Experimental Section

Samples of complex **1** were synthesized as previously described.[15]

$[Mn_{12}(\mu_3\text{-}O)_{12}(\mu\text{-}RCOO)_{16}(H_2O)_4]$, R = C_6H_4-2-Cl, C_6H_4-2-Br: A slurry of $[Mn_{12}(\mu_3\text{-}O)_{12}(\mu\text{-}MeCOO)_{16}(H_2O)_4]$ (0.50 g, 0.25 mmol) in CH_2Cl_2 (50 mL) was treated with an excess of the corresponding carboxylic acid RCOOH (8.0 mmol). The mixture was stirred overnight in a closed flask and filtered to remove any undissolved solid. Hexanes were added to the filtrate until precipitation of a dark brown solid was observed. The resulting solid was collected by filtration and the above treatment was repeated. The resulting filtrate was layered with hexanes (100–150 mL) and stored at room temperature for several days. Since the acid was highly soluble in diethyl ether but the Mn_{12} complex was only partially soluble in this solvent, a diethyl ether/hexane(s) mixture (1:4) was used to wash the resulting solid, which was finally dried in air. Recrystallization from CH_2Cl_2/hexane(s) gave crystals of complex **2** suitable for X-ray structure analysis. Complex **2:** Elemental analysis calcd for $[Mn_{12}O_{12}(O_2CC_6H_4\text{-}2\text{-}Cl)_{16}(H_2O)_4]\cdot 4H_2O$, $C_{112}H_{80}O_{52}Cl_{16}Mn_{12}$: C 38.58, H 2.30, Cl 16.30; found: C 38.4, H 2.4, Cl 16.2%. FT-IR (KBr): $\tilde{\nu}$ = 1589, 1560, 1544, 1519, 1473, 1412, 1164, 1054, 750, 725, 702, 651, 614, 552, 522 cm^{-1}. Complex **3:** Elemental analysis calcd for $[Mn_{12}O_{12}(O_2CC_6H_4\text{-}2\text{-}Br)_{16}(H_2O)_4]\cdot 3H_2O$, $C_{112}H_{78}O_{51}Br_{46}Mn_{12}$: C 32.17, H 1.88, Br 30.64; found: C 32.1, H 1.9, Br 30.7%. FT-IR (KBr): $\tilde{\nu}$ = 1585, 1543, 1518, 1470, 1411, 1161, 1045, 1028, 747, 695, 644, 614, 552, 518 cm^{-1}.

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[12] Crystal data for $[Mn_{12}O_{12}(O_2CC_6H_4\text{-}o\text{-}Cl)_{16}(H_2O)_4]\cdot(CH_2Cl_2)\cdot 5(H_2O)$ (complex **2**): $C_{113}H_{82}Cl_{18}Mn_{12}O_{56}$, noncentrosymmetric space group *Pnn*2, $T = -175\,^{\circ}C$, $a = 18.033(3)$, $b = 22.752(4)$, $c = 17.319(3)$ Å, $V = 7105.62$, $Z = 2$, $6.0^{\circ} \le 2\theta \le 45^{\circ}$. There were 4197 unique reflections with 3702 unique reflections with $F > 2.33\sigma(F)$; $R(F) = 0.0880$; $R_w(F) = 0.0872$. Several of the 2-chlorobenzoate ligands exhibited disorder in the position of the chlorine atom. The CH_2Cl_2 and five H_2O solvate molecules were present at about 50% occupancy. Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-100605. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: int. code + (44) 1223 336-033; e-mail: deposit@ccdc.cam.ac.uk).
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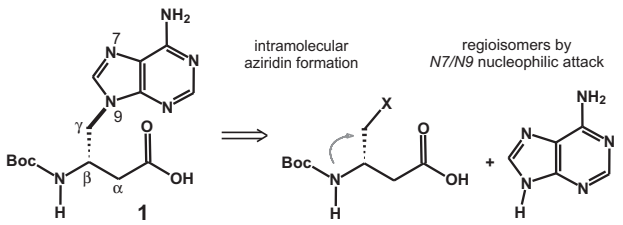
β-Homoalanyl PNAs: Synthesis and Indication of Higher Ordered Structures**

