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Synthesis of differentially protected/functionalised acetylenic building blocks from *p*-benzoquinone and their use in the synthesis of new enediynes †

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Received 3rd March 2003, Accepted 20th May 2003
First published as an Advance Article on the web 4th June 2003

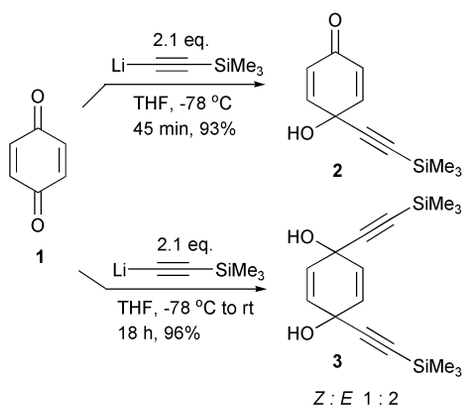
Sequential addition of two different lithium acetylides to *p*-benzoquinone yielded diastereomeric mixtures of 1,4-diethynylcyclohexa-2,5-diene-1,4-diols wherein the two ethynyl groups bear different protective/functional groups. Selective deprotection to the terminal acetylene followed by Pd(0) mediated coupling with *Z*-1,2-dichloroethene yielded new enediynes bearing cyclohexa-2,5-diene units.

Introduction

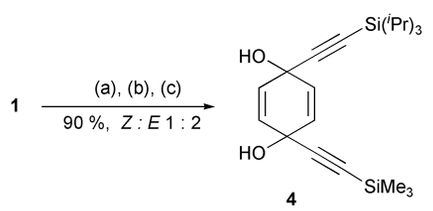
The recent past has witnessed tremendous growth in acetylene chemistry, fuelled by the discovery of new carbon–carbon bond forming reactions mediated by metal complexes.[1] Several novel acetylenic building blocks have been synthesized.[2] The building block approach is very useful for molecular scaffolding for the synthesis of *n*-cyclocarbons, dehydroannulenes, pericyclynes, graphyne subunits, enediynes and cyclophynes, to name a few.[3] Recently we have synthesized *Z*-1,4-diethynyl-1,4-dimethoxycyclohexa-2,5-diene from *p*-benzoquinone and demonstrated its use as an acetylenic building block for the synthesis of macrocyclic compounds bearing acetylenic bridges.[4] In the building block approach it is often necessary to selectively protect the terminal acetylenes with various protecting groups so that they can be deprotected at an appropriate step to carry out carbon–carbon bond forming reactions.[5] During the course of our investigation we have developed methods for the sequential addition of differentially protected lithium acetylides to *p*-benzoquinone for the synthesis of 1,4-diethynylcyclohexa-2,5-diene systems bearing two acetylenic groups that are either differentially protected or differentially functionalized at the termini.[6] Herein we report the synthesis of derivatives of cyclohexa-2,5-diene bearing two acetylenic groups, selective deprotection of one of the acetylenic groups to the corresponding terminal acetylene and subsequent coupling of the terminal acetylene with *Z*-1,2-dichloroethene for the synthesis of new enediynes. The derivatives of 1,4-diethynylcyclohexa-2,5-diene reported in this article are potentially useful as acetylenic building blocks for the synthesis of macrocycles and cyclophanes bearing enediyne and acetylenic bridges.

Results and discussion

Our investigation began with an interesting observation that the addition of two equivalents of lithium trimethylsilylacetylide to *p*-benzoquinone occurred stepwise. At −78 °C the reaction stopped cleanly at the mono addition stage to yield dienone **2** as the only product in nearly quantitative yield. It was necessary to warm up the reaction mixture above −40 °C in order for the second addition to take place to yield diol **3**. The dienone **2** was isolated in 93% yield as a colorless solid. Addition of two equivalents of lithium trimethylsilylacetylide to the dienone **2** at −78 °C and subsequent warming of the reaction mixture to rt yielded the diol **3** in 96% yield (Scheme 1).[4] These results prompted us to investigate the sequential addition of two different lithium acetylides to *p*-benzoquinone. Accordingly one equivalent of lithium triisopropylsilylacetylide was added at −78 °C to *p*-benzoquinone and the solution was stirred at −30 °C for 5 h and cooled back to −78 °C. Addition of one equivalent of lithium trimethylsilylacetylide to the same pot followed by slow warming to rt over a period of 16 h yielded the corresponding diol **4** as a mixture of *Z* and *E* isomers in the ratio 1 : 2, respectively (Scheme 2).



