Synthesis and Structure of Carbomethoxyethynyl[2.2]paracyclophane Derivatives

Assunta Marrocchi,* Aldo Taticchi, Selvaggia Landi

Dipartimento di Chimica, Università degli Studi di Perugia, via Elce di Sotto 8, 06123 Perugia, Italy
Fax +39(075)5855560; E-mail: assunta@unipg.it

Received 12 November 2007; revised 2 January 2008

Abstract: The synthesis of the three ethynyl esters and three ethynyl[2.2]paracyclophane derivatives is described. All of the compounds were fully characterized.

Key words: cyclophanes, synthesis, Diels–Alder reaction, cross-coupling, alkynes

There is a great deal of interest in the synthesis of [2.2]paracyclophane derivatives and their application in asymmetric catalysis and materials chemistry.[1] The face-to-face arrangement of the benzene rings, distorted into boat-like shapes, determines three-dimensional structures with peculiar electronic properties due to the interaction between the π-electron systems of the two benzene rings.[1a–c] It is the wide variety of cyclophane structural arrangements that affords such a rich field for research into synthesis, molecular design and supramolecular architecture. Conjugated derivatives of [2.2]paracyclophane are of particular interest as novel molecules for organic electronics. In a continuation of our study on the synthesis of [2.2]paracyclophanes,[2] we report the preparation of the novel ethynyl esters **1**–**3** and their use as building blocks for the synthesis of cyclophanes (Figure 1).

Esters **1** and **2**, characterized by an acetylenic bond conjugated with the electron-attracting carbomethoxy group, may be useful dienophiles for synthesizing substituted biaryl-like cyclophanes by a two-step approach based on intermolecular Diels–Alder cycloaddition reaction,[3] followed by aromatization of the cycloadducts. Biaryls are important subunits in a broad range of ligands used in asymmetric catalysis and in the material structures.[4] Ester **3**, for example, is a building block for the preparation of *pseudo-gem*-substituted polyethynylaryl derivatives through the Sonogashira heterocoupling reaction, which are interesting compounds in organic electronics.

Ester **1** has been prepared by treating 4-ethynyl[2.2]paracyclophane[2d,5] with butyllithium and then quenching the acetylide with methyl chloroformate (76% yield). The same procedure allowed *gem*-diester **2** to be prepared, starting from compound **3**, but using lithium diisopropylamine as the base for the anionization (83% yield). Finally, *pseudo-gem*-ethynylcarbomethoxy derivative **3** has been prepared starting from the previously described[6] 4-formyl-15-carbomethoxy[2.2]paracyclophane, following a procedure developed by Hopf to convert an aldehyde carbonyl group into an ethynyl group.[5] When ethynyl esters **1** and **2** were allowed to interact with the electron-rich open-chain dienes 2,3-dimethyl-1,3-butadiene and 2,3-dimethoxy-1,3-butadiene under a broad variety of thermal and Lewis acid ($EtAlCl_2$, Et_2AlCl, $AlCl_3$) catalyzed conditions,[3] no Diels–Alder reaction was observed. Arylacetylenes are known to be poor dienophiles; nevertheless, the complete lack of reactivity was unanticipated. In fact, Pearson and Kim[7] reported the Diels–Alder reaction of methylphenylpropiolate with a substituted cyclopentadienone. The reaction occurred, even at high temperature, in only low yield (25%). Better results (75% yield) were obtained when phenyl-*p*-toluenesulfonylacetylene was used as dienophile. Unfortunately this functionalization is not of great interest in materials chemistry. The behavior of ester **2** was still more surprising in view of the increased carbon–carbon triple bond activation due to the transannular interaction with the carbomethoxy group on the non-ethynylated benzene ring.

Starting from *pseudo-gem*-carbomethoxy ethynyl[2.2]paracyclophane (**3**) we have succeeded in carry-

