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Synthesis of a Dicarboxylic Acid Receptor Organized Around a Dioxomolybdenum Core

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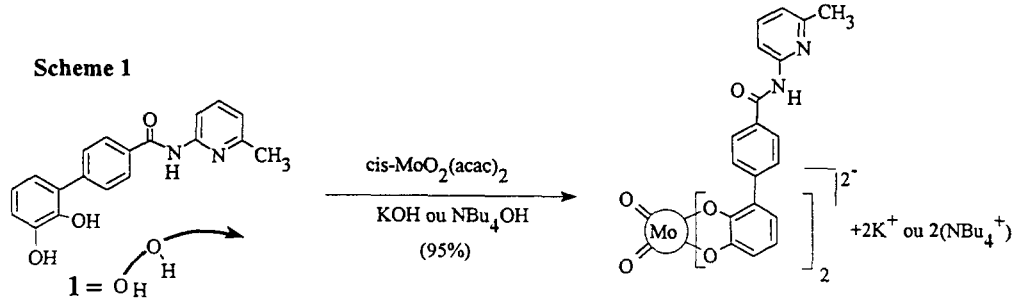
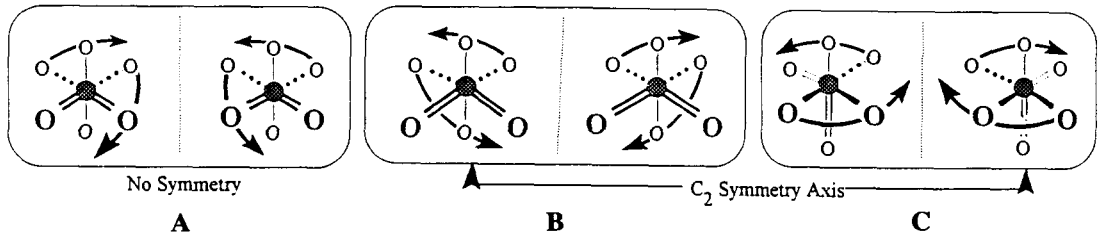
During the last decade, many receptors for neutral molecules based on properly oriented hydrogen bonding sites have been reported. In particular, numerous receptors for dicarboxylic acids[1] have been prepared by adequate spacing of 2-acylamino pyridine units.[1b-3] Since the geometrical control applied to the H-bonding sites often requires several synthetic steps, the spontaneous assembling of smaller constituents to form receptors has been investigated.[4] As transition metals have demonstrated their ability to gather and orient organic fragments,[5] self assembly of half receptors around metallic templates has been used to build specific receptors for neutral molecules.[6-9] The ability of catechols to form complexes with a large variety of transition metals[10] has prompted us to investigate the potential use of half receptors containing this coordinating moiety.

We describe hereafter the first receptor built by assembling two catecholate ligands around molybdenum as depicted in Scheme 1.

Scheme 1



Three pairs of possible enantiomers



A **B** **C**

The subunit **1** by itself exhibits poor affinity for mono- or dicarboxylic acids, however, binding of diacids is effective once the two H-bonding sites are rigidly preorganized around the MoO_2 template. Due to the two possible orientations of each catechol around the molybdenum, three pairs of enantiomers **A**, **B**, and **C** could be obtained, but only one racemate has been isolated. The synthesis of the half receptor **1** was performed as depicted in Figure 1, starting from veratrole **2** and 4-bromobenzoic acid. Low temperature lithiation of veratrole followed by quenching with trimethylborate and acidic work-up afforded the boronic acid **3** (58% after

chromatography over silica gel). The acid chloride **4**, prepared from 4-bromobenzoic acid was readily condensed with 2-amino 6-methylpyridine **5** in the presence of DBU to afford **6** in 90% yield after chromatography (SiO_2, CH_2Cl_2/traces of MeOH). The catecholate precursor **3** was coupled to the phenyl spacer bearing the amide **6** by "Suzuki" coupling reaction in 95% yield, using $Pd(PPh_3)_4$ in alkaline heterogeneous medium (MeOH/2 M aqueous Na_2CO_3/toluene, 1/1/5). Finally, deprotection of the catecholate chelating site was achieved using stoichiometric amounts of boron tribromide in CH_2Cl_2, affording the half receptor **1** in 85% yield. Synthesis of the fully assembled receptor was realized starting from bis(acetylacetonato)dioxomolybdenum(VI).

