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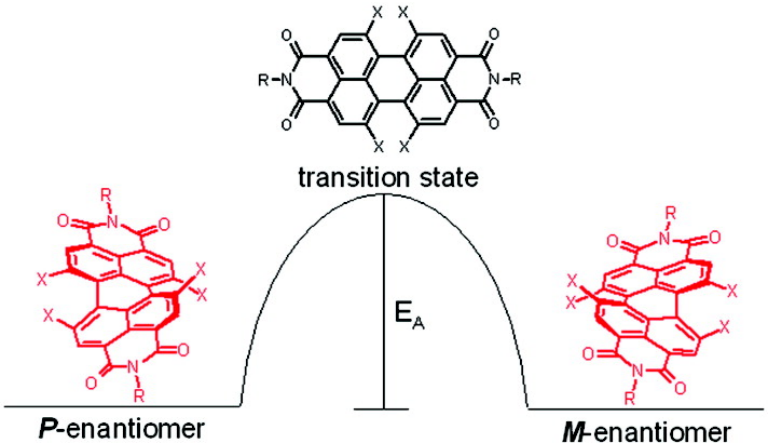

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Effects of Bay Substituents on the Racemization Barriers of Perylene Bisimides: Resolution of Atropo-Enantiomers

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Abstract: The activation parameters for the interconversion of atropisomers (*P*- and *M*-enantiomer) of core-twisted perylene bisimides have been determined by dynamic NMR spectroscopy (DNMR) and time- and temperature-dependent CD spectroscopy. By comparing the activation parameters of a series of perylene bisimides containing halogen or aryloxy substituents in the bay area (1,6,7,12-positions), a clear structure−property relationship has been found that demonstrates that the kinetic and thermodynamic parameters for the inversion of enantiomers are dependent on the apparent overlap parameter $\sum r^*$ of the bay substituents. This study reveals a high stability ($\Delta G^{\ddagger}_{368\ K} = 118$ kJ/mol) for the atropo-enantiomers of tetrabromo-substituted perylene bisimide in solution. Accordingly, the enantiomers of this derivative could be resolved by HPLC on a chiral column. These enantiomers do not racemize in solution at room temperature and, thus, represent the first examples of enantiomerically pure core-twisted perylene bisimides.

Introduction

In recent years, bay-functionalized perylene bisimides (PBIs) have received considerable attention for a wide range of applications, for example, as fluorescent dyes for single molecule spectroscopy[1] and bio-imaging[2] and as organic semiconductors for organic and polymeric light-emitting diodes (OLEDs and PLEDs), organic field-effect transistors (OFETs), and solar cells.[3] The molecular properties that enable all these applications are the high fluorescent quantum yield, fairly persistent radical anion state, easy accessibility, and outstanding stability of these dyes against environmental influences.[4] For most of the applications, aryloxy-, cyano-, or pyrrolidino-substituted PBIs have been employed, whereas the readily available halogen-substituted PBIs, such as 1,7-dibromo and 1,6,7,12-tetrachloro derivatives, have been used as intermediates for the synthesis of these functionalized perylene bisimides.[4] In the past few years, the utility of tetrahalogen-substituted PBIs, especially the tetrachloro derivatives, has also been demonstrated for a variety of applications, for example, as organic semiconductor;[5] in multichromophoric systems containing tetrathiafulvalene,[6] fullerenes,[7] or oligo(phenylenevinylene)s;[8] and as liquid crystals,[9] laser

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dyes,[10] g-quartet binder,[11] and functional units in polymers.[12] Recently, the successful synthesis of tetrabromo-substituted derivatives[13] as well as of di- and tetrafluoro-substituted perylene bisimides[14] has enlarged the number of available halogen-substituted PBIs and raised our expectations with regard to their application as starting materials for the next generation of functional PBIs. Apart from the functional diversity of bay-substituted PBIs, they also exhibit interesting structural features, in particular, a twisted π-system that results in a conformational chirality of these dyes.[4d] The distortion of the π-system results from repulsive interactions between the sterically encumbered bay substituents and can significantly vary depending on the size of the bay substituents from 4° (for the difluoro-substituted derivatives) up to 35° (for the tetrachloro derivatives), as revealed by X-ray analysis.[5a,6,15] However, despite significant distortion of the perylene core a fast interconversion process between the atropo-enantiomers (*P*- and *M*-enantiomer) had been found, for example, for tetraaryloxy-substituted PBIs, which prohibited the isolation of enantiopure derivatives.[16] Only very recently, we have reported the isolation of diastereomerically (epimerically) pure tetraaryloxy-substituted PBIs by restricting the interconversion of atropo-diastereomers through incorporation of the aryloxy substituents into a macrocyclic structure.[17] However, to our knowledge, at ambient temperature, conformationally stable enantiopure perylene bisimides are unprecedented to date. Such enantiomerically pure perylene bisimide fluorophores are potentially interesting for chiral recognition and sensory application. Thus, in this work we have made efforts to achieve atropo-enantiomerically pure perylene bisimides.

For the resolution of atropo-enantiomers of perylene bisimides, derivatives with high activation barriers (>93 kJ mol^{-1}) for racemization are required.[18] Our literature survey revealed that the racemization process of PBIs has not been systematically investigated so far. Nevertheless, the interconversion barrier for a tetrachloro derivative was reported to be larger than 87 kJ mol^{-1}.[16] Encouraged by this result, we have searched for conformationally more stable perylene bismides, which may enable the separation of atropo-enantiomers. As it is known that the activation parameters for conformational chiral systems, for example, in biaryl compounds,[19] are strongly influenced by the size of the substituents, it appears to be possible to obtain enantiopure perylene bisimides by proper choice of bay substituents.

