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Diastereoselective reaction of (*MP*)-pentahelicene-7,8-dione with *trans*-cyclohexane-1,2-diamine. Thermal and photochemical transformations of its product†

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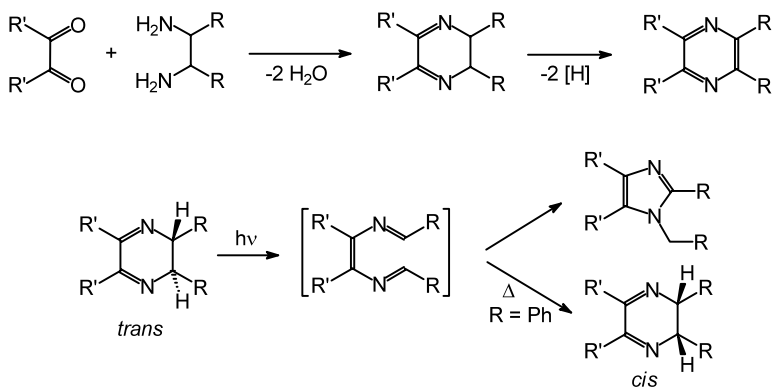
Abstract—The reaction of the title compounds and the transformations of the product, **3** were investigated with an emphasis on the stereochemistry. The primary interaction of the title compounds is feebly stereoselective. The diastereoisomers of product **3** exhibit free energies differing by ca. 16 kJ/mol; diastereoisomerization by helix inversion takes place during the reaction. The most stable diastereoisomers of the intermediate **8** and the product **3** show opposite helicities, which allows isolation of the product **3** in diastereoisomeric ratios from 19:81 to >99:1 depending on solvent and temperature. The free energies of activation for helix inversions of **3** were determined by time-dependent ^{1}H NMR. The predicted configuration of the more stable diastereoisomer of **3** was confirmed by chemical correlation to be (*M*,*R*,*R*). The four stereoisomers of **3** were separated by analytical enantioselective HPLC and characterized by on-line circular dichroism. Irradiation of **3** afforded the 2-substituted benzimidazole derivative **9**.

1. Introduction

The condensation of α-diketones with vicinal diamines (including subsequent dehydrogenation) represents a classical method for the synthesis of pyrazines,[2] especially symmetrically substituted ones (Scheme 1). Quinoxalines or phenazines are formed in this reaction sequence depending on the vicinal diamine used, when the α-diketone is replaced by an *o*-quinone. Alternatively, the intermediate 2,3-dihydropyrazines can be photochemically rearranged via the enediimine to the corresponding imidazole derivatives[3] (Scheme 1). Ther-



Scheme 1.

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† Helical phenanthrenes, part 6, for part 5 see Ref. 1.

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mal cyclization of particular enediimines yields *cis*-2,3-dihydropyrazines.[4]

Diastereoselective reduction (explored for the synthesis of enantiopure C_2-symmetric vicinal diamines) as a stereoselective transformation of the intermediate 2,3-dihydropyrazines has been reported.[5] Nevertheless, the steric course of the formation of 2,3-dihydropyrazines themselves has not yet been investigated in detail. The combination of a chiral *o*-quinone and a chiral vicinal diamine, in particular helicenequinone **1**[1] and *trans*-diamine **2** (Scheme 2), both showing C_2-symmetry, should serve as a representative system for the stereochemical study of their mutual condensation reaction.

2. Results and discussion

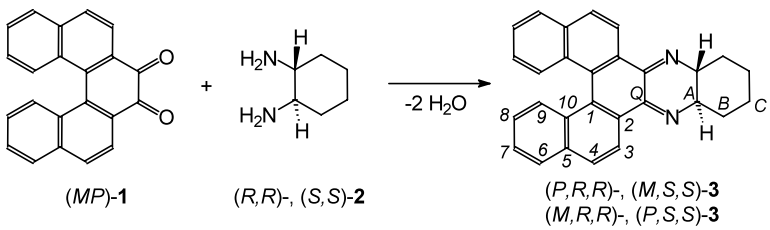
2.1. The two diastereoisomers of 3

The structure of the racemic diastereoisomers of **3** are given in Scheme 3. From these formulae and the corresponding molecular models (Fig. 1) the following characteristic difference between the diastereoisomers can be seen: While in (*M*,*R*,*R*)-, (*P*,*S*,*S*)-**3** each of the halves of the molecule (divided by the C_2-symmetry axis) is almost planar (overall scissors shape), in (*M*,*S*,*S*)-, (*P*,*R*,*R*)-**3** each half is bent (overall double U shape), most probably resulting in additional intramolecular strain. This expectation was supported by the results of semi-empirical calculations (AM1, PM3, SAM1), giving 12.5–14.2 kJ/mol in favor of the more stable (*M*,*R*,*R*)-, (*P*,*S*,*S*)-**3** diastereoisomer on the left hand side of Scheme 3, compared to the one on the right hand side.

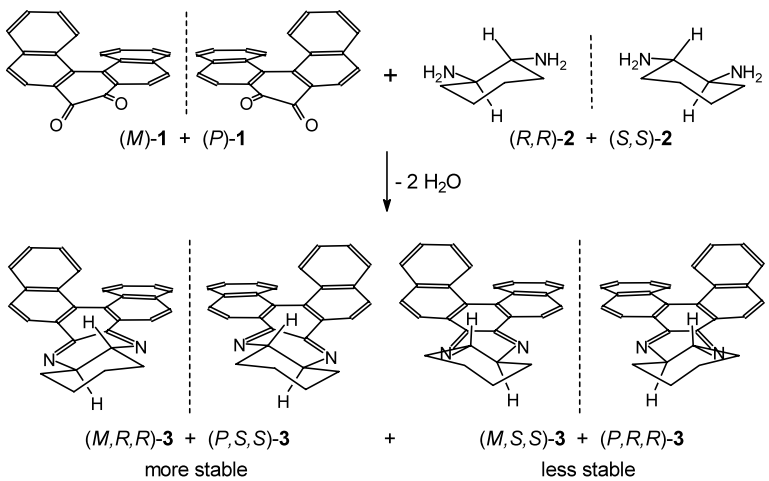
2.2. Diastereoselective reactions of (*MP*)-1 with *trans*-2

The reaction of (*MP*)-**1** with a slight excess of (±)-*trans*-**2** (Scheme 3; Table 1, entries 1 and 2) at −78°C with subsequent warming to room temperature resulted in an orange–yellow solid in 91–96% yield. The course of the reaction as well as the diastereomeric ratio of the isolated **3** depend on the solvent used. The reaction performed in ethanol proceeded directly from red **1** to orange–yellow **3** without visible formation of an intermediate. In THF as well as in other aprotic organic solvents (MeCN, CH_2Cl_2, PhMe), a yellowish precipitate was formed at first, slowly turning orange–yellow at room temperature. The observed difference is most probably caused by the contribution of the ethanol as a protic solvent in aiding the elimination of water in the later steps of the reaction. Both **1** and **3** were more soluble in THF than in EtOH. ^{1}H NMR analysis of the obtained product showed that two diastereoisomers of **3** had formed in ratios of 19:81 in EtOH and 60:40 in THF, the origin of different results in EtOH and THF is discussed later. The reaction times given (conditions **A**, **B**) were required for the complete conversion into **3**. In boiling THF, the diastereomeric ratio (d.r.) increased to >99:1 (Table 1, entry 3).

