A Diiminoplatinum(II) Complex of 4-Ethynylbenzo-15-crown-5 as a Luminescent Sensor for Divalent Metal Ions

Phyllis K. M. Siu,[a] Siu-Wai Lai,[a] Wei Lu,[a] Nianyong Zhu,[a] and Chi-Ming Che*[a]

Keywords: Crown compounds / Platinum / Luminescence / Magnesium / Sensors

The binding of a diiminoplatinum(II) complex of 4-ethynylbenzo-15-crown-5 to divalent metal ions such as Mg^{2+} or Zn^{2+} is accompanied by substantial enhancement of emission intensity (1035- and 870-fold increase, respectively, with 40 equivalents of metal salt) at $\lambda_{max} \approx 555$ nm; H^{+}, Cd^{2+} and alkali-metal ions cause minor enhancement of the photoluminescence ($\leq$ 10-fold) under similar conditions.

(© Wiley-VCH Verlag GmbH & Co. KGaA, 69451 Weinheim, Germany, 2003)

Introduction

The design of new luminescent sensors for metal ions has continued to attract considerable interest.[1,2] An efficient luminescent probe should exhibit a substantial "switch-on" effect upon binding to metal ions. Using emission as a signalling reporter, luminescent metal complexes are of interest due to their long emission lifetimes, tunable emission energies in the visible region and large Stokes shifts between absorption and emission spectra.[3] In our design of luminescent sensors for metal ions, we were attracted to the following: (1) encapsulation of divalent metal ions such as Zn^{2+} by $[(\eta^5\text{-}C_5H_4SiMe_3)_2Ti(C{\equiv}CR)_2]$ [R = SiMe$_3$ or (η^5-C$_5$H$_4$)FeCp] via side-on coordination of alkynyl ligands has been reported;[4] (2) crown ethers are known to complex metal ions;[5] (3) neutral organoplatinum(II) complexes are known to form dative bonds with divalent metal ions;[6] and (4) square-planar cyclometalated[7] and aromatic[8,9] diiminoplatinum(II) complexes possess rich photoluminescent properties that are sensitive to the microenvironment. Herein we describe the synthesis of [Pt(4-ethynylbenzo-15-crown-5)$_2$(*t*Bu$_2$bpy)] (**1**) (*t*Bu$_2$bpy = 4,4′-di-*tert*-butyl-2,2′-bipyridine) and [Pt(4-ethynylbenzo-15-crown-5)(C^N^N)] (**2**) (HC^N^N = 6-phenyl-2,2′-bipyridine), and their luminescence responses towards metal ions. A dramatic photoluminescence switch-on effect has been observed for **1** in the presence of Zn(ClO$_4$)$_2$ and Mg(ClO$_4$)$_2$ and the binding of Mg^{2+} to **1** found to be selective in the presence of alkali or alkaline earth metal ions.

Results and Discussion

Treatment of [PtCl$_2$(*t*Bu$_2$bpy)][10] with two molar equivalents of 4-ethynylbenzo-15-crown-5 (**L**)[11] in the presence of copper(I) iodide and diisopropylamine afforded **1**. The molecular structure of **1** (Figure 1) shows that the Pt^{II} core is *cis*-coordinated by two 4-ethynylbenzo-15-crown-5 moieties and the *t*Bu$_2$bpy ligand. The cyclometalated counterpart **2** was similarly synthesised by reacting equimolar amounts of [PtCl(C^N^N)][12] and **L** (Figure 2).