For this purpose, we have investigated the racemization process of a series of bay-substituted PBIs **2**−**5** (see Scheme 1) bearing three different types of halogen substituents in bay positions and the tetra(3-methoxyphenoxy)-substituted perylene bisimide **1** as reference system by dynamic NMR spectroscopy (DNMR) and CD spectroscopy. The series of halogen-substituted perylene bisimides facilitates the variation of the size of the bay substituents and thus the structural properties of PBIs in a defined way,[20] as the size of these substituents is tunable from fluorine (r_{vdW} = 1.35 Å) to bromine (r_{vdW} = 1.86 Å).

Experimental Section

Methods and Materials. 1-(*R*)-Phenylethylamine with an *ee* value of >99% was purchased from Fluka (Buchs, Switzerland). Perylene bisimides **1**,[16] **2**,[14] **3**,[21] **4**,[16] and **5**[13] were synthesized according to the literature.

Analytical HPLC was performed on a system with a photodiode array detector equipped with a ternary gradient unit and line-degasser. Semipreparative HPLC was carried out on a system with a photodiode array detector. HPLC grade solvents were used except for chloroform, which was distilled prior to use. Reprosil 100 Chiral-NR chiral columns from Trentec (Gerlingen, Germany) were used in the analytical (Ø = 4.6 mm) as well as semipreparative size (Ø = 20 mm).

Spectroscopy. For UV/vis measurements, spectroscopic grade solvents were used. UV/vis spectra were recorded with a Perkin-Elmer PE 950 under ambient conditions. Circular Dichroism (CD) measurements were carried out on a JASCO J-810 spectrometer equipped with a CDF 426-S temperature control unit.

Temperature-Dependent ^{1}H NMR Spectroscopy. Temperature-dependent ^{1}H NMR spectra were recorded on a 500 MHz instrument (for compounds **2** and **3**) and 600 MHz spectrometer (for compound **1**). Temperature was calibrated to the temperature-dependent chemical shift of methanol. Coalescence temperature was determined from the signal broadening, and the data evaluation was performed by using the coalescence method according to the eqs 3 and 4 (see below).

Kinetic Measurements. For the kinetic measurements by time-dependent CD spectroscopy, the atropo-diastereomers of **4** and the atropo-enantiomers of **5** were separated by semipreparative HPLC using chloroform as eluent (details are given in the Results and Discussion section). The separation was done directly before each kinetic measurement, and only the amount necessary for one measurement was separated (<0.5 mg). As starting time for the kinetic measurements of **4**, the peak maximum of the first eluted fraction was used. The first CD spectrum was measured after ~90 s. The obtained fraction was diluted with chloroform (spectroscopic grade) to adjust the concentration suitable for the CD measurement. For the kinetic measurements of **5**, either the first or the second eluted fraction was used. The solvent was removed in a nitrogen flow, and the obtained solid was dissolved in 1,1,2,2-tetrachloroethane (1,1,2,2-tetrachloroethane used for the CD measurements was fractionally distilled under vacuum prior to use). The Peltier element was calibrated to the starting temperature and as starting time, the beginning of the measurement was chosen. The purity of the samples was checked by HPLC. For data evaluation, the Eyring (eqs 3 and 4) and Arrhenius equation (eq S6) were applied as outlined in the Supporting Information. The errors for the rate constant k (Table 1), activation energy E_A, enthalpy $\Delta H^{\ddagger}$ and entropy of activation $\Delta S^{\ddagger}$ are the standard deviation obtained by linear regression analysis. The errors for $\Delta G^{\ddagger}$ and $\tau_{1/2}$ were calculated by main error estimation (also see the Supporting Information).

Results and Discussion

Determination of Activation Parameters for the Racemization Barriers of Bay-Substituted Perylene Bisimides. The

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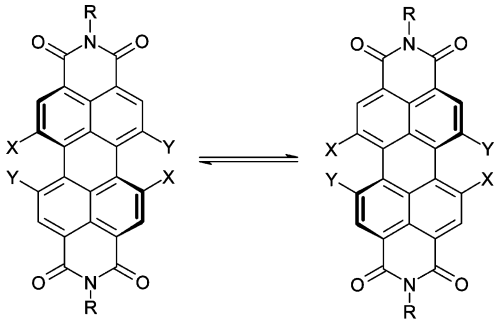
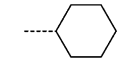
Table 1. Kinetic Data for the Racemization Process of **4** in Chloroform and **5** in 1,1,2,2-Tetrachloroethane at Different Temperatures

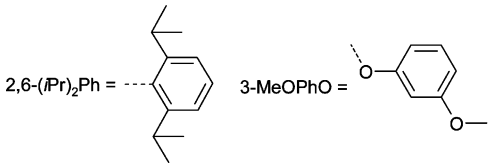
4				**5**			
T/K	$k/10^{-5}s^{-1}$	$t_{1/2}$[a]/min	$\Delta G^{\ddagger}$/kJ mol^{-1}	*T*/K	$k/10^{-5}s^{-1}$	$t_{1/2}$[a]/min	$\Delta G^{\ddagger}$/kJ mol^{-1}
293	1.40 ± 0.03	825 ± 14	97.3 ± 0.1	363	3.54 ± 0.08	326 ± 7	118.2 ± 0.1
303	4.54 ± 0.08	255 ± 5	97.7 ± 0.1	368	6.33 ± 0.19	183 ± 6	118.1 ± 0.1
313	15.30 ± 0.40	76 ± 2	97.8 ± 0.1	373	10.50 ± 0.30	110 ± 4	118.1 ± 0.1
323	50.68 ± 1.30	23 ± 1	97.8 ± 0.1	378	17.87 ± 0.60	67 ± 2	118.2 ± 0.1
				383	32.55 ± 1.00	36 ± 1	117.8 ± 0.1

[a] Calculated according to $t_{1/2} = \ln 2/k$.

