Oxidative N-dealkylation in cobalt-bispidine-H₂O₂ systems

Peter Comba*, Shigemasa Kuwata, Gerald Linti, Hans Pritzkow, Máté Tarnai and Hubert Wadepohl

Universität Heidelberg, Anorganisch-Chemisches Institut, Im Neuenheimer Feld 270, D-69120 Heidelberg, Germany, Fax: +49-6221-546617,

E-mail: peter.comba@aci.uni-heidelberg.de
Table S1. Electrochemical, spectroscopic and kinetic data

<table>
<thead>
<tr>
<th></th>
<th>$E_0$ / mV (Ag/AgNO$_3$ in MeCN)</th>
<th>$\lambda(\varepsilon)$ Co$^{II}$ (MeOH)</th>
<th>$\lambda(\varepsilon)$ Co$^{III}$ (MeOH)</th>
<th>$k_{ox}^{app}$ (10$^{-3}$ s$^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>L$^1$</td>
<td>653</td>
<td>425(13.8)</td>
<td>420(177)</td>
<td>1.86</td>
</tr>
<tr>
<td></td>
<td></td>
<td>486(19.0)</td>
<td>508(124)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>533(16.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L$^2$</td>
<td>250</td>
<td>458(41)</td>
<td>513(138)</td>
<td>3.44</td>
</tr>
<tr>
<td></td>
<td></td>
<td>499(61)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>542(44)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L$^4$</td>
<td>530</td>
<td>463(18.9)</td>
<td>499(79)</td>
<td>0.875</td>
</tr>
<tr>
<td></td>
<td></td>
<td>517(19.1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>551(14.4)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L$^5$</td>
<td>300</td>
<td>500(131.4)</td>
<td>342(1345)</td>
<td>&gt;12</td>
</tr>
<tr>
<td></td>
<td></td>
<td>560(87)</td>
<td>504(285)</td>
<td></td>
</tr>
<tr>
<td>L$^6$</td>
<td>519</td>
<td>383(37.3)</td>
<td>481(216)</td>
<td>9.28</td>
</tr>
<tr>
<td></td>
<td></td>
<td>483(34.6)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>542(17.9)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>L$^7$</td>
<td>75</td>
<td>480(147)</td>
<td>544(1050)</td>
<td>7.00</td>
</tr>
<tr>
<td></td>
<td></td>
<td>517(118)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>553(121)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Kinetics

Oxidation kinetics were followed by UV-vis spectroscopy. To the methanolic solution of the corresponding Co$^{II}$ complexes (11 mM) was added 30% aqueous H$_2$O$_2$ (170 eq) at 25°C. Time-dependent spectra were recorded over a period of 2 h. Absorbance values at absorption maxima were recorded as a function of times and pseudo-first order rate constants were determined from the slope of the semilogarithmic plots ($\ln(A_{\text{inf}}-A_t)$ vs t). In case of [Co$^{II}$L$^7$H$_1$(OH$_2$)]$^{+1}$ only a 2 mM concentration was used due to the high absorption coefficient of the oxidized complex; also, 40 eq H$_2$O$_2$ were used here, due to the relatively fast oxidation rate. The rates are reported in Table S1; these are interpreted as the oxidation of cobalt(II) to cobalt(III). Note that there is a fast initial reaction step (approx. first 5 minutes, see Fig. S2). This has not yet been analyzed.
Figure S1. Time-dependent UV-vis spectra for the oxidation of 11 mM [Co$^{II}$(L)$^1$(OH$_2$)$_2$](ClO$_4$)$_2$ with 170 eq H$_2$O$_2$ in MeOH, anaerobic conditions, T = 25 °C, spectra every 5 minutes.

$$k = 2.12 \times 10^{-3} \text{ s}^{-1}$$

Figure S2. Half-logarithmic plot for the oxidation of 11 mM [Co$^{II}$(L)$^1$(OH$_2$)$_2$](ClO$_4$)$_2$ with 170 eq H$_2$O$_2$ in MeOH, anaerobic conditions, T = 25 °C.
Labeling studies

Oxidation of \([\text{Co}^{II}(L_1)(\text{OH}_2)_2]^{2+}\) in MeOH was also carried out with \(\text{H}_2^{18}\text{O}_2\) as oxidant. ESI-MS spectra of the reaction mixtures were recorded and were compared to those with unlabeled \(\text{H}_2^{16}\text{O}_2\) under otherwise identical conditions. These studies were done to confirm the assignment of the mass spectra of the oxygenated complexes.

