Synthesis of Buta-1,3-diyne-Bridged Macrocycles with (*Z*)-1,4-Diethynyl-1,4-dimethoxycyclohexa-2,5-diene as the Building Block

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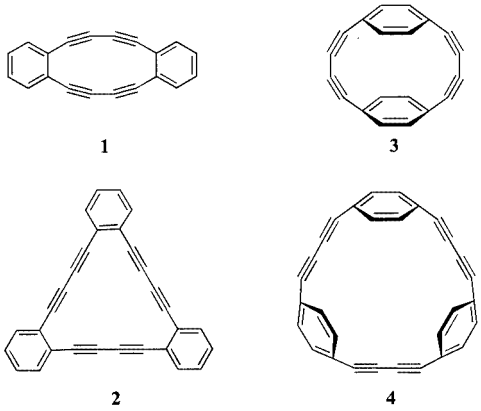
(Z)-1,4-Diethynyl-1,4-dimethoxycyclohexa-2,5-diene has been used as a building block for the synthesis of two novel macrocycles containing buta-1,3-diyne units as bridges. The tetrayne derivative **5c** has been structurally characterized by single crystal X-ray crystallographic data.

Introduction

The oxidative dimerization of a terminal acetylene to the corresponding diacetylene − the Glaser coupling[1] − is a very powerful tool for the synthesis of a variety of molecular frameworks containing acetylenic units. The recent past has witnessed the synthesis of several novel acetylenic building blocks which are potentially useful for molecular scaffolding for the synthesis of *n*-cyclocarbons, dehydroannulenes, pericyclynes, graphyne subunits, and cyclophynes, to name but a few.[2] Cyclophynes are an interesting class of compounds in which the aromatic units are connected by acetylenic bridges. The simplest cyclophyne is [2.2]paracyclophyne, a hydrocarbon in which one ethano bridge has been replaced by a triple bond. This compound was generated as a highly reactive intermediate as early as 1982 and the term cyclophyne was also introduced for the first time.[3] Oda has reported the synthesis of a highly strained [2.2.2]metacyclophane-1,9,17-triyne in which the sp bond angles are 158.6°.[4] Haley has recently reported the synthesis of an octacobalt complex of [8.8]paracyclophane octayne.[5] However, the parent hydrocarbon of this cobalt complex has eluded isolation, presumably due to the strain-induced high reactivity of the tetrayne bridges. Tobe has reported spectroscopic evidence for the formation of [12.12]paracyclophane dodecayne.[6] The hexakis(octayne)-bridged all-carbon cage compound C_{60} with C_i point group symmetry, proposed by Rubin, is the ultimate goal of the cyclophyne series.[7]

Although dehydrobenzannulenes **1**[8] and **2**[9] have been reported, the corresponding *para* isomers, cyclophynes **3** and **4**, are unknown in the literature (Scheme 1). [2_6]- and [2_8]Paracyclophane hexayne and octayne, respectively, have been reported by Oda.[10] These are belt-shaped molecules in which the paraphenylene units are connected by a single acetylenic unit.



Scheme 1. A selection of cyclophynes containing diacetylenic bridges

As a part of our ongoing efforts to synthesize cyclophanes and related macrocycles bearing polyyne bridges,[11] we have devised a new methodology for the synthesis of novel macrocycles bearing 1,4-cyclohexadiene units instead of aromatic rings. The 1,4-hexadiene-based macrocycles are worthwhile targets because they could serve as potential

