Designed molecular propellers based on tetraarylterephthalamide and their chiroptical properties induced by biased helicity through transmission of point chirality†

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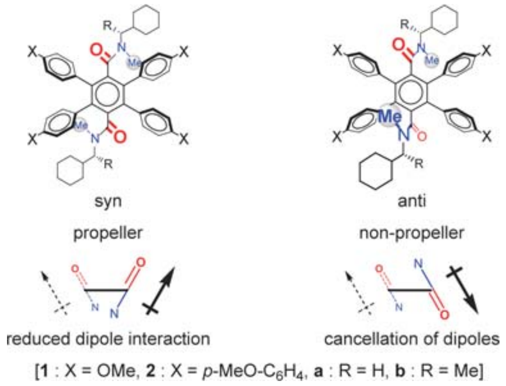
The *syn*-atropisomers of the title bis(tertiary amide)s were designed as six-bladed molecular propellers based on the “directing effects” of amide dipoles; the helicity of the propeller is biased to prefer one handedness upon the attachment of point chirality to the amide nitrogens to attain stronger circular-dichroism activity than for the non-propeller-shaped *anti*-isomers.



Scheme 1

Persubstituted benzenes have attracted much attention as promising motifs in the design of molecular rotors, gears and propellers.[1] One of the most-studied classes of molecules is hexaarylbenzenes,[1a,2] which cannot adopt a conformation with all aryl blades lying on the same plane as the central core due to the steric repulsion among neighboring substituents. Instead, substituents are twisted almost perpendicularly, and slight skewing about the $C_{central}$–C_{aryl} bond in either direction induces numerous conformations, including several chiral ones. The propeller-shaped conformation occurs when all blades are skewed in a conrotatory manner, which is interesting in terms of its mobile chirality with an easy inversion of helicity. While the parent hexaphenylbenzene[2b,e] was shown to adopt a propeller conformation in the crystal, it is difficult to force the molecule to maintain this same structure in solution. The control of propeller helicity is also challenging to bias the (*P*)/(*M*)-stereoisomer.

We envisaged that the rational design of persubstituted benzenes would provide a significant preference for the propeller geometry even in solution, and the mobile helicity could be biased to a single handedness through the effective transmission of point chiralities on the periphery. Based on our detailed conformational studies on terephthalamides,[3] we have designed here 2,3,5,6-tetraarylated bis(tertiary amide)s **1**/**2** as promising compounds for adopting a propeller geometry. As in the case of hexaarylbenzenes, all of the blades in **1**/**2** are twisted nearly perpendicularly, which gives two atropisomers (*syn* and *anti*) in terms of the relative direction of the two amide groups. Both isomers must prefer the conformation with the amide dipoles reduced/canceled to minimize the electrostatic disadvantage: a conrotatory-skewed C_2-symmetric structure for *syn* and a centrosymmetric structure for *anti* (Scheme 1). Such “directing effects” by the amide groups in the former should endow the *syn*-isomers with a preference for the propeller-shape by forcing conrotatory skewing of the four aryl blades. This is the central point of our concept toward “designed molecular propellers”, and we report here the details of a successful demonstration. The point chirality on the amide nitrogen is transmitted to the helicity-preference of the propellers to attain much stronger chiroptical signals for the *syn*-isomers of **1**/**2** than for the non-propeller-shaped *anti*-isomers.

For detailed conformational analyses, 4-methoxyphenyl (**1**) and 4′-methoxybiphenyl-4-yl (**2**) groups are selected as the aryl blade to simplify the aryl region of the NMR spectrum. The cyclohexylmethyl (**a**) or (*R*)-1-cyclohexylethyl (**b**) group is attached to each amide nitrogen, which of the latter was anticipated to act as a chiral handle to control the mobile helicity of the propellers. Further substitution on nitrogens to bis(tertiary amide)s would be necessary to suppress interconversion between *syn*- and *anti*-atropisomers. The larger substituent on the amide may preferentially occupy the “lateral” position (s-*trans* to the benzene core), whereas the smaller one may be located at the “vertical” position (s-*cis* to the core). The rotational freedom about the $C_{central}$–C_{aryl} bond depends on the steric bulkiness of the vertical group.