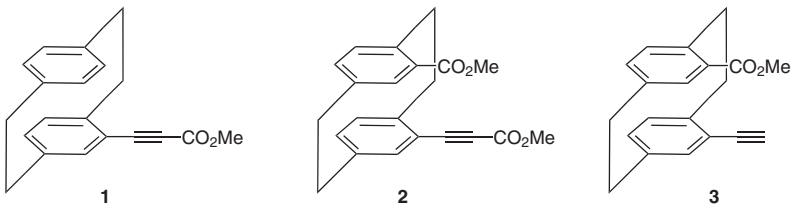
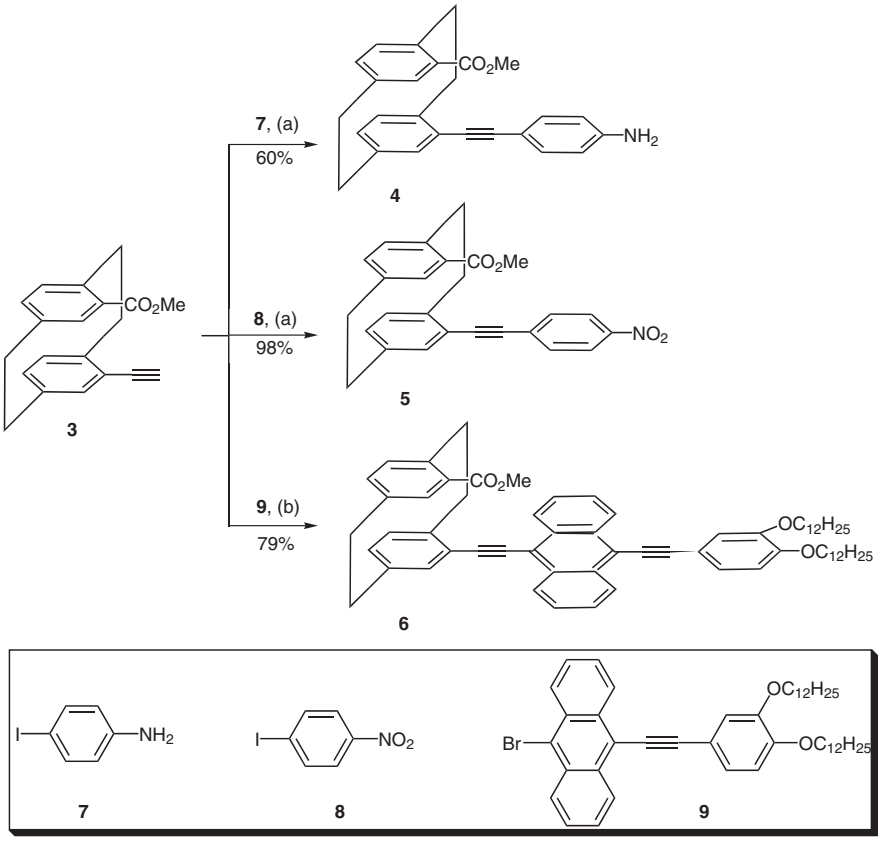


Figure 1

SYNTHESIS 2008, No. 7, pp 1045–1048
Advanced online publication: 06.03.2008
DOI: 10.1055/s-2008-1032122; Art ID: T17407SS



Scheme 1 *Reagents and conditions*: (a) $Pd(PPh_3)_2Cl_2$, CuI, PPh_3, Et_3N, THF; (b) $Pd(PPh_3)_4$, CuI, *i*-Pr_2NH, toluene.

ing out the synthesis of the *pseudo-gem*-carbomethoxyarylethynyl compounds **4**–**6** by Pd/Cu catalyzed Sonogashira heterocoupling reaction[8] (Scheme 1).

This methodology is known to be a powerful tool for the preparation of both terminal and internal acetylenes. Coupling of ethynyl ester **3** with *p*-iodoaminobenzene (**7**) and *p*-iodonitrobenzene (**8**) led to amino- and nitro-carbomethoxy ethynylcyclophanes **4** (60% yield) and **5** (98% yield), respectively. Cyclophane **6** was obtained (79% yield) by Sonogashira reaction between **3** and bromoanthracene derivative **9**, prepared from 9-bromo-10-iodoanthracene[9] and 3,4-bis(dodecyloxy)ethynylbenzene.[10] Conjugated compounds **4**–**6** are of interest for their potential applications in photovoltaic devices[11] in view of the presence of chromophores that allow good light harvesting to be obtained. Moreover, a variety of derivatives may be prepared by converting the *pseudo-gem*-methyl ester groups into other functionalities. The structures of all original compounds have been assigned on the basis of the known outcome of the reaction used for their preparation and on the analysis of ^1H and ^{13}C NMR spectra.

In summary, the synthesis of three novel carbomethoxy arylethynyl [2.2]paracyclophanes by Pd/Cu-catalyzed Sonogashira coupling reaction starting from ethynyl ester **3** has been reported. These compounds may be of interest for application in organic electronics.