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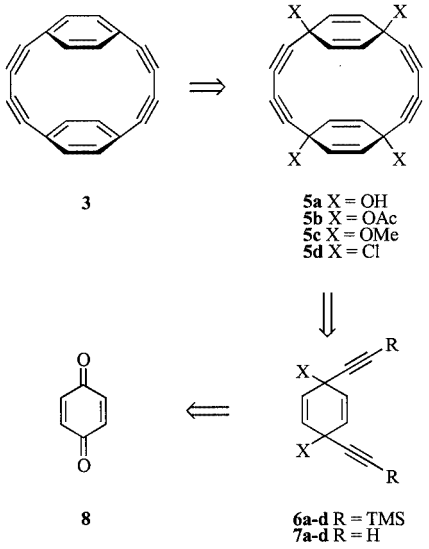
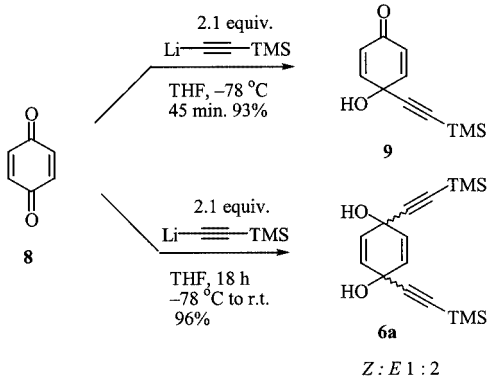
precursors for the synthesis of paracyclophynes, as shown in the retrosynthetic analysis (Scheme 2). Because of its linear geometry 1,4-diethynylbenzene is an unsuitable starting material for the synthesis of **3** and **4** using Glaser-coupling conditions. In the literature two methodologies are commonly used to "bend" the otherwise linear buta-1,3-diyne unit in order to construct macrocycles bearing polyyne bridges. The first one involves the formation of an η^2-dicobalt hexacarbonyl derivative of the alkyne by the reaction of the alkyne with dicobalt octacarbonyl. After the construction of the macrocycle the alkyne is regenerated by oxidative demetallation of the cobalt complex.[12] The second approach involves the use of cyclobutene-based precursors which serve as masked alkynes. In this method the alkyne is restored by a photochemical [2+2] cycloreversion.[6] In the *Z*-isomer of the diol **7a** the two terminal acetylenic groups point at an angle of 128° from the nearly planar cyclohexadiene unit.[13] The disposition of the two acetylenic groups at this angle makes **7a** and its derivatives amenable for the synthesis of macrocycles bearing buta-1,3-diyne bridges by a Glaser coupling reaction. Although diol **7a** was reported by Ried in 1957,[14] it has not been used as a building block for the synthesis of macrocyclic structures. The crucial step in Scheme 2 is the conversion of **5** by a reductive 1,4-elimination of X groups to the aromatic system **3**. To carry out this conversion it would be desirable to have X as a good leaving group such as halide or acetate. Herein we report the synthesis and characterization of two new macrocycles **5c** and **12** using (*Z*)-1,4-diethynyl-1,4-dimethoxycyclohexa-2,5-diene as the building block. We describe our attempts to synthesize **5a−b** and **5d** from the corresponding precursors **7a−b** and **7d**, respectively. We also report the calculated energy minimized structures of the hypothetical cyclophynes **3** and **4** along with their strain energies.



Scheme 2. Cyclophane-tetrayne **3**: retrosynthesis

Results and Discussion

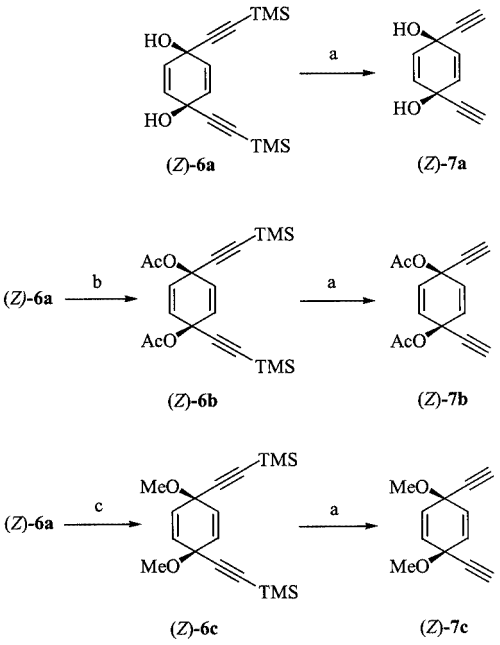
Addition of two equivalents of lithium trimethylsilylacetylide in THF to *p*-benzoquinone (**8**) furnished the diol **6a** as a mixture of *Z*- and *E*-diastereomers in a 1:2 ratio, respectively (Scheme 3). It is interesting to note that the addition of lithium trimethylsilylacetylide stopped at the monoaddition stage to yield the dienone **9** as the only product in nearly quantitative yield when the reaction was carried out at −78 °C. It was necessary to warm the reaction mixture to above −40 °C in order for the second addition to take place to yield **6a**. The diastereomers of **6a** were separated by column chromatography. The *E*-isomer was also obtained in pure form by fractional crystallization of the crude product from a mixture of CH_2Cl_2 and pentane, leaving behind a mother liquor that was enriched in the *Z*-isomer. The structure of the *E*-isomer was established by single-crystal X-ray crystallographic data.[15] Since the *E*-isomer is not useful for the synthetic route presented in Scheme 2, further transformations of the diol **6** were performed only with the *Z*-isomer. Deprotection of the TMS groups proceeded smoothly when the diol **6a** was treated with K_2CO_3 in methanol. Although the synthesis of diol **7** has been reported in 30−45% yield,[14,16] the two-step strategy presented here gives the diol in 85−90% overall yield starting from *p*-benzoquinone.



