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# Handy Protocols using Vinyl Nosylates in Suzuki–Miyaura Cross-Coupling Reactions

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**Abstract:** Vinyl nosylates derived from 1,3-dicarbonyl compounds could be engaged in Suzuki–Myaura cross coupling reactions with aryl-, vinyl- and methylboronic acids or trifluoborate derivatives at room temperature in the presence of 2 mol% of [1,1′-bis(diphenylphosphino)ferrocene]dichloropalladium(II) [$PdCl_2$(dppf)]. *One-pot* procedures have been set up for practical and efficient nosylation–cross-coupling reactions. Nosylate, as a cheap novel pseudo-halide, gives very stable compounds and is very efficient in Suzuki–Myaura cross coupling reactions (21 examples, 44–99%).

**Keywords:** cross-coupling; palladium; Suzuki–Miyaura reaction; vinyl nosylates

## Introduction

Cross-coupling reactions are among the most powerful and reliable reactions using transition metals, for the formation of carbon-carbon or carbon-heteroatom bonds.[1] Mostly based on palladium complex catalysts,[2] these reactions offer high efficiency and broad functional tolerance, leading to numerous applications.[3]

Among palladium-catalyzed cross-coupling reactions, the Suzuki–Miyaura coupling probably is the most popular due to its mildness, the stability and non-toxicity of the boron coupling partner, together with its tolerance to $sp^3$ coupling partners. This has led to the widespread use of this reaction in synthesis,[4] as well as in industrial processes.[5] Since its discovery in 1979,[6] efforts have been maintained to develop more efficient catalysts[7] and ligands.[8]

In contrast, the electrophilic partners have been less investigated. Nevertheless, the traditional use of halides has been expanded to the so-called pseudo-halides[9] such as some ethers,[10] esters,[9a,b,d] carbamates,[9a,b,d] sulfamate,[9a,b] and of course sulfonates. In the latter family, triflate derivatives[11] are now very popular but alternatives, such as mesylate,[12] tosylate,[13] nonaflate,[14] fluorobenzenesulfonate,[15] have also been explored and some are currently under development.

## Results and Discussion

Recently, we demonstrated that *para*-nitrobenzenesulfonate (nosyloxy or NsO) derivatives exhibit all the required properties to act as new electrophilic partners. Indeed, nosylates could be engaged *for the first time* in palladium-catalyzed Suzuki–Miyaura, Stille, Mirozoki–Heck and Sonogashira reactions.[16] In the continuation of this work, we describe here, in more detail, the scope and limitations of the preparation of vinyl nosylates and of their utilization in Suzuki–Miyaura reaction (Scheme 1, *top*). We also describe here the development of a *one-pot procedure* to get cross-coupling products, directly from a non-activated electrophilic partner using *in situ* C–O activation (Scheme 1, *bottom*).

### Vinyl Sulfonate Formation/Nosylation

Setting up novel electrophilic partners in palladium cross-coupling reactions imposed the necessity to get smooth, practical and easy to scale up access to such compounds.

In our preliminary work, we used the commercially available and cheap 4-nitrobenzenesulfonyl (*p*-nosyl) chloride for the sulfonylation reaction.[16] Nosyl chlo-

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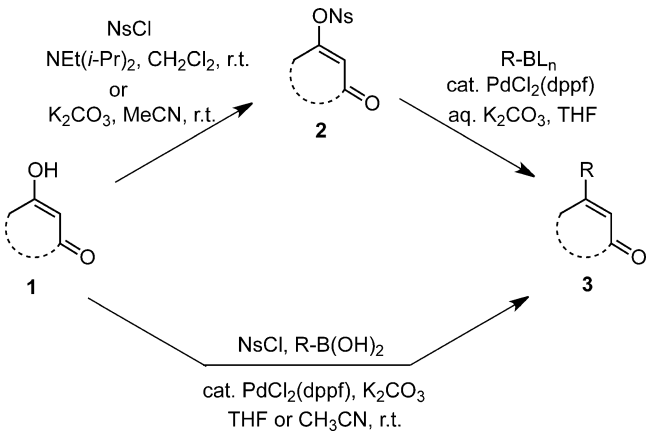



**Scheme 1.** Two-step or one-pot protocols for Suzuki–Miyaura cross-coupling with vinyl nosylate partners.

ride rapidly reacted with 1,3-diketones in the presence of diisopropylethylamine in dichloromethane at room temperature, giving the corresponding nosylates in yields higher than 90% in most cases (Table 1, conditions **A**). Looking for a one-pot sulfonylation–coupling process, we also checked the effect of bases commonly used in Suzuki–Miyaura reactions. A rapid screening revealed that potassium carbonate in acetonitrile presented the best conditions for sulfonylating various 1,3-diketones (Table 1, conditions **B**).

