Available online at www.sciencedirect.com
ScienceDirect
Tetrahedron 63 (2007) 10330–10336
Tetrahedron

Synthesis of *N*-tetrasubstituted cyclam derivatives appended with sulfonyl or sulfinyl groups via aza-Michael addition

Augustin de Castries, Aude Escande, Hélène Fensterbank, Emmanuel Magnier, Jérôme Marrot and Chantal Larpent*

Institut Lavoisier, CNRS UMR 8180, Université de Versailles Saint-Quentin, 45 avenue des Etats-Unis, 78035 Versailles Cedex, France

Received 21 June 2007; revised 16 July 2007; accepted 18 July 2007
Available online 26 July 2007

Abstract—Azamacrocycles bearing four arylsulfonyl or arylsulfinyl pendant arms have been synthesised with good yields through nucleophilic addition of 1,4,8,11-tetraazacyclotetradecane (cyclam) to phenylvinylsulfone, phenylvinylsulfoxide or (*R*)-tolylvinylsulfoxide in isopropanol/water media. The crystal structure of the tetraethylsulfonylphenyl substituted macrocycle has been determined by X-ray crystallography. Preliminary studies of the coordination properties of these functionalised macrocyles towards Cu(II) and Eu(III) indicate that pendant sulfoxide groups act as oxygen donor coordinating groups.

1. Introduction

Macrocyclic ligands and in particular polyazamacrocycles have received a great deal of research interest since they find various applications in numerous fields such as coordination chemistry, biomedical uses, ion sequestration and extraction or catalysis.[1–7] Among them, cyclam (1,4,8,11-tetraazacyclotetradecane) has attracted a widespread attention owing to its high affinity for transition metals.[1–6,8] Numerous cyclam derivatives have been reported and the presence of additional functionalities on one or several pendant arms has been found to enlarge the recognition and complexation properties.[1–6,9–14] The grafting of pendant arms has also been used to modulate the solubility as well as the solution behaviour: cyclam derivatives with appended perfluorinated tails have been used as ligands in fluorous biphasic catalysis,[15,16] macrocyclic surfactants have been designed by linking amphiphilic groups onto the cyclam.[17,18]

Functionalisation of cyclam is usually performed by N-alkylation of its secondary amines via nucleophilic substitution with halogenated or tosylated reagents. Alternatively, some cyclam derivatives have been obtained through nucleophilic additions of cyclam to Michael acceptors:[13,15,17,19–22] among them reactions with acrylic derivatives (like acrylonitrile, acrylic esters or acrylamides) have been the most widely studied and used to obtain a variety of appended cyclam derivatives.[17,19–22]

Vinyl- and alkenylsulfones and sulfoxides are excellent Michael acceptors and have been found to react with a number of nucleophiles.[23–35] Among them vinyl- and divinylsulfones have been the most widely studied and aza-Michael additions to vinylsulfones have proven to be useful synthetic tools for the functionalisation of various amines[15,24–32] as well as in the synthesis of nitrogen heterocycles.[33] Except for the reaction of cyclam with divinylsulfone, that has been found to lead to a 1,8-*N*,*N*-bisethylsulfonyl bridged macrocycle,[30] and with perfluorinated acceptors,[15] the synthesis of cyclam derivatives with appended sulfinyl or sulfonyl groups, through aza-Michael additions, has never been investigated before. We anticipated that conjugate additions of cyclam to vinylsulfones or sulfoxides would give a straightforward access to new families of *N*-ethylsulfinyl and *N*-ethylsulfonyl substituted macrocycles. Such functionalised cyclam derivatives may present interesting binding properties since the appended SO groups may act as auxiliary ligands in the formation of coordination complexes. Furthermore, reaction with enantiomerically pure vinylsulfoxides could give access to optically active ligands or organocatalysts usable in asymmetric catalysis. Moreover, electrophilic substitutions in the alpha-position to the sulfonyl groups, well known and widely used in the chemistry of β-aminosulfones,[25] might permit further functionalisations.

Herein, we describe the straightforward synthesis of *N*-tetrasubstituted cyclam derivatives with ethylarylsulfonyl and

Keywords: Azamacrocycles; Vinylsulfone; Vinylsulfoxide; Coordination complexes.
* Corresponding author. Tel.: +33 139254413; fax: +33 139254452; e-mail: larpent@chimie.uvsq.fr

0040–4020/$ - see front matter © 2007 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2007.07.067

ethylarylsulfinyl pendant arms, via aza-Michael additions as well as preliminary studies of their coordination properties towards Cu(II) and Eu(III).

2. Results and discussion

2.1. Synthesis of the *N*-tetrasubstituted macrocycles appended with sulfinyl and sulfonyl groups

The synthesis of tetrasubstituted macrocycles was investigated via nucleophilic addition of cyclam to phenyl vinyl sulfone **1**, phenyl vinyl sulfoxide **2** as well as to the enantiomerically pure (*R*)-*p*-tolyl vinyl sulfoxide **3** (Scheme 1). The latter has been prepared via the nucleophilic substitution of vinyl magnesium bromide on (*S*) menthyl-*p*-toluenesulfinate following Kagan's experimental conditions.[36]

The reactions were performed with an excess of Michael acceptors in protic solvents. The different sets of experimental conditions tested are summarised in Table 1.

The choice of the solvent *i*-PrOH or *i*-PrOH/water was made according to published results that demonstrated that hetero-Michael additions are favoured in protic medium with remarkable rate accelerations in water presumably due to a faster proton transfer.[17,37] For instance in the case of sulfinyl and sulfonyl substituted acceptors, addition of amines to vinylsulfoxide and vinylsulfone derivatives was found to be faster in ethanol than in benzene[28,34] and reaction of isobutylamine with a bis-vinylsulfone acceptor proceeded in methanol but did not occur in chloroform.[31] In the formation of bridged macrocycles involving aza-Michael additions to divinylsulfone, best results were obtained in protic media (isopropanol or isopropanol/water).[30] Furthermore, we recently found that addition of the amines of cyclam to perfluorinated Michael acceptors is readily achieved in an *i*-PrOH/water medium.[15]

