Supporting Information

A chiral indolocarbazole foldamer displaying strong circular dichroism responsive to anion binding

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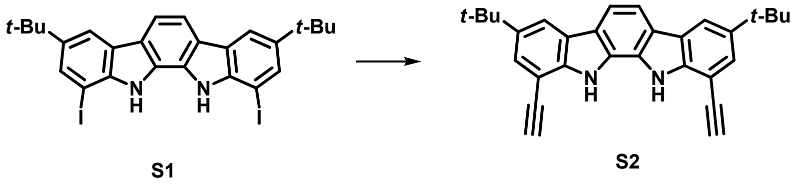
Contents

1. Synthesis and characterization.

General: Air- or moisture-sensitive reactions were carried out under nitrogen. Reagents and anhydrous solvents obtained from commercial suppliers were used without further purification. Thin layer chromatography (TLC) was performed on Merck (silica gel 60, F-254, 0.25 mm). Silica gel 60 (230–240 mesh, Merck) was used for column chromatography. NMR spectra were recorded by using Bruker DRX 500, Avance II instruments, the chemical shifts were reported using residual protonated solvent peaks (for ^{1}H NMR spectra, CD_2Cl_2 5.32 ppm; CD_3CN 1.94 ppm; DMSO-d_6 2.50 ppm and for ^{13}C NMR spectra, DMSO-d_6 39.52 ppm; CD_2Cl_2 54.00 ppm). Melting points were determined with a Barnstead Electrothermal (IA9100) apparatus. The UV-Vis spectra were recorded by using an Agilent 8453 UV-Visible spectrophotometer. And FT-IR spectra were measured by using a Nicolet Impact-400 FT-IR spectrometer. Circular dichroism (CD) spectra were conducted on a JASCO (J-810). Optical rotation values were measured with the RUDOLPH (III-589). The elemental analysis data were obtained from *the Organic Chemistry Research Center* at Sogang University.



S2: A Schlenk tube containing indolocarbazole **S1**[S1] (0.6 g, 0.96 mmol), $Pd(PPh_3)_2Cl_2$ (34 mg, 0.05 equiv), and CuI (9 mg, 0.05 equiv) was evacuated under vacuum and back-filled with nitrogen. Anhydrous THF (8 mL), Et_3N (8 mL), and ethynyltrimethylsilane (7 mL, 5 equiv) were sequentially added, and the solution was stirred at 56-58 °C for 24 h. After cooled ambient temperature, the mixture was filtered through Celite and concentrated. The residue was dissolved in ethyl acetate and the organic solution was washed with distilled water, dried over anhydrous Na_2SO_4 and concentrated. After concentration, the crude mixture was dissolved in CH_2Cl_2 (6 mL) at room temperature without purification. Tetra-*n*-butylammonium fluoride (1 M solution in THF, 2.1 equiv) was sequentially added at 0 °C,

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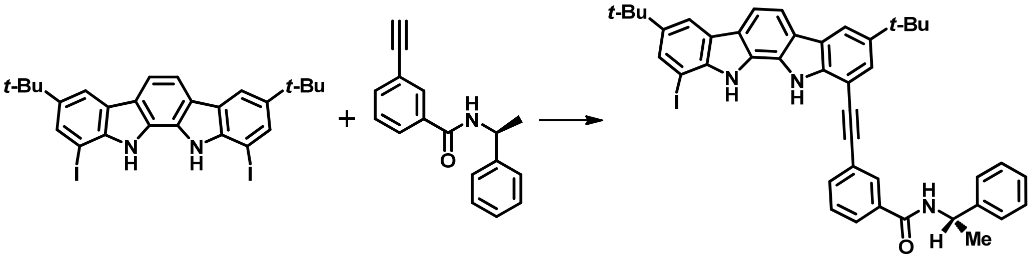
[S1] K.-J. Chang, D. Moon, M. S. Lah and K.-S. Jeong, *Angew. Chem. Int. Ed.,* 2005, **44**, 7926.

and the solution was stirred for 10 min at room temperature. The mixture was concentrated, and the product was purified by flash column chromatography (silica gel, 1/3 (v/v) = CH_2Cl_2/hexane) to give **S3** as a white solid (0.37 g, 94%). mp: 166-167 °C; IR (thin film): $\tilde{\nu}$ (cm^{-1}) 3367 (NH), 2158 (C≡C), 3253 (C(sp)–H); ^{1}H NMR (400 MHz, DMSO-d_6, 298 K) δ (ppm) 11.15 (s, 2H, NH), 8.25 (s, 2H, ArH), 7.98 (s, 2H, ArH), 7.57 (s, 2H, ArH), 4.71 (s, 2H, C≡CH), 1.42 (s, 18H, *t*-Bu); ^{13}C NMR (100 MHz, DMSO-d_6, 298 K): δ (ppm) 141.7, 138.2, 125.7, 125.6, 123.6, 120.4, 117.6, 112.2, 103.8, 84.6, 80.9, 34.4, 31.7; elemental analysis calcd (%) for $C_{30}H_{28}N_2$: C 86.5, H 6.8, N 6.7; found C 86.5, H 6.8, N 6.7.



