# A Light-operated Pillar[6]arene-based Molecular Shuttle

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# A Light-operated Pillar[6]arene-based Molecular Shuttle

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**A molecular shuttle comprising a pillar[6]arene macrocyclic ring and an axle with two equal-energy-level stations connected by an azobenzene unit was synthesised. The *E* isomer of the azobenzene functioned as "open gate", allowing the pillar[6]arene ring to rapidly shuttle back-and-forth between the two stations. Ultraviolet irradiation induced photo-isomerisation of the azobenzene from *E* to *Z* form. The *Z* isomer of the azobenzene functioned as a "closed gate", inhibiting shuttling of the pillar[6]arene ring.**

Molecular shuttles are mechanically interlocked molecules (MIMs) in which a macrocyclic ring is able to move back-and-forth between two recognition sites (stations).[1] The constitution and length of the linker connecting the two stations dominate the ring movement. Insertion of groups sensitive to external stimuli (pH,[2] redox reactions[3] and light[4]) into the linker is a useful approach to control the ring movement. Among these stimuli, light is especially useful because it functions quickly, efficiently, and reversibly. Azobenzene derivatives are widely used as photo-responsive compounds. Their conformational change between *E* and *Z* isomers in response to visible light or ultraviolet (UV) can be exploited to construct light-operated molecular shuttles. Examples include shuttles based on macrocyclic rings such as cyclodextrins,[4c-e] cucurbit[n]urils[4a] and cyclobis(paraquat-*p*-phenylene)[4b]. However, few light-operated molecular shuttles have been designed because of the need to match the sizes of the macrocyclic ring and azobenzene derivatives. In this study, we synthesised a new light-operated molecular shuttle, [2]rotaxane, consisting of a pillar[6]arene ring and an azobenzene derivative. Pillar[n]arenes, which were reported by our group in 2008,[5] are pillar-shaped macrocyclic hosts in supramolecular chemistry.[6] Based on their superior functionality,[7] host-guest property,[8] symmetric structures,[9] and facile synthesis,[10] various pillar[n]arene-based supramolecular assemblies and systems have been reported.[11] In this study, we designed a pillar[n]arene-based photo-responsive molecular shuttle using a photo-responsive host-guest complexation between azobenzene derivatives and pillar[6]arenes. From previous reports,[12] the smaller size of the *E* isomers of azobenzene derivatives permits them to thread pillar[6]arene cavity (**Fig. 1a**).

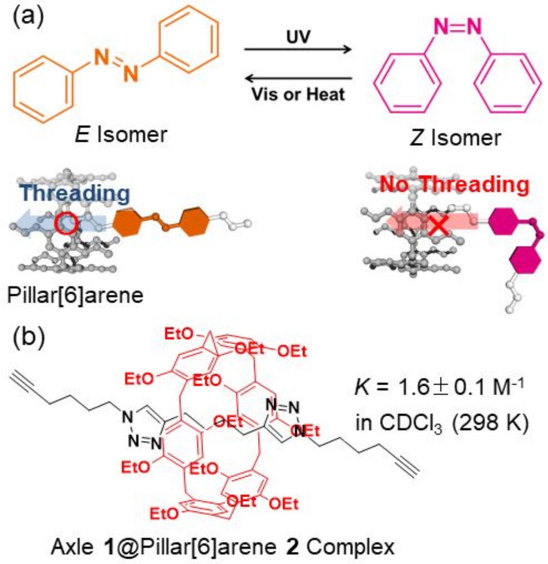

**Fig. 1** (a) Photo-responsive host-guest system based on an azobenzene guest and a pillar[6]arene. (b) Host-guest complexation between C4 methylene station (axle **1**) and pillar[6]arene **2**.

