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π-Stacking Induced NMR Spectrum Splitting in Enantiomerically Enriched Ru(II) Complexes: Evaluation of Enantiomeric Excess

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Several chiral octahedral complexes of the general formula $[Ru(bpy)_2(Lig)][PF_6]_2$ (Lig = a ligand that can participate in π-stacking interactions such as eilatin, isoeilatin, and tpphz) were synthesized in both the racemic and enantiomerically pure/enriched forms. Nonracemic mixtures of enantiomers of all these complexes exhibit splitting of the ^{1}H NMR spectra (NMR nonequivalence); i.e., each spectrum contains a major and a minor set of peaks. The origin of this phenomenon is attributed to a fast equilibrium between monomers and discrete dimers held together by π-stacking interactions, and it is observed for a wide range of π-stacking interaction strengths. The NMR spectrum splitting exhibited by these complexes can be exploited for the evaluation of their enantiomeric excess simply from the integral ratio, without addition of chiral shift reagents.

Introduction

Interaction between chiral species in solution is of pivotal importance in many biological and chemical systems, e.g., biomolecule recognition,[1] supramolecular assembly,[2] and enantioselective catalysis.[3] An important application of the interaction of a chiral compound with a chiral auxiliary (e.g., chiral solvent or chiral complexing agent) is the determination of enantiomeric purity by NMR.[4−8] However, using such chiral auxiliaries is not an absolute requirement: In several reports, enantiomeric discrimination was achieved by employing achiral auxiliary compounds, e.g., dialkyltin(IV) reagents, a self-assembled cylindrical host, phosphorus trichloride, and lanthanide ions.[9] The addition of the auxiliary agent results in diastereoisomeric differentiation, either permanent or transient.

Self-association of chiral species in solution has received less attention. There are several reports in the literature of chiral organic compounds that self-associate principally via intermolecular hydrogen bonds.[10] Nonracemic mixtures of enantiomers of these compounds exhibited two sets of resonances (^{1}H NMR nonequivalence), without addition of any "external" auxiliary. In solution, these compounds are

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in equilibrium between monomeric species and aggregates, which is fast on the NMR time scale. Thus, the NMR signals represent a weighted average of all the species present in solution, and for nonracemic mixtures, each of the two sets of peaks represents the weighted average of all the present species of a given enantiomer. For compounds that exhibit such NMR splitting, the enantiomeric excess can be calculated directly from the ^{1}H NMR data, with no need of prior knowledge of their physiochemical properties.

Recently, we have been studying octahedral complexes of the general formula $[Ru(bpy)_2(Lig)][PF_6]_2$ (bpy = 2,2′-bipyridine; Lig = eilatin, isoeilatin, dibenzoeilatin), which form discrete dimers in solution held solely by the seemingly weak and nondirectional $\pi-\pi$ stacking interactions via the eilatin-type ligand.[11−13] These complexes are chiral, existing as noninterconverting Δ and Λ enantiomers, and the discrete dimers they form are in fast equilibrium on the NMR time scale with their corresponding monomers, as evidenced by concentration dependence of the NMR chemical shifts. We therefore postulated that nonracemic samples of these complexes, and perhaps other complexes that tend to π-stack in solution, might exhibit ^{1}H NMR nonequivalence. In this report we demonstrate, for the first time, that such splitting does indeed take place in enantiomerically enriched mixtures whose sole intermolecular interaction is π-stacking. We show that the self-association of Ru(II) complexes featuring a wide range of π-stacking interaction tendencies in solution can be exploited to determine their enantiomeric purity by NMR, without addition of chiral-shift reagents.

Experimental Section

Materials. Isoeilatin,[14] Δ-$[Ru(bpy)_2(eil)][PF_6]_2$ (Δ-**1**),[11b] Λ-$[Ru(bpy)_2(eil)][PF_6]_2$ (Λ-**1**),[11b] *rac*-$[Ru(bpy)_2(ieil)][PF_6]_2$ (*rac*-**2**),[13] Δ-$[Ru(bpy)_2(py)_2]$[di-*O*,*O*′-benzoyl-(+)-tartrate]·$12H_2O$,[15] Λ-$[Ru(bpy)_2(py)_2]$[di-*O*,*O*′-benzoyl-(−)-tartrate]·$12H_2O$,[15] 1,10-phenanthroline-5,6,-dione (phendione),[16] 5,6-diamino-1,10-phenanthroline (phendiamine),[17] Δ-$[Ru(bpy)_2(phen)][PF_6]_2$,[15] Λ-$[Ru(bpy)_2(phen)][PF_6]_2$,[15] and *rac*-$[Ru(bpy)_2(tpphz)][PF_6]_2$ (*rac*-**4**)[18] were synthesized according to the literature procedures (eil = eilatin; ieil = isoeilatin). All other chemicals and solvents were of reagent grade and used without further purification. All the reactions were performed under an argon atmosphere.

Instrumentation. ^{1}H NMR spectra were recorded on a Bruker Avance 400 spectrometer using the residual protons of the solvent (CD_3CN) as an internal standard at $\delta = 1.93$ ppm. CD spectra in acetonitrile were measured on an Aviv model 202 circular dichroism spectrometer. Elemental analyses were performed in the microanalytical laboratory of the Hebrew University of Jerusalem.