Tetraarylterephthalamides **1a,b** were prepared by Suzuki–Miyaura coupling[4] of 2,3,5,6-tetrabromoterephthalamides **3a,b** and 4-methoxyphenylboronic acid followed by *N*-methylation of the intermediary secondary amides **4a,b**. The tetrakis(biphenylated) derivatives **2a,b** were similarly prepared by using 4′-methoxybiphenyl-4-yl-boronic acid[5] in the Pd-catalyzed coupling step. The *syn*- and *anti*-atropisomers were formed as mixtures, which were readily separated in pure form by column chromatography since they exhibit quite different R_f (relative to front) values. The isomers with a smaller R_f value were tentatively assigned as *syn*, and this was later confirmed by X-ray analyses on *syn*- and *anti*-**1** (*vide infra*). The atropisomers **1**/**2** were non-interconvertible even after heating at 338 K for 24 hours in

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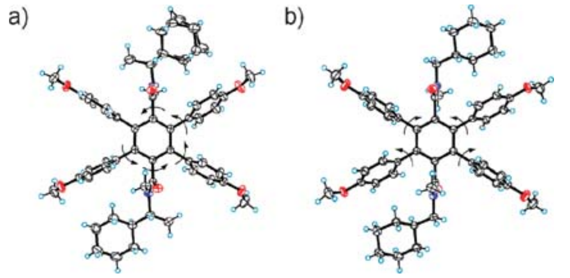

Fig. 1 X-Ray structures of (a) (*R*,*R*)-*syn*-**1b** ($P1$, Z = 1) and (b) *anti*-**1a** ($P\bar{1}$, Z = 1). One of the aryl blades in (a) is almost perpendicular to the central core. Solvated benzene molecule in the crystal in (b) is omitted for clarity. Thermal ellipsoids are shown at 50% probability level.

$CDCl_3$. For the bis(secondary amide)s **4a,b** without vertical methyl substituents, interconversion is much faster than the NMR time-scale, even at room temperature, as predicted.

Single-crystal X-ray analysis‡ demonstrated that (*R*,*R*)-*syn*-**1b** adopts the propeller geometry in crystal, as desired. The aryl blades are skewed in a conrotatory manner, which must be induced by the directing effects of amide dipoles at the *para*-positions (Fig. 1a). Preliminary investigation indicates this is also the case for achiral *syn*-**1a** (Fig. S1;† $P\bar{1}$, Z = 2). In the latter case, the enantiomeric propellers exist in pairs whereas in the former with a chiral auxiliary on each amide nitrogen, only propellers with (*M*)-helicity exist in the crystal and thus the point chiralities are perfectly transmitted to the mobile helicity, at least in a crystalline state of (*R*,*R*)-*syn*-**1b**.

On the other hand, the electrostatic interaction of the amide "directing effects" must be the major reason why *anti*-**1a** adopts a centrosymmetric structure with full cancellation of the dipole, and thus the *anti*-isomer is not propeller-shaped at all (Fig. 1b). Even with the attachment of chiral auxiliaries, the *anti*-isomer prefers the pseudo-centrosymmetric geometry to minimize dipole repulsion, as shown by the similarity of the non-propeller structure of (*R*,*R*)-*anti*-**1b** (Fig. S1;† $P1$, Z = 1) and *anti*-**1a**.

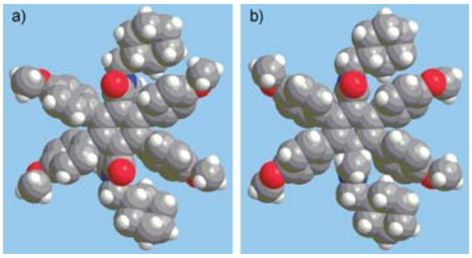

Fig. 2 Energy-minimized structures for (a) *syn*-**1a** and (b) *anti*-**1a** according to Monte Carlo simulations in $CHCl_3$.

Conformational searches on achiral **1a** using Macromodel software[6] indicated that the propeller conformation is the most stable geometry for the *syn*-isomer among numerous conformations (Fig. 2a). This theoretical examination suggests that the propeller-shaped geometry must also be the major contributor in solution for the *syn*-isomers of **1a,b**. The centrosymmetric non-propeller-shaped structure was predicted for the *anti*-isomer in accordance with the observed geometry in crystal (Fig. 2b).

