

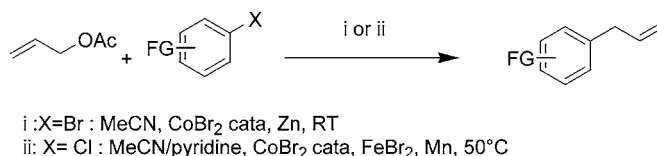
New Chemical Cross-Coupling between Aryl Halides and Allylic Acetates Using a Cobalt Catalyst

Paulo Gomes, Corinne Gosmini,* and Jacques Périchon

Laboratoire d'Electrochimie, Catalyse et Synthèse Organique, UMR 7582,
Université Paris 12—CNRS 2, Rue Henri Dunant, F-94320 Thiais, France
gosmini@glvt-cnrs.fr

Received January 14, 2003

ABSTRACT



The cobalt-catalyzed coupling reaction of aromatic halides and allylic acetates proceeds readily under mild conditions in the presence of the appropriate reducing agent to produce allyl aromatic derivatives either in pure acetonitrile (aryl bromides) or in an acetonitrile/pyridine mixture (aryl chlorides).

Many natural products exhibit allylbenzene and propenylbenzene skeletons.¹ Substitution reactions of allylic halides with various aromatic organometallic reagents have provided an important route for the synthesis of these compounds. Indeed, aromatic Grignard reagents have received much attention, but their use² precludes the presence of most reactive functional groups on the aromatic nuclei such as aldehydes, esters, ketones, or nitriles except in the case of low-temperature iodine–magnesium exchange reaction.³ Alternatively, arylzinc compounds are convenient reagents due to their high functional group tolerance and their good reactivity toward allylic halides in the presence of the soluble salt CuCN·2LiCl to activate the arylzinc.⁴ Similarly, aryl-palladium species prepared in situ from arylmercuric and Pd(II) salts react with allylic halides to produce allyl aromatic compounds⁵ in moderate yields. Allylic acetates, which are

less reactive than allylic halides, can be coupled with aryl bromides by palladium catalysis either directly in the presence of hexa-*n*-butylditin⁶ or from allylic stannanes.⁷ More recently, a variety of arylboronic acids were found to be efficient in cross-coupling also with allylic acetates⁸ under neutral conditions using the palladium catalyst. However, this catalyst remains expensive.

Among the numerous topics developed in our laboratory, the synthesis of arylallyl compounds is of current interest. In the past few years, these compounds have been successfully synthesized from aryl halides under mild conditions by two electrochemical procedures. The first one was based on the catalytic activity of a nickel complex in DMF as a solvent and allowed the electrochemical allylation of aryl halides.⁹ More recently, we have developed a simpler catalytic system involving CoX₂ in DMF or acetonitrile associated to pyridine.¹⁰ The use of cobalt allowed us to

(1) Wenkert, E.; Fernandes, J. B.; Michelotti, E. L.; Swindell, C. S. *Synthesis* **1983**, 701.

(2) (a) Kharasch, M. S.; Reinmuth, O. In *Grignard Reactions of Nonmetallic Substances*; Coustable: London, 1954. (b) Hayashi, T.; Konishi, M.; Yokota, K.-i.; Kumada, M. *J. Chem. Soc., Chem. Commun.* **1981**, 313. (c) Hayashi, T.; Konishi, M.; Yokota, K.-i.; Kumada, M. *J. Organomet. Chem.* **1985**, 285, 359.

(3) Rottländer, M.; Boymond, L.; Bérillon, L.; Leprêtre, A.; Varchi, G.; Avolio, S.; Laaziri, H.; Quéguiner, G.; Ricci, A.; Cahiez, G.; Knochel, P. *Chem. Eur. J.* **2000**, 6, 767.

(4) (a) Majid, T. N.; Knochel, P. *Tetrahedron Lett.* **1990**, 31, 4413. (b) Zhu, L.; Wehmeyer, R. M.; Rieke, R. D. *J. Org. Chem.* **1991**, 56, 1445.

(5) Heck, R. F. *J. Am. Chem. Soc.* **1968**, 90, 5531.

