JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

COMMUNICATION

pubs.acs.org/JACS

# A Stereodynamic Probe Providing a Chiroptical Response to Substrate-Controlled Induction of an Axially Chiral Arylacetylene Framework

Daniel P. Iwaniuk and Christian Wolf*

Department of Chemistry, Georgetown University, Washington, D.C. 20057, United States

Supporting Information

**ABSTRACT:** A stereodynamic probe containing a central 1,4-di(phenylethynyl)benzene rod and two 2-formylphenylethynyl branches has been prepared through a series of Sonogashira cross-coupling reactions with 62% overall yield. This CD silent diarylacetylene-based framework carries two terminal aldehyde groups and provides a strong chiroptical response to substrate-controlled induction of three chiral axes upon diimine formation. The chiral amplification results in intense Cotton effects that can be used for in situ ICD analysis of the absolute configuration and ee of a wide range of amines.

The unique structure and stereodynamic properties of axially chiral biaryls have been exploited in asymmetric synthesis, and chiral amplification and for the development of fascinating technomimetic devices, including molecular propellers and switches.[1] The use of internal or external means to control the energy barrier to rotation, such as incorporation of steric bulk, metal complexation, or photochemical activation, often plays a crucial role in these applications. Elongation of the biaryl axis with an acetylene unit increases the aryl−aryl distance to approximately 4.0 Å. Because of the extended separation of the two aryl rings, the steric hindrance to rotation about the pivotal axis in diarylacetylenes is generally low, and conformational isomers cannot be isolated at room temperature.[2] This intrinsic rotational freedom is a key feature of diarylacetylene-derived molecular turnstiles[3] and gyroscopes.[4]

The design of chromophoric stereodynamic receptors that report a molecular recognition event through substrate-controlled induction of axial or helical chirality has received increasing attention in recent years.[5] The amplification of central chirality in supramolecular assemblies,[6] molecular bevel gears,[7] propellers,[8] and other well-defined arrangements[9] is often expressed by characteristic induced circular dichroism (ICD) signals which can be used for configurational and conformational analysis.[10] Berova, Nakanishi, Canary, and others have introduced practical ICD probes that are based on chiral amplification via formation of hydrogen bond adducts[11] and metal complexes[12] exhibiting fluxional porphyrin or other aromatic ligands. Rosini and Toniolo have demonstrated that the covalent attachment of a conformationally flexible biphenyl unit to chiral amino acids, carboxylic acids, and alcohols followed by isolation of the adduct and CD analysis provides a reliable means for the assignment of the absolute configuration of these important substrates.[13]

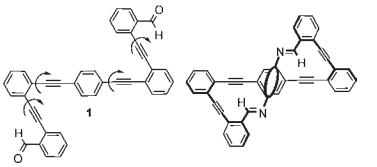


**Figure 1.** Structure of **1** and schematic illustration of a conformationally locked diimine analogue.

Despite the advance of stereodynamic biphenyl probes, a rationally designed enantioselective sensor exhibiting a diarylacetylene-based framework capable of "frictionless" central-to-axial chirality induction has not been reported to date.[14] Herein, we describe that the central chirality of amines and diamines can be imprinted on a conformationally flexible dialdehyde receptor, resulting in remarkable chirality amplification, and intense Cotton effects. The CD measurements of the corresponding diimines provide a convenient entry for in situ determination of the absolute configuration and enantiomeric excess of amines.

In recent years, we have investigated the stereodynamics of a wide range of axially chiral compounds[15] and demonstrated the usefulness of triaryl probes[16] in several applications including quantitative analysis of the enantiomeric composition of scalemic mixtures of carboxylic acids, amino acids, and amino alcohols. We have now designed a fluxional chromophoric scaffold **1** containing a central 1,4-di(phenylethynyl)benzene axis and two 2-formylphenylethynyl branches. On the basis of the relatively free rotation about the alkyne rods one can assume that **1** exists as a mixture of rapidly interconverting conformers in solution. However, the molecular geometry, i.e. the relative orientation and the length of the central axis and the branches, was carefully chosen to provide a platform for two subsequent condensation reactions between a diamine, such as 1,2-diaminocyclohexane, and the terminal aldehyde functions. The underlying idea was that, upon diimine formation, **1** would be locked into a macrocyclic structure in which the central chirality of the substrate dictates the axial chirality of the diarylacetylene-based framework, Figure 1. This substrate-controlled stereoselective cyclization was thus anticipated to result in distinct chiral amplification and generate a highly CD active compound, providing quantifiable

