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Reactivity of *tert*-butanesulfinamides in palladium-catalyzed allylic substitutions

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ABSTRACT

The performance of *tert*-butanesulfinamides as nitrogen nucleophiles in Pd(0)-catalyzed allylic substitution reactions has been investigated. Metalated *N*-alkyl and *N*-acetyl sulfinamides have been identified as suitable partners for the reaction with π-allyl–palladium complexes. The cross-coupling of *N*-acetyl *tert*-butanesulfinamide with 2- or 3-substituted linear allylic carbonates is achieved in the presence of $Pd(OAc)_2$ (5 mol%) and dppe (7.5 mol%) and does not require an additional base. The reaction proceeds in high yields (59–98%) to produce the corresponding *E*-configured linear allylic sulfinamides in a totally regioselective and highly diastereoselective manner. The sulfur atom remains configurationally stable throughout the allylation process, and thus the coupling products are obtained in enantiomerically pure form.

1. Introduction

The use of the chiral amine reagent *tert*-butanesulfinamide **1a** (Scheme 1) has attracted a great deal of attention over the last decade and has found applications in an increasingly growing number of research fields [1]. In the context of asymmetric synthesis, it is now a well-established tool for the preparation of chiral non-racemic amines. Rapid access to both enantiomeric forms of *tert*-butanesulfinamide, high levels of stereodiscrimination and easy removal of the sulfinyl moiety under mild acidic conditions constitute major advantages to the use of the *N*-*tert*-butanesulfinyl group as chiral auxiliary. Furthermore, *tert*-butanesulfinamides have also found promising applications in the field of asymmetric catalysis, where they have been successfully used as ligands for transition metal catalysts or organocatalysts [1].

An impressive body of work has been devoted to the preparation of elaborated enantiopure *tert*-butanesulfinamides and the area has been recently reviewed extensively [1,2]. The vast majority of synthetic approaches entails the condensation of **1a** with a carbonyl derivative and the subsequent reaction at the electrophilic carbon atom of the corresponding sulfinimine thereby produced [2]. Quite surprisingly, the complementary synthetic strategies utilizing *tert*-butanesulfinamides as chiral nitrogen nucleophiles have received far less attention [3]. Furthermore, their use as partners in metal-catalyzed amination reactions is an interesting prospect that has only been successfully exploited very recently. Arylation of *tert*-butanesulfinamide with aryl- and heteroaryl halides has been reported using Cu [4] and Pd [5] catalysts. *tert*-Butanesulfinamides have also been shown to be efficient partners for the Pd-catalyzed Wacker-type aerobic oxidative cyclization of tethered alkenes [6]. Finally, the Pd-catalyzed [3 + 2] cycloaddition of *N*-*tert*-butanesulfinimines with trimethylenemethane is as well a related process that involves a carbon–nitrogen bond formation [7].

In this context, and given the recent interest in allylic *N*-*tert*-butanesulfinamides as hybrid ligands for asymmetric catalysis [8], we have considered the use of *tert*-butanesulfinamides as nitrogen

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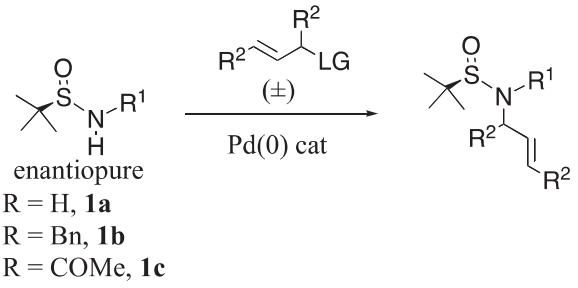


Scheme 1. Proposed strategy to prepare enantiopure allylic sulfinamides.

nucleophiles in Pd(0)-catalyzed allylic substitution reactions [9] (Scheme 1). To the best of our knowledge, the only precedent for such a transformation is that of Pyne and co-workers. These authors reported that lithiated **1a** reacts with cyclohex-2-enyl ethyl carbonate in the presence of 5 mol% [$Pd(PPh_3)_4$] to afford the corresponding sulfinamide, albeit in poor yield and diastereoselectivity [10]. Furthermore, the substitution product was described to undergo rapid hydrolysis in the presence of silica-gel. Intrigued by this reported unstability, we decided to reinvestigate this reaction using other nitrogen-substituted sulfinamides and acyclic electrophiles. Hereafter, we disclose our first findings concerning this approach.

