Pergamon

SCIENCE @ DIRECT®

Tetrahedron Letters 44 (2003) 5415–5418

TETRAHEDRON
LETTERS

Synthesis, characterization of a novel calixarene having dipyridyl pendants and study of its complexes with Cu(II) and Co(II)

Giuseppe Arena,* Annalinda Contino, Elisa Longo, Domenico Sciotto, Carmelo Sgarlata and Giuseppe Spoto

Dipartimento di Scienze Chimiche, Viale Andrea Doria 6, 95125 Catania, Italy

Received 25 March 2003; revised 26 May 2003; accepted 26 May 2003

Abstract—Two dipyridyl pendants were attached to the 1,3 positions of a calix[4]arene, with the purpose of having a ligand able to complex Cu(II) and Co(II). Indeed, the new ligand, fixed in its 1,3-alternate conformation, forms stable complexes with both Co(II) and Cu(II), as shown by UV–vis titrations carried out in acetonitrile. However, the data analysis clearly shows that the ligand forms with the two metal ions complexes having different stoichiometries. © 2003 Elsevier Science Ltd. All rights reserved.

It is well known that calixarenes are an extremely versatile class of macrocyclic receptors able to complex various metal ions as well as to selectively recognize both neutral and charged inorganic as well as organic species in solution.[1] When a metal ion is complexed, the simultaneous presence of a metal center and a cavity within the backbone makes it possible to obtain synthetic model systems able both to bind small molecules via the coordination of a substrate by unoccupied sites of the metal ion coordination sphere and to include the same substrate into the calixarene cavity. In this context, the complexes formed by calixarenes with suitable metal ions, as cobalt(II)[2] or copper(I)/(II),[3] might be exploited to bind, transport and activate simple molecules such as molecular oxygen[4] or other small molecules of biological interest. Investigations have to be carried out in solvents that, while ensuring the solubility of reactants, are as far as possible similar to water. To this end we have synthesized a new calix[4]arene functionalized with two dipyridyl groups at the lower rim and fixed in a 1,3 alternate conformation (compound **5**, Scheme 1) and have investigated its Co(II) and Cu(II) complexes in CH_3CN. Bipyridyl containing calixarenes have been extensively used to complex various metal ions.[5] The importance of this class of complexes also stems from the possibility to oxidize/reduce these systems and thus to exploit these properties at the nanoscale level. Ligand **5** was chosen because it offers a fairly pre-organized scaffold where only the donating bipyridine chelating groups are relatively free to rotate around the $C_{bipyridyl}$–CH_2–O_{calix} bond as shown by CPK models as well as by molecular mechanics calculations.[6] Thus, at least in principle, **5** should be able to form both mononuclear and binuclear complexes.[7]

To synthesize **5**, **1** was first refluxed under nitrogen with K_2CO_3 and 1-iodopropane in anhydrous CH_3CN. **2**, fixed in its *cone* conformation, was obtained from the reaction mixture by extraction with CH_2Cl_2 and subsequent precipitation with methanol (yield of 70%). The reaction of 6-methyl-2,2′-dipyridyl (**3**) with *N*-bromosuccinimide and azobis(isobutirronitrile) in CCl_4 afforded compound **4** that was purified by column chromatography on silica gel (yield 40%). Finally, compounds **2** and **4** were refluxed in anhydrous CH_3CN in presence of Cs_2CO_3 under nitrogen to obtain compound **5**, which was purified by extraction with CH_2Cl_2 and trituration in methanol (yield 60%).[8] The ^1H NMR data of **5** in $CDCl_3$ clearly shows that this calixarene has a 1,3 alternate blocked conformation. The pattern of the bridging methylene protons reproduces a typical AB system, resulting from the small anisochrony of the axial and equatorial protons.

