Syntheses of 5-(2-arylazenyl)-1,2,4-triazoles and 2-amino-5-aryl-1,3,4-oxadiazoles

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Dedicated to Charles Rees on the occasion of his 75th anniversary and 50 years of friendship

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Abstract

Di(benzotriazolyl)methanimine **1** was used for convenient preparation of previously unknown triazoles **11a,b** and **15a-d** and as a new reagent for the synthesis of oxadiazoles **17a-j**.

Keywords: Di(benzotriazolyl)methanimine, triazoles, oxadiazoles, synthesis, hydrazine, hydrazide

Introduction

Di(benzotriazol-1-yl)methanimine **1** is useful for the preparation of carboximidamides **2**, guanidines **3**,[1] triazoles **5**,[2] and triazinones and triazinthiones **6**[3] (Scheme 1). We now extend the reported preparation of 2-amino-5-phenyl-1,3,4-oxadiazole **17a** from imine **1** and benzenecarbohydrazide[2] to other hydrazides, thus providing a general route to 2-amino-5-aryl-1,3,4-oxadiazoles **17a-j**. These compounds, which are antidiabetic,[4] antiarthritic and antiinflammatory,[5] were previously prepared in high yield from arylhydrazides but this required toxic cyanogen bromide.[6-10] We also report the use of **1** for the preparation of novel triazoles **11a,b** and **15a-d.**

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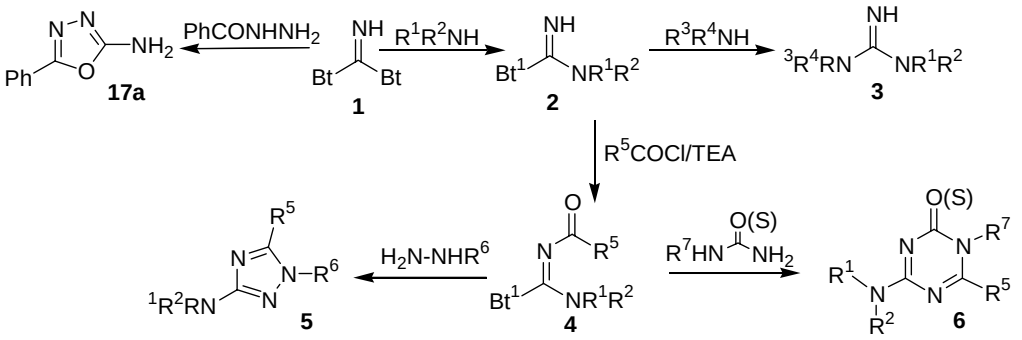
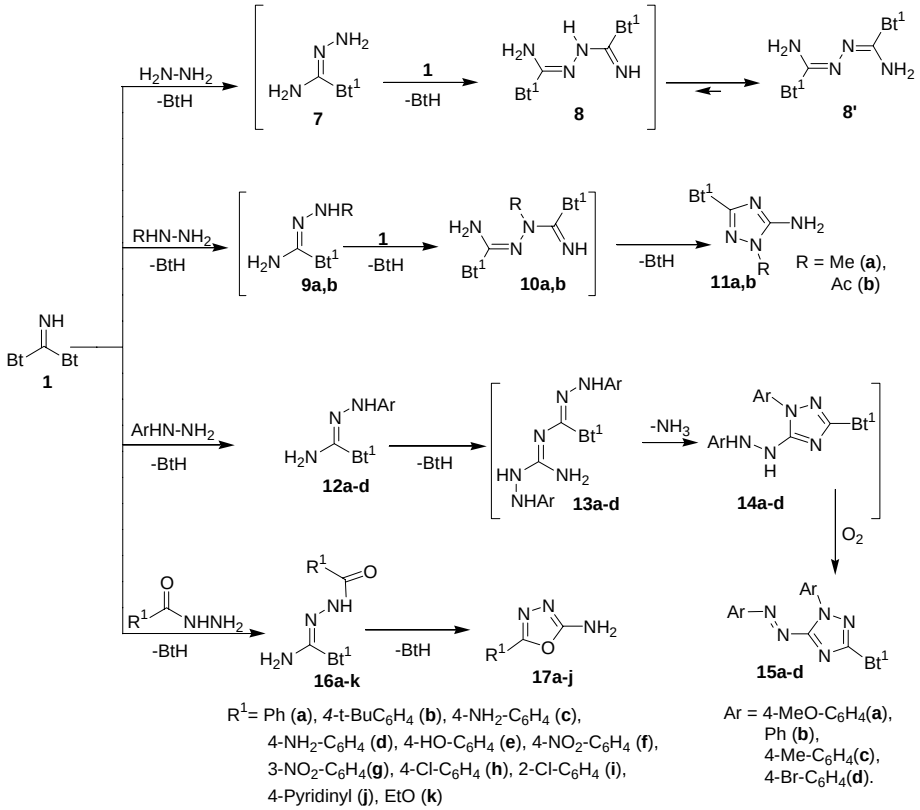