In contrast, pillar[6]arenes rarely form stable complexes with *Z* isomers because the latter are too bulky.[12] Therefore, the

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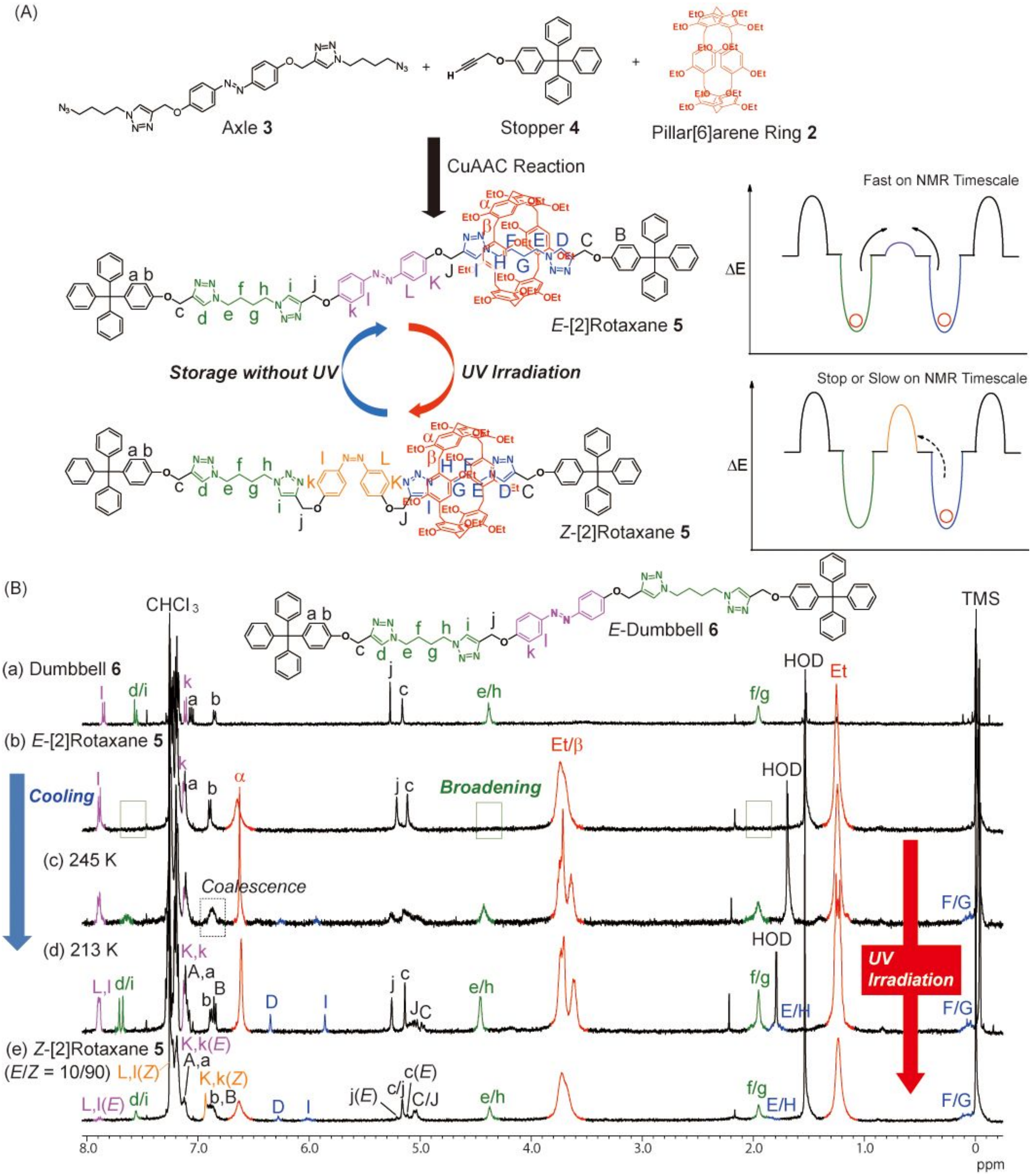