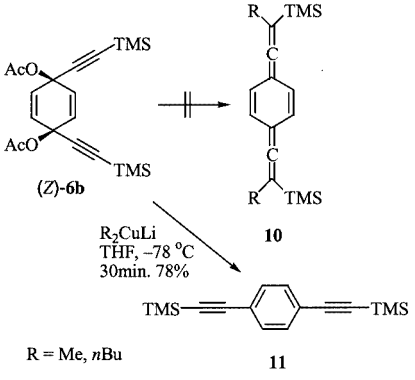
Scheme 3. The ethynylation of *p*-benzoquinone (**8**)

The *Z*-diol **6a** was converted into the corresponding diacetate *Z*-**6b** and dimethyl ether *Z*-**6c** using standard procedures in high yields. The silyl protecting groups were then removed with K_2CO_3 in methanol to yield the desired terminal acetylene derivatives *Z*-**7b** and *Z*-**7c**, respectively, in good yields (Scheme 4). Attempts to synthesize the dichloro derivative *Z*-**6d** from *Z*-**6a** and *Z*-**7d** from *Z*-**7a**, respectively, by using $SOCl_2$ and pyridine were unsuccessful due to the propensity of the diols **6a** and **7a** to undergo aromatization under strong acidic conditions.

Initially our attention was focused on the synthesis of the tetraacetate derivative **5b** because the acetate functions could be made to undergo reductive 1,4-elimination to yield the target cyclophyne **3**. The idea that the 1,4-elimination of these groups could be performed gained support from a serendipitous observation. The fact that propargylic acetates undergo (S_N2') substitution, with propargylic re-



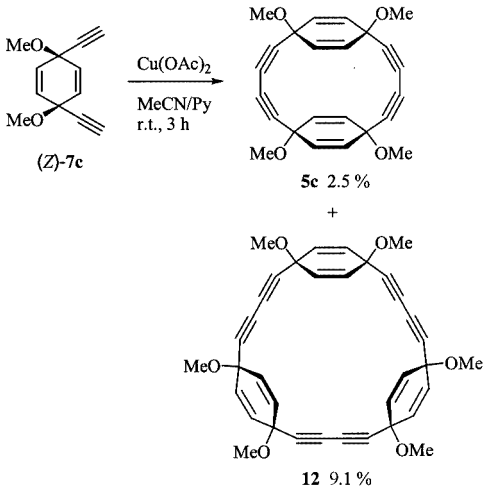
Scheme 4. Preparation of the building blocks **7**; Reagents and conditions: a. K_2CO_3, MeOH, room temp., 1 h, 95−100%; b. Ac_2O, Py, 60 °C, 4 h, 74%; c. NaH, THF, MeI, −30 °C to room temp., overnight, 94%



Scheme 5. Reaction of (*Z*)-**6b** with R_2CuLi

arrangement to give allenes, when reacted with dialkylcuprates[17] under appropriate conditions led us to an independent investigation of the reactions of the diacetate **6b** with dialkylcuprates for the synthesis of extended quinodimethides, as shown in Scheme 5.

Treatment of the diacetate **6b** with either lithium dimethylcuprate or lithium di-n-butylcuprate at −78 °C did not yield the expected compound **10**. Instead, a very clean reductive elimination of the acetate groups was observed leading to the formation of 1,4-bis(trimethylsilylethynyl)-benzene **11** as the sole product in 78% yield. This observation encouraged us to investigate the synthesis of **5b** from *Z*-**7b**. The diacetate *Z*-**7b** was subjected to a Glaser−Eglinton coupling reaction under a variety of conditions.[11a] None of these reactions gave any tractable material. In all the cases along with major amounts of insoluble polymeric materials, aromatic compounds were obtained in small amounts which were not fully characterized. Similar observations were made when the diol *Z*-**7a** was subjected to Glaser−Eglinton coupling conditions. In sharp contrast, however, the dimethoxy derivative *Z*-**7c**, when subjected to an Eglinton coupling reaction in the presence of $Cu(OAc)_2$ and pyridine, gave a crude product which was completely soluble in common organic solvents such as $CHCl_3$, CH_2Cl_2, and diethyl ether (Scheme 6). Careful chromatographic separation yielded **5c** and **12** in 2.5% and 9.1% yields, respectively. In spite of the low yields, compounds **5c** and **12** were isolated and purified by column chromatography and repeated crystallization and were thoroughly characterized by spectroscopic and analytical data (see Exp. Sect.).



