MOLECULAR KNOTS

Topological molecular nanocarbons: All-benzene catenane and trefoil knot

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The generation of topologically complex nanocarbons can spur developments in science and technology. However, conventional synthetic routes to interlocked molecules require heteroatoms. We report the synthesis of catenanes and a molecular trefoil knot consisting solely of *para*-connected benzene rings. Characteristic fluorescence of a heterocatenane associated with fast energy transfer between two rings was observed, and the topological chirality of the all-benzene knot was confirmed by enantiomer separation and circular dichroism spectroscopy. The seemingly rigid all-benzene knot has rapid vortex-like motion in solution even at -95° C, resulting in averaged nuclear magnetic resonance signals for all hydrogen atoms. This interesting dynamic behavior of the knot was theoretically predicted and could stimulate deeper understanding and applications of these previously untapped classes of topological molecular nanocarbons.

arbon nanostructures such as fullerenes (1), carbon nanotubes (CNTs) (2), and graphene (3) and their partial molecular substructures (molecular nanocarbons) (4–9) have revolutionized the research fields of chemistry, physics, materials science, and nanoscience (Fig. 1A). Historically, these studies have shown that the emergence of distinct geometries and morphologies of carbon leads to the discovery of functions and applications that are not initially predicted nor expected (10-12). Currently, the known variations of nanocarbon structure are all topologically simple. There are numerous theoretically proposed nanocarbons with unexplored topologies, such as carbon nanotori (Fig. 1A) (*13–15*), nanocoils (*13–15*), and Mackay crystals (*16*). However, the lack of methods for creating such carbon topologies hampers the advancement of this field. In particular, mechanically interlocked molecules (MIMs) such as catenanes and molecular knots (*17–20*) are interesting motifs that provide heretofore unrealized topologies in the context of nanocarbon structures.

We report the synthesis of all-benzene catenanes **1a** and **1b** and trefoil knot **2** (Fig. 1B). These molecules are cycloparaphenylenes (CPPs) (7, 8) a class of molecular nanocarbon that comprises a sidewall segment structure of CNTs—with the topology of catenanes and trefoil knots. They retain the high symmetry and radial π -conjugation modes characteristic of CPPs, but also demonstrate distinctive intramolecular electronic interactions and dynamic motion. Geometrically, trefoil knots are in the class of torus knots (21),

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Fig. 1. Topological molecular nanocarbons. (A) Structures of fullerene, CNT, carbon nanotorus, and their segmental molecules (corannulene, CPP, and all-benzene trefoil knot). (B) Structures of all-benzene catenane 1a and all-benzene trefoil knot 2. (C and D) Strategy for the synthesis of all-benzene catenane (C) and the trefoil knot (D). F⁻, fluoride anion; ROH, alcohol.

which can be placed on the surface of a torus. As shown in Fig. 1A, the all-benzene trefoil knot **2** is a partial segment of a carbon nanotorus.

Conventionally, MIMs have been synthesized by using several types of reversible interactions such as metal–ligand coordination (22), electrostatic and π - π stacking interactions (23, 24), as well as hydrogen bonding (25). All-hydrocarbon structures have been left behind in the history of MIMs since the report on the synthesis of a cycloalkane catenane in 1983 (26), presumably because of the lack of an efficient synthetic method. In 2016, the existence of all-benzene catenanes and possibly trefoil knots was suggested from a detailed mass spectral analysis of a mixture of CPPs. However, results of further spectral or structural investigations were not reported, as individual components were diffi-

cult to isolate (27). Two recent reports of MIMs with nitrogen-containing CPP derivatives rely on the metal-ligand coordination strategy (28, 29). Thus, a distinct synthetic method to access allbenzene catenanes and knots is necessary to explore this exciting field. Our strategy (Fig. 1, C and D) drew inspiration from the known quantitative conversion of a spirobi(dibenzosilole) to two biphenyls upon treatment with fluoride in





(v) *n*-Bu₄NF, THF/EtOH. (vi) Sodium naphthalenide, THF, and then I₂. THF, tetrahydrofuran; cod, 1,5-cyclooctadiene; DMF, *N*,*N*-dimethylformamide; TMEDA, *N*,*N*,*N*',*N*'-tetramethylethylenediamine; pinB, 4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl.



