Metallamacrocycles

A Simple, One-Step Procedure for the Formation of Chiral Metallamacrocycles**

*Katie Campbell, Charles A. Johnson II, Robert McDonald, Michael J. Ferguson, Michael M. Haley, and Rik R. Tykwinski**

Dedicated to Professor Larry Scott on the occasion of his 60th birthday

Metal-directed self-assembly reactions have become a powerful method used for the construction of supramolecular architectures including molecular squares, cages, and other polygons, as well as numerous polymeric and dendrimeric species.[1] In the last decade, scientists have become particularly intrigued with the effect of incorporating chiral ligands/groups into metallosupramolecular systems. These materials have demonstrated potential in numerous enantioselective processes including asymmetric catalysis,[2] chemical sensing,[3] and selective guest inclusion.[4]

[*] K. Campbell, Prof. Dr. R. R. Tykwinski
Department of Chemistry
University of Alberta
Edmonton, AB, T6G 2G2 (Canada)
Fax: (+1) 780-492-8231
E-mail: rik.tykwinski@ualberta.ca

C. A. Johnson II, Dr. R. McDonald, Dr. M. J. Ferguson
X-Ray Crystallography Laboratory
Department of Chemistry
University of Alberta
Edmonton, AB, T6G 2G2 (Canada)

Prof. Dr. M. M. Haley
Department of Chemistry
University of Oregon
Eugene, OR 97403-1253 (USA)

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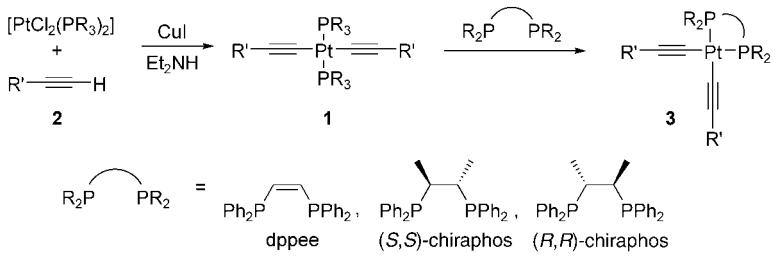
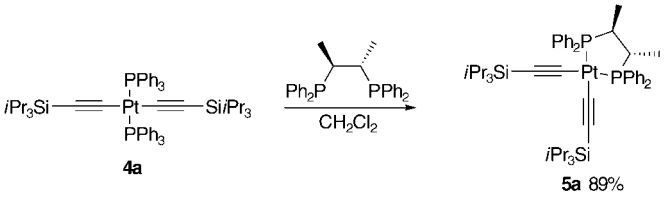
In most cases, the synthesis of metal-containing chiral supramolecules involves derivatization of an enantiopure building block, as in the numerous chiral binaphthyl-based molecules. Using a typically step-wise process, these chiral segments are elaborated with functionality capable of binding to a metal or metal ion, such as pyridyl and alkynyl moieties.[5] These larger segments are then assembled into the desired supramolecule, and this ultimately provides a chiral metal-containing architecture of predictable size, shape, and function.



Scheme 1. Construction of achiral and chiral *cis* platinum acetylide complexes by ligand exchange.

