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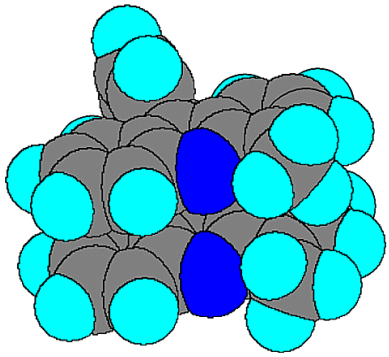

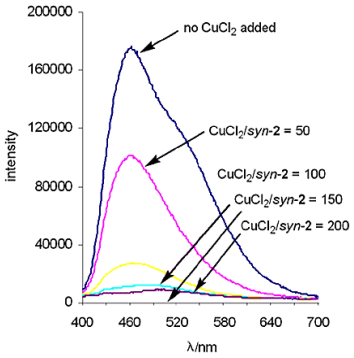

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Synthesis of Conformationally Stable 1,8-Diarylnaphthalenes: Development of New Photoluminescent Sensors for Ion-Selective Recognition

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Abstract: Highly constrained 1,8-diarylnaphthalenes exhibiting stability to isomerization have been prepared utilizing two consecutive CuO-promoted Stille cross-couplings of 1,8-dibromonaphthalene and 4-alkyl-9-trimethylstannylacridines. Screening of Pd catalysts $Pd(PPh_3)_4$, $PdCl_2$dppf, or $Pd_2(dba)_3$/*t*-Bu_3P and bases such as Cy_2NMe, *t*-BuOK, K_3PO_4, and Cs_2CO_3 in DME or DMF revealed superior results of Stille over Suzuki coupling with acridylboronic acids or pinacolate derivatives. The meso syn- and C_2-symmetric anti-isomers of 1,8-bis(4,4′-dimethyl-9,9′-diacridyl)naphthalene, **2**, and 1,8-bis(4,4′-diisopropyl-9,9′-diacridyl)-naphthalene, **3**, did not show any sign of syn/anti-interconversion after heating to 180 °C for 24 h. Using the Eyring equation, we calculated the Gibbs standard activation energy for isomerization, $\Delta G^{\circ\ddagger}$, to be higher than 180 kJ/mol. PM3 calculations of **2** and **3** suggest a highly congested structure exhibiting two parallel acridyl moieties perpendicular to the naphthalene ring. UV and fluorescence spectroscopy studies of **2** and **3** revealed remarkable quantum yields of these blue and green light emitters. Fluorescence titration experiments with the syn-isomer of **2** showed highly efficient quenching by Cu(II) ions, whereas almost no quenching effects were observed with Cu(I) and Zn(II) salts. The striking difference in fluorescence quenching was attributed to significant photoinduced electron transfer, resulting in nonradiative relaxation of excited Cu(II)-*syn*-**2**. Stern−Völmer plots of *syn*-**2** in the presence of $CuCl_2$ showed a sigmoidal quenching curve indicating cooperative recognition, whereas a linear response was observed with CuCl and $ZnCl_2$. Fluorescence experiments in the presence of various amounts of CuCl, CuBr, and $Cu(ACN)_4BF_4$ proved that the quenching is cation selective and independent of the nature of counteranions.

Introduction

The unique stereochemical, electronic, and photochemical properties of sterically congested aromatic compounds has attracted considerable attention during recent years because they afford promising optoelectronic devices, rotors, and chemical sensors.[1] The preparation of conformationally stable 1,8-diarylnaphthalenes has been an unresolved challenge since Clough and Roberts reported the synthesis of atropisomeric 1,8-bis(2,2′-dimethyl-1,1′-diphenyl)naphthalene, **1**, almost 30 years ago (Figure 1).[2] Exhibiting an energy barrier to isomerization of 100 kJ/mol, **1** remains the most stable atropisomer of this class of compounds reported to date. Despite the variety of cross-coupling procedures that has been developed for the synthesis of biaryls in recent years, coupling reactions using highly hindered aromatic compounds has rarely been achieved.[3] A number of aryl[4] and hetaryl[5] groups has been introduced into the peri-positions of naphthalene by us and others to study the energy barrier to rotation about the naphthyl-aryl bond. Incor-

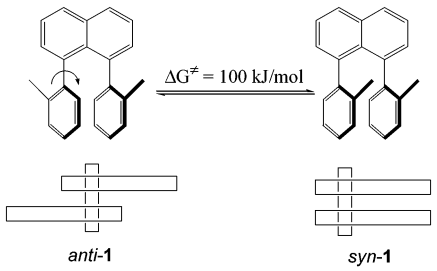

Figure 1. Structure of **1** exhibing antiparallel (anti-isomer) or parallel (syn-isomer) 2-methylphenyl moieties.

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poration of ortho- or meta-substituted aryl moieties into both peri-positions of naphthalene results in two chiral anti-isomers and one meso syn-isomer. Computational studies and X-ray analysis have shown that the peri-aryl rings are coplanar and almost perpendicular to the naphthalene moiety in the ground state. In contrast to the significant steric hindrance to isomerization suggested by CPK models, 1,8-diarylnaphthalenes such as **1** are not stable to interconversion at room temperature. The development of a synthetic route toward conformationally stable, atropisomeric 1,8-diarylnaphthalenes would facilitate studies of intramolecular interactions between stacked aryl groups[6] and has been considered an entry to a new class of chiral ligands for asymmetric catalysis.[7]

To date, all attempts to prepare 1,8-diarylnaphthalenes exhibiting conformational stability have been unsuccessful because of the severe steric repulsion that one can expect during the construction of such a highly constrained framework. On the basis of ab initio calculations, Thirsk et al. recently predicted a rotational energy barrier of approximately 160 kJ/mol to isomerization for ortho-substituted 2,7-diisopropoxy-1,8-diarylnaphthalenes. However, their attempts to synthesize such conformationally stable atropisomers using Suzuki cross-coupling were not successful.[8]

Herein, we wish to report the synthesis of 1,8-diarylnaphthalenes exhibiting conformational stability to isomerization even at high temperatures. We assumed that introduction of acridyl moieties into the peri-positions of naphthalene would result in a rigid scaffold that renders rotation of the aryl rings about the acridylnaphthalene axis impossible. Careful incorporation of substitutents into the fluorescent acridyl rings was expected to afford bidentate selectors exhibiting well-defined pockets for coordination to Lewis or Bronsted acids. Selective interactions between this new class of chemosensors and metal ions or other substrates would be measurable by sensitive fluorescence spectroscopy and allow real-time monitoring of trace analytes. Although a variety of fluorescent sensors for alkali, alkaline earth, and transition metals has been developed, high ion selectivity and the ability to differentiate between different oxidation states remain a challenge.[9]