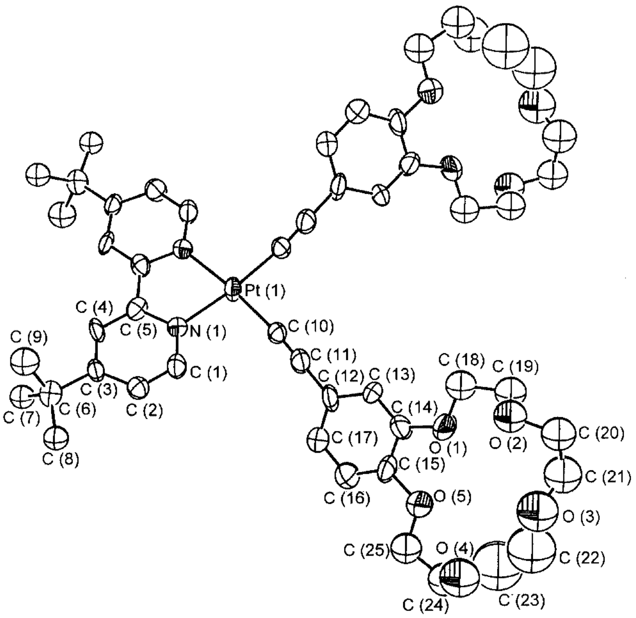
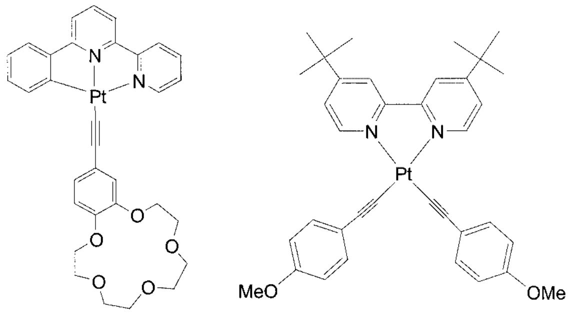


Figure 1. Perspective view of **1** (30% probability ellipsoids); selected bond lengths (Å) and angles (°): Pt(1)−C(10) 1.98(1), Pt(1)−N(1) 2.062(8), C(10)−C(11) 1.12(1); C(10)#1−Pt(1)−C(10) 90.0(6), N(1)#1−Pt(1)−N(1) 78.3(5), C(11)−C(10)−Pt(1) 172(1)

---

[a] Department of Chemistry and the Open Laboratory of Chemical Biology of the Institute of Molecular Technology for Drug Discovery and Synthesis, The University of Hong Kong, Pokfulam Road, Hong Kong SAR, China
Fax: (internat.) + 852-2857-1586
E-mail: cmche@hku.hk

Supporting information for this article is available on the WWW under http://www.eurjic.org or from the author.



2 **3**

Figure 2. Structures of **2** and **3**

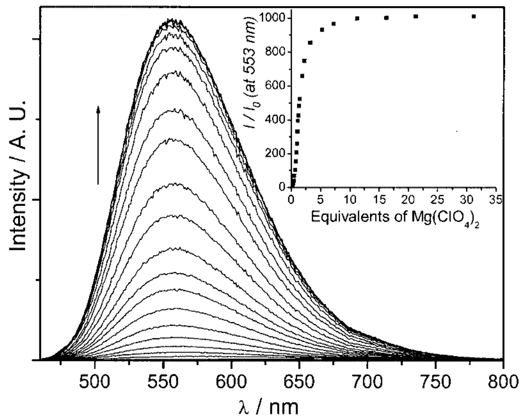


Figure 3. Emission spectral traces and (inset) luminescence enhancement factor ($\equiv I/I_o$; monitored at 553 nm) of **1** at increasing equivalents of Mg^{2+} in 0.1 M $n$$Bu_4NPF_6$ acetonitrile solution at 298 K ($\lambda_{ex} = 405$ nm, [**1**] $= 1.0 \times 10^{-5}$ mol dm^{-3})