Scheme 1

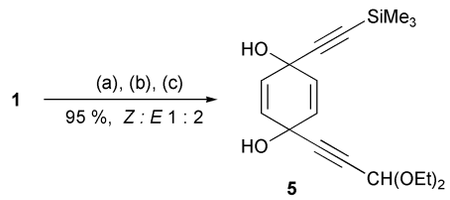


Scheme 2 (a) 1.0 eq. lithium triisopropylsilylacetylide, THF, 5 h, −78 °C to −30 °C; (b) 1.0 eq. lithium trimethylsilylacetylide, THF, −78 °C to rt, 16 h; (c) aq. NH_4Cl.

The diastereoisomers were separated by column chromatography and characterized by spectroscopic data. Similarly, sequential addition of one equivalent of lithium acetylide derived from 3,3-diethoxypropyne followed by one equivalent of lithium trimethylsilylacetylide yielded the corresponding diol **5** as a pair of *Z* and *E* isomers in the ratio 1 : 2, respectively (Scheme 3). In the above two reactions reversal of the sequence of addition of the two acetylides did not affect the yield of the

† Electronic supplementary information (ESI) available: 400 MHz ^1H NMR and ^{13}C NMR spectra. See http://www.rsc.org/suppdata/ob/b3/b302323k/

DOI: 10.1039/b302323k



Scheme 3 (a) 1.0 eq. lithium 3,3-diethoxypropyne, THF, 5 h, −78 °C to −30 °C; (b) 1.0 eq. lithium trimethylsilylacetylide, THF, −78 °C to rt, 16 h; (c) aq. NH_4Cl.

diols. The isomer ratios reported for diols **3**–**5** are based on the ^{1}H-NMR spectral integration of the cyclohexadiene protons. The stereochemistry of the *E* isomer of diol **3** was established by single crystal X-ray crystallographic data.[7] The structure of the *E* isomer of diol **3** in the crystal is shown in Fig. 1. During the chromatographic separation of the diastereomers of **3**, the *E* isomer was eluted first followed by the *Z* isomer. During our earlier studies, several derivatives of **3** also showed the same trend during chromatographic separation, in that the *E* isomer was always eluted first.[4] In general the *E* isomer was less polar than the *Z* isomer in this series of compounds. On the basis of these observations, based on the chromatographic elution order we have assigned the relative stereochemistry of the diastereomers of diols **4** and **5**. The *Z* isomer of diols **4** and **5** were converted to the corresponding methyl ethers *Z*-**6** and *Z*-**7** using NaH and methyl iodide in good yields (Scheme 4). The methyl ethers were generally found to be more stable than the diols towards acid catalyzed decomposition leading to aromatic compounds. Therefore further transformations were carried out with the methyl ether derivatives **6** and **7**. In order to demonstrate the synthetic utility of the acetylenic building blocks **6** and **7** where the acetylenic functional groups are differentially protected in case of **6** and differentially functionalized in case of **7**, selective deprotection of the TMS group followed by Pd(0) mediated Sonogashira coupling was taken up. The selective deprotection of the TMS group proceeded smoothly in high yields when *Z*-**6** and *Z*-**7** were treated with K_2CO_3 in MeOH under nitrogen atmosphere to yield the corresponding terminal acetylene *Z*-**8** and *Z*-**9**, respectively. Under these conditions the TIPS group is unaffected. The terminal acetylenic hydrogen appeared as a singlet at δ 2.55 ppm in the ^{1}H-NMR spectra of *Z*-**8** and *Z*-**9**. The coupling of *Z*-**8** and *Z*-**9** with *Z*-1,2-dichloroethene, mediated by $Pd(PPh_3)_4$ gave the corresponding enediyne derivatives *Z*-**10** (49%) and *Z*-**11** (25%), respectively (Scheme 5). The olefinic hydrogens of the newly formed enediyne moiety appeared as a singlet at δ 5.75 ppm in *Z*-**10** and at 5.81 ppm in *Z*-**11**, respectively in the corresponding ^{1}H-NMR spectrum. Finally the deprotection of the TIPS groups in *Z*-**10** was effected by treating it with *n*-Bu_4NF in THF to yield the terminal acetylene *Z*-**12** in 75% yield (Scheme 6). Attempted deprotection of the acetal groups in *Z*-**11** to the corresponding aldehyde under a variety of conditions[8] (98% HCOOH–$CHCl_3$, rt; 3 M HCl–THF, rt; $LiBF_4$–MeCN, rt and DDQ–MeCN–H_2O, rt) was unsuccessful. Under strongly acidic conditions the cyclohexadiene units in *Z*-**11** underwent aromatization, the products of which were not investigated further. Coupling of *Z*-**8** with excess *Z*-1,2-dichloroethene using $Pd(PPh_3)_4$ yielded the corresponding mono coupled product **13**. Deprotection of the TIPS group using TBAF yielded the terminal acetylene **14** in 85% yield (Scheme 7). Both *Z*-**12** and **14** are potentially useful starting materials for the construction of acetylenic macrocycles bearing cyclohexadiene moieties and enediyne and polyyne bridging units which are being currently investigated in our laboratory.

