Synthesis of [5]-, [6]-, and [7]Helicene via Ni(0)- or Co(I)-Catalyzed Isomerization of Aromatic *cis,cis*-Dienetriynes

Filip Teplý, Irena G. Stará,* Ivo Starý,* Adrian Kollárovič, David Šaman,
Lubomír Rulíšek,[†] and Pavel Fiedler

*Contribution from the Institute of Organic Chemistry and Biochemistry and Center for Complex
Molecular Systems and Biomolecules, Academy of Sciences of the Czech Republic,
Flemingovo nám. 2, 166 10 Prague 6, Czech Republic*

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Abstract: An original approach to helicene frameworks exploiting atom economic *isomerization* of appropriate energy-rich aromatic *cis,cis*-dienetriynes has been developed. The new paradigm provides nonphotochemical syntheses of helicenes based on the easy, convergent, and modular assembly of key *cis,cis*-dienetriynes and their nickel(0)-catalyzed [2+2+2] cycloisomerization. The potential of the methodology is underlined by the syntheses of the parent [5]helicene (**2**), 7,8-dibutyl[5]helicene (**23**), [6]helicene (**24**), and [7]helicene (**25**). The approach can be adapted to prepare functionalized helicenes as exemplified by the eight-step synthesis of 7,8-dibutyl-2,3-dimethoxy[6]helicene (**34**). Density functional theory (DFT) calculations showed that bis[2-((1*Z*)-1-buten-3-ynyl)phenyl]acetylene (**1**) and isomeric [5]helicene (**2**) differ enormously in the Gibbs energy content ($\Delta G = -136.6$ kcal.mol^{-1}) to favor highly the devised intramolecular simultaneous construction of three aromatic rings.

Introduction

Isomerizations, besides ultimate addition reactions, perfectly fulfill criteria of atom economy[1] and, when cleverly used,[2] reflect art in organic synthesis. The simple, photochemically mediated isomerization of stilbene-like precursors to ortho fused aromatics[3] is almost in full harmony with this concept, but it has been hampered by fundamental drawbacks to evolve into a really convenient method for preparing helicenes.[4] Despite further remarkable progress in helicene chemistry that has been recorded in the past decade,[5] namely due to the revolutionary Diels−Alder approach invented and exploited by Katz,[6] the task of developing novel strategies for the preparation of helicenes remains a challenge to state-of-the-art synthesis. In this paper, we report an original approach to helicene frameworks based on pure atom economic *isomerization* of appropriate energy-rich aromatic *cis,cis*-dienetriynes under transition metal catalysis.

Results and Discussion

Devising Helicene Precursors. Being inspired by photodehydrocyclization of *cis/trans*-1,2-diaryl ethenes relying on the UV-mediated six-electron electrocyclization followed by in situ oxidation, we sought a similar but more efficient alternative pathway based on a simple isomerization of a suitable precursor under transition metal catalysis to build up a helicene framework. As the preparation of [5]helicene **2** (Scheme 1) might be called a "benchmark process" in helicene chemistry to test the

* Corresponding author. E-mail: stary@uochb.cas.cz.
† Center for Complex Molecular Systems and Biomolecules.

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Scheme 1. Calculated Gibbs Energy Content of *cis,cis*-Dienetriyne **1** and [5]Helicene **2**
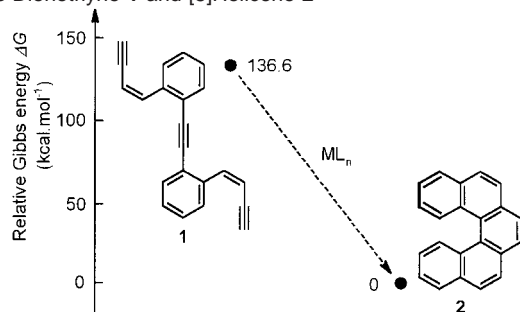

feasibility of a synthetic strategy,[7] we proposed the model isomeric *cis,cis*-dienetriyne **1** as a potential precursor of [5]-helicene **2**.

Computational Study. For the reaction **1** → **2** in tetrahydrofuran, the value of $\Delta G^0_{298}(THF) = -136.6$ kcal·mol^{-1} has been calculated (for details, see the Experimental Section). It can be decomposed into three significant contributions: $\Delta E = -148.0$ kcal·mol^{-1} (difference between potential energies of reactant and product), ΔG^0_{298}(gas phase) $- \Delta E = 14.3$ kcal·mol^{-1} (difference in the gas-phase corrections to Gibbs energy), and $\Delta G_{solv} = -2.9$ kcal·mol^{-1} (difference in the solvation energies of reactant and product in tetrahydrofuran). It can be seen that dominant energy contribution comes from the decay of three triple bonds and the formation of three aromatic rings.[8] The calculations support the idea of "energy-rich" intermediate **1** and demonstrate that its conversion into [5]helicene **2** is thermodynamically highly favored.[9]