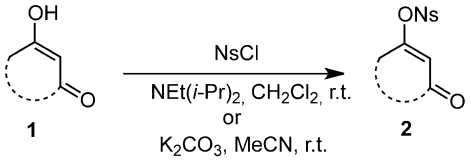
The role of the nitro group's position on the sulfonylation reaction was also evaluated with hydroxycoumarin **1** as model compound (entries 1–6).[17] Irrespective of the *para*, *ortho*, or *meta* nosyl isomers and the conditions (**A** or **B**), short reaction times (~0.5 h) were achieved for the sulfonylation of hydroxycoumarin **1** (entries 1–6). In this series, conditions **B** proved slightly, but consistently, more efficient than the conditions **A** (entries 2 *vs.* 1, 4 *vs.* 3 and 6 *vs.* 5). The *para*-nitrophenylsulfonyl was thus always used and thereafter referred to as the "nosyl" group (Ns).

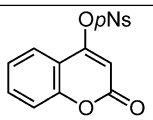
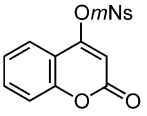
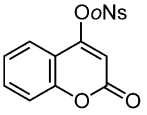
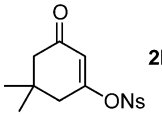
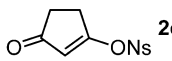
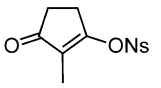
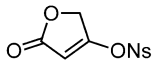
Whatever the position of the nitro group, the so-obtained nitrobenzenesulfonates proved to be highly crystalline and stable compounds.

Both nosylation conditions were then applied to other 1,3-diketones. Five- and six-membered cyclic diketones gave the expected nosylates, usually in high to quantitative yields (entries 7–15). Conditions **A** usually required longer reaction times than conditions **B**, but overall within 1 h. In some cases, product stability might be mostly responsible for the observed variations. For example, the less substituted nosylate **2c** is less stable than the methylated **2d**,[18] and conditions **A** were clearly not the most appropriate for such a sensitive substrate (entry 9 *vs.* 11), although reasonable yields of **2c** could be obtained using conditions **B** (entry 10 *vs.* 9). Similar trends were observed for tetronic acid **1e**, which readily polymerized under basic conditions. Conditions **A** only led to polymerization, while conditions **B** allowed us to get the corresponding nosylate **2e** in reasonable yield (entry 13 *vs.* 15). Slight modifications, with triethylamine in THF at 0 °C (conditions **A′**), and final precipitation of the product with ethanol offered a significant improvement (entry 14 *vs.* 13). Once isolated, the nosylate proved very stable like all the other nosylates.

It is worth noting that purification by flash chromatography was in most cases not necessary for vinyl nosylates **2**, in sharp contrast to their triflate analogues. Here, simple recrystallization yielded analytical grade

**Table 1.** Nosylation of cyclic diketones.




| Entry | Product | Conditions[a] | Time [h] | Yield[b] [%] |
|---|---|---|---|---|
| 1 |  **2aa** | **A** | 1 | 96 |
| 2 | | **B** | 0.5 | 97 |
| 3 |  **2ab** | **A** | 0.5 | 92 |
| 4 | | **B** | 0.5 | 95 |
| 5 |  **2ac** | **A** | 0.5 | 94 |
| 6 | | **B** | 0.5 | 97 |
| 7 |  **2b** | **A** | 1 | 88 |
| 8 | | **B** | 0.5 | 79 |
| 9 |  **2c** | **A** | 1 | 58 |
| 10 | | **B** | 0.5 | >95[c] |
| 11 |  **2d** | **A** | 1 | 79 |
| 12 | | **B** | 0.5 | 95 |
| 13 |  **2e** | **A** | 0.3 | -[d] |
| 14 | | **A'** | 0.3 | 74[e] |
| 15 | | **B** | 0.5 | 73 |

