A New Template Encapsulation Strategy for Larger Cavity Metal Ion Cages

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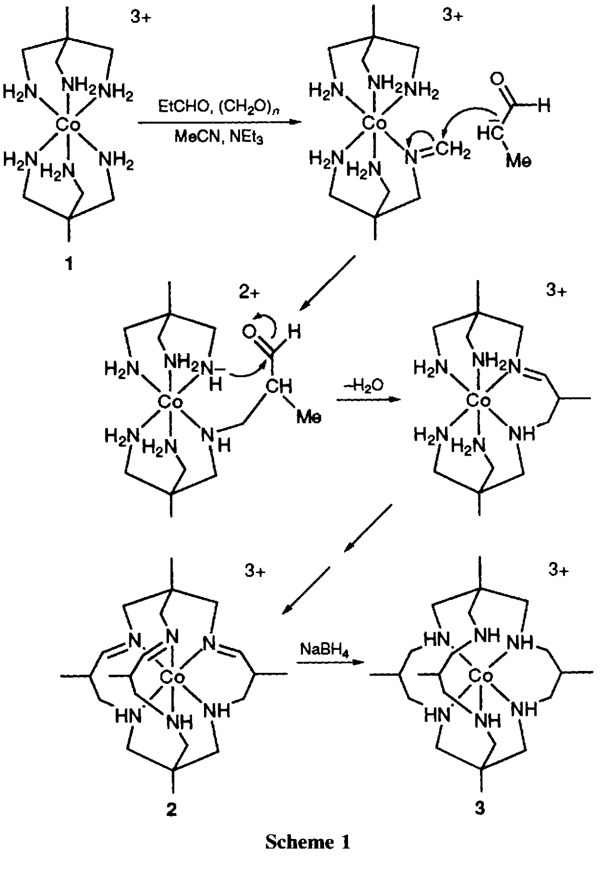
Stereospecific sequential condensation of paraformaldehyde and propionaldehyde with a tripodal bis(triamine)cobalt(III) template rapidly encapsulates the metal, and a subsequent facile reduction of imine functions gives an expanded cavity hexaazabicyclic cage system with unusual structural and chromophore electron properties, complemented by an exceptional stability and relatively fast $Co^{II/III}$ electron exchange rates.

The relatively stable cobalt(III) templates $[Co(en)_3]^{3+}$ (en = 1,2-ethanediamine),[1] $[Co(chxn)_3]^{3+}$ (chxn = *trans*-1,2-cyclohexanediamine)[2] and $[Co(pn)_3]^{3+}$(pn = 1,2-propanediamine)[3] have been used to obtain encapsulated species with typical $Co^{II/III}N_6$ dimensions but with unusual stabilities and electron transfer rates. This promoted a study of the striking effects of chelate ring conformation on spectroscopic, electrochemical and electron transfer properties.[3] Contracting and distorting the CoN_6 cavity strongly influences these as well as the electronic absorption intensities, and cobalt cages demonstrating these effects were synthesised using the $[Co(tame)_2]^{3+}$ [tame = ethylidynetris(methanamine)] and $[Co(tach)_2]^{3+}$ (tach = 1,3,5-*cis*-cyclohexanetriamine)-templates.[4]

Another important way of modulating the potential energy surfaces for CoN_6 electronic states and therefore the chromophore electron chemistry is to increase the preferred cage cavity size. However it is difficult to do this by using cobalt(III) templates which have oversized CoN_6 dimensions and associated properties that are anomalous for such systems. Often such complexes {*e.g.* $[Co(stn)_3]^{3+}$, stn = 5,5′5″-ethylidynetris-(4-azapentan-1-amine)} are somewhat unstable to begin with,[5] and may require even less stable intermediate conformations to satisfy stereoelectronic needs in the course of a capping process. Other reactions, sometimes including dissociative steps, then become more favourable[6] and thwart the desired result. It occurred to us that the more robust $[Co(tame)_2]^{3+}$ template might instead be encapsulated by connecting the donor atoms through three hydrocarbon straps, each containing one Co^{III}–N=CH– link. This would give an unsaturated cobalt(III) cage with a near optimal CoN_6 size, which could then be rapidly expanded by reducing the imines under conditions where metal exchange is repressed. In this way a stable cobalt(III) template, typically with a relatively small CoN_6 dimension, may be used to engineer a bicyclic cage assembly with a larger preferred cavity, to stabilize larger metal ions and lower oxidation states, and to develop new chemistry. Here we describe an implementation of this idea and some properties of the cobalt cage complexes obtained when $[Co(tame)_2]^{3+}$ **1** is condensed with paraformaldehyde in the presence of propanal.

