Interconversion between Möbius Chiroptical States Sustained by Hexaphyrin Dynamic Coordination

Bernard Boitrel, and Stéphane Le Gac

SUPPORTING INFORMATION

1. Experimental part

General

Characterization of 1.Zn_{L1}^{L2}

Figure S1. Selected ¹H NMR Complexation Induced Shift for $1.2n_{L1}^{L2}$.

Typical procedures for the switching between $1.Zn_{L1}$ and $1.Zn_{L1}^{L2}$

2. Selected ¹H NMR spectra for the optimization of the Boc protection sequence

Figure S2. ¹H NMR spectra corresponding to the interconversion between **1.Zn**_{OAc} and **1.Zn**_{OAc}^{NH2Bu}, performed at RT.

Figure S3. ¹H NMR spectra corresponding to the interconversion between **1.Zn**_{OAc} and **1.Zn**_{OAc}^{NH2Bu}, the backward process being performed at 50 °C.

Figure S4. Comparison of the ¹H NMR spectra of **1.Zn**_{OAc}, before and after interconversion with **1.Zn**_{OAc}^{NH2Bu}, with the backward process performed at RT or at 50 °C.

Figure S5. ¹H NMR spectra corresponding to the interconversion between **1.Zn**_{OAc} and **1.Zn**_{OAc}^{NH2Bu}, the backward process being performed at RT with different amounts of Boc₂O.

3. Selected ¹H NMR spectra for the switching between 1.Zn_{L1} and 1.Zn_{L1}^{L2}

Figure S6. Partial ¹H NMR spectra related to the *in situ* interconversion between **1.Zn**_{OAC} and **1.Zn**_{OAC}^{NH2Bu}.

Figure S7. Partial ¹H NMR spectra related to the *in situ* interconversion between **1.Zn**_{L1} and **1.Zn**_{L1}^{NH2Bu} (L₁ = (*S*)BocProO⁻).

Figure S8. Partial ¹H NMR spectra related to the *in situ* interconversion between **1.Zn**_{OAC} and **1.Zn**_{OAC}^{(S)MBA}.

4. Selected ECD spectra for the switching between $1.Zn_{L1}$ and $1.Zn_{L1}^{L2}$

Figure S9. ECD spectra (general overview) related to the *in situ* interconversion between **1.Zn**_{L1} and **1.Zn**_{L1}^{L2}: (a) with $L_1 = (S)BocProO^{-}/L_2 = BuNH_2$; (b) with $L_1 = (R)BocProO^{-}/L_2 = BuNH_2$.

Figure S10. ECD spectra (detailed steps) related to the *in situ* interconversion between $1.Zn_{L1}$ and $1.Zn_{L1}^{L2}$, with $L_1 = (S)BocProO^{-}/L_2 = BuNH_2$.

Figure S11. ECD spectra (general overview) related to the *in situ* interconversion between **1.Zn**_{OAc} and **1.Zn**_{OAc}^{(S)MBA} or **1.Zn**_{OAc}^{(R)MBA}.

Figure S12. ECD spectra (detailed steps) related to the *in situ* interconversion between **1.Zn**_{OAc} and **1.Zn**_{OAc}^{(S)MBA}.

Figure S13. ECD spectra (detailed steps) related to the *in situ* interconversion between $1.Zn_{OAC}$ and $1.Zn_{OAC}$ ^{(S)MBA} or $1.Zn_{OAC}$ ^{(R)MBA}.

1. Experimental part

General

All chemicals were commercial products used as received. ¹H NMR spectra were recorded at 298 K (unless otherwise stated), at 500 MHz. Residual traces of solvent were used as internal standard. The NMR experiments were conducted in 5 mm standard NMR tubes. The ECD spectra were recorded in a quartz glass cuvette of 2 mm optical path length, at ca. 20 °C. The synthesis of **1** and the ¹H NMR characterization of the various complexes **1Zn**_{L1} and **1Zn**_{L1}^{L2} were previously reported.¹ It is worth to note that these metal complexes exhibit hindered rotation of the 2-acetamidophenyl *meso* substituents, and thus correspond to dynamic mixtures of atropisomers.