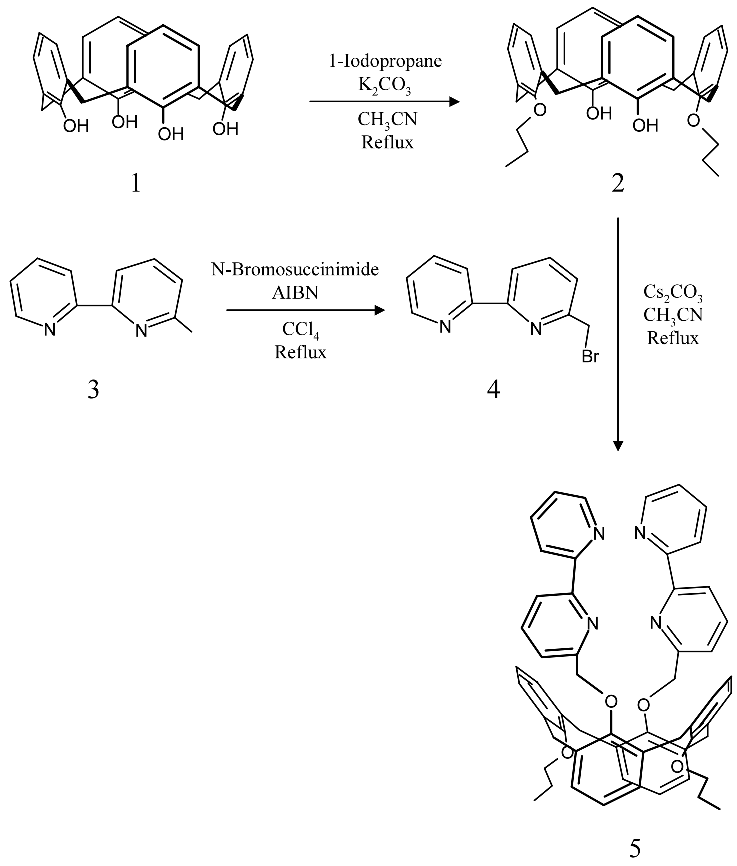
The complexes of **5** with both Co^{2+} and Cu^{2+} were investigated by UV–vis titrations. The spectrophotometric measurements were carried out at 25°C and at an ionic strength of 0.1 mol dm^{-3} ($NaClO_4$) (**Caution!** *Perchlorates may be explosive and should be handled with caution*) in acetonitrile, using a Hewlett–Packard 8542 diode array spectrophotometer. Unfortunately,

---

Keywords: calixarenes; cobalt(II); copper(II); spectrophotometric titrations.

* Corresponding author.

0040-4039/03/$ - see front matter © 2003 Elsevier Science Ltd. All rights reserved.
doi:10.1016/S0040-4039(03)01319-4



Scheme 1.

safer anions, such as tetrafluoroborate, could not be used since the anion absorbs significantly from 200 to 400 nm, i.e. in the region used to refine the complex formation constants (260–400 nm). Increasing amounts of cobalt or copper perchlorate were added by a precision burette (Hamilton, 1 ml) into the measuring cell containing a known volume (usually 2 ml) of the ligand solution and the solution was allowed to equilibrate for 3 (or 4) min. Usually a solution of the metal ion (6.0×10^{-4}–8.0×10^{-4} mol dm^{-3}) was added to a solution of the host (3.6×10^{-5}–6.0×10^{-5} mol dm^{-3}); 60–70 points were recorded for each independent titration run. The data were subsequently analyzed by using two different software packages (Specfit[9] and Hyperquad[10]) that make use of a multiwavelength and multivariate treatment of spectral data but use a different algorithm. Titration curves for both Co(II)–**5** and Cu(II)–**5** are shown in Figures 1 and 2, respectively.

The free ligand (**5**) shows two absorption bands in the UV–vis region centered at 202 and 286 nm, due to the absorption of the phenyl and 2,2′-dipyridyl moieties. The addition of cobalt or copper solutions induced a clear change of the free ligand UV–vis spectrum (inserts of Figs. 1 and 2). In particular, the addition of Co^{2+} or Cu^{2+} to compound **5** causes a batochromic shift of the ligand absorption band centered at 286 nm; this band is shifted to 308 and 314 nm, for Co^{2+} and Cu^{2+}, respectively. No CT bands were detected in the concentration range indicated above; such transitions (477 nm) become significant when working at concentrations that are ten times those we employed in the present study to have optimal absorbance values.

