

# BIOINORGANIC CHEMISTRY

## Annual Research Review

### (1) “Efficient Incorporation of A Metal-Mediated Base Pair into Duplex and Triplex DNAs”

Replacement of the hydrogen-bonded base pairing of natural DNA by alternative base pairing modes is expected to lead not only to expansion of the genetic alphabet but to novel DNA structures and functions based on the controlled and periodic spacing of the building blocks along the helix axis. We have recently reported the first artificial nucleoside for alternative DNA base pairing through metal complexation (*J. Org. Chem.*, **64**, 5002-5003 (1999)). In this context, we have accomplished a Ag(I)-mediated base pair or a base triplet in a double- or triple-stranded DNA, respectively, by introducing a pair of pyridine nucleobases in the middle of the sequence. As a result, the incorporated Ag(I) complex significantly stabilized the DNA duplex and triplex (A-7). Along this strategy, we have also designed a novel hydroxypyridone nucleobase (**H**) as a planar bidentate ligand (FIG. 1). Since hydroxypyridone forms, with concomitant deprotonation, a stable, neutral complex with a divalent transition metal ion such as  $\text{Cu}^{2+}$ , the resulting square-planar complex should replace hydrogen-bonded natural base pairs. We reported a single-site incorporation of **H** into DNA, and the influence of the  $\text{Cu}^{2+}$ -mediated base pairing on the thermal stability of DNA duplex (A-10).

A-7) *J. Am. Chem. Soc.*, **124**, 8802-8803 (2002)

A-10) *J. Am. Chem. Soc.*, **124**, 12494-12498 (2002)

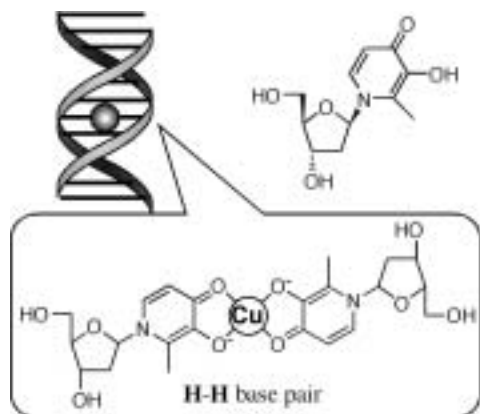


FIG. 1 Efficient single-site incorporation of a hydroxypyridone base pair into DNA.

### (2) “Dynamic Control of Coordination Equilibrium of Metal Complexes”

Multi-metal array, controlled by predesigned multidentate ligands, has received increasing attention with respect not only to supramolecular architecturing but also to equilibrium control of prototypical dynamic library. With an interest in finding new multidentate ligand frameworks, we set out to synthesize a novel disk-shaped tridentate ligand **1**, which is capable of arranging to metal centers in a variety of fashions (FIG. 2). This tripodal ligand was designed so that three methyl groups could force the neighboring benzimidazolyl groups out of the plane of the central aromatic ring. As the consequence, metal ions were arrayed on the disk plane with metal-metal distances of several angstroms. We found the ability of **1** to arrange  $\text{Ag}^+$  ions reversibly in a triangular and a tetrahedral fashion. The  $\text{Ag}^+$  complexes of **1** were proven to assume both sandwich-shaped  $\text{Ag}_3\mathbf{1}_2$  and tetrahedral  $\text{Ag}_4\mathbf{1}_4$  structures which are in a controllable dynamic equilibrium in solution depending on the ratio of **1** to  $\text{Ag}^+$  ions. The structure of the latter tetrahedral complex was also confirmed by its single-crystal X-ray analysis.

A-11) *J. Am. Chem. Soc.*, **124**, 14510-14511 (2002)

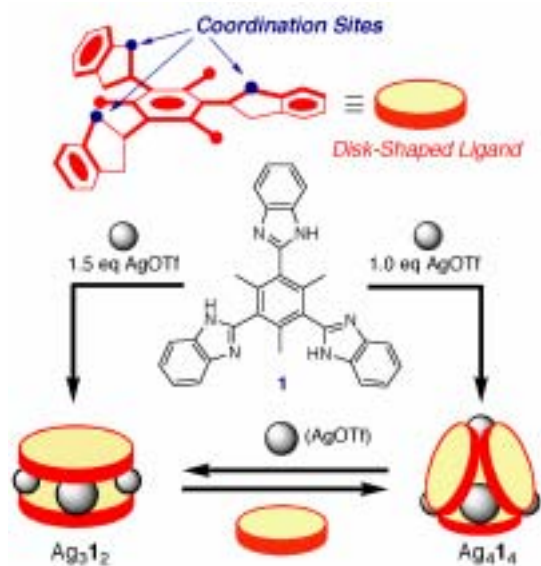


FIG. 2 Schematic representation of the reversible conversion between tetrahedral  $\text{Ag}_4\mathbf{1}_4$  and sandwich-shaped  $\text{Ag}_3\mathbf{1}_2$  complexes.

