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Synthesis and Self-aggregation of Cyclic Alkynes Containing Helicene

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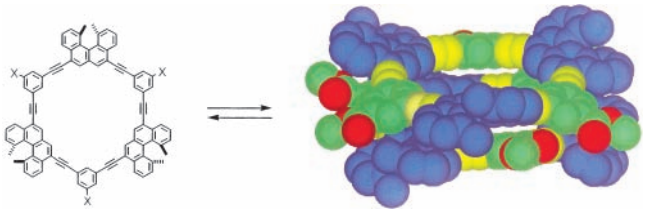
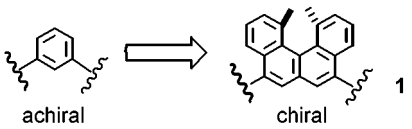
ABSTRACT



All stereoisomers of a cyclic alkyne containing three helicene units, 1,12-dimethylbenzo[*c*]phenanthrene, are synthesized using a building block. Isomeric [3 + 3]cycloalkynes aggregate in organic solvents. Vapor pressure osmometry reveals dimer formation of (*M*,*M*,*M*)-[3 + 3]-cycloalkynes in chloroform and benzene at concentrations above 2 mM. No higher aggregation is observed. The chirality of helicenes plays an important role in self-aggregation, and diastereomeric (*M*,*P*,*M*)-[3 + 3]cycloalkyne forms a dimer only above 15 mM. Aggregation of racemic (*M,*M**,*M**)-[3 + 3]cycloalkyne or (*M**,*P**,*M**)-[3 + 3]cycloalkyne is much weaker than that of a single enantiomer.**

Helicenes are polycyclic aromatic compounds possessing nonplanar helical structures and, accordingly, are chiral.[1] We previously developed a method to prepare an optically pure helicene, 1,12-dimethylbenzo[*c*]phenanthrene-5,8-dicarboxylate.[2] Of various potential uses of this low molecular weight helical compound, we regard here the helicene **1** as a chiral equivalent of *m*-phenylene (Scheme 1). Many functionally

Scheme 1



interesting compounds contain *m*-phenylene, and replacing this unit with helicene converts achiral compounds to chiral ones. In addition, if an achiral compound originally possesses more than one *m*-phenylene unit, this manipulation produces a series of stereoisomers. The diversity of chiral derivatives generated from a single achiral aromatic compound may prove useful in controlling their properties.

(1) For examples, see:Yamamoto, K.; Ikeda, T.; Kitsuki, T.; Okamoto, Y.; Chikamatsu, H.; Nakazaki, M. *J. Chem. Soc., Perkin Trans.1* **1990**, 271. Osuga, H.; Suzuki, H.; Tanaka, K. *Bull. Chem. Soc. Jpn*. **1997**, *70*, 891. Dai, Y.; Katz, T. J.; Nichols, D. A. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2109. Katz, T. J.; Liu, L.; Willmore, N. D.; Fox, J. M.; Rheingold, A. L.; Shi, S.; Nuckolls, C.; Rickman, B. H. *J. Am. Chem. Soc.* **1997**, *119*, 10054. Pischel, I.; Grimme, S.; Kotila, S.; Nieger, M.; Vögtle, F. *Tetrahedron: Asymmetry* **1996**, *7*, 109. Also see ref 6.

(2) Okubo, H.; Yamaguchi, M.; Kabuto, C. *J. Org. Chem*. **1998**, *63*, 9500. Formation of LB films of the helicene derivative. Feng, F.; Miyashita, T.; Okubo, H.; Yamaguchi, M. *J. Am. Chem. Soc*. **1998**, *120*, 10166. Okubo, H.; Feng, F.; Nakano, D.; Hirata, T.; Yamaguchi, M.; Miyashita, T. *Tetrahedron* **1999**, *55*, 14855. CT complexation of the helicene derivative. Okubo, H.; Nakano, D.; Yamaguchi, M.; Kabuto, C. *Chem. Lett*. **2000**, 1316. Okubo, H.; Nakano, D.; Anzai, S.; Yamaguchi, M. *J. Org. Chem.* **2001**, *66*, 557.

