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Ion pair recognition by Zn–porphyrin/crown ether conjugates: visible sensing of sodium cyanide†

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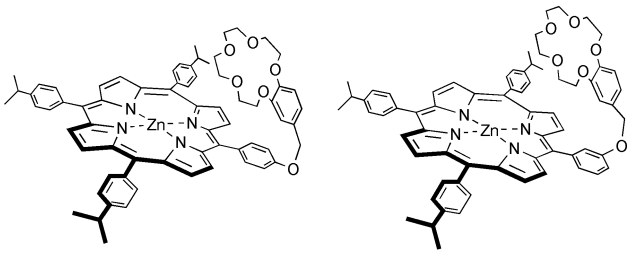
Synthesis and complexation behavior of ditopic neutral receptors composed of both a Lewis-acidic binding site (zinc porphyrin moiety) and a Lewis-basic binding site (crown ether moiety) are reported; the receptors bound only NaCN in a ditopic fashion with a color change, and in contrast other sodium salts bound to the receptors in a monotopic fashion without a color change.

The simultaneous complexation of cationic and anionic guest species by ditopic receptors is a rapidly growing area of supramolecular chemistry due to the need to develop selective extraction and membrane transport reagents for metal salts of environmental and biological significance.[1–5] The process of cellular respiration in mammalian cells is inhibited by the cyanide anion which is known to interact strongly with a heme in the active site of cytochrome a_3.[6] Therefore it is important to sense highly toxic and lethal cyanide. We have been interested in developing a new class of selective Zn–porphyrin receptors, which are capable of ion pair recognition of metal salts containing the cyanide anion using different binding sites within the receptor. The new receptor molecules contain binding sites for anionic and cationic guest species covalently linked together and fashioned to be selective for target ion pair species. Herein we report two new ditopic receptors (**3a**, **3b**) based on zinc porphyrins, as Lewis acidic metal centers, covalently linked to Lewis basic crown ether groups. We show that **3a** and **3b** are capable of selective visual sensing of NaCN.



3a = ZnTPP-15C5(p) **3b** = ZnTPP-15C5(m)

Synthesis of **3a** and **3b** is described in Fig. S1, ESI.† Interestingly, **3a** and **3b** were found to be in equilibrium with their dimeric forms in nonpolar organic solvents on the NMR time scale (Fig. S2, ESI†). We expect that in their dimeric forms the crown ether groups of **3a** and **3b** are mutually coordinated to the zinc of the other molecule (Fig. S3, ESI†).