Characterization of $1.Zn_{\text{L1}}^{\text{L2}}$



¹H NMR (CDCl₃/CD₃OD 9:1, 298 K, partial descriptions because of a strong overlapping and/or highly broaden signals; selected complexation induced shifts are displayed Figure S1):

1.Zn _{OAc} ^a	β-pyr <i>inner</i>	β-pyr <i>twisted</i>			
	M: -2.60 (s _b , 1H), -1.95 (d, <i>J</i> = 4.7 Hz, 1H) m: -2.81 (s _b , 1H), -1.79 (d, <i>J</i> = 4.5 Hz, 1H)	5.2 to 5.9: broad signals with strong overlapping			
	HAr ^{ortho} inward	OAc			
	M: 4.17 (d <i>, J</i> = 7.1 Hz, 1H)	-0.99 (s _b)			
	m: 4.19 (d <i>, J</i> = 6.1 Hz, 1H)	-0.95 (s _b)			
a "M" and "m" stand for major and minor.					

β-pyr <i>inner</i>	β-pyr <i>twisted</i>	
A : -2.68 (d, <i>J</i> = 4.6 Hz, 1H),	A : 4.84 (d, <i>J</i> = 4.3 Hz,	1H),
-1.66 (d, J = 4.8 Hz, 1H)	4.87 (d <i>, J</i> = 4.5 Hz,	1H)
B : -2.57 (d, <i>J</i> = 4.4 Hz, 1H),	B : 4.89 (d, <i>J</i> = 4.4 Hz, 1H),	
-1.51 (d, <i>J</i> = 4.4 Hz, 1H)	4.99 (d, J = 4.3 Hz,	1H)
C : -2.42 (d, <i>J</i> = 4.9 Hz, 1H),	C : 4.95 (d, <i>J</i> = 4.5 Hz,	1H),
-1.60 (d, <i>J</i> = 4.7 Hz, 1H)	5.05 (d, J = 4.4 Hz, 1H)	
HAr ^{ortho} inward	OAc	BuNH ₂ (α-CH ₂) ^b
A : 4.61 (d, <i>J</i> = 7.5 Hz, 1H)	A: -1.16 (s, 3H)	1.76/2.00
B : 4.62 (d, <i>J</i> = 7.2 Hz, 1H)	B: -1.12 (s, 3H)	
C : 4.44 (d, <i>J</i> = 7.2 Hz, 1H)	C: -1.20 (s, 3H)	
	β-pyr inner A: -2.68 (d, J = 4.6 Hz, 1H), -1.66 (d, J = 4.8 Hz, 1H) B: -2.57 (d, J = 4.4 Hz, 1H), -1.51 (d, J = 4.4 Hz, 1H) C: -2.42 (d, J = 4.9 Hz, 1H), -1.60 (d, J = 4.7 Hz, 1H) HAr ^{ortho} inward A: 4.61 (d, J = 7.5 Hz, 1H) B: 4.62 (d, J = 7.2 Hz, 1H) C: 4.44 (d, J = 7.2 Hz, 1H)	β -pyr inner β -pyr twistedA: -2.68 (d, J = 4.6 Hz, 1H), -1.66 (d, J = 4.8 Hz, 1H)A: 4.84 (d, J = 4.3 Hz, 4.87 (d, J = 4.5 Hz, B: -2.57 (d, J = 4.4 Hz, 1H)B: -2.57 (d, J = 4.4 Hz, 1H), -1.51 (d, J = 4.4 Hz, 1H)B: 4.89 (d, J = 4.4 Hz, 4.99 (d, J = 4.3 Hz, C: -2.42 (d, J = 4.9 Hz, 1H)C: -2.42 (d, J = 4.9 Hz, 1H), -1.60 (d, J = 4.7 Hz, 1H)C: 4.95 (d, J = 4.5 Hz, 5.05 (d, J = 4.5 Hz, 5.05 (d, J = 4.4 Hz,HArortho inwardOAcA: 4.61 (d, J = 7.5 Hz, 1H)A: -1.16 (s, 3H) B: 4.62 (d, J = 7.2 Hz, 1H)B: 4.62 (d, J = 7.2 Hz, 1H)C: -1.20 (s, 3H)

^{*a*} At 278 K. The labeling "A", "B" and "C" corresponds to the three major species retaining the characteristic resonances of Zn(II) Möbius complexes (see ref [1]).^{*b*} Average values obtained from 2D ROESY experiment.

