A Conformationally Programmable Ligand

Yong S. Chong, Mark D. Smith, and Ken D. Shimizu*

University of South Carolina
Department of Chemistry and Biochemistry
Columbia, South Carolina 29208

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Metals are well-known to induce conformational changes upon ligand systems.[1] This attribute has been utilized in sensors,[2] molecular machines,[3] synthetic receptors,[4] and stabilization of protein structures.[5] However, these metal-induced conformations are normally dependent on the presence of the metal ion. For example, chelation of a metal by 2,2′-bipyridine stops rotation about the C−C bond and leads to a planar conformation.[6] Upon removal of the metal ion the 2,2′-bipyridine "forgets" and reverts to its conformationally flexible state. Demonstrated herein is a ligand that can remember or retain its metal-induced conformation even in the absence of the metal ion. In effect, the ligand can be "taught" to hold a specific conformation.

Our strategy utilizes a ligand that is conformationally flexible at elevated temperatures yet is conformationally rigid at room temperature (Figure 1). This is achieved via restricted rotation, which leads to two stable and separable conformational isomers: a convergent *syn*- and a divergent *anti*-rotamer.[7] Control over ligand conformation can be exerted by heating the ligand in the presence of a metal ion.[8] The chelating *syn*-conformer is preferred, and on cooling to room temperature, this conformer or shape is locked in, even upon removal of the metal ion.

The specific ligand that was designed and synthesized was bis(pyridine) **1** (Scheme 1). Restricted rotation is present about the two $C_{aryl}-N_{imide}$ bonds due to the steric interactions of the ether oxygens with the imide carbonyls.[9,10] As a consequence, the ligand adopts stable *syn*- and *anti*-rotamers.

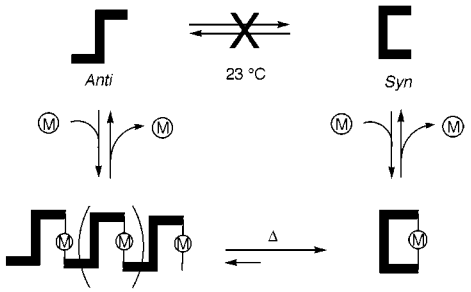
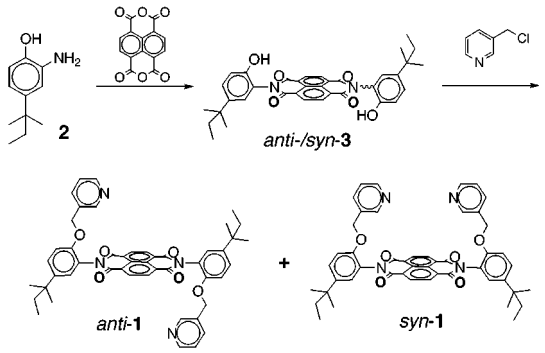


Figure 1. Schematic representation of a "programmable" ligand. At room temperature the ligand adopts one of two conformations: *syn*- or *anti*-. On heating in the presence of a metal, the *syn*-isomer is preferred. On cooling this conformational preference is "locked-in" even on removal of the metal ion.

Scheme 1[a]



[a] (a) DMF, reflux, 12 h (99%), (b) K_2CO_3, DMF, 18 h (55%).

The ligand was readily assembled in two steps from amino phenol **2** (Scheme 1). Condensation with 1,4,5,8-naphthalenetetracarboxylic dianhydride in DMF yielded *syn*-/*anti*-**3**.[11] Subsequent alkylation with 3-chloromethylpyridine gave *syn*-**1** and *anti*-**1** which were separated by column chromatography. The rotamers were assigned on the basis of their dipole moments as measured by their R_f on silica gel[12] and later by an X-ray structure of the *anti*-isomer.[13] The stability of the conformational isomers was determined by following the equilibration of the respective isomers by ^{1}H NMR, yielding a rotational barrier of 27.0 kcal/mol,[14] which corresponds to a half-life of 71 days at room temperature (23 °C).[15]

Differences in coordination abilities of *syn*- and *anti*-**1** were evident by their differential solubilities in $CDCl_3$ on addition of 1 equiv of $[PdCl_2(PhCN)_2]$. The convergent *syn*-bis(pyridine) **1** forms a soluble monomeric chelate complex; whereas the divergent *anti*-**1** forms an insoluble coordination polymer. Similar differences in solubility have been demonstrated for macrocyclic versus oligomeric supramolecular assemblies.

