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Synthesis of Oligopyridines and Their Metal Complexes as Precursors to Topological Stereoisomers

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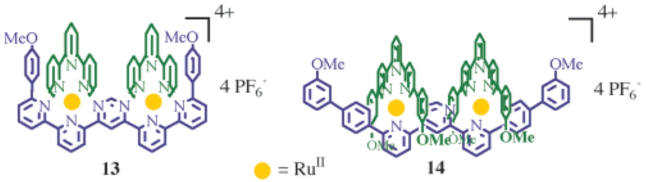
ABSTRACT



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Palladium-based carbon–carbon coupling reactions in sequence with halogen-exchange chemistry on a series of heterocycles lead to an efficient synthetic strategy for oligopyridines that bind metal ions such as ruthenium to form coordination racks. The particular structures are designed to form terpyridine subunits for octahedral binding. Reaction of 4,6-diiodopyrimidine produces a "double-bay" terpyridine from which binuclear coordination complexes have been formed.

Synthesis of topologically[1] interesting metal complexes requires efficient synthetic methods for polydentate ligand preparation.[2] Within the realm of aromatic nitrogen heterocycles these complex ligands comprise polypyridines such as oligo-bipyridines and terpyridines, which have found application in the construction of two classes of entwined molecules.[3] Molecular racks,[4] grids,[5] and helices[6] typify Class 1 and do not require the formation of a macrocycle, whereas rotaxanes,[7] catenanes,[8] and knots[9] that represent Class 2 do. In this manner, Class 1 compounds can be conceived as precursors to Class 2 (Figure 1). In order for this design strategy to work, the subcomponents of Class 1 molecules must contain functional groups and geometric dispositions amenable to macrocycle formation. We report the synthesis of two new ligands with characteristics suitable for the creation of highly organized supramolecular assemblies and describe preliminary studies of the complexation of these ligands with ruthenium(II).

Although **1** and terpyridine **2** have been used to form racks and grids, these complexes do not qualify as Class 2 precursors because they lack functional group "hooks" at which macrocyclic connections could be made. Appropriate

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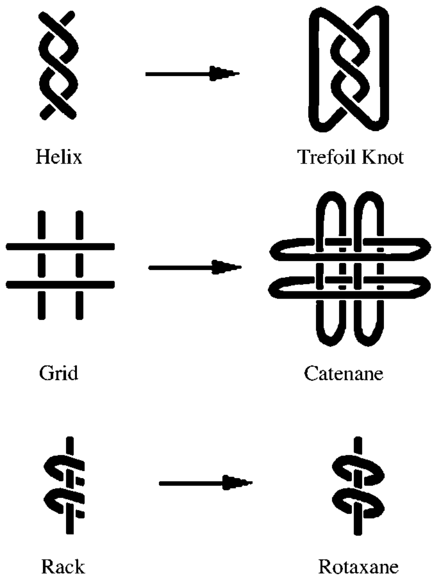


Figure 1. Examples of Class 1 (left) complexes as precursors to Class 2 (right) complexes.

modifications of these systems can be seen in the design of ligands **3**−**8** (Figure 2).

Ligands **3** and **4** are characterized by the presence of two tridentate binding sites (double-bay), whereas **2** and **5**−**8** are single tridentate ligands (single-bay). Mixed complexation of single- and double-bay ligands leads to molecular racks with octahedral metals.[10]