[a] *Reaction conditions, method **A**:* substrate (1 equiv.), (*i*-Pr)$_2$EtN (1.2 equiv.), NsCl (1.05 equiv.) in DCM (0.125 M) at room temperature; *method **B**:* substrate (1 equiv.), $K_2CO_3$ (1.8 equiv.), NsCl (1.1 equiv.) in MeCN (0.1 M).
[b] Isolated pure material.
[c] Estimated from NMR spectra; see text and ref.[18]
[d] Polymerization occurred.
[e] $Et_3N$ was used as base in THF at 0 °C.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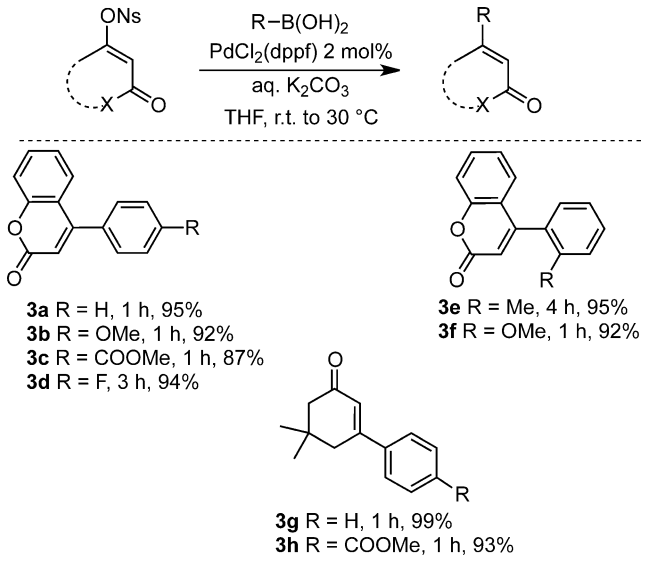
nosylates, which were stable over months at room temperature without any precaution.

## Suzuki–Miyaura Coupling from Nosylates

In our previous work, we focused our interest on the preparation of 4-arylcoumarins (Scheme 2), compounds that are reported to exhibit interesting properties, especially pharmaceutical activities.[19] To access to such compounds, we privileged the Suzuki–Miyaura cross-coupling with arylboronic acids (Scheme 2).[16] However, other boron reagents could also be engaged in similar coupling reactions (Table 2).

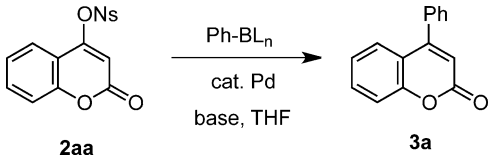
Due to their structure, boronic acids are always in equilibrium with their anhydride and cyclic trimer (boroxine), which can affect the reactivity due to competitive reactions.[20] In contrast, pinacol boranes, borabicyclononane derivatives[21] and the more recently introduced trifluoroborates[22] only exist as the monomeric form, often providing better reactivity in Suzuki–Miyaura coupling.

For mechanistic reasons,[23] the presence of hydroxy or alkoxy group is mandatory in such couplings. They are usually produced by adding base to the reaction mixture in the presence of water. However, competitive reactions could occur. Indeed, in our case, strong aqueous bases induced a rapid hydrolysis of the starting material (e.g., entry 1, Table 2). Milder bases also led to such competitive hydrolysis, but tuning the base nature and the conditions allowed to slow such side reaction, although not enough for useful results (entries 2 and 3). More interestingly, adjusting the catalyst nature alleviated this side reaction, the coupling being faster than hydrolysis, and diphenylphosphinoferrocene dichloropalladium proved to be the best catalyst, very efficiently furnishing the coupling product within one hour (entry 4 *vs.* 3).