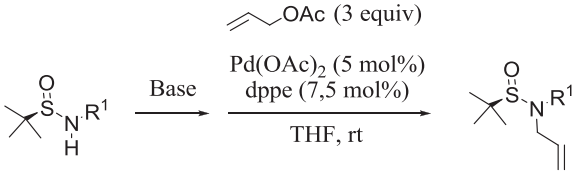
2. Results and discussion

2.1. Allylic substitution with allyl acetate

Initially, we decided to identify nucleophiles derived from *tert*-butanesulfinamide that would be well-suited to react with standard π-allyl–palladium complexes. Towards this end, we selected as archetypal reaction the allylic substitution of allyl acetate (3 equiv), using as catalytic system a combination of $Pd(OAc)_2$ (5 mol%) and dppe [1,2-bis(diphenylphosphino)ethane] (7.5 mol%) in THF (Table 1). In the presence of K_2CO_3, allylation of sulfinamides **1a** or **1b** was at most very sluggish (entries 1 and 3), thereby indicating that *N*-alkyl *tert*-butanesulfinamides are not nucleophilic enough to intercept the π-allyl complex intermediate in these conditions. By contrast, their corresponding lithium salts, obtained by treatment with 1 equiv ^{n}BuLi, took part readily in the nucleophilic substitution. For unsubstituted sulfinamide **1a**, the expected product **2a** was only obtained in 8% yield as the process was hampered by the competitive acylation reaction of the lithium salt of **1a** with the ester moiety of allyl acetate (entry 2). However, in the case of substituted sulfinamide **1b**, the allylated compound **2b** was isolated in 83% yield (entry 4). Finally, starting from acetyl-substituted pronucleophile **1c**, the allylation product **2c** was obtained in good 70–95% yields either by reacting the pre-formed lithium or sodium salts of **1c** (entries 5 and 6), or in the presence of K_2CO_3 (entry 7). For these last reaction conditions, it is likely that the carbonate base is strong enough to deprotonate **1c** (quantitatively or at least to a great extent), thereby generating *in situ* the reactive nucleophile.

Worthy of mention, the unforeseen acylation of the lithium salt of **1a** in the presence of allyl acetate led us to consider a one-pot strategy leading to the sequential acylation/allylation of *tert*-butanesulfinamide **1a** (Scheme 2). Treatment of **1a** with ^{n}BuLi, followed by the addition of methyl acetate led to the formation of the lithium salt **3** that was then engaged directly in the palladium(0)-catalyzed allylation. Product **2c** was obtained in excellent 95% yield using only a slight excess of allyl acetate.

Table 1
Pd(0)-catalyzed allylic substitution of allyl acetate by metalated sulfinamides.



Entry	Substrate	R^1	Base	Product	Yield[a]
1	**1a**	H	K_2CO_3[b]	**2a**	11%
2	**1a**	H	^{n}BuLi[c]	**2a**	8%[d]
3	**1b**	Bn	K_2CO_3[b]	**2b**	No reaction
4	**1b**	Bn	^{n}BuLi[c]	**2b**	83%
5	**1c**	COMe	^{n}BuLi[c]	**2c**	83%
6	**1c**	COMe	NaH[e]	**2c**	95%
7	**1c**	COMe	K_2CO_3[b]	**2c**	70%

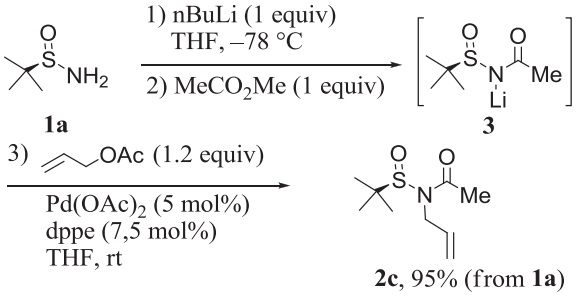
[a] Yield of isolated product after column chromatography.
[b] K_2CO_3 (3 equiv) was added to the reaction medium.
[c] Deprotonation conditions: ^{n}BuLi (1 equiv), THF, −30 °C, 0.5 h.
[d] 85% of acetylated product **2c** was also isolated.
[e] Deprotonation conditions: NaH (1 equiv), THF, 0 °C, 0.5 h.

Having identified metalated sulfinamides as competent nucleophiles for allylic substitution, we considered to use the BSA [*N*,*O*-bis(trimethyl)acetamide]/AcOK system [11] as an alternative to the discrete pre-formation of the metalated nucleophiles (Table 2). Pleasingly, sulfinamide **1a** underwent allylation with allyl acetate in refluxing THF using the $Pd(OAc)_2$/dppe catalytic system in the presence of BSA (1.1 equiv) and AcOK (10 mol%). *N*-Allyl *tert*-butanesulfinamide **2a** was isolated in 56% yield, despite the formation of 16% of *N*,*N*-diallyl *tert*-butanesulfinamide (entry 1). While no reaction was observed with benzyl-substituted sulfinamide **1b** (entry 2), efficient allylic substitution was restored in the case of the acetyl-substituted sulfinamide **1c** (entry 3).

