

Regioselective, Stereoselective, and Conformationally Controlled Synthesis of (η^4 -Tetraarylcyclobutadiene)-(η^5 -carbomethoxycyclopentadienyl)-cobalt Metallocenes

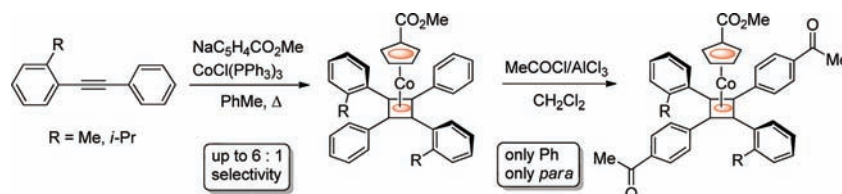
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ABSTRACT



The Friedel–Crafts reaction of (η^4 -tetraphenylcyclobutadiene)(η^5 -carbomethoxycyclopentadienyl)cobalt with acid chlorides/aluminum chloride resulted exclusively in *para*-phenyl acylation. Both monoacylated (1.1 equiv of $\text{RCOCl}/\text{AlCl}_3$) and tetraacylated products (>4 equiv of $\text{RCOCl}/\text{AlCl}_3$) were synthesized. Reaction of $\text{PhCC}(o\text{-RC}_6\text{H}_4)$ ($\text{R} = \text{Me}, i\text{-Pr}$) with $\text{Na}(\text{C}_5\text{H}_4\text{CO}_2\text{Me})$ and $\text{CoCl}(\text{PPh}_3)_3$ gave predominantly (η^4 -1,3-diaryl-2,4-diphenylcyclobutadiene)(η^5 -carbomethoxycyclopentadienyl)cobalt metallocenes (1,3-[*trans*] vs 1,2-[*cis*] selectivity up to 6:1). Conformational control of Friedel–Crafts reactions on the major isomers gave exclusively *para*-acylation of the unsubstituted phenyl groups.

(η^4 -Tetraphenylcyclobutadiene)(η^5 -cyclopentadienyl)-cobalt **1** is an air and moisture stable metallocene readily synthesized from diphenylacetylene (Scheme 1).¹ The size and geometry of **1**, together with the relatively electron-deficient cyclopentadienyl ring, differ from ferrocene and

have resulted in a number of specific applications. Examples include the use of 1,2-disubstituted planar chiral derivatives of **1** as reagents and catalysts in asymmetric synthesis,² and the incorporation of cobalt metallocenes into dendrimers,³ square-grid monomers,⁴ and molecular rotors⁵ and gears.⁶ Some of these studies have employed tetraaryl derivatives of **1**, readily synthesized from the corresponding diarylacetylene.^{3,4,7}

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(1) (a) Nakamura, A.; Hagihara, N. *Bull. Chem. Soc. Jpn.* **1961**, *34*, 452. (b) Rausch, M. D.; Genetti, R. A. *J. Org. Chem.* **1970**, *35*, 3888.

(2) (a) Arrayás, R. G.; Mancheño, O. G.; Carretero, J. C. *Chem. Commun.* **2004**, 1654. (b) Roca, F. X.; Motevalli, M.; Richards, C. J. *J. Am. Chem. Soc.* **2005**, *127*, 2388. (c) Review: Nomura, H.; Richards, C. J. *Chem. Asian J.* **2010**, *5*, 1726. (d) Cannon, J. S.; Kirsch, S. F.; Overman, L. E. *J. Am. Chem. Soc.* **2010**, *132*, 15185. (e) Cannon, J. S.; Kirsch, S. F.; Overman, L. E.; Sneddon, H. F. *J. Am. Chem. Soc.* **2010**, *132*, 15192.

(3) Waybright, S. M.; McAlpine, K.; Laskoski, M.; Smith, M. D.; Bunz, U. H. F. *J. Am. Chem. Soc.* **2002**, *124*, 8661.