Ulf Diederichsen* and Harald W. Schmitt

Peptide nucleic acids (PNAs) are oligomers possessing a polyamide backbone in which the nucleobases of DNA/RNA function as recognition units. The interaction of PNAs with DNA double strands or RNA have increased in importance because of their potential use in antigene or antisense therapy.[1] In contrast, helical[2] or linear PNA–PNA self-pairing complexes[3] are uncharged models that are appropriate for investigating interactions between nucleobases or between nucleobases and amino acids[4] and for examining intercalation.[5] The linearity of two complementary strands is an important structural feature of our previous investigations on α-alanyl and α-homoalanyl PNAs. It is based on the 3.6-Å distance between two consecutive amino acid side chains in the β-sheet conformation, which is similar to the stacking distance of base pairs in DNA. Here we describe the synthesis of Boc-β-homoalanyladenine (**1**) and its oligomerization to β-PNAs. UV and CD spectra suggest that the hexamer and pentamer are self-organized in higher ordered structures, which can be rationalized from model studies as being structurally inevitable.

Although there are many methods to synthesize β-amino acids[6], nucleo-β-amino acids have not been described to date. The following difficulties have to be considered in linking the nucleobase to the γ position of the side chain (Scheme 1): 1) Nucleobases are poorly soluble in most organic solvents. 2) The desired nucleophilic attack by the *N*9 nitrogen atom of



Scheme 1. Side reactions in the synthesis of nucleo-β-amino acid **1**.

[*] Dr. U. Diederichsen, H. W. Schmitt
Institut für Organische Chemie und Biochemie der
Technischen Universität München
Lichtenbergstrasse 4, D-85747 Garching (Germany)
Fax: Int. code + (49) 89 2891-3210
E-mail: ud@linda.org.chemie.tu-muenchen.de

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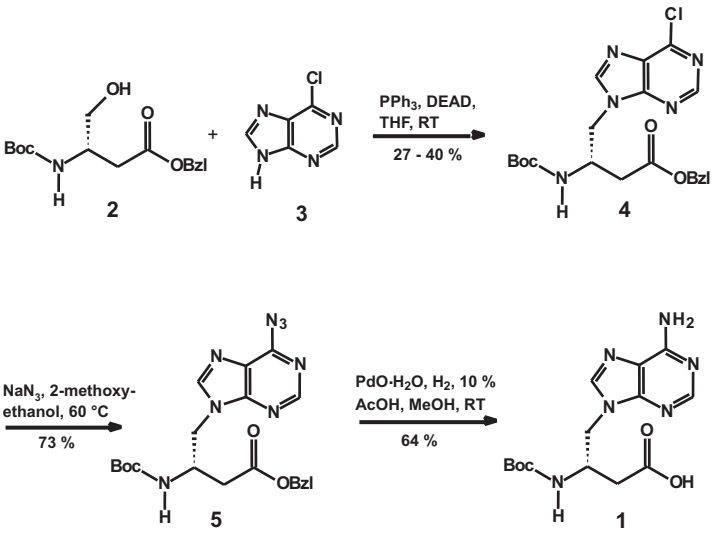
the purine competes with that by the *N*7 nitrogen atom and with intramolecular azridine formation. 3) In situ generation of the leaving group at the γ position of the amino acid appears significant. 4) Arndt–Eistert homologization of aromatic α-amino acids is expected to proceed with racemization.[6d]

The desired coupling to provide a purine attached through the *N*9 nitrogen atom to the γ position of the β-homoalanine was performed with the Mitsunobu reaction[7] (Scheme 2).



Scheme 2. Synthesis of nucleo-β-amino acid **1**: The key step is the attachment of amino acid **2** with **3** under Mitsunobu conditions (DEAD = diethyl azodicarboxylate).