Synthesis. Δ-Enriched-$[Ru(bpy)_2(ieil)][PF_6]_2$ (Δ_e-2). Δ-$[Ru(bpy)_2(py)_2]$[di-*O*,*O*′-benzoyl-(+)-tartrate]·$12H_2O$ (104.1 mg, 0.091 mmol) and isoeilatin (30.0 mg, 0.084 mmol) were added to 16 mL of ethylene glycol and heated in the dark to 120 °C for 6 h under argon atmosphere. The dark green reaction mixture obtained was cooled to RT, and a sat. KPF_6(aq) solution was added until precipitation of a solid occurred. The solid was isolated by centrifugation and washed several times with water to remove traces of salts. The solid was dried in vacuo, and then purified by chromatography on a Sephadex-CM C-25 column using a gradient of NaCl(aq)/CH_3OH = 1/1 as eluent. The mononuclear complex eluted out of the column as an emerald-green band at ionic strength 0.1−0.15 M NaCl(aq). An additional olive-green band eluted out at higher ionic strength (0.2−0.25 M NaCl(aq)) and was identified as the dinuclear complex.[19] The appropriate fraction was precipitated by addition of a saturated aqueous KPF_6 solution, filtered, and dried in vacuo. Δ_e-**2** is obtained as a green solid, in a yield of 45% (39.8 mg). Anal. Calcd (Found) for $C_{44}H_{28}F_{12}N_8P_2Ru$·$2.5H_2O$: C, 47.83 (47.78); H, 3.01 (2.96); N, 10.14 (10.16). CD [λ_{max}, nm ($\Delta\epsilon$, cm^{-1} M^{-1})] 235 (−7.2), 267 (39.2), 288 (−82.8), 356 (−6.3), 386 (0.1), 415 (−6.6), 432 (3.0), 455 (−1.3), 608 (−2.9).

Λ-Enriched-$[Ru(bpy)_2(ieil)][PF_6]_2$ (Λ_e-2). This complex was prepared by the same method described for Δ_e-**2**, using Λ-$[Ru(bpy)_2(py)_2]$[di-*O*,*O*′-benzoyl-(−)-tartrate]·$12H_2O$ (102.4 mg, 0.090 mmol), and isoeilatin (29.8 mg, 0.084 mmol). The dark green-brown reaction mixture obtained was handled and purified as described for Δ_e-**2**. Again, the grass-green dinuclear complex was obtained as a byproduct,[19] which was successfully separated from Λ_e-**2** by ion-exchange chromatography utilizing the same conditions described for Δ_e-**2**. Λ_e-**2** is obtained as a green solid, in a yield of 70% (61.9 mg). Anal. Calcd (Found) for $C_{44}H_{28}F_{12}N_8P_2Ru$·$1.5H_2O$: C, 48.62 (48.61); H, 2.88 (2.95); N, 10.31 (10.37). CD [λ_{max}, nm ($\Delta\epsilon$, cm^{-1} M^{-1})] 235 (5.6), 267 (−39.2), 287 (80.8), 354 (6.0), 384 (−0.4), 414 (5.7), 432 (−3.5), 455 (2.0), 608 (2.2).

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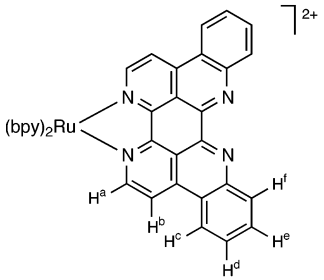

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Figure 1. Structure and proton numbering of $[Ru(bpy)_2(eil)][PF_6]_2$ (**1**).

Δ-[Ru(bpy)$_2$(phendione)][PF$_6$]$_2$ (Δ-3). This known complex was prepared using a modification of a published procedure:[20] To a cooled solution of Δ-$[Ru(bpy)_2(phen)][PF_6]_2$ (100.0 mg, 0.113 mmol) in 3 mL of concd H_2SO_4 were added NaBr (119.7 mg, 1.163 mmol) and 2.5 mL of concd HNO_3. The reaction mixture was heated to 110 °C for 20 min, and then poured into 50 mL of cold sat. KPF_6(aq) solution. The mixture was cooled for 12 h to ensure full precipitation. The brown precipitate was isolated by filtration, washed with water, and dried in vacuo. The desired complex was obtained in a yield of 57% (59.2 mg).

Λ-[Ru(bpy)$_2$(phendione)][PF$_6$]$_2$ (Λ-3). This complex was prepared as described for Δ-**3**, using Λ-$[Ru(bpy)_2(phen)][PF_6]_2$ (77.8 mg, 0.088 mmol), 3 mL of concd H_2SO_4, NaBr (110.8 mg, 1.077 mmol), and 2.5 mL of concd HNO_3. The desired complex was obtained in a yield of 76% (61.4 mg).

Both Δ-**3** and Λ-**3** products featured spectroscopic properties identical to those reported in the literature.[20c]

Δ-[Ru(bpy)$_2$(tpphz)][PF$_6$]$_2$ (Δ-4). This complex was prepared using a modification of the procedure reported for the racemic compound:[18] To a refluxing solution of Δ-**3** (44.4 mg, 0.049 mmol) in 3 mL of CH_3CN was added a hot solution of phendiamine (20.8 mg, 0.099 mmol) in 10 mL of CH_3OH, and the reaction mixture was stirred at 80 °C for 6 h. The red reaction mixture was cooled to RT and filtered and the solvent removed in vacuo. The solid residue obtained was triturated with CH_3CN and the filtered red solution evaporated to dryness to yield the desired complex in a yield of 99% (52.3 mg). Anal. Calcd (Found) for $C_{44}H_{28}F_{12}N_{10}P_2Ru\cdot 1.5H_2O$: C, 47.41 (47.56); H, 2.80 (3.08); N, 12.56 (12.26). CD [λ_{max}, nm ($\Delta\epsilon$, M^{-1} cm^{-1})] 268 (26.1), 297 (−86.5), 413 (18.1), 465 (−12.4).

Λ-[Ru(bpy)$_2$(tpphz)][PF$_6$]$_2$ (Λ-4). This complex was prepared as described for Δ-**4**, using Λ-**3** (39.0 mg, 0.043 mmol), 3 mL of CH_3CN, phendiamine (20.0 mg, 0.095 mmol), and 10 mL of CH_3OH. The desired complex was obtained in a yield of 96% (44.7 mg). Anal. Calcd (Found) for $C_{44}H_{28}F_{12}N_{10}P_2Ru\cdot 1.5H_2O$: C, 47.41 (47.30); H, 2.80 (2.86); N, 12.56 (12.51). CD [λ_{max}, nm ($\Delta\epsilon$, M^{-1} cm^{-1})] 267 (−21.1), 298 (83.8), 413 (−17.9), 465 (15.1).