These results suggest that the *in situ* generated *N*-(trimethylsilyl)acetamide is basic enough to deprotonate unsubstituted *tert*-butanesulfinamide **1a** and *N*-acyl-substituted **1c**, thereby efficiently generating a nucleophile suitable for the substitution to occur. Conversely, this silylated base does not metalate *N*-benzyl *tert*-butanesulfinamide **1b**.

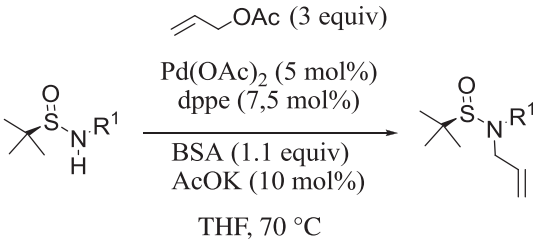
2.2. Allylic substitution with allylic carbonates

We considered next to use allylic carbonates as electrophilic partners. Given that *N*-acetyl *tert*-butanesulfinamide **1c** undergoes allylation in the presence of K_2CO_3, we reasoned that in this case an additional base might be avoided as the carbonate leaving group could be basic enough to deprotonate the starting material and thus generate the nucleophile for the coupling reaction (Scheme 3).



Scheme 2. One-pot acylation/allylation of *tert*-butanesulfinamide **1a**.

Table 2
Pd(0)-catalyzed allylic substitution of allyl acetate by sulfinamides in the presence of BSA/AcOK.

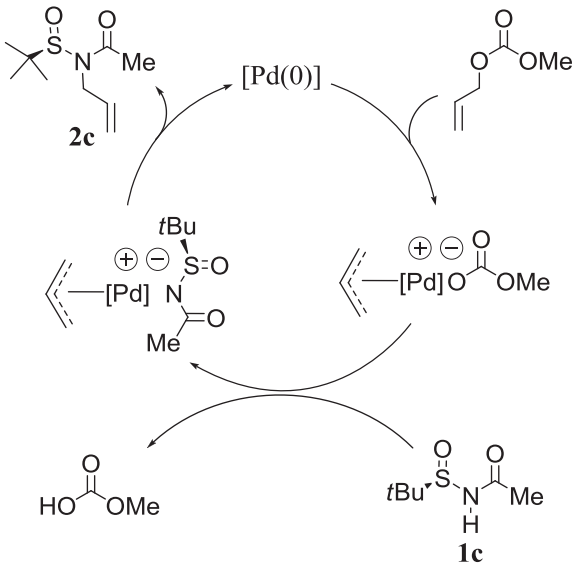


Entry	Substrate	R^1	Product	Yield[a]
1	**1a**	H	**2a**	56%[b]
2	**1b**	Bn	**2b**	0%
3	**1c**	COMe	**2c**	84%

[a] Yield of isolated product after column chromatography.
[b] 16% of *N*,*N*-diallyl *tert*-butanesulfinamide **2d** (R^1 = allyl) were also isolated.

Gratifyingly, *N*-acetyl *tert*-butanesulfinamide was found to undergo allylation in THF at 70 °C by reaction with allyl methyl carbonate in the presence of $Pd(OAc)_2$ (5 mol%) and dppe (7.5 mol%). Using only 1.2 equiv of electrophile, **2c** was isolated in 94% yield (Table 3, entry 1). Encouraged by this positive result we then studied the scope of the transformation (Table 3).

We first considered a range of primary carbonates. Under the same conditions as above, methallyl carbonate underwent allylic substitution smoothly and allylic sulfinamide **4** was isolated in 86% yield (entry 2). 1,2-Disubstituted allylic carbonates behaved efficiently, in a totally regioselective and highly diastereoselective way. In the case of 3-alkyl-substituted allyl carbonates (entries 3–6), the corresponding linear allylic sulfinamides **5**–**7** were isolated in 59–98% yield and *E*/*Z* ratio higher than 94:06 [12]. The process was stereoconvergent, as the same diastereoselectivity in favor of the *E* isomer was obtained regardless of the configuration of the starting alkene (compare entries 3,5 *vs* 4,6). A similar behavior was also observed with cinnamyl carbonate, the linear *E*-configurated allylation product **8** being isolated in 81% yield without *Z* isomer detection. By contrast, the process could not be applied to allylic



Scheme 3. Proposed mechanism for the Pd(0)-catalyzed allylic substitution of allylic carbonates by *N*-acetyl *tert*-butanesulfinamide.

carbonates incorporating 1,1′,2-trisubstituted alkenes such as prenyl carbonate (entry 8), for which no reaction was observed.