At room temperature the β-homoserine derivative **2**[8] was added to 6-chloropurine (**3**) together with the Mitsunobu reagents. The direct use of adenine was not successful; the 6-chloropurine nucleo amino acid **4** could be converted into the azidopurine derivative **5**, which then was reduced and deprotected to yield **1**.[9] The presence of the *N*9 regioisomer was proven by HMQC and HMBC NMR experiments.[10] Nucleo amino acid **1** was oligomerized by solid-phase peptide synthesis (SPPS) on a 4-methylbenzhydrylamine (MBHA)–polystyrene support loaded with R-lysine(Z)-OH (Z = benzyloxycarbonyl; lysine was introduced at the C terminus for solubility reasons). The coupling was activated by *O*-(7-azabenzotriazol-1-yl)-1,1,3,3-tetramethyluronium hexafluorophosphate (HATU) and proceeded with at least 95% yield. After the oligomers were purified with HPLC (RP-C18), they were characterized with electrospray ionization mass spectrometry (ESI-MS) and ^{1}H NMR spectroscopy.

Although adenine–adenine pairing is not observed in DNA because of the helix topology, it is well established for oligomer pairing complexes[11] with a linear backbone. High stability of hexamer double strands based on A–A base pairs is known for the homo-DNA series (which contain 2′,3′-dideoxyglucopyranosyl sugar moieties, $T_m = 47\,^\circ$C)[12] as well as for α-alanyl PNA ($T_m = 31\,^\circ$C).[3] We investigated the pairing of β-homoalanyl PNAs by examining hexamer H-(β-HalA)$_6$-Lys-NH$_2$ (β-HalA = γ-(adenin-9-yl)-β-(*S*)-homoalanine, Lys-NH$_2$ = (*R*)-lysine amide). Cooperative depairing of a double strand can be recognized in UV melting curves by the sigmoidal increase in absorption upon raising the temperature. The extraordinary high stability of H-(β-HalA)$_6$-Lys-NH$_2$ was surprising; it was not possible to detect a melting point up to 95 °C (Figure 1). Furthermore, the unusual high hyperchromicity ($A_{rel.} > 40\%$) is striking. We also observed this effect with alternating G/C sequences in the alanyl PNA series for the formation of higher ordered structures.[13] The shorter oligomers H-(β-HalA)$_5$-Lys-NH$_2$ and H-(β-HalA)$_4$-Lys-NH$_2$ were synthesized to obtain UV melting curves within a measurable temperature range. Indeed, the pentamer melts at $T_m = 72\,^\circ$C ($A_{rel.} > 60\%$), and the tetramer at $T_m = 26\,^\circ$C ($A_{rel.} = 16\%$). The remarkable difference in stability and hyperchromicity of the two species (Figure 1) indicates that the structural organizations are not identical. The CD spectra of pentamer H-(β-HalA)$_5$-Lys-NH$_2$ measured at different temperatures confirm the UV melting curve. The nucleobases display a strong Cotton effect when conformationally restricted in a double strand, which begins to diminish at 40 °C when the number of flexible single strands increases. The high stabilities of adenine β-PNA oligomers is only partly the result of depairing of double strands, because the formation of higher ordered structures is indicated for the pentamer and hexamer. β-Homoalanyl PNA has a particular potential for

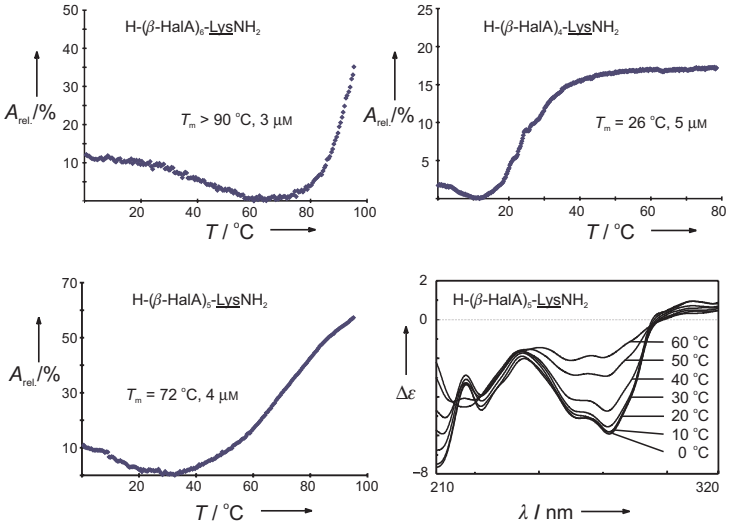


Figure 1. UV melting curves of β-PNA oligomers H-(β-HalA)$_n$-Lys-NH$_2$ ($n = 4-6$) and CD spectra of H-(β-HalA)$_5$-Lys-NH$_2$ (0.1 M NaCl, 0.01 M Na_2HPO_4/H_3PO_4, pH 7).

