

## New synthetic routes to hexa-aza cages using cobalt(III) tris(1,2-diamine) templates

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Received 19th November 2002, Accepted 17th December 2002

First published as an Advance Article on the web 8th January 2003

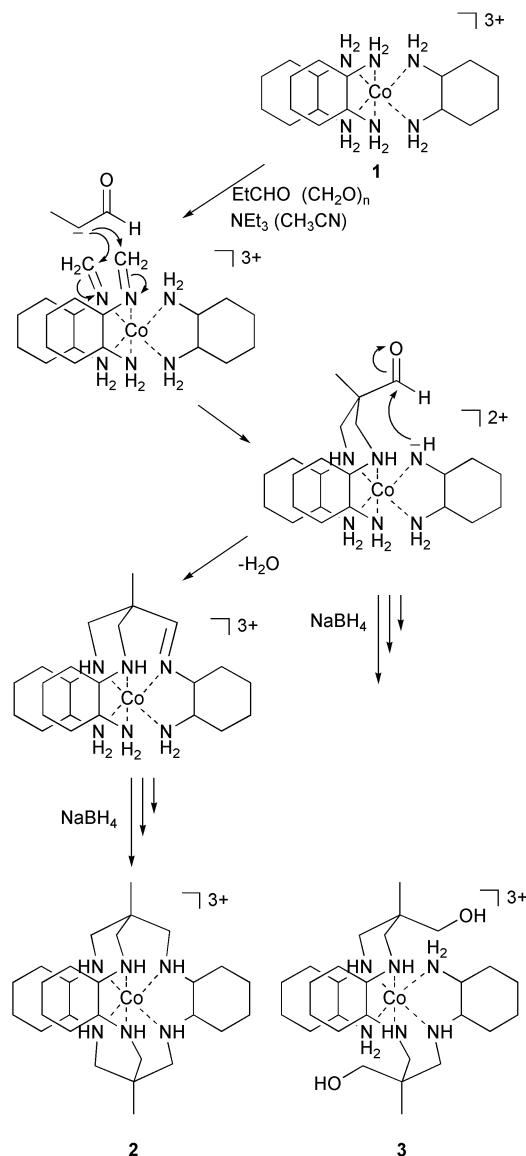
A new template synthetic route to hexa-aza macropentacyclic cobalt(III) complexes is described together with the X-ray crystal structure of a new conformationally rigid cobalt cage complex.

The  $\Delta$ -*le*<sub>3</sub>-[Co((*R,R*)-chxn)<sub>3</sub>]<sup>3+</sup> cation (**1**) {(*R,R*)-chxn = 1*R,2R*-cyclohexanediamine}, and related substitutionally inert metal tris-1,2-diamine complexes, condense with formaldehyde and nitromethane (or ammonia) in basic aqueous solution to give hexa-aza<sup>1</sup> (or octa-aza)<sup>2</sup> macropolycyclic cage complexes. Encapsulation is achieved by a series of inter- and intramolecular condensation reactions between the organic reagents and the coordinated deprotonated primary amines, to form bridgehead 'caps' over both trigonal faces of the starting ion.<sup>1</sup> A significant advance in this type of encapsulation chemistry has been the introduction of non-aqueous synthetic methodology, which has greatly increased the range of acids, particularly weak CH-acids, which can participate in the template organic reactions.<sup>3-5</sup> This strategy has been used to synthesise new and previously inaccessible cage ligand complexes which display some interesting photophysical,<sup>6,7</sup> redox<sup>7</sup> and stereochemical<sup>7</sup> properties. Some of this chemistry is based on cage complexes derived from tripodal amine<sup>4,8</sup> and bis triamine<sup>5,7</sup> templates, but novel cage complexes with new properties are also anticipated from capping reactions involving weak CH-acids and metal tris-1,2-diamine templates including **1**.

The base-catalysed co-condensation of propanal and formaldehyde with **1** in acetonitrile gave the macropentacyclic cobalt(III) cage complex  $\Delta$ -(*R,R*)-*le*<sub>3</sub>-[Co((CH<sub>3</sub>)<sub>2</sub>-char)]<sup>3+</sup> (**2**) {(CH<sub>3</sub>)<sub>2</sub>-char = 1,12-dimethyl-3,10,14,21,24,31-hexaazapentacyclo-[10.10.10.0<sup>4,9</sup>0<sup>15,20</sup>0<sup>25,30</sup>]dotriacontane} after reduction of the intermediate di-imine cage ligand complexes with NaBH<sub>4</sub> (Scheme 1).<sup>†</sup>