(6) Yokoyama, Y.; Ito, S.; Takahashi, Y.; Murakami, Y. *Tetrahedron Lett.* **1985**, 26, 6457.

(7) Kosugi, M.; Sasazawa, K.; Shimizu, Y.; Migita, T. *Chem. Lett.* **1977**, 301.

(8) Bouyssi, D.; Gerusz, V.; Balme, G. *Eur. J. Org. Chem.* **2002**, 2445.

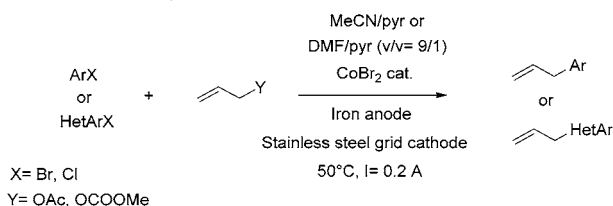
(9) Durandetti, M.; Nédélec, J.-Y.; Périchon, J. *J. Org. Chem.* **1996**, 61, 1748.

(10) Gomes, P.; Gosmini, C.; Périchon, J. *J. Org. Chem.* **2003**, 68, 1142.

(b) Gomes, P.; Gosmini, C.; Périchon, J. Fr. Pat. Appl. 01/08808, July 3, 2001.

achieve the arylation of allylic acetates from aryl halides by introducing all the allylic substrate in the cell at the beginning of the reaction (unlike the electrochemical process using a nickel complex as a catalyst) and to use a less toxic catalyst (Scheme 1).

Scheme 1. Arylation of Allylic Acetate Catalyzed by CoBr_2 by the Electrochemical Method



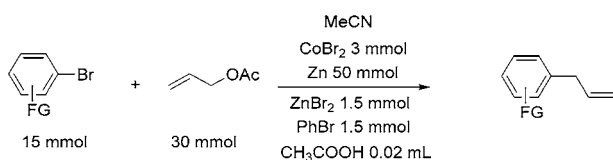
These electrochemical methods favorably compare with known chemical processes. However, all the electrochemical reactions are generally considered more difficult to handle than conventional chemical methods. As a result, electrochemical syntheses are poorly applied by organic chemists and are not used in a larger scale than in the laboratory.

Recently, we have demonstrated that in some cases a purely chemical reaction could be extended from our initial electrochemical process. Indeed, we have established that the low-valent cobalt generated from the chemical reduction of cobalt halide can unprecedently activate aryl bromide in acetonitrile to form arylzinc species.¹¹

Herein, we describe that the cobalt catalyst is suitable for the efficient arylation of allylic acetate not only with aryl bromides but also with aryl chlorides, using a different reducing agent in the appropriate medium.

Aryl bromides react with allylic acetate in the presence of zinc dust in pure acetonitrile (Scheme 2). However, aryl

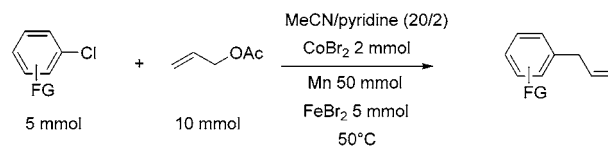
Scheme 2. Aryl Bromide Allylation by Allyl Acetate with Co–Zn



chlorides require stronger reducing metal (manganese powder) in a mixture of acetonitrile–pyridine with a stoichiometric amount of iron salt to carry out the same reaction (Scheme 3).

We first investigated the reaction between an aryl bromide and allyl acetate. To an acetonitrile solution (20 mL) was successively added zinc dust (3.25 g, 50 mmol), CoBr_2 (0.657 g, 3 mmol), ZnBr_2 (0.338 g, 1.5 mmol), and bromobenzene

Scheme 3. Aryl Chloride Allylation by Allyl Acetate with Co–Fe–Mn



(0.16 g, 1.5 mmol). The reaction medium was activated by adding acetic acid (0.024 g, 4×10^{-4} mmol) and stirred for 30 min at room temperature until bromobenzene was totally consumed. Allyl acetate (3.03 g, 30 mmol) and ethyl 4-bromobenzoate (2.427 g, 15 mmol) were then introduced into the solution. After being stirred for 3 h at room temperature, the reaction mixture was poured into a solution of 2 M HCl (40 mL) and extracted with diethyl ether (3 \times 40 mL). The combined extracts were dried over MgSO_4 . Evaporation of ether and purification by column chromatography on silica gel (pentane/ether, 99/1) afforded 1.852 g (65%) of 4-(2-propenyl)ethyl benzoate as a colorless oil.