Scheme 1

Results and Discussion

By analogy to reactions with amines (Scheme 1), reactions of **1** with hydrazines are expected to give compounds of types **7**, **9** and **12**. However, after reaction of imine **1** with hydrazine hydrate in THF at 20 ^{o}C, we detected only carbohydrazonamide **8'a** (isolated yield 41%). Methylhydrazine (from 0.5 to 1.0 equivalent), under similar conditions, formed triazole **11a** (isolated yield 57%) probably because intermediate **10a** cannot tautomerize to give a product with a conjugated structure, and instead eliminates benzotriazole to form the aromatic triazole **11a**.



Scheme 2

Reactions of imine **1** with 4-methoxyphenylhydrazine in THF at rt for 18 h led to triazole **15a** in 86% yield. Analogous reactions of phenylhydrazine, 4-methylphenylhydrazine and 4-bromophenylhydrazine gave mainly products of simple substitution **12b-d,** while triazoles **15b-d** were detected as minor products. Compound **12b** was isolated and purified (yield 85%). However, treatment with *t*-BuOK (rt, 18 h, 1 eq.) converts intermediates **12b-d** quantitatively into triazoles **15b-d** (isolated yields 80–85%). The formation of unexpected compounds **15a-d** (Scheme 2) suggests condensation of intermediates **12a-d** into compounds **13a-d** followed by evolution of ammonia to give triazoles **14a-d**.

Table 1. Reactions of imine **1** with compounds RNH-NH_2

Etntry	R	Conditions	Product #	Yield %
1	H	(i)	**8**	41
2	Me	(i)	**11a**	57
3	4-MeO-C_6H_4	(ii)	**15a**	86
4	Ph	(i)	**12b**	85
5		(iii)	**15b**	82
6	4-Me-C_6H_4	(iii)	**15c**	84
7	4-Br-C_6H_4	(iii)	**15d**	78
8	MeCO	(iv)	**11b**	42
9	PhCO-	(v)	**17a**	93
10	4-tert-Butyl-C_6H_4CO-	(v)	**17b**	92
11	4-NH_2-C_6H_4CO-	(v)	**17c**	82
12	2-NH_2-C_6H_4CO-	(v)	**17d**	92
13	4-HO-C_6H_4CO-	(v)	**17e**	93
14	4-NO_2-C_6H_4CO-	(v)	**17f**	97
15	3-NO_2-C_6H_4CO-	(v)	**17g**	96
16	4-Cl-C_6H_4CO-	(v)	**17h**	96
17	2-Cl-C_6H_4CO-	(v)	**17i**	95
18	4-pyridinyl-CO-	(v)	**17j**	97
19	COOEt	(v)	**16k**	99

(i) THF, rt, 24 h; (ii) THF, rt, 4d; (iii) THF, rt, 24 h, *t*-BuOK; (iv) PhH, refl, 48 h;

(v) THF, refl, 3–6 h.

