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Synthesis and Structures of 1,2,4-Triazoles Derivatives[1]

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Abstract—A series of novel 1,2,4-triazole derivatives were synthesized, and their structures were characterized by IR, UV-Vis, FL, NMR, ESI-MS, and elemental analysis. In the meanwhile, the single crystal structures of 3,4-diethyl-5-(4-pyridyl)-1,2,4-triazole and 3,4-dimethyl-5-(*o*-hydroxyphenyl)-1,2,4-triazole were determined by X-ray diffraction.

Keywords: 1,2,4-triazole derivatives, 3,4-diethyl-5-(4-pyridyl)-1,2,4-triazole, 3,4-dimethyl-5-(*o*-hydroxyphenyl)-1,2,4-triazole, X-ray diffraction

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INTRODUCTION

In the last few years, considerable attention had been paid to the synthesis of 1,2,4-triazoles and their derivatives due to their significant pharmacological activities and specific magnetic properties [1–3], and wide application as antitumor drugs, pesticide, weedicide, fungicide and so on [4, 5]. 1,2,4-Triazole and their derivatives are important five-membered heterocyclic structures [6], which have a lower toxicity than imidazole as pharmacophores. Moreover, 1,2,4-triazoles and their derivatives have a large conjugate planarity and exhibited good electronic transmission performance, which can be used extensively as electron transport materials, such as small organic molecule electron transport materials [7–9]. However, more details about the crystal design and crystal engineering, prediction and computation of molecular crystal structures through inter molecular interactions also had an aroused attention [10–12]. There are various methods for the preparation of 1,2,4-triazoles and their derivatives. A generally used method for the preparation of substituted 1,2,4-triazoles is by the cyclization reaction of hydrazide with hydrazine derivatives, hydrazide or amide derivatives [13–16].

Herein, we described the procedure of the reaction of *N*-substituted acetamide and oxalylchloride to form imide chloride derivatives, which can easily react with hydrazides. After the cyclization, a series of 1,2,4-triazoles derivatives were designed and synthesized as the target compounds [17].

In addition, the compounds were characterized by IR, UV-Vis, FL, NMR, ESI-MS, and elemental analysis. The single crystal of **VIIc** and **VIId** had been obtained, and their structures were characterized by X-ray diffraction analyses.

RESULTS AND DISCUSSION

The carboxylic acids **I** were easily converted into the hydrazides **III** following the known procedure. Then the *N*-substitued acetamide **IV** reacted with oxalylchloride to form imide chloride **V**, and subsequently cyclized to form 1,2,4-triazole compounds **VII**. The general procedure for the synthesis is given in Experimental. The synthesis of the targets is described in the Scheme 1.

In order to determine the spatial structure of the synthesized compound, we performed the X-ray diffraction analysis of 3,4-dimethyl-5-(4-pyridyl)-1,2,4-triazole and 3,4-dimethyl-5-(*o*-hydroxyphenyl)-1,2,4-triazole. The spatial structure of **VIIc** and **VIId** are shown in the figures.

The data of **VIIc** obtained show that both of the triazole ring and pyridine ring have planar structures, while they are not coplanar. The molecular structure of **VIIc** was shown in Fig. 1. There are a dihedral angle between them, such as a dihedral angle of 37.29(7)° between the triazole ring (C^2, N^1, N^2, C^3, and N^3) and pyridine ring (C^4, C^5, C^6, N^4, C^7, and C^8). The selected bond lengths and angles were listed in Table 1.

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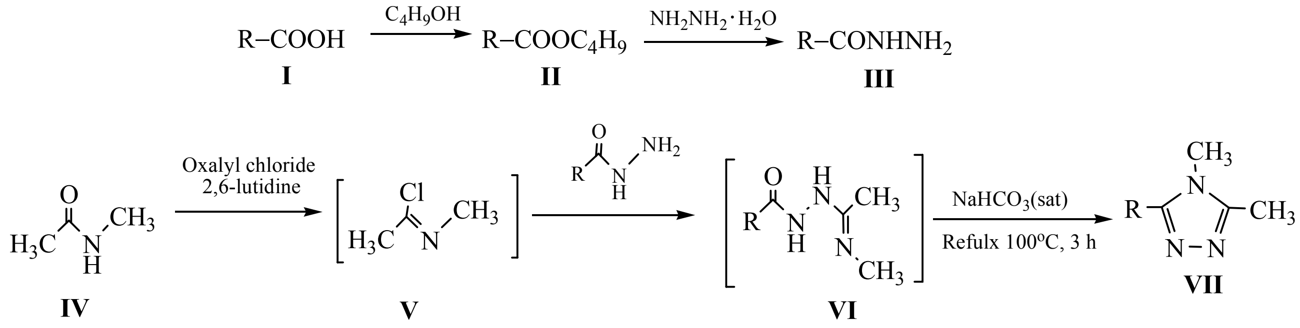
[1] The text was submitted by the authors in English.

