

Photoresponsive Phosphate Coordination Using Azobenzene-Spaced Bis-tris(urea) Ligand

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Abstract. Given the nondestructive nature and high spatiotemporal resolution of the light source, studies of photoresponsive systems have gained great attention and made considerable progresses in the past decades. By incorporating photoswitch molecules with noncovalent interaction, photoresponsive, supramolecular systems can be designed for tailored properties, e.g., guest delivery, catalysis, sensing, and information processing. Here, we introduced a new photoresponsive ligand (**L**) comprised of azobenzene spacer and two tris(urea) binding moiety. The latter component displayed characteristic coordination property with anions. Upon light irradiation, we observed reversible photoswitching of free ligand. The *Z/E* thermal relaxation half-life of free ligand **L** was determined to be 3.4 h at room temperature. By coordinating to phosphate anion, double helicate structure was believed to form and can be subsequently regulated by light and heat.

Keywords: anion coordination; photoresponsive; double helicate, azobenzene.

1. Introduction

Supramolecular chemistry has obtained a new cutting edge with the incorporation of stimuli-responsive modulation^[1-2]. By comparing to other stimuli (chemical inputs^[3], pH^[4-5], and temperature^[6-8]), use of light source is thought to be elegant as of its nondestructive nature and controllable spatiotemporal resolution. Such photoresponsive systems have been well-programmed for the application of transmembrane transport^[9-11], gel materials^[12], catalysis^[13] and other fields^[14]. Among commonly utilized photoswitches, azobenzene is one of the most widely studied groups in the design of photoresponsive supramolecular systems due to its feasible synthetic method and reversible photoisomerization quantum yield^[15]. Upon light irradiation, azobenzene unit can undergo trans/cis isomerization with distinct geometric change. Typically, the two isomers display different absorption spectra. The *E*-isomer mainly absorbs UV light in the range of 360-370 nm and converts to *Z*-isomer. The absorption of *Z*-isomer is concentrated in the visible region of 430-440 nm. Irradiation with visible light in this region will trigger the reduction of *Z*-isomers, which can also be achieved by heating. These absorption nature of two isomers can be finely tuned by modifying the substitution with available synthetic procedures, consequently regulating its thermal kinetics.

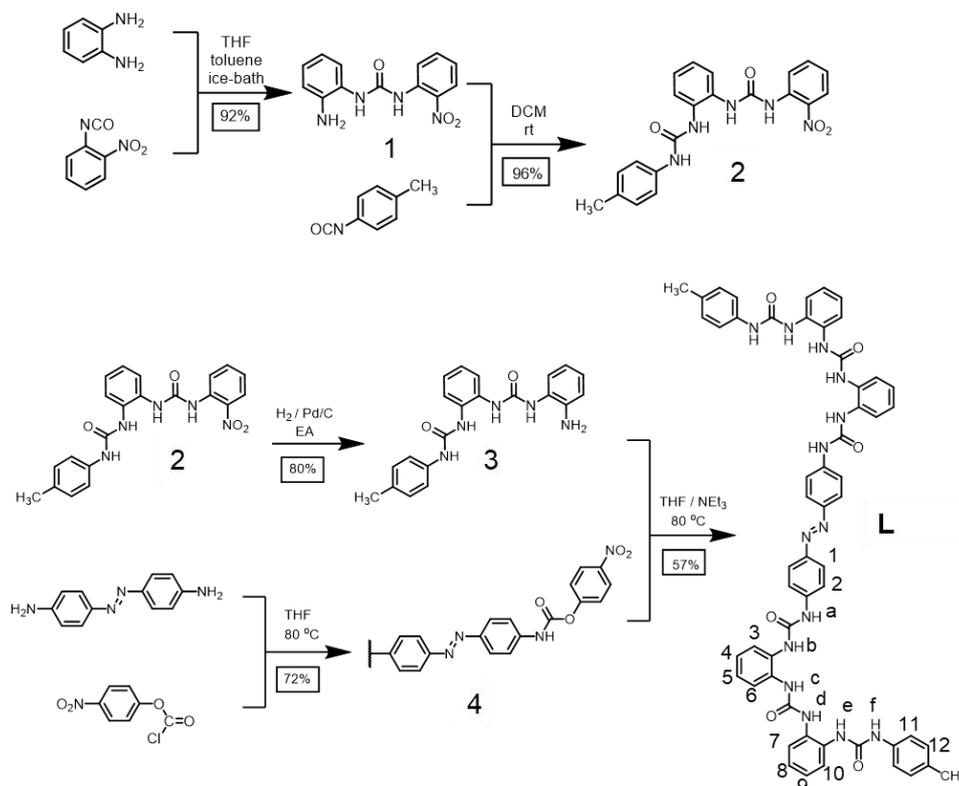
Photoresponsive supramolecular architectures used to be prepared through metal coordination^[16]. A series of metal square complexes bridged by a photoactive 4,4'-azopyridine ligand had been reported by Lees group^[17]. The tetranuclear square can be converted to di-nuclear macrocycle thus thermally switching back to the initial tetranuclear square. Hardie and co-workers^[18] reported the first example of metal-coordinated cage showing reversible photoisomerization with retaining the compositional integrity. Beves and co-workers^[19] reported a photoswitchable ligand, which is self-assembled with palladium (II) to form a $[Pd_2(E-L)_4]^{4+}$ cage. The cage can be switched to $Pd(Z-L)_2]^{2+}$ by visible light. Although photoresponsive assemblies have been widely demonstrated by metal coordination, very few examples formed by anionic coordination with azobenzene bridged ligand. Azobenzene-based anion supramolecular systems are mostly focused on small complexes of supramolecular tweezer to regulate substrate binding upon isomerization.

