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Efficient synthesis of metallated thioporphyrazines in task specific ionic liquids and their spectroscopic investigation of binding with selected transition metal ions

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Abstract. Tetramerization of substituted maleonitriles in task specific 2-hydroxylethyl based imidazolium ionic liquids at 120°C gave corresponding electron rich peripheral substituted thioporphyrazines in moderate yield. The 2-hydroxylethyl imidazolium ionic liquids gave better yields of peripheral substituted thioporphyrazines in comparison with non-hydroxyl functionalized ionic liquids. Further, these peripherally functionalized porphyrazines containing sulphur are used to investigate spectroscopically the binding studies with palladium(II) and mercury(II) ions. These metal ions are toxic in nature and deserve serious attention in the area of design of effective separation and efficient micro-sensing techniques. The UV–Vis absorption spectroscopy and fluorescence signalling are mainly used to study peripheral binding of transition metal ions.

Keywords. Thioporphyrazines; tetramerization; metal salts; ionic liquids; transition metal; sensors.

1. Introduction

Porphyrazines[1] are porphyrin variants in which the carbon at *meso* positions are replaced with nitrogen. Porphyrazines have found wide applications in diverse areas such as elaboration of chemical sensors,[2–4] nonlinear optical materials,[5,6] biomedical agents for diagnosis, therapy[7] and as sensitizers in dye-sensitized solar cell applications.[8–11] The structure–property relationship of these materials in their redox properties, conductivity and photoconductivity makes them promising materials within a number of devices and also for singlet oxygen production in photodynamic therapy.[12] Porphyrazines substituted with long alkyl or alkyloxy chains result in suitable soluble products for applications in liquid crystals and Langmuir–Blodgett layers, and fusion of heterocyclic or macrocyclic units onto the core enables them to enhance their physical properties[13–16] The presence of soft S donor atoms in porphyrazines plays an important role in affecting the solid state interactions.[17]

In this paper, we are reporting the novel methodology for the synthesis of thiaporphyrazines-based receptors under milder conditions for selective binding with transition metal ions that are toxic in nature. Peripherally functionalized porphyrazines have been prepared in moderate yields using task specific ionic liquids from a range of maleonitriles *via* cyclotetramerization around a metal in hydroxylated ionic liquid using hexamethyldisilazane (HMDS) at 120°C. Thiaporphyrazines of the form M[pz(X_n:Y_{4-n})], in which X and Y symbolize functional groups fused directly to the β-positions of the pyrrole rings are synthesized.

The peripheral X moieties mainly involving sulphur as a heteroatom appended to the porphyrazine ring are designed in order to bind toxic metal ions, such as mercury(II) and palladium(II). These metal ions are highly toxic in nature and deserve serious attention in the area of design of effective separation and efficient micro-sensing techniques. Several approaches such as atomic absorption, inductively coupled plasma-mass atomic emission, fluorescence and UV–Vis absorption are known to detect trace amount of metal ions. Among these techniques, UV–Vis absorption spectroscopy and fluorescence signalling are foremost choices as they are highly sensitive and simple to distinguish the chemical and physical changes associated with metal binding with excellent selectivity, shorter response times and low detection limits.

2. Experimental

2.1 *Materials and Methods*

The ^{1}H NMR and ^{13}C NMR spectra were recorded on Jeol 400 MHz spectrometer using TMS as internal

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standard and the chemical shifts (δ) are expressed in ppm. IR spectra were recorded on a Perkin–Elmer Spectrum 2000 infrared spectrophotometer. UV/Vis spectra were recorded on a Perkin–Elmer Lambda 35 UV/Vis Spectrophotometer. The flourscence spectra were recorded on Cary Eclipse Flourscence Spectrophotometer. The mass spectra (EI-MS) were recorded on a Jeol SX-102DA-6000 (6 kV, 10 mA) spectrometer and ESI-MS spectra were recorded on a Micromass LCT KC 455 spectrometer (+ve mode). All the melting points were determined on a Thomas Hoover unimelt capillary melting point apparatus. Dimethyformamide, sodium cyanide, carbon disulphide, diaminomaleonitrile, α-diketone, HMDS and zinc chloride were obtained from Spectrochem Pvt. Ltd. Thiophosgene, palladium chloride were obtained from Aldrich. bmim[OH] and bmim[Br] were prepared according to the literature methods.[18] 1,2-Dicyano-1,2-bis(methylthio)ethylene was prepared by reaction of methyl iodide with Sodium maleonitrile dithionate (Na_2mnt) by literature procedure.[19]

