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Nickel-Catalyzed Coupling Reaction of Lithium Organoborates and Aryl Mesylates Possessing An Electron Withdrawing Group

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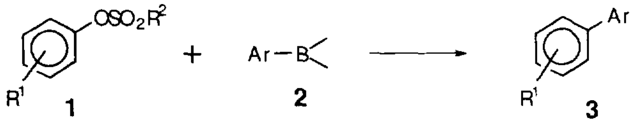
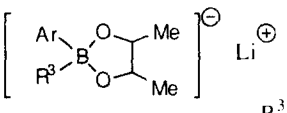
Abstract: *In the presence of* $NiCl_2(PPh_3)_2$ *as catalyst, p-methoxycarbonylphenyl mesylate* ***(5)*** *and tosylate* ***(6)*** *react with lithium arylborates* ***4*** *(Ar = 2-furyl, Ph, p-Me-Ph, p-MeO-Ph) at room temperature to afford the coupling products in high yields. Similarly, mesylates* ***9-11*** *coupled with these borates* ***4*** *efficiently.* Copyright © 1996 Elsevier Science Ltd

Palladium-catalyzed coupling of aryl halides and organoboranes in the presence of bases is known as the Suzuki reaction.[1,2] Usually aryl iodides and bromides participate in the reaction and a number of applications using these halides have been reported.[3] From a synthetic point of view, however, the use of aryl sulfonates has some advantages. They are easily prepared from phenols and the phenolic group can be used as a means to install the functionalities in the aromatic ring.[4] Triflates **1** ($R^2 = CF_3$) are the only example which are reactive enough to couple with organoboranes (eq 1).[5] However, the propensity of triflates to readily hydrolyze to starting phenols and higher price of triflating agents such as Tf_2O, TfCl, Tf_2NPh reduce the advantages mentioned above.[6] Recently Percec revealed for the first time that though mesylates **1** ($R^2 = Me$) are marginally reactive substrates in a palladium-catalyzed coupling, nickel complexes catalyze the coupling reaction.[7] Mesylates are generally more stable than triflates and MsCl is a much more inexpensive reagent than the triflating agents, thus the mesylate methodology seems to have some advantages. However, moderate yields in most cases, even under forcing conditions of higher temperatures and the use of a certain amount of Zn (1.7 equiv based on the mesylate) to prepare the Ni(0) catalyst from 0.1 equiv of the Ni(II) salt seem to be improved. They ascribe such results to the slow oxidative addition of the mesylates to Ni(0) complexes. Recently we have reported[8] that lithium organoborates **4** possessing the methyl ligand ($R^3 = Me$) in combination with use of the nickel catalyst are highly reactive reagents in the coupling with allyl carbonates: the reaction goes to completion at room temperature or at 5 °C within 12 h. We envisioned that the Percec's sluggish reaction is



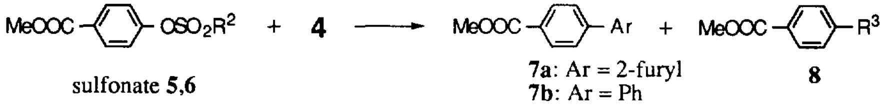
(1)



4

R^3 = Me, *n*-Bu

Table 1. Nickel-Catalyzed Reaction of Mesylate 5 or Tosylate 6 with Borates 4[a]