Scheme 1. Racemization Equilibrium and Structures of Bay-Substituted Perylene Bisimides **1**−**5** Used in the Present Investigation



	X	Y	R
1	3-MeOPhO	3-MeOPhO	2,6-(*i*Pr)$_2$Ph
2	F	F	2,6-(*i*Pr)$_2$Ph
3	Br	H	2,6-(*i*Pr)$_2$Ph
4	Cl	Cl	
5	Br	Br	



bay-substituted perylene bisimides **1**−**5** used for this investigation are shown in Scheme 1. To determine the activation parameters for perylene bisimide **1** bearing four aryloxy substituents in the bay position, dynamic NMR experiments were performed in deuterated chloroform. For data evaluation, the resonances of the diastereotopic methyl groups of the 2,6-diisopropylphenyl substituents were used. The temperature-dependent changes of these signals are shown in Figure 1. At room temperature, the methyl protons of the diisopropyl groups show one doublet, which suggests that the interconversion process is faster than the spin-relaxation at this temperature. Upon decreasing the temperature, this signal is broadened, and at low temperature (230 K), two doublets (overlapped to a triplet) arose for the two atropo-enantiomers, namely (*P*)-**1** and (*M*)-**1**. The coalescence temperature was determined from the line broadening to 270 K, and the difference in chemical shift $\Delta\nu$ of the two enantiomers at low temperature (230 K) was

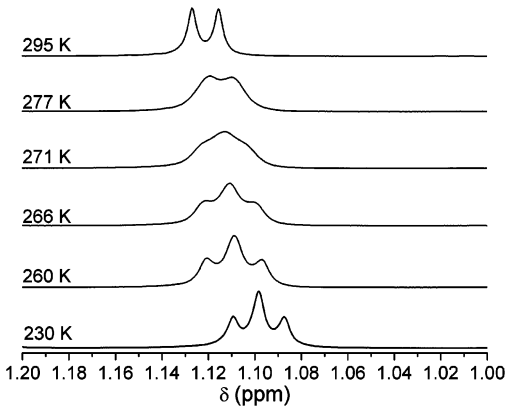


Figure 1. Sections of the temperature-dependent ^{1}H NMR spectra of **1** (600 MHz) in $CDCl_3$. The signals of the diastereotopic methyl groups of the diisopropylphenyl imide substituents are shown.

estimated to 6.3 Hz. With these data, the free enthalpy of activation was calculated as 60 kJ mol^{-1} according to the coalescence method (eqs 1 and 2).[22]

$$k_C = \frac{\pi}{\sqrt{2}}|\Delta\nu| \tag{1}$$

$$\Delta G^{\ddagger} = R\cdot T_C \cdot \ln\left(\frac{R\cdot T_C}{k_C\cdot N_A\cdot h}\right) \tag{2}$$

From eq 1, the half-lifetime for PBI **1** at the coalescence temperature (270 K) was estimated to be approximately 10 s, under the assumption of a first-order kinetic. Thus, the interconversion process for **1** is very fast, and therefore, the resolution of the atropo-enantiomers is not possible at room temperature.

For perylene bisimide **2** bearing four fluorine substituents in the bay position, dynamic NMR experiments were performed in deuterated dichloromethane. As can be seen from Figure S1 (left), the changes of the methyl resonances are similar to those observed for the tetraaryloxy-substituted PBI **1**. Unfortunately, the static case in the slow exchange region could not be realized, owing to the experimental limitations (melting point of dichloromethane), and only the coalescence temperature of 180 K could be determined from this experiment. However, as the signal splitting $\Delta\nu$ in the static region is not significantly different for similar perylene bisimides, for example, for **1** (6.3 Hz) as shown before, it can be assumed that the differences in the chemical shift $\Delta\nu$ of the two atropo-enantiomers of **2** should be similar as well. Therefore, the free enthalpy of activation $\Delta G^{\ddagger}$ is estimated according to the eqs 1 and 2 as 40 kJ mol^{-1} at 180 K.

In the series of 1,7-dihalogenated PBIs, only the bromo and fluoro derivatives are available.[4a,4d,14] Owing to the only slightly

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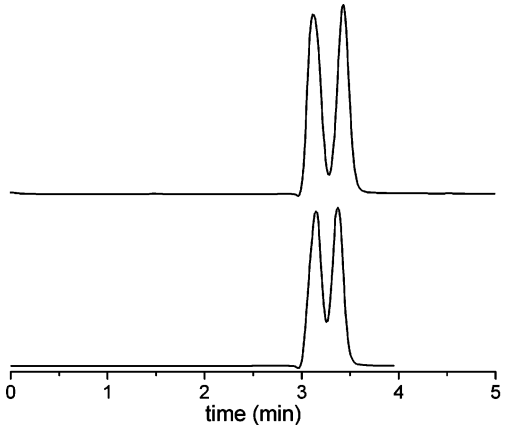


Figure 2. HPLC traces of racemic **4** (bottom) and **5** (top) on a Trentec Reprosil 100 chiral-NR column at ambient conditions using dichloromethane as eluent (flow rate: 1 mL/min).

twisted perylene core of 1,7-difluoro-substituted derivative (4°)[14] and comparatively low activation barrier for the tetrafluoro derivative **2**, the torsional barrier for the difluoro compound is expected to be rather small. For the dibromo-substituted PBI **3,** similar temperature-dependent changes as for the tetrafluoro derivative **2** were observed and the coalescence of the methyl resonances was reached at 180 K (Figure S1, right). Thus, the free energy of activation is similarly estimated to 40 kJ mol^{-1}. This very closely related behavior strongly suggests that similar steric constraints are given with regard to the planarization of the π-conjugated system of PBIs **2** and **3**, despite their pronounced structural differences.

