Pfeiffer effect on Configurationally Labile Dyes within Ternary Complexes with Metal Ions and Enantiopure Macrocycles

Dávid Pál and Jérôme Lacour*

Department of Organic Chemistry, University of Geneva, 30 quai Ernest Ansermet, CH-1211 Geneva, Switzerland

Supporting Information

Contents

1. Overview of compounds S3
2. Experimental methods S4
2.1. Synthesis and characterizationS4
2.2. UV-vis and electronic circular dichroism measurements
3. Synthesis of the compounds S5
3.1. Oximate salts
3.1.1. Potassium 2,4,5,7-tetranitro-9H-fluoren-9-one oximate [K][1]
3.2. Macrocycles
4. UV-vis and electronic circular dichroism (ECD) studies
4.1. UV–vis and ECD spectra of enantiopure ${f 2}$ with Bu ₄ N ⁺ ion (control experiments)S9
4.2. UV-vis and ECD titration of (<i>R</i> , <i>R</i>)- 2 and (<i>S</i> , <i>S</i>)- 2 with alkali metal ionsS10
4.3. UV-vis and ECD titration of (<i>R</i> , <i>R</i>)- 2 and (<i>S</i> , <i>S</i>)- 2 with alkaline earth metal ionsS12
4.4. UV-vis and ECD titration of [Bu ₄ N][1] with (<i>R</i> , <i>R</i>)- 2 S13
4.5. UV-vis and ECD titration of 1 with (<i>R</i> , <i>R</i>)- 2 in the presence of alkali metal ionsS14
4.6. UV-vis and ECD titration of 1 with (R,R)- 2 in the presence of Ba ²⁺ ionsS16
5. ¹ H NMR experiments S17
6. Temperature-dependent equilibrium between ternary complexes
7. References

1. Overview of compounds



(S)- and (R)-2-(((2,4,5,7-tetranitro-9H-fluoren-9-ylidene)amino)oxy)propanoic acid

Figure S1.

2. Experimental methods

2.1. Synthesis and characterization

Starting materials were purchased from Sigma-Aldrich unless otherwise noted. Compounds [Bu₄N][1].^[S1] [Na][1].^[S1] and 2^[S2] were prepared as reported in the literature. Lithium perchlorate (Fluka), sodium perchlorate monohydrate (Fluka), potassium perchlorate (Acros Organics), rubidium perchlorate (abcr), cesium perchlorate (Sigma-Aldrich), magnesium perchlorate (Fluka), calcium perchlorate tetrahydrate (Acros Organics), strontium perchlorate trihydrate (Thermo Scientific), and barium perchlorate (Acros Organics) were purchased from commercial sources and used without further purification. Enantiomers of rac-2 were separated by HPLC using a Daicel Chiral Technologies CHIRALPAK[®] IG (inner diameter × length; particle size: 10 mm \times 250 mm; 5 µm) semi-preparative column as chiral stationary phase and CH₂Cl₂-MeCN 70:30 (0.1% Et₂NH) as eluent (2.0 mL/min flow rate, 25 °C). 23 mg of rac-2 dissolved in CH₂Cl₂ (1.5 mL), inj.: 500 µL. Ratios of solvents for the eluents are given in volumes (mL/mL). NMR spectra were measured using a Bruker Avance III HD Nanobay 400 MHz spectrometer equipped with a 5 mm CPP BBO probe, or using a Bruker Avance III 500 MHz spectrometer equipped with a 5 mm CPP DCH ¹³C-¹H/D helium-cooled cryogenic probe. NMR solvent: MeCN- d_3 (Apollo Scientific). All signals were internally referenced to the solvent residue (MeCN- d_3 : 1.940 ppm for ¹H NMR).

2.2. UV-vis and electronic circular dichroism measurements

UV-visible spectra were taken using a Jasco V-650 spectrophotometer equipped with a programmable temperature control system. Electronic circular dichroism (ECD) spectra were measured using a Jasco J-815 spectrometer equipped with a Peltier cuvette holder and a programmable temperature control system with the following parameters: 200 nm/min scan speed, 1 nm slit width, 1 sec integration time, 10 accumulations. Temperature was set to 20 °C. All spectra were baseline corrected by subtraction of the solvent spectrum. All spectra were recorded in analytical grade acetonitrile. Quartz cuvettes with path length of 1 cm were used. Software: Spectra Manager.