forming higher associations, as shown by a single-strand model (Figure 2): A homochiral β-homoalanyl PNA strand with an extended conformation provides a uniform orientation of all the side chains, and all adenine bases are aligned in the same way. This leads to pairing planes based on all Watson–Crick and Hoogsteen sites, respectively.

Adenine–adenine self-pairing can be achieved in three pairing modes: the symmetrical reverse Watson–Crick and reverse Hoogsteen modes as well as the Hoogsteen mode (Scheme 3). A chain of H-(β-HalA)$_n$-Lys-NH$_2$ oligomers based on adenine self-pairing with simultaneous participation

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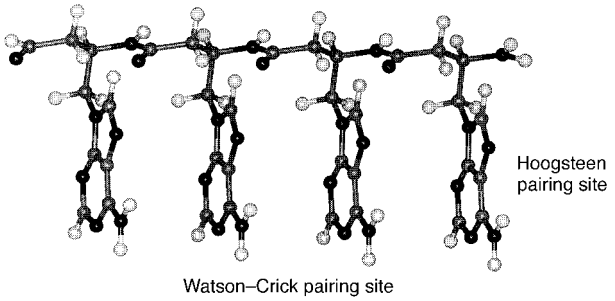
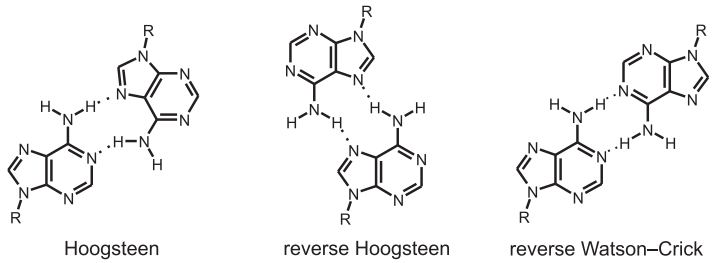


Figure 2. Model of a homochiral β-homoalanyl PNA single strand: In the extended backbone conformation, all nucleobases are uniformly aligned. This creates a pairing plane at the Watson – Crick and the Hoogsteen site.



Scheme 3. Possible adenine – adenine pairing modes.

of the Watson – Crick and Hoogsteen site is possibly responsible for the strong aggregation indicated by the melting curves.

We introduced nucleo amino acid **1** as a new building block for the synthesis of β-PNA oligomers. β-PNA is a special case of β-peptides.[14] Nevertheless, differences in structure are expected because the aggregates of β-PNA are defined by the β-peptide backbone and base-pair stabilization. The uniform alignment of all nucleobases in the extended conformation could be causal for the exceptional self-pairing of adenine oligomers in higher ordered structures. We are presently investigating the pairing possibilities and selectivities of the other canonical nucleobases as well as the influence of heterochiral base pairs.

