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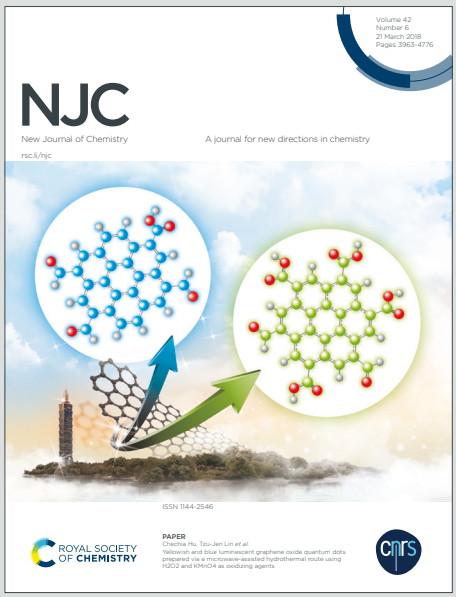

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COMMUNICATION

Synthesis of A New Solvent-driven Pillar[5]arene-Based [1]Rotaxane Molecular Machine

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Huasheng Tian, Runan Li, Po-Han Lin, Kamel Meguellati*

In this work, we designed a new pillar[5]arene-based molecular machine responsive to the polarity of different solvents which can exist in an interlocked structure in $CDCl_3$ and CD_3OD, and can exist in an extended form in DMSO and was studied by 1H and 2D NMR spectroscopy, HR(MS) and fluorescence spectroscopy.

With the development of supramolecular chemistry[1] and the emergence of macrocycles such as crown ethers[2], cyclodextrins[3], calixarenes[4] and pillar[5]arenes[5-10], *etc.* mechanically interlocked molecules (MIMs)[11-14] such as rotaxanes[15-17], catenanes[18, 19] and molecular knots[20, 21], have attracted attention due to their broad applications in self-assembly[12, 22], drug delivery[23], light harvesting[24], *etc*. Rotaxane, composed of one or more macrocycles threading one or more axles with two stoppers at the ends [25] and sensitive to the tunability of the host and guest interactions, has potential applications in the design of molecular shuttles[26], molecular machines[27] and ion recognitions[28]. Depending on the number of building units, it can be defined as [1]rotaxane[29], [n]rotaxane[9] and poly[n]rotaxane[30]. [1]rotaxane is a key member in the rotaxane family, and has attracted more chemists to find special architectures and applications.

Pillar[5]arene[31] was first reported by Ogoshi in 2008. They are composed of five hydroquinone units linked by methylene bridges at the 2- and 5- positions. Pillar[5]arene has an electron-rich cavity which makes it as an excellent container to host various electron-poor guests[32]. The synthesis and functionalization on both rims spotlight them as a macrocycle of choice for the design of a series of hydrophobic, hydrophilic and amphiphilic derivatives which could be applied in molecular shuttles[33], nano-containers[34], ion recognitions[35], supramolecular gels[36], drug delivery[37], *etc*. Mono-substituted pillar[5]arene is usually used to construct more complicated nanomaterials such as fluorescent probes[38], ion recognition[39], gels[40] *and so on*. However, pillar[5]arene-based (pseudo)[1]rotaxane or [1]rotaxane made up of one macrocycle and one axle have been poorly reported mainly due to their lower synthetic yield and the relative instability of the self-assembled structures. Ogoshi *et al.* reported the first mono-substituted pillar[5]arene-based pseudo[1]rotaxane, which indicated that mono-guest-functionalized pillar[5]arene can be self-included in $CDCl_3$ and in an open form in acetone[41]. Xue *et al*. reported a new strategy for the design and the synthesis of [1]rotaxane via the condensation of a carboxylic acid containing pillar[5]arene and with an amine in one step[42]. Yang *et al.* reported a light-driven molecular machine, which can display different conformations by light triggered Z/E isomerization of stiff stilbene[43]. The aforementioned approaches represent very convenient strategies for the design of multi-functionalized (pseudo)[1]rotaxane or [1]rotaxane.