The encapsulation reaction was carried out under non-aqueous conditions in which formaldehyde, derived from the solid polymer, paraformaldehyde, was used to generate coordinated methanimines by reaction with deprotonated primary amines of the template. Two coordinated methanimine intermediates are activated electrophiles poised for reaction with the carbanion of propanal. Two of the apical ring systems arise in this manner. Finally, the pendant aldehyde condenses with a deprotonated primary amine of the template to complete one cap containing an *endo*-cyclic imine. Repetition of the process on the opposite side yields a mixture of imine diastereoisomers which were characterised by <sup>13</sup>C NMR, but proved relatively unstable in neutral and basic aqueous solution. They were therefore reduced to the same stable saturated cage ligand complex (**2**) with BH<sub>4</sub><sup>-</sup>. The other major product isolated was a novel cobalt(III) linear hexaamine complex **3**. Incomplete formation of bridgehead caps in this complex linked the three 1*R,2R*-cyclohexanediamine units of the template together to form the open chain polyamine ligand.

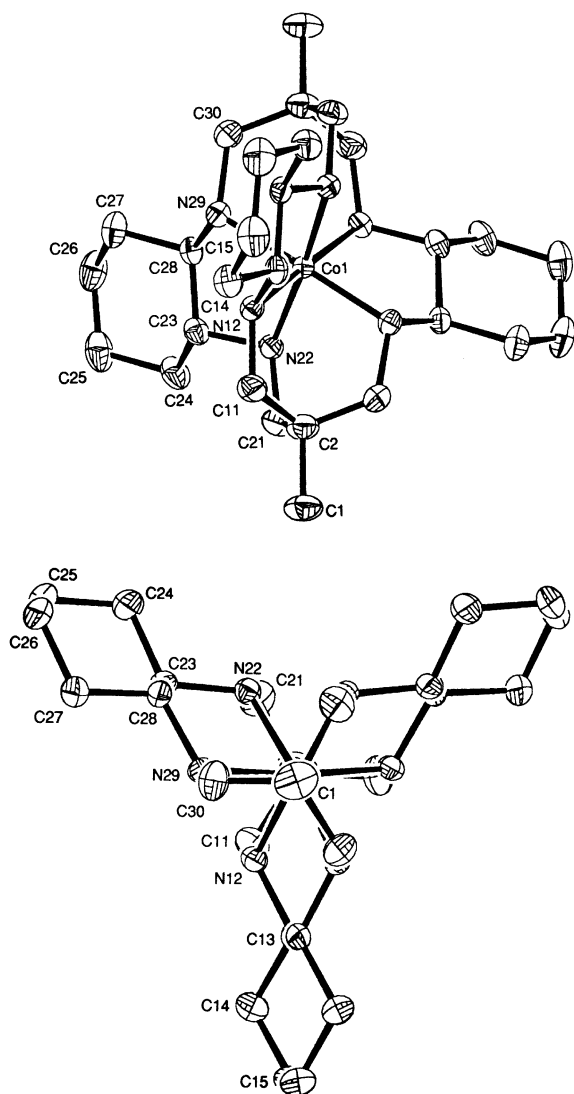
The reduced products of the template reaction were identified by a combination of NMR spectroscopy (<sup>1</sup>H, <sup>13</sup>C, and C-H-HETCOR) and elemental and X-ray crystallographic



Scheme 1

analysis.<sup>‡</sup> Thus, the hexa-aza cage ligand complex **2**, which has average *D*<sub>3</sub>-symmetry on the <sup>13</sup>C NMR timescale, gives rise to six <sup>13</sup>C resonances for a complex that analyses correctly for a Co : N : C ratio of 1 : 6 : 28. The tris(methylene)ethane caps of the cage complex **2** were readily identified in the <sup>13</sup>C NMR spectrum by diagnostic resonances for the quaternary carbon ( $\delta$  43.2) and methyl carbon ( $\delta$  20.8) of the trigonal caps.

The X-ray structure of the anhydrous mixed chloride-perchlorate salt,  $\Delta$ -*le*<sub>3</sub>-[Co((CH<sub>3</sub>)<sub>2</sub>-char)]Cl<sub>2</sub>ClO<sub>4</sub>§ (Fig. 1) reveals an encapsulated cobalt(III)-ion coordinated to the six secondary amine nitrogen donors of the hexadentate ligand in a near



**Fig. 1** ORTEP<sup>13</sup> plots for the non-hydrogen atoms of the  $\Delta(R,R)_3\text{-}lel_3\text{-}[\text{Co}((\text{CH}_3)_2\text{-char})]^{3+}$  cation. Principal bond lengths (Å) and angles ( $^\circ$ ): Co–N(12) 1.995(4), Co–N(22) 1.985(4), Co–N(29) 1.986(4); N(22)–Co–N(29) 86.3(2), N(12)–Co–N(22) 92.1(1), N(12)–Co–N(29) 93.2(2), N(29)–C(28)–C(23)–N(22) –52.2(4).

