Tandem Michael Addition/Imino-Nitrile Cyclization Synthesis of 2-Amino-6-(1-aryl-5-methyl-1*H*-1,2,3-triazol-4yl)-4-phenylpyridine-3-carbonitrile

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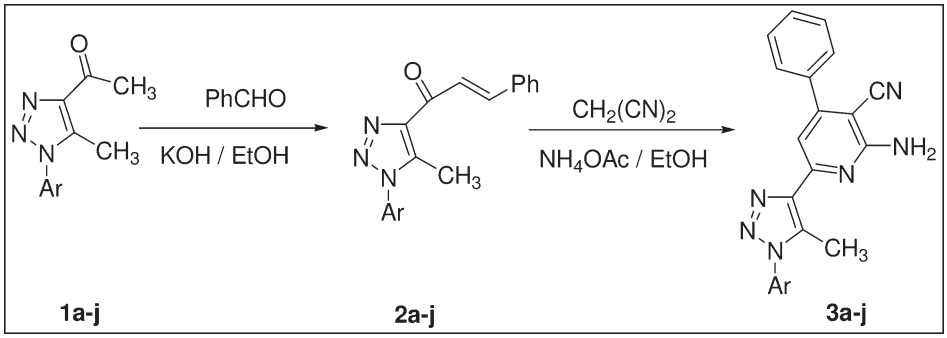

Several 2–amino-6-(1-aryl-5-methyl-1*H*-1,2,3-triazol-4-yl)-4-phenylpyridine-3-carbonitrile have been synthesized by Tandem Michael addition/imino-nitrile cyclization and the structures of these compounds were established by MS, IR, CHN, and ^{1}H NMR spectral data. The crystal structure of 2-amino-6-[1-(4-methoxyphenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl]-4-phenylpyridine-3-carbonitrile was established by X-ray diffraction.

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INTRODUCTION

The pyridine ring is one of the most well-known systems among the naturally occurring heterocycles [1]. Pyridine and fused pyridine moieties was shown in numerous natural products such as quinoline and isoquinoline alkaloids [2], and nicotine and its analogs [3], 2-aminopyridines are promising substituted pyridines which have been shown to be biologically active molecules [4]. Additionally, because of their chelating abilities, 2-aminopyridines are commonly used as ligands in inorganic and organometallic chemistry [5]. If substituted with optically active groups, they could potentially serve for chiral auxiliaries or chiral ligands in asymmetric reactions. For this reaction, 2-aminopyridine derivatives are valuable synthetic target compounds. The synthesis of 2-aminopyridine derivatives has been extensively reviewed [4–10]. In addition there have been some reports concerning biological interest for 1,2,3-triazole nucleus have been reported as antibacterial [11], antifungal [12], antiviral [13], anti-inflammatory and analgesic [14] and 1,2,3-triazole derivatives have been synthesized to inhibit tumor proliferation, invasion, and metastasis [15]. However, there is a little data describing compounds containing the two heterocyclic moieties, thiazoline and 1,2,3-triazole. Interest in this class of compounds prompted the synthesis, several new 2-amino-6-(1-aryl-5-methyl-1*H*-1,2,3-triazol-4-yl)-4-phenylpyridine-3-carbonitrile have been synthesized by Tandem Michael addition/amino-nitrile cyclization.

RESULTS AND DISCUSSION

The some new 2-amino-6-(1-aryl-5-methyl-1*H*-1,2,3-triazol-4yl)-4-phenylpyridine-3-carbonitrile (**3a–j**) have been synthesized by Tandem Michael addition/imino-nitrile cyclization [16] with (*E*)-1-(1-aryl-5-methyl-1*H*-1,2,3-triazol-4-yl)-3-phenylprop-2-en-1-one from 1-(1-aryl-5-methyl-1*H*-1,2,3-triazol-4-yl)-ethanone derivatives (Scheme 1).

Our own interest in the development of new 2–amino-6-(1-aryl-5-methyl-1*H*-1,2,3-triazol-4-yl)-4-phenylpyridine-3-carbonitrile derivatives and in extending this type of tandem reaction prompted us to examine potential applications and generalizations to the synthesis of substituted pyridine. The reactivity of (*E*)-1-(1-aryl-5-methyl-1*H*-1,2,3-triazol-4-yl)-3-phenylprop-2-en-1-one would be regarded particularly closely during the cyclization step to shed further light on the course of this short transformation and, also, to gain further insight into the mechanistic aspects of this tandem reaction.

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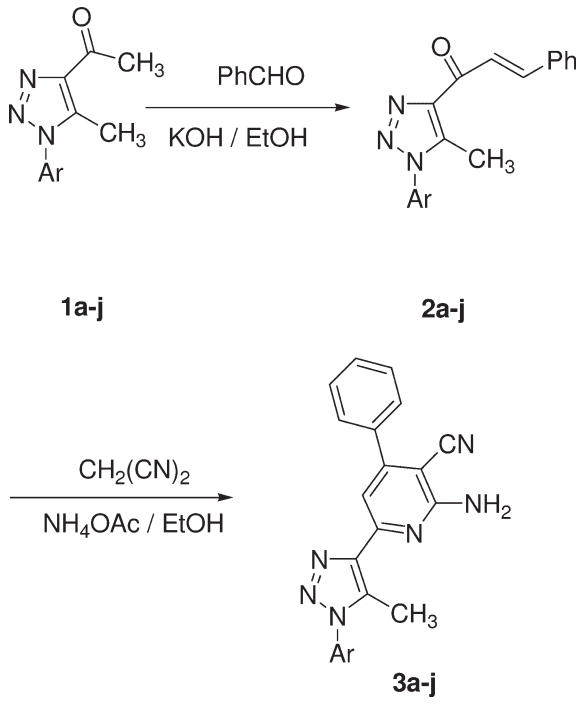
Scheme 1



1a-j **2a-j** **3a-j**

2a, 3a Ar=4-$CH_3C_6H_4$-; **2b, 3b** Ar=Ph; **2c, 3c** Ar=4-ClC_6H_4-; **2d, 3d** Ar=2,5-diClC_6H_3-; **2e, 3e** Ar=3-ClC_6H_4-; **2f, 3f** Ar=2-ClC_6H_4-; **2g, 3g** Ar=4-BrC_6H_4-; **2h, 3h** Ar=β-$C_{10}H_7$-; **2i, 3i** Ar=3-BrC_6H_4-; **2j, 3j** Ar=4-$MeOC_6H_4$-