The structures of *syn*-isomers in solution were experimentally verified by ^1H NMR spectroscopy (Fig. S2).† The chemical shifts of their aromatic protons in $CDCl_3$ at 298 K are summarized in Table 1. The observed spectrum of achiral *syn*-**1a** was C_{2v}-symmetric, which can be accounted for by assuming a rapid inversion of helicity between two energetically equivalent propeller structures. Some broadening is related to rotational motion about the $C_{central}$–C_{aryl} bond ($\Delta G^{\ddagger}$ = 15.3 kcal mol^{-1}, coalescence temperature = 313 K), but there is no indication of $C_{central}$–C_{amide} bond rotation. In the case of (*R*,*R*)-*syn*-**1b** with chiral auxiliaries, the spectrum is C_2-symmetric, as expected for rapidly interconverting diastereomeric propellers (Fig. S2).† Slight broadening is again induced by the $C_{central}$–C_{aryl} rotation. There are four sets of resonances (H^C: 7.18–6.87 ppm in $CDCl_3$ at 298 K) that correspond to anisyl protons close to the central benzene core. The other four (H^X: 6.77–6.48 ppm) are *ortho* to the methoxy group, and are not well separated from each other. The energy barrier for propeller inversion seems to be too low to observe the diastereomeric propellers as two independent sets of signals, even when the temperature is lowered to 223 K. Although the above NMR features might be alternatively rationalized by assuming a single geometry with all substituents twisted perpendicular to the central core, only one of four anisyl signals (H^C) showed a correlation with the vertical methyl group in an ROE measurement (Fig. S3),† which is readily accounted for by assuming a propeller geometry. Furthermore, as shown in Fig. S4,† the temperature-dependent shift of resonances while maintaining the spectral symmetry in (*R*,*R*)-*syn*-**1b** shows that there are

Table 1 Chemical shifts[a] for the aromatic protons in **1**/**2**[b] in $CDCl_3$ at 298 K

	δ/ppm					Observed symmetry
syn-**1a**	7.09^C (4H)	6.87^C (4H)	6.64^X (4H×2)			C_{2v}
(*R*,*R*)-*syn*-**1b**	7.18^C (2H)	7.02^C (2H)	6.93^C (2H)	6.87^C (2H)	6.74–6.49^X (2H×4)	C_2
anti-**1a**	7.55^C (4H)	6.79^X (4H)	6.66^C (4H)	6.48^X (4H)		C_{2h}
(*R*,*R*)-*anti*-**1b**	7.59^C (2H×2)	6.81^X (2H)	6.66^C (2H)	6.49^X (2H)		C_2
		6.79^X (2H)	6.63^C (2H)	6.45^X (2H)		
syn-**2a**	7.31^{C,X} (4H×3)	7.07^C (4H)				C_{2v}
(*R*,*R*)-*syn*-**2b**	—					—
anti-**2a**	7.74^C (4H)	7.50^X (4H)	7.17^X (4H)	6.86^C (4H)		C_{2h}
(*R*,*R*)-*anti*-**2b**	7.80^C (2H×2)	7.53^X (2H)	7.17^X (2H)	6.89^C (2H)		C_2
		7.50^X (2H)	7.11^X (2H)	6.81^C (2H)		

[a] Assignment is indicated by superscripts C and X. Superscript C denotes the aromatic protons close to the central benzene ring. Superscript X denotes the aromatic protons close to X (X = MeO for **1**, and 4′-$MeOC_6H_4$ for **2**). The aromatic protons in (*R*,*R*)-*syn*-**2b** could not be fully assigned due to peak overlap and broadening. [b] Only the protons on four phenylene rings attached on the core are shown.

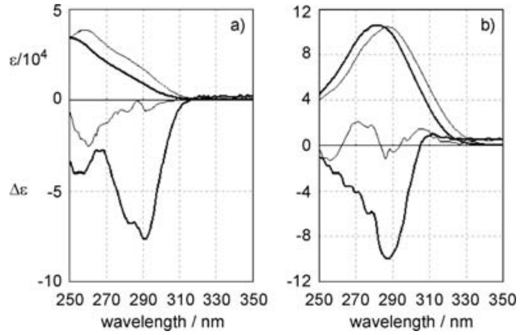

Fig. 3 UV and CD spectra of (a) (*R*,*R*)-*syn*-**1b** (bold line), (*R*,*R*)-*anti*-**1b** (thin line), and (b) (*R*,*R*)-*syn*-**2b** (bold line), (*R*,*R*)-*anti*-**2b** (thin line) in CH_2Cl_2 at room temperature respectively.

energetically-nonequivalent and rapidly-interconverting (*P*)- and (*M*)-propellers, the diastereomeric ratio of which is a function of temperature.

In the case of tetrakis(biphenylated) derivatives *syn*-**2a,b**, the NMR spectra show similar characteristics (Table 1; Fig. S2),† suggesting that they also prefer the propeller shape. This idea was supported by the chiroptical properties of (*R*,*R*)-*syn*-**2b**, which resemble those of propeller-shaped (*R*,*R*)-*syn*-**1b** (*vide infra*). The NMR data of *anti*-isomers of **1a,b**/**2a,b** are also listed in Table 1 and Fig. S2,† and can be readily explained by assuming the (pseudo)centrosymmetric geometries observed in crystal.

