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Carbon–Carbon Bond-Forming Reaction through a η^5-Pentadienylchromium Complex

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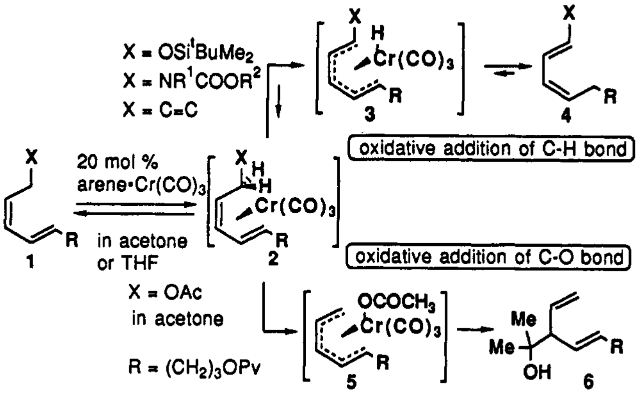
Summary: Arene•$Cr(CO)_3$-mediated coupling reactions of pentadienyl esters (**7a–d**, **11**, and **13**) with carbonyl compounds via η^5-pentadienylchromium intermediates gave the γ-adducts regioselectively.

Previously, we reported that the naphthalene•$Cr(CO)_3$ complex could catalyze a stereospecific 1,5-hydrogen shift in butadiene derivatives through a U-shaped η^5-pentadienylhydridochromium intermediate **3**.[1–5] This isomerization reaction has been successfully used in the stereocontrolled syntheses of silyl dienol ethers,[3] dienamine derivatives,[4] and aromatic ring-substituted exocyclic olefins[5] (Scheme 1). In connection with these projects, we have found that treatment of pentadienyl acetate **1** (X = OAc) with 20 mol % of naphthalene•$Cr(CO)_3$ in acetone at 20 °C for 4 h gave the coupling product **6**, albeit in low yield (7%), along with recovered **1** (85%) (Scheme 1). Under these reaction conditions, none of the isomerized product **4** (X = OAc) was detected. The formation of a η^5-pentadienylacetoxychromium intermediate **5** with nucleophilic character is suggested. Presumably, after coordination of the diene in the cisoid conformation (**2**), oxidative addition of the C–OAc bond, not the C–H bond, to "$Cr(CO)_3$" occurs as shown in Scheme 1. In spite of many structural studies on η^5-pentadienylchromium species and other group VIB metal complexes,[6] not much attention has been paid to their reactivity and synthetic potential.[7]

Scheme 1



These facts prompted us to investigate the reaction of pentadienyl ester derivatives with arene•$Cr(CO)_3$ complexes. Here, we report a novel coupling reaction of pentadienyl esters with carbonyl compounds mediated by arene•$Cr(CO)_3$ complexes which proceeds through a η^5-pentadienylacetoxychromium complex.

First, we examined the coupling reaction of the pentadienyl acetate **7a**[8] and found that treatment of **7a** with (methyl benzoate)$Cr(CO)_3$ (2 equiv) and butanal (2 equiv) at 120 °C for 43 h in the presence of K_2CO_3 (1.5 equiv)[9] gave the coupling product **8a** in 63% yield together with **9** (26%) (Table 1, entry 1). Similarly, reaction of **7a** with benzaldehyde and *o*-methylbenzaldehyde under the same conditions afforded **8b** and **8c** in 51% and 48% yields, respectively (entries 2 and 3). In all cases, the C–C bond formation occurred at the γ-position regiospecifically, but no diastereoselectivity (*syn, anti*) was observed. Ketones were also studied as substrates, and reaction of acetate **7a** with 4-methyl-2-pentanone gave the coupling product **8d** in only 22% yield. A regioisomeric mixture of dienes **9** was obtained as the major product (63%). These formal reduction products **9** are presumably formed by protonation of the nucleophilic η^5-pentadienylacetoxychromium intermediate, and this pathway seems to become significant in the case of a less reactive bulky ketone such as 4-methyl-2-pentanone. In an attempt to improve the yield of coupling product **8d**, we investigated Lewis acid activation of the carbonyl group. While Lewis acids such as TMSOTf, BF_3•OEt_2, $TiCl_4$, and Et_2AlCl did not increase the yield of the coupling product, the addition of 2 equiv

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(1) For a review, see: Sodeoka, M.; Shibasaki, M. *Synthesis* **1993**, 643.

