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Three-Component Palladium-Catalyzed Tandem Suzuki-Miyaura/Allylic Substitution: A Regioselective Synthesis of (2-Arylallyl) Aryl Sulfones

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Abstract: A one-pot Pd-catalyzed tandem process to prepare (2-arylallyl) aryl sulfones has been developed. This strategy is based on the modular assembly of a boronic acid, a sodium sulfinate and 2-bromoallyl acetate. The reaction is completely regioselective towards the terminal alkene, yielding (2-arylallyl) aryl (or alkyl) sulfones with yields ranging from 56 to 93%. Control experiments together with DFT calculations allowed to propose a plausible reaction mechanism of the tandem reaction. The usefulness of this methodology has been demonstrated with the formal synthesis of the marketed drug Apremilast and of several natural products by asymmetric hydrogenation. Using the commercially available UbaPHOX iridium complex, chiral β-methyl sulfones with up to 98% ee were obtained

Keywords: Multicomponent reactions; Homogeneous catalysis; Palladium; Iridium; Sulfones; Ab initio calculations

Introduction

Sulfones are present in many drugs and biologically active compounds (Figure 1).[1] They are also of great relevance in organic synthesis. As chemical intermediates, sulfones are widely used building blocks due to their exclusive reactivity and chemical versatility;[2] being able to react as nucleophiles, electrophiles, radicals,[3] or in Pd-catalyzed desulfonative cross couplings.[4] Moreover, unsaturated sulfones can be asymmetrically reduced[5] or hydrogenated,[6] to afford chiral sulfones which are present in many drugs and synthetic intermediates.[7]

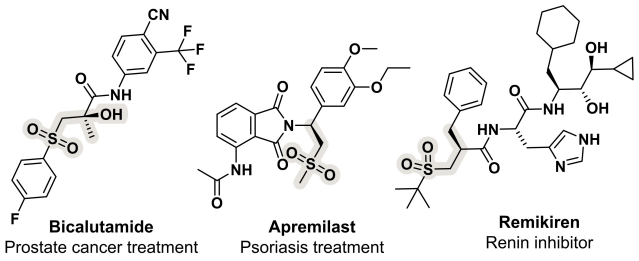


Figure 1. Examples of pharmaceutical compounds bearing sulfone groups and their use.

In particular, (2-arylallyl) aryl sulfones **1** have found many uses in the field of photochemistry.[8] Despite all the interesting applications of these compounds in novel chemical transformations, as well as in traditional reactions, their preparation has several drawbacks. For instance, contemporary methods for their synthesis involve the use of stoichiometric amounts of NBS,[9] NO_2,[10] ZnI_2,[11] TBAI,[12] or I_2,[13]

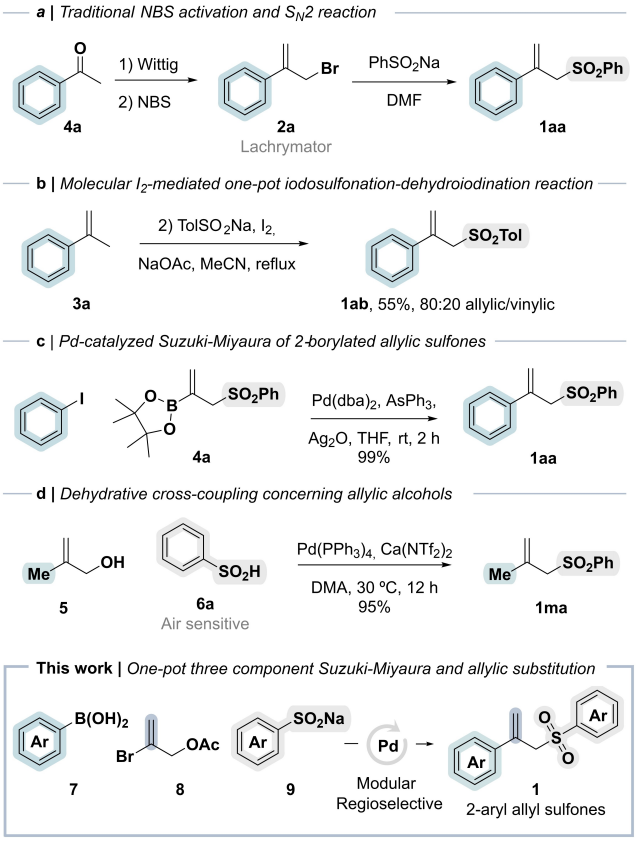
among others. Catalytic approaches have also emerged, which include examples using photoredox chemistry with Rh[14] or Co,[15] as well as transition-metal catalysis employing Cu[16] or Pd.[17] Nevertheless, most of these strategies have limitations because they usually involve several steps, hazardous by-products or reagents, harsh or unpleasant conditions, or are low atom economy processes. Selected reports for the preparation of **1** are given in Scheme 1.

