Synthesis, crystal structure and Cu^{2+} recognition of novel azobenzene derivatives

Wei Wang[a], Mingzhu Li[a], Xiaolong Yu[a], Qiang Zhang[a], Xiaoyu Jiang[a], Junwu Wang[a] and Yan Gao[b]*

[a]*School of Perfume and Aroma Technology, Shanghai Institute of Technology, Shanghai 200235, P.R. China*

[b]*Department of Chemical Engineering, University of Science and Technology Liaoning, Anshan, 114051, P.R. China*

Three novel azobenzene derivatives have been synthesised from (E)-4,4'-bischloroformyl azobenzene and arylamines. The crystal structure of (E)-[{diazene-1,2-diylbis(4,1-phenylene)}bis{(3,5-dimethyl-1H-pyrazol-1-yl)methanone}] has been obtained The UV-Vis and fluorescence spectral data of (E)-[{diazene-1,2-diylbis(4,1-phenylene)}bis-{(1H-imidazol-1-yl)methanone}] show that it can recognise selectively Cu^{2+} and a 1 : 2 stoichiometric complex is formed between the receptor and the cation.

Keywords: azobenzene, aromatic heterocyclic, X-ray crystal structure, recognition, copper ion

Copper, an essential trace element for plants and animals, is the third most abundant transition metal following zinc and iron in human bodies and plays a crucial role in many fundamental physiological processes in organisms.[1] However, exposure to a high level of copper even for a short period of time can cause gastrointestinal disturbance, while long-term exposure can cause liver or kidney damage. Due to this Janus-faced property of copper ion in organisms, considerable attention has been devoted to the design of efficient and selective fluorescence chemosensors for Cu^{2+}.[2–7]

Azobenzene derivatives, as ligands for transition metal ions, have been widely employed in coordination chemistry and supra-molecular chemistry. Although there are a few reports of azobenzene derivatives in selective detection of heavy metal cations,[8,9] there still is a need for alternative systems to selectively recognise Cu^{2+} for environmental or biological applications. We describe here a comprehensive study of several azobenzene derivatives bearing aromatic heterocyclic substituents (Scheme 1). Their metal-binding properties toward cations showed that compound **3a** displays a highly selective and sensitive response towards Cu^{2+} in DMF and H_2O.

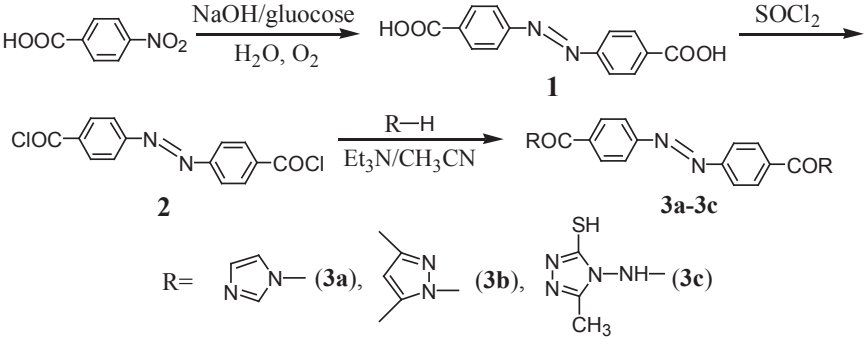
Results and discussion

The target products were synthesised using a three-step procedure as shown in Scheme 1: (i) synthesis of (E)-4,4′-bicarboxyl azobenzene **1** *via* the reduction reaction of 4-methylbenzoic acid; (ii) synthesis of (E)-4,4′-bischloroformyl azobenzene **2** by chlorination reaction of **1** with thionyl chloride; (iii) synthesis of azobenzene derivatives (**3a–c**) by nucleophilic substitution reaction of **2** with different arylamines. The crude products were purified by column chromatography and the differently coloured, solid products were obtained. The target compounds were characterised by elemental analysis, ^{1}H NMR, ^{13}C NMR, IR, and MS; the spectral data were in agreement with the proposed structures.