(2) Several $CrH(\eta^5$-pentadienyl$)L_3$ complexes have been isolated and characterized. See: (a) Blackborow, J. R.; Eady, C. R.; Grevels, F.-W.; von Gustorf, E. A. K.; Scrivanti, A.; Wolfbeis, O. S.; Benn, R.; Brauer, D. J.; Krüger, C.; Roberts, P. J.; Tsay, Y.-H. *J. Chem. Soc., Dalton Trans.* **1981**, 661. (b) Michael, G.; Kaub, J.; Kreiter, C. G. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 502. (c) Michael, G.; Kaub, J.; Kreiter, C. G. *Chem. Ber.* **1985**, 3994.

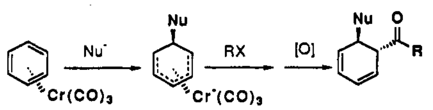
(3) Sodeoka, M.; Yamada, H.; Shibasaki, M. *J. Am. Chem. Soc.* **1990**, *112*, 4906.

(4) Yamada, H.; Sodeoka, M.; Shibasaki, M. *J. Org. Chem.* **1991**, *56*, 4569.

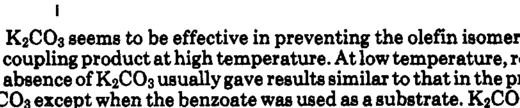
(5) Sodeoka, M.; Sato, S.; Shibasaki, M. *J. Am. Chem. Soc.* **1988**, *110*, 4823.

(6) For a review, see: (a) Ernst, R. D. *Chem. Rev.* **1988**, *88*, 1255 and references cited therein. (b) Djukic, J.-P.; Rose-Munch, F.; Rose, E.; Dromzee, Y. *J. Am. Chem. Soc.* **1993**, *115*, 6434.

(7) To our knowledge, only one synthetically useful C–C bond-forming reaction employing a η^5-pentadienylchromium species has been reported. However, this η^5-pentadienylchromium anion, generated by the reaction of arene•$Cr(CO)_3$ with a strong nucleophile such as alkyllithium, failed to react with carbonyl compounds. See: (a) Semmelhack, M. F.; Clark, G.; Garcia, J. L.; Harrison, J. J.; Thebtaranonth, Y.; Wulff, W.; Yamashita, A. *Tetrahedron* **1981**, *37*, 3957. (b) Kündig, E. P.; Desobry, V.; Simmons, D. P.; Wenger, E. *J. Am. Chem. Soc.* **1989**, *111*, 1804. (c) Kündig, E. P.; Do Thi, N. P.; Paglia, P.; Simmons, D. P.; Spichiger, S.; Wenger, E. *Organometallics in Organic Synthesis;* de Meijere, A., tom Dieck, H., Eds.; Springer-Verlag: Berlin Heidelberg, 1987. (d) Kündig, E. P.; Cunningham, A. F., Jr.; Paglia, P.; Simmons, D. P. *Helv. Chim. Acta* **1990**, *73*, 386. (e) Kündig, E. P.; Ripa, A.; Bernardinelli, G. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1071 and references cited therein.



(8) Pentadienyl esters **7a-7d** were easily prepared from the corresponding alcohol **i**.[4]



(9) K_2CO_3 seems to be effective in preventing the olefin isomerization of the coupling product at high temperature. At low temperature, reaction in the absence of K_2CO_3 usually gave results similar to that in the presence of K_2CO_3 except when the benzoate was used as a substrate. K_2CO_3 seems to enhance the reaction rate of the benzoate substrate (Table 2, entries 5 and 6).

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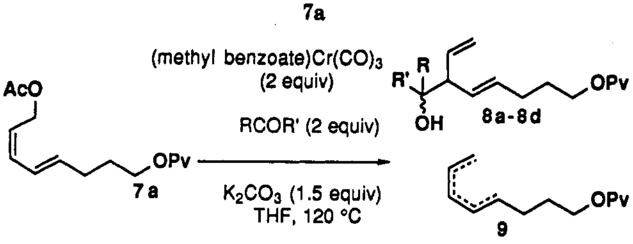
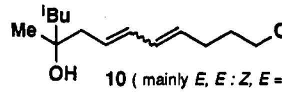
Table 1. (Methyl benzoate)Cr(CO)$_3$-Mediated Reaction of 7a



entry	carbonyl compd R′ =	R =	time (h)	coupling product (%)	reduced products (%)
1	H	^{n}Pr	43	**8a** (63)	**9** (26)
2	H	Ph	48	**8b** (51)	**9** (30)
3	H	*o*-MePh	45	**8c** (48)	**9** (30)
4	Me	^{i}Bu	48	**8d** (22)	**9** (63)
5^a	Me	^{i}Bu	12	**10**^{b} (63)	**9** (33)

^{a} ZnCl$_2$ (2 equiv) was used as an additive. ^{b} No γ-product **8d** was obtained.