sulfonate **5**,**6**

7a: Ar = 2-furyl
7b: Ar = Ph

8

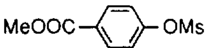
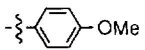
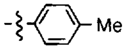
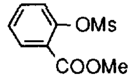
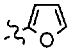
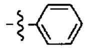
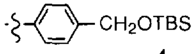
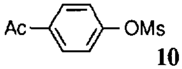
entry	sulfonate	SO$_2$R^2	borate 4[b]	Ar	R^3	Ni cat.	temp. (°C)	time (h)	yield[c] of product 7		ratio[d] 7 : 8
1	**5**	Ms	**4a**	2-furyl	Me	NiCl$_2$(PPh$_3$)$_2$	20	11	**7a**	82	100 : 0[e]
2	**5**	Ms	**4a**	2-furyl	Me	NiCl$_2$(dppf)	20	14	**7a**	91	100 : 0[e]
3	**5**	Ms	**4b**	Ph	Me	NiCl$_2$(PPh$_3$)$_2$	20	11	**7b**	24[f]	57 : 43
4	**5**	Ms	**4b**	Ph	Me	NiCl$_2$(dppf)	20	11	**7b**	32[f]	55 : 45
5	**5**	Ms	**4c**	Ph	CH$_2$-TMS	NiCl$_2$(PPh$_3$)$_2$	20	12	**7b**	84	90 : 10
6[g]	**5**	Ms	**4d**	Ph	*n*-Bu	NiCl$_2$(PPh$_3$)$_2$	20	12	**7b**	95	>95 : <5
7	**5**	Ms	**4d**	Ph	*n*-Bu	NiCl$_2$(dppf)	20	12	**7b**	60[f]	>95 : <5
8	**5**	Ms	**4d**	Ph	*n*-Bu	NiCl$_2$(PPh$_3$)$_2$	60	6	**7b**	90	>95 : <5
9	**6**	Ts	**4b**	Ph	Me	NiCl$_2$(PPh$_3$)$_2$	20	11	**7b**	21[f]	50 : 50
10	**6**	Ts	**4b**	Ph	Me	NiCl$_2$(dppf)	20	14	**7b**	33[f]	70 : 30
11	**6**	Ts	**4c**	Ph	CH$_2$-TMS	NiCl$_2$(PPh$_3$)$_2$	20	12	**7b**	17[f]	85 : 15
12	**6**	Ts	**4d**	Ph	*n*-Bu	NiCl$_2$(PPh$_3$)$_2$	20	14	**7b**	83	>95 : <5

[a] Reactions were carried out using sulfonates (**5** or **6**) and 3 equiv of the borates **4** in the presence of 10 mol % of the nickel catalyst unless otherwise noted. [b] Borates **4** were prepared *in situ* from the corresponding boronates and R^{3}Li (at 0 °C for 15 min). [c] Isolated yields. [d] Determined by ^{1}H NMR (300 MHz) spectroscopy. [e] Production of **8** was not detected by NMR spectroscopy. [f] Starting mesylate was recovered. [g] Reaction carried out with 1.5 equiv of **4d** also gave **7b** in 93% yield with a high selectivity (**7b** : **8** = >95 : <5).

rather due to the slow transmetalation process and that use of borates **4** instead of organoboranes might accelerate the overall reaction. Herein we report our results along these lines with a new finding that the butyl group in **4** (R^3 = *n*-Bu) is a more effective ligand than the original methyl ligand.[9,10]

Initially, we examined the coupling of *p*-methoxycarbonylphenyl mesylate (**5**) with 3 equiv of lithium 2-furyl- or phenylborates **4a,b** possessing a methyl ligand (Ar = 2-furyl, Ph; R^3 = Me) in the presence of 10 mol % of NiCl$_2$(PPh$_3$)$_2$ or NiCl$_2$(dppf) (dppf = 1,1'-bis(diphenylphosphino)ferrocene). With furylborate **4a**, the reaction proceeded smoothly at room temperature (ca 20 °C) to furnish product **7a** (Ar = 2-furyl) in good yields (entries 1 and 2). To the best of our knowledge it is the first example of both the oxidative addition of mesylates to Ni(0) species and the subsequent transmetalation proceeding at room temperatures with reasonable rates. However the coupling of **5** with phenylborate **4b** with the methyl ligand (Ar = Ph, R^3 = Me) did not proceed completely and product-selectivity was poor; starting mesylate **5** was recovered and the by-product **8** (R^3 = Me) was co-produced in fairly large quantity with **7b** (Ar = Ph) (entries 3 and 4). Attempted reactions at higher temperatures and/or in other solvents such as DMF, CH$_3$CN did not improve the situation. In light of the results obtained with furylborate **4a**, we imputed the unsatisfying result to the lower transmetallating ability of the phenyl group from boron to nickel.[11] Thus, ligands which are thought to be more electron donating and more bulky than the methyl ligand were investigated so as to gain higher reactivity and selectivity for phenyl transfer. Phenylborates possessing trimethylsilylmethyl ligand (**4c**; entry 5) or *tert*-butyl ligand (R^3 = *t*-Bu; data not shown) improved the yield of **7b** and the product-selectivity, but these were still far from satisfactory. However, in the presence of NiCl$_2$(PPh$_3$)$_2$, borate **4d** with the butyl ligand (R^3 = *n*-Bu, Ar = Ph) gave the coupling product **7b** in good yield and with a high product-selectivity of **7b** / **8** (>95 : <5) (entry 6). With