Crystal data for compound **3b** are shown in Table 1. Single crystal X-ray diffraction studies were performed on a Bruker Smart 1000 CCD diffractometer with MoKα radiation (λ = 0.71073 Å). The structures were solved by direct methods and semi-empirical absorption corrections were applied. All

Table 1 Crystal data and structure refinement for compound **3b**

Molecular formula	$C_{24}H_{22}N_6O_2$
Molecular weight	426.48
Temperature/K	113(2)
Radiation λ	0.71073
Crystal system	Monoclinic
Space group	P2(1)/n
a/Å	3.8560(3)
b/Å	20.0439(17)
c/Å	26.915(2)
V/Å^3	2079.3(3)
Z	4
D calcd/g cm^{-3}	1.362
Crystal size/mm	0.18 × 0.05 × 0.04
Crystal colour	Colourless
Absorption coefficient/mm^{-1}	0.091
Absorption correction T_{min} and T_{max}	0.9838 and 0.9964
F(000)	896
Reflections collected/unique	13446/3690 [R(int) = 0.0550]
Range/indices (*h*, *k*, *l*)	−4,4; −21,23; −32,32
θ limit (°)	1.51 to 25.02
No. of observed data, $I > 2\sigma(I)$	3690
No. of restraints	0
Goodness of fit on F^2	1.1816
R^1, wR^2 [$I \geq 2\sigma(I)$]	0.0618, 0.1191
R^1, wR^2 (all data)	0.0768, 0.1261



Scheme 1 Synthesis of azobenzene derivatives **3a–c**.

* Correspondent. E-mail: gys20080901@126.com

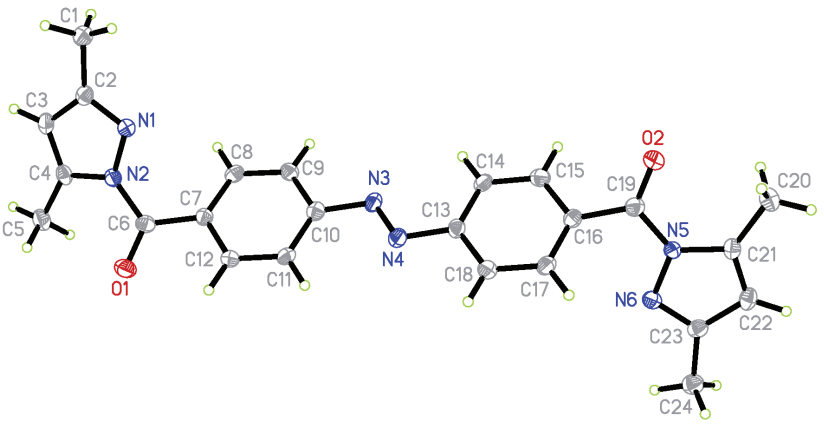


Fig. 1 ORTEP structure of compound **3b**, showing 50% probability ellipsoids.