Finally, we considered the prospect of taking advantage of the *tert*-butanesulfinyl group as stereodirecting group in the reaction with racemic secondary allylic carbonates. Most disappointingly, in this case the process was hampered by a significant lack of reactivity. Out of several allyl carbonates tested, only 1,3-diphenyl-3-ethoxycarbonyloxy-propene (±)-**9** led to somewhat interesting results (Scheme 4). The best conditions, resulting from an extended screening of catalytic systems, reaction conditions and solvents (see Supporting information) consisted in the use of 3 equiv of (±)-**9** in DMF at 80 °C in the presence of $Pd(OAc)_2$ (5 mol%), dppe (7.5 mol%), and gave the substitution product **10** in 41% yield as a mixture of diastereoisomers [13].

2.3. Orthogonal deprotection of *N*-allylic *N*-acetyl *tert*-butanesulfinamide

An interesting aspect of *N*-acetyl *tert*-butanesulfinamides is the possibility to orthogonally cleave each of the nitrogen-protecting groups. As illustrated in the case of **8**, treatment with dry HCl in methanol provides the corresponding allylic acetamide **12** in excellent yield. Alternatively, cleavage of the acetyl moiety with NaOH in MeOH leads to the corresponding allylic *tert*-butanesulfinamide **11**. Therefore, from a synthetic standpoint, in the context of Pd-catalyzed allylic substitution reactions, *N*-acetyl *tert*-butanesulfinamide **1c** can thus be regarded either as a chiral equivalent of acetamide or as an equivalent of *tert*-butanesulfinamide.

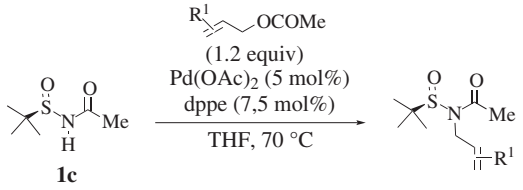
Moreover, the preparation of allylic sulfinamide **11** provided us with a means to check the stereochemical integrity of the *tert*-butanesulfinyl moiety in the Pd(0)-catalyzed allylic substitution reaction conditions. We were concerned by this issue because we reasoned that the acetyl group could stabilize a putative *O*-metalated imidate-type tautomeric form [14] of metalated **1c** and thereby possibly cause its racemization. There are only a few reports on the use of metalated enantiopure *N*-acyl *tert*-butanesulfinamides [15,16] and their configurational stability at the temperature required to perform the allylic substitution reaction is a matter that has not been addressed.

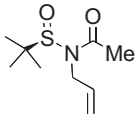
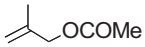
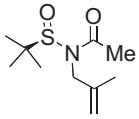
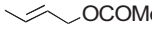
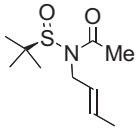
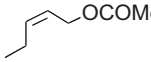
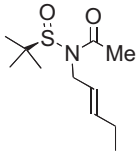
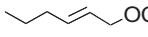
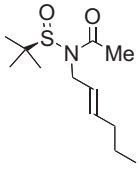
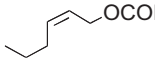
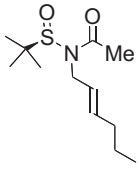
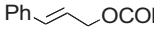
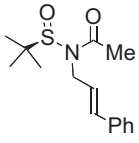
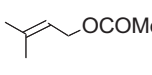
The specific optical rotation value of allylic sulfinamide **11** prepared according to our methodology was $[\alpha]_D^{25}$ −49.4 (*c* 0.89, $CHCl_3$). As the reported specific optical rotation values for enantiopure **11** are much lower and not consistent [8d,e], we decided to synthesize an enantiomerically pure sample of it from enantiopure (*R*)-*tert*-butanesulfinamide **1a** and cinnamaldehyde, following a reported protocol [8e] (Scheme 6). The $[\alpha]_D^{25}$ value of −48.7 (*c* 0.90, $CHCl_3$) measured for this sample was the same within experimental error as the one measured for that prepared using our methodology (Scheme 5). As a consequence, we can conclude that **11** deriving from the present allylation procedure is enantiomerically pure and, as a corollary, that the sulfur atom remains configurationally stable throughout the allylation process.

3. Conclusion

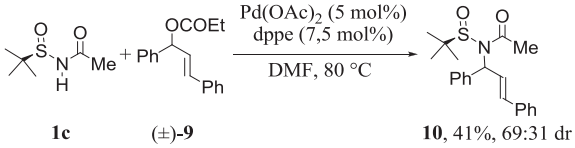
In summary, we have investigated the use of *N*-*tert*-butanesulfinamides as coupling partners in Pd(0)-catalyzed allylic substitution reactions. From a fundamental viewpoint, we have identified metal salts of *N*-substituted *tert*-butanesulfinamides as excellent nucleophiles for the reaction with π-allyl–palladium complexes. From a synthetic perspective, we have developed a mild and simple catalytic system to perform the cross-coupling of *N*-acetyl *tert*-butanesulfinamide with linear allylic carbonates in the absence of added base. The acetyl group of the coupling products

Table 3
Pd(0)-catalyzed allylic substitution of allylic carbonates by *N*-acetyl *tert*-butanesulfinamide.