10 (mainly *E*, *E* : *Z*, *E* = 4 : 1)

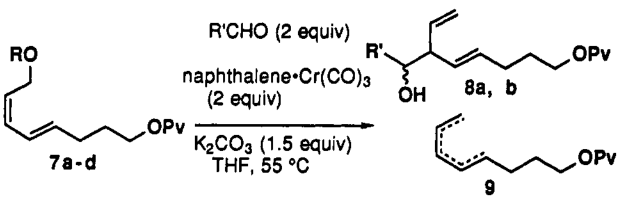
of ZnCl$_2$ accelerated the reaction to give the α-substituted product **10** in 63% yield (entry 5).[10] Since this drastic change of regiochemistry is quite interesting from a mechanistic point of view, we also examined the reaction of **7a** in the presence of ZnCl$_2$ with various aldehydes or ketones.[11] In all cases, rate enhancement was observed; however, the regioselectivity (α vs γ) varied depending on the structure of the carbonyl compound. The observed change in regioselectivity and the isomerization of the stereochemistry of the double bond in the coupling products suggest the intermediacy of a pentadienyl zinc species[12] produced by the transmetalation from Cr to Zn.

We also studied the coupling reaction using naphthalene·Cr(CO)$_3$, a complex that is expected to give the active "Cr(CO)$_3$" species at lower temperature (Table 2). On treatment of pentadienyl acetate **7a** with 2 equiv of naphthalene·Cr(CO)$_3$ and butanal in THF at 55 °C, the coupling product **8a** was formed in 47% yield. The major byproduct of this reaction was again the regioisomeric mixture of dienes **9**. It is possible that the acidic α-hydrogen of the acetoxy group is protonating the proposed intermediate **5** to give **9**, and in an effort to improve the yield of the coupling product, we investigated the coupling reaction of various esters **7b–7d**[8] having no acidic α-hydrogen. When the benzoate **7d** was used as a substrate, the yields of the coupling products **8a** or **8b** were increased to 75% (entries 4–6). In addition, the pivaloate **7b** and carbonate **7c** afforded increased yields of coupling products (entries 2 and 3). However, it is still not clear that the α-hydrogen of the acetoxy group is the only proton source, since significant amounts of the reduction products **9** are still formed in some cases. It is also noteworthy that the reaction rate of the benzoate **7d** is significantly faster than that of other esters studied.

This methodology has also been successfully applied to an intramolecular coupling reaction. The requisite aldehyde **11** was readily prepared as shown in Scheme 2. Treatment of this substrate with naphthalene·Cr(CO)$_3$ (2 equiv) in THF at 90 °C for 5 h was found to give the cyclized product **12** in 66% yield. It is notable that the relative stereochemistry of the vinyl and the hydroxy group in the cyclized product was exclusively *cis*, although no selectivity in the stereochemistry of the ring-juncture carbon was observed.[13]

We investigated the chemoselectivity of this coupling reaction. Our studies of the arene·Cr(CO)$_3$-catalyzed hydrogenation and isomerization reactions have shown that "Cr(CO)$_3$" has a strong preference to form 18-electron complexes such as **3** and **5**. Thus, this reagent should be able to discriminate a pentadienyl acetate from a simple allylic acetate. To test this hypothesis a substrate **13** which has both a pentadienyl and allyl acetate group in the same

Table 2. Naphthalene·Cr(CO)$_3$-Mediated Reaction of 7a–7d



entry	ester	R =	aldehyde R′ =	time (h)	coupling product (%)	reduced products (%)	recovery of SM (%)
1	**7a**	Ac	^{n}Pr	68	**8a** (47)	**9** (36)	12
2	**7b**	Pv	^{n}Pr	49	**8a** (60)	**9** (trace)	21
3	**7c**	COOMe	^{n}Pr	49	**8a** (68)	**9** (12)	17
4	**7d**	Bz	^{n}Pr	25	**8a** (75)	**9** (trace)	
5	**7d**	Bz	Ph	25	**8b** (70)	**9** (20)	
6^a	**7d**	Bz	Ph	50	**8b** (75)		

^{a} No K$_2$CO$_3$ was used.