S1 **S3** **S4**

S4: Previously a Schlenk flask containing **S1** (1.97 g, 3.16mmol, 1.1 equiv). Under N_2, CuI (2 mg, 0.005 mmol), $Pd(PPh_3)_2Cl_2$ (7 mg, 0.005 equiv) were added to a Schlenk flask. The Schlenk flask was fitted with a rubber stopper, and evacuated under vacuum and back-filled with N_2 (repeated three times). After addition of anhydrous THF (15 mL), Et_3N (15 mL) and compound **S3**[S2] (720 mg, 2.88 mmol, 1 equiv), the rubber stopper was replaced with a screw stopper and the solution was stirred at 55-58°C for 12.5 h. After cooled ambient temperature, filtered through Celite and concentrated. The residue was dissolved in EtOAc, washed with brine, and dried over anhydrous Na_2SO_4. After concentration under reduced pressure, the residue was purified by flash column chromatography (silica gel, 1/2 (v/v) = CH_2Cl_2/hexane) to give **S4** (0.8 g, 37%) as ivory solid. Mp>240 ºC (dec); IR (thin film): $\tilde{\nu}$ (cm^{-1}) 3334(NH), 1644(C=O); ^{1}H NMR (400 MHz, DMSO-d_6): δ (ppm) 11.26 (s, 1H), 10.85 (s, 1H), 9.01 (d, 1H), 8.32(s, 1H), 8.30(s, 1H), 8.22 (s, 1H), 8.00 (m, 3H), 7.92 (d, 1H), 7.80 (s, 1H), 7.68 (s 1 H) 7.64 (t, 1H), 7.43 (d, 1H), 7.35 (t, 1H), 7.24 (t, 2H), 5.23 (qn, 1H), 1.52 (d, 3H), 1.45 (s, 9H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, DMSO-d_6): δ (ppm) 164.6, 144.7, 143.9, 142.0,

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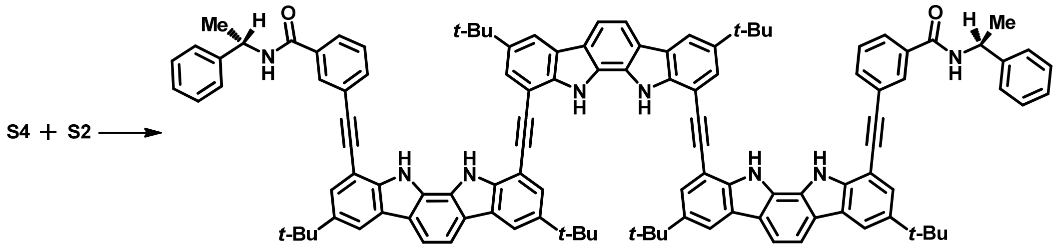
[S2] (a) V. R. Naidu, M. C. Kim, J.-m. Suk, H.-J. Kim, M. Lee, E. Sim and K.-S. J eong, *Org. Lett.* 2008, **10**, 5373.

139.0, 137.5, 135.0, 134.1, 130.7, 130.2, 128.9, 128.2, 127.9, 126.6, 126.0, 125.7, 125.5, 125.4, 123.8, 123.7, 122.6, 121.0, 120.5, 117.7, 116.2, 112,5, 112.4, 104.1, 92.3, 87.0, 76.7, 48.6, 34.5, 34.4, 31.7, 22.1; LRMS (FAB) *m/z* calcd. $C_{43}H_{40}IN_3O$ 741, found 741; $C_{43}H_{40}IN_3O$: calcd. C 69.6, H 5.4, N 5.7; found: C 69.5, H 5.5, N 5.6.