研究レビュー

(1) 二重鎖および三重鎖 DNA への金属誘起型塩基対の効率的導入

天然DNAの水素結合型塩基対を他の塩基対様式に置き換えることは、遺伝子アルファベットの拡張ばかりでなく、ビルディングブロックがらせん軸に沿って制御された形で周期的に並ぶことに基づく、DNAの新しい構造や機能の構築につながる。最近我々は、金属錯形成により塩基対をつくる人工DNAヌクレオシドの最初の例を報告した (*J. Org. Chem.*, **64**, 5002-5003 (1999))。これと関連して、我々は銀イオンが誘起するプリン型塩基対(或いは、塩基トリプレット)を二重鎖および三重鎖DNAの中央部分において実現することができた。その結果、導入されたプリン-銀型塩基対は、二重鎖および三重鎖DNAの熱力学的安定性を有意に増大させた(A-7)。これをもとに、さらに安定化効果が期待できる、平面二座配位子のヒドロキシピリドン(H)を新しい塩基として設計した(FIG. 1)。DNAの中央に導入されたヒドロキシピリドン塩基は脱プロトン化を伴いながら銅イオンと安定な塩基対を形成し、二重鎖DNAの熱力学的安定性に対して、プリン型塩基対の場合よりもはるかに高い効果を示した(A-10)。これらの金属誘起型塩基対を複数導入することにより、DNA中に金属イオンを配列化できることが期待される。

A-7) *J. Am. Chem. Soc.*, **124**, 8802-8803 (2002)

A-10) *J. Am. Chem. Soc.*, **124**, 12494-12498 (2002)

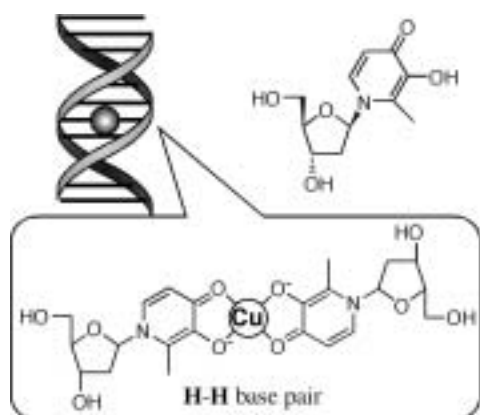


FIG. 1 Efficient single-site incorporation of a hydroxypyridone base pair into DNA.

(2) 金属錯体の配位平衡の動的制御

多座配位子を用いて複数の金属イオンを精密に配列化することは、超分子体の構築や動的ライブラリーの平衡状態のコントロールなど様々な観点から高い関心が集まっている。我々は金属イオンを様々な形式に配列化するための新たな多座配位子骨格として、新規のディスク状三座配位子 1 をデザインした(FIG. 2)。この三座配位子は隣接するベンズイミダゾール環が中心ベンゼン環に対し垂直方向を向くように交互にメチル基が導入されている。その結果、金属イオンはディスク状配位子の面上に数オングストロームの間隔で配置される。三座配位子 1 と銀イオンから作られる錯体は、サンドイッチ型  $Ag_3I_2$  と四面体型  $Ag_4I_4$  の両錯体間は配位子:金属イオン比に応じてそれぞれ定量的に形成され、四面体型錯体  $Ag_4I_4$  についてはX線構造解析の結果その詳細な構造が明らかになった。

A-11) *J. Am. Chem. Soc.*, **124**, 14510-14511 (2002)

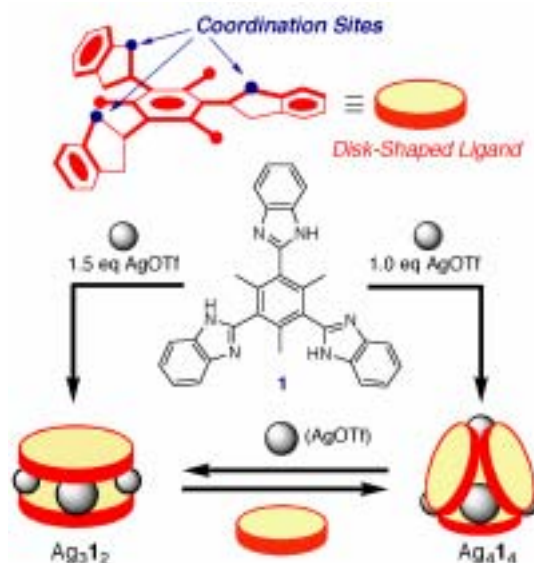


FIG. 2 Schematic representation of the reversible conversion between tetrahedral  $Ag_4I_4$  and sandwich-shaped  $Ag_3I_2$  complexes.