When the reaction of (*MP*)-**1** was performed with (*R*,*R*)-**2** (Table 1, entries 4 and 5) under the same conditions (**A** or **B**, respectively, although conditions **D** would be sufficient for complete conversion), ratios of



Scheme 2. Given numbering of atoms in **3** is relevant for the assignment of NMR spectra.



Scheme 3.

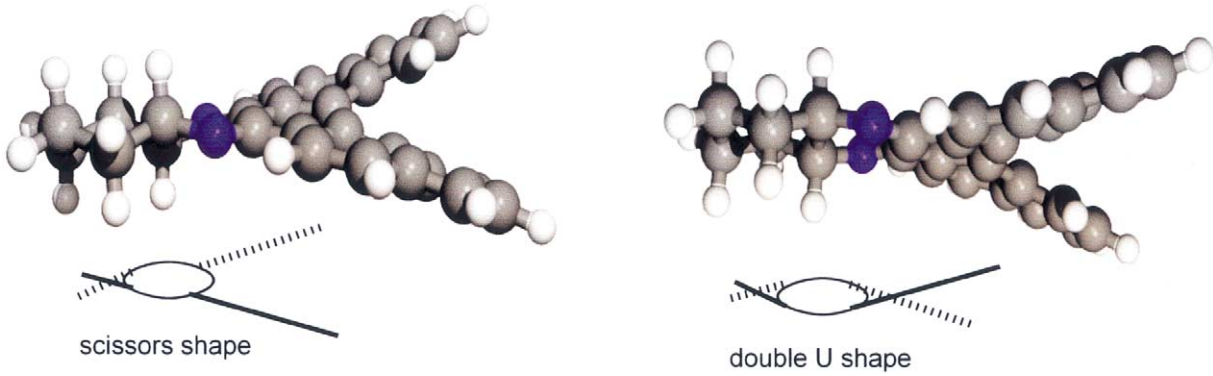


Figure 1. Molecular models of the more (left) and less stable (right) diastereoisomers of 2,3-dihydropyrazine **3**. Geometry optimization was performed using the AM1 method.

Table 1. Stereoselectivity of the reactions of (*MP*)-**1** with *trans*-**2**

Entry	Molar ratio (*MP*)-**1**:*trans*-**2**	Configuration of *trans*-**2**	Solvent	Conditions	Resulting ratio of stereoisomers	
					(*M*,*R*,*R*)-**3**:(*P*,*R*,*R*)-**3**[a]	(*M*)-**1**:(*P*)-**1**[b]
1	1:1.3	*rac*	EtOH	**A**	19:81[c]	–
2	1:1.3	*rac*	THF	**B**	60:40[c]	–
3	1:1.3	*rac*	THF	**C**	>99:1[c]	–
4	1:1.3	(*R*,*R*)	EtOH	**A**	46:54	–
5	1:1.3	(*R*,*R*)	THF	**B**	64:36	–
6	1:1.3	(*R*,*R*)	THF	**C**	>99:1	–
7	2:1	(*R*,*R*)	EtOH	**D**	41:59	55:45
8	2:1	(*R*,*R*)	THF	**D**	53:47	55:45
9	2:1	(*R*,*R*)	THF	**C**	>99:1	50:50

[a] Determined by ^{1}H NMR.
[b] Determined by ^{1}H NMR in the presence of Eu(hfbc)$_3$.
[c] Ratio of pairs of diastereoisomers (*M*,*R*,*R*)-, (*P*,*S*,*S*)-**3**: (*M*,*S*,*S*)-, (*P*,*R*,*R*)-**3**.
A: −78°C→rt overnight, then 3 h at rt.
B: −78°C→rt overnight, then 8 h at rt.
C: Reflux for 4 h.
D: −78°C→rt overnight.

diastereoisomers of **3** differed from the ones observed in the reactions with (±)-*trans*-**2** (entries 1 and 2), being shifted more in favor of the most stable diastereoisomer. In addition, the solubilities of the intermediate and the product **3** were significantly higher in the case of the reaction with (*R*,*R*)-**2**.

The reaction of (*MP*)-**1** with (*R*,*R*)-**2** in a molar ratio of 2:1 (Table 1, entries 7–9) afforded additional information about the steric course of the formation of **3**. Unreacted **1** was not significantly enriched (entries 7 and 8), enantiomer (*P*)-**1** (which should yield the less stable diastereoisomer of **3**) being slightly more reactive towards (*R*,*R*)-**2**. The stereoselectivity of this early step of the reaction does not depend on the solvent in which the reaction is performed. When the reaction was run at elevated temperature (entry 9), despite the low stereoselectivity of the primary interaction of (*MP*)-**1** with (*R*,*R*)-**2**, the isolated unreacted **1** was completely racemic, since it underwent complete racemization at elevated temperature. In addition. product **3** (entries 7 and 8) was of low diastereomeric purity, in a way analogous to the 1:1 experiments (entries 4 and 5), the predominance of one diastereoisomer being solvent dependent.

2.3. Thermal interconversion of the diastereoisomers of 3 and assignment of their configurations

The experimental diastereomeric ratio of **3**, isolated from the reactions of (*MP*)-**1** with *trans*-**2** performed at elevated temperatures (>99:1; Table 1, entries 3, 6 and 9), brought us to the idea that thermal diastereoisomerization of **3** is possible. Indeed, heating a solution of the diastereoisomeric mixture of **3** (19:81), obtained from the reaction in EtOH (Table 1, entry 1) to 40°C for 30 h resulted in the same ratio of diastereoisomers of **3** (>99:1). In addition, the experimental ratios of the diastereoisomers of **3**, isolated from the reactions of (*MP*)-**1** with *trans*-**2** performed under different conditions (Table 1, entries 1, 2, 4, 5, 7 and 8), are consistent with the observation of thermal interconversions of the diastereoisomers of **3**, if the different solubility of **3** (depending also on the enantiomeric purity of the diastereoisomers of **3**) and different reaction times are taken in account (see discussion in Section 2.4).

