Mechanochemistry

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Mechanochemical Tuning of the Binaphthyl Conformation at the Air–Water Interface**

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Abstract: *Gradual and reversible tuning of the torsion angle of an amphiphilic chiral binaphthyl, from −90° to −80°, was achieved by application of a mechanical force to its molecular monolayer at the air–water interface. This 2D interface was an ideal location for mechanochemistry for molecular tuning and its experimental and theoretical analysis, since this lowered dimension enables high orientation of molecules and large variation in the area. A small mechanical energy (<1 kcal mol*$^{-1}$*) was applied to the monolayer, causing a large variation (>50%) in the area of the monolayer and modification of binaphthyl conformation. Single-molecule simulations revealed that mechanical energy was converted proportionally to torsional energy. Molecular dynamics simulations of the monolayer indicated that the global average torsion angle of a monolayer was gradually shifted.*

Mechanochemistry[1] is a growing field that involves the use of mechanical forces for operation and control of molecular structures and their resulting properties, instead of the more usually applied stimuli of heat, light, or electric potential.[2,3] Recent advances have been partly derived from a shift towards the use of soft materials (for example, polymers and liquid crystals) rather than hard materials (crystals).[4] Although mechanical forces can be applied to oriented molecules in the crystal state,[5,6] only minor structural (or conformational) changes involving only an up to 1% change in volume are possible, in most cases, prior to loss of crystal integrity (Figure 1a).[7] In contrast, polymers[8–12] and liquid crystals[13,14] are flexible, permitting dynamic variation of their structures and those of their constituent molecules (Figure 1b). Although the flexible nature of soft materials makes their structures capable of undergoing deformation, a molec-

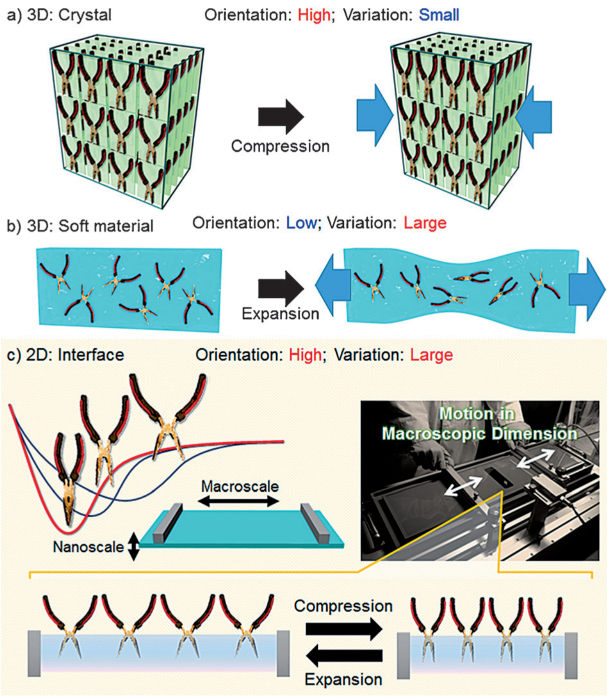

Figure 1. Mechanochemical control of molecular structures. a) Molecules contained in a 3D crystal: minimal dynamic variation is allowed. b) Molecules contained in a 3D soft material: relatively wide dynamic range is possible, but molecules are randomly oriented and any applied force is dispersed. c) Molecules at the 2D interface. Molecules are oriented and dynamic conformational variation is allowed: external force is transferred efficiently to individual molecules.

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ular-level understanding of these processes under an applied force is lacking. Because these systems are not highly ordered (in contrast to crystalline materials), control of the effects of an applied force is less effective, which is due to the wide range of different conformations and orientations of the molecules. Despite the difficulty presented by the transfer of macroscopic force to molecular force in polymer mechanochemistry, recent work on force-affected reactions, including their theoretical consideration, has helped to provide a quantitative understanding of molecular force.[15] On the other hand, the measurement of applied force or energy in relation to mechanochemical phenomena has been limited to single-molecule investigations using atomic force microscopy (AFM).[16–19] We have investigated dynamic molecular structures and their assemblies by applying a force (mechanical energy) to such a structure at the 2D air–water interface (Figure 1c). At the air–water interface, amphiphilic molecules can assemble to form molecularly oriented films, which are known as Langmuir monolayers. The area of the film interface can be varied dynamically at the macroscopic level by applying an external force, although the film thickness is maintained at a nanoscopic molecular level. Application of an external force to the film causes changes in the local minima in the potential energy and can be used quantitatively to tune the molecular structures and hence their properties.[20] Recently, we have reported that molecular properties can be tuned by applying a mechanical force to a monolayer at the air–water interface.[21–23] However, although variation of properties should originate from changes at the molecular level, at that time these could be only inferred.

