VII-C Bio-Inspired Molecular Architecture

Nature has produced a limited number of molecular modules such as nucleosides and nucleotides, amino acids, and lipids. However, the chemical diversity of these biomolecules and the different ways they can be polymerized or assembled into precisely-defined three-dimensional shapes provide a wide range of possible structures and functions. Furthermore, owing to advances in chemical synthesis and biotechnology we can combine or chemically modify these molecular building blocks, almost at will, to produce new functional molecules that have not yet been made in Nature. Based on these concepts, we have been working on the following research projects. Our research programs also consciously focus on structures and functions that have been unknown in living, biological systems.

VII-C-1 Synthesis of a Novel Nucleoside for Alternative DNA Base Pairing through Metal Complexation

TANAKA, Kentaro; SHIONOYA, Mitsuhiko

[*J. Org. Chem.* **64**, 5002 (1999)]

A novel artificial nucleoside was synthesized, in which artificial bases are introduced as metal coordination sites for alternative base-pairing through metal complexation instead of hydrogen bonding in natural DNA. The artificial β-C-nucleoside (4-[1,2-dideoxy-β-D-ribofuranos-1-yl)-*o*-phenylenediamine) **1** which has a phenylenediamine moiety as a metal coordination site was prepared by coupling reaction of a lithiated *o*-phenylenediamine derivative and 2,3,5-tri-*O*-benzyl-D-ribonic γ-lactone followed by several reactions to remove 2'-hydroxyl group. ^{1}H NMR and ESI mass spectroscopic studies clearly showed that **1** and Pd^{2+} form a stable 2:1 complex in aqueous media (Figure 1).

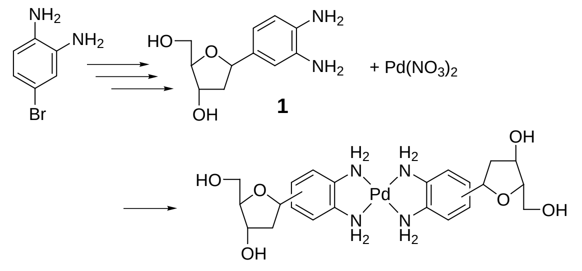

Figure 1. Complex formation of phenylenediamine-nucleoside **1** with Pd^{2+}.

VII-C-2 An Approach to Metal-Assisted DNA Base Pairing: Novel β-C-Nucleosides with a 2-Aminophenol or a Catechol as the Nucleobase

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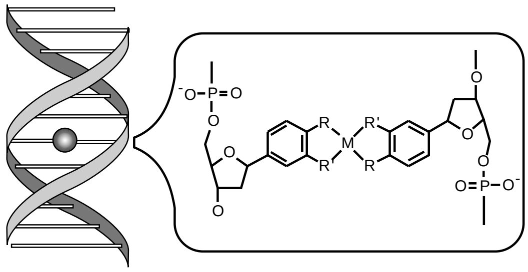
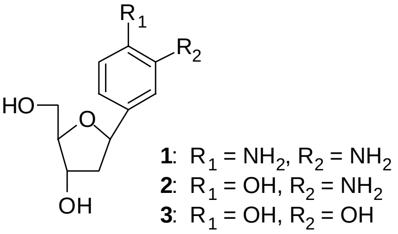
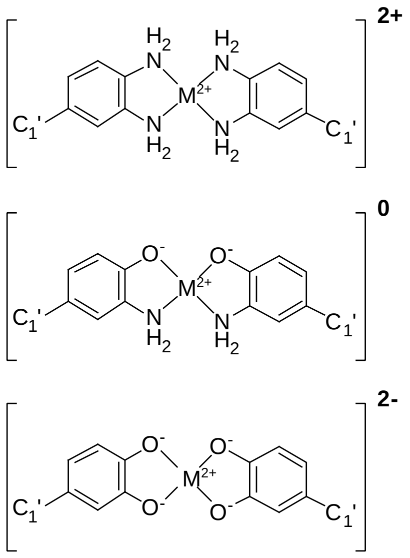
[*Eur. J. Pharm. Sci.* in press]

The metal-chelating β-C-nucleoside having a phenylenediamine moiety as the nucleobase was previously found to form a stable 2:1 complex with a Pd^{2+} ion in aqueous media, where hydrogen bonding is replaced by metal coordination in the base pairing thereby creating a novel hybridization motif in duplex DNA. In this regard, we have further designed two types of artificial β-C-nucleosides possessing a metal-chelating site (a 2-aminophenol or a catechol) as the nucleobase moiety. These artificial nucleosides are directed toward controlling the net charges of the metal-assisted base pairs. This paper describes convenient syntheses of the artificial nucleosides bearing a 2-aminophenol or a catechol moiety. Each nucleoside was directly synthesized through 2'-deoxy derivative via a Friedel-Crafts coupling reaction as the key step between the aromatic ring and ribose moiety, whereas the nucleoside having a phenylenediamine moiety was prepared in rather longer steps through an RNA type intermediate followed by the removal of 2'-hydroxy group.