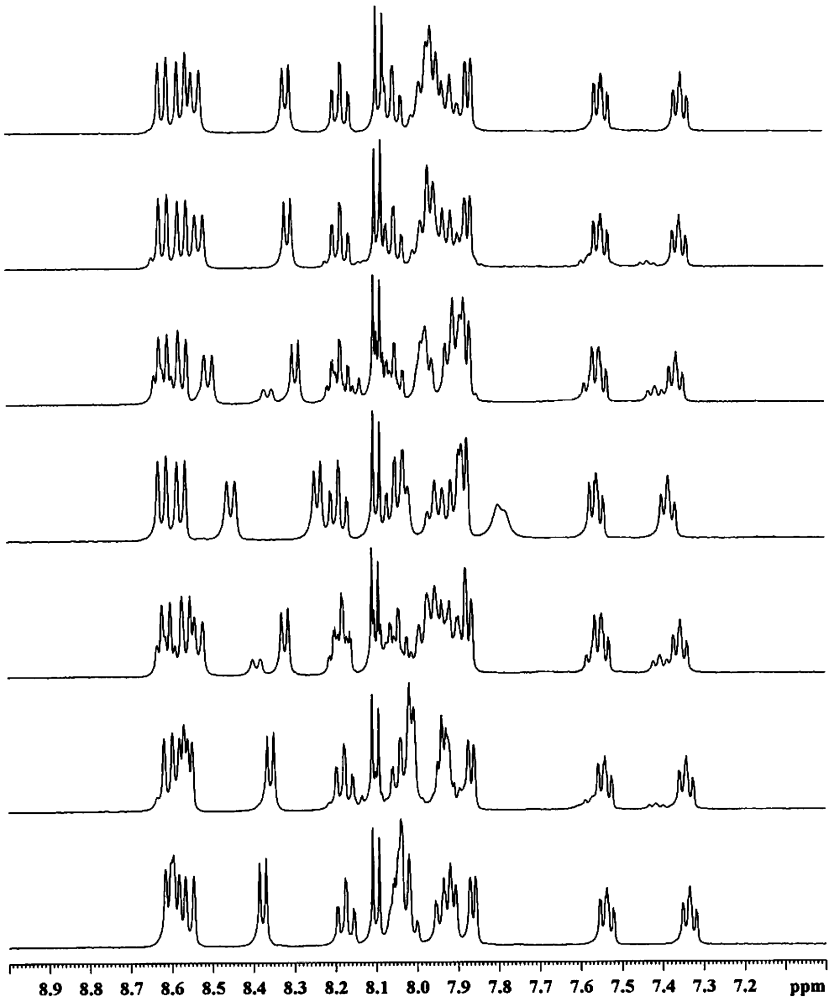

Figure 2. ^1H NMR spectra of 3.5 mM solutions of **1** in CD_3CN at various Δ/Λ ratios, from top to bottom: Λ, Δ/Λ = 1/9, Δ/Λ = 1/3, Δ/Λ = 1/1, Δ/Λ = 3/1, Δ/Λ = 9/1, and Δ. The slight differences between the spectra of the two enantiomers and respective mixtures result from minor concentration variation.

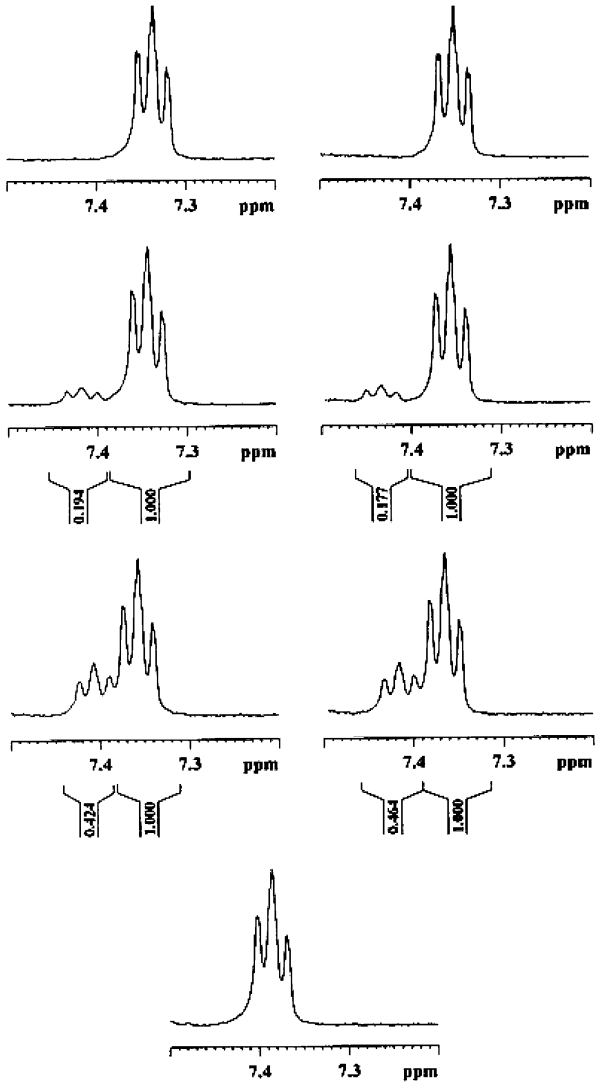

Figure 3. NMR signal of the bpy H^5 proton of 3.5 mM solutions of **1** in CD_3CN at various Δ/Λ ratios, from top to bottom (left and right): Δ and Λ before mixing, $\Delta/\Lambda = 9/1$ and $\Delta/\Lambda = 1/9$, $\Delta/\Lambda = 3/1$ and $\Delta/\Lambda = 1/3$, and $\Delta/\Lambda = 1/1$.

