Tetrahedron Letters,Vol.27,No.45,pp 5541-5544,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

PALLADIUM-CATALYZED TRIETHYLAMMONIUM FORMATE REDUCTION OF ARYL TRIFLATES. A SELECTIVE METHOD FOR THE DEOXYGENATION OF PHENOLS

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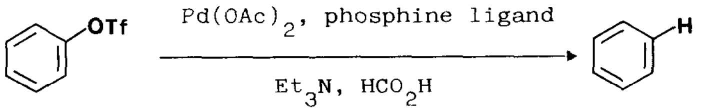
Abstract: Phenols can be selectively deoxygenated by reduction of the corresponding aryl triflates with triethylammonium formate in the presence of a homogeneous palladium catalyst.

Current methods for the deoxygenation of phenols, an important synthetic objective in the field of natural products, involve conversion of the phenol into a suitable phenolic ester or ether and reduction of the latter with molecular hydrogen, hydrogen donors, and dissolving metal techniques.[1]

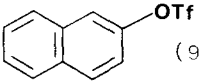
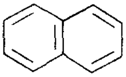
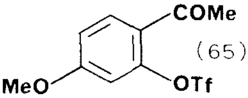
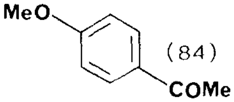
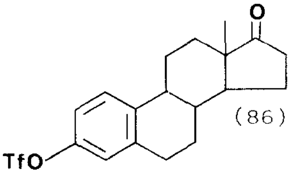
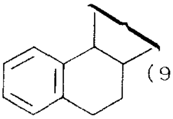
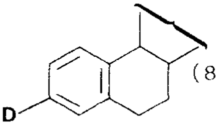
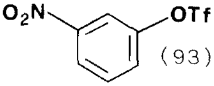
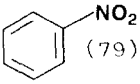
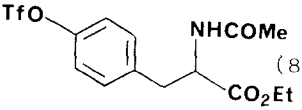
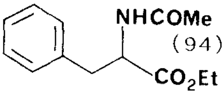
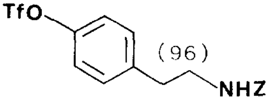
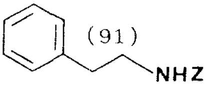
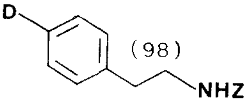
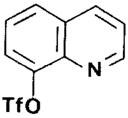
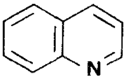
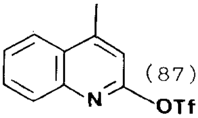
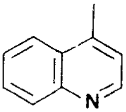
Most of these procedures are unfortunately subject to substantial limitations as concerns the presence of reducible functional groups and lack therefore the desired generality for true synthetic utility.

Following recent findings by us[2] and other authors[3] that arylpalladium(II) species produced from the oxidative addition of aryl triflates to palladium (0) complexes readily undergo carbonylation and Heck reactions, we wish to report herein a new and selective method for reducing aryl triflates to aromatic hydrocarbons in high yield utilizing triethylammonium formate[4] as hydrogen donor in the presence of a homogeneous palladium catalyst.



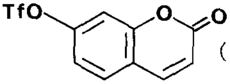
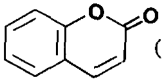
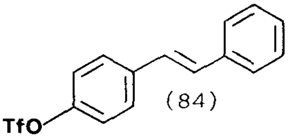
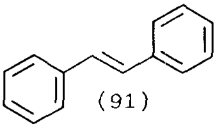
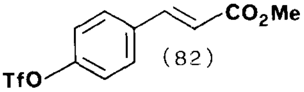
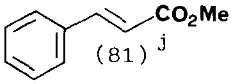
In a typical procedure (entry 1), to a mixture of 2-naphtyl triflate (276 mg, 1 mmol), triethylamine(0.42 ml, 3 mmol), palladium acetate(4 mg, 0.02 mmol), and triphenylphosphine (10 mg, 0.04 mmol) in DMF (2 ml) was added 99% formic acid (0.075 ml, 2 mmol). The mixture was stirred at 60 °C for 1 h under nitrogen, diluted with brine, extracted with ether, washed twice with brine, dried

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

Entry	Aryl Triflate[b,c] (% yield)[d]	Phosphine (mol%)	Reaction time, h	Reduction Product[c] (% yield)[d]
1	 (95)	PPh_3(4)	1	 (91)
2	 (65)	"	2	 (84)
3	 (86)	DPPF(2)[e]	1	 (93)
4	"	"	"	 (87)[f]
5	 (93)	"	0.5[g]	 (79)
6	 (89)	"	1	 (94)
7	 (96)	"	"	 (91)
8	"	"	"	 (98)
9	 (94)	PPh_3(4)	2.5	 (89)
10	 (87)	DPPF(2)	1	 (82)