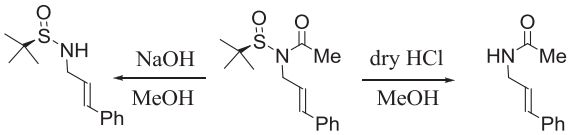


Entry	Carbonate	Product	Yield[a]	*E*/*Z* ratio
1		 **2c**	94%	–
2		 **4**	86%	–
3		 **5**	76%	94:6
4		 **6**	98%	97:3
5		 **7**	67%	96:4
6		 **7**	59%	96:4
7		 **8**	81%	>98:2
8		–	No reaction	–

[a] Yield of isolated product after column chromatography.



Scheme 4. Pd(0)-catalyzed allylic substitution of (±)-**9** by *N*-acetyl *tert*-butanesulfinamide **1c**.



$[\alpha]_D^{25} = -49.4$ (c 0.89, $CHCl_3$)

Scheme 5. Orthogonal deprotection of **8**.

can be readily removed, thereby providing a new entry to enantiopure linear allylic *tert*-butanesulfinamides that are promising hybrid ligands for asymmetric catalysis [8b–e,g]. By contrast, racemic secondary carbonates were found to be rather poor coupling partners, affording low overall yields (up to 41%) and low levels of asymmetric induction (dr up to 69:31).

4. Experimental section

Experiments involving organometallic compounds were carried out in dried glassware under a positive pressure of dry argon. All solvents were distilled to remove stabilizers and dried with a Solvent Purification System. ^{1}H NMR and ^{13}C NMR spectra were recorded with a Bruker AM 300 MHz or a Bruker AVANCE 400 spectrometer. Chemical shifts are reported in δ relative to an internal standard of residual chloroform (δ = 7.27 for ^{1}H NMR and 77.16 for ^{13}C NMR). IR spectra were recorded with an ATR diamond spectrophotometer. High resolution mass spectra (HRMS) were obtained on a Bruker MicrOTOF. $[\alpha]_D$ were measured on a JASCO P-2000 polarimeter.

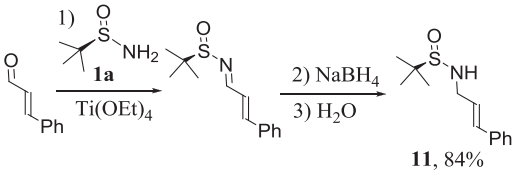
4.1. (R_S)-N-Acetyl tert-butanesulfinamide (*1c*)

Under argon, ^{n}BuLi (8.8 mL, 1.9 M in hexanes, 16.5 mmol) was added drop wise to a solution of (R_S)-*tert*-butanesulfinamide (2.0 g, 16.5 mmol) in THF (80 mL) kept at −35 °C. Methyl acetate (4.0 mL, 49.5 mmol) cooled at 0 °C was then added. The cooling bath was removed and the reaction was stirred overnight. The reaction was quenched with solid $Na_2SO_4 \cdot 10H_2O$ (5 g), filtered (solid rinsed with CH_2Cl_2) and concentrated under reduced pressure. The crude was recrystallized in THF and washed with pentane to afford (R_S)-*N-acetyl tert-butanesulfinamide* (**1c**) (2.23 g, 83%) as a white solid. Spectroscopic data were in good agreement with previously reported data [16]. $[\alpha]_D^{20}$ −379.2 (c 1.0, $CHCl_3$).

4.2. Pd(0)-catalyzed allylic substitution of allyl acetate by metalated sulfinamides, preparation of *2b* from *1b* is representative [Table 1, entry 4]

4.2.1. Metalation

Under argon, to a stirred solution of (R_S)-*N*-benzyl-2-methylpropane-2-sulfinamide [17] (**1b**) (211 mg, 1 mmol) in THF (5 mL) kept at −30 °C, ^{n}BuLi (2.1 M in hexane, 0.48 mL, 1 mmol),



$[\alpha]_D^{25} = -48.7$ (c 0.89, $CHCl_3$)

Scheme 6. Synthesis of the allylic sulfinamide **11** in enantiomerically pure form by reduction of the parent α-β unsaturated imine [8e].

was added drop wise. The reaction mixture was stirred for 30 min at 0 °C.