2.2 *Synthesis of porphyrazine derivatives*

To a mixture of derivative of maleonitrile (**1a**–**1c**, **2**–**6)** (2 mmol), metal salts (1 mmol) and HMDS (8 mmol), functional ionic liquid (1 mL) was added and the reaction mixture was stirred at 120°C under a nitrogen atmosphere for the appropriate time (see Tables 1 and 2). The progress of the reaction was monitored by TLC and UV/Vis spectroscopic analysis. After the reaction was complete, the mixture was extracted with chloroform and the filtrate was concentrated under reduced pressure. The resulting oily liquid was chromatographed over silica gel (60–120 mesh) and the column was eluted with petroleum ether–chloroform (9:1). The front running blue color band was collected and evaporated to dryness under reduced pressure to get the corresponding Zn-porphyrazine.

3. Results and Discussion

3.1 *Synthesis and characterization*

The tetramerization of substituted maleonitriles in the presence of base HMDS and various template metal salts has been carried out in basic ionic liquids to give different metalloporphyrazines in good yields (Scheme 1). The reaction of maleonitrile **1a**, various template metal salts and base (HMDS) in functional ionic liquids (bmim[Br] and bmim[OH]) at 120°C gave zinc(II) porphyrazine **7a** as blue-green color solid in 28% and 45% yield, respectively (Table 1). The formation of **7a** was confirmed by various spectroscopic analysis. The UV-Vis spectra of 7**a** in $CHCl_3$ showed the Soret and Q-bands at 369 nm and 666 nm arising from $\pi - \pi*$ and $n - \pi*$ transitions of the tetraazamacrocycle ring, respectively mention (Figure S1, in S1).[20] In the IR spectrum of metallated porphyrazine **7a**, the disappearance of the intense -CN stretching vibration of precursor maleonitrile at ~2200 cm^{-1} gave the clear evidence for tetrapyrrole formation. Further, the characteristic NH stretching vibration of the inner core at 3285 cm^{-1} for unmetallated porphyrazine was also absent which further confirmed the formation of metallated porphyrazine. In the ^{1}H NMR spectrum of **7a**, the S–CH_3 protons were observed at 3.04 ppm. Further, ESI-MS spectrum of **7a** showed a peak at m/z 744.92 corresponding to [M + H^+], confirming the formation of **7a**.

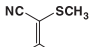
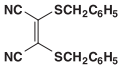
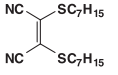
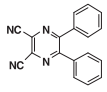
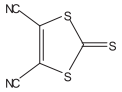
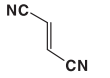
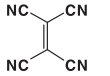
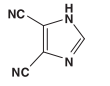
To explore the role of functional ionic liquids and HMDS, the reactions of **1a** were performed in DMF,

Table 1. Reactions of 1,2-Dicyano-1,2-*bis*(methylthio)-ethylene **1a** in presence of metal salts under different reaction conditions at 120°C.

