Angewandte
Chemie

Reprogrammable Ligands

Allosteric and Electrostatic Reprogramming of a Ditopic Ligand**

*Christian J. Baylies, Lindsay P. Harding, John C. Jeffery, T. Riis-Johannessen, and Craig R. Rice**

The ability of ligands to partition into different binding domains is instrumental in the formation of transition-metal supramolecular architectures. For this reason ligands are designed and synthesized to contain binding sites of differing nature and number. Hence, on reacting such ligands with metal ions, a desired supramolecular architecture assembles as a result of the particular disposition of the binding sites.[1] The information stored within a ligand strand can lead to a variety of supramolecular species, such as helicates,[2] grids,[3] and cages.[4] Once a ligand has been synthesized the information is permanently stored within it and the ligand can therefore be thought of as being "preprogrammed".[5] Herein, we describe a remarkable new ditopic ligand L^1, whose binding modes can be changed or "reprogrammed" by the addition of barium ions to a crown ether moiety. This is related to the allosteric effect demonstrated by Rebek et al.,

---

[*] Dr. C. J. Baylies, L. P. Harding, Dr. C. R. Rice
Department of Chemical and Biological Sciences
University of Huddersfield
Huddersfield HD1 3DH (UK)
Fax: (+44) 148-447-2182
E-mail: c.r.rice@hud.ac.uk

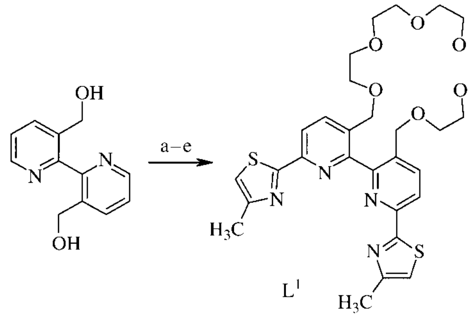
Dr. J. C. Jeffery, T. Riis-Johannessen
School of Chemistry, University of Bristol
Cantocks Close, Bristol BS8 1TS (UK)

[**] We thank the EPSRC and the University of Huddersfield for financial support.

DOI: 10.1002/ange.200460424

who used a derivative of 2,2′-bipyridine in which the twist between the two pyridyl rings was influenced by remote conformational changes in a crown ether fragment joining the backs of the rings.[6] However, in the case of L^1 reported herein, there is a fundamental difference in that the cation that binds to the crown ether moiety changes the gross molecular structure.

The ditopic ligand L^1 was prepared from 2,2′-bipyridine-3,3′-dimethanol as outlined in Scheme 1. L^1 contains a potentially tetradentate pyridyl–thiazole ligand chain and an additional "external" crown ether binding site that connects the two halves of the bipyridyl moiety. On treating L^1 with an equimolar amount of $Hg(ClO_4)_2{\cdot}3H_2O$ in MeCN a colorless solution was produced, and ESI MS showed the formation of a dinuclear double helicate with an ion at m/z 1924 corresponding to $[Hg_2(L^1)_2](ClO_4)_3^+$. The ^{1}H NMR spectrum of $[Hg_2(L^1)_2]^{4+}$ in CD_3CN shows only three aromatic resonances for the pyridyl–thiazole moiety which is consistent with a highly symmetrical, double-helicate complex. Furthermore, the benzylic $-CH_2O-$ fragment has a diastereotopic methylene group, which, as expected, gives rise to two doublets ($\delta = 4.50$ and 4.39 ppm; Figure 1 a).



Scheme 1. Reagents and conditions: a) penta(ethylene glycol) di-*p*-toluenesulfonate, DMF, NaH, 60%; b) *m*CPBA, CH_2Cl_2, 70%; c) TMSCN, PhCOCl, CH_2Cl_2, 83%; d) H_2S, Et_3N, EtOH, 90%; e) chloroacetone, EtOH,76%.

