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ARTICLE TYPE

Intramolecular C–H...F hydrogen bonding-induced 1,2,3-triazole-based foldamers

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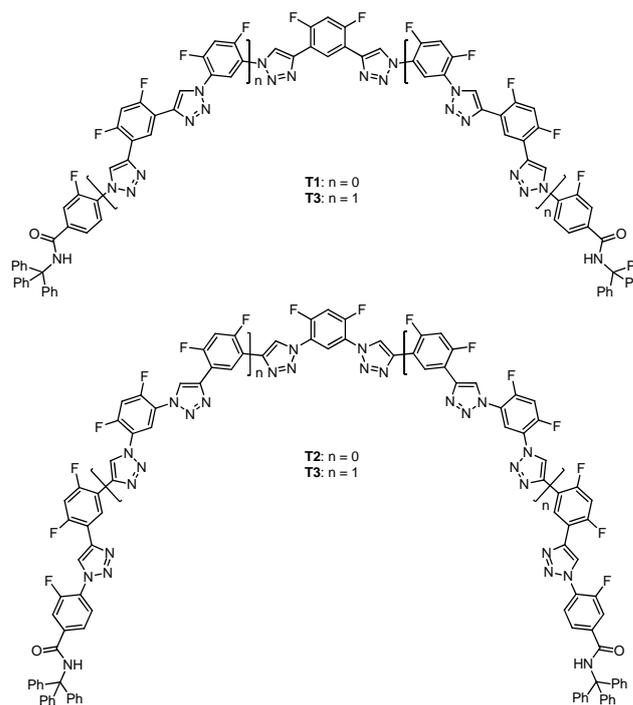
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This paper reports the first kind of artificial secondary structures that are induced by intermolecular C–H...F hydrogen bonding. Oligomers that contain two, four, six, and eight 1,2,3-triazole units have been designed and prepared by connecting the neighbouring 1,2,3-triazole units with 4,6-difluoro-*m*-phenylene linker(s). Two triphenylmethyl groups are appended at the ends of the backbones to suppress the stacking of the backbones and provide solubility. X-Ray analysis and ¹H NMR and two-dimensional ¹H-¹⁹F heteronuclear Overhauser enhancement spectroscopic (HOESY) experiments support that the 1,2,3-triazole backbones adopt folded or helical conformations due to the formation of continuous three-centred C–H...F hydrogen bonding. Quantum chemical calculations reveal that the longest 8-mer foldamer can form a one-turn helical cavity with a diameter of ca. 1.7 nm. Halide anion competition experiments show that the intramolecular C–H...F hydrogen bonding is more stable than the well-established intermolecular C–H...X⁻ (X = Cl and I) hydrogen bonding.

Introduction

In the last two decades, chemists have considerable interest in constructing foldamers, the artificial secondary structures that are stabilized by non-covalent interactions.^{1–3} Particularly, foldamers of aromatic backbones have found extensive applications as synthetic receptors for various molecules and ions.⁴ They are also useful preorganized frameworks for assembling advanced supramolecular architectures,⁵ facilitating the formation of macrocyclic and capsular structures,⁶ and developing new biologically active molecules.⁷ Due to its strength and directionality, hydrogen bonding has been most widely used to drive the formation of folded conformations for aromatic oligomers.³ In this context, oligomeric aromatic amides have been extensively investigated because of the structural diversity and modifiability of the aromatic segments and the high ability of the amide unit to serve as hydrogen bonding donor.^{3,8} In most cases, the folding of the backbones is driven by strong intramolecular N–H...O or N–H...N hydrogen bonding.³ However, N–H...F or N–H...Cl hydrogen bonding has also been demonstrated to realize this process.^{8c,9–11}



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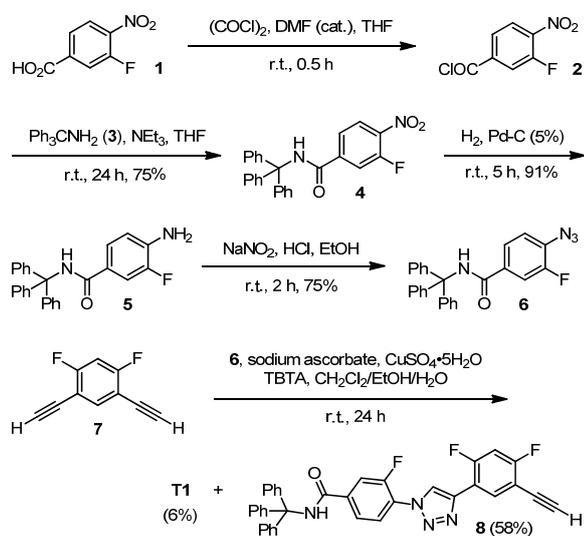
† Electronic Supplementary Information (ESI) available: Synthesis and characterization of new compounds, calculation details, crystal data, ¹H, ¹⁹F and ¹³C NMR spectra, and additional 2D ¹H NOESY and ¹H-¹⁹F HOESY NMR spectra. See DOI: 10.1039/b000000x/