The absorption spectrum of **1** in acetonitrile features a moderately intense band at $\lambda_{max} = 393$ nm ($\varepsilon \approx 7900$ dm^3 mol^{-1} cm^{-1}) which is attributed to the [5d(Pt) → π*($t$$Bu_2$bpy)] metal-to-ligand charge transfer (MLCT) transition. This absorption occurs at the same energy as that reported for $[Pt(C{\equiv}CC_6H_4OMe\text{-}4)_2(t\text{Bu}_2\text{bpy})]$ (**3**; Figure 2) in acetonitrile.[13] Complex **2** shows an intense ^{1}MLCT [5d(Pt) → π*(C^N^N)] absorption in the 400−450 nm range similar to that typically observed for cyclometalated Pt^{II} derivatives.[7] Addition of 20 equivalents of $M(ClO_4)_2$ ($M^{2+} = Zn^{2+}$, Mg^{2+}) to a 0.1 M $n$$Bu_4NPF_6$ acetonitrile solution of **1** (3.2×10^{-5} mol dm^{-3}) blue-shifts the MLCT absorption band from $\lambda_{max} = 393$ to 383 nm ($\varepsilon \approx 9600$ dm^3 mol^{-1} cm^{-1}); no significant change in the absorption at $\lambda_{max} = 284$ nm is observed. In contrast, addition of up to 100 equivalents of $M(ClO_4)_2$ to a 0.1 M $n$$Bu_4NPF_6$ acetonitrile solution of **2** or **3** results in no significant shift of the MLCT absorption. Thus, the presence of the *cis* crown ether moieties in **1** appears to be critical to affect the shifting of the MLCT absorption upon interaction with Mg^{2+}/Zn^{2+}.

The weak emission of **1** ($\varphi_o = 1.1 \times 10^{-4}$) in acetonitrile at $\lambda_{max} = 635$ nm is assigned as being ^{3}MLCT [5d(Pt) → π*($t$$Bu_2$bpy)] in nature.[13] Addition of M^{2+} (as a perchlorate salt) to a 0.1 M $n$$Bu_4NPF_6$ acetonitrile solution of **1** induces a substantial enhancement of the emission intensity at 553 and 560 nm for Mg^{2+} and Zn^{2+}, respectively, and reaches a maximum of 1035-fold (Figure 3) and 870-fold, respectively, at 40 equivalents of M^{2+}. With reference to previous work,[14] the emission at $\lambda_{max} \approx 555$ nm may be an admixture with both ^{3}MLCT and $^3\pi\pi^*$ character.

The effect of different Zn^{2+} salts upon binding properties was also examined. Addition of 100 equivalents of $ZnCl_2$ or $Zn(NO_3)_2$ to an acetonitrile solution of **1** (3.2×10^{-5} mol dm^{-3}) shows a similar blue shift in the emission maximum from 635 to approx. 560 nm, but the emission intensity was enhanced by only 105- and 250-fold, respectively. This indicates that the binding of **1** to Zn^{2+} ions weakens as the anion nucleophilicity increases in the order: $ClO_4^- < NO_3^- < Cl^-$ in acetonitrile. The effect of protons was investigated by addition of 200 equivalents of HBF_4 to a 0.1 M $n$$Bu_4NPF_6$ acetonitrile solution of **1**; no emission enhancement was detected. The binding properties of **1** with other metal ions have also been studied. Addition of 100 equivalents of $KClO_4$, $NaClO_4$, or $Cd(ClO_4)_2$ induces a relatively insignificant increase (≤ 10-fold) in the emission intensity of **1**. However, a 300-fold luminescence enhancement at $\lambda_{max} = 563$ nm was observed for **1** in the presence of 100 equivalents of $Ca(ClO_4)_2$. As depicted in Figure 4, the luminescence enhancement factor (LE $\equiv I/I_o$) induced by 40 equivalents of Mg^{2+} decreases by less than 20% in the presence of 40 equivalents of other cations, such as Na^+, K^+, Cd^{2+} and H^+, indicating that the binding of Mg^{2+} to **1** remains selective in their presence. For the binding of Zn^{2+} to **1**, the LE is reduced from 870 to 736 and 160 in the presence of K^+ and Na^+ respectively. This indicates that Na^+ is able to bind to **1** even in the presence of Zn^{2+}.

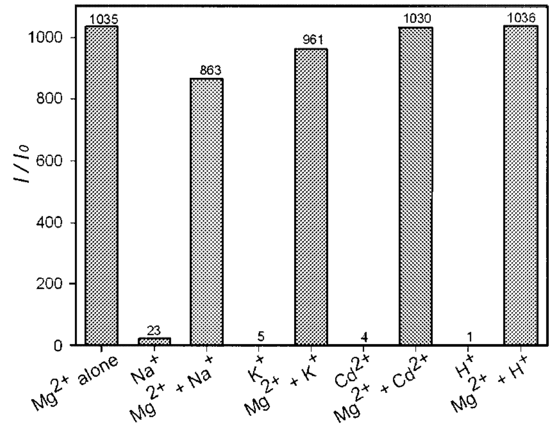


Figure 4. Luminescence enhancement factor induced by 40 equivalents of Mg^{2+} with or without the presence of M^{x+} ions in a 0.1 M $n$$Bu_4NPF_6$ acetonitrile solution of **1** (3.2×10^{-5} mol dm^{-3}) at 298 K