**Scheme 2.** Our preliminary Suzuki–Miyaura cross-couplings with vinyl nosylate partners.[16]

**Table 2.** Suzuki–Miyaura coupling of coumarin nosylate with various boron derivatives.




| Entry | Borane | Conditions | Time [h] | Yield [%][a] |
|---|---|---|---|---|
| 1 | $PhB(OH)_2$ | $Pd(PPh_3)_4$ 3 mol% aq. NaOH, 30 °C | 0.5 | 0[b] |
| 2 | $PhB(OH)_2$ | $Pd(PPh_3)_4$ 3 mol% aq. $Na_2CO_3$, 30 °C[c] | 0.5 | 0[b] |
| 3 | $PhB(OH)_2$ | $Pd(PPh_3)_4$ 2 mol% aq. $K_2CO_3$, 30 °C | 10 | 20[b] |
| 4 | $PhB(OH)_2$ | $PdCl_2$(dppf) 2 mol% aq. $K_2CO_3$, 30 °C | 1 | 95 |
| 5 | $PhB(OH)_2$ | $Pd(PPh_3)_4$ 3 mol% CsF, 60 °C | 0.5 | 0[d] |
| 6 | $PhB(OH)_2$ | $PdCl_2$(dppf) 2 mol% CsF, 60 °C | 1 | 0[d] |
| 7 | PhB(pin) | $PdCl_2$(dppf) 2 mol% aq. $K_2CO_3$, 30 °C | 24 | 8 |
| 8 | $PhBF_3K$ | $PdCl_2$(dppf) 2 mol% aq. $K_2CO_3$, 30 °C | 16 | 57 |

[a] Isolated pure material.
[b] Hydrolysis was observed.
[c] Performed in toluene-ethanol at 60 °C.
[d] Fluorolysis was observed.

Fluoride salts are also known as a boron activator, promoting fluoroborate formation and transmetallation.[23c,24] However, only fluorolysis of the nosyl group occurred whatever the conditions and catalyst used (entries 5 and 6).

Under the optimized conditions, pinacol boranes readily reacted with nosylates, cleanly furnishing the coupling products (entry 7). Reaction times were much longer, although high yields were nevertheless obtained (entry 7 *vs.* 4). Trifluoroborates also readily reacted with nosylates, but again slowly compared to boronic acids (entry 8 *vs.* 4), although less than pinacol boranes (entry 8 *vs.* 7). The yield proved to be lower (entry 8 *vs.* 7 *vs.* 4), mostly due to fluorolysis as a side reaction.

The scope and limitations of Suzuki–Miyaura cross-coupling with nosylates were then examined (Scheme 2 and Table 3). We first looked for the best nosylates to use for coupling, since the *ortho*, *meta* or *para*-nosyl chlorides are commercially available[17] and all readily gave the corresponding nosylates (see Table 1). Nosylates **2aa**, **2ab** and **2ac** were thus sub-

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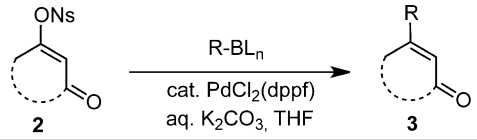
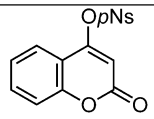
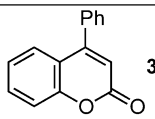
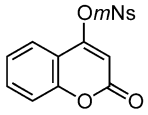
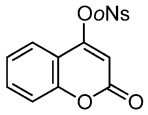
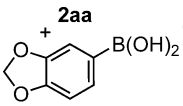
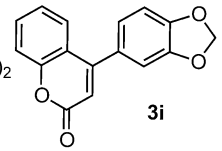
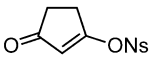
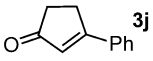
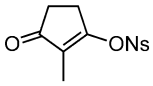
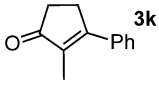
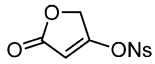
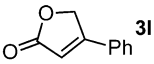
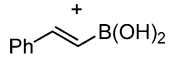
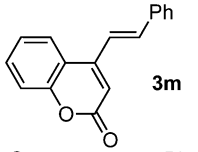
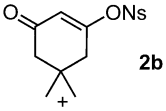
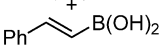
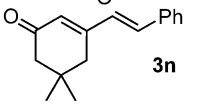
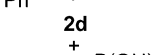
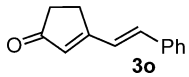
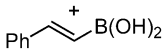
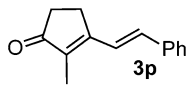
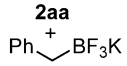
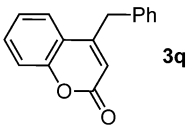
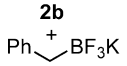
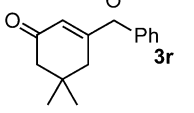
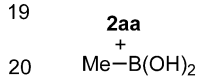
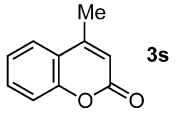
**Table 3.** Scope and limitations of the Suzuki–Miyaura coupling of nosylates.[a]