Experimental Section

General Procedures. All reaction were carried out under nitrogen. Commercially available reagents and solvents were used without further purification. Flash chromatography was carried out on silica gel (particle size 0.032−0.063 mm). NMR spectra were obtained at 300 MHz (^{1}H NMR) and 75 MHz (^{13}C NMR), using $CDCl_3$ as the solvent. Chemical shifts are reported in ppm relative to TMS. Elemental analysis data were collected using a Perkin-Elmer 2400 CHN. UV measurements were performed on an Agilent 8453 UV−visible spectrometer. Extinction coefficients were determined from five different measurements in CH_2Cl_2. Absorption and emission spectra were collected under nitrogen. Fluorescence experiments were conducted using a Fluoromax-2 from Instruments S. A., Inc. Quantum yields of **2** and **3** were determined in benzene following literature procedures.[10] 1,8-Bis(4,4′-dialkyl-9,9′-diacridyl)naphthalenes were excited at 381 nm, and relative integrated intensities of the emission spectra were compared to anthracene. The quantum efficiency of anthracene in benzene (25.6%) was taken from the literature.

Synthetic Procedures. 1,8-Bis(4,4′-dimethyl-9,9′-diacridyl)naphthalene, 2. A mixture of 1,8-dibromonaphthanene **1** (92 mg, 0.32 mmol), tetrakis(triphenylphosphine)palladium(0) (0.11 g, 0.10 mmol, 30 mol %), and CuO (51 mg, 0.64 mmol) in 10 mL DMF was stirred at 140 °C. After 5 min, a solution of 4-methyl-9-trimethylstannanyl acridine **12** (0.46 g, 1.29 mmol) dissolved in 2 mL of DMF was added in one portion. After 16 h, the reaction mixture was quenched with 10% aqueous ammonium hydroxide, extracted with diethyl ether, dried over $MgSO_4$, and concentrated in vacuo. Purification of the orange residue by flash chromatography (100:5:1 hexanes/ethyl acetate/triethylamine) afforded **2** (41 mg, 25%) as a yellow solid. The diastereoisomers were separated on a phenylglycine column (250 mm × 4.6 mm) using hexanes/EtOH (98:2) as the mobile phase. The anti- and syn-conformation of the two isomer of **2** was determined by ^{1}H NMR spectroscopy using 1.2 mol equivalents of (+)-Eu(tfc)$_3$ as a chiral shift reagent.[11]

anti-Isomer: ^{1}H NMR δ = 2.72 (s, 6H), 6.50 (d, J = 8.8 Hz, 1H), 6.52 (d, J = 8.8 Hz, 1H), 6.58−6.78 (m, 6H), 7.18 (d, J = 6.6 Hz, 2H), 7.22−7.27 (m, 2H), 7.35 (ddd, J = 1.7 Hz, J = 7.8 Hz, J = 8.8 Hz, 2H), 7.68−7.73 (m, 4H), 8.25 (dd, J = 1.3 Hz, J = 8.8 Hz, 2H). ^{13}C NMR δ = 18.87, 123.75, 124.67, 125.00, 125.70, 125.74, 128.18, 128.37, 129.72, 129.87, 130.58, 130.73, 134.37, 135.10, 135.90, 146.73, 146.81, 146.04, 146.32. LC/APCI/MS: m/z = 511 (M + H).

syn-Isomer: ^{1}H NMR δ = 2.67 (s, 6H), 6.45−6.52 (m, 2H), 6.58−6.70 (m, 4H), 6.80 (d, J = 8.8 Hz 2H), 7.20−7.40 (m, 6H), 7.65−7.78 (m, 4H), 8.25 (dd, J = 1.3 Hz, J = 8.8 Hz, 2H). ^{13}C NMR δ = 18.94, 123.42, 124.67, 125.00, 125.73, 125.76, 128.21, 128.41, 129.73, 129.85, 130.58, 130.73, 134.37, 135.10, 135.90, 146.72, 146.81, 146.04, 146.32. LC/APCI/MS: m/z = 511 (M + H). Anal. Calcd for *syn*- and *anti*-$C_{38}H_{26}N_2$: C, 89.38; H, 5.13; N, 5.49. Found: C, 89.80; H, 5.57; N, 4.99.

1,8-Bis(4,4′-diisopropyl-9,9′-diacridyl)naphthalene, 3. A mixture 1,8-dibromonaphthanene **1** (0.25 g, 0.89 mmol), tetrakis(triphenylphos-

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(11) See Supporting Information.

phine)palladium(0) (0.31 g, 0.27 mmol, 30 mol %), and CuO (0.14 g, 1.78 mmol) in 18 mL DMF was stirred at 140 °C. After 5 min, a solution of 4-isopropyl-9-trimethylstannanyl acridine **12** (1.45 g, 3.8 mmol) dissolved in 2 mL DMF was added in one portion. After 16 h, the reaction mixture was quenched with 10% aqueous ammonium hydroxide, extracted with diethyl ether, dried over $MgSO_4$, and concentrated in a vacuum. Purification of the orange residue by flash chromatography (100:5:1 hexanes/ethyl acetate/trimethylamine) afforded **3** (126 mg, 25%) as a yellow solid. The diastereoisomers were separated on a phenylglycine column (250 mm × 4.6 mm) using hexanes/EtOH (98.4:1.6) as the mobile phase.

Isomer 1: ^{1}H NMR δ = 1.22 (d, J = 6.9 Hz, 6H), 1.52 (d, J = 6.9 Hz, 6H), 4.23 (sept, J = 6.9 Hz, 2H), 6.60−6.70 (m, 6H), 6.85 (d, J = 8.4 Hz, 2H), 7.18−7.30 (m, 6H), 7.60−7.78 (m, 4H), 8.26 (dd, J = 1.6 Hz, J = 8.4 Hz, 2H). ^{13}C NMR δ = 24.38, 27.25, 27.33, 123.58, 123.96, 124.68, 124.74, 124.74, 125.54, 125.58, 125.87, 128.21, 129.72, 129.90, 130.92, 134.93, 135.10, 144.95, 145.01, 145.61, 145.97, 146.79. LC/APCI/MS: m/z = 567 (M + H).

Isomer 2: ^{1}H NMR δ = 1.22 (d, J = 6.9 Hz, 6H), 1.52 (d, J = 6.9 Hz, 6H), 4.23 (sept, J = 6.9 Hz, 2H), 6.59−6.78 (m, 6H), 7.20−7.37 (m, 8H), 7.64−7.72 (m, 4H), 8.26 (dd, J = 1.6 Hz, J = 8.4 Hz, 2H). ^{13}C NMR δ = 24.62, 26.98, 27.08, 123.54, 123.95, 124.60, 124.71, 125.16, 125.52, 125.74, 128.09, 129.69, 129.93, 130.79, 134.59, 134.70, 144.95,145.01, 145.57, 145.77, 146.79. LC/APCI/MS: m/z = 567 (M + H). Anal. Calcd for *syn*- and *anti*-$C_{42}H_{34}N_2$: C, 89.01; H, 6.05; N, 4.94. Found: C, 89.38; H, 6.25; N, 4.67.

