Stereoselective Sensing by Substrate-Controlled *syn*/*anti* Interconversion of a Stereodynamic Fluorosensor

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A stereoselective sensing method that is based on the unique stereodynamic and photochemical properties of 1,8-diquinolylnaphthalenes has been developed. The ability to undergo substrate-induced *syn*/*anti* interconversion and the striking difference in the fluorescence intensity of the *syn* and *anti* isomers of 1,8-bis(2-isopropyl-4-quinolyl)naphthalene (**1**) have been utilized for stereoselective sensing of the isomers of 1,2-diaminocyclohexane (**5**). The conformational stability of **1** at room temperature greatly facilitated spectroscopic and crystallographic studies of this new prototype of stereodynamic fluorosensors. Fluorescence measurements of the *anti* and *syn* isomer of **1** revealed a quantum yield of 11.6% and 2%, respectively. NMR spectroscopy experiments confirmed that *trans*-**5** stabilizes the C_2-symmetric *anti* isomers of **1**, whereas *cis*-**5** favors formation of the less fluorescent meso *syn*-**1** isomer, which results in a reduced fluorescence response.

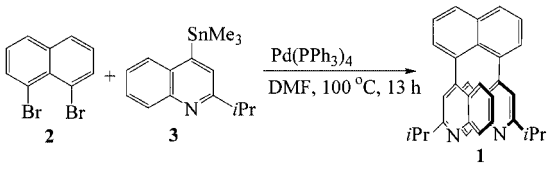
Introduction

Sterically crowded aromatic compounds have been incorporated into optoelectronic devices, rotors, and chemical sensors because of their unique stereochemical, electronic, and photochemical properties.[1] Recently, the stereodynamics of congested atropisomeric 1,8-disubstituted naphthalene derivatives have received considerable attention.[2] Alkyl,[3] aryl,[4] and heteroaryl[5] groups have been introduced into the *peri* positions of naphthalene to determine the energy barrier for rotation about the naphthyl−alkyl or naphthyl−aryl axis and to investigate intramolecular interactions between stacked aryl groups.

Fluorescent 1,8-bis(heteroaryl)naphthalenes exhibiting conformational stability and rigidity at room temperature as well as the ability to undergo hydrogen bonding to organic compounds have been considered to afford new chiroptical switches that undergo photoenantiomerization upon irradiation of circularly polarized light.[6] Stereoselective fluorosensors have received increasing attention because fluorescence spectroscopy provides different detection modes (fluorescence quenching, enhancement, and lifetime), high sensitivity, low cost of instrumentation, waste reduction, time efficiency, and the possibility of performing real-time analysis. As a consequence of the high sensitivity inherent to fluorescence spectroscopy only a very small amount of the sensor is required, which makes this technique cost-effective and practicable. To date, few stereoselective fluorescence sensors[7] including chiral macrocycles,[8] dendrimers,[9] or oligomers[10] have been reported. Enantioselectivity in energy transfer reactions between a variety of chiral quencher molecules and photoexcited chiral lanthanide chelates has also been observed by time-resolved or steady-state circularly polarized luminescence measurements.[11] Stereoselective luminescent sensing based on indicator-displacement assays has been recently reported to provide a promising entry to high-throughput screening of chiral catalysts.[12] Herein, we wish to report the use of sterically crowded 1,8-bis(2-isopropyl-4-quinolyl)naphthalene (**1**) as a prototype of stereodynamic fluorosensors capable of stereoselective recognition.

Results and Discussion

According to a synthetic strategy towards atropisomeric 1,8-diacridylnaphthalenes developed in our laboratory,[13] we recently reported the synthesis of axially chiral 1,8-bis(2-isopropyl-4-quinolyl)naphthalene (**1**) by $Pd(PPh_3)_4$-catalyzed and CuO-promoted cross-coupling of 1,8-dibromonaphthalene (**2**) and 2-isopropyl-4-(trimethylstannyl)quinoline (**3**) in 42% yield (Scheme 1).[14]



Scheme 1. Synthesis of 1,8-bis(2-isopropyl-4-quinolyl)naphthalene (**1**)

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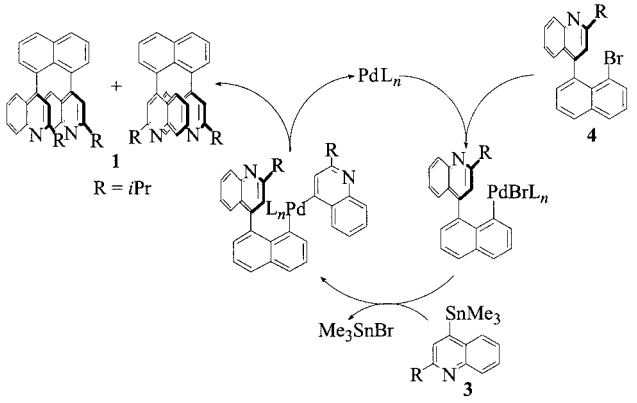
The formation of **1** requires two consecutive Stille couplings involving sterically crowded Pd complexes, in particular during the Pd-catalyzed reaction between the intermediate 1-bromo-8-(2-isopropylquinolyl)naphthalene (**4**) and a second equivalent of stannane **3** (Scheme 2). During the first and presumably less hindered coupling step, quinolylstannane **3** and dibromide **2** give bromide **4**, which enters another coupling cycle. Diquinolylnaphthalene **1** is produced by oxidative addition of bromide **4** to the Pd^0 catalyst and subsequent transmetallation with stannane **3** to afford a crowded Pd complex, which undergoes reductive elimination. The overall yield of this procedure is remarkably high considering the steric repulsion during the two catalytic steps and the strain inherent to **1**.