Melting points were determined on a Büchi melting point apparatus and are uncorrected. Adsorption chromatography was carried out on Riedel de Haën silica gel (32–63 μm; 230–400 mesh ASTM). UV/Vis spectra were recorded on a Kontron Uvikon 923 spectrophotometer. NMR spectra were recorded on a Varian Associates VXR-400 multinuclear instrument (internal TMS). Petroleum ether (PE) as 40–60 °C boiling fraction was used.

4-Carbomethoxyethynyl[2.2]paracyclophane (1)

To a solution of 4-ethynyl[2.2]paracyclophane (0.7 g, 3 mmol) in anhydrous Et_2O (9 mL) at –30 °C was added, dropwise, *n*-BuLi (1.6 M in hexane, 2.44 mL, 3.9 mmol). The reaction mixture was stirred at –30 °C for 3 h, then a solution of methyl chloroformate (0.23 mL, 3 mmol) in anhydrous Et_2O (1.5 mL) was added dropwise. The reaction mixture was stirred at –30 °C for 30 min, then warmed to r.t., filtered and concentrated in vacuo to afford the crude ethynyl ester **1**. Column chromatography (SiO_2; PE–CH_2Cl_2, 2:1) gave the pure product.

Yield: 76%; pale-orange solid; mp 67–68 °C (MeOH).

IR ($CHCl_3$): 1705 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.95–3.15 (m, 6 H), 3.24 (dd, *J* = 13.0, 10.4 Hz, 1 H), 3.58 (dd, *J* = 12.2, 10.4 Hz, 1 H), 3.88 (s, 3 H, OMe), 6.45 (dd, *J* = 7.7, 1.8 Hz, 1 H), 6.51 (d, *J* = 7.9 Hz, 1 H), 6.49–6.54 (m, 2 H), 6.61 (dd, *J* = 7.9, 1.9 Hz, 1 H), 6.70 (d, *J* = 1.9 Hz, 1 H), 6.88 (dd, *J* = 7.7, 1.7 Hz, 1 H).

^{13}C NMR ($CDCl_3$): δ = 34.5, 34.6, 35.3, 35.6, 52.9, 84.0, 87.2, 121.3, 130.8, 132.8, 132.9, 133.6, 134.4, 135.5, 138.4, 139.5, 139.6, 140.4, 145.0, 155.0.

Anal. Calcd for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 82.63; H, 6.26.

4-Carbomethoxyethynyl-15-carbomethoxy[2.2]paracyclophane (2)

To a solution of *i*-Pr_2NH (0.21 mL, 1.4 mmol) in anhydrous THF (3.5 mL) at –30 °C was added, dropwise, *n*-BuLi (1.6 M in hexane, 0.79 mL, 1.3 mmol). The reaction mixture was stirred at –30 °C for 30 min then allowed to warm to r.t. over 2 h. The mixture was again cooled to –30 °C and a solution of cyclophane **3** (0.24 g, 0.84 mmol) in THF (13.5 mL) was added. After 40 min, the mixture was allowed to warm to 0 °C and stirring was continued for 1.5 h. Methyl chloroformate (0.08 mL, 1.05 mmol) was then added dropwise at –30 °C. The reaction mixture was stirred for 30 min, then warmed to r.t., filtered and concentrated in vacuo to afford the crude ethynyl ester **2**. Column chromatography (SiO_2; PE–EtOAc, 9:1) afforded the pure product.

Yield: 83%; pale-yellow solid; mp 104–105 °C (MeOH).

IR ($CHCl_3$): 1711 (s, C=O) cm^{-1}.

^1H NMR ($CDCl_3$): δ = 3.00–3.16 (m, 7 H), 3.71–3.80 (m, 1 H), 3.84 (s, 3 H), 3.87 (s, 3 H), 6.52–6.77 (m, 5 H), 7.29 (d, *J* = 2.0 Hz, 1 H).

^{13}C NMR ($CDCl_3$): δ = 33.4, 34.6, 34.8, 35.4, 51.6, 52.6, 83.7, 86.0, 120.7, 129.5, 133.9, 134.8, 135.5, 136.2, 136.5, 136.8, 139.5, 139.8, 142.5, 144.5, 154.5, 166.6.

Anal. Calcd for $C_{22}H_{20}O_4$: C, 75.84; H, 5.79. Found: 75.60; H, 5.80.