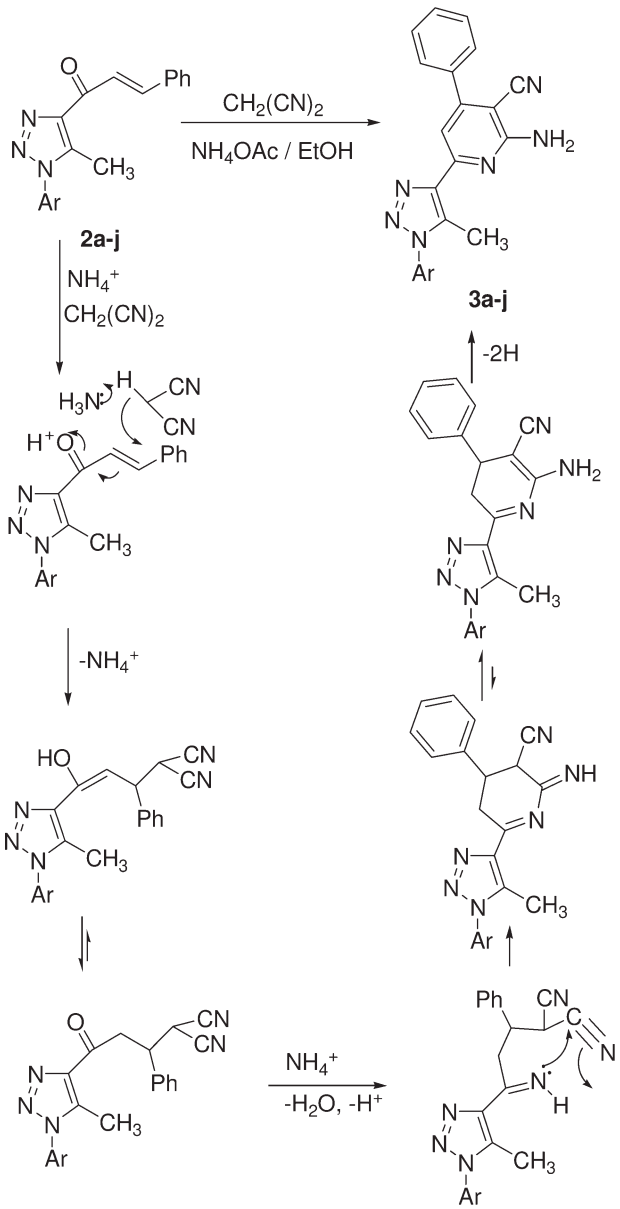
Identified as a cyano compound showing IR absorption at 2207–2213 cm^{-1} and amino at 3436–3494, 3353–3374 cm^{-1} of **3a–j**, as a carbonyl compound showing strong IR absorption at 1679–1683 cm^{-1} of **1a–j** and 1659–1666 cm^{-1} of **2a–j**. ^{1}H NMR —CO—CH_3 peak at 2.694–2.778 ppm of **1a–j** and showing  ^{1}H NMR dual peak 8.057–8.173 ppm, 7.809–8.076 ppm, J = 15.6–15.9 Hz of **2a–j** but it is disappearance in compounds **3a–j** (Scheme 2).

Compound 2-amino-6-[1-(4-methoxyphenyl)-5-methyl-1*H*-1,2,3-triazol-4-yl]-4-phenylpyridine-3-carbonitrile. This consists of a substituted triazolyl ring and a phenyl ring is not planar (torsion angles is shown for dihedral angle of $C_{triazolyl}$—$N_{triazolyl}$—C_{phenyl}—C_{phenyl} is 48.6(4)° by the hindering of triazole ring C9—CH_3 and benzene ring C2—H or C6—H, and so dihedral angle of $C_{pyridyl}$—$C_{pyridyl}$—C_{phenyl}—C_{phenyl} is 38.3(4)° in stable conformation of the crystal). The substituted triazolyl ring and substituted pyridyl ring is an approximation planar (torsion angles is shown for dihedral angle of $N_{triazolyl}$—$C_{triazolyl}$—$C_{pyridyl}$—$N_{pyridyl}$ is 176.5(3)°) by the π–π conjugation of triazole ring π bond and pyridine ring π bond, C10—C11 bond 1.475 Å is shorter than nonconjugation Csp^2-Csp^2 bond C13—C17 1.484 Å (Fig. 1; Table 1).

On pyridine ring, the p-π conjugation was indicated between amino N5 and ring C15, N5—C15 length is 1.343(4) Å, C15—N5—H, H—N5—H angle is 120°, dihedral angle of C11—N4—C15—N5 is 179.4°, dihedral angle of N5—C15—C14—C13 is 178.2°, N5 is came under the action of sp^2 hybridized.

On pyridine ring, 2-amino has two N—H bond and two intermolecular hydrogen bonds as the superamolecular structure in the crystal. The intermolecular O′1···H5A-N5 hydrogen-bond between the O1 atoms of the CH_3O group and N5—H, intermolecular N′6···H5A—N5 hydrogen bond between the N atoms of the CN group and N5—H was given (Fig. 2; Table 2). The orderly range of the structure forms stratification polymer in the crystal. The intermolecular hydrogen bond connects the translated molecules into an infinite chain on a layer.