Treatment of $[Hg_2(L^1)_2]^{4+}$ with an excess of $NaClO_4$ (3 equiv) followed by crystallization afforded the complex $[Hg_2(L^1)_2Na_2](ClO_4)_6{\cdot}4MeCN$, whose structure has been established by a single-crystal X-ray diffraction studies.[7] In the crystal, the ligand splits into two bis-bidentate binding domains with two Hg^{2+} ions coordinated by two bridging ligands in a double-helicate arrangement (Figure 2). Each of the Hg^{2+} centers has a distorted tetrahedral geometry formed

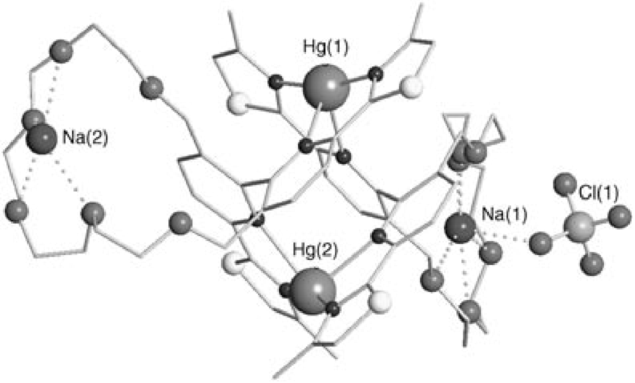


Figure 2. Structure of the complex cation of $[Hg_2(L^1)_2Na_2]^{6+}$.

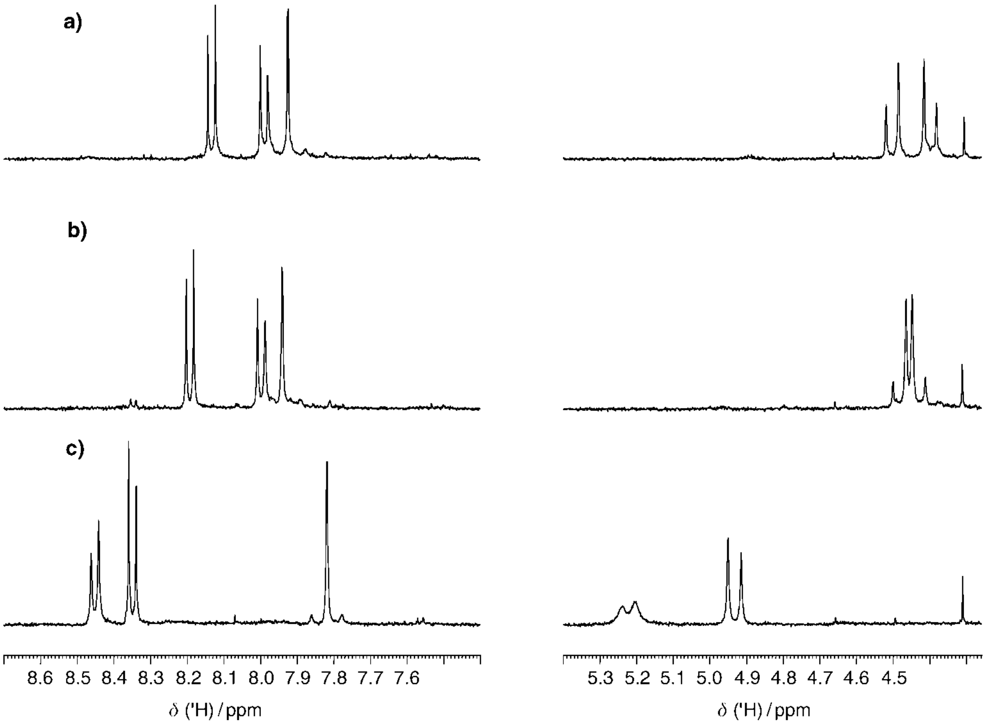


Figure 1. Selected regions of the ^{1}H NMR spectra (CD_3CN) of a) $[Hg_2(L^1)_2]^{4+}$, b) $[Hg_2(L^1)_2]^{4+} + Na^+$, c) $[Hg_2(L^1)_2]^{4+} + Ba^{2+}$.

by coordination of two thiazole–pyridyl bidentate N-donor units [2.107(5)–2.535(5) Å], one from each ligand. Each ligand is twisted about the central bond between the two pyridyl rings [92.2 and 93.7°]. In theory, L^1 can act as either a bis-bidentate or a tetradentate N-donor ligand. However, in this case, owing to the preference of Hg^{2+} for tetrahedral geometry, the ligand acts as a bis-bidentate donor and forms a dinuclear double helicate.