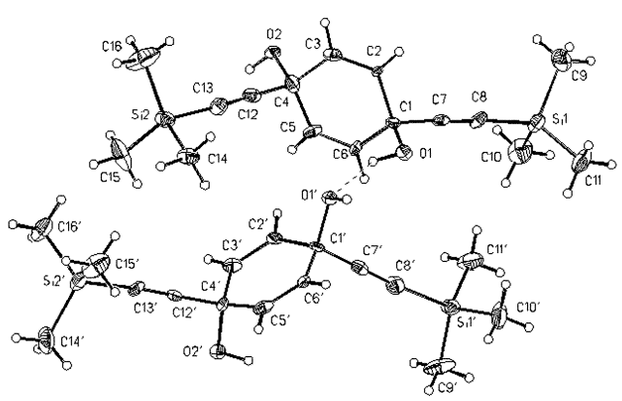
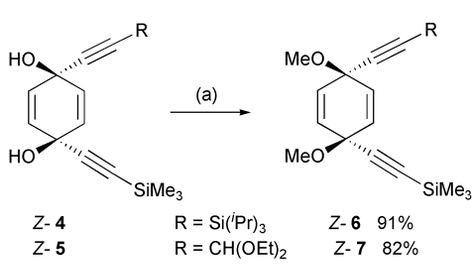
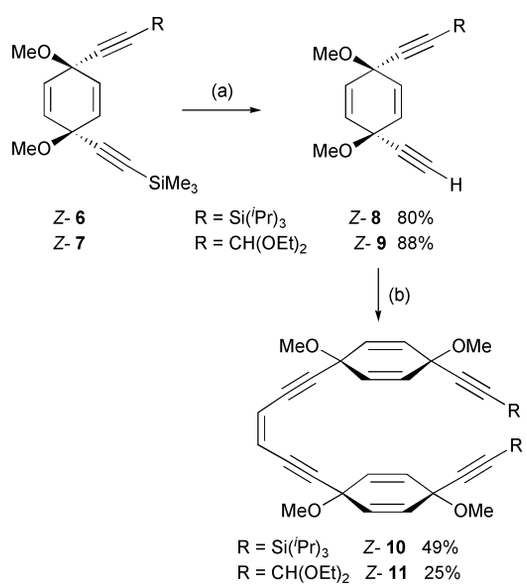


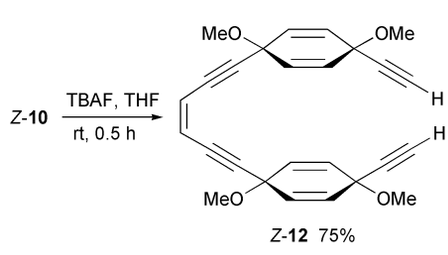
Fig. 1 Structure of the *E* isomer of diol **3** in the crystal showing the H-bonding between two molecules.



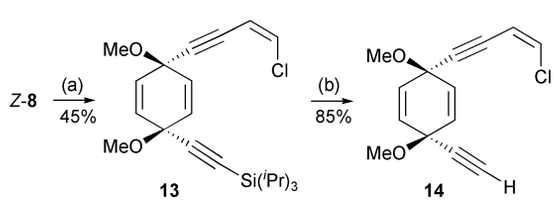
Scheme 4 (a) NaH, MeI, THF, −78 °C to rt, 16 h.



Scheme 5 (a) K_2CO_3, MeOH, rt, N_2, 1 h; (b) *Z*-ClCH=CHCl, $Pd(PPh_3)_4$, CuI, *n*-$BuNH_2$, THF, rt, N_2, 18 h.



Scheme 6



Scheme 7 (a) *Z*-ClCH=CHCl, $Pd(PPh_3)_4$, CuI, *n*-$BuNH_2$, THF, rt, 18 h; (b) TBAF, THF, rt, 0.5 h.

Conclusion

We have shown that the addition of lithium acetylides to *p*-benzoquinone occurs in a stepwise manner, thus providing a method for the synthesis of cyclohexa-2,5-dienes bearing different ethynyl substituents. Sequential addition of two different lithium acetylides to *p*-benzoquinone gave cyclohexa-2,5-diene-1,4-diols bearing ethynyl groups with different protective/functional groups. Using selective deprotection followed by Pd(0) mediated coupling reaction we have prepared enediynes **10**–**12** and eneynes **13**–**14** that are potentially useful as acetylenic building blocks.