Scheme 2



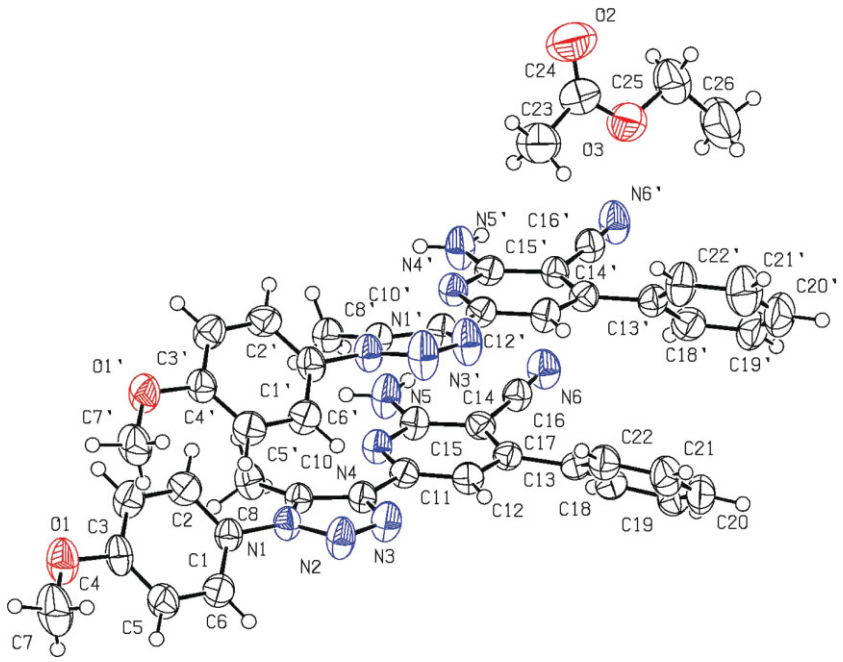


Figure 1. A *PLATON* (Spek, 2001) view of the molecular structure of (*I*), the asymmetric unit showing 50% probability displacement ellipsoids. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

EXPERIMENTAL

All melting points were determined on an XT4-100× microscopic melting point apparatus and are uncorrected. Mass spectrum was performed on a ESQ6K esquire6000 spectrometer (**3a–j**) and HP-5988A (**2a–j**) spectrometer (EI at 70 eV). IR spectra were obtained in KBr discus using a Nicolet NEXUS 670 FTIR spectrometer. ^{1}H NMR spectroscopy ($CDCl_3$) was recorded on Avance Mercury plus-300 with TMS as an internal standard. Elemental analyses were carried out on a Yanaco CHN Corder MT-3 analyzer.

General procedure for the preparation of 1-(1-aryl-5-methyl-1*H*-1,2,3-triazol-4-yl)-ethanone derivatives (1a–j). 1-(1-Aryl-5-methyl-1*H*-1,2,3-triazol-4-yl)-ethanone **1a–j** was prepared following condensation methods of 1-azido-4-methylbenzene [17] with pentane-2,4-dione. A cold solution of sodium methanolate (0.23 mol, in 120 mL absolute methanol) was added to the mixture of pentane-2,4-dione (17 mL, 0.165 mol) and 1-azido-4-methylbenzene (about 0.15 mol) and stirred for 1 h at 0–5°C. Then the mixture was heated under reflux on an oil-bath for 10 h. Finally the mixture was neutralized with concentrated hydrochloric acid. 1-(1-Aryl-5-methyl-1*H*-1,2,3-triazol-4-yl)ethanone **1a–j** was separated and crystallized from methanol.

1-(5-Methyl-1-p-tolyl-1H-1,2,3-triazol-4-yl) ethanone (1a). Yield: 52.6%; buff crystals; mp: 105–107°C (Lit 106–107°C); ^{1}H NMR: 7.360–7.384(d, 2H, J = 7.2 Hz, Ar-2,6), 7.306–7.333(d, 2H, J = 8.1 Hz, Ar-3,5), 2.757(s, 3H, CH_3CO), 2.573(s, 3H, TRZ-CH_3), 2.468(s, 3H, Ar—CH_3); MS: 215(M^+,19); CA 194478-14-3 [17].

1-(5-Methyl-1-phenyl-1H-1,2,3-triazol-4-yl)ethanone (1b). Yield: 58.5%; buff crystals; mp: 99–100°C (Lit 108°C); ^{1}H NMR: 7.552–7.578(m, 3H, J = 7.8 Hz, Ar-3,4,5), 7.408–7.432(m, 2H, J = 7.2 Hz, Ar-2,6), 2.729(s, 3H, CH_3CO), 2,571(s, 3H, TRZ-CH_3); MS: 201(M^+, 13) CA 51118-32-2 [18].

1-[1-(4-Chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]ethanone (1c). Yield: 53.2%; white crystals; mp: 108–110°C (Lit 119°C); ^{1}H NMR: 7.546–7.564(d, 2H, J = 5.4 Hz, Ar-2, 6), 7.399–7.429(d, 2H, J = 9.0 Hz, Ar-3,5), 2.757(s, 3H, CH_3CO), 2.599(s, 3H, TRZ-CH_3); MS: 235(M^+, 4). Found: C, 56.47; H, 4.42; N, 17.57 CA 33821-38-4 [18].

Table 1

Selected geometric parameters (Å, °).

Atom-atom	Bond (Å, °)	Atom-atom	Bond (Å, °)
C10—C11	1.475 (4)	C15—N5	1.343 (4)
C13—C17	1.484 (4)		
C15—N5—H5A	120.0	H5A—N5—H5B	120.0
C15—N5—H5B	120.0		
N3—C10—C11—N4	−176.5 (3)	C2—C1—N1—C9	−48.6 (4)
C13—C14—C15—N5	−178.2 (3)	N5—C15—N4—C11	−179.4 (3)
C12—C13—C17—C22	−38.3 (4)		

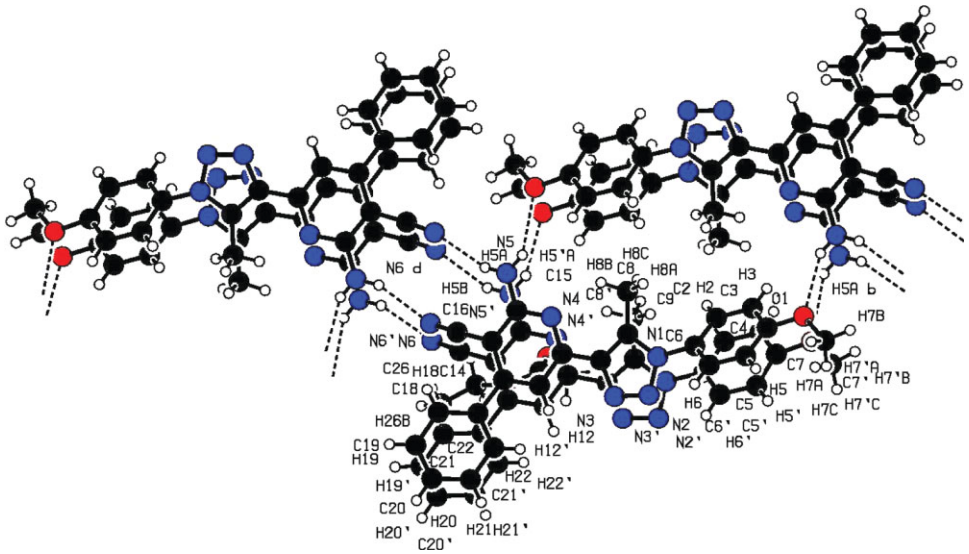


Figure 2. A *PLATON* (Spek, 2001) view of the hydrogen-bonded motif of the superamolecular structure. Hydrogen bonds are shown as dashed lines (Symmetry codes: (i) −x + 1, −y + 1, −z; (ii) −x, −y, −z). [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

