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Chiral Self-Recognition and Self-Discrimination of Strapped Perylene Bisimides by π-Stacking Dimerization

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The importance of self-assembly and self-organization for the creation of higher order functional structures is evident in natural systems.[1] Both in biological processes and in organic synthesis, chiral recognition,[2] that is, the ability of a chiral molecule to differentiate between two enantiomers, is of great significance as demonstrated in asymmetric catalysis[3] and enantioselective recognition by enzymes and protein-receptor sites.[4] Chiral recognition between enantiomeric pairs can lead to self-recognition[5] or self-discrimination,[6] depending on whether an enantiomer preferentially recognizes itself or its mirror image to generate homochiral or heterochiral self-assemblies, respectively. Such stereoselective recognition events may have intriguing consequences such as the formation of homochiral compounds from racemates in autocatalytic reactions.[7] Accordingly, a better understanding of chiral recognition phenomena will ultimately enable a more rational catalyst design for asymmetric synthesis and may even contribute to a better understanding of the origin of homochirality in biological molecules (e.g., L-amino acids and D-sugars and the biopolymers derived thereof). Despite such important prospects, little attention has been paid to the elucidation of self-recognition versus self-discrimination phenomena of chiral compounds in supramolecular systems. Most of the known examples for chiral recognition are based on the rather strong "inorganic" metal–ligand[5a–c,6a–f] and cation–anion interactions,[8] whereas examples based on weak "organic" interactions like hydrogen bonding and π–π interactions remain relatively rare.[5d,e,6g,h] Notably, some interesting examples of self-association by metal-ion coordination or hydrogen bonding have been reported for chiral helicates,[9] calix[4]arenes,[10] and peptides.[11]

Perylene bisimide (PBI) dyes have attracted considerable attention during the past years as fluorophores and organic semiconductor materials due to their unique optical and electrochemical properties.[12a] Moreover, the concurrence of a large π-surface and a pronounced quadrupole moment of PBIs enables exceptionally strong π–π-stacking interactions between these dyes.[12b] PBIs containing substituents in the bay positions (1, 6, 7, 12-positions) are of particular interest as they possess chirality due to the twisting of the perylene core leading to *atropo*-enantiomers (*P* and *M* enantiomers).[13]

Very recently, Li and co-workers elegantly explored the influence of core-twisting on dynamic self-assembly (DSA) of congigurationally flexible PBIs and their covalent cyclodimerization.[14] However, for the investigation of chiral recognition properties of this important class of functional dyes, enantiopure PBIs with stable configuration are required. Due to the fast interconversion process between *atropo*-enantiomers of PBIs, such enantiopure derivatives are rather scarce.[13a] Recently, we obtained epimerically pure tetra-aryloxy-substituted PBIs by restricting the interconversion of atropisomers through bridging the aryloxy bay substituents.[13b] However, these chiral PBIs are not suitable for self-assembly studies to explore the chiral recognition properties since both π-faces of the perylene core are blocked by bridging units. Therefore, to enable such studies, we have synthesized the chiral, at the bay position 1,7-disubstituted macrocyclic PBIs **2a,b** and resolved the *atropo*-enantiomers (*P*)-**2a,b** and (*M*)-**2a,b** (Figure 1). The bridging unit on one π-face of these strapped PBIs **2** allows only dimerization by interaction of free π-faces and restricts the interconversion between *M* and *P* enantiomers. Self-assembly studies with these new chiral PBIs revealed that self-recognition, that is, formation of homochiral dimers, prevails over self-discrimination, that is, formation of heterochiral dimers, by π–π stacking. One unexpected finding of our present studies is that the formation of minor amounts of heterochiral dimers enables the determination of *P*/*M* enantiomeric ratios of

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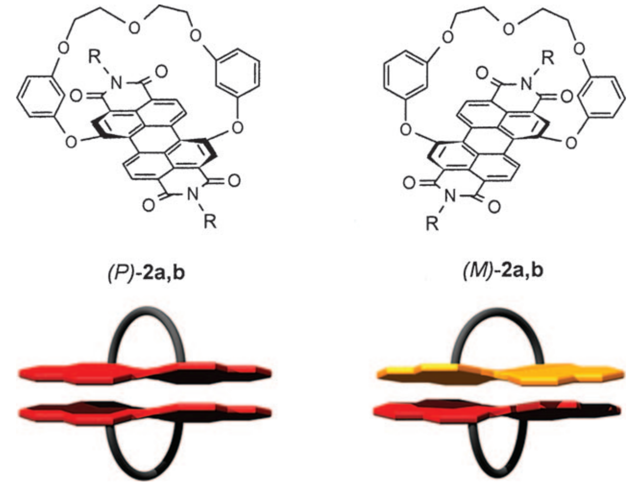