Experimental Section

4: DEAD (1.69 g, 14.55 mmol) was added at room temperature under argon to PPh_3 (3.82 g, 14.55 mmol) in THF (18 mL) within 10 min. 6-Chloropurine (**3**, 1.45 g, 9.70 mmol) was added, and the suspension heated to 40 °C until a clear yellow solution was obtained. A solution of **2** (3.00 g, 9.70 mmol) in THF (10 mL) was added dropwise within 10 min at room temperature. After the reaction mixture was stirred for 2 d, it was heated for 4 h at 60 °C. The product was purified by consecutive flash chromatography with hexanes:ethyl acetate (1:3), hexanes:ethyl acetate (1:1), and hexanes:acetone (7:3); yield: 1.15 g (27 %). Further experiments improved the yield up to 40 %. M.p. 131 – 132 °C; $\alpha_D^{25} = 31$ ($c = 5$ in $CHCl_3$); $R_F = 0.27$ (hexanes:acetone 7:3); ^{1}H NMR (250 MHz, $CDCl_3$): $\delta = 1.21 - 1.45$ (m, 9H, *t*Bu), 2.70 (d, 2H, ^3J(H,H) = 6 Hz, α-CH_2), 4.33 – 4.43 (m, 1H, β-CH), 4.43 – 4.55 (m, 2H, γ-CH_2), 5.14 (s, 2H, CH_2–Ph), 5.30 (m, 1H, NH), 7.35 (m, 5H, Ph), 8.04 (s, 1H, H8), 8.68 (s, 1H, H2); ^{13}C NMR (62 MHz, $CDCl_3$): $\delta = 28.0$, 36.0, 46.5, 47.6, 66.8, 80.1, 128.3, 128.5, 128.6, 131.3, 135.0, 145.7, 150.9, 151.8, 152.0, 154.8, 170.4; MS: *m*/*z*: 446.3 (*M*H)$^+$; elemental analysis calcd for $C_{21}H_{24}N_5O_4Cl$: C 56.57, H 5.42, N 15.71; found: C 56.60, H 5.36, N 15.71.

5: A solution of **4** (690 mg, 1.547 mmol) and sodium azide (1.10 g, 16.92 mmol) in 2-methoxyethanol (8 mL) was heated for 5 h at 60 °C. The solvent was evaporated, and the residue suspended in ethyl acetate. After the salts were removed by filtration, the product was purified by flash chromatography with silica gel (110 g) and hexanes:ethyl acetate (3:1); yield: 512 mg (73 %); m.p. 76 – 78 °C, $[\alpha]_D^{25} = 40$ ($c = 1$ in $CHCl_3$); $R_F = 0.30$ (hexanes:ethyl acetate 1:3); ^{1}H NMR (250 MHz, [D$_6$]DMSO): $\delta = 1.15 - 1.23$ (m, 9H, *t*Bu), 2.54 – 2.86 (m, 2H α-CH_2), 4.28 – 4.42 (m, 2H, γ-CH_2), 4.44 – 4.68 (m, 1H, β-CH), 5.09 (s, 2H, CH_2–Ph), 7.00 (d, 1H, ^3J(H,H) = 8 Hz, NH), 7.33 (m, 5H, Ph), 8.48 (s, 1H, H8), 10.13 (s, 1H, H2); ^{13}C NMR (62 MHz, [D$_6$]DMSO): $\delta = 27.8$, 36.4, 47.5, 47.6, 65.7, 78.0, 119.5, 127.8, 127.9, 128.3, 135.4, 135.9, 142.7, 144.8, 145.4, 154.7, 170.1; MS: *m*/*z*: 904.8 (M_2H)$^+$, 453.2 (*M*H)$^+$; elemental analysis calcd for $C_{21}H_{24}N_8O_4$: C 55.75, H 5.35, N 24.76; found: C 55.60, H 5.52, N 24.53.

1: A solution of **5** (457 mg, 1.02 mmol) in methanol:acetic acid (9:1, 110 mL) was treated with palladium oxide hydrate (220 mg, 1.80 mmol) under argon and saturated with hydrogen. After 105 min the catalyst and the partially precipitated nucleo amino acid were separated by centrifugation, and the solid phase was extracted several times with ethyl acetate:acetic acid (9:1). Subsequent flash chromatography (ethyl acetate:methanol:water:acetic acid 40:7:3:1). Yield: 218 mg (64 %). M.p. 286 °C (decomp); $[\alpha]_D^{25} = 41$ ($c = 1$ in DMSO); $R_F = 0.36$ (ethyl acetate:methanol:water:acetic acid 10:1:1:0.5, NaCl saturated); ^{1}H NMR (500 MHz, [D$_6$]DMSO): $\delta = 0.95 - 1.03$ (m, 1.5H, *t*Bu), 1.15 – 1.30 (m, 7.5H, *t*Bu), 2.36 – 2.52 (m, 2H, α-CH_2), 4.05 – 4.20 (m, 2H, γ-CH_2), 4.21 – 4.30 (m, 1H, β-CH), 6.42 (m, 0.2H, NH), 6.90 (d, 0.8H, J = 7.1 Hz, NH), 7.13 (s, 2H, NH_2), 7.92 (s, 1H, H8), 8.12 (s, 1H, H2); ^{13}C NMR (125 MHz, [D$_6$]DMSO): $\delta = 27.6$ (*t*Bu), 37.1 (Cα), 45.8 (Cβ), 47.3 (Cγ), 77.5 (*t*Bu), 118.3 (C5), 140.6 (C8), 149.5 (C4), 152.0 (C2), 154.5 (CO of Boc), 156.0 (C6), 171.7 (COOH); the ^{13}C NMR signals were assigned with HMBC and HMQC experiments; MS: *m*/*z*: 337.1 (*M*H)$^+$; UV (H_2O): $\lambda_{max} = 263$ nm (14000).