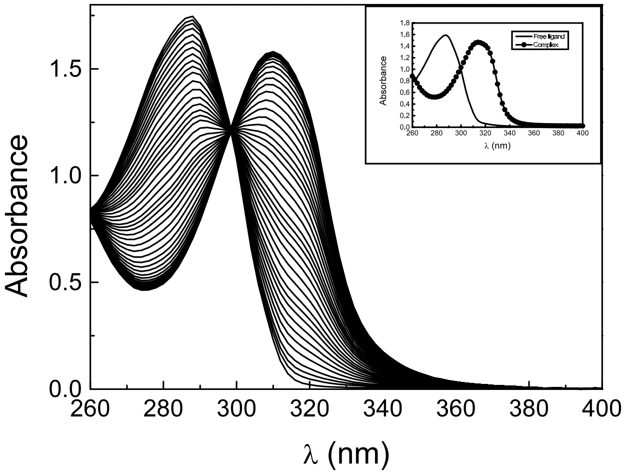


Figure 1. UV–vis titration curves for the Co–**5** system in CH_3CN; the insert shows the ligand spectrum before (—) and after (–•–) the metal ion addition.

The stoichiometries of Co–**5** and Cu–**5** main species were initially determined by both the mole-ratio[11] and the Job plot[12] methods. Both methods indicated the presence of only one complex species (ML) (Fig. 3a and

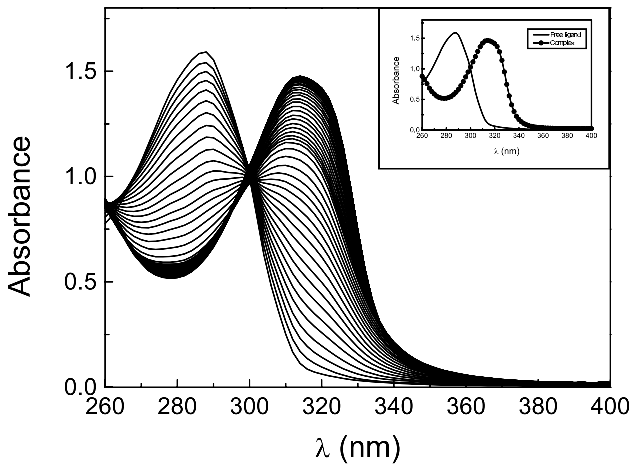


Figure 2. UV–vis titration curves for the Cu–**5** system in CH_3CN; the insert shows the ligand spectrum before (—) and after (–•–) the metal ion addition.

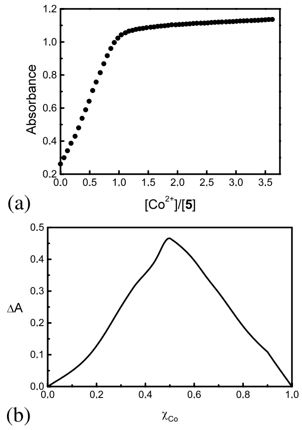


Figure 3. (a) A_{max} (308 nm) values versus Co^{2+}/**5** molar ratio. (b) Job Plot for mixtures of **5** and $Co(ClO_4)_2$ in CH_3CN. ΔA at 310 nm is plotted against the cobalt molar fraction (χ_{Co}).

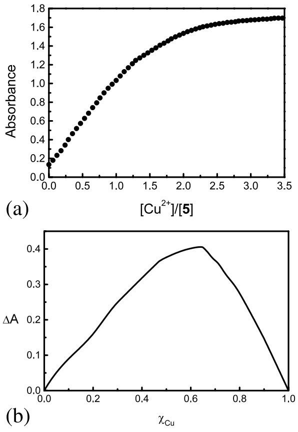


Figure 4. (a) A_{max} (314 nm) values versus Cu^{2+}/**5** molar ratio. (b) Job Plot for mixtures of **5** and $Cu(ClO_4)_2$ in CH_3CN. ΔA at 322 nm is plotted against the copper molar fraction (χ_{Cu}).

Table 1. log β values[a] for the complex formation of Co^{2+} and Cu^{2+} with host **5** at 25°C in CH_3CN

Reaction		log β	
		SPECFIT	HYPERQUAD
Co^{2+}+**5** ⇄	$[Co(\mathbf{5})]^{2+}$	7.0(2)	7.0(2)
Cu^{2+}+**5** ⇄	$[Cu(\mathbf{5})]^{2+}$	6.9(3)	7.3(2)
$2Cu^{2+}$+**5** ⇄	$[Cu_2(\mathbf{5})]^{4+}$	12.2(2)	12.6(2)

[a] 2σ in parentheses.