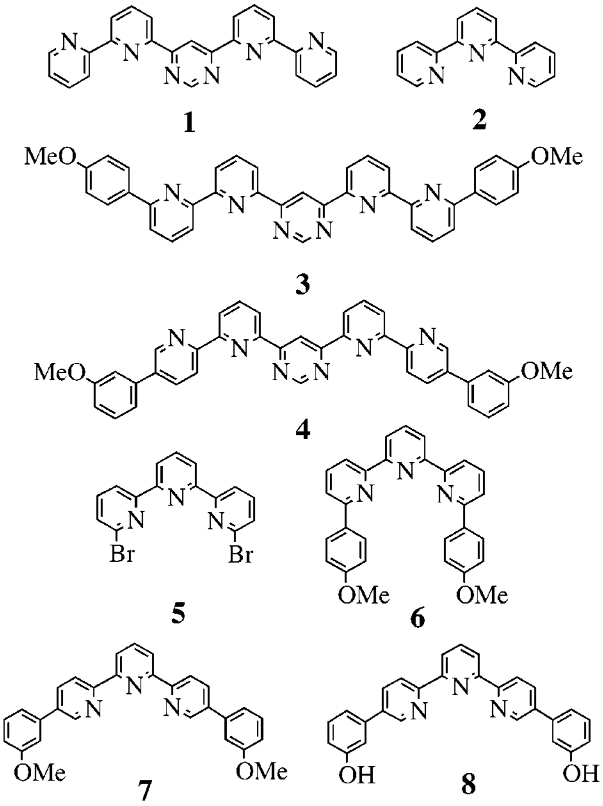
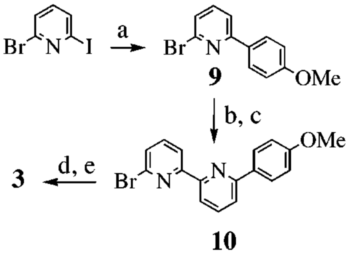


Figure 2. Single- and double-bay ligands **1**−**8**.

The synthesis of **3** starts with the Suzuki coupling[11] of *p*-methoxyphenylboronic acid and 2,6-dibromopyridine to give **9**. The tin derivative of **9**, generated via the lithium salt quenched by trimethylchlorostannane, couples with 2,6-dibromopyridine under Stille conditions[12] to yield **10**. Alternatively, **10** can be synthesized by Suzuki coupling of *p*-methoxyphenylboronic acid with 6,6′-dibromo-2,2′-bipyridine.[13] Finally, the palladium-catalyzed coupling of the tin derivative of **10** with 4,6-diiodopyrimidine in dimethoxyethane (DME) gives the desired **3** in 55% yield after chromatographic purification (Scheme 1).[14]

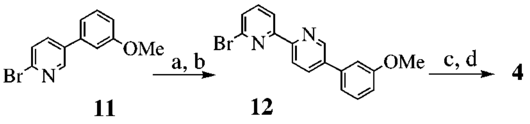
Scheme 1. Synthesis of **3**[a]



[a] (a) 4-Methoxyphenylboronic acid, $Pd(PPh_3)_4$, Na_2CO_3, toluene, reflux, 74%; (b) (1) BuLi, Et_2O, −78 °C, (2) Me_3SnCl, 85%; (c) 2,6-dibromopyridine, $Pd_2(dba)_3$, Ph_3As, DME, reflux, 80%; (d) $Me_3Sn{-}SnMe_3$, $Pd(PPh_3)_4$, DME, 91%; (e) 4,6-diiodopyrimidine, $Pd_2(dba)_3$, Ph_3As, DME, reflux, 55%.

The synthesis of ligand **4** proceeds in a manner similar to that of **3**. After the cross coupling between 3-(trimethylstannyl)-6-bromopyridine and *m*-iodoanisole, **11** was obtained and used in a further coupling reaction to give intermediate **12**. Here every attempt to use the lithiation/trimethylchlorostannane protocol to obtain the tin derivative was unsuccessful; but using the palladium/hexamethyldistannane methodology,[15] the tin compound was synthesized in 80% yield. Finally, Stille coupling with tris(dibenzylideneacetone)-dipalladium ($Pd_2(dba)_3$) in DME afforded ligand **3** in 64% yield (Scheme 2).[16]

Scheme 2. Synthesis of **4**[a]



[a] (a) (1) BuLi, Et_2O, −78 °C, (2) Me_3SnCl, 77%; (b) 2-iodo-6-bromopyridine, $Pd_2(DBA)_3$, Ph_3As, DME, reflux, 60%; (c) $Me_3Sn{-}SnMe_3$, $Pd(PPh_3)_4$, DME, 90%; (d) 4,6-diiodopyrimidine, $Pd_2(DBA)_3$, Ph_3As, DME, reflux, 64%.

