

## The influence of the ancillary ligand on the potential of cobalt(III) complexes to act as chaperones for hydroxamic acid-based drugs

Bradley P. Green, Anna K. Renfrew, Alexandra Glenister, Peter Turner, Trevor W. Hambley

### Supporting Information

#### Single Crystal X-ray Diffraction

Data were collected using a Rigaku Oxford Diffraction SuperNova Dual diffractometer equipped with an Atlas CCD detector and employing mirror monochromated Mo-K $\alpha$  or Cu-K $\alpha$  radiation generated from a micro-source. The crystals were each attached with Exxon Paratone N to a nylon loop and quenched in a cold nitrogen gas stream from an Oxford Cryosystems Cryostream. Data processing was undertaken with CrysAlisPro<sup>1</sup> software and included a multi-scan absorption correction. Subsequent computations were carried out with the assistance of the WinGX<sup>2</sup>, ShelXle<sup>3</sup> and Olex2<sup>4</sup> interfaces. Structures were solved by direct methods using SIR97<sup>5</sup> or SHELXS-97<sup>6</sup> were extended and refined with SHELXL-2016/6.<sup>7</sup>

In general non-hydrogen atoms were modelled with anisotropic displacement parameters and a riding atom model was used for the hydrogen sites. The amine hydrogens were located in final difference maps and modelled with isotropic displacement parameters. Crystallographic details are provided in Table 1.

#### [Co(aha)(cyclen)]ClO<sub>4</sub> (1)

Data were collected at 150(1) Kelvin from a dark red prismatic crystal with  $\omega$  scans to 66° 2 $\theta$  using Mo(K $\alpha$ ) radiation. Cell constants were obtained from a least squares refinement against 50,138 reflections located between 5 and 66° 2 $\theta$ . The structure was solved in the space group  $P2_1/n$ (#14) by direct methods with SHELXS-97.<sup>6</sup> The asymmetric unit contains two crystallographically independent cobalt complex cations together with four perchlorate anions. One of the anions exhibits rotational disorder about an oxygen – chlorine bond and this was modelled with three orientations for the other three oxygen sites, with occupancies refined and then fixed at 0.45, 0.3 and 0.25. The partially occupied perchlorate sites were modelled with isotropic displacement parameters. The amine hydrogen sites were located in final difference maps and modelled with isotropic displacement parameters.

An Olex2<sup>4</sup> depiction of the molecule with 50% displacement ellipsoids is provided in Figure S1.

### [Co(bha)(cyclen)]ClO<sub>4</sub> (2)

Data were collected at 100(1) Kelvin with  $\omega$  scans to 60° 2 $\theta$  from a dark purple irregular crystal using Mo(K $\alpha$ ). Cell constants were obtained from a least squares refinement against 6,405 reflections located between 5 and 65° 2 $\theta$ . The structure was solved in the space group  $P2_1/c$ (#14) by direct methods with SHELXS-97<sup>5</sup>, and extended and refined with SHELXL-2016/6.<sup>6</sup> The asymmetric unit contains the cobalt complex cation together with two perchlorate anions. One of the anions exhibits a significant degree of disorder, which was modelled with three orientations having occupancies refined and then fixed at 0.5, 0.4 and 0.1. In general the non-hydrogen sites were modelled with anisotropic displacement parameters and a riding atom model was used for the hydrogen sites. The minor occupancy perchlorate sites were modelled with isotropic displacement parameters. The amine hydrogen sites were located in final difference maps and modelled with isotropic displacement parameters.

An Olex2<sup>4</sup> depiction of the molecule with 50% displacement ellipsoids is provided in Figure S2.

