A Novel Orthogonal Joint by Hydrogen Bonding. Pybox Ligand and Secondary Dialkylammonium Cation Complexes

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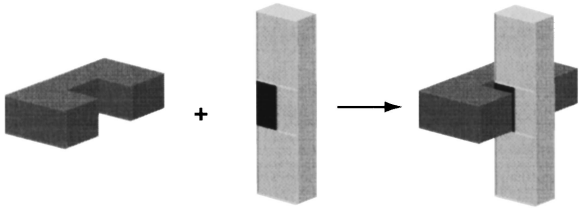
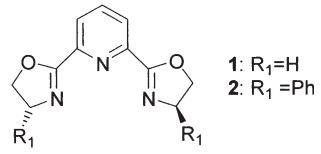
A novel supramolecular orthogonal joint via hydrogen bonds was constructed by a molecular complex between 2,6-bis(2-oxazolyl)pyridnes (pybox) and secondary dialkylammonium tetraphenylborates.

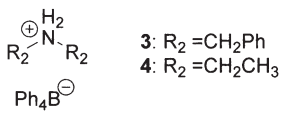
Constructions of multi-component supramolecular assemblies have been received considerable interests as a bottom-up approach of nano-technology.[1] Many basic supramolecular building blocks that connect two or more molecules or ions afford various molecular assemblies with planar, interlocked and orthogonal connections, by means of metal-ligand interactions and hydrogen bonds.[2] Accumulation and combination of these building blocks provide various complex molecular architectures.[3,4] Developments of new building blocks with unique geometries are important to access a new series of supramolecular structures.



Tetrahedral coordinations of metal complexes have been received much attention as supramolecular building blocks for complex supramolecular assemblies, such as helices, ladders, grids and boxes.[4] They are attributed to the orthogonal connections of the two ligands via metal coordination. However, it is not so easy to use these building blocks to construct orthogonal connections between two different ligands, because of difficulty in controlling coordinations of mixed ligands. In this report, we present a novel orthogonal building block that connects two different compounds. The molecular design lays on unsymmetrical nature of hydrogen bonding and tetraheral geometry of seconday ammonium cations. As far as we know, no supramolecular building blocks have been described for orthogonal joints via hydrogen bonding.



1: R_1=H
2: R_1 =Ph



3: R_2 =CH_2Ph
4: R_2 =CH_2CH_3

Secondary dialkylammonium cations are well known as a building block for interlocked molecules by complex formations with crown ethers.[5–7] The complexes are caused by N^+H–O and CH–O hydrogen bonds, as well as dipole-cation interactions. The macrocyclic structures restrict the conformations, and the oxygen atoms are pre-organized to form the stable complexes. More recently, non-macrocyclic tripodal host compounds have been reported to have high affinities with primary alkylammonium cations by N^+H–O hydrogen bonds.[8] These results led us to design novel supramolecules from secondary dialkylammonium cations and non-cyclic 2,6-bis(2-oxazolyl)pyridine (pybox) derivatives, which are well-known ligands for catalytic asymmetric reactions.[9,10] The former have tetrahedral geometry with two alkyl groups and two polarized N^+H's that are expected to form two strong hydrogen bonds. The latter have convergent molecular structures with two imino groups ca. 5 Å apart. The imino groups are directed to central cleft sandwiched by the two oxazoline rings and expected to act as hydrogen bond-accepting sites The hydrogen bonds between them would give an orthogonal hetero-conjunction.

Unsubstituted pybox (**1**) was prepared by the reported method,[11] and the complexation with a few secondary dialkylammonium cations was investigated by X-ray crystallography in crystalline state and by ^{1}H NMR and ESI-MS in solution. A crystal structure of a 1:1 complex of **1** and **3** is depicted in Figure 1.[12] Two oxazoline rings in the pybox ligand are mostly

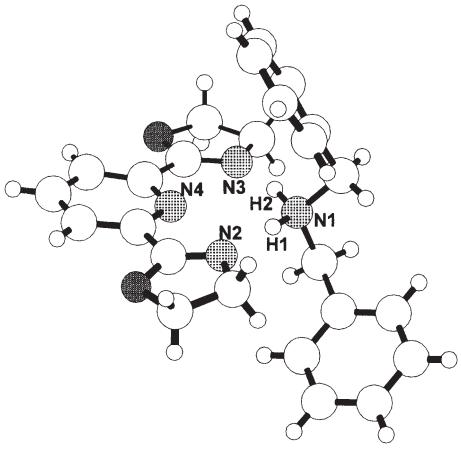


Figure 1. Molecular structure of a 1:1 complex of **1** with **3**. A tetraphenylborate anion is omitted for clarity. Small, open, shadowed, and filled circles represent hydrogen, carbon, nitrogen, and oxygen atoms, respectively. Selected intermolecular distances; N1-N2 2.906(4) Å, N1-N3 2.991(3) Å, N1-N4 2.887(3) Å.

co-planar to the pyridine ring. The dialkylammonium cation is included in the cleft between them, and the ammonium nitrogen atom (N1) is located on the same plane of the pybox. As expected, intermolecular distances between N1 and imino nitrogen atoms (N2 or N3) of **1** are in the range of NH–N hydrogen bonds (<3.0 Å).[5,6] This indicates that the two hydrogen atoms of the secondary ammonium cation form hydrogen bonds with the two imino groups. Pyridine nitrogen atom (N4) of **1** interacts weakly with the ammonium cation, but the angles are too bent to give stable hydrogen bonds. Tetraphenylborate anion does not interfere with these hydrogen bonds because of weak interaction to cations. As the result, the pre-organized hydrogen bond acceptors of **1** can entrap the secondary dialkylammonium cation in the cleft.