## A. Original Papers

- 1) (M. Du), (X.-H. Bu), (K. Biradha) and M. Shionoya: "An Extended Network *via* Hydrogen Bond Linkage of Linear Coordination Polymer  $[\text{Cd}(\mu\text{-dptz})(\text{NO}_3)_2]_\infty$  (Dptz = 3,6-di-2-pyridyl-1,2,4,5-tetrazine)", *J. Chem. Res.*, 247-249 (2002).
- 2) (X.-H. Bu), (H. Liu), (M. Du), (L. Zhang), (Y.-M. Guo), M. Shionoya and (J. Ribas): "New Mononuclear, Cyclic Tetranuclear and 1-D Helical-Chain Cu(II) Complexes Formed by Metal-assisted Hydrolysis of 3,6-Di-2-pyridyl-1,2,4,5-tetrazine (DPTZ): Crystal Structures and Magnetic Properties", *Inorg. Chem.*, **41**, 1855-1861 (2002).
- 3) (M. Du), (X.-H. Bu), M. Shionoya and (M. Shiro): "Metal Assisted Rearrangement of 2,2'-Pyridil with  $\text{M}(\text{ClO}_4)_2 \cdot 6\text{H}_2\text{O}$  (M =  $\text{Co}^{\text{II}}$ ,  $\text{Ni}^{\text{II}}$  and  $\text{Cu}^{\text{II}}$ ) : Syntheses, Characterization and Crystal Structures", *J. Mol. Struct.*, **607**, 155-161 (2002).
- 4) K. Tanaka, (M. Tasaka), (H. Cao) and M. Shionoya: "Toward Nano-Assembly of Metals through Engineered DNAs", *Supramol. Chem.*, **14**, 255-261 (2002).
- 5) (A. Hatano), K. Tanaka, (M. Shiro) and M. Shionoya: "Synthesis of Nucleic Acid Mimics Designed for Metal-Induced Strand Formation on DNA", *Tetrahedron*, **58**, 2965-2972 (2002).
- 6) (M. Du), (X.-H. Bu), (K. Biradha) and M. Shionoya: "A Novel Two Dimensional Non-interpenetrating Coordination Polymer  $[\text{Ag}_{2.5}\text{L}(\text{NO}_3)_{2.5}]_\infty$  with Three Different Coordination Modes of  $\text{Ag}^{\text{I}}$  (L = diquinoxalino[2,3-a:2',3'-c]phenazine)", *J. Chem. Res.*, 493-495 (2002).
- 7) K. Tanaka, Y. Yamada and M. Shionoya: "Formation of Silver(I)-Mediated DNA Duplex and Triplex through an Alternative Base Pair of Pyridine Nucleobases", *J. Am. Chem. Soc.*, **124**, 8802-8803 (2002).
- 8) (D.-L.An),(M.Du),(X.-H.Bu),(K.Biradha)andM.Shionoya:"[5-Amino-6,8-dichloro-2,3-bis(2-pyridyl)-quinoxaline ]dichlorozinc(II)", *Acta Cryst.*, **E58**, m436-m438 (2002).
- 9) S. Aketani, K. Tanaka, (K. Yamamoto), (A. Ishihama), (H. Cao), A. Tengeiji, S. Hiraoka, (M. Shiro) and M. Shionoya: "Syntheses and Structure-Activity Relationships of Nonnatural  $\beta$ -C-Nucleoside 5'-Triphosphates Bearing an Aromatic Nucleobase with Phenolic Hydroxy Groups: Inhibitory Activities against DNA Polymerases", *J. Med. Chem.*, **45**, 5594-5603 (2002).
- 10) K. Tanaka, A. Tengeiji, (T. Kato), (N. Toyama), (M. Shiro) and M. Shionoya: "Efficient Incorporation of A Copper Hydroxypyridone Base Pair in DNA", *J. Am. Chem. Soc.*, **124**, 12494-12498 (2002).
- 11) S. Hiraoka, T. Yi, (M. Shiro) and M. Shionoya: "Triangular and Tetrahedral Array of Silver(I) Ions by a Novel Disk-Shaped Tridentate Ligand: Dynamic Control of Coordination Equilibrium of the Silver(I) Complexes", *J. Am. Chem. Soc.*, **124**, 14510-14511 (2002).

## B. Reviews

- 1) (T. Takeuchi) and M. Shionoya: "Synthetic Receptors Prepared by Organized Assembly of Organic Molecules", *IEEE Engineering in Medicine and Biology Magazine*, **21**(6), 144-150 (2002).

## D. Books

- 1) 塩谷光彦, 田中健太郎: 「金属錯体型塩基対をもった人工 DNA の創製」, オレオサイエンス, **2**, 451-457 (2002).