(3) For examples, see: Zhang, J.; Pesak, D. J.; Ludwick, J. L.; Moore, J. S. *J. Am. Chem. Soc*. **1994**, *116*, 4227. McCallien, D. W. J.; Sanders, J. K. M. *J. Am. Chem. Soc*. **1995**, *117*, 6611. Anderson, S.; Neidlein, U.; Gramlich, V.; Diederich, F. *Angew. Chem., Int. Ed. Engl*. **1995**, *34*, 1596. Wu, Z.; Moore, J. S. *Angew. Chem., Int. Ed. Engl*. **1996**, *35*, 297. Kawase, T.; Ueda, N.; Darabi, H. R.; Oda, M. *Angew. Chem., Int. Ed. Engl*. **1996**, *35*, 1556. Boese, R.; Matzger, A. J.; Vollhardt, K. P. C. *J. Am. Chem. Soc*. **1997**, *119*, 2052. Haley, M. M.; Bell, M. L.; English, J. J.; Johnson, C. A.; Weakley, T. J. R. *J. Am. Chem. Soc*. **1997**, *119*, 2956. Rubin, Y.; Parker, T. C.; Pastor, S. J.; Jalisatgi, S.; Boulle, C.; Wilkins, C. L. *Angew. Chem., Int. Ed.* **1998**, *37*, 1226. Tobe, Y.; Nakagawa, N.; Naemura, K.; Wakabayashi, T.; Shida, T.; Achiba, Y. *J. Am. Chem. Soc*. **1998**, *120*, 4544.

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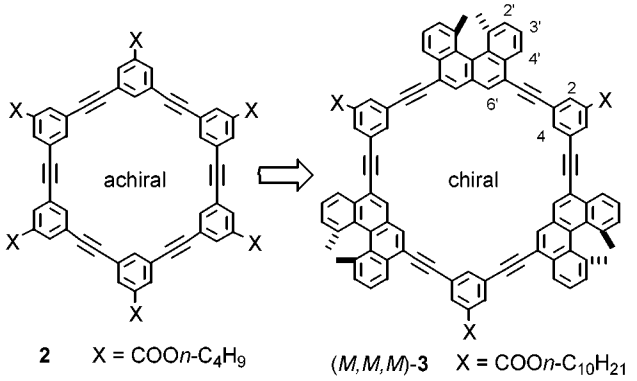
Cyclic oligoalkynes such as **2** have recently attracted much attention.[3,4] Since many of them contain more than one *m*-phenylene unit, chiral compounds generated by the substitution of the achiral unit with **1** appear interesting (Scheme 2).[5] Described here is the synthesis of optically

Scheme 2

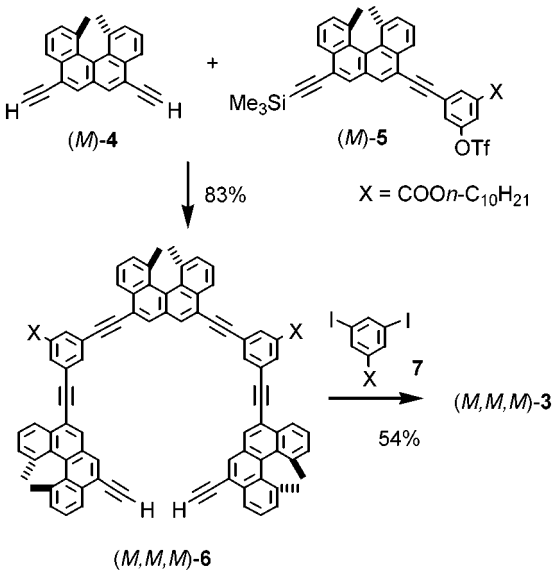


active [3 + 3]cycloalkyne **3**, which possess three units of **1** and three units of *m*-phenylene spacer moieties, and their self-aggregation behavior in organic solvents. The self-aggregation of chiral **3** is considerably affected by the stereochemistry of the helicene moiety.[4,6]

The cycloalkynes are synthesized using the building block (*M*)-**5** containing a helicene unit and a spacer unit (Scheme 3). Coupling of (*M*)-**4** and (*M*)-**5** via the Sonogashira coupling developed in this laboratory[7] followed by desilylation gives the (*M*,*M*,*M*)-[3 + 2]dialkyne (*M*,*M*,*M*)-**6**. Cyclization of (*M*,*M*,*M*)-**6** with *m*-phenylene diiodide **7** under conditions of high dilution gives (*M*,*M*,*M*)-**3** in 54% yield. Analogously, a diastereomeric (*M*,*P*,*M*)-[3 + 3]cycloalkyne, (*M*,*P*,*M*)-**3**, is obtained from (*P*)-**4** and (*M*)-**5**. As expected from its structure, NMR spectra of (*M*,*M*,*M*)-**3** show only one aromatic methyl proton and four aromatic protons. In contrast, (*M*,*P*,*M*)-**3** exhibits aromatic protons in a 2:1 ratio. Since the symmetry of the compound requires three distinct peaks in a 1:1:1 ratio, two of the peaks may be overlapped. Many of the aromatic carbons as well as the carbonyl carbons behave similarly. The antipodes (*P*,*P*,*P*)-**3** and (*P*,*M*,*P*)-**3** are also synthesized, and the racemic (*M**,*M**,*M**)-**3** and (*M**,*P**,*M**)-**3** are prepared by mixing equal amounts of the enantiomers.