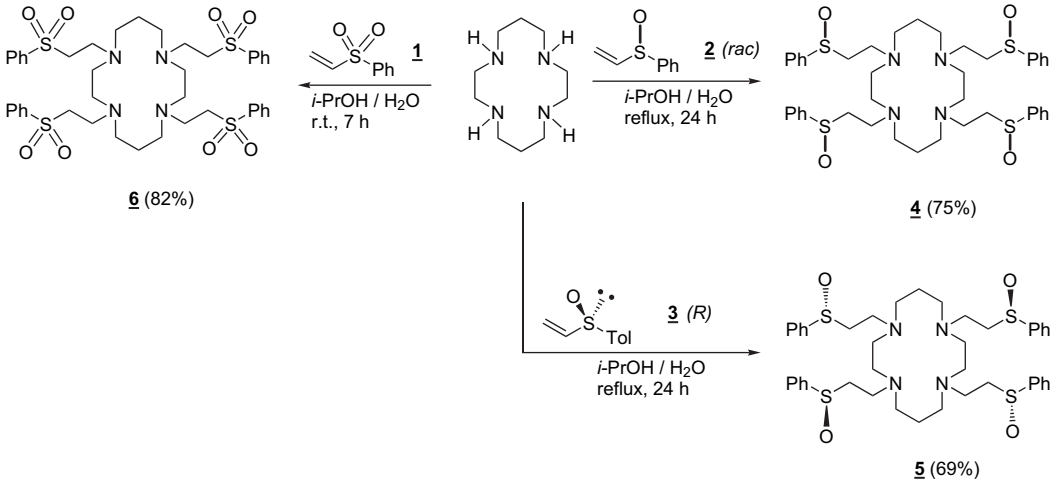
In the present case, the reaction of cyclam with a slight excess of phenyl vinyl sulfoxide **2** (5 equiv per cyclam) proceeded sluggishly in isopropanol and the reaction rate significantly increased in isopropanol/water (Table 1, entries 1–3). Heating up the reaction mixture improved the yield and best conversions were obtained at 65 °C. The tetrasubstituted macrocycles **4** and **5** have been isolated after purification by column chromatography in 70–75% yields from **2** and **3** (Table 1, entries 4,5). These experimental conditions within this range of temperatures do not induce racemisation of the sulfinyl groups since the optical activity of the macrocycle **5** is the same as when the reaction was run at room temperature (Table 1, entries 5,6). The tetrasubstituted macrocycles **4** and **5** have been fully characterised. Elemental analyses and mass spectra confirmed the grafting of four arylethylsulfinyl pendant arms. The observed number of ^{1}H and ^{13}C NMR signals and the relative integration of the corresponding ^{1}H signals are in agreement with the tetrasubstitution pattern.

Table 1. Reaction conditions for the synthesis of sulfinyl and sulfonyl appended macrocycles **4–6**

Entry	Michael acceptor	Solvent	*T*/°C	Reaction time	Product	Yield/%
1	**2** (5 equiv)[a]	*i*-PrOH	rt	3 days	**4**	16[b]
2	**2** (5 equiv)[a]	*i*-PrOH/H_2O (2/1)	rt	24 h	**4**	56[b]
3	**2** (5 equiv)[a]	*i*-PrOH/H_2O (2/1)	rt	5 days	**4**	55[b]
4	**2** (5 equiv)[a]	*i*-PrOH/H_2O (2/1)	65	24 h	**4**	75[b]
5	**3** (5 equiv)[a]	*i*-PrOH/H_2O (2/1)	65	15 h	**5**	69[b,d]
6	**3** (5 equiv)[a]	*i*-PrOH/H_2O (2/1)	rt	15 h	**5**	13[b,d]
7	**1** (6 equiv)[a]	*i*-PrOH/H_2O (2/1)	rt	17 h	**6**	68[c]
8	**1** (10 equiv)[a]	*i*-PrOH/H_2O (2/1)	rt	7 h	**6**	82[c]

[a] Number of equivalent per cyclam.
[b] Isolated yield after purification by column chromatography.
[c] Isolated yield after recrystallisation.
[d] The optical rotation is identical for the products obtained at 65 °C or at rt.

The tetrasubstituted macrocycle **6** with sulfonyl pendant arms was obtained similarly from phenyl vinyl sulfone **1** (Table 1, entries 7,8). The reaction went to completion at room temperature provided that an excess of Michael acceptor (6–10 equiv per cyclam) was used. Room temperature reaction of cyclam with phenyl vinyl sulfone **1** proceeds more rapidly than with aryl vinyl sulfoxides **2** and **3**, in agreement with the known higher reactivity of a double bond activated with a sulfone compared to that substituted with a sulfoxide.[24–26] The macrocycle **6** conveniently precipitated out of the reaction mixture and was crystallised by slow diffusion of methanol through a chloroform solution of **6** in



Scheme 1. Synthesis of sulfinyl and sulfonyl appended macrocycles **4–6**.

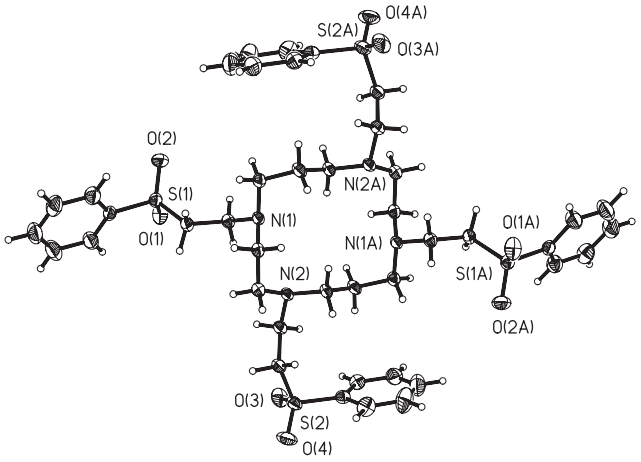


Figure 1. Molecular structure of **6**. ORTEP diagram.

82% overall yield. The crystals were suitable for X-ray diffraction analysis and the resulting crystallographic structure confirms the tetrasubstituted structure with a trans relative arrangement of the pendant groups (Fig. 1). As observed for compounds **4** and **5**, the symmetry of the molecule can be inferred from the number of signals in the ^{1}H NMR (five signals for the methylene protons vs three aromatic signals) and ^{13}C NMR spectra.

2.2. Coordination properties of macrocycles 4–6

The coordination chemistry of cyclam has been widely studied, owing to its high binding affinity for transition metals and its marked selectivity for cupric ions.[1,2,8] A number of tetra-*N*-alkylated ligands derived from cyclam and their copper complexes, in which the metal is coordinated to the four nitrogen atoms, have been described in the literature.[1,2,8,21,38] In some cases, axial coordination of Cu by one or two auxiliary coordinating groups like amide, carboxylate, amine or pyridine attached on the side chains has been reported.[1,2,9,22,39,40] On the other hand, cyclam does not form complexes with rare earth cations[12] and Ln complexes have only been described with cyclam derivatives appended with additional oxygen donor coordinating groups on side chains.[1–6,9,10] like carboxylates,[3–5,9,10] amides[9,12] or phosphonates[6] groups. SO groups are known strong oxygen donor coordinating groups and numerous coordination compounds of transition metals and rare earth elements with various sulfoxides have been reported.[41–46] We have therefore investigated the coordination properties of macrocycles **4–6** appended with four sulfinyl or sulfonyl groups, that might act as auxiliary ligands, towards Cu(II) and Eu(III).