Due to its planarity and strong dipole moment, the 1,2,3-triazole functions bear a physicochemical resemblance to the amide bond. One such function is its ability for acting as both hydrogen bonding donor and acceptor.^{12,13} Since 2008, several groups have reported that 1,2,3-triazole oligomers can complex

chloride anion by forming multiple C–H...Cl⁻ hydrogen bonds.¹⁴⁻¹⁷ It was also demonstrated that intrinsically disordered 1,2,3-triazole oligomers can be induced to fold into helical conformations by solvophobicity.¹⁸ We recently reported that intramolecular C–H...OR hydrogen bonding can induce 1,2,3-triazole oligomers to form folded or helical secondary structures.¹⁹ To explore the application of the recently established intramolecular C–H...F hydrogen bonding motif,²⁰ we have prepared oligomers **T1–T4**, which contains two, four, six, or eight 1,2,3-triazole units. We herein describe that these oligomers can form continuous intramolecular three-centred C–H...F hydrogen bonding to drive the backbones to produce stable foldamers, which, to the best of our knowledge, represent the first series of artificial secondary structures that are stabilized by the C–H hydrogen bonding.

Results and discussion

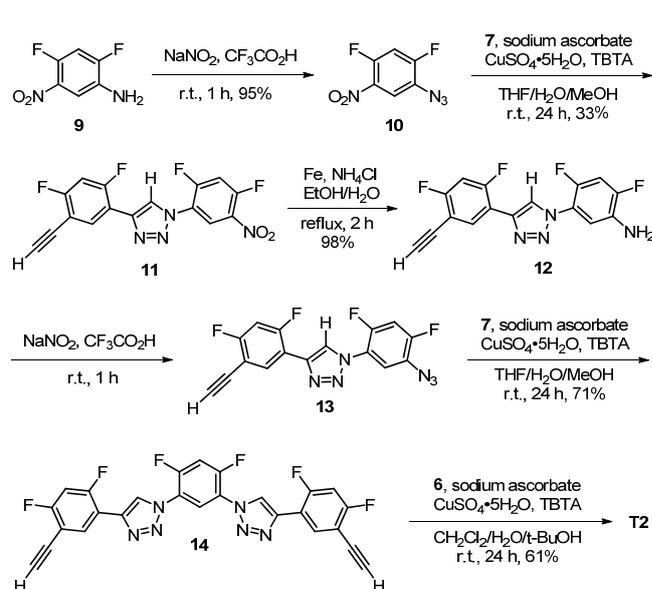
Because the newly designed 1,2,3-triazole backbones bear no flexible chains, two bulky triphenylmethyl groups were appended at the ends of the backbones to suppress their stacking and provide solubility in organic solvents. The synthetic route for 2-mer **T1** is shown in Scheme 1. Thus, acid **1** was first treated with oxalyl chloride to afford acyl chloride **2**, which then reacted with amine **3** to produce **4**. This nitro derivative underwent Pd-catalyzed hydrogenation to give amine **5**, which was treated with sodium nitrite in hydrochloric acid to produce azide **6**. Finally, the “click” 1,3-cycloaddition reaction of **6** with diacetylene **7** afforded both **T1** and **8**.



Scheme 1. The synthesis of compounds **T1** and **8**.

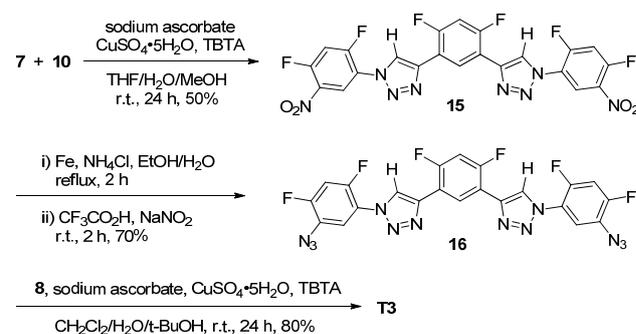
For the synthesis of 4-mer **T2** (Scheme 2), amine **9** was first converted to azide **10** by treating with sodium nitrite in trifluoroacetic acid (TFA). The azide was then reacted with **7** to afford triazole derivative **11**, which was further reduced with iron and ammonium chloride in aqueous ethanol to give amine **12**. The amine was then reacted with sodium nitrite in TFA to produce azide **13**. The 1,3-cycloaddition of **13** with excess of **7**

afforded diacetylene **14**. Compound **T2** was finally prepared from its reaction with azide **6**.



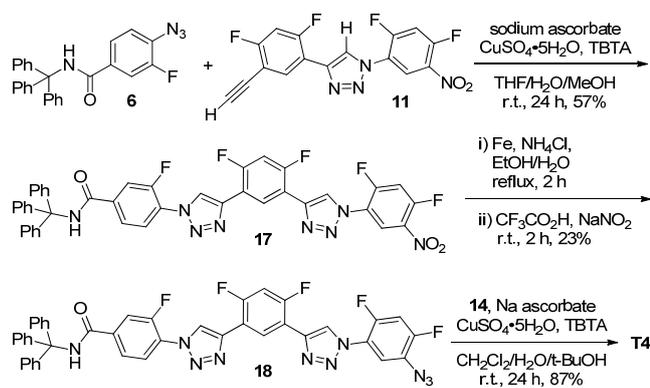
Scheme 2. The synthesis of compound **T2**.

