Asian Journal of Chemistry; Vol. 26, No. 21 (2014), 7109-7112

ASIAN JOURNAL OF CHEMISTRY

http://dx.doi.org/10.14233/ajchem.2014.16507

Synthesis, Spectroscopic Properties of Boc-*L*-alanine Modified 1,8-Naphthyridine Ligands

GAOZHANG GOU[1,2], BO ZHOU[1], HEPING YAN[1], NA WU[1], SHIJUAN XU[1] and WEI LIU[1,2,*]

[1]School of Science, Honghe University, Mengzi 661100, Yunnan Province, P.R. China
[2]Key Laboratory of Natural Pharmaceutical & Chemical Biology of Yunnan Province, Mengzi 661100, Yunnan Province, P.R. China

*Corresponding author: Tel/Fax: +86 873 3694919; E-mail: liuwei4728@126.com

Received: 9 October 2013; *Accepted*: 15 January 2014; *Published online*: 30 September 2014; AJC-16081

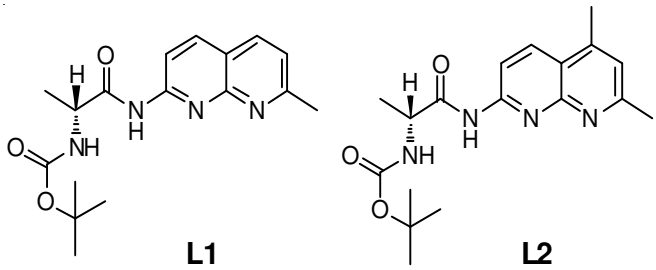
Two 1,8-naphthyridine derivatives containing amino acid by amido bond, Boc-*L*-alanine-2-methy-1,8-naphthyridine (**L1**) and Boc-*L*-alanine-2,4-dimethy-1,8-naphthyridine (**L2**) were synthesized and characterized. And there absorption and fluorescence spectra in various solvents and solid are presented comprehensively. The two ligands exhibit similar electronic absorption spectra with λ_{max} at about 330 nm, which can be tentatively assigned to $\pi \rightarrow \pi^*$ transition. A comprehensive study of spectroscopic properties upon titration of **L1**, **L2** with HBF_4 as a proton source in CH_3OH was investigated. Compounds **L1** and **L2** can use as acid-controlled molecular switching on from the luminescence intensity change caused by proton source.

Keywords: 1,8-Naphthyridine derivatives, Boc-*L*-alanine, Amino acid, Acid-controlled molecular switching on, Spectroscopic properties.

INTRODUCTION

1,8-Naphthyridine compounds have been extensively investigated not only due to their special conjugate π electronic structures, good coordination capabilities[1] and favourable photophysical and photochemical properties[2-6] but also their potential applications as functional materials in the fields of solar energy conversion, sensors[7-9], supramolecular assemblies[10-12], photocatalysis[13,14], nonlinear optical materials, biological activities[15,16] and optical molecular devices[17-19] *etc*. A number of 1,8-naphthyridine derivatives[20,21] have been synthesized since the first 1,8-naphthyridine compound was prepared in the 1920s. Numerous complexes with naphthyridine-based ligands in different coordination modes have also been reported since 1969[22,23].

Additional research effort on luminescent 1,8-naphthyridine derivatives and their Cu(I) complexes has focused on emissive $\pi \rightarrow \pi^*$ or metal-to-ligand charge-transfer (MLCT) excited states which can be tuned by hydrogen-bonding sites leading to intra- or intermolecular interactions[24]. However, the studies on 1,8-naphthyridyl derivatives modified with amino acid is rare. The amino acids enable the ligand to rotate freely, thereby resulting in various coordination modes and interesting spectroscopic properties. Herein, we report on the synthesis and characterization of two new 1,8-naphthyridine ligand **L1** and **L2** in which a 1,8-naphthyridinyl segment and a Boc-*L*-alanine group are connected by a amido bond (**Scheme-I**). their spectroscopic properties are comprehensive studied.