2-(2′-Methylphenylamino)benzoic Acid, 7. A mixture of 2-methylaniline (2.68 g, 25 mmol), 2-chlorobenzoic acid (3.8 g, 24 mmol), K_2CO_3 (4.1 g, 30 mmol), Cu powder (0.05 g), Cu_2O (0.05 g), and 5 mL of 2-methoxyethanol was refluxed for 2 h. The cooled reaction mixture was poured into 30 mL of water. Charcoal was then added, and the solution was filtrated through Celite. The crude product was obtained by acidification of the filtrate with diluted HCl at ambient temperature, and subsequent recrystallization from acetone/water (1:8). The crystals were dissolved in 100 mL of 5% aqueous Na_2CO_3. The solution was filtered through Celite, and the product was precipitated by acidification to afford acid **7** (3.0 g, 55%) as a white powder. ^{1}H NMR δ = 2.29 (s, 3H), 6.72 (bs, 1H), 6.85 (d, J = 8.2 Hz, 1H), 7.12 (dd, J = 7.2 Hz, J = 7.4 Hz, 1H), 7.20−7.34 (m, 5H), 8.05 (d, J = 7.2 Hz, 1H), 9.18 (bs, 1H). ^{13}C NMR δ = 18.96, 114.4, 117.3, 125.67, 125.98, 127.22, 127.49, 131.61, 131.85, 134.10, 135.79, 135.97, 139.16, 150.35.

2-(2′-Isopropylphenylamino)benzoic Acid, 8. A mixture of 2-isopropylaniline (3.4 g, 25 mmol), 2-chlorobenzoic acid (3.8 g, 24 mmol), K_2CO_3 (4.1 g, 30 mmol), Cu powder (0.05 g), and Cu_2O (0.05 g) in 5 mL of 2-methoxyethanol was refluxed for 2 h. The cooled reaction mixture was poured into 30 mL of water. Charcoal was then added, and the solution was filtrated through Celite. The crude product was obtained by acidification of the filtrate with diluted HCl at ambient temperature and by subsequent recrystallization from acetone/water (1:8). The crystals were dissolved in 100 mL of 5% aqueous Na_2CO_3 and filtered through Celite, and the crystals were recrystallized by acidification to yield acid **8** (4.4 g, 73%) as a white powder. ^{1}H NMR δ = 1.22 (d, J = 6.9 Hz, 6H), 3.21 (sept, J = 6.9 Hz, 1H), 4.68 (bs, 1H), 6.68 (dd, J = 7.2 Hz, J = 7.4 Hz, 1H), 6.81 (d, J = 8.2 Hz, 1H), 7.22−7.40 (m, 4H), 8.1 (dd, J = 1.7 Hz, J = 8.2 Hz, 1H), 9.18 (s, 1H). ^{13}C NMR δ = 23.97, 28.83, 114.38, 117.09, 126.72, 126.90, 127.13, 127.31, 133.08, 135.68, 136.04, 137.84, 145.09, 151.20, 174.73.

9-Bromo-4-methylacridine, 9. 2-(2′-Methylphenylamino)benzoic acid **7** (1.0 g, 4.4 mmol) was suspended in 11.0 g (38 mmol) of phosphorus oxybromide, and the mixture was heated to 120 °C for 2 h. Excess phosphorus oxybromide was removed by distillation, and the residual solution was poured into a 1:1 mixture of aqueous ammonium hydroxide/CH_2Cl_2. The CH_2Cl_2 solution was separated, dried, and filtered, and the combined organic layers were dried in vacuo to give **9** (1.0 g, 85%) as a yellow powder. ^{1}H NMR δ = 2.94 (s, 3H), 7.53 (dd, J = 8.5 Hz, J = 8.8 Hz, 1H), 7.59−7.69 (m, 2H), 7.78 (ddd, J = 1.4 Hz, J = 8.5 Hz, J = 8.5 Hz, 1H), 8.28 (dd, J = 8.5 Hz, J = 8.5 Hz, 2H), 8.43 (dd, J = 1.4 Hz, J = 8.8 Hz, 1H). ^{13}C NMR δ = 19.48, 126.37, 128.49, 128.76, 129.07, 129.28, 129.72, 130.95, 131.15, 131.88, 135.87, 138.12, 148.43, 148.71. Anal. Calcd for $C_{14}H_{10}NBr$: C, 61.79; H, 3.70; N, 5.15. Found: C, 61.40; H, 3.72; N, 5.05.

9-Bromo-4-isopropyl-acridine, 10. 2-(2′-Isopropylphenylamino)-benzoic acid **8** (1.0 g, 3.9 mmol) was suspended in 11.0 g (38 mmol) of phosphorus oxybromide, and the mixture was heated to 120 °C for 2 h. Excess phosphorus oxybromide was removed by distillation, and the residual solution was poured into a 1:1 mixture of aqueous ammonium hydroxide/CH_2Cl_2. The CH_2Cl_2 solution was separated, dried, and filtered, and the combined organic layers were dried in a vacuum to give **10** (1.2 g, 79%) as yellow powder. ^{1}H NMR δ = 1.45 (d, J = 6.9 Hz, 6H), 4.56 (sept, J = 6.9 Hz, 1H), 7.56−7.70 (m, 3H), 7.78 (ddd, J = 1.5 Hz, J = 6.6 Hz, J = 6.6 Hz, 1H), 8.24 (d, J = 8.4 Hz, 1H), 8.29 (dd, J = 1.5 Hz, J = 8.5 Hz, 1H), 8.41 (d, J = 8.8 Hz, 1H). ^{13}C NMR δ = 24.00, 28.21, 125.20, 125.62, 125.86, 126.49, 127.38, 127.64, 129.90, 130.58, 130.83, 135.69, 147.44, 148.01, 148.14. Anal. Calcd for $C_{16}H_{14}NBr$: C, 64.02; H, 4.70; N, 4.67. Found: C, 64.23; H, 4.78; N, 4.59.