1-[1-(2,5-Dichlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl] ethanone (1d). Yield: 54.9%; white crystals; mp: 100–102°C; IR: 3458, 3356, 3098(—CH_3), 1895, 1682(C=O), 1557, 1487(Ar), 1395, 1360, 1280, 1231, 1092, 955(N—N=N), 877, 810(Ar—H), 680; ^{1}H NMR: 7.534–7.545(d, 2H, J = 3.3 Hz, Ar-3,4), 7.448(s, 1H, Ar-6), 2.735(s, 3H, CH_3CO), 2.451(s, 3H, TRZ-CH_3); MS: 269(M+, 3), 241(1), 226(4), 199(11), 186(3), 172(3), 145(9), 109(14), 74(10), 43(100); Anal. Calcd. for $C_{11}H_9Cl_2N_3O$: C, 48.91; H, 3.36; N, 15.56; Found: C, 48.67; H, 3.21; N, 15.86 CA 668471-36-1.

1-[1-(3-Chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]ethanone (1e). Yield: 57.5%; white crystals; mp: 78–80°C; IR: 3422, 3334, 3061(—CH_3), 1896, 1679(C=O), 1554, 1489(Ar), 1436, 1413, 1370, 1290, 1240, 1084, 955(N—N=N), 869, 792(Ar-H), 683; ^{1}H NMR: 7.503–7.528(m, 3H, J = 7.5 Hz, Ar-4,5,6), 7.325–7.354(s, 1H, J = 8.7 Hz, Ar-2), 2.733(s, 3H, CH_3CO), 2.598(s, 3H, TRZ-CH_3); MS: 235(M+,3), 207(1), 192(4), 178(1), 164(16), 130(3), 111(20), 75(33), 65(1), 43(100); Anal. Calcd. for $C_{11}H_{10}ClN_3O$: C, 56.06; H, 4.28; N, 17.83; Found: C, 56.53; H, 4.33; N, 17.67 CA 1017399-61-9.

1-[1-(2-Chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]ethanone (1f). Yield: 58.5%; buff crystals; mp: 92–94°C; IR: 3441, 3344, 3069(—CH_3), 1936, 1681(C=O), 1552, 1489(Ar), 1420, 1365, 1282, 1216, 1080, 951(N—N=N), 764(Ar-H), 654; ^{1}H NMR: 7.374–7.606(m, 4H, Ar-3,4,5,6), 2.753(s, 3H, CH_3CO), 2.428(s, 3H, TRZ-CH_3); MS: 235(M+,9), 207(2), 192(15), 178(2), 164(35), 130(5), 111(32), 75(49), 65(1), 43(100); Anal. Calcd. for $C_{11}H_{10}ClN_3O$: C, 56.06; H, 4.28; N, 17.83; Found: C, 56.47; H, 4.39; N, 17.57 CA 1017471-30-5.

1-[1-(4-Bromophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]ethanone (1g). Yield: 64.2%; yellow crystals; mp: 108–110°C (Lit 120°C); ^{1}H NMR: 7,720–7.751(d, 2H, J = 9.3 Hz, Ar-2,6), 7.364–7.396(d, 2H, J = 9.6 Hz, Ar-3,5), 2.739(s, 3H, CH_3CO), 2.601(s, 3H, TRZ-CH_3); MS: 279(M+,3). Found: C, 47.46; H, 3.24; N, 15.31 CA 33722-11-1 [18].

1-[5-Menthyl-1-(naphthalene-2-yl)-1H-1,2,3-triazol-4-yl] ethanone (1h). Yield: 73.8%; buff crystals; mp: 146–148°C; IR: 3429, 3346, 3057(—CH_3), 1927, 1681(C=O), 1598, 1557(Ar), 1420, 1363, 1272, 1215, 1079, 951(N—N=N), 865, 826(Ar-H), 755; ^{1}H NMR: 7.896–8.038(m, 4H, Ar-1,4,5,8), 7.501–7.624(m, 3H, Ar-3,6,7), 2.778(s, 3H, CH_3CO), 2.642(s, 3H, TRZ-CH_3); MS: 251(M^+, 17), 222(3), 208(9), 194(3), 180(61), 153(14), 127(63), 101(12), 77(22), 63(10), 51(13), 43(100); Anal. Calcd. for $C_{15}H_{13}N_2O$: C, 71.70; H, 5.21; N, 16.72; Found: C, 71.57; H, 5.45; N, 16.56.

1-[1-(3-Bromophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]ethanone (1i). Yield:59.8%; white crystals; mp: 102–104°C; IR: 3444, 3348, 3073(—CH_3), 1683(C=O), 1554, 1494(Ar), 1420, 1365, 1282, 1219, 1066, 1029, 952(N—N=N), 765(Ar-H), 671; ^{1}H NMR: 7.790(s, 1H, Ar-2), 7.505–7.528(m, 3H,Ar-4,5,6), 2.728(s, 3H, CH_3CO), 2.452(s, 3H, TRZ-CH_3); MS: 279(M+, 5), 251(1), 236(7), 211(13), 196(4), 182(3), 157(18), 144(7), 102(8), 75(25), 63(9), 50(22), 43(100); Anal. Calcd. for $C_{11}H_{10}BrN_3O$: C, 47.16; H, 3.60; N, 15.00; Found: C, 47.36; H, 3.19; N, 15.13.