3. Synthesis of the compounds

3.1. Oximate salts

A straightforward synthesis of oximate salts was carried out as outlined in Scheme S1. Condensation of tetranitrofluorenone $3^{[S3]}$ with hydroxylamine hydrochloride afforded oxime $4^{[S4]}$. Then, various ion pairs were prepared by quantitative reactions with hydroxide/methoxide bases to afford the sodium, potassium and tetrabutylammonium salts, namely [Na][1],^[S1] [K][1] and [Bu₄N][1].^[S1]



Scheme S1. Synthesis of salts [Na][1], [K][1], and [Bu₄N][1].

3.1.1. Potassium 2,4,5,7-tetranitro-9H-fluoren-9-one oximate [K][1]

To a solution of 2,4,5,7-tetranitro-9*H*-fluoren-9-one oxime (**4**, 20.0 mg, 0.0533 mmol) in methanol (1.5 mL) was added a 0.1 N methanolic solution of potassium methoxide (0.0533 mmol, 0.533 mL). The resulting dark red mixture was stirred at room temperature for 2 hours then the volatile components were removed under reduced pressure to obtain dark red crystals. Yield: 22 mg (100%) dark red (burgundy) crystals. M. p.: 290 °C (decomposition). ¹H NMR (MeCN-*d*₃, 500 MHz, 298 K) δ (ppm): 9.77 (d, *J* = 2 Hz, 1H), 9.58 (d, *J* = 2 Hz, 1H), 8.57 (d, *J* = 2 Hz, 1H), 8.55 (d, *J* = 2 Hz, 1H). ¹³C NMR (MeCN-*d*₃, 125 MHz, 298 K) δ (ppm): 152.2, 149.7, 146.9, 146.9, 145.9, 145.8, 127.0, 122.4, 119.8, 119.8, 119.0, 115.1, 114.2. IR (solid) v_{max} (cm⁻¹): 3091, 1573, 1518, 1451, 1336, 1321, 1234, 1162, 1134, 1097, 1062, 1015, 930, 845, 726. HR-MS (ESI–) calculated for C₁₃H₄N₅O₉⁻ [M]⁻ (*m/z*) 374.0009, found 374.0005.



Figure S2. A) ¹H NMR (MeCN-*d*₃, 500 MHz, 298 K) and **B**) ¹³C NMR (MeCN-*d*₃, 125 MHz, 298 K) spectra of compound [K][**1**].

3.2. Macrocycles

The two-step synthesis of constrained polyether macrocycle *rac*-2 was developed in our group (Scheme S2). The rhodium(II)-catalyzed 3+6+3+6 reaction of α -diazo- β -ketoester **5** and 1,4-dioxane enabled the efficient large-scale preparation of macrocycle **6**.^[S5,S6] Chiral 18-crown-6 ether-based *rac*-**2** was then formed through a *syn* diastereoselective (d.r. > 49:1) double and tandem amidation-olefin transposition process of diester **6**.^[S2,S7] The enantiomers of *rac*-**2** were separated by semi-preparative CSP-HPLC.



Scheme S2. Synthesis of functionalized macrocycle 2.

4. UV-vis and electronic circular dichroism (ECD) studies

Perchlorate salts were used in the UV-visible and ECD studies.

4.1. UV-vis and ECD spectra of enantiopure **2** with Bu₄N⁺ ion (control experiments)



Figure S3. A) UV–vis and B) ECD spectra of enantiopure 2 (20 μ M), and the spectra in the presence of 1000 equiv Bu₄N⁺ in MeCN.



4.2. UV-vis and ECD titration of (R,R)-2 and (S,S)-2 with alkali metal ions

Figure S4. UV–vis (A–C) and ECD (D–F) spectra of (R,R)-2 (20 µM), (S,S)-2 (20 µM), and their spectra in the presence of Li⁺, Na⁺ or K⁺ in MeCN.



Figure S5. UV–vis (**A** and **B**) and ECD (**C** and **D**) spectra of (*R*,*R*)-**2** (20 μM), (*S*,*S*)-**2** (20 μM), and their spectra in the presence of Rb⁺ (solution saturated with RbClO₄) or Cs⁺ in MeCN.



4.3. UV-vis and ECD titration of (R,R)-2 and (S,S)-2 with alkaline earth metal ions

Figure S6. UV–vis (A–D) and ECD (E–H) spectra of (*R*,*R*)-2 (20 μ M), (*S*,*S*)-2 (20 μ M), and their spectra in the presence of Mg²⁺, Ca²⁺, Sr²⁺ or Ba²⁺ in MeCN.