Scheme-I: Synthetic routes and chemical structures of **L1**, **L2**

EXPERIMENTAL

All of commercially available reagents and solvents are analytically pure used in the experiment without any further purification unless stated otherwise. The solvents used for photophysical measurements were of HPLC grade. Silica gel (200-300 mesh) was used for column chromatography and thin layer chromatography was performed on Merck silica gel plates (GF-254). 7-Amino-2,4-dimethyl-1,8-naphthyridine, 7-amino-2-methyl-1,8-naphthyridine were prepared according to the reported literatures[25].

^{1}H NMR spectra were run on a Bruker Avance 400/500 spectrometer with tetramethylsilane (^{1}H) as an internal standard. Electrospray ionization (ESI) mass spectra were performed on a Finnigan LCQ quadrupole ion trap mass spectrometer (samples were dissolved in HPLC grade methanol). Elemental analyses were performed on by Beijing Institute of Chemistry, Chinese Academy of Sciences. UV-visible absorption spectra

were recorded using a Hitachi U-3010 spectrophotometer. Emission and excitation spectra were obtained on a Hitachi F-4500 fluorescence spectrophotometer. The fluorescence quantum yields in solution were measured relative to quinine sulfate in 0.1 N sulfuric acid aqueous solution (λ_{ex} = 345 nm, Φ_F = 0.546) at room temperature and calculated by $\Phi s = Fr(B_r/B_s)(n_s/n_r)^2(D_s/D_r)$, where the subscripts s and r refer to the sample and reference standard solution respectively, n is the refractive index of the solvents, D is the integrated intensity and Φ is the luminescence quantum yield. The quantity B is calculated by $B = 1\text{-}10^{-AL}$, where A is the absorbance at the excitation wavelength and L is the optical path length. Errors for wavelength values (1 nm) and F (10 %) are estimated.

Syntheses of L1: To a 50 mL flask were added 7-amino-2-methy-1,8-naphthyridine (0.8534 g, 5.4 mmol) in 40 mL freshly distilled CH_2Cl_2, then added Boc-*L*-alanine (1.70 g, 9 mmol) and *N,N'*-dicyclohexylcarbodiimide (1.75 g, 9 mmol) under electromagnetic stirring. The mixture was stirred for 24 h under nitrogen atomsphere at room temperature and monitored by TLC. After the reaction is finished, the solvent was removed under reduced pressure after freezing and filtering to obtain a pale yellow solid. The crude product was purified by chromatography on silica gel (CH_2Cl_2:EtOH = 100:1) to give **L1** as white solid (0.8 g, Yield: 45 %). ^{1}H NMR (500 MHz, CD_3CN) δ (ppm): 9.68 (s, 1H NH), 8.40 (d, *J* = 8.8 Hz, 1H Napy-H), 8.29 (d, *J* = 8.8 Hz, 1H Napy-H), 8.16 (d, *J* = 8.2 Hz, 1H Napy-H), 7.37 (d, *J* = 8.2 Hz, 1H Napy-H), 5.98 (s, 1H CH), 4.39 (s, 1H NH), 2.71 (s, 3H CH_3), 2.29 (s, 9H CH_3), 1.43 (s, 3H CH_3). ESI-MS (*m/z*): 331.18 $[M + H]^+$. Elemental analysis calcd (%) for $C_{17}H_{22}N_4O_3$: C, 61.80; H, 6.71; N, 16.96; found: C, 61.75; H, 6.77; N, 17.03.

