Article

JOURNAL OF THE CHINESE CHEMICAL SOCIETY

One-pot Synthesis of 2,5-Disubstituted-1,3,4-oxadiazoles Based on the Reaction of *N,N*-Dimethyl Amides with Acid Hydrazides

Qiang Li,[a,b] Yi Tao,[b] Dongfang Xu,[a]* Haobing Zhang[b] and Liping Duan[b]*

[a]*Shanghai Normal University, Shanghai 200025, China*

[b]*National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention, WHO Collaborating Centre for Malaria, Schistosomiasis, and Filariasis, Key laboratory of Parasitology and Vector Biology at National Institute of Parasitic Diseases, Shanghai 200005, China*

(Received: Nov. 14, 2013; Accepted: Jan. 22, 2014; Published Online: ??; DOI: 10.1002/jccs.201300598)

Convenient and efficient one pot method for the synthesis of 2,5-disubstituted-1,3,4-oxadiazoles based on the reaction of *N,N*-dimethyl amides with acid hydrazides has been developed. The methodology is applied to a wide range of difference aryl hydrazide and difference *N,N*-dimethyl amides to 2,5-disubstituted-1,3,4-oxadiazoles yield the in good to excellent yields. It will be possible wide useful application in synthesis.

Keywords: One pot method; Synthesis; 1,3,4-Oxadiazoles derivatives.

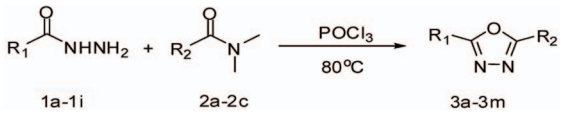
INTRODUCTION

1,3,4-Oxadiazoles have been the subject of intensive interest in medicinal chemistry, due to a wide variety of their biological activities including antifungal, antimitiotic, antimycobacterial and antibacterial activities.[1-3] Thus, numerous methods have been explored for the synthesis of this class of heterocycles. The commonly used synthetic route for 1,3,4-oxadiazoles involves the cyclization of the carboxylic acid hydrazides with a variety of dehydrating reagents under harsh reaction conditions[4-7] or the oxidation of hydrazones using various oxidizing agents. The former require long reaction times and high temperature.[8] As to the latter, these protocols use expensive catalysts.[9-10] There are a few reliable and operationally simple examples for the one-step synthesis of 1,3,4-oxadiazoles using acid or orthoformate as raw materials.[11-13] However, to the best of our knowledge, preparation of 1,3,4-oxadiazoles utilizing *N,N*-dimethyl amide as the reagent has not been reported yet. Herein we reported in one pot synthesis of 2,5-disubstituted-1,3,4-oxadiazoles based on the reaction of *N,N*-dimethyl amides with acid hydrazides by phosphorous oxychloride as coupling reagent and cyclo-dehydration catalyst in the absence of any solvent.

RESULTS AND DISCUSSION

Typically, compounds **(3)** were prepared by the reaction of corresponding hydrazide **(1)** with difference *N,N*-dimethyl amide **(2)** and phosphorus oxychloride in one pot in good yield. The details for the syntheses are shown in Scheme 1 and Table 1.

Scheme 1



The structures of **(3)** were characterized by mass spectrometry and NMR. Elemental analyses of all compounds were in agreement with the calculated values. The molecular structure of 2-methyl-5-(4-nitrophenyl)-1,3,4-oxadiazole (3g) was confirmed by X-ray analysis (Figure 1). From the crystal packing picture, a large variety of hydrogen-bonded networks was observed; a three-dimensional network was formed by hydrogen bonding of the benzene group with oxadiazole ring. Some selected bond lengths and bond angles are listed in Table 2. The O(3)-C(7) bond (1.3596(17) Å) and O(3)-C(8) bond (1.3663(18) Å) are shorter than the typical C-O bond (1.43 Å)[14] because of the P-π conjugate effect, similarly, the N(2)-C(7) bond (1.282(2) Å) and N(3)-C(8) bond (1.277(2) Å) is shorter than the typical C=N bond (1.35 Å), respectively. The angles containing unsaturated bond C(8)-N(3)-N(2), O(1)-N(1)-O(2) and N(2)-C(7)-O(3) correspond to 106.24(13)°, 118.88(14)° and 112.38(13)° respectively. The torsion angles of C(2)-C(3)-C(4)-C(7), C(9)-C(8)-O(3)-C(7) were equal to -179.68(11)° and -179.48(15)°, respectively.