The most common strategy to generate terminal allylic sulfones is through substitution of allyl bromides **2** by sulfinate salts (Scheme 1.a). The main drawback here is the strong lachrymogenic activity of allyl bromides **2**. In addition, bromides are prepared from their corresponding styrenes **3** which are, in turn, prepared by Wittig olefination of acetophenones **4**, in a poor atom-economy process.[18] A safer procedure was recently described by the Kuhakarn's group, which reported on the iodine-mediated one-pot iodosulfonation-dehydroiodination reaction starting from styrenes **3** (Scheme 1.b).[19] However, this reaction was not completely regioselective towards the terminal sulfone **1 ab**. The formation of substantial quantities of regioisomer **1 ab'** ((*E*)-((2-phenylprop-1-en-1-yl)sulfonyl)benzene) can be detrimental for subsequent transformations, such as hydrogenation. Harmata's group reported the Pd-catalyzed synthesis of **1 aa** by a Suzuki-Miyaura reaction (Scheme 1.c).[17] Although they obtained high yields, the procedure required silver oxide and triphenylarsine as additives, as well as the previous preparation of the 2-borylated allylic sulfone **4 a**. Finally, Loh's group described a dehydrative cross-coupling (Scheme 1.d) that had to be performed with sulfinic acids **6**, which are not air-stable and have to be freshly prepared.[20]

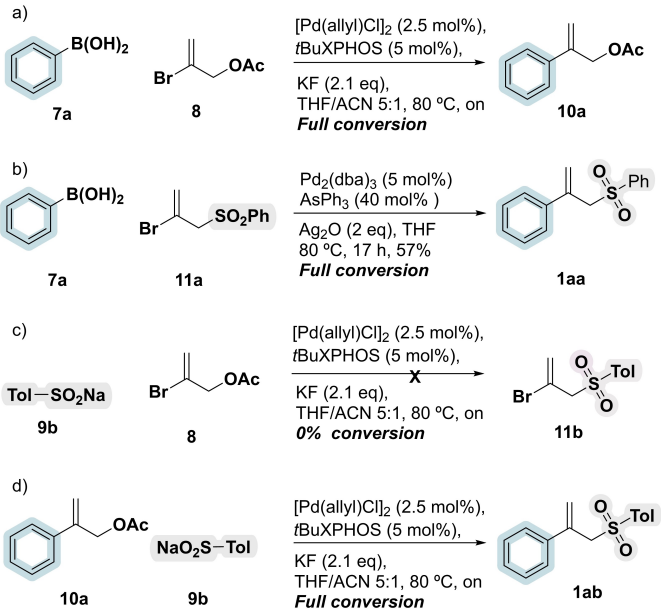
To develop an efficient and simpler route to (2-arylallyl) aryl sulfones avoiding harsh conditions and inconvenient intermediates, we have developed a one-step multicomponent reaction (MCR) using 2-bromoallyl acetate **8** as a central scaffold (Scheme 1). We envisioned introducing both aromatic groups **7** and **9** through a two-reaction cascade (Suzuki-Miyaura[21] and Tsuji-Trost[22]) using the same Pd catalyst. We describe herein a MCR that combines these three starting materials to furnish **1** in one step, catalytic conditions and good yields.

Our initial experiments started exploring both reactions independently. The reaction between 2-bromoallyl acetate **8** with phenylboronic acid **7 a** took place uneventfully affording **10 a** with full conversion using a Pd pre-catalyst, *t*BuXPHOS as ligand and KF as a base (Scheme 2.a).

The Suzuki-Miyaura (S–M) reaction of **7 a** and **11 a** afforded **1 aa** in full conversion by ^{1}H NMR spectroscopy, using the reaction conditions developed by Harmata's group (Scheme 2.b).[17] Very recently, the same reaction has been described using nickel-catalysis in water.[23] However, under Pd-catalysis, the allylic



Scheme 1. Previous preparations of terminal (2-arylallyl) aryl sulfones **1** and our approach.



Scheme 2. Initial studies of the S–M and AS reactions. Conversions were analyzed by ^{1}H NMR spectroscopy.

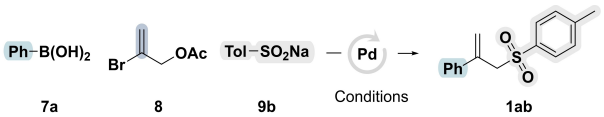
substitution (AS) on **8** using sodium tolylsulfinate **9b** as a nucleophile did not take place at all (Scheme 2.c). Conversely, it is worth noting that the substitution did work when using **10a** as the starting material and **9b** as the nucleophile (Scheme 2.d). This reaction takes place even at room temperature (90% conv. after 18 h). We then concluded that it would be feasible to find the reaction conditions where the same catalyst could perform a three-component tandem reaction.[24]

The first attempt of the one-pot reaction was performed under standard Pd (0) conditions (entry 1, Table 1). The reaction afforded the desired allyl sulfone **1ab** in 43% yield. The regioselectivity was excellent, but the yield was low. The main by-product of the reaction was the homocoupling between two boronic acid molecules. Since it is known that oxygen catalyzes the homocoupling of arylboronic acids,[25] the side reaction was minimized using strictly anhydrous solvents and nitrogen sparging the reaction mixture.