Relatively fast and efficient reaction was achieved by firstly stirring $[Co(tame)_2]Cl_3$ (2 g) with $NaClO_4 \cdot H_2O$ (6 g) dissolved in acetonitrile (30 ml), and then adding paraformaldehyde (4 equiv.), propanal (10 equiv.) and triethylamine (6 equiv.). Stirring was continued for 2 h at *ca.* 20 °C, and after quenching the intense dark green reaction mixture with HCl, a main orange–yellow complex was isolated cleanly (20–25% yield) by cation-exchange chromatography on SP-Sephadex C-25 and crystallization as its chloride tetrachlorozincate or triperchlorate salt. Elemental microanalysis (C, H, N, Cl and Co), ^1H and ^{13}C NMR spectra, and Dreiding models served to identify the complex ion as a racemate of Λ-(5*R*,13*R*,20*R*)- and Δ-(5*S*,13*S*,20*S*)-$[Co\{(Me)_5\text{-}C_{3v}\text{tricosatrieneN}_6\}]^{3+}$ (**2**, Scheme 1) {$(Me)_5\text{-}C_{3v}\text{tricosatrieneN}_6$ = 1,5,9,13,20-pentamethyl-3,7,11,15,18,22-hexaazabicyclo[7.7.7]tricosa-3,14,18-triene}.† This diastereoisomer has a bond framework with C_3 symmetry when all saturated nitrogen centres have the same chirality, and its ^{13}C NMR spectrum,‡ which shows nine signals in D_2O, is consistent with an average C_3 symmetry in solution. The assignment of individual carbon resonances is also in agreement with the nominated structure of **2** which shows that three formaldehyde and three propanal molecules have cocondensed to produce the desired encapsulation topology. The visible electronic spectrum in H_2O has absorption bands at λ_{max} (ε_{max}) 468 nm (107 $mol^{-1}\ dm^3\ cm^{-1}$) and 343 nm (135 $mol^{-1}\ dm^3\ cm^{-1}$), whose positions are similar to those for corresponding bands of $^1A_{1g} \rightarrow {}^1T_{1g}$ and $^1A_{1g} \rightarrow {}^1T_{2g}$ parentage in other $Co^{III}N_6$ (amine, imine) type complexes with nearly optimal chromophore geometries.[1–4,7–10] Isomers of **2** were not evident among the many minor products of the reaction,[7] which implies that its formation is stereospecific under the current conditions. Also the identification of intermediates and by-products in control experiments indicates that the individual straps knit together by the sequence depicted in Scheme 1. Despite its ordinary spectroscopic features the tri-imine complex **2** promises to be a rather useful molecule. For example, the methine carbons are sufficiently acidic to facilitate the stereospecific introduction of functional groups for a variety of chemical, physical and biological applications, and these aspects are being explored.

$[Co\{(Me)_5\text{-}C_{3v}\text{tricosatrieneN}_6\}]^{3+}$ was readily converted into the saturated species $[Co\{fac\text{-}(Me)_5\text{-}D_{3h}\text{tricosaneN}_6\}]^{3+}$ **3** {*fac*-$(Me)_5\text{-}D_{3h}\text{tricosaneN}_6$ = *facial*-1,5,9,13,20-pentamethyl-3,7,11,15,18,22-hexaazabicyclo[7.7.7]tricosane}† by stirring with $NaBH_4$ in aqueous solution (pH 9–10) at 20 °C for 20 min. After the removal of salts by using Dowex 50W-X2



Scheme 1

cation exchange resin the crimson [Co{*fac*-(Me)$_5$-D_{3h}tricosaneN$_6$}]$^{3+}$ ion was isolated (>95%) as its trichloride or tris(hexafluorophosphate) salt and characterized by its elemental microanalysis (C, H, N, Cl and Co) and ^{1}H and ^{13}C NMR spectra. Only one of the possible 92 diastereoisomeric forms of **3** (64 *meridional* and 28 *facial*) has so far been observed. The ten signals of the ^{13}C NMR spectrum‡ show that this form averages rigorous C_3 symmetry in solution, and that the ligand has the facial (C_3 symmetric) configuration.