As mentioned before, for a tetrachloro PBI derivative, an activation energy of more than 87 kJ mol^{-1} was reported previously,[16] which is markedly higher than the activation barriers of the above-mentioned tetrafluoro-substituted PBI **2** and dibromo-substituted derivative **3**. Thus, we anticipated that the atropisomers of tetrachloro PBI **4** would be separable. Indeed, the atropo-diastereomers of PBI **4** and also the atropo-enantiomers of tetrabromo-substituted PBI **5** could be separated by HPLC on a chiral column. The isolation of the atropisomers of **4** and **5** facilitated the investigation of the racemization process of these PBIs by kinetic measurements using CD spectroscopy as a complementary method to the dynamic NMR used for PBIs **1**−**3**. Before we present the details of the kinetic measurements, we briefly describe the HPLC separation of the atropisomers of PBIs **4** and **5** and report their chiroptical properties, as these are the first examples of enantiomerically pure (in the case of **5**) perylene bisimides. Conformationally stable atropo-diastereomers of nonmacrocyclic PBIs are not reported before;[17] thus, **4** is a unique example of conformationally flexible perylene bisimide, whose atropo-diastereomers are separable.

Separation and Chiroptical Properties of the Atropisomers of 4 and 5. The diastereomers of **4** (more precisely epimers as **4** contains two *R*-configured chiral substituents) and enantiomers of **5** were resolved by HPLC using a semipreparative chiral column at room temperature (Figure 2). In the case of PBI **4**, the two epimers are not completely separated (no baseline separation) with chloroform as eluent, but the separation was good enough to isolate epimerically enriched (de > 90%) (*P*,*R*,*R*)-**4** and (*M*,*R*,*R*)-**4** to investigate their chiroptical properties. A better resolution was achieved for the enantiomers of **5** providing almost enantiopure **5** (97% ee). Notably, the atropo-enantiomers of PBIs **1**−**3** could not be separated by HPLC as the inversion barriers in these cases are too low for resolving the enantiomers at ambient temperature.[18]

The successful resolution of the atropisomers of **4** and **5** enabled the investigation of their chiroptical properties. Figure 3 shows the absorption and circular dichroism (CD) spectra of the two eluted fractions of **4** and **5**, respectively, in chloroform. On the basis of previously accomplished stereochemical assignment of epimerically pure macrocyclic PBI systems,[17] the positive signal for the longest wavelength transition (λ_{max} = 527 nm) in the CD spectrum of the first eluted fraction of **4** can be attributed to a *P*-configuration of the perylene core, and thus, this atropo-diastereomer can be assigned to (*P*,*R*,*R*)-**4**. Likewise, the negative sign for the longest wavelength transition therefore reveals the *M*-configuration of the perylene core and, accordingly, the second eluted fraction can be assigned as (*M*,*R*,*R*)-**4**. The observed mirror image relation for the CD spectra of both fractions of **4** reveals the pseudo-enantiomeric behavior for these compounds as previously discussed for macrocyclic aryloxy-substituted derivatives.[17]

Similarly, the first eluted fraction of **5** shows a positive signal for the lowest energy transition (λ_{max} = 535 nm). This reveals a *P*-configuration of the perylene core, and the first eluted fraction of **5** can thus be assigned to (*P*)-**5**. The CD spectrum of the second eluted fraction shows a mirror image relation and, therefore, can be assigned to the *M*-configuration of **5**.

Racemization Barrier of PBIs 4 and 5. To determine the activation parameters for the racemization of **4** and **5**, time-dependent CD measurements were performed at different temperatures in the range of 293−323 K for **4** in chloroform and 363−383 K for **5** in 1,1,2,2-tetrachloroethane. For the racemization process, a first-order kinetic can be assumed ($-d[\mathbf{4}]/dt = kt$).[23] Accordingly, the rate constants were determined from the time dependence of the CD amplitude at 500 nm (for **4**) and 510 nm (for **5**). The kinetic parameters for the racemization at each temperature are collected in Table 1.

PBI **4** showed a half-lifetime of 23 min at 323 K, and almost complete racemization was observed after 3 h. Upon decreasing the temperature to 293 K, the half-lifetime increased to 825 min and the racemization was not complete even after 1 day, as can be seen from Figure 4. The free activation enthalpy $\Delta G^{\ddagger}_{303\,K}$ for the racemization process of **4** was determined according to the Eyring equation (eq 3) to 98 ± 1 kJ mol^{-1}, which is very similar to the activation barrier reported for pentahelicene or unsubstituted 1,1′-binaphthyl.[24] The temperature dependence of the rate constant could also be used to determine the thermodynamic activation parameters $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ by linear regression analysis according to the Eyring equation (eq 4).

$$\Delta G^{\ddagger} = -RT \ln\left(\frac{hk}{\kappa\, k_b T}\right) \tag{3}$$

$$k = \kappa \frac{k_B T}{h} \exp\left[\frac{\Delta S_0^{\ddagger}}{R} - \frac{\Delta H_0^{\ddagger}}{RT}\right] \tag{4}$$

The parameter κ was taken as 0.5 since the probability of the transition state to transform into one or the other stereoisomer

(23) Wolf, C.; König, W. A.; Roussel, C. *Liebigs Ann. Chem.* **1995**, 781−786.
(24) (a) Laarhoven, W. H.; Prinsen, W. J. C. *Top. Curr. Chem.* **1984**, *125*, 63−130. (b) Cooke, A. S.; Harris, M. M. *J. Chem. Soc.* **1963**, 2365−2373.