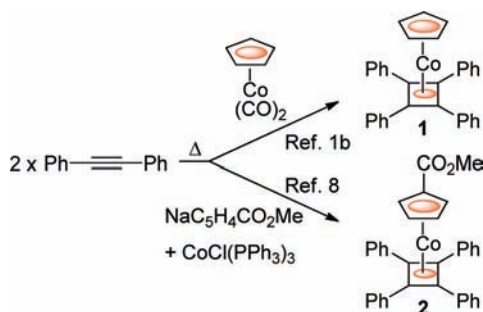
(4) (a) Harrison, R. M.; Brotin, T.; Noll, B. C.; Michl, J. *Organometallics* **1997**, *16*, 3401. (b) Brotin, T.; Pospíšil, L.; Fiedler, J.; King, B. T.; Michl, J. *J. Phys. Chem. B* **1998**, *102*, 10062.

(5) Zheng, X.; Mulcahy, M. E.; Horinek, D.; Galeotti, F.; Magnera, T. F.; Michl, J. *J. Am. Chem. Soc.* **2004**, *126*, 4540.

(6) Stevens, A. M.; Richards, C. J. *Tetrahedron Lett.* **1997**, *38*, 7805.

(7) Nguyen, H. V.; Yeamine, M. R.; Amin, J.; Motevalli, M.; Richards, C. J. *J. Organomet. Chem.* **2008**, *693*, 3668.

Scheme 1. Synthesis of Cobalt Metallocenes **1** and **2**



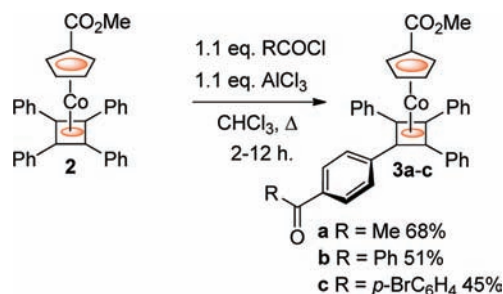
The generation of differentially substituted aryl derivatives is significantly more challenging. For example, reaction of diphenylacetylene, 4-bromodiphenylacetylene, and (η^5 -cyclopentadienyl)cobaltdicarbonyl resulted in an essentially statistical mixture of the four expected metallocenes, and thus a low yield of the metallocene required, in this instance, (η^4 -4-bromophenyltriphenylcyclobutadiene)-(η^5 -cyclopentadienyl)cobalt (25%).⁵ In this Letter we report on a Friedel–Crafts substitution method for the synthesis of monoaryl and tetraaryl derivatized cobalt metallocenes and a stereoselective complexation method for the synthesis of isomers containing a 1,3-[*trans*] arrangement of substituted aryl groups attached to the η^4 -cyclobutadiene ligand.

In contrast to ferrocene, cobalt metallocene **1** is a very poor substrate for Friedel–Crafts substitution, and attempts to perform this reaction on **1** have been reported to result in only a trace amount of cyclopentadienyl ring acylated product.^{1b} In our hands, heating **1** at reflux with 1.1 equiv each of acetyl chloride and aluminum chloride in CHCl_3 for 2 h resulted only in metallocene decomposition. We reasoned that this might be prevented by deactivation of the metallocene by introduction of an ester group on the cyclopentadienyl ring resulting in selective Friedel–Crafts substitution of a phenyl group.

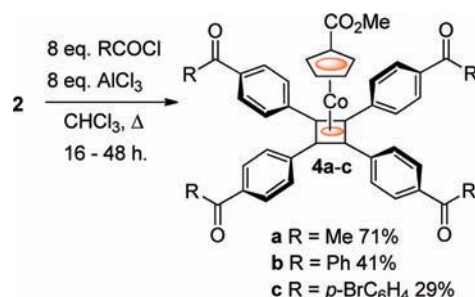
Friedel–Crafts reaction of cobalt metallocene **2**⁸ under the same conditions resulted in a 1:4.6:1 ratio of **2**, **3a**, and diacylated products respectively. The major monoacylated *para*-substituted product **3a** was isolated in 68% yield by chromatography, with no trace of monosubstituted regioisomers (Scheme 2). The disubstituted products, which can be either *cis* or *trans*, were obtained as a 2:1 ratio of *para*-substituted isomers revealing the absence of stereoselectivity in the second substitution reaction. This monosubstitution methodology was extended to the introduction of benzoyl and *para*-bromobenzoyl groups to give **3b** and **3c** respectively, the bromine substituent of the latter providing an additional handle for further functionalization.