The observed thermal conversion of the less stable diastereoisomer of **3** to the more stable one in agreement with the above calculations (Section 2.1), resulted in the assignment of the most representative signals

$\delta(H^A) = 2.92$ ppm and $\delta(H^3) = 8.35$ ppm (Fig. 2, top) to the more stable diastereoisomer (*M*,*R*,*R*)-, (*P*,*S*,*S*)-**3**, and $\delta(H^A) = 3.04$ ppm and of $\delta(H^3) = 8.51$ ppm (Fig. 2, bottom) to (*M*,*S*,*S*)-, (*P*,*S*,*S*)-**3**, the less stable one. The time-dependence of the partial ^{1}H NMR spectrum (Fig. 2) of **3** gave access to the following data for the thermal diastereoisomerization in $CDCl_3$ at 40°C: $k_+ = 50\times10^{-6}$ s^{-1}, $k_- = 0.1\times10^{-6}$ s^{-1}, $\Delta G_+^{\neq} = 103\pm1$ kJ/mol, $\Delta G_-^{\neq} = 119\pm2$ kJ/mol. The result of the AM1 method (14.2 kJ/mol) for the energy difference between the diastereoisomers was closest to the experimental value of $\Delta G = 16\pm3$ kJ/mol.

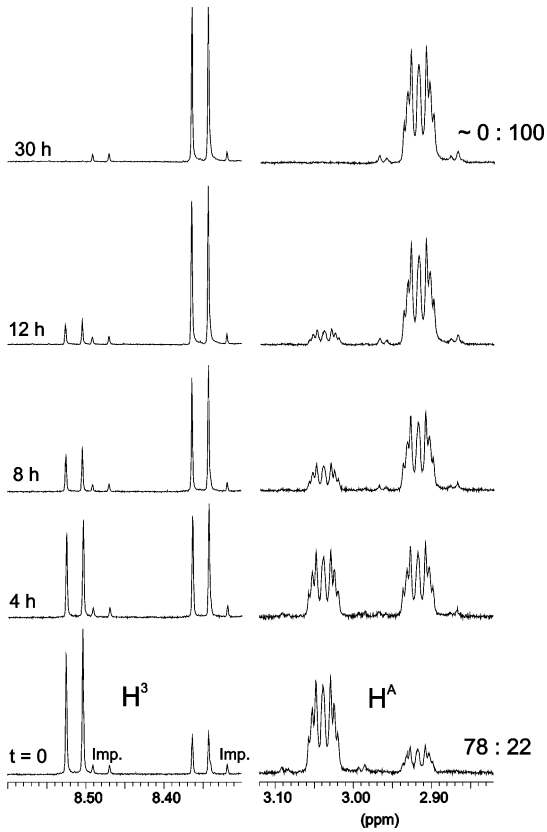
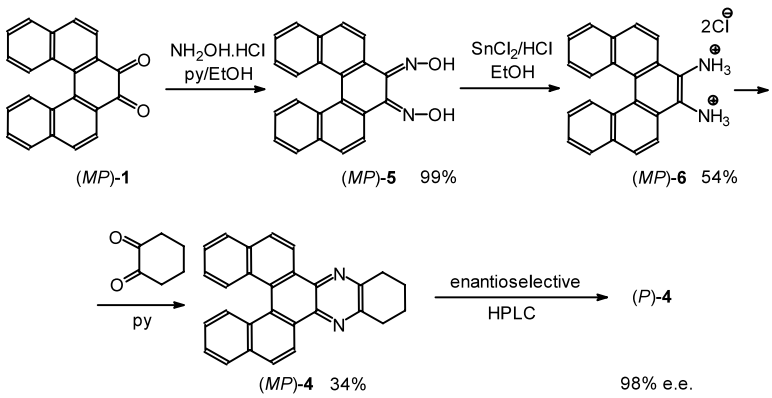


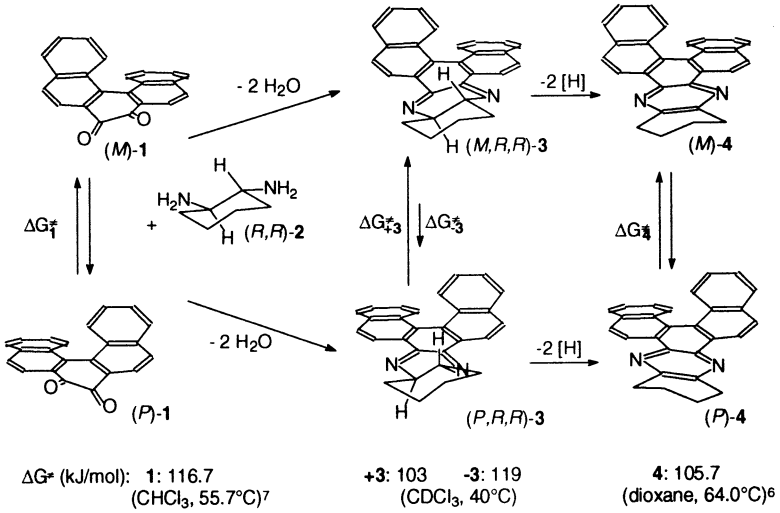
Figure 2. ^{1}H NMR of H^3 and H^A of the mixture of diastereoisomers of **3** in $CDCl_3$ under a nitrogen atmosphere at 400 MHz. This mixture had been prepared by the reaction (Scheme 3) in EtOH and shows the ratio of the diastereoisomers of 78:22 (bottom). After 30 h at 40°C in $CDCl_3$, the ratio has changed to almost 0:100 (top). For spectral assignment see text.

Dehydrogenation of enantiopure (*M*,*R*,*R*)-**3**, obtained from the reaction of (*MP*)-**1** with (*R*,*R*)-**2** in boiling THF (Table 1, entry 6), gave $(-)_{578}$-(*M*)-**4** in 76% e.e. (Scheme 5). The partial loss of enantiomeric purity is due to racemization during the oxidation (24 h at rt). This experiment allowed us to confirm the predicted configuration of the more stable diastereoisomer of **3** by chemical correlation, since the assignment of the sign of the specific rotation to the absolute configuration of **4** was known from anomalous X-ray diffraction of $(+)_{436}$-(*P*)-**4**.[6] The latter compound was also prepared according to Scheme 4 as part of an independent study.[6] For this purpose, dione (*MP*)-**1** was converted into a mixture of the three diastereoisomers of dioxime (*MP*)-**5** which was reduced to diammonium chloride (*MP*)-**6** according to a known method.[7] (*MP*)-**6** was heated with cyclohexane-1,2-dione to form tetrahydrophenazine (*MP*)-**4** in 34% yield. These three steps correspond to known types of reactions. Micropreparative HPLC resulted in $(+)_{436}$-(*P*)-**4** with 98% e.e.

Scheme 5 summarizes the reaction of (*MP*)-**1** with (*R*,*R*)-**2** and compares the above barriers to helix inversion of **3** with those of the starting quinone **1**,[8] and **4**,[6] the dehydrogenation product of **3**. While barriers for helix inversions in the cases of **1** and **4** represent barriers to enantiomerization and are the same in both $(M) \rightleftharpoons (P)$ directions, in the case of **3** they represent diastereoisomerization barriers and are unequal. Although the temperatures and solvents for the measurements were different, isomerization of **3** to the more stable diastereoisomer is clearly the process requiring the lowest activation energy among the helix inversions of the molecules presented. In any case, taking into account the results of the reactions (Section 2.2), the diastereoisomerization barriers of the intermediates **8** should most probably be even lower and should prefer the conversion to the diastereoisomers of the intermediates affording the less stable diastereoisomer of **3**.