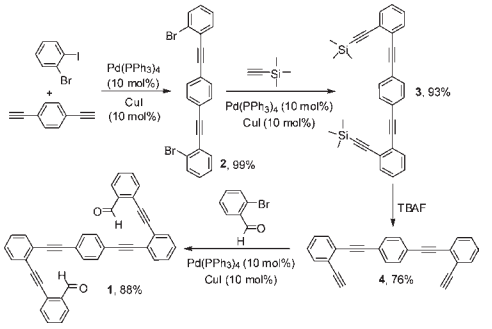
**Received:** December 23, 2010
**Published:** February 9, 2011





dx.doi.org/10.1021/ja111583e | J. Am. Chem. Soc. 2011, 133, 2414–2417

**Scheme 1. Synthesis of Probe 1**




information on the absolute configuration and the enantiomeric composition of the diamine used.

We were able to prepare 1,4-bis(2(2-formylphenylethynyl)-phenylethynyl)benzene, **1**, in four steps and 62% overall yield, Scheme 1. Sonogashira coupling of 2-bromoiodobenzene and 1,4-diethynylbenzene gave 1,4-bis((2-bromophenyl)ethynyl)-benzene, **2**, in almost quantitative yields. Alkynylation with trimethylsilylacetylene followed by deprotection of **3** using TBAF then afforded precursor **4**. Finally, 1,4-bis((2-ethynylphenyl)ethynyl)benzene, **4**, was converted to **1** in 88% yield by palladium-catalyzed Sonogashira coupling with 2-bromobenzaldehyde.

Sensor **1** was then tested with aliphatic and aromatic diamines **5**−**7**. Condensation with one diamine equivalent toward the expected macrocycle was evident by NMR spectroscopy showing quantitative disappearance of the formyl protons of **1** and ESI-MS analysis revealing exclusive dimerization (see Supporting Information). We were pleased to find that the corresponding diimines have very strong Cotton effects even at micromolar concentrations. The CD spectra of the cyclic diimines obtained from the enantiomers of *trans*-1,2-diaminocyclohexane, **6**, (*m*/*z* 612) at $3.76 \times 10^{-5}$ M are shown in Figure 2.

Apparently, cyclocondensation of the CD silent probe generates a rigid ring topology that is controlled by the structure of the diamine. Computational analysis suggests that **6** adopts a diaxial chair conformation upon cyclization, Figure 3. The chirality of the substrate is thus imprinted into the previously fluxional diarylacetylene-based probe, and the high CD activity can be attributed to the induction of three chiral axes represented by the central 1,4-di(phenylethynyl)benzene rod and the two 2-iminophenylethynyl branches. According to the MM2 calculation of the diimine derived from (1*S*,2*S*)-**6**, the central rod of the sensor accepts a (*P*)-conformation, whereas the two branches are locked into (*M*)-axes. Interestingly, this probe is also suitable for the CD analysis of monoamines **8**−**14**. A representative example obtained with two equivalents of **13** proves that this diimine (*m*/*z* 804) affords distinctive Cotton effects, Figure 2. The general CD activity of the acyclic condensation products derived from **8**−**14** is quite remarkable since one can assume that these acyclic diimines can populate a complex mixture of discrete conformations.

