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Synthesis of cyclophanetetrayne complexes from bis(propargyldicobalt) dication equivalents†

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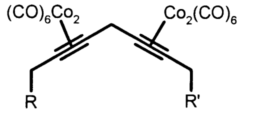
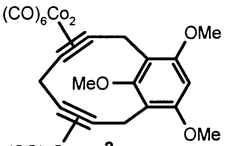
Nicholas reactions of the *p*-phenyl linked bis(propargyl acetate) complex (3a) with electron rich arenes give cyclophanetetrayne complexes (5). The use of bis(propargyl ether) complex (8) with (3a) allows formation of a mixed cyclophanetetrayne complex (9), and in addition gives retro-Nicholas/intramolecular Nicholas reaction product (2).

Alkyne-containing cyclophane molecules have been the subject of intense recent research activity. Reasons for this attention include their syntheses as enediyne antitumour analogues/Bergman cyclization precursors,[1] the design of cyclophanes with shape persistent cavities,[2] the metal complexation or self aggregation abilities of these compounds,[3] interest in systems containing extended π-conjugation,[4] their use as fullerene precursors,[5] and questions of stability *versus* angle strain on the alkyne unit. [6,7]

The synthetic chemistry of hexacarbonyldicobalt alkyne complexes also has been a topic of widespread interest,[8] due to the ability of the group to participate in novel cycloaddition reactions,[9,10] to enable the facile formation and trapping of cations in the propargylic position (the Nicholas reaction),[11] and to allow bond geometries not available to the metal free alkyne function. We have been engaged in the study of the use of these complexes, predominantly in their use in tandem Nicholas reactions towards a number of synthetic ends.[12,13] One of the most significant manifestations of this work has been the discovery that electron rich arenes and heteroarenes react with complex **1** to rapidly assemble [7]metacyclophanediyne tetracobalt complexes (*i.e.*, **2**). We have developed an interest in systems containing an aryl group as a spacer between propargyl cation units,[14] and as a result have begun investigation of the Nicholas reaction chemistry of bis(propargyl acetate) complex **3a** with electron rich arenes.



1 R = OBn, R' = OMe
8 R = R' = 2,4,6-(MeO)$_3$Ph



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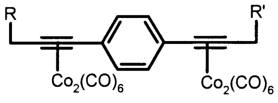
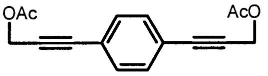
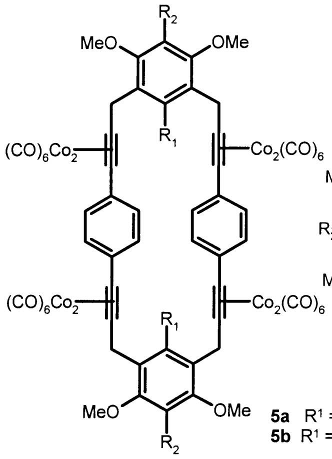


3a R = R' = OAc
4a R = R' = 2,4,6-(MeO)$_3$Ph
4b R = R' = 2,3,4-(MeO)$_3$Ph

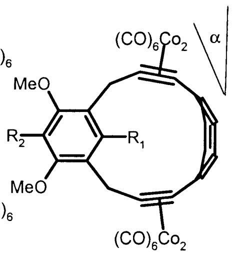


3b

Compound **3a** was readily accessible by complexation of **3b**[15] with $Co_2(CO)_8$ under standard reaction conditions (75% yield). The bis(propargyl acetate) complex was then added to 1,3,5-trimethoxybenzene in the presence of BF_3–OEt_2. Reaction was found to occur by one of two pathways, depending on reagent stoichiometry and concentration. At 5×10^{-2} M concentration of **3a** (CH_2Cl_2, 0 °C, 12 h), with an excess (4 equiv.) of 1,3,5-trimethoxybenzene and 3 equiv. of BF_3–OEt_2, diarylation product **4a** was formed in 90% yield. In contrast, at 2×10^{-3} M of **3a** (CH_2Cl_2, 5 °C, 12 h), with 1.0 equiv. of 1,3,5-trimethoxybenzene and a large excess of BF_3–OEt_2 (9 equiv.), a different predominant discrete product, the [3.3.3.3]*m*,*p*,*m*,*p*-cyclophanetetrayne complex **5a**, was isolated (20% yield).‡ The observation of Na^+ and K^+ ion adducts (*m*/*z* 1803 and 1819, respectively) in the electrospray mass spectrum of this compound was central to the assignment as **5a**. No evidence of the smaller cyclophanediyne complex **6** could be detected.



5a R^1 = OMe, R^2 = H
5b R^1 = H, R^2 = OMe



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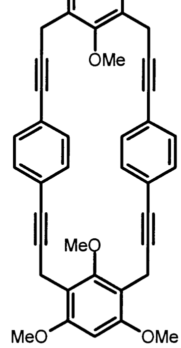
The reaction chemistry between **3a** and 1,2,3-trimethoxybenzene was studied, and afforded similar results. Under the analogous 5×10^{-2} M reaction conditions, diarylation product **4b** resulted (89% yield). Under the high dilution conditions, cyclophanetetrayne complex **5b** was the major isolated product (15% yield).

The possibility of decomplexation of cyclophanetetrayne **5a** has been investigated. Reaction with an excess of Me_3NO (acetone, 0 °C, 1 h) gave metal-free cyclophanetetrayne **7** in 62% yield.



