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Acid-mediated sulfonylation of arylethynylene bromides with sodium arylsulfinates: synthesis of (*E*)-1,2-bis(arylsulfonyl)ethylenes and arylacetylenic sulfones†

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A solvent-dependent sulfonylation of arylethynylene bromides with sodium arylsulfinates has been developed. The (*E*)-1,2-bis(arylsulfonyl)ethylenes were formed in DMSO, while the arylacetylenic sulfones were obtained in toluene. Utilizing simple and readily available starting materials, the sulfonylation products were generated with good selectivities and yields without the need for a metal catalyst or oxidant.

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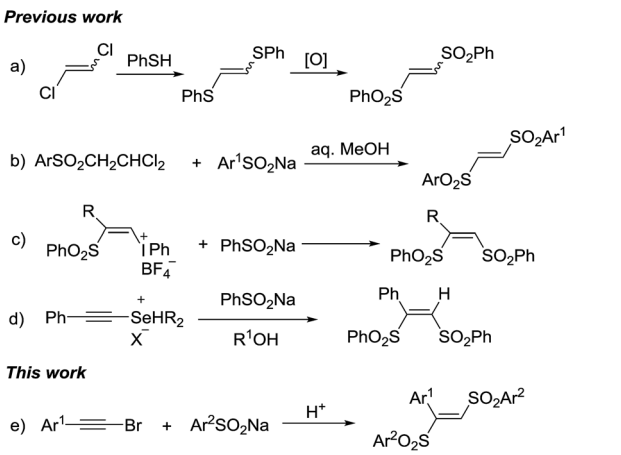
Organosulfone compounds are of great importance in organic chemistry, due to their widely existing in natural products and drug molecules.[1] Meanwhile, the sulfonyl group is also extensively used as versatile synthon for other organosulfur compounds synthesis.[2] 1,2-Bis(arylsulfonyl)ethylenes are important organosulfone compounds and widely studied in synthetic applications. Firstly, they can act as π-deficient alkenes for cycloaddition reaction to synthesize cyclic compounds.[3] Secondly, they play the role as leaving group in radical alkenylation reaction, in which various radicals add into the C–C double bond and then eliminate a sulfonyl radical.[4] Thirdly, in the presence of organocatalyst, they are able to undergo 1,2-sulfone rearrangement to form various other organosulfone compounds.[5] Due to their importance, synthetic chemists have exploring their synthetic methods. However, the methods for synthesis of 1,2-bis(arylsulfonyl)ethylenes are still rarely. The most common method was the reaction of the 1,2-dichloroethylene with phenylthiolate to give 1,2-bis(arylthio) ethylene which was followed by oxidation to furnish 1,2-bis(arylsulfonyl)ethylenes (Scheme 1a).[6a] While those multi-step synthesis was even impeded by limited symmetric 1,2-bis(arylsulfonyl)ethylenes formation. Reddy *et al.* reported a one-pot method, through the condensation of 1-arylsulfonyl-2,2-dichloroethanes with sodium sulfinates in aqueous alcohol (Scheme 1b).[6b] The β-((phenylsulfonyl)alkenyl)iodonium tetrafluoroborates were used as starting materials to form (*Z*)-1,2-bis(arylsulfonyl)ethylenes by nucleophilic vinylic substitutions with sodium arylsulfinates. Except the multi-step preparation of vinyl-iodonium salts, stoichiometric amount of iodine benzene as a by-product placed this method in an unfavourable position (Scheme 1c).[6c] Kataoka *et al.* also developed a method for 1,2-bis(phenylsulfonyl)ethylene *via* the reaction of alkynylselenonium salt with sodium benzenesulfinate (Scheme 1d).[6d–f] In the above methods, all have some obvious disadvantages such as multi-step processes, strong oxidants, unavailable starting materials, toxic by-products and so on. Hence, it is attractive and meaningful to develop a new method for synthesis of 1,2-bis(arylsulfonyl)ethylenes in a direct, simple and green way.

