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Room temperature Ni-catalyzed reduction of aryl tosylates by borane hydrides

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Abstract—Mild Ni-catalyzed homogeneous reductions of aryl tosylates are described for the first time. The catalytic system $Ni(PPh_3)_2Cl_2$ and PCy_3 is shown to be general for hydrogenolysis of a wide range of tosylates, including hindered, deactivated, heterocyclic, and bifunctional examples.

1. Introduction

Deoxygenation of phenols has aroused considerable scientific interest, as it is an important transformation in synthetic organic chemistry.[1] This interest is certainly well-grounded: replacement of the hydroxy group on an aryl ring with hydrogen was a key step in the synthesis of the vancomycin aglycon,[2a] linarin,[2b] angelecin,[2c] calothrixin B,[2d] metacyclophanes,[2e] and partially reduced polysubstituted calixarenes,[2f] liquid crystals dopands,[2g] etc. To date, almost all reports have described palladium catalyzed deoxygenation of phenols via triflates or nonaflates,[3] usually employing ammonium formate as the reducing agent. Aryl tosylates have not been reported as synthetically useful substrates for the deoxygenation of phenols. However, aryl tosylates are more stable, operationally convenient, and cheaper than triflates.

It has been shown that tosylates can serve as coupling partners in Suzuki–Miyaura cross-coupling reactions catalyzed by Ni complexes,[4] however, palladium catalyzed coupling processes of tosylates have been investigated in detail.[5] In this letter, we demonstrate Ni-catalyzed reduction of aryl tosylates.

2. Results and discussion

Pd complexes were found to be ineffective for the reduction of 2-naphthyl tosylate with $NaBH_4$ at room temperature. Palladium acetate and $Pd_2(dba)_3$ in the presence of 4 equiv of triphenylphosphine gave good yields (81% and 85%, respectively) of naphthalene in DMF only at 75 °C. Bidentate ligands (2 equiv): dppf, dppb, dppe, and dppp in combination with palladium acetate resulted in similar conversions of 2-naphthyl tosylate. These results were consistent with previously published data describing Pd-catalyzed reduction of strongly activated aryl sulfonates.[6]

In the present study, we report a novel method for the Ni-catalyzed hydrogenolysis of aryl tosylates using the borane hydrides $NaBH_4$ and dimethylamine–borane complex under mild conditions.

Commercially available $Ni(PPh_3)_2Cl_2$ was used in this research. PCy_3 was found to be the best ligand leading to excellent conversions as shown in Table 1. Surprisingly, electron-rich ligands (entries 7 and 12) were less effective; triarylphosphines, PPh_3 and $P(o\text{-tolyl})_3$ demonstrated low activity. The bidentate ligands dppb, dppe, dppp, and dppf afforded low conversions of the model tosylate (10–23%).

Among the solvents screened, THF and DMF were found to be the best. In acetonitrile the reaction time was slightly longer and nonpolar solvents (toluene, dioxane and dichloromethane) also gave slow reactions. The borane hydrides play a dual role: they reduce the Ni(II) complex to a Ni(0) complex in situ and serve as a hydrogen donor in the hydrogenation process. A number of hydride donors reported for triflate reductions[7] were also examined: tributyltin hydride, triethylsilane, and

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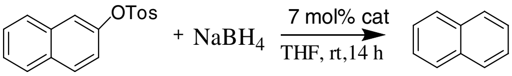
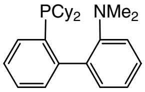
Table 1. Room temperature Pd(0) and Ni(0)-catalyzed reduction of 2-naphthyl tosylate with sodium borohydride[a]