* Corresponding author. Tel: +021-64377008-2606; Email: lipingduan@yahoo.com

Table 1. Synthesis of 1,3,4-oxadiazoles derivatives using *N,N*-dimethyl amides and acid hydrazides

Entry	Substrate (1a-1i)	Substrate (2a-2c)	Product (3a-3m)
1		2a	3a
2	1a	2b	3b
3		2c	3c
4	1b		3d
5	1c		3e
6	1d		3f
7	1e	2a	3g
8	1f		3h
9	1g		3i
10	1h		3j
11		2a	3k
12	1i	2b	3l
13		2c	3m

In order to further investigate the generality of this methodology, the reaction of difference subsutited benzoic acid hydrazide with difference *N,N*-dimethyl amides were performed under similar condition (Table 3). Firstly, we have tested variations of benzoic acid hydrazide moiety participating in the formation of oxadiazoles, preserving the same *N,N*-dimethyl acetyl amide. As the results shown in Table 3, a variety of substituents such as F, Cl, Br, NO_2, CN, OMe, Me on the aromatic ring are compatible with this reaction condition. Similarly the cyclization of hetercyclic hydrazide such as 3-pyridyl led to the desired oxadizaole in modest yield. Compared to substrates bearing electron–donating groups, electron-withdrawing substrates gave better yields. It appears that the electronic property of the acid hydrazide plays certain roles in the cyclization.

Subsequently, we also reacted benzoic acid hydrazide as well as 3-pyridyl acid hydrazide with several *N,N*-dimethyl amides to give the corresponding oxadiazoles. These results showed that the best substrates was *N,N*-dimethyl acetamide, the reaction preceded smoothly in high yield separately (92%; 83%). *N,N*-dimethyl benzamide showed poor activity (79%; 72%) in one hour. In general, when the *N,N*-dimethyl amides section contains a large substituted group, the yields are lower than those of *N,N*-dimethyl amides. It demonstrated that steric effect is also an important influence on a reaction's course or rate.

The possible mechanism of this reaction is shown in

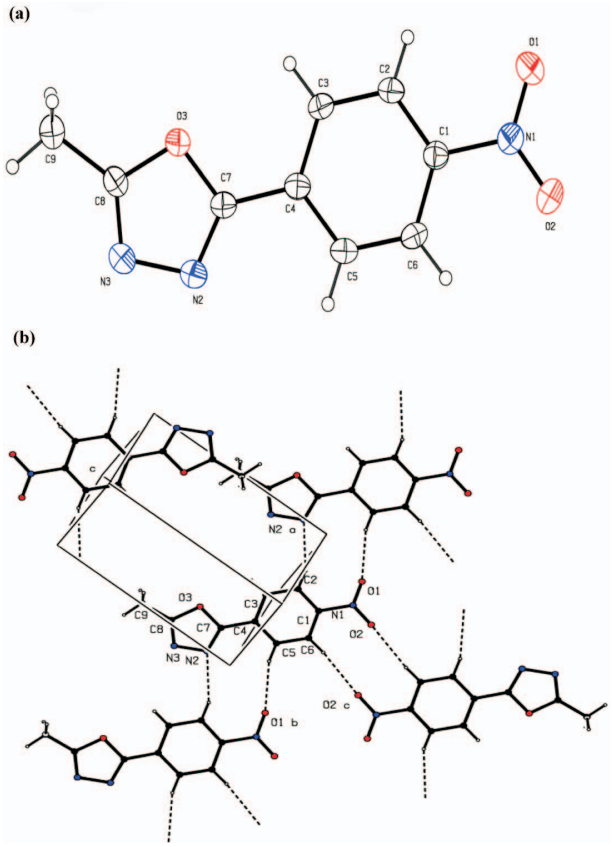


Fig. 1. (a) Molecular structure of (3g), (b) crystal packing of compound (3g).

