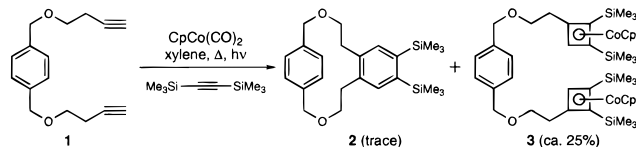


Regiocontrolled Synthesis of CpCo-Cyclobutadienyl-Bridged *p*-Cyclophanes via Annulation of Acyclic Diynes

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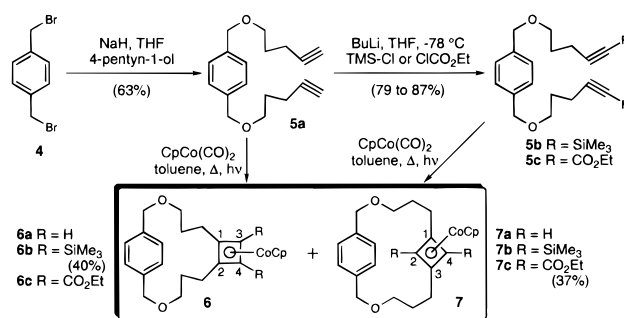
Noncovalent interactions between aromatic units are key facets of host–guest chemistry¹ and are thought to be important in protein folding.² In the extreme, two aromatic moieties can orient either π -face to π -face or π -face to π -edge. In order to examine the degree to which such interactions can constrain conformational mobility, we initiated a program of research directed toward the synthesis of *o,p*-cyclophanes derived from a structural core which remains conformationally dynamic (on the NMR time scale) even at low temperature.³ Along with classical approaches⁴ to this series of compounds, we have also probed Co-mediated [2 + 2] aromatic annulations⁵ on bis-alkyne **1** as a potential means of maximizing synthetic convergence (eq 1). The required closure of the



medium/large bridging ring was very inefficient and unreproducible;⁶ however, an interesting compound (**3**), containing bis-CpCo-cyclobutadienyl moieties, was isolated and characterized.⁷ We were motivated by this result to redirect a portion of our efforts to the synthesis and characterization of mixed aryl/CpCo-cyclobutadienyl cyclophanes via a highly convergent, Co-mediated [2 + 2] annulation of readily accessible acyclic diyne precursors (Scheme 1).

Gleiter and co-workers have reported elegant work on the Co-mediated conversion of cyclic diyne precursors to CpCo-cyclobutadienyl superphanes.⁸ We viewed the

Scheme 1



specific opportunity/challenge of working with *acyclic diynes* as a function of the two possible regiochemical outcomes in the Co-mediated [2 + 2] annulation: *1,2-tethered* (**6**) and/or *1,3-tethered* (**7**) products. Either through careful separation of regioisomers or by regiocontrol in the Co-mediated [2 + 2] annulation, mixed cyclophanes with π -face (aryl)/ π -edge (CpCo-cyclobutadienyl) or π -face (aryl)/ π -face (CpCo-cyclobutadienyl) geometries could, in principle, be obtained. We report here our preliminary results.

The first case we investigated (**5a**) featured five-atom tethering chains to ensure a high degree of conformational freedom and allow for the formation of either cyclophane **6** or **7**. The attempted annulation of **5a** was inconclusive, yet encouraging, because an extremely unstable product mixture was obtained which we tentatively assigned as an unknown ratio of **6a** and **7a**. Our experience in isolating and handling the stable compound **3**, along with literature precedent,^{7b} suggested investigation of acyclic diyne **5b**. Reaction of **5b** proceeded smoothly to afford only the *1,2-tethered* product **6b** in 40% yield. Gleiter and co-workers have observed similar regiocontrol in the reaction of cyclic silyl-substituted diynes.^{8f} Our repeated attempts to isolate/characterize the corresponding *1,3-tethered* product **7b** have proven fruitless thus far. Mixed cyclophane **6b** is highly crystalline and readily yielded crystals suitable for X-ray analysis. A synopsis of some key structural features of **6b** is provided in Figure 1.⁹

The next case we investigated provided a gratifying result. Annulation of acyclic diyne **5c** afforded only the *1,3-tethered* product **7c** in 37% yield. Mixed cyclophane **7c** is also highly crystalline, and structural details are provided in Figure 1.⁹ Multiple attempts to isolate/characterize the corresponding *1,2-tethered* product **6c** have been unsuccessful. Clearly, the CO₂Et group manifests its own unique mode of regiocontrol in the Co-mediated [2 + 2] annulation.