Figure 1. Structures of *atropo*-enantiomeric (*P*)-**2a**,**b** and (*M*)-**2a**,**b** and schematic representation of homo- and heterochiral dimer aggregates derived thereof.

chiral PBIs by ^{1}H NMR spectroscopy without using any external chiral auxiliary.[15]

The strapped PBIs **2a**,**b** were synthesized by macrocyclization of the corresponding 1,7-di(3-hydroxyphenoxy)-substituted PBIs **1a**,**b** through etherification with di(ethylene glycol) ditosylate in the presence of cesium carbonate in DMSO (for **1a**) or THF (for **1b**) (Scheme 1).[13b,c] The details of the synthesis and characterization of (*rac*)-**2a**,**b** and the precursors **1a**,**b** are given in the Supporting Information.

Single crystals of (*rac*)-**2a** suitable for X-ray diffraction were obtained by dissolving the compound in dichloromethane, followed by addition of equal amounts of methanol, and subsequent slow evaporation of the solvent. The molecular structure of (*rac*)-**2a** determined by single-crystal X-ray analysis (Figure 2) unequivocally confirms the macrocyclic structure of these PBIs with the diethylene glycol bridge shielding one π-face of the perylene core. The twist angle between the two naphthalene units of this molecule (which leads to atropisomers) is about 17° (for further structural and crystallographic data, see the Supporting Information).

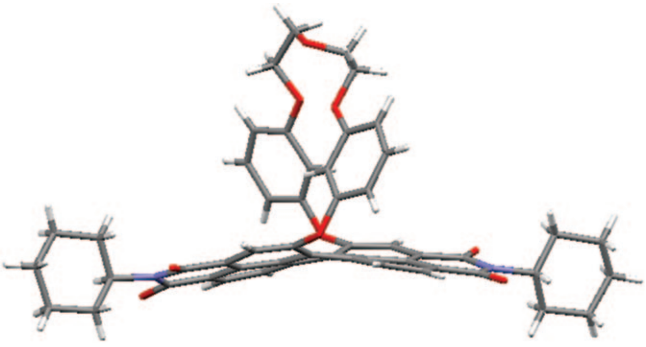
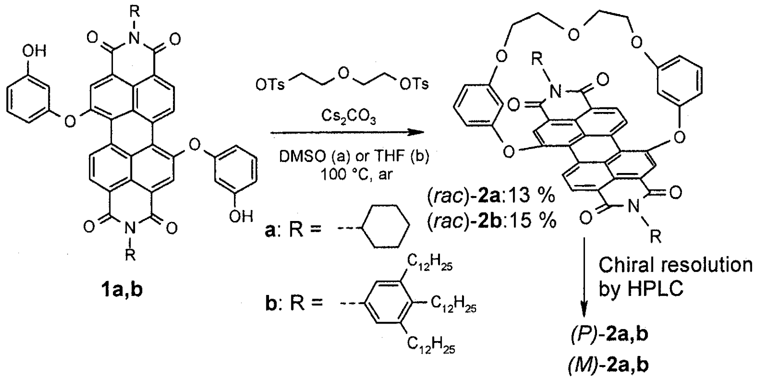


Figure 2. Molecular structure of racemic PBI **2a**, as observed by single-crystal X-ray analysis. (*P*)-enantiomer is depicted, view along the short axis of the PBI showing the bowl-like distortion of the perylene core.

