RSC Advances

This article can be cited before page numbers have been issued, to do this please use: J. Gao, J. Lai and G. Yuan, *RSC Adv.*, 2015, DOI: 10.1039/C5RA10896A.

Volume 1 | Number 1 | Jan 2013 | Pages 1–100

RSC Advances

www.rsc.org/advances

ROYAL SOCIETY OF CHEMISTRY

Dynamic Article Links ►
View Article Online
DOI: 10.1039/C5RA10896A

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

Iodine-mediated synthesis of (*E*)-vinyl sulfones from sodium sulfinates and cinnamic acids in aqueous medium

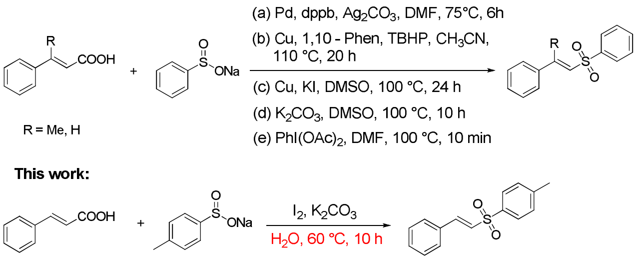
Jian Gao, Junyi Lai and Gaoqing Yuan*

Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

With water as the reaction medium, a green and efficient method has been developed for the synthesis of (*E*)-vinyl sulfones via I_2-mediated decarboxylative cross-coupling reactions of sodium sulfinates with cinnamic acids. This synthetic route could effectively avoid the use of toxic organic solvents and transition metal catalysts, and the target products could be obtained with moderate to excellent yields under green and mild conditions.

Since 1960s, transition metal catalysts have increasingly attracted one's attention owing to their versatile reactivity and practical applications in organic synthesis,[1] especially for the formation of carbon-carbon and carbon-heteroatom bonds.[2] Nevertheless, transition-metal-catalyzed coupling reactions have long been plagued by instinctive drawbacks of the catalytic systems, such as expensive, toxic catalysts and ligands, extra additives or co-catalysts, harsh reaction conditions and so on.[3] So chemists desire to look for greener and more efficient synthetic routes,[4] and recent researches have revealed the feasibility to replace transition metal catalysts with greener and cheaper iodine or iodide reagents.[5] For example, Yotphan and co-workers recently reported iodine-catalyzed oxidative amination of sodium sulfonates.[5h]

Vinyl sulfones, as key functional units, exhibit a broad range of biological and parmaceutical activities in biological and medicinal chemistry,[6] and show great synthetic value as building blocks in organic transformations.[7] To date various synthetic methods have been developed,[8] mainly including (1) direct coupling reaction of alkenes or alkynes with sulfone resources (sulfinic acid,[9] sodium sulfinate,[10] sulfonyl hydrazide,[11] thiols[12] and dimethyl sulfoxide[5b,13]), and (2) decarboxylative coupling reaction of cinnamic acids with sodium sulfinate (Scheme 1).[14] In Scheme 1, there have been some new and efficient Pd- or Cu-catalyzed decarbocylative coupling reactions for the synthesis vinyl sulfones from cinnamic acid and sodium sulfinate. However, all of them need toxic metals, ligands, oxidants and high temperature (Scheme 1a–c).



Scheme 1 Methods for synthesis of vinyl sulfones.

It is noteworthy that Jiang's group has reported a simple and efficient route for the synthesis of vinyl sulfones without any catalysts (Scheme 1d), and very recently Kuhakarn's group has reported a highly efficient method by $PhI(OAc)_2$ mediated decarboxylative sulfonylation in a very short time (Scheme 1e). However, both of them still suffer from toxic organic solvents and high temperature. It is well known that water as green reaction medium has practical advantages over organic solvents and attracted increasing attention in organic synthesis.[15] Herein, we reported a green and efficient method for the synthesis of vinyl sulfones via I_2-mediated decarboxyative cross-coupling reaction of sodium sulfinates with cinnamic acids, using water as a solvent at lower temperature.

