

## [2.2]Paracyclophanes: The Interaction of *Pseudo-Geminal* Bisacetylene with Water and Electrophiles

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**Abstract:** The acid catalyzed interaction of 4,15-bisethynyl[2.2]paracyclophane with water has been investigated in the presence of cerium sulfate. Besides the expected addition product, a cyclic ketone has been formed by intramolecular cyclization of *pseudo-geminal* substituents. The reaction mechanism has been proved by the structure of the addition product of bromine to 4,15-bisethynyl[2.2]paracyclophane. The addition of iodine monochloride follows a similar route leading to a third bridge in cyclophane.

**Keywords:** [2.2]Paracyclophane; Acetylenes; Cerium sulfate, Iodine monochloride.

### Introduction

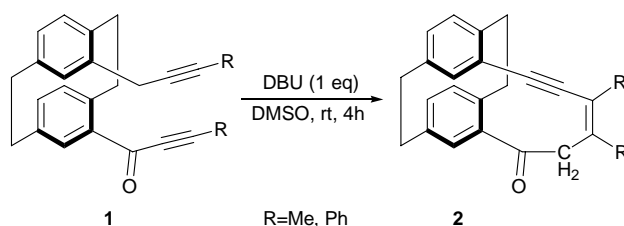
The chemistry of [2.2]paracyclophanes has been focused so far on the structural characteristics, particularly the geometry and the steric

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properties, transannular interactions, and ring strain; the electronic interaction between the aromatic rings having a sandwich form, their influence on reactivity in electrophilic aromatic substitution reactions, and their implications for charge-transfer complex formation have also been investigated.<sup>1-3</sup> As far as the chemical behavior is concerned the vast majority of the reported reactions has been carried out at the benzene rings. However, the chemistry of the molecular bridges of these molecules should also be interesting, especially when the bridges carry important functional groups. Whereas we have described the introduction of various functional groups into the ethano bridges of [2.2]paracyclophanes<sup>4</sup> and the generation of new types of unsaturation by isomerization<sup>5</sup> previously, we now report on a novel process which not only generates a new bridge in a *pseudo-geminally* substituted [2.2]paracyclophane, but also produces new, and possibly widely usable functionality in this new bridge simultaneously. In *pseudo-geminally* substituted [2.2]paracyclophanes functional groups are often held in such a position as to allow highly specific reactions to take place between them in near quantitative yield. In one such application unsaturated cyclophane bisesters undergo intramolecular photocyclization to the corresponding ladderane isomers.<sup>6</sup> Because of the rigid molecular framework provided by the paracyclophane unit and its short interannular distance, functional groups in *pseudo-geminally* substituted [2.2]paracyclophanes are often held in such a position as to allow highly specific reactions to take place between them. In one such application, unsaturated cyclophane bisesters undergo intramolecular photocyclization to the corresponding ladderane isomers.<sup>7-9</sup> Following our interest for the investigation of the chemistry of new unsaturated *pseudo-geminally* substituted [2.2]paracyclophanes, we recently have reported a new way to

generate functionalized bridges in [2.2]cyclophanes.<sup>10</sup> This was accomplished by base catalysed intramolecular cyclization of pinacolone type compounds **1**. (Scheme 1).

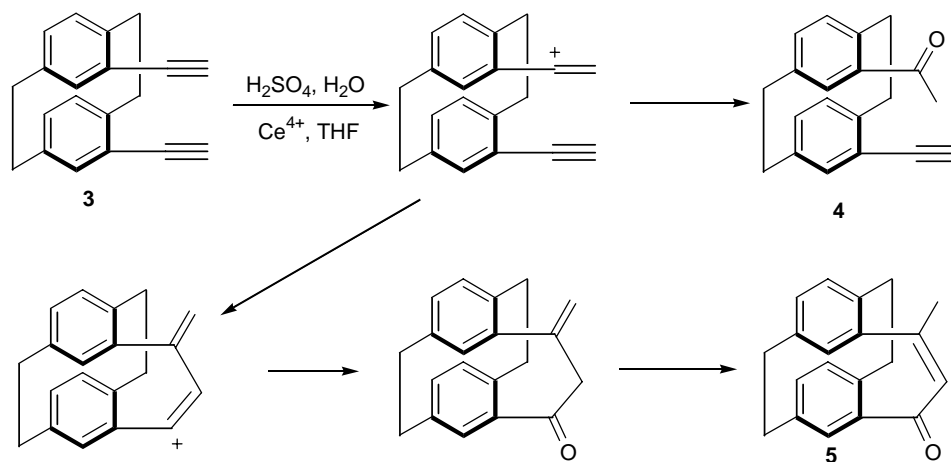


**Scheme 1**

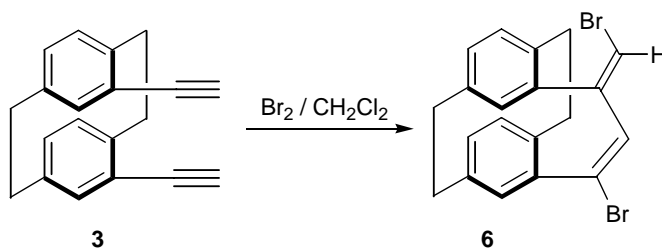
We wish to report here our preliminary results on the addition of water and electrophiles to 4,15-bisethynyl[2.2]paracyclophane.