Scheme 6. Preparation of the macrocyclic polyynes **5c** and **12**

Additionally, the structure of **5c** was confirmed by single-crystal X-ray crystallographic data (Figure 1). In each of the cyclohexadiene rings the sp^2 carbon atoms form an almost ideal plane and the sp^3 carbons lie 0.304 Å above the plane towards the cavity of the macrocycle. The distance between the centers of the cyclohexadiene rings is 7.27 Å and the distance between the centers of the two acetylenic

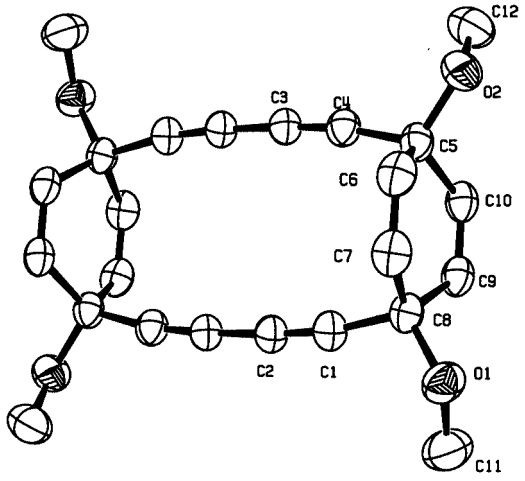


Figure 1. Structure of **5c** in the crystal

bridges is 3.70 Å. The acetylenic bridges are bow shaped. The average sp angles are 176 and 170° for the sp carbon atoms at the center of the bridge C(1)−C(2)−C(3)′ and the sp carbon atoms connected to the sp^3 carbon of the cyclohexadiene ring C(2)−C(1)−C(8), respectively (Figure 1). In comparison with the sp bond angle of 158.6° reported by Oda[4] for [2.2.2]metacyclophane-1,9,17-triyne, the macrocycle **5c** is relatively strain free. Recently Fallis[18] has reported sp bond angles of 163° and 153.4° in highly strained cyclophane polyyne systems.

Energy-Minimized Structures of 3 and 4 Based on Semiempirical Calculations

The energy-minimization calculations on the structures of the hypothetical cyclophynes **3** and **4** were carried out by semiempirical AM1 and PM3 methods.[19] The energy-minimized structures A and B are shown in Figure 2, from which it is clear that cyclophynes **3** and **4** are belt-shaped molecules. According to these calculations **3** possesses D_{2h} symmetry while **4** prefers D_{3h} symmetry. The average sp angle in **3** is approximately 155°; that in **4** is 163°. As expected, the aromatic rings are not planar. In the case of structure **3**, carbon atoms 1 and 4 of the aromatic rings are 19° above the plane containing the rest of the ring carbons, whereas in **4** this deviation amounts to 12°. The strain energies of **3** and **4** based on AM1 (PM3) calculations are 106 (93) and 69 (60) kcal·mol^{-1}, respectively.

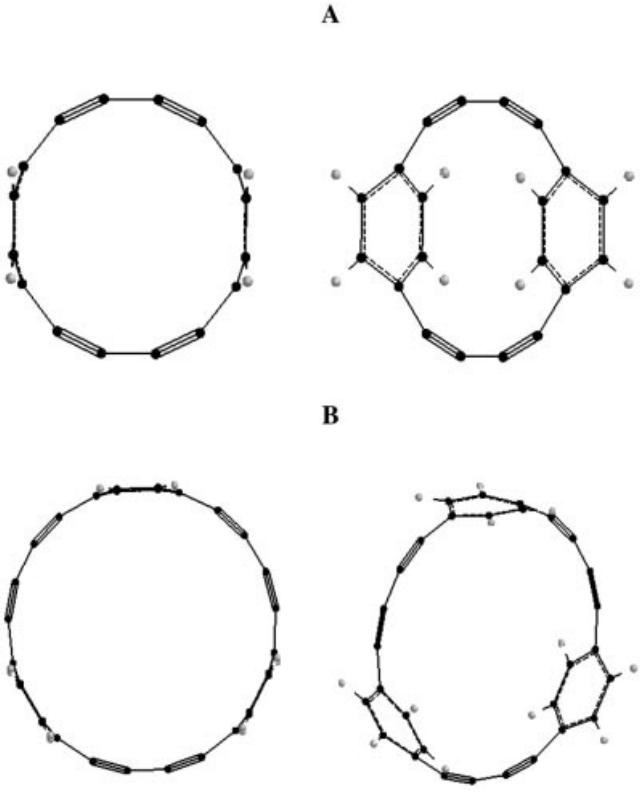


Figure 2. Calculated energy-minimized structures of **3** (A) and **4** (B) in different perspective views

Conclusion

The synthesis of two new macrocycles **5c** and **12** with buta-1,3-diyne bridges derived from (*Z*)-1,4-diethynyl-1,4-dimethoxycyclohexa-2,5-diene (*Z*-**7c**) as the building block has been accomplished. Macrocycle **5c** has been structurally characterized by single-crystal X-ray crystallographic data. The derivatives of **5c** and **12** are promising candidates for the synthesis of cyclophynes by the methodology outlined in Scheme 2; this work is currently in progress.