Firstly, we chose trans-cinnamic acid (**1a**) and sodium 4-methyl benzenesulfinate (**2a**) as model substrates to examine various reaction conditions, and the results were shown in Table 1. We did not get the desired product when the reaction of **1a** with **2a** was performed with 1 equiv. of I_2 in the absence of a base at room temperature for 5 h (entry 1). In the presence of base K_2CO_3 (1.0 equiv.), (*E*)-1-methyl-4-(styrylsulfonyl)benzene (**3a**) could be obtained with 10% yield (entry 2). We attempted to prolong reaction time to 10 h, but the yield of **3a** was not obviously improved (only 23%, entry 3). Luckily, when the reaction temperature was raised to 40 ºC, the yield of **3a** was drastically increased to 72% (entry 4). Higher temperatures (50 ºC, 60 ºC and 70 ºC, entries 5–7)

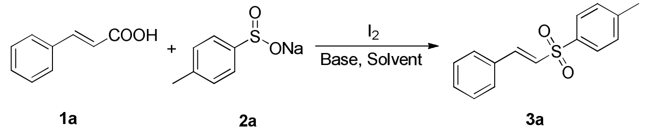
School of Chemistry and Chemical Engineering, South China University of Technology, Guangzhou, 510640, P. R. China
E-mail: gqyuan@scut.edu.cn

† Electronic Supplementary Information (ESI) available: Detailed experimental procedures, characterization of products, and NMR spectral charts. See DOI: 10.1039/b000000x/

View Article Online
DOI: 10.1039/C5RA10896A

were further tested, and a best yield was obtained (91%, entry 6). When 0.5 equiv. of I_2 or 0.5 equiv. of K_2CO_3 was added to the reaction system, the yield of **3a** declined to approximately half of the best yield (entries 8 and 9). Besides, the reaction efficiency was not improved when excess K_2CO_3 (2.0 equiv.) was used (entry 10). At last, various bases (Cs_2CO_3, NaOAc, KOH, CH_3ONa and Et_3N) and solvents (CH_3CN, DMF, EtOAc, CH_3OH and DMSO) were screened, respectively. These results showed that K_2CO_3 was an optimal base and water was the most suitable solvent in this process (entries 11–20).

Table 1 Optimization of reaction conditions. [a]