foldamer 1

Foldamer**1:** A dry Schlenk flask containing **S7** (0.21 g, 0.29 mmol), $Pd(PPh_3)_2Cl_2$ (7 mg, 0.1 equiv) and CuI (2.5 mg, 0.1 equiv) was evacuated under vacuum and back-filled with nitrogen three times. Anhydrous THF (6 mL), Et_3N (6 mL) and **S2** (0.05 g, 0.13 mmol) were sequentially added and the solution was stirred at 55-60°C for 15 h. The mixture was filtered through Celite and the filtrate was concentrated. The residue was dissolved in CH_2Cl_2, and was washed with distilled water, dried over anhydrous Na_2SO_4 and concentrated. The residue was purified by flash column chromatography (silica gel, 1/3 (v/v) = EtOAc/hexane) to give foldamer **1** as an ivory solid (0.90 g, 42%). Mp> 290 °C (dec); IR (KBr): $\tilde{\nu}$ (cm^{-1}) 3376(NH overlapped), 2956(ArCH), 1642(C=O); ^1H NMR (400 MHz, DMSO-d_6, 298 K) δ (ppm) 11.25 (s, 1H, NH), 11.16 (s, 1H, NH), 11.13 (s, 1H, NH), 8.88 (d, 1H, NH), 8.36 (s, 1H, ArH), 8.29 (s, 1H, ArH), 8.24 (s, 1H, ArH), 8.17 (s, 1H, ArH), 8.10 (s, 1H, ArH), 8.02 (s, 2H, ArH), 7.86 (d, 1H, ArH), 7.78 (s, 1H, ArH), 7.75 (d, 1H, ArH), 7.63 (d, 1H, ArH), 7.43 (t, 1H, ArH), 7.27 (d, 1H, ArH), 7.20 (t, 2H, ArH), 7.13 (t, 1H, ArH), 5.05 (t, 1H, benzyllic H), 1.46 (s 9H, *t*-Bu), 1.43 (s 9H, *t*-Bu), 1.34 (d, 3H, Me), 1.23 (s, 9H, *t*-Bu); ^{13}C NMR (100 MHz, DMSO-d_6, 298 K) δ (ppm) 164.4, 144.6, 144.5, 142.1, 142.0, 141.9, 140.6, 140.5, 140.4, 137.9, 137.7, 137.5, 134.8, 133.9, 130.0, 128.1, 127.8, 126.5, 126.0, 125.9, 125.8, 125.7, 125.6, 123.9, 123.8, 122.5, 120.7, 120.6, 120.5, 117.8, 117.7, 117.6, 112.4, 112.3, 104.6, 104.4, 104.1, 92.2, 89.9, 89.6, 86.9, 48.4, 34.6, 34.5, 34.3, 31.8, 31.7, 31.6, 21.9; MALDI-TOF ($M+H^{+}$, *m/z*): calcd for $C_{116}H_{106}N_8O_2$ 1644.86, found 1644.44; elemental analysis calcd (%) for $C_{116}H_{106}N_8O_2$: C 84.7, H 6.5, N 6.8; found C 84.6, H 6.5, N 6.9.

2. Computer modeling.

Computer modeling studies was conducted by MacroModel 9.1 implemented with OPLS2005[S3] force field. The minimized structure of **1** was obtained in the gas phase via 3000 separated search steps in Monte Carlo conformational search.[S4].

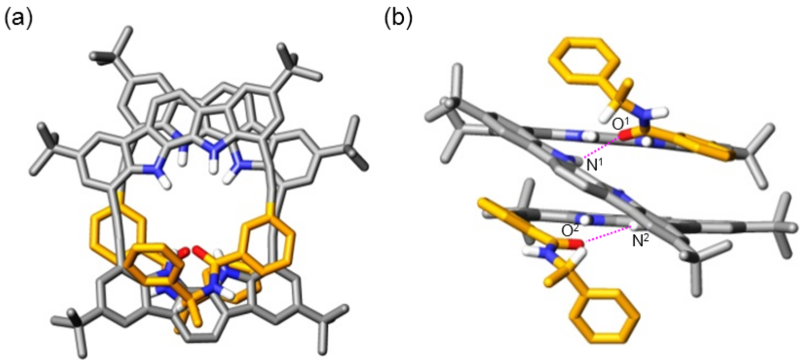


Fig. S1 Two views of the energy-minimized structure of **1** wherein amide residues at ends were shown as yellow colors for clarity and intramolecular hydrogen bonds are marked as red-dotted lines in (b) Hydrogen atoms except NH protons are omitted for clarity.

3. Specific rotations and circular dichroism (CD) spectra.

3.1 CD values ($\Delta\varepsilon$) and optical rotation of **1** in organic solvents.

Each solution of **1** (3.0×10^{-5} M) was prepared in different organic solvents and the CD spectra recorded at 24 °C. On the other hand, specific rotations of **1** were measured with the concentration (*c*, mg/mL) of 0.5-1.0 at 24 ± 1 °C.

Table S1 Magnitudes of molar CD values ($\Delta\varepsilon$) at 366 nm and Optical Rotation $[\alpha]_D$ of **1** in different solvents (24 ± 1 °C).

Solvent	$\Delta\varepsilon$/M·cm	$[\alpha]_D$
toluene	– 263	– 765°
chloroform	– 129	– 556°
dichloromethane	– 117	– 514°
acetonitrile	– 5.4	– 0.3°
acetone	+ 1.2	– 0.3°
DMSO	– 14	+ 6.5°

[S3] (a) W. L. Jorgensen and J. J. Tirado-Rives, *Am. Chem. Soc.*, 1988, **110**, 1657; (b) W. L. Jorgensen, D. S. Maxwell and J. J. Tirado-Rives, *Am. Chem. Soc.*, 1996, **118**, 11225; (c) G. A. Kaminski, R. A. Friesner, J. Tirado-Rives and W. J. Jorgensen, *J. Phys. Chem. B.*, 2001, **105**, 6474.