4-Methyl-9-trimethylstannanylacridine, 11. A solution of 9-bromo-4-methylacridine **9** (1 g, 3.7 mmol) in 50 mL of anhydrous diethyl ether was cooled to −78 °C under nitrogen. To the solution were added 1.6 M *n*-BuLi in hexanes (0.74 mmol, 0.46 mL) dropwise over a period of 15 min and a 1.0 M solution of Me_3SnCl in hexanes (0.81 mL, 0.81 mmol). The reaction solution mixture was allowed to warm to room temperature, stirred for 18 h, and concentrated in vacuo. Purification of the orange residue by flash chromatography (100:10:1 hexanes/ethyl acetate/triethylamine) afforded **11** (1.1 g, 84%) as a yellow solid. GC−MS revealed contamination of the product with 5−10% 4-methylacridine that could not be separated by chromatography. The stannane was therefore employed in the Stille coupling with 1,8-dibromonaphthalene without further purification. ^{1}H NMR δ = 0.67 (s, 9H), 2.95 (s, 3H), 7.41 (dd, J = 6.9 Hz, J = 8.8 Hz, 1H), 7.52 (ddd, J = 1.4 Hz, J = 6.5 Hz, J = 6.5 Hz, 1H), 7.61 (d, J = 6.9 Hz, 1H), 7.74 (ddd, J = 1.4 Hz, J = 7.4 Hz, J = 7.4 Hz, 1H), 7.97 (d, J = 7.9 Hz, 1H), 8.12 (d, J = 9.3 Hz, 1H), 8.28 (d, J = 7.9 Hz, 1H). ^{13}C NMR δ = −4.63, 19.51, 125.33, 125.56, 128.42, 128.94, 129.30, 129.93, 131.38, 133.49, 133.62, 138.58, 147.36, 147.53, 156.78.

4-Isopropyl-9-trimethylstannylacridine, 12. Stannane **12** (1.4 g, 3.5 mmol) was obtained in 90% yield using 9-bromo-4-isopropyl-acridine **10 (**1.2 g, 3.9 mmol), 1.6 M *n*-BuLi in hexanes (2.6 mL, 4.2 mmol), and a 1.0 M solution of Me_3SnCl in hexanes (4.5 mL, 4.5 mmol), following the procedure described for the preparation of **11**. GC−MS revealed contamination of the product with 5−10% 4-isopropylacridine that could not be separated by chromatography. The stannane was therefore employed in the Stille coupling with 1,8-dibromonaphthalene without further purification. ^{1}H NMR δ = 0.71 (s, 9H), 1.51 (d, J = 6.9 Hz, 6H), 4.69 (sept, J = 6.9 Hz, 1H), 7.48−7.60 (m, 2H), 7.67 (d, J = 6.4 Hz, 1H), 7.76 (ddd, J = 1.4 Hz, J = 6.0 Hz, J = 6.0 Hz, 1H), 8.02 (dd, J = 1.1 Hz, J = 8.6 Hz, 1H), 8.16 (d, J = 8.5 Hz, 1H), 8.33 (d, J = 8.8 Hz, 1H). ^{13}C NMR δ = −4.05, 24.05, 28.02, 124.77, 125.37, 125.50, 128.05, 129.05, 129.95, 131.71, 133.33, 133.72, 146.16, 147.18, 148.72, 156.59.

Results and Discussion

Retrosynthetic analysis of 1,8-bis(4,4′-dimethyl-9,9′-diacridyl)-naphthalene, **2**, and 1,8-bis(4,4′-diisopropyl-9,9′-diacridyl)-naphthalene, **3**, suggested Stille or Suzuki cross-coupling of 1,8-dibromo- or 1,8-diiodonaphthalene with a 4-substituted-9-acridyl stannane or boronic acid derivative, which can be formed via ring construction from 2-substituted anilines. We have found that 1,8-bis(4,4′-dialkyl-9,9′-diacridyl)naphthalenes **2** and **3** can be synthesized from readily available 2-chlorobenzoic acid, **4**,

Scheme 1. Synthesis of 1,8-Diacridylnaphthalenes **2** and **3**

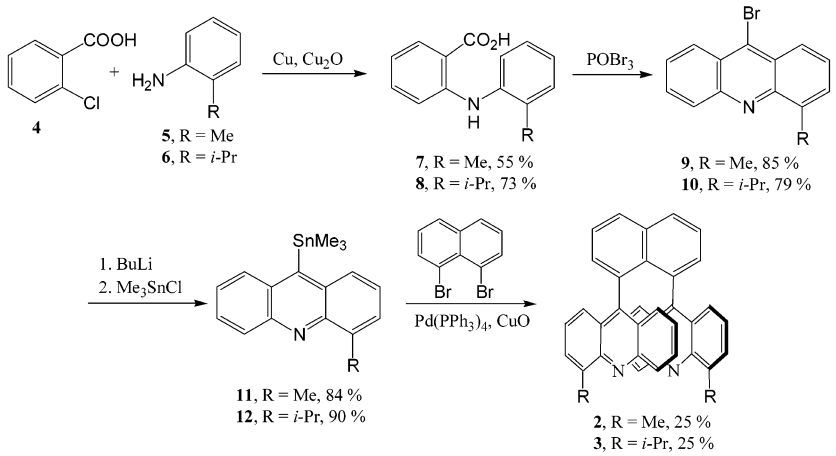
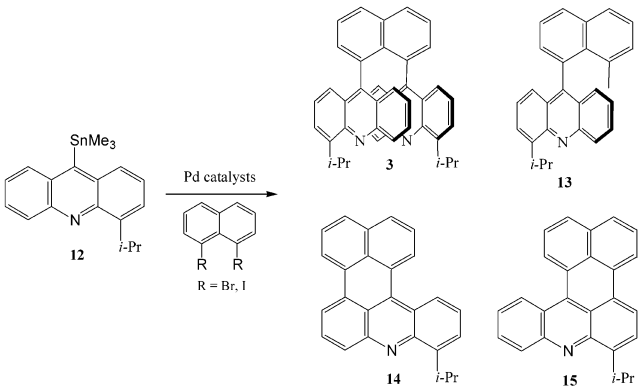


Table 1. Optimization Results of the Pd-Catalyzed Cross-Coupling Reactions

entry		stannane	Catalyst (mol%)	additives	yield of major product (%)
1	R = I	**12**	$Pd(PPh_3)_4$ (10)[a]	/	**14** + **15** (17)
2	R = I	**12**	$Pd(PPh_3)_4$ (10)[a]	Cy_2NMe	**14** + **15** (17)
3	R = Br	**12**	$Pd(PPh_3)_4$ (10)[b]	CuO	**3** (5)
4	R = Br	**12**	$Pd(PPh_3)_4$ (10)[c]	CuO	**3** (5)
5	R = Br	**12**	$Pd(PPh_3)_4$ (10)[a]	CuO	**3** (10)
6	R = Br	**12**	$Pd(PPh_3)_4$ (20)[a]	CuO	**3** (18)
7	R = Br	**12**	$Pd(PPh_3)_4$ (30)[a]	CuO	**3** (25)
8	R = Br	**12**	$Pd(PPh_3)_4$ (40)[a]	CuO	**3** (25)
9	R = Br	**12**	$Pd(PPh_3)_4$ (50)[a]	CuO	**3** (25)
10	R = Br	**11**	$Pd(PPh_3)_4$ (30)[a]	CuO	**2** (25)

[a] DMF, 140 °C, 18 h. [b] DMF, 100 °C, 18 h. [c] DMF, 140 °C, 5 h.