Why do the SiMe₃ and CO₂Et groups exert *opposite* modes of regiocontrol in the Co-mediated annulation? Gleiter^{8f} and Vollhardt⁵ have discussed the importance

[†] NSF-Presidential Faculty Fellow, 1993–97.

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(9) The authors have deposited atomic coordinates for structures depicted in Figure 1 with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, upon request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

(10) A number of cobaltacyclopentadienes have been isolated and characterized. (a) McAlister, D. R.; Bercaw, J. E.; Bergman, R. G. *J. Am. Chem. Soc.* **1977**, *99*, 1666. (b) McDonnell Bushnell, L. P.; Evitt, E. R.; Bergman, R. G. *J. Organomet. Chem.* **1978**, *157*, 445. (c) Yamazaki, H.; Wakatsuki, Y. *J. Organomet. Chem.* **1977**, *139*, 157. (d) Yamazaki, H.; Wakatsuki, Y. *J. Am. Chem. Soc.* **1980**, *102*, 4363.

(11) (a) Comparison of the acidities of (*i*-Pr)₂NH ($pK_a \approx 40$) and (Me₃Si)₂NH ($pK_a \approx 28$) provides an example which can be used to advantage in enolate generation. See: Brown, C. A. *J. Org. Chem.* **1974**, *39*, 3913. Danheiser, R. L.; Miller, R. F.; Brisbois, R. G.; Park, S. Z. *J. Org. Chem.* **1990**, *55*, 1959 and references cited therein. (b) Colvin, E. *Silicon in Organic Synthesis*; Springer-Verlag: Berlin, 1983.

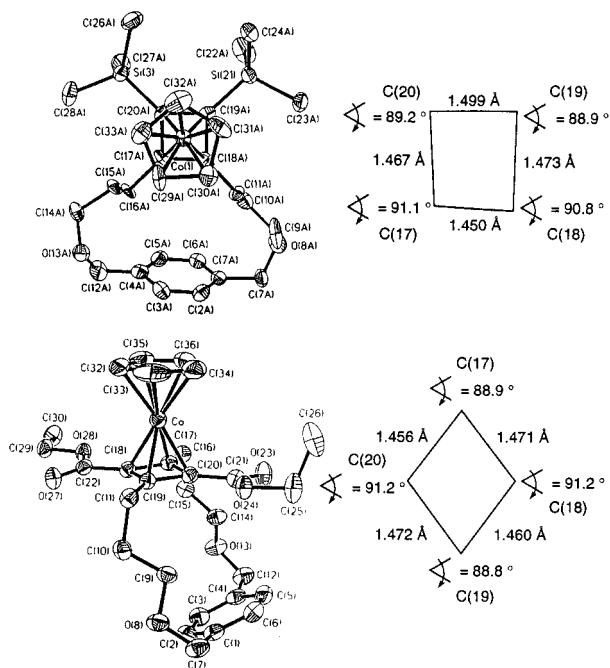


Figure 1. 1,2-Tethered cyclophane **6b** (top) and 1,3-tethered cyclophane **7c** (bottom), with key aspects of the cyclobutadienyl moiety summarized.

