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Indolophanetetrayne Cobalt Complexes via Nicholas Reactions

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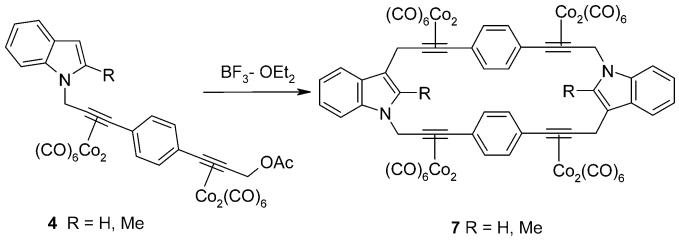
ABSTRACT



4 R = H, Me **7** R = H, Me

Indole *N*-substituted diyne tetracobalt complexes (4) undergo a Lewis acid mediated dimerization–cyclization reaction through the indole 3-position to afford indolophanetetrayne cobalt complexes (7). Substitution of the indole fragment of (4) with a 3-methyl function allows analogous formation of indolophanetetrayne complex (9), linked through the indole 2-position.

Alkyne-containing cyclophane molecules, or cyclophynes, have been the subject of much recent interest. The ability of the alkyne unit(s) to give the cyclophanes cavities with shape persistence[1] has often been reflected in an ability to complex metals or organic molecules,[2] or to self-aggregate in some cases.[3] In addition, cyclophynes have often been prepared as systems with extended π-conjugation[4] or as fullerene precursors.[5] On occasion, they have been studied as enediyne antitumor analogues or Bergman cylization precursors.[6] They have also been subjects for studying the consequences of angle strain on the alkyne function.[7]

Our interest in these systems stems for our work on the synthetic chemistry of hexacarbonyldicobalt alkyne complexes, which we have employed predominantly for the tandem formation and nucleophilic substitution of their propargylic cations (the Nicholas reaction).[8,9] The widespread

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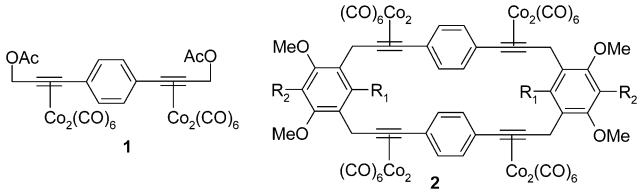
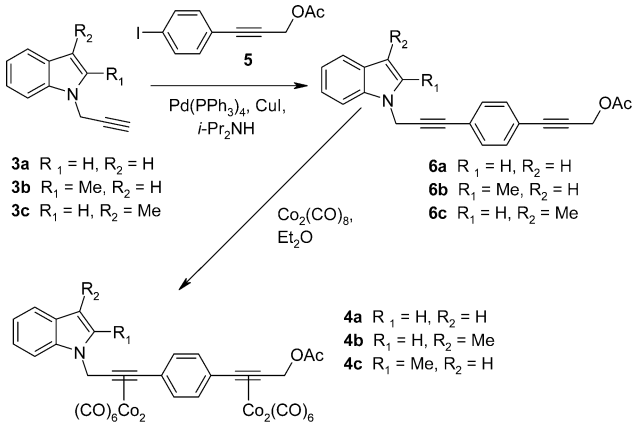


Figure 1. Cyclophanetetraynes (**2**) and precursor complex (**1**).

applicability of Nicholas reaction chemistry on these complexes,[10] the ability of the group to allow nonconventional alkyne geometries, and their ability to participate in novel cycloaddition reactions[11,12] make them excellent candidates as intermediates for the preparation and modification of many types of cyclophynes.[13,14] Recently, we have discovered that derivatives of bis(propargyl alcohol) tetracobalt complexes are capable of reaction with electron-rich arenes to afford cyclophanediynes or cyclophanetetraynes in a single synthetic operation, depending upon the spacer between the two alkyne units.[15,16] In particular, we have reported recently that *p*-phenyl-linked bis(propargyl acetate) complex **1** is capable of assembling cyclophanetetrayne complexes **2**.[16] We were interested in applying this chemistry to the synthesis of indole-containing cyclophanes (indolophanes), due to a recent increase of interest in these infrequently encountered systems.[17−19]