### [Co(nha)(cyclen)](ClO<sub>4</sub>)<sub>2</sub> (3)

Data were collected at 150(1) Kelvin with  $\omega$  scans to 153° 2 $\theta$  from a purple prismatic crystal using Cu(K $\alpha$ ) radiation. Cell constants were obtained from a least squares refinement against 30,968 reflections located between 7 and 152° 2 $\theta$ . The structure was solved in the space group  $P2_1/c$ (#14) by direct methods with SIR97.<sup>5</sup> The non-hydrogen atoms in the asymmetric unit were modelled with anisotropic displacement parameters and in general a riding atom model was used for the remainder. The amine hydrogen sites were located in final difference maps. An Olex2<sup>4</sup> depiction of the molecule with 50% displacement ellipsoids is provided in Figure S3.

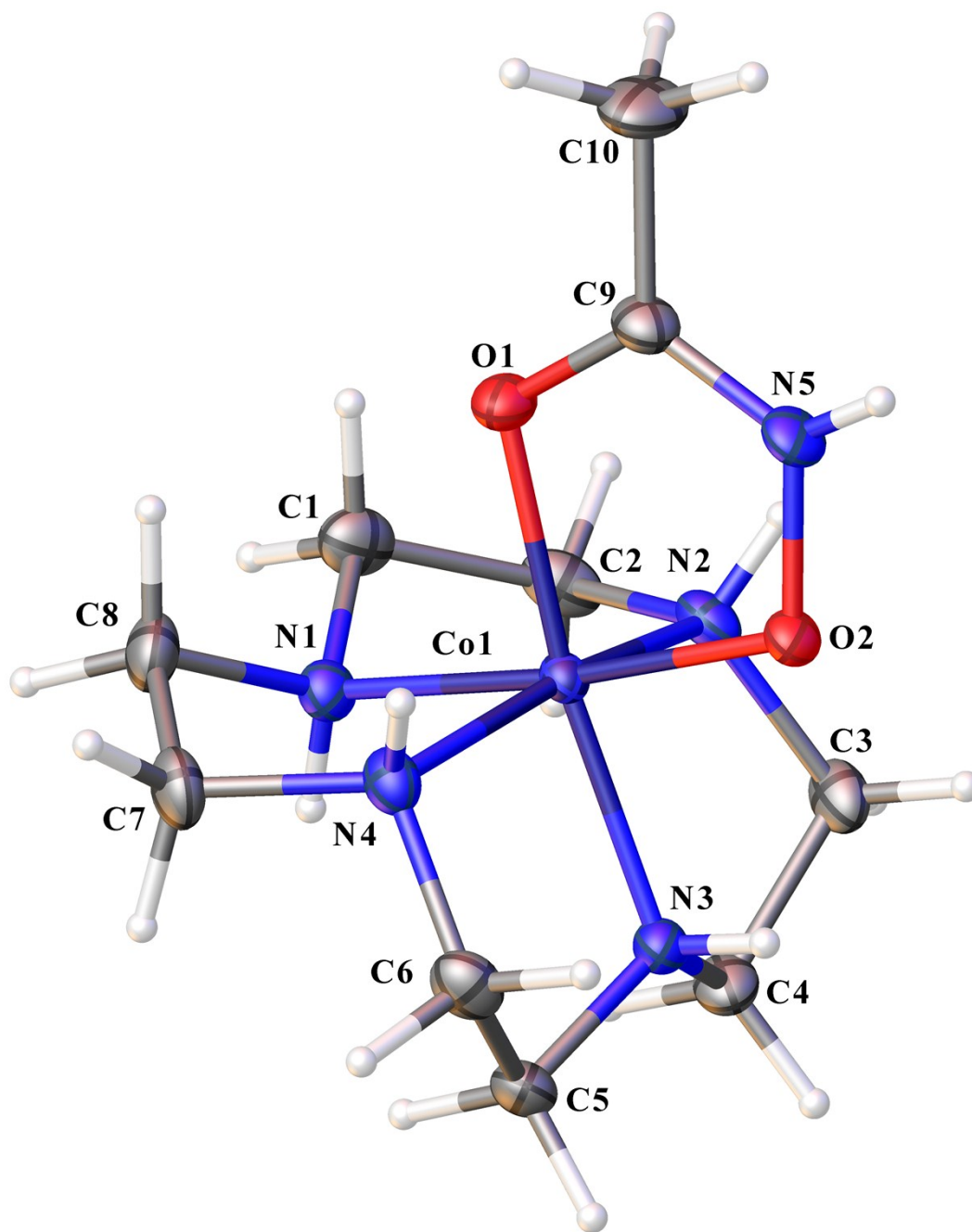
### References

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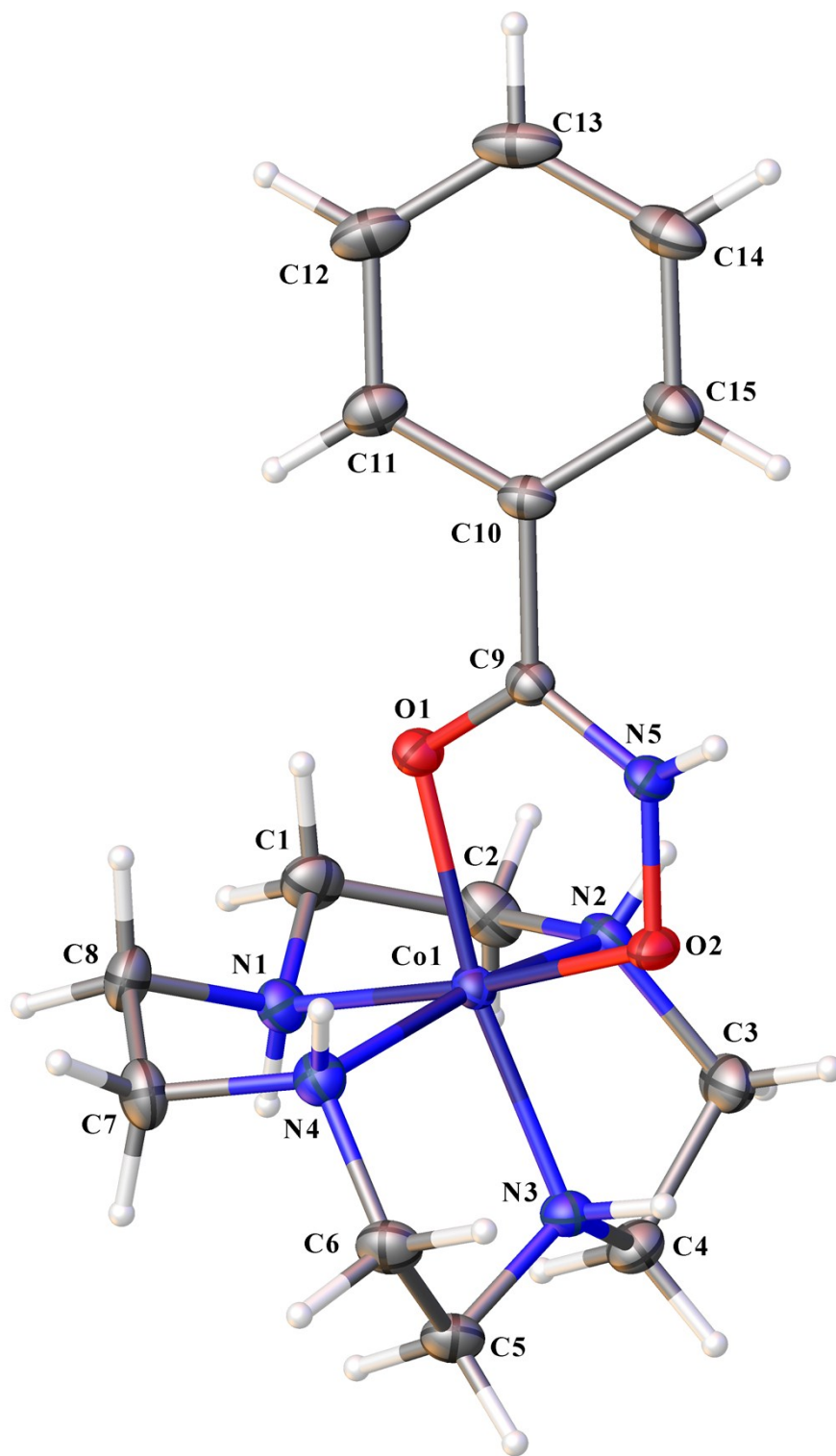
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6. Sheldrick, G.M. (2015), *Acta Cryst.* A71 3-85.
7. (a) Sheldrick, G. M. (2015), *Acta Cryst.* C71, 3-8. (b) G. M. Sheldrick, *Acta Crystallogr., Sect. A: Found. Crystallogr.*, 2008, 64, 112-122.