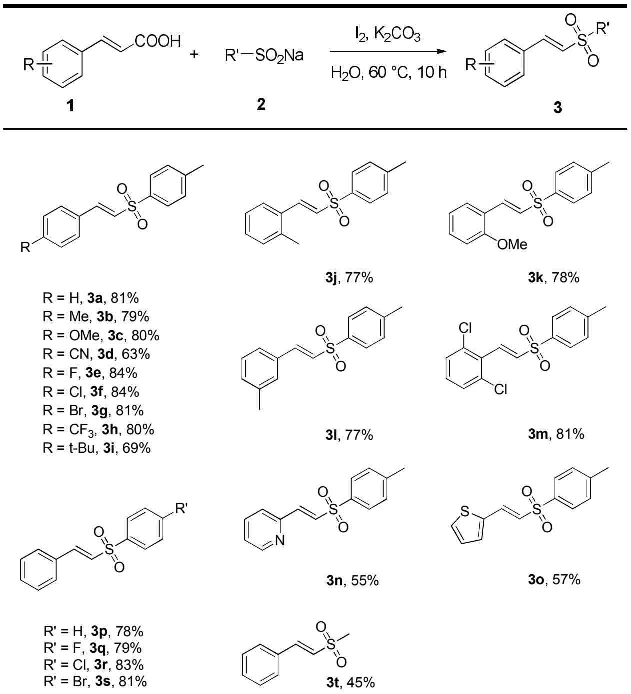


Entry	I_2 (equiv.)	Base (equiv.)	Solvent	Time (h)	Temp. (ºC)	Yield[b] (%)
1	1.0	no	H_2O	5	r t	trace
2	1.0	K_2CO_3 (1.0)	H_2O	5	r t	10
3	1.0	K_2CO_3 (1.0)	H_2O	10	r t	23
4	1.0	K_2CO_3 (1.0)	H_2O	10	40	72
5	1.0	K_2CO_3 (1.0)	H_2O	10	50	80
6	**1.0**	**K_2CO_3 (1.0)**	**H_2O**	**10**	**60**	**91**
7	1.0	K_2CO_3 (1.0)	H_2O	10	70	84
8	0.5	K_2CO_3 (1.0)	H_2O	10	60	40
9	1.0	K_2CO_3 (0.5)	H_2O	10	60	41
10	1.0	K_2CO_3 (2.0)	H_2O	10	60	80
11	1.0	Cs_2CO_3(1.0)	H_2O	10	60	90
12	1.0	NaOAc (1.0)	H_2O	10	60	14
13	1.0	KOH (1.0)	H_2O	10	60	30
14	1.0	CH_3ONa(1.0)	H_2O	10	60	35
15	1.0	Et_3N (1.0)	H_2O	10	60	22
16	1.0	K_2CO_3 (1.0)	CH_3CN	10	60	7
17	1.0	K_2CO_3 (1.0)	DMF	10	60	5
18	1.0	K_2CO_3 (1.0)	EtOAc	10	60	3
19	1.0	K_2CO_3 (1.0)	CH_3OH	10	60	52
20	1.0	K_2CO_3 (1.0)	DMSO	10	60	5
21 [c]	1.0	K_2CO_3 (1.0)	H_2O	10	60	87

[a] Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), base (1.0 equiv.), I_2 (1.0 equiv.), H_2O (2 mL) at 60 ºC for 10 h. [b] Determined by GC-MS using dodecane as the internal standard. [c] Under N_2 atmosphere.

With the optimal reaction conditions in hand, the scope of substrates was investigated and the results are summarized in Table 2. On one hand, we examined the reaction of sodium 4-methyl benzenesulfinate (**2a**) with cinnamic acid derivatives in the standard reaction conditions. Some cinnamic acids which have electron-withdrawing substituents on the phenyl ring (4-CN, 4-F, 4-Cl, 4-Br, 4-CF_3 and 2,6-2Cl) could proceed smoothly to afford the corresponding products in available yields (63%–84%) (**3d–h**, **3m**). Also, cinnamic acids with electron-donating substituents on the phenyl ring (4-Me, 4-MeO, 4-*t*-Bu, 2-Me, 2-MeO and 3-Me) were examined, and the yields of the corresponding products ranged from 69% to 81% (**3b–c**, **3i–l**). These results did not obviously change in comparison with those of substrates having electron-withdrawing substituents. In addition, (*E*)-2-(2-tosylvinyl)pyridine (**3n**) and (*E*)-2-(2-tosylvinyl)thiophene (**3o**) could be obtained with 55% and 57% yields, respectively. On the other hand, the reactions of trans-cinnamic acid (**1a**) with various sodium sulfinates were tested. Various sodium sulfinates with 4-H, 4-F, 4-Cl and 4-Br groups substituted on phenyl rings all proceeded smoothly to give good yields (78%–83%) (**3p–s**). Moreover, (*E*)-(2-(methyl sulfonyl)vinyl)benzene (**3t**) was obtained with 45% yield.

Table 2 Synthesis of (*E*)-vinyl sulfones. [a,b]



[a] Reaction conditions: **1** (0.5 mmol), **2** (0.6 mmol), I_2 (1.0 equiv.), K_2CO_3 (1.0 equiv.), H_2O (2 mL) at 60 ºC for 10 h. [b] Isolated yields.

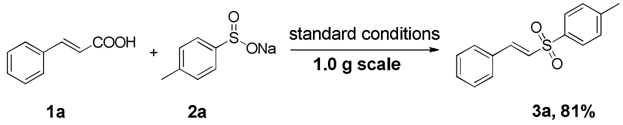
It is worth noting that the reaction was performed on a 1.0 g scale to afford **3a** with 81% yield, indicating that the reaction is scalable and practical (Scheme 2).

