Switchable *trans–cis* interconversion of an amphiphilic anthracene trimer†

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Received (in Cambridge, UK) 23rd June 2009, Accepted 18th August 2009
First published as an Advance Article on the web 3rd September 2009
DOI: 10.1039/b912365b

Three anthracene rings connected by *m*-phenylene spacers with hydroxy groups generate isolable *trans*- and *cis*-atropisomers whose interconversion is solvent sensitive and can be activated at room temperature by an external stimulus (base).

Rotation around an aryl–aryl single bond is a fundamental molecular motion.[1] Unsubstituted biphenyl rotates freely at room temperature but bulky *ortho*-substituents effectively restrict and hinder bond rotation due to steric repulsion between the substituents.[2] Most aryl–aryl atropisomers require elevated temperatures to interconvert, and switching between freely rotating and non-rotating states at a moderate temperature is rare. Controlling the rotation around an aryl–aryl single bond by external stimuli is a fascinating subject in terms of basic stereochemistry as well as potentially useful for molecular-based switches and machines.[3,4]

Here we report that anthracene trimer **1** shows solvent- and pH-controllable *trans–cis* atropisomerism (Fig. 1).[5] Compound **1** consists of three anthracene moieties connected by *m*-phenylene spacers functionalized with hydroxy groups, providing both hydrophobic and hydrophilic surfaces. The aryl–aryl bonds of **1** are hindered by the three *ortho*-substituents, which restrict the bond rotation and force the aryl subunits to adopt orthogonal conformations. As a result, the tape-like structure of **1** can take on a zig–zag (*trans*-**1**) or curved (*cis*-**1**) form. In this communication, we report that the *trans–cis* interconversion of **1** occurs at *room temperature* in a basic aqueous solution. Not only is the free bond rotation activated in the presence of base, but the *cis* isomer becomes thermodynamically favored in an aqueous solution.

Anthracene trimer **1** was synthesized by the following four-step reaction sequence (Fig. 2). First, treatment of anthraquinone with 2,4-dimethoxyphenyllithium and immediate reduction gave 9,10-bis(2,4-dimethoxyphenyl)anthracene (**2**; R_1 = H) in 54% yield.[6] After bromination, the Suzuki–Miyaura coupling of brominated **2** (R_1 = Br) with 9-anthrylboronic acid yielded **3** in 59%. Demethylation of **3** by BBr_3 quantitatively afforded **1**. Compound **1** was fully characterized by MS, NMR, and EA. The FAB-MS spectrum showed a single peak at m/z = 746.8 ($[M]^+$), but the ^{1}H NMR spectrum revealed the formation of a mixture of the *trans* and *cis* isomers of **1** in *ca.* 2 : 1 ratio. The proton signals derived from hydroxy groups and anthracene rings ($H_{a\sim g}$) appeared around 4.7–4.9 and 7.5–8.6 ppm, respectively. The atropisomers were separated by recycled gel permeation chromatography (GPC) (Fig. 2A,B).[7] After isolation, no interconversion between the isomers was observed in organic solvents at room temperature after several months due to steric interactions between the bulky anthracene units and the *ortho*-hydroxy groups.

Interconversion between the atropisomers of **1** could be controlled with solvent and was activated at room temperature in a basic solution. At room temperature in THF no interconversion was observed but, as expected, upon heating *trans*-**1** (1.0 mM) at 80 °C torsional rotation occurred and afforded a 3 : 2 *trans* : *cis* equilibrium mixture after 12 hours (Table 1). Similar behavior was observed in a benzene solution. In pyridine at 80 °C, the equilibrium favors the *trans*-atropisomer to a greater extent (*trans* : *cis* = 4 : 1) but after heating a methanol solution in a sealed tube at 120 °C, the equilibrium slightly favored the *cis* form (*trans* : *cis* = 2 : 3). In an aqueous 1 M NaOH solution, *trans*-**1** almost fully converted to *cis*-**1** at *room temperature* in a 1 : 9 *trans* : *cis* equilibrium mixture after one week.[8]

The remarkable effects of the basic aqueous solution on the bond rotation[9] and the equilibrium distribution are rationalized as follows: typically, steric interactions with the *ortho*-hydroxy group prevent anthracene rotation (Fig. 3A); after deprotonation, there exists a quinoid resonance form with the carbanion located on the anthracene part, stabilizing the planar transition station state (Fig. 3B) and thus lowering the rotation barrier.