Herein, we have designed and synthesized an amphiphilic chiral binaphthyl[24] molecule (Figure 2a), the circular dichroic (CD) activity of which is directly related to the torsion angle subtended between the planes of its two naphthyl moieties (Figure 2b,c).[25,26] This feature enabled us to monitor precisely structural changes due to any force applied to its monolayer films prepared at the air–water interface. Ultimately, we demonstrate that the structures of molecules contained in such a monolayer can be precisely controlled by applying only a small mechanical energy (ca. 1 kcal mol^{-1}; Figure 2d).

Chiral amphiphilic binaphthyl *R*-**1** (Figure 2a) was synthesized from commercially available (*R*)-1,1′-bi-2-naphthol (see the Supporting Information). A monolayer of *R*-**1** on a water surface was prepared and it was mechanically compressed in situ, thus decreasing the area per molecule. A plot of surface pressure vs. molecular area (π–A) of *R*-**1** on pure water (Figure 3a) indicates a well-condensed phase with a collapse pressure of 42 mN m^{-1} at a molecular area of 0.68 nm^2. This area is smaller than the molecular area estimated for *R*-**1** (0.9 nm^2 with the optimized structure), which is attributed to its structural variation and partial overlapping of molecules. The molecular area of *R*-**1** in the monolayer varied in the range 1.4 to 0.68 nm^2, which

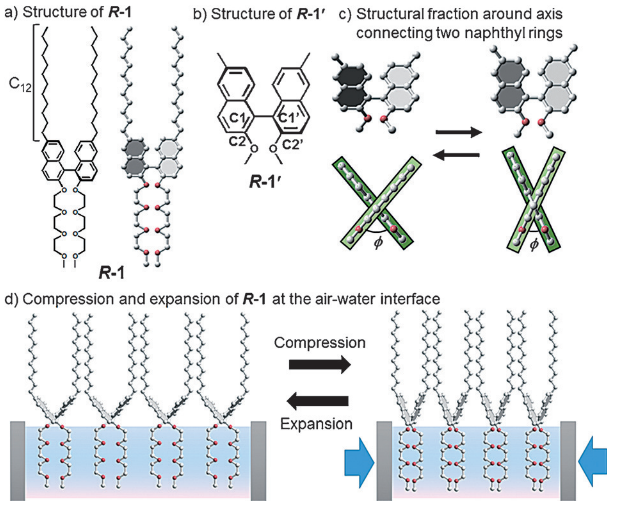

Figure 2. a) The structure of binaphthyl *R*-**1**. b) A model structure of *R*-**1** (*R*-**1′**). c) Representation of structural fluctuation around axis connecting two naphthalene rings. Torsion angles of two naphthalene rings are show as ϕ. d) Representation of compression/expansion of a monolayer of *R*-**1** at the air–water interface.