Table 2. Selected Bond Lengths (Å) and Bond Angles (°)

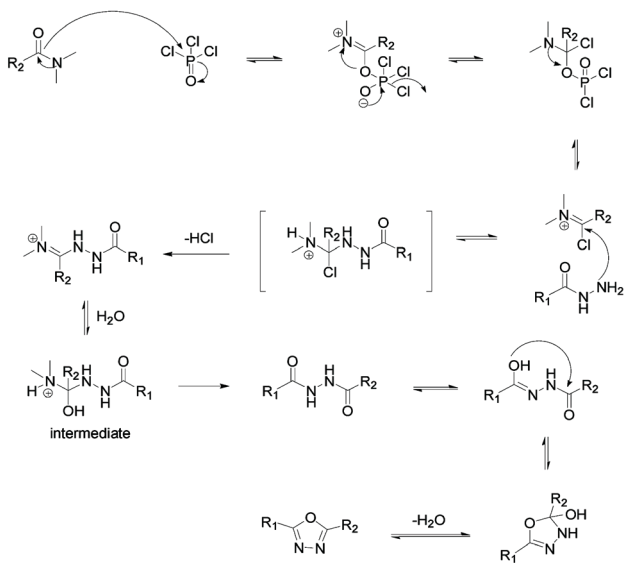
Bond	Dist.	Bond	Dist.	Bond	Dist.
C(7)-O(3)	1.3596(17)	C(7)-N(2)	1.282 (2)	C(1)-N(1)	1.469(2)
C (8)-O(3)	1.3663(18)	C(8)-N(3)	1.277(2)	C(8)-C(9)	1.478(2)
Angle	(°)	Angle	(°)	Angle	(°)
C(2)-C(1)-C(6)	122.95(14)	C(6)-C(5)-C(4)	119.95(13)	N(1)-C(1)-C(2)-C(3)	-179.75(12)
C(2)-C(1)-N(1)	118.41(13)	N(2)-C(7)-O(3)	112.38(13)	C(2)-C(3)-C(4)-C(7)	-179.68(11)
C(6)-C(1)-N(1)	118.64(13)	O(1)-N(1)-O(2)	122.93(16)	N(1)-C(1)-C(6)-C(5)	179.84(12)
C(1)-C(2)-C(3)	118.21(13)	O(3)-C(8)-C(9)	118.16(14)	O(3)-C(7)-N(2)-N(3)	-0.47(16)
C(3)-C(4)-C(5)	120.42(14)	O(1)-N(1)-C(1)	118.88(14)	C(3)-C(4)-C(7)-O(3)	6.78(19)
C(3)-C(4)-C(7)	121.16(13)	C(7)-O(3)-C(8)	102.62(11)	C(2)-C(1)-N(1)-O(1)	-0.8(2)
C(5)-C(4)-C(7)	118.42(13)	C(8)-N(3)-N(2)	106.24(13)	C(9)-C(8)-O(3)-C(7)	-179.48(15)

Symmetry transformation: a: *x*, *y*+1, *z*; b: –*x*, *y*, –*z*+1/2; c: –*x*, –*y*+1, –*z*

Table 3. Synthesis of 1,3,4-oxadiazoles (3a-3m)

Entry	R^1	R^2	Product	Time (min)	Yield (%)
1	Ph	CH_3	3a	35	92
2	Ph	CH_3CH_2	3b	40	88
3	Ph	Ph	3c	45	79
4	4-F-C_6H_4	CH_3	3d	30	93
5	4-Cl-C_6H_4	CH_3	3e	32	90
6	4-Br- C_6H_4	CH_3	3f	30	88
7	4-NO_2- C_6H_4	CH_3	3g	20	96
8	4-CN- C_6H_4	CH_3	3h	20	95
9	4-MeO- C_6H_4	CH_3	3i	60	54
10	4-Me- C_6H_4	CH_3	3j	60	57
11	3-pyridyl	CH_3	3k	40	83
12	3-pyridyl	CH_3CH_2	3l	45	79
13	3-pyridyl	Ph	3m	55	72

