Palladium Catalysed Alkoxycarbonylation of Phenols to Benzoate Esters

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The methoxycarbonylation of aryl trifluoromethanesulphonates with CO and aliphatic alcohols is catalysed by $Pd(OAc)_2$–1,3-bis(diphenylphosphino)propane in high yield at 70 °C and ambient CO pressure.

We recently reported the efficient decarbonylation of indole-2-carbaldehydes under mild conditions with 1—3 mol% of (dppp)Rh(CO)Cl catalyst.[1] The high turnover number and rate acceleration observed with this rhodium complex results from the 1,3-bis(diphenylphosphino)propane (dppp) ligand.[2] During a particular synthetic programme the direct conversion of a phenolic hydroxy into an alkoxycarbonyl group [(I) into (II)] was required. It was expected that a palladium-catalysed alkoxycarbonylation of the activated phenol would lead directly to the benzoate ester, by analogy with the known palladium-catalysed carbonylation of aryl bromides and iodides.[3] However, attempted carbonylation of even the very reactive phenyl triflates (triflate = trifluoromethanesulphonate) with the previously employed $(Ph_3P)_2Pd(OAc)_2$ catalyst was found to be unsatisfactory. We have been prompted by a recent report[4] which described a related carbonylation to

Table 1. Palladium-catalysed methoxycarbonylation of aryl triflates.

Triflate[a]	Time/h(Temp./°C)	Yield/%[b]
(1a)	0.75(70)	95
(1b)	1(70)	84
(1c)	1(60)	98
(1d)	1(60)	98
(1e)	2(70)	84[c]
(1f)	2(60)	93
(1g)	2(70)	87
(2)	1(70)	96
(3)	2(70)	72[d]
(4)	2(70)	75
(5)	1(70)	85
(6)	1(70)	80[d]
(7)	1(70)	91[d,e]

[a] All triflates prepared by method (a) except entries **(1g)** and **(3)**, see text. [b] Yields determined by capillary g.c. unless otherwise noted. [c] A 12% yield of terephthalate was also obtained. [d] Isolated yield. [e] 1,2-Dichloroethane added as co-solvent.

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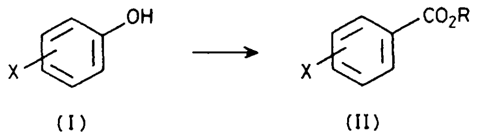
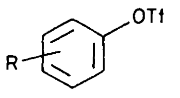
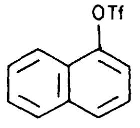


(I) (II)

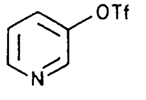


(**1**)

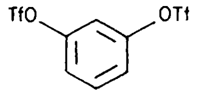
a; R = 4-Me
b; R = 4-OMe
c; R = 4-CN
d; R = 4-CO$_2$Me
e, R = 4-Br
f; R = 2,6-F$_2$
g; R = 2,6-Me$_2$



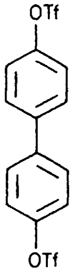
(**2**)



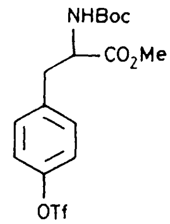
(**3**)



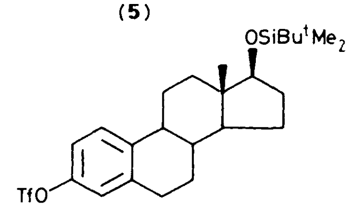
(**4**)



(**5**)



(**6**)



(**7**)

Tf = CF$_3$SO$_2$

disclose our use of dppp as a ligand in a new palladium complex which affords *ca.* 500-fold rate enhancement in the palladium-catalysed alkoxycarbonylation of aryl triflates. The preparation of the aryl triflates and subsequent methoxycarbonylation can be conveniently carried out on a large scale under very mild conditions which are compatible with many sensitive functional groups.‡