[S4] (a) M. Saunders, K. N. Houk, Y. D. Wu, W. C. Still, M. Lipton, G. Chang. W. C. Guida, *J. Am. Chem. Soc.,* 1990, **112**, 1419.

3.2 Changes in CD and UV-visible spectra of **1** upon addition of tetrabutylammonium (TBA) anions in CH_2Cl_2.

Stock solutions of TBA anions were also prepared with the concentrations of 2.0-3.0 × 10^{-3} M in CH_2Cl_2 at 24 ± 1 °C. To a solution (3.0 × 10^{-5} M, 2.0 mL) of **1**, small portions of the guest solution, and the spectrum was recorded after each addition. (Scanning rate: 500 nm/min, bond width: 0.1 nm, response time: 1.0 sec, accumulations: 2 scan).

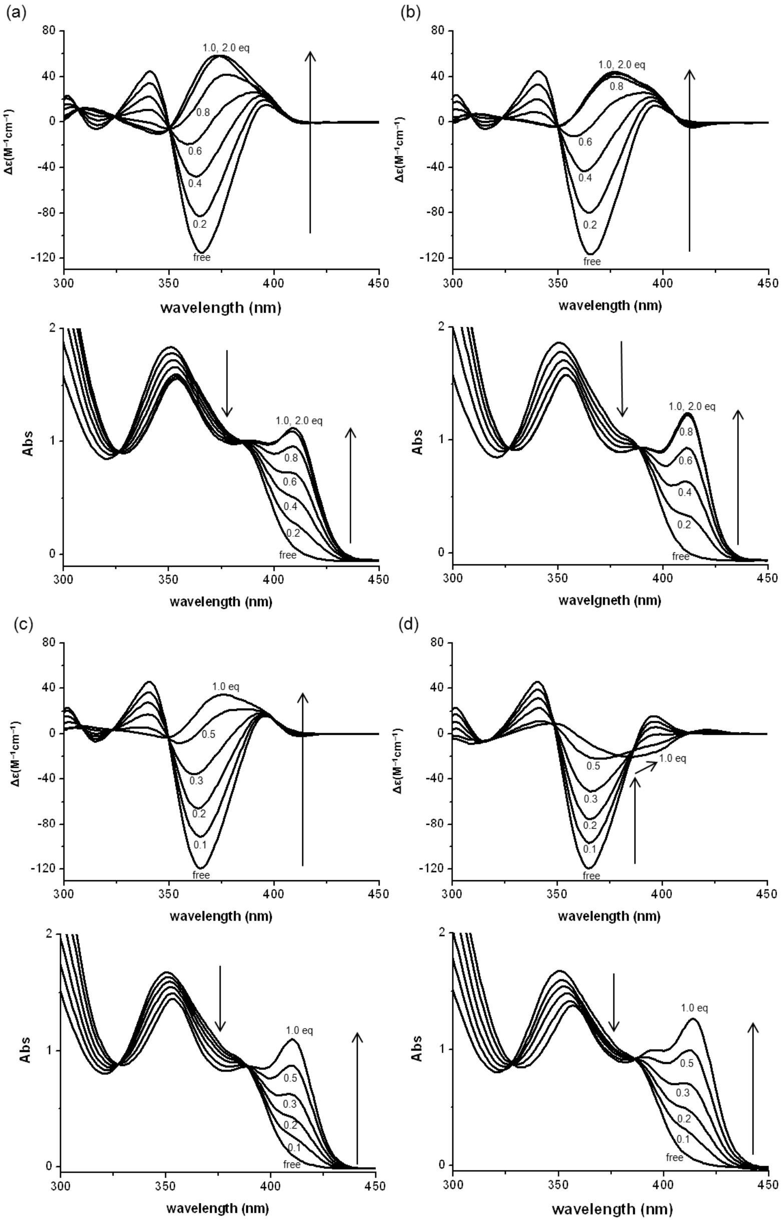
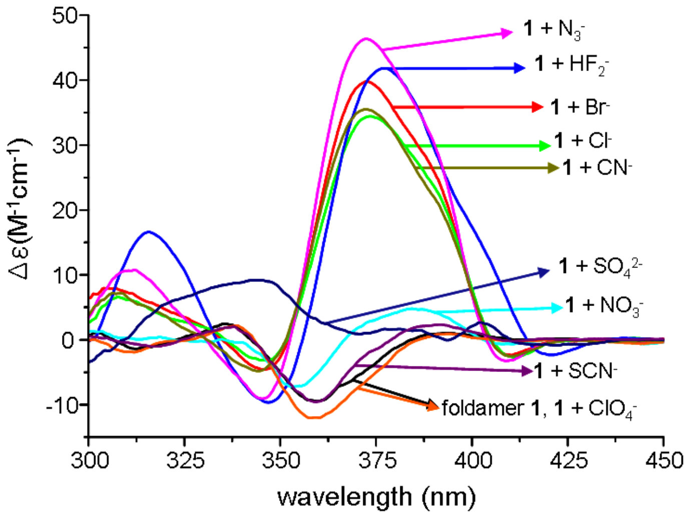


Fig. S2 Changes in the CD (top) and UV-visible spectra (bottom) of **1** (3.0 × 10^{-5} M in CH_2Cl_2) upon addition of TBA anions, (a) AcO^-, (b) Cl^-, (c) Br^- and (d) SO_4^{2-}.