Scheme 2 The possible mechanism of this reaction



Scheme 2. We speculated that Schiff base formed first through $POCl_3$-assisted coupling, followed by elimination of $HN(CH_3)_2$ and thus resulted in diaroyl hydrazines, finally the generated diaroyl hydrazines was dehydration leading to formation of a stable oxadiazole ring. In the present study intermediate was identified by LC/MS. According to the mass spectrum, it was identified as *N*′-((dimethylamino)(hydroxy)(phenyl)methyl)nicotinohydrazide in 3-pyridyl acid hydrazide reaction of *N,N*-dimethyl benzamide (Figure 2). The molecular ion was *m/z* 289.25 [M + H^+]. The positively charged *m/z* = 244.20 of *N*′-benzoylnicotinohydrazide was also proved referring to Figure 2. This agent $POCl_3$ promotes coupling and cyclization at the same time: firstly, the conversion of acid hydrazide into Schiff base as coupling reagent, then as catalyst provide for acidic environment, which helps Schiff base lead to oxadiazole derivatives. This reaction process might provide the first example of using *N,N*-dimethyl amides to synthesize 1,3,4-oxadiazoles.[15-19]

In summary, a convenient and efficient one pot method for the synthesis of 2,5-disubstituted-1,3,4-oxadiazoles based on the reaction of *N,N*-dimethyl amides with acid hydrazides has been developed. The methodology is applied to a wide range of difference aryl hydrazide and difference *N,N*-dimethyl amides to 2,5-disubstituted-1,3,4-oxadiazoles yield the in good to excellent yields.

EXPERIMENTAL

All solvents and other reagents were of high purity (Aldrich and Sigma) and were used without further purification. Elemental analysis was performed on a PE-2400 Elemental Analyzer, the C, H and N analysis were repeated twice. ^{1}H-NMR

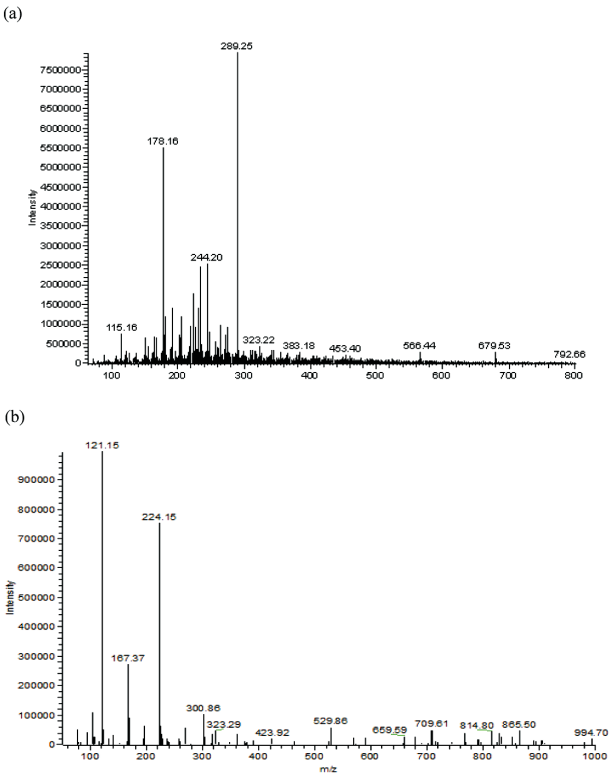


Fig. 2. (a) MS data of (3m) intermediate. (b) MS data of (3m).

and ^{13}C-NMR spectra were obtained in $CDCl_3$ or DMSO-d6 with TMS as internal standard on a Bruker AM-400 spectrometer. Chemical shifts were reported as ppm. Mass spectra were measured on a LCQ LC-MS spectrometer. Melting points were determined by an BÜCHI melting point B-540 apparatus and were uncorrected.

