Palladium(II)-induced Alkali Metal Ion Incorporation of 2,6-Disubstituted Pyridines with Bis(alkoxyethyl) Malonate Subunits

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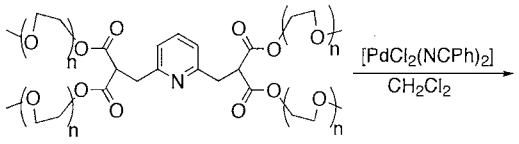
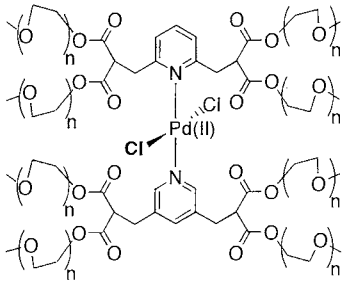
A series of 2,6-bis(2,2'-dicarbalkoxyethyl)pyridine ligands were prepared. A couple of the ligands linked by a *trans*-$PdCl_2$ unit extracted alkali metal ions from an aqueous media into a chloroform media, while a single pyridine ligand did not work as an extractive reagent.

Supramolecular systems with significant allosteric effects are a topic of recent chemistry because of their elegant and potential usefulness.[1] In artificial approach, complexation with a selected metal ion at a well-defined place has been applied successfully to control the function of another binding site in the molecule.[2] In a previous paper we described the preparation and inclusion phenomenon of a trinuclear complex of 2,6-bis(acetylacetoxymethyl)pyridine with Pd(II) and Cu(II) ions.[3] In the study, pyridine ligands possessing metal-chelation subunits were suggested to be effective for the systematic syntheses of hetero polymetallic complexes, and the formation of inclusion compounds were also expected. In order to generate a new series of 2,6-difunctionalized pyridine ligands to construct a new type of supramolecular system, we planned to introduce polyether groups as functional pyridine substituents. By the support with a Pd(II) ion to link two pyridine ligands, the juxtaposed alkoxy groups might hold an alkali metal ion between them like a pair of chopsticks. To serve this purpose we employed bis(alkoxyethyl) malonate moieties as pyridine substituents. Here we report the synthesis and preliminary incorporation properties of the Pd(II) complexes of 2,6-bis(2,2'-dicarbalkoxyethyl)pyridines.

Starting malonic diesters of 2-methoxyethanol, 3,6-dioxaheptan-1-ol, and 3,6,9-trioxadecan-1-ol were prepared by heating a mixture of diethyl malonate and appropriate poly(ethylene glycol) monomethyl ether with a trace amount of acid to cause trans-esterification. When a mixture of resultant malonic diester and 2,6-bis(chloromethyl)pyridine was stirred with anhydrous potassium carbonate in dry dimethylformamide at room temperature for 1 day,[4] the desired ligand was obtained in a moderate yield (70%) as a colorless liquid, which was purified by flash column chromatography on silica-gel eluting with ethyl acetate/hexane (4/1 v/v). The ligands (**1a-c**: L) were reacted with 1/2 molar amount of $[PdCl_2(NCPh)_2]$ in CH_2Cl_2 at room temperature. Evaporation of the solvent and workup with ethyl acetate gave analytically pure *trans*-$[PdCl_2L_2]$ complexes (**2a-c**, yield 80%).[5]



n = 1: **1a**
n = 2: **1b**
n = 3: **1c**



n = 1: **2a**
n = 2: **2b**
n = 3: **2c**

Literature shows that Pd(II) complexes with aromatic *N*-heterocycles display tilting of the coordination and heterocycle planes.[6] The angles between the coordination plane ($PdCl_2N_2$) and those of the pyridine rings are at ca. 90 °C due to a repulsive interaction between the chlorine atoms and the 2,6-pyridine substituents. Thus, two pyridine rings of the Pd(II) complex **2** must be on the same plane, and the pyridyl methylene protons are thrust directly into the coordinated metal environment. The geometrical structure of the obtained complex was confirmed by a single Cl-Pd-Cl IR band at around 353-356 cm^{-1} due to the antisymmetric stretching mode for *trans*-$PdCl_2$ configuration along with the absence of a symmetric Cl-Pd-Cl stretching band which is observed for a *cis*-$PdCl_2$ complex.[7] In support of the desired structure, ^1H NMR peaks due to the pyridyl methylene protons (at around δ 3.3 ppm) and β-methine protons (at around δ 4.2 ppm) of the ligands shifted remarkably downfield (Δδ = 1.63 and 0.31 ppm, respectively) as the result of the Pd(II) complexation.[3] The pyridine ^1H NMR peaks (at around δ 7.0 and δ 7.5 ppm) exhibited moderate downfield shifts (Δδ = 0.22 - 0.14 ppm), and characteristic IR peaks (1750 and 1733 cm^{-1}) due to the carbonyl bonds were scarcely shifted on Pd(II) complex formation. The ^1H NMR signals for the pyridine ring protons appeared as AB_2 patterns for the free ligands as well as their Pd(II) complexes, suggesting clearly that the pyridine ligands adopted C_2 symmetry in solution at NMR time scale.