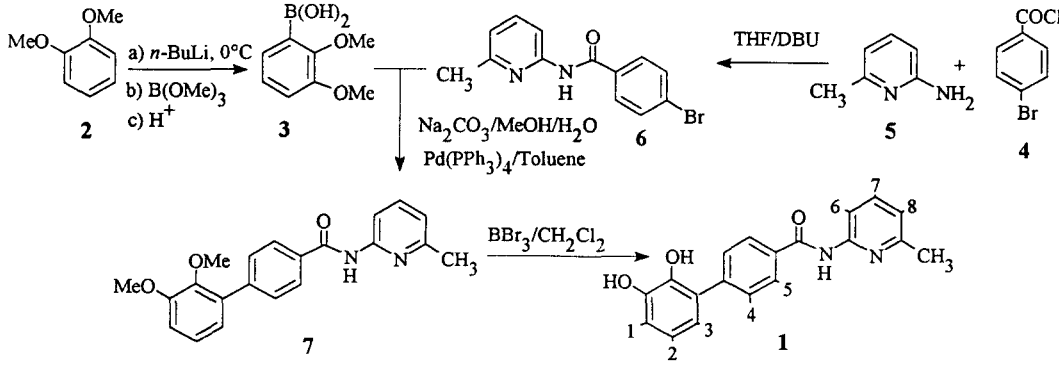
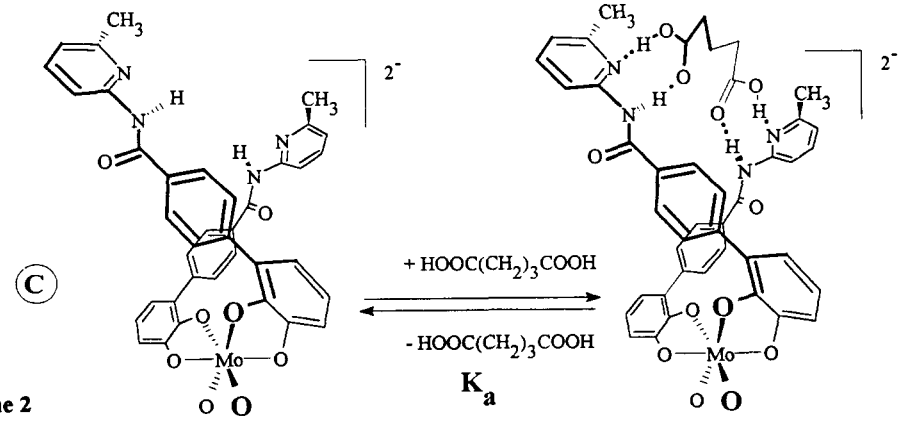


Figure 1

Reaction with two equivalents of half-receptor **1** in ethanol in presence of a base afforded the fully assembled receptor[11] in high yield (88-95%). Depending on the base used at this stage of the synthesis, the solubility of the target dianionic molybdenum complex in organic solvents can be controlled, the use of $(n\text{Bu})_4N^+$ cation (*vs.* K^+) considerably enhancing the solubility of the receptor in halogenated organic solvents. Regardless of the base used, only one pair of enantiomers out of the three possible was obtained. The reasons for ruling out the two other structures are briefly discussed hereafter.