Experimental

General remarks

^{1}H and ^{13}C NMR spectra ($CDCl_3$ solution) were recorded with a JEOL GSX-400 spectrometer at 400 MHz and 100 MHz or on a Bruker AM-200 at 200 MHz and 50 MHz, respectively. Chemical shifts are reported in ppm from TMS. Mass spectra were recorded either on a Finnigan MAT 8439 or a Finnigan MAT 8230 spectrometer. IR spectra were recorded either on a Nicolet 320 FTIR or on a Shimadzu IR470 spectrometer. All reactions were carried out under nitrogen unless indicated otherwise. Column chromatography was performed on silica gel (60–120 or 240–400 mesh) with various mixtures of diethyl ether, ethyl acetate, and hexane. TLCs were run on Macherey-Nagel polygram sil G/UV_{254} plates. Melting points are uncorrected. THF was distilled from calcium hydride.

1-Triisopropylsilanylethynyl-4-trimethylsilanylethynylcyclohexa-2,5-diene-1,4-diol (4)

n-BuLi (38 cm³ of a 1.6 M solution in hexane, 0.06 mol) was added to a stirred solution of triisopropylsilylacetylene (11.0 g, 13.5 cm³, 0.06 mol) in dry THF (100 cm³) at −78 °C. The resulting pale yellow solution was stirred for 45 min at the same temperature. It was added drop wise using a stainless steel needle to a stirred yellow viscous suspension of *p*-benzoquinone (5.93 g, 0.06 mol) in dry THF (300 cm³) at −78 °C. The dark blue reaction mixture was stirred at −30 °C for 5 h and then cooled to −78 °C. In another schlenck flask lithium trimethylsilylacetylide was prepared from *n*-BuLi (38 cm³ of a 1.6 M solution in hexane, 0.06 mol) and trimethylsilylacetylene (5.93 g, 8.5 cm³, 0.06 mol) in dry THF (100 cm³) at −78 °C. It was added drop wise using a stainless steel needle to the above dark blue reaction mixture at −78 °C and allowed to attain 10 °C over a period of 16 h. It was cooled to 0 °C and quenched with aqueous saturated NH_4Cl solution (300 cm³). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (4 × 100 cm³). The combined organic extract was washed with ice cold water (200 cm³) followed by ice cold saturated brine solution (200 cm³). After drying over $MgSO_4$, solvent was removed and the resulting solid product was separated by column chromatography using silica gel and ether–hexane mixture (3 : 7, v/v) as the eluant to yield first the pure *E*-isomer (*E*-**4**) (10.8 g, 51%) followed by the *Z*-isomer (*Z*-**4**) (9.17 g, 43%). *Z*-**4**: mp 186–188 °C; ν_{max} (KBr)/cm^{-1} 3345 (OH), 2181, 2153 (C≡C); δ_H (400 MHz) 5.81 (4H, s), 2.34 (2H, br, s), 0.91 (21H, s), 0.00 (9H, s); δ_C (100 MHz) 129.3 (d), 129.0 (d), 104.3 (s), 100.0 (s), 89.9 (s), 86.7 (s), 61.3 (s), 61.25 (s), 18.5 (q), 11.0 (d), −0.3 (q); *m*/*z* (EI) 388.2190 (M^+, 10%, $C_{22}H_{36}Si_2O_2$ requires 388.2254), 370 (20), 327 (58), 311 (40), 257 (42), 73 (100); *E*-**4**: mp 56–58 °C; ν_{max} (KBr)/cm^{-1} 3413 (OH), 2164 (C≡C); δ_H (400 MHz) 5.86 (4H, s), 2.20 (1H, br s), 2.1 (s, 1H), 0.89 (21H, s), 0.00 (9H, s); δ_C (100 MHz) 130.3 (d), 129.9 (d), 107.2 (s) 104.9 (s), 90.2 (s), 86.8 (s), 61.5 (s), 61.47 (s), 18.8 (q), 11.3 (d), −0.12 (q).

1-(3,3-Diethoxypropynyl)-4-trimethylsilanylethynylcyclohexa-2,5-diene-1,4-diol (5)