octahedral configuration. The analysis also shows that the cage complex retains the  $\Delta$ -absolute configuration of the template ion and that the configuration about each coordinated secondary nitrogen atom is the same (*S*). The conformations of the C–C bonds in the equatorial five-membered chelate rings are fixed parallel (*lel*) to the  $C_3$ -axis of the cage complex by the rigid (*R,R*)-*trans*-1,2-cyclohexanediamine units in this  $\Delta$  configurational stereoisomer. The cyclohexane rings fused to these equatorial chelate rings each assume the same chair conformation. The fused six-membered chelate rings of the cage bridge-heads appear conformationally somewhat more flexible and could adopt a right or left handed helical arrangement with respect to the molecular three-fold axis.<sup>1</sup> In the structure, however, both trigonal caps adopt slight right-handed conformations that are nearly eclipsed. The cage cation is therefore assigned the  $\Delta\text{-}D_3\text{-}lel_3$  configuration.

The visible absorption spectrum of complex **2** has two d–d bands at  $\lambda_{\text{max}}$  ( $\text{e}/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$ ) 476 (131) and 348 nm (121) that have their respective origins in the  $^1A_{1g} \rightarrow ^1T_{1g}$  and  $^1A_{1g} \rightarrow ^1T_{2g}$  electronic transitions of a  $\text{Co(III)}N_6$  chromophore with  $O_h$  symmetry. The optical rotatory dispersion (ORD) spectrum for complex **2** features two wings of opposite sign with maxima at  $\lambda_{\text{max}}$  ( $[M]/\text{deg M}^{-1} \text{ m}^{-1}$ ) 503 ( $6535 \pm 65$ ) and 437 nm ( $-5812 \pm 58$ ). However, they are inverted in sign and blue-shifted relative

to the ORD of the template-ion<sup>1</sup> and this result pinpoints the hazards in making absolute configuration assignments solely from ORD or CD spectra in solution. The sign of the A or E symmetry component needs to be established from a single crystal study.

The mixed aldehyde encapsulation strategy described here has the potential to install many types of substituents in the cap and it should apply to a wide variety of other cobalt(III),<sup>9,10</sup> rhodium(III),<sup>11</sup> iridium(III),<sup>11</sup> and platinum(IV)<sup>12</sup> tris-1,2-diamine complexes at least.

We thank the Microanalytical Section of the Research School of Chemistry (ANU) for the elemental analyses.

## Notes and references

† A solution of  $\Delta\text{-}lel_3\text{-}[\text{Co}((R,R)\text{-chxn})_3](\text{CF}_3\text{SO}_3)_3 \cdot 2\text{H}_2\text{O}^1$  (8.88 g, 10 mmol) in acetonitrile (160 mL) was treated with paraformaldehyde (3.0 g, 100 mmol), propanal (5.76 g, 100 mmol), and triethylamine (2.0 g, 20 mmol) for 3 hours at 20  $^\circ\text{C}$ . The crude products of the reaction were collected together by cation-exchange chromatography (SP Sephadex C-25,  $\text{H}^+$  form, 0.5 M HCl), concentrated to dryness and reduced with  $\text{NaBH}_4$  (0.76 g, 20 mmol) in an aqueous buffer solution ( $\text{NaHCO}_3$ , 8.4 g in 400 mL  $\text{H}_2\text{O}$ ). The products of the reaction were separated by cation-exchange chromatography (Sephadex,  $\text{Na}^+$  form, 0.1 M tri-sodium citrate) into a lead orange fraction containing the cage complex **2** and a trailing orange–pink fraction containing the by-product complex **3**, which were separately desalted (Dowex AG 50W-X2,  $\text{H}^+$  form, 6 mol  $\text{dm}^{-3}$  HCl). Complex **2** was further purified by cation-exchange chromatography (Sephadex,  $\text{Na}^+$  form, 0.2 M  $\text{Na}_3\text{-PO}_4$ ), desalted as above and crystallised from concentrated aqueous HCl solution as the trichloride salt. Yield (1.0 g, 12%). Complex **2** was also obtained as the sparingly soluble mixed chloride–perchlorate salt by addition of excess 70%  $\text{HClO}_4$  to a solution of the tri-chloride salt in  $\text{H}_2\text{O}$ . Complex **3** was further purified by cation-exchange chromatography (Sephadex,  $\text{Na}^+$  form, 1 mol  $\text{dm}^{-3}$  NaCl) and desalted on Dowex (1 : 1 ethanol : HCl). The complex was precipitated from solution as the tetrachlorozincate salt by addition of excess  $\text{ZnCl}_2$  to an aqueous solution of the trichloride salt of **3**. Yield (0.60 g, 6.8%). The open chain structure of the ligand in **3** was confirmed by the facile demetallation of the complex in concentrated aqueous HCl solution at room temperature after reduction of cobalt(III) to cobalt(II) over zinc dust. The cobalt(II) form of the macropentacyclic complex **2** was substitutionally inert and completely resistant to demetallation under these conditions.