Our approach to indolophanetetraynes linked through their nitrogen atoms required a change from our cyclophanetetrayne synthetic pathway, as a consequence of the fact that the N-atoms of indoles are known to participate only poorly in Nicholas reactions.[20] Therefore, *N*-propargylindoles (**3**)

Scheme 1. Indolophane Precursor Synthesis



were chosen as starting points for these syntheses. The propargyl acetate−hexacarbonyldicobalt function for the final dimerization−cyclization would then be built upon this unit. Specifically, preparation of the N-functionalized indole cyclization precursor **4a** was initiated by Sonogashira coupling of *N*-propargylindole **3a**[21] with iodoarylpropargyl acetate **5**[22] to give **6a** in 88% yield. Both alkyne units of diyne **6a** could be converted to their $Co_2(CO)_6$ complexes in the presence of excess $Co_2(CO)_8$, giving **4a** in 84% yield; no evidence of single alkyne complexation products could be detected under these conditions. Treatment of a solution of **4a** (0 °C, 10^{-2} M, CH_2Cl_2, 5.5 h) with excess $BF_3{-}OEt_2$ (6.5 equiv) gave two chromatographically separable main products. The initially eluting compound possessed highly characteristic H^+, Na^+, and K^+ positive ion adducts (*m*/*z* 1679, 1701, 1717, respectively) and the Cl^- negative ion adduct (*m*/*z* 1713) in its electrospray mass spectra, identifying it as the dimerized indolophanetetrayne complex **7a** (55% yield). The other major product (28% yield) possessed no ions of significant abundance in the 1600−1800 *m*/*z* region of its positive ion electrospray mass spectrum. X-ray crystallographic analysis showed the compound to be **8**, the trimerized indolophanehexayne complex linked through the indole 3-position, and this was confirmed by the presence of $M + Cl^- - nCO$ ($n = 2$, 4−11) ions in the negative ion electrospray mass spectrum, the most intense of which was the $M + Cl^- - 5CO$ ion (*m*/*z* 2412).

We wished to determine whether this synthetic route could be applied to the individual preparations of analogous indolophanetetraynes linked through the C-2 and C-3 positions. As a result, we chose C-2 methylated, C-3 linked **7b** and the C-3 methylated, C-2 linked **9** as targets. For access to **7b**, 2-methylindole was propargylated under conventional conditions (NaH, propargyl bromide + Bu_4NI, THF) to give **3b** (71%). In a fashion analogous to that for **3a**, propargylindole **3b** was subjected to Sonogashira coupling with **5** to give **6b** (85% yield), and both alkyne functions complexed

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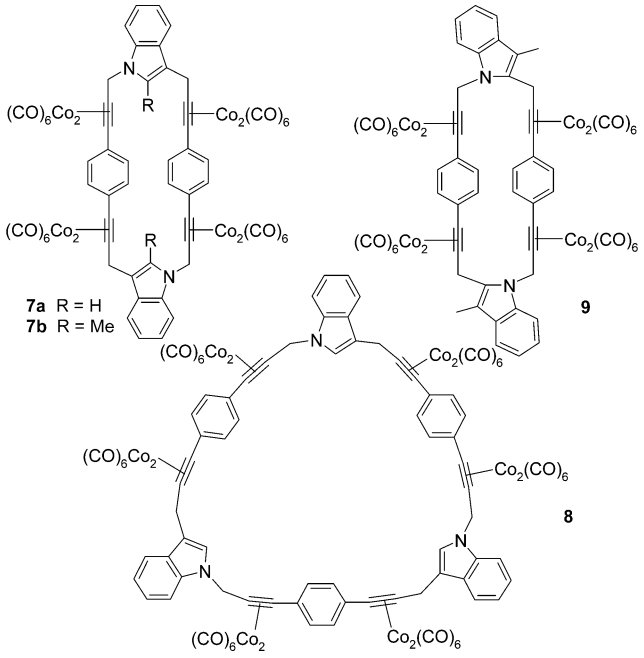