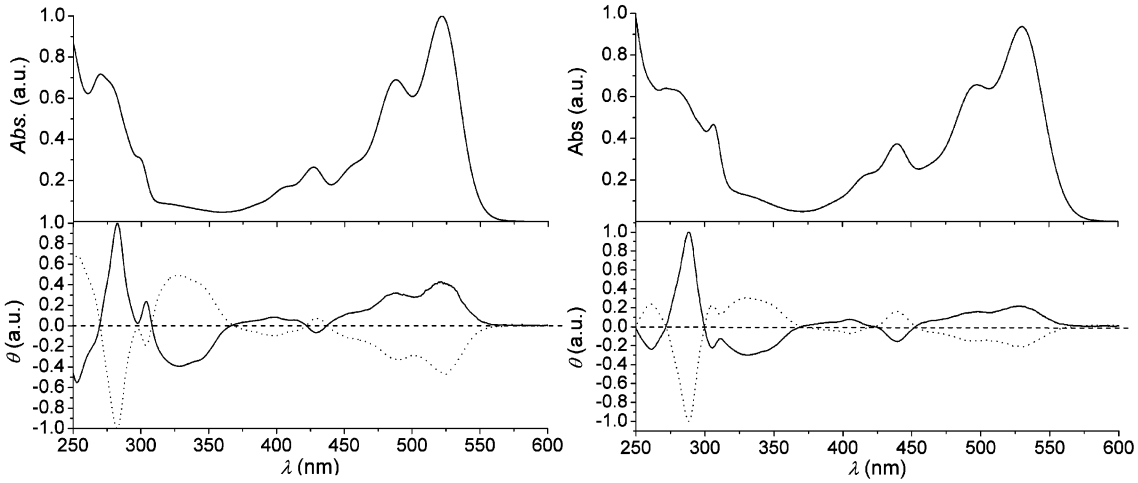


Figure 3. Normalized absorption and circular dichroism spectra of both epimers of **4** (left) and enantiomers of **5** (right) in chloroform at 20 °C; first eluted fraction (solid line), second eluted fraction (dotted line).

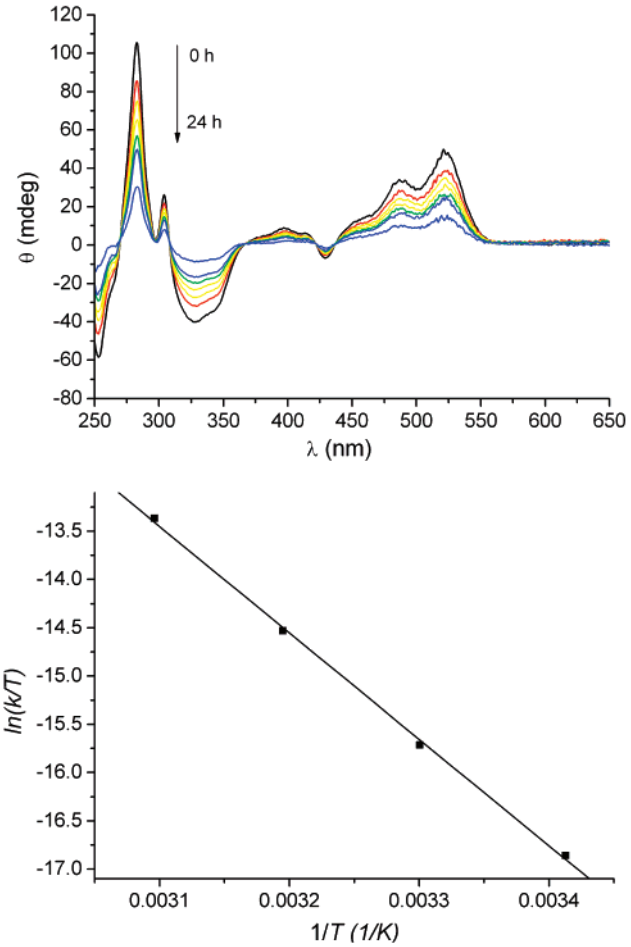


Figure 4. Time-dependent CD spectra of (*P*,*R*,*R*)-**5** in chloroform at 20 °C and Eyring plot for **5**.

is equal.[25] For PBI **4**, the activated complex exhibited an enthalpy $\Delta H^{\ddagger}$ of 92 ± 2 kJ mol^{-1} and only a slightly negative entropy $\Delta S^{\ddagger}$ of −20 ± 15 J mol^{-1}K^{-1}. Furthermore, the activation energy E_A of 94 ± 2 kJ mol^{-1} was determined according to Arrhenius equation. This value is in good agreement with the activation enthalpy $\Delta H^{\ddagger}$ (92 ± 2 kJ mol^{-1}) determined by Eyring equation as these two parameters are related by $E_A = \Delta H^{\ddagger} + RT$.

Table 2. Free Enthalpy of Activation for the Racemization of PBIs **1**−**5**

PBI	**1**	**2**	**3**	**4**	**5**
$\Delta G^{\ddagger}$/kJ mol^{-1}	60 ± 3[a]	40 ± 5[b]	40 ± 5[b]	98 ± 1[c]	118 ± 1[d]

[a] At 270 K. [b] At 183 K. [c] At 303 K. [d] At 368 K.