1: $R_1 = NH_2$, $R_2 = NH_2$
2: $R_1 = OH$, $R_2 = NH_2$
3: $R_1 = OH$, $R_2 = OH$



VII-C-3 Cyclic Metallopeptides, *cyclo*[-Gly-L-Cys(terpyPt^{II})-]$_n$Cl$_n$

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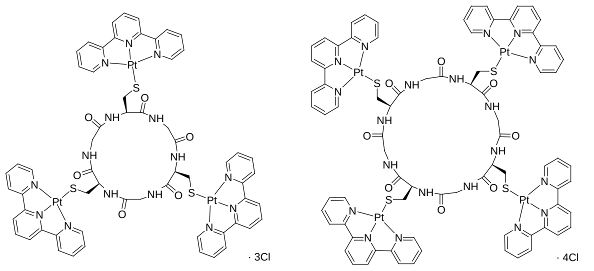
[*Chem. Commun.* in press]

A new efficient synthetic methodology has been developed that can be utilized for the iterative construction of a new family of cyclohexa and cycloocta metallopeptides of the general formula, *cyclo*[-Gly-L-Cys(terpyPt^{II})-]$_n$Cl$_n$, **1** (n = 3) and **2** (n = 4). The linear peptides, TFA·H-[Gly-L-Cys(terpyPt^{II})]$_n$-OH·$(CF_3CO_2)_n$, (n = 3) and (n = 4), were cyclized in H_2O-CH_3CN (7:3) at 25 ˚C to the corresponding cyclopeptides, **1** and **2**, in the presence of excess HOBt and EDC in 58% yield in both cases. The ring size of each cyclopeptide was determined by high-resolution ESI mass spectroscopy. The cyclohexapeptide **1** selectively separated benzene 1,3,5-tricarboxylate from a mixture of three tricarboxylates (benzene 1,3,5-tricarboxylate and its 1,2,4- and 1,2,3-isomers) in neutral water. The ^{1}H NMR and ESI mass spectra of the precipitate immediately appeared clearly evidenced the 1:1 complexation of **1** and benzene 1,3,5-tricarboxylate. The Pt^{II}-terpyridine complex moieties of **1** were readily removed by acid treatment to afford the corresponding cyclohexapeptides, *cyclo*[-Gly-L-Cys-]$_3$. The synthetic strategy developed in this work would provide a powerful tool for arraying functional metal complexes on cyclopeptide frameworks.



1 **2**

Figure 1. Chemical structures of the cyclic metallopeptides newly synthesized in this study.

VII-C-4 Construction of a Unique Alternating-Chain Array with Copper(II) and a New Diazamesocycle Bearing One Functional Pendant

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[*Inorg. Chem. Commun.* submitted]

The polymeric Cu^{II} complex of 1-[(1-methylimidazol-2-yl)methyl]-1,5-diazacyclooctane (**L**), $\{[Cu_2(\mathbf{L})_2(\mu\text{-}Cl)_2](ClO_4)_2\}_\infty$ (***I***), has been constructed from the self-assembling reaction of Cu^{II} perchlorate and **L** in water; and the X-ray crystallographic analysis of the complex showed that it has a zigzag alternating-chain structure consisting of two distinct coordination geometries.

VII-C-5 Spontaneously Resolved Chiral Molecular Box: A Cyclic Tetranuclear Zn(II) Complex with DPTZ (DPTZ = 3,6-Di-2-Pyridyl-1,2,4,5-Tetrazine)

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[*J. Am. Chem. Soc.* submitted]

Interest in coordination architectures constructed by metal ions and bridging ligands has been driven by the expectation of developing new materials with unique electronic, magnetic, and optical properties, or catalytic activities. Their structure and functions have a close relationship with the geometry and chemical properties of the metal ions and bridging ligands used in the architectures. Our recent studies make clear that 3,6-di-2-pyridyl-1,2,4,5-tetrazine (DPTZ) is a promising ligand which can be used in the construction of highly organized supramolecular structures.

We report herein a novel tetranuclear Zn(II) molecular square complex that exhibits a chiral structure in the crystal state. The reaction of Zn-$(ClO_4)_2 \cdot 6H_2O$ with DPTZ in a 1:1 ratio in a mixed solvent of $CHCl_3$ and CH_3CN at room temperature produced a tetranuclear zinc(II) complex as orange prisms in *ca.* 90% yield. Its X-ray crystal structure is shown in Figure 1. This compound crystallizes in the chiral space group $C222_1$. In contrast, a similar reaction of DPTZ with Cd(II) in a 1:1 ratio afforded a linear complex of Cd(II) with 1D chain structure almost quantitatively.

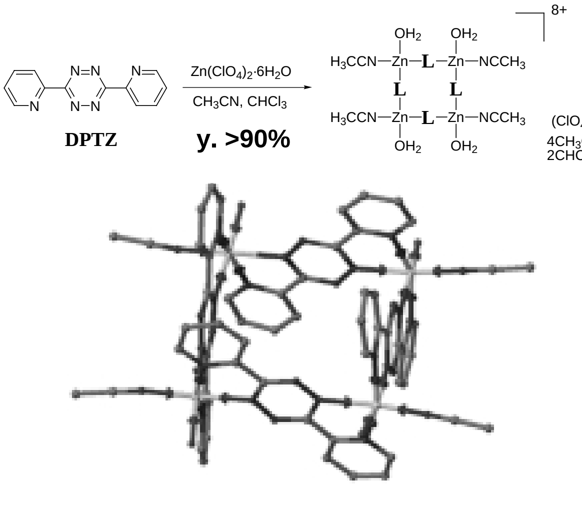

Figure 1. A chiral molecular box Zn(II) complex.