| Entry | Starting Material | Product | Cat. Loading Time [h] | Yield[b] [%] |
|---|---|---|---|---|
| 1 |  **2aa** |  **3a** | 2 mol% 1 | 95 |
| 2 | | | 4 mol% 1 | 93 |
| 3 |  **2ab** | **3a** | 2 mol% 2 | 96 |
| 4 | | | 4 mol% 1 | 94 |
| 5 |  **2ac** | **3a** | 2 mol% 10 | 90 |
| 6 | | | 4 mol% 1 | 96 |
| 7 | **2aa** +  |  **3i** | 2 mol% 1 | 83 |
| 8 |  **2c** |  **3j** | 2 mol% 2 | 88 |
| 9 |  **2d** |  **3k** | 2 mol% 4 | 52 |
| 10 | | | 6 mol% 3 | 77 |
| 11 |  **2e** |  **3l** | 2 mol% 1 | 99 |
| 12 | **2aa** +  |  **3m** | 2 mol% 1 | 71 |
| 13 |  **2b** +  |  **3n** | 2 mol% 1 | 91 |
| 14 | **2c** +  |  **3o** | 2 mol% 1 | 74 |
| 15 | **2d** +  |  **3p** | 6 mol% 2 | 67 |
| 16 | **2aa** +  |  **3q** | 9 mol% 14 | 81[c] |
| 17 | **2b** +  |  **3r** | 2 mol% 14 | 35 |
| 18 | | | 9 mol% 14 | 77[c] |
| 19 | **2aa** +  |  **3s** | 5 mol% 5 | 44[d] |
| 20 | | | 10 mol% 5 | 22[d] |

jected to cross-coupling with phenylboronic acid under our best coupling conditions. They all gave the coupling product in high yields, with similar efficiency in the presence of 4 mol% of $PdCl_2$(dppf) (Table 3, entries 6 *vs.* 2 *vs.* 4). By decreasing the catalyst loading, the *ortho*-nosyloxy coumarin **2ac** was clearly less efficient than its *meta*- **2ab** and *para*-analogues **2aa**, inducing a long reaction time, probably due to the steric hindrance brought by the *ortho*-substituent during the key oxidative addition (Table 3, entry 5 *vs.* 3 *vs.* 1). Being less expensive than its *meta* isomer,[17] the *para*-nosylate thus turned to be the best choice and was later always used in Suzuki–Miyaura reactions.

Interestingly, an *ortho*-substituent did not alter the reaction efficiency when placed on the boronic acid partner. A slower reactivity was nevertheless observed with the *ortho*-methylphenylboronic acid (Scheme 2, **3e** *vs.* **3f**). Except for the *para*-fluorophenyl, which required a longer reaction time (Scheme 2, **3d** *vs.* **3a–c**), other substituents, even electron-withdrawing ones, did not much affect the reaction time or its efficiency (Table 3, entry 7). This trend was also observed with other nosylates, such as the one derived from dimedone **2b** (Scheme 2, **3g** *vs.* **3h**).

Other nosylates, such as those derived from cyclopentane-1,3-dione, 2-methylcyclopentane-1,3-dione and 4-hydroxy-2-furanone, **2c–e**, also gave with phenylboronic acid the corresponding coupling products in high, sometimes quantitative, yields (Table 3, entries 8–11). It is worth noting that the methylated cyclopentenyl derivative **2d** required increased catalyst loading and longer reaction time in order to obtain the desired product in slightly lower yield (entries 9 and 10 *vs.* 8).

Arylboronic acids thus represent a useful and very effective class of partners for Suzuki–Miyaura cross-coupling with nosylates. To fully show the viability of the latter in cross-coupling reactions, we also examined other types of boron reagents.

The behaviour of boronic acids carrying a non-aryl $sp^2$-transferable group has been explored with the *E*-2-phenylethenylboronic acid. The latter was successfully engaged in Suzuki–Miyaura cross-coupling with various nosylates (entries 12–15). These couplings were overall slightly less efficient than those with ar-

[a] *Conditions:* nosylate (1 equiv.), $RB(OH)_2$ (1.02 equiv.), $PdCl_2$(dppf) and $K_2CO_3$ (2.4 equiv., 2 M aqueous solution) in THF (6 M) at room temperature.