Complex **3** displays a weak ^{3}MLCT [5d(Pt) → π*($t$$Bu_2$bpy)] emission at $\lambda_{max} = 610$ nm in acetonitrile.[13] Addition of $Zn(ClO_4)_2$ to **3** yields virtually no change in emission intensity with or without the presence of the free crown-ether ligand **L**. The ^{3}MLCT emission of the mono-crown derivative **2**, which appears at $\lambda_{max} = 560$ nm, undergoes around a 10-fold increase in intensity, together with a slight red-shift to $\lambda_{max} = 581$ nm upon addition of 100 equivalents of $Zn(ClO_4)_2$. This signifies that, as observed in the absorption studies, the two crown ether moieties in **1** are essential for the dramatic ion-induced luminescence enhancement.

In order to elucidate the ion-binding nature of **1**, we have attempted to fit the emission data to stepwise equilibrium equations, where M^{x+} ions are consecutively bound by the platinum complex.

$$\begin{array}{lll} \mathrm{Pt} + \mathrm{M}^{x+} \rightleftharpoons \mathrm{PtM}^{x+} & & K_{11} \\ \mathrm{PtM}^{x+} + \mathrm{M}^{x+} \rightleftharpoons \mathrm{Pt(M}^{x+})_2 & & K_{12} \\ \vdots & & \vdots \\ \mathrm{Pt(M}^{x+})_{n-1} + \mathrm{M}^{x+} \rightleftharpoons \mathrm{Pt(M}^{x+})_n & & K_{1n} \end{array}$$

The stepwise (K_{11}, K_{12}, K_{13}) and overall (β) binding constants for the complexation of Na^+, Mg^{2+} and Zn^{2+} ions to **1** were determined under the assumptions stated in the supporting information and compared to the total number of M^{x+} ions bound by **1** (n) and the β value obtained from the Hill equation (Table 1).[15] In the case of $n = 3$, the discrepancy of β values between the nonlinear least-squares fits and Hill plots for these ions suggests unreasonable data fitting, and that this can be disregarded in the analysis. The similarity in β values determined by stepwise equilibrium binding reactions and Hill plots for the case of $n = 2$ imply that two M^{x+} ions are bound per molecule of **1**. For Na^+, the values of K_{11} and K_{12} are similar, whereas for Zn^{2+} and Mg^{2+}, the K_{12} values are around 20 and 54 times larger, respectively, than the corresponding K_{11} values. The electrospray mass spectra of **1** in the presence of 20 equivalents of $M(ClO_4)_x$ ($M^{x+} = Mg^{2+}$, Na^+) in acetonitrile reveal peaks attributable to [**1** + nM^{x+}] species (n = 1 and 2). For Mg^{2+}, the intensity ratio of peaks for [**1** + M^{x+}]:[**1** +2M^{x+}] is about 2:1, whereas that for Na^+ is about 1:3.

Table 1. Stepwise and overall equilibrium constants of **1** with Na^+, Mg^{2+}, Zn^{2+}

Ions	Nonlinear least-squares fits (n = 2)			Hill equation	
	K_{11}	K_{12}	β[a]	n	β
Na^+	7.27×10^3	1.08×10^4	7.9×10^7	1.7	6.5×10^6
Mg^{2+}	3.11×10^3	1.69×10^5	5.3×10^8	2.2	3.7×10^9
Zn^{2+}	2.11×10^3	4.41×10^4	9.3×10^7	2.0	5.5×10^7

[a] β is the overall equilibrium constant = $\Pi^n K_{1n}$

We suggest that the electrophilic M^{2+} ion functions as a Lewis acid that can be bound by the crown ether moieties. This type of interaction induces substantial perturbation upon the luminescence but is prone to competitive interaction of M^{2+} with counteranions. The switching on of substantial emission intensity in **1** with added M^{2+} may be rationalised by the destabilisation of the ^{3}MLCT excited state, leading to an increase in ^{3}IL character for the excited state. Binding of the first M^{2+} ion by **1** may widen the *cis*-$[Pt(C{\equiv}CR)_2]$ angle, which could facilitate subsequent chelation of the second M^{2+} ion by the crown ether and/or bisalkynyl moieties. This is consistent with the increase of the K_{12} binding constant relative to K_{11}.