Table S1: Crystallographic data for **1 - 3**

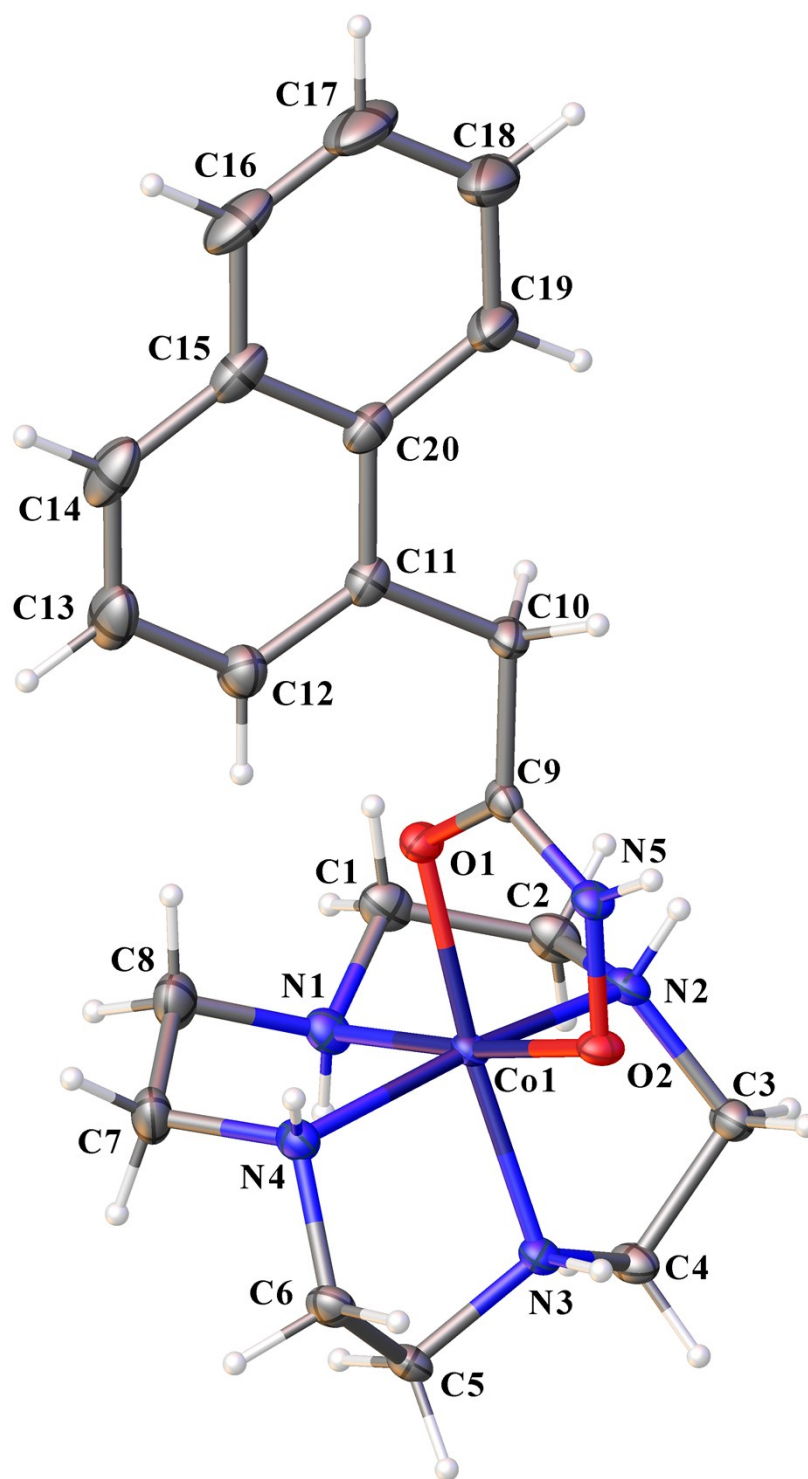
| Compound   | <b>1</b>   | <b>2</b>   | <b>3</b>   |
|--|--|--|--|
| Formula  | C <sub>10</sub> H <sub>24</sub> Cl <sub>2</sub> CoN <sub>5</sub> O <sub>10</sub> | C <sub>15</sub> H <sub>26</sub> Cl <sub>2</sub> CoN <sub>5</sub> O <sub>10</sub> | C <sub>20</sub> H <sub>30</sub> Cl <sub>2</sub> CoN <sub>5</sub> O <sub>10</sub> |
| Molecular weight                                   | 504.17   | 566.24   | 630.32   |
| Crystal system                                     | Monoclinic   | Monoclinic   | Monoclinic   |
| Space group  | P2 <sub>1</sub> /n   | P2 <sub>1</sub> /c   | P12 <sub>1</sub> /c1   |
| a/Å  | 11.07286(9)  | 16.7154(4)   | 15.74190(10)   |
| b/Å  | 22.07939(15)   | 8.95880(10)  | 17.22010(10)   |
| c/Å  | 16.02544(13)   | 16.7610(4)   | 9.39560(10)  |
| β (°)  | 106.0005(9)  | 118.994(3)   | 92.7320(10)  |
| V (Å <sup>3</sup> )                                | 3766.15(5)   | 2195.39(10)  | 2544.04  |
| D <sub>c</sub> (g cm <sup>-3</sup> )               | 1.778  | 1.713  | 1.646  |
| Z  | 8  | 4  | 4  |
| Crystal size (mm)                                  | 0.167 × 0.160 × 0.098  | 0.207 × 0.152 × 0.100  | 0.122 × 0.053 × 0.047  |