Scheme 2

A symmetrical ^1H NMR spectrum rules out the unsymetrical structure **A** which would give two sets of signals for each half of the assembled receptor. Evidence for C_2 symmetry was obtained from ^1H and ^{13}C NMR. Complexation studies provide evidence necessary to rule out structure **B**. Although forms **B** and **C** afford the

same spacing between the H-bonding sites, **B** is sterically disfavored due to the presence of the cis-dioxo ligands. Monitoring dicarboxylic acid complexation by ^1H NMR does not show significant displacement of chemical shifts for the protons located on the C_5 chain of glutaric acid, which affords good evidence that the diacid binding occurs far from the cis-dioxo moiety. Also, previously reported structures of MoO_2 species with substituted catechols[12] have shown structures similar to **C**. Thus, the complexation of dicarboxylic acids with the receptor **C** is likely to occur as depicted in Scheme 2.

The receptor **C** has been characterized by standard techniques. FTIR clearly shows that the cis-MoO_2 geometry has been retained as two bands corresponding to the ν(Mo=O) are observed.[11] In addition to the correct molecular mass, mass spectrometry measurements confirmed in each case, the presence of the counter cations K^+ or $(n\text{Bu})_4N^+$. The use of potassium as counter cation causes the inclusion of nine water molecules in the crystal lattice of the receptor, which should decrease its H-bonding ability towards dicarboxylic acids. UV-visible titrations were performed to assay the receptor affinity for diacids ranging from C_4 to C_7. As it has been reported previously,[8] significant changes in the electronic absorption spectrum of receptors assembled around transition metal render UV-visible titrations more accurate than NMR for the determination of binding constants. Titration curves, an example of which is given in Figure 2 for adipic acid, were analyzed with the help of the LETAGROP program (ver. 2.4.93). For each titration, the 1/1 stoichiometry of the complex formation was confirmed by Job's method. Binding constants in acetonitrile (K^+ as counter cation) and also in CH_2Cl_2 ($(n\text{Bu})_4N^+$ as counter cation) are collected in Table 1.

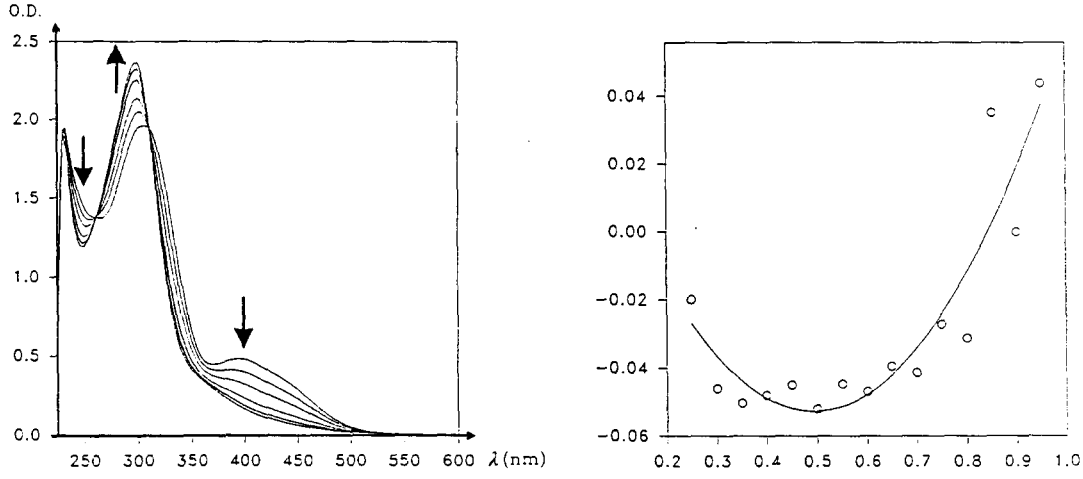


Figure 2: UV-visible Titration Curves and Job Plot for adipic acid with receptor C.