Scheme 3 provides the synthetic route for 6-mer **T3**. Compound **15** was first prepared from the 1,3-cycloaddition reaction of compounds **7** and **10**. The dinitro derivative was then reduced with iron and ammonium chloride by refluxing in aqueous ethanol to afford diamine **16**, which was further converted into diazide **16** by being treated with sodium nitrite in TFA. Finally, this precursor was reacted with acetylene **8** to afford compound **T3**.



Scheme 3. The synthesis of compound **T3**.

The synthetic route of 8-mer **T4** is shown in Scheme 4. Compound **17** was first prepared from the 1,3-cycloaddition reaction of **6** and **11** and then reduced to the corresponding amine **17** by iron and ammonium chloride in aqueous ethanol. The amine intermediate was further treated with sodium nitrite in TFA to afford azide **18**. Further 1,3-cycloaddition reaction of **18** with diacetylene **14** gave rise to **T4**.



Scheme 4. The synthesis of compound **T4**.

The crystal structures of compounds **8** and **11** were obtained. In the crystal, compound **8** existed in two conformers. For both conformers, the C²-H atom of the 1,2,3-triazole ring was involved in three-centred C–H...F hydrogen bonding. The structures of the two conformers are provided in Fig 1a. For one conformer, the CH...F distances were 2.32 and 2.27 Å, respectively. For another conformer, the distances were 2.38 and 2.28 Å, respectively. The crystal structure of compound **11** is shown in Fig 1b, which shows that this compound also formed the similar three-centred C–H...F hydrogen bonding, and the CH...F distances were 2.42 and 2.34 Å, respectively. All these values are considerably shorter than the sum (2.67 Å) of the van der Waals radius of the F and H atoms, supporting the stability of this three-centred hydrogen bonding motif.

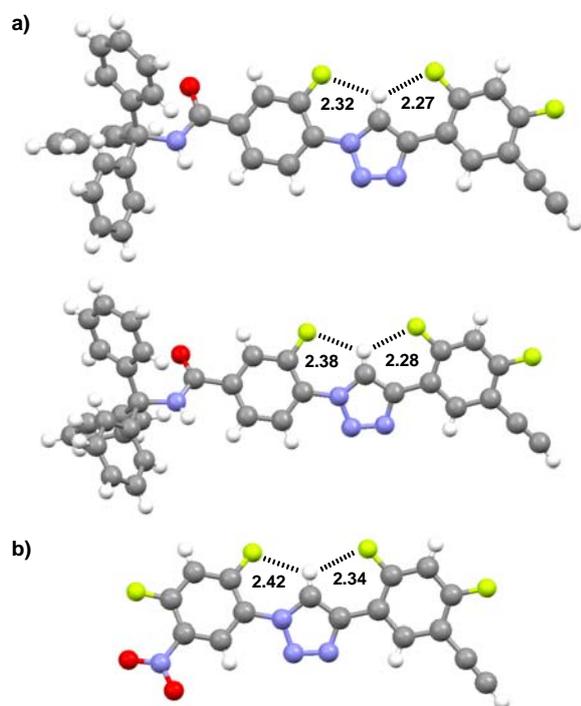


Fig 1 The crystal structures of compounds **8** (two conformers, CCDC 986427) and **11** (CCDC 986426), highlighting the formation of the three-centred C–H...F hydrogen bonding.

The ¹H NMR spectrum of compounds **8** and **11** in CDCl₃ displayed a dd signal for the C²-H atoms. For compound **8**, the coupling constant (*J*) was 3.1 Hz, and for compound **11**, the coupling constants were 2.7 and 3.2 Hz, respectively. The splitting should be attributed to the proximity of the two F atoms at the *ortho*-position of the two attached benzene rings.^{9a} This through-space coupling also supported that the C²-H atoms were engaged in three-centred C–H...F hydrogen bonding. The fact that compound **8** gave rise to a triplet implied that the two F atoms approached the C²-H atom to a very comparable extent. Similar triplets were also observed for **17**. Adding DMSO-*d*₆ caused the signals to coalesce into singlets, reflecting that the hydrogen bonding was weakened or destroyed in the highly polar solvent. Compounds **T1**, **T2**, **T3**, and **14** also displayed splitting for the signals of their C²-H atoms. However, coupling constants could not be obtained due to signal overlapping or broadening.

The signals of the H atoms on the difluorobenzene rings of the triazole oligomers were also split by the neighbouring F atoms. However, these split signals did not coalesce into singlets in DMSO-*d*₆. For **T2** and **T3**, the continuous three-centred hydrogen bonding should force their backbones to form folded conformations (*vide infra*). Considering the similarity of the backbones, the longest oligomer **T4** should also form similar three-centred C–H...F hydrogen bonding. The ¹H NMR spectrum of **T4**, however, displayed broad signals of low resolution. This result suggested that a helical conformation should be formed, which might undergo intramolecular stacking and P/M conformational exchange to lead to the decrease of the resolution of the ¹H NMR spectrum. The ¹H NMR spectrum in DMSO-*d*₆ is of high resolution (ESI), indicating of the formation of a flexible conformation due to the breaking of the C–H...F hydrogen bonding in a highly polar medium.