NMR Dimerization Experiments. Typically, a concentrated stock solution (ca. 10 mM) of a complex was prepared by accurately weighing out the dried complex and dissolving it in an accurately measured volume of CD_3CN (2.00 mL). The concentration dependence of the chemical shifts was studied at constant temperature, measured by the chemical shift of MeOH. Aliquots (50 μL) of the stock solution were added to an NMR tube initially containing 0.40 mL of CD_3CN, and 50 μL aliquots of CD_3CN were added to an NMR tube initially containing 0.40 mL of the stock solution to obtain a wide concentration range. The NMR spectra were recorded after several minutes of thermal equilibration time, following each addition. The dimerization constants were calculated, on the basis of the chemical shifts of selected protons, by the method of Horman and Dreux.[21]

NMR Forced Racemization Experiments. Typically, a stock solution (ca. 3.5 mM) of each enantiomer was prepared by accurately weighing out the dried complex and dissolving it in an accurately measured volume of CD_3CN (2.00−3.00 mL). The opposite enantiomers were mixed in different ratios while maintaining the overall concentration and sample volume constant (500 μL). The ^{1}H NMR spectra of the various mixtures, and of the pure enantiomers, were recorded at constant temperature, measured by the chemical shift of MeOH. The enantiomeric excess was calculated directly from the integral ratios of the major and minor peaks.

Table 1. Summary of ^{1}H NMR Data of the "Forced Racemization" Experiment of Complex **1**[a]

composition	δ^b [ppm] major	minor	$\Delta\delta$ [ppm]	integral ratio major/minor	% ee[c]	expected % ee
Δ	7.336					100
$\Delta/\Lambda = 9/1$	7.343	7.418	0.075	5.15	68	80
$\Delta/\Lambda = 3/1$	7.357	7.407	0.050	2.36	40	50
$\Delta/\Lambda = 1/1$	7.385					0
$\Delta/\Lambda = 1/3$	7.365	7.416	0.051	2.16	37	50
$\Delta/\Lambda = 1/9$	7.355	7.434	0.079	5.65	70	80
Λ	7.351					100

[a] Measured for 3.5 mM CD_3CN solutions of constant volume (500 μL). [b] Chemical shift of the bpy H^5 proton. [c] Calculated from the integral ratio.

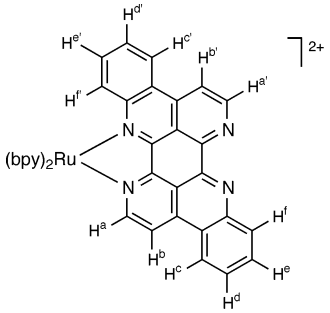

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Figure 4. Structure and proton numbering of $[Ru(bpy)_2(ieil)][PF_6]_2$ (**2**).

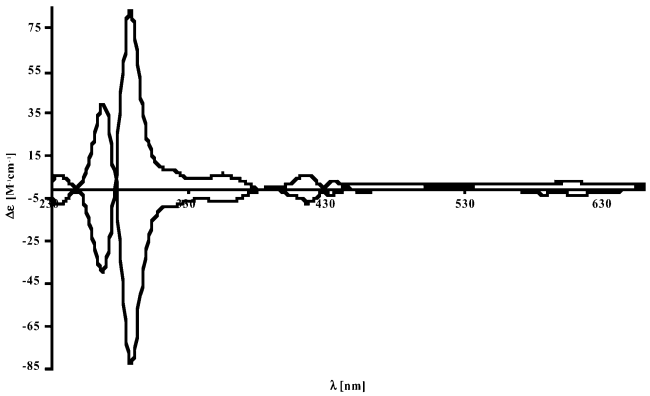

Figure 5. CD spectra of the two isoeilatin complexes derived from Δ-$[Ru(bpy)_2(py)_2]^{2+}$ (fine line) and Λ-$[Ru(bpy)_2(py)_2]^{2+}$ (bold line), recorded in acetonitrile.

Results and Discussion

Eilatin Complexes. The synthesis, characterization, and dimerization experiments of both the racemic and enantiomerically pure forms of the eilatin complex $[Ru(bpy)_2(eil)][PF_6]_2$ (**1**) (Figure 1) have been reported previously.[11b] As expected, both the racemic and the enantiomerically pure complexes exhibited a single set of peaks in all concentra-

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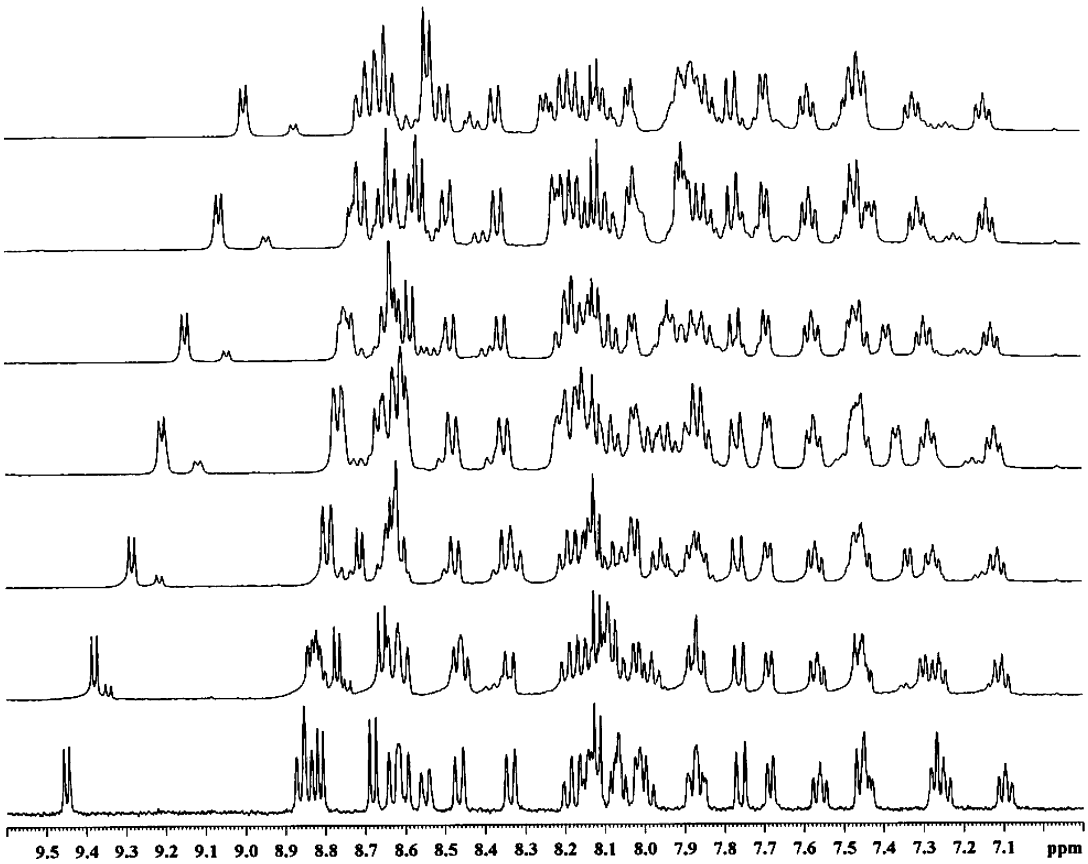