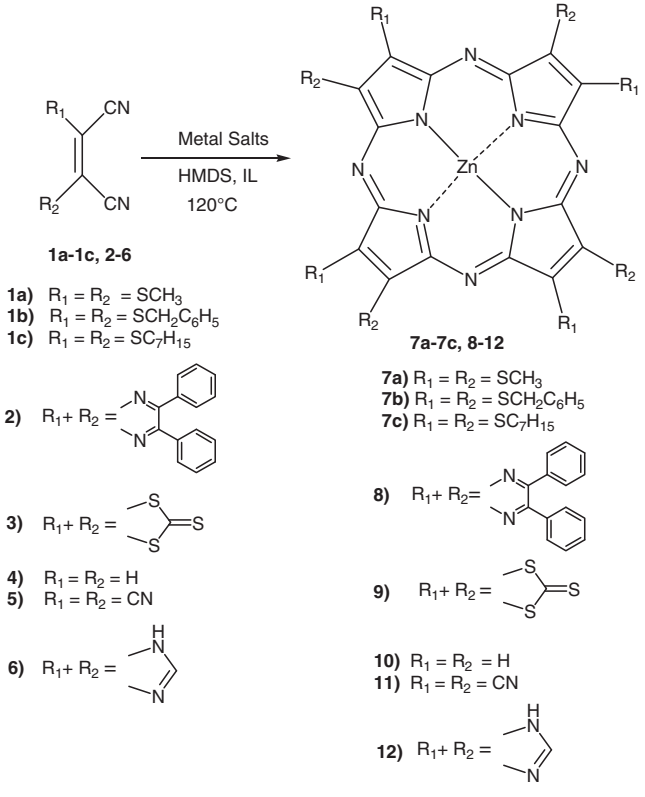
Entry	Substrate	Reaction medium	Metal Salt	HMDS (equiv.)	Time h	Product	Yield[a](%)
1.	**1a**	DMF	$Zn(OAc)_2.2H_2O$		24	**7a**	–
2.	**1a**	DMF	$Zn(OAc)_2.2H_2O$	4.0	24	**7a**	–
3.	**1a**	bmim [Br]	$Zn(OAc)_2.2H_2O$		24	**7a**	–
4.	**1a**	bmim [Br]	$Zn(OAc)_2.2H_2O$	4.0	24	**7a**	28[23]
5.	**1a**	bmim [OH]	$Zn(OAc)_2.2H_2O$		24	**7a**	8
6.	**1a**	bmim [OH]	$Zn(OAc)_2.2H_2O$	2.0	8	**7a**	35
7.	**1a**	bmim [OH]	$Zn(OAc)_2.2H_2O$	4.0	8	**7a**	45
8.	**1a**	bmim [OH]	$Zn(OAc)_2.2H_2O$	4.0	24	**7a**	48
9.	**1a**	bmim [OH]	$Zn(OAc)_2.2H_2O$	6.0	8	**7a**	50
10.	**1a**	bmim [OH]	–	6.0	24	**7a**	–
11.	**1a**	bmim [OH]	$Co(OAc)_2.7H_2O$	4.0	8	**13a**	38[23]
12.	**1a**	bmim [OH]	$Ni(OAc)_2.2H_2O$	4.0	8	**14a**	41[23]

[a] isolated yield.

Table 2. Synthesis of functional Zn(II)porphyrazines (**7–12**) in bmim[OH] in presence of $Zn(OAc)_2$ at 120°C.

Entry	Maleonitrile derivatives	Time h	Product	Yield[a](%)
1.		8	**7a**[32]	48
2.		8	**7b**[32]	41
3.		8	**7c**	44
4.		8	**8**[33]	28
5.		8	**9**	22
6.		24	**10**	–
7.		24	**11**	–
8.		24	**12**	–

[a] isolated yield.



Scheme 1. Synthesis of substituted porphyrazines.

bmim[Br] and bmim[OH], using different molar ratio of HMDS. The formation of Zn(II)porphyrazine was not observed in the reaction using DMF or bmim[Br] in the absence of HMDS (Table 1, Entries 1 and 3), while the similar reaction in presence of bmim[OH] and $Zn(OAc)_2.2H_2O$ at 120°C gave **7a** in 8% yield (Table 1, Entry 5). On addition of HMDS upto 4.0 equiv., the yield of **7a** increased from 0 to 28% in bmim[Br] (Table 1, Entry 4) and 8 to 45% in bmim[OH] (Table 1, Entry 7). On the other hand, formation of product was not observed on addition of 4.0 equiv. of HMDS using DMF as solvent (Table 1, Entry 2). Therefore, the ionic liquid bmim[OH] is the more effective reaction medium in comparison to bmim[Br] and promotes the synthesis of metal porphyrazine in absence or presence of HMDS. Further, on increasing the amount of HMDS to 6.0 equiv in bmim[OH], the yield of **7a** increased to 50% (Table 1, Entry 9), and no further increase in the yield of Zn(II)porphyrazine was observed on increasing further the amount of HMDS.