The structure of [Co{*fac*-(Me)$_5$-D_{3h}tricosaneN$_6$}]$^{3+}$ (Fig. 1) was established by a single crystal X-ray analysis of its $(PF_6)_3$ salt§ clearly revealing that all six nitrogen centres have the same *S* (or *R*) configuration linked to the Λ (or Δ) arrangement of the three 1,3-propanediamine (tn) straps. The Co-tn rings display flattened chair conformations which accommodate equatorial orientations for the three facial methyl substituents, and the structure is essentially C_3 symmetric. An important molecular feature is illustrated by the unusually long Co–N distances which range from 2.010(4) to 2.032(4) Å. They are 0.05–0.06 Å longer than those of [Co(NH$_3$)$_6$]$^{3+}$ (1.965(1) Å),[11] [Co(en)$_3$]$^{3+}$ (1.964 ± 0.004)[12], [Co(tame)$_2$]$^{3+}$ (1.972 ± 0.004)[8] and [Co(sen)]$^{3+}$ [1.971 ± 0.009, sen = 4,4′,4″-ethylidynetris (3-azabutan-1-amine)],[13] all of which have typical CoN$_6$ dimensions. Also they are longer than those for several other cobalt(III) amine species with oversized cores and average distances of 1.99 to 2.00 Å.[5,14] These results imply that the conformation of *fac*-(Me)$_5$-D_{3h}tricosaneN$_6$ with the smallest preferred cavity size markedly expands the natural Co^{III}N$_6$ chromophore. This largely arises from steric overcrowding and is supported by molecular mechanics potential energy surface calculations using recently refined force fields.[3,6] The twist angles (ϕ) defined by the torsion angles N(*n*2)···C(2)···C(3)···N(*n*6) (*n* = 1–3) are 67 (±0.8)°, and show that for the same chelate ring arrangement the distortion of CoN$_6$ away from octahedral geometry in **3** has the opposite chirality to that found in homologous smaller cavity cobalt cage systems.[15]