Figure 6. ^{1}H NMR spectra of Λ_e-**2** in CD_3CN at various concentrations, from top to bottom: 6.34, 5.28, 3.96, 3.24, 2.38, 1.32, and 0.50 mM.

tions (the chemical shift values were concentration-dependent due to the variation in monomer/dimer composition). To test our "π-stacking induced spectrum splitting" hypothesis, we performed a "forced racemization" experiment: Stock solutions of Δ-**1** and Λ-**1** (3.5 mM in CD_3CN each) were prepared and their ^{1}H NMR spectra recorded. Then, mixtures in different Δ-**1**/Λ-**1** ratios (9/1, 3/1, 1/1, 1/3, 1/9) were prepared and their ^{1}H NMR spectra recorded (Figure 2). Contamination of one enantiomer with the other resulted in splitting of the spectra into two peak sets, being most easily observed for the bpy H^5 proton,[22] as shown in Figure 3. Finally, the 1:1 mixture exhibited a single set of peaks, as expected from a racemic mixture (Figure 3, bottom). This experiment demonstrates that indeed nonracemic samples of **1** exhibit ^{1}H NMR nonequivalence induced by their dimerization via π-stacking interactions.

Enantiomeric Excess. In solution, three equilibrium processes take place:

$$\Delta + \Delta \rightleftharpoons \Delta\Delta \qquad (1)$$

$$K_{hom} = K_{\Delta\Delta} = K_{\Lambda\Lambda} = \frac{[\Delta\Delta]}{[\Delta]^2} = \frac{[\Lambda\Lambda]}{[\Lambda]^2}$$

$$\Lambda + \Lambda \rightleftharpoons \Lambda\Lambda \qquad (2)$$

$$\Delta + \Lambda \rightleftharpoons \Delta\Lambda \quad K_{het} = K_{\Delta\Lambda} = \frac{[\Delta\Lambda]}{[\Delta]\cdot[\Lambda]} \qquad (3)$$

Since each peak in the spectrum represents the weighted average of all three species containing a given enantiomer (i.e., the major peak representing Δ, $\Delta\Delta$, and $\Delta\Lambda$ and the minor peak representing Λ, $\Lambda\Lambda$, and $\Delta\Lambda$, assuming that the mixture is enriched with the Δ enantiomer), the integral is proportional to the total concentration of a given enantiomer, defined as Δ_T and Λ_T, respectively:

$$I_1 = \alpha([\Delta] + 2[\Delta\Delta] + [\Delta\Lambda]) = \alpha\Delta_T$$

$$I_2 = \alpha([\Lambda] + 2[\Lambda\Lambda] + [\Delta\Lambda]) = \alpha\Lambda_T$$

In these equations, I_1 and I_2 are the integrals of the major and minor peaks, respectively, and α is an unknown proportionality constant. The enantiomeric excess is defined by the following equation:

$$\%\ \text{ee} = \frac{|\Delta_T - \Lambda_T|}{|\Delta_T + \Lambda_T|}\cdot 100$$

Substituting $\Delta_T = I_1/\alpha$ and $\Lambda_T = I_2/\alpha$ yields

$$\%\ \text{ee} = \frac{|I_1 - I_2|}{|I_1 + I_2|}\cdot 100$$

Significantly, no prior knowledge of K_{hom} and K_{het} is required for evaluating the enantiomeric excess, which can be directly calculated from the integral ratios in the ^{1}H NMR spectra. To the best of our knowledge, this is the first time that such

(22) The splitting is most easily observed for the bpy H^5 proton because it is relatively separated from the rest of the spectrum, not because it exhibits the largest splitting.