Scheme 4.

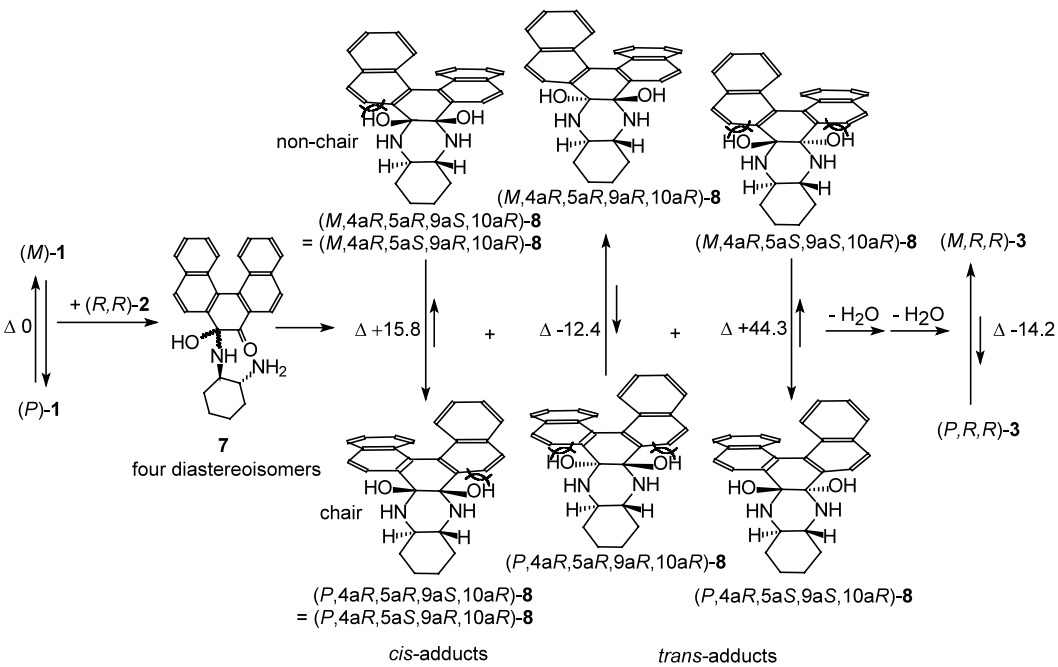


Scheme 5.

2.4. Mechanistic considerations with respect to the diastereoselectivity of the reaction of (*MP*)-1 with *trans*-2

The results of our experiments (Section 2.2) showed that the more stable diastereoisomer of **3** is not the preferred product in the reaction of quinone **1** with *trans*-diamine **2** (up to 62% d.e. of the less stable diastereoisomer of **3**; Table 1, entry 1). This means that the difference of the free energies of the diastereoisomers of the final product **3** does not determine the stereochemical outcome of the reaction. The reaction pathway is definitely multistep and its last step does not determine the configuration of the product. However, this is also true for its first step, since the primary interaction of (*MP*)-**1** with *trans*-**2** shows low stereoselectivity (10% d.e. in favor of the direction to the less stable diastereoisomer of **3**; Table 1, entries 7 and 8). The stereoselectivity of the first step is clearly not solvent dependent.

Using molecular modeling, we examined possible intermediates in the reaction of (*MP*)-**1** with (*R*,*R*)-**2** on the pathway consisting of stepwise double nucleophilic attack and then stepwise elimination of two molecules of water. For the semi-empirical calculations of energy differences between diastereoisomers we used the AM1 method, which had proven to be reliable with respect to experimental results (Section 2.3). In our opinion, based on consideration of molecular models, the second nucleophilic attack (from **7** to **8**; Scheme 6) is crucial to the diastereoselectivity of the reaction, since it affords preferentially the diastereoisomers of bis(aminol) **8** which correspond to formal *cis*-, not *trans*-addition.



Scheme 6. Δ values are energy differences calculated by the AM1 method, given in kJ/mol.

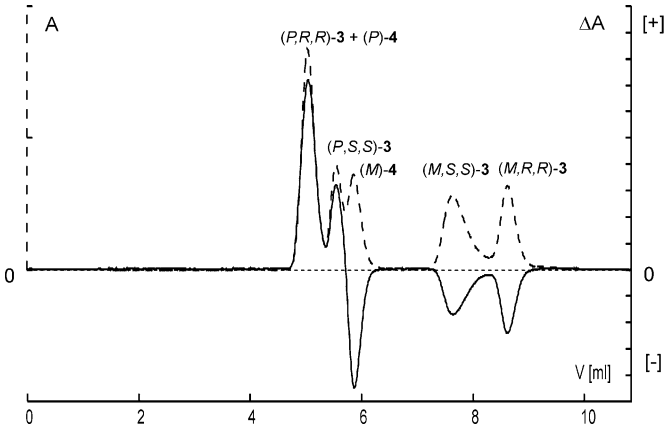


Figure 3. Liquid chromatogram of the reaction product (Scheme 3) of (*MP*)-**1** and racemic *trans*-**2** in THF, after removal of THF without further treatment. Eluent: *n*-hexane/EtOH, 85:15. Sorbent: tris(3,5-dimethyl-phenylcarbamoyl)amylose/SiO_2 (Chiralpak AD). A and ΔA: absorbance and differential absorbance, respectively, at 230 nm in arbitrary units. V: Retention volume, referred to injection at $V=0$. Retention factors k' from the left to right: 0.2, 0.4, 0.5, 0.9, 1.1. For the assignments see text.

The overall number of diastereoisomers of bis(aminol) **8** (given in Scheme 6) is reduced to six because there are only two diastereoisomers of **8** resulting from *cis*-addition, since they are *meso*-like (this term was used to denote the diastereoisomers of *ansa*-metallocenes with analogous specific stereochemistry[9]). Among all diastereoisomers, the *cis*-adduct with (*P*)-helicity (yielding the less stable (*P*,*R*,*R*)-**3** diastereoisomer) is the most stable one. This most stable (*P*,4a*R*,5a*R*,9a*S*,10a*R*)-**8** diastereoisomer has a chair conformation of the perhydropyrazine ring in contrast to the less stable *cis*-adduct (*M*,4a*R*,5a*R*,9a*S*,10a*R*)-**8** (calculated energy difference +15.8 kJ/mol). *cis*-Adducts are possibly the key intermediates controlling final stereochemistry. Racemic-like diastereoisomers (*trans*-adducts) of **8** are expected to be less favored; non-bonding interactions between hydroxy and naphthyl groups determine which diastereoisomers, interconvertible by helix inversions, are more stable.