Spontaneous oxidation of hydrazo derivatives **14a-d** with atmospheric oxygen afforded deep orange to red colored azo derivatives **15a-d**. The ready formation and strong color of these compounds is explained by their highly conjugated planar structure, as confirmed by X-ray analysis for compound **15b**. Figure 1 shows a perspective view of the crystal structure of **15b**, which has bond lengths and angles similar to those previously reported for a closely related structure.[11] Overall, the molecule is close to planar, with the triazole ring meanplane subtending angles of 10.4, 8.2 and 29.7 ^{o} to the planes of the benzotriazole, phenylazo and phenyl substituents, respectively. As is often the case with planar aromatic compounds, the molecules pack in a herringbone fashion. Spontaneous oxidation of a hydrazo substituent to form a triazole ring was described by Fromm in his preparation of 1-phenyl-5-[(*E*)-2-phenyldiazenyl]-1,2-dihydro-3*H*-1,2,4-triazole-3-thione.[12] Azotriazoles similar to compounds **15a-d** have been described as dyes.[13]

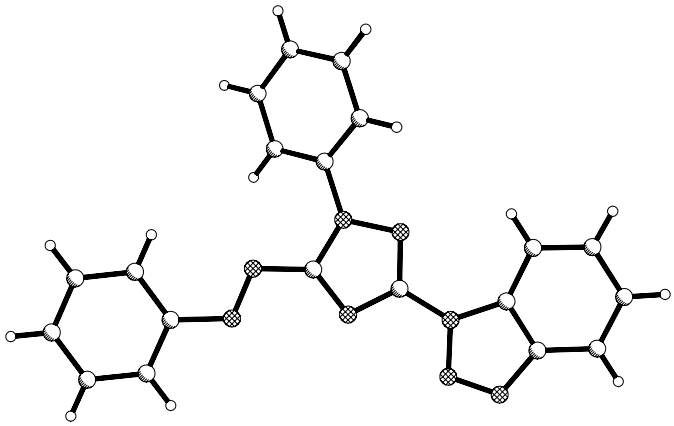


Figure 1. X-Ray structure of compound **15b**.

We also investigated reactions of imine **1** with acyl hydrazides. Similar to methyl hydrazine, acetyl hydrazide readily reacts with imine **1** to give triazole **11b** in 42% yield (Scheme 2). In contrast, aryl hydrazides gave oxadiazoles **17a-j** in 82–97% yields, independent of the nature of the aryl group (Scheme 2, Table 1). In order to unambiguously confirm the structures of these compounds, an X-ray determination was carried out for compound **17a**. Figure 2 shows a perspective view of the molecule, which has the phenyl ring inclined to the plane of the oxadiazole ring at an angle of 12.6 ^{o}. The geometry of the oxadiazole ring is similar to that previously observed in other 2-amino-1,3,4-oxadiazoles.[14] The molecules pack in infinite sheets governed by intermolecular hydrogen bonds between each of the amino group hydrogens and oxadiazole nitrogens of adjacent molecules.

Conclusions

In summary we have developed the use of di(benzotriazolyl)methanimine **1** for the convenient preparation of previously unknown triazoles **11a,b** and **15a-d** and as a new reagent for the synthesis of oxadiazoles **17a-j**.

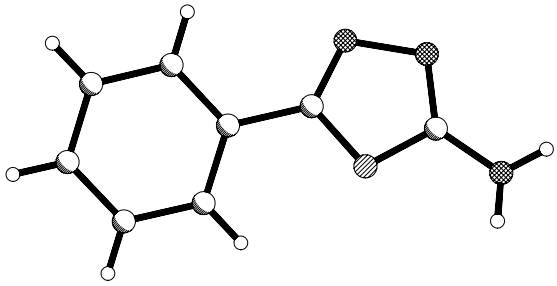


Figure 2. X-Ray structure of compound **17a**.

Experimental Section

General Procedures. Melting points were determined using a capillary melting point apparatus equipped with a digital thermometer and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a 300 MHz NMR spectrometer (300 and 75 MHz respectively) using $CDCl_3$ or DMSO-d_6 as solvents with tetramethylsilane as an internal standard. Tetrahydrofuran (THF) was distilled under nitrogen from sodium/benzophenone immediately before use. Column chromatography was conducted with silica gel grade 230–400 mesh. All other reagents were of reagent grade and were used without purification.

