the cyclodextrin channel, which can only be explained by strong intermolecular interactions.

Very surprising was our observation that these polyamide inclusion compounds are water-soluble. The ^{1}H NMR spectrum of $[\mathbf{2}\cdot(\mathbf{1a})_2]_n$ in D_2O (Fig. 1 b) shows the signals of cyclodextrin and polyamide. Although these are slightly broader than the corresponding signals of the monomers, they indicate the existence of a real solution. The signals of $[\mathbf{2}\cdot(\mathbf{1a})_2]_n$ in [D$_6$]DMSO/CD$_3$COOD are better resolved, and the sharp signal for H-1 of **1a** proves that the C_6-symmetry of the α-cyclodextrin has been retained. Thus a reaction between the guest and cyclodextrin can be ruled out. The integration supports a coverage of the polyamide chain with two cyclodextrin units per repeating unit. This very high coverage explains the good solubility.

If the solution of the polyamide inclusion compound $[\mathbf{2}\cdot(\mathbf{1a})_2]_n$ is allowed to stand for several hours, a precipitate forms in which the cyclodextrin content is reduced by 30% with respect to $[\mathbf{2}\cdot(\mathbf{1a})_2]_n$. Apparently, the solubilizing cyclodextrins slowly unthread, with the result that free polymer chain ends can aggregate to allow the inclusion compound to precipitate. Due to the lack of mobility, the rings that are still threaded cannot slip off. The inclusion compound of polymer $[\mathbf{4}\cdot(\mathbf{1a})_2]_n$ is soluble in water for an unlimited time. Thus the methyl substituents of the piperazine moiety seem to prevent the rings from slipping off the polymer chain.

The pure polyamides were isolated by cleaving the threaded cyclodextrins with dilute HCl. The yields of the pure polyamides, for example, polyamide-11 from $[\mathbf{2}\cdot(\mathbf{1a})_2]_n$, was greater than 90%. The molecular masses were determined by gel permeation chromatography after N-trifluoroacylation.[10] The molecular mass of $M_w = 4500$ g mol^{-1}, which was obtained for **2**, corresponds to about 16 repeating units.[11]

With this solid-state polycondensation it is, in principle, possible to synthesize polyrotaxanes on any scale. Furthermore, this methodology might be applicable for the synthesis of rigid-chain, aromatic polyamides. Due to their good water-solubility, polymeric inclusion compounds could, for instance, be used for the coating of metals, polymers or textile surfaces with polyamides. Composite materials of the polyamide inclusion compounds and hydrophilic polymers, such as starch, might also be obtained.

Experimental Procedure

General: The ^{1}H NMR spectra were obtained at 400 MHz, and the X-ray powder diffractograms performed on a Siemens-WAXS-S-5000 diffractometer at 22 °C.

$[\mathbf{2}\cdot(\mathbf{1a})_2]$: **2** (5 g, 24.9 mmol) and **1a** (125 g, 129 mmol) were dissolved in water (250 mL) and heated to 80 °C upon stirring. The clear solution was then quickly cooled to 5 °C. The resulting white precipitate was filtered, washed with water (400 mL), and dried in vacuo. Yield: 39.8 g (65%). ^{1}H NMR ([D$_6$]DMSO/CD$_3$COOD, 10/1): $\delta = 4.78$ (d, ^3J(H,H) = 1.73 Hz, 12 H, H-1), 3.74 (t, ^3J(H,H) = 7.9 Hz, 12 H, H-3), 3.63 (m, 36 H, H-5, H-6), 3.37 (t, ^3J(H,H) = 7.86 Hz, 12 H, H-4), 3.26 (dd, ^3J(H-1,H-2) = 1.73, ^3J(H-2,H-3) = 7.86 Hz, 12 H, H-2), 2.73 (t, ^3J(H,H) = 7.38 Hz, 1.7 H, H-a), 2.15 (t, ^3J(H,H) = 7.39 Hz, 1.7 H, H-j), 1.47 (m, 3.7 H, H-b, H-i), 1.225 (s, 12 H, H-c through H-h); IR (KBr): $\tilde{\nu} = 3408$ s, 2925 s, 1635 m, 1410 w, 1362 w, 1291 w, 1246 w, 1202 w, 1162 s, 1095 s, 938 m cm^{-1}.