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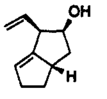
[10] ZnBr$_2$ and ZnI$_2$ also have similar effects on the reaction affording **10** in 40% and 54% yields, respectively, together with **9** (41% and 33%).

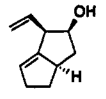
[11] Reaction of **7a** with various carbonyl compounds in the presence of ZnCl$_2$ gave the coupling products at the α-position and γ-position in the following yields: butanal, α 0%, γ 50%; benzaldehyde, α 0%, γ 70%; 4-methyl-2-pentanone, α 63%, γ 0%; 1-phenyl-2-propanone, α 0%, γ 75%; 1-phenyl-2-butanone, α 27%, γ 14%; phenyl trimethylsilyl ketone, α 57%, γ 17%.

[12] (a) G'erard, F.; Miginiac, P. *Bull. Soc. Chim. Fr.* **1974**, 1924. (b) Gérard, F.; Miginiac, P. *Bull. Soc. Chim. Fr.* **1974**, 2527. (c) Yasuda, H.; Nakamura, A. *J. Organomet. Chem.* **1985**, *285*, 15. (d) Yasuda, H.; Ohnuma, Y.; Nakamura, A.; Kai, Y.; Yasuoka, N.; Kasai, N. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1101.

[13] The two diastereomers of **12** (**12a**:**12b** = 1.3:1) were separated after conversion to the *tert*-butyldimethylsilyl ethers (^{t}BuMe$_2$SiCl, imidazole, DMF, rt, quant). The stereochemistry of each diastereomer was determined by NOE experiments and analysis of coupling constants in its ^{1}H-NMR spectra.

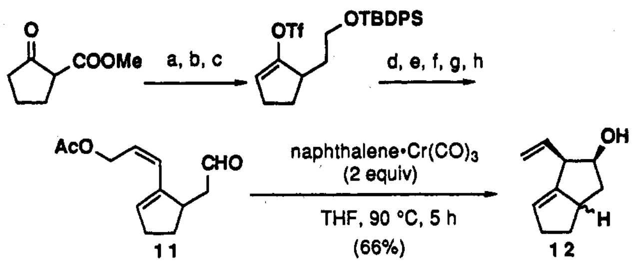


12a



12b

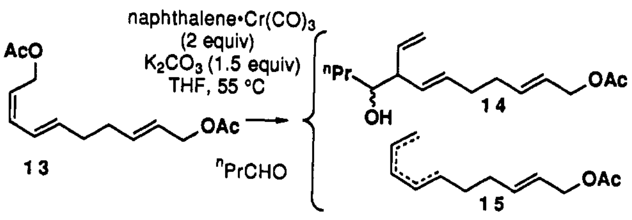
Scheme 2[a]



[a] Key: (a) $ICH_2CH_2OTBDPS$, Cs_2CO_3, DMF, 70 °C (62%); (b) p-NH_2PhSH, Cs_2CO_3, DMF, 85 °C (100%); (c) LDA, Tf_2NPh, THF, 0 °C (99%); (d) propargyl alcohol, cat. $PdCl_2(PPh_3)_2$, CuI, Et_2NH, DMF, rt (91%); (e) $(Sia)_2BH$, 0 °C then AcOH, 65 °C, NaOH–H_2O_2 (75%); (f) Ac_2O, DMAP, NEt_3, CH_2Cl_2, rt (91%); (g) TBAF, THF, rt (75%); (h) $(COCl)_2$, DMSO, NEt_3, CH_2Cl_2, −78 to −30 °C (95%).

molecule was prepared.[14] As expected, treatment of **13** with 2 equiv of naphthalene•$Cr(CO)_3$ and 2 equiv of butanal afforded the coupling product **14** (40%) as well as the reduction product **15** (45%). No coupling or reduction of the allylic acetate functionality was observed under these reaction conditions.[15–17] Thus, the pentadienyl acetate was selectively activated by naphthalene•$Cr(CO)_3$ in the presence of an allylic acetate. This represents a unique character of this chromium reagent (Scheme 3).