3.3 CD spectra of **1** in the presence of TBA anions (1 equiv) in CH_3CN.

CD spectra of **1** in the presence of TBA anions (1 equiv) were recorded with the concentration of 3.0 × 10^{-5} M in CH_3CN at 24 ±1 °C. (Scanning rate: 500 nm/min, bond width: 0.1 nm, response time: 1.0 sec, accumulations: 2 scan). The spectra remained nearly unchanged when more than 1 equiv of the anion were added.



Anion	$\lambda_{(max)}$	Δε
free	359.7	-9.47
N_3^-	372.5	46.37
HF^{2-}	377.2	41.84
Br^-	372.5	39.79
Cl^-	373.4	34.42
CN^-	372.2	35.52
SO_4^{2-}	344.0	9.19
NO^{3-}	384.2	4.78
SCN^-	359.2	-9.55
ClO_4^-	357.9	-12.06

Fig. S3 CD spectral data of **1** in the presence of TBA anions (1 equiv) at 24 ± 1 °C in CH_3CN.

4. ^{1}H NMR spectra of complex between **1** and tetrabutylammonium chloride (TBACl).

4.1 ^{1}H NMR spectral changes of **1** with increasing TBACl.

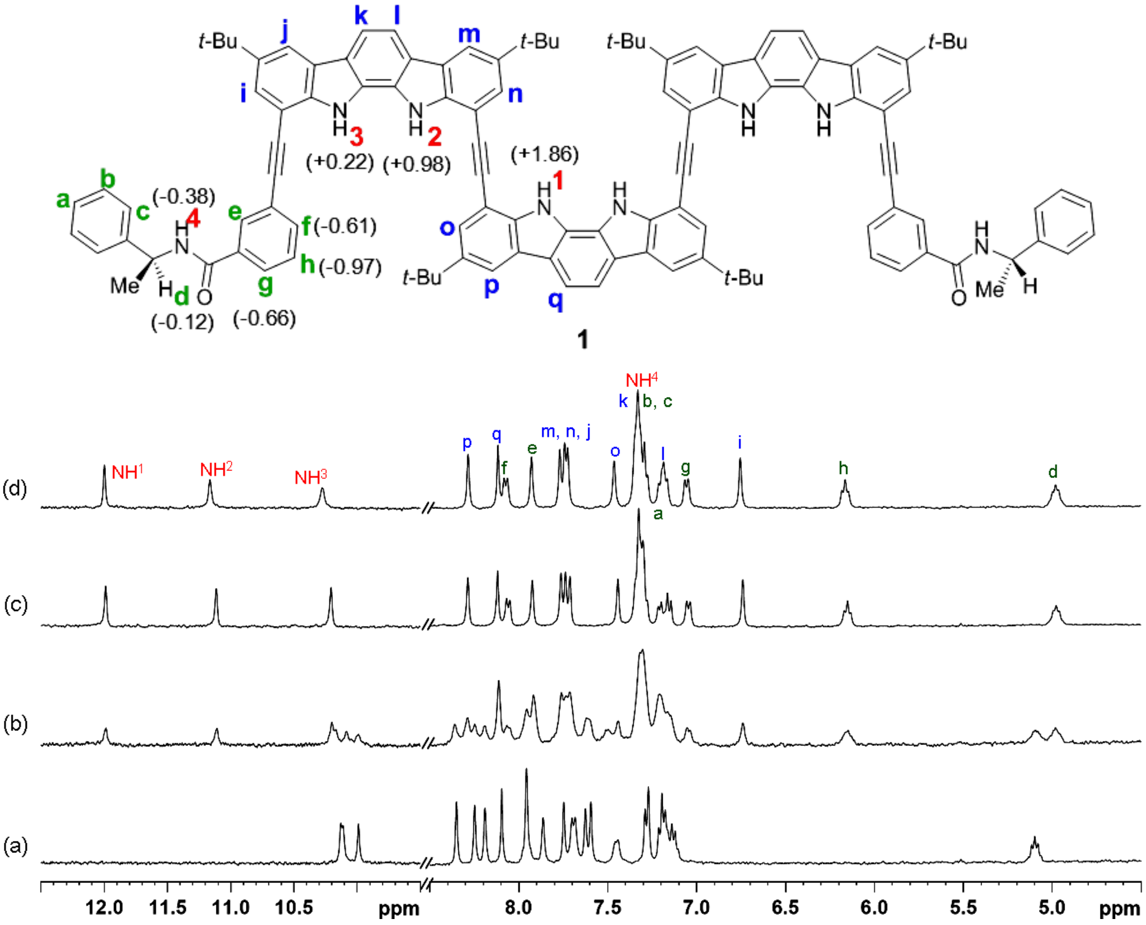