The solvent plays a role for the rate of transformation of intermediate **8** to product **3**, a protic solvent facilitating it. The solvent has a significant effect on the ratio of diastereoisomers in isolated **3**, via its solubility. Product **3** conserves the ratio of diastereoisomers in EtOH, where it is sparingly soluble, better than in THF, where it is more soluble; therefore, diastereoisomerization to the more stable diastereoisomer takes place (Table 1, entry 1 versus 2). In the reactions with enantiopure (*R*,*R*)-**2**, where the enantiopure diastereoisomers of **3** are more soluble compared to the racemic ones, the composition of the isolated product is closer to the equilibrium of the diastereoisomers of **3**, particularly in EtOH (Table 1, entries 4, 5, 7 and 8).

2.5. The four stereoisomers of 3—enantioselective HPLC and circular dichroism

Liquid chromatograms of the reaction product (Fig. 3) of (*MP*)-**1** with (±)-**2** in THF and of its pure dehydrogenation product **4** under similar conditions result in the distinction of the peaks for **3** and **4**. (*M*)-**4** and (*P*)-**4** were assigned via anomalous X-ray diffraction[6] of $(+)_{436}$-(*P*)-**4**. The remaining peaks at retention factors $k'=0.2$ and 0.4 show positive ΔA detections, the peaks at 0.9 and 1.1 negative ones. Their absolute assignments to the four stereoisomers of **3** result from the selective formation, starting from (*MP*)-**1** and **2** under various conditions (Section 2.2, Table 1) and from their on-line circular dichrograms,[10] most of which are shown in Fig. 4. On the left side of Fig. 4, (*M*,*R*,*R*)- and (*P*,*S*,*S*)-**3** show a mirror image relationship and are therefore enantiomers. On the right side, (*M*,*S*,*S*)- and (*M*,*R*,*R*)-**3** show differences below 260 nm and should therefore be diastereoisomers. At the same time, it is evident that the dichrograms are not dominated by central chirality, but by helicity (as shown by the similarity of spectra in Fig. 4, right part).

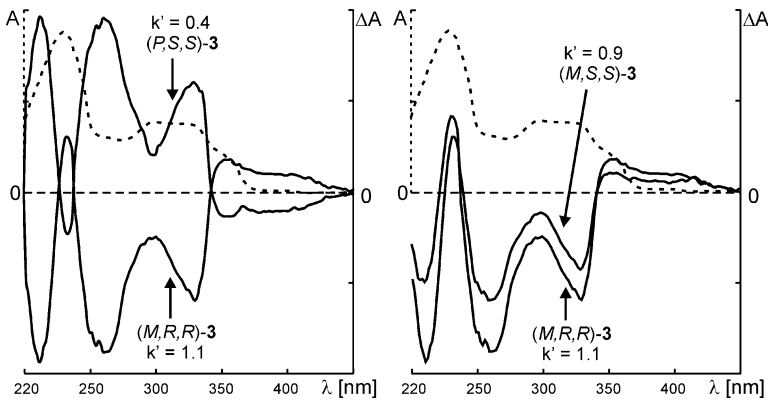


Figure 4. On-line circular dichrograms ΔA (λ) and ultraviolet spectra A (λ) in arbitrary units for the stereoisomers of **3** (Scheme 3), obtained during HPLC (Fig. 3) in *n*-hexane/EtOH, 85:15. For assignments see text. Left: the dichrograms of the enantiomers (*M*,*R*,*R*)- and (*P*,*S*,*S*)-**3** show a mirror-image relationship. Right: the dichrograms of the diastereoisomers (*M*,*S*,*S*)- and (*M*,*R*,*R*)-**3** with identical (*M*) helicity show differences below 260 nm. (In order to show these differences more clearly, unequal arbitrary units of ΔA were chosen for these diastereoisomers.)

In an attempt to analyze and assign the observed Cotton effects and to correlate them to molecular absolute configurations of the stereoisomers of **3**, the wavelengths of the extrema were compared with the ones of the dehydrogenation product **4** (Table 2). Indeed, the signs and relative intensities of the bands between 220 and 275 nm appear to be the same for (*M*)-**3** and (*M*)-**4** (Table 2) and may correspond to known π→π* transitions in the pentahelicene hydrocarbons.[11] However, safe assignments of the observed Cotton effects to the electronic transitions (and also to the absolute helicity) would require quantum chemical calculations. The bands at 297 nm and above (Table 2), partly arising from n→π* transitions of the nitrogen atoms, differ considerably, including the signs, for (*M*)-**3** and (*M*)-**4** and, therefore, cannot be assigned without calculations. To the best of our knowledge, no circular dichroism information is available[12] about suitable heterosubstituted helicene or 1,1′-binaphthyl derivatives which might be helpful for the assignments of the Cotton effects and absolute configurations of **3** and **4**.

These absolute configurations were obtained by X-ray diffraction[6] and chemical correlation and could not be determined by circular dichroism. However, the latter method, on line with HPLC, turned out to be an excellent enantioselective method for characterization of the stereoisomers of **3** by use of their mixture, because the individual isomers are not easily obtained in quantities required for conventional characterization, e.g. by mp, elemental analysis and polarimetry.

2.6. Photolysis of 3

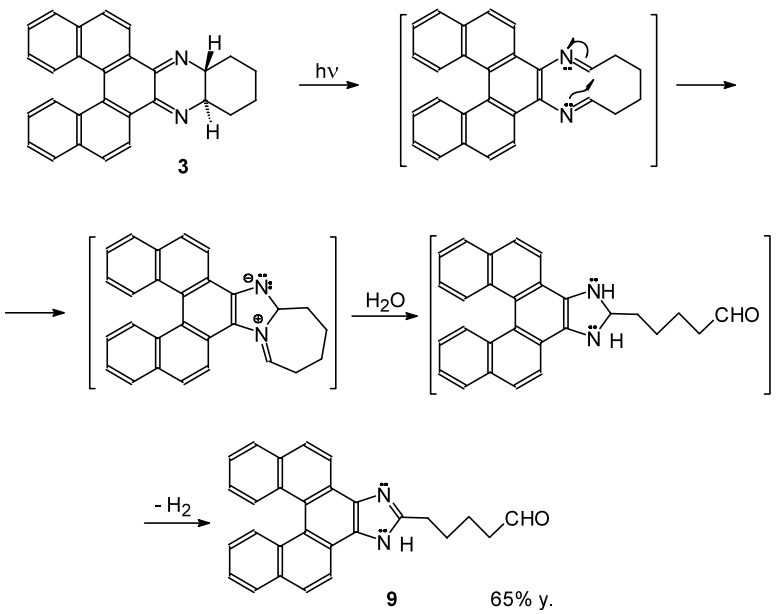
When irradiated with a UV-lamp or left in sunlight, compound **3** in dilute solution undergoes photochemical rearrangement (Scheme 7) analogous to the one observed for 2,3-dihydropyrazines[3] (Scheme 1). Contrary to the general scheme, the 2-substituted imidazole derivative **9** was isolated as the final product in 65% yield instead of 1,2-disubstituted one. This can be explained by the proposed mechanism (Scheme 7), where, after the expected cleavage of the C(2)–C(3) bond to an enediimine, its intramolecular nucleophilic addition, and the formation of the 1,2-disubstituted imidazol-1-ium-3-ide derivative, the latter is hydrolyzed to a 2,3-dihydro-1*H*-imidazole derivative substituted in position 2 with the aliphatic chain terminated by the aldehyde group. Finally, the imidazole ring is stabilized (aromatized) by spontaneous dehydrogenation. In the photochemical rearrangements affording 1,2-disubstituted imidazole derivatives described in the literature,[3] the 1,2-disubstituted imidazol-1-ium-3-ide is most probably aromatized primarily by proton transfer and then does not undergo hydrolysis.