Our team is committed to the study of anion-coordination-driven assembly (ACDA), which has been proven to be an effective approach to prepare various supramolecular architectures^[20]. For

example, macrocycles^[21], foldamers^[22], cage structure^[23] and helicate structure^[24]. Previously, we synthesized a bis-bis(urea) ligand spaced by azobenzene unit that can form tetrahedral cages or helicate structure upon phosphate coordination. Upon light irradiation, topology of assembled structure can be regulated^[25]. In contrast, the use of tri(urea) moiety instead of bis(urea) unit to build up discrete supramolecular architectures is largely unexplored.^[26] Herein, we synthesized an azobenzene-spaced bis-tris(urea) ligand, which was found to display comparable photoswitching and thermal relaxation properties like the bis-bis(urea) ligand. In addition, by phosphate coordination, the structure of double helicate can be prepared and regulated by light.

2. Results and discussion

2.1 Preparation of the bis-tris(urea) ligand L



Scheme 1 Synthetic procedure of making bis-tris(urea) ligand **L**. THF denotes tetrahydrofuran, DCM denotes dichloromethane, rt denotes room temperature.

The preparation of azobenzene spaced bis-tris(urea) ligand **L** was shown in Scheme 1. Synthetic details of key intermediate and final product are shown followingly. Notably, all the compounds are isolated by recrystallization without using any column purification.

Compound 2: compound **1** was synthesized based on previously reported procedure^[27]. Under N_2 atmosphere, compound **1** (0.50 g, 1.8 mmol) was placed in a 100 mL three-necked, round-bottomed flask and suspended in dry DCM (45 mL), *p*-methylbenzene isocyanate (2.9 mL, 2.3 mmol) in dry DCM (10 mL) was added dropwise over 30 mins. Stir the reaction mixture at room temperature for 5 hours until compound **1** is consumed. The precipitates were separated by filtration and washed with DCM and diethyl ether. Compound **2** was isolated as a yellow powder (0.7 g), yield: 96%. ¹H NMR (400 MHz, 298K, DMSO-*d*₆): δ 9.74 (s, 1H), 9.21 (s, 1H), 9.02 (s, 1H), 8.33 (d, $J = 8.6$ Hz, 1H), 8.09 (d, $J = 9.9$ Hz, 1H), 8.02 (s, 1H), 7.82 (d, $J = 9.7$ Hz, 1H), 7.74 – 7.64 (m, 1H), 7.41 (d, $J = 9.5$ Hz, 1H), 7.34 (d, $J = 8.4$ Hz, 2H), 7.24 – 7.11 (m, 2H), 7.07 (t, $J = 8.3$ Hz, 3H), 2.23 (s, 3H).