Scheme 1.



R = 2-pyridyl (**VIIa**), 3-pyridyl (**VIIb**), 4-pyridyl (**VIIc**), *o*-hydroxyphenyl (**VIId**).

The crystal water molecules involve several hydrogen bond interactions in **VIIc** (Table 2). There are five edge-to-face C–H···π interactions and four face-to-face π···π interactions that exist between the triazole rings and pyridine rings. The compound **VIIc** is stabilized through all these interactions and forms a three-dimensional network (Fig. 2).

The data of **VIId** obtained show that the triazole and phenyl rings were not in the same plane, and the dihedral angle between them was 50.15(6)°.The molecular structure of **VIId** was shown in Fig. 3. The selected bond lengths and angles were listed (Table 3).

There are one intramolecule hydrogen bond (C^4–H^{4C}···O^1) and two inter– molecule hydrogen bonds (O^1–H^1···N^1 and C^9–H^9···N^2) in **VIId** (Table 4). In addition, there are several C–H···π interactions. All these interactions link the compound **VIId** into a network structure (Fig. 4).

EXPERIMENTAL

Reagents and all solvents were analytically pure grade and used without further purification. Melting points were determined using a X-4 digital microscopic melting point apparatus and uncorrected. UV-Vis were recorded on a UV–6000PC spectrophotometer. Fluorescence spectra were recorded on a F-2700 FL fluorescence spectrophotometer. IR spectra were recorded on a prestige-21 infrared spectrometer using KBr pellets. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AV300 magnetic resonance spectrometer in $CDCl_3$ solution. MS were determined on a thermofisher Finnigan LCQ Advantage Max. Elemental analysis was performed by the Perkin-Elmer 24 elemental analyzer.

X-Ray diffraction analysis of compound VIIc. The crystal data were collected at 296(2) K on a

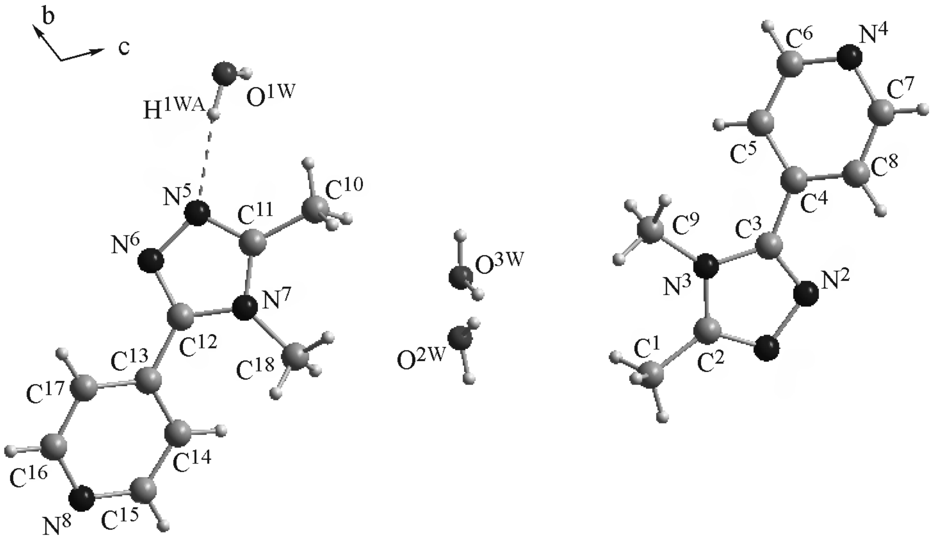


Fig. 1. The molecular structure of **VIIc**.