Table 2. Wavelengths (nm) of circular dichroism extrema for compound **3** and its dehydrogenation product **4** (Scheme 5). Relative intensities of the extrema indicated by w (weak), m (medium) and s (strong). See text for absolute helicities

(*M*)-**3**[a]	220	230	260			330	350		420
	−s	+m	−s			−m	+w		+w
(*M*)-**4**[b]	224	247	270	275	297	342	375	380	395
	−s	+s	−m	−m	−s	+m	−w	−w	−w

[a] Solvent *n*-hexane/EtOH 85:15. (*M*,*R*,*R*)-**3** and (*M*,*S*,*S*)-**3** were measured on line with HPLC (Fig. 4, right part); approximate wavelengths, averaged for these diastereoisomers, are given.

[b] Solvent CH_2Cl_2/*n*-hexane 75:25 with 5% MeCN. Absolute intensities for (*P*)-**4** are given in Section 3.



Scheme 7.

3. Experimental

Melting points were determined using a Kofler melting point apparatus and are uncorrected. The IR spectra were scanned from KBr pellets using a Mattson FTIR spectrometer. The NMR spectra were recorded with Bruker AC-250 (250 MHz), Varian Gemini 300 (300 MHz) and Bruker ARX-400 (400 MHz) instruments with tetramethylsilane as an internal standard. Mass spectra were measured on a Finnigan MAT 90 spectrometer at 70 eV. Flash column chromatography was performed on 30–60 μm silica gel and thin-layer chromatography on Silufol UV 254 foils. HPLC analysis was done on a Chiralpak AD column using a Jasco CD-1595 detector[10] (UV and CD detection). HPLC analysis and micropreparative separations of the enantiomers of **4** were performed on a column[13,14] containing chemically bonded (+)-(*S*)-2-(2,4,5,7-tetranitrofluorenylideneaminooxy)propanoic acid (TAPA), using a photometer ERC 7210, ERMA Optical Works Ltd., and a polarimeter Perkin–Elmer 241 (UV and polarimetry detections). Specific rotations were measured on a Perkin–Elmer 241 polarimeter and are given in 10^{-1} deg cm^2 g^{-1}. CD spectra were obtained by the circular dichrograph Jasco J-40A. Elemental analysis was determined on an Erba Science 1106 instrument.

All reactions were performed in freshly distilled dried solvents under nitrogen atmosphere. Compound **1** was synthesized according to Ref. 1.

3.1. 1,2,3,4,4a,10a-Hexahydrodinaphtho[2,1-*h*;1′,2′-*j*]-phenazine 3

3.1.1. Preparation of (*M*,*R*,*R*)-, (*M*,*S*,*S*)-, (*P*,*R*,*R*)- and (*P*,*S*,*S*)-3. In ethanol: A solution of (*R*,*R*)-**2** and (*S*,*S*)-cyclohexane-1,2-diamine **2** (15 mg, 0.13 mmol) in ethanol (2 mL) was added dropwise to a stirred suspension of finely powdered (*MP*)-**1** (31 mg, 0.10 mmol) in ethanol (3 mL) at room temperature in the dark. The color of the reaction mixture turned from red to orangish yellow. After being stirred for 3 h, the reaction mixture was opened to the air, and the solvent was evaporated under vacuum at room temperature. The residue was washed twice with a small amount of hexane, and dried under vacuum. Yield: 37 mg (96%) of orangish yellow solid with 62±3% d.e. of diastereoisomers (*M*,*S*,*S*)-**3**, and (*P*,*R*,*R*)-**3** (determined by ^{1}H NMR). D.e. of the product was found to be in the same range, if the reactants had been mixed at −78°C (reaction takes place above −50°C). The product is slightly air and light sensitive even in the solid state.

In THF: A solution of (*R*,*R*)-**2** and (*S*,*S*)-**2** (15 mg, 0.13 mmol) THF (2 mL) was added dropwise to a stirred suspension of finely powdered (*MP*)-**1** (31 mg, 0.10 mmol) in THF (3 mL) at −78°C in the dark. The color of the reaction mixture turned yellowish within a minute and a yellowish white precipitate slowly formed. The reaction mixture was allowed to warm to room temperature, being kept in the former cooling bath overnight. Then it was stirred for 8 h at room temperature. The precipitate turned orangish yellow. Work-up was the same as described above. Yield: 36 mg (91%) of orangish yellow solid with 20±3% d.e. of diastereoisomer (*M*,*R*,*R*)-, and (*P*,*S*,*S*)-**3** (^{1}H NMR). If the reaction was started at room temperature and stirred for 12 h, the isolated product was of 14±3% d.e. of diastereoisomer (*M*,*R*,*R*)-, and (*P*,*S*,*S*)-**3**.

^{1}H and ^{13}C NMR spectra are given in Tables 3 and 4. IR (cm^{-1}): 3070, 3050 (C_{ar}-H), 2920, 2850 (C_{al}-H). Mp: 253–255°C with decomposition. Elemental analysis: $C_{28}H_{22}N_2$ (386.50); found/calcd (%): C, 86.78/87.01; H, 5.62/5.74; N, 7.14/7.25. MS: $M^{\bullet+}$ 386. HPLC separation of stereoisomers of **3** on Chiralpak AD [eluent hexane/ethanol, 85:15, temp. 22°C, flow 0.50 mL min^{-1}, λ (UV, CD) 230 nm]; k': 0.2 {[+]-(*P*,*R*,*R*)-**3**}, 0.4 {[+]-(*P*,*S*,*S*)-**3**}, 0.9 {[−]-(*M*,*S*,*S*)-**3**}, 1.1 {[−]-(*M*,*R*,*R*)-**3**}; Fig. 3.