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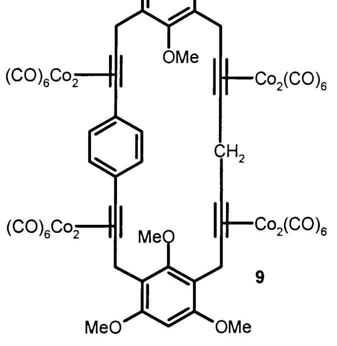

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The availability of the diarylated diyne complexes **4** afforded an alternative possible route to the preparation of **5**. Subjecting **4a** to reaction with 1.0 equiv. of diacetate complex **3a** (2×10^{-3}

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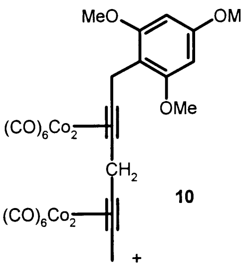
† Electronic supplementary information (ESI) available: experimental conditions and new compounds. See http://www.rsc.org/suppdata/cc/b2/b203187f/

M, CH_2Cl_2, 0 °C, 12 h) in the presence of BF_3–OEt_2 (4 equiv.) did successfully result in the formation of **5a** (24% yield), along with recovered **3a** (31%) and **4a** (31%). The analogous reaction with **4b** with **3a** gave **5b** (18% yield), with no recovered **3a** or **4b**.

This alternative cyclization procedure opened the possibility for the synthesis of mixed cyclophanetetraynes. In order to investigate the feasibility of such an approach, we employed bis(propargyl ether) complex **1**[13] and the diarylated diyne complex **8**, the latter prepared from **1** and 1,3,5-trimethoxybenzene in 82% yield under conditions analogous to **4a** and **4b**. Compound **4a** was then subjected to BF_3–OEt_2 mediated reaction with diyne complex **1**. Unfortunately, under a variety of conditions, this reaction afforded only trace amounts of **9**. Conversely, the condensation of **8** and an equimolar amount of **3a** was more successful. In the presence of Lewis acid Bu_2BOTf (2.5 equiv.) in CH_2Cl_2 (4×10^{-3} M, 0 °C, 15 h) two main new products could be isolated. The compound eluting second proved to be the target mixed cyclophanetetrayne **9** (26% yield). Preceding **9** chromatographically was cyclophanediyne complex **2**[13] (25% yield).§

The formation of cyclophanediyne complex **2** is the result of a retrograde Nicholas reaction of **8** followed by an intramolecular Nicholas reaction of putative cation **10** on the remaining arene. The facility with which **2** is formed by Nicholas reaction chemistry has been previously reported by our group,[13] but this is to our knowledge the first example of a retro-Nicholas reaction involving the cleavage of a carbon–carbon bond.¶ [16,17] We believe that its appearance in this case stems from a combination of the high stability of propargyl cation dicobalt complexes[11] and the very electron rich nature of the trimethoxyaryl unit.

The cyclophanetetraynes **5** and **7** are to our knowledge the first examples of the [3.3.3.3]*m,p,m,p*-cyclophanetetrayne ring system. They may be seen as alkyne extended homologues of the known [1.1.1.1]*m,p,m,p*-cyclophanes, which have been termed ‘calix[4]arenoids’ by Finocchiaro.[18] Their occurrence is likely a consequence of the difficulty of formation of the corresponding cyclophanediyne **6**. MM3 (CAChe) calculations reveal that a substantial (α = *ca.* 15 °) bending of the *para*-disubstituted arene ring would be necessary to form **6**. As a result, **5**, which requires no such bond angle deformations, is instead formed either through dimerization of **11**, the demonstrated reaction of **3a** with **4**, or both.‖ Each of these cyclophanetetraynes, including metal-free **7**, give a single resonance for their benzylic methylene protons, indicating any fluxional processes are at their fast exchange limit; this is consistent with the expected larger cavity relative to the calix[4]arenoids. Each of **5a**, **7**, and **9** is also characterized by a small but noticeable upfield shift in the ^{1}H NMR spectrum for the *para*-disubstituted aryl ring protons, which may be the result of shielding by the other arene rings in each molecule.** This effect is absent or minuscule for **5b**.



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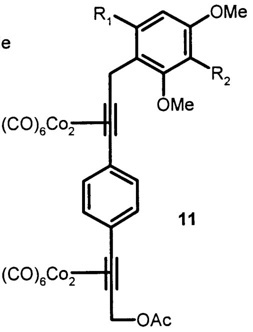

11

The pursuit of a deeper understanding of the conformational properties of these molecules, and synthetic work towards cyclophanetetraynes with other aromatic bridging groups, are in progress and will be reported in due course.

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Notes and references

‡ The use of 2.5 equiv of BF_3–OEt_2 gave **5a** in lower (9–10%) yield.

§ Small amounts of **3a** (15%) and **8** (17%) were also recovered.

¶ Dimethyl sulfonium adducts of propargyldicobalt cations are known to regenerate the cations in solution *via* C–S bond cleavage.[16] Propargyl ether exchange reactions must involve reversible C–O bond cleavage.[17]

‖ The reaction of **3a**, 1,3,5-trimethoxybenzene, and BF_3–OEt_2 (1 equiv. each) is unselective for monocondensation.

** The *para*-disubstituted aryl ring protons are isochronous in each case, with the following chemical shifts: δ (ppm); **3a**, 7.43; **3b**, 7.34; **4a**, 7.44; **4b**, 7.47; **5a**, 7.21; **5b**, 7.43; **7**, 7.10; **9**, 7.19.

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