Hydrazine test

\([\text{Co}(L_1)(\text{OH}_2)_2]^{2+}\) /\([\text{Co}(L_4)(\text{OH}_2)_2]^{2+}\) (0.27 mmol) in MeOH (3 mL) was mixed with 30% aqueous \(\text{H}_2\text{O}_2\) (0.5 g). After 20 h at RT, the reaction mixture was added to the hydrazine reagent solution (10 mL; preparation of the hydrazine reagent solution: 2,4-dinitrophenylhydrazine in 1 g \(\text{H}_2\text{SO}_4\) (5 mL cc) was added slowly to a mixture of \(\text{H}_2\text{O}\) (10 mL) and 95% EtOH (35 mL)). The resulting orange precipitate was extracted with toluene (5 mL) and dried in vacuum. ESI(-) for the solid hydrazones from the reaction with \(L_1\): 209.2 [M-1], from the reaction with \(L_4\): 283.2 [M-3] (due to the extended delocalization chinoidal oxidation occurs).

Syntheses and characterization

Synthesis of \(L_4\): To the suspension of the piperidone\(^1\) (10.0 g 26.08 mmol) in EtOH (110 mL) aqueous formaldehyde 5.08 g (62.6 mmol) 37 w/w% was added dropwise, followed by benzylamine (3.35 g, 31.3 mmol). The reaction mixture was stirred under reflux for 3 h. Partial solvent removal under reduced pressure led to precipitation of the product. Yield: 7.44 g (55%). Elemental analysis: measured C 67.54, H 5.83, N 10.97; calculated for \(\text{C}_{29}\text{H}_{30}\text{N}_4\text{O}_5\), MW 514.54: C 67.89, H 5.87, N 10.89. FAB(+) (NBA): 515.5 [M+H]\(^+\), 537.5 [M+Na]\(^+\) \(^1\)H NMR (200 MHz, CDCl\(_3\)): 8.56 (d, 2H, Py-H, \(J = 4.2\) Hz), 7.87 (d, 2H, Py-H, \(J = 7.9\) Hz), 7.46 (td, 2H, Py-H, \(J = 7.7\) Hz and 1.7 Hz), 7.38 (s, 5H, \(\text{C}_6\text{H}_5\)), 7.11 (td, 2H, Py-H, \(J = 6.1\) Hz, 1.6
Supplementary Material (ESI) for Chemical Communications

This journal is (c) The Royal Society of Chemistry 2006

$^1$H NMR (200 MHz, CDCl$_3$): 4.68 (s, 2H, NCH), 3.81 (s, 6H, OCH$_3$), 3.35 (s, 2H, CH$_2$Ph), 3.05 (d, 2H, NCH$_2$, $J = 12.8$ Hz), 2.53 (d, 2H, NCH$_2$, $J = 12.8$ Hz), 1.96 (s, 3H, NCH$_3$) $^{13}$C NMR (200 MHz, CDCl$_3$): 52.5 (2C, NCH$_2$), 59.0 (2C, OCH$_3$), 62.1 (2C, NCH), 73.8 (2C, COC$_{\text{quat}}$CO), 122.9 (2C, C$_{\text{py-β}}$), 123.4 (2C, C$_{\text{py-δ}}$), 127.6 (1C, C$_{\text{ph-para}}$), 128.4 (2C, C$_{\text{ph-meta}}$), 130.4 (2C, C$_{\text{ph-ortho}}$), 136.1 (2C, C$_{\text{py-g}}$), 136.9 (1C, C$_{\text{ph-quat}}$), 149.0 (2C, C$_{\text{py-α}}$), 158.4 (2C, C$_{\text{py-quat}}$), 168.5 (2C, COOMe), 203.7 (1C, C=O) IR(KBr) [cm$^{-1}$]: 3425 (br,s), 3085 (w), 3057 (w), 3008 (m), 2987 (m), 2953 (m), 2855 (w), 2844 (m), 1739 (vs), 1589 (s), 1571 (m), 1465 (m), 1435 (vs), 1349 (s), 1279 (vs), 1159 (s), 1097 (s), 982 (m), 751 (s), 704 (m), 619 (m)