Fig. 3. Structures and properties of all-benzene catenanes 1a and 1b.
(A and C) Oak Ridge thermal ellipsoid plot (ORTEP) drawings of 1a (A) and 1b (C) with thermal ellipsoids set to 50% probability. Hydrogen atoms and solvent molecules are omitted for clarity.
(B and D) Packing structures of 1a (B) and 1b (D); carbon: gray, blue, or green; hydrogen: white. Solvent molecules are omitted for clarity.



(**E**) Ultraviolet-visible absorption (solid lines) and fluorescence (dashed lines) spectra of the dichloromethane solutions of **1b**, [9]CPP, and [12]CPP. The fluorescence spectra were measured upon excitation at 340 nm for [12]CPP and [9]CPP or 360 nm for **1b**. (**F**) Hypothetical illustration of the fluorescence mechanism of **1b**. Orange color with asterisk (*) represents excited moieties. hv, light irradiation; FL, fluorescence.

first fraction



 $\frac{25 \circ C}{25 \circ C}$ $\frac{95 \circ C}{25 \circ C}$

Fig. 4. Structure and properties of all-benzene knot 2. (A) ORTEP drawing of **2** with thermal ellipsoids set to 50% probability. Hydrogen atoms and solvent molecules are omitted for clarity. (**B**) Packing structures of **2**; carbon: gray or orange; hydrogen: white. Solvent molecules are omitted for clarity.

(C) CD spectra of the enantiomers of 2 and their assignment. (D) ¹H-NMR spectra of **1a**, 2, and [12]CPP in CD₂Cl₂ at 25°C and -95°C. (E) Snapshots of the DFTB-MD simulation of 2 (carbon: gray or orange; hydrogen: white). See the supplementary materials and methods and movie S1 for details.

ethanol (*30*). We envisioned that the spirosilane moiety could similarly be used as a traceless template for the synthesis of all-benzene catenanes and trefoil knots, which would contain no remnants of it.

The synthetic route to [12]CPP-based [2] catenane (1a) is shown in Fig. 2A. According to the synthetic protocol reported by Jasti and colleagues (31), dialkoxycyclohexadiene moieties were selected as bent paraphenylene precursors, whereas n-butoxy groups were used instead of methoxy groups to increase the solubility of the intermediates. The starting material, 2,2'dibromo-4,4'-diiodobiphenyl (3), was converted into a dibrominated U-shaped unit 4a in four steps that included an iodo-selective lithiation, a nucleophilic addition to a *p*-quinone derivative, a nucleophilic addition of *p*-halolithiobenzenes, and an *n*-butylation of the resulting hydroxy groups. A Suzuki-Miyaura coupling of 4a and L-shaped unit 5, which bears chloro and boryl groups (31), took place selectively at the iodo moieties of 4a to form C-shaped unit 6a in moderate yield. For the formation of spirosilane 7a, conventional reaction conditions (dilithiation with *n*-BuLi, followed by spirosilylation with SiCl₄) were not applicable because of the high Lewis acidity of SiCl₄, which reacts quickly with the *n*-butoxy moieties. After screening the reaction conditions using a model reaction (compare table S1), we discovered that the complex of SiHCl₃ and TMEDA (*N*,*N*,*N*,*N*'-tetramethylethylenediamine) (32) was suitable for this spirosilylation step. Sequential lithiation of **6a** and addition of SiHCl₃ and TMEDA afforded spirosilane 7a in 57% vield.