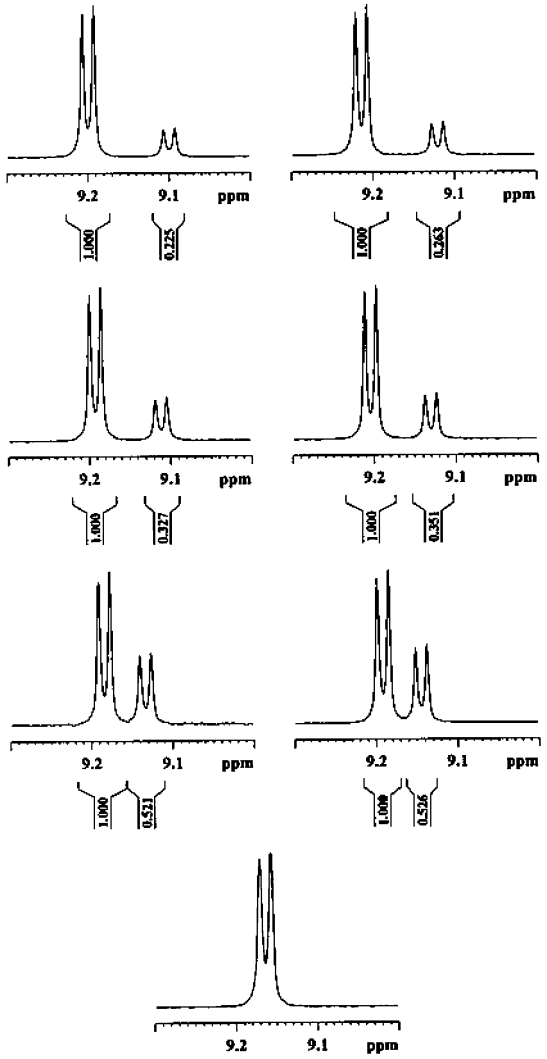


Figure 7. NMR signal of the $H^{a'}$ proton for 3.5 mM solutions of **2** in CD_3CN at various Δ/Λ ratios, from top to bottom (left and right): Δ_e and Λ_e before mixing, $\Delta_e/\Lambda_e = 9/1$ and $\Delta_e/\Lambda_e = 1/9$, $\Delta_e/\Lambda_e = 3/1$ and $\Delta_e/\Lambda_e = 1/3$, and $\Delta_e/\Lambda_e = 1/1$.

a phenomenon is observed for systems that associate solely by π-stacking interactions.

We employed this method to calculate the % ee of the nonracemic samples of **1**; the results are summarized in Table 1. It is important to point out that while the calculated % ee values are not in perfect agreement with the expected values according to the formal Δ/Λ ratio taken, they represent, within the accuracy limits of NMR, the true % ee of the mixture. The inconsistency between the calculated and expected values arises from the errors in dilution and volume measurement, which are estimated to be ca. 10%, and lead to Δ/Λ mixtures whose real composition differs from that taken formally. An additional source of inaccuracy is partial overlap of the major and minor peak sets, which can be overcome by deconvolution.

Isoeilatin Complexes. Recently, we have reported that the mononuclear isoeilatin complex *rac*-$[Ru(bpy)_2(ieil)][PF_6]_2$ (*rac*-**2**, Figure 4) exhibits substantially weaker solution stacking than *rac*-**1**, although the two ligands are structurally related.[13] Thus, **2** is a suitable compound for determining whether the NMR spectrum splitting may be observed for

Table 2. Summary of ^{1}H NMR Data of the "Forced Racemization" Experiment of Complex **2**[a]

composition	δ[b] [ppm] major	minor	$\Delta\delta$ [ppm]	integral ratio major/minor	% ee[c]	calcd % ee[d]
Δ_e	9.200	9.100	0.100	4.44	63	60
$\Delta_e/\Lambda_e = 9/1$	9.193	9.112	0.081	3.06	51	48
$\Delta_e/\Lambda_e = 3/1$	9.184	9.134	0.050	1.92	32	30
$\Delta_e/\Lambda_e = 1/1$	9.164					0
$\Delta_e/\Lambda_e = 1/3$	9.191	9.145	0.046	1.90	31	30
$\Delta_e/\Lambda_e = 1/9$	9.204	9.131	0.073	2.85	48	48
Λ_e	9.214	9.121	0.093	3.80	58	60

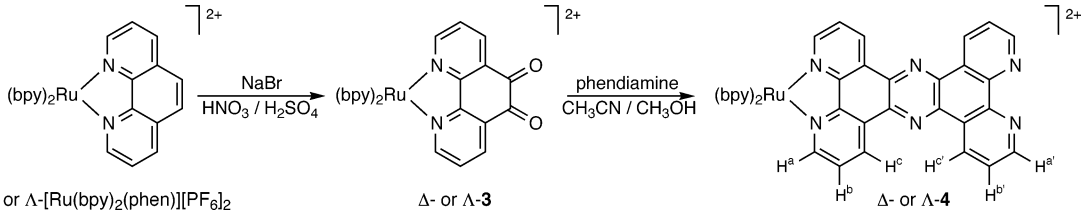
[a] Measured for 3.5 mM CD_3CN solutions of constant volume (500 μL). [b] Chemical shift of the isoeilatin $H^{a'}$ proton. [c] Calculated from the integral ratio. [d] Calculated from the mixing ratio, assuming an enantiomeric excess of 60% for the Δ and Λ forms.

weakly interacting species. The synthesis, characterization, and dimerization data of *rac*-**2** have been reported previously.[13] The synthesis of the Δ and Λ enantiomers of **2** was attempted employing the methodology introduced by von Zelewsky et al.,[15] by reacting isoeilatin with the enantiomerically pure starting materials Δ- and Λ-$[Ru(bpy)_2(py)_2]$-[di-*O*,*O*′-benzoyl-(±)-tartrate]·$12H_2O$. As previously reported for the racemic complex,[13] a mixture of mononuclear and dinuclear species was obtained, and their separation was achieved using cation-exchange chromatography. The mononuclear complexes were isolated as the PF_6^- salts, and characterized by circular dichroism (CD) measurements. The assignments of the Cotton effects are in agreement with the expected absolute stereochemistry, as predicted by the exciton theory.[23] The CD spectra demonstrate that the two mononuclear complexes are of identical optical purity (Figure 5).