General procedure for the synthesis of the Co$^{	ext{II}}$ complexes: 1.94 mmol ligand in 30 mL MeOH was mixed with 1.94 mmol Co(ClO$_4$)$_2$ × 6 H$_2$O in 10 mL MeOH, and stirred for 1 h at room temperature. After partial solvent removal under reduced pressure a precipitate was formed, which was removed by filtration and air dried.

[Co$^{	ext{II}}$(L$_1$)(OH)$_2$](ClO$_4$)$_2$ × H$_2$O: Elemental analysis: measured C 36.97, H 4.20, N 7.39, calculated for C$_{23}$H$_{32}$N$_4$O$_{14}$Cl$_2$Co, MW 732.36: C 36.81, H 4.29, N 7.47. IR(KBr) [cm$^{-1}$]: 3428 (s, br), 3040 (w), 2955 (w), 2846 (w), 1722 (s), 1646 (m), 1605 (s), 1479 (m), 1449 (m), 1434 (m), 1261 (s), 1093 (vs), 961 (m), 783 (m), 626 (s), 516 (m). ESI-MS (in MeOH): 514.2 [Co$^{	ext{II}}$(L$_1$)(OH)]$^+$, 614.1 [Co$^{	ext{II}}$(L$_1$)(OH)$_2$(ClO$_4$)]$^+$. UV-vis ($\lambda_{\text{max}}$/nm ($\varepsilon$) in MeOH): 425(13.8), 486(19.0), 533(16.6)

[Co$^{	ext{II}}$(L$_4$)(OH)$_2$](ClO$_4$)$_2$: Elemental analysis: measured C 41.61, H 4.55, N 6.58; calculated for C$_{29}$H$_{37}$N$_4$O$_{16.5}$Cl$_2$Co, MW 835.44: C 41.69, H 4.46, N 6.71. FAB(+)-MS (NBA): 672.4 [Co$^{	ext{II}}$(L$_4$)(ClO$_4$)]$^+$, 690.4 [Co$^{	ext{II}}$(L$_4$)(OH$_2$)(ClO$_4$)]$^+$ IR(KBr) [cm$^{-1}$]: 3431 (br,s), 3030 (w), 2954
6

[Co\(^{II}\)(L\(^5\))(OH\(_2\))](ClO\(_4\))\(_2\) \(\times\) 2 H\(_2\)O:  
**Elemental analysis:** measured C 40.43, H 4.26, N 8.29;  
calculated for C\(_{29}\)H\(_{34}\)N\(_5\)O\(_{16}\)Cl\(_2\)Co, MW 827.43: C 40.64, H 4.26, N 8.47.  
**ESI-MS** in MeOH:  
287.1 [Co\(^{II}\)N\(_2\)Py\(_3\)u]\(^2+\), 296.1 [Co\(^{II}\)N\(_2\)Py\(_3\)u(OH\(_2\))]\(^2+\)

[Co\(^{II}\)(L\(^6\))(OH\(_2\))](ClO\(_4\))\(_2\) \(\times\) 1.5 H\(_2\)O:  
**Elemental analysis:** measured C 41.00, H 4.18, N 8.45;  
calculated for C\(_{28}\)H\(_{34}\)N\(_5\)O\(_{15.5}\)Cl\(_2\)Co, MW 818.42: C 41.09, H 4.18, N 8.56.  
**ESI-MS** in MeOH:  
287.1 [Co\(^{II}\)(L\(^6\))]\(^2+\), 303.1 [Co\(^{II}\)(L\(^6\))(MeOH)]\(^2+\).  
**IR(KBr) [cm\(^{-1}\)]:** 3438 (s, br), 2954 (w), 2846 (w), 1729 (s), 1606 (m), 1474 (m), 1449 (s), 1436 (m), 1275 (s), 1088 (vs), 966 (m), 785 (m), 768 (m), 624 (s), 515 (m).  
**UV-vis (\(\lambda_{\text{max}}/\text{nm} (\varepsilon)\) in MeOH):** 383(37.3), 446(23.5), 483(34.6), 542(17.9).