The two-dimensional (2D) ¹H-¹⁹F heteronuclear Overhauser enhancement spectroscopy (HOESY) is a robust technique which allows for the detection of through-space NOE connectivity between non-bonded H and F nuclei.²¹ Thus, systematic HOESY experiments were performed in chloroform-*d* to characterize the folded conformations of the new series of triazole derivatives. The 2D HOESY spectra of compounds **8** and **11** were first recorded and are provided in Fig 2. For both compounds, intramolecular NOE contacts were observed between the triazole C²-H atom and the neighbouring F-2 and F-3 atoms, supporting the formation of the intramolecular three-centred C–H...F hydrogen bonding. In DMSO-*d*₆, similar contacts were not observed, indicating that the hydrogen bonding was weakened or destroyed in this highly polar solvent. In principle, the electrostatic repulsions between the N-2 and N-3 atoms of the 1,2,3-triazole ring and the two adjacent F atoms and the intrinsic co-planarity of the 1,4-diphenyl-1,2,3-triazole backbone should also facilitate the formation of the two NOE contacts. However, the above results indicate that the intramolecular three-centred C–H...F hydrogen bonding should play a key role in driving the formation of the NOE contacts, as supported by the DFT calculation for the torsion energies (Fig 6, *vide infra*). The 2D NOESY spectrum of compound **8** (40 mM) in CDCl₃ was also recorded (ESI), which did not exhibit any NOE contact between H-2 and H-4 or H-5, which further supports that the hydrogen bonded conformation existed exclusively.

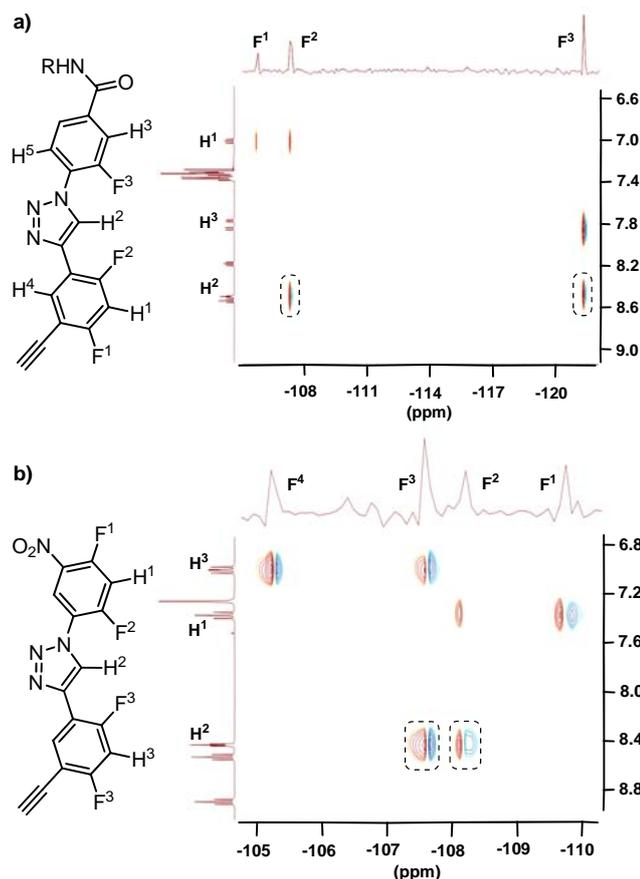


Fig 2 2D ^1H - ^{19}F HOESY spectra (500 MHz) of compounds **8** (a) and **11** (b) in CDCl_3 (5 mM), highlighting the heteronuclear NOE contacts in the dashed boxes.

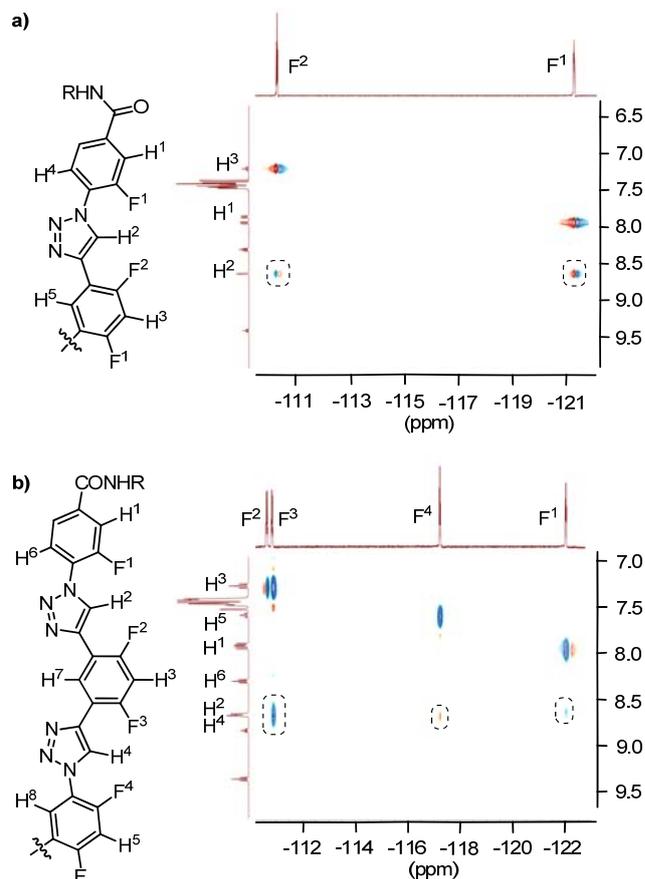


Fig 3 2D ^1H - ^{19}F HOESY spectra (500 MHz) of compounds **T1** (a) and **T2** (b) in CDCl_3 (5 mM), highlighting the heteronuclear NOE contacts in the dashed boxes.