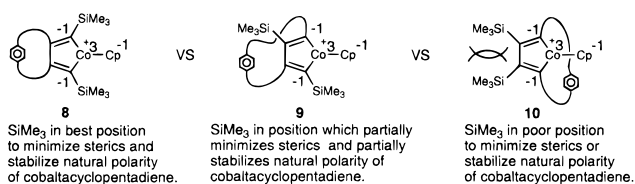
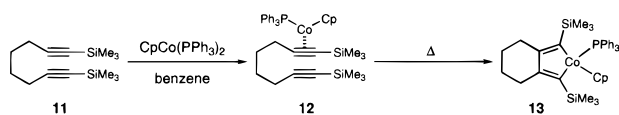


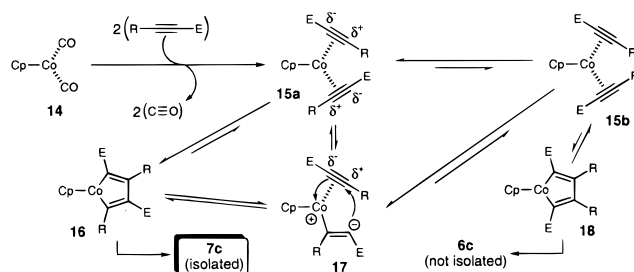
Figure 2. Regiochemical permutations for the cobaltacyclopentadiene formed upon oxidative addition.

of having the bulky SiMe₃ groups positioned α to cobalt in the cobaltacyclopentadiene formed upon oxidative addition (Figure 2).¹⁰ In this regard, Bergman and co-workers reported the synthesis and characterization of **13** (eq 2).^{10b} Although diyne **11** lacks the conformational



flexibility of diyne **5b**, its conversion to **13** clearly demonstrates that the steric size of the SiMe₃ group does not preclude the formation of intermediate **8**. Additionally, we believe that the ability of silicon to stabilize α -anion character¹¹ plays an important role and, in the conversion of **5b** to **6b**, works with steric factors in positioning the SiMe₃ groups upon oxidative addition (Scheme 2), such that reductive elimination provides only the 1,2-tethered product **6b** via intermediate **8**. A recent report by Tilley and Mao supports this conclusion, given their observation of the same regiodirecting effect in a Zr-mediated polymerization/cyclization reaction sequence

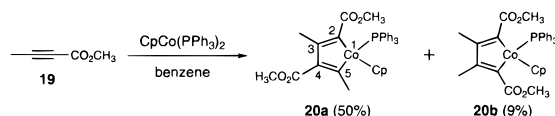
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Scheme 2^a

^a For clarity, E = CO₂Et and R = tethering chains to benzene moiety.

which yielded a zirconacyclopentadiene-based cyclophane macrocycle.¹²

Although the CO₂Et group is not as bulky as SiMe₃, it is better at stabilizing α -anion character. Therein, perhaps, is the key to its regiodirecting effect. As outlined in Scheme 2, the increased ability of the CO₂Et group to polarize intermediates, in a push-pull fashion, might lead to an oxidative addition process that features—in the extreme—charge character akin to 1,4-nucleophilic addition (**15a** to **16**). Alternatively, the oxidative addition might be proceeding stepwise, wherein a 1,4-nucleophilic addition effectively does take place (**15a/15b** to **17** to **16**). We have no direct evidence for this speculation; however, in work related to that of Bergman (eq 2), Yamazaki and Wakatsuki observed a strong preference for 2,4-positioning of CO₂CH₃ moieties in cobaltacyclopentadiene formation (eq 3), leading them to discuss a possible competition between concerted and stepwise oxidative addition processes which might be substituent dependent.^{10c}



We have demonstrated that mixed CpCo-cyclobutadienyl-bridged *p*-cyclophanes can be prepared easily from acyclic diynes. Most importantly, we have found that, under the reaction conditions used, judicious choice of the diyne (*terminal*) substituent allows for complete regiocontrol in the key Co-mediated [2 + 2] annulation, giving either a π -face (aryl)/ π -edge (CpCo-cyclobutadienyl) (**6b**) or π -face (aryl)/ π -face (CpCo-cyclobutadienyl) (**7c**) geometry in the product. We are currently investigating the regiodirecting effects of other substituents, different tether lengths, and alternative bridging orientations on the aryl moiety. Results will be reported in due course.

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Supporting Information Available: Experimental procedures for the synthesis of compounds **5a–c**, **6b**, and **7c**, as well as ¹H NMR spectra (9 pages).

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