It was prepared by following the procedure described for diol **4** from *p*-benzoquinone (12.6 g, 0.12 mol). Lithium 3,3-diethoxypropylide [prepared from *n*-BuLi (0.140 mol, 88 mL of a 1.6 M solution in hexane) and 3,3-diethoxypropyne (15.0 g, 0.12 mol)] was added first followed by the addition of lithium trimethylsilylacetylide [prepared from *n*-BuLi (0.140 mol, 88 mL of a 1.6 M solution in hexane) and trimethylsilylacetylene (11.5 g, 0.12 mol)] The tan colored crude product was separated by column chromatography using silica gel and ether–hexane mixture (3 : 7, v/v) as the eluant to yield first the pure *E*-isomer (*E*-**5**) (16.7 g, 43%) followed by the *Z*-isomer (*Z*-**5**) (11.9 g, 30%). *Z*-**5**: viscous liquid; ν_{max} (film)/cm^{-1} 3355 (OH), 2176 (C≡C); δ_H (400 MHz) 5.80 (4H, s), 5.12 (1H, s), 3.55 and 3.40 (4H, quartet of AB pattern, *J* 9.5 and 7.1), 3.2 (1H, br, s), 2.93 (1H, br, s), 1.06 (6H, t, *J* 7.1), 0.00 (9H, s); δ_C (100 MHz) 129.6 (d), 128.7 (d), 104.2 (s), 91.2 (d), 90.2 (s), 84.9 (s), 80.2 (s), 61.01 (s), 61.00 (t), 60.6 (s), 15.0 (q), −0.3 (q); *m*/*z* (EI) 334.1600 (M^+, 1%, $C_{18}H_{26}SiO_4$ requires 334.16008), 317 (1), 301 (2), 255 (4), 246 (5), 231 (28), 215 (40), 191 (62), 73 (100); *E*-**5**: mp 88–90 °C; ν_{max} (KBr)/cm^{-1} 3355 (OH), 2176 (C≡C); δ_H (400 MHz) 5.88 (4H, s), 5.11 (1H, s), 3.5 and 3.4 (4H, quartet of AB pattern, *J* 9.5 and 7.1), 2.32 (1H, br, s), 2.20 (1H, br s), 1.06 (6H, t, *J* 7.1), 0.00 (9H, s); δ_C (100 MHz) 130.1 (d), 129.3 (d), 104.4 (s), 91.1 (d), 90.2 (s), 84.9 (s), 80.3 (s), 61.1 (t), 61.0 (s), 15.0 (q), −0.3 (q); *m*/*z* (EI) 335 (<1%), 334 (M^+,<1), 333 (1), 289 (M^+ − OEt, 1), 246 (5), 231 (12), 215 (15), 191 (20), 169 (100), 73 (90).

General procedure for the methylation of diols 4 and 5

The pure *Z* diol (*Z*-**4** or *Z*-**5**) (0.02 mol) in THF (100 cm³) was added to a stirred suspension of NaH (0.9 g, 0.04 mol) in THF (200 cm³) at −78 °C. The yellow colored suspension was stirred for 30 min at the same temperature. Methyl iodide (14.9 g, 6.6 cm³, 0.11 mol) was added drop wise from a syringe and the resulting mixture was allowed to warm to room temperature overnight (18 h). The reaction mixture was poured into ice cold saturated NH_4Cl solution (500 cm³). The organic layer was separated and the aqueous portion was extracted with ether (3 × 200 cm³). The combined organic extract was washed thoroughly with water (2 × 200 cm³) and finally with saturated brine solution (200 cm³). After drying over $MgSO_4$, solvent was removed to give the crude product as a viscous liquid. It was purified by column chromatography on silica gel with ether–hexane mixture (1 : 4, v/v) to afford the dimethyl ether as a colorless viscous liquid.

***Z*-1,4-Dimethoxy-1-(3,3-diethoxyprop-1-ynyl)-4-trimethylsilanylethynylcyclohexa-2,5-diene (*Z*-7).** Yield (4.46 g, 82%), viscous liquid, ν_{max} (film)/cm^{-1} 2977, 2899, 2166 (C≡C); δ_H (400 MHz) 5.87 and 5.84 (4H, AA′BB′pattern, *J* 10.2), 5.15 (1H, s), 3.57 and 3.43 (4H, quartet of AB pattern, *J* 9.5 and 7.1), 3.13 (3H, s, OMe), 3.10 (3H, s, OMe), 1.05 (6H, t, *J* 7.1), 0.00 (9H, s); δ_C (100 MHz) 129.4 (d), 128.7 (d), 102.8 (s), 91.2 (s), 91.1 (d), 83.3 (s), 81.3 (s), 66.6 (s), 66.2 (s), 60.9 (t), 51.7 (q), 51.5 (q), 15.1 (q), −0.3 (q); *m*/*z* (EI) 364 (1%), 363 (4), 362.2089 (M^+, 22, $C_{20}H_{30}SiO_4$ requires 362.1914), 331 (30), 317 (18), 289 (20), 273 (19), 255 (38), 241 (22), 227 (50), 183 (23), 113 (50), 103 (20), 73 (100).