Scheme 2. Catalytic cycle of the Stille coupling step between 1-bromo-8-(2-isopropylquinolyl)naphthalene (**4**) and stannane **3**

NMR spectroscopy and HPLC studies, in conjunction with crystallographic identification of the *anti* conformer, reveal that the C_2-symmetric *anti* isomers of **1** are thermodynamically more stable than the *meso-syn* isomer, vide infra. The ratio of the two enantiomeric *anti* atropisomers to the *syn* isomer was determined as 8.6:1 in DMSO by NMR analysis. The atropisomers of **1** proved to be conformationally stable at room temperature but showed slow *syn*/*anti* interconversion at elevated temperature (Figure 1).[15] Kinetic studies revealed a Gibbs activation energy, $\Delta G^{\neq}$, of 115.2 (111.1) kJ/mol for the conversion of the *anti* (*syn*) to the *syn* (*anti*) isomer at 66.2 °C.[14]

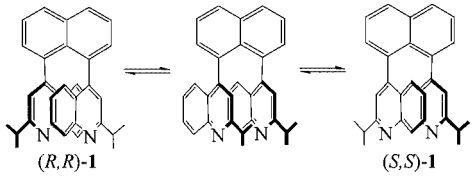


Figure 1. Interconversion of *anti* and *syn* isomers of **1**

We were able to grow a monoclinic single crystal of racemic *anti*-**1** belonging to the *C*2 space group through slow diffusion of diethyl ether into a dichloromethane solution of the chromatographically purified atropisomer at room temperature (Table 1).[16] Crystallographic analysis revealed a C_2-symmetric structure exhibiting two antiplanar quinolyl rings that are almost perpendicular to the naphthalene moiety (Figure 2). The quinolyl moieties are slightly splayed and twisted to reduce electronic repulsion and dipole−dipole interactions between the rings. The distance between the two quinolyl nitrogen atoms was determined to be 3.86 Å. The close proximity of the two heteroaryl rings is a consequence of the highly congested structure of **1**, albeit it might partly be attributed to packing forces.

Table 1. Selected crystallographic data of **1**

Empirical formula	$C_{34}H_{30}N_2$
Formula mass	466.60
Crystal system	monoclinic
Space group	*C*2
Unit cell dimensions	*a* = 15.540(2) Å *b* = 12.2484(15) Å *c* = 14.8766(19) Å β = 117.288(2)°
Volume	2516.4(6) Å^3
Z	4
Density (calculated)	1.232 g cm^{-3}
Crystal size	0.50 × 0.50 × 0.30 mm

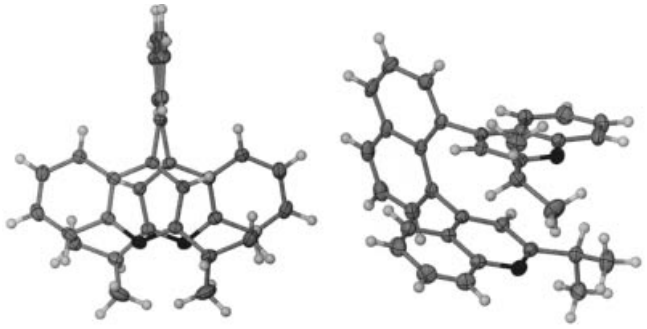


Figure 2. Single crystal structure of *anti*-**1**; the view along the naphthalene ring (left) shows the twisting of the quinolyl rings; the side view (right) reveals the splaying of the heteroaryl rings

Atropisomer **1** combines three important features invaluable for developing stereodynamic fluorosensors: (1) a sufficient conformational stability for the determination of photochemical and stereochemical properties of isolated stereoisomers at room temperature by NMR and fluorescence spectroscopy and single-crystal X-ray crystallography; (2) structural simplicity that facilitates studies of the stereoselective recognition mechanism; (3) the ability to undergo temperature-controlled interconversion. The geometry of the *syn* and *anti* isomers of 1,8-diquinolylnaphthalene (**1**) exhibits a unique bidentate ligand structure. The spatial arrangement of the 2-isopropylquinolyl rings affords a well-defined binding environment for stereoselective recognition of hydrogen-bond-donating compounds. Fluorescence studies reveal an emission maximum of 380 nm for both isomers of **1**, and a considerably higher quantum yield for *anti*-**1** than for its *syn* isomer. The quantum yield of *syn*-**1** and *anti*-**1** were determined as 2.0 and 11.6%, respectively. Because we were not able to obtain a single crystal of the *syn* isomer, we used PM3 calculations to compare the ground state structure of the diastereoisomers of **1**. The

computations of *anti*-**1** show a slightly twisted and splayed orientation of antiparallel heteroaryl rings, which is in good agreement with its single crystal structure (Figure 3).