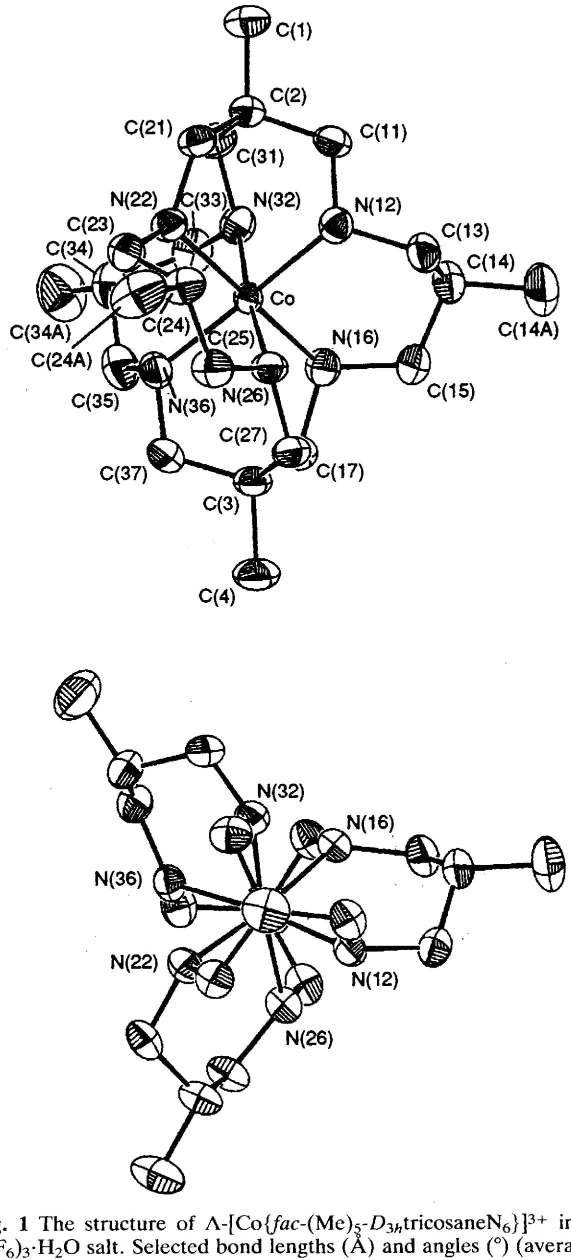


Fig. 1 The structure of Λ-[Co{*fac*-(Me)$_5$-D_{3h}tricosaneN$_6$}]$^{3+}$ in its $(PF_6)_3 \cdot H_2O$ salt. Selected bond lengths (Å) and angles (°) (averaged assuming C_3 symmetry): Co–N(*n*2) 2.021 (±0.004), Co–N(*n*6) 2.024 (±0.013), N(*n*2)–Co–N(*n*6) 95.2 (±0.7), Co–N(*n*2)–C(*n*3) 120.1 (±0.5), Co–N(*n*6)–C(*n*5) 120.7 (±0.7), N(*n*6)–Co–N(*n*2)–C(*n*3) −19.9 (±1.8), N(*n*2)–Co–N(*n*6)–C(*n*5) 15.9 (± 2.2).

The electronic absorption spectrum of [Co{*fac*-(Me)$_5$-D_{3h}tricosaneN$_6$}]$^{3+}$ is especially interesting, with the low energy spin-allowed ligand field bands occurring at λ_{max} (ε_{max}) 516 nm (80 mol^{-1} dm^3 cm^{-1}) and 370 (102) for the trichloride salt in water. This involves red shifts of 2000–2500 cm^{-1} from the corresponding bands of the more typical cobalt(III) amines [Co(en)$_3$]$^{3+}$ [467 (93), 339 (85)],[10] [Co(tame)$_2$]$^{3+}$ [472 (81), 342 (73)],[8] [Co(sen)]$^{3+}$ [467 (113), 340 (103)][9] and the smaller bicyclic homologue [Co(sar)]$^{3+}$ {471 (135), 343 (108), sar = 3,6,10,13,16,19-hexaazabicyclo[6.6.6]icosane}.[1] The effect is more pronounced than those observed in other red-shifted instances[5,14,16,17] even when there are significant orbital mismatch contributions.[14] A reversible Co^{III}/Co^{II} reduction at *E* + 0.08 V (*vs.* normal hydrogen electrode at 100 mV s^{-1}) was observed for **3** using CV in aqueous 0.1 mol dm^{-3} NaCl. This is 560 mV more positive (equivalent to a change of −54.0 kJ mol^{-1} in Δ*G*) than the Co^{III}/Co^{II} reduction potential for the smaller cavity [Co{(Me)$_2$-sar}]$^{3+}$ (sar substituted at 1,8 positions) cage[7] (*E* −0.48 V). When the chloride salt of **3** was reduced by shaking with Zn dust in N$_2$ saturated neutral aqueous solution, a pale yellow solution of the cobalt(II) cage complex was obtained. The visible absorption spectrum of this species is very similar to those of the smaller high spin cobalt(II) sar type cage systems[18] which can adopt conformations with nearly optimal Co^{II}N$_6$ sizes. Overall the structural and spectroscopic results show that the leading contribution to the more favourable Co$^{III/II}$ reduction in [Co{*fac*-(Me)$_5$-D_{3h}tricosaneN$_6$}]$^{3+}$ arises from the destabilization of the Co^{III} oxidation state. This is supported by molecular mechanics calculations[6] coupled with results from previous work on the properties of the smaller cobalt cage homologues.