In order to appraise the functionality of the pyridine substituents, extraction experiments of alkali metal picrates from an aqueous medium into a chloroform medium containing each pyridine ligand or its Pd(II) complex as a receptor were undertaken. The degree of extraction of metal picrates was calculated from the standard absorbance data of the aqueous solution at 355 nm. The extraction percentage data are summarized in Table 1. In every case, a single ligand itself had little extractability for each picrate ion into the chloroform phase; whereas its Pd(II) complex exhibited significant degree of extraction, irrespective of side-chain long. These results are explained plausibly in terms of a molecular chopsticks way for preorganizing the binding site. In the case of a free ligand, the

2,6-disubstituents of the pyridine ring are kept apart from each other and a single substituent is not sufficient to catch any alkali metal ion; thus, formation of an alkali metal adduct is of entropic disadvantage for a single ligand. Ligand **1a** with the shortest side chain exhibited the lowest extractability. By the support of a Pd(II) ion to link two pyridine ligands, the juxtaposed functional groups of the opposite side of the ligands come close to each other. Such a parallel arrangement of the binding sites is essential for a linear system to work well as a host molecule for holding a guest species between them just like a pair of chopsticks work to pick up a grain. The reason of the poor guest-selectivity of the hosts is not obvious. The carbonyl oxygens may play an important role to extract alkali metal ions; however, there is no valid reason to exclude the possibility for the host systems to extract picrate anions or water molecules accompanied by alkali metal ions.

Table 1. Extraction of alkali metal picrates for free ligands **1a-c** and Pd(II) complexes **2a-c** [a]

	Li^+	Na^+	K^+	Rb^+	Cs^+
1a	1	0.3	0.4	1	0.6
1b	1.6	1	0.3	1	0.9
1c	2.4	1.7	0.6	1.4	1.3
2a	11	12	12	14.6	13.6
2b	14.6	15.9	15.4	16.8	15.3
2c	15.5	15.9	15.8	16.6	15.7

[a] Conditions: [alkali picrate] = 1.0×10^{-2} mol dm^{-3}, H_2O = 1 ml; [receptor] = 1.0×10^{-2} mol dm^{-3} for **1** or 0.5×10^{-2} mol dm^{-3} for **2**, $CHCl_3$ = 1 ml.

In general, acyclic host molecules have the advantage of easy synthesis and high versatility of the structure.[8] In the present work, we employed two simple host molecules as a pair of molecular chopsticks to hold guest alkali metal ions. Thus, 2,6-difunctionalized pyridines and related derivatives are expected to develop into a new type of supramolecular systems to pick up selected chemical species by the aid of *trans*-metal complexation, which grips the coupled host molecules in the right way. Of the potential variations on our general strategy, a study on the inclusion of a neutral molecule into such a Pd(II) complex with condensed-ring subunits is now under investigation.

References and Notes

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5 All the compounds prepared in this study were characterized *via* their ^1H NMR (270 MHz, $CDCl_3$) and IR spectra and correct elemental analyses. Selected data are as follows.
1a: a colorless oil. ^1H NMR: δ 3.35 ppm (s, 12H, CH_3), 3.36 (d, J = 7.4 Hz, 4H, Py-CH_2), 3.57 (t, J = 4.6 Hz, 8H, CH_2-OMe), 4.19-4.32 (m, 10H, $COOCH_2$, CH), 7.02 (d, J = 7 Hz, 2H, 3,5-Py-H), 7.48 (t, J = 7 Hz, 1H, 4-Py-H). IR (neat): 2890, 1751(C=O), 1733(C=O), 1457, 1130, 1038, 864 cm^{-1}. Anal. Calcd for $C_{25}H_{37}NO_{12}$: C, 55.24; H, 6.86; N, 2.58%. Found: C, 55.03; H, 6.82; N, 2.56%.
1b: ^1H NMR: δ 3.34 ppm (d, J = 7.5 Hz, 4H, Py-CH_2), 4.17 (t, J = 7.5 Hz, 1H, CH). IR: 1751, 1733 cm^{-1}.
1c: ^1H NMR: δ 3.34 ppm (d, J = 7.7 Hz, 4H, Py-CH_2), 4.16 (t, J = 7.7 Hz, 1H, CH). IR: 1750, 1733 cm^{-1}.
2a: yellow fibers; mp 90.5-91.5 °C. ^1H NMR: δ 3.32 ppm (s, 24H, CH_3), 3.58 (t, J = 4.6 Hz, 16H, CH_2OCH_3), 4.24-4.38 (m, 16H, $COOCH_2$), 4.49 (t, J = 7 Hz, 4H, CH), 5.01 (d, J = 7 Hz, 8H, Py-CH_2), 7.24 (d, J = 7 Hz, 4H, 3,5-Py-H), 7.59 (t, J = 7 Hz, 2H, 4-Py-H). IR (KBr): 2883, 1752(C=O), 1725(C=O), 1610, 1245, 1128, 1031, 851, 353 (Pd-Cl) cm^{-1}. Anal. Calcd for $C_{50}H_{74}Cl_2N_2O_{24}Pd$: C, 47.50; H, 5.90; N, 2.22%. Found: C, 47.50; H, 5.89; N, 2.22%.
2b: ^1H NMR: δ 4.97 ppm (d, J = 7 Hz, 8H, Py-CH_2), 4.48 (t, J = 7 Hz, 2H, CH). IR: 1750, 1734, 356 cm^{-1}.
2c: ^1H NMR: δ 4.96 ppm (d, J = 7 Hz, 8H, Py-CH_2), 4.46 (t, J = 7 Hz, 2H, CH). IR: 1749, 1734, 356 cm^{-1}.

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