Solvent-responsive smart molecular machines have been poorly reported. Wang *et al.* reported a self-locked solvent responsive pseudo[1]catenane containing one pillar[5]arene motif linked to an alkyl chain with two urea groups. However, the structure of synthetic self-locked pseudo[1]rotaxane cannot be changed by the modification of solvent[14]. Jiang *et al*. reported a kind of pillar[5]arene based [2]rotaxane constructed with 1,4-diethoxypillar[5]arene as a wheel that can slide depending on the solvent along a long alkyl axle where a bodipy chromophore was used as a stopper[44]. There are a very few reported mono-substituted pillar[5]arene based molecular machine that can exist in the form of self-included [1]rotaxane in $CDCl_3$ and dissociated in DMSO. Herein, A new strategy to construct stimuli-responsive [1]rotaxane is described (**Scheme 1**). Firstly, we prepared a mono-guest functionalized pillar[5]arene **P3** via click reaction from a monohydroxy-pillar[5]arene and 1-

[a] *Huasheng Tian, Runan Li, Po-Han Lin, Prof. Kamel Meguellati*
International Joint Research Laboratory of Nano-Micro Architecture Chemistry (NMAC), College of Chemistry, Jilin University, 2699 Qianjin Street, Changchun 130012, (PR China).

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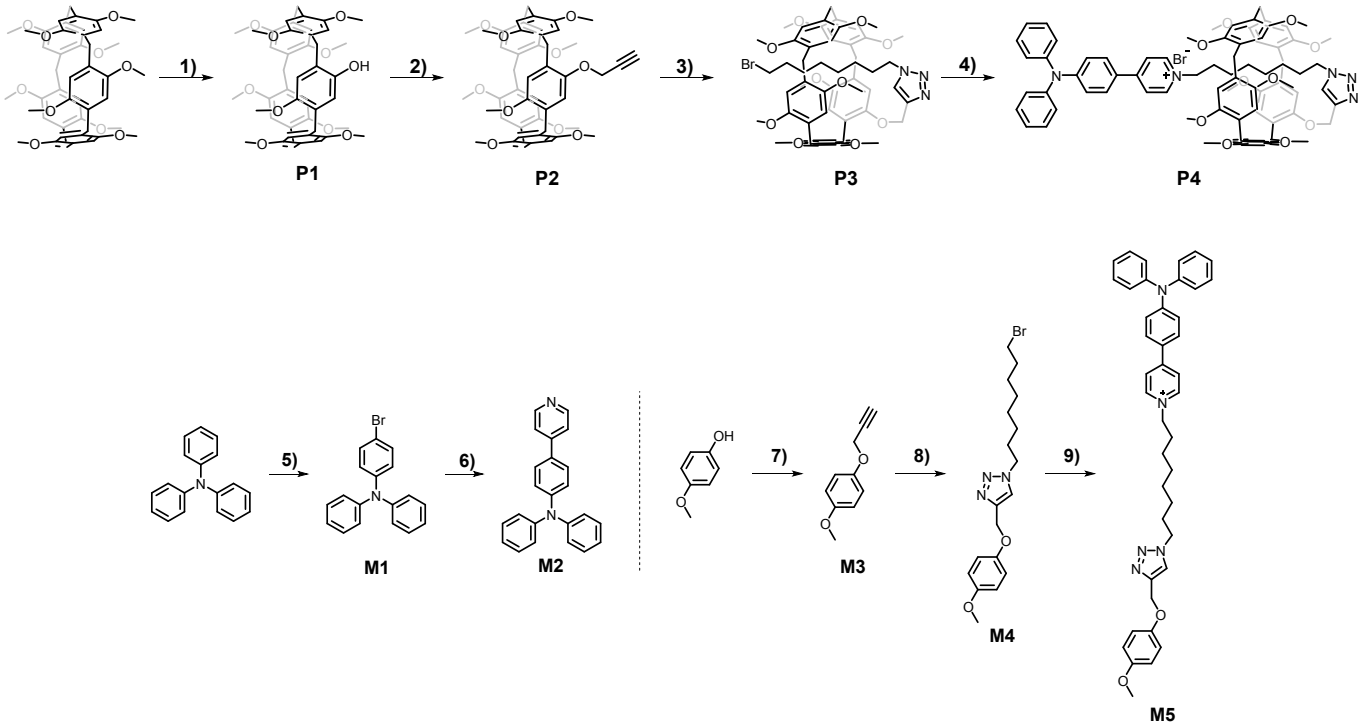