Macrocycles **4–6** readily form complexes with copper nitrate: the tetrasulfinyl macrocycles **4** and **5** furnished Cu(II) complexes, **4**·Cu(II) and **5**·Cu(II), as green powders after concentration of the reaction mixtures whereas the sulfonyl complex **6**·Cu(II) conveniently precipitated out of the reaction medium as a blue powder. Elemental analyses are consistent with a 1:1 stoichiometry for the complexes. The ESI-MS spectra show the base peaks, with the expected isotopic pattern, at *m*/*z* 435.5 and 436.5 for **4**·Cu^{2+} and 463.5 and 464.5 for **5**·Cu^{2+}. The mass spectrum of **6**·Cu(II) shows the monocharged ion **6**·Cu^{+}, resulting from a reduction of Cu(II) in the ESI source, as a small cluster of peaks centred at *m*/*z* 936.5. The visible spectra display absorption bands consistent with copper(II)–N_4 chromophores for these complexes.[15,21,38,39] Their λ_{max} and ε are given in Table 2 and compared to those of the tetra-*N*-methylcyclam copper complex (TMC·Cu(II)). The red shifts of absorption bands ($\Delta\lambda_{max}$ 67–74 nm) observed in the case of complexes **4**·Cu(II) and **5**·Cu(II) when compared to the TMC complex are consistent with an axial coordination of one or two sulfoxide groups to the central metal ion.[15,21,38,39,47] On the other hand, the absorption band of complex **6**·Cu(II) is close to that of TMC·Cu(II) suggesting that the sulfonyl pendant groups do not coordinate to Cu.

Table 2. UV–vis data of Cu(II) complexes with sulfinyl and sulfonyl appended macrocycles **4–6** and tetra-*N*-methylcyclam (TMC)

Complex	Colour	Solvent	λ/nm (ε/L mol^{-1} cm^{-1})
TMC·Cu(II)	Blue	MeOH	645 (161)
TMC·Cu(II)	Blue	EtOH	664 (287)
6·Cu(II)	Blue	MeOH	659 (244)
4·Cu(II)	Green	EtOH	731 (316)
5·Cu(II)	Green	EtOH	738 (297)

Reaction of either tetrasulfinyl macrocycles **4** or **5** with 1 equiv of europium nitrate in ethanol led to the formation of insoluble brown powders. The IR spectra of the two solids, **4**·Eu(III) and **5**·Eu(III), showed bands at 1030 cm^{-1} resulting from the stretching vibration of the S=O group. The shift of ν(S=O) to lower wavenumbers compared to that of free ligands **4** and **5** (1038 cm^{-1})[48] suggests coordination through the oxygen atoms of the S=O moieties of the pendant arms, as was already reported with classical sulfoxides.[42] The IR spectra also reveal the presence of nitrate anions coordinated in a bidentate and monodentate manner at 1480, 1385 and 1300 cm^{-1}.[49] The fluorescence spectra of the solids, recorded at room temperature, further demonstrate the presence of europium. These spectra show the three characteristic emission bands for Eu(III) at 593, 619 and 696 nm, corresponding to the $^{5}D_0 \rightarrow {}^{7}F_J$ (J=1, 2, 4) transitions, upon excitation at 466 or 396 nm (Fig. 2).[11,43,49,50] Elemental analyses of the solid **4**·Eu(III) are consistent with a $Eu_3L_2(NO_3)_3$ composition and are indicative of the coordination of two or three sulfoxide groups and three nitrates per

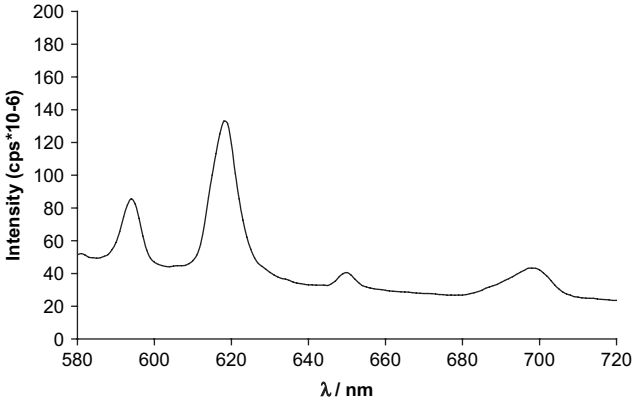


Figure 2. Solid state fluorescence emission spectrum (room temperature) of coordination compound **4**·Eu(III) with excitation at 396 nm.

Eu. This 1.5 Eu-per-macrocycle stoichiometry strongly suggests that the macrocyclic tetrasulfoxide ligands act as bridges to link adjacent Eu(III) ions giving rise to polymeric assemblies, similar to those recently reported in lanthanide coordination polymers with bis and tris sulfoxides.[44,45] A close composition is obtained with ligand **5** with a slightly higher Eu-to-macrocycle molar ratio. All these characteristics are indicative of the coordination of Eu(III) by ligands **4** and **5** through the oxygen atoms of their pendant sulfoxide groups.

On the other hand, when macrocycle **6**, bearing four ethylphenylsulfonyl pendant arms, was reacted with $Eu(NO_3)_3$ no precipitate was formed and there was no spectroscopic evidence for the formation of coordination complexes. These latter features indicate that sulfonyl groups do not coordinate to Eu ions.

3. Conclusions

Aza-Michael addition is a very convenient method to prepare substituted cyclam derivatives appended with four sulfonyl and sulfinyl groups. Since numerous vinylsulfones and vinylsulfoxides are readily accessible through well-documented synthetic processes, this strategy is expected to be quite general and should give access to a variety of functionalised azamacrocycles. Interestingly, optically active macrocycles are easily obtained from enantiomerically pure vinylsulfoxides.

The preliminary studies of the coordination properties of the cyclam derivatives bearing ethylphenysulfonyl and ethylarylsulfinyl pendant arms indicate that the sulfoxides act as coordinating groups whereas we do not get any evidence for the participation of sulfonyl groups. In copper(II) complexes, the sulfoxide pendant arms act as auxiliary coordinating groups in addition to the four macrocyclic nitrogen atoms. In coordination compounds with europium(III) the sulfinyl functionalised macrocycles act as polydentate ligands and lead to supramolecular assemblies.

Potential applications of the macrocyclic ligand **5** appended with enantiomerically pure sulfinyl groups in asymmetric catalysis are currently under investigation.