4.2.2. Allylic substitution

Under argon, THF (250 μL) was added to a mixture of $Pd(OAc)_2$ (11 mg, 0.05 mmol) and dppe [1,2-bis(diphenylphosphino)ethane] (30 mg, 0.075 mmol). The white slurry was stirred until it became yellow and allyl acetate (0. 33 mL, 3.0 mmol) was added. Metalated **1b** was next added via cannula and the resulting solution was stirred at rt overnight. AcOEt (10 mL) and aqueous HCl (1 M, 4 mL) were then added. The layers were separated, the aqueous one being extracted with AcOEt (×3). The combined organic layers were washed with brine (×3), dried over $MgSO_4$ and the solvents evaporated under reduced pressure. Purification by flash chromatography (AcOEt/cyclohexane = 20:80 then 30:70) afforded (*R*$_S$)-*N-allyl-N-benzyl-2-methylpropane-2-sulfinamide* (**2b**) (208 mg, 83%) as a white solid. IR (neat): 1495, 1476, 1416, 1360 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.33–7.26 (m, 5H), 5.80 (m, 1H), 5.18 (d, 1H, *J* = 10.1 Hz), 5.12 (d, 1H, *J* = 17.1 Hz), 4.32 (AB system, 1H, *J* = 17.1 Hz), 4.14 (AB system, 1H, *J* = 17.1 Hz), 3.72 (dd, 1H, *J* = 15.8, 5.7 Hz), 3.39 (dd, 1H, *J* = 15.8, 6.8 Hz), 1.20 (s, 9H); ^{13}C NMR ($CDCl_3$, 75 MHz): δ 137.4, 134.4, 129.0 (2C), 127.7, 118.3, 59.0, 51.8, 50.3, 23.5; HRMS (ESI): *m*/*z* $[M - Na]^+$ calcd for $C_{14}H_{21}NOSNa$: 274.1242; found: 274.1236.

*4.3. Pd(0)-catalyzed allylic substitution of allyl acetate by sulfinamides in the presence of BSA/AcOK, preparation of **2a** from **1a** is representative [Table 2, entry 1]*

In a sealed-tube under argon, THF (250 μL) was added to a mixture of $Pd(OAc)_2$ (11 mg, 0.05 mmol) and dppe [1,2-bis(diphenylphosphino)ethane] (30 mg, 0.075 mmol). The white slurry was stirred until it became yellow and allyl acetate (0. 33 mL, 3.0 mmol) was added. A solution of (*R*$_S$)-2-methyl-2-propanesulfinamide (**1a**) (121 mg, 1.0 mmol) in THF (5 mL) was introduced via cannula at rt. *N*,*O*-Bis(trimethyl)acetamide (BSA) (0.27 mL, 1.1 mmol) and AcOK (9.8 mg, 0.1 mmol) were added and the reaction mixture was heated at 70 °C overnight. AcOEt (5 mL) and aqueous HCl (1 M, 4 mL) were then added. The layers were separated, the aqueous one being extracted with AcOEt (×3). The combined organic layers were washed with brine (×3), dried over $MgSO_4$ and the solvents evaporated under reduced pressure. Purification by flash chromatography (AcOEt/cyclohexane gradient) afforded (*R*$_S$)-*N-allyl-2-methylpropane-2-sulfinamide* (**2a**) (90 mg, 56%) as a colorless oil. Spectroscopic data were in good agreement with previously reported data [8d,e].

*4.4. Pd(0)-catalyzed allylic substitution of allylic carbonates by N-acetyl tert-butanesulfinamide, preparation of **2c** from **1c** is representative [Table 3, entry 1]*

In a sealed-tube under argon, THF (250 μL) was added to a mixture of $Pd(OAc)_2$ (11 mg, 0.05 mmol) and dppe [1,2-bis(diphenyl phosphino)ethane] (30 mg, 0.075 mmol). The white slurry was stirred until it became yellow and allyl methyl carbonate (0.14 mL, 1.2 mmol) was added. A solution of (*R*$_S$)-*N*-acetyl-*tert*-butanesulfinamide (**1c**) (163 mg, 1.0 mmol) in THF (5 mL) was introduced via cannula at rt. The reaction mixture was heated at 70 °C overnight. AcOEt (5 mL) and aqueous HCl (1 M, 4 mL) were then added. The layers were separated, the aqueous one being extracted with AcOEt (×3). The combined organic layers were washed with brine (×3), dried over $MgSO_4$ and the solvents evaporated under reduced pressure. Purification by flash chromatography (AcOEt/cyclohexane 50:50) afforded (*R*$_S$)-*N-acetyl-N-allyl-2-methylpropane-2-sulfinamide* (**2c**) (190 mg, 94%) as a white solid. IR (neat): 2960, 1669, 1083 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, 300 K): δ 5.82 (m, 1H), 5.21–5.16 (m, 2H), 4.02 (m, 1H), 3.99 (m, 1H), 2.24 (s, 3H), 1.25 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz, 300 K): δ 172.4, 134.3, 118.0, 60.7, 41.4, 23.8, 23.3; HRMS (ESI): *m*/*z* $[M - Na]^+$ calcd for $C_9H_{17}NO_2SNa$: 226.0872; found: 226.0874. $[\alpha]_D^{20}$ +77.6 (*c* 0.92, $CHCl_3$).