Once the feasibility of the tandem reaction was confirmed, the conditions were optimized to increase the yield. A screening of various palladium catalysts was first undertaken (Table 1). We chose KF instead of Cs_2CO_3 because Suzuki reactions are known to be faster in the presence of KF.[26] The use of bulky monocoordinated phosphines, such as XPhos[27] or Gphos,[28] clearly increased the yield by generating a more unstable and reactive catalytic species.[29] Sterically hindered P*t*Bu$_3$ showed the best result of the entries 1–5, but it is an air sensitive ligand that needs to be handled in the glove box. To avoid it, we proposed the air-stable sterically demanding *t*BuXPhos[28,30] which afforded sulfone **1ab** in 93% yield (entry 6). Modification of the temperature and solvent did not improve the results (*see Supporting Information*). Therefore, the optimized conditions (entry 6) were used in a gram scale experiment obtaining **1ab** in 87% yield (entry 7).

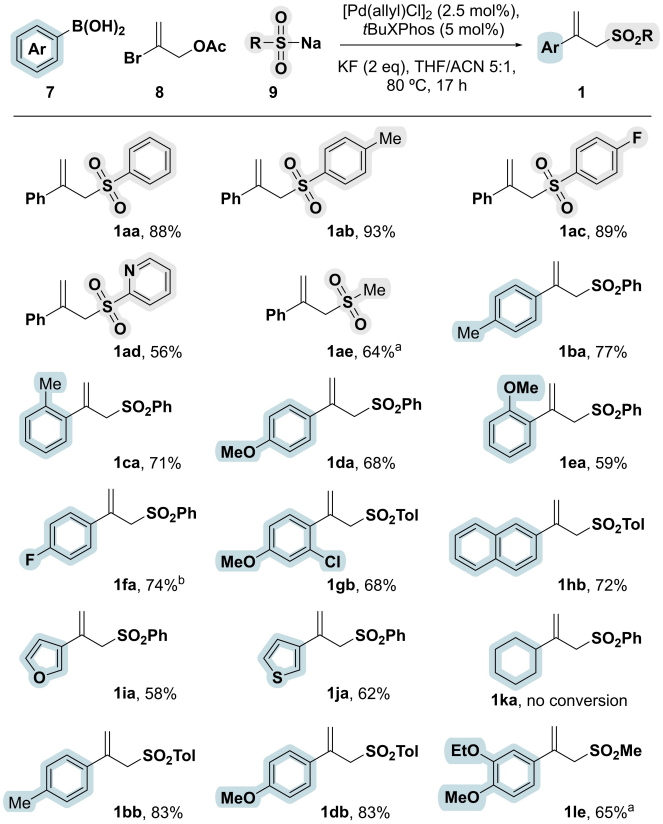
With the optimal conditions in hand, we explored the scope of the reaction (Scheme 3). As we planned it to be modular, boronic acids **7a–j** and sulfinates **9a–e** were reacted to afford the family of allyl sulfones **1aa-le**. Both **1aa** and **1ab**, electron-deficient aromatic sulfones **1ac** and heterosubstituted **1ad** were obtained in good to excellent yields, ranging 56–93%. The aliphatic sulfone **1ae** had to be prepared in DMF for 41 h due to its insolubility in THF. The scope of boronic acids was very wide and a diverse array of substituents could be incorporated to the vinylic position. We successfully synthetized electron rich **1ba** and **1da**, as well as sterically hindered *ortho*-substituted **1ca** and **1ea**. Boronic acids with EWG such as *p*-F, *p*-Cl or *p*-NO_2 showed low conversions and would require harsher conditions. Specifically, the *p*-F sub-

Table 1. Optimization of the tandem reaction conditions.



	Conditions	T(°C)	Conv (%)[a]	Yield (%)[b]
1[c]	$Pd(PPh_3)_4$, Cs_2CO_3	80	100	43
2[d]	$Pd[P(tBu)_3]_2$	80	69	n.d.
3	$[Pd(allyl)Cl]_2$, XPhos	80	100	77
4	GPhos Pd G3	80	100	70
5[c]	$[Pd(allyl)Cl]_2$, $P(tBu)_3$	80	100	83
6	$[Pd(allyl)Cl]_2$, *t*BuXPhos	80	100	93
7[h]	$[Pd(allyl)Cl]_2$, *t*BuXPhos	80	100	87

The reactions were run on a 1 mmol scale of **8**, **7a** (1.5 equiv.), **9b** (1.1 equiv.), Pd complex (2.5 mol%) ligand (5 mol%), KF (2 equiv.), in 6 mL of a THF/ACN (5:1) solvent mixture for 17 h.
[a] Conversions were determined by NMR spectroscopy.
[b] Yields correspond to isolated products.
[c] Cesium carbonate was used instead of KF.
[d] Using a glove box.
[h] 1 gram scale.

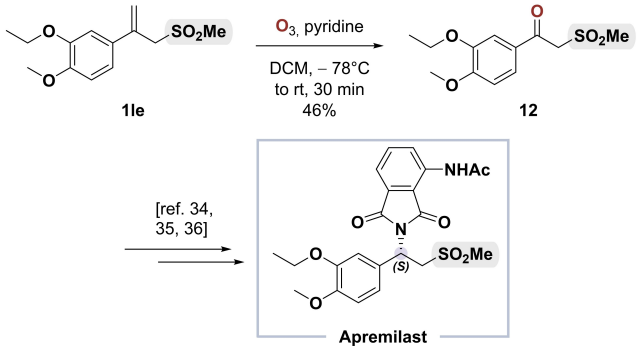


Scheme 3. Reaction scope. The reactions were run on a 1 mmol scale of **8**, **7** (1.5 equiv.), **9** (1.1 equiv.), Pd complex (2.5 mol%) ligand (5 mol%), KF (2.2 equiv.), in 6 mL of a THF/ACN (5:1) solvent mixture for 17 h. [a] Using DMF/ACN 5:1 as solvent and 41 h. [b] Using 2 equiv. of boronic acid in 3 mL of ACN and 41 h.