Catenane 1a was synthesized from 7a in three steps including a Ni(0)-mediated intramolecular aryl-aryl coupling reaction at the C-Cl moieties, a fluoride-mediated desilylation, and a reductive aromatization of the dialkoxycyclohexadiene units (Fig. 2A). As a result, the desired catenane 1a was isolated in 16% yield (9.0 mg) from 7a by column chromatography and preparative thinlayer chromatography (PTLC), along with the generation of pristine [12]CPP (14% yield, 8.0 mg). Although intermediates were neither isolated nor characterized, precursors 8a and 9a were expected to be generated from the aryl-aryl coupling step and the desilylation step, respectively (see fig. S1 for the plausible intermediate of [12] CPP). The ¹H-nuclear magnetic resonance (NMR) spectrum of 1a in CD₂Cl₂ showed a singlet peak at 7.35 parts per million (ppm), which indicates fast mutual rotation of the two [12]CPP components of **1a** in solution.

By applying this strategy, the all-benzene catenanes consisting of two different-sized rings could also be synthesized (Fig. 2B). Starting from C-shaped unit **6b** in addition to **6a**, heterospirosilylation successfully occurred to furnish **7b** in 41% yield together with relatively small amounts of the homo-spirosilylation products **7a** and **7c**, which is a possible precursor for [9]CPP catenane. The thus-obtained hetero-spirosilane **7b** was converted into [9]CPP-[12]CPP heterocatenane **1b** in 1.5% yield (2.0 mg) by sequential homocoupling

reaction, desilylation, and reductive aromatization reactions. The ¹H-NMR signals of **1b** in CD₂Cl₂ were observed at 7.29 and 7.38 ppm, with the integral ratio of 9:12 indicating 1:1 catenated structure of [9]CPP and [12]CPP in **1b**.

The catenated structures of ${\bf 1a}$ and ${\bf 1b}$ were confirmed by x-ray crystallography (Fig. 3, A and C). In the solid state, catenanes 1a and 1b stack in one dimension to form void channels (Fig. 3, B and D), wherein solvent molecules used for recrystallization (hexane and chloroform for 1a and 1,4-dioxane and chloroform for **1b**) were incorporated. Intramolecular π - π interactions are evident, with the C-C distance of the nonbonding benzene rings ~3.4 to 3.6 Å (see fig. S2 for details). Absorption and fluorescence measurements of 1b (Fig. 3E) revealed unusual features of this heterocatenane compared with [9]CPP and [12]CPP as reference molecules (33). The fluorescence spectrum of **1b** is almost identical to that of [9]CPP without any trace of the fluorescence peaks that originated from [12]CPP, whereas the absorption spectrum of **1b** is the simple combination of those of [9]CPP and [12]CPP. The fluorescence lifetime of 1b (10.9 ns) is also similar to that of [9]CPP (10.6 ns) (33). Judging from the fact that the solution of the mixture of [9]CPP and [12]CPP shows the fluorescence peaks of both [9]CPP and [12]CPP (fig. S4), the complete fluorescence quenching of the [12]CPP moiety in 1b seems to be a consequence of the catenated structure. As depicted in Fig. 3F, fast energy transfer from the excited [12]CPP moiety to the [9]CPP moiety in **1b** would account for these observations (fig. S5). This result clearly demonstrates the effect of the catenated structure on the photophysical properties of fully conjugated rings, in that catenation is the only way to connect the all-benzene rings without breaking their high symmetry.

We hypothesized that our traceless synthetic strategy could be extended to the generation of an even more challenging, all-benzene trefoil knot 2, as shown in Fig. 1C. Inspired by the report of Dietrich-Buchecker and Sauvage, who constructed the trefoil-knot-type topology using two phenanthroline-Cu moieties as template units (34), we designed 11 (Fig. 2C) as the key intermediate, in which a loop consisting of 16 paraphenylenes and 8 cyclohexadiene-diyl units is knotted through two spirosilane joints. As the key intermediate 11 was a dimerized product of spirosilane 10, we started with the synthesis of 10. The U-shaped unit 4c was lithiated and silylated under the aforementioned conditions (SiHCl₃ and TMEDA) to afford **10** in 86% yield. In a manner similar to the synthesis of **1a** and 1b, 10 was subjected to a sequence of Ni(0)mediated aryl-aryl coupling, desilylation, and reductive aromatization without isolating the intermediates. Fortunately, after extensive chromatographic separation of the crude mixture, the all-benzene trefoil knot 2 was isolated by PTLC and preparative high-performance liquid chromatography (HPLC) in 0.3% yield (0.8 mg), along with [12]CPP (17.3 mg, 6.1%) and 1a (0.5 mg, 0.2%; see fig. S1 for the plausible intermediate of **1a** from **10**).