Typical experimental procedure: A solution of difference acid hydrazide (1) (0.01 mol) was stirred in difference *N,N*-dimethyl amide (2) (10 mL) solution. The reaction mixture was heated up to 80 ^{o}C, phosphorus oxychloride (0.011 mol) was added into the reaction mixture. After the reaction was completed, the reaction mixture was added with cold water (50 mL) and neutralized with Na_2CO_3 aqueous solution, the solution was extracted with CH_2Cl_2. The organic layer was then dried over sodium sulfate and evaporated under vacuo. The crude material was purified by chromatography on silica gel column using ethyl acetate +petroleum ether (1+4 by volume) as eluent. The solvent was removed under reduced pressure to give 2,5-disubstituted-1,3,4-oxadiazoles.

3a: White solid, m.p. 67-68 ^{o}C IR (KBr) *v*: 3440, 3335, 1640, 1630, 1500, 1422, 1300 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.70 (d, *J* = 7.0, 2H), 7.19 (t, *J* = 7.0, 2H), 7.18 (t, *J* = 7.0, 1H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.66, 163.43, 130.61, 127.18, 122.25, 120.45, 11.36; LC-MS [M+H$^+$]: 161.14. Anal. Calcd for $C_9H_8N_2O$: C, 67.49; H, 5.03; N, 17.49. Found: C, 67.40, H, 5.00; N, 17.51. **3b**: White solid, m.p.105-107 ^{o}C IR (KBr) *v*: 3443, 3330, 1639, 1632, 1512, 1423, 1299 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.71 (d, *J* = 7.2, 2H), 7.20 (t, *J* = 7.2, 2H), 7.19 (t, *J* = 7.2, 1H), 2.21 (m, 2H), 1.37 (t, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.67, 163.46, 130.61, 127.18, 123.25, 121.45, 11.59, 9.18; LC-MS [M+H$^+$]: 175.15. Anal. Calcd for $C_{10}H_{10}N_2O$: C, 68.95; H, 5.79; N, 16.08. Found: C, 68.91; H, 5.80; N, 16.09. **3c**: White solid, m.p. 136-138 ^{o}C IR (KBr) *v*: 3441, 3328, 1636, 1628, 1501, 1421, 1308 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.73 (d, *J* = 7.2, 4H), 7.18 (t, *J* = 7.2, 4H), 7.16 (t, *J* = 7.2, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.69, 163.56, 129.67, 128.19, 123.27, 121.47; LC-MS [M+H$^+$]: 223.16. Anal. Calcd for $C_{14}H_{10}N_2O$: C, 75.66; H, 4.54; N, 12.60. Found: C, 75.66; H, 4.52; N, 12.53. **3d**: White solid, m.p. 100-101 ^{o}C IR (KBr) *v*: 3445, 3338, 1638, 1629, 1495, 1420, 1298 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.05-8.01 (d, *J* = 8.0, 2H), 7.26-7.22 (d, *J* = 8.0, 2H), 2.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.45, 163.59, 129.27, 129.18, 116.70, 116.48, 11.35; LC-MS [M+H$^+$]: 179.16. Anal. Calcd for $C_{10}H_7FN_2O$: C, 60.67; H, 3.96; N, 15.72. Found: C, 60.61; H, 4.00; N, 15.80. **3e**: White solid, m.p. 109-110 ^{o}C IR (KBr) *v*: 3440, 3335, 1640, 1630, 1498, 1422, 1307 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.98-7.94 (d, *J* = 8.0, 2H), 7.49-7.45 (d, *J* = 8.0, 2H), 2.63 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.00, 163.99, 138.03, 129.63, 128.22, 122.70, 11.32; LC-MS [M+H$^+$]: 195.13. Anal. Calcd for $C_{10}H_7ClN_2O$: C, 55.54; H, 3.63; N, 14.39. Found: C, 55.50; H, 3.60; N, 14.41. **3f**: Brown solid, m.p. 118-119 ^{o}C IR (KBr) *v*: 3442, 3337, 1643, 1638, 1503, 1423, 1301 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.90-7.86 (d, *J* = 8.0, 2H), 7.65-7.61 (d, *J* = 8.0, 2H), 2.62 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 164.66, 163.47, 130.61, 129.18, 120.25, 119.45, 11.38; LC-MS [M+H$^+$]: 239.10. Anal. Calcd for $C_{10}H_7BrN_2O$: C, 45.22; H, 2.95; N, 11.72. Found: C, 45.25; H, 3.00; N, 11.80. **3g**: Brown solid, m.p. 209.0-210.8 ^{o}C IR (KBr) *v*: 3441, 3338, 1642, 1623, 1498, 1427, 1291 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.39-8.37 (d, *J* = 8.0, 2H), 8.25-8.23 (d, *J* = 8.0, 2H), 2.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.66, 163.43, 130.67, 127.87, 124.62, 11.40; LC-MS [M+H$^+$]: 206.12. Anal. Calcd for $C_9H_7N_3O_3$: C, 52.69; H, 3.44; N, 20.48. Found: C, 52.70; H, 3.44; N, 20.49. **3h**: Brown solid, m.p. 141.5-142.8 ^{o}C IR (KBr) *v*: 3440, 3335, 1640, 1630, 1500, 1422, 1300 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.16-8.14 (d, *J* = 8.0, 2H), 7.81-7.79 (d, *J* = 8.0, 2H), 2.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.79, 163.65, 133.09, 128.04, 127.41, 118.13, 115.28, 114.26, 11.36; LC-MS [M+H$^+$]: 186.15. Anal.