[Co\(^{II}\)(L\(^7\)H\(_{-1}\))(OH\(_2\))ClO\(_4\) \(\times\) 1.5 H\(_2\)O:  
**Elemental analysis:** measured C 47.31, H 4.83, N 7.46;  
calculated for for C\(_{29}\)H\(_{35}\)N\(_4\)O\(_{13}\)ClCo, MW 741.96: C 47.51, H 4.67, N 7.64.  
**UV-vis (\(\lambda_{\text{max}} (\varepsilon)\) in MeOH):** 480(147), 519(118), 553(121).  
**FAB(+)–MS:** 588.6 [Co\(^{II}\)(L\(^7\)H\(_{-1}\))]\(^+\), 606.6 [Co\(^{II}\)(L\(^7\)H\(_{-1}\))(OH\(_2\))]\(^+\).  
**IR(KBr) [cm\(^{-1}\)]:** 3474 (s, br), 2950 (w), 2834 (w), 1720 (vs), 1606 (s), 1478 (s), 1450 (s), 1272 (vs), 1084 (vs), 1020 (s), 974 (m), 790 (s), 764 (s), 622 (m).

[Co\(^{III}\)(L\(^3\))(CO\(_3\))](PF\(_6\)) \(\times\) 3 H\(_2\)O:  
L\(_1\) (1.0 g, 2.28 mmol) dissolved in MeOH (20 mL), was added to 1 M aqueous solution of K\(_3\)[Co(CO\(_3\))\(_3\)] (2.28 mL).  
This solution was stirred under reflux for 30 min, and the products separated on a Sephadex CM25 ion-exchange column, using 0.1 M NaCl as eluant.  
To the main fraction was added NaPF\(_6\) (1.5 eq), the solvent was partially removed under reduced pressure, the precipitate main fraction was collected and dried in vacuo.  
**Elemental analysis:** measured C 32.54, H 3.48, N 7.00; calculated for
C$_{21}$H$_{28}$N$_4$O$_{11}$PF$_6$Co, MW 716.35: C 32.12, H 3.43, N 6.81. ESI-MS: 567.2 [Co$_{\text{III}}$(L$_3$)(CO$_3$)]$^+$

$^1$H NMR: (200 MHz, DMSO): 1.80 (d, 2H, CH$_2$), 2.51 (d, 2H, CH$_2$), 2.51 (s, 3H, NCH$_3$), 3.50 (s, 3H, NCH$_3$), 5.25 (s, 2H, NCH), 7.85-8.85 (m, 8H, Ar-H). IR(KBr) [cm$^{-1}$]: 3430 (s), 2356 (m), 1618 (s), 1450 (m), 1352 (s), 1266 (m), 1244 (m), 1158 (w), 1102 (w), 1052 (m), 1038 (m), 986 (w), 840 (s), 782 (m), 750 (m), 562 (m)

**General procedure of the synthesis of the Co$^{\text{III}}$ chloro complexes:** The Co$^{\text{II}}$-complex (0.54 mmol) was dissolved in MeOH (20 mL) and 30% aqueous H$_2$O$_2$ (17 µL, 3 eq) was added dropwise. After 1 day stirring at room temperature the product was separated on a Dowex 50 Wx2 ion exchange column, eluting with 1 M HCl. NaClO$_4$ (1.2 eq) was added to the major fraction, the solvent was partially removed under reduced pressure, and the precipitate was collected and dried.