| Crystal Colour                                     | Dark Red   | Purple   | Purple   |
| Crystal Habit                                      | Prism  | Block  | Prism  |
| Temperature (K)                                    | 150(2)   | 100(2)   | 150(2)   |
| λ  | 0.71073 (Mo Kα)  | 0.71073 (Mo Kα)  | 1.5418 (Cu Kα)   |
| μ (mm <sup>-1</sup> )                              | 1.257  | 1.089  | 7.799  |
| T <sub>min,max</sub>                               | 0.985, 1.00  | 0.708, 1.00  | 0.609, 1.00  |
| 2θ <sub>max</sub> (°)                              | 65.8   | 60.0   | 152.98   |
| hkl range  | -16 16, -33 32, -23 23   | -23 23, -12 12, -23 23   | -19 19, -21 21, -9 11  |
| N <sub>obs</sub> (N <sub>var</sub> )               | 120107 (516)   | 101780 (344)   | 50246 (360)  |
| N <sub>ind</sub> (R <sub>merge</sub> )             | 13463 (-0.0312)  | 6405 (0.0349)  | 5324 (0.0273)  |
| N <sub>obs</sub> - (I > 2σ(I))                     | 11684  | 6081   | 5188   |
| Residuals  | 0.0368, 0.0941   | 0.0383, 0.0937   | 0.0270, 0.0856   |
| GoF  | 1.032  | 1.116  | 1.350  |
| Residual extrema (e <sup>-</sup> Å <sup>-3</sup> ) | -0.749, 1.027  | -0.909, 1.798  | -0.596, 0.364  |



**Fig S1.** [Co(aha)(cyclen)]ClO<sub>4</sub> (1). Olex2 generated thermal ellipsoid depiction with ellipsoids shown at the 50% level.