The *atropo*-enantiomers (*P* and *M*) of PBIs **2a**,**b** were resolved by semi-preparative HPLC on a chiral column (Trentec, Reprosil 100 chiral-NR) using a mixture of dichloromethane and *n*-hexane as eluent (for details, see the Supporting Information). The stereochemical assignment of the isolated enantiomers was achieved by comparison of their circular dichroism (CD) spectra with those of the previously reported structurally similar epimerically pure *P*- and *M*-configured macrocyclic PBIs.[13b]

For the investigation of chiral recognition process of these PBIs in solution, PBI **2b** containing six long alkyl chains in imide substituents was used. This derivative is soluble in nonpolar solvents such as *n*-hexane or *n*-heptane, in which aggregation of PBIs can be observed at rather low concentrations.[16] Chiral recognition in the self-assembly of PBIs **2b** was studied by CD, UV/Vis, and ^{1}H NMR spectroscopy. The CD spectra of monomeric (*P*)-**2b** and (*M*)-**2b** enantiomers in dichloromethane ($c = 5\times10^{-6}$ M) show monosignated spectra in the visible region (400–600 nm) in a mirror image relation (Figure 3, top panel, blue lines) due to intrinsic molecular chirality.[13b] In nonpolar *n*-hexane a bisignate Cotton effect (zero crossing at 542 nm) is observed for both enantiomers at a concentration of 5×10^{-4} M (Figure 3, upper panel, red lines), which can be attributed to chiral exciton coupling[17] of the transition dipole moments of the chromophores and thus the formation of dimer aggregates with a helical π–π-stacking arrangement. The negative sign of the exciton couplet (at 555 nm) for (*P*)-**2b** indicates a left-handed helicity (the opposite for (*M*)-**2b**) of the respective dimer aggregate according to exciton chirality method.[17,18]

The binding constants K_D for dimerization of (*rac*)-**2b**, (*P*)-**2b**, and (*M*)-**2b** were determined by concentration-dependent UV/Vis absorption studies at 331 K in *n*-heptane. The con-



Scheme 1. Synthesis of racemic PBIs **2a**,**b** and resolution of *atropo*-enantiomers (*P*)-**2a**,**b** and (*M*)-**2a**,**b**.

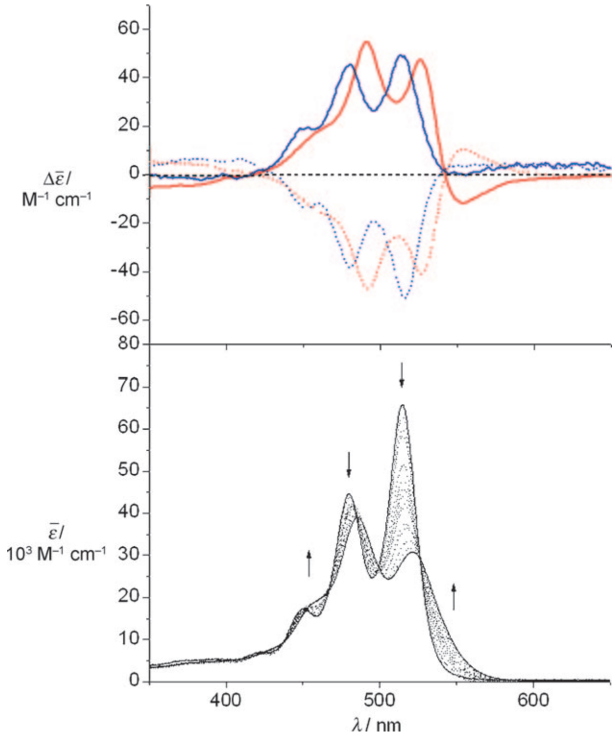


Figure 3. Top: CD spectra of (*P*)-**2b** (solid lines) and (*M*)-**2b** (dashed lines) in CH_2Cl_2 (5×10^{-6} M) (blue lines) and in *n*-hexane (1×10^{-3} M) (red lines) at 298 K. Bottom: concentration-dependent UV/Vis absorption spectra of (*rac*)-**2b** in *n*-heptane at 331 K; arrows indicate spectral changes with increasing concentration from 5×10^{-6} M to 1×10^{-3} M.

centration-dependent UV/Vis absorption spectra (all experiments were repeated twice) of these three samples are virtually identical, indicating similar aggregation behavior (see Figure S3–S8 in the Supporting Information). In all cases, isosbestic points are observed at 526 and 466 nm, suggesting the presence of thermodynamic equilibrium between two species.[19] The experimental data obtained from the concentration-dependent UV/Vis absorption studies can be adequately fitted by nonlinear regression analysis using the dimerization model (see Figure S3–S8 in the Supporting Information).[20,21] The dimerization constants K_D of (*rac*)-**2b** and enantiomers (*P*)-**2b** and (*M*)-**2b** at 331 K are collected in Table 1 (and Table S1 in the Supporting Information). It is remarkable that the K_D values determined for the pure enantiomers are significantly larger than that for the racemate, implying that the formation of homochiral dimers is thermodynamically more favored.