On the basis of this result, complexation experiments have been carried out. Excess dry sodium salts (NaF, NaCl, NaBr, NaI, NaSCN, NaCN, NaH_2PO_4) were added to a 15 mM $CDCl_3$ solution of **3a** (or **3b**), respectively. After all the mixtures were sonicated for 3 h and centrifuged for 20 min at room temperature, the excess salt in each mixture was filtered out and the filtrate investigated by NMR, UV-visible spectroscopy (Fig. S4, ESI†) and mass spectrometry. In ^{1}H NMR spectra, the proton signals of the crown ether ethylenes of **3a** moved downfield upon complexation with the sodium salts, indicating the presence of a cation–dipole interaction between Na^+ and the crown ether oxygens. Among the sodium salts, NaF, NaCl, and NaH_2PO_4 caused smaller downfield shifts upon complexation with **3a** (or **3b**). However, complexation of **3a** and **3b** with NaBr, NaI and NaSCN caused the crown ether ethylene protons to move to a more downfield region, which indicates that these salts interact with **3a** and **3b** more strongly than hydrophilic salts such as NaF and NaCl. NaF and NaCl seemed to be slightly extracted through monotopic binding of Na^+ to the crown ether moiety. NaBr, NaI and NaSCN were mostly extracted by monotopic binding presumably due to the better lipophilic character of the counter anions. Among the various sodium salts, only NaCN caused a dramatic change in the aromatic region of the porphyrin.[7] The aromatic proton signals broadened indicating that the porphyrin macrocycle is frozen due to CN^- binding to the zinc. In addition, in the case of the binding of **3a** to NaCN, the crown ether ethylene protons undergo smaller downfield shift compared to binding with NaBr, NaSCN and NaI. Similarly, complexation of **3b** with NaCN resulted in an upfield shift of the crown ether ethylene protons. This is because the crown ring of **3a** (or **3b**) complexed with Na^+ folds over the porphyrin surface due to the interaction of $Zn–CN^-$ with an Na^+–crown ring. This implies that NaCN is complexed by **3a** and **3b** in ditopic fashion. Sodium salts other than NaCN were extracted into the organic phase by **3a** and **3b** in monotopic fashion (Fig. S3, ESI†). The extractability of the sodium salts presumably depends upon the lipophilicity of the counter anions of each salt. Because the cyanide anion is basic enough to coordinate Zn metal, **3a** and **3b** are likely to prefer ditopic complexation of NaCN despite charge separation. Further evidence for the ditopic binding of NaCN comes from the ^{13}C NMR spectra of NaCN–**3a** or NaCN–**3b**, in which all the carbon signals of the crown ether ethylenes show characteristic upfield shifts ($\Delta\delta$ = *ca.* 2 ppm) in comparison with the free receptors. UV-visible spectra of the complexes between the receptors and NaCN also provided further evidence for ditopic binding. Cyanide complexation to the zinc caused a red shift (*ca.* 15 nm) of the Soret band, which is the origin of the color change from red to green. However, F^- and Cl^-, which both have an affinity for Zn–porphyrins, do not result in color changes upon complexation with **3a** and **3b**.[8] Liquid/liquid extraction from saturated aqueous solutions of the sodium salts to nonpolar organic phases containing **3a** and **3b** gave the same results. FAB and MALDI mass spectra of the filtrates were also checked and gave similar results. In all cases a peak corresponding to **3a** (or **3b**) + sodium (M + Na^+) was observed in the positive ion mode spectrum. Complexes of NaF and NaCl with **3a** (or **3b**) show an intense peak for the free receptor (M^+) along with a relatively small peak for M + Na^+. In the complexes with NaBr, NaSCN and NaCN, only a peak for the complex (M + Na^+) was observed without that of the free receptor. This indicates that these salts are extracted better than the relatively hydrophilic salts such as NaF and NaCl. Furthermore, the quantitative extractabilities of **3a** and **3b** for NaCN were investigated by solid/liquid extraction experiments. For comparison, extraction by ZnTPP‡ and benzo-15-crown-5 was also carried out under the same conditions.

† Electronic supplementary information (ESI) available: selected spectral data for **3a** and **3b**, detailed dimerization phenomena, and Fig. S1–8. See http://www.rsc.org/suppdata/cc/b1/109596j/

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Extraction of NaCN into **3a** and **3b** in CH_2Cl_2 gave kinetically stable complexes on the NMR time scale in DMSO-d_6. Without benzo-15-crown-5, NaCN was not extracted into the CH_2Cl_2 solution of ZnTPP. Addition of 1 mol equivalent benzo-15-crown-5 to ZnTPP did not cause a significant increase in the β-H signal intensity of the NaCN–ZnTPP complex. Therefore a mixture of 3 mol equivalents benzo-15-crown-5 and ZnTPP (co-receptor) was used to estimate the extractability. The extractability was quantified by comparison of the relative intensities of the β-H signals of free and complexed receptors in the ^{1}H NMR titrations of these receptors with organic soluble cyanide in DMSO-d_6 (Fig. S5, ESI†). In all ^{1}H NMR titration spectra, the β-H signal of the free receptor gradually decreases and that of the CN^-/Zn–porphyrin complex starts to appear in a region 0.1 ppm upfield upon addition of an increasing amount of cyanide. Extraction of NaCN with these receptors in CH_2Cl_2 yielded similar ^{1}H NMR spectra, in which two β-H signals of free and complexed receptors were observed as shown in Fig. 1. The extractabilities ([complexed]/[free + complexed] × 100%) were estimated to be respectively 50% for the co-receptor, 80% for **3a** and 80% for **3b** under the same conditions. In this solid/liquid extraction experiment, UV-visible spectra of various filtrates in CH_2Cl_2 also showed a large red shift and an absorption change of λ_{max}, consistent with the result in Fig. 2 (Fig. S4, ESI†).[9] This indicates that covalently linked receptors extract NaCN more efficiently than a co-receptor system. These receptors also showed color changes after the solid/liquid extraction of NaCN into various host systems. As expected from the strong interaction of heme with cyanide in the biosystem, the more efficient extraction ability of only NaCN by these Zn–porphyrin/crown ether conjugates (**3a** and **3b**) compared to the co-receptor results from the ditopic binding of NaCN to **3a** and **3b** in organic media. This caused a color change from red to green suitable for the 'naked-eye' selective monitoring of the highly toxic cyanide ion existing in a heterophase. However, extraction of NaCN with ZnTPP without a crown ether moiety does not show any color change. This means that ZnTPP itself is not capable of extracting NaCN. The fact that a mixture of ZnTPP and 3 mol equiv. 15-crown-5 can extract NaCN less efficiently than ZnTPP–15C5 conjugates was reflected in the color change of the extracted solution from red to violet (Fig. S6, ESI†).