Table 2. Nickel-Catalyzed Coupling of Mesylates with Borates 4[a]

entry	mesylate	borate 4[b]		yield[c]
		Ar	R^3	%
1	 **5**	 **4e**	*n*-Bu	85[d]
2	**5**	 **4f**	*n*-Bu	85[d]
3	 **9**	 **4a**	Me	94
4	**9**	 **4d**	*n*-Bu	83[d]
5	**9**	 **4g**	*n*-Bu	88[d]
6	 **10**	**4a**	Me	80
7	**10**	**4d**	*n*-Bu	95[d]
8	 **11**	**4d**	*n*-Bu	80[d]

[a] Reactions were carried out using mesylatess **5**,**9**,**10**, and **11** with 3 equiv of the borates **4** in the presence of 10 mol % of the nickel catalyst at room temperature for 12 h unless otherwise noted. [b] The borates **4** were prepared *in situ* from the corresponding boronates and R^3Li (0 °C for 15 min). [c] Isolated yields. [d] A trace amount (<5%) of the butyl coupling product was detected by ^1H NMR (300 MHz) spectroscopy.

$NiCl_2$(dppf) the reaction proceeded selectively but slowly (entry 7). The reaction with 1.5 equiv of **4d** gave a similarly good result (note g of entry 6). In this examination, methyl benzoate produced via β-hydride elimination of the butyl ligand was not detected by ^1H NMR spectroscopy. Even at elevated temperatures such a side reaction was not observed at all (entry 8).

Similar results were observed in the coupling of tosylate **6** (entries 9-12 of Table 1): the best result was obtained with the phenylborate of the butyl ligand (**4d**; Ar = Ph, R^3 = *n*-Bu) as indicated in entry 12. For tosylate **6**, $NiCl_2(PPh_3)_2$ also showed higher catalytic activity than $NiCl_2$(dppf).

Next, we applied the best conditions mentioned above to other combinations of mesylates and lithium borates. The mesylates we selected were **5**, sterically more congested mesylate **9**, and *p*-acetyl- and *p*-cyanophenyl mesylates **10** and **11**, which were submitted to the reaction with 2-furylborate **4a**, phenylborate **4d**, and substituted phenylborates **4e-g** possessing the butyl ligand (R^3 = *n*-Bu) in the presence of 10 mol % of $NiCl_2(PPh_3)_2$. The results are presented in Table 2. All the reactions were completed at room temperature within 12 h to give the desired products in high yields and no starting mesylates were recovered. In the case of the phenylborates, the by-products of the butyl ligand transfer were less than 5% of the desired products (entries 1,2,4,5,7, and 8), while furylborate **4a** did not afford such by-products (entries 3 and 6). Difference in reactivity was not observed among the entries.

In conclusion we have shown that the efficient coupling of aryl mesylates takes place with lithium borates in the presence of the nickel catalyst under mild conditions, thus furnishing coupling products in high yields. Although the mesylates we examined possess an electron withdrawing group, the mesylate methodology will open economical routes to biologically important biaryl compounds.[2,5,12] Coupling of aryl mesylates without such an activating substituent and lithium borates are now under investigation.[13]

Typical experimental procedure: To an ice cold suspension of $NiCl_2(PPh_3)_2$ (17 mg, 0.027 mmol) and 4,5-dimethyl-2-phenyl-1,3,2-dioxaborolane (200 mg, 1.1 mmol) in THF (2 mL) was added *n*-BuLi (0.51 mL, 1.6 M in hexane, 0.81 mmol). The suspension immediately turned to a dark brown solution. After 15 min of stirring at the same temperature, the ice bath was removed and *p*-methoxycarbonylphenyl mesylate (**5**) (62 mg, 0.27 mmol) in THF (1 mL) was added to the solution. After stirring for 6 h at 60 °C, sat. $NaHCO_3$ was added and the mixture was extracted with AcOEt twice. Purification by chromatography (AcOEt/hexane) afforded methyl 4-phenylbenzoate (**7b**) as a white solid (90%): mp 115-116 °C (recrystallized from hexane); lit.[14] 117.5 °C).

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