(6) For the syntheses of helicenes and heterohelicenes based on Diels−Alder approach, see: (a) Phillips, K. E. S.; Katz, T. J.; Jockusch, S.; Lovinger, A. J.; Turro, N. J. *J. Am. Chem. Soc.* **2001**, *123*, 11899. (b) Weix, D. J.; Dreher, S. D.; Katz, T. J. *J. Am. Chem. Soc.* **2000**, *122*, 10027. (c) Paruch, K.; Vyklický, L.; Katz, T. J.; Incarvito, C. D.; Rheingold, A. L. *J. Org. Chem.* **2000**, *65*, 8774. (d) Paruch, K.; Katz, T. J.; Incarvito, C.; Lam, K. C.; Rhatigan, B.; Rheingold, A. L. *J. Org. Chem.* **2000**, *65*, 7602. (e) Thongpanchang, T.; Paruch, K.; Katz, T. J.; Rheingold, A. L.; Lam, K. C.; Liablesands, L. *J. Org. Chem.* **2000**, *65*, 1850. (f) Dreher, S. D.; Katz, T. J.; Lam, K. C.; Rheingold, A. L. *J. Org. Chem.* **2000**, *65*, 815. (g) Dreher, S. D.; Paruch, K.; Katz, T. J. *J. Org. Chem.* **2000**, *65*, 806. (h) Fox, J. M.; Katz, T. J.; Van Elshocht, S.; Verbiest, T.; Kauranen, M.; Persoons, A.; Thongpanchang, T.; Krauss, T.; Brus, L. *J. Am. Chem. Soc.* **1999**, *121*, 3453. (i) Nuckolls, C.; Katz, T. J.; Katz, G.; Collings, P. J.; Castellanos, L. *J. Am. Chem. Soc.* **1999**, *121*, 79. (j) Dreher, S. D.; Weix, D. J.; Katz, T. J. *J. Org. Chem.* **1999**, *64*, 3671. (k) Fox, J. M.; Katz, T. J. *J. Org. Chem.* **1999**, *64*, 302. (l) Nuckolls, C.; Katz, T. J. *J. Am. Chem. Soc.* **1998**, *120*, 9541. (m) Fox, J. M.; Goldberg, N. R.; Katz, T. J. *J. Org. Chem.* **1998**, *63*, 7456. (n) Katz, T. J.; Liu, L. B.; Willmore, N. D.; Fox, J. M.; Rheingold, A. L.; Shi, S. H.; Nuckolls, C.; Rickman, B. H. *J. Am. Chem. Soc.* **1997**, *119*, 10054. (o) Dai, Y. J.; Katz, T. J. *J. Org. Chem.* **1997**, *62*, 1274. (p) Nuckolls, C.; Katz, T. J.; Castellanos, L. *J. Am. Chem. Soc.* **1996**, *118*, 3767. (q) Dai, Y. J.; Katz, T. J.; Nichols, D. A. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 2109. (r) Shi, S.; Katz, T. J.; Yang, B. V.; Liu, L. *J. Org. Chem.* **1995**, *60*, 1285. (s) Willmore, N. D.; Hoic, D. A.; Katz, T. J. *J. Org. Chem.* **1994**, *59*, 1889. (t) Willmore, N. D.; Liu, L. B.; Katz, T. J. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1093. (u) Liu, L.; Katz, T. J. *Tetrahedron Lett.* **1990**, *31*, 3983.

(7) Synthesis of parent pentahelicene **2** by photocyclization of stilbene-type precursors is difficult without using a bromine auxiliaries trick, see: (a) Liu, L.; Katz, T. J. *Tetrahedron Lett.* **1991**, *32*, 6831. For other preparations of pentahelicene **2**, see refs 5j−l,w and: (b) Bestmann, H. J.; Both, W. *Chem. Ber.* **1974**, *107*, 2923. (c) Bestmann, H. J.; Both, W. *Angew. Chem.* **1972**, *84*, 293. (d) Mukharji, P. C.; Ray, S. B.; Ghosh, A. *Indian J. Chem.* **1971**, 408. (e) Bestmann, H. J.; Armsen, R.; Wagner, H. *Chem. Ber.* **1969**, *102*, 2259. (f) Altman, Y.; Ginsburg, D. *J. Chem. Soc.* **1959**, 466.

(8) The studied reaction is anisodesmic. The local electronic environments of most of the atoms change significantly in the course of the reaction. Therefore we carried out model calculations for the simple reaction $(3C_2H_2 \rightarrow C_6H_6)$ to ascertain the accuracy of the calculated data. It was found that the ΔE value calculated at B3LYP/6-311++G(d,p) level ($\Delta E = -151.7$ kcal·mol^{-1}) was in a very good agreement with reference CCSD(T)/6-311++G(d,p) values ($\Delta E = -148.6$ kcal·mol^{-1}). The B3LYP method performed even better than MP2/6-311++G(d,p), which yielded $\Delta E = -153.6$ kcal·mol^{-1}. In this respect, we consider the adopted computational scheme as reasonably accurate and estimate the error in the calculated value of $\Delta G^0_{298}(THF)$ for reaction **1** → **2** to be 5−10 kcal·mol^{-1}.