The NMR spectra of the two isoeilatin complexes were recorded in CD_3CN. As previously described for *rac*-**2**,[13] the ^{1}H NMR chemical shifts of the mononuclear complexes change as a function of concentration and temperature, due to $\pi-\pi$ stacking of the complexes via the isoeilatin moiety. Surprisingly, when we performed the dimerization experiment for the two complexes, we observed two sets of peaks with integral ratios ca. 4/1 in the concentration range 1−10 mM, as demonstrated in Figure 6. The two sets of peaks exhibit different concentration dependence, the smaller set exhibiting greater shifts. Further dilution of the samples leads to a single set of peaks, reminiscent of that observed for the racemic complex. On the basis of the above, this phenomenon is best explained by incomplete enantiomeric purity of the two isoeilatin complexes; i.e., they are enantiomerically enriched, not enantiomerically pure. To support this hypothesis, we performed a "forced racemization" experiment: 3.5 mM stock solutions in CD_3CN of Δ_e-**2** and Λ_e-**2** (where Δ_e and Λ_e represent the corresponding Δ and Λ enriched forms), as well as mixtures of the two in different ratios (9/1, 3/1, 1/1, 1/3, 1/9), were prepared and their ^{1}H NMR spectra recorded. As shown in Figure 7, the gradual contamination of one stock solution with the other results in a smaller integral ratio between the two peak sets, and the separation between them is somewhat diminished. Finally, the 1:1

(23) Bosnich, B. *Acc. Chem. Res.* **1969**, *2*, 266.

Scheme 1. Synthesis and Proton Numbering of Δ- and Λ-$[Ru(bpy)_2(tpphz)][PF_6]_2$ (**4**)



Δ- or Λ-$[Ru(bpy)_2(phen)][PF_6]_2$ Δ- or Λ-**3** Δ- or Λ-**4**

Table 3. Summary of ^{1}H NMR Dimerization Data of Complex **4**[a]

	Δ-**4**		Λ-**4**		*rac*-**4**	
	H^c	$H^{c'}$	H^c	$H^{c'}$	H^c	$H^{c'}$
$\delta_{0(calc)}$	10.045	9.956	10.047	9.953	10.436	10.089
$\delta_{\infty(calc)}$	8.758	9.034	8.696	8.956	8.485	8.779
$K_{D(calc)}$[b]	$122 \pm 3\ M^{-1}$	$75 \pm 5\ M^{-1}$	$115 \pm 5\ M^{-1}$	$67 \pm 3\ M^{-1}$	$260 \pm 5\ M^{-1}$	$110 \pm 5\ M^{-1}$
$K_{D(av)}$	$99 \pm 24\ M^{-1}$		$91 \pm 24\ M^{-1}$		$185 \pm 75\ M^{-1}$	
K_{hom}[c]	$95\ M^{-1}$					
K_{het}[d]	$550\ M^{-1}$					

[a] Measured in CD_3CN; calculated chemical shifts at infinite dilution (δ_0) and at infinite concentration (δ_∞) are reported in ppm. The dimerization constants were calculated on the basis of the concentration dependence of the chemical shifts of the tpphz H^c and $H^{c'}$protons, which are well separated throughout the entire concentration range. [b] The error was estimated as the range of linearity of the graph ($R^2 \geq 0.996$). This also includes the error in concentration. [c] Calculated as the average between the $K_{D(ave)}$ values obtained for Δ- and Λ-**4**. [d] Calculated using the relationship $K_{het} = 4K_{D(ave)} - 2K_{hom}$, as outlined in ref 11b.

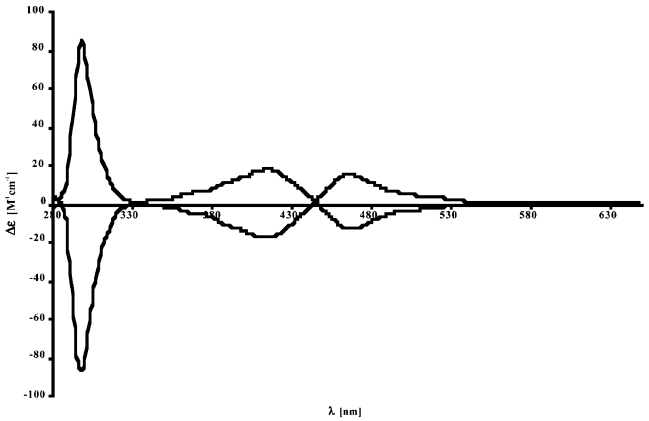


Figure 8. CD spectra of Δ-**4** (fine line) and Λ-**4** (bold line), recorded in acetonitrile.

mixture exhibits a single set of peaks, as expected from a racemic mixture. This experiment demonstrates that the observed phenomenon indeed results from incomplete enantiomeric purity of the complexes, and indicates that weak π-stacking interactions are sufficient to induce the NMR spectrum splitting. Also, the data show that in the conversion of the enantiomerically pure starting materials to the isoeilatin complexes partial racemization has occurred, probably due to the greater steric hindrance at the coordination site of the isoeilatin ligand.

Since we could not prepare the enantiomerically pure complexes of **2**, we do not know the exact values of K_{hom} and K_{het}.[24] However, prior knowledge of these values is not necessary for the calculation of % ee; the results are summarized in Table 2. Apparently, Δ_e-**2** and Λ_e-**2** are prepared by the method of von Zelewsky et al.[15] with 63 and 58% ee, respectively.

Table 4. Summary of ^{1}H NMR Data of the "Forced Racemization" Experiment of Complex **4**[a]

	δ^b [ppm]					
composition	major	minor	Δδ [ppm]	integral ratio major/minor	% ee[c]	expected % ee
Δ	9.573					100
Δ/Λ = 9/1	9.568	9.450	0.118	7.69	77	80
Δ/Λ = 3/1	9.549	9.480	0.069	2.43	42	50
Δ/Λ = 1/1	9.517					0
Δ/Λ = 1/3	9.549	9.477	0.072	2.58	44	50
Δ/Λ = 1/9	9.562	9.453	0.109	5.35	69	80
Λ	9.568					100

[a] Measured for 3.5 mM CD_3CN solutions of constant volume (500 μL). [b] Chemical shift of the tpphz H^c proton. [c] Calculated from the integral ratio.