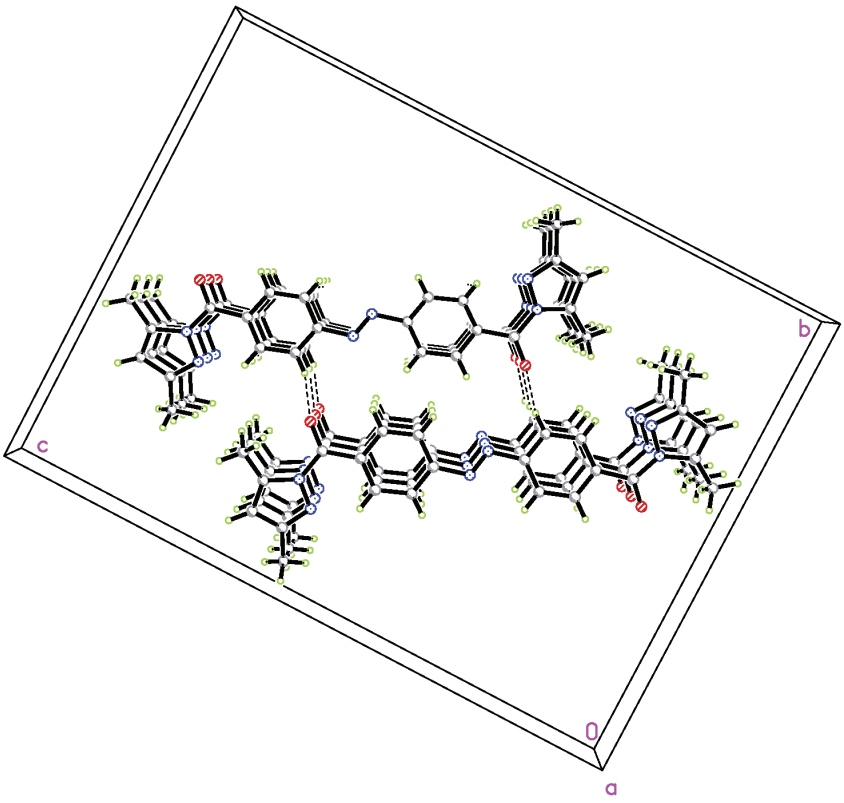


Fig. 2 A section of the crystal packing of the title compound, viewed down the *a*-axis. Dashed lines denote the intermolecular C18–H18···O1 hydrogen bonds.

H atoms were geometrically positioned and refined as riding (C–H = 0.95–0.98 Å) and allowed to ride on their parent atoms, with Uiso (H) = 1.2 or 1.5 Ueq (parent). Further details of the structural analyses are summarised in Table 1. The molecular structure of **3b** and atom-numbering scheme are shown in Fig. 1.

In the structure of compound **3b**, the diphenyldiazene section was almost coplanar with a mean derivation of 0.0293 Å. At the end of the structure, two planar pyrazole rings (mean derivations of 0.0035 Å for the ring C2/C3/C4/N1/N2 and 0.0005 Å for the ring C21/C22/C23/N5/N6, respectively) lie to the opposite sides of the plane with a dihedral angle of 13.0°. In the crystal (Fig. 2), inversion-related molecules are linked by pairs of intermolecular C18–H18···O1 hydrogen bonds, forming a cyclic dimer with an R22(30) graph-set motif, which further stabilises the molecular structure.

The complexation properties of compound **3a** were investigated toward various heavy and transition metal cations (Ca^{2+}, Cd^{2+}, Cu^{2+}, Hg^{2+}, Mn^{2+}, Ni^{2+}, Pb^{2+}, Zn^{2+}, Mg^{2+}, Na^{+}, Al^{3+}, Fe^{3+}, Ag^{+}) by UV-Vis spectroscopy. As shown in Fig. 3, the maximum band of compound **3a** occurs at 340 nm. When Cu^{2+} was added, the original peak was increased, whereas negligible changes were observed with the other metal ions. Thus, it may be concluded that compound **3a** has special selectivity and sensitivity to Cu^{2+}.

The fluorescence enhancement effects of Cu^{2+} ions on compound **3a** in DMF/aqueous media were investigated as shown in Fig. 4.

In the fluorescence spectrum, compound **3a** exhibits a weak fluorescence emission at 436 nm in aqueous DMF media. When Cu^{2+} was added to compound **3a**, the fluorescence intensity was enhanced remarkably. An emission change of nine-fold was observed for Cu^{2+}. The fluorescence enhancement observed for **3a** is attributed to the formation of the **3a**–Cu^{2+} complex as a result of which the PET from sulfur atoms to the

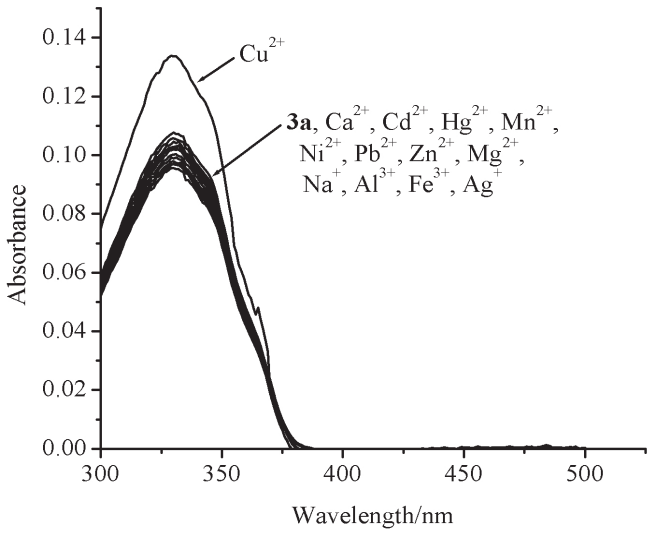


Fig. 3 UV-Vis spectra of compound **3a** (10 μM) upon addition of various ions (20 μM) in DMF and H_2O (v/v = 1/1).