4. Experimental section

4.1. General

All chemicals were purchased from Sigma, Aldrich or Fluka and were used without further purification. Organic solvents were purchased from SDS. IR spectra were recorded on an Impact 400D Nicolet spectrophotometer. ^{1}H NMR and ^{13}C NMR spectra were acquired on a Bruker AC300 (300, 75 MHz) or on a Bruker AC200 (200, 50 MHz) spectrometer using the residual peak of $CHCl_3$ or $CDCl_3$ (7.27, 77 ppm) as internal standards. Electrospray mass spectra (positive mode) were obtained on an HP MS Engine 5989B spectrometer. Elemental analyses were obtained from the Service Central d'Analyses du CNRS (Vernaison, France) or ICSN (Gif-sur-Yvette, France). Optical rotations were measured on a Perkin–Elmer 341 digital polarimeter at λ=589, 578, 546 and 436 nm at 25 °C. TLC analyses were performed on silica plates (Merck $60F_{254}$) with $Cu(NO_3)_2\cdot 3H_2O$ (0.2% in absolute ethanol) as the revelator for the free ligands. Column chromatography was carried out with silica gel Chromagel 60 A C.C (70–200 μm) from SDS. Melting points were determined on a Mettler FP61 melting point apparatus. The UV–vis spectra were recorded on a Lambda 19 spectrophotometer (Perkin–Elmer). Fluorescence measurements were made at 25 °C using a FluoroMax®-3 spectrofluorometer equipped with 150 W xenon lamp. Solid fluorescence spectra were measured with a reflexion angle of 45° with a recording rate adjusted to 10 nm/s upon excitation at 396 and 466 nm.

4.1.1. (*R*)-*p*-Tolyl vinyl sulfoxide 3. (*R*)-*p*-Tolyl vinyl sulfoxide was prepared using an experimental procedure slightly adapted from Ref. 36. A solution of (1*R*,2*S*,5*R*)-menthyl (*S*)-*p*-toluenesulfinate (33.9 mmol, 10 g) was dissolved in 100 mL of distilled diethyl ether and placed under argon. Vinyl magnesium bromide (33.9 mmol, 1 M in THF, 33.9 mL) was rapidly added at room temperature. After stirring the reaction mixture for 10 min, a saturated solution of ammonium chloride (30 mL) was added. The aqueous layer was extracted with dichloromethane (4×150 mL) and the combined organic layers were washed with brine (100 mL), dried with $MgSO_4$, filtered and rotary evaporated. The crude product was distilled off at 67–70 °C under reduced pressure (0.25 mbar) to yield a yellow oil (5.65 g, 59%). R_f: 0.5 (pentane/ethyl acetate 1/1; revelator: $KMnO_4$). $[\alpha]_D^{25}$ 413 (*c* 1.65, acetone) (lit.[36] $[\alpha]_D^{25}$ 446 (*c* 1.65, acetone)). The ^{1}H NMR spectrum is in agreement with the literature.[36]

4.1.2. 1,4,8,11-Tetrakis-(2-phenylsulfinyl-ethyl)-1,4,8,11-tetraazacyclotetradecane 4. Phenyl vinyl sulfoxide **2** (2.5 mmol, 0.33 mL) was added to a solution of cyclam (0.5 mmol, 100 mg) in a mixture of isopropanol and water (1.3 mL/0.6 mL). The reaction mixture was refluxed for 24 h, concentrated and purified through column chromatography (ether followed by dichloromethane/methanol 1/1) to yield a brownish powder (0.38 mmol, 309 mg, 75% yield). R_f: 0.8 (CH_2Cl_2/MeOH 65/35); mp 132.1 °C. Anal. Found: C, 60.30; H, 7.10; N, 6.68. Calcd for $C_{42}H_{56}N_4O_4S_4\cdot 2H_2O$: C, 60.30; H, 7.15; N, 6.62%; λ_{max} (DMF)/330 nm (ε/dm^3 mol^{-1} cm^{-1} 166), 280 (968); ν_{max}/cm^{-1} (KBr pellet): 3050, 2955, 1640, 1439, 1038 (S=O), 748, 691, 518 cm^{-1}; δ_H (200 MHz; $CDCl_3$) 1.64 (4H, m, $CH_2CH_2CH_2$), 2.60–2.99 (32H, m, CH_2N, CH_2SO), 7.49–7.50 (CH_{Ar}); δ_c (75 MHz; $CDCl_3$) 23.9 ($CH_2CH_2CH_2$), 47.3, 51.2, 51.3, 55.0, 123.8, 129.8, 130.7 ($C_{Ar}H$), 144.0 ($C_{Ar}S$); *m*/*z* (ESI pos) 809 [(M+H)$^+$] (100%), 831 [(M+Na)$^+$] (50).

4.1.3. 1,4,8,11-Tetrakis-(2-*p*-tolylsulfinyl-ethyl)-1,4,8,11-tetraazacyclotetradecane 5. (*R*)-*p*-Tolyl vinyl sulfoxide **3** (2.5 mmol, 380 mg, 0.33 mL) reacted with cyclam (0.5 mmol, 100 mg) following the above procedure for **4**. Purification by column chromatography (ether followed by dichloromethane/methanol 1/1) gave **5** as a brownish powder (0.39 mmol, 298 mg, 69% yield). R_f: 0.8 (CH_2Cl_2/MeOH 65/35); mp: 135–137 °C; $[\alpha]_D^{25}$ 157, $[\alpha]_{578}^{25}$ 165, $[\alpha]_{546}^{25}$ 192, $[\alpha]_{436}^{25}$ 383 (*c* 5.76, ethanol). Anal. Found: C, 62.34; H, 7.38; N, 6.19. Calcd for $C_{46}H_{64}N_4O_4S_4\cdot 1H_2O$: C, 62.55; H, 7.53; N, 6.34%; ν_{max}/cm^{-1} (KBr pellet) 3448,

2949, 1644, 1493, 1455, 1084, 1038 (S═O), 811; δ_H (200 MHz; $CDCl_3$) 1.66 (4H, m, $CH_2CH_2CH_2$), 2.42 (12H, s, PhMe), 2.61 (16H, m, NCH_2), 3.00 (16H, m, NCH_2 and CH_2SO), 7.30 (8H, d, J=8.1, CH_{Ar}), 7.54 (8H, d, J=8.1, CH_{Ar}); δ_c (75 MHz; $CDCl_3$) 21.2 (CH_3), 23.7 ($CH_2CH_2CH_2$), 47.4, 51.2, 51.5, 55.1 (CH_2N), 123.7, 129.9 ($C_{Ar}H$), 144.8, 141.4 ($C_{Ar}S$, $C_{Ar}Me$); *m/z* (ESI pos) 865 [(M+H)$^+$] (100%), 887 [(M+Na)$^+$] (20).