In order to evaluate the practical use of sensor **1** for quantitative ee determination of an amine substrate, a calibration curve was constructed using diamine **6** in varying ee. The diimine mixtures were obtained at 3.75 mM, and the samples were diluted to $1.88 \times 10^{-5}$ M for CD analysis. The CD amplitudes (mdeg) at 288 nm were plotted versus % ee, showing a perfectly linear relationship. Five scalemic samples of **6** were then prepared

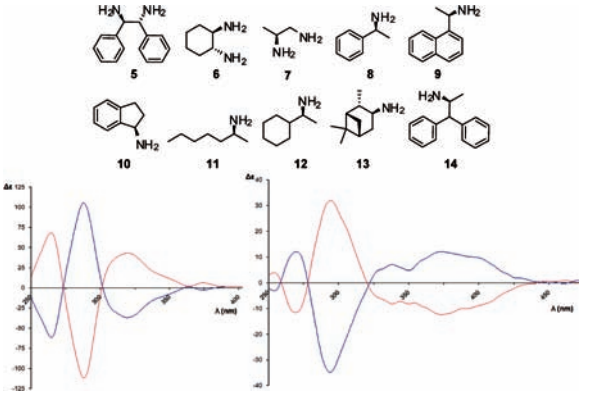



**Figure 2.** (Top) Structures of amines tested. (Bottom) ICD spectra of the diimines formed from **1** (3.75 mM in chloroform) and (1*R*,2*R*)-**6** (blue) and (1*S*,2*S*)-**6** (red) (left) and (1*R*,2*R*,3*R*,5*S*)-**13** (blue) and (1*S*,2*S*,3*S*,5*R*)-**13** (red) (right) at room temperature. For CD analysis the samples were diluted to $3.76 \times 10^{-5}$ M and $7.52 \times 10^{-5}$ M, respectively.

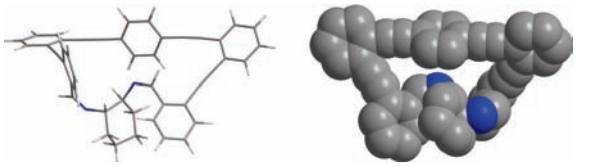


**Figure 3.** MM2 computation of the structure of the diimine derived from **1** and (1*S*,2*S*)-**6**. For better clarity, the hydrogens are omitted in the space filling model.

and treated with sensor **1** as described above. Using the linear regression equation calculated from the calibration curve and the measured CD amplitudes at 288 nm, the enantiomeric excess of these samples was determined. Experimentally obtained data were within 3.9% of the actual values (see Supporting Information).[17] While the stereochemical outcome of the cyclocondensation between **1** and diamines such as **6** is well-defined and predictable, the reaction with two equivalents of a scalemic monoamine can potentially result in a mixture of homochiral and heterochiral adducts. The formation of a diastereomeric mixture would be likely to complicate quantitative ee analysis due to smaller Cotton effects and a nonlinear relationship between the observed CD amplitude and the enantiomeric composition of the amine used. However, we obtained very similar results, i.e. a linear calibration curve and experimentally obtained ee's within 5.5% of the actual values, when the sensor was applied in the enantioselective analysis of monoamine **13**; see Supporting Information. MS examination of a mixture containing an acyclic diimine of **1** in the presence of stoichiometric amounts of another monoamine showed that the condensation is reversible under the conditions used in our assay. Accordingly, the linear relationship between the CD amplitude of the diimines obtained and the enantiomeric composition of **13** may be attributed to highly stereoselective formation of thermodynamically favored homochiral products.

In summary, we have introduced a fluxional, CD silent probe **1** that shows substrate-controlled induction of three chiral axes upon diimine formation. Dialdehyde **1** can be used for metal-free enantioselective CD analysis of a wide range of chiral amines, and it eliminates the need to prepare an enantiomerically pure, chiral


dx.doi.org/10.1021/ja111583e |*J. Am. Chem. Soc.* 2011, 133, 2414–2417

sensor. The intense Cotton effects of the diimines obtained with **1** occur at high wavelengths which excludes misinterpretation due to overlapping CD signals of the substrate and interference with chiral impurities. The extensive induction of axial chirality results in a distinct CD output which allows determination of the absolute configuration and the enantiomeric composition of amines.

## ■ ASSOCIATED CONTENT

**Supporting Information.** Synthetic details, compound characterization, and MS, CD, and NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

## ■ AUTHOR INFORMATION

**Corresponding Author**
cw27@georgetown.edu

## ■ ACKNOWLEDGMENT

This material is based upon work supported by the NSF under CHE-0910604.