Table 1. Dimerization constants K_D determined for (*rac*)-**2b**, (*P*)-**2b** and (*M*)-**2b** in *n*-heptane at 331 K by multilinear fit of the concentration-dependent UV/Vis absorption data to the dimerization model.

Sample	(*P*)-**2b**	(*M*)-**2b**	(*rac*)-**2b**
[a]K_D [M^{-1}]	2800	2800	1500

[a] Details for the determination of these binding constants are given in the Supporting Information. The error is ±15%.

Quantitative information about the ratio of homochiral and heterochiral dimers can be obtained from the K_D values of PBI **2b**. The K_D value obtained for enantiopure (*P*)-**2b** (or (*M*)-**2b**) is obviously related to the formation of homochiral dimers (i.e., $K_D = K_{D(homo)}$), whereas in the case of the racemate (*rac*)-**2b**, the obtained $K_{D(rac)}$ is the average value of homo- and hetero-dimerization processes. According to Kol and co-workers,[22] for racemates the binding constant can be expressed as given in Equations (1) and (2),

$$K_{D(rac)} = \frac{[D]}{[M]^2} \qquad (1)$$

$$K_{D(rac)} = \frac{K_{D(hetero)} + 2K_{D(homo)}}{4} \qquad (2)$$

where [D] is the total dimer concentration (homo- and heterochiral dimers) and [M] is the free monomer concentration. By applying the respective K_D values obtained for the enantiopure ($K_{D(homo)}$) and racemic ($K_{D(rac)}$) PBI samples to Equation (2), $K_{D(hetero)}$ can be calculated as 400 M^{-1}. From these binding constants it can also be concluded that heterodimers account for less than 7% of the total dimer concentration (for details, see the Supporting Information), confirming the prevalence of chiral self-recognition (homodimerization) over self-discrimination (heterodimerization) of these PBIs by π-stacking. Moreover, with $K_{D(homo)}$ and $K_{D(hetero)}$, the equilibrium constant (K') and related Gibbs energy ($\Delta G'$) for the formation of heterodimers from a racemic mixture of homodimers can be calculated as 5×10^{-3} and 14.5 kJ mol^{-1}, respectively (details are given in the Supporting Information). Note that the obtained Gibbs energy has a positive sign as the formation of heterodimers from homodimers is an energetically disfavored process.

To get more insights into the chiral recognition behavior of PBIs **2b**, ^{1}H NMR investigations in deuterated *n*-hexane at 331 K were performed. As expected, identical NMR spectra were obtained for (*P*)-**2b** and (*M*)-**2b** enantiomers ($c = 10^{-3}$ M). However, significant differences were observed in spectra of (*rac*)-**2b** ($c = 2\times10^{-3}$ M).[23] As can be seen in Figure 4, the superposed spectra of racemate (*rac*)-**2b** and enantiopure (*P*)-**2b** (or (*M*)-**2b**) show significant differences in chemical shift, particularly of the protons in the aromatic region. For the concentration and temperature used in the ^{1}H NMR experiments, at least 60% of dimeric species should be present as estimated from UV/Vis studies (Figure S3–S8 in the Supporting Information). Thus, the observed differences between the spectra of (*rac*)-**2b** and enantiopure (*P*)-**2b** (or (*M*)-**2b**) should be related to the contemporaneous presence of homo- and heterochiral dimers in the case of racemate.

To clarify the observed differences in chemical shifts of racemate and pure enantiomers, a series of solutions in [D_{14}]*n*-hexane with varying enantiomeric excess (*ee*) ranging from 18 to 90% *ee* at $c = 2\times10^{-3}$ M were investigated by ^{1}H NMR. The spectra in Figure 4 show two sets of signals for the aromatic protons of perylene core (denoted as