4.4. UV-vis and ECD titration of [Bu₄N][1] with (R,R)-2



Figure S7. UV–vis (**A**) and ECD (**B**) spectra of $[Bu_4N][1]$ (200 μ M), and the spectra in the presence of (*R*,*R*)-2 in MeCN.



4.5. UV-vis and ECD titration of 1 with (*R*,*R*)-2 in the presence of alkali metal ions

Figure S8. Series of absorption spectra upon titration of A) [Li][1], B) [Na][1], C) [K][1], D) [Rb][1] or E) [Cs][1] (200 μ M) with (*R*,*R*)-2 in MeCN.



Figure S9. Series of ECD spectra upon titration of **A**) [Li][**1**], **B**) [Na][**1**], **C**) [K][**1**], **D**) [Rb][**1**] or **E**) [Cs][**1**] (200 μM) with (*R*,*R*)-**2** in MeCN.

4.6. UV-vis and ECD titration of **1** with (R,R)-**2** in the presence of Ba²⁺ ions

Note: to compare ε molar extinction coefficients and $\Delta \varepsilon$ differential molar extinction coefficients globally, values are given for formula [Ba]_{1/2}[1].



Figure S10. A) Series of absorption spectra, and **B)** ECD spectra upon titration of $[Ba]_{\frac{1}{2}}[1]$ (200 μ M) with (*R*,*R*)-2 in MeCN.

5. ¹H NMR experiments



Figure S11. A) ¹H NMR (MeCN-*d*₃, 500 MHz, 298 K) and **B**) ¹³C NMR (MeCN-*d*₃, 125 MHz, 298 K) spectra of compound [Bu₄N][**1**].



Figure S12. A) ¹H NMR (MeCN-*d*₃, 500 MHz, 298 K) and **B**) ¹³C NMR (MeCN-*d*₃, 125 MHz, 298 K) spectra of compound [Na][1].



Figure S13. A) ¹H NMR (MeCN-*d*₃, 500 MHz, 298 K) and **B**) ¹³C NMR (MeCN-*d*₃, 125 MHz, 298 K) spectra of compound **2**.



Figure S14. ¹H NMR (MeCN-d₃, 400 MHz, 298 K) spectra upon titration of 2 (2 mM) with [Na][1].



Figure S15. ¹H NMR (MeCN-d₃, 400 MHz, 298 K) spectra upon titration of 2 (2 mM) with [Bu₄N][1].



Figure S16. ¹H NMR (MeCN-*d*₃, 400 MHz, 298 K) spectra of **A**) the ternary complex *i.e.* **2** (2 mM) in the presence of 7.2 equiv [Na][**1**] and **B**) **2**•Na⁺ *i.e.* **2** (2 mM) in the presence of 4.0 equiv NaClO₄.



Figure S17. Variable temperature ¹H NMR (MeCN-*d*₃, 500 MHz) of 1:2 mixture of [Na][**1**] (1 mM) and **2** (2 mM).



Figure S18. A) NOESY (MeCN- d_3 , 500 MHz, 343 K, $d_8 = 500$ ms) of [Na][1] (1 mM) and 2 (2 mM), B) one of the plausible conformations in accordance.

6. Temperature-dependent equilibrium between ternary complexes



7. References

- S1. D. Pál, C. Besnard, A. de Aguirre, A. I. Poblador-Bahamonde, G. Pescitelli, J. Lacour Chem. Eur. J. 2023, e202302169.
- S2. Z. Jarolímová, M. Vishe, J. Lacour, E. Bakker Chem. Sci. 2016, 7, 525–533.
- S3. M. S. Newman, W. B. Lutz J. Am. Chem. Soc. 1956, 78, 2469–2473.
- S4. S. B. Strashnova, O. V. Avramenko, A. V. Churakov, V. S. Sergienko, O. V. Koval'chukova, B. E. Zaitsev *Russ. J. Inorg. Chem.* **2008**, *53*, 1586–1589.
- S5. D. Poggiali, A. Homberg, T. Lathion, C. Piguet, J. Lacour ACS Catalysis 2016, 6, 4877–4881.
- S6. W. Zeghida, C. Besnard, J. Lacour Angew. Chem. Int. Ed. 2010, 49, 7253-7256.
- S7. A. Homberg, J. Lacour Chem. Sci. 2020, 11, 6362–6369.