Experimental Section

General Remarks: ^{1}H and ^{13}C NMR spectroscopy: Jeol GSX-400 at 400 MHz and 100 MHz or Bruker AM-200 at 200 MHz and 50 MHz, respectively; in $CDCl_3$ solution unless otherwise stated, TMS as internal standard. All reactions were carried out under nitrogen unless indicated otherwise. Column chromatography: silica gel (60−120 or 240−400 mesh) with various mixtures of diethyl ether (Et_2O), ethyl acetate (EtOAc), and hexane. TLC: Macherey−Nagel polygram sil G/UV_{254} plates. Melting points are uncorrected. THF was distilled from calcium hydride.

(*Z*)-1,4-Bis(trimethylsilylethynyl)cyclohexa-2,5-dien-1,4-diol (*Z*-6a): *n*BuLi (0.25 mol, 156 mL of a 1.6 M solution in hexane) was added at −78 °C to a stirred solution of trimethylsilylacetylene (35 mL, 0.25 mol) in anhydrous THF (300 mL). The resulting pale yellow solution was stirred for 45 min at the same temperature before it was added dropwise through a stainless steel needle to a stirred yellow viscous suspension of *p*-benzoquinone (10.8 g, 0.1 mol) in anhydrous THF (500 mL) at −78 °C. The mixture initially turned dark blue and then became dark brown. The reaction was allowed to reach +10 °C (ca. 16 h) and was cooled to 0 °C before it was quenched with aqueous saturated NH_4Cl solution (600 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extract was washed with ice-cold water (200 mL) and once with ice-cold saturated brine solution (200 mL). After drying with $MgSO_4$, the solvent was removed and the resulting tan colored solid was used for the next step. The ^{1}H NMR spectrum of the crude product indicated a mixture of *Z* and *E* diastereomers of **6a** in a 1:2 ratio (29.1 g, 96%). The mixture (5.0 g) was separated by silica-gel column chromatography with diethyl ether/hexane (20:80, v/v) to yield the pure *E*-isomer (2.6 g) and the *Z*-isomer (1.9 g). The synthesis and spectroscopic characterization of the *E*-diastereomer has been reported earlier.[16] *Z*-**6a**: m.p. 152−154 °C. ^{1}H NMR: δ = 0.00 ppm (s, 18 H), 3.17 (br. s, 2 H), 5.79 (s, 4 H). ^{13}C NMR: δ = −0.3 ppm (CH_3), 61.1 (Cq), 90.1 (Cq), 104.3 (Cq), 129.3 (CH). IR: $\tilde{\nu}$ = 3328 cm^{-1}, 2160, 1248. MS (EI): *m*/*z* = (%) = 304 [M$^+$] (12), 286 (22), 271 (78), 255 (98), 73 (100). HRMS: calcd. 304.1315; found 304.1304.

(*Z*)-1,4-Dimethoxy-1,4-bis(trimethylsilylethynyl)cyclohexa-2,5-diene (*Z*-6c): The crude diol **6a** containing a mixture of the *Z*- and *E*-isomers (29.0 g, 0.095 mol) in anhydrous THF (300 mL) was added to a stirred suspension of NaH (6.0 g, 0.24 mol) in anhydrous THF (300 mL) at −78 °C. The yellow suspension was stirred for 30 min at the same temperature. Methyl iodide (68.1 g, 30 mL, 0.48 mol) was added dropwise slowly with a syringe and the mixture was allowed to warm to room temp. overnight (18 h). The reaction mixture was poured into ice-cold saturated NH_4Cl solution (500 mL). The organic layer was separated and the aqueous portion was repeatedly extracted with diethyl ether (3 × 200 mL). The combined

organic extract was washed thoroughly with water (2 × 200 mL) and finally with saturated brine solution (200 mL). After drying with $MgSO_4$, the solvent was removed in vacuo to give a pale yellow solid (29.7 g, 94%). The ^1H NMR spectrum of the crude product indicated a mixture of *Z*- and *E*-diastereomers of **6c** in a 1:2 ratio. The diastereomers were separated and purified by silica-gel column chromatography with diethyl ether/hexane (1:19, v/v) to yield the *E*-isomer (13.6 g) and the *Z*-isomer (8.6 g) of **6c**. *Z*-**6c**: Low-melting solid. ^1H NMR: δ = 0.00 ppm (s, 18 H), 3.10 (s, 6 H), 5.85 (s, 4 H). ^{13}C NMR: δ = −0.2 ppm (CH_3), 51.5 (OCH_3), 66.7 (Cq), 90.8 (Cq), 102.9 (Cq), 129.3 (CH). IR: $\tilde{\nu}$ = 2242 cm^{-1}, 2146. MS (EI): *m*/*z* = (%) = 332 [M^+] (12), 301 (18), 270 (18), 255 (70), 213 (42), 73 (100). *E*-**6c**: pale yellow solid; m.p. 102−104 °C. IR: $\tilde{\nu}$ = 2176 cm^{-1}. ^1H NMR: δ = 0.00 ppm (s, 18 H), 3.07 (s, 6 H), 5.89 (s, 4 H). ^{13}C NMR: δ = −0.3 ppm (CH_3), 51.2 (OCH_3), 66.8 (Cq), 90.7 (Cq), 103.0 (Cq), 130.1 (CH). MS (EI): *m*/*z* = (%) = 332 [M^+] (80), 317 (15), 301 (100), 270 (10), 255 (70), 213 (62), 73 (85).