Compound 3: Under H_2 atmosphere, compound **2** (0.10 g, 0.2 mmol) and 10 mg Pd/C were placed in double-necked, round-bottomed flask and suspended in 30 mL ethyl acetate. After stirring

overnight at room temperature, white precipitates were obtained. The precipitates were separated by filtration and washed with ethanol and diethyl ether. Compound **3** was isolated as a white powder (0.06 g), yield: 80%. $^1\text{H NMR}$ (400 MHz, $\text{DMSO-}d_6$): δ 8.96 (s, 1H), 8.15 (s, 1H), 8.09 (s, 1H), 8.00 (s, 1H), 7.60 – 7.53 (m, 2H), 7.35 (d, $J = 8.4$ Hz, 3H), 7.07 (dd, $J = 9.1, 6.5$ Hz, 4H), 6.84 (t, $J = 7.6$ Hz, 1H), 6.73 (d, $J = 6.4$ Hz, 1H), 4.82 (s, 2H), 2.24 (s, 3H).

Ligand **L**: Compound **4** was synthesized based on our previous work^[28]. Under N_2 atmosphere, compound **3** (0.16 g, 0.4 mmol) and compound **4** (0.10 g, 0.2 mmol) were placed in a 50 mL double-necked, round-bottomed flask and suspended in dry THF (25 mL). The solution was heated to 80 °C, and triethylamine (0.15 mL, 0.73 mmol) was added dropwise. Stir the reaction mixture overnight at 80°C until compound **3** is consumed. The precipitates were separated by filtration and washed with THF and diethyl ether. Ligand **L** was isolated as a brown solid powder (0.12 g), yield: 57%. $^1\text{H NMR}$ (400 MHz, 298K, $\text{DMSO-}d_6$): δ 9.52 (s, 1H), 8.99 (s, 1H), 8.48 (d, $J = 11.2$ Hz, 2H), 8.20 (s, 1H), 8.04 (s, 1H), 7.80 (d, $J = 8.7$ Hz, 2H), 7.65 (d, $J = 8.9$ Hz, 2H), 7.63 – 7.53 (m, 4H), 7.33 (d, $J = 8.4$ Hz, 2H), 7.13 – 7.02 (m, 7H), 2.22 (s, 3H).

2.2 Photoisomerization of the free ligand

The reversible photoisomerization of free ligand was firstly investigated, which displayed solvent-dependent property as recorded by $^1\text{H NMR}$ (Fig. 1). Specifically, in $\text{DMSO-}d_6$, 66% of *Z*-isomer was produced upon irradiation of 365 nm light (3 W). Comparing to the NMR signature of *E*-isomer, all urea protons of *Z*-isomer were up-field shifted deriving from twisting of two phenyl rings on the azobenzene unit. The protons of H_1 and H_2 were also observed to up-field shift, these are all consistent with previous results seen for the bis-bis(urea) ligand and indicated the photoisomerization *E*-isomer to *Z*-isomer. In 20% v/v $\text{DMSO-}d_6/\text{CD}_3\text{CN}$, higher conversion of *Z*-isomer of 85% was seen suggesting that less polar solvent of acetonitrile is beneficial for photoswitching.

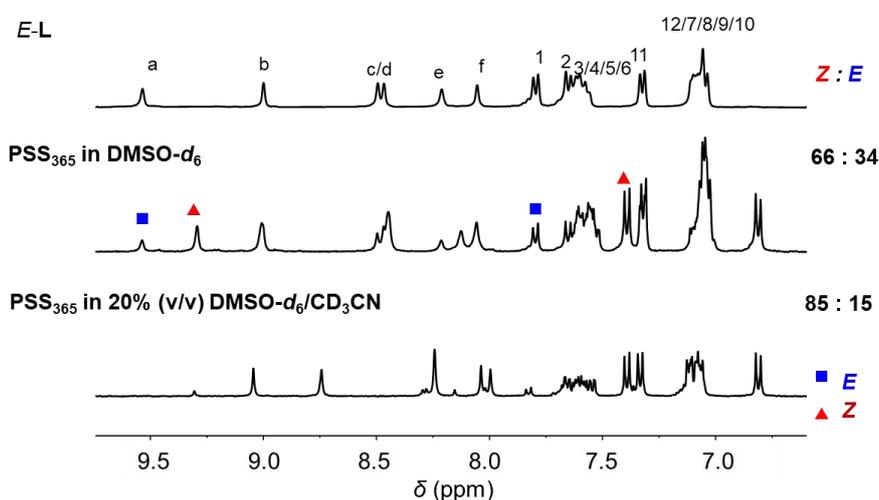


Fig. 1 Stacked partial $^1\text{H NMR}$ spectra of **L** upon 365 nm light irradiation (1 mM, 400 MHz, 298 K, $\text{DMSO-}d_6$ or 20% v/v $\text{DMSO-}d_6/\text{CD}_3\text{CN}$). Relative ratio of isomers is shown on the right.

