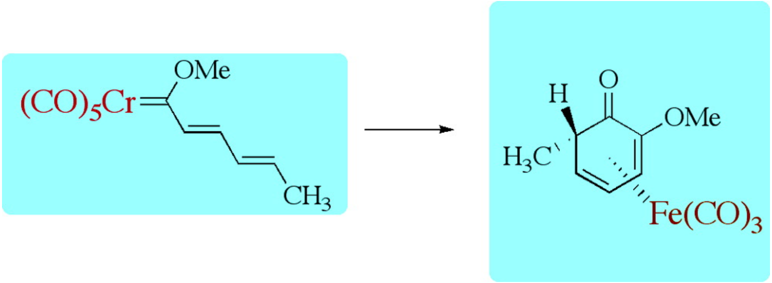
Communication

Iron in the Service of Chromium: The *ortho*-Benzannulation of *trans*,*trans*-Dienyl Fischer Carbene Complexes

Yiqian Lian, and William D. Wulff

J. Am. Chem. Soc., **2005**, 127 (49), 17162-17163• DOI: 10.1021/ja0540268 • Publication Date (Web): 17 November 2005



Journal of the American Chemical Society is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

J|A|C|S
COMMUNICATIONS

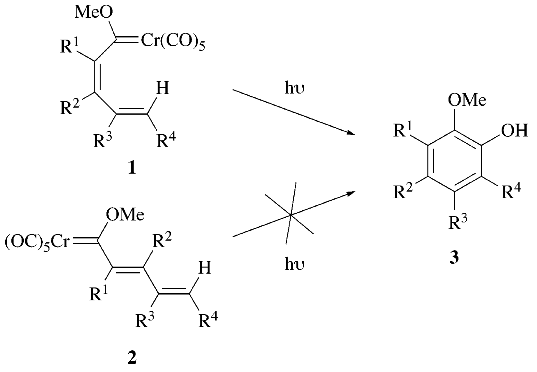
Published on Web 11/17/2005

Iron in the Service of Chromium: The *ortho*-Benzannulation of *trans*,*trans*-Dienyl Fischer Carbene Complexes

Yiqian Lian and William D. Wulff*
Department of Chemistry, Michigan State University, East Lansing, Michigan 48824
Received June 17, 2005; E-mail: wulff@chemistry.msu.edu

The synthesis of *o*-alkoxyphenols by the photoinduced CO insertion and cyclization (*ortho*-benzannulation) of dienyl Fischer carbene complexes was originally reported from our laboratories[1] and later improved by Merlic and co-workers (Scheme 1).[2] This reaction has been explored and developed as a synthetic method and has been utilized in the total synthesis of Carbazoquinocin C,[3] a member of a family of compounds possessing neuronal cell protecting activity, and in the total synthesis of Calphostins A−D, inhibitors of protein kinase C.[4] The reaction requires that the α,β-double bond in **1** has a cis-disposition of the carbene complex and the second double bond. As a consequence of synthetic expediency, most of the complexes of the type **1** that have been examined either have the α,β-unsaturated double bond incorporated into an aryl ring or were those that could be directly prepared from a [4 + 2] or [2 + 2] cycloaddition onto the alkyne function of an enynyl carbene complex. In a few rare cases where the substituents R^1 and R^2 were embedded into a strained four-membered ring, the formation of *o*-alkoxyphenols from complex **1** could be induced thermally.[5] The corresponding carbonylative cyclization of *trans*,*trans*-dienyl complex **2** to *o*-alkoxyphenols is not known and has been reported to fail under photochemical conditions.[2]

