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Allylsulfones through Palladium-Catalyzed Allylic C–H Sulfonylation of Terminal Alkenes

Tingting Chen,[a] Jassmin Lahbi,[a, b] Gianluigi Broggini,[b] Alexandre Pradal,*[a] and Giovanni Poli*[a]

In memory of Professor Gaetano Zecchi

Two previously unknown protocols for Pd-catalyzed allylic C–H sulfonylation of terminal alkenes have been developed. While the former consists of a direct Pd(II)-catalyzed oxidative C–H allylic sulfonylation in the presence of sulfinate anions, the latter involves a sequential one-pot Pd(II)-catalyzed C–H allylic acetoxylation followed by a Pd(0)-catalyzed sulfonylation. The scope of both protocols was studied on 25 examples.

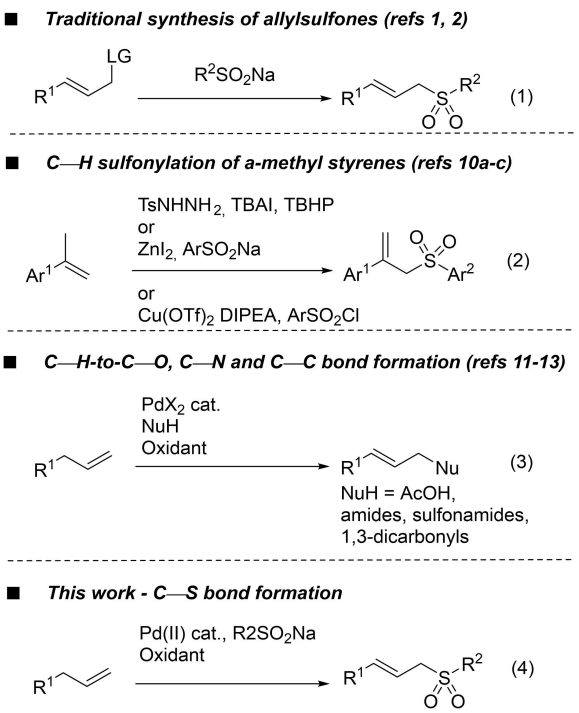
Introduction

Organosulfur compounds represent an important class of molecules that play a key role in a number of organic reactions, and find applications in various fields of chemistry. In particular, the relevance and versatility of sulfones[1] is so high that B. M. Trost[2] defined them as chemical *chameleons*, and P. L. Fuchs[3] as *pluripotent*. In addition, sulfones are intermediates in synthetically relevant reactions such as the Julia-Lythgoe olefination, the modified Julia,[4] and the Julia-Kociensky olefination,[5] the Ramberg-Bäcklund reaction,[6] as well as a number of other desulfonylative transformations.[7]

In the course of a project directed toward the synthesis of conjugated polyenes, we became interested in the preparation of allylsulfones. The classic way to access these compounds involves the coupling between substrates bearing an allylic leaving group (LG) and sulfinate anions.[8,9] This well-known strategy (Scheme 1, equation 1), although normally effective, often implies several synthetic steps, as the required allylic precursors are not always commercially available. Conversely, the direct C–H sulfonylation of alkenes, which, thanks to its step-economy and the abundance of the alkenes would represent a much more elegant access to allylsulfones, has been so far reported only for the very restricted case of α-methylstyrenes (Scheme 1, equation 2).[10]

Considering the recent studies by us and others on the Pd-catalyzed allylic C–H activation of alkenes to form C–O,[11] C–N[12] and C–C bonds (Scheme 1, equation 3),[13] we decided to investigate the direct C–H sulfonylation of terminal alkenes.[14]

We describe in this article the development of two protocols of Pd-catalyzed direct C–H sulfonylation of terminal alkenes (Scheme 1, equation 4).



Scheme 1. Previous works related to the synthesis of allylsulfones (equations 1–3), and this work (equation 4).

[a] *T. Chen, J. Lahbi, Dr. A. Pradal, Prof. G. Poli*
Sorbonne Université
Faculté des Sciences et Ingénierie, CNRS
Institut Parisien de Chimie Moléculaire, IPCM
4 place Jussieu, 75005 Paris (France)
E-mail: alexandre.pradal@sorbonne-universite.fr
giovanni.poli@sorbonne-universite.fr
[b] *J. Lahbi, Prof. G. Broggini*
Dipartimento di Scienza e Alta Tecnologia
Università dell'Insubria
via Valleggio 11, 22100 Como (Italy)

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Results and Discussion

We started our study choosing for our model reaction the coupling between allylbenzene (**1a**) and sodium *p*-toluenesulfinate (**2a**). Gratifyingly, reacting **1a** (1.0 equiv.) with **2a** (2.0 equiv.) in the presence of palladium acetate (10 mol%) and 2,6-dimethylbenzoquinone (2,6-DMBQ) (2.0 equiv.) as the terminal oxidant, in freshly distilled acetonitrile (0.2 M), at 80 °C under argon, gave after 72 h of reaction the expected allylsulfone **3aa** in 42% yield (Table 1, entry 1). Performing the reaction under aerobic conditions led to the same result.

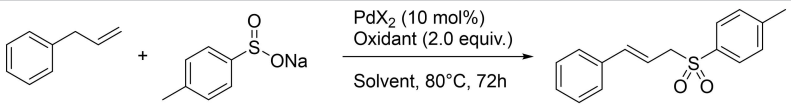
We then studied the influence of several parameters on the outcome of the reaction. A screening of polar solvents (propionitrile, DMF, DMSO, THF, 1,4-dioxane, MTBE, HFIP) showed that none of them gave a better yield than acetonitrile (Table 1, entries 2–8). With propionitrile, a similar result was obtained when the reaction was performed at 110 °C (Table 1, entry 2, note c). Suspecting that the moderate yield and the long reaction time could be due to a poor solubility of the sulfinate salt in acetonitrile, we tested methanol as a cosolvent. However, performing the reaction in CH_3CN/MeOH 4:1 v/v gave a poor yield of 29% (Table 1, entry 9). We next investigated the influence of the oxidant while keeping acetonitrile as the solvent. The use of other quinones such as benzoquinone (BQ), 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), duroquinone (DQ) and 2,5-dimethyl-1,4-benzoquinone (2,5-DMBQ) proved to be unfruitful (Table 1, entries 10–13).[15] We thus decided to keep 2,6-DMBQ as the oxidant and screened other palladium(II) sources. However, except for palladium(II) acetylacetonate, which gave results similar to palladium(II) acetate (Table 1, entry 16), none of the other catalysts provided better yields (Table 1, entries 14–18). We finally decided to retain palladium(II) acetylacetonate, as some reproducibility problems were encountered with palladium(II) acetate due to the variable purity of commercial batches. The use of ancillary ligands was also evaluated. However, none of those tested (bis-sulfoxide, pyridine-type, phenanthroline, pyridones, *N*-acetyl amino acids) gave allylsulfone **3aa** with a better yield than without ligands (See Supporting Information). Finally, changing the concentration of the reaction to 0.66 M increased slightly the yield of **3aa** to 47% (Table 1, entry 19).