***N'*-[Amino(1*H*-1,2,3-benzotriazol-1-yl)methylidene]-1*H*-1,2,3-benzotriazole-1-carbohydrazonamide (8).** Di(benzotriazol-1yl)methanimine **1** (2g, 7.6 mmol), hydrazine hydrate (191 mg, 3.8 mmol) and THF (30 mL) were stirred at rt for 24 h. The residue obtained after removal of THF was recrystallized from acetone to give 500 mg (41%) of *N'*-[amino(1*H*-benzotriazol-1-yl)methylidene]-1*H*-benzotriazole-1-carbo-hydrazonamide **8**, mp 244–245 °C; ^{1}H NMR δ 7.29 (br. s, 4H), 7.58 (t, *J* = 7.5 Hz, 2H), 7.74 (t, *J* = 7.4 Hz, 2H), 8.22 (d, *J* = 8.2 Hz, 2H), 8.61 (d, *J* = 8.4 Hz, 2H); ^{13}C NMR δ 115.5, 119.6, 125.6, 129.5, 130.8, 145.9, 148.8. Anal. Calcd for $C_{14}H_{12}N_{1014}$: C, 52.50; H, 3.78; N, 43.73. Found: C, 52.56; H, 3.89; N, 43.83.

3-(1*H*-Benzotriazol-1-yl)-1-methyl-1*H*-1,2,4-triazole-5-amine (11a). Compound **1** (1.5 g, 5.7 mmol), methyl hydrazine (150 mg, 3.3 mmol) and THF (50 mL) were stirred at rt for 24 h. The residue obtained after removal of THF was dissolved in DCM and washed with 10% aqueous Na_2CO_3. The organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*

to give 0.35 g (57%) of compound **11a** as pink prisms, mp 240–242 °C (decomp.) ^{1}H NMR (DMSO d_6) δ 3.66 (s, 3H), 6.79 (s, 2H), 7.51 (t, J = 7.8 Hz, 1H), 7.68 (t, J = 7.8 Hz, 1H), 8.16 (d, J = 8.7 Hz, 2H); ^{13}C NMR (DMSO d_6) δ 33.8, 112.8, 119.7, 125.2, 129.1, 131.3, 145.2, 151.7, 156.1. Anal. Calcd for $C_9H_9N_7$: C, 50.23; H, 4.21; N, 45.56. Found: C, 49.84; H, 4.13; N, 45.17.

3-(1*H*-Benzotriazol-1-yl)-1-acetyl-1*H*-1,2,4-triazole-5-amine (11b). Compound **1** (1.50 g, 5.7 mmol) and acetohydrazide (0.22 g, 3.0 mmol) were dissolved in dry benzene (40 mL) and heated under reflux for 48 h. After concentration of the reaction mixture, the crude residue was dissolved in CH_2Cl_2 and washed with 10% aqueous Na_2CO_3. The organic layer was dried (Na_2SO_4), filtered and evaporated to yield pure product **11b** as white flakes 0.29 g (42%), mp 232–234°C (decomp.). ^{1}H NMR (DMSO d_6) 2.49 (s, 3H), 7.61 (t, J = 7.8 Hz, 1H), 7.80 (t, J = 7.8 Hz, 1H), 8.26 (d, J = 8.2 Hz, 1H), 8.45 (d, J = 8.2 Hz, 1H), 8.81 (br, s, 1H), 9.96 (br, s, 1H); ^{13}C NMR (DMSO d_6) 11.7, 115.8, 120.9, 126.9, 131.2, 131.6, 146.9, 151.1, 160.8, 166.1. Anal. Calcd for $C_{10}H_9N_7O$: C, 49.38; H, 3.73; N, 40.31. Found: C, 49.67; H, 3.57; N, 40.54.