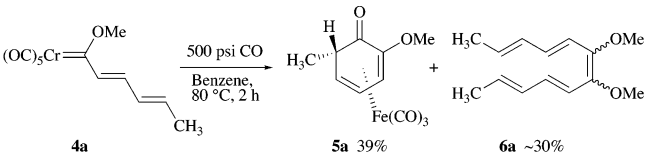
Scheme 1



In the course of a control experiment for a cyclopropanation reaction, we had occasion to heat the *trans*,*trans*-pentadienyl carbene complex **4a** in benzene at 80 °C under 500 psi of carbon monoxide (Scheme 2). As expected, the pentaene **6a** resulting from dimerization of the carbene ligand was observed,[6] but what was most certainly not expected was the η^4-dienyl iron complex **5a**. The structure of this product was determined by its NMR spectra, X-ray diffraction analysis, mass spectra, and the presence of iron was confirmed by SEM/EDS. The reaction was performed in a Monel Paar reactor which is composed of 65% nickel, 33% copper, and only 2% iron and did not look corroded. The mechanical stirrer, on the other hand, appeared to be quite corroded and was suspected to be the source of iron.

With the mass of the stirrer rapidly diminishing, we decided to pursue other sources of iron for this reaction. In addition, for the purpose of convenience and to be able to maintain rigorous control over the source of iron, conditions were sought where the reaction could be carried out in glass under 1 atm of carbon monoxide.

Scheme 2



Sources of iron tricarbonyl that were successful include diiron nonacarbonyl and benzylidene acetone iron tricarbonyl, both of which were superior to triirondodecacarbonyl. It was of interest to note that the yields of **5a** and **7a** were only slightly better under a carbon monoxide atmosphere than under argon (Table 1). The best solvent for this reaction was THF, which gave an 81% total yield of **5a** and **7a**. The dienone complex **5a** could be converted to the *o*-methoxyphenol **7a** in 91% yield upon stirring in Et_3N/H_2O at room temperature for 5 h. The control reaction under argon without a source of iron does produce a small amount of **7a** (8% yield) but only after 144 h. After 144 h under a CO atmosphere, a 70% recovery of **4a** is obtained, and only trace of **7a** is observed. Clearly, iron is playing the key role in this carbonylative cyclization.

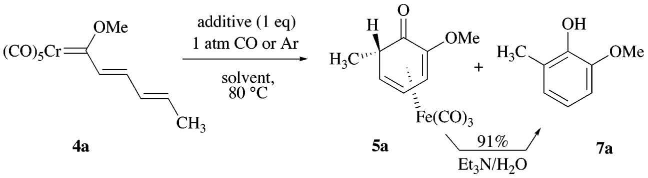


Table 1. Optimization with Added Iron Tricarbonyl Sources

additive	solvent	CO/Ar	time, h	**5a**, % yield	**7a**, % yield
	benzene	CO	144		<0.5[a]
		Ar	144		8
$Fe_2(CO)_9$	benzene	CO	18	70	8
		Ar	28	58	6
$Fe_2(CO)_9$	heptane	CO	36	68	7
		Ar	20	54	5
$Fe_2(CO)_9$	THF	CO	36	61	20
		Ar	20	50	10
$Fe_2(CO)_9$	CH_3CN	CO	17	68	12
		Ar	20	34	8
$Fe(CO)_3(ba)$[b]	benzene	CO	48	60	7

[a] With 70% recovery of **4a**. [b] Benzylideneacetone iron tricarbonyl.

In an effort to explore the scope of this reaction, a number of different *trans*,*trans*-dienyl carbene complexes were investigated, all of which (except **4d**) were directly prepared by an aldol reaction of the methyl carbene complex **8** with unsaturated aldehydes and ketones (Scheme 3).[7,8] For many of the substrates, THF was the optimal solvent, and cyclization gave high to excellent yields of dienone iron tricarbonyl complexes and/or *o*-methoxyphenols (Table 2). The dienone complexes could be converted to their corresponding phenols by treatment with base (**7a**, Table 1) or by stirring with silica gel in the presence of air (**7b**, Table 2). In all cases, only a single diastereomer of the dienone iron tricarbonyl complex was formed, and the stereochemistry of each was assigned as syn based