(continued)

Table (continued)

Entry	Aryl Triflate[b,c] (% yield)[d]	Phosphine (mol%)	Reaction time, h	Reduction Product[c] (% yield)[d]
11	 (79)	DPPF(2)	2	 (82)
12	 (84)	PPh_3(4)	1.5	 (91)
13	 (82)	DPPF(4)	1[i]	 (81)[j]
14	"	" (2)	2	" (60)[k]

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[a] Carried out in the same manner as described in the text, unless otherwise noted. [b] Preparation of aryl triflates used in entries 1,2,5,9-14 was carried out according to ref. 6b; aryl triflate used in entries 3 and 4 was prepared according to: D.O. Kiesewetter, J.A. Katzenellenbogen, M.R. Kilbourn, and M.J. Welch, J. Org. Chem., 49, 4900 (1984); aryl triflates of entries 6-8 were prepared using N-phenyltriflimide (1.1 equiv) and Et_3N (1.1 equiv) in CH_2Cl_2 at room temperature. [c] All new compounds were adequately characterized spectroscopically (IR, NMR, MS). [d] Yields of isolated products unless otherwise indicated. [e] DPPF refers to 1,1'-bis(diphenylphosphino)ferrocene. [f] DCO_2D was used. [g] Reaction carried out at 70 °C. [h] Z refers to benzyloxycarbonyl group. [i] Reaction carried out at 80 °C. [j] Also present in the product was 3% of methyl hydrocinnamate. [k] Yield determined by ^1H NMR analysis; 21% of starting material and 19% of methyl hydrocinnamate were also present.

(Na_2SO_4), and evaporated. Chromatography of the residue (150 mg) on silica gel (5g, hexane as eluant) provided 116 mg (91%) of naphtalene.

The hydrogenolysis of aryl triflates with molecular hydrogen over an heterogeneous transition-metal catalyst (e.g. Pd/C) has been recently described.[5] However, this nonselective procedure for the deoxygenation of phenols appears to be incompatible with several functional groups.

The replacement of molecular hydrogen by triethylammonium formate as a hydrogen donor in a homogeneous catalyzed hydrogen transfer reaction provides therefore an efficient and chemoselective route for the reductive cleavage of carbon-oxygen bonds in aryl triflates. Typical results are given in the Table.

Unsaturated functional groups like nitro, ketones, esters, and olefins are found to tolerate well the reaction conditions. N-benzyloxycarbonyl protecting group survives as well (entries 7 and 8) and no appreciable reduction of the quinoline heterocyclic ring occurs (entries 9 and 10).

The use of dideuterioformic acid eventually allows a regioselective introduction of deuterium into aromatic rings (entries 4 and 8).

As in the case of carbonylation reactions, reductions of aryl triflates, too, are somewhat dependent upon phosphine ligand. The recourse to 1,1'-bis(diphenylphosphino)ferrocene (DPPF) reveals to be benefical to those reactions that do not proceed in the presence of triphenylphosphine.

The mechanism of the reduction reactions most likely involves oxidative addition of the aryl triflate to a palladium(0)-phosphine catalyst followed by displacement of triflate on the metal by formate ion. Loss of carbon dioxide generates arylpalladium(II) hydride from which arene and catalytically active palladium species are formed by reductive elimination.

$$\mathrm{Pd(PR_3)_2} + \mathrm{ArOTf} \longrightarrow \mathrm{ArPd(PR_3)_2OTf} \xrightarrow{\mathrm{HCO_2^-}} \mathrm{ArPd(PR_3)_2HCO_2}$$

$$\mathrm{ArPd(PR_3)_2HCO_2} \xrightarrow{-\mathrm{CO_2}} \mathrm{ArPd(PR_3)_2H} \longrightarrow \mathrm{ARH} + \mathrm{Pd(PR_3)_2}$$

The present paper represents a further demonstration of the synthetic usefulness of the palladium-catalyzed reactions of enol and aryl triflates we have been investigating for the last two years.[2,6]

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4. For the use of the trialkylammonium formate-palladium reagents in the reduction of various functional groups, see: J.R. Weir, B.A. Patel, and R.F. Heck, J. Org. Chem., 45, 4926 (1980) and references therein.
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(Received in UK 9 September 1986)