Fig. S4 Partial ^{1}H NMR spectra (400 MHz, 1:1(v/v) acetone-d_6/CD_3CN, 25 °C of (a) free **1** (0.5 mM) and in the presence of TBA chloride (b) 0.5 equiv, (c)1.1 equiv and (d) 2.1 equiv The values in the parentheses of a molecular structure (top) are chemical shift changes, Δδ (ppm) = δ (complex) - δ (free), upon saturation.

4.2 ^{1}H-^{1}H 2D NMR (COSY and NOESY) spectra of **1** in the presence of TBACl (1 equiv).

A solution of **1** (1.5×10^{-3} M) and tetrabutylammonium chloride (1 equiv) was prepared in 1:1(v/v) actone-d_6/CD_3CN. The COSY spectrum was taken using the pulse programs of cosygpqf at 298 K and the NOESY experiment was carried out using the pulse programs of roesyph and the mixing time was 600 ms at 25 °C.

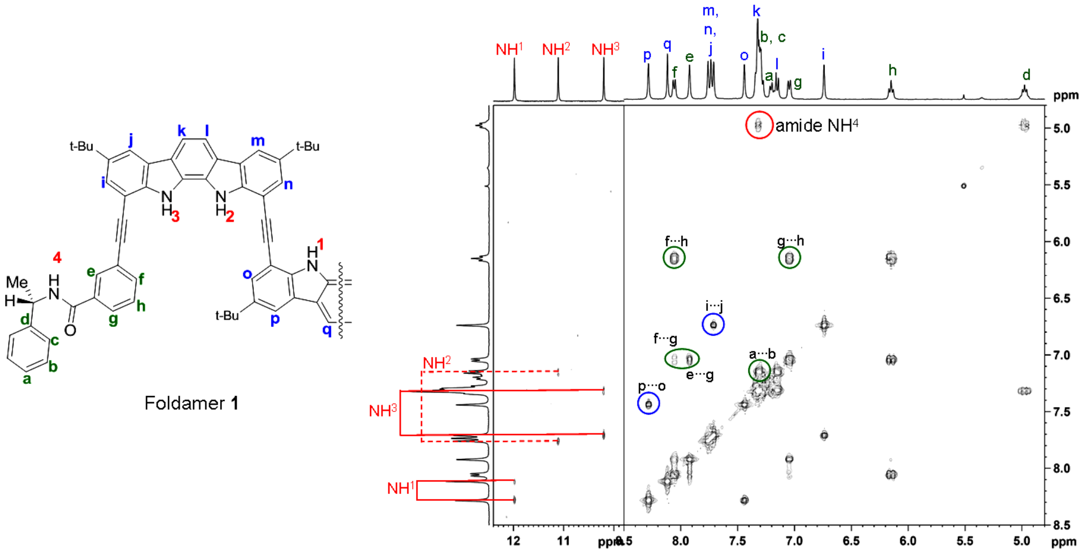


Fig. S5 Peak assignments based on the COSY spectrum (400 MHz, 1:1(v/v) acetone-d_6/CD_3CN, 25 °C).