Haloalkynes are easily available building blocks which can be prepared in quantitative yield in mol-scale on the bench top. Due to the electron-deficiency of haloalkyne, it usually used as an activated alkyne for addition reaction to give the sole regioselectivity.[7] In recent years, some practical synthetic methods



Scheme 1 Synthetic methods for 1,2-bis(arylsulfonyl)ethylenes.

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† Electronic supplementary information (ESI) available: Experimental section, characterization of all compounds, Fig. S1, copies of ^{1}H and ^{13}C NMR spectra for all target compounds. CCDC 1502249. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c7ra07105a

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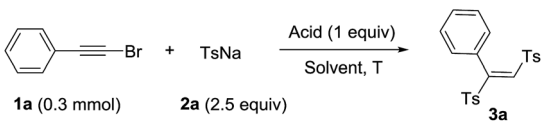
involving haloalkynes have been developed, including nucleophilic addition,[8] cross-coupling reactions[9] and cycloaddition reactions.[10] In comparison with sulfonyl chlorides, sodium sulfinates as mild sulfone moieties have many advantages, such as low toxicity, ready accessibility and stability. The sodium sulfinates are not only used as the simple nucleophilic reagents but also sulfonyl radicals to participate in the sulfonylation reaction. Recently, many endeavors have been made towards utilizing sodium sulfinates to synthesize organosulfone compounds.[11] Based on the reaction development of haloalkynes and sodium sulfinates, we developed a direct synthesis of 1,2-bis(arylsulfonyl)ethylenes through tandem reaction between haloalkynes and sodium sulfinates under acidic conditions. Herein, we presented a acid-mediated synthesis of 1,2-bis(arylsulfonyl)ethylenes from bromoalkynes and sodium sulfinates (Scheme 1e).

We used the reaction between phenylethynyl bromide (**1a**) and sodium *p*-tolylsulfinate (**2a**) as a model to examine various reaction parameters and the results were summarized in Table 1. On the first trial, **1a** and **2a** (2.5 equiv.) were treated with 1 M HCl (1 equiv.) in DMSO as solvent at 60 °C for 12 h. To our delight, the target product 1,2-bis(tolylsulfonyl)phenylethene (**3a**) was obtained in 60% yield (entry 1). And the structure was confirmed by single-crystal X-ray analysis, in which the double bond is *E*-type configuration.[12] Afterwards, we examined the concentration of hydrochloric acid and the results indicated that the yields increased with higher concentration HCl (entries 2–5). The yield was raised up to 91% when 12 M HCl was used (entry 5). Next, the screening of reaction temperature showed that neither increasing nor decreasing the temperature led to a lower yield of product (entries 6–9). Other Brønsted acids such as H_2SO_4, TsOH, TfOH, TFA and HOAc were tested to give the product in decent yields (entries 10–14). Control experiment indicated that acid was essential for this transformation (entry 15). The screening of different solvents showed that the solvents played a critical role, the polar solvents were beneficial for the transformation (entries 16–24).

With the optimal reaction condition in hand, we next conducted a survey of various substrates to explore the scope of this transformation. As listed in Table 2, the reaction had a good substrate suitability and various substituted (*E*)-1,2-bis(arylsulfonyl)ethylenes were obtained in moderate to excellent yields. We firstly evaluated the scope of bromoalkynes. Various alkyl and halogen substitutions on benzene ring of