**Fig. 2** (A) Synthesis of pillar[6]arene-based [2]rotaxane **5** from pillar[6]arene ring **2**, stopper **4** and azobenzene axle **3**. (B) $^1$H NMR spectra ($CDCl_3$) of (a) dumbbell **6** at 298 K, (b-d) *E*-[2]rotaxane **5** at different temperatures and (e) *Z*-[2]rotaxane **5** (*E*/*Z* = 10/90) at 298 K.

pillar[6]arene ring can only accommodate *E* isomer azobenzenes. We thus introduced the azobenzene group as a photo-responsive gate to control pillar[6]arene shuttling between two stations. A C4 methylene chain group flanked by *N*-substituted triazoles, axle **1** (**Fig. 1b**) was used as a station. Axle **1** forms a 1:1 host-guest complex with the pillar[6]arene **2** at 298 K in $CDCl_3$ ($K$ = 1.6 ± 0.1 $M^{-1}$, see ESI for detail), that is notably weaker than its corresponding complexes with pillar[5]arenes ($K > 10^4$ $M^{-1}$)[13] because of the lager cavity size of pillar[6]arenes (ca. 6.7 Å) compared with pillar[5]arenes (ca. 4.7 Å). The weak binding of the C4 station by pillar[6]arenes enables rapid shuttling between two such stations. Thus, we designed [2]rotaxane **5**, a pillar[6]arene ring **2**, encircling axle **3** (a central photo-responsive azobenzene gate connecting two C4 stations), capped by a pair of bulky trityl stoppers **4**. The pillar[6]arene-based [2]rotaxane **5** was synthesised using a stepwise copper(I)-catalysed alkyne–azide cycloaddition (CuAAC) reaction, previously developed in our laboratory (**Fig. 2A**).[13] In the rotaxane synthesis, first CuAAC reaction between axle **3** and stopper **4** produced an intermediate containing one C4 station *in situ*, then *pseudo*[2]rotaxane structure forms. The second

CuAAC reaction produces the second C4 station. However, wheel **5** cannot slip over the stopper ends, resulting in formation of [2]rotaxane **5** with two C4 stations (yield 39%). We used a large excess of the pillar[6]arene **2** to promote the complex formation, thus [2]rotaxane **5** was obtained relatively high yield despite the low association constant.

**Fig. 2B** shows $^1$H NMR spectra of dumbbell **6** (**Fig. 2B(a)**) and [2]rotaxane **5** with the *E* isomer azobenzene (*E*-[2]rotaxane **5**, **Fig. 2B(b)**) at 298 K. Both dumbbell **6** and *E*-[2]rotaxane **5** showed clear proton signals from the *E* isomer azobenzene gate (k, l; shown in purple), pillar[6]arene ring ($\alpha$, $\beta$, Et; red), stopper and methylene linkers (a, b, c, j; black); however, proton signals from C4 stations and triazole groups (d-i; green, **Fig. 2B(a)**) were so strongly broadened in the spectra of *E*-[2]rotaxane **5** at 298 K that they are not visible, indicating that shuttling of the pillar[6]arene ring between the two C4 stations occurs on the NMR time scale.[14] To clarify this, we obtained $^1$H NMR spectra of *E*-[2]rotaxane **5** at lower temperatures. At 213 K (**Fig 2B(d)**), new proton signals appeared because the ring shuttling was now slow on the NMR time scale. New peaks (d-i; green) were observed at the same position as the signals from the C4 station and triazole moieties of dumbbell **6** (**Fig. 2B(a)**), confirming that they originate from the un-covered C4 station and triazole moieties. Other new peaks were attributed to proton signals from the C4 station and triazole groups covered by the pillar[6]arene ring (D-I; blue). Proton signals ($\alpha$, $\beta$, Et; red) from pillar[6]arene ring were broadening even at low temperature due to the rotation of the units. The same trend was observed in the pillar[6]arene-based [2]rotaxane.[15] All proton signals were completely assigned using 2D NMR experiments. NOE cross peaks were observed between proton signals of pillar[6]arene ring and axle (details in ESI). Proton signals from the trityl stopper (signals b and B) were individually observed at 213 K because of the slow ring shuttling on the NMR time scale, and coalesced at 245 K (**Fig. 2B(c)**). The ring motion was evaluated using the coalescence temperature, from which the rate of ring shuttling in *E*-[2]rotaxane **5** at 298 K was determined to be $k = 4.7 \times 10^3$ s$^{-1}$ (ESI).[16] The value of $k$ at 213 K estimated by EXSY measurements (ESI) was 0.86±0.02 s$^{-1}$, which is consisted with the extrapolated value of $k$ at 213 K by variable temperature $^1$H NMR measurements (0.8 s$^{-1}$). The pillar[6]arene ring in *E*-[2]rotaxane **5** rapidly moves back-and-forth between the two C4 stations because the *E* isomer azobenzene functions as an "open gate" (**Fig. 3a**).