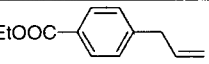
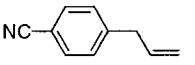
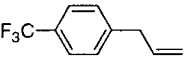
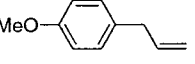
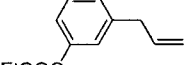
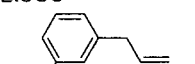
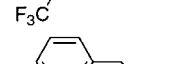
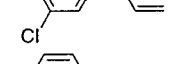
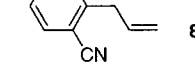
Acetic acid was necessary to activate the zinc dust. Iodine or trifluoroacetic acid could also play this part. Nevertheless, with iodine as an activating agent, ethyl 4-bromobenzoate is totally consumed only after 48 h and the amount of zinc dust must be increased to 100 mmol. The presence of the zinc bromide is not necessary but enhances the yield of the reaction. To decrease the amount of the reduction product, a catalytic amount of bromobenzene is added to the solution before the introduction of the functionalized aryl bromide. Bromobenzene is readily converted into the reduced product. This procedure is the same as described before for the formation of the aryl zinc species¹¹ except that allylic acetate is present in the medium and reacts directly by substitution with this compound without a supplementary catalyst. The byproducts of this reaction are the reduction product and the dimer of the aryl bromide. The results of the allylation of various aryl bromides by allyl acetate are reported in Table 1.

Good yields are obtained with several aryl bromides substituted either by an electron-withdrawing group in the para, meta, and ortho positions (Table 1, entries 1–3 and 5–8) or by an electron-donating group (Table 1, entry 4). It can be pointed out that the position of the substituent has a slight influence on the yield. For all aryl bromides, the reaction time was ca. 3 h. However, the yield decreases with a substituted allyl acetate, and the cross-coupling of crotyl acetate or cinnamyl acetate with *p*-BrPhCOOEt leads to 21 or 30%, respectively, of the corresponding coupling products. Undoubtedly, these yields can be improved through optimization of the process toward substituted allylic acetates. When the halogen on ArX is chlorine instead bromine, the aryl chloride is not consumed even if the aromatic nucleus is substituted by an electron-withdrawing group as we have already observed in the formation of the aryl zinc species in this medium.

However, this process has been successfully extended to aryl chlorides by changing several experimental conditions.¹²

(11) (a) Fillon, H.; Gosmini, C.; P  richon, J. Fr. Pat. Appl. 01/08880, July 4, 2001. (b) Fillon, H.; Gosmini, C.; P  richon, J. *J. Am. Chem. Soc.* **2003**, in press.

Table 1. Aryl Bromide Allylation by Allyl Acetate with Co–Zn

entry	FG	product	yield, ^a %	other products
1	<i>p</i> -COOEt		65	ArH 20% ArAr 15%
2	<i>p</i> -CN		75	ArH 25%
3	<i>p</i> -CF ₃		50	ArH 40% ArAr 10%
4	<i>p</i> -OMe		60	ArH 27% ArAr 13%
5	<i>m</i> -COOEt		51	ArH 36% ArAr 13%
6	<i>m</i> -CF ₃		31	ArH 54% ArAr 15%
7	<i>m</i> -Cl		54	ArH 34% ArAr 12%
8	<i>o</i> -CN		66	ArH 29% ArAr 5%
9 ^b	H		35	ArH 50% ArAr 15%

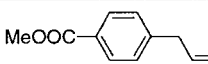
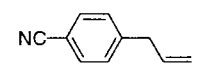
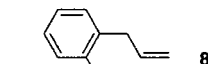
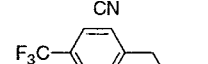
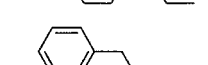
^a Yields of isolated pure products. ^b Although used as additive in all other experiments (allowing the initial reduction into ArH to proceed on an unsubstituted ring), bromobenzene undergoes coupling with allyl acetate if used in a stoichiometric amount.