10.1021/ja0540268

Scheme 3

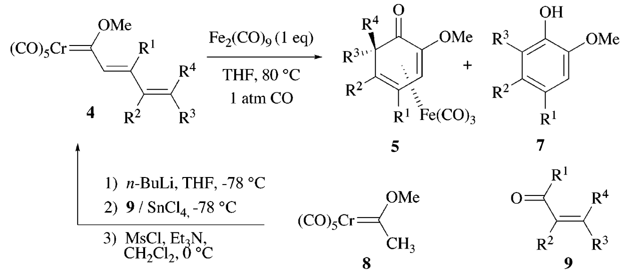
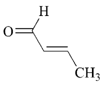
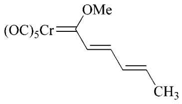
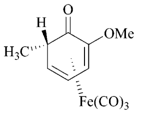
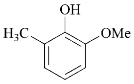
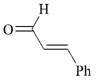
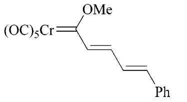
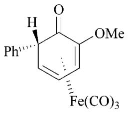
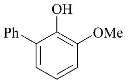
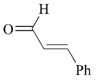
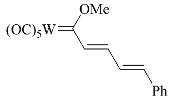
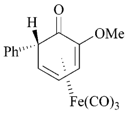
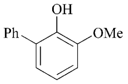
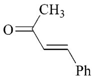
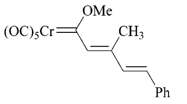
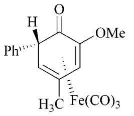
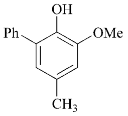
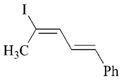
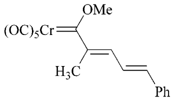
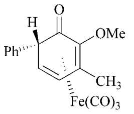
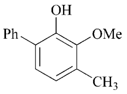
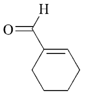
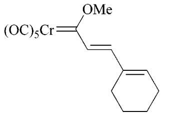
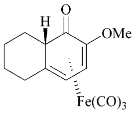
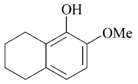
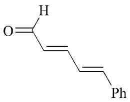
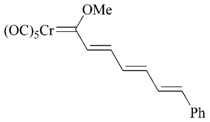
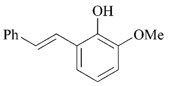
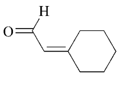
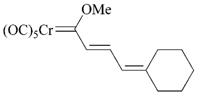
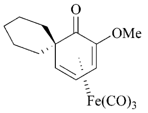
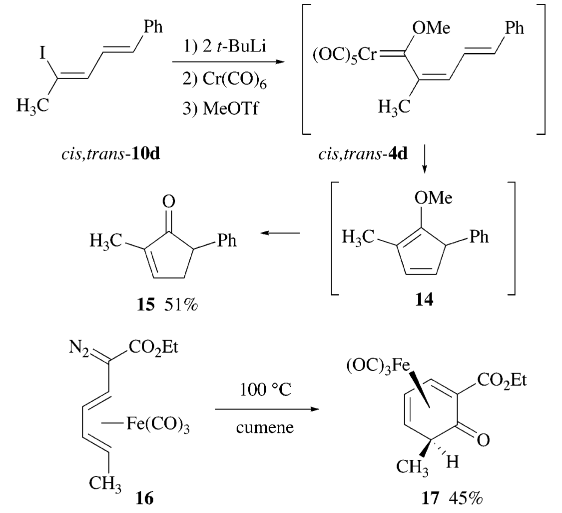


Table 2. Iron-Mediated Reactions of Dienyl Fischer Carbene Complexes[a]

aldehyde	carbene complex [b]	dienone	phenol
 **9a**	 **4a** 52% (63%)	 **5a** 81% (75:25)	 **7a**
 **9b**	 **4b-Cr** 68%	 **5b** 82% (40:60) 78% (0:100) [c]	 **7b**
 **9b**	 **4b-W** 65%	 **5b** 92% (25:75)	 **7b**
 **9c**	 **4c** 43% (51%)	 **5c** 89% (67:33) [d]	 **7c**
 **10d**	 **4d** 62%	 **5d** 87% (83:17) [d]	 **7d**
 **9e**	 **4e** 31% (61%)	 **5e** 91% (93:7)	 **7e**
 **9f**	 **4f** 72%		 **7f** 70%
 **9g**	 **4g** 51% (72%)	 **5g** 85%	

[a] Unless otherwise specified, all reactions were carried out in THF at 80 °C with 1 equiv of $Fe_2(CO)_9$ under 1 atm of CO at 0.02 M in **4**. [b] Yields in parentheses are based on unrecovered starting material. [c] The crude reaction mixture was stirred with silica gel for 2−3 days. [d] In benzene.