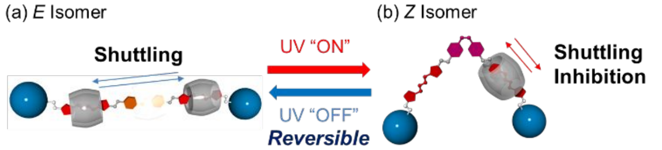

**Fig. 3** Illustration of the photo-regulated molecular shuttle by [2]rotaxane **5** with (a) *E* and (b) *Z* azobenzene isomers.

Shuttling of the pillar[6]arene ring in [2]rotaxane **5** after photo-isomerisation of the azobenzene gate between its *E* and *Z* isomers was investigated using $^1$H NMR (**Fig. 2B(e)**) at 298 K. When *E*-[2]rotaxane **5** was irradiated with UV (365 nm), new peaks appeared at 6.9 ppm, which were attributed to the *Z* isomer of the azobenzene gate (orange). At equilibrium, the *E*-/*Z*-azobenzene ratio was 10/90, which was determined from the relative intensity of the $^1$H signals corresponding to *E*-azobenzene (peaks c and j) and *Z*-azobenzene (peaks C and J) in **Fig. 2B(e)**. The new peaks at 7.55, 4.45 and 1.95 ppm were attributed to un-covered C4 stations and triazole groups (green). The other set of signals at 6.3, 6.0, 1.8 and 0.2 ppm could be attributed to C4 station and triazole groups covered by the pillar[6]arene ring (blue), because they were found at the same position in the spectra of *E*-[2]rotaxane **5** at 213 K (**Fig. 2B(d)**). These peaks were observed in the spectra of *Z*-[2]rotaxane **5** even at 298 K indicating that the *Z* isomer of the azobenzene gate restricted the ring to reside over one C4 station. The $^1$H NMR spectra of *Z*-[2]rotaxane **5** did not change even upon cooling to 213 K (ESI), indicating that the *Z*-azobenzene functions as a "closed gate" that inhibits shuttling of pillar[6]arene ring (**Fig. 3b**). Photo-isomerisation of the azobenzene group between its *E* and *Z* isomers in [2]rotaxane **5** was also monitored using UV-vis absorption measurements (**Fig. 4**).