[Co$^{\text{III}}$(L$^2$)Cl$_2$]ClO$_4$ × 1.5 H$_2$O: **Elemental analysis:** measured C 38.87, H 4.01, N 8.01; calculated for C$_{22}$H$_{27}$N$_4$O$_{10.5}$Cl$_3$Co, MW 680.76: C 38.81, H 3.99, N 8.23. ESI-MS: 553.3 [Co$^{\text{III}}$(L$^2$)Cl$_2$]$^+$, 571.3 [Co$^{\text{III}}$(L$^2$)Cl$_2$(H$_2$O)]$^+$. $^1$H NMR (200 MHz, DMSO): 2.25 (d, 2H, CH$_2$), 2.80 (d, 2H, CH$_2$), 3.55 (s, 6H, OCH$_3$), 3.95 (s, 3H, NCH$_3$), 5.25 (s, 2H, NCH), 7.25-9.25 (m, 8H, Ar-H). IR(KBr) [cm$^{-1}$]: 3168 (s), 2958 (w), 1756 (m), 1738 (s), 1608 (s), 1476 (s), 1438 (w), 1364 (s), 1286 (s), 1252 (m), 1214 (w), 1108 (s), 1102 (s), 1050 (s), 954 (m), 924 (w), 902 (w), 788 (m), 778 (m), 758 (m), 740 (w), 624 (w)

[Co$^{\text{III}}$(L$_5$)Cl]Cl$_2$: ESI-MS: 296.4 [Co(III)N$_2$Py$_3$(OH)]$^{2+}$. IR(KBr) [cm$^{-1}$]: 3424 (s), 2358 (m), 1732 (s), 1606 (s), 1472 (m), 1440 (s), 1280 (s), 1256 (s), 1086 (s), 958 (w), 774 (m), 668 (w), 622 (w), 536 (w). $^1$H NMR: (200 MHz, D$_2$O) 2.11 (s, 3H, NCH$_3$), 2.21 (d, 2H, CH$_2$), 2.55 (d, 2H, CH$_2$), 3.47 (s, 6H, OCH$_3$), 3.77 (s, 2H, NCH$_2$), 5.93 (s, 2H, NCH), 7.15-9.26 (m, 12H, Ar-H)
[Co\textsuperscript{III}(L\textsuperscript{6})Cl]\textsubscript{2} \times 6 \text{H}_2\text{O}: \textit{Elemental analysis}: measured C 42.59, H 5.24, N 8.88; calculated for C\textsubscript{28}H\textsubscript{41}N\textsubscript{5}O\textsubscript{11}Cl\textsubscript{3}Co, MW 788.97: C 42.63, H 4.66, N 8.85. \textit{ESI-MS}: 313.9 [Co(III)N\textsubscript{2}Py\textsubscript{3}O\textsubscript{Cl}]\textsuperscript{2+}. \textit{IR(KBr)} [cm\textsuperscript{-1}]: 3388 (s), 2358 (m), 1726 (s), 1608 (s), 1474 (w), 1436 (m), 1262 (s), 1156 (w), 1108 (w), 1060 (m), 1030 (w), 950 (w), 770 (m). \textit{1H NMR} (200 MHz, DMSO): 2.60 (d, 2H, CH\textsubscript{2}), 2.75 (s, 3H, NCH\textsubscript{3}), 3.05 (d., 2H, CH\textsubscript{2}), 3.75 (s, 6H, OCH\textsubscript{3}), 4.80 (s, 2H, NCH\textsubscript{2}), 5.28 (s, 2H, NCH), 7.50-9.72 (m, 12H, Ar-H)