¹ B. Boitrel and S. Le Gac, *Chem. Commun.*, 2020, **56**, 9166.

1.Zn _{(S)-BocProO} NH2Bu a	β-pyr <i>inner</i>	β-pyr <i>twisted</i>		
	M: -2.61 (d, <i>J</i> = 4.7 Hz, 1H),	M: 4.52 (d, <i>J</i> = 4.4 Hz, 1H),		
	-1.68 (d, <i>J</i> = 4.9 Hz, 1H)	4.70 (d, J = 4.6 Hz, 1H)		
	m: -2.58 (d, <i>J</i> = 4.6 Hz, 1H),	m: 4.63 (d <i>, J</i> = 4.3 Hz, 1H),		
	-1.61 (d, <i>J</i> = 4.4 Hz, 1H)	4.74 (d, J = 4.3 Hz, 1H)		
	HAr ^{ortho} inward	BuNH₂ (α-CH₂) ^b		
	M: 5.09 (d, J = 7.5 Hz, 1H)	1.79/2.04		
	m: 5.04 (d <i>, J</i> = 7.6 Hz, 1H)			
g (NA) and (m) atom of far major and minor h Average values a lateined from 2D DOFGV superiment				

^a "M" and "m" stand for major and minor. ^b Average values obtained from 2D ROESY experiment.

1.Zn_{OAc}^{(S)-MBA} a	β-pyr inner	β-pyr <i>twisted</i>		
	 A: -2.70 (d, J = 4.0 Hz, 1H), -1.69 (d, J = 4.1 Hz, 1H) B: -2.64 (d, J = 4.9 Hz, 1H), -1.60 (d_b, 1H) C: -2.85 (d, J = 4.8 Hz, 1H), -1.65 (d_b, 1H) 	4.8 to 5.15: broad signals with strong overlapping		
	HAr ^{ortho} inward	OAc	(S)-MBA (α-CH) ^b	
	A : 4.61 (d, <i>J</i> = 7.8 Hz, 1H) B : 4.58 (d, <i>J</i> = 7.3 Hz, 1H) C : 4.46 (d, <i>J</i> = 7.8 Hz, 1H)	A: -1.22 (s, 3H) B: -1.20 (s, 3H) C: -1.25 (s, 3H)	2.76 (q _b , J = 7.0 Hz, 1H) 2.92 (broad signal)	

^{*a*} The labeling "A", "B" and "C" corresponds to the three major species retaining the characteristic resonances of Zn(II) Möbius complexes (in total, five Möbius-type NMR patterns are observed). ^{*b*} Average values obtained from 2D ROESY experiment.



Figure S1. Selected ¹H NMR Complexation Induced Shift (CIS in ppm, $\Delta \delta = \delta_{\text{bound}} - \delta_{\text{free}}$) for **1.Zn**_{L1}^{L2} (CDCl₃/CD₃OD 9:1, 298 K). Because of the presence of multiple species, the CISs are given for the major species as single values or, for complex spectra, as a range of values.

Typical procedures for the switching between 1.Zn_{L1} and 1.Zn_{L1}^{L2}

¹H NMR monitoring of the switching between **1.Zn**_{OAc} and **1.Zn**_{OAc}^{NH2Bu} (approach A)

The two following solutions were prepared:

- **S1**: 8.0 mg of Zn(OAc)₂ in 9:1 CDCl₃/CD₃OD (500 μL).
- **S2**: 125.0 mg of Boc₂O in 9:1 CDCl₃/CD₃OD (500 μL).

In a NMR tube, hexaphyrin 1 (3.0 mg, 2.2 μ mol) was dissolved in 9:1 CDCl₃/CD₃OD (500 μ L). To this solution, 2 µL of DIPEA (11.5 µmol, 5 equiv.) and 45 µL of S1 (3.3 µmol, 1.5 equiv.) were successively added at room temperature. A ¹H NMR spectrum was immediately recorded showing formation of 1.Zn_{OAc}.