4.1.4. 1,4,8,11-Tetrakis-(2-phenylsulfonyl-ethyl)-1,4,8,11-tetraazacyclotetradecane 6. Phenyl vinyl sulfone **1** (1.67 g, 10 mmol) was added to a solution of cyclam (200 mg, 1 mmol) in a mixture of isopropanol and water (8 mL/4 mL). The reaction mixture was stirred at room temperature for 7 h. The desired product precipitated out of the reaction mixture and was collected by filtration. It was washed with 15 mL of methanol. Crystallisation by slow diffusion of 15 mL of methanol carefully added to 773 mg of the white powder in 70 mL of chloroform gave white crystals (709 mg, 82%). R_f: 0.8 ($CHCl_3$/MeOH 9/1); mp 178 °C. Anal. Found: C, 57.51; H, 6.85; N 6.32. Calcd for $C_{42}H_{56}N_4O_8S_4$: C, 57.77; H, 6.46; N, 6.42%; ν_{max}/cm^{-1} (KBr pellet) 3059, 2962, 2936, 2817, 1583 (C═C), 1475, 1440, 1301 (SO_2 asym), 1142 (SO_2 sym); δ_H (200 MHz; $CDCl_3$) 1.35 (4H, m, $CH_2CH_2CH_2$), 2.31 (16H, m, $CH_2CH_2CH_2N$, NCH_2CH_2N), 2.79–2.84 (m, 8H, NCH_2CH_2SO), 3.13–3.18 (m, 8H, CH_2SO), 7.59 (m, 8H, H_m), 7.68 (4H, m, H_p), 7.91 (8H, m, H_o); δ_c (75 MHz; $CDCl_3$) 24.2 ($CH_2CH_2CH_2$), 47.1 ($NCH_2CH_2SO_2$), 50.7 ($CH_2CH_2CH_2N$, NCH_2CH_2N), 52.6 (CH_2SO_2), 127.9 (C_o), 129.4 (C_m), 133.8 (C_p), 139.6 (C_{ipso}); FAB (pos mode) *m/z*: 873 [(M+H)$^+$] (100).

4.1.5. Crystal structure determination. A white platelet (0.50×0.10×0.02 mm^3) was analysed with a Siemens SMART three-circle diffractometer equipped with a CCD bidimensional detector with Mo Kα monochromatised radiation (λ=0.71073 Å). Slightly more than one hemisphere of data was collected in 1271 frames with ω scans (width of 0.30° and exposure time of 30 s per frame). Data reduction was performed with SAINT software. Data were corrected for Lorentz and polarisation effects and the absorption correction was based on multiple and symmetry-equivalent reflections in the data set by using the SADABS[51] program based on the method of Blessing. Lattice parameters were obtained from least-squares analysis of all reflections. The structure was solved by direct method and refined by full matrix least-squares, based on F^2, using the SHELX-TL software package.[52] All non-hydrogen atoms were refined with anisotropic displacement parameters. All hydrogen atoms were located with geometrical restraints in the riding mode.

Crystallographic data for the structure reported in this paper have been deposited at the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 644941. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Monoclinic, space group $P2_1/c$, a=5.6755(2) Å, b=11.3204(1) Å, c=33.2829(5) Å, β=91.021(1)°, V=2138.05(8) Å^3, Z=2, ρ_{calcd}=1.356 g cm^{-3}, μ(Mo Kα)=0.279 mm^{-1}, F(000)=928, 14,871 reflections measured, of which 5663 were independent (2589 $F_o>4\sigma(F_o)$), 263 refined parameters, R_1=0.0586, wR_2=0.1057, GOF=0.996; max./min. residual electron density 0.229/−0.284 e Å^{-3}.

4.1.6. 1,4,8,11-Tetrakis-(2-phenylsulfinyl-ethyl)-1,4,8,11-tetraazacyclotetradecane copper(II)nitrate 4·Cu(II). Copper nitrate trihydrate (0.177 mmol, 42.8 mg) was added to a solution of macrocycle **4** (0.177 mmol, 143 mg) in a mixture of dichloromethane and methanol (3 mL/1 mL). The resulting reaction mixture was stirred at room temperature over a period of 18 h and concentrated to dryness to yield a green powder (0.177 mmol, 179 mg); mp: decomposition at 148–150 °C. Anal. Found: C, 46.58; H, 5.73; Cu, 6.51; N, 8.05. Calcd for $C_{42}H_{56}N_6O_{10}S_4Cu\cdot 4H_2O$ (CuL-$(NO_3)_2\cdot 4H_2O$) C, 46.81; H, 6.07; Cu, 5.90; N, 7.80%; λ_{max} (EtOH)/731 nm (ε/dm^3 mol^{-1} cm^{-1} 316), 327 nm (6312), 247 nm; ν_{max}/cm^{-1} (KBr pellet) 2940, 1640, 1480, 1383, 1086, 1040 (S═O), 748, 697 cm^{-1}; ESI (pos mode) *m/z*: 435.5–436.5 [(**4**·Cu)$^{2+}$] (100), 373–374 [(**4**·Cu)–SOC_6H_5]$^{2+}$ (25), 933–935 [**4**·$CuNO_3$]$^+$ (10).

4.1.7. 1,4,8,11-Tetrakis-(2-*p*-tolylsulfinyl-ethyl)-1,4,8,11-tetraazacyclotetradecane copper(II) nitrate 5·Cu(II). Prepared as described above from **5** (0.486 mmol, 420 mg). A green powder (0.486 mmol, 520 mg) was obtained. Mp: decomposition at 154–156 °C; $[\alpha]_D^{25}$ 78, $[\alpha]_{578}^{25}$ 102, $[\alpha]_{546}^{25}$ 194 (*c* 1.0, ethanol). Anal. Found: C, 51.08; H, 6.14; N, 7.77; Cu, 5.92. Calcd for $C_{46}H_{64}N_6O_{10}S_4Cu\cdot 1.5H_2O$ ($CuL(NO_3)_2\cdot 1.5H_2O$): C, 51.17; H, 6.25; N, 7.78; Cu, 5.88%; λ_{max} (EtOH)/738 nm (ε/dm^3 mol^{-1} cm^{-1} 297), 321 nm (4160), 256 nm; ν_{max}/cm^{-1} (KBr pellet) 3421, 2925, 2720, 1644, 1480, 1379 (NO_3), 1086, 1040 (S═O), 1014, 815 cm^{-1}; ESI (pos mode) *m/z*: 463.5–464.5 [**5**·Cu^{2+}] (100), 394–395 [**5**·Cu–SOTol]$^{2+}$ (25), 989–991 [**5**·$CuNO_3$]$^+$ (10).