[Co\textsuperscript{III}(L\textsuperscript{7})Cl]\textsubscript{2} \times 5.5 \text{H}_2\text{O}: \textit{Elemental analysis}: measured C 43.85, H 4.99, N 7.27, calculated for C\textsubscript{29}H\textsubscript{40}N\textsubscript{4}O\textsubscript{11.5}Cl\textsubscript{3}Co, MW 793.92: C 43.87, H 5.07, N 7.06. \textit{ESI-MS}: 641.3 [Co\textsuperscript{III}(L\textsuperscript{7})(Cl)(OH)]\textsuperscript{+}. \textit{IR(KBr)}: 3384 br, s (OH), 2954 w (CH\textsubscript{2}), 1734 s (C=O), 1608 m, 1478 m, 1452 m, 1274 s, 1062 m, 954 m, 774 m. \textit{UV-vis} (MeOH): 394 nm (\(\varepsilon = 1400\)), 557 nm (\(\varepsilon = 860\)). \textit{1H NMR}(D\textsubscript{2}O): 8.54 (br, 2H, ar-H), 8.03 (br, 2H, ar-H), 7.64 (d, 1H, ar-H, \(\text{3J} = 7.95 \text{ Hz}\)), 7.58 (br, 4H, ar-H), 7.30 (t, 1H, ar-H, \(\text{3J} = 7.7 \text{ Hz}\)), 7.00 (d, 1H, ar-H, \(\text{3J} = 7.4 \text{ Hz}\)), 6.82 (t, 1H, ar-H, \(\text{3J} = 7.4 \text{ Hz}\)), 5.37 (s, br, 2H, NCH), 3.63 (s, br, 8H, NCH\textsubscript{2}C\textsubscript{6}H\textsubscript{4}OH), 2.52 (s, br, 4H, NCH\textsubscript{2}), 2.24 (s, br, 3H, NCH\textsubscript{3})

[Co\textsuperscript{II}(L\textsuperscript{2})(OH\textsubscript{2})\textsubscript{2}][ClO\textsubscript{4}]\textsubscript{2} \times 4 \text{H}_2\text{O} was prepared by H\textsubscript{2}O\textsubscript{2} addition (10 eq) to a solution of [Co\textsuperscript{II}(L\textsuperscript{1})(OH\textsubscript{2})\textsubscript{2}][ClO\textsubscript{4}]\textsubscript{2} \times \text{H}_2\text{O} (15 mg, 20.48 \text{µmol}) in MeOH (0.8 mL) methanol. Pink crystals suitable for X-ray studies formed after 5 days (ether diffusion). \textit{Elemental analysis}: measured C 34.99, H 4.30, N 7.11, calculated C 35.03, H 4.27, N 7.43. \textit{UV-vis}: (\(\lambda_{\text{max}}/\text{nm}\)) 456, 496, 534

[Co\textsuperscript{III}(L\textsuperscript{7})(Cl)(OH\textsubscript{2})\textsubscript{2}][ClO\textsubscript{4}]\textsubscript{2}: [Co\textsuperscript{III}(L\textsuperscript{2})Cl\textsubscript{2}]ClO\textsubscript{4} \times 1.5 \text{H}_2\text{O} (14.7 mg, 21.61 \text{µmol}) was dissolved in water (3 mL). To this solution was added AgClO\textsubscript{4} (8.9 mg, 43.2 \text{µmol}) in water
(1 mL), and was left under stirring and in the dark overnight. AgCl was then removed by filtration and the clear solution was fully evaporated. MeOH (0.75 mL) was then added to the solid, and was treated with 30% aqueous H₂O₂ (30 eq, 61.6 µL). Crystals were grown by ether diffusion (violet needles, obtained after 2 days).

Crystal structure determination:
Data were collected at 100 K with a Bruker-AXS CCD diffractometer (Mo-Kα radiation, λ = 0.71073 Å, ω-scans). Structures were solved by direct methods and refined against F² (SHELXTL V5.10).

DFT calculations
DFT calculations were carried out using Gaussian 03 with the three-parameter hybrid exchange and correlation functional, B3LYP. Geometry optimizations were made at 6-31G(d) level. Optimized structures of [Co⁺²(L¹)(OH₂)₂]²⁺ and [Co⁺²(L²)(OH₂)₂]²⁺ show elongated axial axis, along the Co-N7 bond (see entries a´ and b´ in Table 1). Although the bite distance N3····N7 is overestimated in the optimized structures, the trend observed in the crystal structures is nicely followed.

References

1 Haller, R.; Ashauer, U.; Arch. Pharm. 1985, 318, 405