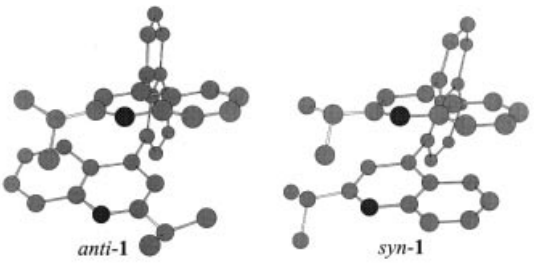


Figure 3. Ground state of *syn*- and *anti*-**1** optimized by PM3 calculations

Comparison of the geometry of *syn*- and *anti*-**1** shows strikingly different coordination environments. The isopropyl groups occupy two quadrants on the same side of the quinolyl nitrogen atoms in the *meso* form and two opposite quadrants in the C_2-symmetric *anti* isomers (Figures 2 and 3). We anticipated that *syn*-**1** would undergo stronger interactions with a bidentate hydrogen-bond donor exhibiting *cis* configuration, whereas *anti*-**1** would undergo stronger hydrogen bonding to a *trans* isomer. The *cis* and *trans* isomers of 1,2-diaminocyclohexane (**5**) were therefore employed in fluorescence titration experiments with *anti*-**1** in acetonitrile. We did not observe any significant change of the fluorescence emission intensity of *syn*- and *anti*-**1** in the presence of *cis*- or *trans*-**5**. Because of the striking difference in the fluorescence quantum yield of *syn*- and *anti*-**1** and its ability to undergo isomerization at elevated temperature, we decided to heat the sensor in the presence of either *cis*- or *trans*-**5** in order to investigate its use as a stereodynamic sensor. We observed a linear Stern−Volmer plot indicating moderate quenching after heating *anti*-**1** in the presence of a commercially available mixture of 95% *trans*- and 5% *syn*-**5** (Figure 4). The thermodynamic *anti*/*syn* equilibrium of **1** in acetonitrile in the absence of **5** was determined as 5:1 (83.3% *anti*-**1** and 16.7% *syn*-**1**) by NMR spectroscopy.[17] Accordingly, thermal isomerization to 16.7% *syn*-**1** thus accounts for approximately 14% quenching as a consequence of the inherently lower quantum yield of the *syn* isomer.[18] The small additional quenching effect observed in the presence of 95% *trans*-**5** can be attributed to some *anti*/*syn* isomerization of **1** induced by the 5% *cis*-**5** impurity.

We were pleased to find that heating of **1** in the presence of *cis*-**5** results in significantly stronger fluorescence quenching. The nonlinear Stern-Volmer plot exhibiting a sigmoidal curve can be explained by substrate-induced isomerization of *anti*-**1** to considerable amounts of less fluorescent *syn*-**1**. A comparison of the structure of the sensor and substrate isomers suggests that the amino groups of *cis*-**5** can participate in simultaneous hydrogen bonding to the two quinolyl nitrogen atoms of *syn*-**1**, whereas coordination to *anti*-**1** is impeded by steric repulsion between the cyclohexyl backbone of the approaching diamine and one isopropyl group of the sensor (Figure 5). The different thermodynamic stabilities of the two complexes, which are interconverting at 80 °C, therefore favors formation of *syn*-**1** during isomerization.

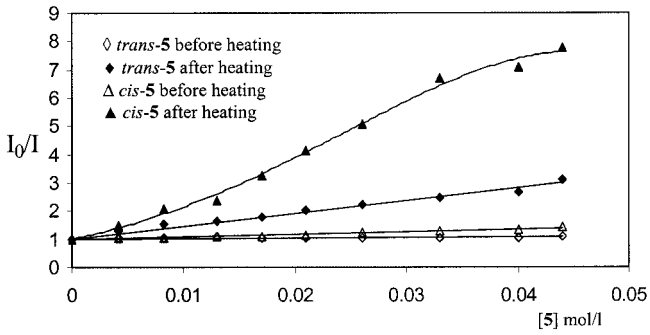


Figure 4. Fluorescence titration of *anti*-**1** in the presence of *cis*- or *trans*-**5** before and after heating in acetonitrile at 80 °C for 12 h; the concentration of **1** was 4.3×10^{-5} M; excitation wavelength: 320 nm, emission wavelength: 380 nm

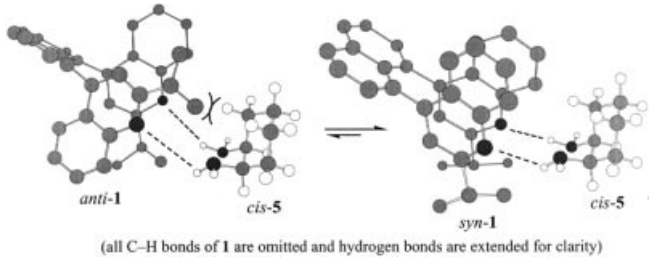


Figure 5. Interconversion of *anti*- to *syn*-**1** induced by *cis*-**5**

By contrast, *trans*-**5** can avoid significant steric repulsion during hydrogen bonding to *anti*-**1** by placing the axial hydrogen atoms attached to the stereogenic centers into the unoccupied quadrants of the sensor molecule (Figure 6). Exhibiting the same C_2 symmetry as *anti*-**1**, *trans*-**5** thus stabilizes the more fluorescent *anti* isomer of the sensor, which explains the moderate quenching effect after heating. The stereoselective fluorescence sensing of *cis*- and *trans*-**5** is therefore a consequence of substrate-controlled *syn*/*anti* interconversion of the stereodynamic sensor combined with a striking difference in the quantum yield of the *syn* and *anti* isomers of **1**.

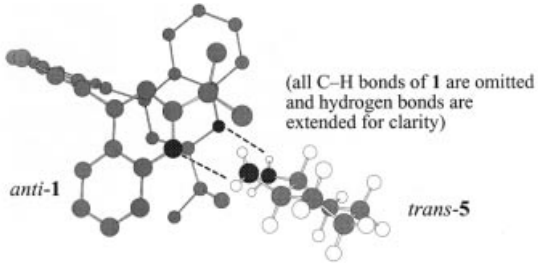


Figure 6. Hydrogen bonding between (*R*,*R*)-*anti*-**1** and (*R*,*R*)-*trans*-**5**

To verify the proposed substrate-induced isomerization of **1** observed by fluorescence spectroscopy, we heated a solution of sensor **1** and 10 equiv. of *trans*-**5** to 80 °C for 12 h in acetonitrile, and determined the isomer interconversion by NMR analysis. We found that the *anti*/*syn* ratio of **1** increases from 5.0:1 to 6.3:1. By contrast, we observed that the *anti*/*syn* ratio of the diquinolylnaphthalene decreases to 4.2:1 in the presence of *cis*-**5** under the same conditions, i.e. NMR results are in good agreement with the fluorescence measurements (Figure 7).[19] It should be noted that the configurational isomers of **5** do not exhibit sterically demanding groups near their hydrogen-bonding sites and are expected to engage **1** in energetically similar interactions. The low steric demand of *cis*- and *trans*-**5** should therefore result in moderate stereodynamic sensing selectivity. The isomerization of sensor **1** induced by the *cis* and *trans* isomers of **5** at elevated temperature is therefore quite remarkable and indicates the potential of this sensing method.