Moreover, the complex acts as an orthogonal joint of two molecules. The two alkyl groups of the secondary ammonium spread to the orthogonal directions from the pybox plane because of the tetrahedral geometry of the secondary ammonium. The angle of the two planes is about ca. 86° on the basis of the dihedral angle of C(benzyl)-N1-N4-C(pyridyl). The similar geometry of the complex has been reported for interlocked complexes of crown ethers with secondary ammonium cations.[5] However, the pybox complexes do not require 'threading' through the macrocyclic strutcures, due to open molecular structure of the pybox ligand. This would expand utility of secondary ammonium cations as a supramolecular building block.

In order to confirm complexation in less polar solvents, we carried out ^{1}H NMR titrations by **1** or **2** as a host. In the presence of **1**, no apparent chemical shift changes of the guest **3** or **4** were observed in $CDCl_3$. However, addition of the host **2** to a solution of the guest **4** in $CDCl_3$:CD_3CN = 9:1 (v/v) causes the methyl protons resonance of the alkylammonium to shift upfield from 0.843 ppm to 0.802 ppm due to shielding of the phenyl ring of **2**. Broad NH proton resonance around 7 ppm moves to 9.601 ppm because of formation of hydrogen bonds. The guest **3** provides slight upfield shifts of 4-oxazolyl protons of the hosts due to shielding of the phenyl ring of **3**. In all cases, proton resonances on the pyridine ring at 3 and 4 positions show downfield and upfield shifts, respectively. These chemical shift changes are saturated nearly at a 1:1 stoichiometry. Non-linear curve fitting indicates the binding constants $K = 14900$ (mol dm^{-3}) for **2**+**4** in $CDCl_3$:CD_3CN = 9:1 (v/v) and $K = 14000$ (mol dm^{-3}) for **2**+**3** in $CDCl_3$, respectively. These binding constants have similar magnitudes to pseudo-rotaxane complexes of the secondary ammonium cations with crown ethers,[5] and are much smaller than those of tripodal hosts with primary alkylammonium cations.[8] Moreover, they are much larger than those of complexes with 1,1′-bi-2-naphthols.[13] These results indicate that the open architecture of the pybox ligand does not decrease the binding constants and that the high affinities are ascribed to pre-organization of the hydrogen bond acceptors toward the secondary ammonium cation. Therefore, complementary two hydrogen bonds from a secondary ammonium cation to a pybox ligand plays an important role for the complexation.

Moreover, ESI mass spectrum of a 1:1 mixture between **1** and **4** in acetonitrile (10 μmol dm^{-3}) illustrated the peak of the corresponding 1:1 complex at $m/z = 291.2$. This supports the 1:1 complexation of pybox ligands and secondary ammonium cations.

In conclusion, we demonstrated novel orthogonal supramolecular assemblies by hydrogen bonding between secondary ammonium cations and pybox ligands. Compared with tetrahedral coordination of metal complexes,[4] this system provides a hetero-dimeric connection via DD-AA type hydrogen bonds. Moreover, the open molecular structure of the pybox ligands provides the orthogonal complexes without interlocking. A wide variety of secondary ammonium cations as well as pybox ligands provide various well-defined supramolecular architectures, such as helices, ladders and grids. In addition, chiral pybox ligands should be chiral selectors and chiral shift reagents for racemic mixtures of secondary dialkylamines with asymmetric centers.

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12 Crystal data for **1**+**3**: $C_{49}H_{47}BN_4O_2$, colorless prism (0.70 × 0.40 × 0.10 mm, chloroform, mp 159.9-160.3 °C, $M_r = 734.75$, monoclinic space group $P2_1$ (#4), $a = 9.728(1)$ Å, $b = 18.527(2)$ Å, $c = 11.423(1)$ Å, $\beta = 93.999(4)$°, $V = 2053.7(4)$ Å^3, $Z = 2$, $D_{calcd} = 1.188$ g/cm^{-3}, $\mu = 0.563$ (cm^{-1}), Cu Kα radiation ($\lambda = 1.5418$ Å), $\theta_{max} = 68.3$°. 3428 reflections ($I > 2\sigma(I)$), $R1 = 0.045$ and $Rw = 0.107$, GOF = 1.24 (CCDC-208219).

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