Other Systems. To obtain further information on the generality of this phenomenon, i.e., the range of stacking strengths for which it is observed, we examined other complexes known to exhibit similar solution aggregation, i.e., tetrapyrido[3,2-a:2′,3′-c:3″,2″-h:2‴,3‴-j]phenazine (tpphz)[18] and dibenzoeilatin (dbneil)[12] complexes. The complex *rac*-$[Ru(bpy)_2(tpphz)]^{2+}$ (*rac*-**4**) was previously reported to participate in π-stacking induced dimerization in solution via the tpphz ligand; however, it was never synthesized in an enantiomerically pure form. We synthesized enantiomerically pure tpphz complexes Δ-**4** and Λ-**4** by reacting 5,6-diamino-1,10-phenanthroline (phendiamine) and the appropriate Ru−phendione (Δ-**3** and Λ-**3**) complexes, which were prepared by oxidation of the corresponding enantiomerically pure Δ- and Λ-$[Ru(bpy)_2(phen)][PF_6]_2$ complexes, as outlined in Scheme 1. The complexes were isolated as the PF_6^- salts, and CD spectra recorded in acetonitrile confirmed that the two enantiomers are obtained in identical optical purity (Figure 8). The racemic form of **4** was synthesized as described in the literature.[18] Simple ^{1}H NMR chemical shift-concentration dependence experiments were performed for

(24) The K_{hom} and K_{het} values can be estimated as each peak in the spectrum represents the weighted average of all three species containing a given enantiomer, so that the dimerization constants calculated from the concentration dependence of the chemical shifts of the major and minor peaks roughly correspond to the homochiral and heterochiral dimers, respectively. For the estimated values, refer to the Supporting Information.

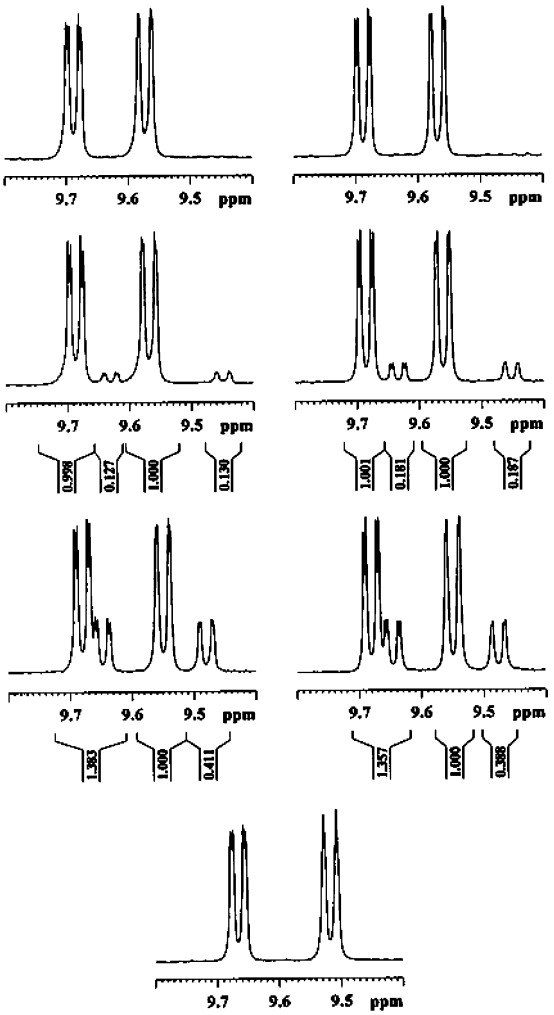


Figure 9. NMR signals of the $H^{c'}$ and H^{c} protons for 3.5 mM solutions of **5** in CD_3CN at various Δ/Λ ratios, from top to bottom (left and right): Δ and Λ before mixing, $\Delta/\Lambda = 9/1$ and $\Delta/\Lambda = 1/9$, $\Delta/\Lambda = 3/1$ and $\Delta/\Lambda = 1/3$, and $\Delta/\Lambda = 1/1$.

both racemic and enantiomerically pure **4**, as no such data is available in the literature;[25] the results are summarized in Table 3. The results clearly show a similar trend previously observed for the analogous eilatin complexes: There is a preference for the formation of a heterochiral, as opposed to a homochiral, dimer in solution.[11b] We performed a "forced racemization" experiment, as shown in Figure 9; the results are summarized in Table 4. These results indicate that the NMR nonequivalence is a general phenomenon that may be observed for any complex that self-associates, even by weak π-stacking interactions. Thus, the enantiomeric purity of these complexes can be easily assessed by a simple ^{1}H NMR spectrum.

To gain insight on the degree of racemization that may occur when the chiral Ru(II) center in $[Ru(bpy)_2(py)_2]^{2+}$ interacts with a sterically demanding ligand, we reacted Λ-$[Ru(bpy)_2(py)_2]^{2+}$ with dibenzoeilatin; the harsh reaction conditions required (140 °C, 48 h) for the binding of this ligand resulted in complete racemization, as evidenced from the lack of splitting of the NMR spectrum, and its complete chemical shift identity to a racemic sample of this complex at identical concentration.

Conclusions

In this work we have demonstrated that splitting of NMR spectra of enantiomerically enriched systems that undergo self-association processes is a general phenomenon not limited to hydrogen-bond interactions. Several systems that self-associate via π-stacking interactions, either weak or strong, clearly exhibit this behavior. Most importantly, a direct assessment of enantiomeric purity of such systems can be obtained simply from the integral ratio of the ^{1}H NMR spectrum, without the addition of any external agents or comparison to an enantiomerically pure standard. A second outcome of the current work is the insight it gives on the degree of racemization around a $[Ru(bpy)_2(py)_2]^{2+}$ chiral center interacting with sterically demanding bpy-type ligands. We expect that such NMR splitting will be observed for systems interacting via other types of intermolecular forces as well.

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Supporting Information Available: Concentration dependence of ^{1}H NMR chemical shifts, calculation of dimerization constants, ^{1}H NMR spectra of nonracemic mixtures. This material is available free of charge via the Internet at http://pubs.acs.org.

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(25) Gourdon et al.[18] have noted that *rac*-**4** exhibits π-stacking in solution; however, numerical data (*K*) had not been reported.