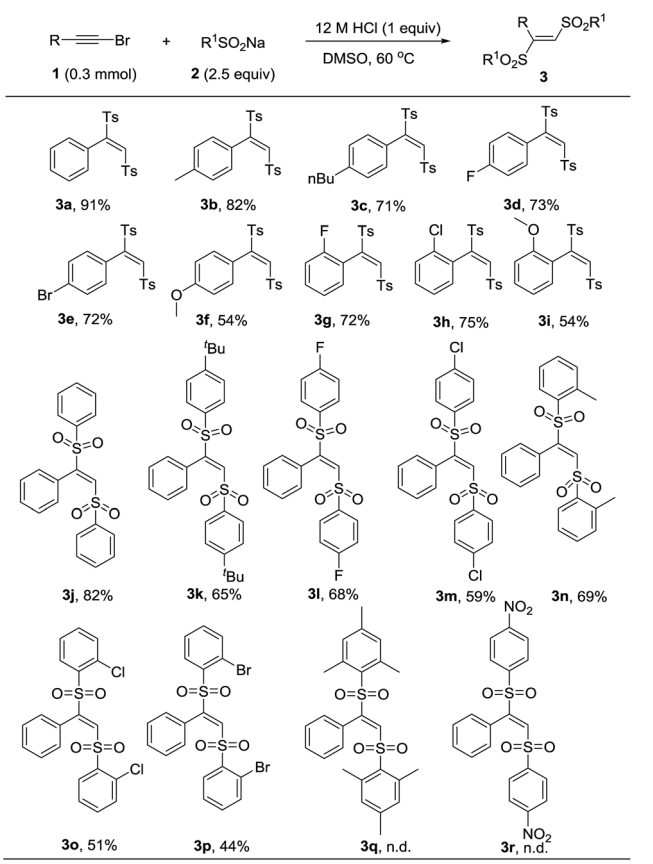
Table 1 Optimization of the reaction conditions[a]



Entry	Acid	Solvent	*T* (°C)	Yield (%)
1	1 M HCl	DMSO	60	60
2	3 M HCl	DMSO	60	68
3	6 M HCl	DMSO	60	74
4	9 M HCl	DMSO	60	83
5	**12 M HCl**	**DMSO**	**60**	**91**
6	12 M HCl	DMSO	40	42
7	12 M HCl	DMSO	rt	13
8	12 M HCl	DMSO	80	80
9	12 M HCl	DMSO	100	78
10	H_2SO_4	DMSO	60	71
11	TsOH	DMSO	60	58
12	TfOH	DMSO	60	68
13	TFA	DMSO	60	65
14	HOAc	DMSO	60	10
15	—	DMSO	60	n.d.
16	12 M HCl	CH_3CN	60	61
17	12 M HCl	DMF	60	50
18	12 M HCl	Acetone	60	38
19	12 M HCl	CH_3NO_2	60	27
20	12 M HCl	1,4-Dioxane	60	15
21	12 M HCl	$CHCl_3$	60	n.d.
22	12 M HCl	EtOAc	60	n.d.
23	12 M HCl	Toluene	60	n.d.
24	12 M HCl	DCE	60	n.d.

[a] Reaction were performed with **1a** (0.3 mmol), **2a** (0.75 mmol), acid (0.3 mmol) in solvent (3.0 mL) for 12 h. Isolated yield. n.d. = not determined.

Table 2 Substrate scope for the synthesis of substituted (*E*)-1,2-bis(arylsulfonyl) ethylenes[a]



[a] Reactions were performed with **1** (0.3 mmol), **2** (0.75 mmol), 12 M HCl (0.3 mmol), and DMSO (3 mL) at 60C for 12 h. Yields was referred to isolated yields.

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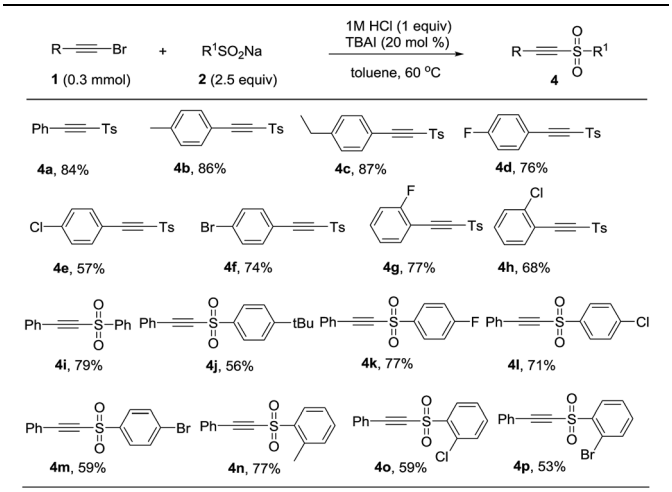
phenylacetylene bromides were tolerated for this reaction. Strong electron-donating substitute such as methoxyl slightly decreased the yield of desired product (Table 2, **3f** and **3i**). For the substrate scope of sodium sulfinates, different *para*-substituted sodium phenylsulfinates could be converted into the corresponding products in moderate to good yields (Table 2, **3j–3m**). Even the steric hindered *ortho*-substituted sodium phenylsulfinates also worked efficiently to give the products in 44% to 69% yields (Table 2, **3n–3p**). Unfortunately, more steric hindered mesitylenesulfinate and electron-deficient nitrobenzenesulfinate were failed to transform into the corresponding products (Table 2, **3q** and **3r**).