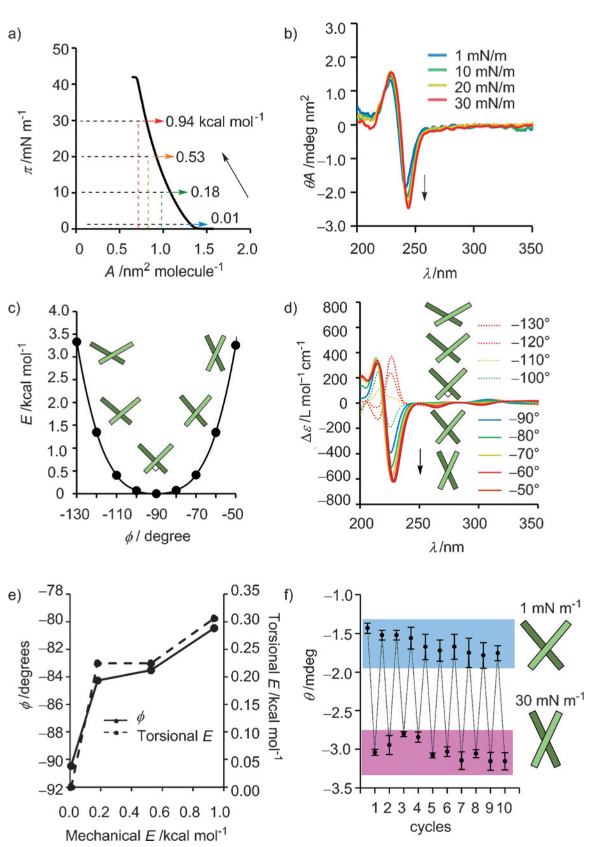

Figure 3. Analysis of the monolayer of *R*-**1**. a) Surface-pressure–molecular-area (π–A) curve of the monolayer. Applied total energies of compression were estimated by integration of the π–A curve. b) CD spectra of monolayers of *R*-**1** at different surface pressures multiplied by molecular area. c) Estimated energies (DFT) required for changing the torsion angle (ϕ) of binaphthyls *R*-**1′**. d) TD DFT based CD spectral simulations of a model structure *R*-**1′** as a function of ϕ. e) Estimated ϕ and obtained torsional energies are shown as a function of applied mechanical force. Torsional energy was estimated from the torsional energy of *R*-**1′** (single-point SCS-MP2). f) CD intensity during cycles of compression (30 mN m^{-1}) and expansion (1 mN m^{-1}) of *R*-**1** at the air–water interface. Each point is shown as an average with standard deviations ($n=3$).

corresponds to a 50% compression of area. Integration of the π–A curve leads to quite precise estimation of the energy of compression (Supporting Information, Figure S8, Table S1). The monolayer gradually increased in energy: 0.179 ± 0.002, 0.526 ± 0.003, and $0.937 \pm 0.009\,\mathrm{kcal\,mol^{-1}}$ at 10, 20, and $30\,\mathrm{mN\,m^{-1}}$, respectively.

A surface-pressure-dependent increase in the intensity of the CD signal was observed for monolayers transferred to a quartz substrate (Figure 3b). The intensities of CD signals were normalized according to occupied molecular area at the corresponding surface pressure taking into account the effect of the increasing lateral density of the monolayer at higher surface pressures. From the normalized CD spectra of *R*-**1**, the absolute intensity of the negative peak around 242 nm increased gradually up to 1.3 during compression of the monolayer from 1 to $30\,\mathrm{mN\,m^{-1}}$. CD activity of binaphthyls is known to be dependent on the torsion angle between the naphthalene planes.[25,27] Binaphthyls can occupy either *cisoid* or *transoid* configurations, where torsion angles are less than $|90°|$ or greater than $|90°|$, respectively. The shape of the CD spectra obtained from the transferred monolayers corresponds to a *cisoid* form, which is similar to that observed in solution phase. The enantiomer of *R*-**1** (*S*-**1**) showed a mirror image of CD spectra upon compression (Supporting Information, Figure S7).

Energies necessary for structural variations were estimated by using density functional theory (DFT) calculations (Figure 3c) and single-point energies estimated using spin-component-scaled (SCS)-MP2[28] calculations (Supporting Information, Table S2). Considering that thermal energy is estimated to be $kT = 0.6\,\mathrm{kcal\,mol^{-1}}$ at 20°C, *R*-**1′** fluctuates with a torsion angle in the range −110° to −70°.[29]

The relationship between structure and CD spectrum based on the torsion angle of the naphthalene planes was investigated using theoretical calculations (Figure 3d). The experimental spectrum of *R*-**1** in solution matches that simulated based on an optimized structure (Supporting Information, Figure S9) obtained using time-dependent density functional theory (TD DFT) calculations using B3LYP/6-31G(d,p). Simulation of CD spectra as a function of the torsion angle was performed for the model compound *R*-**1** (= *R*-**1′**, Figure 2b). A comparison of simulated (Figure 3d) and experimental (Figure 3b) CD spectra indicates that an increase in the absolute intensity for *R*-**1** originates from a structural change in the *cisoid* direction. It suggests that the torsion angle $|\phi|$ gradually decreases and that the torsional energy gradually accumulates with applied mechanical energy (Figure 3e). The torsion angles ϕ gradually increased from −90° to −80° upon compression (see the Supporting Information, Figure S10 for details). Variation in intensity of the CD signals was reversible upon compression and expansion of *R*-**1** in monolayer (Figure 3f), indicating that the tuning of molecular structure is also reversible at the dynamic air–water interface.