[b] Isolated pure material.

[c] *Conditions:* nosylate (1 equiv.), $BnBF_3K$ (1.02 equiv.), $PdCl_2$(dppf) and $K_2CO_3$ (3 equiv., 5 M aqueous solution) in THF (0.17 M) at 60 °C.

[d] *Conditions:* nosylate (1 equiv.), $MeB(OH)_2$ (1.5 equiv.), $PdCl_2(PPh_3)_2$ and $K_2CO_3$ (3.5 equiv., $H_2O$ (1 mL mmol$^{-1}$) in THF (0.1 M) at 60 °C.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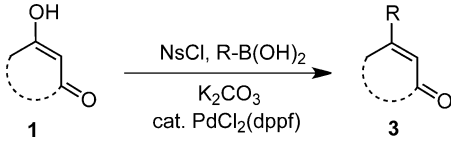
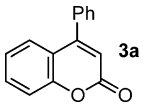
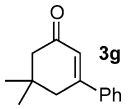
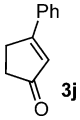
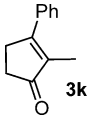
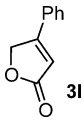
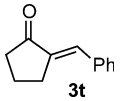
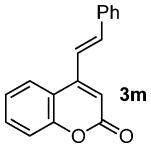
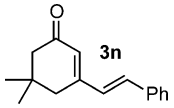
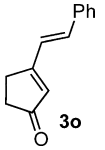
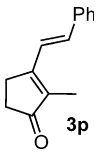
ylboronic acids (entry 12 *vs.* 1, 14 *vs.* 8, 15 *vs.* 10), but nevertheless high yields (67–91%) were achieved within 1 to 3 h. It is worth noting again that the methylated cyclopentenyl derivative **2d** were less reactive, with lower yield (entry 15 *vs.* 14).

**Table 4.** One-step nosylation–Suzuki–Miyaura coupling from β-keto carbonyls and comparison with the classical optimized two-step protocol.[a]




| Entry | Product | Conditions[a] | Yield [%][b,c] |
|---|---|---|---|
| 1 |  **3a** | **C**, *p*NsCl, 3.5 h | 94 (92) |
| 2 | | **D**, *p*NsCl, 1.5 h | 85 |
| 3 | | **C**, *m*NsCl, 7 h | 84 (91) |
| 4 | | **C**, *o*NsCl, 18 h | 84 (93) |
| 5 |  **3g** | **C**, *p*NsCl, 3.5 h | 76 (87) |
| 6 |  **3j** | **C**, *p*NsCl, 4 h | 81 (87) |
| 7 |  **3k** | **C**,[d] *p*NsCl, 45 h | 57 (73) |
| 8 | | **D**,[d] *p*NsCl, 29 h | 54 |
| 9 |  **3l** | **C**, *p*NsCl, 4.5 h | 62 (73) |
| 10 | | **D**, *p*NsCl, 3.5 h | 56[e] |
| 11 |  **3t** | **C**, *p*NsCl, 22 h | 52 (0) |
| 12 |  **3m** | **C**, *p*NsCl, 20 h | –[f] |
| 13 | | **D**, *p*NsCl, 3 h | 91 (69) |
| 14 |  **3n** | **D**, *p*NsCl, 3 h | 92 (80) |
| 15 |  **3o** | **D**, *p*NsCl, 9 h | 67 (73) |
| 16 |  **3p** | **D**, *p*NsCl, 72 h | 26 (64) |

Alkylboronic acids and their derivatives represent an important class of reagents, allowing a simple alkyl chain to be introduced onto various substrates.[25] They are however less reactive than their aryl or vinylic counterparts, not only due to the presence of the $sp^3$-transferable group, but also due to their easier equilibration to the corresponding boroxines.

We nevertheless briefly explored such couplings with nosylates. Under our standard conditions, benzyl trifluoroborate readily reacted with various nosylates, but only with higher catalyst loading. Despite longer reaction times, the desired coupling products were obtained in low to good yields (entries 16–18). The same problem arose for introducing a simple methyl group (entry 19). Here, increasing the catalyst loading was detrimental to the yield (entry 20).