Conclusion

In summary, we have developed a stereodynamic fluorosensor that undergoes selective recognition of the *cis* and *trans* isomers of 1,2-diaminocyclohexane (**5**), through substrate-controlled interconversion between its *syn* and *anti* isomers exhibiting strikingly different fluorescence quantum yields. The conformational stability of **1** at room temperature greatly facilitates the spectroscopic and crystallo-

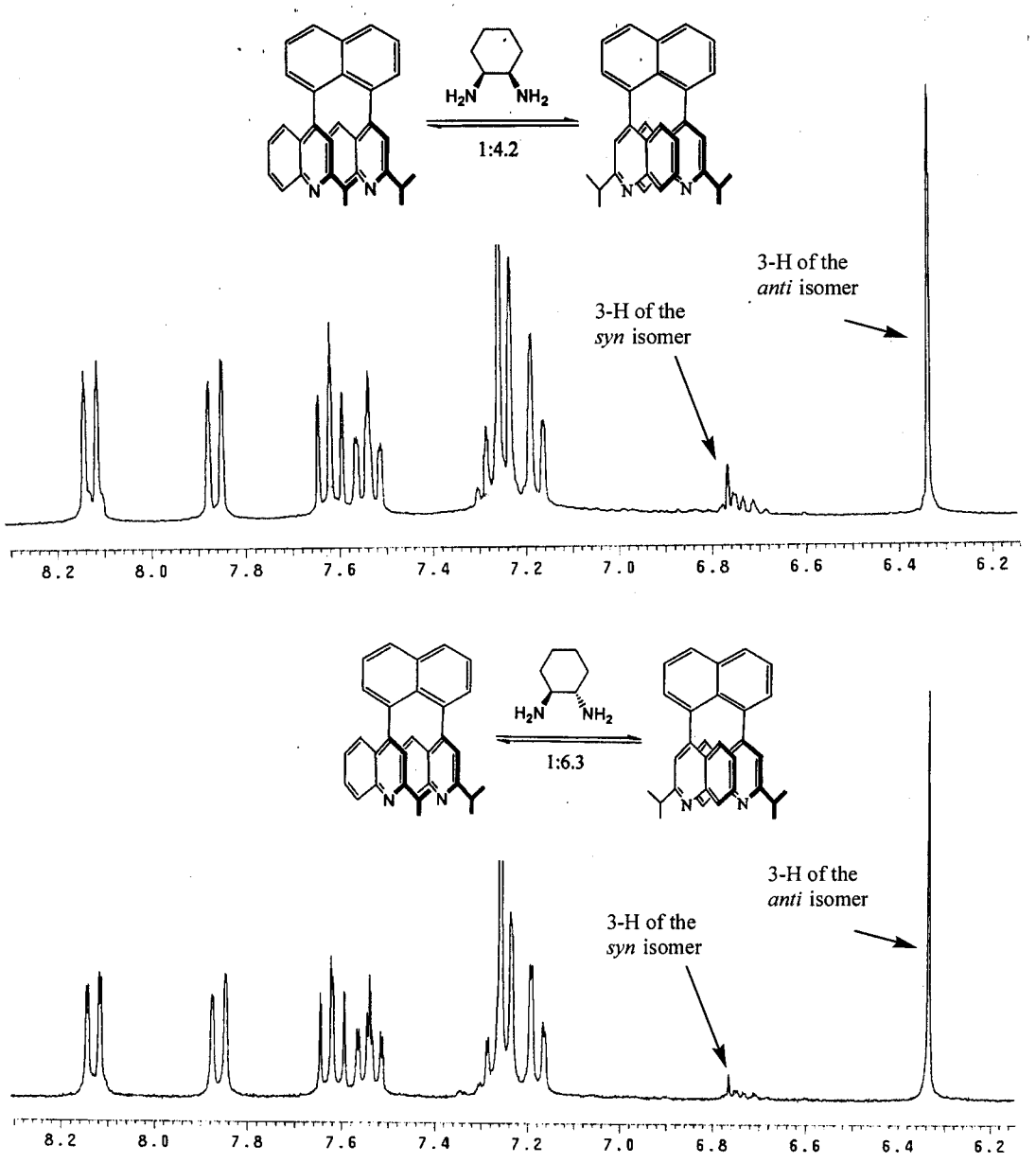


Figure 7. ^{1}H NMR spectra of the aromatic signals of sensor **1** after heating in acetonitrile to 80 °C for 12 h in the presence of *cis*- (top) and *trans*-**5** (bottom); the concentration of **1** was 8.0×10^{-5} M and the concentration of **5** was 8.0×10^{-4} M

graphic analysis of the unique photochemical and stereochemical properties of this class of compounds, which will be invaluable for the design of stereodynamic sensors that operate at lower temperature. The development of conformationally less stable analogs of diquinolylnaphthalene **1** for stereodynamic sensing of diastereoisomers, such as *cis*- and *trans*-**5** or enantiomers of chiral compounds, based on fluorescence spectroscopy or induced circular dichroism is currently underway in our laboratories.

Experimental Section

Materials and Methods: All commercially available reagents and solvents were used without further purification. 4-Iodo-2-isopropylquinoline was prepared as described previously.[20] 1,8-Dibromonaphthalene was prepared from 1,8-diaminonaphthalene as described in the literature.[21] All reactions were carried out under nitrogen and under anhydrous conditions. Sensor **1** and stannane **3** were purified by flash chromatography on SiO_2 (particle size 0.032−0.063 mm). Organostannanes are highly toxic and should only be used in a vented hood, and when wearing eye and skin protection. NMR spectra were obtained at 300 MHz (^1H NMR) and 75 MHz (^{13}C NMR) with a Varian FT NMR spectrometer using $CDCl_3$ as the solvent. Chemical shifts are reported in ppm relative to TMS. Atmospheric pressure chemical ionization (APCI) mass spectra were collected with a YMC-Pack CN column (4.6 × 250 mm) using an HPLC/MSD system equipped with electrospray and atmospheric pressure chemical ionization MS detection and hexane/EtOH (9:1) as the mobile phase. Elemental analysis data were collected using a Perkin−Elmer 2400 CHN.