Forward process: 1.0 µL of BuNH₂ (10.1 µmol, 5 equiv.) was added, and a ¹H NMR spectrum was immediately recorded showing formation of ${\bf 1.Zn}_{OAc}{}^{\rm NH2Bu}$ [for the second and third forward processes, 1.5 μ L of BuNH₂ (15.1 μ mol, 7 equiv.) were added].

Backward process: 16 μL of S2 (14.2 μmol, 7 equiv.) were added and the NMR tube was left at RT; ¹H NMR spectra were regularly recorded showing completion of the backward process after 2 hours (only the signature of **1.Zn**_{OAc} was observed).

These two steps were repeated three times (see text, Figure 2A).

¹H NMR monitoring of the switching between $1.Zn_{L1}$ and $1.Zn_{L1}^{NH2Bu}$ (L₁ = (S)BocProO⁻)

The following solutions were prepared:

- **S3**: 20 mg of Zn(OTf)₂ in 9:1 CDCl₃/CD₃OD (500 μL).
- **S4**: 58 mg of (S)BocProOH in 9:1 CDCl₃/CD₃OD (500 μL).

In a NMR tube, hexaphyrin 1 (3.0 mg, 2.2 μ mol) was dissolved in 9:1 CDCl₃/CD₃OD (500 μ L). To this solution, 5 μL of DIPEA (28.7 μmol, 13 equiv.), 30 μL of **S3** (3.1 μmol, 1.5 equiv.), 20 μL of **S4** (9.7 μmol, 4 equiv.) were successively added at room temperature. A ¹H NMR spectrum was immediately recorded showing almost no metalation of 1.

Forward process: 1.0 µL of BuNH₂ (10.1 µmol, 5 equiv.) was added and the NMR tube was heated at 50 °C for 30 min [for the second and third forward processes, 1.5 μ L of BuNH₂ (15.1 μ mol, 7 equiv.) were added]. A ¹H NMR spectrum was recorded showing the formation of $1.Zn_{L1}^{NH2Bu}$ (L₁ = (S)BocProO⁻) as major product(s).²

Backward process: 16 μ L of **S2** (14.2 μ mol, 7 equiv.) were added and the NMR tube was left at RT; ¹H NMR spectra were regularly recorded showing completion of the backward process after 2 hours (the signature of $1.Zn_{L1}^{NH2Bu}$ (L₁ = (S)BocProO⁻) was no longer observed).

These two steps were repeated three times (Figure S7).

ECD monitoring of the switching between $1.Zn_{L1}$ and $1.Zn_{L1}^{NH2Bu}$ ($L_1 = BocProO^-$) and between $1.Zn_{OAC}$ and **1.Zn**OAc^{MBA}

Same procedure as for the NMR studies (same concentration of ca. 4 mM), but non-deuterated solvents were used, and NMR tubes were replaced by sealed vials with screw caps. For ECD

² A mixture of isomers is formed; note that an incomplete metalation is observed, which is likely due the steric hindrance of BocProO⁻ larger than that of AcO⁻ (see ref 1).

measurements, aliquots of 5 μL were diluted in 500 μL of CHCl₃/MeOH 9 :1 and ECD spectra immediately recorded.

For the switching between $\mathbf{1.Zn_{L1}}$ and $\mathbf{1.Zn_{L1}}^{NH2Bu}$ (L₁ = BocProO⁻), short time heating at 50 °C (15-30 min) was needed to complete the forward and backward processes (Figure S10).

For the switching between **1.Zn**_{OAc} and **1.Zn**_{OAc}^{MBA}, no heating was required, all processes were realized at RT.

2. Selected ¹H NMR spectra for the optimization of the Boc protection sequence



Figure S2-A. ¹H NMR spectra (CDCl₃/CD₃OD 9:1, 298 K, selected parts) corresponding to the interconversion between **1.Zn**_{OAc} and **1.Zn**_{OAc}^{NH2Bu}, performed at RT: a) **1**, 5 eq. DIPEA; b) upon addition of 1.5 eq. Zn(OAc)₂; c) upon addition of 5 eq. BuNH₂; d-g) respectively 5 min, 40 min, 2h15 and 5h30 upon addition of 5 eq. of Boc₂O. S = solvent, G = grease.