The complete control of *para*-regioselectivity observed in these monoacylation reactions gave us the confidence to investigate tetraacylation. Use of 8 equiv each of acetyl chloride and aluminum chloride and an extended 16 h reaction time resulted in the generation of a single major

Scheme 2. Mono-Friedel–Crafts Acylation of **2**



Scheme 3. Tetra-Friedel–Crafts Acylation of **2**



product, with ^1H NMR spectroscopy revealing only trace amounts of other acylation compounds. Following chromatography, tetra-*para*-acetyl substituted metallocene **4a** was isolated in 71% yield (Scheme 3). Use of benzoyl chloride and *para*-bromobenzoyl chloride similarly resulted in tetraacyl products **4b** and **4c**, with the latter requiring a longer 48 h reaction time. The structure of **4b** was confirmed by X-ray crystallography (Figure 1). Steric prevention of *ortho*-substitution results in the selective formation of just one of the six possible tetraacyl isomers.

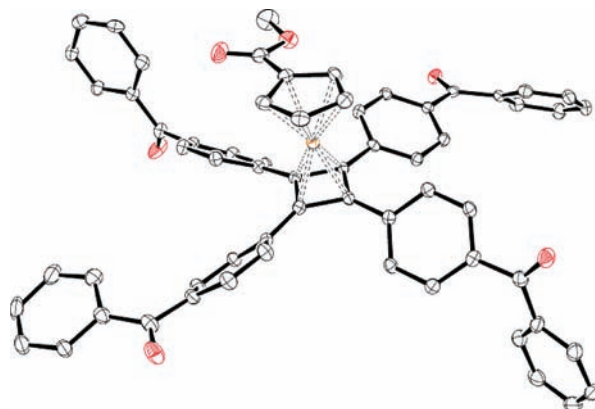
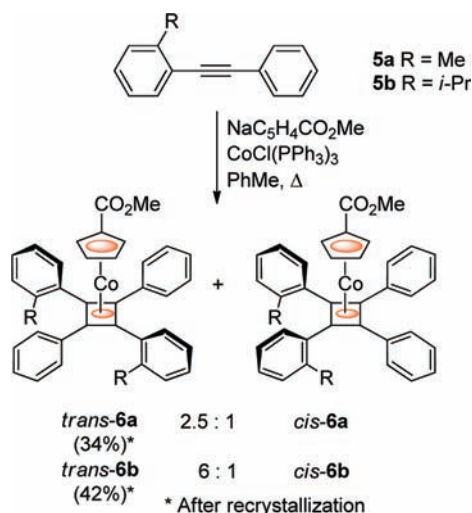


Figure 1. Representation of the X-ray structure of tetra-benzoyl substituted metallocene **4b**.

(8) (a) Stevens, A. M.; Richards, C. J. *Organometallics* **1999**, *18*, 1346. (b) Anderson, C. E.; Overman, L. E.; Richards, C. J.; Watson, M. P.; White, N. *Org. Synth.* **2007**, *84*, 139.