***Z*-1,4-Dimethoxy-1-triisopropyl-silanylethynyl-4-trimethylsilanylethynylcyclohexa-2,5-diene (*Z*-6).** In case of *Z*-**6**, its formation was confirmed only by ^{1}H- and ^{13}C-NMR spectral data. After purification it was directly converted to *Z*-**8** and compound *Z*-**8** was fully characterized. Yield *Z*-**6** (91%) viscous liquid, δ_H (400 MHz) 5.80 (4H, s), 3.12 (6H, s), 0.88 (21H, s), 0.00 (9H, s); δ_C (100 MHz) 129.5 (d), 127.1 (d), 104.7 (s), 102.7

(s), 91.5 (s), 90.2 (s), 61.5 (s), 61.3 (s), 56.0 (q), 18.8 (q), 11.3 (d), 0.0 (q).

General procedure for the deprotection of the TMS group

To a stirred solution of the column purified dimethoxy derivative (*Z*-**6** and *Z*-**7**) (0.01 mol) in degassed MeOH (200 cm^3), solid K_2CO_3 (5.45 g, 0.04 mol) was added under a nitrogen atmosphere at room temperature and stirring was continued for 1 h. After completion of the reaction, about 150 cm^3 of MeOH was removed under reduced pressure then the resulting slurry was poured into ice cold water (700 cm^3) and extracted with ether (3 × 100 cm^3). The combined organic extract was washed thoroughly with water (2 × 100 cm^3) and once with saturated brine solution (200 cm^3). After drying over anhydrous $MgSO_4$, solvent was removed to get a yellow viscous liquid. The crude product was column chromatographed on silica gel with ether–hexane mixture (1 : 9, v/v) to afford the desilylated product as colorless viscous liquids.

***Z*-1,4-Dimethoxy-1-triisopropylsilanylethynyl-4-ethynylcyclohexa-2,5-diene (*Z*-8).** Yield (5.95 g, 0.017 mol, 85% from 0.02 mole of *Z*-**6**), colorless liquid, ν_{max} (film)/cm^{-1} 3311 (C≡C–H), 2944, 2866, 2163 (C≡C); δ_H (400 MHz) 6.12 and 6.03 (4H, AA′BB′pattern, *J* 10.1), 3.38 (3H, s), 3.32 (3H, s), 2.55 (1H, s), 1.08 (21H, s); δ_C (100 MHz) 129.8 (d), 128.2 (d), 104.7 (s), 88.1 (s), 82.1 (d), 73.6 (s), 66.8 (s), 66.3 (s), 51.7 (q), 51.6 (q), 18.5 (q), 11.1 (d); *m*/*z* (EI) 346 (5%), 345 (10), 344.2084 (M^+, 38, $C_{21}H_{32}SiO_2$ requires 344.2173), 313 (M^+ − OMe, 25), 286 (M^+ − $CH(CH_3)_2$, 30), 75 (100).

***Z*-1,4-Dimethoxy-1-(3,3-diethoxyprop-1-ynyl)-4-ethynylcyclohexa-2,5-diene (*Z*-9).** Yield (3.37 g, 0.009 mol, 90% from 0.01 mol of *Z*-**7**), colorless liquid, ν_{max} (film)/cm^{-1} 3288 (C≡C–H), 2978, 2889, 2114 (C≡C); δ_H (400 MHz) 5.99 and 5.96 (4H, AA′BB′pattern, *J* 10.3), 5.22 (1H, s), 3.65 and 3.52 (4H, quartet of AB pattern, *J* 9.5 and 7.1), 3.23 (3H, s), 3.22 (3H, s), 2.55 (1H, s), 1.14 (6H, t, *J* 7.1); δ_C (100 MHz) 128.8 (d), 128.7 (d), 90.9 (d), 82.8 (s), 81.6 (d), 81.3 (s), 74.1 (s), 65.9 (s), 65.8 (s), 60.6 (t), 51.4 (q), 51.3 (q), 14.8 (q); *m*/*z* (EI) 290 (M^+, 1%), 289 (2), 273 (5), 259 (M^+ − OCH_3, 18), 245 (M^+ − OC_2H_5, 20), 231 (18), 217 (20), 201 (M^+ − $2OC_2H_5$, 20), 185 (M^+ − $CH(OEt)_2$, 40), 139 (100), 127 (40), 113 (65), 85 (28), 75 (30).