## Towards a One-Pot Nosylation–Suzuki–Miyaura Coupling

As mentioned above, it was tempting to develop a one-pot protocol for domino nosylation–cross-coupling reactions, especially since nosylations were always fast ($\leq$30 min) in the presence of potassium carbonate, while the coupling reactions proceeded in 1 to 3 h.[26]

To look for such a one-pot process, we examined two sets of conditions (Table 4), one in which all reagents were mixed in the reaction flask (method **C**), and a sequential one, in which the nosylated products were *in situ* prepared prior to the addition of the boronic acid and the palladium catalyst (method **D**).

Starting with the 4-coumarinyl *para*-nosylate and phenylboronic acid, both methods afforded the expected 4-phenylcoumarin **3a** in high yields. Although slower, method **C** provided the better yield compared to the sequential protocol (method **D**) (Table 4, entry 1 *vs.* 2). It is worth noting that this one-pot protocol is slightly better than the optimized two-step sequence already reported (94% *vs.* 92%; entry 1).

[a] *Reaction conditions:* method **C**: substrate (1 equiv.), NsCl (1.1 equiv.), $RB(OH)_2$ (1.2 equiv.), $PdCl_2$(dppf) (4 mol%) and $K_2CO_3$ (7 equiv.) in MeCN (0.17 M) at room temperature; method **D**: substrate (1 equiv.), NsCl (1.1 equiv.), $K_2CO_3$ (4 equiv.) in THF (0.17 M) at room temperature then $RB(OH)_2$ (1.2 equiv.), $H_2O$ (1.4 mL mmol$^{-1}$) and $PdCl_2$(dppf) (4 mol%).

[b] Yields of isolated pure material.

[c] In brackets, overall yields obtained with our optimized two-step protocol (see Table 1 and Table 3).

[d] Modified coupling conditions using 12 mol% $PdCl_2$(dppf) and 2.4 equiv. Ph-$B(OH)_2$.

[e] 10% of the starting nosylate were recovered.

[f] Decomposition occurred.

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This method was also applied to the other *ortho*- and *meta*-isomers (entries 3 and 4). With these isomeric nosyl reagents, the desired coupling product was still obtained but with lower yields and longer reaction time (entries 3 and 4 *vs.* 1). These results paralleled those achieved in the independent nosylation step (see Table 1) and confirmed again the superiority of the *para*-nosyl derivative compared to its *ortho*- and *meta*-analogues.

Other substrates, like dimedone, cyclopentane-1,3-dione, 2-methylcyclopentane-1,3-dione and 4-hydroxy-2-furanone were also successfully engaged in such protocols with phenylboronic acid as the coupling partner (entries 5–10). The major asset of this one-pot procedure came from its successful application to unstable electrophilic partners. For example, (*E*)-(2-oxocyclopentylidene)methyl nitrobenzenesulfonate is stable only in solution during a short period of time, and its one-pot formation and direct *in situ* coupling solved the problem of its handling (entry 11). With phenylethenylboronic acid, the fully one-pot protocol did not proceed smoothly and led to decomposition, while the one-pot but sequential protocol proved really efficient, giving better results than the two-step route described above (entry 13 *vs.* 12, entry 14). Although the coupling of cyclopentenyl **2c** was achieved in good yield in our conditions **D** (entry 15), its methylated analogue **2d** afforded the dienone **3p** only in low yield (entry 16).

Whatever the conditions, it is worth noting that in all those reactions we never detected sulfone derivatives showing the chemoselective palladium insertion.[23]

## Conclusions

In summary, we have demonstrated here that nosylates are ideal substrates for Suzuki–Miyaura cross-coupling reactions with aryl-, vinyl- and methylboronic acids, boronates and trifluoroborates. Furthermore, we showed that a one-pot nosylation–cross coupling reaction could be achieved at room temperature. The *para*-nitrobenzenesulfonyl chloride, a cheap, air stable, inexpensive and commercially available reagent, provided the best results. Furthermore, the corresponding nosylates are very stable, almost always crystalline, coupling partners.