**Scheme 2.** Preparation of *cis,cis*-Dienetriynes **1** and **9**[a]
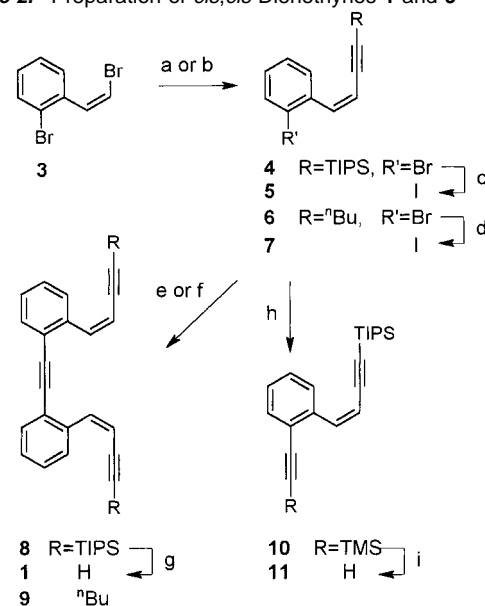
[a] Conditions: (a) TIPS−C≡CH (1.0 equiv), Pd(PPh₃)₄ (5%), CuI (10%), ^{i}Pr₂NH, 0 °C to room temperature, 2 h, 99%. (b) ^{n}Bu−C≡CH (2.1 equiv), Pd(PPh₃)₄ (5%), CuI (10%), ^{i}Pr₂NH, 0 °C to room temperature, 12 h, 99%. (c) ^{t}BuLi (2.0 equiv), ether, −90 °C, 10 min, then I₂ (1.7 equiv), −90 °C, 10 min, 98%. (d) ^{t}BuLi (2.0 equiv), ether, −90 °C, 10 min, then I₂ (1.7 equiv), −90 °C, 10 min, 97%. (e) HC≡CH (gaseous), Pd(PPh₃)₄ (5%), CuI (10%), piperidine, room temperature, 3 h, 79%. (f) HC≡CH (gaseous), Pd(PPh₃)₄ (5%), CuI (10%), piperidine, room temperature, 1 h, 78%. (g) ^{n}Bu₄NF (2.4 equiv), THF, room temperature, 5 min, 71%. (h) TMS−C≡CH (1.1 equiv), Pd(PPh₃)₄ (5%), CuI (10%), ^{i}Pr₂NH, room temperature, 50 min, 99%. (i) CH₃ONa (2.4 equiv), methanol, room temperature, 2 h, 98%.

Despite the encouraging fact that thermodynamic factors stood on our side, the basic questions about synthetic availability/ stability of energy-rich, fully unsaturated *cis,cis*-dienetriynes and, most importantly, about kinetics of the key isomerization to helicenes under transition metal catalysis primarily still has to be answered.

Synthesis of *cis,cis*-Dienetriynes. The synthesis of *cis,cis*-dienetriynes **1** and **9** began from known *cis*-dibromide **3** (Scheme 2).[10] Sonogashira coupling with TIPS−C≡CH or ^{n}Bu−C≡CH proceeded smoothly under Pd^0/Cu^I catalysis with excellent regioselectivity at the vinyl part of **3** to deliver *cis*-enyne **4** and **6**, respectively. To ensure further clean Sonogashira coupling with acetylene or TMS−C≡CH without participation of the ortho enyne moiety, we converted bromide **4** and **6** to iodide **5** and **7**, respectively, by routine lithiation with ^{t}BuLi and subsequent quenching aryllithiums with iodine. Then, on reaction with gaseous acetylene under Pd^0/Cu^I catalysis, we obtained the symmetrical *cis,cis*-dienetriynes **8** and **9**. Smooth desilylation of **8** with ^{n}Bu₄NF ensued to provide *cis,cis*-dienetriyne **1**. In addition, iodide **5** was treated with TMS−C≡ CH under Pd^0/Cu^I catalysis to afford *cis*-endiyne **10**. The

(9) The difference between the potential energy $\Delta E = -148.0$ kcal·mol^{-1} for the simultaneous formation of three aromatic rings in **2** and the enthalpy value $\Delta H = -143.1$ kcal·mol^{-1} (calculated from tabulated data, see ref 24) for the formation of benzene from three acetylenes is not so significant as expected. This incongruity may be attributed to the presence of a torsional strain in pentahelicene **2**. Its value calculated at the B3LYP/6-31+G(d) level as the difference in thermodynamic stability of **2** and picene is 11.9 kcal·mol^{-1}, in agreement with the previous findings of Schulman for [n]-helicenes and [n]phenacenes (ref 25).