Experimental Section

General Remarks: Acetonitrile for photophysical measurements was distilled over potassium permanganate and calcium hydride. All other solvents were of analytical grade and purified according to conventional methods.[16] 4,4′-Di-*tert*-butyl-2,2′-bipyridine,[17] $[PtCl_2(tBu_2bpy)]$,[10] 4-ethynylbenzo-15-crown-5,[11] 6-phenyl-2,2′-bipyridine,[18] and [PtCl(C^N^N)][12] were prepared by published methods. Fast atom bombardment (FAB) and electrospray mass spectra were obtained on a Finnigan MAT 95 (3-nitrobenzyl alcohol matrix) and LCQ quadrupole ion trap mass spectrometers, respectively. ^{1}H (500 MHz) NMR spectra were recorded on DPX 500 Bruker FT NMR spectrometers; chemical shift (in ppm) are quoted relative to tetramethylsilane. Elemental analysis was performed by the Institute of Chemistry at the Chinese Academy of Sciences, Beijing. IR spectra were recorded on a BIO RAD FT-IR spectrophotometer. UV/Vis spectra were recorded on a Perkin−Elmer Lambda 19 UV/Vis spectrophotometer.

Steady-state emission spectra were recorded on a SPEX 1681 Fluorolog-2 series F111AI spectrophotometer. The emission spectra were corrected for monochromator and photomultiplier efficiency and for xenon lamp stability.

Solutions for titration experiments were prepared by mixing 5 mL of **1** (6.4×10^{-5} mol dm^{-3}) in a 0.1 M nBu_4NPF_6 acetonitrile solution with the required molar equivalents of M^{x+} in the same supporting electrolyte and made up to a total of 10 mL with a 0.1 M nBu_4NPF_6 acetonitrile solution. All the sample solutions were degassed with at least four freeze-pump-thaw cycles. The emission quantum yield was measured by the method of Demas and Crosby.[19] Errors for λ values (± 1 nm) and φ (± 10%) are estimated.

[Pt(4-ethynylbenzo-15-crown-5)$_2$(*t*Bu$_2$bpy)] (1): Reaction of $[PtCl_2(tBu_2bpy)]$ and two equivalents of 4-ethynylbenzo-15-crown-5 (**L**) in the presence of copper(I) iodide and diisopropylamine afforded **1** (85%). ^{1}H NMR (CD_3CN): δ = 1.45 (s, 18 H, *t*Bu), 3.61−3.67 (m, 16 H, CH_2), 3.78−3.81 (m, 8 H, CH_2), 4.05−4.12 (m, 8 H, CH_2), 6.82−6.98 (m, 6 H, C_6H_3), 7.75 (dd, J = 6.0, J = 2.0 Hz, 2 H), 8.30 (d, J = 1.7 Hz, 2 H), 9.54 (d, J = 6.0 Hz, 2 H) ppm. MS (FAB, +ve): *m/z* (%) = 1047 (15) [M^+ + H], 1069 (60) [M^+ + Na], 1085 (8) [M^+ + K]. IR (KBr disc): $\tilde{\nu}$ = 2101 cm^{-1} (C≡C). $C_{50}H_{62}N_2O_{10}Pt$ (1046.14): calcd. C 57.41, H 5.97, N 2.68; found C 57.59, H 5.82, N 2.92.