It was surprising that when **1a** and **2a** was treated with 12 M HCl (1 equiv.) in toluene as solvent at 60 °C for 12 h, the product acetylenic sulfone (**4a**) was formed in 48% yield.[13] Though some methods have been reported for the synthesis of acetylenic sulfones, they had some disadvantages such as unavailable starting materials and strong oxidant.[14] Thus, we optimized the reaction conditions and the best reaction conditions were as followed: **1a** (0.3 mmol), **2a** (0.75 mmol), 1 M HCl (0.3 mmol), TBAI (20 mol%), in toluene (3 mL) at 60 °C for 12 h (see the ESI† for details). After establishing the optimized reaction conditions, the generality and limitations of various substrates were investigated. Firstly, sodium *p*-tolylsulfinate (**2a**) was treated with different substituted phenylacetylene bromides. Different *para*-substituted phenylacetylene bromides including alkyl group (Me, Et) and halides (F, Cl, Br) were well tolerated under the optimized condition to afford the products in 57% to 87% (Table 3, **4a–4f**). Subsequently, the effect of *ortho*-substituents on the phenyl ring of phenylacetylene bromides were investigated. The product **4g** and **4h** were formed in 77% and 68% yields, respectively. Further investigating the scope of this transformation included various substitutions effect on sodium phenylsulfinates. Various sodium sulfinates could be proceeded smoothly and afforded the corresponding products in moderate to good yields (Table 3, **4i–4p**). It was a pity that sodium alkylsulfinates was not appropriate for the transformation at this stage.

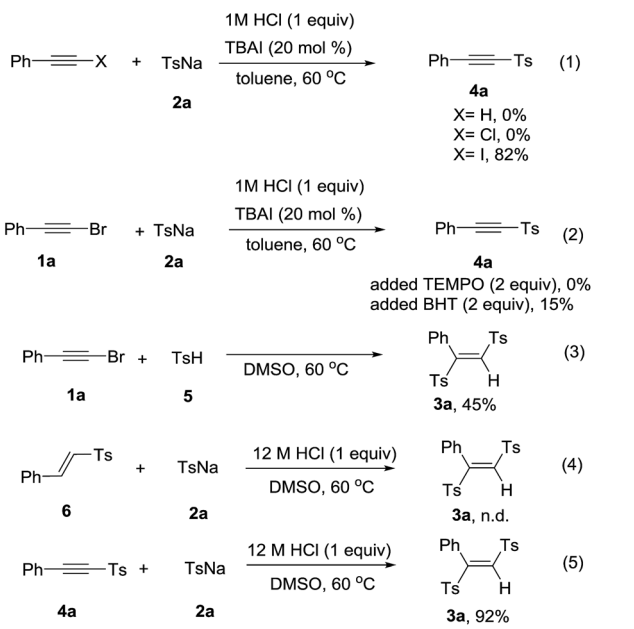
To gain more insight into the mechanism, the control experiments were carried out and shown in Scheme 2. When we utilized phenylacetylene, phenylethynyl chloride or phenylethynyl iodine to react with **2a** under the standard conditions. Phenylethynyl iodide gave the product **4a** in 82% yield, while phenylacetylene and phenylethynyl chloride were failed to convert into the product (Scheme 2, eqn (1)). The presence of TEMPO or BHT strongly suppressed the product formation, respectively gave the product **4a** in 0% and 15% yields (Scheme 2, eqn (2)). These results indicated that a radical pathway may be involved. However, we did not detect the additive products of radicals coupling with TEMPO or BHT. When the 4-methylbenzenesulfinic acid **5** reacted with **2a** in absence of 12 M HCl, the product **3a** was obtained in 45% yield (Scheme 2, eqn (3)). The vinyl sulfone **6** could not transformed into the product with **2a** under standard reaction condition (Scheme 2, eqn (4)). We next investigated whether **4a** was the reaction intermediate for the formation product **3a**. Sodium sulfinates could add into **4a** to form **3a** in excellent yield in the presence of 12 M HCl (Scheme 2, eqn (5)).