$[\mathbf{2}\cdot(\mathbf{1a})_2]_n$: $[\mathbf{2}\cdot(\mathbf{1a})_2]$ (203 mg) was tempered at 230 °C and 0.1 mbar for 5 h. Yield: 196 mg (97.4%), light brown powder. ^{1}H NMR ([D$_6$]DMSO/CD$_3$COOD, 10/1): $\delta = 4.78$ (d, ^3J(H,H) = 1.73 Hz, 12 H, H-1), 3.74 (t, ^3J(H,H) = 7.9 Hz, 12 H, H-3), 3.62 (m, 36 H, H-5, H-6), 3.36 (t, ^3J(H,H) = 7.86 Hz, 12 H, H-4), 3.26 (dd, ^3J(H-1,H-2) = 1.73, ^3J(H-2,H-3) = 7.86 Hz, 12 H, H-2), 2.98 (t, ^3J(H,H) = 7.38 Hz, 1.7 H, H-a), 2.13 (t, ^3J(H,H) = 7.39 Hz, 1.7 H, H-j), 1.44 (m, 3.7 H, H-b, H-i), 1.35–1.15 (br., 12 H, H-c through H-h); IR (KBr): $\tilde{\nu} = 3399$ s, 2925 s, 2362 w, 1733 m, 1646 m, 1410 w, 1362 w, 1161 s, 1087 s, 938 m cm^{-1}; elemental analysis (%): calcd: C 46.83, H 6.68, N 0.66; found: C 46.61, H 6.96, N 1.14.

$(\mathbf{2})_n$: $[\mathbf{2}\cdot(\mathbf{1a})_2]_n$ (1.172 g) was stirred in 1% HCl (60 mL) at 80 °C for 25 h. The resulting precipitate was filtered and washed several times with water and methanol. Yield: 103.1 mg (93.9%). For the molecular mass determination, $(\mathbf{2})_n$ (90 mg, 0.49 mmol) was added to absolute CH_2Cl_2 (15 mL) and stirred with trifluoroacetic anhydride (0.21 g, 1.0 mmol) at 25 °C for 24 h [10]. After removal of the solvent by distillation, the residue was dried at 0.1 mbar. Yield: 139 mg (96%) N-trifluoroacylated nylon-11. The soluble product was subjected to size exclusion chromatography on Styralgel columns (Waters, calibration with polystyrene standards [10]) in absolute THF.

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Molecular Recognition of Cyanide by a Dicopper(II) Macrocyclic Ionophore: Construction of a Cyanide-Selective Liquid-Membrane Electrode

Benedikt Ahlers, Karl Cammann,* Sabine Warzeska, and Roland Krämer*

Over the years various types of synthetic receptors for the efficient and selective binding of anions have been developed.[1] A particularly interesting application of such compounds is their use as ionophores in potentiometric sensors.[2] There are only few examples of anion-selective microelectrodes that are based on the specific interaction of the target anion with a transition metal complex. Lipophilic metalloporphyrins[3] and alkyltin compounds[4] are selective carriers for various anions in liquid-membrane electrodes; they show a correlation between the selectivity sequence of the electrode and the strength of the coordinative bond between metal and anion.

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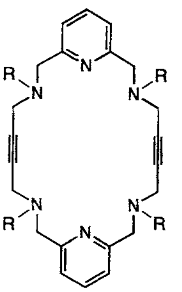
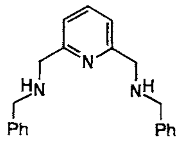
Here we present the first potentiometric anion sensor in which the dinuclear metal complex of a polyaza macrocycle acts as an ion-selective ionophore. Complexes of macrocycles that have two sites for ligation to metal centers coordinate bridging anions in a shape-selective, molecular recognition process.[5]

The lipophilic bis(tridentate) macrocycles L^1 and L^2 are readily available by alkylation of the secondary amino groups of a previously described ligand.[6] For a comparative study the related monotopic ligand L^3 was prepared by Schiff base condensation of pyridine-2,6-dicarbaldehyde and benzylamine, followed by $NaBH_4$ reduction of the imino groups. The crystalline complexes $[(L^1)Cu_2(NO_3)_4]$, $[(L^2)Cu_2(NO_3)_4]$,[7] and $[(L^3)Cu(NO_3)_2]$ were obtained by reaction of the ligands with $Cu(NO_3)_2 \cdot 3H_2O$ in appropriate stoichiometry.