Single crystals of 2 were obtained from a hexane and 1,2-dichloroethane solution of 2, and x-ray crystallography unambiguously corroborated the trefoil-knot structure (Fig. 4A). Similar to **1a** and **1b**, intramolecular π - π stacking was observed (see the supplementary materials for details). Trefoil knot 2 is chiral, and both enantiomers (gray and orange) were incorporated in a 1:1 ratio in the crystal (Fig. 4B). Separation of the enantiomers of **2** was achieved by chiral HPLC, and the circular dichroism (CD) spectra of both enantiomers were successfully recorded. Judging from the simulated CD spectra by density functional theory (DFT) calculations, the first and second HPLC fractions could be assigned to the left-handed (-) and right-handed (+) (35) trefoil-knot structures, respectively (Fig. 4C).

The seemingly rigid knot 2 was demonstrated to have rapid dynamic motion in solution. The ¹H-NMR spectrum for **2** in CD_2Cl_2 exhibited a sharp singlet at room temperature (7.14 ppm), and even at -95°C, a slightly broadened peak was present, similar to those of 1a and [12]CPP (Fig. 4D). This result clearly indicates that all benzene rings of 2 were equivalent on the NMR time scale even at -95°C because of the rapid dynamic motion of the molecule (see fig. S7 for simulated NMR spectra). The dynamic behavior of 2 was simulated by density-functional tightbinding (DFTB) with molecular dynamics (MD) methods. In this simulation, we observed the intrinsic dynamics whereby the paraphenylene chains of **2** coil around a thin torus like the typical motion of trefoil-knot vortices (36). Because this dynamic motion seamlessly shifts the benzene rings (orange in Fig. 4E) from the undercrossing to the overcrossing regions of the knot (see movie S1), it plausibly accounts for the averaged NMR signals of 2.

These catenane and trefoil-knot molecules represent the cornerstone objects for topological molecular nanocarbons. The properties of these π -conjugated molecules raise further scientific questions such as how the structural features (size, components, substituents) affect their dynamic motions, physical properties, π -conjugation, and optoelectronic properties. We anticipate that this traceless synthetic method will generate a broader variety of topological molecular nanocarbons and open the door to expanded research areas in nanocarbon science.

REFERENCES AND NOTES

- H. W. Kroto, J. R. Heath, S. C. O'Brien, R. F. Curl, R. E. Smalley, Nature **318**, 162–163 (1985).
- 2. S. lijima, Nature **354**, 56–58 (1991).
- K. S. Novoselov et al., Science 306, 666–669 (2004).
 W.F. Barth, R.G. Lawton, J. Am. Chem. Soc. 88, 380–381.
- W. E. Barth, R. G. Lawton, J. Am. Chem. Soc. 88, 380–381 (1966).
 L. T. Scott et al., Science 295, 1500–1503 (2002).
- 5. H. Sakurai, T. Daiko, T. Hirao, Science **301**, 1878 (2003).
- K. Tahara, Y. Tobe, Chem. Rev. 106, 5274–5290 (2006).
- 8. Y. Segawa, A. Yagi, K. Matsui, K. Itami, Angew. Chem. Int.
- Ed. 55, 5136-5158 (2016).
- G. Povie, Y. Segawa, T. Nishihara, Y. Miyauchi, K. Itami, *Science* 356, 172–175 (2017).
- M. F. L. De Volder, S. H. Tawfick, R. H. Baughman, A. J. Hart, Science 339, 535–539 (2013).
- Y.-T. Wu, J. S. Siegel, in *Polyarenes i*, J. S. Siegel, Y.-T. Wu, Eds. (Springer, 2014), pp. 63–120.