Scheme 1 Synthetic route of [1]rotaxane **P4** and the related monomer **M5**. 1) BBr_3, $CHCl_3$, 0 °C, 1 h, 22%; 2) propargyl bromide, NaH, DMF, 80 °C, 24 h, 56%; 3) 1-aza-8-bromooctane, sodium ascorbate, $CuSO_4 \cdot 5H_2O$, THF, H_2O, 24 h, 87%; 4) **M2**, $CHCl_3$, 90 °C, 24 h, 18%. 5) NBS, DMF, 0 °C, 4 h, 60%; 6) pyridine-4-boronic acid, K_2CO_3, $Pd(PPh_3)_4$, DMF, 120 °C, 24 h, 67%; 7) propargyl bromide, K_2CO_3, CH_3CN, 85 °C,24 h, 56%; 8) 1-aza-8-bromooctane, sodium ascorbate, $CuSO_4 \cdot 5H_2O$, THF, H_2O, 24 h, 75 %; 9) **M2**, $CHCl_3$, 90°C, 24h, 84%.

aza-8-bromooctane, which is self-included in $CDCl_3$. The final mechanically interlocked molecules were prepared from **P3** and a triphenylamine derivative. The equilibrium between the self-included structure and its extended form depends on the environment. By introducing two different electron deficient positions, that act as stations, solvent responsive mechanically interlocked molecules can change conformation and move upon addition of a stimuli. Furthermore, by introducing a triphenylamine moiety as a fluorescent group in the molecule, the solvent-dependent transformation of the structure can be monitored via NMR analysis and fluorescence analysis.

It is well known that the host-guest interactions can be affected by changing the polarities of solvents[45], by increasing the temperature[8], by adding guests that have stronger interactions with the host[14]. In this study, a solvent responsive mechanically interlocked molecule **P4** was prepared according to the procedure described in **Scheme 1**. Firstly, the self-included compound **P3** was synthesized from the monohydroxy-substituted pillar[5]arene **P1**, propargyl bromide and 1-aza-8-bromooctane. Then, the mechanically interlocked molecule **P4** was prepared directly through a reaction of substitution between **P3** and **M2**. For a better understanding of the switchability of compound **P4**, the related monomer **M5** was synthesized according to a similar method than compound **P4.**

As compound **P3** is a precursor of the mechanically interlocked molecule **P4**, so the preliminary dynamic study of **P3** was very important to prepare **P4**. When it was dissolved in $CDCl_3$, we noticed that some peaks were below 0 ppm from the ^1H NMR studies (**Fig. 1**), which indicated that these protons were shielded by pillar[5]arene. This phenomenon was certified by 2D ^1H-^1H NOESY NMR studies. From the 2D ^1H-^1H NOESY NMR spectrum of **P3** in $CDCl_3$ (**Fig. 2**), we can see correlation peaks between aromatic protons of pillar[5]arene and aliphatic protons of the axle which confirmed the interlocked structure of **P3**. Furthermore, to determine the intermolecular assembly or the process of dynamic interlocked assembly of compound

P3, the concentration related NMR titration experiments were conducted in $CDCl_3$ (**Fig. S25**). From the concentration related NMR spectra of compound **P3**, we can notice similar chemical shifts of **P3** by increasing the concentration of **P3** from 4 mM to 64 mM, which indicated that the structure of compound **P3** in $CDCl_3$ is attributed to an intramolecular assembly.

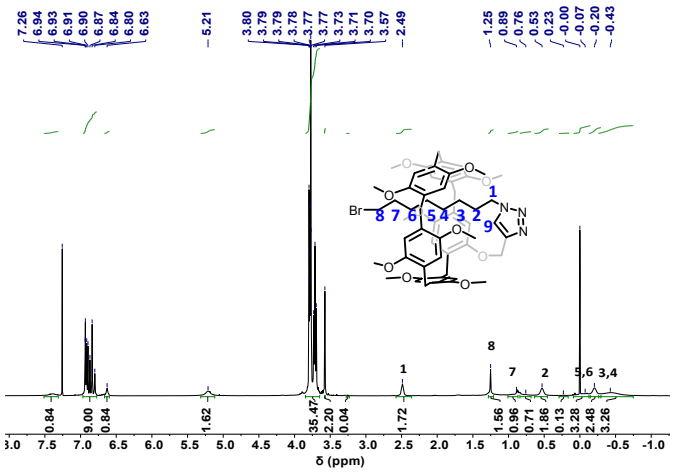


Fig. 1 ^{1}H NMR spectroscopy of compound **P3** (300 MHz, $CDCl_3$, 298 K).