Figure S2-B. Same ¹H NMR experiment, selected part 3.5-0.7 ppm, scale/20, showing disappearance of BuNH₂ and formation of BuNHBoc.

Figure S2-C. Same ¹H NMR experiment, selected part 1.45-1.15 ppm, scale/200, showing disappearance of Boc_2O and formation of BuNHBoc along with tBuOH.



Figure S3. ¹H NMR spectra (CDCl₃/CD₃OD 9:1, 298 K, selected parts) corresponding to the interconversion between **1.Zn**_{OAc} and **1.Zn**_{OAc}^{NH2Bu}, the backward process being performed at 50 °C: a) **1**, 5 eq. DIPEA; b) upon addition of 1.5 eq. $Zn(OAc)_2$; c) upon addition of 5 eq. $BuNH_2$; d-g) respectively 20 min, 40 min, 80 min and 110 min upon addition of 5 eq. of Boc₂O. S = solvent, G = grease.



Figure S4. Comparison of the ¹H NMR spectra of **1.Zn**_{OAc} (CDCl₃/CD₃OD 9:1, 298 K, selected parts), before (a) and after interconversion with **1.Zn**_{OAc}^{NH2Bu} (addition of 5 eq. BuNH₂, then reaction with 5 eq. of Boc₂O), with the backward process performed at RT for 5h30 (b) or at 50 °C for 110 min (c). Dashed circle: apparition of a complex set of signals in the "non-aromatic" region, which might correspond to hexaphyrin degradation. S = solvent, G = grease.



Figure S5. ¹H NMR spectra (CDCl₃/CD₃OD 9:1, 298 K, selected parts) corresponding to the interconversion between **1.Zn**_{OAc} and **1.Zn**_{OAc}^{NH2Bu}, the backward process being performed at RT with different amounts of Boc₂O: a) **1**, 5 eq. DIPEA and 1.5 eq. Zn(OAc)₂; b) upon addition of 5 eq. BuNH₂; c-d) respectively 17 min and 60 min upon addition of 20 eq. of Boc₂O. e) **1**, 5 eq. DIPEA and 1.5 eq. Zn(OAc)₂; f) upon addition of 5 eq. BuNH₂; g-h) respectively 28 min and 120 min upon addition of 7.5 eq. of Boc₂O. S = solvent, G = grease.

3. Selected ¹H NMR spectra for the switching between $1Zn_{L1}$ and $1Zn_{L1}^{L2}$



Figure S6. Partial ¹H NMR spectra (CDCl₃/CD₃OD 9:1, 298 K) related to the *in situ* interconversion between **1.Zn**_{OAc} and **1.Zn**_{OAc}^{NH2Bu} (approach "B", forward and backward processes performed at RT): a) **1.Zn**_{OAc}, formed by addition of 1.5 eq. of Zn(OAc)₂ to **1**, in the presence of 5 eq. of DIPEA; b) upon addition of 5 eq. of BuNH₂; c) upon addition of 20 eq. of Boc₂O/17 min; d-e) upon addition of 5 eq. of BuNH₂/3 min and 40 min; f-g) upon addition of 5 eq. of BuNH₂/4 min and 48 min; h) upon addition of 5 eq. of BuNH₂/4 min; i) upon addition of 15 eq. of BuNH₂/4 min and 53 min. S = solvent, G = grease.



Figure S7. Partial ¹H NMR spectra (CDCl₃/CD₃OD 9:1, 298 K) related to the *in situ* interconversion between **1.Zn**_{L1} and **1.Zn**_{L1}^{NH2Bu} (L₁ = (*S*)BocProO⁻): a) **1**, 1.5 eq. Zn(OTf)₂, 4 eq. (*S*)BocProOH, 13 eq. DIPEA; b) upon addition of 5 eq. BuNH₂/50°C 30 min; c) upon addition of 7 eq. Boc₂O/RT 2h; d) upon addition of 7 eq. BuNH₂/RT 10 min then 50°C 30 min; e) upon addition of 7 eq. Boc₂O/RT 1h30; f) upon addition of 7 eq. BuNH₂/RT 15 min then 50°C 30 min; g) upon addition of 7 eq. Boc₂O/RT 1h. S = solvent.