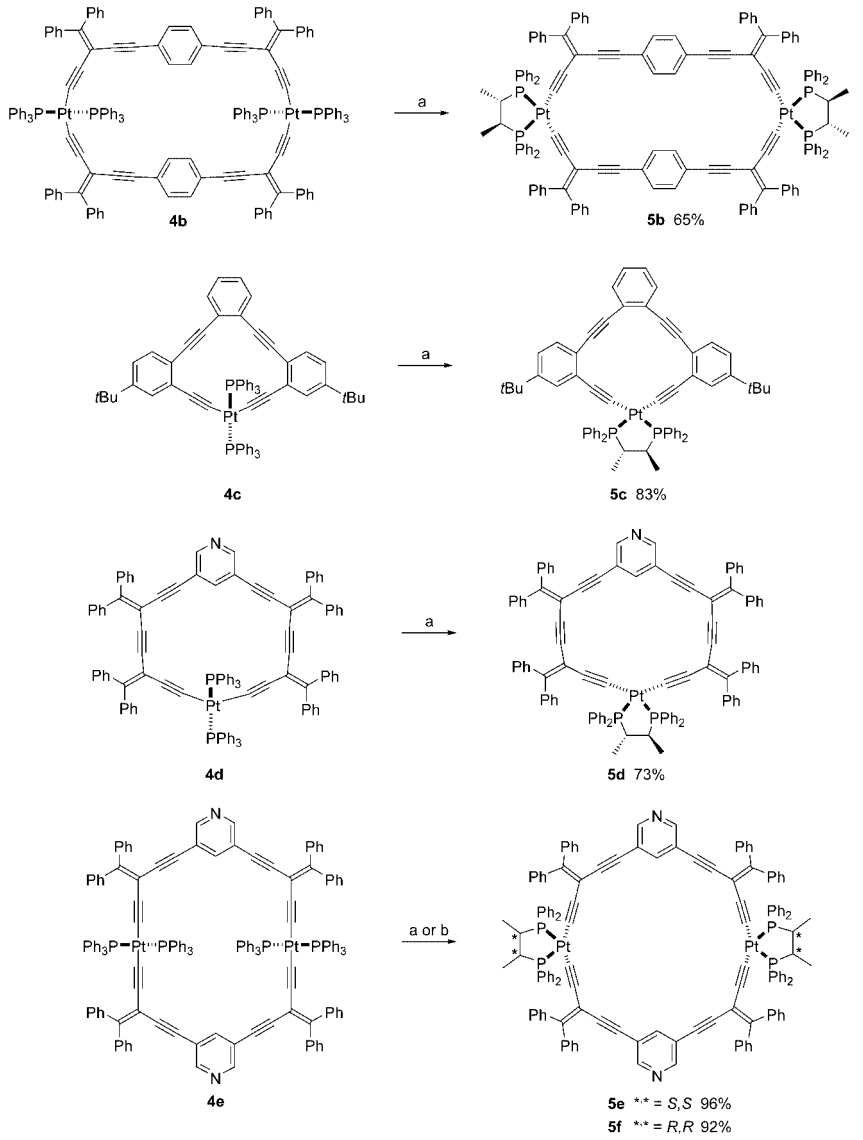
The most costly component of a chiral framework is nearly always the optically pure building block. Thus, a synthetic sequence that initiates from a chiral building block will inherently suffer from losses due to subsequent synthetic and purification steps.[2,3] A more attractive approach would be a method that introduced chirality after construction of the desired supramolecular assembly. This approach would not only circumvent waste of the chiral building block prior to the ultimate synthetic step, but would also facilitate the divergent preparation of both enantiomers of a given target from a common precursor. Described herein is a simple and general protocol that provides economical access to chiral metal-containing molecules by ligand exchange between *trans* platinum acetylide complexes (**1**) and the chiral diphosphine ligands (*R*,*R*)- and (*S*,*S*)-chiraphos (Scheme 1).



Scheme 2. Synthesis of chiral *cis* acetylide complex **5a**.

Metal-organic frameworks can be expediently accessed by the conversion of terminal acetylenes (**2**) into *trans* platinum acetylide complexes (**1**) by reaction with $[PtCl_2(PR_3)_2]$.[6] It has been established that transformation of *trans* complexes **1** into their *cis* counterparts **3** can be readily accomplished by ligand exchange with a chelating diphosphine ligand,[7] provided the lability of the exiting phosphine ligand is carefully controlled. In the case of *trans* acetylides with PEt_3 ligands (e.g., **1**, R = Et), ligand exchange to give the *cis* derivatives **3** is either extremely slow or completely retarded in reactions with dppee.[7] The *trans* complexes **1** with pendant PPh_3 ligands, on the other hand, are readily converted to their *cis* counterparts **3** in good to excellent yield, when using dppee to effect ligand exchange.