Syntheses of L2: To a 50 mL flask were added 7-amino-2,4-dimethy-1,8-naphthyridine (0.8661 g, 5 mmol) in 40 mL freshly distilled CH_2Cl_2, then added Boc-*L*-alanine (1.70 g, 9 mmol) and *N,N'*-dicyclohexylcarbodiimide (1.75 g, 9 mmol) under electromagnetic stirring. The mixture was stirred for 24 h under nitrogen atomsphere at room temperature and monitored by TLC. After the reaction is finished, the solvent was removed under reduced pressure after freezing and filtering to obtain a pale yellow solid. The crude product was purified by chromatography on silica gel (CH_2Cl_2:EtOH = 100:1) to give **L2** as white solid (0.83 g, Yield: 48 %). ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 9.26 (s, 1H NH), 8.51 (d, *J* = 9 Hz, 1H Napy-H), 8.35 (d, *J* = 9 Hz, 1H Napy-H), 7.16 (s, 1H Napy-H), 5.07 (s, 1H CH), 4.45 (s, 1H NH), 2.74 (s, 3H CH_3), 2.68 (s, 3H CH_3), 1.52 (d, *J* = 7.2 Hz, 3H CH_3), 1.48 (s, 9H CH_3). ESI-MS (*m/z*): 345.19 $[M + H]^+$. Elemental analysis calcd. (%) for $C_{18}H_{24}N_4O_3$:C, 62.77; H, 7.02; N, 16.27; found: C, 62.74; H, 6.98; N, 17.21.

RESULTS AND DISCUSSION

As outlined in **Scheme-I**, the naphthyridine precursor was prepared starting from 2,6-diaminopyridine in a one-step synthetic route with reference to literature methods[25-29]. The reaction of naphthyridine precursor with a excess of Boc-*L*-alanine and *N,N'*-dicyclohexylcarbodiimide in dry CH_2Cl_2 at room temperature yielded **L1** or **L2** as the product (about 45 %). Both of **L1** and **L2** synthesized were fully characterized by ^{1}H NMR spectroscopy, mass spectroscopy and elemental analyses. This was the first time to synthesis new ligands Boc-*L*-alanine-1,8-naphthyridine that containing amino acid by amido bond. A broad peak in the ^{1}H NMR spectrum, which is an indication of the NH proton of the 7-amido1,8-naphthyridine group, was found after 9 ppm for **L1** and **L2**. And the CH protons are found at about 6 ppm in the ^{1}H NMR spectrum. The other one broad peak in the ^{1}H NMR spectrum, which is an indication of the NH proton of the amino acid group, was found at about 4.3 ppm for **L1** and **L2**. Also, mass spectrum and elemental analyses revealed that compound **L1** and **L2** should contain Boc-*L*-alanine groups. Notably, compound **L1** and **L2** were prepared in a high yield by directly reacting the naphthyridine precursor with Boc-*L*-alanine in dry CH_2Cl_2 at room temperature which dewatered by *N,N'*-dicyclohexylcarbodie.

Electronic absorption spectroscopy and photoluminescence: The spectral properties of compounds **L1** and **L2** were examined under various conditions and the results are summarized in Table-1. Fig. 1 showed the compounds **L1** and **L2** in dichloromethane moderately intense absorptions at 319-333 nm and exhibit intense bands between 225 and 250 nm. And the intense absorptions expressed the characteristic absorption peak of 1,8-naphthyridine which emerged abruption. The structured low-energy absorption bands with a large extinction coefficient (about 1.5×10^4 mol^{-1} dm^{-3} cm^{-1}) may be assigned to the 0→0 vibrational band of the strong S0→S1 transition with some charge-transfer character, as evidenced by the slight sensitivity towards solvent polarity (Fig. 2). On going from **L1** to **L2**, the introduction of the Me unit caused a unconspicuous shift (3 nm) in the absorption maximum.

Upon excitation at 330 nm, the emission spectra of **L1** and **L2** in CH_2Cl_2 feature a broad and structureless peak, with λ_{max} (Quantum yield; Stokes shift) of 374 nm (3 %; 41 nm), 378 nm (11 %; 43 nm), respectively (Table-1). Although the emission bands in **L1** and **L2** occur at almost the same position, but the quantum yield of the latter is obviously higher relative to the former. It may be due to their analogous-extended structures but distinct photoluminescence mechanism (the Me group in **L2** can push electrons). The emission intensity of L2 is dependent on solvents and increases markedly with an increase in solvent polarity (Fig. 2). More than 25-fold enhancement in fluorescence intensity was recorded when

