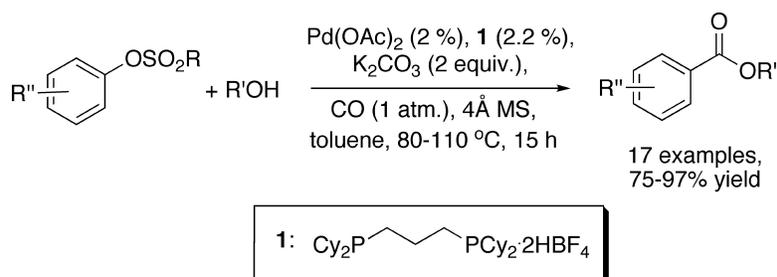


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Palladium-Catalyzed Carbonylation of Aryl Tosylates and Mesylates

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The Heck carbonylation¹ is a powerful method for the synthesis of aryl carboxylic acid derivatives. There are many published protocols for the carbonylation of aryl iodides, bromides, and triflates;² however, cheaper, more readily available aryl chlorides and tosylates have proved more recalcitrant. Methods have been developed for the carbonylation of unactivated aryl chlorides³ using bulky, electron-rich, bidentate ligands which both facilitate oxidative addition and prevent catalyst decomposition by carbon monoxide,⁴ including a recently published protocol from our laboratories which addresses previous limitations with respect to scope and the requirement to employ harsh reaction conditions.⁵

Aryl tosylates are easily prepared from cheap, readily available starting materials and are convenient to handle, stable, crystalline solids. Use of these compounds can have advantages over the corresponding aryl halides in that the phenol is a useful directing group for the introduction of other functional groups on the aromatic ring and as such can allow access to a wider substrate scope. Aryl mesylates have seen limited use in cross-coupling processes⁶ and to the best of our knowledge have never been used in carbonylation reactions. The relative acidity of the methyl group renders them incompatible with procedures that require strong base. They, however, are also easy to prepare and a procedure that could utilize these substrates would have the advantage of being more atom economical than one employing the corresponding aryl tosylates due to their significantly lower molecular weight.⁷ This is of increasing importance as greener processes are sought because of environmental concerns.

There is only limited precedent for the carbonylation of aryl tosylates, with only two publications to date.⁸ The most general procedure was recently published by Cai and co-workers for the carbonylation of aryl arenesulfonates to form esters.^{8b} A catalyst system derived from Pd(OAc)₂ and a Josiphos-type ligand was employed at 90 psi pressure of carbon monoxide and elevated temperatures which were required to allow oxidative addition of the relatively inert C–O bond. The more reactive aryl *p*-fluorobenzene sulfonates gave good yields of esters (70–96%) for a wide variety of aryl substituents at 135 °C; however, a single example of an electron-rich aryl tosylate was included and its carbonylation proceeded in lower yield. Therefore the need to develop a general procedure for the carbonylation of unactivated aryl tosylates under mild conditions still exists. Herein we report a general catalytic process for the carbonylation of aryl tosylates that also allows carbonylation of aryl mesylates for the first time. This process proceeds at 80–110 °C and one atmosphere (balloon pressure) of carbon monoxide.

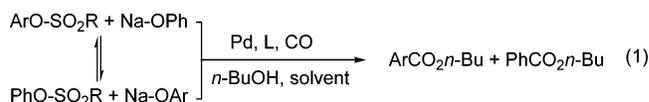
We recently reported an improved method for the carbonylation of aryl chlorides that employed the electron-rich chelating ligand **1**.⁵ Central to the success of this work was the use of sodium phenoxide as the supporting base; it was demonstrated that phenyl esters are key intermediates in this process. Our initial approach to

Table 1. Butoxycarbonylation of Aryl Sulfonates Using Ligand **1**^a

entry	R	1 (mol %)	conversion (%)	yield (GC)
1	<i>p</i> -tol	4	100	>99
2	Ph	4	100	>99
3	Me	4	100	>99
4	<i>p</i> -tol	2.2	100	>99
5	<i>p</i> -tol	2.2	95	85 ^b

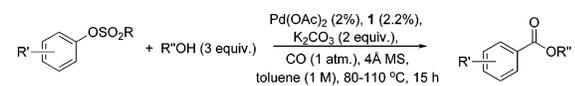
^a **1**: Cy₂P(CH₂)₃PCy₂·2HBF₄. ^b No 4 Å MS.