With the optimized reaction conditions in hand (Method A), the scope of the reaction was then evaluated, starting with the couplings between allylbenzene **1a** and various sulfinates (Scheme 3). Electron-rich *p*-toluene-, phenyl- and 4-methoxyphenylsulfinates **2a**, **2b** and **2c** provided the corresponding allylsulfones **3aa**, **3ab** and **3ac** in 47%, 58% and 41% isolated yield. Sodium α-naphthylsulfinate gave only degradation products. Electron-poor arylsulfinates reacted too, although their coupling was much more sluggish. For example, only 57% conversion was measured by quantitative ^{1}H NMR analysis after 72 h of reaction of sodium 4-nitrobenzenesulfinate **2f**. Nevertheless, the desired allylsulfones **3ae** and **3af** could be obtained with 11% yield and 37% yield, respectively. Sodium 4-bromophenylsulfinate **2g** gave the corresponding allylsulfone **3ag** with 45% isolated yield. Worthy of note, the C–Br bond was not affected. Sodium thiophene-2-sulfinate gave only degradation products.

Alkylsulfinates proved also to be reactive. Indeed, reaction between sodium propane-2-sulfinate **2h**, or sodium cyclopropanesulfinate **2i**, gave allylsulfones **3ah** and **3ai** in 22% and 51% yield, respectively. Sodium methylsulfinate, sodium camphorsulfinate and sodium benzylsulfinate, gave no conversion or degradation products. Therefore, cyclopropylsulfinate **2i** turned out to be the only alkylsulfinate able to give the coupling. The reaction was also totally ineffective with very electron-poor sulfinates such as sodium trifluoromethylsulfinate (Langlois' reagent).

On the basis of previous reports on Pd-catalyzed allylic C–H activation reactions, a tentative mechanism is proposed (Scheme 2).[11e,12d,14] After coordination of the alkene to the Pd(II) catalyst, an allylic proton is abstracted via a likely concerted

Table 1. Optimization of the reaction conditions.[a]



1a **2a** **3aa**

entry[a]	PdX_2	Oxidant	Solvent	Yield **3aa** [%][b]	entry[a]	PdX_2	Oxidant	Solvent	Yield **3aa** [%][b]
1	$Pd(OAc)_2$	2,6-DMBQ	CH_3CN	42	10	$Pd(OAc)_2$	BQ	CH_3CN	3
2	$Pd(OAc)_2$	2,6-DMBQ	EtCN	35[c]	11	$Pd(OAc)_2$	DDQ	CH_3CN	<2
3[d]	$Pd(OAc)_2$	2,6-DMBQ	DMF	13	12	$Pd(OAc)_2$	DQ	CH_3CN	10
4[d]	$Pd(OAc)_2$	2,6-DMBQ	DMSO	13	13	$Pd(OAc)_2$	2,5-DMBQ	CH_3CN	36
5	$Pd(OAc)_2$	2,6-DMBQ	THF	12	14	$Pd(OPiv)_2$	2,6-DMBQ	CH_3CN	12
6	$Pd(OAc)_2$	2,6-DMBQ	1,4-dioxane	2	15	$Pd(TFA)_2$	2,6-DMBQ	CH_3CN	26
7	$Pd(OAc)_2$	2,6-DMBQ	MTBE	<2	16	$Pd(acac)_2$	2,6-DMBQ	CH_3CN	42
8	$Pd(OAc)_2$	2,6-DMBQ	HFIP	26	17	$PdCl_2(CH_3CN)_2$	2,6-DMBQ	CH_3CN	23
9	$Pd(OAc)_2$	2,6-DMBQ	MeCN/MeOH (4:1)	29	18	$PdCl_2$	2,6-DMBQ	CH_3CN	15
					19[e]	$Pd(acac)_2$	2,6-DMBQ	CH_3CN	47

[a] Reaction conditions: allylbenzene **1a** (0.2 mmol), sodium *p*-toluenesulfinate **2a** (2.0 equiv.), $Pd(OAc)_2$ (10 mol%), 2,6-DMBQ (2.0 equiv.), CH_3CN (0.2 M) were heated at 80 °C in a sealed tube under Ar. [b] Yields were determined by quantitative ^{1}H NMR analysis, using 1,4-dinitrobenzene as an internal standard. [c] Allylsulfone **3aa** was obtained with 33% NMR yield when heating at 110 °C instead of 80 °C. [d] The reaction was finished after 45 h. [e] CH_3CN (0.66 M); 2,6-DMBQ: 2,6-dimethyl-1,4-benzoquinone; BQ: 1,4-benzoquinone; DDQ: 2,3-dichloro-5,6-dicyano-1,4-benzoquinone; DQ: duroquinone (2,3,5,6-tetramethyl-1,4-benzoquinone); 2,5-DMBQ: 2,5-dimethyl-1,4-benzoquinone; acac: acetylacetonate.

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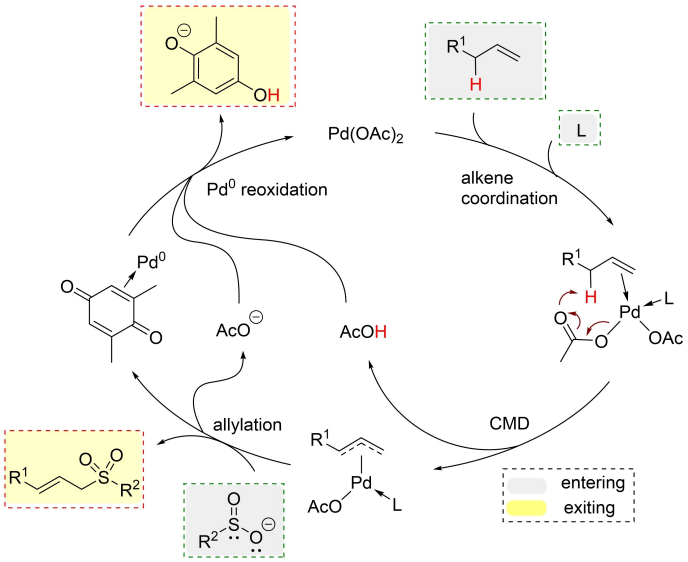