(*Z*)-1,4-Diethynyl-1,4-dimethoxycyclohexa-2,5-diene (*Z*-7c): Column purified *Z*-**6c** (6.6 g, 0.02 mol) was dissolved in degassed MeOH (100 mL). K_2CO_3 (6.9 g, 0.05 mol) was added and the mixture stirred under argon at room temp. for 1 h. The reaction mixture was poured into a large excess of ice-cold water (700 mL) and extracted with diethyl ether (3 × 100 mL). The combined organic extracts were again washed thoroughly with water (2 × 100 mL), followed by a saturated brine solution (200 mL). After drying with anhydrous Na_2SO_4, the solvent was removed to obtain *Z*-**7c** as a colorless crystalline solid, which was used for the next step without further purification. Yield: 3.7 g (0.02 mol, 100%); m.p. 94−96 °C. ^1H NMR: δ = 2.62 ppm (s, 2 H), 3.32 (s, 6 H), 6.08 (s, 4 H). ^{13}C NMR: δ = 51.6 ppm (OCH_3), 66.0 (Cq), 74.2 (Cq), 81.8 (CH), 129.1 (CH). IR: $\tilde{\nu}$ = 2113 cm^{-1}. MS (EI): *m*/*z* = (%) = 188 [M^+] (< 5) 173 (10), 157 (52), 142 (40), 127 (100), 114 (50).

(*Z*)-1,4-Diacetoxy-1,4-bis(trimethylsilylethynyl)cyclohexa-2,5-diene (*Z*-6b): A mixture of diol *Z*-**6a** (1.54 g, 0.005 mol), acetic anhydride (5 mL, 0.05 mol) and pyridine (1.5 mL) was stirred at room temp. overnight and at 60−70 °C for 4 h. The progress of the reaction was monitored by TLC. The reaction mixture was cooled to −5 °C, quenched with aqueous ammonia solution (28% 20 mL) and extracted with diethyl ether (3 × 100 mL). The combined organic phases were washed with 1 N HCl (2 × 100 mL), followed by saturated $NaHCO_3$ (200 mL), water (200 mL), and once with saturated brine solution (100 mL). After drying with anhydrous Na_2SO_4, the solvent was removed to yield a colorless solid, which was used for the next step without further purification. *Z*-**6b:** colorless solid, m.p.118−120 °C. ^1H NMR: δ = 0.00 ppm (s, 18 H), 1.89 (s, 6 H), 6.12 (s, 4 H). ^{13}C NMR: δ = −0.4 ppm (CH_3), 21.7 (CH_3), 67.0 (Cq), 92.4 (Cq), 101.0 (Cq), 128.0 (CH), 168.7 (Cq). MS(EI): *m*/*z* = (%) = 329 [M^+ − 59], (80), 286 (100), 271 (90), 255 (92), 73 (65).

(*Z*)-1,4-Diacetoxy-1,4-diethynylcyclohexa-2,5-diene (*Z*-7b): Deprotection of *Z*-**6b** by the standard procedure with K_2CO_3 in degassed methanol gave *Z*-**7b** in quantitative yield as a pale yellow solid. ^1H NMR: δ = 2.07 ppm (s, 6 H), 2.70 (s, 2 H), 6.36 (s, 4 H). Compound *Z*-**7b** was found to be unstable in the solid state and in solution ($CDCl_3$) and decomposed to yield an aromatic compound which has been tentatively identified as 2-acetoxy-1,4-diethynylbenzene.

4-Hydroxy-4-trimethylsilylethynylcyclohexa-2,5-dienone (9): *n*BuLi (26.5 mL, 0.03 mol of a 1.6 M solution in hexane) was added at −78 °C to a stirred solution of trimethylsilylacetylene (6.0 mL, 0.04 mol) in anhydrous THF (50 mL). The resulting pale yellow solution was stirred for 45 min at the same temperature before it was added to a yellow viscous solution of *p*-benzoquinone (2.2 g, 0.02 mol) in anhydrous THF (50 mL) at −78 °C. The mixture was stirred for 45 min and quenched with aqueous saturated NH_4Cl solution (300 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic extracts were washed with water (200 mL) and once with saturated brine solution (200 mL). After drying with $MgSO_4$, the solvent was removed in vacuo to furnish a colorless solid; yield: 3.8 g (0.02 mol, 93%), m.p. 98−100 °C. ^1H NMR: δ = 0.00 ppm (s, 9 H), 3.36 (br. s, 1 H), 6.73 and 5.99 (AA′BB′-q, *J* = 10.04 Hz, 4 H). ^{13}C NMR: δ = −0.5 ppm (CH_3), 62.4 (Cq), 91.9 (Cq), 100.4 (Cq), 126.8 (CH), 147.2 (CH), 185.1 (Cq) ppm. IR $\tilde{\nu}$ = 3281 cm^{-1}, 1665. MS (EI): *m*/*z* = (%) = 206 [M^+] (10), 190 (12), 175 (50), 73 (100).