## ■ REFERENCES

(1) Wolf, C., Ed. *Dynamic Stereochemistry of Chiral Compounds*; RSC Publishing: Cambridge, 2008. Selected examples of stereodynamic analysis of biaryls: (a) Adams, R.; Kornblum, N. *J. Am. Chem. Soc.* **1941**, *63*, 188–200. (b) Rieger, M.; Westheimer, F. H. *J. Am. Chem. Soc.* **1950**, *72*, 19–28. (c) Hall, D. M.; Harris, M. M. *J. Chem. Soc.* **1960**, 490–494. (d) Mislow, K.; Hyden, S.; Schaefer, H. *J. Am. Chem. Soc.* **1962**, *84*, 1449–1455. (e) Mislow, K.; Gordon, A. J. *J. Am. Chem. Soc.* **1963**, *85*, 3521–3521. (f) Melander, L.; Carter, R. E. *J. Am. Chem. Soc.* **1964**, *86*, 295–296. (g) Ling, C. K.; Harris, M. M. *J. Chem. Soc.* **1964**, 1825–1835. (h) Oki, M.; Yamamoto, G. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 266–270. (i) Mislow, K.; Gust, D. *J. Am. Chem. Soc.* **1973**, *95*, 1535–1547. (j) Irie, M.; Yoshida, K.; Hayashi, K. *J. Phys. Chem.* **1977**, *81*, 969–972. (k) Irie, M.; Yorozu, T.; Yoshida, K.; Hayashi, K. *J. Phys. Chem.* **1977**, *81*, 973–976. (l) Kyba, E. P.; Gokel, G. W.; de Jong, F.; Koga, K.; Sousa, L. R.; Siegel, M. G.; Kaplan, L.; Sogah, G. D. Y.; Cram, D. J. *J. Org. Chem.* **1977**, *42*, 4173–4184. (m) Bott, G.; Field, L. D.; Sternhell, S. *J. Am. Chem. Soc.* **1980**, *102*, 5618–5626. (n) Meyers, A. I.; Himmelsbach, R. J. *J. Am. Chem. Soc.* **1985**, *107*, 682–685. (o) Biali, S. E.; Kahr, B.; Okamoto, Y.; Aburatani, R.; Mislow, K. *J. Am. Chem. Soc.* **1988**, *110*, 1917–1922. (p) Wolf, C.; König, W. A.; Roussel, C. *Liebigs Ann.* **1995**, 781–786. (q) Wolf, C.; Hochmuth, D. H.; König, W. A.; Roussel, C. *Liebigs Ann.* **1996**, 357–363. (r) Superchi, S.; Casarini, D.; Laurita, A.; Bavoso, A.; Rosini, C. *Angew. Chem., Int. Ed.* **2001**, *40*, 451–454. (s) Meca, L.; Reha, D.; Havlas, Z. *J. Org. Chem.* **2003**, *68*, 5677–5680. (t) Wolf, C.; Pirkle, W. H.; Welch, C. J.; Hochmuth, D. H.; König, W. A.; Chee, G.-L.; Charlton, J. L. *J. Org. Chem.* **1997**, *62*, 5208–5210. (u) Ohmori, K.; Kitamura, M.; Suzuki, K. *Angew. Chem., Int. Ed.* **1999**, *38*, 1226–1229. (v) Bringmann, G.; Heubes, M.; Breuning, M.; Göbel, L.; Ochse, M.; Schöner, B.; Schupp, O. *J. Org. Chem.* **2000**, *65*, 722–728. (w) Spivey, A. C.; Charbonneau, P.; Fekner, T.; Hochmuth, D. H.; Maddaford, A.; Malardier-Jugroot, C.; Redgrave, A. J.; Whitehead, M. A. *J. Org. Chem.* **2001**, *66*, 7394–7401. (x) Tochtermann, W.; Kuckling, D.; Meints, C.; Kraus, J.; Bringmann, G. *Tetrahedron* **2003**, *59*, 7791–7801. (y) Bringmann, G.; Mühlbacher, J.; Reichert, M.; Dreyer, M.; Kolz, J.; Speicher, A. *J. Am. Chem. Soc.* **2004**, *126*, 9283–9290.