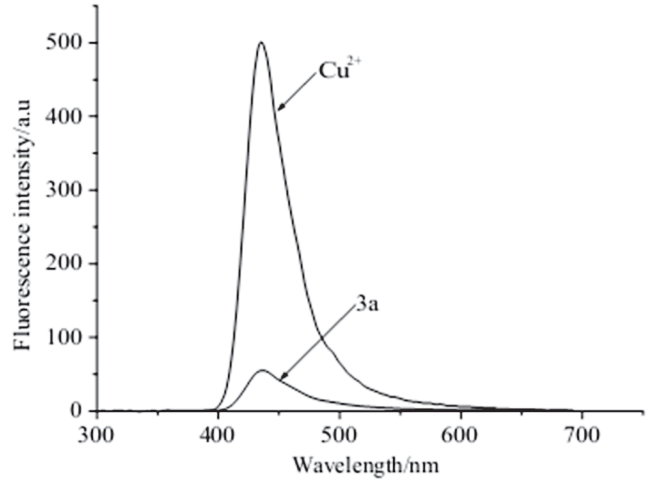


Fig. 4 Fluorescence emission spectra of compound **3a** (10 μM) upon addition of Cu^{2+} (20 μM) in DMF and H_2O (v/v = 1/1).

imidazole moiety was suppressed, resulting in the fluorescent enhancement.

The titration of compound **3a** by Cu^{2+} with an excitation at λ_{ex} = 393 nm, given in Fig. 5 as an example, exhibited an increase of its emission intensity at 436 nm. According to the titrations, we determined an association constant of compound **3a** ($Ka = 2.49 \times 10^5\ M^{-2}$) for Cu^{2+}.

Fitting the changes in fluorescence spectra of compound **3a** with Cu^{2+} ions, we applied the method of continuous variation (Job's plot) to prove the complexation ratio between compound **3a** and Cu^{2+} ions. As shown in Fig. 6, the maximum point at the mole fraction of 0.67 indicates that the complexation ratio of compound **3a** and Cu^{2+} is 1 : 2.

In conclusion, we have synthesised three novel azobenzene derivatives **3a–c** with different arylamines. The structures of target compounds were clearly identified by ^1H NMR, ^{13}C NMR spectroscopy, elemental analysis and the structure of **3b** has been unambiguously confirmed by X-ray crystallography. The UV and fluorescence spectra data indicated that compound **3a** could recognise $Cu^{2+}$and a 1 : 2 stoichiometric complex was formed between the receptors and the cation.

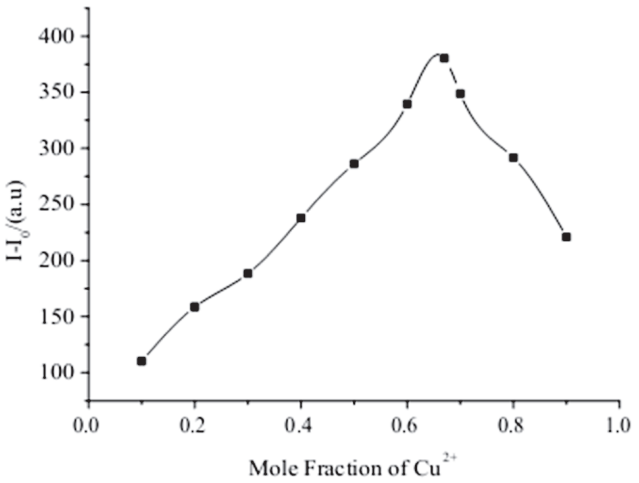
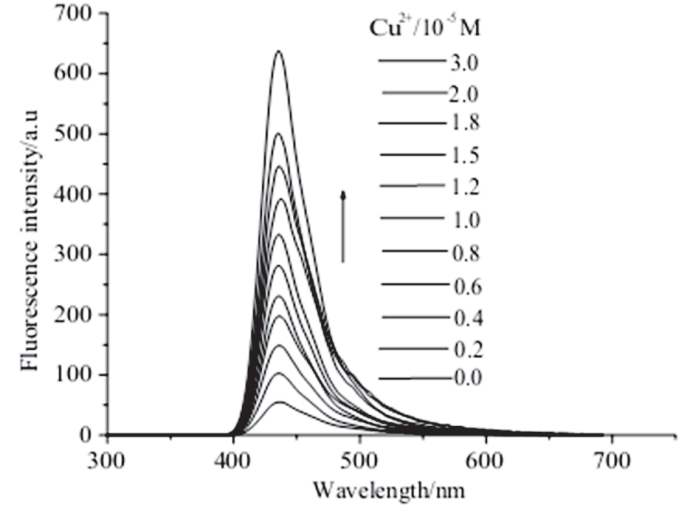