### Results and Discussion

The reaction of *pseudo-geminal* bisethynyl **3** with one equivalent of water has been performed in the presence of sulfuric acid and cerium sulfate as catalyst. The reaction progress has been monitored by TLC. Purification on silica gel provided an inseparable mixture of mono ketone **4** and cyclic compound **5** in a 2 : 3 ratio. The structural assignment for both compounds has been performed using the 2D NMR analysis. While the formation of mono ketone **4** should follow a known mechanism, the synthesis of compound **5** involves an intramolecular interaction between the *pseudo-geminally* functionalities (Scheme 2). The formation of the third bridge appears to be followed by the addition of water. In a final step the exocyclic double bond undergoes isomerization to a more stable  $\alpha,\beta$ -unsaturated ketone **5**.

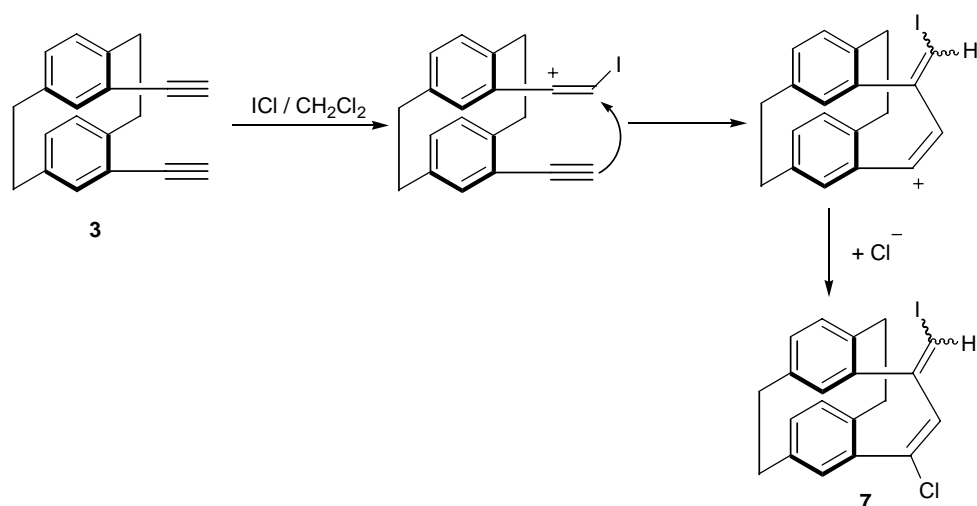


The above described mechanism is supported by the result of bromination of the *pseudo-geminal* bisethynyl[2.2]paracyclophane (Scheme 3).<sup>6b</sup> The structure of compound **6** is very similar with that of compound **5**. Since the mechanism must be identical the enol-ketone tautomerization and the isomerization of the exocyclic double bond do not operate in the case of bromine addition.



An extension of these studies has been performed by the addition of iodine monochloride to the *pseudo-geminal* bisethynyl[2.2]paracyclophane **3** (Scheme 4). The structure of compound **7** has been established by 2D

NMR analysis. Mass spectrometric analysis of compound **7** using ESI technique has indicated a molecular ion ( $m/z = 418$ ) consistent with molecular formula of the addition product ( $C_{20}H_{16}ClI$ ).



Scheme 4

The structure of compound **7** also support the reaction mechanism proposed above.

### Conclusions

The addition of water and iodine monochloride to 4,15-bisethynyl[2.2]paracyclophane has been investigated. The formation of a third bridge in cyclophane has been described as the result of an intramolecular interaction between a triple bond and a vinyl-type cation. The reaction mechanism has been proved by the structure of the addition product of bromine to 4,15-bisethynyl[2.2]paracyclophane.

### Acknowledgments

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### Experimental

Melting points were obtained on a Mel-Temp II apparatus. IR spectra were recorded on a Bruker Tensor 27 instrument. NMR spectra were recorded on a Bruker DRX-400 spectrometer. Chemical shifts are reported in ppm downfield from TMS. Elemental analyses (C, H) were conducted using the CE440 Elemental Analyser. Mass spectra were recorded on a Finnigan MAT 90X spectrometer.