Both crown ethers partially coordinate sodium ions. In one case the Na^+ is seven-coordinate and bonds to five oxygen atoms (2.351(5)–2.693(5) Å) from the [16]crown-6 fragment, leaving one of the benzylic oxygen atoms uncoordinated. The remaining two coordination sites incorporate an acetonitrile molecule and a perchlorate anion. The other Na^+ ion is five-coordinate and is only coordinated by the four "outer" oxygen atoms (2.319(7)–2.545(6) Å) of the crown ether ring, leaving both benzylic oxygen atoms uncoordinated. A single monodentate perchlorate anion completes the coordination environment. The inability of the sodium ions to coordinate all of the crown oxygen atoms is to be expected, given that a crown-6 type fragment is known to be too big to coordinate optimally to the Na^+ cation.

The weak Na^+ cation binding observed in the solid state is maintained in solution. Thus ESI MS shows ions at *m/z* 2046 and 2168, which correspond to $[\{Hg_2(L^1)_2Na\}(ClO_4)_4]^+$ and $[\{Hg_2(L^1)_2Na_2\}(ClO_4)_5]^+$, respectively. Similarly, the ^{1}H NMR spectrum of the sodium species in CD_3CN is similar to that of $[Hg_2(L^1)_2]^{4+}$, but in this case a shift in the -CH_2O- region of approximately 0.02 ppm confirms that the crown ether is weakly coordinated to Na^+ in solution (Figure 1 b).

In marked contrast, reaction of $[Hg_2(L^1)_2]^{4+}$ with $Ba(ClO_4)_2$ affords a colorless solution for which ESI MS shows only an ion that corresponds to the mononuclear complex $[\{Hg(L^1)Ba\}(ClO_4)_3]^+$. Additionally, the ^{1}H NMR spectrum in CD_3CN showed a marked change in the signals that arise from both the benzylic -CH_2O- and the aromatic regions (Figure 1 c). These signals are substantially shifted relative to those for $[Hg_2(L^1)_2]^{4+}$ (-CH_2O- average $\Delta\delta =$ 0.63 ppm) or its Na^+ derivative. Chemical-shift changes of this order in the aromatic region are more indicative of a change in molecular structure rather than the relatively small changes that would be observed with coordinative perturbation of the crown. The formation of the mononuclear species was confirmed by X-ray crystallography,[7] which showed a six-coordinate Hg^{2+} complex with a distorted octahedral environment (Figure 3). The ligand acts as a near-planar tetradentate "equatorial" ligand, with two perchlorate anions acting as bidentate axial ligands. The Hg–N bonds range from 2.24(1) to 2.47(1) Å. The ligand is almost planar but exhibits a shallow helical twist caused by the unfavorable steric interactions between the methylene substituents on the central bipyridyl core (33.1°). The barium ion is ten-coordinate and strongly bonded to all *six* of the crown ether oxygen atoms (2.76(1)–2.90(1) Å), with the oxygen atoms of two perchlorate anions acting as bidentate O-donor ligands. Unlike the sodium analogue, all of the oxygen atoms in the crown ether moiety form bonds to Ba^{2+}, reflecting the good size match between the ion and the crown-6 fragment and the electron-deficient character of the Ba^{2+} dication.

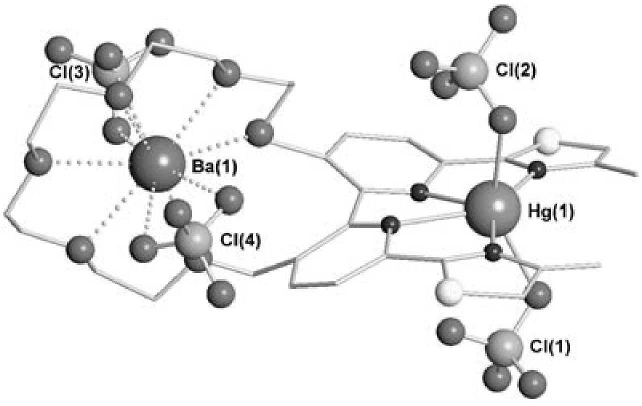


Figure 3. Structure of the complex cation of $[Hg(L^1)Ba]^{4+}$.