4.5. (R$_S$*)-N-Acetyl-N-methylallyl-2-methylpropane-2-sulfinamide (**4**)*

IR (neat): 2969, 1668, 1072 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, 325 K): δ 4.88 (m, 1H), 4.74 (s, 1H), 3.92 (m, 1H), 3.84 (AB system, 1H, *J* = 17.2 Hz), 2.17 (s, 3H), 1.67 (s, 3H), 1.19 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz, 325 K): δ 172.3, 140.8, 111.2, 60.7, 43.8, 23.2, 22.8, 20.3; HRMS (ESI): *m*/*z* $[M - Na]^+$ calcd for $C_{10}H_{19}NO_2SNa$: 240.1029; found: 240.1025. $[\alpha]_D^{20}$ +91.2 (*c* 1.0, $CHCl_3$).

4.6. (R$_S$*)-N-Acetyl-N-((E)-but-2-enyl)-2-methylpropane-2-sulfinamide (**5**)*

Isolated as a *E*/*Z* = 94:06 mixture of isomers. IR (neat): 2963, 1673, 1088 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, 325 K) *E isomer*: δ 5.60 (dqt, 1H, *J* = 15.2, 6.4, 1.2 Hz), 4.82 (m, 1H), 3.96–3.85 (m, 2H), 2.18 (s, 3H), 1.63 (dq, 3H, *J* = 6.4, 1.2 Hz), 1.20 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz, 325 K) *E isomer*: δ 171.9, 129.1, 126.9, 60.3, 40.5, 23.3, 23.0, 17.3; HRMS (ESI): *m*/*z* $[M - Na]^+$ calcd for $C_{10}H_{19}NO_2SNa$: 240.1029; found: 240.1026. $[\alpha]_D^{20}$ +68.8 (*c* 1.0, $CHCl_3$).

4.7. (R$_S$*)-N-Acetyl-N-((E)-pent-2-enyl)-2-methylpropane-2-sulfinamide (**6**)*

Isolated as a *E*/*Z* = 97:03 mixture of isomers. IR (neat): 2965, 1677, 1092 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, 325 K) *E isomer*: δ 5.62 (dtt, 1H, *J* = 15.6, 6.4, 1.2 Hz), 5.42 (m, 1H), 4.00–3.80 (m, 2H), 2.19 (s, 3H), 2.00 (m, 2H), 1.21 (s, 9H), 0.93 (t, 3H, *J* = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, 325 K) *E isomer*: δ 171.9, 136.1, 124.7, 60.2, 40.5, 25.1, 23.3, 23.1, 13.2; HRMS (ESI): *m*/*z* $[M - Na]^+$ calcd for $C_{11}H_{21}NO_2SNa$: 254.1185; found: 254.1188. $[\alpha]_D^{20}$ +71.9 (*c* 1.0, $CHCl_3$).

4.8. (R$_S$*)-N-Acetyl-N-((E)-hex-2-enyl)-2-methylpropane-2-sulfinamide (**7**)*

Isolated as a *E*/*Z* = 96:04 mixture of isomers. IR (neat): 2958, 1675, 1091 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz, 325 K) *E isomer*: δ 5.58 (m, 1H), 5.42 (m, 1H), 4.00–3.85 (m, 2H), 2.18 (s, 3H), 1.97 (m, 2H), 1.34 (m, 2H), 1.21 (s, 9H), 0.84 (t, 3H, *J* = 7.6 Hz); ^{13}C NMR ($CDCl_3$, 100 MHz, 325 K) *E isomer*: δ 171.9, 134.4, 125.8, 60.2, 40.5, 34.1, 23.3, 23.0, 22.1, 13.4; HRMS (ESI): *m*/*z* $[M - Na]^+$ calcd for $C_{12}H_{23}NO_2SNa$: 268.1342; found: 268.1347. $[\alpha]_D^{20}$ +68.6 (*c* 1.1, $CHCl_3$).

4.9. (R$_S$*)-N-Acetyl-N-((E)-cinnamyl)-2-methylpropane-2-sulfinamide (**8**)*

Isolated as a *E*/*Z* >98:02 mixture of isomers. 7.35–7.14 (m, 5H), 6.52 (d, *J* = 16.0 Hz, 1H), 6.17 (dt, *J* = 16.0, 6.1 Hz, 1H), 4.24–4.08 (m, 2H), 2.24 (s, 3H), 1.25 (s, 9H); ^{13}C NMR ($CDCl_3$, 100 MHz, 325 K) *E isomer*: δ 172.0, 136.7, 133.6, 128.7, 127.9, 126.6, 125.6, 60.6, 40.9, 29.8, 23.6, 23.3. HRMS (ESI): *m*/*z* $[M - Na]^+$ calcd for $C_{15}H_{21}NO_2SNa$: 302.1185; found: 302.1187. $[\alpha]_D^{20}$ +32.6 (*c* 1.1, $CHCl_3$).