Glaser−Eglinton Coupling of *Z*-7c; Synthesis of Macrocycles 5c and 12: Cu $(OAc)_2 \cdot H_2O$ (1.86 g, 0.01 mol) was added to a degassed mixture of CH_3CN and pyridine (4:1, v/v 100 mL), and the mixture stirred at room temp. for 30 min. A solution of *Z*-**7c** (0.7 g, 0.004 mol) in CH_3CN (5 mL) was added slowly to the suspension and the mixture stirred for another 3 h at room temp. The color of the solution changed from deep blue to brown within 10 min. The reaction was monitored by TLC. After 3 h the mixture was poured slowly into an ice-cold 5% HCl solution (500 mL) with constant stirring, then extracted repeatedly with diethyl ether (3 × 100 mL). The combined organic extracts were washed with ice-cold 5% HCl solution (2 × 100 mL), followed by saturated $NaHCO_3$ (200 mL), water (200 mL), and finally with saturated brine solution (100 mL). The organic layer was dried with anhydrous Na_2SO_4, filtered, and the solvent was removed in vacuo. The crude product was chromatographed on silica gel and eluted with hexane/ethyl acetate (8:2 v/v) to afford a mixture of **5c**, **12**, and some higher oligomers. This was rechromatographed on silica gel with hexane/ethyl acetate (9:1 v/v) to yield pure fractions of **5c** and **12**. Repeated crystallization from a diethyl ether/hexane mixture gave pure **5c** and **12** as colorless crystalline solids.

1,6,9,14-Tetramethoxytricyclo[12.2.2.2^{6,9}]icosa-7,5,17,19-tetraene-2,4,10,12-tetrayne (5c): Yield 0.02 g (2.5%); colorless crystalline solid, m.p. 205 °C (decomp.). ^1H NMR: δ = 3.36 ppm (s, 12 H), 6.15 (s, 8 H). ^{13}C NMR: δ = 52.4 ppm (OCH_3), 68.9 (Cq), 69.6 (Cq), 130.6 (CH). IR: $\tilde{\nu}$ = 2240 cm^{-1}, 2136. MS (EI): *m*/*z* = (%) = 372 [M^+] (5), 357 (10), 341 (10), 327 (30). HRMS calcd. 372.1362; found 372.1358. $C_{24}H_{20}O_4$ (372.1): calcd. C 77.39, H 5.42; found C 77.27, H 5.45.

1,6,9,14,17,22-Hexamethoxytetracyclo[20.2.2.2^{6,9}.2^{14,17}]triaconta-7,15,23,25,27,29-hexaene-2,4,10,12,18,20-hexayne (12): Yield 0.06 g (9.1%); colorless solid, m.p. 180 °C (decomp.). ^1H NMR: δ = 3.22 ppm (s, 18 H), 5.93 (s, 12 H). ^{13}C NMR: δ = 51.9 ppm (OCH_3), 66.6 (Cq), 70.2 (Cq), 77.6 (Cq), 128.3 (CH). IR: $\tilde{\nu}$ = 2251 cm^{-1}. MS (EI): *m*/*z* = (%) = 558 [M^+] (2), 527 (30), 497 (10), 481 (15). HRMS calcd. 558.2042; found 558.2048.

X-ray Crystallographic Data for Compound 5c: Data were collected with an Enraf−Nonius CAD4 diffractometer by using Cu-K_α radiation (λ = 1.54180 Å) at 293 K. Crystal data: monoclinic, space group *P*21/*n*, *a* = 9.6894 (17), *b* = 5.8296 (13), *c* = 17.343 (4) Å, *V* = 979.2 (4) Å^3, *Z* = 2. Data collection: a crystal of ca. 0.3 × 0.3 × 0.4 mm was used to record 1768 intensities, $2\theta_{max}$ = 67.75°, completeness to θ = 67.75 was 99.9%. Structure refinement: the structure was refined anisotropically by full-matrix least-squares on F^2 to *wR*2 = 0.0922, *R*1 = 0.0347 for 144 parameters and zero restraints. CCDC-193339 contains the supplementary crystallographic data for this paper. These data can be obtained free of

charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: (internat.) + 44-1223/336-033; E-mail: deposit@ccdc.cam.ac.uk].