Thus, in the presence of Hg^{2+} and Na^+, the ligand L^1 forms a dinuclear double helicate complex, whereas in the presence of Hg^{2+} and Ba^{2+} a mononuclear species is formed exclusively. Such control of self-assembly can be attributed to one of two factors: First, an electrostatic effect as coordination of barium to the helicate would lead to a highly charged $8+$ ion. Subsequent disassembly to the mononuclear species would then lower the extent of electrostatic repulsion and increase the entropy of the system. However, the change in structure could also be attributed to an allosteric effect. Thus, in the helicate $[Hg_2(L^1)_2Na_2]^{6+}$ the sodium ions are coordinated by the crown ether moieties but, owing to the poor fit of the Na^+ in the [16]crown-6 fragment, at least one of the benzylic oxygen atoms remains uncoordinated. This poor fit allows the ligand to twist about the central bipyridyl unit, enabling it to partition into two bidentate domains and assemble into a dinuclear double helicate. In contrast, upon reaction with Ba^{2+} the mononuclear species $[Hg(L^1)Ba]^{4+}$ is formed. In this system both benzylic oxygen atoms are coordinated, thus restricting the previously observed conformational mobility of the ligand. This prerequisite for helicate formation being absent means that the ligand does not partition into separate bridging units but instead acts as a simple tetradentate donor.

In an effort to ascertain which effect controls the self-assembly, systematic ^{1}H NMR studies were carried out to monitor the effect of addition of different Group 1 and 2 metal ions to the ditopic helicate $[Hg_2(L^1)_2]^{4+}$. This revealed that dinuclear double helicates are formed in the presence of smaller metal ions of both Group 1 and 2 (i.e. $[Hg_2(L^1)_2M_2]^{6+/8+}$, $M = Li^+$, Na^+, or Mg^{2+}), whereas mononuclear species are formed with Ba^{2+} and Sr^{2+} (i.e. $[Hg(L^1)M]^{4+}$, $M = Ba^{2+}$ or Sr^{2+}). Upon addition of K^+, which is similar in size to Ba^{2+} but only singly charged, a mixture of species is formed ($[Hg_2(L^1)_2K_2]^{6+}/[Hg(L^1)K]^{3+} = 1{:}2$) whereas with Ca^{2+}, which is doubly charged but is smaller than K^+, a mixture of species is also observed, but the ratios are the reverse of that found with K^+ ($[Hg_2(L^1)_2Ca_2]^{8+}/[Hg(L^1)Ca]^{4+} = 2{:}1$). Given these results, it would appear that no one factor is dominant in this control of self-assembly and that both electrostatic and allosteric effects play important roles.

So far, this system represents a unique example of how ligand-binding domains can be changed or "reprogrammed" by a combination of electrostatic and allosteric effects.

Experimental Section

L^1 was prepared in five steps from 2,2′-bipyridine-3,3′-dimethanol (24% overall yield): ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 8.23$ (2H, d, $J = 8.14$; pyridyl H), 8.11 (2H, d, $J = 8.14$; pyridyl H), 6.91 (2H, s; thiazole H), 4.84 (4H, s; OCH_2), 3.55–3.35 (20H, m; $O(CH_2)_2O$), 1.55 ppm (6H, s; Me); ^{13}C NMR (100.6 MHz, $CDCl_3$): $\delta = 168.6$, 155.3, 154.6, 149.3, 138.3, 135.3, 119.1, 116.5 (pyridyl and thiazole), 71.1, 71.0, 70.7, 70.6, 70.3, 66.3 (CH_2), 17.8 ppm (Me); elemental analysis: calcd for $C_{30}H_{36}N_4O_6S_2$ (%): C 58.8; H 5.9; N 9.1; found: C 58.6, H 5.6, N 8.6; MS ESI: m/z: 613 [MH^+].

Both $[Hg_2(L^1)_2Na_2](ClO_4)_6$ and $[Hg(L^1)Ba](ClO_4)_4$ were prepared in an analogous manner: $Hg(ClO_4)_2{\cdot}3H_2O$ (0.007 g. 0.016 mmol) was added to a suspension of L^1 (0.010 g, 0.016 mmol) in MeCN, and the solution was stirred until dissolution was complete. $NaClO_4$ or $Ba(ClO_4)_2$ (3 equiv) was then added, and the complexes were isolated by slow diffusion of Et_2O.

$[Hg_2(L^1)_2Na_2](ClO_4)_6$ (65% yield): ^{1}H NMR (400 MHz, CD_3CN): $\delta = 8.16$ (d, $J = 8.2$ Hz, 2H; pyridyl-H), 7.96 (d, $J = 8.2$ Hz, 2H; pyridyl-H), 7.90 (s, 2H; thiazole-H), 4.48 (d, $J = 14.3$ Hz, 2H; OCH_2), 4.42 (d, $J = 14.3$ Hz, 2H; OCH_2), 3.7–3.3 (m, (overlapping), 20H; $O(CH_2)_2O$), 2.59 ppm (3H, s, Me); MS ESI: m/z: 2168 [M^+].