stituted **1 fa** had to be prepared adding 2 equiv. of its corresponding boronic acid for 41 h. Different substitution patterns such as **1 gb** (*o*-Cl and *p*-OMe) and **1 hb** (naphthyl) in the boronic acid were well tolerated. Moreover, both furan **1 ia** and thiophene **1 ja** groups were incorporated with moderate yields. Under our conditions cyclohexylboronic acid did not furnish the desired product **1 ka** and only starting material was recovered.[31] We also prepared allylic sulfones **1 db** and **1 bb** which were substituted with EDG both at the boronic acid fragment and at the sodium sulfinate. Finally, we also prepared **1 le** using the same conditions as **1 ae**, due to the low solubility of $MeSO_2Na$. In summary, the developed methodology has been successfully applied up to 17 examples and it tolerates a wide variety of functional groups.

This tandem reaction was applied to the preparation of a synthetic intermediate of Apremilast, a marketed drug used in psoriasis treatment.[32] Ketone **12** has been converted into the desired product by means of enzymatic resolution,[34] the use of a chiral auxiliary,[35] and asymmetric hydrogenation (AH).[36] In our approach, ketone **12** was easily prepared from **1 le** (Scheme 3, last example) by a reductive ozonolysis catalyzed by pyridine (Scheme 4).[33] Although the yield was not optimized, full conversion and clean reaction were observed.

The synthesis of chiral sulfones has attracted significant attention over the past 30 years due to their presence in many biologically active compounds and drugs.[7] Regarding asymmetric and catalytic transformations, AH constitutes one of the most elegant strategies to afford chiral fragments with great atom economy.[37] In fact, several groups have synthetized and hydrogenated vinylic, allylic and homoallylic sulfones by using Ir[6a–c] or Rh complexes.[6d–g] However, they used tri- and tetra-substituted olefins, which often encounter *E*/*Z*-selectivity issues in their preparation steps and may be hard to separate. In addition, they often require high H_2 pressure (up to 60 bar) to reduce the internal olefin. Our tandem reaction gave us the opportunity to readily perform the asymmetric hydrogenation on the convenient 1,1-disubstituted olefins. Based on the previous results of the group[38] we thought that (2-arylallyl) aryl sulfones **1** might be suitable candidates to undergo AH. At first, the hydrogenation of substrate **1 ab** was screened with complexes Ir-MaxPHOX **C1**,[39] Ir-PepPHOX **C2**,[40] and Ir-(*S*,*S*)-UbaPHOX **C3** (Figure 2).[41]



Scheme 4. Preparation of a synthetic intermediate of Apremilast.

The detailed screening results in the hydrogenation of **1 ab** can be found in the *Supporting Information*. The best results were obtained using Ir-Ubaphox **C3** (1 mol%) which showed an outstanding 98% ee in the hydrogenation of the model substrate in DCM at −20 °C and 10 bar (1000 kPa) of H_2. This optimized protocol was applied to some substrates obtained by the tandem reaction as shown in Scheme 5. It is worth noting that compound **13 ba** is an interesting intermediate for the synthesis of several natural products.

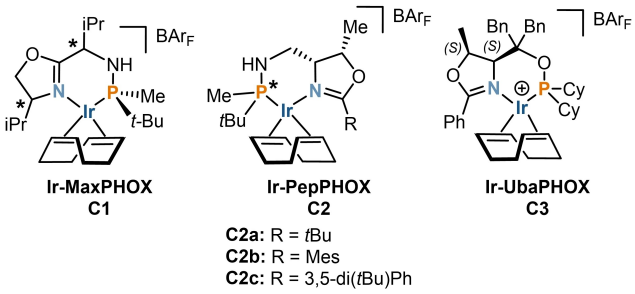
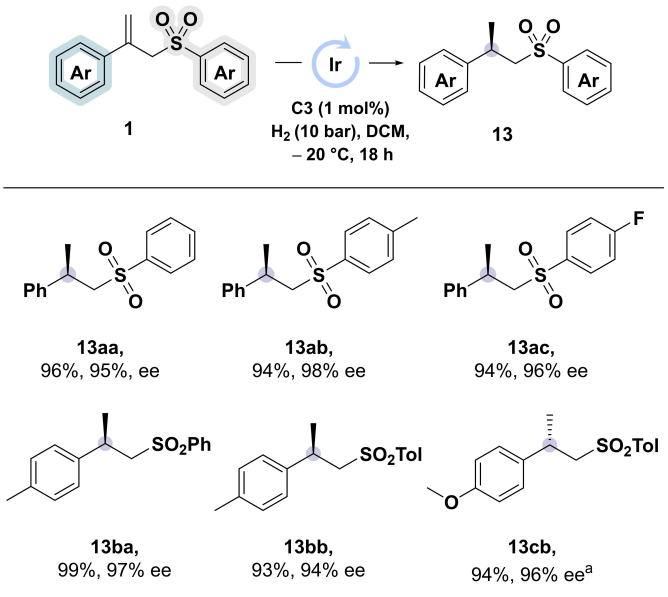


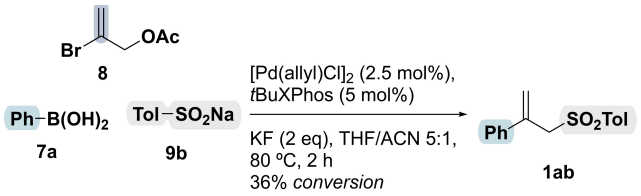
Figure 2. Screening of Ir-catalysts for the asymmetric hydrogenation of sulfone **1**.