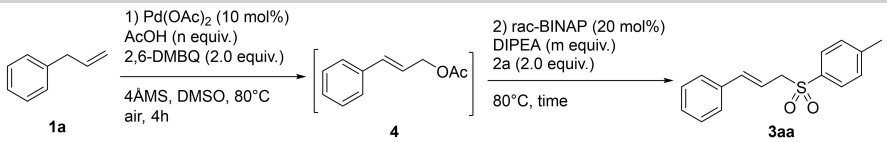
Scheme 2. Proposed mechanism for the direct Pd-catalyzed allylic C–H sulfonylation of terminal alkenes. L = 2,6-DMBQ.

metalation deprotonation (CMD) mechanism, and the thus generated η^3-allylpalladium intermediate undergoes substitution by the sulfinate anion. Finally, after product decoordination, the generated Pd(0) complex, is reoxidized by the coordinated benzoquinone.

Given the moderate yields associated to some of the direct C–H sulfonylations, we decided to study an alternative protocol. Accordingly, on the basis of our previous work on the amination of but-3-enoic acids,[12h] we envisioned to perform a sequential one-pot doubly Pd-catalyzed procedure consisting in an initial oxidative Pd(II)-catalyzed allylic C–H alkene acetoxylation, followed by a redox-neutral Pd(0)-catalyzed allylic sulfonylation. The major challenge of this process consists in the use of the same palladium source for both the transformations. In the event, reacting allylbenzene (1.0 equiv.) with acetic acid (10.0 equiv.), in the presence of 2,6-DMBQ (2.0 equiv.) and $Pd(OAc)_2$ (10 mol%), in DMSO (0.2 M) at 80 °C gave the corresponding allylic acetate, which was not isolated (TLC verification). Subsequent in situ addition of *rac*-BINAP (20 mol%), DIPEA (11.5 equiv.), and sodium *p*-toluenesulfinate (2.0 equiv.) with further stirring at 80 °C under air gave the desired allylsulfinate **3 aa** in 82 % yield (Table 2, entry 1). When 10.0 equivalents of both acetic acid and base were used, the allylsulfone **3 aa** was obtained with a similar yield (83 %), but in a much longer reaction time for the second step (Table 2, entry 2). Reducing this amount to 7.0, 5.0 or 3.0 equivalents resulted in generally longer reaction times for the second step accompanied with lower yields (Table 2, entries 3–5). We thus decided to keep our first conditions for the one-pot sequential protocol (Method B).

With the new one-pot sequential protocol in hand for the model coupling **1 a** + **2 a**, we re-evaluated the sulfonylation of allylbenzene with the sulfinate salts previously used in the direct procedure (method A). The couplings turned out to be equally efficient with electron-rich sulfinates **2 a**–**2 c** as well as with electron poor sulfinate **2 e**, affording satisfactory isolated

Table 2. Optimization attempt for the one-pot sequential C–H acetoxylation/sulfonylation.[a]



1a 4 3aa

entry	AcOH (n equiv.)	DIPEA (m equiv.)	Time step 2 [h]	Yield **3 aa** [%][b]
1	10.0	11.5	25	82
2	10.0	10.0	48	83
3	7.0	7.0	38	64
4	5.0	5.0	38	56
5	3.0	3.0	66	48

[a] Reaction conditions: allylbenzene **1 a** (0.2 mmol), $Pd(OAc)_2$ (10 mol%), AcOH (n equiv.), 2,6-DMBQ (2.0 equiv.), 4 Å MS (50 mg), DMSO (0.2 M) were heated at 80 °C in a sealed tube for 4 h (until complete conversion) then were introduced DIPEA (m equiv.), sodium *p*-toluenesulfinate **2 a** (2.0 equiv.), *rac*-BINAP (20 mol%) and the mixture was heated at 80 °C until complete conversion of the cinnamylacetate intermediate. [b] Yields were determined by quantitative ^{1}H NMR analysis, using 1,4-dinitrobenzene as an internal standard; 2,6-DMBQ: 2,6-dimethyl-1,4-benzoquinone; DIPEA: N,N-di-*iso*propylethylamine; BINAP: 2,2′-bis(diphenylphosphino)-1,1′-binaphthyl.

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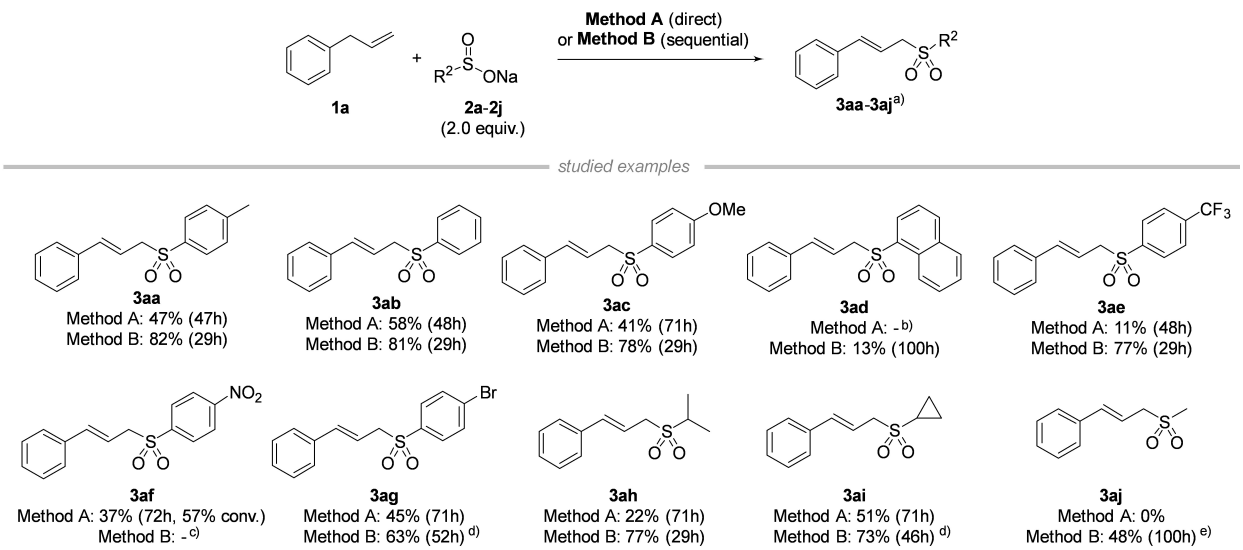
yields, ranging from 77% to 82% (Scheme 3). Such increases in yield when switching from Method A to Method B with reduced reaction times underscore the synthetic importance of the sequential one-pot procedure. However, with this protocol sodium α-naphtylsulfinate **2d** gave a low yield of cinnamylsulfone **3ad**, and sodium 4-nitrobenzenesulfinate **2f** did not sulfonylate the intermediate cinnamylacetate **4**, which was recovered in 75% yield. When utilizing 2.0 equivalents of sodium 4-bromophenylsulfinate **2g**, only a partial conversion of intermediate cinnamylacetate **4** was detected (40% recovered) and the allylsulfone **3ag** was isolated with 45% yield. Such a low reactivity might be due to competitive oxidative addition of the carbon-bromine bond of the sulfinate to Pd(0). However, increasing the amount of sulfinate **2g** to 3.0 equivalents, the second step of the sequential procedure was complete and allylsufone **3ag** was isolated with 63% yield. Alkylsulfinates **2h**, **2i** and **2j** were also relatively efficient with this one-pot protocol, affording the corresponding allylsulfones **3ah**, **3ai** and **3aj** in 77%, 73% and 48% yield, respectively (Scheme 3). In the case of sodium cyclopropylsulfinate **2i**, 3.0 equivalents were also needed to obtain a satisfactory yield of cinnamylsulfone **3ai**, as only 28% yield was obtained when using 2.0 equivalents of the sulfinate. Also, 4.4 equivalents of sodium methylsulfinate **2j** were necessary to obtain cinnamylmethylsulfone **3aj**.