For the current study, formation of requisite *trans* platinum complexes **4a–e** (Schemes 2 and 3) was effected by treating the appropriate terminal acetylene with $[PtCl_2(PPh_3)_2]$ in degassed Et_2NH with a catalytic amount of CuI.[8] In the case of cyclic derivatives such as **4b–e**,



Scheme 3. Synthesis of chiral macrocycles **5b–f**. a) (*S*,*S*)-chiraphos, CH_2Cl_2, RT; b) (*R*,*R*)-chiraphos, CH_2Cl_2, RT.

high dilution was used to facilitate closure of the macrocyclic skeleton. All *trans* complexes were readily purified by either selective precipitation or flash chromatography on silica gel.

To probe the transformation of the achiral complexes into chiral supramolecules, the acyclic system **4a** was used as a model system. Treatment of **4a** with (*S*,*S*)-chiraphos in CH_2Cl_2 at RT for 14 h cleanly formed the chiral *cis* complex **5a** in 89% yield (Scheme 2). This protocol was next applied to a structurally diverse selection of metallamacrocycles **4b–e**.[9] Gratifyingly, the reaction of these *trans* acetylide complexes with (*S*,*S*)-chiraphos under analogous conditions led to the *cis* acetylide macrocyclic complexes **5b–e** in good to excellent yields. The reaction of **4e** with the ligand (*R*,*R*)-chiraphos to give **5f** was equally successful, highlighting the economy of our methodology which allows for the divergent generation of both enantiomeric macrocycles, **5e** and **5f**, from **4e** by simply changing the ligand system in the final step of the synthesis. Thus, this one-step transformation is equally effective for carbocyclic systems such as **5b,c** and complexes with pyridine rings containing one (**5d**) or two metal centers (**5e**,**f**). The successful formation of **5d–f** is noteworthy as they are excellent candidates for use as chiral building blocks in self-assembly reactions, through coordination through the pyridine unit(s).[10]

The formation of **5a–f** is easily monitored by ^1H and ^{31}P NMR spectroscopy. The alkyl protons of the free ligand, (*S*,*S*)-chiraphos, appear as a multiplet (methine) and quartet (methyl) at $\delta = 2.50$–2.43 and 1.17 ppm, respectively. Upon binding to the metal center, these protons are shifted upfield and appear as broad multiplets centered at $\delta = 2.49$–2.16 and 0.95–0.84 ppm, respectively. Even more diagnostic are the ^{31}P NMR spectra. The free chiraphos ligand gives rise to a singlet at $\delta = -8.7$ ppm that diminishes in intensity as ligand exchange proceeds, while the resonance of uncoordinated PPh_3 emerges at $\delta = -4.4$ ppm. Concurrently, the intensity of the ^{31}P NMR resonance from the ligated PPh_3 of the *trans* acetylide complex **4**, observed at $\delta = 18$–21 ppm, disappears as the reaction proceeds. It is replaced by a new resonance at $\delta = 42$–47 ppm from the chiraphos ligand bound to platinum in complex **5**. As the coordination geometry about the platinum center changes from *trans* to *cis*, a diagnostic change in the coupling constant $J_{P\text{-}Pt}$ is also observed (2600–2720 Hz for **4a–e**, 2190–2250 Hz for **5a–f**).

It is well known that five-membered chelate rings can adopt two puckered, chiral conformations (Figure 1).[11] In the presence of stereogenic centers (as is the case with chiraphos), these two conformations become diastereomeric, and one conformation is therefore energetically more favorable. For (*S*,*S*)-chiraphos, the most stable conformation is the one in which the substituents of the chelate ring are equatorially disposed (the δ conformation). As a result of this conformational preference, the phenyl groups on the phosphorus centers are locked into a chiral arrangement. It is through this arrangement that the chiraphos ligand can convey chirality to the entire molecular framework by the steric influence of the phenyl groups of the phosphine, which is relayed to other ligands bonded to platinum.

