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Letter

Efficient Synthesis of Vinyl Sulfones by Manganese-Catalyzed Decarboxylative Coupling of Cinnamic Acids with Aromatic Sulfinic Acid Sodium Salts

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Abstract An efficient synthesis of vinyl sulfones is described. Reactions of cinnamic acids with aromatic sulfinic acid sodium salts in the presence of a catalytic amount of manganese(II) acetate tetrahydrate (5 mol%) in dimethyl sulfoxide (DMSO) afforded the desired vinyl sulfones in good to excellent yields. Notably, the reaction does not need any base or iodide as additive. The use of DMSO as the solvent and running the reaction under air are critical in achieving good yields.

Key words manganese catalysis, decarboxylation, coupling, cinnamic acids, sodium arenesulfinates, vinyl sulfones

Vinyl sulfones (α , β -unsaturated sulfones) are important organic molecules and they are crucial structural scaffolds in many bioactive compounds and drugs.¹ In addition, they are also widely used as Michael acceptors² in organic chemistry. Because of their synthetic utility and their potential biological activities, the synthesis of vinyl sulfones has received considerable attention in organic synthesis and medicinal chemistry. Conventionally, vinyl sulfones are synthesized either by the oxidation of thioethers³ or through condensation of aldehydes with sulfonylacetic acids.⁴ However, two of the most straightforward approaches to vinyl sulfone synthesis involve the addition of sulfinates to alkenes⁵ or alkynes.⁶ Because alkenes and alkynes are basic building blocks and can be easily prepared, their use as starting materials for the synthesis of vinyl sulfones can be highly advantageous. Alternatively, vinyl sulfones can be synthesized by transition-metal-catalyzed cross-coupling reactions of sulfinates with vinyl halides,⁷ triflates,⁸ or boronic acids.⁹ More recently, chemists have begun to synthesize vinyl sulfones by decarboxylative coupling of cinnamic acids with sulfinates.¹⁰ because a variety of cinnamic acids are commercially available. Along this line, metal-catalyzed or metal-free decarboxylative coupling reactions of cinnamic acids with sulfinates have been developed by several groups. For example, Guo and co-workers demonstrated that vinyl sulfones can be efficiently synthesized from cinnamic acids and benzenesulfinates through catalysis by CuI in the presence of KI as an additive.¹¹ Tan and co-workers have shown that by using Pd as a catalyst and Ag₂CO₃ as an oxidant, vinvl sulfones can be efficiently constructed from various cinnamic acids and arenesulfinates.¹² The same transformation can also be effected with a stoichiometric amount of $PhI(OAc)_2^{13}$ or under Cu catalysis by using tertbutyl hydroperoxide (TBHP) as the oxidant.¹⁴ Note that the same reaction can also be accomplished in the presence of I₂ and TBHP.¹⁵ More impressively, Jiang and co-workers were able to carry out the same transformation without any catalyst.¹⁶ All the reaction needed was 0.5 equivalents of a simple inorganic base, such as K₂CO₃. It is proposed that the solvent DMSO is the actual oxidant.^{16,17} Interestingly, a similar reaction can also be run in water by using I_2 as the oxidant.¹⁸ Even though these methods provide efficient routes for the synthesis of vinyl sulfones from cinnamic acids, the need to use iodides is a disadvantage. Here, we disclose a novel and efficient synthesis of vinyl sulfones by decarboxylative coupling of cinnamic acids with arenesulfinates without the need for any base or iodide additive. Instead, only a catalytic amount of a simple Mn(II) salt is reauired.

We began the study by using cinnamic acid (**1a**; 1 equiv) and sodium benzenesulfinate (**2a**; 3 equiv) as our model reactants. Inspired by Guo's method, we wondered whether

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other transition metals might catalyze the decarboxylative coupling of cinnamic acids with arenesulfinates, so we tested the coupling of acid **1a** with sulfinate **2a** in the presence of various transition-metal catalysts (5 mol%) under air with KI (20 mol%) as an additive in DMSO at 110 °C for 12 hours (Table 1, entries 1-3). With Co(OAc)₂, or FeCl₃ as catalyst, the desired vinyl sulfone 3a was isolated in 26% and 8% yield, respectively (entries 1 and 2). The stereochemistry of the product **3a** was determined to be *trans*, because the coupling constant between the two olefinic hydrogens was 15.5 Hz. Much to our delight, when the catalyst was switched to $Mn(OAc)_2$, the yield improved to 76% (entry 3). As a result, we chose $Mn(OAc)_2$ as the catalyst to screen other reaction parameters. Interestingly, we found that the coupling reaction occurred even in the absence of KI, and this gave an even better yield of **3a** (86%; entry 4).