To understand the reaction mechanism better, some control experiments have been explored. The desired product **3a** was obtained with a good yield under nitrogen atmosphere, which eliminated the influence of oxygen on this reaction very well (Table 1, entry 21). The reaction of **1a** with **2a** was proceeded under the standard conditions in the presence of 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO), and no **3a** was detected by GC, which implied a radical pathway should be involved (Scheme 3a). When using 4-methylbenzene-1-sulfonyl iodide as the substrate instead of **2a** and iodine, the yield of **3a** was almost unchanged (Scheme 3b). The result suggested that 4-methylbenzene-1-sulfonyl iodide should be an intermediate in this transformation. The synthetic procedure of 4-methylbenzene-1-sulfonyl iodide was given in the Supporting Information. In addition, it should be pointed out that I_2 is almost converted to iodine anions after the reaction in two steps (i.e., the reaction of $ArSO_2Na$ with I_2, and the reaction of $ArSO_2I$ with cinnamic acid) in the present standard conditions, which is confirmed by iodometric

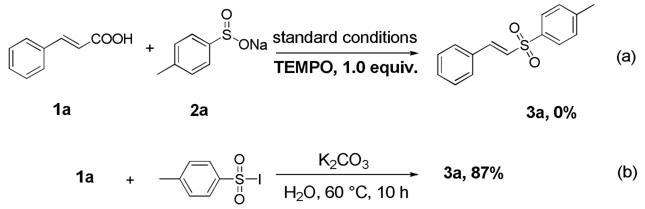
View Article Online
DOI: 10.1039/C5RA10896A

titration.

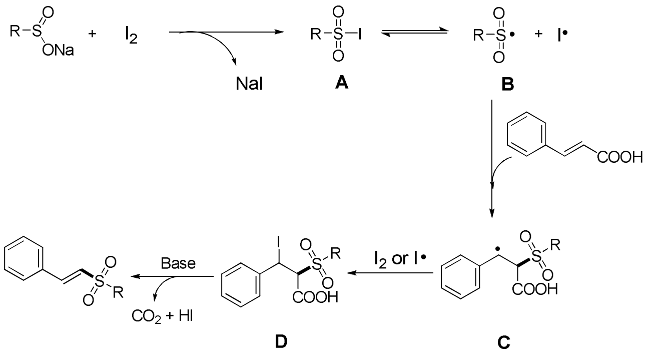
Based on the results of control experiments, a possible reaction mechanism was proposed in Scheme 4. It is easy to generate intermediate **A** from sodium sulfinate and iodine, and the intermediate **A** undergoes homolysis to give a sulfonyl radical (**B**) and an iodine radical.[16] Subsequently, the radical **B** is added to the double bond of cinnamic acid to afford intermediate **C**,[14b-e,17] which is combined with iodine or iodine radical to generate intermediate **D**.[10b,d] Finally, the intermediate **D** undergoes the elimination of carbon dioxide and hydrogen iodide to provide the desired vinyl sulfones with the help of a base.[14c,17]



Scheme 2 Reaction on a 1.0 gram scale.



Scheme 3 Control experiments.



Scheme 4 Possible reaction mechanism.

In conclusion, we have developed a green and efficient method for the synthesis of vinyl sulfones via I_2-mediated decarboxylative coupling reaction using environmentally friendly water as the reaction medium. This reaction shows its fascinating application prospect in organic synthesis. Compared with the reported methods, this route seems to be greener and more efficient.

Acknowledgements

We are grateful to the National Natural Science Foundation of China (21172079) and the Science and Technology Planning Project of Guangdong Province (2011B090400031) for financial support.