Further, the conditions for the synthesis of metal porphyrazines in bmim[OH] were optimized. The reaction was sluggish at room temperature or temperature below 100°C. In the absence of either the metal template (Table 1, Entry 10) or the ionic liquid (Table 1, Entries 1–2), the reaction did not occur. The reaction, after workup and column purification through neutral alumina, afforded the symmetrical porphyrazine Zn in 22–50% yield. The change in the molar equivalents of HMDS, reaction time and reaction temperature affects the yield of Zn(II)porphyrazine **7a** (Table 1, Entries 3–9). The maximum yield (50%) of **7a** was obtained

when a mixture of one equivalent of **1a**, 6 equivalents of HMDS, 0.5 equivalent of $Zn(OAc)_2$, in 1 g (for 250 mg) of bmim[OH] was heated at 120°C for 8 h (Table 1, Entry 9). By using this method, metalloporphyrazines can be directly synthesized in higher yields under milder conditions, which was not possible in any of the earlier methods.[21,22] The present method was also utilized for the synthesis of porphyrazines containing different transition metals (M = Zn, Co, Ni) in bmim[OH]. By changing the divalent metal ion from Zn, Co to Ni at the centre of porphyrazine 48%, 38%, 41% yield of **7a, 13a, 14a** were obtained, respectively (Table 1, Entries 8–12).

The same reaction procedure was extended to substituted maleonitriles such as 2,3-*bis*(benzylthio) maleonitrile **1b**, 2,3-*bis*(heptylthio)maleonitrile **1c**, 2,3-dicyano-5,6-diphenylpyrazine **2**, 4,5-dicyano-1,3-dithiole-2-thione **3**, fumaronitrile **4**, tetracyanoethylene **5**, and 1*H*-imidazole-4,5-dicarbonitrile **6**, with $Zn(OAc)_2$ using HMDS in presence of bmim[OH] at 120°C. It was observed that, fumaronitrile **4**, tetracyanoethylene **5** and the five-membered maleonitrile such as 1*H*-imidazole-4,5-dicarbonitrile **6** showed no formation of the corresponding porphyrazines,[24] while 2,3-*bis*(methylthio)maleonitrile **1a**, 2,3-*bis*(benzylthio) maleonitrile **1b**, 2,3-*bis*(heptylthio)maleonitrile **1c**, 2,3-dicyano-5,6-diphenylpyrazine **2** and 4,5-dicyano-1,3-dithiole-2-thione **3** gave symmetrical Zn porphyrazine in 48%, 41%, 44%, 28% and 22% yields, respectively (Table 2). The structures of the products were characterized by various spectroscopic analysis.

The exact mechanism for the formation of a porphyrazine from a dinitrile is still unknown as no formal studies on the mechanism have been reported so far. At 120°C, HMDS can act as a source of nucleophilic nitrogen and react with dialkylmaleonitrile to give 5-amino-2-imino-3,4-dialkyl-2*H*-pyrrole which can more actively participate in tetramerization in presence of metal template leading to the formation of metal porphyrazine.