We next studied the influence of the nature of the alkene on the reaction outcome with the two sets of conditions. For this study, sodium benzenesulfinate **2b** was chosen as the reaction partner, because it is the nucleophile that gave the best results and the corresponding allylsulfones are synthetic intermediates for Julia olefinations. Thus, submission of the electron-rich allylarenes **1b** and **1c** to the coupling with sodium benzenesulfinate provided the corresponding allylsulfones **3bb** and **3cb** in 41% and 42% yield by Method A, and 48% and 44% yield by Method B (Scheme 4), respectively. *Ortho*-substituted allylbenzene **1d** gave allylsulfone **3db** in 40% yield with Method A, while no product was observed when using the sequential procedure of Method B. The phenolic derivatives benzyleugenol **1e** and 2-*O*-benzylallylbenzene **1f** gave the corresponding allylsulfones **3eb** and **3fb** in 33% and 24% yields with Method A, and in 67% and 42% yields with Method B. The electron-poor allylarene **1g** bearing a *para*-trifluoromethyl substituent afforded the expected allylsulfone **3gb** in 20% yield with Method A and in 23% yield with Method B (Scheme 4).[16]

We next evaluated terminal aliphatic alkenes in the developed reaction conditions (Scheme 5). Undec-1-ene **1h**, dec-1-ene **1i**, non-1-ene **1j**, oct-1-ene **1k**, and hex-1-ene **1l** were engaged in the presence of sodium benzenesulfinate **2b**, providing with total regioselectivity the linear allylsulfones **3hb**–**3lb** with yields ranging between 30% and 45% with Method A. In most cases, the pure (*E*)-configurated allylsulfones were isolated, although minor amounts of the (*Z*) isomers could be detected in the ^{1}H NMR spectra of the crude reaction products. Only in the case of allylsulfone **3jb**, both (*E*)- and (*Z*)-isomers could be isolated separately.

Unfortunately, with these aliphatic substrates the reaction conditions of Method B do not allow the generation of the intermediate allylacetate. Since the Pd(II)-catalyzed C–H allylic acetoxylation of terminal alkenes has been reported,[11e] we decided to adopt these reaction conditions



Scheme 3. Evaluation of the reactivity of aryl- and alkylsulfinates in the developed reaction conditions (Methods A and B). [a] Typical reaction conditions: Method A: allylbenzene **1a** (0.5 mmol), **2a**–**2j** (2.0 equiv.), $Pd(acac)_2$ (10 mol%), 2,6-DMBQ (2.0 equiv.), CH_3CN (0.66 M), 80 °C in a sealed tube under Ar, 48–72 h. Method B: allylbenzene **1a** (0.5 mmol), $Pd(OAc)_2$ (10 mol%), AcOH (10.0 equiv.), 2,6-DMBQ (2.0 equiv.), 4 Å MS (50 mg), DMSO (0.2 M) were heated at 80 °C under air in a sealed tube for 4 h (until complete conversion of allylbenzene into the allylic acetate, TLC check). Then DIPEA (11.5 equiv.), **2a**–**2j** (2.0 equiv.), *rac*-BINAP (20 mol%) were introduced, and the mixture was heated at 80 °C until disappearance (TLC check) of the cinnamylacetate **4** intermediate. Reaction time for Method B corresponds to the sum of the reaction times for the two steps. Indicated yields refer to isolated, after silica gel column chromatography purification. [b] Only degradation products were formed. [c] No allylsulfone was formed. The intermediate cinnamylacetate **4** was obtained with 75% yield (measured by quantitative ^{1}H NMR with 1,4-dinitrobenzene as internal standard). [d] 3.0 equivalents of sodium 4-bromophenylsulfinate **2f** or sodium cyclopropylsulfinate **2i** were used. [e] 4.4 equivalents of sodium methylsulfinate **2j** were used.