Notes and references

1 For reviews on transition-metal-catalyzed coupling reactions, please see: (*a*) C. C. C. J. Seechurn, M. O. Kiching, T. J. Colacot and V. Snieckus, *Angew. Chem., Int. Ed.*, 2012, **51**, 5062; (*b*) X. F. Wu, H. Neumann and M. Beller, *Chem. Soc. Rev.*, 2011, **40**, 4986; (*c*) F. S. Han, *Chem. Soc. Rev.*, 2013, **42**, 5270; (*d*) R. Jana, T. P. Pathak and M. S. Sigman, *Chem. Rev.*, 2011, **111**, 1417; (*e*) K. C. Nicolaou, P. G. Bulger and D. Sarlah, *Angew. Chem., Int. Ed.*, 2005, **44**, 4442; (*f*) I. Bauer and H. J. Knölker, *Chem. Rev.*, 2015, **115**, 3170.

2 For reviews on transition-metal-catalyzed coupling reactions of C-C bond or C-heteroatom formation, please see: (*a*) W. Shi, C. Liu and A. W. lei, *Chem. Soc. Rev.*, 2011, **40**, 2761; (*b*) B. J. Li and Z. J. Shi, *Chem. Soc. Rev.*, 2012, **41**, 5588; (*c*) R. Kumar and E. V. V. Eycken, *Chem. Soc. Rev.*, 2013, **42**, 1121; (*d*) S. G. Modha, V. P. Mehta and E. V. V. Eycken, *Chem. Soc. Rev.*, 2013, **42**, 5042; (*e*) C. Shen, P. F. Zhang, Q. Sun, S. Q. Bai, T. S. Andy Hor and X. G. Liu, *Chem. Soc. Rev.*, 2015, **44**, 291; (*f*) G. Cahiez and A. Moyeux, *Chem. Rev.*, 2010, **110**, 1435.

3 (*a*) H. Li, L. Wang, Y. Zhang and J. B. Wang, *Angew. Chem., Int. Ed.*, 2012, **51**, 2943; (*b*) H. Zhang, R. Y. Shi, A. X. Ding, L. J. Lu, B. R. Chen and A. W. Lei, *Angew. Chem., Int. Ed.*, 2012, **51**, 12542; (*c*) V. P. Mehta and B. Punji, *RSC Advances*, 2013, **3**, 11957; (*d*) C. L. Sun and Z. J. Shi, *Chem. Rev.*, 2014, **114**, 9219; (*e*) S. Roscales and A. G. Csákÿ, *Chem. Soc. Rev.*, 2014, **43**, 8215.

4 (*a*) B. A. F. Uribe, R. D. Little, J. G. Ibanez, A. Palma and R. V. Medrano, *Green Chem.*, 2010, **12**, 2099; (*b*) Y. L. Gu and F. Jérôme, *Chem. Soc. Rev.*, 2013, **42**, 9550; (*c*) G. L. Sorella, G. Strukul and A. Scarso, *Green Chem.*, 2015, **17**, 644; (*d*) B. H. Lipshutz and S. Ghorai, *Green Chem.*, 2014, **16**, 3660.

5 (*a*) X. J. Pan, J. Gao, J. Liu, J. Y. Lai, H. F. Jiang and G. Q. Yuan, *Green Chem.*, 2015, **17**, 1400; (*b*) J. Gao, X. J. Pan, J. Liu, J. Y. Lai, L. M. Chang and G. Q. Yuan, *RSC Advances*, 2015, **5**, 27439; (*c*) A. K. Banerjee, W. Vera, H. Mora, M. S. Laya, L. Bedoya and E. V. Cabrera, *J. Sci. Ind. Res.*, 2006, **65**, 299; (*d*) T. Nobuta, N. Tada, A. Fujiya, A. Kariya, T. Miura and A. Itoh, *Org. Lett.*, 2013, **15**, 574; (*e*) M. A. Kumar, P. Swamy, M. Naresh, M. M. Reddy, C. N. Rohitha, S. Prabhakar, A. V. S. Sarma, J. R. P. Kumar and N. Narender, *Chem. Commun.*, 2013, **49**, 1711; (*f*) W. Xu, U. Kloeckner and B. J. Nachtsheim, *J. Org. Chem.*, 2013, **78**, 6065; (*g*) P. R. Adiyala, D. Chandrasekhar, J. S. Kapure, C. N. Reddy and R. A. Maurya, *Beilstein J. Org. Chem.*, 2014, **10**, 2065; (*h*) C. Buathongjan, D. Beukeaw and S. Yotphan, *Eur. J. Org. Chem.*, 2015, 1575.