Entry	Metal source	Ligand	Conversion (%)
1	$Pd_2(dba)_3$	PPh_3, PCy_3, dppe, dppf	0
2	$PdCl_2$	dppe, PPh_3	0
3	$PdCl_2(PPh_3)_2$	PPh_3, PCy_3	0
4	$Pd(CH_3COO)_2$	dppf, PPh_3	0
5	$Ni(PPh_3)_2Cl_2$	PPh_3	7
6	$Ni(PPh_3)_2Cl_2$	P(*o*-tolyl)$_3$	11
7	$Ni(PPh_3)_2Cl_2$		45
8	$Ni(PPh_3)_2Cl_2$	dppf	10
9	$Ni(PPh_3)_2Cl_2$	dppe	12
10	$Ni(PPh_3)_2Cl_2$	dppp	15
11	$Ni(PPh_3)_2Cl_2$	dppb	23
12	$Ni(PPh_3)_2Cl_2$	*t*-Bu_3P	57
13	$Ni(PPh_3)_2Cl_2$	PCy_3	100

[a] Reaction conditions: aryl tosylate (1 mmol), 2–4/1 ratios ligand:metal, sodium borohydride (5 mmol), THF (4 ml); conversion determined by GC, using tetrahydronaphthalene as the internal standard.

sodium cyanoborohydride were found to be inactive under these conditions.

In general the reactions with $NaBH_4$ were slow due to the low reactivity of the tosylates and 5 equiv of the reductant were needed to complete this hydrogenolysis. Using sodium borohydride with mild heating permitted decreasing the borohydride loading to 4.2–4.5 equiv. These amounts of reductant are comparable to those reported for triflate reductions.[1,2,6]

As shown in Table 2, a variety of neutral and electron-rich substrates were examined. Entries 1–8 show very high conversions, and products were isolated by flash chromatography. Entries 9–13 demonstrated good conversions as well, despite deactivation by electron-donating substituents on the aromatic ring. In the case of deactivated substrates (entries 10 and 13–15), low conversions were obtained. On reacting these tosylates at 60 °C, moderate to excellent conversions were obtained. Bifunctional tosylates (entries 6 and 7) as well as a heterocyclic tosylate (entry 5) were found to be reactive. In the case of a hindered bistosylate (entry 6), a small amount of mono-reduced product was isolated, but this product was undetectable at 60 °C. Reduction of bistosylates needed almost a double loading of the reductant as expected. Using this protocol competitive Pd-catalyzed hydrolysis of tosylates[6] was never observed.

For a variety of electron-deficient aryl tosylates, the use of sodium borohydride was unsuitable due to the competitive reduction of the carbonyl substituents. For these substrates (entries 1–4 in Table 3) and for nitrile- and ester-containing substituents (entries 5 and 6), dimethylamine–borane complex was used at ambient temperature as the reducting agent. The modified Lipshutz protocol for nonaflate reduction (Ni instead of Pd, DMF as solvent, room temperature) was applied.[8] Due to the strong electron-withdrawing features of these groups, substrates are activated toward insertion of Ni into the C–O bond and a low loading of the reductant (3–3.5 mmol) was sufficient in order to obtain high yields. Thus, using this reagent, chemoselective reductions can be achieved.

During the preparation of this manuscript, a report describing heterogeneous hydrogenolysis was published.[9] Being one of the authors of this paper and recognizing the attraction of a heterogeneous process I note certain drawbacks of this process: (1) harsh reaction conditions (120 °C), (2) hydrolysis and not hydrogenolysis of certain tosylates (substrates 5–7, Scheme 6. Ref. 9). However, tosylate hydrolysis was never observed using mild homogeneous catalysis. So, for example, (substrate 6, Scheme 6, Ref. 9) was smoothly reduced obtaining 2-(2-hydroxyphenyl) benzothiazole).

In conclusion, a novel, efficient and convenient synthetic route for mild dehydroxylation of a wide range of phenols via Ni-catalyzed reduction of their tosylate derivatives is described. Current mechanistic studies on this process as well as a search for new synthetic pathways catalyzed by this Ni(0)/PCy_3 system are underway.