The 2D ^1H - ^{19}F HOESY spectra of oligomers **T1** and **T2** in CDCl_3 also exhibited similar NOE contacts between the C^2 -H atom(s) of the triazole unit(s) and the F atoms on the connected benzene rings (Fig 3). Similar heteronuclear NOEs were also observed for compound **17** (ESI), which may be considered as half of **T2** by the structures. In highly polar DMSO-d_6 , no such NOE contacts were observed. In addition, the ^1H NOESY spectra of **T1** and **T2** in CDCl_3 did not exhibit NOE connects between the triazole C^2 -H atoms and the H atoms at the *ortho* positions of the connected benzene rings (ESI). These results indicated that, similar to the short compounds **8** and **11**, the two oligomers also formed stable intramolecular three-centred $\text{C-H}\cdots\text{F}$ hydrogen bonding in CDCl_3 .

The HOESY spectrum of 6-mer **T3** in CDCl_3 is shown in Fig 4. The ^{19}F signals were identified by comparing the spectrum with those of shorter analogues. Although due to overlapping, the signals of the F-2, F-3, and F-6 atoms could not be assigned completely, the signals of all the six F atoms exhibited the expected NOE contacts with the C^2 -H atoms of the triazole rings. The HOESY spectrum of **T4** in CDCl_3 was not recorded due to the low resolution of its ^1H NMR spectrum. However, considering all the oligomers possess the same backbones, it is reasonable to propose that it also formed the similar continuous intramolecular $\text{C-H}\cdots\text{F}$ hydrogen bonding.

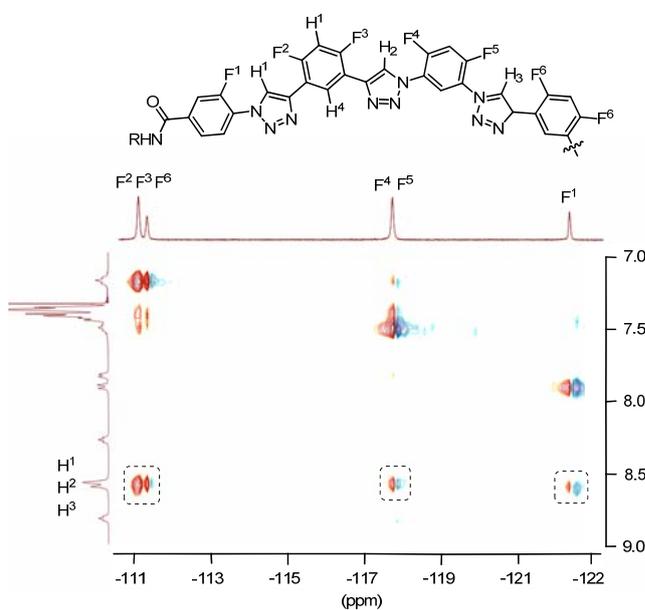


Fig 4 2D ^1H - ^{19}F HOESY spectra (500 MHz) of compound **T3** in CDCl_3 (4 mM), highlighting the heteronuclear NOE contacts in the dashed boxes.

The lowest-energy conformations of the 1,2,3-triazole oligomers were also optimized with the M062X/6-31G(d,p) calculation method,²² using the GAUSSIAN09 program. The obtained lowest-energy conformations of **T2**, **T3** and **T4** are provided in Fig 5. As expected, **T2** and **T3** formed a crescent cavity, while the longest **T4** could form one turn with the diameter of the cavity being about 1.7 nm, although the two appended bulky triphenylmethyl groups forced the 1,2,3-triazole backbone to twist considerably.