H-(β-HalA)$_4$-Lys-NH_2: ^{1}H NMR (500 MHz, D_2O): $\delta = 1.29 - 1.35$ (m, 2H, Lys), 1.50 – 1.71 (m, 4H, Lys), 2.00 (m, 1H, Hα), 2.12 (m, 1H, Hα), 2.18 – 2.38 (m, 4H, Hα), 2.42 (m, 1H, Hα), 2.65 (m, 1H, Hα), 2.85 (m, 2H, Hε-Lys), 3.22 – 3.50 (m, 4H, Hβ, Hγ), 3.55 (m, 1H, Hβ, Hγ), 3.63 – 3.84 (m, 3H, Hβ, Hγ), 3.98 (m, 1H, Hβ, Hγ), 4.11 (m, 1H, Hα-Lys), 4.25 – 4.35 (m, 2H, Hβ, Hγ), 4.42 (m, 1H, Hβ, Hγ), 7.79 (s, 1H, H2, H8), 7.84 (s, 1H, H2, H8), 7.90 (s, 1H, H2, H8), 7.91 (s, 1H, H2, H8), 7.97 (s, 1H, H2, H8), 7.98 (s, 1H, H2, H8), 8.00 (s, 1H, H2, H8), 8.02 (s, 1H, H2, H8); MS: *m*/*z*: 1018.3 (*M*H)$^+$, 511.0 (MH$_2$)$^{2+}$.

H-(β-HalA)$_5$-Lys-NH_2: ^{1}H NMR (500 MHz, D_2O): $\delta = 1.21 - 1.40$ (m, 2H, Lys), 1.50 – 1.75 (m, 4H, Lys), 2.15 – 2.40 (m, 7H, Hα), 2.42 – 2.55 (m, 2H, Hα), 2.68 (m, 1H, Hα), 2.87 (m, 2H, Hε-Lys), 3.70 – 4.50 (m, 16H, Hβ, Hγ, Hα-Lys), 7.95 – 8.20 (m, 10H, H2, H8); MS: *m*/*z*: 1236.4 (*M*H)$^+$, 619.0 (MH$_2$)$^{2+}$.

H-(β-HalA)$_6$-Lys-NH_2: ^{1}H NMR (500 MHz, D_2O): $\delta = 1.25 - 1.38$ (m, 2H, Lys), 1.50 – 1.72 (m, 4H, Lys), 2.11 – 2.40 (m, 9H, Hα), 2.41 – 2.56 (m, 2H, Hα), 2.68 (m, 1H, Hα), 2.87 (m, 2H, Hε-Lys), 3.58 (m, 1H, Hβ, Hγ), 3.61 – 3.75 (m, 2H, Hβ, Hγ), 3.77 – 3.98 (m, 8H, Hβ, Hγ), 4.06 (m, 1H, Hα-Lys), 4.10 – 4.20 (m, 2H, Hβ, Hγ), 4.24 – 4.36 (m, 3H, Hβ, Hγ), 4.38 – 4.49 (m, 2H, Hβ, Hγ), 7.77 (s, 1H, H2, H8), 7.82 (s, 1H, H2, H8), 7.90 (m, 2H, H2, H8), 7.94 (s, 1H, H2, H8), 7.96 (s, 1H, H2, H8), 7.97 (s, 2H, H2, H8), 8.03 (s, 1H, H2, H8), 8.04 (s, 1H, H2, H8), 8.07 (s, 1H, H2, H8), 8.08 (s, 1H, H2, H8); MS: *m*/*z*: 1455.4 (*M*H)$^+$, 727.9 (MH$_2$)$^{2+}$.