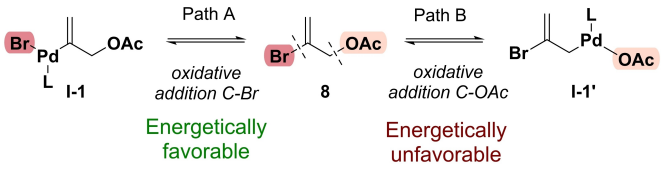
Scheme 5. Ir-catalyzed asymmetric hydrogenation of several (2-arylallyl) aryl sulfones **1**. Reactions were run in a reactor at 10 bar of H_2 pressure, 1 mol% of catalyst loading and −20 °C. [a]Using Ir-(*R*,*R*)-Ubaphox.

The Hou group reported its acylation with 3,3-dimethylacrylic acid methyl ester and $MgBr_2$-Et_2O to afford an intermediate that was converted into (*S*)-(+)-ar-turmerone.[42] Moreover, (*S*)-(+)-ar-turmerone has been used in the asymmetric synthesis of (*S*)-ar-himachalene, a pheromone component of the flea beetle, and (+)-bisacumol, a bisabolane sesquiterpene isolated from the rhizome of *Curcuma xanthorrhiza*.[43]

We then studied the mechanism of the tandem reaction. The previous observation that the allylic substitution does not take place on bromoacetate **8** (Scheme 1.c), led us to hypothesize that the Suzuki-Miyaura reaction occurs first. We then attempted to identify possible intermediates by quenching the reaction of **1 ab** before completion (Scheme 6). With a 36% conversion after 2 h, only starting materials and the final product were observed by ^{1}H-NMR spectroscopy. A possible explanation for this absence of the product of the S–M reaction (**10 a**), could be based on a pathway where the proposed intermediate reacts too rapidly to be detected.



Scheme 6. Control experiment of the standard reaction after two hours.



Scheme 7. Two possible oxidative additions on 2-bromoallyl acetate **8**.

In order to confirm our hypotheses we undertook a DFT study. We started our computational search using P(*t*Bu)$_3$ as ligand (**cat1**, see *Supporting Information* for details). Once viable pathways were identified, we moved to the (computationally more expensive) *t*BuXPhos ligand system (**cat2**). We first explored the oxidative addition step (Scheme 7).

While classical 3-centered oxidative addition of the C–OAc bond (path B) was found to be energetically inaccessible, oxidative addition into the C–Br bond (path A) was low in energy, especially when using the more active *t*BuXPhos ligand (**L2**). This finding was in agreement with the mechanistic studies of Nwokogu[44] and Heathcock,[45] although there was some controversy in the literature.[46]

The sterically congested monophosphane *t*BuXPhos can be considered as a hemilabile bidentate ligand, since the aromatic groups engage in stabilizing interactions with the metal.[47] These interactions combined with the increased steric bulk of the ligand disfavor the formation of bis(phosphine) adducts. Nonetheless, this provokes the formation of *cis*/*trans* isomers for many intermediates, including the oxidative addition intermediates (Figure 3). While these isomers might not be critical from the experimental

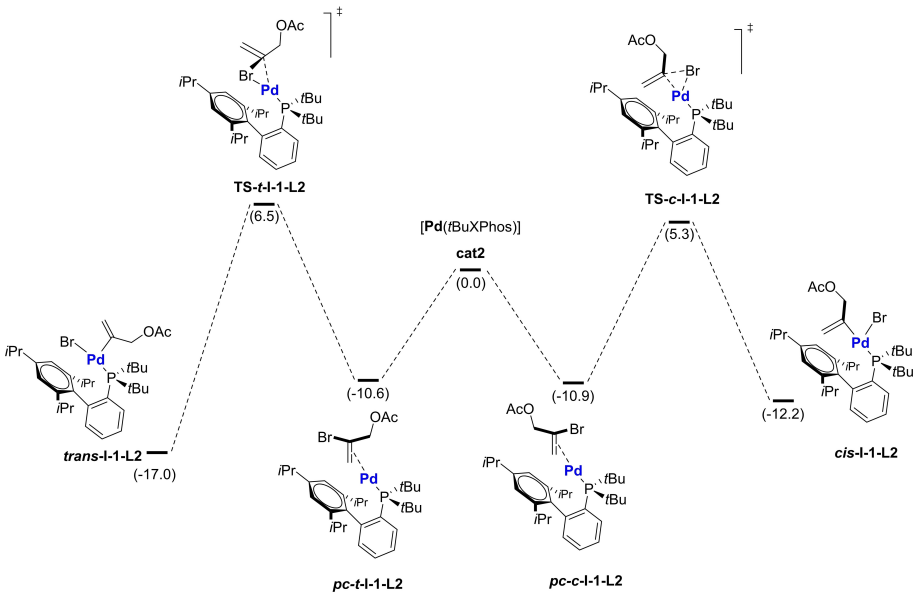


Figure 3. Calculated pathways (ΔG; in kcal·mol^{-1}) for the oxidative addition of [Pd(*t*BuXPhos)] **cat2** to the C–Br bond leading to ***cis*-I-1-L2** (right) and ***trans*-I-1-L2** (left) products.