Scheme 4



on the X-ray structure of **5a**. The reaction can also be used to generate a spiro-cyclohexadienone iron tricarbonyl complex (**5g**, 85%).

Attempts were made to generate the *cis,trans*-dienyl complex **4d** from *cis,trans*-dienyl iodide **10d**; however, *cis,trans*-**4d** underwent spontaneous cyclization to give the cyclopentadiene **14** since the cyclopentenone **15** was isolated from the reaction.[9] In contrast, the *trans,trans*-**4d** complex is stable and, upon treatment with $Fe_2(CO)_9$ at 80 °C, gave an 87% yield of **5d** and **7d** (Table 2).

How does this iron-assisted conversion of the dienyl chromium carbene complexes to *o*-alkoxyphenols occur? In the only related chemistry, thermolysis of **16** gives the dienone complex **17**, demonstrating that a likely iron carbene complexed intermediate can insert CO and cyclize to a dienone (Scheme 4).[10] With regard to how the organic fragment is transferred from chromium to iron, the two most likely possibilities are that the iron tricarbonyl unit becomes complexed to the dienyl unit in **4** followed by loss of chromium or there is a direct trans-metalation to give an iron carbene complex which then undergoes internal coordination to the diene in some fashion such that the α,*β*-*trans*-double bond is isomerized. The transfer of the carbene ligand from chromium Fischer carbene complexes to other metals is an active area of interest and, if it occurs here, would be the first example to iron.[6] Mechanistic and further synthetic studies will be reported in due course.

Acknowledgment. This work was supported by the NIH (GM 33589). We acknowledge the Center for Advanced Microscopy at MSU and Xiuni Wu for assistance with the SEM/EDS experiment. We thank Rui Huang for the X-ray structure of **5a**.

Note Added after ASAP Publication. After this paper was published ASAP on November 17, 2005, structure **7e** in Table 2 was corrected. The corrected version was published ASAP on November 21, 2005.

Supporting Information Available: Experimental procedures and spectral data for all new compounds including X-ray diffraction and SEM/EDS data for **5a**. This material is available free of charge via the Internet at http://pubs.acs.org.

References

(1) Wulff, W. D. In *Advances in Metal-Organic Chemistry*; Liebeskind, L. S., Ed.; JAI Press: Greenwich, CT, 1989; Vol. 1, p 336.
(2) Merlic, C. A.; Xu, D. *J. Am. Chem. Soc.* **1991**, *113*, 7418.
(3) Rawat, M.; Wulff, W. D. *Org. Lett.* **2004**, *6*, 329.
(4) Merlic, C. A.; Aldrich, C. C.; Albaneze-Walker, J.; Saghatelian, A.; Mammen, J. *J. Org. Chem.* **2001**, *66*, 1297.
(5) Barluenga, J.; Aznar, F.; Palomero, M. A. *J. Org. Chem.* **2003**, *68*, 537.
(6) Gomez-Gallego, M.; Mancheno, M. J.; Sierra, M. A. *Acc. Chem. Res.* **2005**, *38*, 44 and references therein.
(7) Wang, H.; Hsung, R. P.; Wulff, W. D. *Tetrahedron Lett.* **1998**, *39*, 1849.
(8) Aumann, R.; Heinen, H. *Chem. Ber.* **1987**, *120*, 537.
(9) For related examples, see citations listed in ref 5.
(10) Franck-Neumann, M.; Geoffroy, P.; Winling, A. *Synlett* **1995**, 341.

JA0540268