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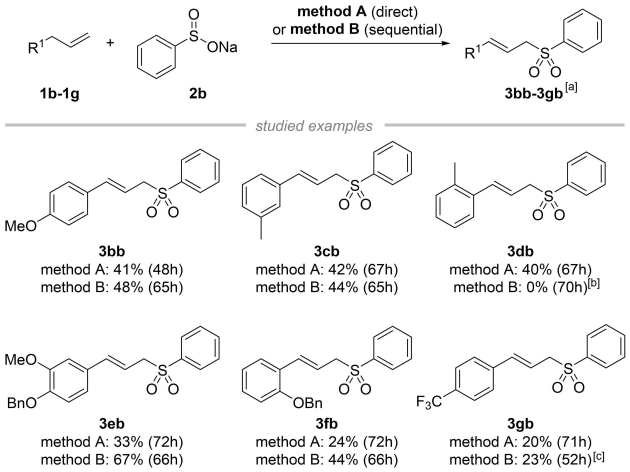
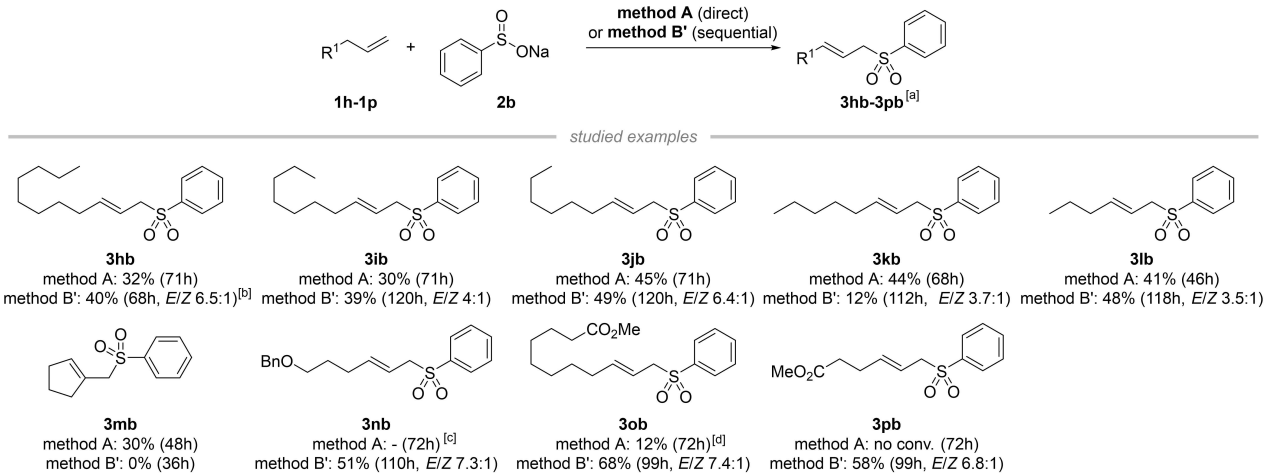


Scheme 4. Evaluation of allylarenes as substrates in the optimized reaction conditions.[a] Typical reaction conditions: **Method A**: allyl-derivative **1 b**–**1 g** (0.5 mmol), **2 b** (2.0 equiv.), $Pd(acac)_2$ (10 mol%), 2,6-DMBQ (2.0 equiv.), CH_3CN (0.66 M), 80 °C in a sealed tube, 48–72 h. **Method B**: allyl-derivative **1 b**–**1 g** (0.5 mmol), $Pd(OAc)_2$ (10 mol%), AcOH (10.0 equiv.), 2,6-DMBQ (2.0 equiv.), 4 Å MS (50 mg), DMSO (0.2 M) were heated at 80 °C under air in a sealed tube until complete conversion of the allyl-derivative. Then DIPEA (11.5 equiv.), sodium benzenesulfinate **2 b** (2.0 equiv.), *rac*-BINAP (20 mol%) were introduced, and the mixture was heated at 80 °C until complete conversion of the allylacetate intermediate. Reaction time for Method B corresponds to the sum of the reaction times for the two steps. Indicated yields refer to isolated, after silica gel column chromatography purification. [b] (*E*)-4-methylcinnamyl acetate was obtained with 26% yield as measured by ^{1}H quantitative NMR with 1,4-dinitrobenzene as internal standard. [c] The cinnamylsulfone **3 gb** was obtained with 67% NMR yield, as measured by ^{1}H quantitative NMR with 1,4-dinitrobenzene as internal standard.

as the first step of Method B. In the event, following a variant of White's protocol, undec-1-ene **1 h** was treated with $Pd(OAc)_2$ (10 mol%), in the presence of phenylvinylsulfoxide (10 mol%) BzOH (10.0 equiv.), benzoquinone (2.0 equiv.), and 4 Å MS (50 mg), in 1,4-dioxane (0.2 M). After 45 h stirring at 43 °C, treatment of the resulting branched allylic allylbenzoate **5** (TLC and ^{1}H NMR verification) with DIPEA (11.5 equiv.), sodium benzenesulfinate **2 b** (2.0 equiv.), *rac*-BINAP (20 mol%) with heating at 80 °C, afforded the desired allylsulfone **3 hb** in 43% NMR yield (Scheme 6). On the other hand, use of 1,2-bis(phenylsulfinyl)ethane (10 mol%) instead of phenylvinylsulfoxide, did not allow the formation of the allyl sulfone, giving only allylbenzoate **5** in 48% spectroscopic yield. We speculate that the disulfoxide ligand may prevent the phosphine promoted Pd(II)-to-Pd(0) reduction, thus halting the second, Pd(0)-catalyzed, step.

With these new conditions in hand, aliphatic terminal alkenes **1 h**–**1 p** were evaluated for the synthesis of the corresponding allylsulfones **3 hb**–**3 pb** (Scheme 5). Besides allylsulfone **3 hb** which was isolated with 40% isolated yield, aliphatic allylsulfones **3 ib**, **3 jb**, **3 kb** and **3 lb** were obtained from dec-1-ene **1 i**, non-1-ene **1 j**, oct-1-ene **1 k** and hex-1-ene **1 l** respectively with 39%, 49%, 12% and 48% isolated yield. Here again, *E*/*Z* mixtures of isomers were detected in the NMR spectra of the crude reaction products, the (*E*)-isomers being always the major ones.

Methylenecyclopentane **1 m** could also be converted into allylsulfone **3 mb** with Method A in a moderate 30% yield, while Method B and B′ failed. More functionalized aliphatic alkenes such as benzylether **1 n** and esters **1 o** and **1 p** gave no or trace amounts of sulfonylated product with Methods A or B. Besides, Method B′ allowed to obtain the corresponding allylsulfones **3 nb**, **3 ob**, and **3 pb** and in 51%, 68% and 58% yields, respectively. In all these cases, *E*/*Z* mixtures were constantly obtained, with the (*E*)-isomer prevailing. This protocol, though requiring a long reaction time (4-5 days), is