(10) *cis*-Bromide **3** was readily available from commercial *trans*-2-bromocinnamic acid in two steps, see: (a) Yasuike, S.; Shiratori, S.-I.; Kurita, J.; Tsuchiya, T. *Chem. Pharm. Bull.* **1999**, *47*, 1108. (b) Tietze, L. F.; Noebel, T.; Spescha, M. *J. Am. Chem. Soc.* **1998**, *120*, 8971.

Scheme 3. Preparation of *cis*,*cis*-Dienetriynes **20** and **22**[a]
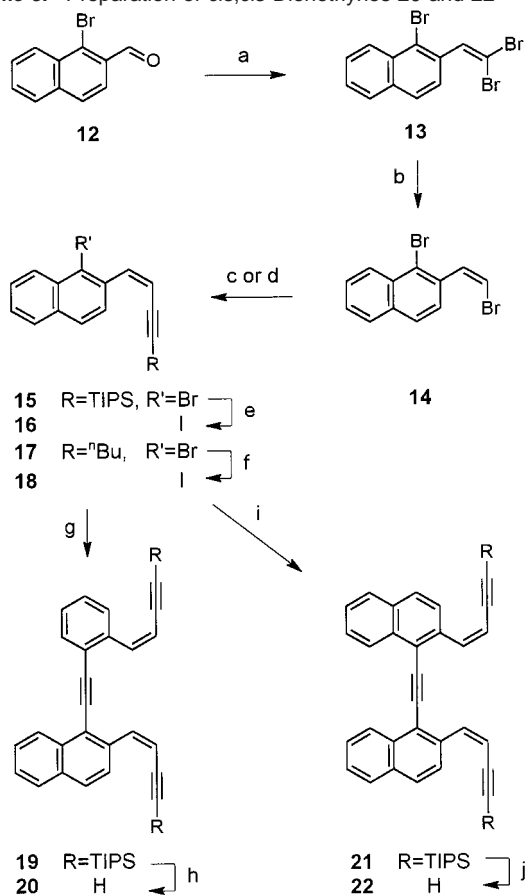
[a] Conditions: (a) CBr$_4$ (2.0 equiv), PPh$_3$ (2.0 equiv), Zn (2.0 equiv), CH$_2$Cl$_2$, room temperature, 14 h, 85%. (b) ^{n}Bu$_3$SnH (1.5 equiv), Pd(PPh$_3$)$_4$ (5%), toluene, room temperature, 3 h, 80%. (c) TIPS−C≡CH (1.1 equiv), Pd(PPh$_3$)$_4$ (5%), CuI (10%), ^{i}Pr$_2$NH, 0 °C to room temperature, 25 min, 99%. (d) ^{n}Bu−C≡CH (1.1 equiv), Pd(PPh$_3$)$_4$ (5%), CuI (10%), ^{i}Pr$_2$NH, 0 °C to room temperature, 1.5 h, 86%. (e) ^{t}BuLi (2.0 equiv), ether, −90 °C, 5 min, then I$_2$ (1.7 equiv), −90 °C, 10 min, 96%. (f) ^{t}BuLi (2.0 equiv), ether, −90 °C, 5 min, then I$_2$ (1.7 equiv), −90 °C, 10 min, 94%. (g) **11** (1.0 equiv), Pd(PPh$_3$)$_4$ (5%), CuI (10%), ^{i}Pr$_2$NH, room temperature, 2 h, 99%. (h) ^{n}Bu$_4$NF (2.4 equiv), THF, room temperature, 5 min, 87%. (i) HC≡CH (gaseous), Pd(PPh$_3$)$_4$ (2.5%), CuI (5%), piperidine, 80 °C, 0.5 h, 57%. (j) ^{n}Bu$_4$NF (2.4 equiv), THF, room temperature 5 min, 63%.

selective removal of the TMS group by CH$_3$ONa accomplished the preparation of the building block **11** that was further used in the synthesis of *cis*,*cis*-dienetriyne **20**, vide infra.

The synthesis of *cis*,*cis*-dienetriynes **20** and **22** relied on a very similar strategy. Starting from known bromo aldehyde **12** (ref 11), we had to install the *cis*-enyne moiety (Scheme 3). The Corey−Fuchs olefination[12] led to tribromide **13** that was subjected to regio- and stereoselective hydrogenolysis on treatment with ^{n}Bu$_3$SnH under Pd^0 catalysis according to the Uenishi−Tsuji procedure[13] to furnish *cis*-vinyl bromide **14**,

leaving the bromine atom at naphthalene untouched. Then the regioselective Pd^0/Cu^I-catalyzed Sonogashira coupling with TIPS−C≡CH gave *cis*-enyne **15**. The synthesis of its more reactive iodo analogue **16** was accomplished by routine halogene exchange with use of the ^{t}BuLi-metalation/iodination protocol. Similarly, *cis*-vinyl bromide **14** was regioselectively coupled with ^{n}Bu−C≡CH to give *cis*-enyne **17** and the following bromine-to-iodine displacement delivered *cis*-enyne **18** that was further utilized in the synthesis of functionalized [6]helicene **34**, vide infra.

