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PALLADIUM-CATALYZED CARBONYLATION OF ARYL TRIFLATES. SYNTHESIS OF ARENECARBOXYLIC ACID DERIVATIVES FROM PHENOLS

Sandro Cacchi,[a] Pier Giuseppe Ciattini,[b] Enrico Morera,[b] and Giorgio Ortar[b*]

[a]Istituto di Chimica Organica dell' Università,
via del Castro Laurenziano 9, 00161 Roma, Italy.
[b]Centro di Studio per la Chimica del Farmaco del C.N.R.,
Istituto di Chimica Farmaceutica dell' Università,
00185 Roma, Italy

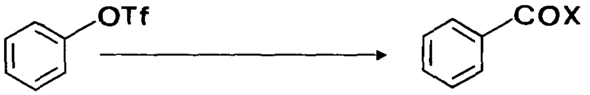
Abstract: Various aryl triflates derived from phenols were converted into aryl esters or amides in good yields by a palladium-catalyzed reaction with carbon monoxide and alcohols or amines.

Recent development by us and other authors of palladium-catalyzed reactions of enol triflates with alkenes,[1] alkynes,[1a,2] trialkylammonium formate,[3] organostannanes,[4] and carbon monoxide plus alcohols,[5] amines,[5] and organostannanes[6] has provided very useful procedures for the homologation of ketones by one or more carbons and for their deoxygenation to olefins.

Even more recently, the palladium-catalyzed olefination and alkynylation reactions have been extended to aryl triflates.[7]

It was therefore to be expected that the arylpalladium(II) species produced from the oxidative addition of aryl triflates to a palladium(0) complex[7] might undergo reaction with carbon monoxide and alcohols or amines to give aryl esters or amides.

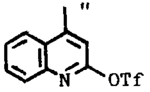
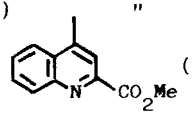
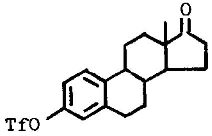
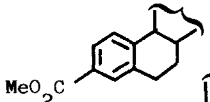
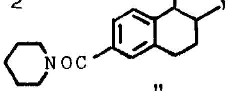
We now report herein that this transformation does indeed take place with a variety of substrates in good yields and under mild conditions.



X = OR, NR_2

In a typical procedure (entry 1), a mixture of 2-naphtyl triflate (276 mg, 1 mmol), triethylamine (0.28 ml, 2 mmol), palladium acetate (7 mg, 0.03 mmol), triphenylphosphine (16 mg, 0.06 mmol), and MeOH (0.9 ml, 20 mmol) in DMF (2 ml) was purged with carbon monoxide for 5 min and stirred under a CO balloon at 60 °C for 2h. The reaction was then diluted with brine, extracted with ether, washed with 1N HCl and then brine until neutral, dried (Na_2SO_4), and

Table. Palladium-Catalyzed Carbonylation of Aryl Triflates[a]

Entry	Aryl Triflate[b,c] (% yield)[d]	Phosphine (mol%)	Alcohol or Amine	Reaction temp, °C	Reaction time, h	Carbonylation Product[c] (% yield)[d]
1	2-Naphtyl triflate (95)	PPh_3 (6)	MeOH	60	2	Methyl 2-naphtalenecarboxylate (78)
2	"	" (12)	iPrOH	"	"	Isopropyl 2-naphtalenecarboxylate (80)
3	"	" (6)	Et_2NH	"	"	N,N-Diethyl-2-naphtalenecarboxamide (78)
4	"	" "	Piperidine	"	1.5	N-Piperidyl-2-naphtalenecarboxamide (70)
5	$4\text{-}MeOC_6H_4OTf$ (89)	DPPF[e] "	"	80	1	$4\text{-}MeOC_6H_4CONC_5H_{10}$ (59)[f]
6	"	" "	"	60	3	" (traces)
7	$3\text{-}MeOC_6H_4OTf$ (68)	" "	"	80	1	$3\text{-}MeOC_6H_4CONC_5H_{10}$ (68)
8	"	PPh_3 (12)	"	"	"	" (47)
9	$4\text{-}MeO_2CC_6H_4OTf$ (88)	DPPF (6)	MeOH	60	"	$4\text{-}MeO_2CC_6H_4CO_2Me$ (77)
10	$4\text{-}BrC_6H_4OTf$ (81)	" "	"	"	"	$4\text{-}BrC_6H_4CO_2Me$ (45) $4\text{-}MeO_2CC_6H_4CO_2Me$ (27)
11	"	" "	"	40	3.5	" (42) " (6)[g]
12	"	" (10)[h]	"	"	20	" (50) " (10)[i]
13	 (87)	" (3)[j]	"	60	1[k]	 (70)[l]
14	 (86)	" (6)	"	"	2	 (81)
15	"	" (9)	Piperidine	80	1	 (61)
16	"	" "	"	60	7	" (24)