1-(4-Methoxyphenyl)-5-((4-methoxyphenyl)diazenyl)-3-(1*H*-benzotriazol-1-yl)-1,2,4-1*H*-triazole (15a). Methoxyphenylhydrazine (4.2 mmol, 0.736 g) was added to a suspension of di(benzotriazolyl)methanimines (3.8 mmol, 1 g) in THF (35 mL). The mixture was allowed to react for 4 days. The precipitate formed was filtered off, washed with cold THF, ethyl ether and dried in vacuum to give 1-(4-methoxyphenyl)-5-((4-methoxyphenyl)diazenyl)-3-(1*H*-benzotriazol-1-yl)-1,2,4-1*H*-triazole **15a** as orange microcrystals in 86% yield, mp 234–235 °C; ^{1}H NMR ($CDCl_3$/TFA) δ 3.93 (s, 3H), 3.96 (s, 3H), 7.01 (d, J = 9.0 Hz, 2H), 7.13 (d, J = 8.9 Hz, 2H), 7.64 (t, J = 7.5 Hz, 1H), 7.76 – 7.81 (m, 3H), 7.92 (d, 9.0 Hz, 2H), 8.19 (d, J = 8.5 Hz, 1H), 8.42 (d, J = 8.5 Hz, 1H); ^{13}C NMR ($CDCl_3$/TFA) δ 55.8, 56.0, 112.6, 114.7, 115.2, 118.9, 126.0, 127.4, 127.5, 128.9, 130.9, 131.4, 143.4, 147.2, 153.4, 157.2, 160.5, 166.0. HRMS (FAB) Calcd for $C_{22}H_{18}N_8O_2$ (M+1): 427.1631. Found: 427.1605.

***N*'-Phenyl-1*H*-1,2,3-benzotriazole-1-carbohydrazonamide (12b).** Imine **1** (1.5 g, 5.7 mmol) and phenylhydrazine (0.87 g, 5.7 mmol) were dissolved in dry THF (40 mL) and heated under reflux overnight. After concentration of the reaction mixture, the crude residue was dissolved in DCM and washed with 10% aqueous Na_2CO_3. The organic layer was dried (Na_2SO_4), filtered and evaporated to yield 1.22g (85%) of compound **12b** as yellow solid; mp 133**–**135°C (decomp.). ^{1}H NMR (DMSO-d_6) δ 5.76 (s, 2H), 6.12 (s, 1H), 6.95 (t, J = 7.3 Hz, 1H), 7.11 (d, J = 7.9 Hz, 2H), 7.30**–**7.35 (m, 2H), 7.48 (t, J = 7.8 Hz, 1H), 7.63 (t, J = 7.8 Hz, 1H), 8.11 (d, J = 8.5 Hz, 1H), 8.51 (d, J = 8.2 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 112.2, 114.2, 118.1, 119.7, 125.3, 129.2, 129.3, 130.4, 138.7, 148.5, 147.3. Anal. Calcd for $C_{13}H_{12}N_6$: C, 61.89; H, 4.79; N, 33.31. Found: C, 61.65; H, 4.67; N, 32.92.

Ethyl2-[(Z)-amino(1*H*-1,2,3-benzotriazol-1-yl)methylidene]-1-hydrazine-carboxylate (16k). Compound **1** (1.5 g, 5.7 mmol) and ethyl carbazate (0.59 g, 5.7 mmol) were dissolved in dry THF (50 mL) and heated under reflux for 6 h. After concentration of the reaction mixture, the crude residue was dissolved in DCM and washed with 10% aqueous Na_2CO_3. The organic layer was dried (Na_2SO_4), filtered and evaporated to yield 1.40g (99%) of compound **16k** as a white solid; mp 163–164°C (decomp.). ^{1}H NMR (DMSO-d_6) δ 1.45 (t, J = 7.0 Hz, 3H), 4.35 (q, J = 7.0

Hz, 2H), 7.42 (s, 2H), 7.79 (t, *J* = 7.7 Hz, 1H), 7.88 (t, *J* = 7.7 Hz, 1H), 8.34 (d, *J* = 8.8 Hz, 1H), 8.62 (d, *J* = 8.2 Hz, 1H), 9.84 (br, s, 1H); ^{13}C NMR (DMSO-d_6) δ 15.6, 61.3, 115.7, 120.3, 126.2, 130.0, 131.4, 142.1, 146.5, 154.9. Anal. Calcd for $C_{10}H_{12}N_6O_2$: C, 48.38; H, 4.87; N, 33.85. Found: C, 48.49; H, 4.84; N, 33.69.