Calcd for $C_{10}H_7N_3O$: C, 64.86; H, 3.81; N, 22.69. Found: C, 64. 79; H, 3.81; N, 22.70. **3i**: White solid, m.p. 91-92.5 °C IR (KBr) *v*: 3444, 3338, 1648, 1631, 1509, 1425, 1308 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.97-7.95 (d, *J* = 8.0, 2H), 7.65-7.63 (d, *J* = 8.0, 2H), 3.87 (s, 3H), 2.67 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.07, 163.98, 130.03, 129.63, 127.22, 48.79, 11.36; LC-MS [M+H$^+$]: 191.13. Anal. Calcd for $C_{10}H_{10}N_2O_2$: C, 63.15; H, 5.30; N, 14.73. Found: C, 63. 16; H, 5.31; N, 14.75. **3j**: White solid, m.p. 136-138 °C IR (KBr) *v*: 3445, 3337, 1640, 1628, 1498, 1421, 1298 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ: 7.97-7.95 (d, *J* = 8.0, 2H), 7.65-7.63 (d, *J* = 8.0, 2H), 3.87 (s, 3H), 2.67 (s,3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.09, 163.47, 130.09, 127.18, 20.78, 11.36; LC-MS [M+H$^+$]: 175.14. Anal. Calcd for $C_{10}H_{10}N_2O$: C, 68.95; H, 5.79; N, 16.08. Found: C, 68. 99; H, 5.81; N, 16.10. **3k**: White solid, m.p. 149.7-150.7 °C IR (KBr) *v*: 3456, 3330, 1639, 1626, 1502, 1422, 1300 cm^{-1}. ^1H NMR (400 MHz, DMSO-d6) δ: 9.30 (s, 1H), 8.80 (d, 1H), 8.47 (d, 1H), 8.23 (d, 2H), 7.70-7.65 (m, 4H), 2.70 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ 164.67, 162.48, 151.98, 146.80, 143.81, 129.69, 127.18, 124.62, 123.75, 121.54, 11.78; LC-MS [M+H$^+$]: 162.12. Anal. Calcd for $C_8H_7N_3O$: C, 59.62; H, 4.38; N, 26.07. Found: C, 59. 66; H, 4.40; N, 26.10. **3l**: White solid, m.p. 136-138 °C IR (KBr) *v*: 3441, 3335, 1645, 1628, 1500, 1420, 1303 cm^{-1}. ^1H NMR (400 MHz, DMSO-d6) δ: 9.28 (s, 1H), 8.89 (d, 1H), 8.43 (d, 1H), 8.17 (d, 2H), 7.73-7.69 (m, 4H), 2.72 (m, 2H), 1.63 (t, 3H); ^{13}C NMR (100 MHz, DMSO-d6) δ: 164.67, 162.43, 152.65, 146.82, 142.67, 129.61, 127.18, 125.26, 122.35, 120.45, 20.14, 11.76; LC-MS [M+H$^+$]: 176.13. Anal. Calcd for $C_9H_9N_3O$: C, 61.70; H, 5.18; N, 23.99. Found: C, 61.68; H, 5.20; N, 23.98. **3m**: White solid m.p. 107.7-109.9 °C IR (KBr) *v*: 3440, 3330, 1638, 1631, 1499, 1428, 1300 cm^{-1}. ^1H NMR (400 MHz, DMSO-d6) δ: 9.31 (s, 1H), 8.82 (d, 1H, *J* = 4.5), 8.49 (d, *J* = 4.2, 1H), 8.15 (d, *J* = 4.1, 2H), 7.69-7.67 (m, 4H); ^{13}C NMR (100 MHz, DMSO-d6) δ: 164.66, 162.43, 151.78, 147.82, 142.67, 130.61, 127.18, 124.24, 122.25, 120.45; LC-MS [M+H$^+$]: 224.14. Anal. Calcd for $C_{13}H_9N_3O$: C, 69.95; H, 4.06; N, 18.82. Found: C, 70.00; H, 4.08; N, 18.98.