Structural characterization of the $[PdCl_2$(*syn*-**1**)] complex was provided by X-ray crystallography, which confirmed the mono-

(1) Eichhorn, G. L. *Coord. Chem. Rev.* **1993**, *128*, 167−173.
(2) For recent example see: (a) Zahn, S.; Proni, G.; Spada, G. P.; Canary, J. W. *Chem.*−*Eur. J.* **2001**, *7*, 88−93. (b) McFarland, S. A.; Finney, N. S. *J. Am. Chem. Soc.* **2001**, *123*, 1260−1261. (c) Matsumoto, H.; Shinkai, S. *Tetrahedron Lett.* **1996**, *37*, 77−80. Liquid crystalline phases: Liebmann, A.; Mertesdorf, C.; Plesnivy, T.; Ringsdorf, H.; Wendorff, J. H. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 1375−1377.
(3) Kelly, T. R.; Bowyer, M. C.; Bhaskar, K. V.; Bebbington, D.; Garcia, A.; Lang, F. R.; Kim, M. H.; Jette, M. P. *J. Am. Chem. Soc.* **1994**, *116*, 3657−3658.
(4) For recent examples, see: (a) Al-Sayah, M. H.; Branda, N. R. *Angew. Chem., Int. Ed.* **2000**, *39*, 945−947. (b) Kubik, S. *J. Am. Chem. Soc.* **1999**, *121*, 5846−5855. For a general review, see: Robertson, A.; Shinkai, S. *Coord. Chem. Rev.* **2000**, *205*, 157−199.
(5) (a) Eichhorn, G. L. *Coord. Chem. Rev.* **1993**, *128*, 167−173. (b) Koshland, D. E. *Angew. Chem., Int. Ed. Engl.* **1995**, *33*, 2375−2378.
(6) Kaes, C.; Katz, A.; Hosseini, M. W. *Chem. Rev.* **2000**, *100*, 3553−3590.
(7) For examples of shape-based memory systems based on restricted rotation, see: (a) Sugasaki, A.; Ikeda, M.; Takeuchi, M.; Robertson, A.; Shinkai, S. *J. Chem. Soc., Perkin Trans. 1* **1999**, 3259−3264. (b) Furusho, Y.; Kimura, T.; Mizuno, Y.; Aida, T. *J. Am. Chem. Soc.* **1997**, *119*, 5267−5268. (c) Yashima, E.; Maeda, K.; Okamoto, Y. *Nature* **1999**, *399*, 449−451.
(8) Examples of induced conformation of atropisomers by organic guests: (a) Hayashi, T.; Asai, T.; Borgmeier, F. M.; Hokazono, H.; Ogoshi, H. *Chem.*−*Eur. J.* **1998**, *4*, 1266−1274. (b) Kuroda, Y.; Kawashima, A.; Urai, T.; Ogoshi, H. *Tetrahedron Lett.* **1995**, *36*, 8449−8452. (c) Bampos, N.; Marvaud, V.; Sanders, J. K. M. *Chem.*−*Eur. J.* **1998**, *4*, 335−343.
(9) (a) Curran, D. P.; Geib, S.; N, D. *Tetrahedron* **1999**, *55*, 5681−5704. (b) Degenhardt, C., III; Shortell, D. B.; Adams, R. D.; Shimizu, K. D. *J. Chem. Soc., Chem. Commun.* **2000**, 929−930. (c) Shimizu, K. D.; Dewey, T. M.; Rebek, J. *J. Am. Chem. Soc.* **1994**, *116*, 5145−5149. (d) Verma, S. M.; Singh, N. D. *Aust. J. Chem.* **1976**, *29*, 295−300. (e) Kishikawa, K.; Yoshizaki, K.; Kohmoto, S.; Yamamoto, M.; Yamaguchi, K.; Yamada, K. *J. Chem. Soc., Perkin Trans. 1* **1997**, 1233−1239. (f) Shimizu, K. D.; Freyer, H. O.; Adams, R. D. *Tetrahedron Lett.* **2000**, *41*, 5431−5434.
(10) For examples of metal complexation to control the conformation of a photoswitchable system, see: (a) Fyles, T. M.; Zeng, B. *J. Org. Chem.* **1998**, *63*, 8337−8345. (b) Shinkai, S.; Ogawa, T.; Kusano, Y.; Manabe, O.; Kikukawa, K.; Goto, T.; Matsuda, T. *J. Am. Chem. Soc.* **1982**, *104*, 4.
(11) The rotational barrier of **3** was too low to enable separation of the isomers at room temperature.
(12) Differences in dipole moments as measured by thin-layer chromatography have been successfully utilized in the assignment of atropisomers in many systems. (a) Sanders, G. M.; Van Dijk, M.; Machiels, B. M.; van Veldhuizen, A. *J. Org. Chem.* **1991**, *56*, 1301−1305. (b) Shimizu, K. D.; Dewey, T. M.; Rebek, J., Jr. *J. Am. Chem. Soc.* **1994**, *116*, 5145−5149.
(13) The crystal structure of *anti*-**1** is in the Supporting Information.
(14) Measured in $CDCl_3$ at 62 °C by ^{1}H NMR.
(15) Calculated from the Arrhenius equation assuming an ideal value of $A = 2.08 \times 10^{10}$ s^{-1} deg^{-1}.