- 12. Y. Segawa, H. Ito, K. Itami, . Nat. Rev. Mater. 1, 15002 (2016).
- 13. B. I. Dunlap, *Phys. Rev. B* **46**, 1933–1936 (1992). E. C. Kirby, R. B. Mallion, P. Pollak, J. Chem. Soc., Faraday 14.
- Trans. 89, 1945-1953 (1993). 15. L. Liu, F. Liu, J. Zhao, Nano Res. 7, 626–657 (2014).
- 16. A. L. Mackay, H. Terrones, Nature 352, 762 (1991).
- 17. J.-P. Sauvage, C. O. Dietrich-Buchecker, Molecular Catenanes, Rotaxanes and Knots: A Journey Through the World of Molecular Topology (Wiley, 2008).
- 18. R. S. Forgan, J.-P. Sauvage, J. F. Stoddart, Chem. Rev. 111, 5434-5464 (2011).
- 19. C. J. Bruns, J. F. Stoddart, The Nature of the Mechanical Bond: From Molecules to Machines (Wiley, 2016).
- 20. S. D. P. Fielden, D. A. Leigh, S. L. Woltering, Angew. Chem. Int. Ed. 56, 11166-11194 (2017).
- 21. W. P. Thurston, Bull. Am. Math. Soc. 6, 357-382 (1982).
- 22. C. O. Dietrich-Buchecker, J.-P. Sauvage, J. P. Kintzinger, Tetrahedron Lett. 24, 5095-5098 (1983).
- 23. P. R. Ashton et al., Angew. Chem. Int. Ed. Engl. 28, 1396-1399 (1989).
- 24. M. Fujita, F. Ibukuro, H. Hagihara, K. Ogura, Nature 367, 720-723 (1994).
- 25. C. A. Hunter, J. Am. Chem. Soc. 114, 5303-5311 (1992).
- 26. G. Schill, N. Schweickert, H. Fritz, W. Vetter, Angew. Chem. Int. Ed. Engl. 22, 889-891 (1983).
- 27. W. Zhang, A. Abdulkarim, F. E. Golling, H. J. Räder, K. Müllen, Angew. Chem. Int. Ed. 56, 2645-2648 (2017).
- 28. Y.-Y. Fan et al., Nat. Commun. 9, 3037 (2018).

- 29. J. M. Van Raden, B. M. White, L. N. Zakharov, R. Jasti,
- Angew. Chem. Int. Ed. 58, 7341-7345 (2019). 30. H. Lenormand, J.-P. Goddard, L. Fensterbank, Org. Lett. 15, 748-751 (2013).
- E. R. Darzi, T. J. Sisto, R. Jasti, J. Org. Chem. 77, 6624–6628 (2012).
 G. W. Fester et al., Inorg. Chem. 49, 2667–2673 (2010).
- 33. Y. Segawa et al., Org. Biomol. Chem. 10, 5979–5984 (2012).
- 34. C. O. Dietrich-Buchecker, J.-P. Sauvage, Angew. Chem. Int. Ed. Engl. 28, 189-192 (1989).
- 35. S. J. Tauber, J. Res. Natl. Bur. Stand. Sect. A 67A, 591-599 (1963). 36. O. Velasco Fuentes, "Quasi-steady endless vortices with
- chaotic streamlines," in Experimental and Computational Fluid Mechanics, J. Klapp, A. Medina, Eds. (Springer, 2014), pp. 111-128.

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SUPPLEMENTARY MATERIALS

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Carbon catenation

Preparing interlocked rings and knots at the molecular scale traditionally relies on preorientation of the building blocks by nitrogen or oxygen substituents. Segawa *et al.* devised a distinct strategy to synthesize catenane and trefoil structures composed exclusively of carbon and hydrogen (see the Perspective by Van Raden and Jasti). They linked phenyl rings end to end into macrocycles that met in the middle at a silicon center. Excision of the silicon with fluoride then yielded the interlocked products.

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