Preparation of 2-Isopropyl-(4-trimethylstannyl)quinoline (3): A solution of 4-iodo-2-isopropylquinoline (2.0 g, 6.7 mmol) in anhydrous ether (25 mL) was cooled to −78 °C under nitrogen. A solution of BuLi in hexane (5.0 mL, 1.6 M in hexane) was added dropwise. After completion of the lithiation reaction, Me_3SnCl (10.0 mL, 1.0 M in hexanes) was added at once, and the reaction mixture was allowed to reach room temperature. The mixture was stirred for another 5 h, quenched with 10% NH_4OH and extracted with CH_2Cl_2. The combined organic layers were dried with $MgSO_4$ and concentrated in vacuo. Purification of the residue by flash chromatography (hexane/ethyl acetate/triethylamine, 150:10:1) afforded **3** (1.7 g, 78%) as a viscous yellow oil. ^1H NMR: δ = 0.46 (s, 9 H), 1.40 (d, *J* = 6.9 Hz, 6 H), 3.22 (sept, *J* = 6.9 Hz, 1 H), 7.44 (s, 1 H), 7.47 (ddd, *J* = 1.4 Hz, 6.9 Hz, 1 H), 7.65 (ddd, *J* = 1.4 Hz, 6.9 Hz, 8.4 Hz, 1 H), 7.72 (dd, *J* = 1.4 Hz, 8.0 Hz, 1 H), 8.04 (dd, *J* = 1.4 Hz, 8.4 Hz, 1 H) ppm. ^{13}C NMR: δ = −8.5, 22.6, 37.4, 125.4, 127.8, 128.7, 129.3, 130.2, 132.4, 147.3, 153.9, 165.2 ppm. EI-MS (70 ev): *m*/*z* (%) = 335 (26) [M^+], 320 (100) [M^+ − Me], 305 (15) [M^+ − 2 Me], 290 (35) [M^+ − Me], 275 (5) [M^+ − 4 Me], 170 (30) [M^+ − Me_3Sn], 155 (10) [M^+ − Me − Me_3Sn]. $C_{15}H_{21}NSn$ (334.0): calcd. C 53.93, H 6.34, N 4.19; found C 53.67, H 6.70, N 4.19.

Preparation of 1,8-Bis(2-isopropyl-4-quinolyl)naphthalene (1): 2-Isopropyl-(4-trimethylstannyl)quinoline (400 mg, 1.2 mmol) was added to a mixture of 1,8-dibromonaphthalene (0.10 g, 0.34 mmol), $Pd(PPh_3)_4$ (44 mg, 11.2 mol %), and CuO (0.10 g, 1.3 mmol) in anhydrous DMF (4 mL). The reaction mixture was stirred at 100 °C for 13 h, cooled to room temperature, quenched with 10% NH_4OH, and extracted with diethyl ether. The combined organic layers were dried with $MgSO_4$ and concentrated under vacuum. The residue was purified by flash chromatography (hexane/ethyl acetate/triethylamine, 100:20:1). ^1H NMR (*anti* isomer): δ = 0.80 (d, *J* = 6.9 Hz, 6 H), 0.98 (d, *J* = 6.9 Hz, 6 H), 2.34 (sept, *J* = 6.9 Hz, 2 H), 6.34 (s, 2 H), 7.18 (dd, *J* = 1.1 Hz, 8.2 Hz, 2 H), 7.23−7.29 (m, 4 H), 7.54 (ddd, *J* = 1.4 Hz, 6.7 Hz, 8.4 Hz, 2 H), 7.62 (dd, *J* = 7.1 Hz, 8.2 Hz, 2 H), 7.87 (d, *J* = 8.5 Hz, 2 H), 8.13 (dd, *J* = 1.4 Hz, 8.4 Hz, 2 H) ppm. ^1H NMR (*syn* isomer): δ = 1.26 (d, *J* = 6.9 Hz, 6 H), 1.31 (d, *J* = 6.9 Hz, 6 H), 2.98 (sept, *J* = 6.9 Hz, 2 H), 6.69−6.79 (m, 4 H), 6.77 (s, 2 H), 7.20 (dd, *J* = 1.1 Hz, 8.2 Hz, 2 H), 7.54 (ddd, *J* = 1.4 Hz, 6.7 Hz, 8.4 Hz, 2 H), 7.62 (dd, *J* = 7.1 Hz, 8.2 Hz, 2 H), 7.87 (d, *J* = 8.5 Hz, 2 H), 8.12 (dd, *J* = 1.4 Hz, 8.4 Hz, 2 H) ppm. ^{13}C NMR (mixture of *syn* and *anti* isomer): δ = 21.1, 21.2, 22.5, 22.7, 36.1, 36.2, 119.8, 120.1, 125.1, 125.3, 125.3, 125.4, 125.6, 125.9, 126.1, 126.4, 126.6, 128.4, 129.2, 129.3, 129.4, 129.5, 129.6, 130.49, 130.6, 130.9, 131.1, 131.6, 134.4, 135.7, 146.7, 147.9, 148.2, 164.9, 165.5 ppm. EI-MS: *m*/*z* (%) = 466 (100) [M^+], 451 (94) [M^+ − Me], 436 (5) [M^+ − 2 Me], 423 (23) [M^+ − *i*Pr], 253 (5) [M^+ − isopropylquinolyl]. LC-APCI-MS: *m*/*z* (%) = 467 (100) [M + H]$^+$. $C_{34}H_{30}N_2$ (466.6): calcd. C 87.52, H 6.48, N 6.00; found C 87.16, H 6.43, N 5.96.