$[Hg(L^1)Ba](ClO_4)_4$ (50% yield): ^{1}H NMR (400 MHz, CD_3CN): $\delta = 8.42$ (d, $J = 8.1$ Hz, 2H; pyridyl-H), 8.31 (d, $J = 8.1$ Hz, 2H; pyridyl-H), 7.78 (s, 2H; thiazole), 5.22 (d, $J = 14.5$ Hz, 2H; OCH_2), 4.93 (d, $J = 14.5$ Hz, 2H; OCH_2), 3.8–3.3 (m, (overlapping), 20H; $O(CH_2)_2O$), 2.78 ppm (3H, s, Me); MS ESI: m/z: 1248 [M^+].

Received: April 23, 2004 [Z460424]

Keywords: allosterism · barium · helical structures · mercury · N ligands

---

[1] J.-M. Lehn, *Supramolecular Chemistry*, VCH, Weinheim, **1995**; J. W. Steed, J. L. Atwood, *Supramolecular Chemistry*, Wiley, Chichester, **2000**.

[2] M. J. Hannon, L. J. Childs, *Supramol. Chem.* **2004**, *16*, 7; M. Albrecht, *Chem. Rev.* **2001**, *101*, 3547; M. Albrecht, *Chem. Soc. Rev.* **1998**, *27*, 281; C. Piguet, G. Bernardinelli, G. Hopfgartner, *Chem. Rev.* **1997**, *97*, 2005; E. C. Constable in *Comprehensive Supramolecular Chemistry, Vol. 9* (Ed.: J.-P. Sauvage), Elsevier, Oxford, **1996**, p. 213.

[3] P. Baxter, J.-M. Lehn, A. DeCian, J. Fischer, *Angew. Chem.* **1993**, *105*, 92; *Angew. Chem. Int. Ed. Engl.* **1993**, *32*, 69; M.-T. Youinou, N. Rahmouni, J. Fischer, J. A. Osborn, *Angew. Chem.* **1992**, *104*, 771; *Angew. Chem. Int. Ed. Engl.* **1992**, *31*, 733; S. T. Onions, A. M. Frankin, P. N. Horton, M. B. Hursthouse, C. J. Mathews, *Chem. Commun.* **2003**, 2864.

[4] P. J. Stang, S. R. Seidel, *Acc. Chem. Res.* **2002**, *35*, 972; S. Leininger, B. Olenyuk, P. J. Stang, *Chem. Rev.* **2000**, *100*, 853; Z. R. Bell, L. P. Harding, M. D. Ward, *Chem. Commun.* **2003**, 2432.

[5] R. Krämer, J.-M. Lehn, A. Marquis-Rigault, *Proc. Natl. Acad. Sci. USA* **1993**, *90*, 3114; B. Hasenknopf, J.-M. Lehn, G. Baum, D. Fenske, *Proc. Natl. Acad. Sci. USA* **1996**, *93*, 1397; S. Floquet, M. Borkovec, G. Bernardinelli, A. Pinto, L.-A. Leuthold, G. Hopfgartner, D. Imbert, J.-C. G. Bünzli, C. Piguet, *Chem. Eur. J.* **2004**, *10*, 1091.

[6] J. Rebek, Jr., J. E. Trend, R. V. Wattley, S. J. Chachravorti, *J. Am. Chem. Soc.* **1979**, *101*, 4333; J. Rebeck, Jr., R. V. Wattley, *J. Am. Chem. Soc.* **1980**, *102*, 4853; J. Rebeck, Jr., *Acc. Chem. Res.* **1984**, *17*, 258; for examples of artificial allosteric systems, see: T. Nabeshima, *Coord. Chem. Rev.* **1996**, *148*, 151; S. Shinkai, M. Ikeda, A. Sugasaki, M. Takeuchi, *Acc. Chem. Res.* **2001**, *34*, 494; Y. Kobuke, Y. Satoh, *J. Am. Chem. Soc.* **1992**, *114*, 789; P. D. Beer, A. S. Rothin, *J. Chem. Soc. Chem. Commun.* **1988**, 52; S. K. Dutta, D. Gan, M. W. Perkovic, *Eur. J. Inorg. Chem.* **2003**, 2812; S. A. McFarland, N. S. Finney, *Chem. Commun.* **2003**. 388; T. Nabeshima, Y. Yoshihira, T. Saiki, S. Akin, E. Horn, *J. Am. Chem. Soc.* **2003**, *125*, 28.