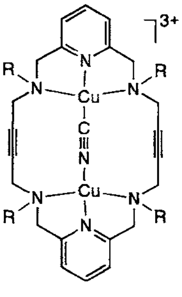


L^1: R = $C_{16}H_{33}$
L^2: R = CH_2Ph

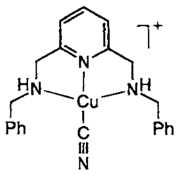


L^3

To our knowledge the reaction of macrocyclic dicopper(II) complexes with cyanide, particularly in solution, has not yet been studied in detail. The green microcrystalline complexes $[(L^n)Cu_2(\mu\text{-}CN)(NO_3)_3]$ are obtained from $[(L^n)Cu_2(NO_3)_4]$ ($n = 1, 2$) and KCN (1 equiv). A weak ν(CN) infrared band at 2205 cm^{-1} for $[(L^1)Cu_2(\mu\text{-}CN)(NO_3)_3]$ and at 2208 cm^{-1} for $[(L^2)Cu_2(\mu\text{-}CN)(NO_3)_3]$ indicate the presence of bridging cyanide.[8] The crystal structure of the cyano-bridged dicopper(II) compound of a related ligand[9] with ν(CN) at 2235 cm^{-1} demonstrates that CN^- fits well into the central cavity defined by the relatively rigid macrocyclic framework. The cleft between the alkyne spacers is only about 6 Å wide,[6,9] which should disfavor the incorporation of bulkier (for example tetrahedral) anions for steric reasons. Addition of KCN to $[(L^3)Cu(NO_3)_2]$ yields purple $[(L^3)Cu(CN)(NO_3)]$. The rather strong ν(CN) infrared band of this complex at 2127 cm^{-1} is typical for terminally coordinated cyano ligands.[8a]



$[(L^n)Cu_2(\mu\text{-}CN)]^{3+}$



$[(L^3)Cu(CN)]^+$

In MeOH-MeCN (1:1 v/v) solution blue $[(L^1)Cu_2]^{4+}$ ($\lambda_{max} = 647$ nm, $\varepsilon_{647} = 480\ M^{-1}cm^{-1}$, $\varepsilon_{400} = 290\ M^{-1}cm^{-1}$) is smoothly converted into blue-green $[(L^1)Cu_2(\mu\text{-}CN)]^{3+}$ ($\lambda_{max} = 617$ nm, $\varepsilon_{617} = 550\ M^{-1}cm^{-1}$, $\varepsilon_{400} = 1200\ M^{-1}cm^{-1}$) by titration with between 0 and 1 equivalent of cyanide (isosbestic point at 665 nm). Similarly, blue $[(L^2)Cu_2]^{4+}$ ($\lambda_{max} = 656$ nm, $\varepsilon_{656} = 590\ M^{-1}cm^{-1}$, $\varepsilon_{400} = 340\ M^{-1}cm^{-1}$) forms green $[(L^2)Cu_2(\mu\text{-}CN)]^{3+}$ ($\lambda_{max} = 635$ nm, $\varepsilon_{635} = 680\ M^{-1}cm^{-1}$, $\varepsilon_{400} = 1100\ M^{-1}cm^{-1}$), with an isosbestic point at 670 nm. The mononuclear complex $[(L^3)Cu]^{2+}$ ($\lambda_{max} = 635$ nm, $\varepsilon = 220\ M^{-1}cm^{-1}$) reacts with between 0 and 1 equivalent of cyanide to yield purple $[(L^3)Cu(CN)]^+$ ($\lambda_{max} = 580$ nm, $\varepsilon = 280\ M^{-1}cm^{-1}$, isosbestic point at 630 nm). Smooth formation of 1:1 complexes shows that the first cyanide molecule is bound with high affinity in all cases.[10] Further changes in the spectra on addition of more than one equivalent of KCN indicate coordination of more than one CN^- ion to the complexes. Thus, for 1-3 equivalents of cyanide the green solutions of the dinuclear complexes turn blue again, due to a significant decrease of 400 nm absorbance.