Table 1. Selected bond lengths (*d,* Å) and bond angles (ω, deg) of crystal **VIIc**

Bond	*d*, Å	Bond angle	ω, deg
N^1–C^2	1.315(3)	N^1–C^2–N^3	110.22(16)
N^1–N^2	1.380(2)	N^2–N^1–C^2	107.51(16)
N^2–C^3	1.313(3)	N^2–C^3–C^4	122.96(16)
N^3–C^2	1.363(3)	C^2–N^3–C^3	104.77(15)
N^3–C^9	1.461(3)	C^4–C^8–C^7	119.32(19)
C^5–C^6	1.379(3)	C^2–N^3–C^9	126.89(15)
N^4–C^6	1.333(3)	C^3–C^4–C^8	118.57(17)
N^4–C^7	1.338(3)	C^5–C^4–C^8	117.58(16)
C^4–C^8	1.391(3)	N^4–C^7–C^8	123.82(19)
C^7–C^8	1.372(3)	N^1–N^2–C^3	107.26(15)

Bruker Smart APEX II CCD diffractometer by using graphite-monochromated MoK_α (λ = 0.71073 Å) radiation. **VIIc** crystallized in triclinic system $P\bar{1}$. Absorption corrections were applied using SADABS program [18]. The structure was solved by direct method and refined by full-matrix least-squares techniques using the SHELXL-97 program [19]. All nonhydrogen atoms were refined anisotropically. All hydrogens were generated geometrically and allowed to ride on their parent atoms. The water hydrogens in **VIIc** were found from the Fourier map, but not refined anisotropically. The coordinates of the atoms are deposited at the Cambridge Crystallographic Data Center (CCDC 1017676).

X-Ray diffraction analysis of compound VIId. According to the same procedures, the structure of **VIId** was solved. **VIId** crystallized in monoclinic

Table 2. The hydrogen bond, C–H···π, and π···π interactions of **VIIc**

D–H···A	D–H, Å	H···A, Å	D···A, Å	∠DHA, deg
O^{1w}–H^{1wA}···N^5	0.865(9)	2.066(17)	2.925(3)	171.9(18)
O^{1w}–H^{1wB}···O$^{3w\ a}$	0.861(10)	1.948(17)	2.800(4)	168(2)
O^{2w}–H^{2wA}···O$^{1w\ a}$	0.842(9)	2.00(2)	2.841(4)	175(2)
O^{2w}–H^{2wB}···N$^{8\ b}$	0.848(9)	2.13(2)	2.909(3)	153(2)
O^{3w}–H^{3wB}···O$^{2w\ c}$	0.857(10)	2.08(3)	2.819(4)	145(3)
O^{3w}–H^{3wA}···N$^{4\ d}$	0.860(10)	2.04(2)	2.874(3)	164.2(19)
C^{18}–H^{18C}···N^{1e}	0.9600	2.5880	3.424(3)	145.73
C^5–H^5···C$^{g2\ f}$	0.9300	3.3230	3.357(3)	84.08
C^9–H^{9B}···C$^{g4\ g}$	0.9600	3.0376	3.468(3)	108.82
C^9–H^{9C}···C$^{g4\ g}$	0.9600	3.3042	3.468(3)	91.72
C^{10}–H^{10A}···C$^{g3\ h}$	0.9600	3.3892	3.967(3)	120.76
C^{15}–H^{15}···C$^{g1\ i}$	0.9300	3.2899	3.466(3)	93.06
C^{g1}···C$^{g4\ g}$	4.080(3)			9.67
C^{g1}···C$^{g4\ f}$	3.707(3)			9.67
C^{g2}···C$^{g3\ h}$	3.842(3)			10.79
C^{g2}···C$^{g3\ i}$	3.776(3)			10.79

[a] Symmetry codes: 1 – *x*, 1 – *y*, 1– *z*; [b] 1 – *x*, –*y*, –*z*; [c] –1 + *x*, *y*, *z*; [d] 1 – *x*,1 – *y*,2 – *z*; [e] 1 – *x*, –*y*,1 – *z*; [f] 1 + *x*, *y*, 1 + *z*; [g] *x*, *y*, 1 + *z*; [h] –1 + *x*, *y*, –1 + *z*; [i] *x*, *y*, –1 + *z*.