‡ Compound **2**: (Found: Co, 7.1; C, 40.4; H, 8.2; N, 10.0; Cl, 19.8.  $\text{CoC}_{28}\text{H}_{54}\text{N}_6\text{Cl}_3 \cdot 1.67\text{HCl} \cdot 7.5\text{H}_2\text{O}$  requires Co, 7.05; C, 40.23; H, 8.52; N, 10.06; Cl, 19.78%;  $\delta_{\text{H}}$  (300 MHz, solvent  $\text{D}_2\text{O}/\text{DCI}$ , standard 1,4-dioxane) 0.93 (6 H, s,  $\text{CH}_3$ ), 1.24 (6 H, m,  $\beta\text{-CH}_2$ ), 1.77 (12 H, m,  $\alpha\text{-CH}_2$ ,  $\beta\text{-CH}_2$ ), 2.59 (18 H, m, 'cap'- $\text{CH}_2$ ,  $\text{CH}$ ,  $\alpha\text{-CH}_2$ ), 2.91 (6 H, AB,  $J_{\text{AB}} = 13$  Hz, 'cap'- $\text{CH}_2$ ), 6.18 (br s, NH);  $\delta_{\text{C}}$  (75.46 MHz, solvent  $\text{D}_2\text{O}$ , standard 1,4-dioxane) 20.8 ( $\text{CH}_3$ ), 24.9 ( $\beta\text{-CH}_2$ ), 30.2 ( $\alpha\text{-CH}_2$ ), 43.2 (quat. C), 52.7 ('cap'- $\text{CH}_2$ ), 69.8 (CH);  $E^\circ$  (in aqueous 0.2 mol  $\text{dm}^{-3}$  NaCl, scan rate 100  $\text{mV s}^{-1}$ ) =  $-0.52$  V (vs. standard hydrogen electrode),  $\Delta E_p = 71$  mV.

Compound **3**: ORD  $\lambda/\text{nm}$  ( $\text{H}_2\text{O}$ ) 497 ( $[M]/\text{deg M}^{-1} \text{ m}^{-1} +8164 \pm 82$ ), 440 ( $-3501 \pm 49$ ) (Found: Co, 6.8; C, 38.0; H, 7.0; N, 9.6; Cl, 20.2.  $\text{CoC}_{28}\text{H}_{58}\text{N}_6\text{Cl}_2\text{ZnO}_2 \cdot 4\text{H}_2\text{O}$  requires Co, 6.66; C, 38.02; H, 7.52; N, 9.50; Cl, 20.04%;  $\lambda_{\text{max}}/\text{nm}$  ( $\text{H}_2\text{O}$ ) 490 ( $\text{e}/\text{dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$  160), 355 (177);  $\delta_{\text{C}}$  ( $\text{D}_2\text{O}$ ) 24.2, 24.4, 25.1 ( $\beta\text{-CH}_2$ ), 25.0 ( $\text{CH}_3$ ), 29.2, 30.4, 33.6 ( $\alpha\text{-CH}_2$ ), 39.4 ( $\text{C}_q$ ), 58.8, 66.1, 70.5 (CH), 46.0, 53.3 ('cap'- $\text{CH}_2$ ), 67.5 ( $\text{CH}_2\text{OH}$ ). § Crystal data for **2**:  $\text{C}_{28}\text{H}_{54}\text{CoN}_6\text{Cl}_3\text{O}_4$ ,  $M_r = 704.07$ , tetragonal, space group  $P4_12_1$ ,  $a = 15.315(2)$ ,  $c = 13.764(3)$  Å,  $U = 3228.5(9)$  Å<sup>3</sup>,  $T = 296$  K,  $Z = 4$ ,  $D_{\text{calc}} = 1.45$  g  $\text{cm}^{-3}$ ,  $\mu(\text{Cu-K}\alpha) = 70.6$   $\text{cm}^{-1}$ . A final value for  $R$  ( $= \sum ||F_o| - |F_c|| / \sum |F_o|$ ) of 0.039 was obtained for the 1752 independent reflections with  $I(h) > 3\sigma(I(h))$ . The diffraction data were collected on a Rigaku AFC6R diffractometer. CCDC reference number 198021. See <http://www.rsc.org/suppdata/dt/b2/b211343k/> for crystallographic data in CIF or other electronic format.

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