(2) (a) Koo Tze Mew, P.; Vögtle, F. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 159–161. (b) Toyota, S.; Yamamori, T.; Asakura, M.; Oki, M. *Bull. Chem. Soc. Jpn.* **2000**, *73*, 205–213. (c) Toyota, S.; Iida, T.; Kunizane, C.; Tanifuji, N.; Yoshida, Y. *Org. Biomol. Chem.* **2003**, *1*, 2298–2302. (d) Toyota, S.; Makino, T. *Tetrahedron Lett.* **2003**, *44*, 7775–7778. (e) Miljanic, O. S.; Han, S.; Holmes, D.; Schaller, G. R.; Vollhardt, K. P. C. *Chem. Commun.* **2005**, 2606–2608. (f) Nandy, R.; Subramoni, M.; Varghese, B.; Sankararaman, S. *J. Org. Chem.* **2007**, *72*, 938–944.

(3) Bedard, T. C.; Moore, J. S. *J. Am. Chem. Soc.* **1995**, *117*, 10662–10671.

(4) (a) Dominguez, Z.; Dang, H.; Strouse, M. J.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **2002**, *124*, 2398–2399. (b) Dominguez, Z.; Dang, H.; Strouse, M. J.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **2002**, *124*, 7719–7727. (c) Khuong, T.-A. V.; Dang, H.; Jarowski, P. D.; Maverick, E. F.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **2007**, *129*, 839–845. (d) Jarowski, P. D.; Houk, K. N.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **2007**, *129*, 3110–3117. (e) Garcia-Garibay, M. A.; Godinez, C. *Cryst. Growth Des.* **2009**, *9*, 3124–3128. (f) Toyota, S. *Chem. Rev.* **2010**, *110*, 5398–5424.

(5) Selected examples:(a) Tumambac, G. E.; Mei, X.; Wolf, C. *Eur. J. Org. Chem.* **2004**, 3850–3856. (b) Kawai, H.; Katoono, R.; Fujiwara, K.; Tsuji, T.; Suzuki, T. *Chem.—Eur. J.* **2005**, *11*, 815–824. (c) Katoono, R.; Kawai, H.; Fujiwara, K.; Suzuki, T. *Tetrahedron Lett.* **2006**, *47*, 1513–1518. (d) Kohmoto, S.; Takeichi, H.; Kishikawa, K.; Masu, H.; Azumaya, I. *Tetrahedron Lett.* **2008**, *49*, 1223–1227. (e) Tartaglia, S.; Pace, F.; Scafato, P.; Rosini, C. *Org. Lett.* **2008**, *10*, 3421–3424. (f) Kim, H.; So, S. M.; Yen, C. P.-H.; Vinhato, E.; Lough, A. J.; Hong, J.-I.; Kim, H.-J.; Chin, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 8657–8660. For a review of supramolecular sensors:Hembury, G. A.; Borovkov, V. V.; Inoue, Y. *Chem. Rev.* **2008**, *108*, 1–73.

(6) Das, N.; Ghosh, A.; Singh, O. M.; Stang, P. J. *Org. Lett.* **2006**, *8*, 1701–1704.

(7) Sciebura, J.; Skowronek, P.; Gawronski, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 7069–7072.

(8) Katoono, R.; Kawai, H.; Fujiwara, K.; Suzuki, T. *J. Am. Chem. Soc.* **2009**, *131*, 16896–16904.

(9) (a) Waki, M.; Abe, H.; Inouye, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 3059–3061. (b) Tartaglia, S.; Pace, F.; Scafato, P.; Rosini, C. *Org. Lett.* **2008**, *10*, 3421–3424. (c) Kim, H.; So, S. M.; Yen, C. P.-H.; Vinhato, E.; Lough, A. J.; Hong, J.-I.; Kim, H.-J.; Chin, J. *Angew. Chem., Int. Ed.* **2008**, *47*, 8657–8660.