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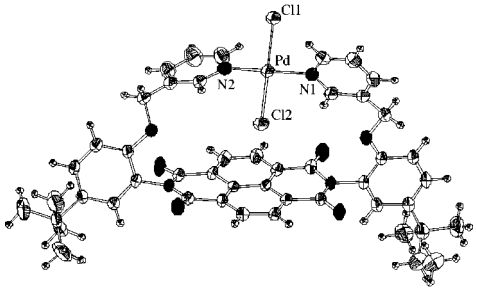

Figure 2. X-ray crystal structure of [$PdCl_2$(*syn*-**1**)]. ORTEP representation with 50% probability.

meric and chelating nature of the complex (Figure 2). The pyridines hold the $PdCl_2$ suspended over the naphthalene diimide surface with N−Pd bond lengths of 2.02 Å. One chlorine atom fills the space below the Pd atom and is poised 3.254 Å above the naphthalene ring. Finally, the aryl rings are nearly perpendicular to the naphthalene diimide surface with dihedral angles of 91° and 81.3°.

The X-ray structure also revealed another unique characteristic of *syn*-**1**, that it is an example of a *trans*-(spanning) bis(pyridine) ligand. The $PdCl_2$ is coordinated from opposite sides in a *trans*-geometry (N−Pd−N bond angle = 176.0°), due to the geometric constrains of the rigid ligand framework. *Trans*-spanning bicoordinate ligands are quite rare.[16] Examples of bis(nitrile),[17] bis(phosphine),[18] and bis(amine)[19] ligands have been reported but to our knowledge, this is the first example of a *trans*-spanning bipyridine ligand.

NMR enabled in situ monitoring of the dynamic properties of ligand **1** and its complexes. The following cycle was performed in a single NMR tube to demonstrate the conformational programmability of ligand **1** by metal chelation. Beginning with *trans*-**1** (Figure 3a), the addition of [$PdCl_2(PhCN)_2$] yielded the corresponding coordination polymer (Figure 3b) as evidenced by the complex and broadened spectra. This species was stable at room temperature but could be transformed quantitatively into [$PdCl_2$(*syn*-**1**)] (Figure 3c), by heating for 25 h at 86 °C (∼15 half-lives) and then cooling to room temperature. The sharp set of new signals were identical to those of the [$PdCl_2$(*syn*-**1**)] complex that was made independently by addition of [$PdCl_2(PhCN)_2$] to *syn*-**1**. Finally, the $PdCl_2$ was removed by addition TMEDA to yield free *syn*-**1** (Figure 3d) with >98% diastereomeric excess.[20] We have also taken mixtures of *syn*-**1**, and *anti*-**1** shifted them entirely to *syn*-**1**, in a similar manner.