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[1] P. Siemsen, R. C. Livingston, F. Diederich, *Angew. Chem. Int. Ed.* **2000**, *39*, 2632−2657; *Angew. Chem.* **2000**, *112*, 2740−2767.

[2] For recent reviews:[2a] F. Diederich, in: *Modern Acetylene Chemistry* (Eds.: P. J. Stang, F. Diederich); VCH, Weinheim **1995**; Ch. 13, pp. 443−471. [2b] L. T. Scott, J. M. Cooney, in: *Modern Acetylene Chemistry* (Eds.: P. J. Stang, F. Diederich); VCH, Weinheim, **1995**; Ch. 9, pp. 321−351. [2c] H. Hopf, *Classics in Hydrocarbon Chemistry*; Wiley-VCH, Weinheim, **2000**; Ch. 15, pp. 457−472. [2d] Y. Rubin, F. Diederich, in: *Stimulating Concepts in Chemistry* (Eds.: F. Vögtle, J. F. Stoddart, M. Shibasaki); Wiley-VCH: Weinheim, **2000**; pp 163−186.[2e]F. Diederich, *Chem. Commun.* **2001**, 219−227.

[3] M. Psiorz, H. Hopf, *Angew. Chem. Int. Ed. Eng.* **1982**, *21*, 623−624; *Angew. Chem.* **1982**, *94*, 639−640.

[4] T. Kawase, N. Ueda, M. Oda, *Tetrahedron Lett.* **1997**, *38*, 6681−6684.

[5] M. M. Haley, L. Langsdorf, *Chem. Commun.* **1997**, 1121−1122.

[6] Y. Tobe, R. Furukawa, M. Sonoda, T. Wakabayashi, *Angew. Chem. Int. Ed.* **2001**, *40*, 4072−4073; *Angew. Chem.* **2001**, *113*, 4196−4198.

[7] [7a] Y. Rubin, T. C. Parker, S. I. Khan, C. L. Holliman, S. W. McElvany, *J. Am. Chem. Soc.* **1996**, *118*, 5308−5309. [7b] Y. Rubin, *Chem. Eur. J.* **1997**, *3*, 1009−1016. [7c] U. H. F. Bunz, Y. Rubin, Y. Tobe, *Chem. Soc. Rev.* **1999**, *28*, 107−119.

[8] R. Wolovsky, F. Sondheimer, *J. Am. Chem. Soc.* **1962**, *84*, 2844−2845; **1965**, *87*, 5720−5727.

[9] [9a] W. B. Wan, S. C. Brand, J. J. Pak, M. M. Haley, *Chem. Eur. J.* **2000**, *6*, 2044−2052. [9b] M. M. Haley, J. J. Pak, S. C. Brand, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 836−838; *Angew. Chem.* **1997**, *109*, 863−866 and refs. cited therein.

[10] T. Kawase, H. R. Darabi, M. Oda, *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 2664−2666; *Angew. Chem.* **1996**, *108*, 2803−2805.

[11] [11a] M. Srinivasan, S. Sankararaman, H. Hopf, I. Dix, P. G. Jones, *J. Org. Chem.* **2001**, *66*, 4299−4303. [11b] M. Srinivasan, S. Sankararaman, I. Dix, P. G. Jones, *Org. Lett.* **2000**, *2*, 3849−3851.

[12] Y. Rubin, C. B. Knobler, F. Diederich, *J. Am. Chem. Soc.* **1990**, *112*, 4966−4968.

[13] Based on the energy-minimized structures obtained from AM1-type semiempirical calculations.

[14] W. Ried, H. J. Schmidt, *Chem. Ber.* **1957**, *90*, 2553−2561.

[15] S. Sankararaman, H. Hopf, unpublished results.

[16] N. N. L. Madhavi, C. Bilton, J. A. K. Howard, F. H. Allen, A. Nangia, G. R. Desiraju, *New J. Chem.* **2000**, *24*, 1−4.

[17] [17a] N. Krause, A. Gerold, *Angew. Chem. Int. Ed. Engl.* **1997**, *36*, 186−204; *Angew. Chem.* **1997**, *108*, 194−213.[17b] S. Thorand, F. Vögtle, N. Krause, *Angew. Chem. Int. Ed.* **1999**, *38*, 3721−3723; *Angew. Chem.* **1999**, *111*, 3929−3931.

[18] [18a] S. K. Collins, G. P. A Yap, A. G. Fallis, *Angew. Chem. Int. Ed.* **2000**, *39*, 385−388; *Angew. Chem.* **2000**, *112*, 393−396.[18b] S. K. Collins, G. P. A. Yap, A. G. Fallis, *Org. Lett.* **2002**, *4*, 11−14.

[19] Calculations were performed using PC Spartan Pro Version 1.1, Wavefunction, Inc., Irvine, CA, U. S. A.

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