Evidence for the particularly efficient binding of bridging cyanide is given by the behavior of the complexes on treatment with strong acid. In a MeOH-MeCN solution (1:1 v/v) of $[(L^n)Cu_2(\mu\text{-}CN)]^{3+}$ (1 mM) λ_{max} and ε of the optical band remain unchanged upon addition of 3 equivalents of *p*-toluenesulfonic acid (TsOH) (with a very large excess of TsOH the complexes are decomposed by ligand protonation rather than by release of HCN). In contrast, treatment of $[(L^3)Cu(CN)]^+$ ($\lambda_{max} = 580$ nm) with TsOH results in protonation of coordinated cyanide to produce 70% $[(L^3)Cu]^{2+}$ ($\lambda_{max} = 635$ nm) on addition of one equivalent of TsOH and 90% $[(L^3)Cu]^{2+}$ on addition of two. Also, TsOH removes the second coordinated cyanide molecule in $[(L^n)Cu_2(CN)_2]^{2+}$ to give 55% $[(L^n)Cu_2(\mu\text{-}CN)]^{3+}$ (1 equiv. TsOH) and 80% $[(L^n)Cu_2(\mu\text{-}CN)]^{3+}$ (2 equiv. TsOH). Based on these observations we can estimate the relative affinities of the complexes for bridging and terminal cyanide ligands. The binding constant of $[(L^n)Cu_2]^{4+}$ for bridging cyanide is at least 10^2 times larger than that of $[(L^3)Cu]^+$ or $[(L^n)Cu_2(\mu\text{-}CN)]^{3+}$ for terminal cyanide.[11] It is well known that dinuclear macrocyclic copper(II) complexes have a much higher affinity for bridging anions of appropriate geometry than related mononuclear complexes.[12]

In the presence of excess cyanide $[(L^n)Cu_2]^{4+}$ ($n = 1,2$) is more stable against reduction than $[(L^3)Cu]^{2+}$. In a MeOH-MeCN solution (1:1 v/v) containing 5 mM KCN the optical absorbance of the dinuclear complex (1 mM) is unchanged for 3 min whereas reduction of Cu^{II} to Cu^{I} in the mononuclear complex (1 mM) is indicated by a complete disappearence of the absorbance around 600 nm in the same period of time.

Application of $[(L^n)Cu_2(NO_3)_4]$ ($n = 1, 2$), $[(L^3)Cu(NO_3)_2]$ and L^2 as ion-selective materials in liquid-membrane electrodes was studied by measuring the potentiometric behavior. The compounds were embedded into a plastisized PVC-membrane (PVC/*o*-nitrophenyl octyl ether/ionophore in a 33/66/1 ratio).[2a] The membranes containing $[(L^n)Cu_2(NO_3)_4]$ and $[(L^3)Cu(NO_3)_2]$ were light blue and transparent when kept in H_2O. Apparently, the $C_{16}H_{33}$ and CH_2Ph substituents anchor the complexes in the lipophilic membrane phase and prevent loss to the aqueous solution.

The membranes were implemented into a potentiometric measuring setup and the potential differences referred to a Ag/AgCl reference electrode were determined.[2a] The electrodes containing $[(L^n)Cu_2(NO_3)_4]$ exhibited fast and reversible near-Nernstian response to aqueous cyanide solutions at pH 10 with a linear working range for cyanide concentrations between 10^{-5} to 10^{-2} M. The response to CN^- is highly selective, in particular for $[(L^1)Cu_2(NO_3)_4]$ (Fig. 1). Alternating current impendance measurements[13] confirmed the interaction of membranes containing $[(L^2)Cu_2(NO_3)_4]$ with cyanide ions. The bulk membrane resistance changed by a factor of 4 on exposure to 1 mM KCN solution in a 0.1 M $Ca(NO_3)_2$ background electrolyte. Furthermore, the bright blue membrane adopts the bright green color of $[(L^2)Cu_2(\mu\text{-}CN)(NO_3)_3]$ when kept in 0.1 M cyanide solution for 5 h.[14]