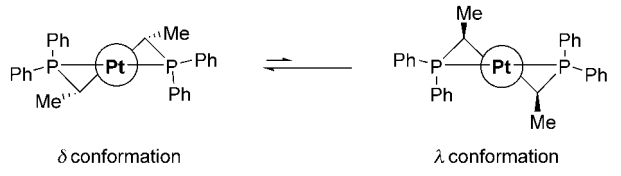


Figure 1. δ and λ conformations resulting from bonding of (*S*,*S*)-chiraphos to platinum.

Conclusive structural proof of the chiral structures of **5a** and **5d** as a result of the chiraphos ligand has been provided by single crystal X-ray crystallographic analysis. The ORTEP drawing of **5a** (Figure 2) shows that the complex is in the expected δ conformation in which the two methyl groups of the chiraphos ligand are pseudoequatorial.[12] The coordination geometry about the platinum center is square planar with angles of 86.29(2)° (P1-Pt-P2) and 87.93(9)° (C3-Pt-C5) which are comparable to other Pt^{II}–chiraphos complexes.[13] All other angles and bond lengths are unremarkable.

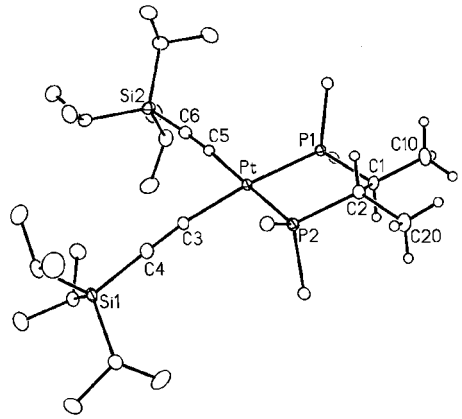


Figure 2. ORTEP drawing of **5a** (20% probability level; solvent molecules and all but the *ipso* carbon atoms of the phenyl rings have been removed).

The solid-state structure of **5d**, by contrast, shows several unexpected features. Complex **5d** crystallizes with two independent molecules in the unit cell (molecule A is shown in Figure 3).[14] While much of the macrocyclic core is nearly planar, the structure pivots dramatically at the alkylidene carbons C17 and C23 to accommodate the *cis* acetylide linkage to platinum. In spite of the inherent strain, the coordination geometry about the platinum center remains unchanged with bond angles about the metal of 87.5(6)° (C20-Pt1-C21) and 86.04(16)° (P1-Pt1-P2). The strain imparted by the *cis* conformation is therefore borne almost exclusively by the enyne core of the macrocycle, as evidenced by the alkylidene and alkyne bond angles, which have mean values of 112.2° and 172.3°, respectively.

The most remarkable feature of the solid-state structure of **5d** is that the Chiraphos ligand has adopted a λ conformation, which places the two methyl groups in pseudodiaxial positions with a dihedral angle C43-C41-C42-C44 between the methyl groups of 166.2° (molecule B is similar, with C43-C41-C42-C44 = 167.4°). This is only the second example of Chiraphos adopting this conformation (in

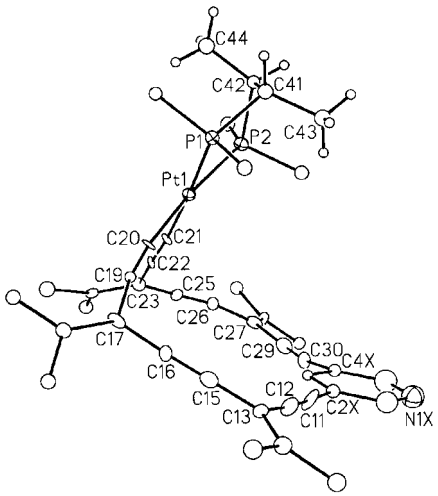


Figure 3. ORTEP drawing of molecule A of **5d** (20% probability level; solvent molecules and all but the *ipso* carbon atoms of the phenyl rings have been removed).

the solid-state) that could be found in the Cambridge structural database.[15] It is speculated that this unusual result is directed by steric interactions between the phenyl groups on the diphosphine ligand and the pendant diphenylalkylidene groups of the macrocycle.