Fig. 6 Job's plot for determining the stoichiometry of receptor **3a** and Cu^{2+} ion in DMF and H_2O (v/v = 1/1). [I and I_0 are the fluorescence intensity of **3a** in the presence and absence of Cu^{2+}, respectively, the total concentration of **3a** and Cu^{2+} ion was 0.1 mM (λ_{ex} = 393 nm)].



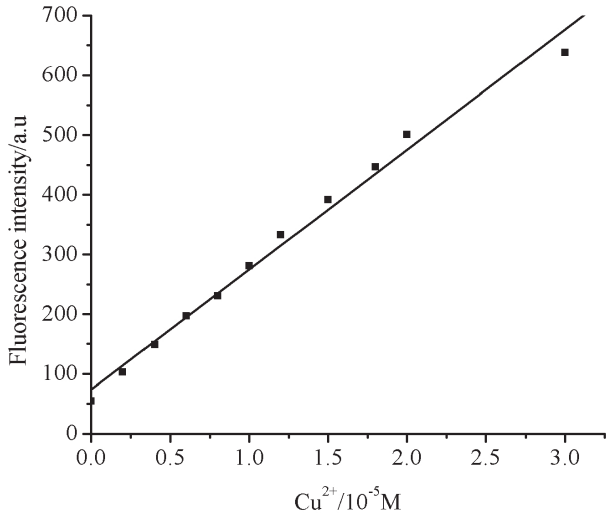


Fig. 5 Fluorescence emission spectra of compound **3a** (10 μM) for Cu^{2+} ion titration in a mixture of DMF/H_2O (v/v = 1/1)(λ_{ex} = 393 nm).

Experimental

3-Methyl-4-amino-5-mercapto-1,2,4-triazole,[10] 3,5-dimethyl-1-H-pyrazole,[11] and (E)-4,4′-bicarboxyl azobenzene[12] were prepared according to literature procedures, other reactants and chemicals were purchased from Aladdin. Solvents were of analytical grade. ^{1}H NMR and ^{13}C NMR spectra were recorded at room temperature on a Bruker Avance-500 NMR spectrometer. DMSO-d6 and $CDCl_3$ were used as solvents and tetramethylsilane (TMS) as internal standard. Mass spectral data were obtained on an Agilent 1100 LC/MS. IR spectra were obtained with a Perkin Elmer spectrophotometer. Elemental analyses were made with a CHN Analyser (Thermo Finnigan Company). UV-Vis absorption spectra were recorded at room temperature on a Lambda-900 spectrometer. The fluorescence emission spectra were measured on a LS-55 spectrometer.

Synthesis of compounds **3a–c***; general procedure*

(E)-4,4′-Bischloroformyl azobenzene **2** (0.8 mmol) was added to a mixture of corresponding arylamine (1.6 mmol), Et_3N (1.6 mmol) in CH_3CN (25 mL) and the mixture was refluxed for 8 h. The mixture was then cooled and filtered and the crude product was purified on a silica gel column using petroleum ether/ethyl acetate (from 10/1 to 4/1, v/v). The products were obtained as differently-coloured solids.

(E)-(Diazene-1,2-diylbis(4,1-phenylene))bis-((1H-imidazol-1-yl) methanone) (**3a**): Yield 69.2%; m.p. 243–245 °C; IR (KBr, cm^{-1}): 3109, 2947, 2883, 1697, 1600, 1464, 1288, 789, 698; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.181 (d, 4H, J = 8.5, PhH), 8.030 (d, 4H, J = 8.5, PhH), 7.847 (s, 2H, imidazole-H), 7.111 (d, 4H, J = 7.5, imidazole-H); ^{13}C NMR (500 MHz, $CDCl_3$): δ_C (ppm) 167.21, 154.61, 135.55, 134.27, 131.11, 123.23, 122.00; MS, *m/z*: 371 (M+H$^+$); Anal. calcd for $C_{20}H_{14}N_6O_2$: C, 64.86; H, 3.81; N, 22.69; found: C, 64.82; H, 3.84; N, 22.73%.