X-ray Crystallography: A single crystal of **1** was obtained by slow diffusion of diethyl ether into a dichloromethane solution of the chromatographically purified *anti* isomer at room temperature. Single crystal X-ray diffractions were collected at −100 °C with graphite-monochromated Mo-K_α radiation (λ = 0.71073 Å). The structures were solved by direct methods and refined with full-matrix least squares/difference Fourier analysis using SHELX-97-2 software. Non-hydrogen atoms were refined with anisotropic displacement parameters, and all hydrogen atoms were placed in calculated positions and refined with a riding model. Data were corrected for the affects of absorption using SADABS.

Fluorescence Spectroscopy: Fluorescence experiments were conducted under nitrogen with a Fluoromax-2 apparatus from Instruments S. A. Inc. All fluorescence experiments were conducted using carefully degassed acetonitrile. The quantum yield of the isomers of **1** was determined according to literature procedures.[22] 1,8-Bis(2-isopropyl-4-quinolyl)naphthalene (**1**) was excited at 320 nm, and relative integrated intensities of the emission spectra were relative to naphthalene, which has a quantum yield of 0.2 in acetonitrile. Fluorescence measurements of the *anti* and *syn* isomer of **1** revealed identical emission spectra in acetonitrile albeit with different intensity (Figure 8). The quantum yield of *anti*- and *syn*-**1** was determined as 11.6% and 2%, respectively. The *cis* and *trans* isomers of 1,2-diaminocyclohexane (**5**) were recrystallized prior to use to rule out any influence of possible oxidation impurities of **5** on the fluorescence response of **1**. Fluorescence experiments with *anti*-**1** in the presence of *cis*- or *trans*-**5** were performed before and after heating in acetonitrile at 80 °C under an inert gas for 12 h. The concentration of the sensor was 4.3×10^{-5} M. The excitation wavelength was 320 nm, and the fluorescence emission maximum was 380 nm. A change in the emission intensity or a shift of the excitation maximum of *syn*- and *anti*-**1** in the presence of diaminocyclohexane **5** was not observed. The observed quenching effects can therefore be attributed to a change in the *syn*/*anti* ratio of the stereodynamic sensor, which was confirmed by NMR spectroscopy. The fluorescence lifetime of *anti*-**1** in acetonitrile was determined to be 1.56 ns. Frequency domain data were obtained with a 10 GHz frequency domain fluorometer.[23] The modulated excitation was provided by the harmonic content of a LASER pulse train with a repetition rate of 3.81326 MHz and a pulse width of 7 ps from a synchronously pumped and cavity dumped pyridine 1 dye LASER. The dye LASER was pumped with a mode-locked Ar ion LASER

(coherent). The dye LASER output was frequency doubled to 340 nm for excitation of **1**. The emitted fluorescence was observed through a glass long-wave pass filter ($\lambda_{obs} > 380$ nm). The fluorescence intensity decay data were fitted to the multi-exponential model $I(t) = \Sigma\alpha_i \exp(-t/\tau_i)$, where τ_i are the individual decay times and α_i are the associated pre-exponential factors. The parameters were recovered by nonlinear least squares using the theory and software described elsewhere.[24]

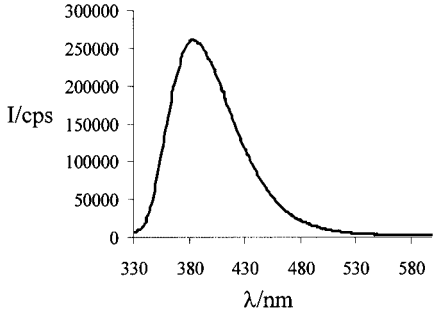


Figure 8. Fluorescence spectrum of 1,8-bis(2-isopropyl-4-quinolyl)-naphthalene (**1**) in acetonitrile; the concentration was 3.2×10^{-5} M and the excitation wavelength was 320 nm

Acknowledgments

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[1] [1a] X. Qiao, M. A. Padula, D. M. Ho, N. J. Vogelaar, C. E. Schutt, R. A. Pascal, Jr., *J. Am. Chem. Soc.* **1996**, *118*, 741−745. [1b] Z. Dominguez, H. Dang, M. J. Strouse, M. A. Garcia-Garibay, *J. Am. Chem. Soc.* **2002**, *124*, 7719−7727. [1c] L. J. Charbonniere, R. Ziessel, M. Montalti, L. Prodi, N. Zaccheroni, C. Boehme, G. Wipff, *J. Am. Chem. Soc.* **2002**, *124*, 7779−7788. [1d] K.-T. Wong, Y.-Y. Chien, R.-T. Chen, C.-F. Wang, Y.-T. Lin, H.-H. Chiang, P.-Y. Hsieh, C.-C. Wu, C. H. Chou, Y. O. Su, G.-H. Lee, S.-M. Peng, *J. Am. Chem. Soc.* **2002**, *124*, 11576−11577. [1e] R. Rathore, M. I. Deselnicu, C. L. Burns, *J. Am. Chem. Soc.* **2002**, *124*, 14832−14833.