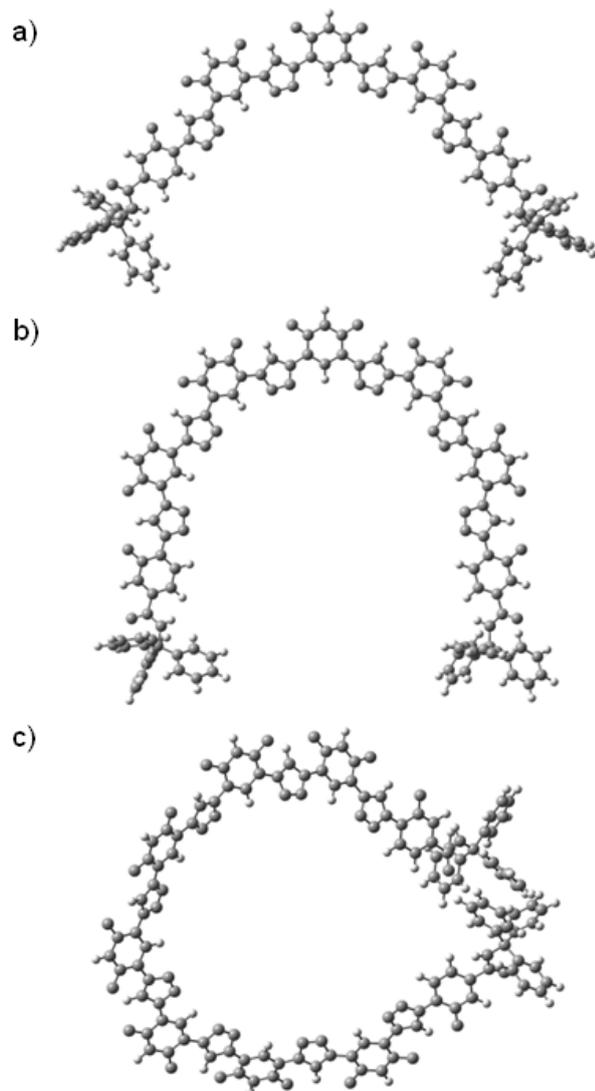


Fig 5 The optimized conformers of oligomers a) **T2**, b) **T3**, and c) **T4**, calculated in chloroform with Gaussian 09 package using 6-31G(d,p) basis set.

DFT calculations were further performed for compound **T1** to obtain the energy difference between different conformers.^{20b} The conformers were produced by changing the torsions between one of the two triazole rings and the two connected benzene rings, while constraining another triazole ring to be co-planar with the connected benzene rings (Fig 6). It can be found that, for both

cases, the conformer at the torsion angle of 180° was of high-energy, which may be attributed to the electrostatic repulsion between the fluorine atoms and the nitrogen atoms of the triazole. For both cases, the minimum-energy conformer was that with the connected benzene rings being closely co-planar with the triazole ring and the fluorine atoms pointing to the C²-H of triazole, even though, at the torsion angles of about 130° for CNCC and 140° for CCCC, there existed other low-energy conformers. These results should be used as evidence that it was the three-centred C-H...F hydrogen bonding that made the main contribution in stabilizing the minimum-energy conformation.

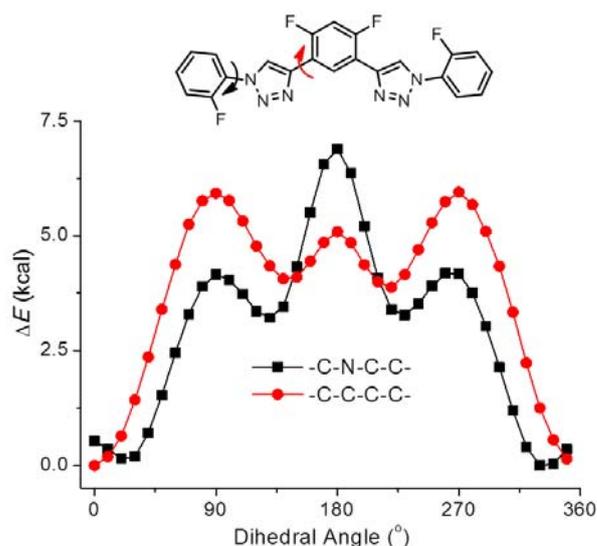


Fig 6 The torsion energies of compound **T1** for turning the two connected benzene rings out of the plane of one of the triazole units by incremental steps of 10°.

To further evaluate the stability of the intramolecular C-H...F hydrogen bonding, the ¹H and ¹⁹F NMR spectra of **T2** were recorded in CDCl₃ in the presence of an incremental amount of tetra(n-butyl)ammonium chloride or iodide (ESI). It was reported that *meta*-phenylene-connected 1,2,3-triazole tetramer can fold to complex chloride or iodide anion by forming four intermolecular C²-H...Cl⁻ or C²-H...I⁻ hydrogen bonds.¹⁵ It was found that, upon adding an excess of tetra(n-butyl)ammonium chloride (up to 140 equiv) or iodide (up to 110 equiv), the ¹H NMR signals of the C²-H atoms of **T2** did not exhibit discernible shifting. In the presence of more amounts of the salts, **T2** began to precipitate. These observations indicate that the folded conformation of **T2**, as shown in Fig 5a, was quite stable and chloride or iodide anion could not induce the backbone to overturn to form another folded state of smaller cavity. Although the electrostatic repulsion between the F atoms and the N-2 and N-3 atoms may play a role in stabilize the intramolecular C-H...F hydrogen bonding, the fact that the chemical shifting of the C²-H atoms did not undergo any change in the presence of an excess of chloride or iodide anion clearly supports the intrinsic stability of this intramolecular hydrogen bonding and the resulting folded secondary structure of this kind of 1,2,3-triazole oligomers.