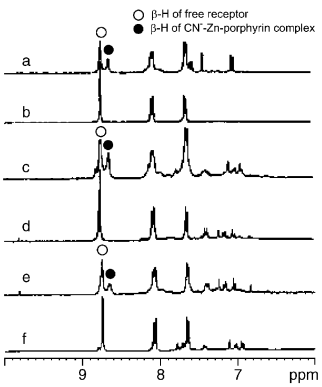

Fig. 1 Partial ^{1}H NMR spectra in DMSO-d_6, checked after solid/liquid extraction of NaCN by the receptors: (a) co-receptor (ZnTPP + 3 equiv. 15BC5) + NaCN, (b) ZnTPP + NaCN, (c) **3a** + NaCN, (d) **3a** only, (e) **3b** + NaCN, (f) **3b** only.

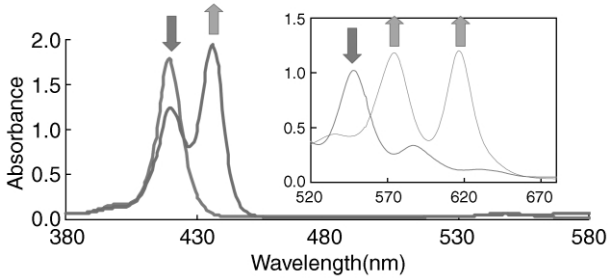

Fig. 2 UV-visible spectra of **3a** (solid line, [**3a**] = 3×10^{-6} M) in CH_2Cl_2, after solid/liquid extraction of NaCN; the dashed line corresponds to free **3a** ([**3a**] = 1.5×10^{-4} M in the inset).

In summary, we have synthesized new ditopic receptors that extracted sodium salts of F^-, Cl^-, Br^-, I^-, SCN^- and $H_2PO_4^-$ into a nonpolar organic phase in a monotopic fashion. With strong ditopic binding, however, NaCN in the heterophase was also able to be extracted into a nonpolar organic phase, which caused a dramatic color change from the orignal red color of the Zn–porphyrin to green. Such a selective color response can be utilized to allow for the easy detection of highly toxic cyanide in nature.

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‡ ZnTPP = Zn(II) 5,10,15,20-tetrakis(4-isopropylphenyl)porphyrin.

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9 According to a referee's comment, we checked the detection limits for NaCN sensing both in liquid/liquid extraction and in a mixed solvent system (DMSO–water); since NaCN is highly solvated in water, in the liquid/liquid extraction, more than 0.5 M aqueous NaCN is required to show the CN^- complex-induced Soret band in the UV-visible spectra. A few mM aqueous NaCN can be detected in the UV-visible spectra by adding aqueous NaCN to a DMSO solution of these receptors (Fig. S7, ESI†). The stability constants of the NaCN complexes in DMSO/water (9:1) were calculated to be 5.7×10^{-4} M for **3a** and 5.1×10^{-4} M for **3b** (Fig. S8, ESI†).