1-[1-(4-Menthoxyphenyl)-5-methyl-1H-1,2,3-triazol-4-yl] ethanone (1j). Yield: 58.4%; buff crystals; mp: 117–119°C (Lit 120°C); ^{1}H NMR: 7.299–7.329(d, 2H, J = 9.0 Hz, Ar-2,6), 7.012–7.032(d, 2H, J = 6.0 Hz, Ar-3,5), 3.837(s, 3H,

Table 2

Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N5′—H5′A···O1[a]	0.86	2.25	3.023 (5)	150
N5′—H5′B···N6[b]	0.86	2.30	3.119 (5)	159
N5—H5A···O1′[a]	0.86	2.42	3.200 (4)	151
N5—H5B···N6′[b]	0.86	2.22	3.039 (5)	160

Symmetry codes:
[a] −x + 1, −y + 1, −z.
[b] −x, −y, −z.

CH_3O), 2.694(s, 3H, CH_3CO), 2.501(s, 3H, TRZ-CH_3); MS: 231(M+, 13) CA 1017399-41-5 [18].

General procedure for the preparation of (*E*)-1-(1-aryl-5-methyl-1*H*-1,2,3-triazol-4-yl)-3-phenylprop-2-en-1-one derivatives (2a–j) [19]. A mixture of the aromatic aldehyde (12 mmol) and compound **1a–j** (10mmol) dissolved in ethanol (70 mL) was added slowly to an aqueous solution of potassium hydroxide (12.8 mmol) in water (10 mL). The reaction mixture was stirred in crushed-ice bath for 2 h, stirred at 20–25°C for 4 h. The mixture was filtrated and the solid was washed with cold water and cold alcohol. The product was crystallized from ethanol to give **2a–j.** All products were new compounds.

(E)-1-(5-Methyl-1-p-tolyl-1H-1,2,3-triazol-4-yl)-3-phenylprop-2-en-1-one (2a). Yield: 92.5%; white crystals; mp: 178–180°C; IR:1664(C=O), 1611(C=C), 1034, 1074, 1110, 997, 979(N—N=N), 899, 855, 838(Ar-H), 815, 789, 684(Ar-H); ^{1}H NMR: 8.080–8.132 (d, 1H, J = 15.6 Hz, CH=C—CO), 7.809–7.862(d, 1H, J = 15.6 Hz, C=CH—CO), 7.721–7.434(m, 2H, Ph-3,5), 7.417–7.434(m, 3H, Ph-2,4,6), 7.376–7.405(d, 2H, J = 8.7 Hz, Ar-2,6), 7.339–7.368(d, 2H, J = 8.7 Hz, Ar-3,5), 2.666(s, 3H, TRZ-CH_3), 2.479(s, 3H, CH_3); MS: 303(M^+, 5), 274(3), 260(3), 247(31), 194(36), 144(13), 132(98), 115(34), 103(65), 91(100), 77(63.3), 65(78.6), 51(35.3), 39(31.5); Anal. Calcd. for $C_{19}H_{17}N_3O$: C, 75.23; H, 5.65; N, 13.85; Found: C, 75.53; H, 5.43; N, 13.76.

(E)-1-(5-Methyl-1-phenyl-1H-1,2,3-triazol-4-yl)-3-phenylprop-2-en-1-one (2b). Yield: 95.2%; white crystals; mp: 123–125°C; IR: 1664(C=O), 1602(C=C), 1554, 1499, 1420, 1276, 1113, 1035, 980 (N—N=N), 765(Ar-H), 687; ^{1}H NMR: 8.101–8.154(d, 1H, J = 15.9 Hz, CH=C—CO), 7.907–7.960(d, 1H, J = 15.9 Hz, C=CH—CO), 7.726–7.757(m, 2H, Ph-2,6), 7.575–7.610(m, 3H, Ar-3,4,5), 7.476–7.509(m, 2H, Ar-2,6), 7.421–7.438(m, 3H, Ph-3,4,5), 2.691(s, 3H, TRZ-CH_3); MS: 289(M^+, 12), 260(4), 233(24), 180(24), 131(31), 118(59), 103(36), 77(100), 65(5), 51(44), 39(9); Anal. Calcd. for $C_{18}H_{15}N_3O$: C, 74.72; H, 5.23; N, 14.52; Found: C, 74.89; H, 5.34; N, 14.15.

(E)-1-[1-(4-Chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]-3-phenylprop-2-en-1-one (2c). Yield: 91.1%; white crystals; mp: 171–173°C; IR: 1665(C=O), 1601(C=C), 1552, 1498, 1427, 1276, 1092, 1032, 990(N—N=N), 844, 776(Ar-H), 733, 690; ^{1}H NMR: 8.074–8.126 (d, 1H, J = 15.6 Hz, CH=C—CO), 7.904–7.956 (d, 1H, J = 15.6 Hz, C=CH—CO), 7.718–7.749 (m, 2H, Ph-2,6), 7.565–7.595 (d, 2H, J = 9.0 Hz, Ar-2,6), 7.456–7.474 (m, 2H, Ar-3,5), 7.419–7.442 (m, 3H, Ph-3,4,5), 2.687(s, 3H, TRZ-CH_3); MS: 323(M^+, 21), 294(3), 267(70), 214(47), 152(66), 131(100), 111(62), 103(59), 77(58), 51(28), 39(9); Anal. Calcd. for $C_{18}H_{14}ClN_3O$: C, 66.77; H, 4.36; N, 12.98; Found: C, 66.34; H, 4.65; N, 12.79.

(E)-1-[1-(2,5-Dichlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]-3-phenylprop-2-en-1-one (2d). Yield: 92.9%; white crystals; mp: 163–165°C; IR: 1659(C=O), 1600(C=C), 1552, 1486, 1448, 1396, 1357, 1282, 1201, 1096, 1032, 984(N—N=N), 815(Ar-H), 682; ^{1}H NMR: 8.075–8.128 (d, 1H, J = 15.9 Hz, CH=C—CO), 7.921–7.974 (d, 1H, J = 15.9 Hz, C=CH—CO), 7.718–7.749 (m, 2H, Ph-2,6), 7.595(s, 1H, Ar-6), 7.554–7.567 (m, 2H, Ph-3,5), 7.493–7.497 (m, 1H, Ph-4), 7.417–7.446 (m, 2H, Ar-3,4), 2.562(s, 3H, TRZ-CH_3); MS: 357(M^+, 6), 328(2), 301(11), 248(28), 186(100), 145(45), 131(58), 115(40), 103(82), 77(79), 51(36), 39(20); Anal. Calcd. for $C_{18}H_{13}Cl_2N_3O$: C, 60.35; H, 3.66; N, 11.73; Found: C, 60.54; H, 3.54; N, 11.63.