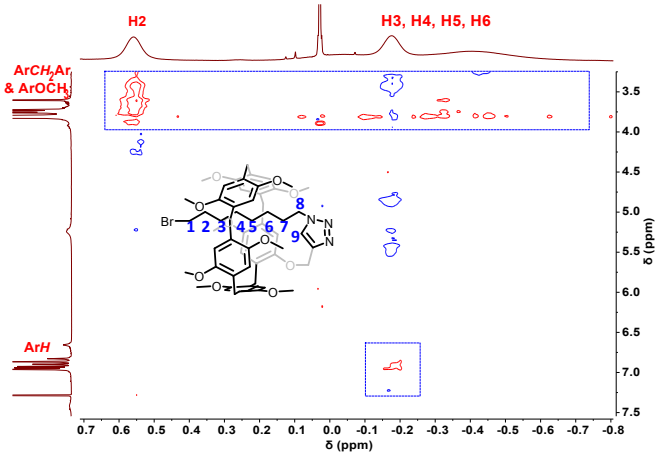


Fig. 2 2D ^{1}H-^{1}H NOESY NMR spectroscopy of compound **P3** (600 MHz, $CDCl_3$, 298 K).

P3 can be defined as an important precursor of self-included [1]rotaxanes by adding a stopper at the end of the axle. In this work, based on the self-included structure of compound **P3**, we constructed a [1]rotaxane **P4** directly via a nucleophilic substitution from **P3** and triphenylamine derivate. To study the self-included structure of compound **P4**, ^{1}H NMR of compounds **P4** (**Fig. 3b**) and **M5** (**Fig. 3a**)were compared in $CDCl_3$, and we can see that some aliphatic protons of the axle and some aromatic protons of triphenylamine shifted to higher magnetic field proving that some protons of the axle were shielded by the cavity of pillar[5]arene, hence the compound **P4** can be described as an interlocked molecule in $CDCl_3$ (**Fig. 3**). From the 2D ^{1}H-^{1}H NOESY NMR spectrum of **P4** in $CDCl_3$ (**Fig. S26**), strong correlation peaks between aromatic protons of pillar[5]arene and aliphatic protons of axle were seen which led us to conclude to a fully interlocked structure for compound **P4**. ^{1}H NMR (**Fig.S13**), 2D ^{1}H-^{1}H COSY NMR (**Fig. 4**) and 2D ^{1}H-^{1}H NOESY NMR (**Fig. 5**) 2D ^{1}H-^{13}C HSQC NMR studies were also conducted in CD_3OD. From the 2D ^{1}H-^{1}H NOESY NMR spectrum of compound **P4** in CD_3OD, a correlation of the corresponding signals between aromatic protons of pillar[5]arene and aliphatic protons of axle can be seen clearly which confirmed a self-interlocked structure for **P4** in CD_3OD.

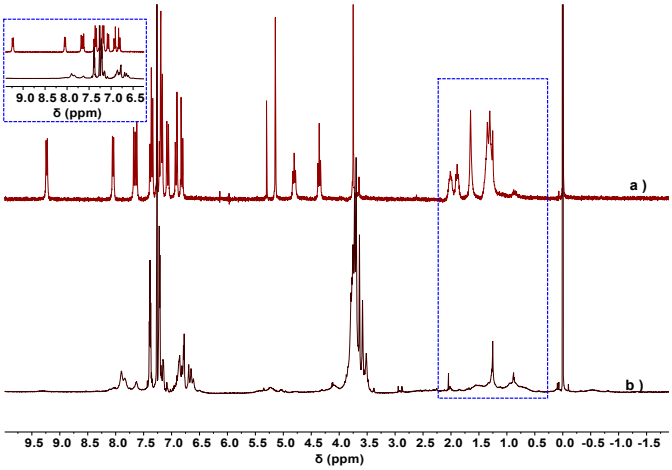


Fig. 3 ^{1}H NMR spectra comparison between **M5** and **P4** in $CDCl_3$ (300 MHz, 298 K).

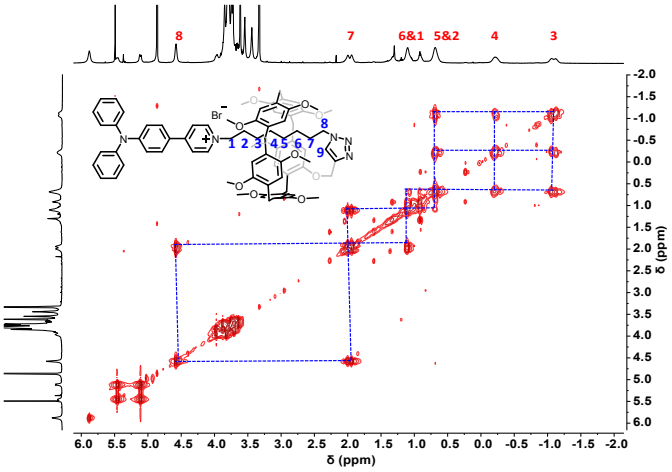


Fig. 4 2D ^{1}H-^{1}H COSY NMR spectroscopy of compound **P4** (600 MHz, CD_3OD-d_4, 298 K).

