dihydro-1*H*-imidazole 3-oxide (3g): Yield (65%). Yellow solid, mp 192-194 ^{o}C (decomp.); IR (KBr, cm^{-1}): 3390, 3311 (NH_2), 3251, 3170 (OH), 2910 (the ring of imidazole), 1690 (C=N), 1609, 1520, 1463 (the ring of benzene), 1350 (N=O), 1309 (NO_2), 1240 (C-N), 968, 933 (N-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 5.98 (s, 1H, H^a), 7.64 (d, J = 8.46 Hz, 2H, H-Ar), 8.27 (d, J = 8.47 Hz, 2H, H-Ar); ^{13}C-NMR (300 MHz, DMSO-d_6): δ 74.2, 74.3, 124.0, 124.4, 124.7, 124.9, 125.3, 125.4, 128.6, 129.4, 131.2, 131.4, 148.6, 150.2, 150.8, 151.3, 151.5, 152.8; Anal. Calcd for $C_9H_9N_5O_4$: C, 43.03; H, 3.61; N, 27.88. Found: C, 42.91; H, 3.65; N, 27.90.

(*Z*)-4-Amino-5-(hydroxyimino)-2-(2-chloro-5-nitrophenyl)-2,5-dihydro-1*H*-imidazole 3-oxide (3h): Yield (67%). Yellow solid, mp 201-203 ^{o}C (decomp.); IR (KBr, cm^{-1}): 3420, 3362, 3251 (NH_2), 3166, 3080 (OH), 2704 (the ring of imidazole), 1712, 1690 (C=N), 1610, 1520, 1472 (the ring of benzene), 1350 (N=O), 1327 (NO_2), 1230 (C-N), 950, 924 (N-O); ^{1}H-NMR (400 MHz, DMSO-d_6): δ 6.30 (d, J = 2.19 Hz, 1H, H^a), 6.72 (s, 2H, H^d), 7.82 (d, J = 8.84 Hz, 1H, H-Ar), 7.83 (d, J = 2.20 Hz, 1H, H^b), 8.07 (d, J = 2.78 Hz, 1H, H-Ar), 8.27 (dd, J = 8.79, 2.81 Hz, 1H, H-Ar), 10.19 (s, 1H, H^c); ^{13}C-NMR (300 MHz, DMSO-d_6): δ 77.5, 90.0, 123.2, 125.0, 126.2, 126.3, 132.2, 136.6, 139.3, 139.7, 141.3, 141.9, 142.7, 143.5, 145.5, 145.6, 147.2, 152.1; Anal. Calcd for $C_9H_8N_5O_4Cl$: C 37.84; H 2.82; N 24.52. Found: C 38.02; H 2.91; N 24.52.

The X-ray data for (*Z*)-4-amino-5-(hydroxyimino)-2-(2-nitrophenyl)-2,5-dihydro-1*H*-imidazole 3-oxide (3e): $C_9H_9N_5O_4$, M_w = 251.21, triclinic, space group *P*-1 / (#2), a = 7.6372(17), b = 7.8628(15), c = 10.0673(15) Å, β = 106.261(19) deg, V = 533.14(18) $Å^3$, Z = 2, $D_{calc.}$ = 1.565 g/cm^3, μ (Mo-$K\alpha$) = 1.24cm^{-1}, 5228 independent reflections, 166 parameters, R = 0.0787, R_w = 0.2242, T = 293(2) K. Crystallographic data excluding structure have been deposited with the Cambridge Crystallographic Data Center as supplementary publication numbers CCDC 703896. A copy of the data can be obtained free of charge from CCDC, 12 Union road, Cambridge CB2 1EZ. UK [DIRECT LINE: +44 1223 762910, Fax:

+44 1223 336033 or e-mail: linstead@ccdc.cam.ac.uk; deposit@ccdc.cam.ac.uk].

REFERENCES

1. (a) E. Colacino, P. Nun, F. M. Colacino, J. Martinez, and F. Lamaty, *Tetrahedron,* 2008, **64**, 5569; (b) W. Benchouk and S. M. Mekelleche, *J. Mol. Struct. THEOCHEM,* 2008, **852**, 46.
2. N. Coskun and B. Yilmaz, *Synth. Commun.*, 2004, **34**, 1617.
3. L. Fisera, 'Topics in Heterocyclic Chemistry: 1,3-Dipolar Cycloadditions of Sugar-Derived Nitrones and their Utilization in Synthesis,' Vol. 7, ed. by R. R. Gupta, Springer-Verlag, Berlin, Heidelberg, 2007, pp. 287-323.
4. L.-C. Li, D.-Z. Liao, L.-J. Bai, Z.-H. Jiang, and S.-P. Yan, *J. Mol. Struct.*, 2001, **569**, 179.
5. (a) M. A. Voinov, I. A. Grigorev, and L. B. T Volodarsky, *Tetrahedron,* 2000, **56**, 4071; (b) A. R. Green, T. Ashwood, T. Odergren, and D. M Jackson, *Pharmacol. Ther.*, 2003, **100**, 195; (c) N. Coskun, H. Mert, and N. Arikan, *Tetrahedron,* 2006, **62**, 1351.
6. R. A Floyd, *Dieases Aging Cell.*, 2006, **5**, 51.
7. (a) G. I Roschupkina, T.V. Rybalova, Yu. V. Gatilov, and V. A Reznikov, *J. Struct. Chem.*, 2004, **45**, 356; (b) L. Catala, R. Feher, D. B. Amabilino, K. Wurst, and J. Veciana, *Polyhedron,* 2001, **20**, 1563; (c) H. Oshio, M. Yamamoto, N. Hoshino, and T. Ito, *Polyhedron,* 2001, **20**, 1621.
8. E. Abele, R. Abele, and E. Lukevics, *Chem. Heterocyl. Comp.*, 2007, **43**, 945.
9. (a) N. Coskun and D. Sumengen, *Synth. Commun.*, 1993, **23**, 1699; (b) N. Coskun, F. T. Tat, and O. O. Guven, *Tetrahedron*, 2001, **57**, 3413; (c) V. V. Martin and L. B. Volodarskii, *Khim. Geterotsikl. Soedin.*, 1979, **1**, 103; (d) I. A. Grigorev, G. I. Shchukin, V. V. Martin, and V. I Mamatyuk, *Khim. Geterotsikl. Soedin.*, 1985, **2**, 252; (e) G. I. Shchukin, I. A. Grigorev, and L. B Volodarskii, *Khim. Geterotsikl. Soedin.*, 1990, **4**, 478; (f) N. Coskun and M. Ay, *Heterocycles,* 1998, **48**, 537; (g) N. Coskun, *Tetrahedron,* 1997, **53**, 13873; (h) S. A. Popov, R. V. Andreev, G. V. Romanenko, V. I. Ovcharenko, and V. A. Reznikov, *J. Mol. Struct.*, 2004, **697**, 49; (i) K. S. Chan, W. L. Yeung, W. K. Chan, R.-J. Wang, and T. C.W. Mak, *J. Org. Chem.*, 1995, **60**, 1741; (j) Y. B. Han, B. Tuccio, R. Lauricella, A. Rockenbauer, J. L. Zweier, and F. A. Villamena, *J. Org. Chem.*, 2008, **73**, 2533.
10. X.-Q. Cao, Z.-X. Li, G.-Q. Chen, and D.-C. Zhang, *Acta Cryst.*, 2007, **C63**, 671.
11. K. Z. Alexander and L. T. Mark, *Heterocyclic Chem.*, 1997, **34**, 1057.