3.1.2. Preparation of (*M*,*R*,*R*)- and (*P*,*S*,*S*)-3. A solution of (*R*,*R*)- and (*S*,*S*)-**2** (69 mg, 0.60 mmol) in THF (10 mL) was added dropwise to a stirred suspension of finely powdered (*MP*)-**1** (154 mg, 0.50 mmol) in THF (20 mL) at room temperature in the dark. The reaction mixture was heated under reflux for 4 h. Work-up was the same as described above. Yield: 186 mg (95%) of orangish yellow solid of pure (*M*,*R*,*R*)-, and (*P*,*S*,*S*)-**3** diastereoisomers (^{1}H NMR).

3.1.3. Preparation of (*M*,*R*,*R*)- and (*P*,*R*,*R*)-3. The procedure was the same as described for the preparations of (*M*,*R*,*R*)-, (*M*,*S*,*S*)-, (*P*,*R*,*R*)- and (*P*,*S*,*S*)-**3**, only (*R*,*R*)-**2** was used instead of (*R*,*R*)- and (*S*,*S*)-**2**. The reactions were started at −78°C. The solubility of the product was higher compared to the reactions with (*R*,*R*)- and (*S*,*S*)-**2**; in THF no precipitate was formed.

Reaction performed in ethanol: Yield: 34 mg (88%) of orangish yellow solid with 8±3% d.e. of diastereoisomers (*P*,*R*,*R*)-**3** (^{1}H NMR).

Reaction performed in THF: Yield: 32 mg (83%) of orangish yellow solid with 28±3% d.e. of diastereoisomers (*M*,*R*,*R*)-**3** (^{1}H NMR).

3.1.4. Preparation of (*M*,*R*,*R*)-3. A solution of (*R*,*R*)-**2** (15 mg, 0.13 mmol) in THF (2 mL) was added dropwise to a stirred suspension of (*MP*)-**1** (31 mg, 0.10 mmol) in THF (3 mL) at room temperature in the dark. The color of the reaction mixture turned yellowish within a minute. The reaction mixture was heated under reflux for 4 h. Work-up was the same as described above. The product was crystallized from hexane. Yield: 28 mg (73%) of orangish yellow solid (*M*,*R*,*R*)-**3** as an enantiopure diastereoisomer (e.e., d.e. >99%, ^{1}H NMR). Mp: from 202°C with decomposition. $[\alpha]_D^{23} = -1400 \pm 25$ ($c = 0.51$, $CHCl_3$).

Table 3. ^{1}H NMR ($CDCl_3$, 400 MHz) spectra of **3** and **4**. For numbering of atoms see Scheme 2

Compound		C(3)H	C(4)H	C(6)H	C(7)H	C(8)H	C(9)H	C(H_a-A)	C(H_e-B)	C(H_a-B)	C(H_e-C)	C(H_a-C)
	δ (ppm) [a]	8.51	7.88	7.88	7.49	7.20	7.48	2.98–3.09	2.48–2.57	1.58–1.72	1.88–2.02	1.42–1.55
(*M*,*S*,*S*)-,	Multiplicity	d (br)	d (br)	d (br)	ddd	ddd	d (br)	m	m	dm	m	m
(*P*,*R*,*R*)-**3**	$\lvert^nJ_{XY}\rvert$ (Hz)	^{3}8.6$_{34}$		^{3}8.1$_{67}$, ^{4}1.3$_{68}$, [b], ^{4}1.1$_{79}$, ^{3}8.5$_{89}$				^{2}13.7$_{Bae}$				
	δ (ppm)[a]	8.35	7.93	7.91	7.52	7.25	7.54	2.86–2.98	2.48–2.57	1.58–1.72	1.88–1.99	1.40–1.52
(*M*,*R*,*R*)-,	Multiplicity	d (br)	d (br)	d (br)	ddd	ddd	d (br)	m	m	dm	m	m
(*P*,*S*,*S*)-**3**	$\lvert^nJ_{XY}\rvert$ (Hz)	^{3}8.6$_{34}$		^{3}8.1$_{67}$, ^{4}1.3$_{68}$, ^{3}6.8$_{78}$, ^{4}1.1$_{79}$, ^{3}8.6$_{89}$				^{2}13.7$_{Bae}$				
	δ (ppm) [a]	9.28	8.13	8.01	7.54	7.28	8.24	–	3.22–3.35 (4H)		2.09–2.13 (4H)	
4	Multiplicity	d (br)	d (br)	dd	ddd	ddd	d (br)		m		m	
	$\lvert^nJ_{XY}\rvert$ (Hz)	^{3}8.7$_{34}$		^{3}8.1$_{67}$, ^{4}1.3$_{68}$, ^{3}6.8$_{78}$, ^{4}1.1$_{79}$, ^{3}8.6$_{89}$								

[a] Each signal corresponds to 2H if not given otherwise.
[b] Not readable $^3J_{78}$.

Table 4. ^{13}C NMR ($CDCl_3$, 100 MHz, δ) spectra of **3** and **4**. For numbering of atoms see Scheme 2

Compound	C(Q)	C-(1,2,5,10)	C(3)	C(4)	C(6)	C(7)	C(8)	C(9)	C(A)	C(B)	C(C)
(*M*,*S*,*S*)-, (*P*,*R*,*R*)-**3**	152.0	135.3, 132.8, 131.9, 130.9	122.7	128.6, 127.9	126.9	124.7	129.0	58.5	33.9	25.9	
(*M*,*R*,*R*)-, (*P*,*S*,*S*)-**3**	154.4	135.4, 132.9, 130.8, 129.7	122.3	128.9	128.2	127.0	125.2	128.5	59.2	33.5	25.7
4	152.6	133.5, 130.7, 129.5, 127.4	121.4	128.2	128.0	126.5	124.5	129.4	138.7	33.0	23.0

3.1.5. Reaction of (*MP*)-1 with (*R*,*R*)-2 in a 2:1 ratio. A solution of (*R*,*R*)-**2** (28.5 mg, 0.25 mmol) in EtOH or THF (10 mL) was added dropwise to the suspension of finely powdered (*MP*)-**1** (154 mg, 0.50 mmol) in the same solvent (20 mL) at −78°C in the dark. The reaction mixture was allowed to warm to room temperature overnight. The solvent was evaporated under vacuum at room temperature. The d.e. of **3** was determined directly from the residue (^{1}H NMR). Unreacted **1** was isolated from the residue by flash chromatography on silica gel, eluted with dichloromethane (R_f=0.65). E.e. of **1** was determined by ^{1}H NMR in the presence of Eu(hfbc)$_3$. Results are given in Table 1, entries 7 and 8.