ACKNOWLEDGEMENTS

The authors wish to acknowledge that this project is supported by Shanghai Municipal Natural Science Foundation (12ZR1434900), the Opening Project of Shanghai Key Laboratory of New Drug Design (Grant No. 11DZ2260600). The crystallographic data have been assigned the deposition numbers at the Cambridge crystallographic data center (CCDC949962).

REFERENCES

1. Chen, C.; Senanayake, C. H.; Bill, T. J.; Larsen, R. D.; Verhoeven, T. R.; Reider, P. J. *J. Org. Chem.* **1994**, *59*, 3738.
2. Holla, B. S.; Gonsalves, R.; Shenoy, S. *Eur. J. Med. Chem*. **2000**, *35*, 267.
3. Laddi, U. V.; Desai, S. R.; Bennur, R. S.; Bennur, S. C. *Ind. J. Heterocycl. Chem*. **2002**, *11*, 319.
4. Baxendale, I. R.; Ley, S. V.; Martinelli, M. *Tetrahedron* **2005**, *61*, 5323.
5. Wang, Y.; Sauer, D. R.; Djuric, S. W. *Tetrahedron Lett.* **2006**, *47*, 105.
6. Somani, R. R.; Shirodkar, P. Y *Asian J. Chem.* **2008**, *20*, 6189; Rajapakse, H. A.; Zhu, H.; Young, M. B.; Mott, B. T. *Tetrahedron Lett.* **2006**, *47*, 4827.
7. Liras, S.; Allen, M. P.; Segelstein, B. E. *Synth. Commun.* **2000**, *30*, 437; Mashrqui, S. H.; Ghadigaonkar, S. G.; Kenny, R. S. *Synth. Commun.* **2003**, *33*, 2541.
8. Baxendale, I. R.; Ley, S. V.; Martinelli, M. *Tetrahedron.* **2005**, *61*, 5323; Brown, B. J.; Clemens, I. R.; Neesom, J. K. *Synlett* **2000**, *1*, 131; Coppo, F. T.; Evans, K. A.; Graybill, K. L.; Burton, G. *Tetrahedron Lett.* **2004**, *45*, 3257; Brain, C. T.; Paul, J. M.; Loong, Y.; Oakley, P. J. *Tetrahedron Lett.* **1999**, *40*, 3275.
9. Dobrota, C.; Paraschivescu, C. C.; Dumitru, L.; Matache, M.; Baciu, I.; Ruta, L. L. *Tetrahedron Lett*. **2009**, *50*, 1886; Yang, R.-Y.; Dai, L.-X. *J. Org. Chem.* **1993**, *58*, 3381.
10. Rao, V. S.; Sekhar, K. *Synth. Commun.* **2004**, *34*, 2153; Shang, Z.; Reiner, J.; Chang, J.; Zhao, K. *Tetrahedron Lett.* **2005**, *46*, 2701.
11. Bentiss, F.; Lagrenee, M. J. *Heterocycl. Chem.* **1999**, *36*, 1029.
12. Chiba, T.; Okimoto, M. *J. Org. Chem.* **1992**, *57*, 1375; Yang, R.; Dai, L. *J. Org. Chem.* **1993**, *58*, 3381.