4-Ethynyl-15-carbomethoxy[2.2]paracyclophane (3)

To a suspension of 4-formyl-15-carbomethoxy[2.2]paracyclophane (2.3 g, 7.78 mmol) and Cs_2CO_3 (16.0 g) in anhydrous MeOH (270 mL), under vigorous stirring at r.t., was added dimethyl-1-diazo-2-oxopropylphosphonate[12] (3.0 g). The mixture was then heated at 40 °C for 12 h, then additional Cs_2CO_3 (8.0 g) and dimethyl-1-diazo-2-oxopropylphosphonate (1.5g) were added. The mixture was stirred at 40 °C for 24 h, then CH_2Cl_2 (70 mL) and H_2O (50 mL) were added. The layers were separated, the aqueous phase was extracted with CH_2Cl_2 (3 × 50 mL) and the combined organic solutions were washed with brine (2 × 100 mL), dried over Na_2SO_4 and evaporated in vacuo. The residue was filtered through SiO_2, (PE–CH_2Cl_2, 1:1) to afford compound **3**.

Yield: 83%; colorless solid; mp 189–190 °C (MeOH).

IR ($CHCl_3$): 1710 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.85–3.04 (m, 7 H), 3.10 (s, 1 H), 3.60–3.67 (m, 1 H), 3.79 (s, 3 H,), 6.42–6.60 (m, 5 H), 7.24–7.25 (m, 1 H);

^{13}C NMR ($CDCl_3$): δ = 33.3, 34.7, 34.8, 34.9, 51.4, 80.3, 83.1, 123.5, 129.0, 133.4, 133.6, 134.7, 136.2, 136.3, 136.4, 139.3, 139.3, 142.8, 142.9, 167.0.

Anal. Calcd for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 82.50; H, 6.25.

Sonogashira Reaction of 4-Ethynyl-15-carbomethoxy[2.2]paracyclophane (3) with Arylhalides 7–9; Typical Procedure

Anhydrous THF (26 mL), 4-ethynyl-15-carbomethoxy[2.2]paracyclophane (**3**; 0.58 g, 2.0 mmol), Ph_3P (0.073 g, 0.28 mmol), CuI (0.026 g, 0.14 mmol), 4-iodoaniline (**7**; 0.57 g, 2.6 mmol), $PdCl_2(PPh_3)_2$ (0.028 g, 0.04 mmol) and Et_3N (11.5 mL) were placed in a flask and degassed at 0 °C with Ar. The mixture was heated at 75 °C for 2 h then the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (PE–CH_2Cl_2, 2:1) to give **4**.

Yield: 0.46 g (60%); colorless solid; mp 109–110 °C (MeOH).

IR ($CHCl_3$): 1708, 1551 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.99–3.13 (m, 6 H), 3.49 (s, 3 H), 3.76–3.83 (m, 1 H), 4.22–4.49 (m, 1 H), 6.53–6.65 (m, 5 H), 7.33–7.36 (m, 3 H), 7.56–7.60 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 33.8, 34.7, 34.8, 34.9, 51.5, 89.2, 93.3, 123.8, 124.9, 128.0, 128.3, 129.3, 131.6, 132.8, 133.6, 134.6, 135.7, 136.2, 136.4, 139.3, 139.4, 142.3, 142.9, 166.9.

UV/Vis ($CHCl_3$): λ_{max} (log ε) = 274 (4.42), 307 nm (4.07).

Anal. Calcd for $C_{26}H_{23}NO_2$: C, 81.86; H, 6.08; N, 3.67. Found: C, 81.65; H, 6.07; N, 3.70.

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Prepared by coupling **3** and **8** following the above procedure. The crude product was purified by column chromatography on silica gel (pentane–CH_2Cl_2, 2:1).

Yield: 98%; yellow solid; mp 154–155 °C (dec).

IR ($CHCl_3$): 1708, 1509, 1338 cm^{-1}.

^1H NMR ($CDCl_3$): δ = 2.91–3.17 (m, 6 H), 3.42 (s, 3 H), 3.61–3.74 (m, 1 H), 4.34–4.45 (m, 1 H), 6.50–6.64 (m, 5 H), 7.25 (d, *J* = 2.1 Hz, 1 H), 7.62–7.67 (m, 2 H), 8.14–8.20 (m, 2 H).