The base-mediated *trans–cis* interconversion of **1** is general and also occurred in a basic methanol solution at room temperature but the *trans–cis* equilibrium ratio matched **1** in non-basic methanol (*trans* : *cis* = 2 : 3). Gas-phase calculations indicated that the two isomers have essentially identical potential energies but the *cis* isomer of **1** is a curved,

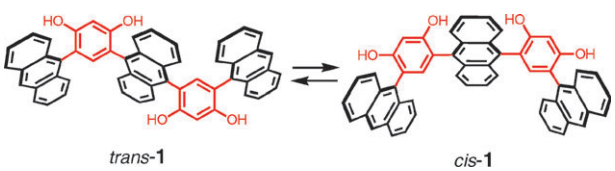

Fig. 1 Schematic representation of *trans–cis* conformational inter conversion of anthracene trimer **1** through the aryl–aryl bond rotations.

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† Electronic supplementary information (ESI) available: Experimental details for the preparation, characterization and properties of **1**. See DOI: 10.1039/b912365b

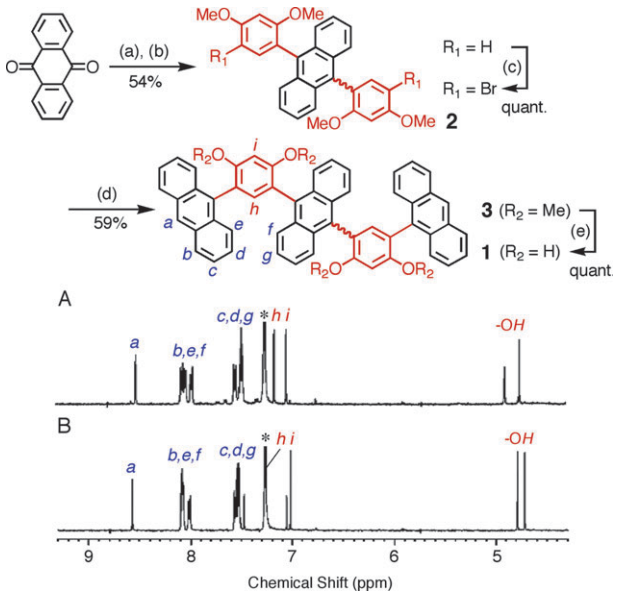

Fig. 2 Synthesis of anthracene trimer **1**: (a) 2,4-dimethoxyphenyllithium, THF, −78 °C; (b) HI (aq), H_3PO_2, AcOH, 80 °C; (c) DBH, THF, 0 °C; (d) 9-anthrylboronic acid, $PdCl_2(PhCN)_2/P(t\text{-}Bu)_3$, DMF, 80 °C; (e) BBr_3, CH_2Cl_2, 0 °C. ^{1}H NMR spectra (500 MHz, $CDCl_3$, r.t.) of (A) *cis*-**1** and (B) *trans*-**1** (*: $CHCl_3$).

Table 1 *Trans–cis* thermodynamic equilibria for **1** starting from *trans*-**1** in various solvents at different temperatures

Run	Solvent	Temperature[a]/°C	*trans* : *cis* ratio[b]
1	THF	80	3 : 2
2	Benzene	70	3 : 2
3	Pyridine[c]	80	4 : 1
4	MeOH	120[d]	2 : 3
5	H_2O + NaOH	30	1 : 9

[a] *trans-cis* interconversion temperatures. [b] *trans-cis* thermodynamic equilibrium ratios determined by ^{1}H NMR in $CDCl_3$ at r.t. [c] Starting from *cis*-**1**. [d] In a sealed tube.

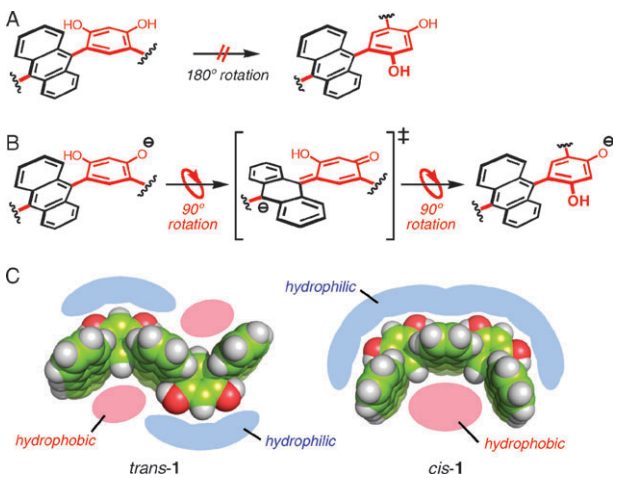

Fig. 3 (A, B) Proposed mechanisms of the *trans–cis* interconversion of **1** under neutral and basic conditions at room temperature. (C) Optimized structures of *trans*-**1** and *cis*-**1**, and their hydrophilic and hydrophobic properties.