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[a] Carried out in the same manner as described in the text, unless otherwise noted. Addition of Et_3N was omitted in the amidation reactions. Disappearance of starting material was monitored by TLC. [b] Preparation of aryl triflates used in entries 1-13 was carried out according to ref. 1b. 3-Triflyloxyestra-1,3,5(10)-trien-17-one (entries 14-16) was prepared according to: D.O. Kiesewetter, J.A. Katzenellenbogen, M.R. Kilbourn, and M.J. Welch, J. Org. Chem., 49, 4900 (1984). [c] All new compounds were adequately characterized spectroscopically (IR, ^1H NMR, MS). [d] Yields of isolated products. [e] DPPF refers to 1,1'-bis(diphenylphosphino)ferrocene. [f] 11% of the chetoamide $4\text{-}MeOC_6H_4COCONC_5H_{10}$ was also isolated. [g] 32% of starting material was recovered. [h] 5 mol% of $Pd(OAc)_2$ were used. [i] 21% of starting material was recovered. [j] 1.5 mol% of $Pd(OAc)_2$ were used. [k] Washing with 1N HCl during work-up was omitted. [l] 21% of the 2-methyl ether was also isolated.

evaporated. Chromatography of the residue (210 mg) on silica gel (7 g, benzene/hexane = 7/3 as eluant) gave 146 mg (78%) of methyl 2-naphtalenecarboxylate: mp 77-77.5 °C (MeOH, lit.[8] mp 77 °C); IR (KBr) 1711 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.98 (3H, s, CO_2Me), 7.2-8.3 (6H, m, aromatics), 8.67 (1H, br s, C-1 H); MS, m/e (relative intensity) 186 (parent, 82), 155 (100), 127(58).

The representative results are collected in the Table which shows that the carbonylation reaction can be successfully applied to aromatic rings containing either electron-withdrawing or electron-donating substituents.

Although a detailed kinetic analysis has not been made, the substituent effects seem to go in the same direction as with aryl halides.[9]

2-Naphtyl triflate (entries 1-4) and 3-methoxyphenyl triflate (entry 8) apart, the use of 1,1'-bis(diphenylphosphino)ferrocene (DPPF) instead of triphenylphosphine proved to be essential for the reactions to proceed significantly. In fact, with PPh_3, palladium precipitation occurred very quickly and only traces of the expected product were obtained.

This trend is reminiscent of that of highly activated aryl bromides in the palladium-catalyzed vinylic substitution[10] and similar explanations may be tentatively invoked.

Tri-o-tolylphosphine doesn't seem to have distinct advantages over PPh_3 as demonstrated by the fact that 3-triflyloxyestra-1,3,5(10)-trien-17-one was completely unchanged in the carbomethoxylation reactions with 12 mol% of either PPh_3 or $P(o\text{-tol})_3$ as ligands.

In the case of 2-naphtyl triflate we found PPh_3 was as good as DPPF with respect to both the rate of the reaction and yield of product.

In most cases, the recourse to more than 2 mol of PPh_3 (entries 2 and 8) or 1 mol of DPPF (entries 5-7 and 9-16) per mole of palladium dramatically improved the yields. Thus, for instance, 2-naphtyl triflate afforded only a 20% yield of isopropyl 2-naphtalenecarboxylate when 6 mol% of PPh_3 were employed and 3-triflyloxyestra-1,3,5(10)-trien-17-one gave only traces of the amide in the treatment with CO and piperidine at 80 °C in the presence of both 3 and 6 mol% of DPPF.

The moderate chemoselectivity that was obtained with 4-bromophenyl triflate (entry 10) could be improved by lowering the reaction temperature (entries 11 and 12) although we were not able to force the reaction to reach completion under these conditions even using 5 mol% of palladium.

Attempts with 4-nitrophenyl triflate met with failure owing to the preponderance of sulphur-oxygen bond cleavage that led to the formation of 4-nitrophenol as the main product in the carbomethoxylation reaction under a variety of conditions.[11]

The palladium-catalyzed carbonylation of aryl triflates appears however to be a quite general reaction and represents a new and expeditious method for a two-steps synthesis of arenecarboxylic acid derivatives from phenols.

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