Scheme 5. Evaluation of aliphatic terminal alkenes as substrates in the optimized reaction conditions. [a] Typical reaction conditions: **Method A**: allyl-derivative **1 h**–**1 p** (0.5 mmol), **2 b** (2.0 equiv.), $Pd(acac)_2$ (10 mol%), 2,6-DMBQ (2.0 equiv.), CH_3CN (0.66 M), 80 °C in a sealed tube, 48–72 h. **Method B′**: allyl-derivative **1 h**–**1 p** (0.2 or 0.5 mmol), $Pd(OAc)_2$ (10 mol%), phenylvinylsulfoxide (10 mol%), BzOH (10.0 equiv.), BQ (2.0 equiv.), 4 Å MS (50 mg), 1,4-dioxane (0.2 M) were heated at 43 °C under air in a sealed tube until complete conversion of the allyl-derivative (48–72 h). Then, DIPEA (11.5 equiv.), sodium benzenesulfinate **2 b** (2.0 equiv.), *rac*-BINAP (20 mol%) were introduced, and the mixture was heated at 80 °C until complete conversion of the allylbenzoate intermediate (usually 48 h). Reaction time for Method B′ corresponds to the sum of the reaction times for the two steps. Indicated yields refer to isolated, after silica gel column chromatography purification. [b] *E*/*Z* ratios were calculated on the ^{1}H-NNR spectra of the crude reaction mixtures. [c] only degradation products were formed. [d] Conversion was 40% (as measured by quantitative ^{1}H NMR using 1,4-dinitrobenzene as internal standard) after 72 h of reaction.

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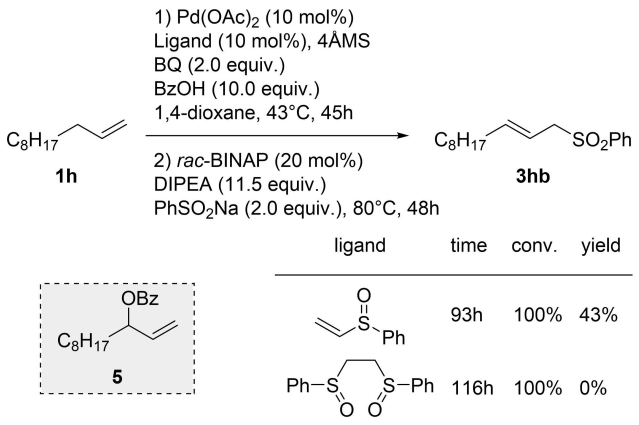


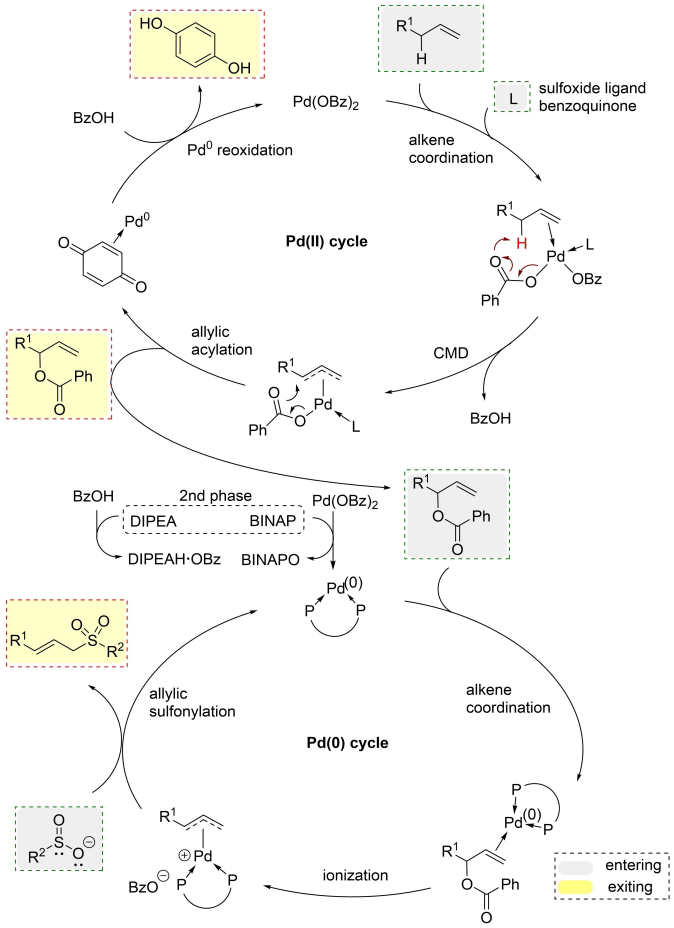
Scheme 6. Adapted sequential conditions for the reaction of undecene **1 h** (Method B').

to date the only way to afford such allylsulfones via allylic C–H functionalization.[17]

The mechanism associated to Method B' is expected to entail two different, but connected, catalytic cycles. Coordination of the terminal alkene and of the sulfoxide ligand to the palladium atom of the in situ formed palladium dibenzoate generates the corresponding η^3-allylpalladium complex via a likely CMD mechanism. Following inner sphere benzoate ligand transfer to the internal terminus of the π-complexed allyl fragment generates the branched allylic benzoate and BQ-complexed Pd(0), which regenerates palladium dibenzoate.[11e,14a] Once the formation of the allylic benzoate is complete, addition of DIPEA and *rac*-BINAP to the reaction mixture sets the stage for the second catalytic cycle. Indeed, the amine quenches the excess of benzoic acid making the corresponding salt, while the diphosphine reduces[18] the palladium diacetate and complexes the thus generated Pd(0) via κ^2-coordination. After coordination of the alkene function of the allylic benzoate to the Pd(0) complex, a new, ionic, η^3-allylpalladium complex is formed. This latter is intercepted by the sulfinate anion, which generates the allylic sulfone product and regenerates the Pd(0) complex (Scheme 7).

Conclusion

In summary, we developed two distinct protocols for the preparation of allylsulfones from commercially available alkenes through allylic C–H activation. The first method consists in the palladium-catalyzed direct allylic C–H sulfonylation of terminal alkenes, while the second procedure deals with a one-pot sequential Pd(II)-catalyzed allylic C–H acetoxylation, followed by a Pd(0)-catalyzed sulfonylation. While the first protocol is more straightforward, the second one gave often higher yields with a broader substrate scope, yet allowing to use the same palladium pre-catalyst for the two steps. A plausible mechanism is proposed in both cases. Future work will be dedicated to the improvement of the



Scheme 7. Proposed mechanism for the sequential Pd-catalyzed allylic C–H sulfonylation of terminal alkenes according to Method B'.

above studied protocols as well as the in situ further reaction of the resulting allylsulfones.