TABLE-1
OPTICAL PROPERTIES OF **L1** AND **L2** IN VARIOUS SOLVENTS AT 298 K

Cpd.	Solvent	λ_{ab} (nm) (ε, mol^{-1} dm^3 cm^{-1})	λ_{em} (nm)	Stokes shift (nm)	[a]λ_{em} (nm)	Φ_f
L1	*n*-hexane	322, 334	361	27	411	0.03
	CH_2Cl_2	319, 333	374	41		0.03
	CH_3CN	318, 331	378	47		0.03
	MeOH	332 (19636)	362	30		0.05
L2	*n*-hexane	336	386, 399	63	475	0.03
	CH_2Cl_2	322, 335	378	43		0.11
	CH_3CN	321, 334	382	48		0.13
	MeOH	334 (15592)	390	56		0.15

[a]Solid state. φ = fluorescence quantum yield, calculated using quinine sulfate as standard (φ = 0.546 in 0.5 mol/L H_2SO_4)

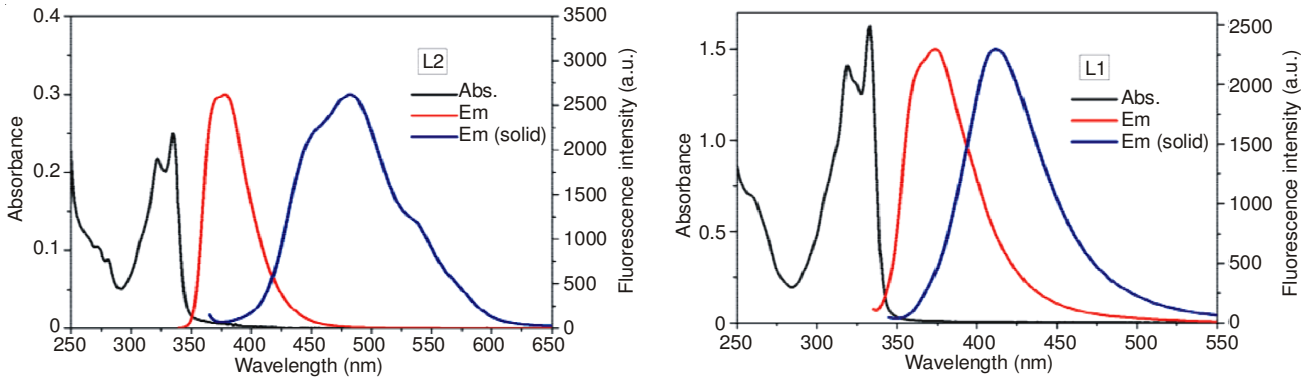


Fig. 1. UV-visible absorption (left) and emission spectra (right) of **L1** and **L2** in CH_2Cl_2 measured at a concentration of 1×10^{-5} mol/L at 25 °C