Scheme 2. Stille Cross-Coupling Products Obtained from Stannane **12** and 1,8-Dihalonaphthalenes



and anilines **5** and **6**, respectively (Scheme 1). Commercially available acid, **4**, was converted to 4-alkyl-9-trimethylstannyl-acridine, **11** and **12**, in three steps with high overall yield. First, we attempted Stille cross-coupling of stannane **12** and 1,8-diiodonaphthalene using $Pd(PPh_3)_4$ as the catalysts. However, **14** and **15** were obtained as the only cross-coupling products in addition to degradation products of stannane **11** (Scheme 2).[12] We therefore decided to use 1,8-dibromonaphthalene[13] in the Stille reaction. Screening of various catalysts such as $Pd(PPh_3)_4$, $PdCl_2$dppf, or $Pd_2(dba)_3$/*t*-Bu_3P and optimization of reaction conditions revealed that employing $Pd(PPh_3)_4$ and CuO in DMF at 140 °C affords 1,8-bis(4,4′-dialkyl-9,9′-diacridyl)naphthalenes **2** and **3** via Stille coupling of stannanes **11** or **12** with 1,8-dibromonaphthalene in remarkable yields. We were pleased to find less than 10% of coupling byproducts **13**, **14**, and **15** under these conditions (Table 1). Notably, Suzuki coupling of 1,8-dibromonaphthalene and 4-isopropyl-9-acridylboronic acid or its pinacolate derivative employing $Pd(PPh_3)_4$, $PdCl_2$dppf, or $Pd_2(dba)_3$/*t*-Bu_3P as the catalyst as well as *t*-BuOK, K_3PO_4, or Cs_2CO_3 as the base in DME and DMF, respectively, did not result in the formation of the desired coupling product.

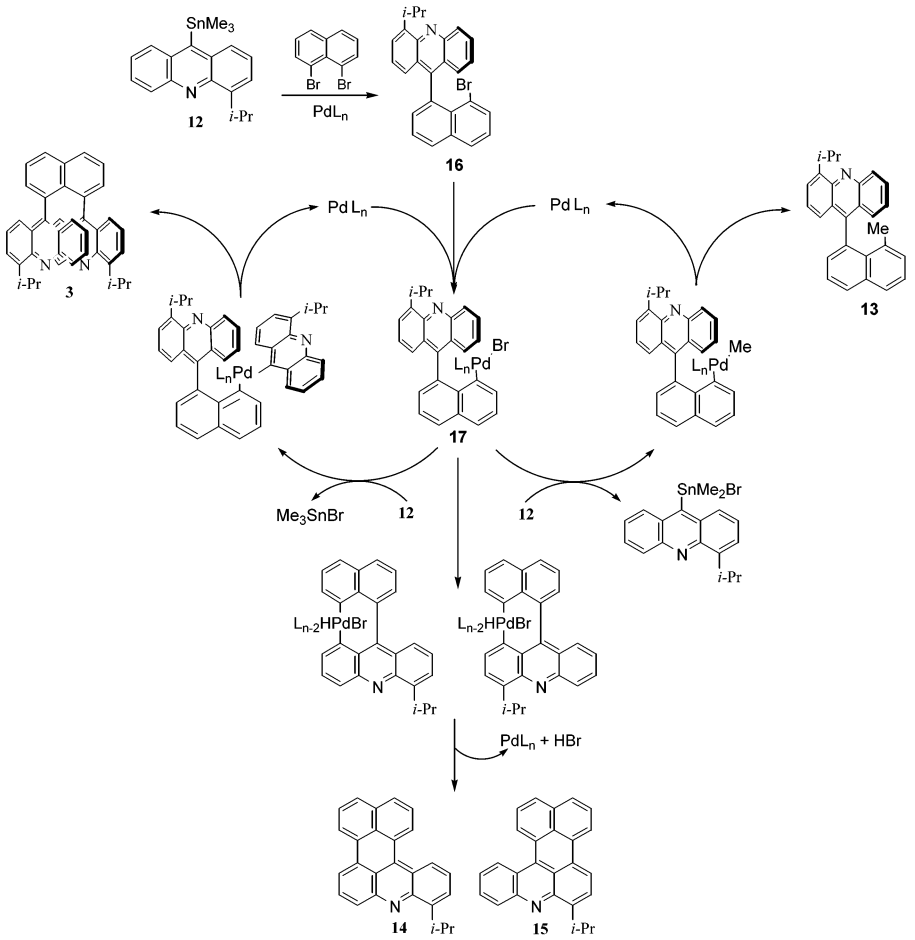
The observed cross-coupling byproducts are indicative of the steric hindrance that occurs during the Pd-catalyzed reaction between the intermediate 1-(4-isopropyl-9-acridyl)-8-bromonaphthalene, **16**, and another stannane, **12** (Scheme 3). Oxidative addition of **16** to the Pd catalysts provides a reactive Pd complex **17** that can undergo transmetalation, followed by reductive elimination to yield Stille products **3** and **13** or intramolecular coupling through Pd-activation of a peri-acridyl C−H bond to form **14** and **15**. The formation of carbon−carbon bonds via metal-mediated C−H bond activation has been reported by others and used as a powerful strategy for the synthesis of complex compounds.[14] Because of the steric hindrance that can be expected between Pd complex **17** and a second stannyl reagent **12**, the transfer of a methyl group instead of the acridyl moiety becomes a competitive side reaction that results in the formation of the undesired coupling product **13**. Since the transmetalation between **17** and **12** is considered to be slow, C−H insertion of **17** and subsequent reductive elimination afford **14** and **15**.

Because of the severe steric hindrance and possible side reactions inherent to their synthesis, highly constrained 1,8-diarylnaphthalenes exhibiting conformational stability have not been reported previously. The preparation of **2** and **3** in 25% yield using our CuO-promoted Stille coupling procedure is quite remarkable since it affords two consecutive coupling steps.

We were pleased to find that the diastereoisomers of **2** and **3** can be separated by HPLC on a (*S*)-phenylglycine column.[15] Semipreparative separation allowed us to determine the anti/syn ratio of **2** and **3** as 4.6:1 and 1:1, respectively.[16] Isomerization via rotation of one acridyl ring about the chiral

(12) The structures of **14** and **15** were determined by NMR and LC/APCI/MS.
(13) Seyferth, D.; Vick, S. C. *J. Organomet. Chem.* **1977**, *141*, 178−187.
(14) (a) Dyker, G. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 103−105. (b) Reetz, M. T.; Wanninger, K.; Hermes, M. *J. Chem. Soc., Chem. Commun.* **1997**, 535−536. (c) Jia, C.; Kitamura, T.; Fujiwara, Y.; *Acc. Chem. Res.* **2001**, *34*, 633−639. (d) Ritleng, V.; Sirlin, C.; Pfeffer, M. *Chem. Rev.* **2002**, *102*, 1731−1769. (e) Dangel, B. D.; Godula, K.; Youn, S. W.; Sezen, B.; Sames, D. *J. Am. Chem. Soc.* **2002**, *124*, 11856−11857.
(15) Using a variety of chiral columns, we were not able to separate the enantiomers of *anti*-**2** and *anti*-**3**, respectively.