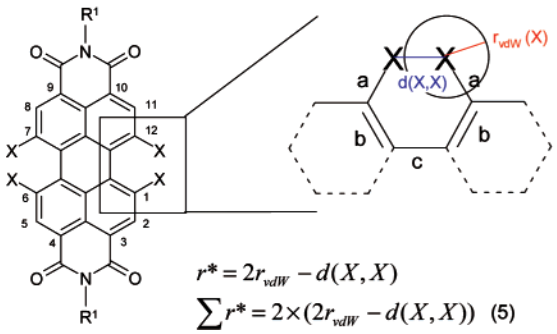
In contrast to the tetrachloro PBI **4**, a significantly decelerated racemization process was observed for the tetrabromo derivative **5**, as can be seen from the half-lifetimes given in Table 1. Thus, **5** exhibited almost the same half-lifetime at 383 K as **4** did at 323 K. For PBI **5**, an almost complete racemization was observed at 363 K after 1.5 days. Upon increasing the temperature to 383 K, a decrease in the half-lifetime of the racemization process to 36 min was observed and a complete racemization took place after 3 h. Furthermore, no significant change of the CD signal of **5** was observed at 323 K over a period of 3 h, demonstrating the high stability of the atropo-enantiomers of **5** at ambient conditions. The free enthalpy of activation for the racemization of **5** at 368 K was determined to be 118 ± 1 kJ mol^{-1}, which is in the same range as the activation barriers observed for hexahelicene[24a] or trisubstituted biphenyl,[26] both being conformationally stable at ambient conditions.

The activation energy E_A according to Arrhenius resulted to 123 ± 3 kJ mol^{-1} and showed again the expected correlation to the activation enthalpy $\Delta H^{\ddagger}$ (126 ± 3 kJ mol^{-1}). The activation entropy of **5** revealed a slightly positive value of 13 ± 10 J mol^{-1}K^{-1}. The negligible entropic contribution to the free enthalpy of activation indicates that the latter can be considered as temperature independent, at least in a particular temperature range.

Table 2 collects the thermodynamic parameters for all investigated PBIs. The comparison of the five bay-substituted perylene bisimides reveals a strong dependence of the free enthalpy of activation for this racemization process on the substituents. Although these $\Delta G^{\ddagger}$ values were determined at different temperatures, their comparison is justified because of the negligible entropic influence.

(25) Schoetz, G.; Trapp, O.; Schuring, V. *Electrophoresis* **2001**, *22*, 3185−3190.

(26) Meyers, A. I.; Himmelsbach, R. J. *J. Am. Chem. Soc.* **1985**, *107*, 682−685.



	r_{vdW}	a	∑r* (Å)
5	1.86	1.92	5.56
4	1.73	1.76	4.76
1	1.52	1.43	3.22
2	1.47	1.38	2.92

Figure 5. Definition of geometrical parameters for 1,6,7,12-tetrasubstituted perylene bisimides and the equations necessary for the calculation of the apparent overlap ∑*r**. The table (right) summarizes the apparent overlap values for PBIs **1**, **2**, **4**, and **5** (ordered according to decreasing overlap value). The apparent overlap of **1** was calculated for a hypothetical PBI bearing only oxygen atoms in the bay positions. For the calculation of apparent overlap values for 1,7-substituted PBIs, see the Supporting Information.

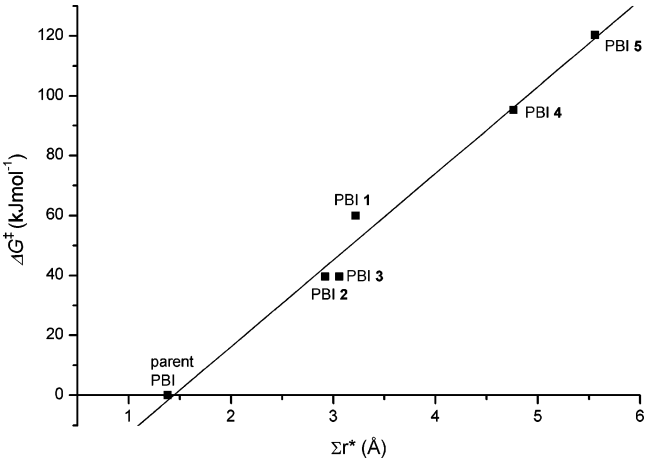


Figure 6. Dependence of the free activation enthalpy of racemization on the apparent overlap ∑*r** for PBIs **1**−**5** (data are taken from Table 2 and Figure 5).

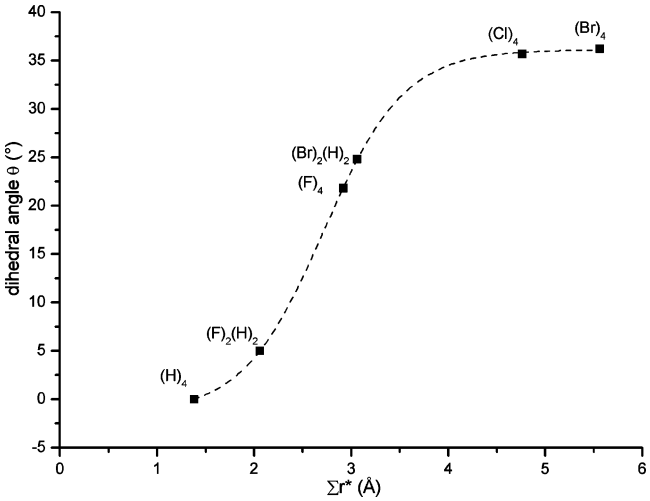


Figure 7. Dependence of the dihedral angle and the apparent overlap for different halogen-substituted perylene bisimides (substituents with numbers are given). The dihedral angles are taken from AM1 calculations and are the average value of two dihedral angles.

Relation between Free Activation Enthalpies and the Size of Bay Substituents. The parameter that has been most frequently applied to account for the steric stress of a distorted system due to the size of the substituents is the apparent overlap parameter ∑*r** of the substituents that cause the distortion.[27] The apparent overlap is defined as the overlap of the substituents in a 2-dimensional projection of a presumably planar transition state, as shown in Figure 5.