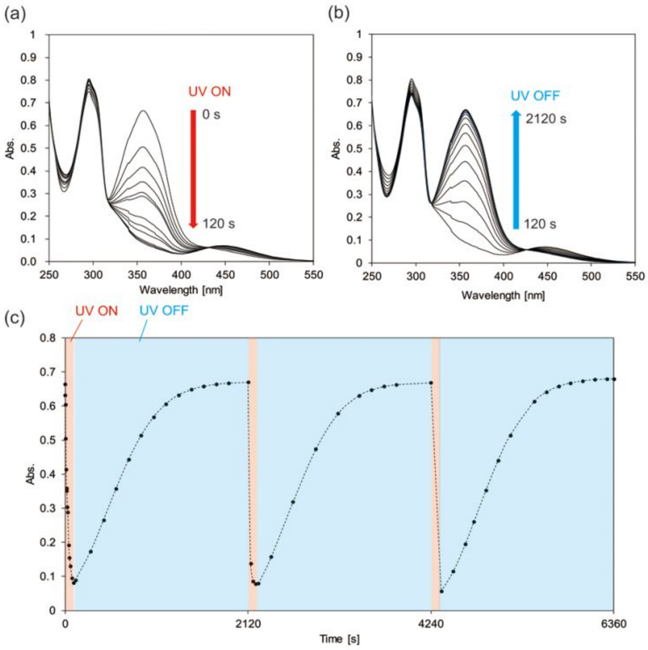

**Fig. 4** Absorption spectra of [2]rotaxane **5** (25 μM in $CHCl_3$ at 298 K) (a) during UV light irradiation, and (b) subsequent recovery in the dark. (c) Absorbance change at 357 nm accompanying the *E*-to-*Z* conversion of [2]rotaxane **5** (25 μM in $CHCl_3$ at 298 K) by UV irradiation in a 120 s/2000 s light-dark cycle.

UV irradiation of *E*-[2]rotaxane **5** caused a decrease in the absorbance of *E*-azobenzene at 357 nm, and an increase in the absorbance of *Z*-azobenzene at 450 nm (**Fig. 4a**), indicating *E*-to-*Z* photo-isomerisation of the azobenzene group. A photostationary state was reached after 120 s. When the solution was left at 298 K in the dark, the absorbance of the *E*-azobenzene completely recovered after 2000 s, with a concomitant decrease in the absorbance of *Z*-azobenzene (**Fig. 4b**), indicating that Z-to-*E* thermal isomerisation occurred at

298 K. The above processes could be reversibly repeated at 298 K (**Fig. 4c**).

In summary, we have synthesised a pillar[6]arene-based photo-responsive molecular shuttle. The azobenzene derivative functions as a photo-gate to control shuttling of the pillar[6]arene ring. In its *E* isomer, the pillar[6]arene ring can shuttle between two stations, while no or slow shuttling on an NMR timescale occurs in the *Z* isomer. To the best of our knowledge, this is first example of a photo-controlled molecular shuttle based on a pillar[n]arene. A fundamental understanding of such simple photo-controlled molecular shuttles will aid the design of more complicated supramolecular assemblies.

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## Conflicts of interest

There are no conflicts to declare.

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14 Proton signals of c/C and j/J are still in the fast exchange limit in **Fig.2(B)b**. This must be because the chemical shift difference is small so that coalescence occurs at much lower temperature than for the proton pairs of which the shielding in the covered part is very strong.

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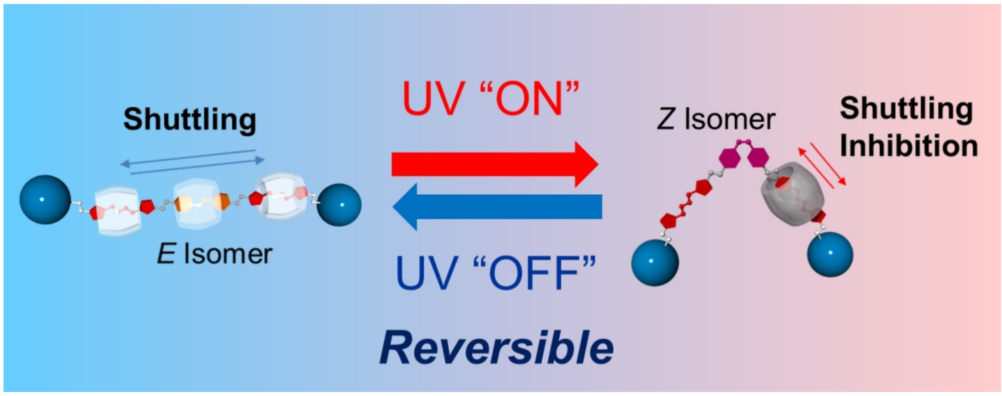

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