Having prepared the suitable building blocks **11** and **16**, vide supra, we could assemble the model *cis*,*cis*-dienetriynes **20** and **22**. Starting from the same *cis*-enyne **16**, the Pd^0/Cu^I-catalyzed reaction with *cis*-endiyne **11** provided the cross-coupled *cis*,*cis*-dienetriyne **19** while the reaction with gaseous acetylene led to the homo-coupled *cis*,*cis*-dienetriyne **21**. Finally, deprotection of terminal acetylene units at **19** and **21** with ^{n}Bu$_4$NF delivered the free *cis*,*cis*-dienetriyne **20** and **22**, respectively.

Isomerization of *cis*,*cis*-Dienetriynes to Helicenes. The [2+2+2] cycloisomerization of alkynes under transition metal catalysis to deliver benzene derivatives is a well-established synthetic tool.[14] As the isomerization of *cis*,*cis*-dienetriynes to helicenes was proposed to follow this mechanistic pathway, we focused on Co(I) and Ni(0) catalysis like that recently applied to the synthesis of helicene-like[15] and tetrahydrohelicene[5j] molecules.

Initial attempts to isomerize **1** with Co$_2$(CO)$_8$ provided only tiny amounts of pentahelicene **2** (Table 1, entry 1) because an undesirable polymerization of the starting material occurred. Changing the catalyst to CpCo(CO)$_2$/PPh$_3$ improved the yield slightly (Table 1, entry 2). Stoichiometric amounts of CpCo-(CO)$_2$ gave only a moderate yield of **2** (Table 1, entry 3).
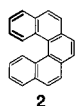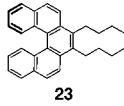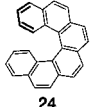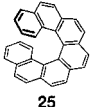
Accordingly, we turned our attention to nickel(0) catalysis, which is usually swifter than cobalt catalysis when six-membered rings are closed.[5j] Indeed, adding an equimolar amount of Ni(cod)$_2$ to **1** gave an instantaneous reaction and led to pentahelicene **2** in high yield (Table 1, entry 4). Gratifyingly, catalytic amounts of Ni(cod)$_2$ also produced **2** in good yield (Table 1, entry 5). The results with nonterminal *cis*,*cis*-dienetriyne **9** were similar. It was smoothly cycloisomerized to bisalkylated pentahelicene **23** (Table 1, entry 6).

Encouraged by the easy formation of the pentahelicene backbone, we focused our attention on the synthesis of higher homologues. In the presence of a stoichiometric amount of Ni(0) complex, a smooth cycloisomerization of both **20** and **22** proceeded to deliver hexahelicene **24** (ref 16) and heptahelicene

(11) For preparation of **12**, see: (a) Clayden, J.; McCarthy, C.; Westlund, N.; Frampton, C. S. *J. Chem. Soc., Perkin Trans. 1* **2000**, 1363. (b) Grissom, J. W.; Klingberg, D.; Meyenburg, S.; Stallman, B. L. *J. Org. Chem.* **1994**, *59*, 7876. (c) Rawal, V. H.; Florjancic, A. S.; Singh, S. P. *Tetrahedron Lett.* **1994**, *35*, 8985. (d) Smith, J. G.; Dibble, P. W.; Sandborn, R. E. *J. Org. Chem.* **1986**, *51*, 3762. (e) Weber, E.; Csoregh, I.; Stensland, B.; Czugler, M. *J. Am. Chem. Soc.* **1984**, *106*, 3297. (f) Trost, B. M.; Liu, G.-J. *J. Org. Chem.* **1981**, *46*, 4617.

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Table 1. [2+2+2] Cycloisomerization of *cis,cis*-Dienetriynes

| Entry	Educt	Co or Ni (mol %)	PPh₃ (mol %)	Product[a,b]	Yield (%)[c]
1	**1**	Co₂(CO)₈ (15)	0	**2**	8
2	**1**	CpCo(CO)₂ (20)	40	**2**	30
3	**1**	CpCo(CO)₂ (100)	200	**2**	43
4	**1**	Ni(cod)₂ (100)	0	**2**	83
5	**1**	Ni(cod)₂ (20)	40	**2**	64
6	**9**	Ni(cod)₂ (20)	40	**23**	76
7	**20**	Ni(cod)₂ (100)	0	**24**	86
8	**20**	Ni(cod)₂ (10)	20	**24**	54
9	**22**	Ni(cod)₂ (100)	0	**25**	60
10	**22**	Ni(cod)₂ (10)	20	**25**	51

[a] The reactions mediated by Co complexes were run in dioxane at 80–90 °C (entries 1 and 2) or in decane at 140 °C (entry 3) until the educt disappeared (1–22 h). When CpCo(CO)₂ was used, the reaction mixture was irradiated by a halogen lamp. [b] The reactions mediated by Ni(cod)₂ were run in THF at room temperature until the educt disappeared (5–15 min). [c] Isolated.