4.1.8. 1,4,8,11-Tetrakis-(2-phenylsulfonyl-ethyl)-1,4,8,11-tetraazacyclotetradecane copper(II) nitrate 6·Cu(II). Prepared by reacting **6** (3.43×10^{-2} mmol, 30 mg) with copper nitrate (3.4×10^{-2} mmol, 8 mg) in 3 mL dichloromethane for 18 h at room temperature. Complex **6**·Cu precipitated as a blue powder (3.3×10^{-2} mmol, 35 mg, 96%). Anal. Found: C, 45.36; H, 5.14; N, 7.68; Cu, 5.82. Calcd for $C_{42}H_{56}N_6S_4O_{14}Cu\cdot 2.5H_2O$ (CuL-$(NO_3)_2\cdot 2.5H_2O$): C, 45.62; H, 5.56; N, 7.60; Cu, 5.74%; λ_{max} (MeOH)/659 nm (ε/dm^3 mol^{-1} cm^{-1} 244); ν_{max}/cm^{-1} (KBr pellet) 2979–2924, 1301 (SO_2 asym), 1146 (SO_2 sym); ESI (pos mode) *m/z*: 873 [**6**·H$^+$] (100), 895 [**6**·Na$^+$] (37), 935 (14)–936 (6)–937 (9)–938 (6) [(**6**·Cu)$^+$].

4.1.9. Coordination complex of Eu with macrocycle 4 4·Eu(III). Europium nitrate pentahydrate (1.84 mmol, 787 mg) was added to a solution of **4** (1.84 mmol, 1.486 g) in absolute ethanol (16 mL) and the resulting solution was stirred at room temperature for 10 min, then diluted with absolute ethanol (21 mL) and stirred for 18 h. The precipitated powder was isolated by filtration, washed with ethanol (100 mL) and then with methanol (100 mL) to yield 605 mg of a brown powder. Mp: decomposition at 153–154 °C. Anal. Found: C, 35.53; H, 4.34; Eu, 15.94; N, 8.02. Calcd for $[Eu_3L_2(NO_3)_9\cdot 12H_2O]$ C, 35.42; H, 4.81; Eu, 16.01; N, 8.36%; ν_{max}/cm^{-1} (KBr pellet) 3416, 2955,

1634, 1480 (NO_3), 1383 (NO_3), 1309 (NO_3), 1086, 1030 (S=O), 748, 682 cm^{-1}.

4.1.10. Coordination complex of Eu with macrocycle 5 5·Eu(III). Prepared as described above from **5** (0.499 mmol, 431 mg). Brown powder (175 mg). Mp: decomposition at 167–169 °C. Anal. Found: C, 33.06; H, 4.34; Eu, 19.93; N, 7.40. Calcd for $[Eu_9L_4(NO_3)_{18}\cdot 12H_2O]$: C, 32.46; H, 5.20; Eu, 20.09; N, 6.99%; ν_{max}/cm^{-1} (KBr pellet) 3398, 1635, 1480 (NO_3), 1384 (NO_3), 1309 (NO_3), 1085, 1030 (S=O), 1004, 813 cm^{-1}.

4.1.11. Attempts to prepare coordination complex of Eu with macrocycle 6. Macrocycle **6** is not soluble in ethanol. Complexation was attempted by addition of europium nitrate pentahydrate to a solution of **6** in a mixture of chloroform and acetonitrile. No precipitate was observed.

Supplementary data

IR spectra of macrocycles **4**, **5** and their coordination compounds with Eu; UV–vis spectra of copper complexes; NMR spectra. Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2007.07.067.