3.2. Dibenzo[*c*,*g*]phenanthrene-3,4-dioxime 5

A solution of (*MP*)-**1** (1.04 g, 3.38 mmol), $NH_2OH{\cdot}HCl$ (16.9 g, 243 mmol) and pyridine (10 mL) in EtOH (100 mL) was heated under reflux for 20 h. The mixture was left at room temperature for 2 h. The needles of pyridinium hydrochloride were removed. Water was added to the filtrate until no further yellow–green precipitate was formed. This precipitate was filtered on silica gel and eluted from it by CH_2Cl_2. This solution was washed twice with highly dilute aq. HCl, then with saturated aq. $NaHCO_3$. After drying over anhydrous $MgSO_4$ and considerable evaporation, yellow crystals formed. Yield: 1.13 g (99%). Three diastereoisomers in a relation 1:2:1 (^{1}H NMR). Mp: 213–216°C (EtOH, then CH_2Cl_2). ^{1}H NMR (d_6-DMSO, δ): 12.46 s (0.5H, OH), 12.23 s (1H, OH), 12.06 s (0.5H, OH), 8.6–7.9 m (6H, CH), 7.6–7.3 m (6H, CH). IR (cm^{-1}): 3600–2600 br (O-H), 3060 (C-H), 1590, 1500 (C=N). MS: M$^{\bullet+}$ 338, 336, 320.

3.3. Dibenzo[*c*,*g*]phenanthrene-3,4-diamminium dichloride 6

According to a known reduction method.[7] A solution of $SnCl_2$ (12 g, 63 mmol) in conc. HCl (44 mL) was added to dioxime **5** (2.0 g, 5.9 mmol) in EtOH (300 mL). After stirring the mixture for 4 h at 60–70°C, the gray–brown precipitate formed was collected and washed several times with EtOH and twice with a small amount of ether. Yield: 1.21 g (54%). Mp: >390°C. ^{1}H NMR (d_{18}-HMPTA, δ): 10.32 br s (6H, NH_3^+), 8.7–7.3 m (12H, CH). IR (cm^{-1}): 3600–2500 br, 3420, 3350, 3270, 3240 (N-H), 3060, 2940 (C-H), 2600. MS: M$^{\bullet+}$ 308, 291, 290, 263.

3.4. 1,2,3,4-Tetrahydrodinaphtho[2,1-*h*;1′,2′-*j*]phenazine 4

3.4.1. Preparation of (*MP*)-4. A mixture of diaminium dichloride **6** (150 mg, 0.39 mmol) and cyclohexane-1,2-dione (150 mg, 1.34 mmol) in dry pyridine (50 mL) was heated under reflux for 1–2 h under nitrogen. The solvent was evaporated and the remaining brown resin submitted to chromatography on silica gel (eluent

CH_2Cl_2). The fraction at $R_f=0.9$ resulted in yellowish crystals. Yield: 51 mg (34%).

Mp: 271–272°C. ^1H and ^{13}C NMR spectra of **4** are given in Tables 3 and 4. IR (cm^{-1}): 3090, 3060 (C_{ar}-H), 2960, 2880 (C_{al}-H). MS: $M^{\bullet+}$ 384, 383, 276, 275, 192. HPLC on Chiralpak AD [eluent hexane/ethanol, 85:15, temp. 22°C, flow 0.50 mL min^{-1}, λ (UV, CD) 230 nm]; k': 0.2 {[+]-(*P*)-**4**}, 0.5 {[−]-(*M*)-**4**}, Fig. 3. HPLC on the column mentioned above, containing (+)-(*S*)-TAPA[13,14] [eluent CH_2Cl_2/hexane, 75:25, with 5% of MeCN, temp. 23°C, 21 bar, λ (polarimetry) 436 nm]; k': 2.3 {[+]-(*P*)-**4**}, 2.7 {[−]-(*M*)-**4**}.

3.4.2. Preparation of (*P*)-4. Under these analytical conditions, a micropreparative separation of the enantiomers was performed. The first fraction resulted in yellowish crystals of (*P*)-**4** with 98±1% e.e. $[\alpha]^{20}$ (CH_2Cl_2/hexane 75:25, with 5% MeCN): +3960±80 (436 nm), +1260±40 (578 nm). CD (CH_2Cl_2/hexane 75:25, with 5% MeCN), λ_{max} [nm] ($\Delta\varepsilon$): 224 (+119), 247 (−104), 270 (+18), 275 (+18), 297 (+105), 342 (−11), 375 (+4), 380 (+3), 395 (+8).

3.4.3. Oxidation of (*M*,*R*,*R*)-3. A suspension of (*M*,*R*,*R*)-**3** (39 mg, 0.10 mmol) and DDQ (25 mg, 0.11 mmol) in toluene (10 mL) was stirred for 24 h at room temperature in the dark (monitored by TLC). The reaction mixture was opened to the air, the solvent was evaporated under vacuum at room temperature and the residue was purified by flash chromatography on silica gel (eluent CH_2Cl_2/hexane 1:1, $R_f=0.5$). Yield: 37 mg (96%) of yellowish crystalline solid with 76±8% e.e. of (*M*)-**4** (polarimetry).

3.5. 5-(Dinaphtho[2,1-*e*;1′,2′-*g*]benzimidazol-2-yl)-pentanal 9

3.5.1. Photolysis of 3. A stirred suspension of the stereoisomeric mixture of **3** (100 mg, 0.26 mmol) in benzene (100 mL) cooled by water was irradiated by a wolfram UV-lamp for 1.5 h. The reaction was monitored by TLC. The solvent was evaporated and the residue submitted to flash chromatography on silica gel, eluted first with CH_2Cl_2/Et_2O, 1:1. A blue shining solution was eluted with CH_2Cl_2/AcOEt, 1:1 ($R_f=0.35$) giving 68 mg (65%) of yellowish solid **9**. Mp: 134–137°C. ^1H NMR ($CDCl_3$, δ): 9.62 s (1H, CHO), 8.50 d (2H, C(5′,14′)-H, $J=8.6$ Hz), 8.38 d (2H, C(6′,13′)-H, $J=8.5$ Hz), 7.97 d (2H, C(4′,15′)-H, $J=8.6$ Hz), 7.90 d (2H, C(9′,10′)-H, $J=7.9$ Hz), 7.44 dd (2H, C(8′,11′)-H, $J=7.9$, 6.8 Hz), 7.23 dd (2H, C(7′,12′)-H, $J=8.5$, 6.8 Hz), 3.05 brt (2H, C(2)-H, $J=6.5$ Hz), 2.38 m (2H, C(5)-H), 1.83 m (2H, C(3)-H), 1.61 m (2H, C(4)-H), N*H* signal could not be detected. ^{13}C NMR ($CDCl_3$, δ): 203.3 C(CHO), 131.7 C(6′,13′), 129.3, 128.2 C(4′,15′, 9′,10′), 125.3 C(8′,11′), 124.6 C(7′,12′), 120.0 C(5′,14′), 43.3 C(2), 28.8 C(5), 26.9 C(3), 21.0 C(4). IR (cm^{-1}): 3465 br (N-H), 2965, 2926, 2857 (C_{al}-H), 2720 (OC-H), 1717 (C=O). Elemental analysis: $C_{28}H_{22}N_2$ (402.50); found/calcd (%): C, 83.24/83.56; H, 5.63/5.51; N, 6.78/6.96. MS: $M^{\bullet+}$ 402.

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