General procedure for the synthesis of enediynes *Z*-10 and *Z*-11

(*Z*)-1,2-Dichloroethene (0.39 g, 4.02 mmol) was added to a dry schlenck flask, containing tetrakis(triphenylphosphine)-palladium(0) (0.193 g, 0.17 mmol) in dry THF (50 cm^3). The mixture was stirred at room temperature for 30 min. To the clear yellow solution thus obtained the acetylenic substrate (*Z*-**8** and *Z*-**9**) (8.4 mmol) and *n*-butylamine (2 cm^3) were added and the resulting mixture was stirred well. After 30 min CuI (0.175 g, 0.921 mmol) was added and stirring was continued for 18 h at room temperature. After completion of the reaction, ice cold saturated aqueous NH_4Cl (300 cm^3) was added to the reaction mixture and it was extracted with CH_2Cl_2 (4 × 100 cm^3). The combined organic extracts were washed with water (200 cm^3) and saturated brine (200 cm^3). The organic layer was dried over $MgSO_4$ and solvent was removed. The crude product was purified by column chromatography on silica gel with ether–hexane mixture (1 : 9 v/v in the case of *Z*-**8** and 3 : 7 v/v in the case of *Z*-**9**) to afford the enediyne as a viscous liquid.

***Z*-1,6-Bis[*Z*-1,4-dimethoxy-4-(triisopropylsilylethynyl)cyclohexa-2,5-dienyl]hexa-3-ene-1,5-diyne (*Z*-10).** Yield (1.41 g, 2 mmol, 49% from 8.4 mmol of *Z*-**8**), viscous liquid, ν_{max} (film)/cm^{-1} 2943, 2866, 2163 (C≡C); δ_H (400 MHz) 5.98 (8H, s), 5.75 (2H, s), 3.30 (6H, s), 3.27 (6H, s), 0.98 (42H, s); δ_C (100 MHz) 128.8 (d), 127.9 (d), 119.6 (d), 104.7 (s), 94.6 (s), 87.6 (s), 82.7 (s), 66.6 (s), 66.5 (s), 51.5 (q), 51.3 (q), 18.2 (q), 10.8 (d). Although, the ^1H and ^{13}C NMR spectroscopic data are consistent with the structure of enediyne *Z*-**10**, mass spectrum (EI) of this substance did not show M^+ ion. However, its desilylated derivative, namely, enediyne *Z*-**12** is fully characterized.

***Z*-1,6-Bis[*Z*-1,4-dimethoxy-4-(3,3-diethoxyprop-1-ynyl)cyclohexa-2,5-dienyl]hexa-3-ene-1,5-diyne (*Z*-11).** Yield (0.77 g, 1.3 mmol, 25% from 10.3 mmol of *Z*-**9**), viscous liquid, ν_{max} (film)/cm^{-1} 2978, 2888, 2146 (C≡C); δ_H (400 MHz) 6.03 and 5.97 (8H, AA′BB′pattern, *J* 10.1), 5.81 (2H, s), 5.23 (2H, s), 3.63 and 3.50 (8H, quartet of AB pattern, *J* 9.5 and 7.1), 3.3 (6H, s), 3.23 (6H, s), 1.14 (12H, t, *J* 7.1); δ_C (100 MHz) 129.1 (d), 128.5 (d), 120.0 (d), 94.8 (s), 91.2 (d), 83.33 (s), 83.29 (s), 81.4 (s), 66.7 (s), 66.2 (s), 60.9 (t), 51.9 (q), 51.7 (q), 15.0 (q). Although, the ^1H and ^{13}C NMR spectroscopic data are consistent with the structure of enediyne Z-**11**, mass spectrum (EI) of this substance did not show M^+ ion.

Z-1,6-Bis[*Z*-4-ethynyl-1,4-dimethoxycyclohexa-2,5-dienyl]hexa-3-ene-1,5-diyne (*Z*-12)

EtOH (10 drops) and *n*-Bu_4NF (1 M solution in THF, 1.5 cm^3) were added to the silyl protected enediyne *Z*-**10** (1.27 g, 2.0 mmol) in dry THF (50 cm^3) with stirring at room temperature. After 0.5 h the reaction mixture was diluted with ether (100 cm^3), washed with water (100 cm^3) followed by saturated brine (2 × 100 cm^3). The organic layer was dried over $MgSO_4$, and solvent was evaporated. The crude product was purified by column chromatography on silica gel with ether–hexane mixture (20 : 80, v/v) to afford *Z*-**12** (0.53 g, 75%) as a colorless solid, mp 118–120 °C; ν_{max} (KBr)/cm^{-1} 3293 (C≡C–H), 2936, 2099 (C≡C); δ_H (400 MHz) 6.04 and 5.97 (8H, AA′BB′pattern, *J* 10.1), 5.83 (2H, s), 3.30 (6H, s), 3.24 (6H, s), 2.53 (2H, s); δ_C (100 MHz) 129.2 (d), 128.6 (d), 120.0 (d), 94.7 (s), 83.3 (s), 82.1 (d), 74.2 (s), 66.6 (s), 66.1 (s), 51.8 (q), 51.6 (q); *m*/*z* (EI) 369.1320 (M^+ − OCH_3, 2%, $C_{25}H_{21}O_3$ requires 369.1491), 338 (19), 307 (38), 276 (42), 263 (100), 250 (50).