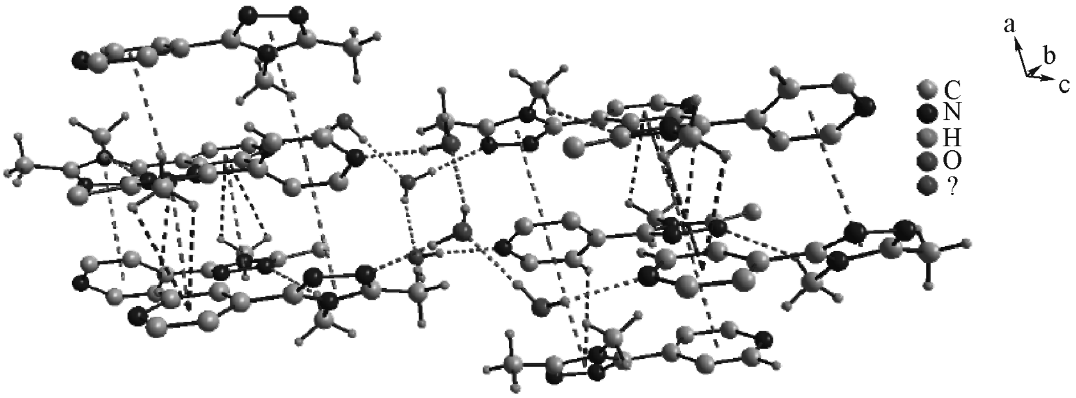


Fig. 2. The 3D network of **VIIc** showing hydrogen bond, C–H···π, and π···π interactions.

system *P*2(1)/*c*. The coordinates of the atoms are deposited at the Cambridge Crystallographic Data Center (CCDC 1017677).

Synthesis of compound III *(general procedure).* To the solution of *n*-butyl alcohol (110 mL) and benzene (30 mL) which contained compounds of **I** (0.2 mol), concentrated sulfuric acid (98%, *d* = 1.84) was added and stirred. The mixture was heated to reflux with a water separator and stirred for 8 hours, then the excess *n*-butyl alcohol and benzene was distillated out, the residuum was pour into ice water (150 mL) and neutralized to pH = 7–8 with saturated sodium carbonate solution. The water solution was extracted with isopropyl ether (3 × 100 mL). The combined extract solution was dried overnight by anhydrous magnesium sulfate and filtered. The filtrate was distillated out first the isopropyl ether then distillated out the ester of **II** under vacuum.

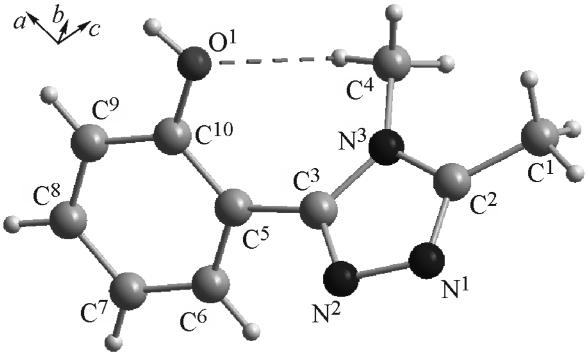


Fig. 3. The molecular structure of **VIId**.

The obtained compounds **II** was dissolved with ethanol (90 mL) and hydrazine hydrate (85%, 30 mL), then the mixture was heated to reflux for 6 h. After the reaction was completed, ethanol and the excess of hydrazine hydrate were distilled out under a reduced pressure, and a white product was left. The crude product was recrystallized from ethanol to afford white crystals **III**.