^{13}C NMR ($CDCl_3$): δ = 33.7, 34.8, 34.9, 51.4, 91.2, 94.7, 123.7, 129.2, 130.7, 132.1, 133.8, 134.0, 134.7, 136.0, 136.4, 136.5, 139.4, 139.7, 142.8, 143.0, 146.8, 166.8.

UV/Vis ($CHCl_3$): λ_{max} (log ε) = 239 (4.24), 367 nm (4.23).

Anal. Calcd for $C_{26}H_{21}NO_4$: C, 75.90; H, 5.14; N, 3.40. Found: C, 75.75; H, 5.15; N, 3.39.

6

Anhydrous toluene (2.5 mL), 4-ethynyl-15-carbomethoxy[2.2]paracyclophane (**3**; 0.05 g, 0.17 mmol), CuI (0.002 g, 0.01 mmol), **9** (0.12 g, 0.17 mmol), $Pd(PPh_3)_4$ (0.005 g, 0.004 mmol) and *i*-Pr_2NH (1.2 mL) were placed in a flask and degassed at 0 °C with Ar. The mixture was heated at 50 °C for 24 h then the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (PE–CH_2Cl_2, 2:1) to afford pure **6**.

Yield: 0.12 g (79%); yellow solid; mp 87–88 °C (MeOH).

^1H NMR ($CDCl_3$): δ = 0.81–0.85 (m, 6 H), 1.14–1.22 (m, 32 H), 1.32–1.50 (m, 4 H), 1.80–1.85 (m, 4 H), 3.06–3.15 (m, 7 H), 3.42 (s, 3 H), 4.00–4.07 (m, 4 H), 4.55–4.56 (m, 1 H), 6.56–6.67 (m, 5 H), 6.88–6.90 (m, 1 H), 7.36 (s, 1 H), 7.61–7.67 (m, 6 H), 8.64 (d, *J* = 8.0 Hz, 2 H), 8.70 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 14.1, 22.7, 26.0, 26.1, 29.2, 29.3, 29.4, 29.43, 29.6, 29.7, 31.9, 34.2, 34.8, 34.9, 51.2, 69.2, 69.5, 85.0, 90.6, 102.3, 103.0, 113.4, 115.5, 116.7, 118.5, 118.6, 124.9, 125.3, 126.7, 126.8, 127.3, 127.4, 130.0, 132.0, 133.4, 133.9, 134.8, 136.0, 136.2, 136.4, 139.4, 139.7, 142.1, 142.8, 149.0, 150.2, 166.8.

UV/Vis ($CHCl_3$): λ_{max} (log ε) = 279 (4.7), 458 (4.4), 482 nm (4.5).

Anal. Calcd for $C_{66}H_{78}O_4$: C, 84.75; H, 8.41. Found: C, 84.50; H, 8.40.

9

Prepared by coupling 9-bromo-10-iodoanthracene with 3,4-bis(dodecyloxy)ethynylbenzene, following the procedure described for reaction between **3** and **9**. Reaction temperature: 30 °C. Reaction time: 3 h. The crude product was purified by column chromatography on silica gel (PE–CH_2Cl_2, 85:15).

Yield: 78%; mp 81–82 °C (MeOH).

^1H NMR ($CDCl_3$): δ = 0.80–0.83 (m, 6 H), 1.22–1.50 (m, 36 H), 1.77–1.84 (m, 4 H), 3.40–4.06 (m, 4 H), 6.87 (d, *J* = 8.0 Hz, 1 H), 7.19–7.20 (m, 1 H), 7.28 (d, *J* = 8.0 Hz, 1 H), 7.55–7.61 (m, 4 H), 8.51 (d, *J* = 8 Hz, 2 H), 8.64 (d, *J* = 8.0 Hz, 2 H).

^{13}C NMR ($CDCl_3$): δ = 14.1, 22.7, 26.0, 29.2, 29.3, 29.3, 29.4, 29.6, 29.7, 31.9, 69.2, 69.5, 84.4, 102.3, 113.4, 115.4, 116.7, 125.2, 126.6, 127.4, 128.2, 130.3, 132.9, 149.0, 150.2.

Anal. Calcd for $C_{46}H_{61}BrO_2$: C, 76.11; H, 8.47. Found: C, 76.31; H, 8.46.

Acknowledgment

The authors thank the MUR (Ministero dell'Università e della Ricerca) Rome, Italy, for financial support.

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