[4-(*Z*-4-Chlorobut-3-en-1-ynyl)-*Z*-1,4-dimethoxycyclohexa-2,5-dienylethynyl]triisopropylsilane (13)

The acetylenic precursor *Z*-**8** (2.9 g, 8.4 mmol) was treated with *Z*-dichloroethene (1.87 g, 19.3 mmol) and the reaction was carried out as described in the synthesis of compounds *Z*-**10** and *Z*-**11**. Chromatographic purification of the crude product on silica gel with ether–hexane mixture (1 : 9, v/v) gave **13** (1.53 g, 45%) as a viscous liquid, ν_{max} (film)/cm^{-1} 2944, 2886, 2163 (C≡C); δ_H (400 MHz) 6.44 (1H, d, *J* 7.5), 6.11 and 6.06 (4H, AA′BB′pattern, *J* 10.2), 5.88 (1H, d, *J* 7.5), 3.37 (3H, s), 3.36 (3H, s), 1.07 (21H, s); δ_C (100 MHz) 129.6 (d), 129.5 (d), 128.1 (d), 111.3 (d), 104.8 (s), 95.3 (s), 88.0 (s), 79.5 (s), 67.0 (s), 66.8 (s), 51.6 (q), 18.5 (q), 11.1 (d); *m*/*z* (EI) 408 (<1%), 407 (2), 406 (8), 405 (5), 404.1893 (M^+, 18, $C_{23}H_{33}SiO_2{}^{35}Cl$ requires 404.1939), 373 (10), 361 (80), 287 (78), 275 (60), 260 (100), 245 (79).

Z-4-(*Z*-4-Chlorobut-3-en-1-ynyl)-6-ethynyl-1,4-dimethoxycyclohexa-2,5-diene (14)

Desilylation of **13** (1.42 g, 4.0 mmol) was carried out in dry THF (50 cm^3) using the same procedure as described in the case of *Z*-**12** using *n*-Bu_4NF. The crude product was purified by column chromatography on silica gel with ether–hexane mixture (1 : 4, v/v) to afford **14** (0.74 g, 85%) as colorless viscous liquid, ν_{max} (film)/cm^{-1} 3293 (C≡C–H), 2938, 2115 (C≡C); δ_H (400 MHz) 6.45 (1H, d, *J* 7.49), 6.10 and 6.05 (4H, AA′BB′-pattern, *J* 10.1), 5.91 (1H, d, *J* 7.49), 3.37 (3H, s), 3.32 (3H, s), 2.61 (1H, s); δ_C (100 MHz) 129.5 (d), 129.1 (d), 128.1 (d), 111.3 (d), 81.9 (s), 81.6 (d), 80.0 (s), 73.7 (s), 66.7 (s), 66.5 (s), 51.74 (q), 51.70 (q); *m*/*z* (EI) 217 (M^+ − OMe, 10%), 181 (100), 150 (80).

Crystal data for compound *E*-3‡

Single crystals of *E*-**3** suitable for X-ray diffraction were obtained by crystallization of the column purified *E*-**3** from a mixture of ether–hexane. The sample was dissolved in minimum amount of ether and then hexane was added until a slight turbidity was seen. The resulting solution was left in the fridge to obtain the crystals. C_{16} H_{24} O_2 Si_2, M = 304.53, Orthorhombic, space group $Pca2(1)$, a = 12.818(7), b = 10.012(5), c = 29.263(14) Å, U = 3756(3) Å^3, T = 115(2) K, Z = 8, λ = 0.71073 Å, m = 0.188 mm^{-1}, 18239 reflections measured, 5904 unique (R_{int} = 0.1206), final $wR(F^2)$ [for 2540 reflections with $I > 2\sigma(I)$] was 0.1745 and $wR(F^2)$ was 0.2075 (all data), refinement method was full-matrix least-squares on F^2 and goodness of fit on F^2 was 0.846.

Acknowledgments

We thank the Volkswagen Stiftung, Hannover, Germany and the Council of Scientific and Industrial Research, India for financial support. We thank Professor H. Hopf, Institute of Organic Chemistry, University of Braunschweig, Germany for his constant support, encouragement and useful discussions and Professor Mikhail Antipin, Director of the X-Ray Structural Center, INEOS, Russian Academy of Sciences, Moscow, for the X-ray crystallographic data and structure refinement. A graduate fellowship from IIT, Madras for MS is gratefully acknowledged. We thank the Regional Sophisticated Instrumentation Centre, IIT, Madras for the spectral data.

‡ CCDC reference numbers 202840. See http://www.rsc.org/suppdata/ob/b3/b302323k/ for crystallographic data in .cif or other electronic format.

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