Scheme 4. Stereoselective Metallocene Formation



An alternative strategy to direct substitution was employed to generate selectively one of the two possible *trans* or *cis* disubstituted aryl isomers. Previous attempts to synthesize an analogue of **2** derived from di(*ortho*-tolyl)acetylene were unsuccessful,⁹ suggesting the unfavorable arrangement in these metallocenes of contiguous *ortho*-substituted aryl groups. Using this observation as the basis of a stereoselective synthesis, the reaction of (*ortho*-tolyl)phenylacetylene **5a** under the standard conditions for cobalt metallocene formation⁸ resulted in a 2.5:1 ratio of stereoisomers **6a** (Scheme 4). Purification of the major isomer was achieved by recrystallization from CH₂Cl₂/hexane, and the *trans* stereochemistry was confirmed by X-ray crystallography. Use of (*ortho*-isopropylphenyl)phenylacetylene **5b** in the same complexation procedure resulted in an increase in selectivity to 6:1, with pure *trans-6b* being obtained by a single recrystallization, and the structure was confirmed by X-ray crystallography (Figure 2). The distance between the two isopropyl methine carbons is only 3.952 Å revealing that accommodation of the additional methyl groups of *tert*-butyl *ortho*-substituents would require a significant distortion. This was therefore not attempted.

The *trans*-stereochemistry of the major isomer of **6a** and **6b** is in agreement with a study on the use of mixed disubstituted acetylenes for the synthesis of η⁵-cyclopentadienyl-(triphenylphosphine)cobaltacyclopentadienes, with the isomer distribution being controlled by the steric requirement of the acetylene substituents.¹⁰ Related coordinatively unsaturated cobaltacyclopentadienes are intermediates in the synthesis of tetraphenylmetallocenes **1** and **2**.⁷ Thus the formation of *trans-6a/b* proceeds *via* oxidative cyclization of bis(η²-alkyne) complex **7** to give cobaltacyclopentadienyl **8** followed by reductive elimination/η⁴-coordination (Scheme 5).

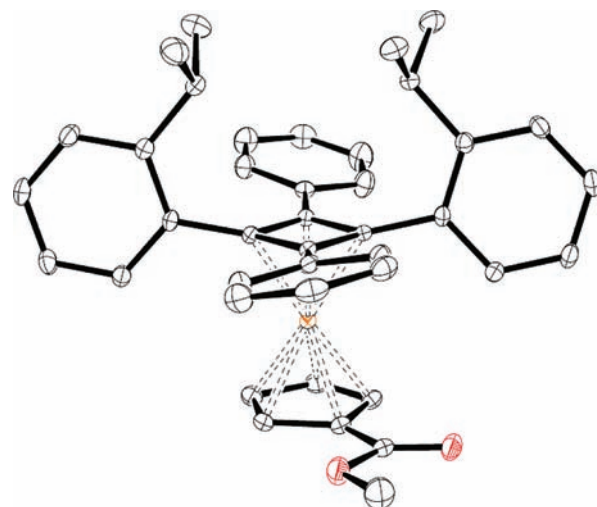
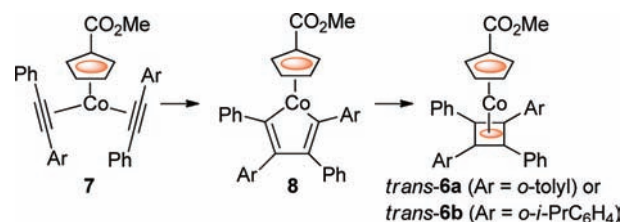


Figure 2. Representation of the X-ray structure of *trans-6b*.

Scheme 5. Stereoselective Metallocene Formation



The X-ray crystal structure of **6b** also reveals a significant difference in the conformation of the substituted and unsubstituted aryl groups; the former lies nearly perpendicular to the cyclobutadiene ring, and the latter almost coplanar (Figure 2). It was anticipated that orbital overlap between the phenyl substituents and the η⁴-cyclobutadiene/cobalt moiety in metallocenes *trans-6a/b* would significantly increase the susceptibility of the phenyl groups toward Friedel–Crafts acylation. Although σ_p⁺ for (η⁴-C₄H₃)Co(η⁵-C₅H₄CO₂Me) is not known, a high σ_p⁺ value of −0.65 has been determined for the ferrocenyl substituent,¹¹ a value similar to that of the methoxy group (σ_p⁺ = −0.78) and consistent with the stability of α-ferrocenylcarbenium ions.¹² In the same manner, a cobalt metallocene substituent will activate a conjugated phenyl group toward electrophilic substitution, overriding the weaker activation of the nonconjugated *o*-tolyl groups by the methyl substituent (σ_p⁺ = −0.31). Indeed, reaction of **6a** with 1.1 equiv of acetyl chloride/aluminum chloride resulted exclusively in *para*-phenyl substitution to give **9a** (Scheme 6), and on use of 2.1 equiv of the reactants, the double *para*-phenyl substituted product **10a** was