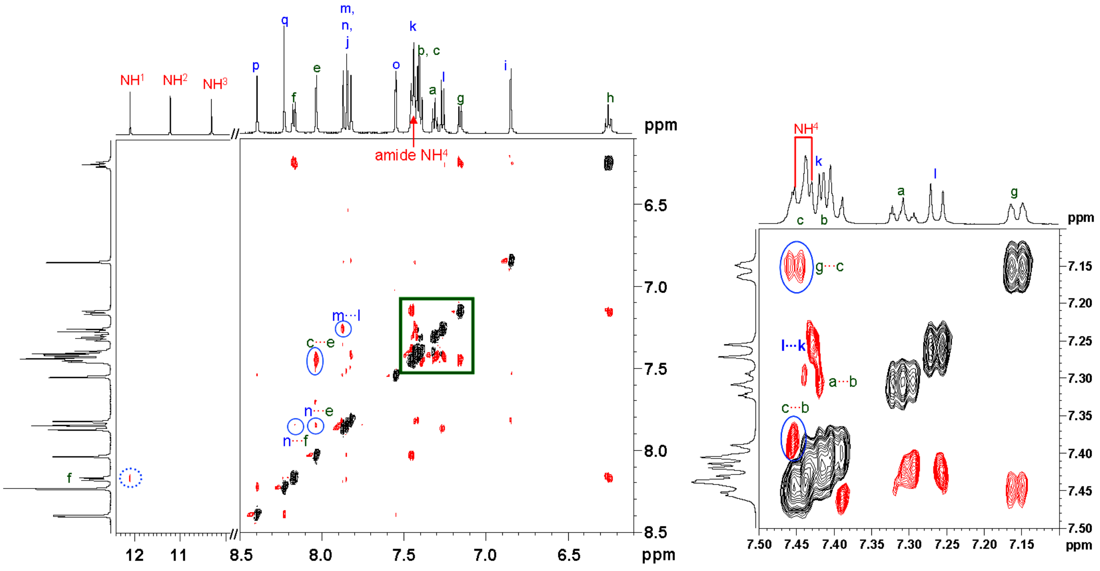


Fig. S6 NOE correlations observed in the ^{1}H-^{1}H 2D NOESY spectra (500 MHz, 1:1(v/v) acetone-d_6/CD_3CN, at 25 °C).

5. UV-visible titrations between **1** and anions.

Binding studies of **1** with tetrabutylammonium anions were conducted in 10% MeOH/CH_3CN by UV-visible spectroscopy. First, a solution of **1** (1.5×10^{-5} M) was prepared in 10% MeOH/ CH_3CN at 23 ± 1°C, with which stock solutions of anions ($1.0 \sim 2.0 \times 10^{-3}$ M) were prepared. A solution (2.0 mL) of free **1** was transferred to a UV cuvette, and an initial spectrum was taken. To this solution added were small portions of the anion solution (initially, 2-50 μL, and later 60 to 500 μL, 9-11 point), and the spectrum was recorded after each addition. The association constants (K_a, M^{-1}) were determined by nonlinear curve fitting of the titration curves[S4], plotting the UV-visible absorbance at against equivalents of an anion added (365, 405, 410 nm). The reported ones are averages calculated at three wavelengths.

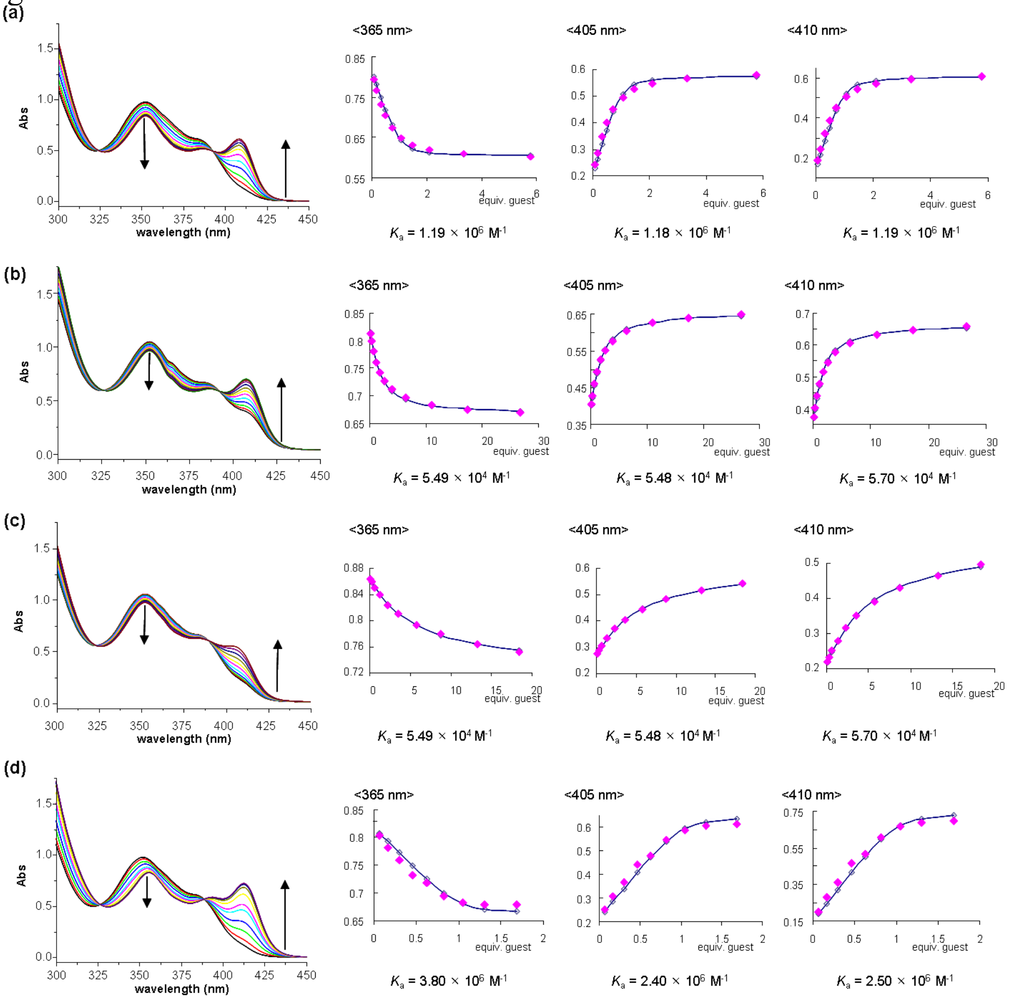


Fig. S7 UV–visible spectra and saturation curves (lines: calculated, dots: experimental) for the titrations of **1** with tetrabutylammonium anions a) Cl^-, b) Br^-, c) AcO^- and d) SO_4^{2-}.