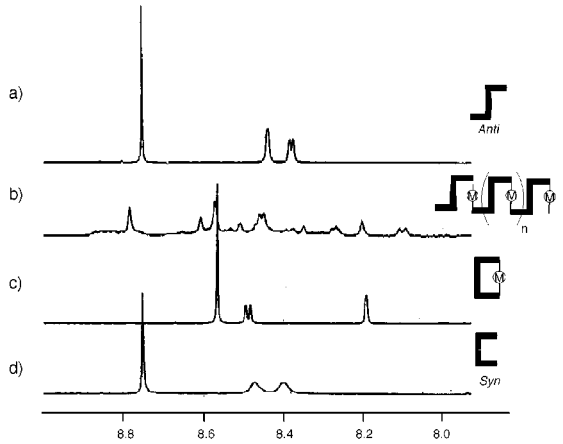

Figure 3. ^{1}H NMR spectra in DMSO-d_6 of (a) *anti*-**1**, (b) [{$PdCl_2$(*anti*-**1**)}$_n$] formed from the addition of 1 equiv of [$PdCl_2(PhCN)_2$] to *anti*-**1**, (c) [$PdCl_2$(*syn*-**1**)] formed by heating [{$PdCl_2$(*anti*-**1**)}$_n$] for 25 h at 86 °C and (d) *syn*-**1** formed by demetalation of [$PdCl_2$(*syn*-**1**)]with TMEDA.

In effect, ligand **1** can be programmed by heating in the presence of the $PdCl_2$ template to form the *syn*-conformer. This conformational preference is retained on cooling to room temperature even on removal of the template. Alternatively, the *anti*-isomer can be favored by heating the TsOH salt in toluene. Again, the conformation is preserved on cooling to room temperature and neutralization to yield 87% *anti*-enriched **1**. The preference for the *anti*-isomer, on protonation, is presumably due to the destabilization of the *syn*-isomer by charge−charge repulsion. In either case, the conformational preferences can be "erased" simply by heating in the absence of metal ion or acid, returning the ligand to an equilibrium mixture of *syn*- and *anti*-**1**.

In summary, ligand **1** can be programmed to adopt either a convergent *syn*-conformer that forms chelates or a divergent *anti*-conformer that forms coordination polymers. Preliminary examinations have also demonstrated that ligand **1** demonstrates similar dynamic characteristics with other metals such as Cu(II) or Ag(I). Potential applications of this structural programmability are as molecular informational storage devices, or materials with programmable properties.

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Supporting Information Available: The contents include synthetic procedures for the synthesis of ligand **1**, characterization data including ^{1}H NMR spectra, and crystallographic tables for [$PdCl_2$(*syn*-**1**)] and *anti*-**1** (PDF). X-ray crystallographic files in CIF format for [$PdCl_2$(*syn*-**1**)] and *anti*-**1.** This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) (a) Bailar, J. C., Jr. *Coord. Chem. Rev.* **1990**, *100*, 1. (b) Ogino, H. *J. Coord. Chem.* **1987**, *15*, 187.

(17) Shimizu, K. D.; Rebek, J., Jr. *Proc. Natl. Acad. Sci. U.S.A.* **1996**, *93*, 4257−4260.

(18) (a) Sawamura, M.; Hamashima, H.; Ito, Y. *J. Am. Chem. Soc.* **1991**, *114*, 8295. (b) Barrow, M.; Bürgi, H. B.; Johnson, D. K.; Venanzi, L. M. *J. Am. Chem. Soc.* **1976**, *98*, 2356.

(19) Mochida, I.; Mattern, J. A.; Bailar, J. C., Jr. *J. Am. Chem. Soc.* **1975**, *97*, 3201.

(20) Interestingly, *syn*-**1** is competitive with TMEDA for $PdCl_2$ as both complexes are observed in ∼1:1 ratio on addition of 1 equiv of TMEDA. Thus, complete demetalation of [$PdCl_2$(*syn*-**1**)] required an excess of TMEDA.