point of view, they both have to be considered from the computational point of view to obtain meaningful results. Most interestingly, the products of oxidative addition of aromatic C–X (X=Cl, I) bonds to [Pd-(*t*BuXPhos)] (**cat2**) have been previously isolated and characterized by X-ray by the Nozaki and Buchwald groups.[48] These structures reveal a *trans* disposition between the phosphorus and halide atoms.

It is worth noting that the barriers for C–Br oxidative addition are very similar for both *cis* and *trans* isomers ($\Delta G^{\ddagger} = 16.2$–$17.4$ kcal·mol^{-1}), the one for the *cis* isomer (***cis*-I-1–L2**; with the P and Br in *cis*) being marginally lower (by 1.2 kcal·mol^{-1}). These barriers are calculated assuming the interconversion between the η^2-olefin complexes is fast. However, the *trans* product (***trans*-I-1–L2**; with the P and Br in *trans*) is significantly more stable (by 4.7 kcal·mol^{-1}), in line with the observations by Nozaki and Buchwald (Figure 3).

After Path A, the obvious steps are the trans-metalation to form **I-2** and the subsequent reductive elimination to furnish intermediate **I-3** (Scheme 8). Because we do not observe intermediate **10 a** in the crude mixture, we proposed that once **I-3** is formed, it rapidly undergoes π-allyl formation to form **I-4** so it does not dissociate the olefin to release **10 a** (Scheme 8). The nucleophilic attack to **I-4** will follow the standard allylic substitution to afford the final product. It is worth noting that the symmetry of the π-allylic intermediate **I-4** would account for the excellent selectivity towards the terminal olefin. This reaction path was located using *t*BuXPhos (**L2**) as a ligand.

With a better understanding of the initial oxidative addition step in hand, we sought to shed light as to why the bromoallyl acetate **8** did not undergo allylic substitution (see Scheme 2.c). For this reason, the step for π-allyl formation was next investigated computationally.

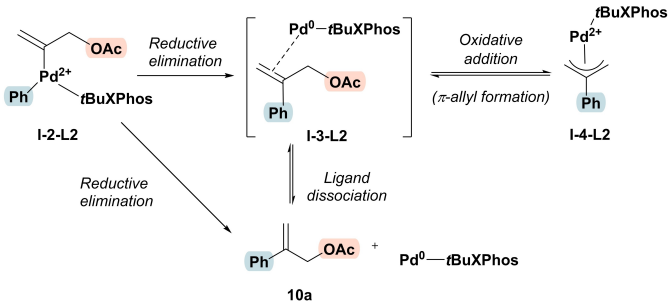
The formation of the π-allyl complex **I-4–L2** from the corresponding η^2 olefin complex **pc-*t*-I-3–L2** was computed. For the sake of comparison, the pathway from the η^2 olefin complex **pc-*t*-I-1'–L2** to intermediate **I-1'–L2** was also studied. Both concerted transition states could be located for the formation of the [(*t*BuXPhos)Pd(π-allyl)] complexes with concomitant loss of acetate (Figure 4.A). It might be worth noting that this pathway (*i.e.* through **TS-I-1'–L2**) is related to the previously discussed path B (*cf.* Scheme 7) for oxidative addition. While that pathway (classical 3-centered oxidative addition of the C–O bond to furnish a η^1-allyl complex) was too high in energy, the pathway located here (S_N2-like oxidative addition to furnish a η^3-allyl complex) has energetically accessible barriers for π-allyl formation ($\Delta G^{\ddagger} = 20.3$–$28.2$ kcal·mol^{-1}, depending on the coordinated face). Analogous TSs (slightly higher in energy) were located with P(*t*Bu)$_3$ (**L1**) as ligand (*see Supporting Information*). Analysis of the NPA charges (from NBO calculations) supports an increase in the oxidation state of Pd from 0 to +2. The electron density lost by the Pd center is transferred to the allyl moiety. Most importantly, the presence of a Ph group in the allyl moiety instead of a Br atom results in a decrease in the local barriers for π-allyl formation (by 4–8 kcal·mol^{-1}, depending on the coordinated face).

This is likely a result of the ability of the Ph group to delocalize the increase in charge of the allyl moiety, leading to an overall stabilization of the transition states and resulting π-allyl complexes. Therefore, the preference for π-allyl formation when a Ph group is present, supports the proposal that π-allyl formation occurs after the S–M steps and why the bromoallyl acetate **8** does not undergo allylic substitution, whereas phenylallyl acetate **10 a** does.

To finalize our computational studies, we then inspected the next step in the catalytic cycle, *i.e.* the nucleophilic attack of the sulfinate anion to the corresponding π-allyl complex. Notably, this step is the microscopic reverse of the π-allyl formation step.