Counter Cation	Solvent	C_4	C_5	C_6	C_7
K^+	CH_3CN	$2.3 \pm 0.2 \times 10^3$	$4.2 \pm 0.4 \times 10^3$	$1.2 \pm 0.2 \times 10^3$	$0.6 \pm 0.1 \times 10^2$
$(n\text{-Bu})_4N^+$	CH_3CN	$5.7 \pm 0.5 \times 10^3$	$3.7 \pm 0.4 \times 10^3$	$1.8 \pm 0.8 \times 10^3$	$1.1 \pm 0.1 \times 10^3$
$(n\text{-Bu})_4N^+$	CH_2Cl_2	*not soluble*	$8.9 \pm 0.1 \times 10^3$	$4.7 \pm 0.4 \times 10^3$	$5.1 \pm 0.5 \times 10^3$

Table 1: K_a values for the titration of C_n dicarboxylic acids from succinic acid to pimelic acid.

Despite the relative rigidity of the $[MoO_2(cat)_2]^{-2}$ framework, only a slight preference for C_4 and C_5 dicarboxylic acids is noticeable, which is, however, consistent with previous observations on $[Cu(phen)_2]^+$ based receptors.[8] This could be explained by the free rotation of the CO-phenyl (spacer) bond enabling the receptor to

adapt to the length of the diacid carbon chain. This free rotation is also responsible for the color changes observed during titrations. Adjustment of the distance between the two aminopyridine units to the length of each diacid leads to partial weakening of the conjugation between the amide bonds and the spacer, thus inducing a redistribution of the electronic density within the (catecholate)MoO_2 moiety, which is responsible for the visible absorption bands. In conclusion, the concept of assembling receptors around metal templates may be extended to metal binding groups other than polyimine ligands. The complexation of chiral dicarboxylic acids has been studied but will be reported elsewhere.

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11. All new compounds have been characterized by standard techniques. The following spectroscopic and analytical data have been obtained for the the fully assembled receptor: **C[(*n*Bu)$_4$N$^+$]$_2$** ^{1}H NMR (CD_3CN): 8.82 (s, 2H, NH), 8.16 (d, J= 7.7Hz, 2H, H_8), 8.15 (d, J= 7.7Hz, 2H, H_6), 7.76 (broad m, 8H, $H_{4,5}$), 7.59 (d, J= 8Hz, 4H, H_7), 6.63 (t, J= 5.5Hz, 2H, H_2), 3.07 (m, 16H, $C\underline{H}_2N^+$), 2.29 (s, 6H, CH_3), 1.59 (m, 16H, $C\underline{H}_2CH_2N^+$), 1.34 (m, 16H, $C\underline{H}_2CH_2CH_2N^+$), 0.96 (t, J=14Hz, 24H, $C\underline{H}_3CH_2CH_2CH_2N^+$); **IR** cm^{-1}: 1669 (νCO), 1602 (δNH), 892 and 843 ν(Mo=O) in cis-[MoO_2]; **UV-vis** in CH_2Cl_2: λ_{max}nm(ε mol^{-1}·l·cm^{-1}): 304 (4.04x10^4), 394 (1.00x10^4); **FAB$^-$ MS**: [M]$^-$ calc.: 764.56, Found: 765.10. **C(K$^+$)$_2$** ^{1}H NMR (CD_3CN): identical to **C(Bu$_4$N)$_2$** except (nBu)$_4$N$^+$ signals; **IR** cm^{-1}: 1660 (νCO), 1598 (δNH), 892 and 841 (νMoO_2 cis); **UV-vis** in CD_3CN: λ_{max}nm(ε mol^{-1}·l·cm^{-1}): 298 (4.04x10^4), 376 (1.08x10^4); **FAB$^+$ MS**: [(M+1)+2K]$^+$ calc.: 843.7, Found: 843.9. **Elem. Anal. :** Calculated for **C(K$^+$)$_2$, (H$_2$0)$_9$** (Found): C 45.42 (45.28), H 4.60 (4.30), N 5.57 (5.58); Calculated for **C(*n*Bu$_4$N$^+$)$_2$** (Found): C 67.32 (67.46), H 8.06 (8.29), N 6.72 (6.14).
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