Compound **3** self-aggregates in organic solvents. The ^{1}H NMR signals of **3** change in $CDCl_3$ at concentrations between 0.1 and 10 mM (Figure 1). For example, 4′-H of (*M*,*M*,*M*)-**3**

Scheme 3



appears at δ 8.59 at concentrations lower than 0.1 mM and at δ 8.18 at higher than 10 mM. The chemical shift is temperature dependent: The same proton is observed in a 2.9 mM solution at δ 8.17 at temperatures lower than −20 °C and at δ 8.40 at 25 °C. CD spectra of (*M*,*M*,*M*)-**3** show changes at approximately 1 mM as in the case of ^{1}H NMR.[8] Vapor pressure osmometry reveals dimer formation of (*M*,*M*,*M*)-**3** in $CHCl_3$ at concentrations higher than 2 mM (Figure 2). Higher aggregation is not observed in the concentration range examined. It is interesting that such an aggregation of a π-compound takes place even in C_6H_6.

Chiral recognition by helicene occurs in the self-aggregation. The dimerization of diastereomer (*M*,*P*,*M*)-**3** takes place at 15 mM, which is considerably higher than that at which dimerization of (*M*,*M*,*M*)-**3** occurs (Figure 2). The racemic (*M**,*M**,*M**)-**3** forms dimers at 20 mM and racemic

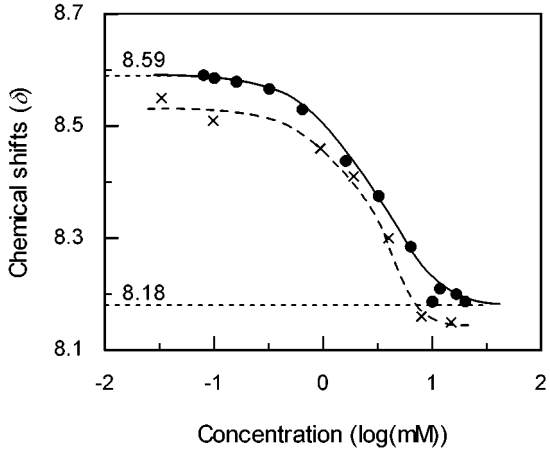


Figure 1. Concentration dependencies of ^{1}H NMR ($CDCl_3$, 22 °C) chemical shift of (*M*,*M*,*M*)-**3** (●) and (*M*,*P*,*M*)-**3** (×) at 4′-H.

(4) Shetty, A. S.; Zhang, J.; Moore, J. S. *J. Am. Chem. Soc.* **1996**, *118*, 1019. Also see: Tobe, Y.; Utsumi, N.; Nagano, A.; Naemura, K. *Angew. Chem., Int. Ed.* **1998**, *37*, 1285.

(5) Synthesis of a cyclic alkyne containing helicene is reported. Fox, J. M.; Lin, D.; Itagaki, Y.; Fujita, T. *J. Org. Chem.* **1998**, *63*, 2031.

(6) Polymerization of helicene by aggregation. Lovinger, A. J.; Nuckolls, C.; Katz, T. J. *J. Am. Chem. Soc.* **1998**, *120*, 264. Nuckolls, C.; Katz, T. J.; Katz, G.; Collings, P. J.; Castellanos, L. *J. Am. Chem. Soc.* **1999**, *121*, 79.

(7) Nakamura, K.; Okubo, H.; Yamaguchi, M. *Synlett* **1999**, 549. Aryl triflates also react rapidly under modified conditions.

(8) See Supporting Information.

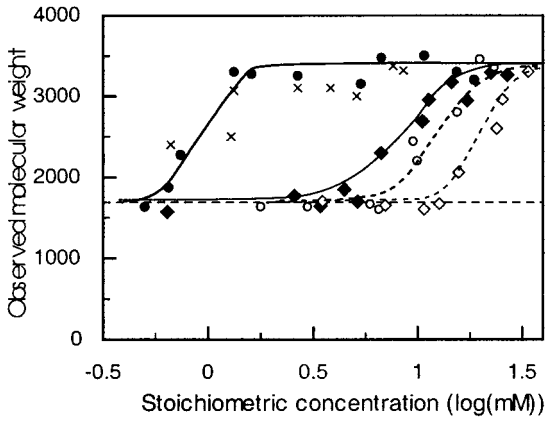


Figure 2. Concentration dependencies of the observed molecular weight and the stoichiometric concentration in chloroform at 35 °C obtained by vapor pressure osmometry: (*M*,*M*,*M*)-**3** (●), (*M*,*M*,*M*)-**3** in benzene (×), (*M*,*P*,*M*)-**3** (◆), (*M*,**M*,**M**)-**3** (○), and (*M**,*P**,*M**)-**3** (◇).