Fig. 3 shows the UV and circular dichroism (CD) spectra of chiral (*R*,*R*)-**1b**/**2b** in CH_2Cl_2 at room temperature. The UV spectra of achiral **1a**/**2a** are quite similar to those of (*R*,*R*)-**1b**/**2b**, respectively (Table S1).† For the atropisomers of (*R*,*R*)-**1b**/**2b**, the amplitude of the Cotton effect in the CD spectra differs significantly: CD signals for *syn*-isomers are much stronger than those for the corresponding *anti*-isomers. An almost 10-fold increase in Δε at the absorption shoulder (291 nm for **1b**)/maximum (286 nm for **2b**) is noteworthy (Table 2). Such differences in chiroptical properties must be due to the propeller-shape preference seen for *syn*-isomers.[7] This is a successful demonstration of the effective transmission of chirality[8] from point asymmetry to the mobile helicity of the propeller structure.

The fluorophoric properties of the tetrakis(biphenylated) derivatives **2** are also interesting. Thus, (*R*,*R*)-*syn*-**2b** represents a new entry into the less-well-developed class of chiral fluorophores.[8b] The large Stokes shifts (*ca.* 100 nm) as well as structureless emission are characteristic of two-dimensional π-conjugated oligoarylenes[9] (Table 2, Fig. S5).†

In conclusion, we have demonstrated "designed" six-bladed molecular propellers based on *syn*-terephthalamides derivatives thanks to the "directing effects" of amide dipoles. A chiral auxiliary on the amide nitrogen gave a preference for skewing the direction of the propeller helicity to realize chiroptical enhancement. We are now studying the complexation properties of the present amides and hydrogen-bonding guests with special focus on guest-induced conformational changes.[3b–d] A preliminary examination shows that the secondary amides **4a,b** prefer a non-propeller *anti*-conformation, but can undergo rapid *syn*–*anti* interconversion to attain the propeller structure upon complexation. Further details will be reported in due course.

Table 2 UV, CD and fluorescence spectral data of (*R*,*R*)-**1b**/**2b** in CH_2Cl_2 at room temperature

	syn-**1b**	*anti*-**1b**	*syn*-**2b**	*anti*-**2b**
λ_{max}/nm	249 (sh.)	259	282	287
(log ε)	(4.54)	(4.59)	(5.02)	(5.02)
λ_{max}/nm	254, 291	261, 291	286, 312	256, 272, 286, 304
(Δε)	(−4.06, −7.67)	(−2.56, −0.608)	(−10.0, 1.04)	(−1.38, 2.11, −1.18, 1.43)
$\lambda_{max,em}$[a]/nm	—	—	378	381

[a] Excited at each absorption maximum.

Notes and references

‡ Crystal data of (*R*,*R*)-*syn*-**1b**: MF $C_{54}H_{64}N_2O_6$, FW 837.11, triclinic $P1$ (No. 1), a = 6.305(2), b = 13.323(5), c = 13.959(5) Å, α = 86.986(10), β = 81.092(9), γ = 85.727(9)°, V = 1154.1(7) Å^3, $\rho(Z = 1)$ = 1.204 g cm^{-3}, T = 153 K, 7239 independent reflections (R_{int} = 0.010), R = 4.3% (6810 data with $F > 2\sigma F$), CCDC 680696.† Crystal data of *anti*-**1a**: MF $C_{58}H_{66}N_2O_6$, FW 887.17, triclinic $P\bar{1}$ (No. 2), a = 9.668(3), b = 11.144(4), c = 11.778(4), α = 106.388(5), β = 96.224(5), γ = 100.015(5)°, V = 1182.0(7) Å^3, $\rho(Z = 1)$ = 1.246 g cm^{-3}, T = 153 K, 5029 independent reflections (R_{int} = 0.031), R = 7.2% (2795 data with $F > 2\sigma F$), CCDC 680697.†

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7 The weaker Cotton effects around 255 nm commonly observed in both atropisomers of (*R*,*R*)-**1b** are also present in the tetrabromic chiral terephthalamides (*R*,*R*)-**5b** derived by *N*-methylation of (*R*,*R*)-**3b** (Table S1),† thus the shorter-wavelength region has nothing to do with the propeller/non-propeller conformation.

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