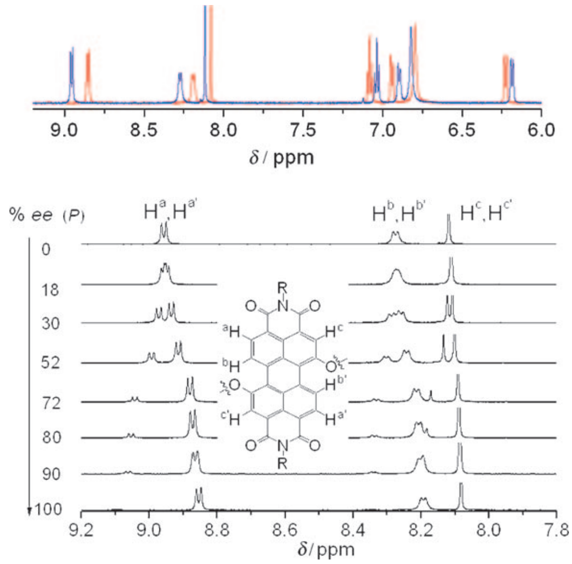


Figure 4. Top: 600 MHz ^{1}H NMR spectra (aromatic region is shown) of (*P*)-**2b** (or (*M*)-**2b**) ($c = 10^{-3}$ M) (red spectrum) and (*rac*)-**2b** ($c = 2 \times 10^{-3}$ M) (blue spectrum). Bottom: 600 MHz ^{1}H NMR spectra (region of PBI core protons) of solutions with different *ee* (%) referenced to the *P* enantiomer ($c = 2 \times 10^{-3}$ M). All spectra were measured in [D$_{14}$]*n*-hexane at 331 K.

H^a,$H^{a'}$, H^b,$H^{b'}$ and H^c,$H^{c'}$) in solutions with *ee* not equal to 0 or 100 %. The relative intensities of the respective signal pairs are directly proportional to the % *ee* applied (see Table S2 in the Supporting Information). This observation can be explained in terms of the different fractions of time spend by the two parent (*M*) and (*P*) enantiomers in the monomeric, homodimeric and heterodimeric state under fast-exchange conditions, giving rise to different averaged diastereotopic enviroments (for further discussion, see the Supporting Information). Obviously, this situation is given under the premise that the composition of enantiomers is not racemic (cp. Figure 4), a sufficient amount of heterochiral dimer is present, and the homo- and heterochiral dimers which are in diastereomeric relationship feature different chemical environments for the H^x and $H^{x'}$ protons (x = a, b or c) leading to magnetic nonequivalence of those protons.[24] We conjecture that the unexpected separation of the perylene H^x and $H^{x'}$ proton signals arises from pronounced differences in the aromatic shielding of these protons in homo- and heterodimers present in the equilibrium, and thus provoke signal split.

To conclude, we have successfully synthesized configurationally fixed chiral 1,7-diaryloxy-substituted PBIs and resolved their *atropo*-enantiomers. The new chiral compounds are adequately characterized by ^{1}H NMR, HRMS, and X-ray analysis. Based on our spectroscopic studies of racemic and enantiopure PBI dyes, we could show for the first time that self-recognition prevails over self-discrimination in the π-stacking dimerization of PBIs. The formation of minor amounts of heterochiral dimers allows the direct determination of the *ee* of chiral PBIs by ^{1}H NMR spectroscopy without using any external chiral auxiliaries. Our findings may initiate activities on π-stacking dimerization of other chiral dyes towards a better understanding of self-sorting phenomena, which is of general interest.

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Keywords: chiral recognition • dyes/pigments • homochirality • self-assembly • pi interactions

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[1] a) J.-M. Lehn, *Supramolecular Chemistry: Concepts and Perspectives*, VCH, Weinheim, **1995**; b) G. M. Whitesides, B. Grzybowski, *Science* **2002**, *295*, 2418–2421.

[2] a) A. Kühnle, T. R. Linderoth, B. Hammer, F. Besenbacher, *Nature* **2002**, *415*, 891–893; b) W.-H. Huang, P. Y. Zavalij, L. Isaacs, *Angew. Chem.* **2007**, *119*, 7569–7571; *Angew. Chem. Int. Ed.* **2007**, *46*, 7425–7427; c) A. Zehnacker, M. A. Suhm, *Angew. Chem.* **2008**, *120*, 7076–7100; *Angew. Chem. Int. Ed.* **2008**, *47*, 6970–6992.