(E)-1-[1-(3-Chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]-3-phenylprop-2-en-1-one (2e). Yield: 91.1%; white crystals; mp: 128–130°C; IR: 1663(C=O), 1612(C=C), 1555, 1489, 1447, 1404, 1306, 1281, 1079, 987(N—N=N), 839(Ar-H), 680; ^{1}H NMR: 8.078–8.131 (d, 1H, J = 15.9 Hz, CH=C—CO), 7.910–7.963 (d, 1H, J = 15.9 Hz, C=CH—CO), 7.725–7.757 (m, 2H, Ph-2,6), 7.538–7.566 (m, 3H, Ar-4,5,6), 7.414–7.446 (m, 4H, Ar-2 and Ph-3,4,5), 2.716(s, 3H, TRZ-CH_3); MS: 323(M^+, 9), 294(3), 267(18), 214(34), 152(100), 131(57), 111(83), 103(67), 77(55), 51(29), 39(14); Anal. Calcd. for $C_{18}H_{14}ClN_3O$: C, 66.77; H, 4.36; N, 12.98; Found: C, 66.29; H, 4.39; N, 12.76.

(E)-1-[1-(2-Chlorophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]-3-phenylprop-2-en-1-one (2f). Yield: 91.2%; white crystals; mp: 116–118°C; IR: 1669(C=O), 1608(C=C), 1553, 1493, 1447, 1393, 1360, 1278, 1200, 1070, 1033, 988(N—N=N), 770; ^{1}H NMR: 8.103–8.156(d, 1H, J = 15.9 Hz, CH=C-CO), 7.925–7.978 (d, 1H, J = 15.9 Hz, C=CH—CO), 7.735–7.751 (m, 2H, Ph-2,6), 7.429–7.640 (m, 7H, Ar-3,4,5,6 and Ph-3,4,5), 2.554(s, 3H, TRZ-CH_3); MS: 323(M^+,1), 294(3), 267(20), 214(33), 152(100), 131(34), 111(73), 103(65), 77(71), 51(49), 39(24); Anal. Calcd. for $C_{18}H_{14}ClN_3O$: C, 66.77; H, 4.36; N, 12.98; Found: C, 66.47; H, 4.56; N, 12.81.

(E)-1-[1-(4-Bromophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]-3-phenylprop-2-en-1-one (2g). Yield: 185–187%; white crystals; mp: 185–187°C; IR: 1662(C=O), 1599(C=C), 1551, 1494, 1443, 1402, 1361, 1275, 1196, 1066, 1031, 987(N—N=N), 838(Ar-H), 687; ^{1}H NMR: 8.057–8.110(d, 1H, J = 15.9 Hz, CH=C—CO) 7.890–7.943 (d, 1H, J = 15.9 Hz, C=CH—CO), 7.708–7.735 (m, 4H, Ar-2,3,5,6), 7.388–7.415 (m, 5H, Ph-2,3,4,5,6), 2.667(s, 3H, TRZ-CH_3); MS: 367(M^+,3), 311(16), 260(24), 217(8), 196(68), 155(56), 131(94), 115(43), 103(100), 77(89), 51(50), 39(25); Anal. Calcd. for $C_{18}H_{14}BrN_3O$: C, 58.71; H, 3.83; N, 11.41; Found: C, 58.47; H, 3.77; N, 11.71.

(E)-1-[5-Methyl-1-(naphthalene-2-yl)-1H-1,2,3-triazol-4-yl]-3-phenylprop-2-en-1-one (2h). Yield: 97.7%; white crystals; mp: 178–180°C; IR: 1664(C=O), 1600(C=C), 1556, 1488, 1446, 1421, 1302, 1269, 1206, 1074, 1033, 989(N—N=N), 826(Ar-H), 689; ^{1}H NMR: 8.120–8.173 (d, 1H, J = 15.9 Hz, CH=C—CO), 8.023–8.076 d, 1H, J = 15.9 Hz, C=CH—CO), 7.919–7.972 (m, 4H, Ar-1,4,5,8), 7.718–7.747 (m, 2H, Ph-2,6), 7.544–7.632 (m, 3H, Ar-3,6,7), 7.409–7.438 (m, 3H, Ph-3,4,5), 2.732(s, 3H, TRZ-CH_3); MS: 339(M^+,1), 310(3), 283(23), 268(3), 251(7), 230(22), 180(27), 168(42), 127(100), 115(20), 103(51), 77(61), 51(24), 39(11); Anal. Calcd. for $C_{22}H_{17}N_3O$: C, 77.86; H, 5.05; N, 12.38; Found: C, 77.65; H, 5.27; N, 12.46.

(E)-1-[1-(3-Bromophenyl)-5-methyl-1H-1,2,3-triazol-4-yl]-3-phenylprop-2-en-1-one (2i). Yield: 89.8%; white crystals; mp: 168–170°C; IR: 1662(C=O), 1599(C=C), 1551, 1494, 1443, 1402, 1361, 1275, 1196, 1066, 1031, 987(N—N=N), 838(Ar-H), 687; ^{1}H NMR: 8.078–8.131 (d, 1H, J = 15.9 Hz, CH=C—CO), 7.910–7.963 (d, 1H, J = 15.9 Hz, C=CH—CO), 7.725–7.757 (m, 2H, Ph-2,6), 7.538–7.566 (m, 3H, Ar-4,5,6), 7.414–7.446 (m, 4H, Ar-2 and Ph-3,4,5), 2.667(s, 3H, TRZ-CH_3); MS: 367(M^+,2), 311(16), 260(24), 217(8), 196(68), 155(56), 131(94), 115(43), 103(100), 77(89), 51(50), 39(25); Anal. Calcd. for $C_{18}H_{14}BrN_3O$: C, 58.71; H, 3.83; N, 11.41; Found: C, 58.57; H, 3.67; N, 11.86.