General procedure for the preparation of 1-aryl-5- (aryldiazenyl)-3-1*H*-benzotriazol-1-yl-1,2,4-triazoles 15b-d

The appropriate arylhydrazine (3.8 mmol) was added to a suspension of compound **1** (3.8 mmol, 1 g) in THF (25 mL). The mixture was allowed to react until the disappearance of **1** (TLC control, about 18 h). Then, potassium tert-butoxide (0.43 g, 3.8 mmol) was added into the reaction mixture. After 18 h the solvent was evaporated and the residue was purified by column chromatography ($CHCl_3$ / ethyl ether : 4 / 1) to give compounds **15b-d**.

1-Phenyl-5-(phenyldiazenyl)-3-(1*H*-benzotriazol-1-yl)-1,2,4-1*H*-triazole (15b). Orange microcrystals (82%), mp 218–219 °C; ^{1}H NMR ($CDCl_3$) δ 7.48–7.70 (m, 8H), 7.92 (d, *J* = 8.2 Hz, 2H), 8.06 (d, *J* = 7.7 Hz, 2H), 8.19 (d, *J* = 8.4 Hz, 1H), 8.44 (d, *J* = 8.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 112.9, 120.1, 124.4, 124.7, 125.1, 129.2, 129.2, 129.3, 129.4, 131.5, 134.1, 136.4, 146.0, 152.8, 155.6, 157.3. Anal. Calcd for $C_{20}H_{14}N_8$: C, 65.56; H, 3.85; N, 30.58. Found: C, 65.63; H, 3.68; N, 30.82.

1-(4-Methylphenyl)-5-((4-methylphenyl)diazenyl)-3-(1*H*-benzotriazol-1-yl)-1,2,4-1*H*-triazole (15c). Orange microcrystals (84%), mp 222–224 °C; ^{1}H NMR ($CDCl_3$) δ 2.47 (s, 3H), 2.49 (s, 3H), 7.35 (d, *J* = 8.3 Hz, 2H), 7.40 (d, *J* = 8.2 Hz, 2H), 7.49 (t, *J* = 7.5 Hz, 1H), 7.67 (t, *J* = 7.4 Hz, 1H), 7.79 (d, *J* = 8.4 Hz, 2H), 7.95 (d, *J* = 8.3 Hz, 2H), 8.17 (d, *J* = 8.3 Hz, 1H), 8.43 (d, *J* = 8.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 21.2, 21.8, 113.0, 120.12, 124.5, 124.6, 125.1, 129.2, 129.8, 130.2, 131.6, 134.1, 139.5, 145.5, 146.1, 151.2, 155.5, 157.5. Anal. Calcd for $C_{22}H_{18}N_8$: C, 66.99; H, 4.60. Found: C, 66.95; H, 4.69.

1-(4-Bromophenyl)-5-((4-bromophenyl)diazenyl)-3-(1*H*-benzotriazol-1-yl)-1,2,4-1*H*-triazole (15d). Orange microcrystals (78%), mp 238–239 °C; ^{1}H NMR ($CDCl_3$) δ 7.51 (t, *J* = 7.5 Hz, 1H), δ 7.66–7.83 (m, 7H), 7.92 (d, *J* = 8.6 Hz, 2H), 8.19 (d, *J* = 8.3 Hz, 1H), 8.41 (d, *J* = 8.3 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 112.8, 120.3, 123.6, 125.3, 125.6, 126.1, 129.4, 129.6, 131.4, 132.5, 133.0, 135.3, 146.1, 151.5, 155.8, 157.2. Anal. Calcd for $C_{20}H_{12}Br_2N_8$: C, 45.83; H, 2.31; N, 21.38. Found: C, 45.95; H, 2.11; N, 21.16.