4.10. (R$_S$*)-N-Acetyl-N-((E)-1,3-diphenylallyl)-2-methylpropane-2-sulfinamide (**10**)*

In a sealed-tube under argon, DMF (250 μL) was added to a mixture of $Pd(OAc)_2$ (14 mg, 0.06 mmol) and dppe [1,2-bis(diphenylphosphino)ethane] (36 mg, 0.09 mmol). The white slurry was stirred until it became yellow and (±)-1,3-diphenyl-3-ethoxycarbonyloxy-propene **9** (1.03 g, 3.66 mmol) was added. A

solution of (*R*)-*N*-acetyl-*tert*-butanesulfinamide (**1c**) (200 mg, 1.22 mmol) in DMF (5 mL) was introduced via cannula at rt. The reaction mixture was heated at 80 °C for 6 h. AcOEt (5 mL) and water (4 mL) were then added. The layers were separated, the aqueous one being extracted with AcOEt. The combined organic layers were washed with water and brine, dried over $MgSO_4$ and the solvents evaporated under reduced pressure. Purification by flash chromatography (AcOEt/cyclohexane 20:80) afforded the title compound (**10**) as a mixture of diastereoisomers (dr = 68:32) as a yellow oil (192 mg, 44%). ^{1}H NMR ($CDCl_3$, 400 MHz, 325 K): δ 7.52–7.21 (m, 10H), 7.00 (dd, $1H_{minor}$, J = 16.4, 8.4 Hz), 6.75–6.74 (m, $2H_{major}$), 6.62 (d, $1H_{minor}$, J = 16.4 Hz), 5.78 (t, $1H_{major}$, J = 2.8 Hz), 5.68 (d, $1H_{minor}$, J = 8.4 Hz), 2.35 (s, $3H_{major}$), 2.17 (s, $3H_{minor}$), 1.38 (s, $9H_{minor}$), 1.22 (s, $9H_{major}$); ^{13}C NMR ($CDCl_3$, 100 MHz, 325 K): δ 172.4, 140.8, 139.7, 137.0, 136.6, 135.5, 134.0, 130.1, 128.9, 128.6, 128.5, 128.3, 128.2, 128.0, 127.8, 127.7, 127.2, 127.1, 126.9, 126.8, 126.6, 61.0, 60.5, 57.1, 55.4, 25.0, 24.8, 23.5, 23.2. HRMS (ESI): m/z $[M - Na]^+$ calcd for $C_{21}H_{25}NO_2SNa$: 378.1498; found: 378.1502.

4.11. (R_S)-*N*-(Cinnamyl)-2-methylpropane-2-sulfinamide (**11**)

In a round-bottom flask, to a solution of (R_S)-*N*-acetyl-*N*-((*E*)-cinnamyl)-2-methylpropane-2-sulfinamide (**8**) (100 mg, 0.36 mmol) in MeOH (5 mL) was added NaOH (43.2 mg, 1.08 mmol). The reaction mixture was refluxed for 4 h and then cooled. AcOEt (5 mL) and aqueous HCl (1 M, 1 mL) were added, the layers separated, and the aqueous one was extracted with AcOEt (×3). The combined organic layers were washed with brine, dried over $MgSO_4$ and the solvents evaporated under reduced pressure. Purification by flash chromatography (AcOEt/cyclohexane 20:80 to 40:60) afforded the title compound **11** (67 mg, 79%) as a white solid. Spectroscopic data were in good agreement with previously reported data [8d,e]. $[\alpha]_D^{25}$ −49.4 (*c* 0.9, $CHCl_3$).

4.12. *N*-Cinnamylacetamide (**12**)

In a round-bottom flask, to a solution of (R_S)-*N*-acetyl-*N*-((*E*)-cinnamyl)-2-methylpropane-2-sulfinamide (**8**) (53 mg, 0.19 mmol) in dry MeOH (5 mL) kept at 0 °C was added HCl (4 M in dioxane, 0.5 mL, 0.5 mmol). The reaction mixture was stirred at 0 °C for 2 h and then sat. $NaHCO_3$ (3 mL) was added. The MeOH was evaporated under reduced pressure and the resulting mixture was extracted with CH_2Cl_2 (×3). The combined organics were washed with brine, dried over $MgSO_4$, and the solvents evaporated under reduced pressure to provide the title compound **12** (33 mg, 99%). Spectroscopic data were in good agreement with previously reported data [18].

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Appendix A. Supplementary data

Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.jorganchem.2013.11.026.

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