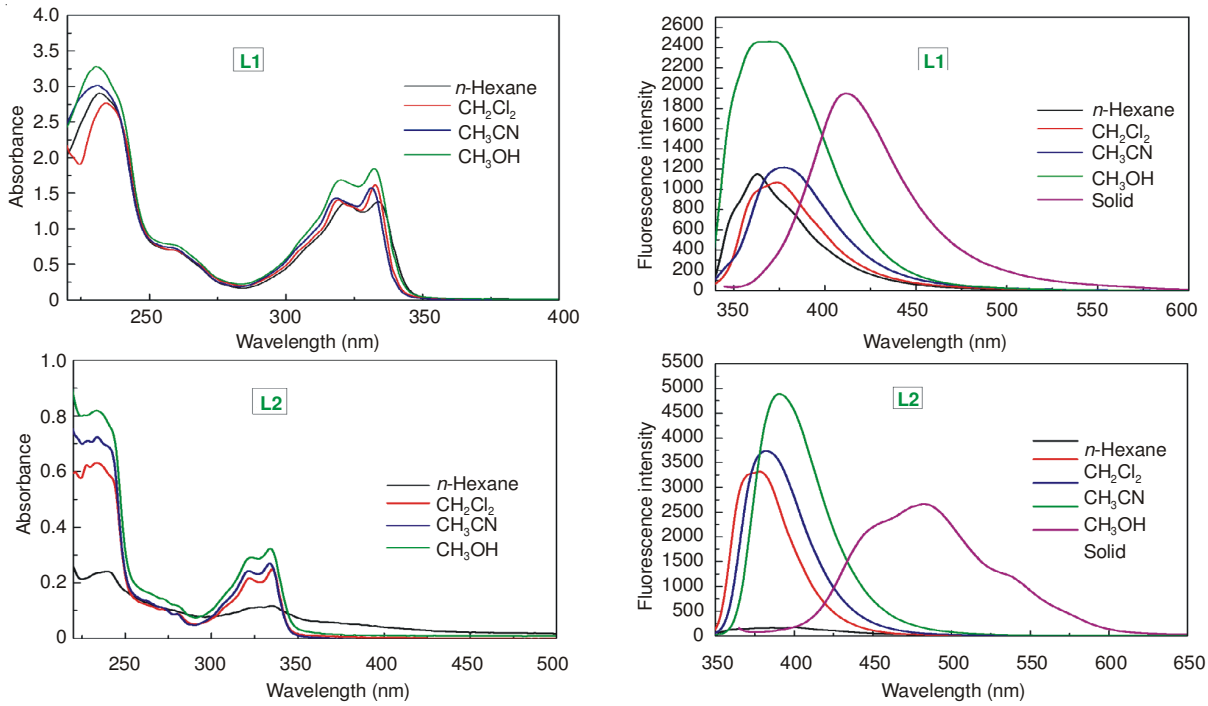


Fig. 2. Absorption (left) and fluorescence (right) spectra of **L1** and **L2** in various solvents and solid

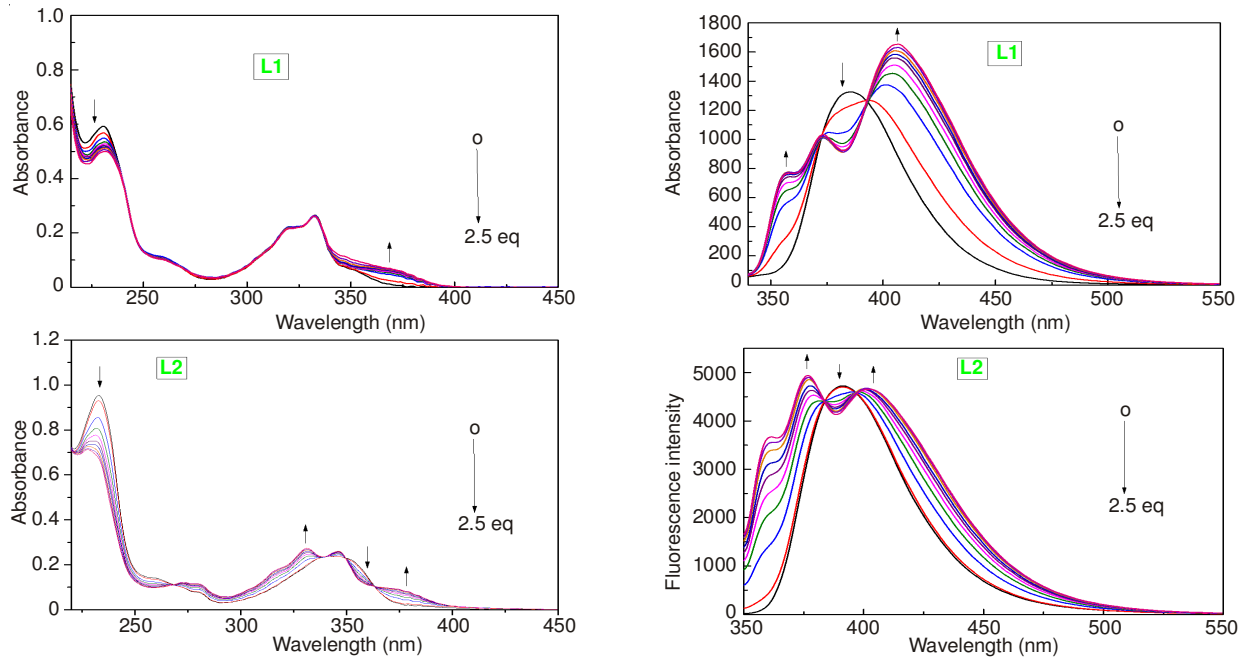


Fig. 3. UV-visible absorption (left) and fluorescence (right) spectra of **L1** and **L2**, upon addition of HBF_4 in CH_3OH. Measured at a concentration of 2×10^{-5} mol/L at 25 °C