(E)-1-[1-(4-Methoxyphenyl)-5-methyl-1H-1,2,3-triazol-4-yl]-3-phenylprop-2-en-1-one (2j). Yield: 92.2%; white crystals; mp: 153–155°C; IR: 1666(C=O), 1604(C=C), 1549, 1511, 1445,

1412, 1363, 1283, 1256, 1036, 987(N—N=N), 837(Ar-H), 627; ^{1}H NMR: 8.087–8.140 (d, 1H, J = 15.9 Hz, CH=C—CO), 7.890–7.947 (d, 1H, J = 15.9 Hz, C=CH—CO), 7.696–7.741 (m, 2H, Ph-2,6), 7.370–7.425 (m, 5H, Ar-2,6 and Ph-3,4,5), 7.050–7.091 (m, 2H, Ar-3,5), 2.638(s, 3H, TRZ-CH_3); MS: 319(M^+,1), 290(2), 263(25), 210(19), 188(8), 161(20), 148(58), 131(77), 115(21), 103(69), 77(100), 51(30), 39(18); Anal. Calcd. for $C_{19}H_{17}N_3O_2$: C, 71.46; H, 5.37; N, 13.16; Found: C, 71.76; H, 5.54; N, 13.02.

General procedure for the preparation of 2-amino-6-(1-aryl-5-methyl-1*H*-1,2,3-triazol-4yl)-4-phenylpyridine-3-carbonitrile derivatives (3a–j) [20]. Chalcone **2a–j** (10 mmol), malononitrile (10 mmol, 0.66 g, 1 equiv.), and ammonium acetate (80 mmol, 0.62 g, 8 equiv.) were dissolved in EtOH (10 mL) and refluxed for 15 h, whereupon no starting material was evident by TLC. The reaction mixture was allowed to cool to RT and the solvent was evaporated to leave a yellow solide, dried, and purified by column chromatography using a mixture of EtOAc /petroleum ether 60–90°C 1:4 as eluent to give the corresponding **3a–j.**

2-Amino-6-(5-methyl-1-p-tolyl-1H-1,2,3-triazol-4yl)-4-phenylpyridine-3-carbonitrile (3a). Yield: 63.5%; yellow crystals; mp: 168–170°C; IR: 3487, 3368(NH_2), 2922(—CH_3), 2212(-CN), 1731, 1619, 1581, 1562, 1516, 1420, 1258(C—N), 1111, 977(N—N=N), 839(Ar-H), 702; ^{1}H NMR: 7.795(s, 1H, Py-), 7.682–7.698 (m, 2H, Ph-2,6), 7.513–7.528 (m, 3H, Ph-3,4,5), 7.392–7.404 (m, 4H, Ar-2,3,5,6), 5.415 (s, 2H, —NH_2), 2.712(s, 3H, TRZ-CH_3), 2.443(s, 3H, Ar-CH_3); MS: 367(M^++1). Anal. Calcd. for $C_{22}H_{18}N_6$: C, 72.11; H, 4.95; N, 22.94; Found: C, 72.43; H, 4.83; N, 22.74.

2-Amino-6-(5-methyl-1-phenyl-1H-1,2,3-triazol-4yl)-4-phenylpyridine-3-carbonitrile (3b). Yield: 60.0%; yellow crystals; mp: 80–82°C; IR: 3471, 3355(NH_2), 2924(—CH_3), 2210(-CN), 1709, 1614, 1589, 1558, 1501, 1419, 1264(C—N), 1114, 977(N—N=N), 765(Ar-H), 696; ^{1}H NMR: 7.827(s, 1H, Py-), 7.480–7.569(m, 10H, Ar-2,3,4,5,6 and Ph-2,3,4,5,6), 5.299(s, 2H, —NH_2), 2.786(s, 3H, TRZ-CH_3); MS: 353(M^++1). Anal. Calcd. for $C_{21}H_{16}N_6$: C, 71.58; H, 4.58; N, 23.85; Found: C, 71.79; H, 4.69; N, 23.53.

2-Amino-6-[1-(4-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4yl]-4-phenylpyridine-3-carbonitrile (3c). Yield: 59.7%; yellow crystals; mp: 192–194°C; IR: 3495, 3369(NH_2), 2923(—CH_3), 2212(-CN), 1730, 1617, 1581, 1560, 1498, 1420, 1259(C-N), 1090, 977(N—N=N), 839(Ar-H), 700; ^{1}H NMR: 7.689(s, 1H, Py-), 7.442–7.591 (m, 9H, Ar-2,3,5,6 and Ph-2,3,4,5,6), 5.420(s, 2H, —NH_2), 2.726(s, 3H, TRZ-CH_3); MS: 387 (M^++1). Anal. Calcd. for $C_{21}H_{15}ClN_6$: C, 65.20; H, 3.91; N, 21.72; Found: C, 65.65; H, 3.75; N, 21.65.

2-Amino-6-[1-(2,5-dichlorophenyl)-5-methyl-1H-1,2,3-triazol-4yl]-4-phenylpyridine-3-carbonitrile (3d). Yield: 52.3%; yellow crystals; mp: 94–96°C; IR: 3464, 3353(NH_2), 2926(—CH_3), 2213(—CN), 1710, 1681, 1588, 1562, 1490, 1426, 1264(C—N), 1097, 979(N—N=N), 770(Ar-H), 700; ^{1}H NMR: 7.663(s, 1H, Py-), 7.528–7.575 (m, 8H, Ar-3,4 and Ph-2,3,4,5,6), 5.422(s, 2H, —NH_2), 2.599(s, 3H, TRZ-CH_3); MS: 421(M^++1). Anal. Calcd. for $C_{21}H_{14}Cl_2N_6$: C, 59.87; H, 3.35; N, 19.35; Found: C, 59.54; H, 3.54; N, 19.19.

2-Amino-6-[1-(3-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4yl]-4-phenylpyridine-3-carbonitrile (3e). Yield: 58.7%; yellow crystals; mp: 164–166°C; IR: 3436, 3354(NH_2), 2923(—CH_3), 2207(-CN), 1733, 1685, 1586, 1544, 1489, 1427, 1261(C—N), 1082, 982(N—N=N), 782(Ar-H), 699; ^{1}H NMR: 7.669(s, 1H, Py-), 7.509–7.591 (m, 9H, Ar-2,4,5,6 and Ph-2,3,4,5,6), 5.434(s, 2H, —NH_2), 2.716(s, 3H, TRZ-CH_3); MS: 387(M^++1). Anal. Calcd. for $C_{21}H_{15}ClN_6$: C, 65.20; H, 3.91; N, 21.72; Found: C, 65.55; H, 3.65; N, 21.59.