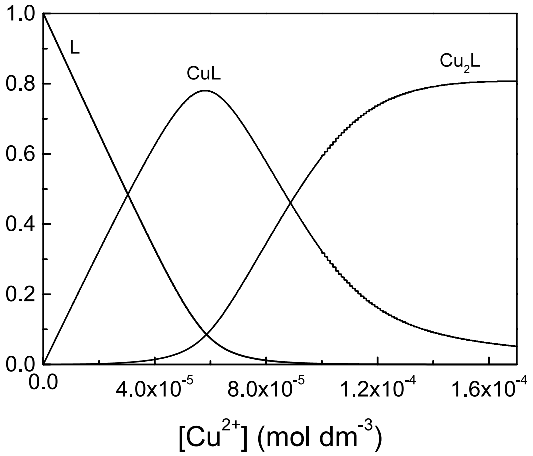


Figure 5. Species distribution diagram for Cu–**5**. [**5**] = 5.60× 10^{-5} mol dm^{-3}.

b) for the Co–**5** system and two species (ML and the M_2L) (Fig. 4a and b), for the Cu–**5** system. This is in line with the titration spectra shown in Figures 1 and 2. In fact the cobalt titration curves show a clear isosbestic point, indicating an equilibrium between two absorbing species, whereas the copper titration spectra indicate the presence of more than two absorbing species (i.e. the ligand and two complex species). The existence of the ML and M_2L was undoubtedly confirmed by the multivariate and multiwavelength treatment of the data. The log *K* values reported in Table 1 show that Co^{2+} and Cu^{2+} form with **5** very stable complexes. As expected for a species having a large stability constant, for the copper system, the ML and M_2L species reach their maximum of formation at the expected stoichiometric ratios (Fig. 5). The good efficiency of the ligand in complexing the target ions makes the cobalt complexes good candidates as di-oxygen carriers.[13] The mononuclear and binuclear copper complexes are good low molecular weight model systems for the study of the catalytic activity of copper enzymes in non aqueous environment.[14] It is noteworthy that the mononuclear Cu–**5** complex can be oxidized/reduced reversibly (ΔE = 110 mV), as shown by a cyclic voltammetry investigation,[15] which makes these systems also good candidates for nano switches.

MIUR (COFIN2002 prot. 2002038825) and CNR are kindly acknowledged for partial financial support.