References and notes

1. Liang, X.; Sadler, P. J. *Chem. Soc. Rev.* **2004**, *33*, 246–265.
2. Izatt, R. M.; Pawlak, K.; Bradshaw, J. S.; Bruening, R. *Chem. Rev.* **1991**, *91*, 1721–2085.
3. Alexander, V. *Chem. Rev.* **1995**, *95*, 273–342.
4. Bottrill, M.; Kwok, L.; Long, N. J. *Chem. Soc. Rev.* **2006**, *35*, 557–571.
5. Helm, L.; Merbach, A. E. *Chem. Rev.* **2005**, *105*, 1923–1959.
6. Lukes, I.; Kotek, J.; Vojtisek, P.; Hermann, P. *Coord. Chem. Rev.* **2001**, *216*, 287–312.
7. (a) Busch, D. H. *Acc. Chem. Res.* **1978**, *11*, 392–400; (b) Parker, D. *Chem. Soc. Rev.* **1990**, *19*, 271–291; (c) Parker, D. *Chem. Britain* **1994**, 818–822; (d) De Clercq, E. *Mini-Rev. Med. Chem.* **2005**, *5*, 805–824; (e) Caravan, P. *Chem. Soc. Rev.* **2006**, *35*, 512–523.
8. (a) Elias, H. *Coord. Chem. Rev.* **1999**, *187*, 37–73; (b) Bakaj, M.; Zimmer, M. *J. Mol. Struct.* **1999**, *508*, 59–72; (c) Thom, V. J.; Boeyens, J. C. A.; McDougall, G. J.; Hancock, R. D. *J. Am. Chem. Soc.* **1984**, *106*, 3198–3207; (d) Thom, V. J.; Hosken, G. D.; Hancock, R. D. *Inorg. Chem.* **1985**, *24*, 3378–3381.
9. Meyer, M.; Dahaoui-Gindrey, V.; Lecomte, C.; Guilard, R. *Coord. Chem. Rev.* **1998**, *178–180*, 1313–1405.
10. Lecomte, C.; Dahaoui-Gindrey, V.; Chollet, H.; Gros, C.; Mishra, A. K.; Barbette, F. P.; Pullumbi, P.; Guilard, R. *Inorg. Chem.* **1997**, *36*, 3827–3838.
11. Liu, W.; Jiao, T.; Li, Y.; Liu, Q.; Tan, M.; Wang, H.; Wang, L. *J. Am. Chem. Soc.* **2004**, *126*, 2280–2281.
12. (a) Moulin, C.; Larpent, C.; Gazeau, D. *Anal. Chim. Acta* **1999**, *378*, 47–54; (b) Corriu, R. J. P.; Embert, F.; Guari, Y.; Reye, C.; Guilard, R. *Chem.—Eur. J.* **2002**, *8*, 5732–5741.
13. Finocchiaro, A.; Failla, S.; Consiglio, G. *Russ. Chem. Bull.* **2005**, *54*, 1355–1372.
14. Svobodova, I.; Lubal, P.; Plutnar, J.; Havlicklova, J.; Kotek, J.; Hermann, P.; Lukes, I. *Dalton Trans* **2006**, *43*, 5184–5197.
15. de Castries, A.; Magnier, E.; Monmotton, S.; Fensterbank, H.; Larpent, C. *Eur. J. Org. Chem.* **2006**, *20*, 4685–4692.
16. Pozzi, G.; Cavazzini, M.; Quici, S. *Tetrahedron Lett.* **1997**, *38*, 7605–7608.
17. Larpent, C.; Laplace, A.; Zemb, T. *Angew. Chem., Int. Ed.* **2004**, *43*, 3163–3167; Larpent, C.; Laplace, A.; Zemb, T. *Angew. Chem.* **2004**, *116*, 3225–3229.
18. Arleth, L.; Posselt, D.; Gazeau, D.; Larpent, C.; Zemb, T.; Mortensen, K.; Pedersen, J. S. *Langmuir* **1997**, *13*, 1887–1896.
19. (a) Fensterbank, H.; Berthault, P.; Larpent, C. *Eur. J. Org. Chem.* **2003**, *20*, 3985–3990; (b) Fensterbank, H.; Zhu, J.; Riou, D.; Larpent, C. *J. Chem. Soc. Perkin Trans. 1* **1999**, 811–816; (c) Gaudinet-Hamann, B.; Zhu, J.; Fensterbank, H.; Larpent, C. *Tetrahedron Lett.* **1999**, *40*, 287–290.
20. (a) Tschudin, D.; Basak, A.; Kaden, T. A. *Helv. Chim. Acta* **1988**, *71*, 100–106; (b) Koshti, N.; Gantla, V. R.; Jacobs, H.; Gopalan, A. *Synth. Commun.* **2002**, *32*, 3779–3790; (c) Wainwright, K. P. *J. Chem. Soc., Dalton Trans.* **1980**, 2117–2120; (d) Freeman, G. M.; Barefield, E. K.; Van Derver, D. G. *Inorg. Chem.* **1984**, *23*, 3092–3103; (e) Gros, C.; Chollet, H.; Mishra, A. K.; Guilard, R. *Synth. Commun.* **1996**, *26*, 35–47; (f) Koshti, N. M.; Jacobs, H. K.; Martin, P. A.; Smith, P. H.; Gopalan, A. S. *Tetrahedron Lett.* **1994**, *35*, 5157–5160; (g) Collman, J. P.; Zhang, X.; Herrmann, P. C.; Uffelman, E. S.; Boitrel, B.; Straumanis, A.; Brauman, J. I. *J. Am. Chem. Soc.* **1994**, *116*, 2681–2682; (h) Bulach, V.; Mandon, D.; Weiss, R. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 572–575.
21. Stephan, H.; Geipel, G.; Appelhans, D.; Bernhard, G.; Tabuani, D.; Komber, H.; Voit, B. *Tetrahedron Lett.* **2005**, *46*, 3209–3212.
22. Bulach, V.; Mandon, D.; Fischer, J.; Weiss, R. *Inorg. Chim. Acta* **1993**, *210*, 7–9.
23. (a) Simpkins, N. S. *Tetrahedron* **1990**, *46*, 6951–6984; (b) Simpkins, N. S. *Sulfones in Organic Synthesis, Tetrahedron Organic Chemistry Series*; Baldwin, J. E., Magnus, P. D., Eds.; Pergamon: Oxford, 1993; Vol. 10; (c) *The Chemistry of Functional Groups: The Chemistry of Sulfones and Sulfoxides*; Patai, S., Rappoport, Z., Stirling, C. J., Eds.; Wiley: Chichester, UK, 1998; (d) Durst, T. *Comprehensive Organic Chemistry*; Barton, D. H. R., Ollis, W. D., Eds.; Pergamon: Oxford, 1979; pp 171–213.
24. Shenhav, H.; Rappoport, Z.; Patai, S. *J. Chem. Soc. B* **1970**, 469–476.
25. Enders, D.; Saint-Dizier, A.; Lannou, M.-I.; Lenzen, A. *Eur. J. Org. Chem.* **2006**, *1*, 29–49 and references therein.
26. Magnier-Bouvier, C.; Blazejewski, J.-C.; Larpent, C.; Magnier, E. *Tetrahedron Lett.* **2006**, *51*, 9121–9124.
27. Enders, D.; Müller, S. F.; Raabe, G.; Runsik, J. *Eur. J. Org. Chem.* **2000**, *6*, 879–892 and references therein.
28. Mc Dowell, S. T.; Stirling, C. J. M. *J. Chem. Soc. B* **1967**, 343–348.
29. (a) Reddick, J. J.; Cheng, J.; Roush, W. R. *Org. Lett.* **2003**, *5*, 1967–1970; (b) Ravindran, B.; Deshpande, S. G.; Pathak, T. *Tetrahedron* **2001**, *57*, 1093–1098; (c) Ravindran, B.; Sakthivel, K.; Cheravakkattu, G. S.; Pathak, T. *J. Org. Chem.* **2000**, *65*, 2637–2641; (d) Das, I.; Pathak, T.; Suresh, C. G. *J. Org. Chem.* **2005**, *70*, 8047–8054; (e) Wu, J.-C.; Pathak, T.; Tong, W.; Vial, J.-M.; Remaud, G.; Chattopadhyaya, J. *Tetrahedron* **1988**, *44*, 6705–6722; (f) Bera, S.; Sakthivel, T.; Pathak, T.; Langley, G. J. *Tetrahedron* **1995**, *51*, 7857–7866; (g) Kroll, F. E.; Morphy, R.; Rees, D.; Gani, D. *Tetrahedron Lett.* **1997**, *38*, 8573–8576; (h) Lutolf, M. P.; Hubbell, J. A. *Biomacromolecules* **2003**, *4*, 713–722; (i) Zhen, G.;