(10) (a) Allenmark, S. *Chirality* **2003**, *15*, 409–422. (b) Gawronski, J.; Grajewski, J. *Org. Lett.* **2003**, *5*, 3301–3303. (c) Berova, N.; Di Bari, L.; Pescitelli, G. *Chem. Soc. Rev.* **2007**, *36*, 914–931.

(11) (a) Kikuchi, Y.; Kobayashi, K.; Aoyama, Y. *J. Am. Chem. Soc.* **1992**, *114*, 1351–1358. (b) Katoono, R.; Kawai, H.; Fujiwara, K.; Suzuki, T. *Tetrahedron Lett.* **2006**, *47*, 1513–1518. (c) Waki, M.; Abe, H.; Inouye, M. *Angew. Chem., Int. Ed.* **2007**, *46*, 3059–3061.

(12) (a) Tsukube, H.; Hosokubo, M.; Wada, M.; Shinoda, S.; Tamiaki, H. *J. Chem. Soc., Dalton Trans.* **1999**, 11–12. (b) Borovkov, V. V.; Lintuluoto, J. M.; Inoue, Y. *J. Am. Chem. Soc.* **2001**, *123*, 2979–2989. (c) Kurtan, T.; Nesnas, N.; Li, Y.-Q.; Huang, X.; Nakanishi, K.; Berova, N. *J. Am. Chem. Soc.* **2001**, *123*, 5962–5973. (d) Kurtan, T.; Nesnas, N.; Koehn, F. E.; Li, Y.-Q.; Nakanishi, K.; Berova, N. *J. Am. Chem. Soc.* **2001**, *123*, 5974–5982. (e) Zhang, J.; Holmes, A. E.; Sharma, A.; Brooks, N. R.; Rarig, R. S.; Zubieta, J.; Canary, J. W. *Chirality* **2003**, *15*, 180–189. (f) Proni, G.; Pescitelli, G.; Huang, X.; Nakanishi, K.; Berova, N. *J. Am. Chem. Soc.* **2003**, *125*, 12914–12927. (g) Yang, Q.; Olmsted, C.; Borhan, B. *Org. Lett.* **2002**, *4*, 3423–3426. (h) Proni, G.; Pescitelli, G.; Huang, X.; Quaraishi, N. Q.; Nakanishi, K.; Berova, N. *Chem. Commun.* **2002**, 1690–1691. (i) Huang, X.; Fujioka, N.; Pescitelli, G.; Koehn, F. E.; Williamson, R. T.; Nakanishi, K.; Berova, N. *J. Am. Chem. Soc.* **2002**, *124*, 10320–10335. (j) Tamiaki, H.; Unno, S.; Takeuchi, E.; Tameshige, N.; Shinoda, S.; Tsukube, H. *Tetrahedron* **2003**, *59*, 10477–10483. (k) Ishii, H.; Chen, Y.; Miller, R. A.; Karady, S.; Nakanishi, K.; Berova, N. *Chirality* **2005**, *17*, 305–315. (l) Balaz, M.; De Napoli, M.; Holmes, A. E.; Mammana, A.; Nakanishi, K.; Berova, N.; Purrello, R. *Angew. Chem., Int. Ed.* **2005**, *44*, 4006–4009. (m) Holmes, A. E.; Das, D.; Canary, J. W. *J. Am. Chem. Soc.* **2007**, *129*, 1506–1507. (n) Berova, N.; Pescitelli, G.; Petrovic, A. G.; Proni, G. *Chem. Commun.* **2009**, 5958–5980. (o) Canary, J. W.; Mortezaei, S.; Liang, J. *Chem. Commun.* **2010**, *46*, 5850–5860.