(E)-(Diazene-1,2-diylbis(4,1-phenylene))bis((3,5-dimethyl-1H-pyrazol-1-yl)methanone) (**3b**): Yield 74.5%; m.p. 193–195 °C; IR (KBr, cm^{-1}): 3028, 2975, 2878, 1702, 1585, 1481, 1439, 1376, 1202, 855, 774; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.166 (d, 4H, J = 8.0, PhH), 8.031 (d, 4H, J = 8.0, PhH), 6.102 (s, 2H, pyrazole-H), 2.666 (s, 6H, CH_3), 2.268 (s, 6H, CH_3); ^{13}C NMR (500 MHz, $CDCl_3$): δ_C (ppm) 167.63, 154.31, 152.52, 145.20, 135.75, 132.33, 122.34, 111.36, 14.32, 13.84; MS, *m/z*: 427(M+H$^+$); Anal. calcd for $C_{24}H_{22}N_6O_2$: C, 67.59; H, 5.20; N, 19.71; found: C, 67.54; H, 5.18; N, 19.75%.

(E)-4,4′-(Diazene-1,2-diyl)bis(N-(3-mercapto-5-methyl-4H-1,2,4-triazol-4-yl)benzamide)(**3c**): Yield 73.8%; m.p. >300 °C; IR (KBr, cm^{-1}): 3362, 3081, 2974, 2878, 1694, 1594, 1499, 1407, 1352, 1205, 854, 721; ^{1}H NMR (500 MHz, DMSO-d6): δ 13.787 (s, 1H, NH), 12.083 (s, 1H, NH), 8.124 (d, 4H, J = 8.5, PhH), 8.027(d, 4H, J = 8.5, PhH), 2.891 (s, 3H, CH_3), 2.732 (s, 3H, CH_3); ^{13}C NMR (500 MHz, DMSO-d6): δ_C (ppm) 167.42, 154.83, 152.59, 133.47, 130.63, 122.85, 121.59; MS, *m/z*: 495(M+H$^+$); Anal. calcd for $C_{20}H_{18}N_{10}O_2S_2$: C, 48.57; H, 3.67; N, 28.32; found: C, 48.52; H, 3.69; N, 28.35%.

We acknowledge the financial support of the Key Laboratory Project (2008S127) and the Initial Fund for Young Teachers of University of Science and Technology Liaoning (008131).

Received 29 September 2013; accepted 19 December 2013
Paper 1302208 doi: 10.3184/174751914X13893754559598
Published online: 5 February 2014

References

1 L.J. Tang, F.F. Li, M.H. Liu and R. Nandhakumar, *Bull. Korean. Chem. Soc*., 2010, **31**, 3212.
2 Y. Xiang, A. Tong, P. Jin and Y. Ju, *Org. Lett*., 2006, **8**, 2863.
3 Y. Xiang, Z. Li, X. Chen and A. Tong, *Tetra. Lett*., 2008, **74**, 1148.
4 Y. Zhou, F. Wang, Y. Kim, S.J. Kim and J. Yoon, *Org. Lett*., 2009, **11**, 4442.
5 M. Royzen, Z. Dai and J.W. Cannry, *J. Am. Chem. Soc*., 2005, **127**, 1612.
6 X. Zhang, Y. Shiraishi and T. Hirai, *Org. Lett*., 2007, **9**, 5039.
7 G.H. Wu, D.X. Wang, D.Y. Wu, Y. Gao and Z.Q. Wang, *J. Chem. Sci*., 2009, **121**, 543.
8 G.K. Lahiri, S. Bhattacharya, M. Mukherjee, A.K. Mukhejee and A. Chakravorty, *Inorg. Chem*., 1987, **26**, 3359.
9 K.E. Besslera, J.A. Santosa, V.M. Deflona, S.S. Lemosa and E. Niquet, *Z. Anorg. Allg. Chem*., 2004, **630**, 742.
10 S.X. Zhang, X.L. Wu, Z.P. Dai, X.C. Liao and J.S. Lu, *Chin. J. Org. Chem*., 2008, **28**, 1111.
11 H.S. Chandak, N.P. Lad and D.S. Dange, *Green Chem. Lett. Rev*., 2012, **2**, 135.
12 Y. Okahata, H. Lim and S. Hachiya, *J. Chem. Soc. Perkin Trans. 2*, 1984, **6**, 989.