Experimental Section

General procedure for direct allylic C–H sulfonylation of alkenes (Method A): An ace pressure tube equipped with a magnetic stirrer was charged with 15.2 mg (0.05 mmol, 10 mol%) of palladium(II) acetylacetonate, 136 mg (1.0 mmol, 2.0 equiv.) of 2,6-dimethyl-1,4-benzoquinone and the sulfinate **2 a**–**2 j** (1.0 mmol, 2.0 equiv.). The tube was placed under vacuum and then backfilled with argon. The vacuum/argon cycles were repeated twice and 0.75 mL of distilled acetonitrile (0.66 M) was introduced. To this suspension was introduced the alkene **1 b**–**1 q** (0.5 mmol, 1.0 equiv.) and the mixture was heated to 80 °C under stirring until conversion was complete as checked by TLC. The mixture was then cooled to rt and filtered over a pad of silica gel with 50 mL of ethyl acetate. The filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel to give the desired products.

General procedure for one-pot sequential allylic C–H sulfonylation of allylarenes (Method B): An ace pressure tube equipped with a magnetic stirrer was charged with 11.2 mg (0.05 mmol, 10 mol%) of palladium(II) acetate, 136.2 mg (1.0 mmol, 2.0 equiv.)

of 2,6-dimethylbenzo-1,4-quinone and 50 mg of 4 Å molecular sieves. The solids were suspended in 1.5 mL of anhydrous DMSO and 0.29 mL (5.0 mmol, 10.0 equiv.) of acetic acid was introduced followed by the alkene **1b**–**1g** (0.5 mmol, 1.0 equiv.). The mixture was heated to 80 °C until complete conversion of the alkene was reached as checked by TLC. The mixture was cooled to rt and 62.0 mg (0.1 mmol, 20 mol%) of *rac*-BINAP followed by 1.0 mL (7.25 mmol, 11.5 equiv.) of N,N-diisopropylethylamine were added to the reaction mixture. The sulfinate **2a**–**2j** (1.0 mmol, 2.0 equiv.) was then introduced and the ace pressure tube was closed. The reaction mixture was then heated to 80 °C until complete conversion of the intermediate allylacetate was seen by TLC. The mixture was then cooled to rt and filtered over a pad of silica gel with 50 mL of ethyl acetate to remove the salts. The filtrate was placed into a separatory funnel and washed with 50 mL of water. The aqueous layer was extracted with 2× 20 mL of ethyl acetate. The combined organic layers were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel to give the desired products.

General procedure for one-pot sequential allylic C–H sulfonylation of terminal aliphatic alkenes (Method B'): An ace pressure tube equipped with a magnetic stirrer was charged with 4.5 mg (0.02 mmol, 10 mol%) of palladium(II) acetate, 2.7 μL (0.02 mmol, 10 mol%) of phenylvinylsulfoxide and 43.3 mg (0.4 mmol, 2.0 equiv.) of 1,4-benzoquinone. The solids were suspended in 0.6 mL of anhydrous 1,4-dioxane and 244.2 mg (2.0 mmol, 10.0 equiv.) of benzoic acid was introduced followed by the alkene **1h**–**1q** (0.2 mmol, 1.0 equiv.). The mixture was heated to 43 °C until complete conversion of the alkene was reached as checked by TLC or ^{1}H NMR (usually 66–72 h). The mixture was cooled to rt and 25.0 mg (0.04 mmol, 20 mol%) of *rac*-BINAP followed by 0.4 mL (2.3 mmol, 11.5 equiv.) of N,N-diisopropylethylamine were added to the reaction mixture. To this mixture was introduced 65.4 mg (0.4 mmol, 2.0 equiv.) of Sodium benzenesulfinate **2b** and the sealed tube was closed. The reaction mixture was then heated to 80 °C until complete conversion of the intermediate allylbenzoate was seen by TLC. The mixture was then cooled to rt and filtered over a pad of silica gel with 25 mL of ethyl acetate to remove the salts. The filtrate was concentrated under reduced pressure and the residue was purified by flash column chromatography on silica gel to give the desired products.

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Conflict of Interest

The authors declare no conflict of interest.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Keywords: allylsulfones · C–H activation · one-pot sequential reactions · palladium catalysis · sulfonylation