#### *Reaction of 4,15-bisethynyl[2.2]paracyclophane 3 with water*

To a solution of bisacetylene **3** (128 mg, 0.5 mmol) in THF (10 mL), Ce(SO<sub>4</sub>)<sub>2</sub>•4H<sub>2</sub>O (0.02g, 0.05 mmol), sulfuric acid (98%, 0.06 mL), and water (0.01 mL, 0.55 mmol) was added and reaction mixture heated to 55 °C. After 36 h the reaction mixture was poured into water and then extracted with CH<sub>2</sub>Cl<sub>2</sub>. The usual work-up (H<sub>2</sub>O, NaHCO<sub>3</sub>, MgSO<sub>4</sub>) and evaporation of the solvent gave the crude product. Purification by column chromatography on silica gel using CH<sub>2</sub>Cl<sub>2</sub>/pentane 1:1 as eluent provided the mono-ketone **4** and compound **5** as an inseparable mixture in a 2 : 3 ratio; 130 mg (95%), R<sub>f</sub>=0.25.

*Mono-ketone 4*: Selected NMR data: <sup>1</sup>H NMR (CDCl<sub>3</sub>): δ = 2.62 (s, 3H, CH<sub>3</sub>), 3.02 - 3.12 (m, 8H, 4CH<sub>2</sub>), 6.15 (s, 1H, CHar), 6.40 (m, 1H, CHar), 6.78 (m, 4H, 4CHar). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ = 28.7 (q), 33.6 (t), 34.5 (t), 34.8 (t), 35.0 (t), 82.2 (d), 83.0 (s), 82.0 (s), 133.3 (d), 133.7 (d),

134.3 (d), 134.5 (d), 135.9 (d), 136.3 (d), 136.9 (s), 139.2 (s), 140.3 (s), 142.1 (s), 142.3 (s), 143.2 (s), 199.1 (s).

*Compound 5*: Selected NMR data:  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta = 2.15$  (d,  $^4J = 1.7$  Hz, 3H,  $\text{CH}_3$ ), 3.02-3.12 (s, 4H,  $2\text{CH}_2$ ), 6.25 (s, 1H, CHar), 6.51 (m, 4H, 4CHar), 6.74 (s, 1H, CHar), 7.10 (q,  $^4J = 1.7$  Hz, 1H, CH);  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta = 27.7$  (q), 32.4 (t), 33.5 (d), 34.5 (s), 34.9 (s), 123.8 (s), 129.4 (s), 131.7 (d), 132.1 (d), 133.3 (d), 133.9 (d), 134.1 (d), 136.1 (d), 136.2 (d), 136.8 (s), 139.1 (s), 139.8 (s), 140.4 (s), 161.4 (s), 200.5 (s).

*Reaction of 4,15-bisethynyl[2.2]paracyclophane 3 with ICl*

To a solution of bisacetylene **3** (128 mg, 0.5 mmol) in  $\text{CH}_2\text{Cl}_2$  (10 mL) a solution of iodine monochloride (1M in  $\text{CH}_2\text{Cl}_2$ , 0.5 mL, 0.5 mmol) was added dropwise at 0 °C. After 2 h the reaction mixture was allowed to warm-up to room temperature. The usual work-up ( $\text{H}_2\text{O}$ ,  $\text{NaHCO}_3$ ,  $\text{MgSO}_4$ ) and evaporation of the solvent gave the crude product. Purification by column chromatography on silica gel using  $\text{CH}_2\text{Cl}_2$  as eluent provided the product **7** as a yellow solid; 141 mg (61%),  $R_f=0.42$ .

IR (ATR): 2958, 2927, 2890, 2847, 1480, 1430, 1338, 876, 829, 780, 618,  $518\text{ cm}^{-1}$ .  $^1\text{H}$  NMR ( $\text{CDCl}_3$ ):  $\delta = 2.85$ -3.13 (m, 6H,  $3\text{CH}_2$ ), 3.30 (m, 2H,  $\text{CH}_2$ ), 6.25 (m, 1H, CHar), 6.31 (s, 1H), 6.46 (m, 2H, Har), 6.49 (s, 2H), 6.62 (s, 1H), 7.01 (s, 1H, CHar).  $^{13}\text{C}$  NMR (100 MHz,  $\text{CDCl}_3$ ):  $\delta = 32.5$  (t), 33.3 (t), 34.8 (t), 35.0 (t), 100.7 (d), 124.7 (s), 132.0 (d), 133.2 (d), 133.5 (d), 134.2 (d), 134.5 (d), 135.0 (d), 135.3 (d), 135.9 (s), 137.4 (s), 138.2 (s), 138.8 (s), 140.3 (s), 140.4 (s), 144.5 (s). MS (ESI):  $m/z = 418$  ( $\text{M}^+$ ). Calcd for  $\text{C}_{20}\text{H}_{16}\text{ClI}$ : C, 57.37; H, 3.85. Found: C, 57.12; H, 3.74.

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