To test how the light wavelength affect photoisomerization, we next test the photoisomerization conversion of free ligand under light irradiation with different wavelengths. Light sources of 380 nm (3 W), 410 nm (3 W), 450 nm (3 W), 480 nm (3 W) and 510 nm (3 W) were chosen for irradiation, and the experiments were monitored by $^1\text{H NMR}$ (Fig. 2). The ratio of *Z/E* configuration at different PSS was obtained through the integrated area of NMR. The results showed that the *Z*-isomer was maximized and enriched under 380 nm wavelength irradiation (*Z*: 98%). As the wavelength moves to the visible light region, the ratio of *Z*-isomer decreases. The *E*-isomer can be

fully recovered by heating (60°C, 40 minutes). By using light and heat, we are able to reversibly regulate the photoisomerization of free ligand.

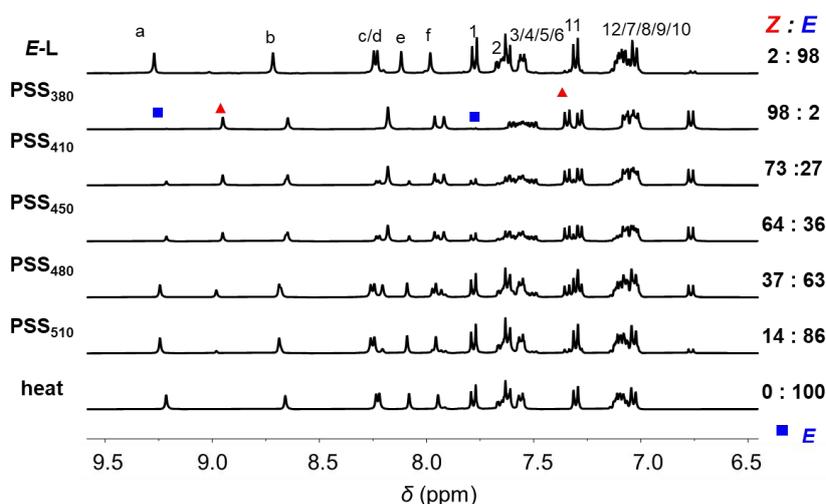


Fig. 2 Stacked partial ^1H NMR spectra of **L** upon light irradiation at different wavelength (1 mM, 20% v/v DMSO- d_6 /CD $_3$ CN, 400 MHz, 298 K).

To gain insight for the photoisomerization properties under light irradiation with various wavelengths, UV-vis absorption spectra of free ligand was recorded (Fig. 3). For the *E*-isomerized free ligand, two absorption peaks at 260 nm and 388 nm were observed, which are assigned to the π - π^* transition band of oligourea backbone and *E*-azobenzene respectively. After exposure to 380 nm light, the absorption at 388 nm significantly decreased and a new absorption at 467 nm emerged that is assigned to the n - π^* transition band of *Z*-azobenzene. The π - π^* transition band of *Z*-azobenzene displayed a clear signature of hypochromic shift to 331 nm. Such distinct UV-vis spectroscopic changes are consistent with previous results and indicate the photoisomerization of azobenzene unit.

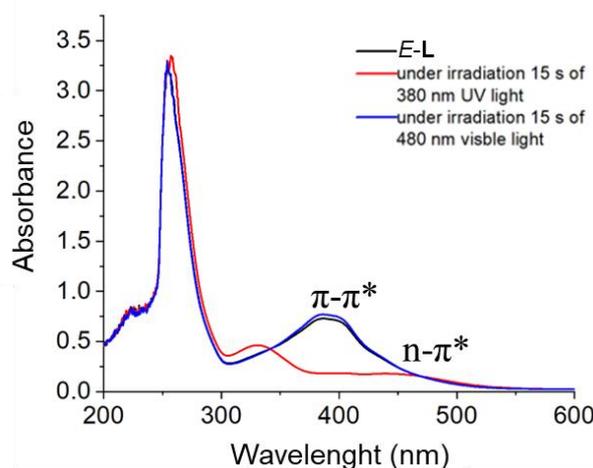


Fig. 3 UV-vis absorption spectra of *E*-**L** (25 μM , 20% v/v DMSO/CH $_3$ CN) under alternating light irradiation (380 nm and 480 nm, 3 W).