Conclusions

In summary, we have demonstrated that intramolecular C–H...F hydrogen bonding can be utilized to induce conjugated 1,2,3-triazole oligomers to form folded or helical secondary structures. The stability of the C–H...F hydrogen bonding is higher than the well-established intermolecular C–H...F hydrogen bonding. As a result, the new folded secondary structures do not undergo a conformational overturn to produce another kind of folded structures of smaller cavity. Different from C–H...OR hydrogen bonding-driven folded systems, the new folded frameworks bear no side chains. Thus, both the F atoms and the N-2 and N-3 atoms of the triazole ring may serve as acceptors to further form intermolecular hydrogen bonding for the assembly of new interlocked architectures.

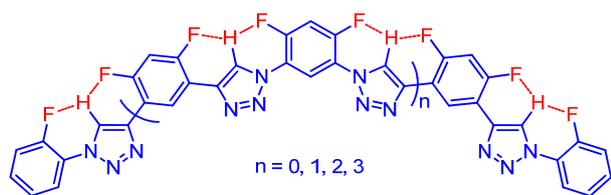
We thank National Natural Science Foundation (91227108 and 21228203) and Ministry of Science and Technology (2013CB834501) of China, and Science and Technology Commission of Shanghai Municipality (13NM1400200) for financial support.

Notes and references

- 1 S. Hecht and I. Huc, (Ed.) *Foldamers: Structure, Properties and Applications*. 431 pp, Wiley-VCH, Weinheim, 2007.
- 2 (a) S. H. Gellman, *Acc. Chem. Res.*, 1998, **31**, 173; (b) D. J. Hill, M. J. Mio, R. B. Prince, T. S. Hughes and J. S. Moore, *Chem. Rev.*, 2001, **101**, 3893; (c) R. P. Cheng, S. H. Gellman and W. F. DeGrado, *Chem. Rev.*, 2001, **101**, 3219; (d) X. Li and D. Yang, *Chem. Commun.*, 2006, 3367; (e) B.-B. Ni, Q. Yan, Y. Ma and D. Zhao, *Coord. Chem. Rev.*, 2010, **254**, 954; (f) H.-Y. Hu and C.-F. Chen, *Methods Mol. Biol.*, 2013, **932**, 219; (g) Y. Zhao, H. Cho, L. Widanapathirana and S. Zhang, *Acc. Chem. Res.*, 2013, **46**, 2763.
- 3 (a) B. Gong, *Chem. Eur. J.* 2001, **7**, 4337; (b) I. Huc, *Eur. J. Org. Chem.* 2004, 17; (c) Q. Gan, Y. Wang and H. Jiang, *Curr. Org. Chem.*, 2011, **15**, 1293; (d) A. Roy, P. Prabhakaran, P. K. Baruah and G. J. Sanjayan, *Chem. Commun.*, 2011, **47**, 11593; (e) D.-W. Zhang, X. Zhao, J.-L. Hou and Z.-T. Li, *Chem. Rev.*, 2012, **112**, 5271; Z. Shi, Y. Song, F. Lu, T. Zhou, X. Zhao, W. Zhang and Z. Li, *Huaxue Xuebao*, 2013, **71**, 51.
- 4 (a) Z.-T. Li, J.-L. Hou, C. Li and H.-P. Yi, *Chem. Asian J.*, 2006, **1**, 766; (b) H. Juwarker, J.-m. Suk and J.- Jeong, *Chem. Soc. Rev.*, 2009, **38**, 3316; (c) Y. Hua and A. H. Flood, *Chem. Soc. Rev.*, 2010, **39**, 1262.
- 5 (a) X. Zhao and Z.-T. Li, *Chem. Commun.*, 2010, **46**, 1601; (b) Q. Gan, Y. Wang and H. Jiang, *Curr. Org. Chem.*, 2011, **15**, 1293; (c) G. Guichard and I. Huc, *Chem. Commun.*, 2011, **47**, 5933; (d) P. Prabhakaran, G. Priya and G. J. Sanjayan, *Angew. Chem. Int. Ed.*, 2012, **51**, 4006.
- 6 (a) B. Gong, *Acc. Chem. Res.*, 2008, **41**, 1376; (b) H. Fu, Y. Liu and H. Zeng, *Chem. Commun.*, 2013, **49**, 4127; (c) W. Q. Ong and H. Zeng, *J. Inclusion Phenom. Macrocycl. Chem.*, 2013, **76**, 1; (d) Y. Yang, W. Feng, J. Hu, S. Zou, R. Gao, K. Yamato, M. Kline, Z. Cai, Y. Gao, Y. Wang, Y. Li, Y. Yang, L. Yuan, X. C. Zeng and B. Gong, *J. Am. Chem. Soc.*, 2011, **133**, 18590.
- 7 (a) C. M. Goodman, S. Choi, S. Shandler and W. F. DeGrado, *Nat. Chem. Biol.*, 2007, **3**, 252; (b) C. G. Cummings and A. D. Hamilton, *Curr. Opin. Chem. Biol.*, 2010, **14**, 341; (c) V. Azzarito, K. Long, N. S. Murphy and A. J. Wilson, *Nat. Chem.*, 2013, **5**, 161.
- 8 (a) H. Jiang, J.-M. Léger and I. Huc, *J. Am. Chem. Soc.*, 2003, **125**, 3448; (b) L. Yuan, H. Zeng, K. Yamato, A. R. Sanford, W. Feng, H. S. Atreya, D. K. Sukumaran, T. Szyperski and B. Gong, *J. Am. Chem. Soc.*, 2004, **126**, 16528; (c) Q. Gan, C. Bao, B. Kauffmann, A. Grélard, J. Xiang, S. Liu, I. Huc and H. Jiang, *Angew. Chem. Int. Ed.*, 2008, **47**, 1715; (d) Y. Yan, B. Qin, C. Ren, X. Chen, Y. K. Yip, R. Ye, D. Zhang, H. Su and H. Zeng, *J. Am. Chem. Soc.*, 2010, **132**, 5869; (e) V. V. E. Ramesh, G. Priya, A. S. Kotmale, R. G. Gonnade,