Synthesis of 3,4-dimethyl-5-(2-pyridyl)-1,2,4-triazole (VIIa). To dichloromethane solution (300 mL) which contained *N*-methylacetamide (4.38 g, 0.06 mol) and 2,6-lutidine (14.0 mL, 0.1 mol), oxalyl chloride (5.2 mL, 0.06 mol) was added, and the mixture was stirred for 40 min at 0°C. Then to the solution 2-

Table 3. Selected bond lengths (*d,* Å) and torsion angles (ω, deg) of crystal **VIId**

Bond	*d,* Å	Bond angle	ω, deg
N^3–C^2	1.3586(17)	N^2–C^3–N^3	109.83(11)
N^1–N^2	1.3907(17)	O^1–C^{10}–C^5	118.22(12)
N^2–C^3	1.3109(17)	N^1–N^2–C^3	106.93(11)
N^3–C^3	1.3692(17)	C^5–C^{10}–C^9	119.28(13)
C^3–C^5	1.4586(19)	O^1–C^{10}–C^9	122.44(12)
C^5–C^6	1.398(2)	N^1–C^2–N^3	109.71(12)
C^6–C^7	1.377(2)	C^3–C^5–C^6	117.56(12)
C^7–C^8	1.378(2)	N^1–C^2–C^1	126.00(13)
C^8–C^9	1.380(2)	C^3–N^3–C^4	128.26(12)
C^9–C^{10}	1.393(2)	N^2–N^1–C^2	107.86(11)

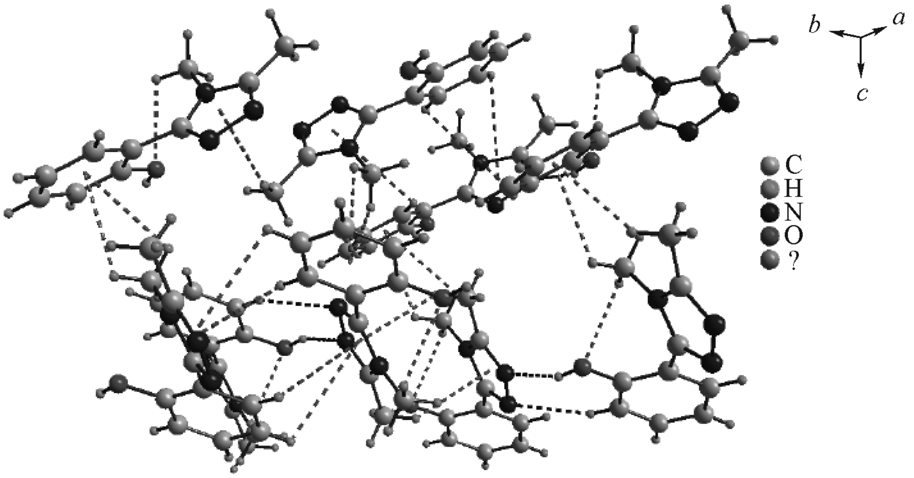


Fig. 4. The hydrogen bonding and C–H···π interactions of **VIId**.

picolinyl hydrazide (8.22 g, 0.06 mol) was added and the mixture was stirred for 5 h at room temperature. After the reaction was completed, the solvent was removed under a reduced pressure and a residue was left. To the residue, a saturated sodium bicarbonate solution (300 mL) was added and the mixture was refluxed for 3 h at 100°C, then cooled to the room temperature, extracted with chloroform (3 × 100 mL). The extract was dried overnight by anhydrous magnesium sulfate. After the filtration chloroform was distilled out and a yellowish solid was separated. The crude product was recrystallized from ethyl acetate to afford white crystals (2.7 g). Yield 25.6 %, mp 113–114°C. IR spectrum, ν, cm^{-1}: 1437, 1491, 1588 (C–C), 2975 (CH_3), 3054 (C–H, 2-pyridyl). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.457 (3H, CCH_3), 3.941 (3H, NCH_3), 7.250–8.581 (4H, 2-pyridyl). ^{13}C NMR spectrum, δ_C, ppm: 10.986, 32.418, 123.494, 123.757, 136.930, 148.174, 148.609, 152.320, 153.665. UV-Vis (CH_2Cl_2), λ_{max}, nm: 233, 269. FL ($CH_3CO_2C_2H_5$), nm: λ_{ex} = 308, λ_{em} = 344. MS (ESI): *m/z* 175.2 $[M + 1]^+$. Found, %: C 62.17; H 5.74; N 32.19. $C_9H_{10}N_4$. Calculated, %: C 62.05; H 5.79; N 32.16.

Compound **VIIb**, **VIIc,** and **VIId** were obtained similarly.