As the π-allyl complex **I-4-L2** is symmetric, addition of a sulfinate anion to either of the two terminal carbons of the allyl moiety will result in the formation of a single product. Nonetheless, from a computational point of view, the two terminal carbons of the palladium π complex are diastereotopic and so the pathways for addition to one or the other will have slightly different energies, and will furnish different products, *i.e.* with the product **1 ab** coordinated either through the *re* or *si* enantiotopic faces of the olefin to Pd (Figure 4.B). Needless to say, these stereochemical considerations have only computational relevance, since simple decoordination makes both pathways converge and release the final (and only) product, **1 ab**.

In order to locate the TS for the addition of sulfinate we exchanged the counterion from acetate (**I-4-L2**) to *p*-toluenesulfinate (***t*-I-4'-L2**) The local barrier for addition of sulfinate, and concomitant reduction from Pd(II) to Pd(0), was found accessible ($\Delta G^{\ddagger} = 14.6$ kcal·mol^{-1}), and lower than the barrier



Scheme 8. Possible pathways from intermediate **I-2-L2** to the π-allyl complex **I-4-L2**.

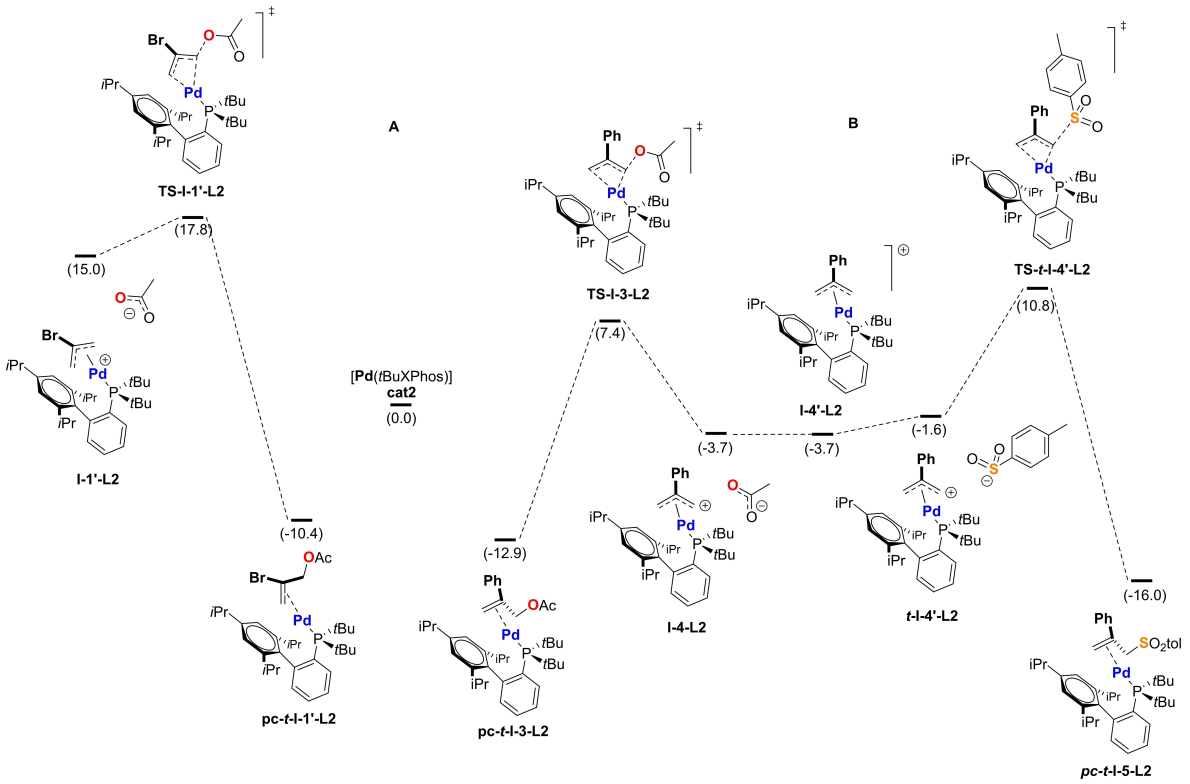


Figure 4. A) Calculated pathways and comparison for the formation of π-allyl complexes **I-4-L2** and **I-1'-L2**. The pathways arising from coordination through the other (less favorable) enantiotopic face of the same olefins can be found in the *Supporting Information.* B) Most favorable pathway for the allylic substitution steps, including π-allyl formation and nucleophilic addition of *p*-tolylsulfinate. The (less favorable) pathway resulting in the product where **1 ab** is coordinated through the *re* face of the olefin can be found in the *Supporting Information.*