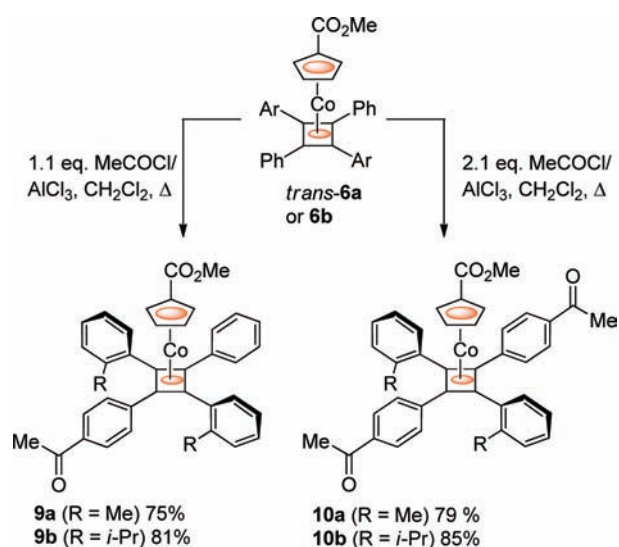
(9) Butler, D. C. D.; Richards, C. J. Unpublished result.

(10) Wakatsuki, Y.; Nomura, O.; Kitaura, K.; Morokuma, K.; Yamazaki, H. *J. Am. Chem. Soc.* **1983**, *105*, 1907.

(11) Nesmeyanov, A. N.; Perevalova, E. G.; Gubin, S. P.; Grandberg, K. I.; Kozlovsky, A. G. *Tetrahedron Lett.* **1966**, 2381.

(12) Allenmark, S. *Tetrahedron Lett.* **1974**, 371.

Scheme 6. Conformationally Controlled Mono- and Diacylation of *trans*-(*ortho*-Substituted) Metallocenes **6a** and **6b**



obtained with no acetylation of the *o*-tolyl groups. The *iso*-propyl substituted congener **6b** also reacted with the same level of conformational control to give monoacetyl derivative **9b** (1.1 equiv of MeCOCl/AI₃) and the di-*para*-acetyl derivative **10b** (2.1 equiv of MeCOCl/AI₃).

In conclusion, the Friedel–Crafts reaction of (η^4 -tetraphenylcyclobutadiene)(η^5 -carbomethoxycyclopentadienyl)-cobalt **2** results in exclusive *para*-substitution of the phenyl groups enabling the efficient synthesis of mono- and tetrasubstituted cobalt metallocenes. Synthesis of a related cobalt metallocene by cyclodimerization of (*ortho*-isopropylphenyl)phenylacetylene results in a *trans/cis* selectivity of 6:1, with the major isomer undergoing conformationally controlled mono- or di-*para*-phenyl Friedel–Crafts acylation. The conformational selectivity as well as regio- and stereoselectivity illustrated in this work, coupled with the synthetic versatility of the cyclopentadienyl ester substituent,⁷ will permit access to a variety of substituted cobalt metallocenes for application in catalyst and materials synthesis.

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Supporting Information Available. Synthesis and characterization data for all compounds reported, and CIF files for **4b**, *trans*-**6a**, and *trans*-**6b**. This material is available free of charge via the Internet at <http://pubs.acs.org>.

The authors declare no competing financial interest.