**Figure S2.** [Co(bha)(cyclen)]ClO<sub>4</sub> (**2**). Olex2 generated thermal ellipsoid depiction with ellipsoids shown at the 50% level.



**Figure S3.** [Co(nha)(cyclen)](ClO<sub>4</sub>)<sub>2</sub> (3). Olex2 generated thermal ellipsoid depiction with ellipsoids shown at the 50% level.

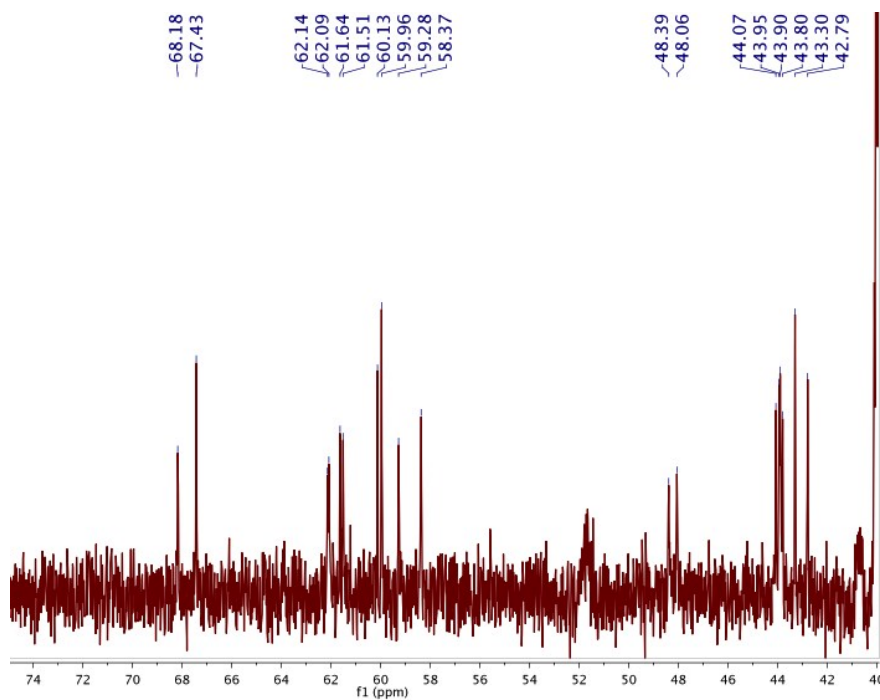


Figure S4a:  $^{13}\text{C}$  NMR spectra of **4b** in the region of the tren ligand.