3,4-Dimethyl-5-(3-pyridyl)-1,2,4-triazole (VIIb) Yield 27.1 %, mp 106–107°C. IR spectrum, ν, cm^{-1}: 1437, 1488, 1599 (C–C), 2972 (CH_3), 3050 (C–H, 2-pyridyl). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 2.51 (3H, CCH_3), 3.62 (3H, NCH_3), 7.42–8.85 (4H, 2-pyridyl). ^{13}C NMR spectrum, δ_C, ppm: 11.065, 31.314, 123.764, 123.864, 136.311, 148.945, 150.930, 152.154, 153.034. UV-Vis (CH_2Cl_2), λ_{max}, nm: 233, 270. FL

Table 4. The hydrogen bond and C–H···π interactions for **VIId**

D–H···A	D–H, Å	H···A, Å	D···A, Å	∠DHA, deg
O^1–H^1···$N^{1\,a}$	0.82	1.9784	2.7546	157.68
C^4–H^{4C}···O^1	0.9600	2.5620	3.0377	110.75
C^9–H^9···N^{2a}	0.9300	2.4986	3.3707	156.25
C^1–H^{1B}···$C^{g1\,b}$	0.9600	2.7492	3.5425	140.44
C^4–H^{4A}···$C^{g2\,c}$	0.9600	3.0843	3.4555	104.73
C^4–H^{4B}···$C^{g2\,c}$	0.9600	2.9948	3.4555	110.88
C^6–H^6···$C^{g1\,d}$	0.9300	3.3958	3.7451	104.95
C^7–H^7···$C^{g1\,d}$	0.9300	3.3915	3.7338	104.45

[a] Symmetry codes: –1 + *x, y, z*; [b] 1 – *x, –y, –z*; [c] *x*, 1/2 – y, –1/2 + *z*; [d] 1 – *x*, 1– *y*, –*z*.

Table 5. Synthesis of compounds **II** and **III**

Product	Yield, %	bp, °C (16 mmHg)	Product	Yield, %	mp, °C
IIa	82	141–142	**IIIa**	80.5	100–102
IIb	80	141–142	**IIIb**	78.7	161–163
IIc	76	141–142	**IIIc**	74.1	170–171
IId	90	145–147	**IIId**	74.4	147–149

($CH_3CO_2C_2H_5$), nm: $\lambda_{ex} = 301$, $\lambda_{em} = 334$. MS (ESI): *m/z* 175.2 $[M + 1]^+$. Found, %: C 62.16; H 5.90; N 31.28. $C_9H_{10}N_4$. Calculated, %: C 62.05; H 5.79; N 32.16.

3,4-Dimethyl-5-(4-pyridyl)-1,2,4-triazole (VIIc). Yield 49.8 %, mp 148–149°C. IR spectrum, ν, cm^{-1}: 1485, 1536, 1610 (C–C), 2971 (CH_3), 3048 (C–H, 2-pyridyl). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.498 (3H, CCH_3), 3.649 (3H, NCH_3), 7.550–8.744 (4H, 2-pyridyl). ^{13}C NMR spectrum, δ_C, ppm: 11.038, 31.443, 122.443, 135.066, 150.488, 152.412, 153.456. UV-Vis (CH_2Cl_2), λ_{max}, nm: 247. FL ($CH_3CO_2C_2H_5$), nm: $\lambda_{ex} = 289$, $\lambda_{em} = 334$. MS (ESI): *m/z* 175.2 $[M + 1]^+$. Found, %: C 61.89; H 5.77; N 32.01. $C_9H_{10}N_4$. Calculated, %: C 62.05; H 5.79; N 32.16.