Parameter *r** depends on the geometry of the system under consideration and can be calculated according to eq 5 by applying standard C(sp^2)-X bond lengths *a* and bond angles, as well as the van der Waals radius r_{vdW} of the substituents.[27] In the present case, the bond lengths and angles were taken from single-crystal X-ray data of the planar parent unsubstituted PBI, which yields a value $d(X,X) = 2.862$ Å $- a$ (for details, see the Supporting Information).[28] The ∑*r** values of the investigated tetrasubstituted perylene bisimides **1**, **2**, **4**, and **5** are collected in Figure 5 (table). The ∑*r** value for the disubstituted PBI **3** was calculated by a similar procedure (see the Supporting Information) to 3.06 Å.

As can be seen from Figure 6, the free enthalpy of activation of the investigated PBI derivatives depends linearly on the apparent overlap of the substituents, indicating a direct relationship of the activation parameters with the size of the substituents and, thus on the steric repulsion imparted by the substituents. For the purpose of comparison, the parent unsubstituted perylene bisimide is also included in Figure 6, which possesses a free enthalpy of activation of zero due to its planar structure.

The observed linear dependence of free enthalpy of activation on the apparent overlap can be expressed by eq 6 (correlation factor r^2 of 0.98).

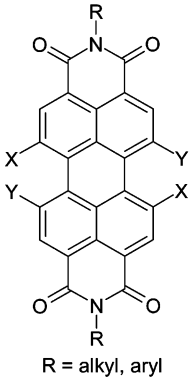
$$\Delta G^{\ddagger}_{180\,\mathrm{K}}\,(\mathrm{kJ/mol}) = 29.0 \sum r^{*} - 41.8 \qquad (6)$$

This demonstrates that the major factor determining the activation energy for the racemization of bay-substituted PBIs is the steric overlap of substituents in the planarized transition state. However, the zero crossing at ∑*r** = 1.40 Å indicates that the planarity can be maintained at small steric encumbering. This is convincingly demonstrated for the parent PBI ($X = Y = H$; ∑*r** = 1.38 Å) as well as for the difluoro-substituted derivative (∑*r** = 2.06 Å).[14]

This aspect is further explored by the relationship between the magnitude of the torsional twist upon attachment of bay substituents and the apparent overlap parameter. If we look at the dependence of the dihedral angles (taken from quantum chemical calculations that are in good accordance with crystal-

(27) (a) Cosmo, R.; Hambley, T. W.; Sternhell, S. *J. Org. Chem.* **1987**, *52*, 3119−3123. (b) Cosmo, R.; Sternhell, S. *Aust. J. Chem.* **1987**, *40*, 35−47.
(28) The planar core-unsubstituted PBI resembles the geometry of the presumably planar transition state. The values were taken as the average value of three different solid state structures: (a) Hino, K.; Mizuguchi, J. *Acta Cryst., Section E* **2005**, *61*, o672−o674. (b) Mizuguchi, J.; Hino, K.; Sato, K.; Takahashi, H.; Suzuki, S. *Acta Cryst., Section E* **2005**, *61*, o437−o439.

Chart 1. Structures, van der Waals Radii r_{vdW}, C(sp^2)-X and C(sp^2)-Y Bond Length *a*, and Apparent Overlap Values ($\sum r^*$) of Different PBIs



PBI	r_{vdw}	a[31]	$\sum r^*$
X = H, Y = NHOctyl	1.20/1.86[30]	1.10/1.47	3.66
X, Y = OH	1.52[30]	1.43	3.22
X, Y = NH_2	1.55[30]	1.47	3.41
X, Y = CH_3	1.80[30,a]	1.54	4.56
X, Y = PH_2	1.80[30]	1.80	5.08
X, Y = SH	1.80[30]	1.81	5.10
X, Y = SiH_3	1.90[30]	1.85	5.48
X, Y = *tert*-Bu	2.40[30]	1.54	6.96
X, Y = $SiMe_3$	2.60[30,a]	1.85	8.37
X, Y = CN	2.71[b]	1.44	8.00
X, Y = ethynyl	3.50[b]	1.53	11.34
X, Y = Ph	3.35	1.53	10.22
X, Y = $P(Ph)_2$	4.05[b]	1.80	14.15

[a] Minimal van der Waals radius. [b] Axial van der Waals radius (for definition, see the Supporting Information).

lographic data) on the apparent overlap in Figure 7, a S-shaped curve can be seen. For apparent overlaps between 2.1 (for 1,7-difluoro-substituted PBI) and 3.1 (for dibromo-substituted PBI **3**), an almost linear increase of the dihedral angle is given. However, on introduction of larger substituents, the dihedral angle saturates at a value of about 37°, whereas for the smallest hydrogen substituents a planarization is apparent.

Obviously, in the most demanding cases of sterical encumbering, other distortions of the π-system come into play rather than a further twisting of the π-system around the central axis. On the other hand, in the region of small apparent overlaps, an increased sterical demand of the respective substituents does not immediately lead to a twist of the perylene core but to slight expansions of the bond angles in such systems. For the unsubstituted perylene bisimide, which was shown to be planar by X-ray crystallography, the bond angles at the two bay areas have to be expanded only slightly to obtain an apparent overlap of zero.

This analysis provides a profound correlation between the interconversion barrier $\Delta G^{\ddagger}$ for known perylene bisimide dyes and the structural parameter $\sum r^*$. Accordingly, with the simple geometrical tool of apparent overlap values, interconversion barriers of known and also unknown bay-substituted perylene bisimide dyes can now be calculated and, with this tool, conformationally stable atropisomers become more predictable. This approach is exemplified below for a variety of bay-substituted perylene bisimides (Chart 1).