2-Amino-6-[1-(2-chlorophenyl)-5-methyl-1H-1,2,3-triazol-4yl]-4-phenylpyridine-3-carbonitrile (3f). Yield: 65.0%; yellow crystals; mp: 98–100°C; IR: 3469, 3354(NH_2), 2926(—CH_3), 2211(—CN), 1710, 1681, 1589, 1544, 1497, 1420, 1262(C-N), 1078, 979(N—N=N), 766(Ar-H), 701; ^{1}H NMR: 7.630(s, 1H, Py-), 7.489–7.560(m, 9H, Ar-3,4,5,6 and Ph-2,3,4,5,6), 5.420(s, 2H, —NH_2), 2.595(s, 3H, TRZ-CH_3); MS: 387(M^++1). Anal. Calcd. for $C_{21}H_{15}ClN_6$: C, 65.20; H, 3.91; N, 21.72; Found: C, 65.61; H, 3.55; N, 21.55.

2-Amino-6-[1-(4-bromophenyl)-5-methyl-1H-1,2,3-triazol-4yl]-4-phenylpyridine-3-carbonitrile (3g). Yield: 54.7%; yellow crystals; mp: 215–217°C; IR: 3494, 3370(NH_2), 2923(—CH_3), 2211(-CN), 1730, 1616, 1580, 1542, 1494, 1418, 1258(C—N), 1070, 977(N—N=N), 837(Ar-H), 699; ^{1}H NMR: 7.794(s, 1H, Py-), 7.673–7.751 (m, 4H, Ar-3,5 and Ph-2,6), 7.507–7.524 (m, 3H, Ph-3,4,5), 7.378–7.407 (m, 2H, Ar-2,6), 5.426(s, 2H, —NH_2), 2.685(s, 3H, TRZ-CH_3); MS: 431(M^++1). Anal. Calcd. for $C_{21}H_{15}BrN_6$: C, 58.48; H, 3.51; N, 19.49; Found: C, 58.84; H, 3.32; N, 19.28.

2-Amino-6-[5-methyl-1-(naphthalene-2-yl)-1H-1,2,3-triazol-4yl]-4-phenylpyridine-3-carbonitrile (3h). Yield: 56.6%; yellow crystals; mp: 104–106°C; IR: 3464, 3374(NH_2), 2923(—CH_3), 2208(—CN), 1732, 1610, 1587, 1542, 1481, 1418, 1263(C—N), 1113, 976(N—N=N), 859(Ar-H), 701; ^{1}H NMR: 7.945–8.040 (m, 6H, Ar-1,4,5,8 and Ph-2,6), 7.685(s, 1H, Py-), 7.517–7.616 (m, 6H, Ar-3,6,7 and Ph-3,4,5), 5.423(s, 2H, —NH_2), 2.712(s, 3H, TRZ-CH_3). MS: 415(M^++1). Anal. Calcd. for $C_{25}H_{18}N_6$: C, 74.61; H, 4.51; N, 20.88; Found: C, 74.86; H, 4.26; N, 20.88.

2-Amino-6-[1-(3-bromophenyl)-5-methyl-1H-1,2,3-triazol-4yl]-4-phenylpyridine-3-carbonitrile (3i). Yield: 61.3%; yellow crystals; mp: 105–107°C; IR: 3466, 3354(NH_2), 2925(—CH_3), 2212(-CN), 1710, 1618, 1590, 1561, 1494, 1422, 1264(C—N), 1119, 976(N—N=N), 767(Ar-H), 701; ^{1}H NMR: 7.825(s, 1H, Py-), 7.487–7.528 (m, 9H, Ar-2,4,5,6 and Ph-2,3,4,5,6), 5.430(s, 2H, —NH_2), 2.642(s, 3H, TRZ-CH_3); MS: 431(M^++1). Anal. Calcd. for $C_{21}H_{15}BrN_6$: C, 58.48; H, 3.51; N, 19.49; Found: C, 58.74; H, 3.52; N, 19.38.

2-Amino-6-[1-(4-methoxyphenyl)-5-methyl-1H-1,2,3-triazol-4yl]-4-phenylpyridine-3-carbonitrile (3j). Yield: 57.2%; yellow crystals; mp: 181–183°C; IR: 3449, 3354(NH_2), 2928(—CH_3), 2210(-CN), 1731, 1633, 1584, 1559, 1516, 1423, 1250(C—N), 1112, 979(N—N=N), 839(Ar-H), 697; ^{1}H NMR: 7.755(s, 1H, Py-), 7.669–7.700 (m, 2H, Ph-2,6), 7.493–7.513 (m, 3H, Ar-2,6 and Ph-4), 7.370–7.384 (m, 2H, Ph-3,5), 7.057–7.085 (d, 2H, J = 8.4 Hz, Ar-3,5), 5.412(s, 2H, —NH_2), 2.565(s, 3H, TRZ-CH_3). MS: 383(M^++1). Anal. Calcd. for $C_{22}H_{18}N_6O$: C, 69.10; H, 4.74; N, 21.98; Found: C, 69.45; H, 4.56; N, 21.87.

X-ray structure determination of **3j**. Colourless Block, $C_{22}H_{18}N_6O$, Mr = 852.95, Triclinic, space group P-1, a = 10.398 (7), b = 14.925 (10), c = 15.475 (10) Å, α = 115.975 (10), β = 94.707 (12), γ = 91.049 (11)°, V = 2148 (3) Å^3, Z = 2, D_x = 1.319 Mg m^{-3}, F_{000} = 896, μ = 0.09 mm^{-1}. Intensity data were collected using a Siemens SMART diffractometer at 293(2) K, graphite monochromator MoKα radiation (λ = 0.071073 nm), using the ω-2θ scan technique to a maximum 1.5–26.5°. A total of 11,896 reflections were collected with 8563 unique ones (R = 0.0732), of which 4049 reflections were observed with $I > 2\sigma(I)$. The final int R and wR values were 0.0732 and 0.1717, s = 0.988,

(Δ/σ) max = 0.000. The maximum peak and minimum peak in the final difference map is 0.20 and -0.32 e $Å^{-3}$.

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