Generally, the increase of the polarity of solvent reduces the host-guest interactions. To further explore the stability of the self-interlocked structure of **P4**, **P4** was dissolved

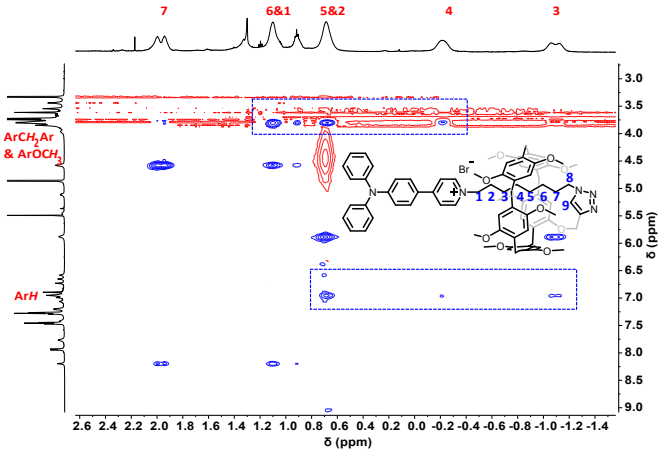


Fig. 5 2D ^{1}H-^{1}H NOESY NMR spectroscopy of compound **P4** (600 MHz, CD_3OD-d_4, 298 K).

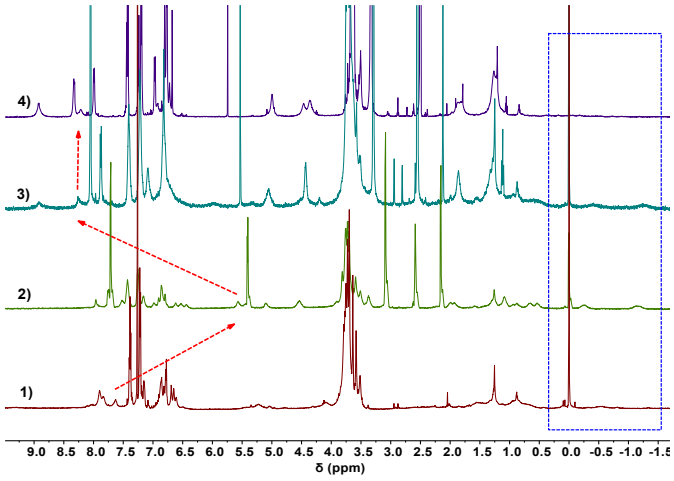
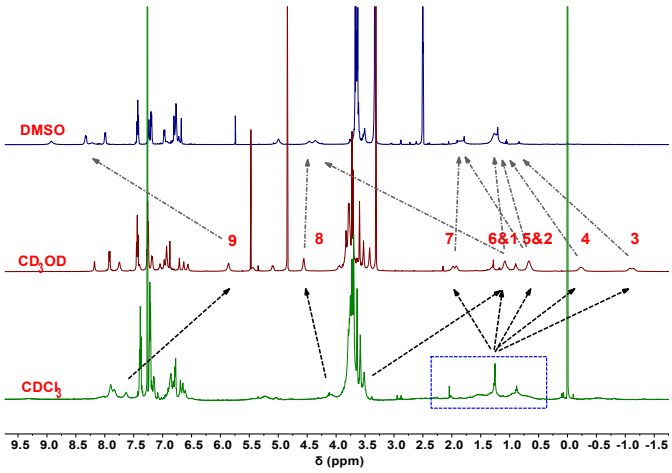


Fig. 6 ^{1}H NMR spectra comparison of compound **P4** by increasing the polarity of solvents: 1) $CDCl_3$; 2) $CDCl_3$/DMSO=3/1; 3) $CDCl_3$/DMSO=1/1; 4) DMSO.