(*M**,*P**,*M**)-**3** at 30 mM. Their aggregation is weaker than those of (*M*,*M*,*M*)-**3** and (*M*,*P*,*M*)-**3**, respectively. This may reflect much weaker aggregation between the antipodes. The extent of the complex formation between the isomeric **3** compounds therefore can be summarized as follows: (*M*,*M*,*M*)-**3** and (*M*,*M*,*M*)-**3** > (*M*,*P*,*M*)-**3** and (*M*,*P*,*M*)-**3** > (*M*,*M*,*M*)-**3** and (*P*,*P*,*P*)-**3** > (*M*,*P*,*M*)-**3** and (*P*,*M*,*P*)-**3**.

Several notable differences are observed in the self-aggregation of achiral **2** and chiral **3**. The extent of the self-aggregation of (*M*,*M*,*M*)-**3** is stronger than that of **2**, and that of (*M*,*P*,*M*)-**3** is comparable with **2**.[8] In addition, (*M*,*M*,*M*)-**3** aggregates in C_6H_6, while the achiral **2** does so only in $CDCl_3$ and not in C_6D_6.[4] It is also noted that (*M*,*M*,*M*)-**3** and (*M*,*P*,*M*)-**3** form only dimers, while **2** shows higher aggregation.[4,8] The observations confirm that the chiral surface of (*M*,*M*,*M*)-**3** plays an important role in the strong and selective dimerization.

The structure of the (*M*,*M*,*M*)-**3** dimer obtained from the Amber* calculations[9] provides information on the role of the chirality (Figure 3). It shows face-to-face dimerization in which the helicene aromatic rings partially overlap each other. This is consistent with the magnitude of the upfield shift in ^{1}H NMR: 4′-H ≫ 2-H > 6′-H > 4-H > 3′-H ≫ 1′-Me > 2′-H.[8] The spacer *m*-phenylene moiety fits in the groove formed by helicene and is slightly bent toward the other cycloalkyne for better stacking. These fittings of the chiral π-surface may be the origin of the strong and selective dimerization of (*M*,*M*,*M*)-**3**.

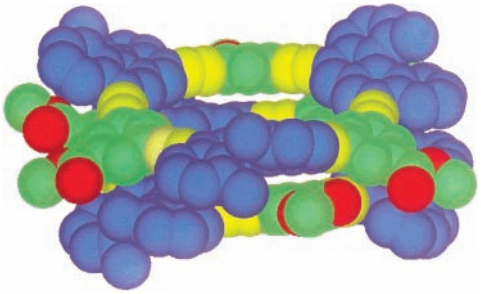


Figure 3. Structure of (*M*,*M*,*M*)-[3 +3]cycloalkyne dimer obtained from Amber* calculations. The helicene moiety is shown in blue and the spacer in green. Hydrogen atoms and decyl groups are omitted for clarity.

To summarize, all the possible stereoisomers of [3 + 3]-cycloalkyne **3** which self-aggregate in organic solvents are synthesized. The configuration of the three helicene units plays an important role in the dimerization. Conversion of the achiral aromatic compounds to chiral ones by replacing their *m*-phenylene units with helicene **1** is an interesting approach, generating new chiral substances.

Acknowledgment. The authors thank JSPS and Toray Science Foundation for financial support. A fellowship to K.N. from JSPS for young Japanese scientists is also gratefully acknowledged.

Supporting Information Available: Experimental procedures for the synthesis of **3**, as well as CD spectra of **3**, and aggregation behavior of **2** and **3** by vapor pressure osmometry. This material is available free of charge via the Internet at http://pubs.acs.org.

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(9) Calculation was performed using the MacroModel Ver 6.0 and the Amber* GB/SA ($CHCl_3$) force field. Monte Carlo searches from several different initial conformations yielded the structure shown in Figure 3 as the global minimum. Amber* (McDonald, D. Q.; Still, W. C. *Tetrahedron Lett.* **1992**, *33*, 7743). MacroModel Ver 6.0. (Mohamadi, F.; Richards, N. G. J.; Guida, W. C.; Liskamp, R.; Lipton, M.; Caulsfield, C.; Chang, G.; Hendrickson, T.; Still, W. C. *J. Comput. Chem.* **1990**, *11*, 440).