According to previous studies[15,16] and our control experiments, the proposed mechanisms were shown in Scheme 3. One proposed mechanism was a addition–elimination process (path a).[15] Firstly, the nucleophilic attack of sulfinate ion to **1a** formed the intermediate **A**, which was followed by protolysis to give the intermediate **B**. Finally, the intermediate **B** eliminated hydrogen bromide to produce the product **4a**. The other mechanism was a radical process (path b). The *p*-tolylsulfonyl radical **C** could be generated from sodium *p*-tolylsulfinate in acid under heated condition.[16a,b] Subsequently, a radical

Table 3 Substrate scope for the synthesis of substituted acetylenic sulfone[a]



[a] Reaction conditions: **1** (0.3 mmol), **2** (0.75 mmol), 1 M HCl (0.3 mmol), TBAI (20 mol%), and toluene (3 mL) at 60 °C for 12 h. Yields was referred to isolated yields.



Scheme 2 Control experiments.

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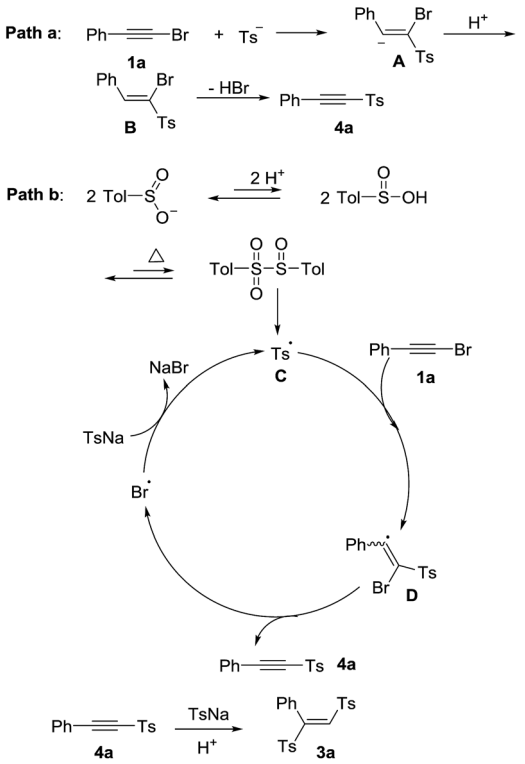

Scheme 3 Possible reaction mechanism.

addition of *p*-tolylsulfonyl radical to **1a** formed a bromovinyl radical **D**.[16c] Then, the product **4a** was obtained *via* bromine radical elimination from **D**.[16c] Finally, the bromine radical oxidized sodium *p*-tolylsulfinate to afford *p*-tolylsulfonyl radical **C** with releasing NaBr.[16c] The **4a** could be transformed into the product **3a** through nucleophilic addition. The polarity of the solvent determined the final product was **4a** or **3a**. The final product was **4a** in the low polar solvents such as toluene, $CHCl_3$, DCE and so on. The high polar solvent was good for nucleophilic addition process. So when the high polar solvents such as DMSO, DMF, CH_3CN were used, the final product was **3a**.

In conclusion, we have developed a practical and novel procedure for the synthesis of (*E*)-1,2-bis(arylsulfonyl)ethylenes and arylacetylenic sulfones by sulfonylation of arylethynylene bromides with sodium arylsulfinates in different solvents. The method obviated the need for unavailable starting materials or strong oxidants with simple operation. Further research for the mechanism and the synthetic applications are ongoing in our laboratory.

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