25 (ref 17), respectively, in excellent or good yield (Table 1, entries 7 and 9). Under catalytic conditions, the yields of **24** and **25** were also reasonable (Table 1, entries 8 and 10). Note, in all cases helicenes were formed as the only low molecular weight products and they were easily separable from the reaction mixture by flash chromatography.

Synthesis of Functionalized Helicenes. To establish the scope of this new approach to helicenes, we embarked on a synthesis of the functionalized [6]helicene **34** (Scheme 4). Starting from commercially available aldehyde **26**, we followed the modular approach developed for the unsubstituted *cis,cis*-dienetriynes **1**, **9**, **20**, and **22**. Dibromoolefination led smoothly to **27**, which was stereoselectively dehalogenated to provide *cis*-vinyl bromide **28**. Regioselective coupling with 1-hexyne afforded *cis*-enyne **29**, which has a nonterminal acetylene unit. Accordingly, after a halogene exchange, iodide **30** could be coupled with TMS–C≡CH to give endiyne **31**. In this reaction, the pendant butyl-substituted acetylene unit participated in undesirable Heck addition to a very low extent, and so pure **31** could be isolated by flash chromatography in good yield. Removal of the TMS group furnished **32**, which was coupled with naphthyl iodide **18** to deliver the key *cis,cis*-dienetriyne **33**. No significant Heck addition interfered. In the final step, Ni(0)/PPh₃ catalyst instantaneously cyclized dienetriyne **33** to substituted [6]helicene **34** in 61% yield.

Conclusions

In summary, the nickel(0)-catalyzed [2+2+2] cycloisomerization of aromatic *cis,cis*-dienetriynes represents a new para-

Scheme 4. Synthesis of Substituted [6]Helicene **34**[a]
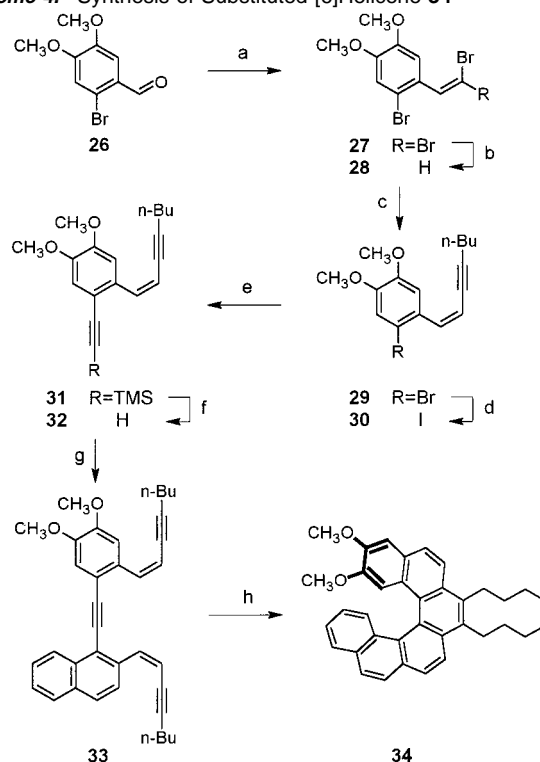
[a] Conditions: (a) CBr₄ (2.0 equiv), PPh₃ (2.0 equiv), Zn (2.0 equiv), CH₂Cl₂, room temperature, 17 h, 99%. (b) ⁿBu₃SnH (1.2 equiv), Pd(PPh₃)₄ (5%), toluene, room temperature, 10 h, 72%. (c) ⁿBu–C≡CH (1.5 equiv), Pd(PPh₃)₄ (5%), CuI (10%), ⁱPr₂NH, 40 °C, 15 min, 95%. (d) ᵗBuLi (2.0 equiv), ether, −90 °C, 5 min, then I₂ (1.7 equiv), −90 °C, 30 min, 81%. (e) TMS–C≡CH (1.4 equiv), Pd(PPh₃)₄ (5%), CuI (10%), ⁱPr₂NH, room temperature 30 min, 77%. (f) CH₃ONa (2.4 equiv), methanol, room temperature, 4.5 h, 99%. (g) **18** (0.98 equiv), Pd(PPh₃)₄ (5%), CuI (10%), ⁱPr₂NH, room temperature, 1 h, 91%. (h) Ni(cod)₂ (20%), PPh₃ (40%), THF, room temperature, 15 min, 61%.

digm for the nonphotochemical preparation of parent [5]-, [6]-, and [7]helicenes. Its bases are the easy, convergent, and modular assembly of energy-rich *cis,cis*-dienetriynes and the high susceptibility of these materials to cyclize to helicenes. It can be applied to synthesize functionalized helicenes. Further studies are therefore underway to extend the syntheses so they give helicenes that are substituted in other ways and helicenes that are nonracemic.