[1] N.-W. Liu, S. Liang, G. Manolikakes, *Synthesis* **2016**, *48*, 1939–1973.
[2] B. M. Trost, *Bull. Chem. Soc. Jpn.* **1988**, *61*, 107–124.
[3] A. El-Awa, M. N. Noshi, X. Mollat du Jourdin, P. L. Fuchs, *Chem. Rev.* **2009**, *109*, 2315–2349.
[4] a) M. Julia, J.-M. Paris, *Tetrahedron Lett.* **1973**, *14*, 4833–4836; b) J.-B. Baudin, G. Hareau, S. A. Julia, O. Ruel, *Tetrahedron Lett.* **1991**, *32*, 1175–1178; For a recent review, see: c) P. R. Blakemore, *J. Chem. Soc. Perkin Trans. 1* **2002**, 2563–2585.
[5] a) P. R. Blakemore, W. J. Cole, P. J. Kocieński, A. Morley, *Synlett* **1998**, 26–28; For reviews, see: b) C. Aïssa, *Eur. J. Org. Chem.* **2009**, 1831–1844; c) B. Chetterjee, S. Bera, D. Mondal, *Tetrahedron: Asymmetry* **2014**, *25*, 1–55.
[6] a) L. Ramberg, B. Bäcklund, *Arkiv Kemi, Minerat. Geol.* **1940**, *13 A*, 50 pp; b) T.-L. Chan, S. Fong, Y. Li, T.-O. Man, C.-D. Poon, *J. Chem. Soc. Chem. Commun.* **1994**, 1771–1772; c) X.-P. Cao, T.-Z. Chan, H.-F. Chow, J. Tu, *J. Chem. Soc. Chem. Commun.* **1995**, 1297–1299.
[7] D. A. Alonso, C. Nájera, in *Organic Reactions Vol. 72*, Ed. S. E. Denmark, John Wiley & Sons, Hoboken, **2008**, pp. 367–656.
[8] Allylsulfones can be prepared from allylic alcohols either by bromination followed by nucleophilic substitution or by acetylation of the alcohol followed by a Pd(0)-catalyzed Tsuji-Trost sulfonylation. For the latter, see for example: a) K. Inomata, T. Yamamoto, H. Kotake, *Chem. Lett.* **1981**, *10*, 1357–1360; b) E. Blart, J.-P. Genêt, M. Safi, M. Savignac, D. Sinou, *Tetrahedron* **1994**, *50*, 505–514; c) F.-X. Felpin, Y. Landais, *J. Org. Chem.* **2005**, *70*, 6441–6446.
[9] When not commercially available, functionalized allylic alcohols can be prepared efficiently in two steps from aldehydes or ketones by HWE olefination followed by reduction with DIBAL–H. See for instance: F. Carlet, G. Bertarini, G. Broggini, A. Pradal, G. Poli, *Eur. J. Org. Chem.* **2021**, 2162–2168
[10] a) X. Li, X. Xu, C. Zhou, *Chem. Commun.* **2012**, *48*, 12240–12242; b) M. Y. Chang, H. Y. Chen, H. S. Wang, *J. Org. Chem.* **2017**, *82*, 10601–10610; c) L. Liu, C. Wang, *Tetrahedron Lett.* **2022**, *88*, 153553–153557.
[11] For a selection of pioneering examples of C–O bond formation, see: a) A. Heumann, B. Åkermark, *Angew. Chem. Int. Ed.* **1984**, *23*, 453–454; *Angew. Chem.* **1984**, *96*, 443–444; b) B. Åkermark, S. Hansson, T. Rein, J. Vågberg, A. Heumann, J.-E. Bäckvall, *J. Organomet. Chem.* **1989**, *369*, 433–444; c) S. Hansson, A. Heumann, T. Rein, B. Åkermark, *J. Org. Chem.* **1990**, *55*, 975–984; d) M. S. Chen, M. C. White, *J. Am. Chem. Soc.* **2004**, *126*, 1346–1347; e) M. S. Chen, N. Prabagaran, N. A. Labenz, M. C. White, *J. Am. Chem. Soc.* **2005**, *127*, 6970–6971; f) K. J. Fraunhoffer, N. Prabagaran, L. E. Sirois, M. C. White, *J. Am. Chem. Soc.* **2006**, *128*, 9032–9033; g) D. J. Covell, M. C. White, *Angew. Chem. Int. Ed.* **2008**, *47*, 6448–6451; *Angew. Chem.* **2008**, *120*, 6548–6551; h) N. A. Vermeulen, J. H. Delcamp, M. C. White, *J. Am. Chem. Soc.* **2010**, *132*, 11323–11328.
[12] For a selection of examples for C–N bond formation, see: a) K. J. Fraunhoffer, M. C. White, *J. Am. Chem. Soc.* **2007**, *129*, 7274–7276; b) S. A. Reed, M. C. White, *J. Am. Chem. Soc.* **2008**, *130*, 3316–3318; c) G. Liu, G. Yin, L. Wu, *Angew. Chem. Int. Ed.* **2008**, *47*, 4733; d) S. A. Reed, A. R. Mazzotti, M. C. White, *J. Am. Chem. Soc.* **2009**, *131*, 11701–11706; e) G. T. Rice, M. C. White, *J. Am. Chem. Soc.* **2009**, *131*, 11707–11711; f) F. Nahra, F. Liron, G. Prestat, C. Mealli, A. Messaoudi, G. Poli, *Chem. Eur. J.* **2009**, *15*, 11078–11082; g) X. Qi, G. T. Rice, M. S. Lall, M. S. Plummer, M. C. White, *Tetrahedron* **2010**, *66*, 4816–4826; h) D. Diamante, S. Gabrieli, T. Benincori, G. Broggini, J. Oble, G. Poli, *Synthesis* **2016**, *48*, 3400–3412; i) R. Ma, M. C. White, *J. Am. Chem. Soc.* **2018**, *140*, 3202–3205.
[13] For a selection of examples for C–C bond formation, see: a) A. J. Young, M. C. White, *J. Am. Chem. Soc.* **2008**, *130*, 14090–14091; b) S. Lin, C.-X. Song, G.-X. Cai, W.-H. Wang, Z.-J. Shi, *J. Am. Chem. Soc.* **2008**, *130*, 12901–12903; c) A. J. Young, M. C. White, *Angew. Chem. Int. Ed.* **2011**, *50*, 6824–6827; *Angew. Chem.* **2011**, *123*, 6956–6959; d) J. M. Howell, W. Liu, A. J. Young, M. C. White, *J. Am. Chem. Soc.* **2014**, *136*, 5750–5754;

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doi.org/10.1002/ejoc.202201493

e) W. Liu, S. Z. Ali, S. E. Ammann, M. C. White, *J. Am. Chem. Soc.* **2018**, *140*, 10658–10662.
[14] For recent reviews, see: a) F. Liron, J. Oble, M. M. Lorion, G. Poli, *Eur. J. Org. Chem.* **2014**, 5863–5883; b) R. A. Fernandes, J. L. Nallasivam, *Org. Biomol. Chem.* **2019**, *17*, 8647–8672.
[15] Several other oxidants such as silver acetate, copper diacetate, diacetoxyiodobenzene, peroxides or molecular oxygen were also tested. However, low yields were obtained in each case together with variable amounts of a desulfonylated by-product (See Supporting Information).
[16] This low isolated yield is very likely due to some problems encountered during the purification process, as the ^{1}H NMR yield was 67%.
[17] Cyclohexene was also tested with Method B, but gave no conversion.
[18] a) F. Ozawa, A. Kubo, T. Hayashi, *Chem. Lett.* **1992**, 2177–2180; b) C. Amatore, A. Jutand, A. Thuilliez, *Organometallics* **2001**, *20*, 3241–3249.

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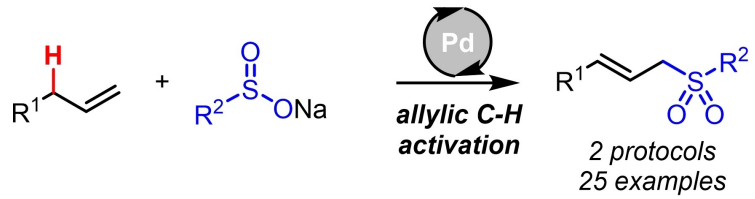

T. Chen, J. Lahbi, Prof. G. Broggini, Dr. A. Pradal, Prof. G. Poli**

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Allylsulfones through Palladium-Catalyzed Allylic C–H Sulfonylation of Terminal Alkenes

We report two distinct protocols for the preparation of allylsulfones via Pd(II)-catalyzed allylic C–H activation. While the former protocol consists of a direct Pd(II)-catalyzed oxidative C–H allylic sulfonylation in the presence of sulfinate anions, the latter involves a sequential one-pot Pd(II)-catalyzed C–H allylic acetoxylation followed by a Pd(0)-catalyzed sulfonylation.