Initial attempts to homologate the triflates in dimethylformamide (DMF) were modelled on the analogous butoxycarbonylation of aryl iodides and bromides with 3 mol% Pd(X)$_2$(Ph$_3$P)$_2$ catalyst with Bu^{n}OH–Bu$^n_3$N at 100 °C.[3] Although carbonylation of the highly reactive triflates did occur under these conditions, problems were encountered which were reminiscent of those encountered in the carbonylations of aryl halides: moderate yields, lengthy reaction times, and poor catalyst turnover, even with high CO pressures. We discovered that the use of 1,3-bis(diphenylphosphino)propane (Aldrich) as the phosphine ligand increased the rate of carbonylation some 500-fold relative to Ph$_3$P.§ The ability of the dppp ligand to accelerate the carbonylation reaction appears not to have been previously recognized. Thus, employing (dppp)Pd(OAc)$_2$ as catalyst, methoxycarbonylation of aryl triflates readily occurred (<2 h) in dimethyl sulphoxide (DMSO) or DMF (the former giving maximum catalyst turnover), methanol, and Et$_3$N under ambient CO pressure at 70 °C in high yield (Table 1). Typically, $\leqslant 5\%$ ester formation was observed after 4 h using Pd(OAc$_2$)(Ph$_3$P)$_2$ as catalyst.¶ In the case of aromatic compounds substituted with electron withdrawing groups, carbonylations may be carried out at even lower temperatures (*ca.* 60 °C, Table 1).||

This mild and efficient homologation of phenols to aryl esters may provide an entry to aryl esters hitherto difficult to prepare.

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‡ The aryl triflates (**1**)—(**7**) were prepared by one of three general methods:[5] (a) treatment of a 0.1—0.2 M CH$_2$Cl$_2$ solution of the phenol at −30 °C with 1.5 equiv. of 2,6-lutidine, 0.2 equiv. of 4-dimethylaminopyridine, and 1.5 equiv. of triflic anhydride then warming to 25 °C for *ca.* 2 h (the majority of triflates in Table 1 were prepared by this method); (b) refluxing (12 h) a 0.2 M CHCl$_3$ solution of the phenol and 1.2 equiv. each of 2,6-t-butyl-4-methylpyridine and triflic anhydride, (**1g**); or (c) reaction of the sodium or potassium salt of the phenol [tetrahydofuran (THF), 0.2 M phenol, 1 equiv. of NaH or KH] with *N*-phenyltrifluoromethanesulphonamide (1.2 equiv., Aldrich) at 40 °C for 12 h, (**1c**). Triflates were purified by flash column chromatography and could be kept for several days at 25 °C without noticeable decomposition.

§ The rate enhancement must, in part, be a consequence of the obligatory *cis* arrangement of the dppp ligand around palladium in the square-planar acyl–palladium complex, in contrast to the *trans* arrangement of the Ph$_3$P ligands in these complexes.[3] Accelerations in rate were also observed with this catalyst during the alkoxycarbonylation of aryl iodides and bromides.

¶ Representative procedure: triethylamine (2.2 mmol) was added to a solution of *p*-methylphenyl trifluoromethanesulphonate in DMSO (3 ml) and MeOH (2 ml) (or other alcohols or amines) followed by Pd(OAc)$_2$ (0.03 mmol) and dppp (0.03 mmol). A stream of CO (Matheson) was passed into the solution for 2—3 min then the reaction vessel and contents were placed in a 70 °C oil bath under a CO balloon. After stirring for 45 min, capillary g.c. (HP model 5890A; 50 m Chrompack Sil 8 column, 115 °C) revealed complete absence of starting triflate and a 95% yield of ester. Following dilution with water (30 ml), the ester was isolated *via* standard procedures. In all cases studied, carbonylation was 100% regiospecific. The corresponding tosylates failed to react.

|| All new compounds showed analytical and spectral properties consistent with their structures.