the extremes of methanol and *n*-hexane were compared in Fig. 2. Moreover, the fluorescence intensity and the maximum of the low-energy absorption band of **L1** is insensitive to solvents. On the other hand, the emission spectra of **L1** and **L2** in solid feature a broad and structureless peak, with λ_{max} of 411 nm, 475 nm, respectively (Table-1). And it has appeared red shift 64 nm compared **L1** with **L2**.

Upon titration of **L1** and **L2** with HBF_4 as a proton source in CH_3OH, the absorptions of **L1** and **L2** have no significant change but all of them appear isosbestic points, (Fig. 3). The hydrogen ion associated with the naphthyrine moiety involves the promotion of the π_{napy}-π_{napy}* transition[22]. But **L1** and **L2** exhibits an attenuate emission with a λ_{max} at about 362 and 390 nm upon excitation at 330 nm at room temperature, respectively. They exhibits two enhanced emission with a λ at about 405 nm, 355 nm for **L1** and 405 nm, 370 nm for **L2** upon excitation at 330 nm at room temperature (Fig. 3). The variation range occurred for **L1** and **L2** though titrating of HBF_4 by 2.5 eq. The luminescence intensity was measured as a function of HBF_4 concentration and decreased with an increase in the degree of protonated nitrogen atoms on the naphthyridine ring. Compounds **L1** and **L2** can use as acid-controlled molecular switching on from the luminescence intensity change caused by proton source.

Conclusion

In summary, two new ligands based on 1,8-naphthyridine and modified with Boc-*L*-alanine named Boc-*L*-alanine-2-methyl-1,8-naphthyridine (**L1**) and Boc-*L*-alanine-2,4-dimethyl-1,8-naphthyridine (**L2**) were synthesized and characterized. Then, there absorption and fluorescence spectra in various solvents and solid are presented comprehensively. The two new ligands exhibit similar electronic absorption spectra with λ_{max} at 318 to 330 nm, which can be tentatively assigned to $\pi \rightarrow \pi^*$ transition. And the intense absorptions expressed the characteristic absorption peak of 1,8-naphthyridine which emerged abruption. And a comprehensive study of spectroscopic properties upon titration of **L1** and **L2** with HBF_4 as a proton source in CH_3OH was investigated.

ACKNOWLEDGEMENTS

This work is supported by the Natural Science Foundation of China (NSFC Grant No. 61361002), the Scientific Research Foundation of Education Department of Yunnan Provience (No. 2013FZ121) and the Chemistry of Key Construction Disciplines for Master Degree Program in Yunnan (No. HXZ1303).