Molecular structure of *R*-**1** at the air–water interface was investigated by using molecular dynamics (MD) calculations (Figure 4, see the Supporting Information for details), with compression of the monolayer being simulated by increasing the number of molecules contained in the unit box (Figure 4a). In MD simulations, individual molecules float at the interface occupying a large molecular area, but stand perpendicular to the interface in a small molecular area when contained in the monolayer, reproducing the common tendency of amphiphilic molecules.[30] The average value of the torsion angle varied gradually (Figure 4b) from −90° to −80° going from the molecular area of $25\,\mathrm{nm^2}$ to $0.60\,\mathrm{nm^2}$. The values estimated by MD calculations are consistent with the values estimated from the experimentally obtained CD signals shown above. The wide ranges of angles under each set of conditions (Figure 4c) are also consistent with binaphthyls according to their broad potential energy profile.[29]

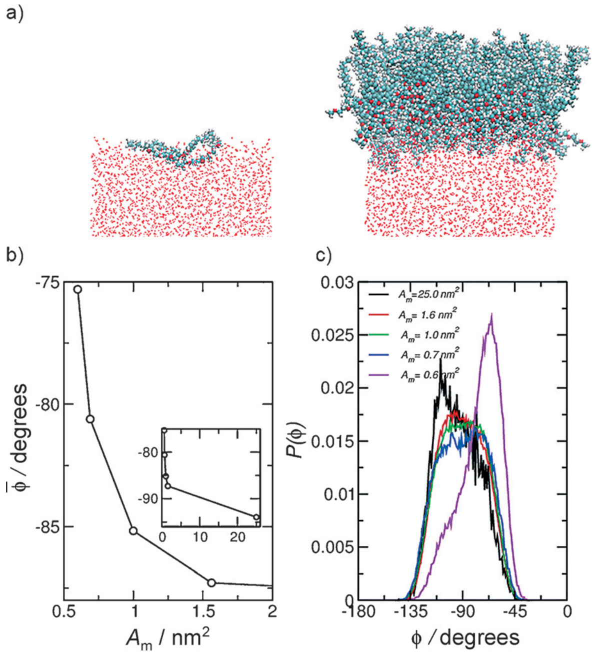

Figure 4. MD calculations of *R*-**1** at the interface. a) Left: a snapshot of the simulation with a large molecular area ($A_m = 25\,\mathrm{nm^2}$, a single molecule in a unit box); right: a small molecular area ($A_m = 0.60\,\mathrm{nm^2}$, 84 molecules in a unit box). The simulation system is displayed with *R*-**1** as CPK model and water molecules as sticks. C sky-blue, H white, O red. Only a half-side of the unit-box is shown. b) Average torsion angle for monolayers of *R*-**1**. c) Torsion angle distributions from molecular dynamics simulations of monolayers of *R*-**1**. Black, red, green, blue, and magenta lines denote molecular area $A_m = 25$, 1.6, 1.0, 0.69, and $0.60\,\mathrm{nm^2}$, respectively. See the Supporting Information for details.

In summary, mechanical tuning of the binaphthyl structure over a range of torsion angles between −90° and −80° was achieved, and is supported by experimental and theoretical analyses of molecular area, energies, and CD intensities. By using the 2D air–water interface where dimensionality is reduced from 3D space, structural changes within molecular assemblies were analyzed as a function of surface pressure and applied mechanical energy. Although the maximum pressure that can be applied is limited by monolayer collapse, we have shown that the 2D air–water interface is indeed a suitable location to perform mechanochemistry for the analysis and control of molecular structures and their assemblies under small applied forces where molecular conformation is an issue. This is because of the unique features of molecular orientation control and dynamically variable area of the medium available using the 2D air–water interface. The former is critical for the transformation of an external force into a structural change while the latter permits dynamic tuning of molecular structure. Although the structural change described here in binaphthyl *R*-**1** is modest (but still larger than available in crystals), this variation in structure (10°) can lead to important effects on molecular recognition processes where only small structural changes can be significant. Small forces that affect conformation are important not only in chemistry but also in biology: pN-level force has been reported to cause changes in the conformations and functions of proteins.[31] We anticipate that the use of the air–water interface as a medium for mechanochemistry will open a new field involving molecular conformational control and consequent control of molecular function. Apart from structural tuning, energy conversion for mechanochemically powered molecular machines[32] is of interest and is currently under investigation in our laboratory (see the Supporting Information).

Keywords: biaryls · chirality · interfaces · lipids · monolayers

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