[7] Crystal data for $[Hg_2(L^1)_2Na_2](ClO_4)_6{\cdot}4\,MeCN$: $M = 2433.57$, triclinic, space group $P\bar{1}$, $a = 13.9240(2)$, $b = 18.4535(2)$, $c = 18.6823(2)$ Å, $\alpha = 107.984(1)$, $\beta = 90.519(1)$, $\gamma = 97.451(1)°$, $V = 4521.13(9)$ Å^3, $Z = 2$; $\rho_{calcd} = 1.788$ Mg m^{-3}, $F(000) = 2424$; crystal dimensions $0.1 \times 0.1 \times 0.05$ mm^3; $\mu(Cu_{K\alpha}) = 9.395$ mm^{-1}, $T = 100$ K. A total of 35433 reflections were measured in the range $2.49 \leq \theta \leq 70.13°$ (*hkl* range indices: $-15 \leq h \leq 16$, $-22 \leq k \leq 22$, $-22 \leq l \leq 22$), 15344 unique reflections ($R_{int} = 0.0576$). The structure was refined on F^2 to $R_w = 0.1053$, $R = 0.0429$ (12005 reflections with $I > 2\sigma(I)$) and GOF = 0.921 on F^2 for 1211 refined parameters, largest difference peak and hole 1.813 and -1.448 e Å^{-3}. Crystal data for $[Hg(L^1)Ba](ClO_4)_4$: $M = 1348.48$, triclinic, space group $P\bar{1}$, $a = 8.785(2)$, $b = 9.619(2)$, $c = 26.409(5)$ Å, $\alpha = 89.95(3)$, $\beta = 88.02(3)$, $\gamma = 77.01(3)°$, $V = 2173.3(8)$ Å^3, $Z = 2$; $\rho_{calcd} = 2.061$ Mg m^{-3}, $F(000) = 1312$; crystal dimensions $0.1 \times 0.1 \times 0.003$ mm^3; $\mu(Mo_{K\alpha}) = 4.858$ mm^{-1}, $T = 100$ K. A total of 20137 reflections were measured in the range $2.17 \leq \theta \leq 25.03°$ (*hkl* range indices: $-10 \leq h \leq 10$, $-11 \leq k \leq 11$, $-31 \leq l \leq 31$), 20142 unique reflections ($R_{int} = 0.0000$, twinned structure solved with Gemini). The structure was refined on F^2 to $R_w = 0.2220$, $R = 0.0924$ (14866 reflections with $I > 2\sigma(I)$) and GOF = 0.998 on F^2 for 549 refined parameters, largest difference peak and hole 3.390 and -2.141 e Å^{-3}. CCDC-236695 and 236694, respectively, contain supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk). For $[Hg_2(L^1)_2Na_2](ClO_4)_6{\cdot}4\,MeCN$, the measurements were carried out on a Bruker PROTEUM CCD area-detector diffractometer with a $Cu_{K\alpha}$ rotating anode and Osmic beam focusing ($\lambda = 1.54178$ Å). For $[Hg(L^1)Ba](ClO_4)_4$, data were collected on a Bruker APEX diffractometer with $Mo_{K\alpha}$ radiation (0.71073 Å). Absorption corrections were applied by using SADABS,[8] and the structure was solved by direct methods using SHELXTL.[9] X-ray data collected for crystals of $[Hg(L^1)Ba](ClO_4)_4$ were of sufficient quality to generate a reliable structure solution by using direct methods; however, problems associated with non-merohedral twinning prevented smooth refinement of atomic parameters. Two twin components, related by a 180° rotation about the direct *c* axis, were identified for a complete array of reflections by using the GEMINI Twinning Solution Program Suite.[10] A subsequent decrease from $R = 0.1474$ to 0.0924 was observed on further refinement.

[8] G. M. Sheldrick. *SADABS: A program for absorption correction with the Siemens SMART system*; University of Göttingen (Germany), **1996**.

[9] *SHELXTL program system version 5.1*, Bruker Analytical X-ray Instruments Inc., Madison, WI, **1998**.

[10] GEMINI, Autoindexing Program for Twinned Crystals Vers. 1.02, Release 5/**2000**.