General procedure for the preparation of 5-aryl-1,3,4-oxadiazol-5-amines 17a-j

Di(benzotriazolyl)methanimine (1.00 g, 3.8 mmol) and the appropriate arylhydrazide (3.8 mmol) were dissolved in dry THF (40 mL) and heated under reflux for 3–6 h. The precipitate formed after cooling of the reaction mixture to rt was filtered off, washed with cold THF and recrystallized from EtOH or THF (compound **17j**) to give the respective 5-aryl-1,3,4-oxadiazol-5-amine **17a-j**. Data for compound **17a** see.[2]

5-[4-(*tert*-Butyl)phenyl]-1,3,4-oxadiazol-2-ylamine (17b). White needles (92%), mp 256–258 °C; ^{1}H NMR (DMSO-d_6) δ 1.29 (s, 9H), 7.22 (s, 2H), 7.54 (d, *J* = 8.5 Hz, 2H), 7.72 (d, *J* = 8.4 Hz,

2H); ^{13}C NMR (DMSO-d_6) δ 31.0, 34.8, 121.9, 125.1, 126.2, 153.3, 157.5, 163.9. Anal. Calcd for $C_{12}H_{15}N_3O$: C, 66.34; H, 6.96; N, 19.34. Found: C, 66.46; H, 7.36; N, 19.33.

5-(4-Aminophenyl)-1,3,4-oxadiazol-2-amine (17c). White prisms (82%), mp 254–255 °C (lit. [6] 273–274 °C); ^{1}H NMR (DMSO-d_6) δ 5.73 (s, 2H), 6.66 (d, J = 8.5 Hz, 2H), 7.01 (s, 2H), 7.48 (d, J = 8.5 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 11.5, 113.8, 126.7, 151.1, 158.4, 163.0. Anal. Calcd for $C_8H_8N_4O$: C, 54.54; H, 4.58; N, 31.80. Found: C, 54.36; H, 4.40; N, 31.67.

5-(2-Aminophenyl)-1,3,4-oxadiazol-2-amine (17d). White microcrystals (92%), mp 184–186 °C; ^{1}H NMR (DMSO-d_6) δ 6.58 (s, 2H), 6.64 (t, J = 7.5 Hz, 1H), 6.85 (d, J = 8.2 Hz, 1H), 7.17 (t, J = 7.3 Hz, 1H), 7.22 (s, 2H), 7.45 (d, J = 8.0 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 105.5, 115.5, 115.6, 126.2, 130.9, 146.8, 158.1, 162.5. Anal. Calcd for $C_8H_8N_4O$: C, 54.54; H, 4.58; N, 31.80. Found: C, 54.88; H, 4.61; N, 31.78.

4-(5-Amino-1,3,4-oxadiazol-2-yl)phenol (17e). White needles (93%), mp 276–278 °C (lit. [7] 274–276 °C); ^{1}H NMR (DMSO-d_6) δ 6.90 (d, J = 8.5 Hz, 2H), 7.11 (s, 2H), 7.63 (d, J = 8.5 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 116.3, 116.9, 127.8, 158.5, 160.3, 164.2. Anal. Calcd for $C_8H_7N_3O_2$: C, 54.24; H, 3.98; N, 23.72. Found: C, 53.96; H, 3.84; N, 23.56.

5-(4-Nitrophenyl)-1,3,4-oxadiazol-2-amine (17f). Yellow needles (97%), mp 255–257 °C (lit.[8] 270 °C); ^{1}H NMR (DMSO-d_6) δ 7.57 (s, 2H), 8.03 (d, J = 8.8 Hz, 2H), 8.37 (d, J = 8.8 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 124.8, 126.1, 130.0, 148.1, 156.2, 164.8. Anal. Calcd for $C_8H_6N_4O_3$: C, 46.61; H, 2.93; N, 27.18. Found: C, 46.52; H, 2.63; N, 27.00.