Scheme 3



In conclusion, selective "umpolung" of pentadienyl esters has been achieved with arene•$Cr(CO)_3$ to afford coupling products at the γ-position with aldehydes in up to 75% yield.[18] Direct pentadienylation of carbonyl compounds with pentadienyl alkali metals has less utility in organic synthesis because a mixture of products is obtained through competitive coupling at the α- and γ-positions of the pentadienyl group.[19] This novel reaction employing a η^5-pentadienylacetoxychromium species has several advantages over those employing alkali metal species such as (1) perfect γ-selectivity, (2) easily preparable and stable esters as pentadienyl precursors, (3) very mild reaction conditions for the generation of a pentadienyl anion equivalent, and (4) unique chemoselectivity for the (Z,E)-pentadienyl acetate. Further mechanistic studies on this novel C–C bond-forming reaction and its application to organic synthesis are in progress.

Supplementary Material Available: General experimental procedures and spectral data for compounds **6**, **7a–d**, **8a–d**, and **9–15** (30 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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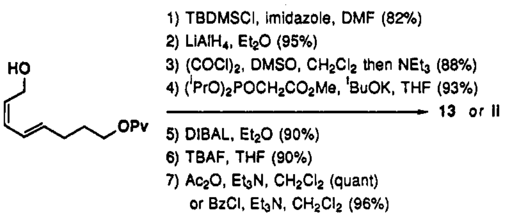
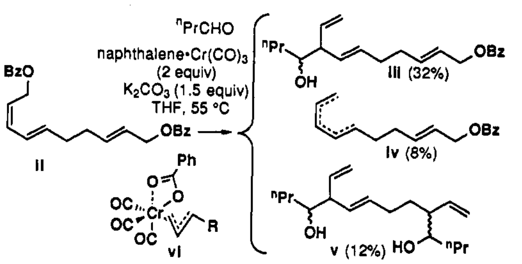
[14] The diacetate **13** and the dibenzoate **ii** were prepared as follows:



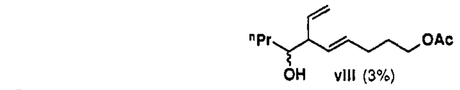
1) TBDMSCl, imidazole, DMF (82%)
2) $LiAlH_4$, Et_2O (95%)
3) $(COCl)_2$, DMSO, CH_2Cl_2 then NEt_3 (88%)
4) $(^iPrO)_2POCH_2CO_2Me$, ^tBuOK, THF (93%)
5) DIBAL, Et_2O (90%)
6) TBAF, THF (90%)
7) Ac_2O, Et_3N, CH_2Cl_2 (quant)
or BzCl, Et_3N, CH_2Cl_2 (96%)

[15] Treatment of **13** with naphthalene•$Cr(CO)_3$ in the absence of carbonyl compound afforded **15** in 95% yield. No reduction of the allylic acetate functionality was observed.

[16] Reaction of the dibenzoate **ii**[14] under similar conditions gave **iii** and **iv** as major products; however, a small amount of diol **v** was also formed in this case. This indicates that the allylic benzoate functionality is sensitive to the reaction conditions, but it is far less reactive than the pentadienyl benzoate. Coordination of the benzoate carbonyl to form a η^3-allyl(benzoyloxy)chromium intermediate with an 18-electron configuration (**vi**) may explain the formation of small amounts of **v**.



[17] Reaction of (E,E)-pentadienyl acetate **vii** with butanal under the same conditions as Table I, entry 1, gave only a 3% yield of **viii** with recovery of 58% of the starting material. This low reactivity of the (E,E)-pentadienyl acetate group supports the fact that formation of the U-shaped η^5-pentadienylacetoxychromium intermediate **5** is a key for this reaction.



[18] Coupling reaction of (E,E)-1-bromo-2,4-hexadiene with benzaldehyde mediated by $CrCl_2$ has been reported by Hiyama et al. to give the γ-adduct. This Cr(II) reagent also reacts with allylic bromides. See: Hiyama, T.; Kimura, K.; Nozaki, H. *Tetrahdron Lett.* **1981**, *22*, 1037.

[19] Paget, W. E.; Smith, K.; Hutchings, M. G.; Martin, G. E. *J. Chem. Res,. Synop.* **1983**, 30. See also ref 12 and references cited therein.