[3] a) J. T. Mohr, M. R. Krout, B. M. Stoltz, *Nature* **2008**, *455*, 323–332; b) J. Lacour, D. Linder, *Science* **2007**, *317*, 462–463; c) B. List, J. W. Yang, *Science* **2006**, *313*, 1584–1586.

[4] a) M. T. Reetz, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5716–5722; b) C. M. Thomas, T. R. Ward, *Chem. Soc. Rev.* **2005**, *34*, 337–346.

[5] a) S. T. Trzaska, H.-F. Hsu, T. M. Swager, *J. Am. Chem. Soc.* **1999**, *121*, 4518–4519; b) J.-M. Vincent, C. Philouze, I. Pianet, J.-B. Verlhac, *Chem. Eur. J.* **2000**, *6*, 3595–3599; c) T. Kamada, N. Aratani, T. Ikeda, N. Shibata, Y. Higuchi, A. Wakamiya, S. Yamaguchi, K. S. Kim, Z. S. Yoon, D. Kim, A. Osuka, *J. Am. Chem. Soc.* **2006**, *128*, 7670–7678; d) S. Ghosh, A. Wu, J. C. Fettinger, P. Y. Zavalij, L. Isaacs, *J. Org. Chem.* **2008**, *73*, 5915–5925; e) for a recent review on chiral recognition in helicenes, see: R. Amemiya, M. Yamaguchi, *Org. Biomol. Chem.* **2008**, *6*, 26–35.

[6] a) T. W. Kim, M. S. Lah, J.-I. Hong, *Chem. Commun.* **2001**, 743–744; b) J. M. Takacs, P. M. Hrvatin, J. M. Atkins, D. S. Reddy, J. L. Clark, *New J. Chem.* **2005**, *29*, 263–265; c) C. G. Claessens, T. Torres, *J. Am. Chem. Soc.* **2002**, *124*, 14522–14523; d) M. Mizumura, H. Shinokubo, A. Osuka, *Angew. Chem.* **2008**, *120*, 5458–5461; *Angew. Chem. Int. Ed.* **2008**, *47*, 5378–5381; e) T. J. Burchell, R. J. Puddephatte, *Inorg. Chem.* **2006**, *45*, 650–659; f) T. Weilandt, U. Kiehne, G. Schnakenburg, A. Lützen, *Chem. Commun.* **2009**, 2320–2322; g) I. Alkorta, J. Elguero, *J. Am. Chem. Soc.* **2002**, *124*, 1488–1493; h) S. D. Bergman, M. Kol, *Inorg. Chem.* **2005**, *44*, 1647–1654.

[7] a) K. Soai, T. Shibata, H. Morioka, K. Choji, *Nature* **1995**, *378*, 767–768; b) D. Blackmond, *Proc. Natl. Acad. Sci. USA* **2004**, *101*, 5732–5736; c) W. L. Noorduin, E. Vlieg, R. M. Kellogg, B. Kaptein, *Angew. Chem.* **2009**, *121*, 9778–9784; *Angew. Chem. Int. Ed.* **2009**, *48*, 9600–9606.

[8] a) O. Maury, J. Lacour, H. Le Bozec, *Eur. J. Inorg. Chem.* **2001**, 201–204; b) J. J. Jodry, R. Frantz, J. Lacour, *Inorg. Chem.* **2004**, *43*, 3329–3331; c) S. D. Bergman, R. Frantz, D. Gut, M. Kol, J. Lacour, *Chem. Commun.* **2006**, 850–852; d) P. Govindaswamy, D. Linder, J. Lacour, G. Süss-Fink, B. Therrien, *Chem. Commun.* **2006**, 4691–4693.

[9] C. Provent, E. Rivara-Minten, S. Hewage, G. Brunner, A. F. Williams, *Chem. Eur. J.* **1999**, *5*, 3487–3494.

[10] a) L. Baldini, F. Sansone, G. Faimani, C. Massera, A. Casnati, R. Ungaro, *Eur. J. Org. Chem.* **2008**, 869–886; b) Y.-S. Zheng, S.-Y. Ran, Y.-J. Hu, X.-X. Liu, *Chem. Commun.* **2009**, 1121–1123.

[11] J. S. Nowick, *Acc. Chem. Res.* **2008**, *41*, 1319–1330.