Electrodes based on $[(L^3)Cu(NO_3)_2]$ or L^1 show only a slight sensitivity to cyanide ions and behave more or less as typical anion exchangers with a selectivity pattern dependent on the lipophilicity of the sample anions (Fig. 1).[2a] Although formation of $[(L^3)Cu(CN)(NO_3)]$ is indicated by the purple color of the membrane after exposure to 0.1 M KCN, cyanide affinity of the mononuclear complex appears to be too weak to induce a selective response.

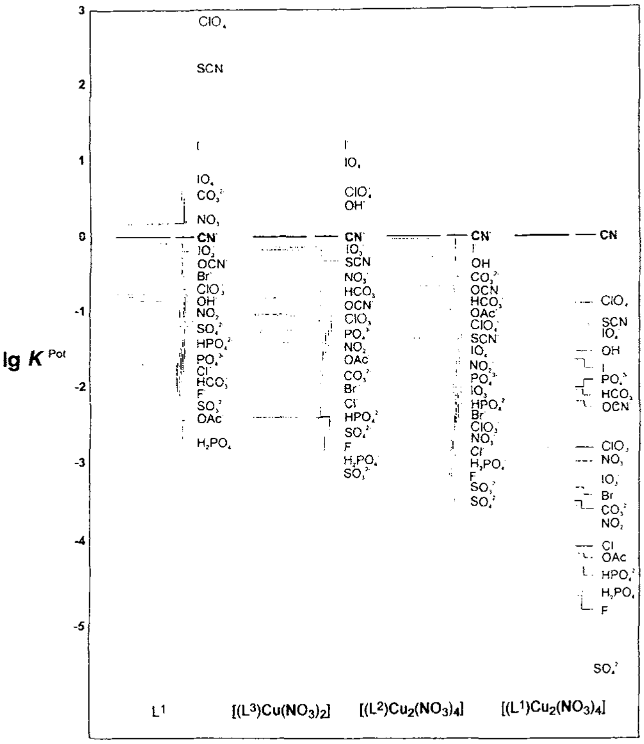


Fig. 1. Selectivity coefficients $\lg K^{\mathrm{Pot}}_{\mathrm{CN^-},A^-}$ of a membrane electrode containing ionophores $[(L^1)Cu_2(NO_3)_4]$, $[(L^2)Cu_2(NO_3)_4]$, $[(L^3)Cu(NO_3)_2]$, and L^2, determined according to the FIM-method.[2a] The selectivity coefficient is given by the weighting factor (K^{Pot}_{ij}) in the Nicolsky Eisenmann equation $\left(E = E^0_i + \frac{2.3\,RT}{z_i \cdot F} \lg\left[a_i + \sum_j K^{\mathrm{Pot}}_{ij} \cdot (a_j)^{z_i/z_j}\right]\right)$.

In conclusion, the first cyanide-selective electrode based on a molecular recognition process was constructed. Dinuclear metal complexes of lipophilic macrocycles represent a novel class of ionophore in liquid-membrane electrodes. By variation of the metal ion and of the macrocyclic framework selective carriers for many different target anions should be available.

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Structure-Directed Synthesis under Thermodynamic Control: Macrocyclic Trimers from Cinchona Alkaloids**

Stuart J. Rowan, Paul A. Brady, and
Jeremy K. M. Sanders*

Covalent organic structures have traditionally been synthesized through kinetically controlled irreversible reactions, whereas noncovalent supramolecular assemblies are generally constructed with thermodynamically controlled reversible interactions.[1,2] Irreversible reactions lack the ability to proofread and repair "incorrect" bond formation, while supramolecular assemblies tend to lack the robust character associated with covalent bonds, so we have been exploring the synthetic potential of covalent chemistry under reversible conditions.[3] We now report the exceptionally efficient synthesis under thermodynamic control of macrocyclic trimers from new supramolecular building blocks derived from the cinchona alkaloids quinine (**1a**) and cinchonidine (**1b**).

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