3.2 *Peripheral binding of transition metal salts with metal porphyrazines*

The Pd(II) complexes are suitable for investigating the self assembly processes in solution *via* titration experiments.[25–27] The formation of the exocyclic Pd(II) adducts of all porphyrazine macrocycles significantly alters the electronic spectra by diminishing $n - \pi*$ transitions and a sharpening of the Q band[28] which is evident in the UV-Vis spectral studies of [2,3,7,8,12,13, 17,18-Octakis(heptylthio)-5,10,15,20-porphyrazinato] zinc(II) **(7c).** The main possibility of the binding of Pd(II) ion to complex **7c** will occur at the thio group.[29–31] On addition of four equivalents of Pd(II) at concentration 1×10^{-5} M to a 1×10^{-5} M solution of **7c** different spectral changes were observed (Figure 1). Initially, a decrease in the Q band intensity at 676 nm in $CHCl_3$ accompanied by broadening and shifting of the band to low energy, at 735 nm was observed on addition of 0.8 equivalents of Pd(II) to a solution of **7c** (Figure S6 a, in Supplementary Information). This broadening with simultaneous splitting of the Q-band which is generally observed for macrocycles of less than D_{4h} symmetry, is most likely due to the overlap of underlying $n - \pi^*$ transitions that arise from the nonbonding electrons associated with the peripheral sulphur atoms. These spectral changes are consistent with formation of aggregates observed on metal binding in thio-substituted MPz complexes. The lack of clear isosbestic points, suggests that there may be more than two species or higher aggregates in solution. Further addition of 2.0 equivalents of Pd(II) resulted in blue shift of the broad peak at 735 nm to 722 nm and the formation of a split peak with maximum at 683 nm (Figure S6 b in SI). The observed split in Q band suggests that the Pd(II) ions are coordinated unsymmetrically with the heptylthio groups present at the periphery of Zn-porphyrazine complex. Again, on further addition of 4.0 equivalents of Pd(II), the gradual disappearance of the split Q bands at 722 nm and 683 nm with decreased absorbance and the simultaneous appearance of a new maximum which is less broad at 648 nm occurred (Figure S6 c, in SI), suggesting the binding of four Pd(II) ions at this stage. The removal of the broadening of the Q-band is directly associated with the peripheral metallation since the sulphur lone pairs can no longer interact with the porphyrazine core.[27]

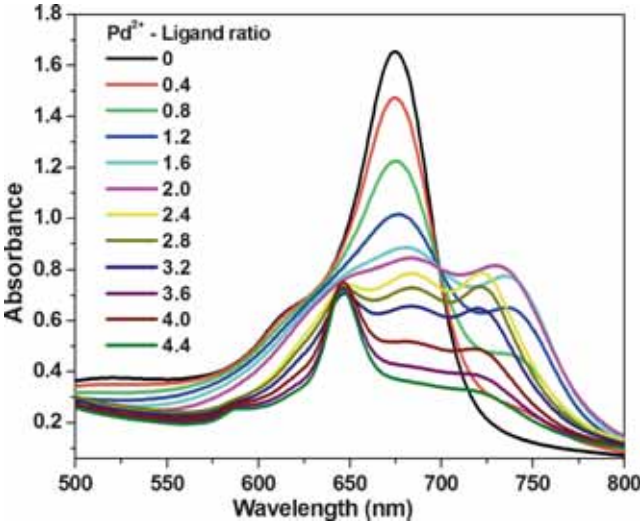


Figure 1. UV–Vis spectral changes observed on addition of Pd(II) [1×10^{-5} M] to **7c** [1×10^{-5} M] in $CHCl_3$.

Further, spectrofluorometric studies were also used for investigation of metal to ligand coordination in ZnPz (**7c**). When excited at 374 nm, the fluorescence spectrum of **7c** in CH_2Cl_2 showed fluorescence peaks at 461, 436, 414 and 749 nm. Upon stepwise addition of $PdCl_2$ to **7c** quenching of peaks at 461, 436, 414 nm were observed. The peak at 749 nm showed a red shift to 751 nm with increase in fluorescence intensity. Apart from all the above changes a new peak at wavelength 655 nm also appeared which on increasing the concentration of $PdCl_2$, red shifted and showed increase in fluorescence intensity with maximum at 659 nm indicating the binding of Pd(II) ion to the heptylthio groups of **7c** (Figure 2).

Similar experiment was performed with **7a** using Pd(II) ion which showed a red shift in Q-band from 666 nm to 680 nm with a decrease in intensity and appearance of a new peak at 732 nm (Figure S7 in Supplementary Information) showing the interaction of Pd(II) ion with the thio groups of ZnPz 7**a** complex. All the changes were the same as in the case of titration studies of **7c**. The Soret band in **7a**, on addition of Pd(II) metal ion also showed a red shift with shift in absorbance from 369 nm to 382 nm, which again confirmed the exocyclic ligand binding to the porphyrazine macrocycle.