The first example is di(NHoctyl)-substituted perylene bisimide,[29] for which the apparent overlap was calculated by taking the van der Waals radius of NH-alkyl substituents from literature (for definitions and the use of group radii, see the Supporting Information).[30] With a value of $\sum r^* = 3.66$ Å, according to the eq 6, a free enthalpy of activation in the order of 64 kJ mol^{-1} is expected for this PBI, which is slightly higher than that of tetraaryloxy-substituted perylene bisimide **3**, implying a fast interconversion of the enantiomers of this dye at room temperature.

More importantly, the presented correlation allows the prediction and the design of conformationally stable core-twisted PBIs. For this purpose, it can be derived from the Eyring equation that the free enthalpy of activation must be in the order of around 106 kJ mol^{-1} at 295 K to obtain at room-temperature stable atropo-enantiomers of PBIs.[18,19,32] Thus, from eq 6, it can be predicted that the apparent overlap $\sum r^*$ has to be larger than 5.1 Å. By comparing the apparent overlap calculated for 1,6,7,12-tetrasubstituted PBIs (Chart 1), it can be proposed that the attachment of sulfur, phosphorus, or silicon substituents would allow the synthesis of conformationally stable atropo-enantiomeric PBIs (estimated $\Delta G^{\ddagger} = 106-118$ kJ mol^{-1}), whereas the attachment of oxygen substituents and primary amines would result in conformationally labile PBIs, as demonstrated for the tetraaryloxy-substituted PBI **1**. On the other hand, tetraarylthio-substituted PBIs, for which a free enthalpy of racemization $\Delta G^{\ddagger}$ of 106 kJ mol^{-1} is estimated from eq 6, seem to be suitable candidates for the synthesis of conformationally stable PBIs. Another reasonable strategy for an effective prevention of the racemization of PBIs would be the introduction of additional bulky substituents at the substituents in the bay area, since for *tert*-butyl and trimethylsilyl substituents $\Delta G^{\ddagger}$ values of 160 and 201 kJ mol^{-1}, respectively, are estimated from eq 6 (see Chart 1). Furthermore, the tetracyano- and

(29) Ahrens, M. J.; Tauber, M. J.; Wasielewski, M. R. *J. Org. Chem.* **2006**, *71*, 2107−2114.
(30) Charton, M. *Top. Curr. Chem.* **1983**, *114*, 57−91.
(31) *CRC Handbook of Chemistry and Physics*, 67th ed.; Weast, R. C., Ed.; CRC Press Inc.: Boca Raton, FL, 1986.
(32) The free enthalpy of activation was calculated by the Eyring equation for a half-lifetime of 100 days.

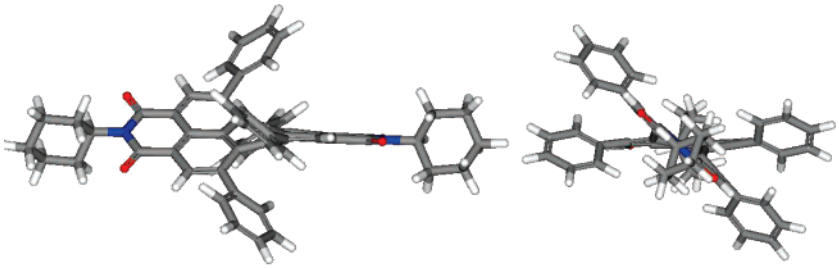


Figure 8. AM1 optimized geometry of tetraphenyl-substituted PBI: Side view (left) and view along the N,N-axis of the *M*-enantiomer (right). Structures were optimized by using the AM1 method as parametrized in CaChe Quantum CaChe workspace 5.0.

tetraalkynyl-substituted PBIs as well as the tetra(diphenylphosphino)-substituted PBI, the latter might be particularly interesting for catalytic purposes, are promising targets for the synthesis of conformationally stable perylene bisimides. But also the known tetraphenyl-substituted perylene bisimide,[13b] (for phenyl substituents an effective van der Waals radius of 3.35 Å was proposed in literature,[30]) should afford stable enantiomers. This can also be seen from an AM1 optimized geometry for this derivative (Figure 8). Here an interconversion of the enantiomers is not easily possible owing to the overlap of the two phenyl substituents in two bay regions, respectively.

Conclusion

Activation parameters for the racemization of five core-twisted perylene bisimides bearing substituents of different sizes in the bay position have been determined. These activation parameters reveal a close correlation with the size of the substituents attached in the bay area and confirm that the transition state in the interconversion process proceeds through an essentially planarized species. Additionally, it was found that four sterically demanding substituents attached to the bay area can prevent the dynamic racemization at ambient temperature. Thus, the atropo-enantiomers of tetrabromo-substituted PBI **5** could be resolved, which represent the first examples of enantiomerically pure core-twisted perylene bisimides. The pronounced stability of these enantiomers allowed us to determine their chiroptical properties. The correlation of substituent size with $\Delta G^{\ddagger}$ values is particularly useful for the prediction of activation barriers for other bay-substituted PBI dyes that might be promising targets for the future research. Conformationally stable atropo-enantiomeric PBIs have potential, especially as chiral building blocks for catalytic and sensory applications. On the basis of the relationship between substituent size and racemization barrier shown here, such conformationally stable perylene bisimide dyes can now be developed by design.

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Supporting Information Available: Temperature-dependent ^{1}H NMR spectra of PBIs **2** and **3**, details for data evaluation of kinetic measurements, calculation of sterical encumbering in bay-substituted perylene bisimides, calculation of group radii, and main error estimation for $\Delta G^{\ddagger}$ and $t_{1/2}$. This material is available free of charge via the Internet at http://pubs.acs.org.

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