[12] For a general review on perylene bisimides and their supramolecular architectures, see: a) F. Würthner, *Chem. Commun.* **2004**, 1564–1579; for a very recent review on dye aggregates focused on binding

strengths, see: b) Z. Chen, A. Lohr, C. R. Saha-Möller, F. Würthner, *Chem. Soc. Rev.* **2009**, *38*, 564–584.

[13] a) P. Osswald, F. Würthner, *J. Am. Chem. Soc.* **2007**, *129*, 14319–14326; b) P. Osswald, M. Reichert, G. Bringmann, F. Würthner, *J. Org. Chem.* **2007**, *72*, 3403–3411; c) P. Osswald, F. Würthner, *Chem. Eur. J.* **2007**, *13*, 7395–7409.

[14] a) W. Wang, A. D. Shaller, A. D. Q. Li, *J. Am. Chem. Soc.* **2008**, *130*, 8271–8279; b) A. D. Shaller, W. Wang, H. Gan, A. D. Q. Li, *Angew. Chem.* **2008**, *120*, 7819–7823; *Angew. Chem. Int. Ed.* **2008**, *47*, 7705–7709.

[15] T. J. Wenzel, *Discrimination of Chiral Compounds Using NMR Spectroscopy*, Wiley, New York, **2007**.

[16] Z. Chen, V. Stepanenko, V. Dehm, P. Prins, L. D. A. Siebbeles, J. Seibt, P. Marquetand, V. Engel, F. Würthner, *Chem. Eur. J.* **2007**, *13*, 433–449.

[17] a) N. Berova, K. Nakanishi in *Circular Dichroism: Principles and Applications* (Eds.: N. Berova, K. Nakanishi, R. W. Woody), Wiley-VCH, Weinheim, **2000**, pp. 337–382; b) N. Berova, L. Di Bari, G. Pescitelli, *Chem. Soc. Rev.* **2007**, *36*, 914–931.

[18] Note that, ideally, the positive and negative signals of bisignate CD couplets should be of similar intensity.[17] However, this situation holds only true if achiral dyes are stacked in a helical fashion. Here, the different amplitudes of the positive and negative parts of the bisignated CD couplets might arise from the intrinsic molecular chirality of these twisted PBIs (see: V. Buß, C. Reichardt, *Chem. Commun.* **1992**, 1636–1638).

[19] Evidently, in the case of (*rac*)-**2b** more than two species are involved due to the possibility of homo- and heterochiral dimers formation. Thus, the dimerization process is either highly stereoselective or both dimers exhibit almost identical UV/Vis absorption spectra.

[20] K. A. Connors, *Binding Constants: The Measurement of Molecular Complex Stability*, Wiley, New York, **1987**.

[21] Additionally, we have performed vapor pressure osmometry (VPO) measurements at 10^{-2} M concentration in *n*-hexane. On the basis of the measured colligative concentrations, aggregation numbers N of 2.5 and 2.3 are estimated for (*rac*)-**2b** and (*P*)-**2b**, respectively. These data again corroborate the formation of dimers in self-assembly of PBIs **2b**.

[22] D. Gut, A. Rudi, J. Kopilov, I. Goldberg, M. Kol, *J. Am. Chem. Soc.* **2002**, *124*, 5449–5456.

[23] To exclude concentration effects as a possible reason for the different chemical shifts of the aromatic protons of (*rac*)-**2b** and (*P*)-**2b** (or (*M*)-**2b**), a double-concentrated solution of (*rac*)-**2b** was measured relative to that of (*P*)-**2b** (or (*M*)-**2b**).

[24] This interesting self-discrimination of enantiomers in the absence of chiral auxiliaries has also been reported for dimer complexes involving metal coordination and hydrogen bonding: a) T. Williams, R. G. Pitcher, P. Bommer, J. Gutzwiller, M. Uskoković, *J. Am. Chem. Soc.* **1969**, *91*, 1871–1872; b) C. Luchinat, S. Roelens, *J. Am. Chem. Soc.* **1986**, *108*, 4873–4878; c) C. Giordano, A. Restelli, M. Villa, R. Annunziata, *J. Org. Chem.* **1991**, *56*, 2270–2272; d) M. J. P. Harger, *J. Chem. Soc. Perkin Trans. 2* **1977**, 1882–1887; e) A. Dobashi, N. Saito, Y. Motoyama, S. Hara, *J. Am. Chem. Soc.* **1986**, *108*, 307–308.

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