3,4-Dimethyl-5-(*o*-hydroxyphenyl)-1,2,4-triazole (VIId). Yield 48.5 %, mp 228–229°C. IR spectrum, ν, cm^{-1}: 1225 (C–O), 1456, 1490, 1609 (C–C), 2926 (CH_3), 3034 (C–H, 2-pyridyl), 3460 (OH). ^1H NMR spectrum ($CDCl_3$), δ, ppm: 2.518 (3H, CCH_3), 3.768 (3H, NCH_3), 6.918–7.497 (4H, 2-pyridyl), 7.381 (1H, OH). ^{13}C NMR spectrum, δ_C, ppm: 11.034, 32.544, 111.219, 118.077, 119.043, 125.983, 131.598, 152.117, 152.861, 157.530. UV-Vis (CH_2Cl_2), λ_{max}, nm: 220, 280. FL ($CH_3CO_2C_2H_5$), nm: $\lambda_{ex} = 286$, $\lambda_{em} = 325$. MS (ESI): *m/z* 190.2 $[M + 1]^+$. Found, %: C 63.57; H 5.85; N 21.99. $C_{10}H_{11}N_3O$. Calculated, %: C 63.48; H 5.86; N 22.21.

CONCLUSIONS

To summarize, a series of new 1,2,4-triazoles derivatives were synthesized and their structures were experimentally characterized by NMR, UV-Vis, FL, IR, ESI-MS, and elemental analysis. The single crystal structures for compound **VIIc** and **VIId** have been determined by X-ray diffraction. The crystal structures showed that the two aromatic rings of **VIIc** and **VIId** were not in a common plane.

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REFERENCES

1. Klingele, M.H., Moubaraki, B., Murray, K.S., and Brooker, S, *Chemistry-A, Eur. J.*, 2005, no. 11, p. 6962. DOI: 10.1002/chem.200500387.
2. Klingele, M.H., Boyd, P.D., Moubaraki, B., Murray, K.S., and Brooker, S, *Eur. J. Inorg. Chem.*, 2005, no. 5, p. 910. DOI: 10.1002/ejic.200400780.
3. Shen, S., Van Khang, P., Chen, Y., Lei, M., and Hu, L, *ARKIVOC*, 2013, no. 3, p. 413.
4. Potts, K.T., *Chem. Rev.,* 1961, no. 61, p. 87. DOI: 10.1021/cr60210a001.
5. Li, Y., Wang, Z.X., Zhang, C.G., Liu, Q., and Liu, L., *Inorg. Chem. Commun.*, 2013, no. 38, p. 58. DOI: 10.1016/j.inoche.2013.09.074.
6. Lindström, J. and Johansson, M.H., *Synt. Commun.,* 2006, no. 36, p. 2217. DOI: 10.1080/00397910600638994.
7. van Koningsbruggen, P.J., *Spin Crossover in Transition Metal Compounds*, 2004, no. 233, p. 123. DOI: 10.1007/b13531.
8. Zhu, D., Xu, Y., Yu, Z.; Guo, Z., Sang, H., Liu, T., and You, X., *Chem. Mater.*, 2002, no. 14, p. 838. DOI: 10.1021/cm010688u.
9. Kitchen, J.A. and Brooker, S., *Coord. Chem. Rev.*, 2008, no. 252, p. 2072. DOI: 10.1016/j.ccr.2007.11.010.
10. McKinnon, J.J., Jayatilaka, D., and Spackman, M.A., *Chem. Commun.*, 2007, no. 37, p. 3814. DOI: 10.1039/b704980c.
11. Rohl, A.L., Moret, M., Kaminsky, W., Claborn, K., McKinnon, J.J., and Kahr, B., *Crystal Growth and Design*, 2008, no. 8, p. 4517. DOI: 10.1021/cg8005212.
12. Luo, Y.H., Xu, J., and Sun, B.W., *J. Chem. Res.*, 2012, no. 36, p. 697. DOI: http://dx.doi.org/10.3184/174751912X13503977364032.
13. Busch, M. and Schneider, C., *J. für Praktische Chemie*, 1914, no. 89, p. 310.
14. Curtius, T., *J. für Praktische Chemie*, 1914, no. 89, p. 508.
15. Herbst, R.M. and Garrison, J.A., *J. Org. Chem.*, 1953, no. 18, p. 872.
16. Pellizzari G., *Gazz Chim Ital*, 1911, no. 41, p. 93.
17. Wang, S.H., Wang, Y., Zhu, Y.Y., Han, J., Zhou, Y.F., Koirala, D., and Hu, C., *ARKIVOC,* 2010, no. 11, p. 204.
18. Sheldrick, G.M., *SADABS*, University of Göttingen, Germany. 2003.
19. Sheldrick, G. M., *Acta Cryst. A,* 2008, no. 64, p. 112.