13. Rostamizadeh, S.; Housanini, G. *Tetrahedron Lett*. **2004**, *45*, 8753; Gavrilyuk, J. I.; Lough, A. J.; Batey, R. A. *Tetrahedron Lett*. **2008**, *49*, 4746; Polshettiwar, V.; Verma, R. S. *Tetrahedron Lett*. **2008**, *49*, 879.
14. Wilson, J. A. C. *International Tables for Crystallography, Vol. C*; Kluwer Academic Publishers: Dordrecht, the Netherlands, 1992.
15. Kaplancikli, Z. A. *Molecules* **2011**, *16*, 7662–7671; Rivera, N. R.; Balsells, J.; Hansen, K. B. *Tetrahedron Lett*. **2006**, *47*, 4889–4891; Dolman, S. J.; Gosselin, F.; O'shea, P. D. *J. Org. Chem.* **2006**, *71*, 9548–9551; Koparır, M.; Çetin, A.; Cansız, A. *Molecules* **2005**, *10*, 475–480; Zheng, X.; Li, Z.; Wang, Y. *J. Fluorine Chem.* **2003**, *123*, 163–169.
16. Amir, M.; Kumar, S. *Acta Pharm*. **2007**, *57*, 31–45; Boström, J.; Hogner, A.; Llinàs, A. *J. Med. Chem*. **2012**, *55*, 1817-1830; Nagendra, G.; Lamani, R. S.; Narendra, N. *Tetrahedron Lett*. **2010**, *51*, 6338–6341; Li, Z.; Zhu, A.; Mao, X. *J. Braz. Chem. Soc*. **2008**, *19*, 1622–1626; Sharma, G. V. M.;

Rakesh, B. A.; Krishna, P. R. *Synth. Commun*. **2004**, *34*, 2387–2391.
17. Yang, Y. H.; Shi, M. *Tetrahedron Lett*. **2005**, *46*, 6285–6288; Pouliot, M. F.; Angers, L.; Hamel, J. D. *Org. Biomol. Chem*. **2012**, *10*, 988–993; Li, C.; Dickson, H. D. *Tetrahedron Lett.* **2009**, *50*, 6435–6439; Mashraqui, S. H.; Ghadigaonkar, S. G.; Kenny, R. S. *Synth. Commun*. **2003**, *33*, 2541–2545; Kumar, G. V. S.; Rajendraprasad, Y.; Mallikarjuna, B. P. *Eur. J. Med. Chem.* **2010**, *45*, 2063–2074.
18. Guin, S.; Ghosh, T.; Rout, S. K. *Org. Lett*. **2011**, *13*, 5976–5979; Pore, D. M.; Mahadik, S. M.; Desai, U. V. *Synth. Commun*. **2008**, *38*, 3121–3128; Dobrotã, C.; Paraschivescu, C. C.; Dumitru, I. *Tetrahedron Lett*. **2009**, *50*, 1886–1888; Jiang, X.; Register, R. A. *Chem. Mater.* **2000**, *12*, 2542–2549; Katritzky, A. R.; Vvedensky, V.; Cai, X. *Arkivoc* **2002**, *6*, 82–90.
19. Martin, P. J.; Bruce, D. B. *Liq. Crystals* **2007**, *34*, 767–774; Yang, R. Y.; Dai, L. X. *J. Org. Chem.* **1993**, *58*, 3381; Brain, C. T.; Paul, J. M.; Loong, Y. *Tetrahedron Lett.* **1999**, *40*, 3275.