Falconnet, D.; Kuennemann, E.; Vörös, J.; Spencer, N. D.; Textor, M.; Zürcher, S. *Adv. Funct. Mater.* **2006**, *16*, 243–251.
30. Teyssot, M.-L.; Fayolle, M.; Philouze, C.; Dupuy, C. *Eur. J. Org. Chem.* **2003**, *1*, 54–62 and references therein.
31. Bera, S.; Langley, G. J. L.; Pathak, T. *J. Org. Chem.* **1998**, *63*, 1754–1760.
32. (a) Padwa, A.; Norman, B. H. *J. Org. Chem.* **1990**, *55*, 4801–4807; (b) Gao, C.; Yan, D. *Chem. Commun.* **2001**, 107–108; (c) Zheng, Z.; Pan, C.; Wang, D.; Liu, Y. *Macromol. Chem. Phys.* **2005**, *206*, 2182–2189.
33. (a) de Vicente, J.; Arrayas, R. G.; Carretero, J. C. *Tetrahedron Lett.* **1999**, *40*, 6083–6086; (b) Alonso, D. A.; Costa, A.; Mancheno, B.; Najera, C. *Tetrahedron* **1997**, *53*, 4791–4814; (c) Back, T. G.; Parvez, M.; Zhai, H. *J. Org. Chem.* **2003**, *68*, 9389–9393.
34. Pyne, S. G.; Griffith, R.; Edwards, M. *Tetrahedron Lett.* **1988**, *29*, 2089–2092.
35. (a) Kahn, S. D.; Hehre, W. J. *J. Am. Chem. Soc.* **1986**, *108*, 7399–7400; (b) Abbot, D. J.; Colonna, S.; Stirling, C. J. M. *J. Chem. Soc., Chem. Commun.* **1971**, 471–471; (c) Matsuyama, H.; Itoh, N.; Matsumoto, A.; Ohira, N.; Hara, K.; Yoshida, M.; Iyoda, M. *J. Chem. Soc. Perkin Trans. 1* **2001**, 2924–2930; (d) Pyne, S. G.; Bloem, P.; Griffith, R. *Tetrahedron* **1989**, *45*, 7013–7022.
36. Ronan, B.; Kagan, H. B. *Tetrahedron: Asymmetry* **1992**, *3*, 115–122.
37. (a) Naidu, B. N.; Sorenson, M. E.; Connolly, T. P.; Ueda, Y. *J. Org. Chem.* **2003**, *68*, 10098–10102; (b) Ranu, B. C.; Banerjee, S. *Tetrahedron Lett.* **2007**, *48*, 141–143; (c) Patin, H.; Larpent, C. *Tetrahedron* **1988**, *44*, 6107–6118; (d) Larpent, C.; Meignan, G.; Patin, H. *Tetrahedron Lett.* **1991**, *32*, 2615–2618; (e) Larpent, C.; Meignan, G.; Patin, H. *Tetrahedron* **1990**, *46*, 6381–6398; (f) Larpent, C.; Patin, H. *Tetrahedron Lett.* **1988**, *29*, 4577–4580; (g) Larpent, C.; Geniès, C.; Delgado, A.-P.; Caminade, A.-M.; Majoral, J.-P.; Sassi, J.-F.; Leising, F. *Chem. Commun.* **2004**, 1816–1817.
38. (a) Dong, Y.; Lawrance, G. A.; Lindoy, L. F.; Turner, P. *Dalton Trans.* **2003**, *8*, 1567–1576; (b) Buxtorf, R.; Kaden, T. A. *Helv. Chim. Acta* **1974**, *57*, 1035–1042.
39. Amatore, C.; Barbe, J.-M.; Bucher, C.; Duval, E.; Guilard, R.; Verpeaux, J.-N. *Inorg. Chim. Acta* **2003**, *356*, 267–278.
40. (a) Bucher, C.; Duval, E.; Barbe, J.-M.; Verpeaux, J.-N.; Amatore, C.; Guilard, R. *C.R. Acad. Sci., Ser. IIc: Chim.* **2000**, *3*, 211–222; (b) El Ghachtouli, S.; Cadiou, C.; Deschamps-Olivier, I.; Chuburu, F.; Aplincourt, M.; Roisnel, T. *Eur. J. Inorg. Chem.* **2006**, *17*, 3472–3481; (c) Comparone, A.; Kaden, T. A. *Helv. Chim. Acta* **1998**, *81*, 1765–1772; (d) Studder, M.; Kaden, T. A. *Helv. Chim. Acta* **1986**, *69*, 2081; (e) Chapman, J.; Ferguson, G.; Gallagher, J. F.; Jennings, M. C.; Parker, D. J. *J. Chem. Soc., Dalton Trans.* **1992**, *3*, 345–353.
41. Calligaris, M. *Coord. Chem. Rev.* **2004**, *318*, 351–375.
42. Niyama, E.; Brito, H. F.; Cremona, M.; Teotonio, E. E. S.; Reyes, R.; Brito, G. E. S.; Felinto, M. C. F. C. *Spectrochim. Acta, Part A* **2005**, *61*, 2643–2649.
43. (a) Malta, O. L.; Brito, H. F.; Menezes, J. F. S.; Goncalves e Silva, F. R.; Alves, S., Jr.; Farias, F. S., Jr.; de Andrade, A. V. M. *J. Lumin.* **1997**, *75*, 255–268; (b) Umeda, K.; Isolani, P. C.; Zaim, M. H.; Vicentini, G. *J. Alloys Compd.* **2002**, *344*, 80–82; (c) Brito, H. F.; Malta, O. L.; Menezes, J. F. S. *J. Alloys Compd.* **2000**, *303–304*, 336–339; (d) Carvalho, A.; Domingos, A.; Isolani, P. C.; Marques, N.; Pires de Matos, A.; Vicentini, G. *Polyhedron* **2000**, *19*, 1707–1712.
44. Li, J. R.; Bu, X. H.; Zhang, R. H. *Inorg. Chem.* **2004**, *43*, 237–244.
45. (a) Li, J.-R.; Bu, X.-H.; Zhang, R.-H.; Duan, C.-Y.; Wong, K. M.-C.; Yam, V. W.-W. *New J. Chem.* **2004**, *28*, 261–265; (b) Zhang, R.-H.; Ma, B.-Q.; Bu, X.-H.; Wang, H.-G.; Yao, X.-K. *Polyhedron* **1997**, *16*, 1123–1127.
46. (a) Li, J. R.; Bu, X. H.; Zhang, R. H. *Eur. J. Inorg. Chem.* **2004**, *8*, 1701–1704; (b) Bu, X.-H.; Weng, W.; Li, J.-R.; Chen, W.; Zhang, R.-H. *Inorg. Chem.* **2002**, *41*, 413–415; (c) Zhang, R.-H.; Ma, B.-Q.; Bu, X.-H.; Wang, H.-G.; Yao, X.-K. *Polyhedron* **1997**, *16*, 1787–1792; (d) Ayala, D.; Bombieri, G.; Del Pra, A.; Vicentin, G. *lnorg. Chim. Acta* **1998**, *274*, 236–238.
47. Prenesti, E.; Daniele, P. G.; Berto, S.; Toso, S. *Polyhedron* **2006**, *25*, 2815–2823.
48. See Supplementary data for comparison of IR spectra.
49. Lei, K.-W.; Liu, W.-S. *Spectrochim. Acta, Part A* **2006**, *65*, 187–190.
50. (a) Leonard, J. P.; dos Santos, C. M. G.; Plush, S. E.; Mc Cabe, T.; Gunnlaugsson, T. *Chem. Commun.* **2007**, 129–131; (b) Gunnlaugsson, T.; Leonard, J. P. *Chem. Commun.* **2005**, 3114–3131.
51. Sheldrick, G. M. *SADABS, Program for Scaling and Correction of Area Detector Data*; University of Göttingen: Göttingen (Germany), 1997; Blessing, R. H. *Acta Cryst A* **1995**, *51*, 33.
52. Sheldrick, G. M. *SHELX-TL, Version 6.14*; University of Göttingen, Bruker AXS: Madison, WI, 2003.