References

1. (a) Gutsche, C. D. In *Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; Calixarenes; Royal Society of Chemistry: Cambridge, 1989; (b) Gutsche, C. D. In *Monographs in Supramolecular Chemistry*; Stoddart, J. F., Ed.; Calixarenes Revisited; Royal Society of Chemistry: Cambridge, 1998; (c) *Calixarenes 2001*; Asfari, Z.; Böhmer, V.; Harrowfield, J.; Vicens, J., Eds.; Kluwer Academic Publishers: Dordrecht, 2001.
2. Niederhoffer, E. C.; Timmons, J. H.; Martell, A. E. *Chem. Rev*. **1984**, *84*, 137–203.
3. Kitajima, N.; Moro-oka, Y. *Chem. Rev*. **1994**, *94*, 737–757.
4. Suzuki, M.; Furutachi, H.; Okawa, H. *Coord. Chem. Rev*. **2000**, *200-202*, 105–129.
5. (a) Beer, P. D.; Martin, J. P.; Drew, M. G. B. *Tetrahedron* **1992**, *48*, 9917–9928; (b) Casnati, A.; Fischer, C.; Guardigli, M.; Isernia, A.; Manet, I.; Sabbatini, N.; Ungaro, R. *J. Chem. Soc*., *Perkin Trans. 2* **1995**, 395–399; (c) Pellet-Rostaing, S.; Regnouf de Vains, J.-B.; Lamartine, R.; Fenet, B. *Inorg. Chem. Commun*. **1999**, *2*, 44–47; (d) Regnouf de Vains, J.-B.; Dalbavie, J.-O.; Lamartine, R.; Fenet, B. *Tetrahedron Lett*. **2001**, *42*, 2681–2684; (e) Psychogios, N.; Regnouf-de-Vains, J.-B. *Tetrahedron Lett*. **2001**, *42*, 2799–2800; (f) Psychogios, N.; Regnouf-de-Vains, J.-B. *Tetrahedron Lett*. **2002**, *43*, 77–80.
6. Hyperchem®; Serial Number 510-10001631.
7. (a) Pellet-Rostaing, S.; Regnouf-de-Vains, J.-B.; Lamartine, R. *Tetrahedron Lett*. **1995**, *36*, 5745–5748; (b) Dalbavie, J.-O.; Regnouf-de-Vains, J.-B.; Lamartine, R.; Lecocq, S.; Perrin, M. *Eur. J. Inorg. Chem*. **2000**, *4*, 683–691; (c) Dalbavie, J.-O.; Regnouf-de-Vains, J.-B.; Lamartine, R.; Perrin, M.; Lecocq, S.; Fenet, B. *Eur. J. Inorg. Chem*. **2002**, *4*, 901–909.
8. Mp 226–228°C. ^{1}H NMR ($CDCl_3$, 500 MHz): δ 8.73 (d,d, 2H, $J_1=4$ Hz, $J_2=1.8$ Hz, 6′-H), 8.43 (d, 2H, $J=8$ Hz, 3′-H), 8.38 (d, 2H, $J=8$ Hz, 3-H), 7.84 (m, 4H, 4-H+4′-H), 7.34 (d,d,d, 2H, $J_1=8$ Hz, $J_2=4$ Hz, $J_3=1.8$ Hz, 5′-H), 7.11 (d, 4H, $J=7.5$ Hz, Ar-H *meta*), 6.98 (d, 2H, $J=7$ Hz, 5-H), 6.86 (t, 2H, $J=7.5$ Hz, Ar-H *para*), 6.71 (d, 4H, $J=7.5$ Hz, Ar-H *meta*), 6.33 (t, 2H, $J=7.5$ Hz, Ar-H *para*), 5.02 (s, 4H, CH_2-bipy), 3.75 and 3.69 (AB, 8H, $J=15$ Hz, Ar-CH_2-Ar), 3.51 (t, 4H, $J=7$ Hz, $OC\mathit{H}_2CH_2CH_3$), 1.60 (tq, 4H, $J_1=J_2=7.5$ Hz $OCH_2C\mathit{H}_2CH_3$), 0.87 (t, 6H, $J=7.5$ Hz, $OCH_2CH_2C\mathit{H}_3$). Anal. calcd for $C_{56}H_{52}O_4N_4$: 79.59% C, 6.20% H, 7.57% O, 6.63% N. Found: 79.43% C, 6.16% H, 6.61% N. This compound was also characterized by ESI-MS (*m*/*z* 846 $(M+1)^+$), UV–vis measurements (λ_{max} (CH_3CN)/nm 286; ε/dm^3 mol^{-1} cm^{-1} 35120) and thermogravimetric analysis. This latter technique indicates that the compound is of the desired degree of purity.
9. Spectrum Software Associates Chapel Hill, NC USA.
10. (a) Sabatini, A.; Vacca, A.; Gans, P. *Coord. Chem. Rev*. **1992**, *120*, 389–405; (b) Gans, P.; Sabatini, A.; Vacca, A. *Talanta* **1996**, *43*, 1739–1753.
11. Yoe, J. H.; Harvey, A. E. *J. Am. Chem. Soc*. **1948**, *70*, 648–654.
12. Job, P. *Ann. Chim*. **1928**, *9*, 113–117.
13. (a) Martell, A. E. *Oxygen Complexes and Oxygen Activation by Transition Metals*; Plenum: New York, 1988; (b) Lindoy, L. F. *The Chemistry of Macrocyclic Ligand Complexes*; Cambridge University Press: Cambridge, 1989.
14. (a) Molenved, P.; Engbersen, J. F. J.; Reinhoudt, D. N. *J. Org. Chem*. **1999**, *64*, 6337–6341; (b) Molenved, P.; Engbersen, J. F. J.; Reinhoudt, D. N. *Chem. Soc. Rev*. **2000**, *29*, 75–86.
15. Arena, G.; Bonomo, R. P.; Contino, A.; Sgarlata, C.; Spoto, G.; Tabbì, G., unpublished results.