in different solvents with different polarities ($CDCl_3$, $CDCl_3$/DMSO=3/1, $CDCl_3$/DMSO=1/1, DMSO), and from the spectra of compound **P4** in four different solvents (**Fig. 6**), it can be seen that with the increase of polarity of the mixed solvents, the aromatic protons close to the pyridinium cation shifted to lower magnetic field, and proton H9 was at higher magnetic field in V_{CDCl3}/V_{DMSO} = 3/1 and then moved to lower magnetic field in V_{CDCl3}/V_{DMSO} = 1/1. Meanwhile, part of aliphatic protons including H_3 and H_4 belonging to the axle were at high magnetic field firstly and then moved to low magnetic field by increasing the ratio of DMSO which indicated that the shield effect of the pyridinium moiety by aromatic protons decreased by increasing the polarity of solvent, and that pillar[5]arene shifted along the axle with the increase of polarity. Furthermore, when **P4** was dissolved in pure DMSO, no proton was found below 0 ppm, as well as the comparison between the ^{1}H NMR spectra of **P4** and **M5**, where the aliphatic protons have almost the same chemical shifts, proved that the self-interlocked structure was destroyed and shifted to an extended form (**Fig. 6 and Fig. S27**). Then $CDCl_3$, CD_3OD and DMSO (respective increased polarity) were used to study the shift effect of **P4**. The compound **P4** was dissolved in these three solvents to see the modification of the chemical shifts by ^{1}H NMR studies (**Fig. 7**). From the spectra of compound **P4**, we can see that the aromatic protons close to the pyridinium moiety shifted to lower magnetic field by increasing the polarity of solvent. Furthermore, proton H9 and some protons of the axle shifted to higher magnetic field in CD_3OD and then shifted to lower magnetic field in DMSO. All of these phenomena indicated that **P4** shifted along the axle with the increase of polarity of solvent until reaching an extended state in DMSO, which led us to conclude to the successful preparation of a new dynamic molecular machine. The self-inclusion is entropically more favorable but the disruption of the cation-π interactions extended the structure. In fact, the solvent responsive feature is dependent on the polarity of the solvent, which can modulate the cation-π interactions between the cavity of the macrocycle and the pyridinium moiety. The lower polarity of $CDCl_3$ promotes the cation-π interactions and the localization of the pyridinium moiety inside the cavity. The increase of polarity disrupts this interaction leading to a progressive dethreading of the macrocycle from the axle into an extended form once we used DMSO.



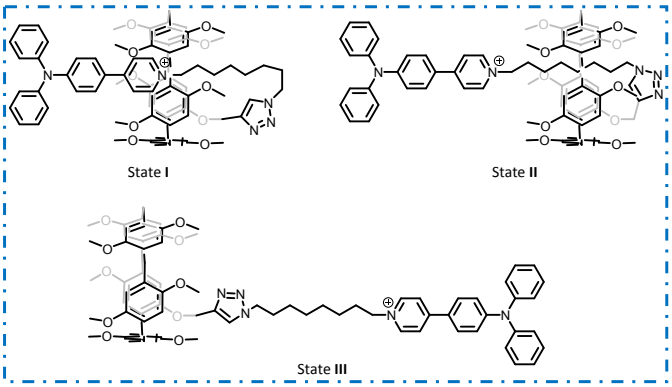


Fig. 7 ^{1}H NMR spectra comparison of compound **P4** by increasing the polarity of solvents: these NMR comparisons helped us to propose different possible conformations for

compound **P4**: $CDCl_3$ (State I), CD_3OD (State II) and DMSO (State III)).

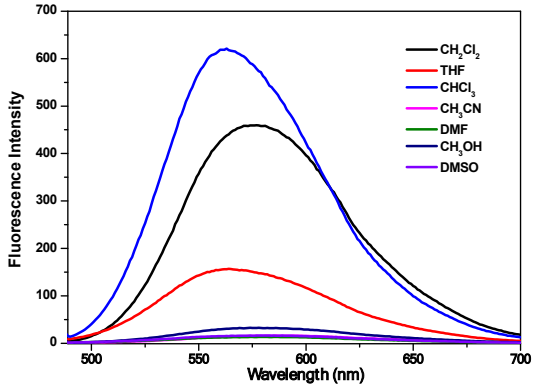


Fig. 8 Fluorescence spectroscopy of compound **P4** in different solvents.