the carbonylation of sulfonates was based on this system and sodium phenoxide was used as the base. This resulted in a mixture of carbonylated products due to a Williamson reaction between the aryl sulfonate and sodium phenoxide (eq 1). To our delight, control experiments revealed that the conditions which originally failed for the carbonylation of aryl chlorides work well with aryl sulfonate substrates. Indeed, the use of Pd(OAc)₂ and **1** (a commercially available,⁹ air stable HBF₄ salt) with either K₂CO₃ or K₃PO₄ in dioxane or toluene provided ≥95% yield (GC) for the butoxyesterification of 4-*t*-butylphenyltosylate.¹⁰ Further, it was found that reaction carried out with K₃PO₄ or K₂CO₃ in DMSO also showed clean formation of ester with electron-rich and electron-neutral substrates.¹¹



We were curious as to whether these conditions could be applied to other classes of aryl sulfonates and found that the analogous benzenesulfonate and mesylate were also converted cleanly to ester (Table 1, entries 2 and 3). Omission of molecular sieves from the reaction mixture led to incomplete conversion of tosylate and reduced yield with the remainder of the material presumably lost as acid (entry 5).

The scope of these carbonylation processes with regard to the aryl tosylate and mesylate and alcohol was next examined (Table 2). Electron-rich and electron-deficient aryl tosylates and mesylates gave good yields of ester products; all substrates shown gave clean conversion to ester with no competing formation of ether byproducts. Heteroaryl substrates were also efficiently transformed and the reaction showed good functional group tolerance. Aryl tosylates and mesylates with aldehyde, ketone, ester and cyano groups all gave high yields of ester as did substrates with acidic hydrogens (entries 3, 5). Esters with ortho substituents could also be obtained in good yield (entries 5, 6, 7).

Table 2. Substrate Scope for the Palladium-Catalyzed Carbonylation of Aryl Sulfonates at Atmospheric CO Pressure

entry	ArOSO ₂ R	product	temp (°C)	yield (%) ^a
1			90	82
2			100	89
3			80	81
4			100	97
5			80	93
6			80	95
7 ^b			100	80 ^c
8			80	84
9 ^d			80	87
10			100	90
11			100	84
12			90	90
13			110	75
14 ^{e,f}			80	86
15 ^{d,e,g}			80	80
16 ^d			80	84

^a Isolated yields (average of two runs). ^b Reaction was performed with 5% Pd(OAc)₂ and 6% **1** for 22h. ^c Reaction proceeded to 88% conversion (GC analysis). ^d Reaction was performed with 10 equiv EtOH. ^e Reaction was performed with 4% Pd(OAc)₂ and 4.4% **1**. ^f Reaction was performed with 5 equiv of EtOH for 20 h. ^g Concentration: 0.67 M toluene.

With regard to the alcohol the reaction was general with a variety of primary alcohols and a secondary alcohol. The synthesis of esters derived from lighter alcohols was limited by the boiling point of the alcohol. Ethyl esters could be synthesized by running the reactions at 80 °C. Carbonylation of modestly activated tosylates and mesylates occurred at this temperature, and their ethyl esters were obtained in good yield (entries 9 and 14); for substrates where the aryl group was unactivated the more reactive *p*-fluorobenzene sulfonate was employed to allow complete conversion to product (entries 15 and 16).

In summary we have developed a mild and general procedure for the carbonylation of aryl tosylates and mesylates at atmospheric pressure of carbon monoxide and relatively low temperatures using commercially available, air stable dccp•2HBF₄ as the supporting ligand.

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Supporting Information Available: Experimental procedures and spectral data for all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- Substrates with certain electron-withdrawing groups (e.g., 3-cyanophenyl methanesulfonate) were transformed into mixtures of butyl ether and ester when the reaction was carried out in DMSO. Ether formation occurred without ligand and Pd in DMSO presumably via a base-mediated sulfonyl transfer mechanism: sulfonyl transfer occurs to form primary sulfonate and phenol, and phenol displaces primary sulfonate in the presence of base. This has been observed previously: Hughes, G.; Kimura, M.; Buchwald, S. L. *J. Am. Chem. Soc.* **2003**, *125*, 11253. This transformation was completely suppressed when the reaction was conducted in toluene or dioxane at 100 °C.

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