Experimental Section

Computational Details. The calculations were performed with a Gaussian 98 program package[18] in the framework of density functional theory (B3LYP functional).[19] Two standard basis sets have been used throughout the calculations: 6-31+G(d) (ref 20) and 6-311++G(2p,d) (ref 21). The optimizations of molecular geometries and vibrational analyses have been carried out at the B3LYP/6-31+G(d) and single point electronic energies computed at the B3LYP/6-311++G(p,d) level. The computed vibrational frequencies have been used for the subsequent thermochemistry calculations, preformed according to the standard

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formulas of statistical thermodynamics in the ideal gas approximation. In this way, ΔG^0_{gas} values have been obtained. Solvation Gibbs energies, ΔG_{solv}, for reactant and product have been computed in the framework of the PCM reaction field model of Tomasi.[22] The standard dielectric constant for tetrahydrofuran has been used ($\epsilon_r = 7.58$). The reference calculations of a simple model reaction described in ref 8 were carried out by using a very accurate CCSD(T) method.[23]

Procedure for Sonogashira Coupling of Aryl Iodides 5, 16, 18, and 30 or Vinyl Bromides 3, 14, and 28 with ^{n}Bu−, TMS−, or TIPS−C≡CH or Aryl Acetylenes 11 and 32. A Schlenk flask was charged with aryl or vinyl halide (1.0 mmol), Pd(PPh$_3$)$_4$ (58 mg, 0.050 mmol, 5 mol %), and CuI (19 mg, 0.100 mmol, 10 mol %) and flushed with argon. Diisopropylamine (10−15 mL) was added and the reaction mixture was briefly heated under stirring to 40−50 °C and then cooled to 0 °C or room temperature. ^{n}Bu−, TMS−, or TIPS−C≡CH or aryl acetylene (1.0−2.4 mmol, 1.0−2.4 equiv) was added and the reaction mixture was stirred at 0 °C or room temperature or 40 °C for 0.25−14 h until the reaction composition did not change (monitored by TLC). The precipitate was filtered off and washed with petroleum ether (5 × 2 mL). The combined fractions were evaporated to dryness in vacuo and the residue was chromatographed on silica gel to obtain the product.

Procedure for Sonogashira Coupling or Aryl Iodides 5, 7, and 16 with Gaseous Acetylene. A Schlenk flask was charged with aryl iodide (1.0 mmol), Pd(PPh$_3$)$_4$ (58 mg, 0.050 mmol, 5 mol %), and CuI (19 mg, 0.100 mmol, 10 mol %) and flushed with argon. Piperidine (10−15 mL) was added and the reaction mixture was briefly heated under stirring to 40−50 °C and then cooled to room temperature. A rubber balloon filled with acetylene was attached to the Schlenk flask and the reaction mixture was stirred at room temperature or 80 °C for 0.5−3 h until the reaction composition did not change (monitored by TLC). The precipitate was filtered off and washed with petroleum ether (5 × 2 mL). The combined fractions were evaporated to dryness in vacuo and the residue was chromatographed on silica gel to obtain the product.

Procedure for Conversion of Bromides 4, 6, 15, 17, and 29 to Corresponding Iodides. *tert*-Butyllithium (1.7 M solution in pentane, 940 µL, 1.60 mmol, 2.0 equiv) was added dropwise (trickling along a cooled flask surface) to a vigorously stirred solution of aryl bromide (0.800 mmol) in ether (4 mL) at −90 °C under argon. After the mixture was stirred at −90 °C for 5−10 min, iodine (345 mg, 1.36 mmol, 1.7 equiv) in ether (3 mL) was added dropwise. The mixture was stirred at −90 °C for 10−30 min and then warmed to room temperature. The reaction mixture was diluted with dichloromethane (4-fold to the amount of ether), washed with Na$_2$S$_2$O$_3$ (2×) and water (1×), and dried over anhydrous Na$_2$SO$_4$. The solvents were removed in vacuo and the residue was chromatographed on silica gel to afford the product.

Procedure for Selective TMS-Deprotection of 10 and 31. Sodium methanolate (0.5 M solution in methanol, 4.80 mL, 2.40 mmol, 2.4 equiv) was added to TMS derivative (1.0 mmol) in methanol (4 mL) under argon and the mixture was stirred at room temperature for 2−4.5 h. The solution was evaporated in vacuo to dryness and the residue was chromatographed on silica gel to obtain the product.

Procedure for TIPS-Deprotection of 8, 19, and 21. Tetrabutylammonium fluoride (1.0 M solution in THF, 720 µL, 0.720 mmol, 2.4 equiv) was added to silylated *cis,cis*-dienetriyne (0.300 mmol) in THF (4 mL) under argon and the mixture was stirred at room temperature for 5 min. The solution was evaporated in vacuo to dryness and the residue was chromatographed on silica gel to obtain the product.