Similar titrations were carried out using equimolar ratio of **7c** with $Hg(ClO_4)_2$ salt (Figure S8 in Supplementary Information). Initially a red shift and decreased intensity of Q-band from 683 nm to 701 nm was observed, accompanied by simultaneous appearance of new peaks at 649 nm and 714 nm showing the interaction of Hg(II) ion with the thio groups of ZnPz **7c** complex.

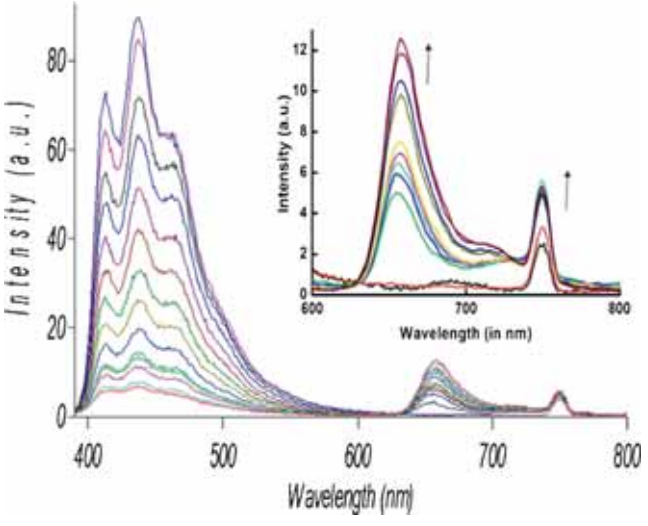


Figure 2. Emission spectral changes observed on addition of $PdCl_2$ [1×10^{-5} M] to **7c** complex [1×10^{-5} M] in CH_2Cl_2. $\lambda_{ex} = 374$ nm.

4. Conclusions

Efficient synthesis of metalloporphyrazines was developed from maleonitrile derivatives using HMDS and metal salts in functional ionic liquids. By using this method metalloporphyrazines have been synthesized in higher yield directly from maleonitrile derivatives, which was not possible by earlier methods. Methylthiozinc(II)porphyrazine and heptylthiozinc(II)porphyrazine have been employed for the binding studies of transition metal ions spectrophotometrically. The spectral changes observed suggest the coordination of four Pd(II) to the peripheral thio groups of zinc(II) porphyrazine macrocycle.

Supplementary Information (SI)

All additional information pertaining to experimental data and characterization of the complexes using UV-Visible spectra (Figures S1, S2, S6, S7 and S8) ESI-MS (Figures S5 and S9), IR spectra (Figure S3) ^{1}H NMR spectra (Figure S4) are given in the Supporting Information, available at www.ias.ac.in/chemsci.

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References

1. Fuchter M J, Zhong C, Zong H, Hoffman B M and Barrett A G M 2008 *Aust. J. Chem.* **61** 235
2. Drain C M, Hupp J T, Suslick K S, Wasielewski M R and Chen X 2002 *J. Porphyrins Phthalocyanines* **6** 243
3. Neelam Singh V, Shankar B, Shanmugam R, Awasthi S K and Gupta R D 2016 *Sens. Actuators, B* **227** 85
4. Zhao L, Chen C, Li Z, Qi D and Jiang J 2014 *J. Porphyrins Phthalocyanines* **18** 715
5. Rao S V and Rao D N 2002 *J. Porphyrins Phthalocyanines* **6** 233
6. Rao S V, Srinivas N N K M, Rao D N, Giribabu L, Maiya B G, Philip R and Kumar G R 2001 *Optics Comm.* **192** 123
7. Trivedi E R, Ma Z, Waters E A, Macrenaris K W, Subramanian R, Barrett A G M, Meade T J and Hoffman B M 2014 *Contrast Media Mol. Imaging.* **9** 313
8. Krasnov P O, Kuzubov A A, Kholtobina A S, Varganov S A and Kuzubova M V 2015 *J. Porphyrins Phthalocyanines* **19** 838
9. Shalabi A S, El Mahdy A M, Assem M M, Taha H O and Soliman K A 2014 *J. Nanopart. Res.* **16** 1
10. Luo J H, Li Q S, Yang L N, Sun Z Z and Li Ze S 2014 *RSC Adv.* **4** 20200
11. Yu L, Zhou X, Yin Y, Liu Y, Li R and Peng T 2012 *Chem. Plus Chem.* **77** 1022