As triphenylamine is a fluorescent molecule with aggregation induced enhanced emission effect, we performed fluorescent spectroscopy studies of compound **P4** by dissolving it in different solvents (CH_2Cl_2, THF, $CHCl_3$, CH_3CN, DMF, CH_3OH, DMSO). From **Fig. 8**, we can see that the emission peak of triphenylamine derivate is around 550 nm and the fluorescent intensity decreased with the increase of polarity of solvent; it can be noticed that the host-guest interactions were enhanced in $CDCl_3$ coupled with a reduction of intramolecular vibrations leading to a fluorescent enhancement. The host-guest interactions which were weakened by the increase of the polarity of solvent and intramolecular vibrations led to the decrease of the fluorescence intensity. These results suggested that this molecular machine is responsive to the polarity of solvents.

Conclusions

In summary, we synthesized a new pillar[5]arene-based molecular machine. This molecular machine can undergo into different self-interlocked structures in $CDCl_3$ and CD_3OD, and in an extended form in DMSO. This new [1]rotaxane solvent-responsive molecular machine was made with a new synthetic route. This machine will be useful for the construction of new stimuli responsive smart materials with applications in biology and material science.

Notes and references

1. J.-M. Lehn, *Science*, 1993, **260**, 1762-1764.
2. B. Zheng, F. Wang, S. Dong and F. Huang, *Chem. Soc. Rev.*, 2012, **41**, 1621-1636.
3. A. Harada, *Acc. Chem. Res.*, 2001, **34**, 456-464.
4. T. Pierro, C. Gaeta, C. Talotta, A. Casapullo and P. Neri, *Org. Lett.*, 2011, **13**, 2650-2653.
5. P. J. Cragg, *Isr. J. Chem.*, 2018, **58**, 1194-1208.
6. J. Sun, B. Hua, Q. Li, J. Zhou and J. Yang, *Org. Lett.*, 2018, **20**, 365-368.
7. F. Zhang, J. Ma, Y. Sun, Y. Mei, X. Chen, W. Wang and H. Li, *Anal. Chem.*, 2018, **90**, 8270-8275.
8. T. Ogoshi, T. Furuta, Y. Hamada, T. Kakuta and T. Yamagishi, *Materials Chemistry Frontiers*, 2018, **2**, 597-602.
9. X. Q. Wang, W. Wang, W. J. Li, L. J. Chen, R. Yao, G. Q. Yin, Y. X. Wang, Y. Zhang, J. Huang, H. Tan, Y. Yu, X. Li, L. Xu and H. B. Yang, *Nature communications*, 2018, **9**, 3190.
10. Y. Wang, Y. Tian, Y. Z. Chen, L. Y. Niu, L. Z. Wu, C. H. Tung, Q. Z. Yang and R. Boulatov, *Chem Commun (Camb)*, 2018.
11. J.-C. Chang, S.-H. Tseng, C.-C. Lai, Y.-H. Liu, S.-M. Peng and S.-H. Chiu, *Nature Chemistry*, 2016, **9**, 128-134.
12. R. Da Silva Rodrigues and K. M. Mullen, *ChemPlusChem*, 2017, **82**, 814-825.
13. J. F. Stoddart, *Angew. Chem. Int. Ed. Engl.*, 2017, **56**, 11094-11125.
14. M. Cheng, Q. Wang, Y. Cao, Y. Pan, Z. Yang, J. Jiang and L. Wang, *Tetrahedron Lett.*, 2016, **57**, 4133-4137.
15. C. J. Bruns and J. F. Stoddart, *Acc. Chem. Res.*, 2014, **47**, 2186-2199.
16. A. Goujon, T. Lang, G. Mariani, E. Moulin, G. Fuks, J. Raya, E. Buhler and N. Giuseppone, *J. Am. Chem. Soc.*, 2017, **139**, 14825-14828.
17. K. Yang, S. Chao, F. Zhang, Y. Pei and Z. Pei, *Chem. Commun.*, 2019, **55**, 13198-13210.
18. K. Kitajima, T. Ogoshi and T. A. Yamagishi, *Chem Commun (Camb)*, 2014, **50**, 2925-2927.
19. S. Mena-Hernando and E. M. Pérez, *Chem. Soc. Rev.*, 2019, **48**, 5016-5032.
20. D. A. Leigh, L. Pirvu and F. Schaufelberger, *J. Am. Chem. Soc.*, 2019, **141**, 6054-6059.
21. J. Zhong, L. Zhang, D. P. August, G. F. S. Whitehead and D. A. Leigh, *J. Am. Chem. Soc.*, 2019, **141**, 14249-14256.
22. W. Yang, Y. Li, H. Liu, L. Chi and Y. Li, *Small*, 2012, **8**, 504-516.
23. Q. Hao, Y. Chen, Z. Huang, J. F. Xu, Z. Sun and X. Zhang, *ACS applied materials & interfaces*, 2018, **10**, 5365-5372.
24. S. Guo, Y. Song, Y. He, X. Y. Hu and L. Wang, *Angew. Chem. Int. Ed. Engl.*, 2018, **57**, 3163-3167.
25. C.-W. Chiu, C.-C. Lai and S.-H. Chiu, *J. Am. Chem. Soc.*, 2007, **129**, 3500-3501.
26. S. Chen, Y. Wang, T. Nie, C. Bao, C. Wang, T. Xu, Q. Lin, D.-H. Qu, X. Gong, Y. Yang, L. Zhu and H. Tian, *J. Am. Chem. Soc.*, 2018, **140**, 17992-17998.
27. G. De Bo, M. A. Y. Gall, S. Kuschel, J. De Winter, P. Gerbaux and D. A. Leigh, *Nature Nanotechnology*, 2018, **13**, 381-385.
28. M. Kimura, T. Mizuno, M. Ueda, S. Miyagawa, T. Kawasaki and Y. Tokunaga, *Chemistry, an Asian journal*, 2017, **12**, 1381-1390.
29. H. Tian, C. Wang, P.-H. Lin and K. Meguellati, *Tetrahedron Lett.*, 2018, **59**, 3416-3422.
30. B. Y. Xia, B. Zheng, C. Y. Han, S. Y. Dong, M. M. Zhang, B. J. Hu, Y. H. Yu and F. H. Huang, *Polymer Chemistry*, 2013, **4**, 2019-2024.
31. T. Ogoshi, T. A. Yamagishi and Y. Nakamoto, *Chem. Rev.*, 2016, **116**, 7937-8002.
32. N. L. Strutt, R. S. Forgan, J. M. Spruell, Y. Y. Botros and J. F. Stoddart, *J. Am. Chem. Soc.*, 2011, **133**, 5668-5671.