Scheme 3. Possible Transmetalation Pathways during the Second Catalytic Cycle of the Pd-Catalyzed Stille Coupling of 1-(4-Isopropyl-9-acridyl)-8-bromonaphthalene **16** and Stannane **12**



acridylnaphthalene axis is highly restricted because of steric hindrance. According to PM3 calculations, diacridyls **2** and **3** afford compact structures in which both acridyl rings are roughly perpendicular to the mean plane of the naphthyl ring, with dihedral angles ranging from 85° to 95°. The acridyl moieties are slightly twisted away from each other and undergo enforced π-stacking (Figure 2).[17]

The isolated isomers were heated in acetonitrile in a closed vessel to 180 °C for 24 h. As expected, rotation of either acridyl moiety about the chiral acridylnaphthalene axis of **2** and **3** is highly sterically hindered, and HPLC analysis did not show any sign of isomerization. Utilizing reversible first-order kinetics and the Eyring equation, we calculated the Gibbs standard activation energy, $\Delta G^{\circ\ddagger}$, for the isomerization of **2** and **3** to be higher than 180 kJ/mol.[18]

Investigation of the photochemical properties of **2** and **3** revealed UV absorption maxima at 246 nm (lg ϵ = 8.02 and 8.06, respectively). The UV spectra proved to be reminiscent of isolated, nonconjugated naphthyl and acridyl chromophores as one would expect for a structure exhibiting both hetaryl rings perpendicular to the naphthalene plane. The UV data are thus in agreement with the results of our PM3 calculations. The fluorescence spectra of **2** and **3** were found to be significantly red-shifted compared to that of acridine, which exhibits an emission maximum around 400 nm in benzene. This may be attributed to the enhanced π-stacking of the two acridyl rings. Fluorescence studies of both isomers of diacridine **3** revealed only one maximum at approximately 530 nm and a quantum yield of 18%. In contrast, the fluorescence of the isomers of **2**

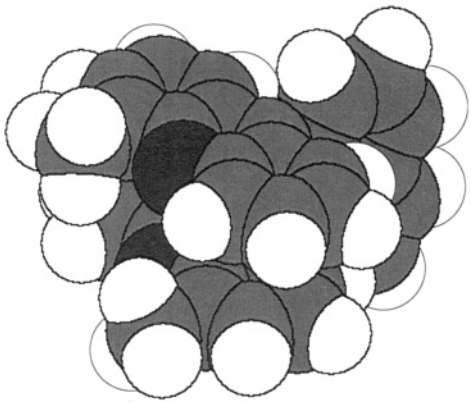


Figure 2. Space-filling model of *anti*-**2** calculated by PM3.

(16) The isomer ratios of **2** and **3** determined after semipreparative HPLC separation are in very good agreement with ^{1}H NMR integration results of the product mixtures. The syn- and anti-conformations of **2** were determined by ^{1}H NMR, using a chiral Lanthanide shift reagent. The formation of diastereomeric complexes of the C_2-symmetric anti-isomers of **2** exhibiting anisochronous signals was observed in the presence of (+)-Eu(tfc)$_3$, whereas the signals of the methyl protons of the meso form are downfield-shifted but are still isochronous; see Supporting Information. The determination of the conformation of the two isomers of **3** using NMR shift reagents or NOESY experiments was not successful.

(17) (a) Hunter, C. A.; Lawson, K. R.; Perkins, J.; Urch, C. J. *J. Chem. Soc., Perkin Trans. 2* **2002**, 651−669. (b) Rashkin, M. J.; Waters, M. L. *J. Am. Chem. Soc.* **2002**, *124*, 1860−1861.

(18) Decomposition of **2** and **3** was observed at 200 °C.

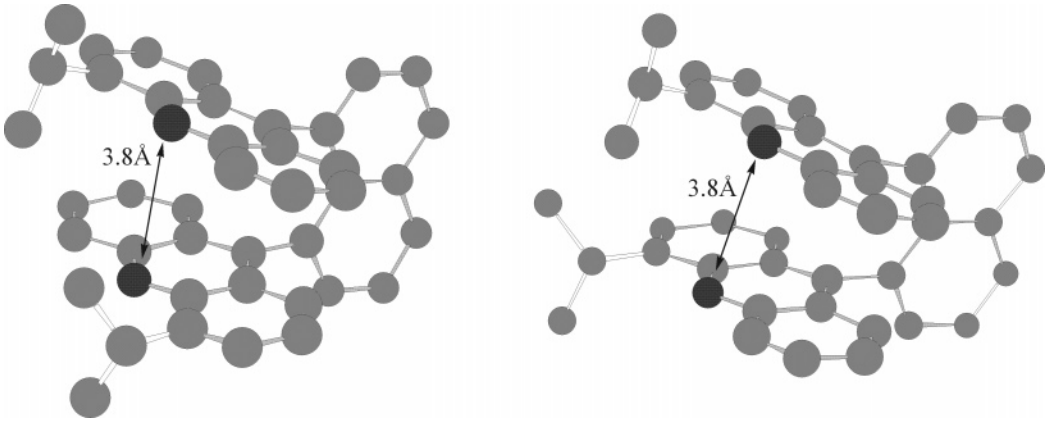


Figure 3. PM3 computation of the ground state of *anti*- (left) and *syn*-**3** (right).

proved to be significantly different. We found that *syn*-**2** is a blue light emitter with a fluorescence maximum at 460 nm, whereas excited *anti*-**2** emits green light at approximately 540 nm. Notably, *syn*-**2** was found to be more fluorescent than its diastereoisomeric anti-isomer. The quantum yields for *syn*- and *anti*-**2** were determined as 22% and 13%, respectively. The striking difference in the flourescence behavior of the isomers of **2** may be attributed to increased $\pi-\pi$ interactions between the anti-parallel acridyl rings of *anti*-**2**. The distance between the acridyl nitrogens of *syn*-**2** was determined as 3.6 Å on the basis of PM3 optimization of the ground state. By contrast, PM3 calculations suggested a N−N distance of only 3.4 Å for *anti*-**2**. We assume that the close proximity of the acridyl rings facilitates nonradiative relaxation of excited *anti*-**2**, resulting in a significantly lower quantum yield than its syn-isomer. Computational studies of the ground state of *syn*- and *anti*-**3** provided a N−N distance of 3.8 Å for both isomers, which explains their indistinguishable fluorescence maximum and quantum yield (Figure 3).