Table 1 Optimization of Reaction Conditions^a

\bigcirc	+ SO ₂	Na <u>catalyst, additive</u> solvent		
1a	2a		~	3a 🗸
Entry	Catalyst (mol%)	Solvent	Additive	Yield ^b (%)
1	Co(OAc) ₂	DMSO	KI	26
2	FeCl ₃	DMSO	KI	8
3	Mn(OAc) ₂ ·4H ₂ O	DMSO	KI	76
4	Mn(OAc) ₂ ·4H ₂ O	DMSO	-	86
5	Mn(OAc) ₂ ·4H ₂ O	DMA ^c	-	47
6	Mn(OAc) ₂ ·4H ₂ O	toluene	-	25
7	Mn(OAc) ₂ ·4H ₂ O	DCE	-	13
8 ^d	Mn(OAc) ₂ ·4H ₂ O	DMSO	-	66
9 ^e	Mn(OAc) ₂ ·4H ₂ O	DMSO	-	47
10 ^f	Mn(OAc) ₂ ·4H ₂ O	DMSO	-	72
11	-	DMSO	-	28
12 ^g	Mn(OAc) ₂ ·4H ₂ O	DMSO	-	12
13 ^h	Mn(OAc) ₂ ·4H ₂ O	DMSO	-	32
14	MnCl ₂ ·4H ₂ O	DMSO	-	27
15	(TCPP)MnCl ⁱ	DMSO	-	19

 a Reaction conditions: 1a (0.5 mmol), 2a (1.5 mmol), catalyst (5 mol %), solvent (2 mL), 110 °C, 12 h, under air.

^b Isolated yield

^c DMA = *N*,*N*-dimethylacetamide d 125 °C.

° 80 °C.

^f Mn(OAc)₂ (3 mol%).

^g Under N₂.

^h Solvent 1 mL.

A screening of solvents revealed that DMSO was better than other solvents such as *N*,*N*-dimethylacetamide (DMA), DCE, or toluene (Table 1, entries 4–7). The effects of the reaction temperature on the decarboxylative coupling reac-

tion in the temperature range 80-125 °C was also investigated, and the reaction performed at 110 °C gave the best result (entry 4); lowering or raising the reaction temperature gave much lower yields (entries 8 and 9). When the amount of the catalyst was reduced to 3 mol%, the yield reached 72% (entry 10). Surprisingly, the vinyl sulfone 3a could be isolated in 28% yield in the absence of a manganese catalyst (entry 11). In addition, the manganese catalvsts MnCl₂ and chloro[tris(4-chlorophenyl)phosphine]manganese [(TCPP)MnCl] gave sulfone 3a in 27% and 19% yield, respectively (entries 14 and 15). On the basis of these results, we decided to set the optimal conditions as follows: **1a** (0.5 mmol), **2a** (1.5 mmol), and Mn(OAc)₂·4H₂O (5 mol%) in DMSO at 110 °C under air for 12 hours.

With the optimized protocol in hand, we explored the substrate scope of the decarboxylation reaction. As shown in Table 2, the reaction worked well for a wide variety of

Table 2 Substrate Scope for the Synthesis of Vinyl Sulfones^{a,19}

	Substrate Scop	be for the synthesis e	n villyi Sulloin	- 5
R ¹	COOH + F	Mn(OAc) ₂ (5 mol%) DMSO, air, 110 2a	► R ¹ .	0 S R ² 3a
Entry	R ¹	R ²	Product	Yield ^b (%)
1	4-Me	Ph	3ab	74
2	4-Cl	Ph	3ac	69
3	4-F	Ph	3ad	64
4	4-Br	Ph	3ae	65
5	2-Cl	Ph	3af	63
6	4-OMe	Ph	3ag	72
7	2-OMe	Ph	3ah	67
8	3-OMe	Ph	3ai	62
9	4-NO ₂	Ph	3aj	80
10	2-NO ₂	Ph	3ak	61
11	3-NO ₂	Ph	3al	73
12	Н	$4-MeC_6H_4$	3am	63
13	Н	$4-BrC_6H_4$	3an	57
14	4-NO ₂	$4-MeC_6H_4$	3ao	53
15	3-NO ₂	$4-MeC_6H_4$	Зар	62
16	4-Me	$4-MeC_6H_4$	3aq	65
17	4-F	$4-MeC_6H_4$	3ar	66
18	4-Cl	$4-MeC_6H_4$	3as	70
19	2-Cl	$4-MeC_6H_4$	3at	57
20	4-Br	$4-MeC_6H_4$	3au	63
21	Н	Me	3av	-c
^a Reactio	on conditions: 1	(0.5 mmol) 2 (1.5 mr	nol) catalyst (5	mol %) sol-

^a Reaction conditions: 1 (0.5 mmol), 2 (1.5 mmol), catalyst (5 mol %), solvent (2 mL), 110 °C, 12 h, under air.

^b Isolated yield.

^c Messy reaction.

TCPP = T(p-CI)PP.