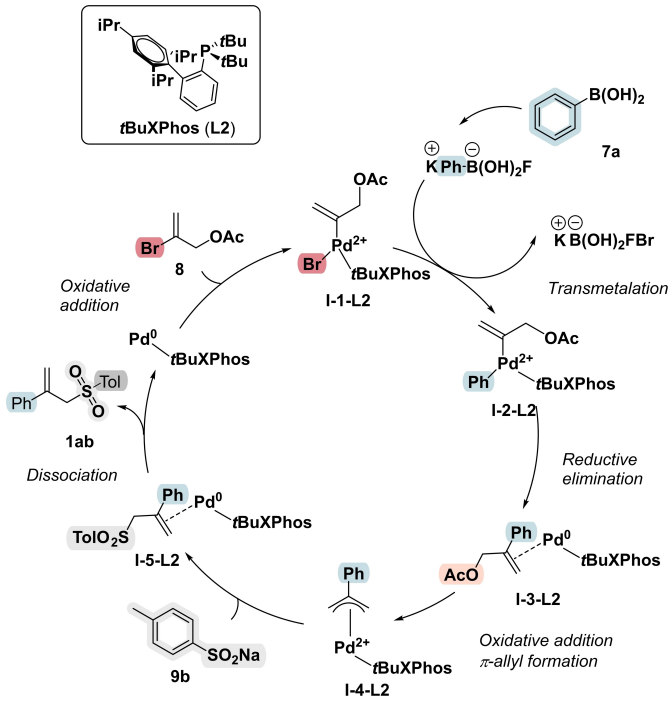
for the formation of the π-allyl complex. However, as π-allyl formation is most likely reversible (as supported by the data), addition of the nucleophile appears to be rate controlling of the allylic substitution steps. In other words, the overall barrier for the allylic substitution (*i. e.* π-allyl formation and sulfinate addition) is $\Delta G^{\ddagger} = 23.8\ \text{kcal}\cdot\text{mol}^{-1}$. As for the rate determining step for the whole tandem process, the current data cannot unambiguously determine it. Experimental interrogation through kinetic studies was hampered by solubility problems, and further computational investigations were deemed insufficient by themselves given the myriad of possible transmetalation pathways that could be operating (on the S–M part of the process). However, the quenching experiment (*cf.* Scheme 6) and the fact that the reaction between **10 a** and **9 b** works even at room temperature, strongly suggests that the Suzuki reaction (either the transmetalation or reductive elimination step) is the rate determining step of the whole process.

While a complete mechanistic study of this process, including the transmetalation step, is beyond the scope of the present study, the current data already allows us to gain valuable insight into this transformation and obtain a general mechanistic picture.

In summary, we propose the catalytic cycle shown in Scheme 9 for the tandem process to obtain compound **1 ab**. The upper half of the cycle contains the S–M steps, while the lower half contains the allylic substitution steps. Starting from Pd(0)-*t*BuXPhos (**cat2**) as the catalytic species, the first step corresponds to the oxidative addition of the C–Br bond of **8**. The resulting Pd(II) complex **I-1-L2** would transmetalate with the boronic acid affording **I-2-L2** and undergo reductive elimination to afford the Pd(0) complex **I-3-L2**. This complex would then undergo π-allyl formation to afford the cationic complex **I-4-L2**, which would then be attacked by the nucleophile. In this case, addition of sulfinate **9 b** leads to intermediate **I-5-L2** and lastly the final product **1 ab** is released by ligand dissociation.

Conclusion

In conclusion, a three-component Pd-catalyzed tandem process involving boronic acids, 2-bromoallyl acetate and sodium sulfinates was developed to prepare (2-



Scheme 9. Proposed catalytic cycle for the tandem reaction.

arylallyl) aryl (or alkyl) sulfones **1**. The process consists of a Suzuki-Miyaura and an allylic substitution reactions. The reaction was completely regioselective towards the terminal sulfone and the yields obtained ranged from 56–93%. It tolerated several functional groups in the boronic acid as well as in the sulfonyl group. Control experiments together with DFT calculations allowed us to postulate a reaction mechanism. The mechanism involves the selective oxidative addition of the C–Br bond (**I-1**), followed by transmetalation of the aryl group from the boronic acid (**I-2**). Reductive elimination of this intermediate gives a palladium complex (**I-3**) that directly evolves through a concerted transition state to the π-allyl complex (**I-4**). Subsequent nucleophilic addition and dissociation afford the final allyl sulfone. A family of allylic sulfones were subsequently hydrogenated by the commercially available UbaPHOX iridium complex affording chiral β-methyl sulfones with up to 98% ee.

Experimental Section

General procedure for the preparation of allylic sulfones. A septum-capped vial, equipped with a magnetic stirring bar, was charged in this specific order with 2-bromoallyl acetate **8** (180 mg, 1 mmol, 1 equiv.), boronic acid **7** (1.5 mmol, 1.5 equiv.), sodium sulfinate **9** (1.1 mmol, 1.1 equiv.), potassium fluoride (128 mg, 2.2 mmol, 2.2 equiv.), *t*BuXPhos (21 mg, 50 µmol, 0.05 equiv.) and allylpalladium (II) chloride dimer (9 mg, 25 µmol, 0.025 equiv.). The vial was sealed, evacuated, and backfilled with nitrogen (x3). Freshly distilled anhydrous THF (5 mL) and sparged anhydrous ACN (1 mL) were consecutively added, and the solution was sparged for 2 min. The reaction mixture was stirred at 80 °C for 16 h. After that time, the crude was filtrated through a short plug of celite and concentrated under reduced pressure. The resulting residue was purified by flash column chromatography (Hexane/EtOAc 8:2) to afford sulfones **1**. Solids were recrystallized from MeOH to obtain white crystals.

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