REFERENCES

1. J.K. Bera, N. Sadhukhan and M. Majumdar, *Eur. J. Inorg. Chem.*, **2009**, 4023 (2009).
2. V. Litvinov, *Adv. Heterocycl. Chem.*, **91**, 189 (2006).
3. W.W. Paudler and R.M. Sheets, *Adv. Heterocycl. Chem.*, **33**, 147 (1983).
4. M. Andrews, R.H. Laye and S.J. Pope, *Transition Metal Chem.*, **34**, 493 (2009).
5. V.P. Litvinov, S.V. Roman and V.D. Dyachenko, *Russ. Chem. Rev.*, **69**, 201 (2000).
6. H. Araki, K. Tsuge, Y. Sasaki, S. Ishizaka and N. Kitamura, *Inorg. Chem.*, **46**, 10032 (2007).
7. C.X. Wang, Y. Sato, M. Kudo, S. Nishizawa and N. Teramae, *Chem. Eur. J.*, **18**, 9481 (2012).
8. Z. Li, W. Zhao, X. Li, Y. Zhu, C. Liu, L. Wang, M. Yu, L. Wei, M. Tang and H. Zhang, *Inorg. Chem.*, **51**, 12444 (2012).
9. Y. Zhou, Y. Xiao and X. Qian, *Tetrahedron Lett.*, **49**, 3380 (2008).
10. Y. Ferrand, A.M. Kendhale, J. Garric, B. Kauffmann and I. Huc, *Angew. Chem.*, **122**, 1822 (2010).
11. S.Z. Hu and C.F. Chen, *Chem. Commun.*, **46**, 4199 (2010).
12. Q. Gan, Y. Ferrand, N. Chandramouli, B. Kauffmann, C. Aube, D. Dubreuil and I. Huc, *J. Am. Chem. Soc.*, **134**, 15656 (2012).
13. H. Yamazaki, T. Hakamata, M. Komi and M. Yagi, *J. Am. Chem. Soc.*, **133**, 8846 (2011).
14. H.W. Tseng, R. Zong, J.T. Muckerman and R. Thummel, *Inorg. Chem.*, **47**, 11763 (2008).
15. D. Bhuniya, D. Umrani, B. Dave, D. Salunke, G. Kukreja, J. Gundu, M. Naykodi, N.S. Shaikh, P. Shitole, S. Kurhade, S. De, S. Majumdar, S.B. Reddy, S. Tambe, Y. Shejul, A. Chugh, V.P. Palle, K.A. Mookhtiar, D. Cully, J. Vacca, P.K. Chakravarty, R.P. Nargund, S.D. Wright, M.P. Graziano, S.B. Singh, S. Roy and T.-Q. Cai, *Bioorg. Med. Chem. Lett.*, **21**, 3596 (2011).
16. A. Capozzi, E. Mantuano, P. Matarrese, G. Saccomanni, C. Manera, V. Mattei, L. Gambardella, W. Malorni, M. Sorice and R. Misasi, *Anti-cancer Agents Med. Chem.*, **12**, 653 (2012).
17. Y. Chen, J.L. Li, G.S.M. Tong, W. Lu, W.-F. Fu, S.-W. Lai and C.-M. Che, *Chem. Sci.*, **2**, 1509 (2011).
18. A. Fernández-Mato, J.M. Quintela and C. Peinador, *New J. Chem.*, **36**, 1634 (2012).
19. Y.Y. Wu, Y. Chen, G.Z. Gou, W.-H. Mu, X.-J. Lv, M.-L. Du and W.-F. Fu, *Org. Lett.*, **14**, 5226 (2012).
20. G. Ligthart, H. Ohkawa, R.P. Sijbesma and E.W. Meijer, *J. Org. Chem.*, **71**, 375 (2006).
21. C.A. Anderson, P.G. Taylor, M.A. Zeller and S.C. Zimmerman, *J. Org. Chem.*, **75**, 4848 (2010).
22. W.F. Fu, L.F. Jia, W.H. Mu, X. Gan, J.-B. Zhang, P.-H. Liu, Q.-Y. Cao, G.-J. Zhang, L. Quan, X.-J. Lv and Q.-Q. Xu, *Inorg. Chem.*, **49**, 4524 (2010).
23. S.M. Chi, Y.F. Wang, X. Gan, D.-H. Wang and W.-F. Fu, *Cent. Eur. J. Chem.*, **7**, 923 (2009).
24. C. He, J.L. DuBois, B. Hedman, K.O. Hodgson and S.J. Lippard, *Angew. Chem. Int. Ed.*, **40**, 1484 (2001).
25. R.A. Henery and P.R. Hammond, *J. Heterocycl. Chem.*, **14**, 1109 (1977).
26. Y. Chen, W.F. Fu, J.L. Li, X.-J. Zhao and X.-M. Ou, *New J. Chem.*, **31**, 1785 (2007).
27. E.V. Brown, *J. Org. Chem.*, **30**, 1607 (1965).
28. W.W. Paudler and T.J. Kress, *J. Org. Chem.*, **32**, 832 (1967).
29. Z. Li, M. Yu, L. Zhang, M. Yu, J. Liu, L. Wei and H. Zhang, *Chem. Commun.*, **46**, 7169 (2010).