## Experimental Section

### General Procedure A – Nosylation of Cyclic Diketones (Table 1, Conditions A)

Diisopropylethylamine (DIPEA) (1.2 equiv.) was dropwise added to a suspension of 1,3-diketone (1 equiv.) in $CH_2Cl_2$ (3 mL mmol$^{-1}$) at room temperature under argon. After 10 min of stirring, a solution of 4-nitrobenzenesulfonyl chloride (1.05 equiv.) in $CH_2Cl_2$ (5 mL mmol$^{-1}$) was added. The mixture was then stirred at room temperature under an inert atmosphere for 30 min to 1 h. The reaction was quenched by addition of 1 M HCl. After extraction with $CH_2Cl_2$, the combined organic layers were dried over $Na_2SO_4$, and evaporated under reduced pressure. The crude was triturated in EtOH (7 mL g$^{-1}$) and filtered; if necessary, the product was recrystallized in EtOH.

### General Procedure B – Nosylation of Cyclic Diketones (Table 1, Conditions B)

To a solution of diketone (1 equiv.) in dry acetonitrile (0.1 M) were added successively nitrobenzenesulfonyl chloride (1.1 equiv.) and potassium carbonate (1.8 equiv.). The mixture was then stirred at 30 °C under an inert atmosphere for 30 min to 2 h. The reaction was quenched by addition of saturated $NH_4Cl$. After extraction with ethyl acetate, the combined organic layers were washed with water, brine and dried over $Na_2SO_4$ and concentrated under reduced pressure. The pure compound was obtained by precipitation in ether or by chromatography on silica gel (cyclohexane/ethyl acetate).

### General Procedure C – Suzuki–Miyaura Cross-Coupling of Nosylated Diketones (Table 3)

To a solution of boron derivative (1.2 equiv., 0.6 mmol) in degassed THF (6 mL mmol$^{-1}$) was added a freshly prepared degassed aqueous solution of potassium carbonate (2 M, 2.4 equiv.). After 5 min of stirring under an inert atmosphere, [1,1′-bis(diphenylphosphino)ferrocene] dichloropalladium(II) [$PdCl_2$(dppf)] (2 or 4 mol%) and the nosylate derivative (1 equiv.) were successively added to the reaction mixture. The mixture was stirred at 30 °C under an inert atmosphere until consumption of the starting material. The reaction was quenched by addition of saturated $NH_4Cl$. After extraction with ethyl acetate, the combined organic layers were washed with water, brine and dried over $Na_2SO_4$ and concentrated under reduced pressure. The crude residue was purified by chromatography on silica gel (cyclohexane/ethyl acetate).

### General Procedure D – *in situ* Nosylation of Cyclic Diketones Followed by Suzuki Coupling (Table 4, conditions C)

To a solution of diketone (1 equiv.) in dry and degassed acetonitrile (6 mL mmol$^{-1}$) were added successively nitrobenzenesulfonyl chloride (1.1 equiv.), phenylboronic acid (1.2 equiv.), $PdCl_2$(dppf) (4 mol%) and potassium carbonate (7 equiv.). The mixture was stirred at 30 °C under an inert atmosphere until consumption of the starting material. The reaction mixture was diluted by addition of ethyl acetate and the resulting suspension was filtered over a pad of Celite®. The filtrate was concentrated under reduced pressure and the crude residue was purified by chromatography on silica gel (cyclohexane/ethyl acetate).


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### General Procedure E – *in situ* Nosylation of Cyclic Diketones Followed by Suzuki Coupling (Table 4, Conditions D)

To a solution of diketone (1 equiv.) in dry and degassed THF (6 mL mmol$^{-1}$) were added successively nitrobenzenesulfonyl chloride (1.1 equiv.) and potassium carbonate (4 equiv.). After 20 min were added degassed water (1.4 mL mmol$^{-1}$), phenylboronic acid (1.2 equiv.) and $PdCl_2$(dppf) (4 mol%). The mixture was stirred at 30 °C under an inert atmosphere until consumption of the starting material. The reaction was quenched by addition of saturated $NH_4Cl$. After extraction with ethyl acetate, the combined organic layers were washed with water and brine, dried over $Na_2SO_4$ and concentrated under reduced pressure. The crude residue was purified by chromatography on silica gel (cyclohexane/ethyl acetate).

### Supporting Information

Experimental details and spectroscopic data of all compounds, as well as copies of their $^1$H and $^{13}$C NMR spectra, are available in the Supporting Information.

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