The thermal isomerization of *Z*-**L** was monitored using ^1H NMR spectroscopy. A sample of photo-switch **L** (500 μL , 1 mM) in 20% v/v DMSO- d_6 /CD $_3$ CN was enriched in *Z*-**L** by irradiating with the 380 nm light. The sample was left in dark at 25°C (298 K) and the relative ratio of isomerization was monitored using ^1H NMR spectroscopy (Fig. 4). Molar fraction was determined based on integrals of H_a and H_1 . The thermal isomerization data can be fitted to the first-order kinetic model. The apparent rate constant was determined to be $5.7 \times 10^{-5} \text{ s}^{-1}$, with a thermal

half-life of 3.4 hours. The apparent thermal barrier was calculated to be $97.2 \text{ kJ}\cdot\text{mol}^{-1}$. All these data were consistent to other azobenzene-based oligourea samples^[29].

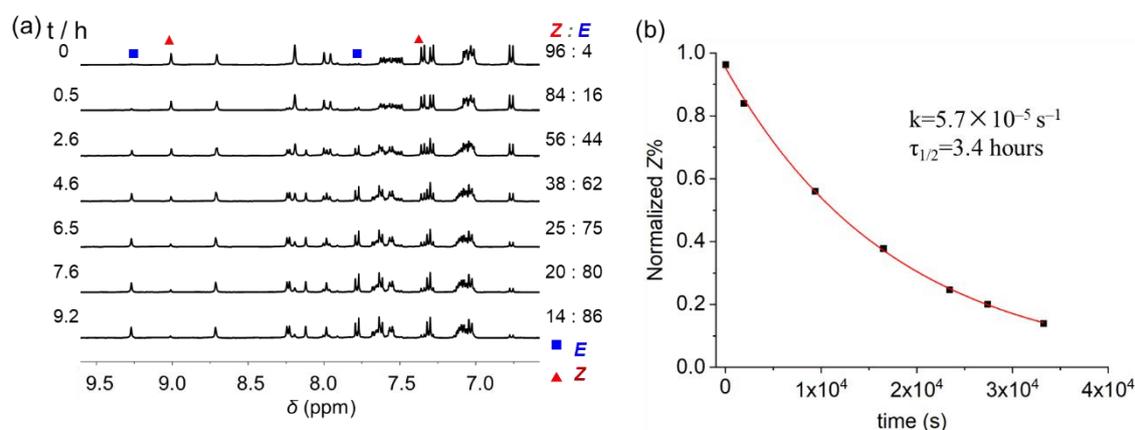


Fig. 4 (a) Stacked ^1H NMR spectra of Z-L upon thermal isomerization at room temperature (1 mM, 20% v/v DMSO- d_6 /CD $_3$ CN, 400 MHz, 298 K). (b) Normalized Z-isomer fraction plots by fitting to the first-order kinetic model.

2.3 Photoresponsive phosphate coordination

The bis-tri(urea) ligand **L** (10 mg, 0.01 mmol) was mixed with 0.67 equivalent of tetrabutylammonium (TBA $^+$) phosphate solution (16 μL , 0.625 M), which was prepared by mixing TBAOH with three equiv. of H $_3$ PO $_4$ in acetonitrile (1 mL). After the mixture was stirred at room temperature overnight, a yellow solution was obtained. Ether slowly diffuses into the solution, providing a yellow powder within a week. The powder was collected and test by NMR. According to the ^1H NMR comparison between the single ligand and the complex (Fig. 5), a clear set of peaks were seen indicating the formation of a well-defined supramolecular architecture driven by phosphate coordination. Based on the peak intensities of ligand and TBA $^+$ counteraction, a double helicate structure was formed. Computational modified structure of presumptive double helicate was shown in Fig 5, where each phosphate anion was stabilized by twelve hydrogen bonding from two tri(urea) binding units.