Terpyridines **2** and **5** are known in the literature; **6** and **7** were prepared via palladium cross-coupling of 2 equiv of the opportune tin derivative and 1 equiv of 2,6-diiodopyridine. Cleavage of the methyl ether bonds in **7** by pyridinium hydrochloride produces **8**.

One-pot complexation of **5**−**7** with **3**, using ruthenium trichloride trihydrate as the octahedral ion, was unsuccessful. Additionally, either complexation of **3** with 2 equiv of ruthenium trichloride trihydrate and reaction with **5**−**7**, or complexation of **5**−**7** with 1 equiv of ruthenium trichloride followed by reaction with **3** gave no rack products; the dimers of **5**−**7** were the only isolated compounds. These results are likely explained in terms of steric hindrance, due to the presence of phenyl groups in ortho position to the nitrogen of the ligand **3**. Indeed, the only molecular rack prepared and isolated from **3** was **13**, the adduct **3** with 2 equiv of **2** (Figure 3).[17]

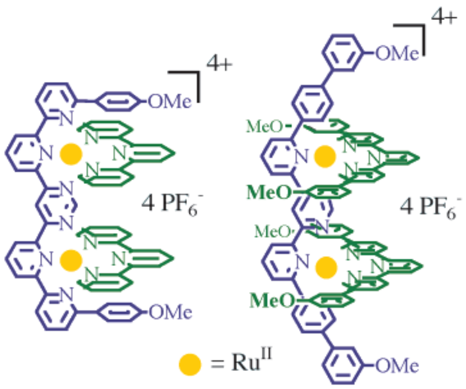


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Figure 3. Bis-ruthenium complexes **13** and **14**. ● = Ru^{II}.

Successful demonstration of Class 1 rack formation resulted from the complexation of **4** with **7**. Positioning the aryl substituents “meta” to the terminal nitrogens reduces the proximal steric hindrance but retains the chemical hook needed for further derivatization. Dichlorotetrakis(dimethyl sufoxide)ruthenium(II)[18] and **4** were heated at reflux in ethanol for 5 h. After cooling, a black precipitate formed and was filtered and used without any purification. This black complex, **4** ($RuCl_2DMSO)_2$, and 2 equiv of **7** were heated at reflux in ethylene glycol for 15 h. After cooling, a deep green solid was induced to precipitate by adding a saturated solution of potassium hexafluorophosphate. This solid was purified by column chromatography on silica gel, using mixtures of dichloromethane and acetonitrile. In this way, the expected bisruthenium complex, **14**, was isolated in 47% yield as a dark green solid and characterized by mass spectroscopy, NMR, COSY NMR, and UV. The complex **14** represents a useful intermediate en route to the synthesis of rotaxanes, catenanes, and structures of additional complexity such as Borromean rings (Figure 4).

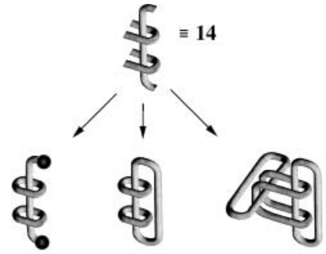

Figure 4. Relationship of **14** (at top center) as a potential precursor to rotaxanes, catenanes, and Borromean rings.

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(17) A mixture of ligand 1 and $RuCl_3{\cdot}3H_2O$ (2 equiv) was heated at reflux in ethanol for 5 h. After cooling the solution to 0 °C for 1 h, the black precipitate was filtered and used without further purification. This solid and 2 equiv of 7 were heated at reflux for 15 h in ethylene glycol. After cooling and the addition of a saturated solution of KPF_6, a deep green solid precipitated and was collected by filtration. Chromatographic purification on silica gel (8:2 dichloromethane:acetonitrile) gave a green solid that was washed with ethanol and then diethyl ether and finally dried under vacuum (51% yield).

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