Figure S8. Partial ¹H NMR spectra (CDCl₃/CD₃OD 9:1, 298 K) related to the *in situ* interconversion between **1.Zn**_{OAc} and **1.Zn**_{OAc}^{(S)MBA}: a) **1.Zn**_{OAc}, formed by addition of 1.5 eq. of $Zn(OAc)_2$ to **1**, in the presence of 5 eq. of DIPEA; b) upon addition of 5 eq. of (*S*)MBA; c) upon addition of 20 eq. of Boc₂O/1h30 RT; d) upon addition of 5 eq. of (*S*)MBA/3 min RT; e) upon addition of 5 eq. of Boc₂O/2h RT; f) upon addition of 5 eq. of (*S*)MBA/4 min RT; g) upon addition of 5 eq. of Boc₂O/1h45 RT; h) upon addition of 5 eq. of Soc₂O/1h45 RT; h) upon addition of 5 eq. of Soc₂O/1h45 RT; h) upon addition of 5 eq. of Soc₂O/1h45 RT; h) upon addition of 5 eq. of Soc₂O/1h45 RT; h) upon addition of 5 eq. of Soc₂O/1h45 RT; h) upon addition of 5 eq. of Soc₂O/1h45 RT; h) upon addition of 5 eq. of Soc₂O/1h45 RT; h) upon addition of 5 eq. of Soc₂O/1h45 RT; h) upon addition of 5 eq. of Soc₂O/1h45 RT; h) upon addition of 5 eq. of Soc₂O/1h45 RT. G = grease .

4. Selected ECD spectra for the switching between $1.Zn_{L1}$ and $1.Zn_{L1}^{L2}$



Figure S9. ECD spectra (general overview) related to the *in situ* interconversion between $1.2n_{L1}$ and $1.2n_{L1}^{L2}$ (CHCl₃/MeOH 9:1): (a) with L₁ = (S)BocProO⁻/L₂ = BuNH₂; (b) with L₁ = (R)BocProO⁻/L₂ = BuNH₂.



Figure S10. ECD spectra (detailed steps) related to the *in situ* interconversion between $1.Zn_{L1}$ and $1.Zn_{L1}^{L2}$ (CHCl₃/MeOH 9:1), with L₁ = (*S*)BocProO⁻/L₂ = BuNH₂: (a) steps 1 and 2; (b) steps 3 and 4.



Figure S11. ECD spectra (general overview) related to the *in situ* interconversion between **1.Zn**_{OAc} and **1.Zn**_{OAc}^{(S)MBA} or **1.Zn**_{OAc}^{(R)MBA} (CHCl₃/MeOH 9:1): (a) starting from **1.Zn**_{OAc}, successive addition of (S)MBA and reaction with Boc₂O, performed twice (steps 1 to 4), then last addition of (S)MBA (step 5); (b) starting from **1.Zn**_{OAc}, addition of (S)MBA and reaction with Boc₂O (steps 1 and 2), followed by addition of (*R*)MBA and reaction with Boc₂O (steps 3 and 4), then last addition of (S)MBA (step 5). Intermediate spectra for each steps are depicted in Figures S12 and S13.



Figure S12. ECD spectra (detailed steps) related to the *in situ* interconversion between $1.Zn_{OAc}$ and $1.Zn_{OAc}$ ^{(S)MBA} (CHCl₃/MeOH 9:1): starting from $1.Zn_{OAc}$, successive addition of (S)MBA (a, c) and reaction with Boc₂O (b, d), performed twice (steps 1 to 4), then last addition of (S)MBA (step 5, e).



Figure S13. ECD spectra (detailed steps) related to the *in situ* interconversion between **1.** Zn_{OAc} and **1.** Zn_{OAc} ^{(S)MBA} or **1.** Zn_{OAc} ^{(R)MBA} (CHCl₃/MeOH 9:1): starting from **1.** Zn_{OAc} , addition of (S)MBA (a) and reaction with Boc₂O (b) (steps 1 and 2), followed by addition of (R)MBA (c) and reaction with Boc₂O (d) (steps 3 and 4), then last addition of (S)MBA (e) (step 5).