[Pt(C^N^N)(4-ethynylbenzo-15-crown-5)] (2): The procedure for the synthesis of **1** was adopted using equimolar amounts of 4-ethynylbenzo-15-crown-5 and [Pt(C^N^N)Cl] (90%). ^{1}H NMR ([D$_6$]DMSO): δ = 3.63 (s, 8 H, CH_2), 3.79 (d, J = 1.9 Hz, 4 H, CH_2), 4.04−4.09 (m, 4 H, CH_2), 6.85−6.94 (m, 3 H, C_6H_3), 7.03−7.15 (m, 2 H), 7.62 (d, J = 7.1 Hz, 1 H), 7.76 (d, J = 7.1 Hz, 1 H), 7.86 (t, J = 6.3 Hz, 1 H), 7.98 (d, J = 7.9 Hz, 1 H), 8.10 (t, J = 7.9 Hz, 1 H), 8.20 (d, J = 7.8 Hz, 1 H), 8.33 (t, J = 7.7 Hz, 1 H), 8.48 (d, J = 7.9 Hz, 1 H), 9.06 (d, J = 4.8 Hz, 1 H) ppm. MS (FAB, +ve): *m/z* (%) = 718 (4) [M^+ + H], 740 (20) [M^+ + Na], 757 (2) [M^+ + K]. IR (KBr disc): $\tilde{\nu}$ = 2097 cm^{-1} (C≡C).

$C_{32}H_{30}N_2O_5Pt$ (717.69): calcd. C 53.55, H 4.21, N 3.90; found C 53.29, H 3.96, N 4.06.

X-ray Crystallographic Study of 1: $C_{50}H_{62}N_2O_{10}Pt$, $M = 1046.11$, orthorhombic, space group *Pccn*, $a = 23.888(5)$, $b = 10.653(2)$, $c = 18.467(4)$ Å, $V = 4699.5(16)$ Å^3, $Z = 4$, $D_c = 1.479$ g cm^{-3}, μ(Mo-K_α) = 3.045 mm^{-1}, $F(000) = 2136$. A crystal of dimensions $0.4 \times 0.2 \times 0.1$ mm^3 mounted in a glass capillary with mother liquor was used for data collection at 20 °C on a MAR diffractometer with a 300 mm image plate detector using graphite-monochromatized Mo-K_α radiation ($\lambda = 0.71073$ Å). Data collection was made with 3° oscillation step of φ, 600 seconds exposure time and a scanner distance of 120 mm; 60 images were collected. The images were interpreted and intensities integrated using the program DENZO.[20] The structure was solved by direct methods employing the SHELXS-97 program suite[21] on a PC. Pt and many non-H atoms were located by direct methods. The positions of other non-hydrogen atoms were found after successful refinement by full-matrix least-squares using SHELXL-97[21] on a PC. The *tert*-butyl group is disordered over two kinds of positions. 2849 independent reflections from a total of 11694 reflections were used in the full-matrix least-squares refinement against F^2. $R_1 = 0.044$ and $wR_2 = 0.103$ with a goodness-of-fit of 0.853 for 1291 observed reflections with $I \geq 2\sigma(I)$. The final difference Fourier map shows maximum residual peaks and holes of 0.457 and −0.642 e·Å^{-3} respectively. CCDC-177975 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

Supporting Information for this article (scheme for synthesis of **1**; emission spectral traces of **1** at increasing equivalents of Zn^{2+}, Ca^{2+}, Na^+ and K^+ ions; table for fluid-state emissions of **1**−**3** in acetonitrile with 100 equivalents of $M(ClO_4)_x$; analysis of the complexation of ions using nonlinear least-squares fits and Hill plots) is available (see footnote on the first page of this article).

Acknowledgments

We are grateful for financial support from the University Development Fund of The University of Hong Kong, the Research Grants Council of the Hong Kong SAR, China, Area of Excellence Scheme (AoE/P-10/01) of the University Grants Committee of the Hong Kong SAR, China, and The Chinese Manufacturers' Association of Hong Kong.

---

[1] S. C. Burdette, G. K. Walkup, B. Spingler, R. Y. Tsien, S. J. Lippard, *J. Am. Chem. Soc.* **2001**, *123*, 7831−7841.

[2] [2a] T. Hirano, K. Kikuchi, Y. Urano, T. Higuchi, T. Nagano, *Angew. Chem. Int. Ed.* **2000**, *39*, 1052−1054. [2b] D. A. Pearce, N. Jotterand, I. S. Carrico, B. Imperiali, *J. Am. Chem. Soc.* **2001**, *123*, 5160−5161.