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DOI: 10.1039/D0NJ01859G

33. Q. Zhao, Y. Chen, B. Sun, C. Qian, M. Cheng, J. Jiang, C. Lin and L. Wang, *Eur. J. Org. Chem.*, 2019, **2019**, 3396-3400.
34. Y. Yao, Y. Wang, R. Zhao, L. Shao, R. Tang and F. Huang, *Journal of Materials Chemistry B*, 2016, **4**, 2691-2696.
35. B. Hua, L. Shao, Z. Zhang, J. Liu and F. Huang, *J. Am. Chem. Soc.*, 2019, **141**, 15008-15012.
36. X.-W. Guan, Q. Lin, Y.-M. Zhang, T.-B. Wei, J. Wang, Y.-Q. Fan and H. Yao, *Soft matter*, 2019, **15**, 3241-3247.
37. X. Wang, J. Yang, X. Sun, H. Yu, F. Yan, K. Meguellati, Z. Cheng, H. Zhang and Y.-W. Yang, *Chem. Commun.*, 2018, **54**, 12990-12993.
38. Q. Lin, X.-M. Jiang, X.-Q. Ma, J. Liu, H. Yao, Y.-M. Zhang and T.-B. Wei, *Sensors and Actuators B: Chemical*, 2018, **272**, 139-145.
39. H. Li, W. Chen, F. Xu, X. Fan, T. Liang, X. Qi and W. Tian, *Macromol. Rapid Commun.*, 2018, **39**, 1800053.
40. X. J. Kuang, A. Wajahat, W. T. Gong, M. K. Dhinakaran, X. H. Li and G. L. Ning, *Soft matter*, 2017, **13**, 4074-4079.
41. T. Ogoshi, K. Demachi, K. Kitajima and T. A. Yamagishi, *Chem Commun (Camb)*, 2011, **47**, 7164-7166.
42. B. Xia and M. Xue, *Chem Commun (Camb)*, 2014, **50**, 1021-1023.
43. Y. Wang, Y. Tian, Y.-Z. Chen, L.-Y. Niu, L.-Z. Wu, C.-H. Tung, Q.-Z. Yang and R. Boulatov, *Chem. Commun.*, 2018, **54**, 7991-7994.
44. N. Sun, X. Xiao, W. Li and J. Jiang, *Advanced science*, 2015, **2**, 1500082.
45. H. Tian, C. Wang, H. Li, R. Deng, R. Li and K. Meguellati, *Eur. J. Org. Chem.*, 2019, **2019**, 2819-2823.