Some aspects of the reactivity of **3** are germane to the potential consequences of this study. A measure of the rate constant (k_{ex}) for electron self-exchange between Co^{II} and Co^{III} forms of the *fac*-(Me)$_5$-D_{3h}tricosaneN$_6$ cage was obtained by monitoring the optical rotation (α) in solutions (under N$_2$) where the Co^{II} and Co^{III} complexes had opposite chiralities and equal concentrations. The data fitted the functional form $d\ln\alpha/dt = -k_{ex}[Co]_{total}$ with k_{ex} 0.40 dm^3 mol^{-1} s^{-1} at 25 °C and *I* 0.2 mol dm^{-3} (as aqueous chloride salts) for several half-lives. A slower reaction involving inversion of the Co^{II} enantiomer was also observed (k_{inv} 0.63 × 10^{-4} s^{-1} at 25 °C, pH 6.2 and *I ca.* 0.2 mol dm^{-3} as aqueous chloride salt). The electron exchange rate constant k_{ex} is only slightly lower than those found for various forms of smaller cage homologues.[2,3,18] Despite the pronounced expansion of its chromophore the cage complex **3** is appreciably more substitution stable than other species having expanded but smaller Co^{III}N$_6$ geometries.[5,14,16] No dissociation or hydrolysis has been observed in aqueous solution from 6 mol dm^{-3} HCl to pH *ca.* 11 at less than 50 °C. The high spin Co^{II} form of **3** also displays an exceptional kinetic stability, and complete ligand removal in aqueous 6 mol dm^{-3} HCl requires minutes of heating at 50 °C. Similar substitution inertness in acid solution is typical of the smaller cobalt(II) sar analogues, but these are usually more difficult to demetallate because of competing redox processes.

This report introduces a strategy for making dramatic changes in chromophore electron properties while retaining the high stability and fast electron transfer rates characteristic of the smaller cavity cage systems. Peripheral and chromophoric properties for the expanded cages may be changed and fine tuned by functional group attachments. Larger metal ions will be stabilized by these expanded cavity molecules and new stable oxidants and reductants should be accessible.

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Footnotes

† The abbreviated nomenclature for the unsubstituted heterobicyclic bases of **2** and **3** broadly follows macrocyclic practice, but includes a prefixed symmetry symbol (C_{3v} and D_{3h}) describing the idealized bonding symmetry of the non-hydrogen frame. This images the three dimensional nature of the polycyclic systems and also distinguishes between several alternative structural isomers. The *facial* notation, for **3** and other derivatives substituted at the special 5,13,20 sites related by idealized C_3 symmetry, distinguishes them from the *meridional* forms where the substitution sites are not symmetry related and follows the usage of J. D. Mather and R. E. Tapscott, *J. Coord. Chem.*, 1981, **11**, 5.

‡ ^{13}C {H} NMR (75.4 MHz in D_2O, δ in ppm *vs.* $SiMe_4$ with internal dioxane at δ 67.6 ppm) **2**: 16.31 (CH–CH_3), 21.09, 21.42 (Cq–CH_3), 33.31 (*C*H), 37.68 (br, possibly d, C_q), 52.75 (CH–CH_2), 53.31 (Cq–CH_2–NH), 67.79 (Cq–CH_2–N=C), 192.03 (N=*C*); **3**: 17.34 (CH–CH_3), 21.76, 22.19 (Cq–CH_3), 28.21 (*C*H), 35.28, 40.59 (*C*q), 56.00, 56.16 (CH–CH_2), 57.68, 64.46 (Cq–CH_2). All assignments were made and confirmed using reported shift data and 2D homonuclear ^{1}H (COSY) and heteronuclear (C-H-HETCOR) experiments.

§ *Crystal data* for **3**: $C_{22}H_{48}CoF_{18}N_6P_3\cdot H_2O$, $M = 908.50$, monoclinic, $P2_1/a$, $a = 10.155(2)$, $b = 19.427(3)$, $c = 18.492(3)$ Å, $\beta = 95.87(1)°$, $U = 3629.0$ Å^3, $Z = 4$, $D_c = 1.663$ g cm^{-3}, μ (Mo-Kα) = 7.2 cm^{-1}. Data comprising 5266 reflections with $I > 3\sigma(I)$ to $2\theta = 55°$ were collected on a Phillips PW-1100/20 diffractometer using graphite monochromated Mo-Kα radiation, and were corrected for absorption. The structure was solved by direct methods and difference Fourier techniques and refined by block-matrix least-squares. Hydrogen atoms were included at calculated positions and not refined; several fluorine atoms of one PF_6^- group and one from another were disordered and the electron density was modelled to accommodate this. Final *R* factor 0.069.

Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

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