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Redox-Switched Exciton-Coupled Circular Dichroism: A Novel Strategy for Binary Molecular Switching**

Steffen Zahn and James W. Canary*

A recent and exciting prospect in the area of information technology lies in the development of molecular switches that operate with efficiency, reversibility, and resistance to fatigue.[1] The development of electrochemical switches has recently attracted much attention due to possible applications such as data storage.[2–8] Redox switches require a) components whose structures and physical properties can be turned on or off electrochemically,[3, 6–8] and b) sufficiently different optical spectra that allow the individual states to be addressed.[2, 4] Here we describe a method for generating a redox switch through redox control of the ligand conformation. This approach resulted in a novel molecular switch with reproducible redox-dependent optical properties; the switch should be easily adaptable to solid-state technology.

Our molecular redox switch is based on a) complexes in which a single metal center can exist in two different oxidation states, and b) chiral ligands having easily distinguishable optical properties. Copper(II) complexes are particularly suitable since they show fast ligand exchange, which potentiates fast signal interchange. The ligand (*S*)-*N*,*N*-bis[(2-quinolyl)methyl]-1-(2-quinolyl)ethylamine, (*S*)-α-MeTQA, was selected for this study because of the steric hindrance and strong chromophoric properties presented by the 2-quinolyl groups and the expected optimal chromophoric orientation provided by the propellerlike geometry of the complexes. Reduction of the sterically hindered Cu^{II} complex was anticipated to result in a change in the orientation of the 2-quinolyl arms with respect to the central axis (Scheme 1). Since the exciton-coupled circular dichroism (ECCD) signal generated from these complexes is critically dependent upon the distance and dihedral angle between the planar chromophores,[9] the magnitude of the ECCD spectrum was expected to vary with the oxidation state of the copper ion.

The preparation of the ligand (*S*)-α-MeTQA began with the asymmetric synthesis of (*S*)-2-(1-aminoethyl)quinoline from the 2-aminomethylquinoline imine of (+)-pinanone.[10] A single recrystallization of the L-(+)-tartrate salt of the chiral primary amine yielded the desired product with 99.7% *ee* in 19% overall yield. Alkylation of the enantiomerically pure amine with 2-bromomethylquinoline provided (*S*)-α-MeTQA in 81% yield. Copper complexes **1** and **2** were prepared by mixing homogeneous solutions of the ligand and the appropriate salt.[11, 12] The UV/Vis spectrum of **2** shows a

$[Cu^{I}\{(S)\text{-}\alpha\text{-MeTQA}\}](PF_6)$ **1**

$[Cu^{II}\{(S)\text{-}\alpha\text{-MeTQA}\}](ClO_4)(PF_6)$ **2**

d–d transition at 691 nm ($\varepsilon = 202$), which is consistent with a coordination geometry for the Cu^{II} ion that is closer to a square pyramid than the desired trigonal bipyramid.[11, 13] However, addition of one equivalent of NH_4NCS (to yield **4**) resulted in two d–d bands (719 nm, $\varepsilon = 202$; 867 nm, $\varepsilon = 296$); this indicates trigonal-bipyramidal geometry.[13] The color change of **4** from turquoise to green-yellow is due to a ligand-to-metal charge transfer (LMCT) at 420 nm ($\varepsilon = 445$).[14] Cyclic voltammograms of the copper complexes in acetonitrile or dimethylformamide were well-behaved and displayed single quasi-reversible one-electron redox waves ($i_{pa}/i_{pc} \approx 1$).[15]

The CD spectra of **1** ($A = 174$) and **2** ($A = 455$) displayed bisignate curves with remarkably large amplitudes (that is, large positive and negative Cotton effects).[16] The split CD

[*] Prof. J. W. Canary, S. Zahn
Department of Chemistry
New York University
New York, NY 10003 (USA)
Fax: Int. code + (1) 212 260-7905
E-mail: james.canary@nyu.edu

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