We chose to investigate the usefulness of this new class of conformationally stable, bidentate 1,8-dihetarylnaphthalenes, combining unique stereochemical and photoluminescent features as selective sensors. The majority of fluorosensors developed to date are macrocyclic structures exhibiting a chelating group and a fluorophore physically separated by a spacer.[19] However, small sensors afford advantageous cell permeability properties and are therefore particularly promising for biomedical trace analysis. Because of its higher quantum yield, we decided to employ the syn-isomer of **2** in metal ion-sensing studies. Fluorescence emission titrations with *syn*-**2** and CuCl and $CuCl_2$ were performed in acetonitrile at room temperature. We did not observe any significant red or blue shifts in the emission spectra of *syn*-**2** in the presence of the metal ions. Addition of CuCl did not result in significant quenching even at high excess (Figure 4). By contrast, titration of the same sensor with $CuCl_2$ revealed highly efficient quenching (Figure 5).

Because of its considerably different fluorescence response to Cu(I) and Cu(II) ions, the syn-isomer of **2** may be used as a highly selective sensor for real-time qualitative and quantitative analysis of the oxidation state of copper ions in solution. Binding to a metal ion opens new vibrational or electronic pathways for nonradiative relaxation of excited *syn*-**2**. Coordination of

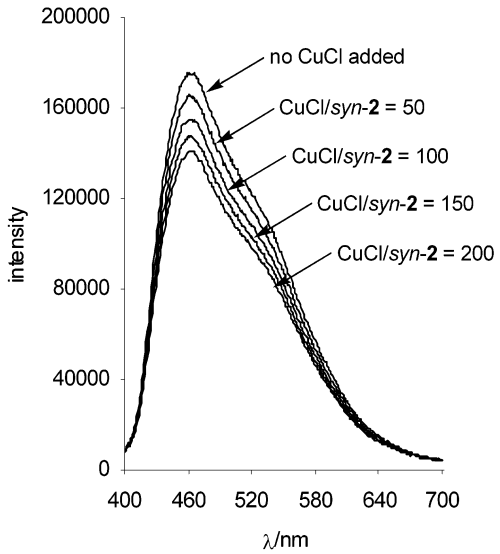


Figure 4. Fluorescence quenching of *syn*-2 using various concentrations of CuCl. Diacridylnaphthalene *syn*-**2** was dissolved in acetonitrile at a concentration of 10^{-6} M.

the diacridylnaphthalene sensor to Cu(II) exhibiting a d^9-electronic configuration is likely to result in considerable fluorescence quenching because of photoinduced electron transfer. Interestingly, we observed nonlinear Stern−Völmer quenching of *syn*-**2** by Cu(II) chloride. A fluorescence titration experiment with $CuCl_2$ gave a sigmoidal quenching curve, indicating cooperative recognition such as formation of less fluorescent agglomerates at a high Cu(II)/sensor ratio (Figure 6). Chemical sensing based on cooperative recognition has rarely been observed and is believed to result in higher selectivity compared to noncooperative sensing exhibiting a linear fluorescence response.[20] By contrast, photoinduced electron transfer is not significant in Cu(I)-*syn*-**2** because of the d^{10}-electronic configuration of the metal ion. Further titration experiments revealed that the selector is also capable of differentiating between $CuCl_2$ and $ZnCl_2$. Stern−Völmer plots of the two salts show that Zn(II) barely induces fluorescence quenching of *syn*-**2** (Figure 7). This may also be attributed to negligible photoinduced electron transfer of excited Zn(II)-*syn*-**2**. We conducted UV titration experiments of *syn*- and *anti*-**2** using Cu(II) chloride for the determination of the stoichiometry of the metal-sensor

(19) de Silva, A. P.; Gunaratne, H. Q. N.; Gunnlaugsson, T.; Huxley, A. J. M.; McCoy, C. P.; Rademacher, J. T.; Rice, T. E. *Chem. Rev.* **1997**, *97*, 1515−1566.

(20) Glass, T. E. *J. Am. Chem. Soc.* **2000**, *122*, 4522−4523 and references therein.

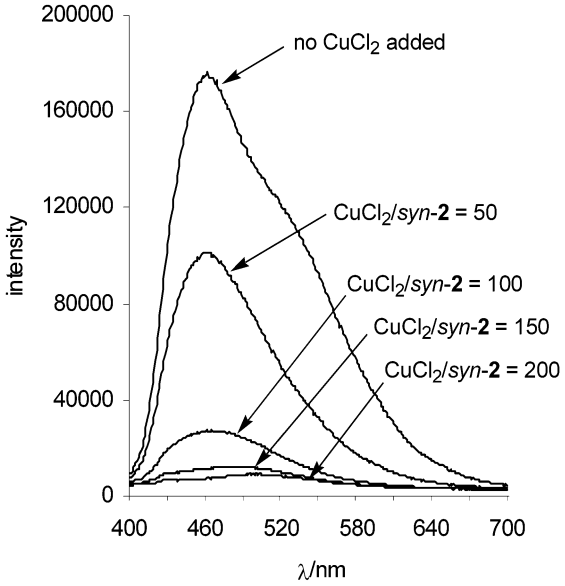


Figure 5. Fluorescence quenching of *syn*-**2** using various concentrations of $CuCl_2$. Diacridylnaphthalene *syn*-**2** was dissolved in acetonitrile at a concentration of 10^{-6} M.

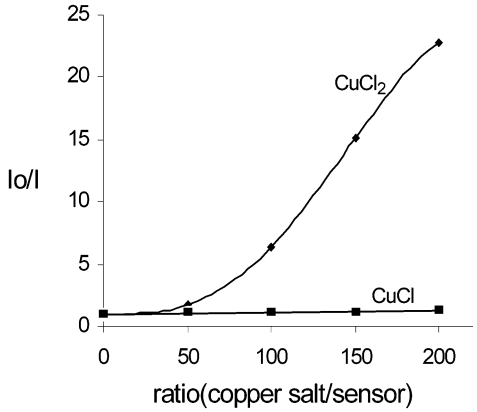


Figure 6. Stern−Völmer plot of *syn*-**2** in the presence of Cu(I) and Cu(II) chloride. The concentration of *syn*-**2** was 10^{-6} M.