5-(3-Nitrophenyl)-1,3,4-oxadiazol-2-amine (17g). Yellow needles (96%), mp 251–253 °C (lit.[8] 262 °C); ^{1}H NMR (DMSO-d_6) δ 7.47 (s, 2H), 7.83 (t, J = 7.9 Hz, 1H), 8.20 (d, J = 7.1 Hz, 1H), 8.33 (d, J = 7.8 Hz, 1H), 8.46 (s, 1H); ^{13}C NMR (DMSO-d_6) δ 119.5, 124.8, 125.9, 131.1, 131.3, 148.4, 155.9, 164.5. Anal. Calcd for $C_8H_6N_4O_3$: C, 46.61; H, 2.93; N, 27.18. Found: C, 46.43; H, 2.56; N, 26.95.

5-(4-Chlorophenyl)-1,3,4-oxadiazol-2-amine (17h). White microcrystals (96%), mp 231–233 °C (lit.[8] 274 °C); ^{1}H NMR (DMSO-d_6) δ 7.36 (s, 2H), 7.61 (d, J = 8.5 Hz, 2H), 7.81 (d, J = 8.5 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 123.4, 126.9, 129.5, 135.0, 156.7, 164.2. Anal. Calcd for $C_8H_6ClN_3O$: C, 49.12; H, 3.09; N, 21.48. Found: C, 49.16; H, 2.83; N, 21.47.

5-(2-Chlorophenyl)-1,3,4-oxadiazol-2-amine (17i). Yellow needles (95%), mp 164–166 °C (lit.[9] 166 °C); ^{1}H NMR (DMSO-d_6) δ 7.34 (s, 2H), 7.47–7.56 (m, 2H), 7.63 (d, J = 7.7 Hz, 1H), 7.81 (d, J = 7.0 Hz, 1H); ^{13}C NMR (DMSO-d_6) δ 123.6, 127.8, 130.4, 131.08, 131.11, 132.0, 155.4, 164.3. Anal. Calcd for $C_8H_6ClN_3O$: C, 49.12; H, 3.09; N, 21.48. Found: C, 48.87; H, 2.73; N, 21.24.

5-(4-Pyridinyl)-1,3,4-oxadiazol-2-amine (17j). White needles (97%), mp 232–234 °C (THF) (lit.[10] 262 °C); ^{1}H NMR (DMSO-d_6) δ 7.57 (s, 2H), 7.72 (d, J = 4.7 Hz, 2H), 8.74 (d, J = 4.7 Hz, 2H); ^{13}C NMR (DMSO-d_6) δ 119.6, 132.0, 151.6, 156.6, 165.4. Anal. Calcd for $C_7H_6N_4O$: C, 51.85; H, 3.73; N, 34.55. Found: C, 51.51; H, 3.49; N, 34.40.

X-ray crystallography

Data were collected with a Siemens SMART CCD area detector, using graphite monochromatized MoKα radiation (λ = 0.71073 Å). The structures were solved by direct methods using SHELXS[15] and refined on F^2, using all data, by full-matrix least-squares procedures using SHELXL.[16] Hydrogen atoms were included in calculated positions, with isotropic displacement parameters 1.2 times the isotropic equivalent of their carrier atoms.

Crystal data for 15b. $C_{20}H_{14}N_8$, MW 366.39, monoclinic, $P2_1/n$, a = 12.686(3), b = 8.366(2), c = 17.310(5) Å, β = 108.152(3) °, V = 1745.8(8) Å ^{3}, Z = 4, T = -105 °C, F(000) = 760, μ (MoKα) = 0.091 mm^{-1}, D_{calcd} = 1.394 $g.cm^{-3}$, $2\theta_{max}$ 53° (CCD area detector, 98% completeness), $wR(F^2)$ = 0.0922 (all 3537 data), R = 0.0346 (3031 data with I > 2σI).

Crystal data for 17a. $C_8H_7N_3O$, MW 161.17, monoclinic, $P2_1/n$, a = 11.290(6), b = 5.983(3), c = 11.654(6) Å, β = 98.892(7) °, V = 777.6(7) Å ^{3}, Z = 4, T = -100 °C, F(000) = 336, μ (MoKα) = 0.097 mm^{-1}, D_{calcd} = 1.377 $g.cm^{-3}$, $2\theta_{max}$ 53° (CCD area detector, 97% completeness), $wR(F^2)$ = 0.1320 (all 1563 data), R = 0.0461 (1270 data with I > 2σI).

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