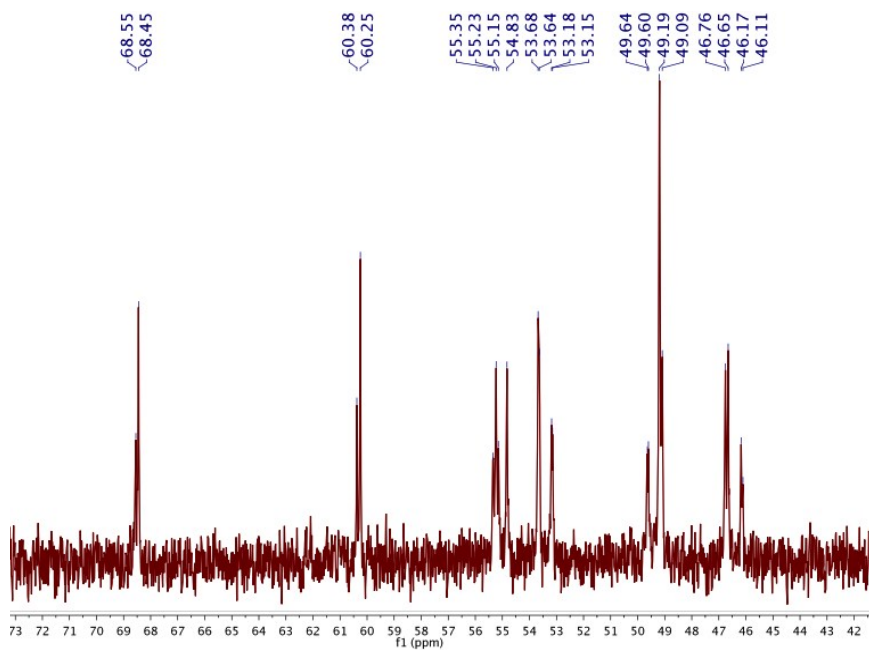


Figure S4b:  $^{13}\text{C}$  NMR spectra of **4c** in the region of the cyclen ligand.

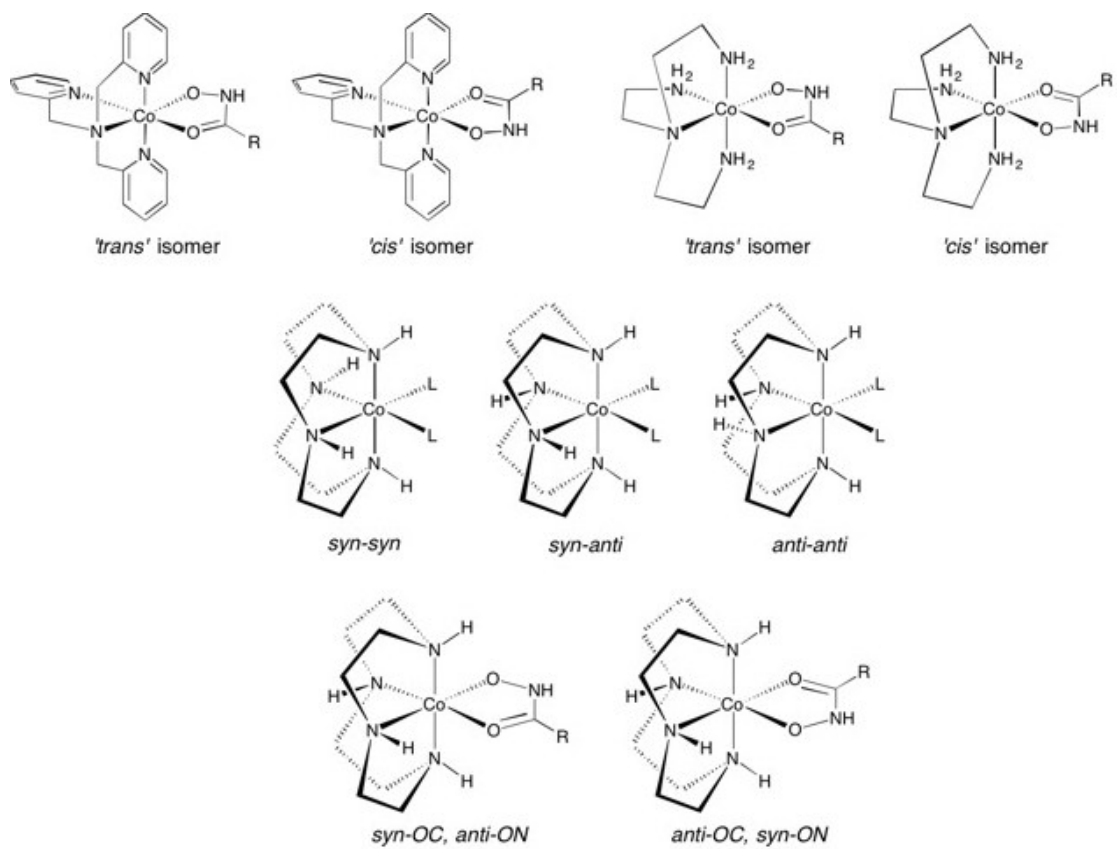


Figure S5: Possible isomers of Co(tpa)(HA), Co(tren)(HA) and Co(cyclen)(HA) complexes