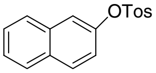
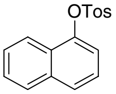
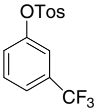
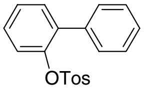
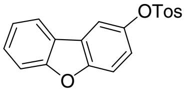
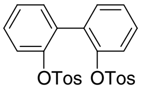
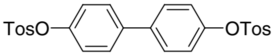
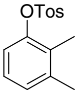
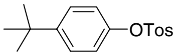
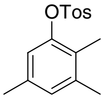
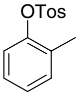
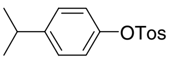
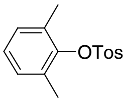
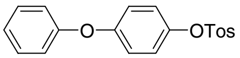
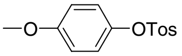
3. Experimental

General method for tosylates hydrogenolysis

A solution of 2-naphthyl tosylate (0.298 g, 1 mmol) in 4 ml of DMF was treated with $Ni(PPh_3)_2Cl_2$ (0.017 g, 0.07 mmol) and tricyclohexylphosphine (0.011 g, 0.28 mmol) and after stirring for 5 min $NaBH_4$ (0.190 g, 5 mmol) was added in one portion. The mixture was stirred at room temperature and the progress of the reaction was monitored by TLC (hexane:ethyl acetate, 8:2). After consumption of the starting material

Table 2. Room temperature Ni(0)-catalyzed reduction of aryl tosylates with sodium borohydride[a]

$$\text{Ar-OTos} + \text{NaBH}_4 \xrightarrow[\text{THF, rt,14 h}]{7\,\%\text{Ni(PPh}_3)_2\text{Cl}_2/28\%\text{PCy}_3} \text{Ar-H}$$

Entry	Ar-OTos	Yield (%)
1		93
2		90
3		100[b]
4		90
5		87
6		81[c,d]
7		88[c]
8		95[b]
9		90
10		93[e]
11		100[b]
12		90
13		81[b,e]
14		70[e]
15		47[b,e]

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[a] Reaction conditions: aryl tosylate (1 mmol), $NaBH_4$ (5 mmol), THF (4 ml).

[b] GC yield, tetrahydronaphthalene was used as the internal standard.

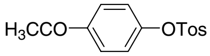
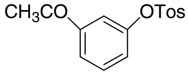
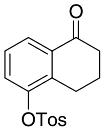
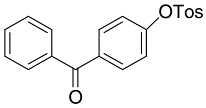
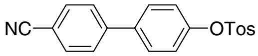
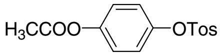
[c] $NaBH_4$ (8.5 mmol).

[d] 5% Mono-reduced product isolated.

[e] Reaction at 60 °C.

Table 3. Room temperature Ni-catalyzed reduction of aryl tosylates with dimethylamine–borane complex[a]

$$\text{Ar-OTos} + \text{BH}_3\text{.N(CH}_3)_2 \xrightarrow[\text{DMF,K}_2\text{CO}_3\text{, rt,14 h}]{7\,\%\text{Ni(PPh}_3)_2\text{Cl}_2/28\%\text{PCy}_3} \text{Ar-H}$$

Entry	Ar-OTos	Yield (%)
1		100[b]
2		90
3		100[b]
4		89
5		87[c]
6		92

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[a] Reaction conditions: aryl tosylate (1 mmol), dimethylamine–borane complex (3 mmol), DMF (4 ml).

[b] GC yield, tetrahydronaphthalene used as the internal standard.

[c] 3.5 mmol of dimethylamine–borane complex, 20 h.

the reaction mixture was diluted with water, extracted with ethyl acetate, dried over $MgSO_4$ and evaporated. The residue was chromatographed on silica gel with hexane–ethyl acetate mixture (99:1) as eluent to give 0.119 g, 93% of naphthalene.

Acknowledgement

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