amphiphilic structure—the solvent exposed, hydrophilic exterior is covered by the hydroxy groups and the concave aromatic interior is hydrophobic (Fig. 3C). In an aqueous solution, solvent–solute interactions and hydrophobic induced self-aggregation thermodynamically favored the *cis* isomer. Self-aggregation was evidenced by ^{1}H NMR; the spectrum of *cis*-**1** was severely broadened in a basic aqueous solution, indicative of aggregation, whereas that of *trans*-**1** displayed sharp signals.[10]

The UV-vis spectrum of **1** in EtOH shows a broadened absorption band (λ_{max} = 390 nm, ε = 1.9 × 10^4) which is red-shifted ($\Delta\lambda$ = 30 nm) compared to anthracene (Fig. 4A). The UV-vis spectrum of 9,10-bis(2,4-dihydroxyphenyl)anthracene, the basic core unit of **1**, was similar to that of **1** indicating that each anthracene unit is electronically isolated due to the orthogonal conformations and limited π-conjugation. In a basic aqueous solution, a broad shoulder band at ~450 nm was present and stems from the phenoxide. In EtOH, **1** is emissive (λ_{max} = 436 nm, ϕ = 0.33) but the emission was completely quenched in a basic aqueous solution due to photoinduced electron transfer (PET) from the phenoxide to the anthracene fragment (Fig. 4B).[11]

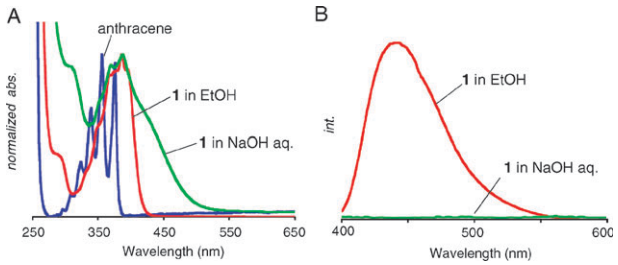

Fig. 4 (A) UV-vis spectra of anthracene trimer **1** (red line) and anthracene (blue line) in EtOH, and **1** in aqueous NaOH solution (green line) at r.t. (B) Fluorescence spectra (λ_{ex} = 385 nm) of anthracene trimer **1** in EtOH (red line) and aqueous NaOH solution (green line) at r.t.

In summary, we have prepared curved, amphiphilic structure **1** with large hydrophobic anthracenes and hydrophilic *m*-phenylene spacers. Rotation about the aryl–aryl bonds is sterically restricted due to the large *ortho*-substituents, and the *trans* and *cis* atropisomers were stable enough to be isolated. The bond rotation and *trans–cis* interconversion at room temperature were activated in basic solution in addition to standard elevated temperatures. Although there is no significant energy difference between the *trans* and *cis* atropisomers, the concave *cis* isomer was thermodynamically favored in aqueous solution and self-aggregated. We expect that the incorporation of this dynamic *trans–cis* switch into static organic and inorganic structures can provide novel molecular switches and machines.

M. Y. is grateful to a Challenging Research Award from Tokyo Institute of Technology and a Grant-in-Aid for Young Scientists from the Ministry of Education, Culture, Sports, Science and Technology of Japan for financial support of this research. K. O. thanks the Japan Society for the Promotion of Science (JSPS) for a Research Fellowship for Young Scientists. The authors would like to thank Dr Jeremy K. Klosterman for his helpful discussions.

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7 Although we examined the *trans–cis* interconversion experiments of **1** in various solutions, the assignment of the *trans–cis* isomers and the thermodynamic equilibrium ratios were determined by ^1H NMR in $CDCl_3$. Due to the efficient shielding effect by the surrounding three anthracene rings, the H_h signal of *cis*-**1** was observed higher up-field than that of *trans*-**1** ($\Delta\delta = -0.1$ ppm). In addition, the GPC retention time of *trans*-**1** (a zig–zag form) is less than that of *cis*-**1** (a curved form).

8 The thermodynamic equilibrium ratios were determined from not only the various solutions of *trans*-**1** but also those of *cis*-**1**.

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10 The NMR spectrum of *cis*-**1** in basic MeOH (and neutral MeOH) display sharp signals (Fig. S13†). The progressive addition of basic water (10, 30, 50%) into the MeOH solutions of **1** produced almost no broadening effects for the *cis*-**1** signals. Only in basic water (due to the insolubility of *cis*-**1** at neutral pH) does *cis*-**1** form aggregates and gives the broadened ^1H NMR signals and UV-vis changes. Concentration-dependent UV-vis spectra (2.5–150 μM) of *cis*-**1** in basic water showed a new broadened band around 420 nm only under higher concentration (150 μM) (Fig. S15†).

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