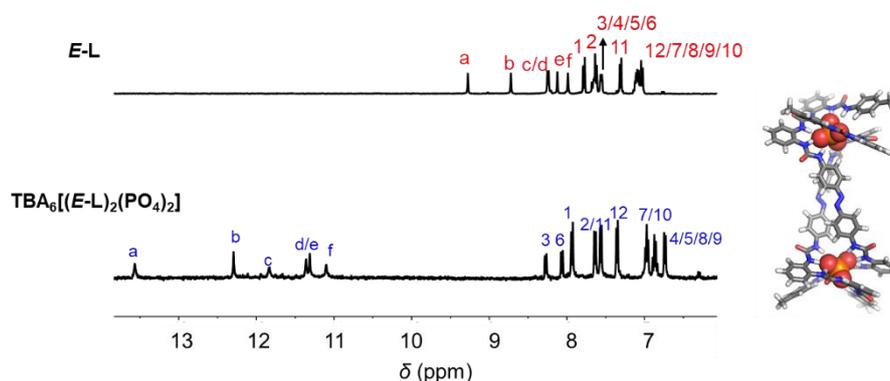


Fig 5. Stacked partial ^1H NMR spectra of free ligand and phosphate-coordinated double helicate, $\text{TBA}_6[(\text{E-L})_2(\text{PO}_4)_2]$ (**L**, in DMSO- d_6 ; $\text{TBA}_6[(\text{E-L})_2(\text{PO}_4)_2]$ in 20% v/v DMSO- d_6 /CD $_3$ CN, 400 MHz, 298 K). Optimized structure of double helicate is shown.

The photoisomerization of the complex was subsequently studied by ^1H NMR (Fig. 6). When $[(\text{E-L})_2(\text{PO}_4)_2]^{6-}$ (counter cation is tetramethylamine, TMA $^+$) was irradiated with a 380 nm light for one hour, a new species was formed. The characteristic peak of the E-isomer disappeared, and an obvious Z-isomer characteristic peak (H $_2$) appeared at 5.5 ppm. Next, we placed the irradiated sample in a water bath (60°C, 4 hours) in dark. The characteristic peak of the Z-isomer disappeared,

and the ^1H NMR spectroscopy showed that the complex reverted to the $[(E-L)_2(\text{PO}_4)_2]^{6-}$. Upon light irradiation and heat, reversible photoisomerization of phosphate-coordinated double helicate was achieved.

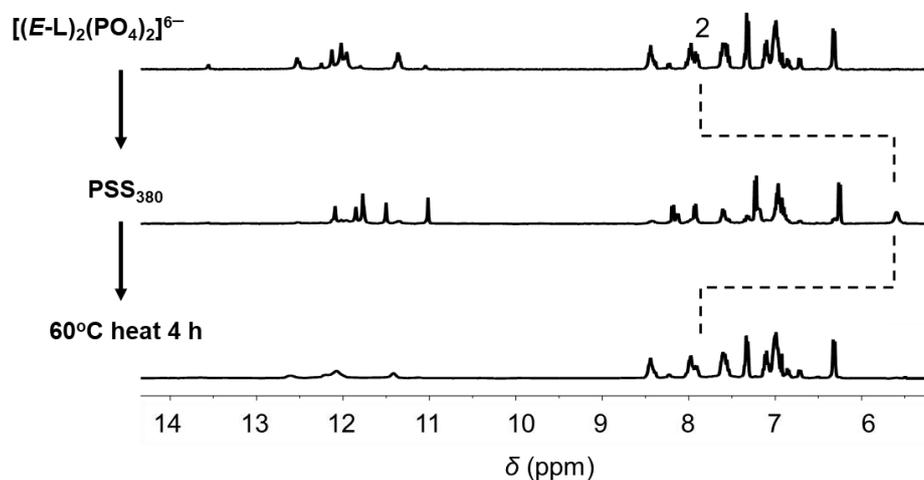


Fig. 6 Stacked partial ^1H NMR spectra of $[(E-L)_2(\text{PO}_4)_2]^{6-}$ (tetramethylamine as counteranion) after irradiating with 380 nm light and the same sample after heating in the dark for 4 hours at 60°C ($\text{DMSO-}d_6$, $\text{TBA}_6[(E-L)_2(\text{PO}_4)_2]$, 400 MHz, 298 K).

3. Summary

In summary, we have synthesized a bis-tris(urea) ligand bridged by azobenzene, which displays efficient photoisomerization performance. Upon irradiation of 380 nm light, over 98% of *Z*-isomer can form, subsequent heating can fully restore the *E*-isomer. In addition, the ligand can form a double helix structure after coordination with phosphate as indicated by ^1H NMR and computational modelling. The reversible photoisomerization was retained for the double helicate structure. Further investigation would focus on the preparation of various supramolecular assemblies by various anion coordination as well as the application for tailored guest delivery.

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