The CD spectra for chiral *cis* complexes **5a–f** are shown in Figure 4. The CD curve for complex **5b** shows the strongest

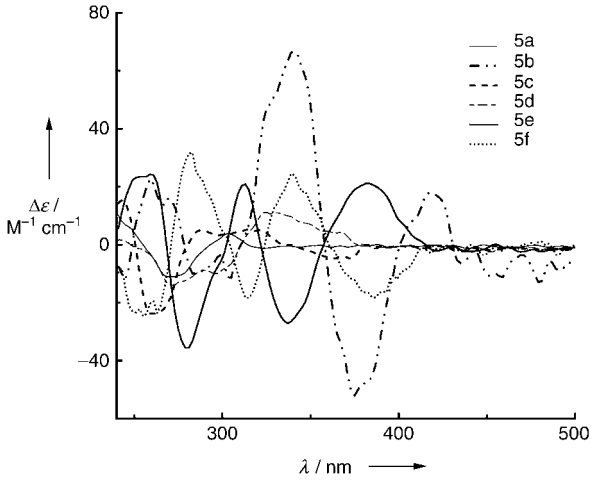


Figure 4. CD spectra for **5a–f** in CH_2Cl_2.

response and is dominated by two intense Cotton effects that form a negative couplet centered at $\lambda = 358$ nm, attributable to the $\pi \rightarrow \pi^*$ transition.[16,17] A third, positive Cotton effect is observed at high energy ($\lambda \approx 260$ nm). The CD curves for complexes **5e** and **5f** demonstrate several moderately strong signals, and the two spectra mirror each other in both form and intensity, consistent with an enantiomeric relationship. More specifically, these spectra show two bisignate signals, centered at $\lambda \approx 360$ and 305 nm. The lower energy couplet likely arises from the MLCT absorption band, whereas the high-energy band is associated with an unassigned transition in the UV/Vis absorption spectrum at $\lambda = 305$ nm. Unlike complexes **5b** and **5e**,**f**, the remaining complexes, acyclic **5a** and the more strained macrocycles **5c** and **5d**, show only weaker, high-energy signals in the lower energy region of the CD spectra.

The solid-state and CD spectroscopic data for **5a–f** unambiguously demonstrate the ability of the chiraphos ligand to efficiently transfer chirality to the conjugated molecular framework of platinum acetylide complexes. There are, however, several important design considerations that appear to govern this process. As demonstrated by CD spectroscopy, the chiral influence from chiraphos is strongest when the acetylenic chromophore attached to the platinum metal center is large and sufficiently rigid to interact with the chiral array of phenyl groups on the diphosphine ligand, as observed for macrocycles **5b** and **5e–f**. The macrocycle must also, however, maintain sufficient conformational mobility to be biased by this interaction, that is, when the macrocycle is too strained or rigid, the chiral influence is minimal, as observed for **5c** and **5d**. Optimization of this process and the formation of chiral, conjugated frameworks using ligand-exchange methodology with other chiral phosphine ligands are currently underway.

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14.1414(6), $b = 14.6660(6)$, $c = 25.5887(11)$ Å; $V = 5307.0(4)$ Å^3; $Z = 4$; $\rho_{calcd} = 1.338\ g\,cm^{-3}$; $\mu(Mo_{K\alpha}) = 2.881\ mm^{-1}$; $T = -80\,°C$; $R_1(F) = 0.0208$ (10217 reflections $F_o^2 \geq 2\sigma(F_o^2)$) and $wR_2(F^2) = 0.0457$ for all 10797 unique data.

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