Figure 2. Indolophanetetrayne complexes and the indolophanehexayne complex prepared from **4**.

with excess $Co_2(CO)_8$ to form **4b** (90% yield). For access to **9**, 3-methylindole was propargylated under conventional conditions to give **3c** (68%).[23] Propargylindole **3c** then was coupled with **5** to form **6c** (81% yield) and complexed with excess $Co_2(CO)_8$ to form **4c** (92% yield). Subjecting **4b** to treatment with excess $BF_3{-}OEt_2$ under high dilution conditions (−10 °C, 10^{-4} M, CH_2Cl_2, 12 h) gave C-3 linked indolophanetetrayne **7b** in 40% yield. Conversely, subjecting **4c** to $BF_3{-}OEt_2$ resulted in a noticeably more sluggish reaction, but at room temperature (10^{-4} M, CH_2Cl_2, 4 h), C-2 linked indolophanetetrayne **9** could be obtained in 25% yield.

The presence of the methyl groups in **7b** and **9** had a noticeable affect on the fluxionality of the C-2 and C-3 linked indolophanetetraynes. While the ^{1}H NMR spectra of unsubstituted **7a** displayed sharp singlets for all methylene groups, **7b** gave two very broadened resonances at room temperature, which decoalesced to four doublets at low *T*, corresponding to a $\Delta G_{283K}^{\ddagger}$ of 12.2 kcal/mol. The methylene protons for **9** in the ^{1}H NMR spectrum were similarly broad, and

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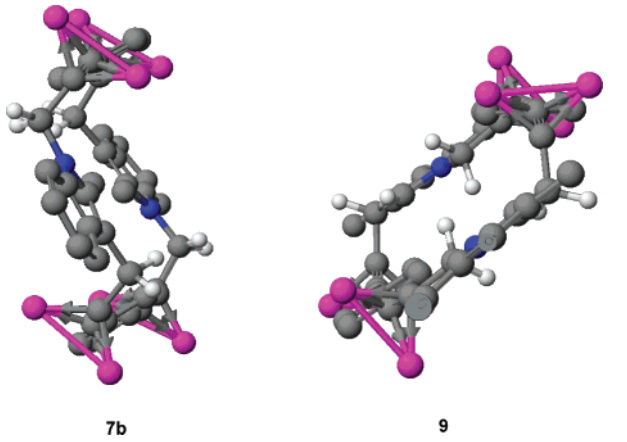

Figure 3. MM3 minimized structures of indolophanetetrayne complexes **7b** and **9**. The carbonyl ligands and nonbenzylic H atoms are removed for clarity. Key: gray = C, white = H, blue = N, violet = Co.

decoalesced to two AB patterns at a higher *T* ($\Delta G_{298K}^{\ddagger}$ = 15.1 kcal/mol). Definitive descriptions of these fluxional processes await suitable crystals for X-ray diffraction studies on **7** and **9**; however, MM3 calculations and molecular models suggest **7a** and **7b** assume a chairlike conformation,[24] with approximately coplanar indole units (Figure 3). The spectral properties are consistent with a chair−chair interconversion, with **7a** at the fast exchange limit and exchange slowed for **7b**. Analogous modeling on **9** supports an antiparallel orientation of the indole units (Figure 3), with the *p*-disubstituted benzenes canted away from a parallel conformation by differing degrees. Nevertheless, only two ^{1}H NMR resonances are observed for these *p*-phenylene units in **9**, as well as in **7a** and **7b**, indicating rotation about the arene−alkyne carbon atoms is rapid over the entire temperature range investigated (−50 to + 40 °C).

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Supporting Information Available: Experimental procedures for the preparation of and characterization data for **4a**−**c**, **6a**−**c**, **7a**,**b**, **8**, and **9**, and crystallographic data for **8**. This material is available free of charge via the Internet at http://pubs.acs.org.

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