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substituted cinnamic acids **1**, and the products were isolated in yields of 57–80% (Table 2, entries 1–8). Substrates with electron-donating or electron-withdrawing groups on the phenyl ring of the cinnamic acids all provided the desired vinyl sulfones in good yields. Cinnamic acids **1** with *ortho-, meta-* or *para*-nitro substituents all gave similar yields of the corresponding products (Table 2, entries 9– 11); these results are important because the nitro group can be easily converted into other functional groups. Additionally, we found that methyl- and bromo-substituted sodium benzenesulfinates **2** gave the desired vinyl sulfones **3** satisfactorily in 53–76% yield (entries 12–20). Unfortunately the reaction was quite messy when a sodium alkanesulfinate, sodium methanesulfinate, was used as the reactant (entry 21).

To shed some light on the reaction mechanism, several control reactions were carried out. When the reaction of **1a** with 2a was conducted under the optimal conditions in the presence of radical inhibitors such as TEMPO or 2,4-di-tertbutyl-4-methylphenol (BHT), the reaction was completely inhibited (Scheme 1, a and b). These results suggested that our reaction might be a free-radical-based process. In addition, when we ran the reaction without the $Mn(OAc)_2 \cdot 4H_2O$ catalyst, the yield of **3a** was only 28% (Scheme 1, c), showing that the catalyst is essential for obtaining **3a** in good vield. On the other hand, when the reaction was performed with a stoichiometric amount of Mn(OAc)₂·4H₂O in DMA under N₂, the product **3a** was only isolated in a trace amount (Scheme 1, d). In comparison, replacing the $Mn(OAc)_2 \cdot 4H_2O$ catalyst with one equivalent of Mn(OAc)₃·2H₂O afforded **3a** in 45% yield (Scheme 1, e). This suggested that the true catalyst in the reaction might be a Mn(III) species. Because a much lower yield was obtained in DMA than in DMSO, we believe that DMSO might play an important role in the reaction in addition to forming complexes with the Mn catalyst.

On the basis of these results and literature precedents,^{10–18} we propose the tentative mechanism shown in Scheme 2.

We believe that the reaction begins with the oxidation of Mn(OAc)₂ by O₂ to give a Mn(III) species that forms intermediate **A** by anion exchange with cinnamic acid. At the same time, sodium benzenesulfinate is oxidized by DMSO or a Mn(III) species to the corresponding sulfinate radical **B**. Next, **B** adds to the double bond of intermediate **A** to form adduct **C**. Subsequently, through homolysis of the Mn–carboxylate bond, adduct **C** is transformed into the biradical intermediate **D**, which, upon loss of one molecule of CO₂, gives the final product **3a**. Because the *trans* product is formed exclusively, this reaction is clearly a thermodynamically controlled process.

In summary, an efficient method has been developed for the synthesis of vinyl sulfones through decarboxylation of various cinnamic acids with sodium benzenesulfinates with air as the oxidant. Unlike other methods, our reaction



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does not use any iodide salt as additive. The success of the reaction is critically dependent on the use of $Mn(OAc)_2$ as catalyst. In addition, the use of DMSO as the solvent is also pivotal. Preliminary mechanistic studies suggest that this reaction is likely to proceed through a radical pathway.

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Supporting Information

Supporting information for this article is available online at http://dx.doi.org/10.1055/s-0035-1562476.

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- (19) General Procedure: To a 25 mL round-bottom flask were added cinnamic acid (0.5 mmol), aromatic sulfinic acid sodium salt (1.5 mmol), Mn(OAc)2·4H₂O (6.13 mg, 0.025 mmol) and DMSO (2 mL). The solution was stirred under air at 110 °C for 12 h. The reaction mixture was cooled to r.t. and washed with sat. aq NaCl (3 ×), extracted with EtOAc, and concentrated in vacuo. The resulting residue was purified by flash column chromatography on silica gel using hexanes–EtOAc (8:1) as the eluent. All compounds are known and were characterized by ¹H NMR, ¹³C NMR, LRMS and their comparison to literature values.

(*E*)-1-Bromo-4-[2-(4-tosyl)vinyl]benzene (3au)^{5c} as a representative product: $C_{15}H_{13}SO_2Br$. Yield: 63%; white solid; mp 163–164 °C. ¹H NMR (400 MHz, CDCl₃): δ = 7.75 (d, *J* = 8.2 Hz, 2 H), 7.51 (d, *J* = 15.4 Hz, 1 H), 7.45 (d, *J* = 8.4 Hz, 2 H), 7.27 (t, *J* = 7.6 Hz, 4 H), 6.77 (d, *J* = 15.4 Hz, 1 H), 2.37 (s, 3 H). ¹³C NMR (101 MHz, CDCl₃): δ = 143.5, 139.4, 136.4, 131.3, 130.3, 128.9, 128.7, 127.3, 126.7, 124.4, 20.6. MS: *m*/*z* = 337 (M⁺).