[2] [2a] D. Casarini, L. Lunazzi, D. Macciantelli, *Tetrahedron Lett.* **1984**, *25*, 3641−3642. [2b] D. Casarini, L. Lunazzi, *J. Org. Chem.* **1988**, *53*, 182−185. [2c] D. Casarini, E. Foresti, L. Lunazzi, D. Macciantelli, *J. Am. Chem. Soc.* **1988**, *110*, 4527−4532. [2d] D. Casarini, S. Davalli, L. Lunazzi, *J. Org. Chem.* **1989**, *54*, 4616−4619. [2e] S. Davalli, L. Lunazzi, *J. Org. Chem.* **1991**, *56*, 1739−1747. [2f] C. Villani, W. H. Pirkle, *Tetrahedron: Asymmetry* **1995**, *6*, 27−30. [2g] D. Casarini, L. Lunazzi, A. Mazzanti, *J. Org. Chem.* **1997**, *62*, 3315−3323. [2h] D. Casarini, L. Lunazzi, A. Mazzanti, *J. Org. Chem.* **1998**, *63*, 4746−4754. [2i] D. Casarini, L. Lunazzi, A. Mazzanti, *J. Org. Chem.* **1998**, *63*, 4991−4995. [2j] D. Casarini, A. Mazzanti, A. M. Alvarez, *J. Org. Chem.* **2000**, *65*, 3200−3206. [2k] R. A. Bragg, J. Clayden, G. A. Morris, J. H. Pink, *Chem. Eur. J.* **2002**, *8*, 1279−1289. [2l] C. Dell'Erba, F. Gasparrini, S. Grilli, L. Lunazzi, A. Mazzanti, M. Novi, M. Pierini, C. Tavani, C. Villani, *J. Org. Chem.* **2002**, *67*, 1663−1668. [2m] C. Wolf, L. Pranatharthiharan, R. B. Ramagosa, *Tetrahedron Lett.* **2002**, *43*, 8563−8567.

[3] [3a] D. L. Fields, T. H. Regan, *J. Org. Chem.* **1971**, *36*, 2986−2990. [3b] D. L. Fields, T. H. Regan, *J. Org. Chem.* **1971**, *36*, 2991−2995. [3c] D. L. Fields, T. H. Regan, *J. Org. Chem.* **1971**, *36*, 2995−3001.

[4] [4a] H. O. House, R. W. Magin, H. W. Thompson, *J. Org. Chem.* **1963**, *28*, 2403−2406. [4b] H. O. House, R. W. Bashe, *J. Org. Chem.* **1965**, *30*, 2942−2947. [4c] H. O. House, R. W. Bashe, *J. Org. Chem.* **1967**, *32*, 784−791. [4d] H. O. House, W. J. Campbell, M. Gall, *J. Org. Chem.* **1970**, *35*, 1815−1819. [4e] H. O. House, D. G. Koepsell, W. J. Campbell, *J. Org. Chem.* **1972**, *37*, 1003−1011. [4f] R. L. Clough, J. D. Roberts, *J. Am. Chem. Soc.* **1976**, *98*, 1018−1020. [4g] F. Cozzi, M. Cinquini, R. Annunziata, T. Dwyer, J. S. Siegel, *J. Am. Chem. Soc.* **1992**, *114*, 5729−5733. [4h] F. Cozzi, M. Cinquini, R. Annunziata, J. S. Siegel, *J. Am. Chem. Soc.* **1993**, *115*, 5330−5331. [4i] F. Cozzi, F. Ponzini, R. Annunziata, M. Cinquini, J. S. Siegel, *Angew. Chem. Int. Ed. Engl.* **1995**, *34*, 1019−1020. [4j] R. G. Pritchard, M. Steele, M. Watkinson, A. Whiting, *Tetrahedron Lett.* **2000**, *41*, 6915−6918. [4k] W. Cross, G. E. Hawkes, R. T. Kroemer, K. R. Liedl, T. Loerting, R. Nasser, R. G. Pritchard, M. Steele, M. Watkinson, A. Whiting, *J. Chem. Soc., Perkin Trans. 2* **2001**, 459−467. [4l] M. Steele, M. Watkinson, A. Whiting, *J. Chem. Soc., Perkin Trans. 1* **2001**, 588−598. [4m] C. Thirsk, G. E. Hawkes, R. T. Kroemer, K. R. Liedl, T. Loertig, R. Nasser, R. G. Pritchard, M. Steele, J. E. Warren, A. Whiting, *J. Chem. Soc., Perkin Trans. 2* **2002**, 1510−1519.

[5] [5a] J. A. Zoltewicz, N. M. Maier, W. M. F. Fabian, *Tetrahedron* **1996**, *52*, 8703−8706. [5b] J. A. Zoltewicz, N. M. Maier, W. M. F. Fabian, *J. Org. Chem.* **1996**, *61*, 7018−7021. [5c] N. M. Maier, J. A. Zoltewicz, *Tetrahedron* **1997**, *53*, 465−468. [5d] J. A. Zoltewicz, N. M. Maier, W. M. F. Fabian, *J. Org. Chem.* **1997**, *62*, 2763−2766. [5e] J. A. Zoltewicz, N. M. Maier, W. M. F. Fabian, *J. Org. Chem.* **1997**, *62*, 3215−3219. [5f] J. A. Zoltewicz, N. M. Maier, S. Lavieri, I. Ghiviriga, K. A. Abboud, *Tetrahedron* **1997**, *53*, 5379−5388. [5g] L. Ernst, P. Sakhaii, *Magn. Reson. Chem.* **2000**, *38*, 559−565. [5h] S. Lavieri, J. A. Zoltewicz, *J. Org. Chem.* **2001**, *66*, 7227−7230. [5i] C. Wolf, B. T. Ghebremariam, *Synthesis* **2002**, 749−752. [5j] C. Wolf, B. T. Ghebremariam, *Tetrahedron: Asymmetry* **2002**, *13*, 1153−1156. [5k] C. Wolf, G. E. Tumambac, *J. Phys. Chem. A.* **2003**, *107*, 815−817.

[6] B. L. Feringa, R. A. van Delden, N. Koumura, E. M. Geertsema, *Chem. Rev.* **2000**, *100*, 1789−1816.