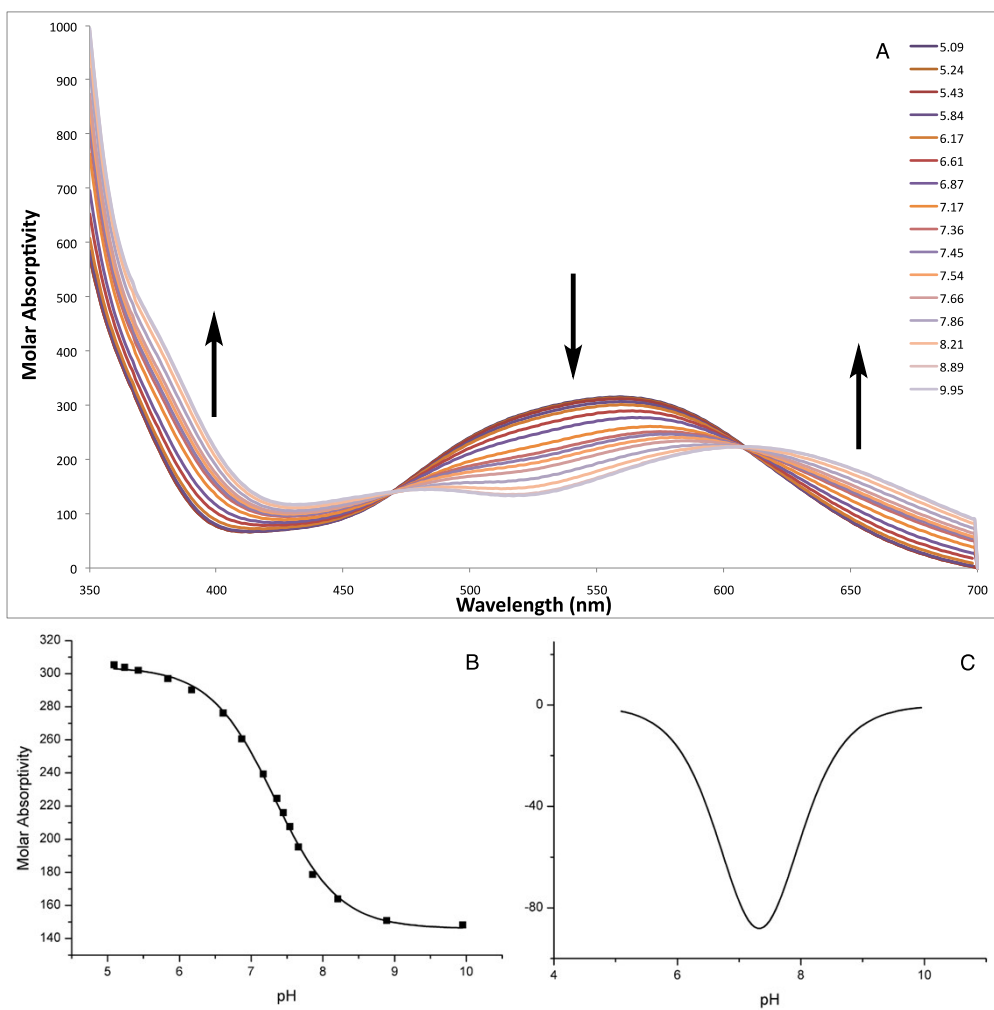


Figure S6: A) UV-vis spectra of **2** at different pH; B) pH against molar absorptivity at 550 nm; C) pH against the first derivative of the sigmoidal line of best fit in B.