[3] [3a] P. D. Beer, O. Kocian, R. J. Mortimer, C. Ridgway, *J. Chem. Soc., Dalton Trans.* **1993**, 2629−2638. [3b] A. P. de Silva, H. Q. N. Gunaratne, T. E. Rice, S. Stewart, *Chem. Commun.* **1997**, 1891−1892.

[4] H. Lang, N. Mansilla, G. Rheinwald, *Organometallics* **2001**, *20*, 1592−1596.

[5] R. M. Izatt, J. S. Bradshaw, S. A. Nielsen, J. D. Lamb, J. J. Christensen, *Chem. Rev.* **1985**, *85*, 271−339.

[6] T. Yamaguchi, F. Yamazaki, T. Ito, *J. Am. Chem. Soc.* **1999**, *121*, 7405−7406.

[7] [7a] K. H. Wong, M. C. W. Chan, C. M. Che, *Chem. Eur. J.* **1999**, *5*, 2845−2849. [7b] C. M. Che, W. F. Fu, S. W. Lai, Y. J. Hou, Y. L. Liu, *Chem. Commun.* **2003**, 118−119.

[8] S. M. Drew, D. E. Janzen, C. E. Buss, D. I. MacEwan, K. M. Dublin, K. R. Mann, *J. Am. Chem. Soc.* **2001**, *123*, 8414−8415.

[9] V. W. W. Yam, R. P. L. Tang, K. M. C. Wong, X. X. Lu, K. K. Cheung, N. Zhu, *Chem. Eur. J.* **2002**, *8*, 4066−4076.

[10] K. D. Hodges, J. V. Rund, *Inorg. Chem.* **1975**, *14*, 525−528.

[11] S. V. Klyatskaya, E. V. Tretyakov, S. F. Vasilevsky, *Mendeleev Commun.* **1998**, *8*, 201−202.

[12] [12a] E. C. Constable, R. P. G. Henney, T. A. Leese, D. A. Tocher, *J. Chem. Soc., Chem. Commun.* **1990**, 513−515. [12b] T. C. Cheung, K. K. Cheung, S. M. Peng, C. M. Che, *J. Chem. Soc., Dalton Trans.* **1996**, 1645−1651.

[13] [13a] M. Hissler, W. B. Connick, D. K. Geiger, J. E. McGarrah, D. Lipa, R. J. Lachicotte, R. Eisenberg, *Inorg. Chem.* **2000**, *39*, 447−457. [13b] S. C. Chan, M. C. W. Chan, Y. Wang, C. M. Che, K. K. Cheung, N. Zhu, *Chem. Eur. J.* **2001**, *7*, 4180−4190.

[14] V. M. Miskowski, V. H. Houlding, C. M. Che, Y. Wang, *Inorg. Chem.* **1993**, *32*, 2518−2524.

[15] *Binding Constants* (Ed.: K. A. Conners), Wiley, New York, **1987**.

[16] D. D. Perrin, W. L. F. Armarego, D. R. Perrin, *Purification of Laboratory Chemicals*; 2nd ed., Pergamon: Oxford, **1980**.

[17] G. M. Badger, W. H. F. Sasse, *J. Chem. Soc.* **1956**, 616−620.

[18] F. Kröhnke, *Synthesis* **1976**, 1−24.

[19] J. N. Demas, G. A. Crosby, *J. Phys. Chem.* **1971**, *75*, 991−1024.

[20] Z. Otwinowski, W. Minor, *Processing of X-ray Diffraction Data Collected in Oscillation Mode*, Methods in Enzymology, Volume 276: Macromolecular Crystallography, part A, 307−326, **1997** (Eds.: C. W. Carter, R. M. Sweet Jr.), Academic Press.

[21] G. M. Sheldrick, *SHELXS-97, Program for Crystal Structure Analysis*, **1997**, University of Göttingen, Germany.

Received April 14, 2003

© 2003 Wiley-VCH Verlag GmbH & Co. KGaA, Weinheim