The zinc dust has been replaced by manganese dust. Moreover, the presence of a stoichiometric amount of iron bromide and pyridine is necessary. In this case, no intermediate aryl zinc species is formed. Therefore, bromobenzene and zinc bromide are not required. Considering the low reactivity of Co(I) toward aryl chloride, the solution should be heated at 50 °C and 40% CoBr₂ is required. However, contrary to the allylation of the aryl bromides, the reaction takes place without the preliminary activation of the metal. The results of the allylation of various aryl chlorides by allyl acetate are reported in Table 2.

Because aryl chlorides are less reactive than corresponding bromides, reaction times are about 24 h. Nevertheless, excellent yields of coupling product are obtained, notably with the chlorinated derivatives of the benzonitrile, and the position of the substituent has no influence (Table 2, entries 11 and 12). As described before for the electrochemical cross-coupling,¹⁰ aryl chlorides need to be activated by the presence of an electron-withdrawing group. Indeed, with chlorobenzene (Table 2, entry 14), the yield of allylbenzene decreased to 14% according to GC analysis and with chloroanisole, only traces of allylated products are detected.

From a mechanistic point of view, in the case of the allylation of aryl bromides, we assume that cobalt bromide is reduced in Co(I) species in the presence of activated zinc

Table 2. Aryl Chloride Allylation by Allyl Acetate with Co–Fe–Zn

entry	FG	product	yield, ^a %	other products
10	<i>p</i> -COOMe		72	ArH 10% ArAr 18%
11	<i>p</i> -CN		83	ArH 17%
12	<i>o</i> -CN		83	ArH 14% ArAr 3%
13	<i>p</i> -CF ₃		50	ArH 26% ArAr 24%
14	H		14 ^b	ArH 48% ArAr 38%

^a Yields of isolated pure products. ^b GC yields.

dust. The role of the bromobenzene added at the beginning is to decrease the proportion of the hydrogenated product (ArH). Recently, we have shown that Co(I) undergoes fast complexation with allylic acetate.¹³ We have established that aromatic halides are reactive toward that latter (η^2 -allylOAc)-cobalt(I) complex. The arylallyl compound is released either through S_N2 from (η^2 -allylOAc)-stabilized arylcobalt or arylzinc species. Further studies are still in progress to elucidate how aryl bromides react with Co(I) complexed to allylic acetate. In the case of the aryl chlorides, the mechanism is more complicated since iron ions are present in the acetonitrile/pyridine solution. Indeed, pyridine is known to be an excellent ligand for cobalt.¹⁴ Manganese dust probably plays the role of a reducing agent, but iron bromide is also susceptible to reduction and to reaction with allyl acetate. This system needs to be studied more deeply.

This transposition of the electrochemical allylation of aromatic halides using cobalt bromide as a catalyst provides a new method for the preparation of allylbenzenes. This reaction requires the Co–Zn system for aryl bromides and Co–Fe–Mn for aryl chlorides. This process is interesting since the presence of several substituents on the aromatic nuclei are compatible. This method does not require the use of electricity, which is an advantage. However, further studies are in progress to extend the reaction to substituted acetates and to other allylic substrates. The mechanism of this process has not yet been completed.

Supporting Information Available: Experimental details and characterization data. This material is available free of charge via the Internet at <http://pubs.acs.org>.

OL0340641

(12) **General Procedure for Aryl Chlorides.** Allyl acetate (10 mmol) and aryl chloride (5 mmol) were introduced into a solution of acetonitrile and pyridine (20 mL/2 mL) containing manganese dust (50 mmol), cobalt bromide (2 mmol), and iron bromide (5 mmol). The solution was heated at 50 °C, and the reaction mixture was stirred until the total consumption of the aryl chloride. Allylbenzenes were purified as described above.

(13) Buriez, O.; Labbé, E.; Périchon, J. *J. Electroanal. Chem.*, in press.

(14) Buriez, O.; Cannes, C.; Nédélec, J.-Y.; Périchon, J. *J. Electroanal. Chem.* **2000**, 495, 57.