Procedure for Corey−Fuchs Olefination of 12 and 26. Triphenylphosphine (525 mg, 2.0 mmol, 2.0 equiv) in dichloromethane (5 mL) was added to a mixture of tetrabromomethane (663 mg, 2.0 mmol, 2.0 equiv) and zinc powder (131 mg, 2.0 mmol, 2.0 equiv) in dichloromethane (3 mL) under argon. After the mixture was stirred at room temperature for 30 min, aldehyde (1.0 mmol) in dichloromethane (5 mL) was added and the suspension was stirred at room temperature for 14−17 h. The crude reaction mixture was passed through a short pad of silica gel using dichloromethane, the solution was evaporated in vacuo to dryness, and the residue was chromatographed on silica gel to get the product.

Procedure for Stereoselective Hydrogenolysis of 13 and 27. A Schlenk flask was charged with dibromovinyl derivative (0.800 mmol) and Pd(PPh$_3$)$_4$ (46.2 mg, 0.040 mmol, 5 mol %) and flushed with argon. Toluene (8 mL) was added and the solution was treated with tributyltin hydride (254 µL, 0.958 mmol, 1.2 equiv) under stirring at room temperature for 0.2−3 h until the reaction composition did not change (monitored by TLC). The reaction mixture was diluted with brine and extracted with dichloromethane (3×). The combined fractions were dried over anhydrous Na$_2$SO$_4$, the solvents were evaporated in vacuo, and the residue was chromatographed on silica gel to obtain the product.

Procedure for Nickel-Mediated [2+2+2] Cycloisomerization of *cis,cis*-Dienetriynes 1, 9, 20, 22, and 33: Stoichiometric Method. A Schlenk flask was charged with *cis,cis*-dienetriyne (0.100 mmol) and flushed with argon. The substrate was dissolved in THF (2 mL), a stock solution of Ni(cod)$_2$ in THF (0.06 M, 1.70 mL, 100 mol %) was added, and the mixture was stirred at room temperature for 15 min. The solvent was evaporated in vacuo and the residue was chromatographed on silica gel to obtain the product. **Catalytic Method.** In a Schlenk flask, triphenylphosphine (10.5 mg, 0.040 mmol, 20 mol %) was dissolved in THF (1 mL) under argon, a stock solution of Ni(cod)$_2$ in THF (0.06 M, 330 µL, 10 mol %) was added, and the mixture was stirred at room temperature for 5 min. *cis,cis*-Dienetriyne (0.200 mmol) in THF (2 mL) was added and the mixture was stirred at room temperature for 5−15 min. The solvent was evaporated in vacuo and the residue was chromatographed on silica gel to obtain the product.

Procedure for Cobalt-Mediated [2+2+2] Cycloisomerization of *cis,cis*-Dienetriyne 1: Cycloisomerization with Co$_2$(CO)$_8$. A Schlenk flask was charged with **1** (52 mg, 0.187 mmol) and flushed with argon. The substrate was dissolved in dioxane (1 mL), a solution of Co$_2$(CO)$_8$ (9.6 mg, 0.028 mmol, 15 mol %) in dioxane (1 mL) was added, and the mixture was stirred at 80 °C for 40 min. The solvent was evaporated in vacuo and the residue was chromatographed on silica gel (petroleum ether-ether 99:1) to obtain **2** (ref 7) (4.4 mg, 8%) as an amorphous solid.

Cycloisomerization with CpCo(CO)$_2$: Stoichiometric Method. A Schlenk flask was charged with **1** (23 mg, 0.083 mmol) and flushed with argon. The substrate was dissolved in decane (5 mL), a solution of triphenylphosphine (43.3 mg, 0.165 mmol, 200 mol %) in decane (1 mL) and CpCo(CO)$_2$ (11 µL, 0.083 mmol, 100 mol %) were added, and the mixture was stirred at 140 °C for 1.2 h under concomitant irradiation with a halogen lamp. The solvent was evaporated in vacuo and the residue was chromatographed on silica gel (petroleum ether−ether 100:0 to 99:1) to obtain **2** (10 mg, 43%) as an amorphous solid. **Catalytic Method.** A Schlenk flask was charged with **1** (52 mg, 0.187 mmol) and flushed with argon. The substrate was dissolved in dioxane (3 mL), a solution of triphenylphosphine (19.6 mg, 0.075 mmol, 40 mol %) in dioxane (1 mL) and CpCo(CO)$_2$ (5 µL, 0.038 mmol, 20 mol %) were added, and the mixture was stirred at 90 °C for 22 h under concomitant irradiation with a halogen lamp. The solvent was evaporated in vacuo and the residue was chromatographed on silica gel (petroleum ether−ether 99:1) to obtain **2** (15.8 mg, 30%) as an amorphous solid.

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Supporting Information Available: Experimental details, characterization data, and ^{1}H NMR spectra for **1, 2, 4−11, 13−25**, and **27−34** (PDF). This material is available free of charge via the Internet at http://pubs.acs.org.

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