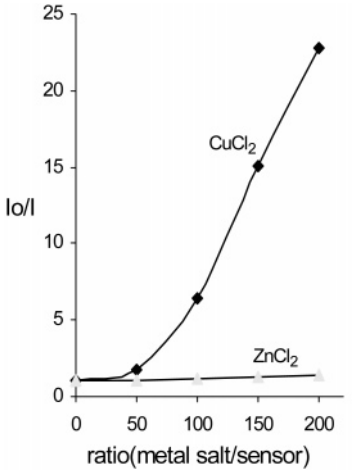


Figure 7. Stern−Völmer plot of *syn*-**2** in the presence of Cu(II) and Zn-(II) chloride. The concentration of *syn*-2 was 10^{-6} M.

complexes formed in acetonitrile (Figures 8 and 9). In accordance with our fluorescence experiments, we did not observe any significant red or blue shifts in the absorption spectra of the diacridylnaphthalenes in the presence of Cu(II). Job analysis

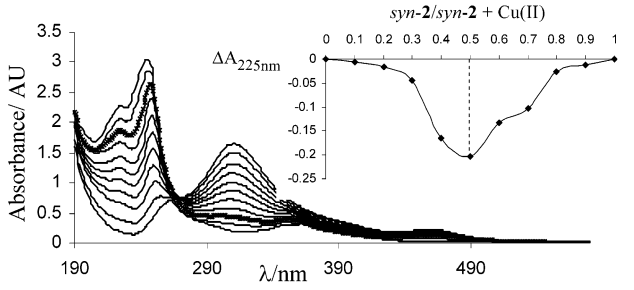


Figure 8. UV titration of *syn*-**2** with $CuCl_2$. Inset: Job plot recorded at 225 nm. Sum of concentrations was fixed at 1.5×10^{-5} M.

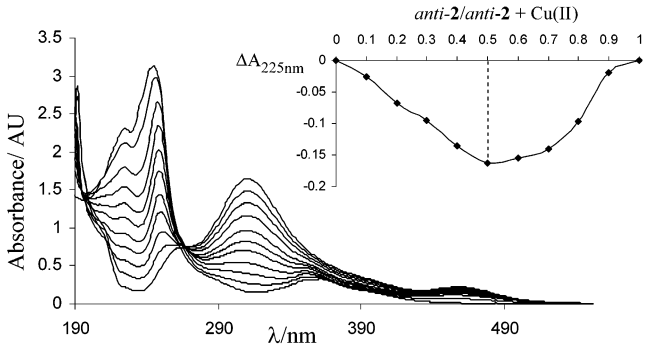


Figure 9. UV titration of *anti*-**2** with $CuCl_2$. Inset: Job plot recorded at 225 nm. Sum of concentrations was fixed at 1.5×10^{-5} M.

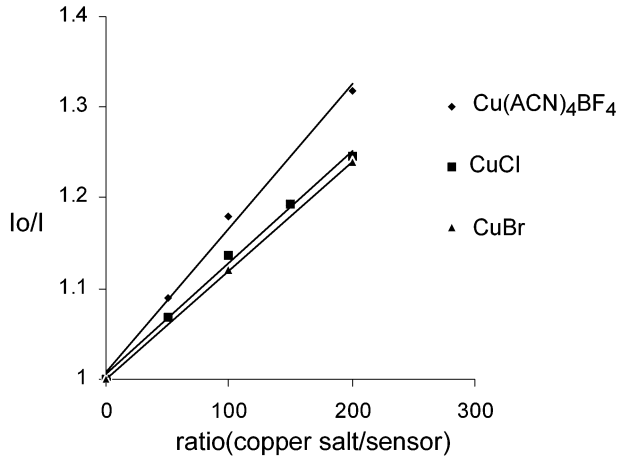


Figure 10. Counterion effect on the fluorescence quenching of *syn*-**2** in acetonitrile. The concentration of *syn*-**2** was 5×10^{-6} M.

of Cu(II) chloride and *syn*-**2** or *anti*-**2** at a total concentration of 1.5×10^{-5} M revealed the existence of one maximum at a molar ratio of 0.5, which is in agreement with the formation of an equimolar complex (Figures 8 and 9).[21] Notably, a job plot affords the sensor/metal ratio but does not differentiate between 1:1 and 2:2 complexation or formation of even higher aggregrates, which would explain the cooperative recognition of Cu-(II) observed with *syn*-**2**.

The selectivity between copper and zinc ions is quite important for bioanalytical and environmental studies. Cu(II) and Zn(II) are essential trace elements that occur in metalloproteins with various biological functions in bacteria, plants, and mammals. Cu(II) is also a significant environmental pollutant. An important requirement for a useful cation-selective

(21) Connors, K. A. *Binding Constants, The Measurement of Molecular Complex Stability*; Wiley: New York, 1987.

sensor is the absence of a significant fluorescence response to anions also present in solution. We therefore selected three different Cu(I) salts for fluorescence titration experiments to determine any counteranion effects on the photochemical properties of the sensor. Indeed, *syn*-**2** did not show any significant fluorescence quenching due to the presence of chloride, bromide, or tetrafluoroborate (Figure 10). The Stern−Völmer plots obtained with CuCl and CuBr are almost superimposable, whereas quenching by $Cu(ACN)_4BF_4$ was found to be approximately 7% more effective.

Conclusions

We have synthesized conformationally stable 1,8-diarylnaphthalenes via CuO-promoted Stille cross-coupling of 1,8-dibromonaphthalene and 4-alkyl-9-trimethylstannylacridines. The syn- and anti-isomers of 1,8-bis(4,4′-dimethyl-9,9′-diacridyl)-naphthalene, **2**, and its diisopropyl analogue, **3**, have been isolated for investigation of their stereodynamic properties. No sign of syn/anti-isomerization was observed even at high temperatures, indicating a rotational energy barrier above 180 kJ/mol. Fluorescence titration experiments with the syn-isomer of **2** revealed highly efficient quenching by Cu(II) ions, which was attributed to cooperative recognition. Job analysis based on UV titration experiments revealed formation of a complex exhibiting equimolar amounts of the sensor and Cu(II). Almost no quenching effects were observed with Cu(I) and Zn(II) salts, which is probably a consequence of negligible photoinduced electron-transfer pathways for nonradiative relaxation. The fluorescence quenching was found to be cation-selective and almost independent of counteranions present in solution. The high sensitivity inherent to fluorescence spectroscopy, combined with the remarkable ion selectivity of this new class of chemosensors, opens new venues for probing small traces of metal ions.

We believe that the development of a synthetic route toward C_2-symmetric and conformationally stable 1,8-diarylnaphthalenes such as *anti*-**2** and *anti*-**3** will allow the exploration of a new class of compounds for enantioselective sensing of chiral molecules. The synthesis and enantioseparation of new axially chiral 1,8-dihetarylnaphthalenes that are capable of participating in diastereomeric interactions that can be quantitatively measured by fluorescence quenching are currently underway in our laboratories.

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Supporting Information Available: NMR, UV, and fluorescence spectroscopy data of compounds **2** and **3** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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