(13) (a) Superchi, S.; Casarini, D.; Laurita, A.; Bavoso, A.; Rosini, C. *Angew. Chem., Int. Ed.* **2001**, *40*, 451–454. (b) Hosoi, S.; Kamiya, M.; Kiuchi, F.; Ohta, T. *Tetrahedron Lett.* **2001**, *42*, 6315–6317. (c) Mazaleyrat, J.-P.; Wright, K.; Gaucher, A.; Toulemonde, N.; Wakselman, M.; Oancea, S.; Peggion, C.; Formaggio, F.; Setnicka, V.; Keiderling, T. A.; Toniolo, C. *J. Am. Chem. Soc.* **2004**, *126*, 12874–12879. (d) Mazaleyrat, J.-P.; Wright, K.; Gaucher, A.; Toulemonde, N.; Dutot, L.; Wakselman, M.; Broxterman, Q. B.; Kaptein, B.; Oancea, S.; Peggion, C.; Crisma, M.; Formaggio, F.; Toniolo, C. *Chem.—Eur. J.* **2005**, *11*, 6921–6929. (e) Superchi, S.; Bisaccia, R.; Casarini, D.; Laurita, A.; Rosini, C. *J. Am. Chem. Soc.* **2006**, *128*, 6893–6902. (f) Dutot, L.; Wright, K.; Gaucher, Wakselman, M.; Mazaleyrat, J.-P.; De Zotti, M.; Peggion, C.; Formaggio, F.; Toniolo, C. *J. Am. Chem. Soc.* **2008**, *130*, 5986–5992.

(14) For a discussion of the general significance of molecular sensing, see: Anslyn, E. V. *J. Am. Chem. Soc.* **2010**, *132*, 15833–15835.

(15) (a) Wolf, C.; Ghebramariam, B. T. *Tetrahedron: Asymmetry* **2002**, *13*, 1153–1156. (b) Wolf, C.; Tumambac, G. E. *J. Phys. Chem. A.* **2003**, *107*, 815–817. (c) Tumambac, G. E.; Wolf, C. *J. Org. Chem.* **2004**, *69*, 2048–2055. (d) Tumambac, G. E.; Mei, X.; Wolf, C. *Eur. J. Org. Chem.* **2004**, 3850–3856. (e) Wolf, C. *Chem. Soc. Rev.* **2005**, *34*, 595–608. (f) Tumambac, G. E.; Wolf, C. *J. Org. Chem.* **2005**, *70*, 2930–2938. (g) Wolf, C.; Xu, H. *Tetrahedron Lett.* **2007**, *48*, 6886–6889.

(16) (a) Mei, X.; Wolf, C. *Chem. Commun.* **2004**, 2078–2079. (b) Mei, X.; Wolf, C. *J. Am. Chem. Soc.* **2004**, *126*, 14736–14737. (c) Tumambac, G. E.; Wolf, C. *Org. Lett.* **2005**, *7*, 4045–4048. (d) Mei, X.; Martin, R. M.; Wolf, C. *J. Org. Chem.* **2006**, *71*, 2854–2861. (e) Liu, S.; Pestano, J. P. C.; Wolf, C. *J. Org. Chem.* **2008**, *73*, 4267–4270. (f) Mei, X.; Wolf, C. *Tetrahedron Lett.* **2006**, *47*, 7901–7904. (g) Wolf, C.; Liu, S.; Reinhardt, B. C. *Chem. Commun.* **2006**, 4242–4244. (h) Mei, X.; Wolf, C. *J. Am. Chem. Soc.* **2006**, *128*, 13326–13327. (i) Liu, S.; Pestano, J. P. C.; Wolf, C. *J. Org. Chem.* **2008**, *73*, 4267–4270. (j) Ghosn, M. W.; Wolf, C. *J. Am. Chem. Soc.* **2009**, *131*, 16360–16361. (k) Ghosn, M. W.; Wolf, C. *Tetrahedron* **2010**, *66*, 3989–3994.

(17) For CD analysis of amines with chiral metal complexes, see: (a) Nieto, S.; Lynch, V. M.; Anslyn, E. V.; Kim, H.; Chin, J. *Org. Lett.* **2008**, *10*, 5167–5170. (b) Nieto, S.; Lynch, V. M.; Anslyn, E. V.; Kim, H.; Chin, J. *J. Am. Chem. Soc.* **2008**, *130*, 9232–9233. (c) Nieto, S.; Dragna, J. M.; Anslyn, E. V. *Chem.—Eur. J.* **2010**, *16*, 227–232.