- 65 P. R. Rajamohan and G. J. Sanjayan, *Chem. Commun.*, 2012, **48**, 11205; (f) S. Zou, L. He, J. Zhang, Y. He, L. Yuan, L. Wu, J. Luo, Y. Wang and W. Feng, *Org. Lett.*, 2012, **14**, 3584; (g) C. Li, X. Zhao, X. Gao, Q. Wang and Z. Li, *Chin. J. Chem.*, 2013, **31**, 582.
- 9 (a) C. Li, S.-F. Ren, J.-L. Hou, H.-P. Yi, S.-Z. Zhu, X.-K. Jiang and Z.-T. Li, *Angew. Chem. Int. Ed.*, 2005, **44**, 5725; (b) C. Li, Y.-Y. Zhu, H.-P. Yi, C.-Z. Li, X.-K. Jiang and Z.-T. Li, *Chem. Eur. J.*, 2007, **13**, 9990.
- 10 Q. Gan, F. Li, G. Li, B. Kauffmann, J. Xiang, I. Huc and H. Jiang, *Chem. Commun.*, 2010, **46**, 297.
- 75 11 C. Ren, S. Xu, J. Xu, H. Chen and H. Zeng, *Org. Lett.*, 2011, **13**, 3840.
- 12 (a) J. M. Holub and K. Kirshenbaum, *Chem. Soc. Rev.*, 2010, **39**, 1325; (b) X. Li, *Chem. Asian J.*, 2011, **6**, 2606.
- 13 (a) Y. Hua, A. H. Flood, *Chem. Soc. Rev.*, 2010, **39**, 1262; (b) K. P. McDonald, Y. Hua, A. H. Flood, *Top. Heterocycl. Chem.*, 2012, **28**, 85.
- 14 R. M. Meudtner and S. Hecht, *Angew. Chem. Int. Ed.* 2008, **47**, 4926.
- 15 (a) H. Juwarker, J. M. Lenhardt, D. M. Pham and S. L. Craig, *Angew. Chem. Int. Ed.*, 2008, **47**, 3740; (b) H. Juwarker, J. M. Lenhardt, J. C. Castillo, E. Zhao, S. Krishnamurthy, R. M. Jamiolkowski, K.-H. Kim and S. L. Craig, *J. Org. Chem.* **2009**, **74**, 8924.
- 16 (a) Y. Wang, F. Bie and H. Jiang, *Org. Lett.*, 2010, **12**, 3630; (b) Y. Wang, J. Xiang and H. Jiang, *Chem. Eur. J.*, 2011, **17**, 613.
- 90 17 (a) Y. Hua and A. H. Flood, *J. Am. Chem. Soc.* **2010**, **132**, 12838; (b) K. P. McDonald, R. O. Ramabhadran, S. Lee, K. Raghavachari and A. H. Flood, *Org. Lett.*, 2011, **13**, 6260.
- 18 (a) Y. Wang, F. Li, Y. Han, F. Wang and H. Jiang, *Chem. Eur. J.*, 2009, **15**, 9424; (b) C.-F. Wu, Z.-M. Li, X.-N. Xu, Z.-X. Zhao, X. Zhao, R.-X. Wang and Z.-T. Li, *Chem. Eur. J.*, 2014, **20**, 1418.
- 19 L.-Y. You, S.-G. Chen, X. Zhao, Y. Liu, W.-X. Lan, Y. Zhang, H.-J. Lu, C.-Y. Cao and Z.-T. Li, *Angew. Chem. Int. Ed.*, 2012, **51**, 1657.
- 20 (a) D. Zornik, R. M. Meudtner, T. E. Malah, C. M. Thiele and S. Hecht, *Chem. Eur. J.*, 2011, **17**, 1473; (b) B.-Y. Lu, Y.-Y. Zhu, Z.-M. Li, X. Zhao and Z.-T. Li, *Tetrahedron*, 2012, **68**, 8857.
- 21 (a) C. Yu and G. C. Levy, *J. Am. Chem. Soc.*, 1984, **106**, 6533; (b) M. A. Hyland, M. D. Morton and C. Brückner, *J. Org. Chem.*, 2012, **77**, 3038.
- 105 22 Y. Zhao and D. G. Truhlar, *Theor. Chem. Acc.*, 2008, **120**, 215.

TOC



⁵ Intramolecular C-H...F hydrogen bonding has been utilized to induce 1,2,3-triazole oligomers to fold into stable artificial secondary structures.