12. Allen C M, Sharman W M and Van Lier J E 2000 *J. Porphyrins Phthalocyanines* **4** 161
13. Van N C F, Benneker F B G, Brussaard H, Kooijman H, Veldman N, Spek A L, Schoonman J, Feiters M C and Nolte R J M 1996 *Inorg. Chem.* **35** 959
14. Kim H S, Choi S M, Pate B D, Kang S H, Sim J B and Lee J K 2015 *Chem. Mater.* **27** 3417
15. Donzello M P, Mori G D, Viola E, Ercolani C and Ricciardi G 2014 *J. Porphyrins Phthalocyanines* **18** 1042
16. Montalban A G, Michel S L J, Baum S M, Vesper B J, White A J P, Williams D J, Barrett A G M and Hoffman B M 2001 *J. Chem. Soc., Dalton Trans*. 3269
17. Miyoshi Y, Takahashi K, Fujimoto T, Yoshikawa H, Matsushita M M, Ouchi Y, Kepenekian M, Robert V, Donzello M P and Ercolani C 2012 *Inorg. Chem.* **51** 456
18. Chauhan S M S, Kumari P and Agarwal S 2007 *Synthesis* **23** 3713
19. Bahr A G and Schleitzer G 1957 *Chem. Ber.* **90** 438
20. Keskin B, Koseoglu Y, Avciata U and Gul A 2008 *Polyhedron* **27** 1155
21. Linstead R P and Whalley M 1952 *J. Chem. Soc.* 4839
22. Donzello M P, Dini D, D'Arcangelo G, Ercolani C, Zhan R, Ou Z, Stuzhin P A and Kadish K M 2003 *J. Am. Chem. Soc.* **125** 14190
23. Prasad R, Kumar R and Prasad S 2009 *Anal. Chim. Acta* **646** 97
24. Bauer E M, Ercolani C, Galli P, Popkova I A and Stuzhin P A 1999 *J. Porphyrins Phthalocyanines* **3** 371
25. Drain C M and Lehn J M 1994 *J. Chem. Soc., Chem. Comm.* 2313
26. Drain C M, Nifiatis F, Vasenko A and Batteas J D 1998 *Angew. Chem. Int. Ed.* **37** 2344
27. Piskorz J, Skupin P, Lijewski S, Korpusinski M, Sciepura M, Konopka K, Sobiak S, Goslinski T and Mielcarek J 2012 *J. Fluorine Chem.* **135** 265
28. Montalban A G, Baum S M, Barrett A G M and Hoffman B M 2003 *J. Chem. Soc., Dalton Trans.* 2093
29. Donzello M P, Mori G D, Viola E, Ercolani C, Bodo E, Mannina L, Capitani D, Rizzoli C, Gontrani L, Aquilanti G, Kadish K M and Angelo P D 2011 *Inorg. Chem.* **50** 12116
30. Donzello M P, Vittoria D, Viola E, Zeng L, Cui Y, Kadish K M, Mannina L and Ercolania C 2015 *J. Porphyrins Phthalocyanines* **19** 904
31. Donzello M P, Viola E, Cai X, Mannina L, Ercolania C and Kadish K M 2010 *Inorg. Chem.* **49** 2447
32. Giribabu L, Chandrasekharam M, MadanMohan S, Rao C S, Kantam M L, Reddy M R, Reddy P Y and Toru T 2006 *Synlett* **10** 16042
33. Maleki A and Rezayan A H 2014 *Organic Chemistry International* **1** Article ID 958951 1