[S4](a) Connors, K. A. *Binding Constants*; John Wiley & Sons: New York, 1987; (b) R. S. Macomber, *J. Chem. Educ.*, 1992, **69**, 375; (c) P. Thordarson, *Chem. Soc. Rev.*, 2011, **40**, 13 05.

6. X-ray crystallographic analysis.

Single crystals were grown as follow: **1** and tetrabutylammounium chloride (TBACl, 2.0 equiv) were dissolved in 1/2 (v/v) EtOAc/CH_2Cl_2. *n*-Hexane was slowly diffused to this solution for a week to afford single crystals suitable for the X-ray diffraction.

A specimen of suitable size and quality was coated with Paratone oil and mounted onto a glass capillary. Reflection data were collected on a Bruker D8 Venture PHOTON 100 area detector diffractometer, with Cu IμS microfocus tube radiation ($\lambda = 1.54178$ Å). The full sphere of reflection data were collected as ω scan frames with 1°/frame and an exposure time of 20 s/frame. Cell parameters were determined and refined by APEX2 program. [S5] Data reduction was performed using SAINT software.[S6] The data were corrected for Lorentz and polarization effects. An empirical absorption correction was applied using the SADABS program.[S7] The structure was solved by direct methods and all nonhydrogen atoms were subjected to anisotropic refinement by full-matrix least-squares on F^2 by using the SHELXTL/PC package.[S8] Hydrogen atoms were placed at their geometrically calculated positions and refined riding on the corresponding carbon atoms with isotropic thermal parameters. Restraint SIMU was applied to methyl groups so that anisotropic displacement parameters of C were similar in the t-butyl group. Restrain for disordered atoms C63A, C63B, C64A, C64B, C65A and C65B was applied so that the Ueq values were adjusted to similar with neighbor atoms. Solvent mask was used to treat highly disordered solvent molecules by Olex 2.[S9]

A summary of the crystal data is given in Table S4 and S5. CCDC-951836. The data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html or from the Cambridge Crystallographic Data Centre, 12, Union Read, Cambridge CB2 1EZ, UK.

[S5] APEX2, version 2012.2-0, Data collection software, Bruker AXS, Inc., Madison, WI, 2011.

[S6] SAINT, version 6.0, Data integration software, Bruker AXS Inc., Madison, WI, 2011.

[S7] G. M. Sheldrick, version 2.05 SADABS, Program for absorption correction with the Bruker SMART system, Universitat Gottingen, Germany, 2011.

[S8] G. M. Sheldrick, SHELXL-93: Program for the refinement of crystal structures; Universitat Gottingen: Germany, 2004.

[S9] O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, OLEX2: a complete structure solution, refinement and analysis program. J. Appl. Cryst. (2009). 42, 339-341.

Table S4 Hydrogen bonds length and bonds angles for **1**·TBACl [Å and °].

D-H…A	d(D-H)	d(H…A)	d(D…A)	∠(DHA)
N(3)-H…Cl^-	0.88	2.71	3.43	140.0
N(6)-H…Cl^-	0.88	2.51	3.22	138.8
N(23)-H…Cl^-	0.88	2.43	3.25	155.9
C(46)-H…Cl^-	0.95	3.93	4.63	132.9

Table S5 Crystal data and structure refinement for Complex **1**• TBACl.

Identification code	Complex **1**•TBACl
Empirical formula	C140H158ClN9O6
Formula weight	2098.19
Temperature/K	170.0
Crystal system	orthorhombic
Space group	P21212
a/Å	37.1603(8)
b/Å	11.1559(3)
c/Å	15.1723(3)
α/°	90
β/°	90
γ/°	90
Volume/Å3	6289.8(2)
Z	2
ρcalcmg/mm3	1.108
m/mm-1	0.709
F(000)	2252.0
Crystal size/mm3	0.2 × 0.1 × 0.1
2Θ range for data collection	4.76 to 159.86°
Index ranges	-46 ≤ h ≤ 47, -14 ≤ k ≤ 14, -17 ≤ l ≤ 18
Reflections collected	60832
Independent reflections	12693[R(int) = 0.0467]
Data/restraints/parameters	12693/36/778
Goodness-of-fit on F2	1.063
Final R indexes [I>=2σ (I)]	R1 = 0.0617, wR2 = 0.1587
Final R indexes [all data]	R1 = 0.0906, wR2 = 0.1816
Largest diff. peak/hole / e Å-3	0.35/-0.23
Flack parameter	0.027(8)