[7] [7a] M. Irie, T. Yorozu, K. Hayashi, *J. Am. Chem. Soc.* **1978**, *100*, 2236−2237. [7b] A. Gafni, *J. Am. Chem. Soc.* **1980**, *102*, 7367−7368. [7c] T. Yorozu, K. Hayashi, M. Irie, *J. Am. Chem. Soc.* **1981**, *103*, 5480−5484. [7d] R. Corradini, G. Sartor, R. Marchelli, A. Dossena, A. Spisni, *J. Chem. Soc., Perkin Trans. 2* **1992**, 1979−1983. [7e] T. D. James, K. R. A. S. Sandanayake, S. Shinkai, *Nature* **1995**, *374*, 345−347. [7f] Y. Yan, M. L. Myrick, *Anal. Chem.* **1999**, *71*, 1958−1962. [7g] G. Beer, K. Rurack, J. Daub, *Chem. Commun.* **2001**, 1138−1139. [7h] M. Reetz, S. Sostmann, *Tetrahedron* **2001**, *57*, 2515−2520. [7i] J. Lin, Q.-S. Hu, M.-H. Xu, L. Pu, *J. Am. Chem. Soc.* **2002**, *124*, 2088−2089. [7j] L. Pu, *Chem. Rev.* **2004**, *104*, 1687−1716.

[8] [8a] P. Tundo, J. H. Fendler, *J. Am. Chem. Soc.* **1980**, *102*, 1760−1762. [8b] T. Grady, S. J. Harris, M. R. Smyth, D. Diamond, *Anal. Chem.* **1996**, *68*, 3775−3782. [8c] F. D'Souza, G. R. Deviprassad, Y.-Y. Hsieh, *Chem. Commun.* **1997**, 533−534. [8d] M. Narita, S. Mima, N. Ogawa, F. Hamada, *Anal. Sci.* **2001**, *17*, 379−385. [8e] C. Lynam, K. Jennings, K. Nolan, P. Kane, M. A. McKervey, D. Diamond, *Anal. Chem.* **2002**, *74*, 59−66. [8f] J. Lin, H.-C. Zhang, L. Pu, *Org. Lett.* **2002**, *4*, 3297−3300. [8g] S. L. Lee, W. Lin, *J. Am. Chem. Soc.* **2002**, *124*, 4554−4555.

[9] [9a] V. J. Pugh, Q.-S. Hu, L. Pu, *Angew. Chem. Int. Ed.* **2000**, *39*, 3638−3641. [9b] l.-Z. Gong, Q.-S. Hu, L. Pu, *J. Org. Chem.* **2001**, *66*, 2358−2367. [9c] V. J. Pugh, Q.-S. Hu, X. Zuo, F. D. Lewis, L. Pu, *J. Org. Chem.* **2001**, *66*, 6136−6140. [9d] M.-H. Xu, J. Lin, Q.-S. Hu, L. Pu, *J. Am. Chem. Soc.* **2002**, *124*, 14239−14246.

[10] [10a] L. Ma, P. S. White, W. Lin, *J. Org. Chem.* **2002**, *67*, 7577−7586. [10b] L. Pu, *J. Photochem. Photobiol. A: Chem.* **2003**, *155*, 47−55.
[11] [11a] D. H. Metcalf, S. W. Snyder, J. N. Demas, F. S. Richardson, *J. Am. Chem. Soc.* **1990**, *112*, 5681−5695. [11b] D. H. Metcalf, J. M. Mc Stewart, S. W. Snyder, C. M. Grisham, F. S. Richardson, *Inorg. Chem.* **1992**, *31*, 2445−2455. [11c] R. B. Rexwinkel, S. C. J. Meskers, H. P. J. M. Dekkers, J. P. Riehl, *J. Phys. Chem.* **1992**, *96*, 5725−5733. [11d] S. C. J. Meskers, H. P. J. M. Dekkers, *J. Am. Chem. Soc.* **1998**, *120*, 6413−6414. [11e] S. C. J. Meskers, H. P. J. M. Dekkers, *J. Phys. Chem. A* **2001**, *105*, 4589−4599 and references cited therein.
[12] L. Zhu, E. V. Anslyn, *J. Am. Chem. Soc.* **2004**, *126*, 3676−3677.
[13] C. Wolf, X. Mei, *J. Am. Chem. Soc.* **2003**, *125*, 10651−10658.
[14] G. E. Tumambac, C. Wolf, *J. Org. Chem.* **2004**, *69*, 2048−2055.
[15] The diastereoisomers of **1** can be separated by preferential crystallization of the *anti* isomers from diethyl ether.
[16] Despite the chiral space group *C*2 no spontaneous resolution of the enantiomers of **1** was observed. CCDC-236848 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.uk/conts/retrieving.htm or from the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223-336033; E-mail: deposit@ccdc.cam.ac.uk).
[17] A solution of *anti*-**1** that was heated to 80 °C for 16 h and the *anti*/*syn* ratio was determined through integration of well-resolved ^{1}H NMR signals.
[18] Calculated based on the 5:1 *anti*/*syn* ratio and the individual quantum yields of each isomer of **1**.
[19] Acetonitrile was removed under vacuum at room temperature to avoid isomerization of **1** and replaced by $CDCl_3$ for NMR analysis. The protons in the 3-position of the two quinolyl moieties of *syn*- and *anti*-**1** exhibit upfield shifted singlets at δ = 6.76 ppm and 6.34 ppm, respectively, and can easily be distinguished. The singlet at δ = 6.76 ppm overlaps with a multiplet of two other protons of the *syn* isomer. For accuracy, all four protons were integrated and the combined area was divided by two prior to determination of the *anti*/*syn* ratio of **1**. The ratio of the isomers of **1** measured by NMR and fluorescence spectroscopy did not change after solvent removal.
[20] C. Wolf, G. E. Tumambac, C. N. Villalobos, *Synlett* **2003**, 1801−1804.
[21] D. Seyferth, S. C. Vick, *J. Organomet. Chem.* **1977**, *141*, 178−187.
[22] G. Jones II, W. R. Jackson, C.-Y. Choi, *J. Phys. Chem.* **1985**, *89*, 294−300.
[23] G. Laczko, I. Gryczynski, Z. Gryczynski, W. Wiczk, H. Malak, J. R. Lakowicz, *Rev. Sci. Instrum.* **1990**, *61*, 2331−2337.
[24] J. R. Lakowicz, G. Laczko, H. Cherek, E. Gratton, H. Linkeman, *Biophys. J.* **1984**, *46*, 463−477.

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