6 (*a*) S. Y. Woo, J. H. Kim, M. K. Moon, S. H. Han, S. K. Yeon, J. W. Choi, B. K. Jang, H. J. Song, Y. G. Kang, J. W. Kim, J. Lee, D. J. Kim, O. Hwang and K. D. Park, *J. Med. Chem.*, 2014, **57**, 1473; (*b*) E. Dunny, W. Doherty, P. Evans, J. P. G. Malthouse, D. Nolan and A. J. S. Knox, *J. Med. Chem.*, 2013, **56**, 6638; (*c*) W. Doherty, J. James, P. Evans, L. Martin, N. Adler, D. Nolan and A. Knox, *Org. Biomol. Chem.*, 2014, **12**, 7561; (*d*) B. A. Frankel, M. Bentley, R. G. Kruger and D. G. McCafferty, *J. Am. Chem. Soc.*, 2004, **126**, 3404.

7 (*a*) J. Aziz, S. Messaoudi, M. Alami and A. Hamze, *Org. Biomol. Chem.*, 2014, **12**, 9743; (*b*) M. N. Noshi, A. El-awa, E. Torres and P.

View Article Online
DOI: 10.1039/C5RA10896A

L. Fuchs, *J. Am. Chem. Soc.*, 2007, **129**, 11242; (*c*) H. M. Li, J. Song, X. F. Liu and L. Deng, *J. Am. Chem. Soc.*, 2005, **127**, 8948.

8 For reviews on other routes of synthesis of vinyl sulfones, please see: (*a*) D. C. Reeves, S. Rodriguez, H. Lee, N. Haddad, D. Krishnamurthy and C. H. Senanayake, *Tetrahedron Lett.*, 2009, **50**, 2870; (*b*) R. Chawla, R. Kapoor, A. K. Singh and D. S. Yadav, *Green Chem.*, 2012, **14**, 1308; (*c*) J. L. G. Ruano, J. Alemán and C. G. Paredes, *Org. Lett.*, 2006, **8**, 2683; (*d*) N. Kamigata, H. Sawada and M. Kobayashi, *J. Org. Chem.*, 1983, **48**, 3793.

9 W. Wei, J. L. Li, D. S. Yang, J. W. Wen, Y. T. Jiao, J. M. You and H. Wang, *Org. Biomol. Chem.*, 2014, **12**, 1861.

10 (*a*) Y. L. Xu, J. W. Zhao, X. D. Tang, W. Q. Wu and H. F. Jiang, *Adv. Synth. Catal.*, 2014, **356**, 2029; (*b*) V. Nair, A. Augustine, T. G. George and L. G. Nair, *Tetrahedron Lett.*, 2001, **42**, 6763; (*c*) Y. C. Luo, X. J. Pan and G. Q. Yuan, *Tetrahedron*, 2015, **73**, 2119; (*d*) N. Zhang, D. S. Yang, W. Wei, L. Yuan, Y. J. Cao and H. Wang, *RSC Advances*, 2015, **5**, 37013; (*e*) N. Taniguchi, *Tetrahedron*, 2014, **70**, 1984; (*f*) N. Taniguchi, *Synlett*, 2012, **23**, 1245; (*g*) P. Katurn, S. Chiampanichayakul, K. Korworapan, M. Pohmakotr, V. Reutrakul, T. Jaipetch and C. Kuhakarn, *Eur. J. Org. Chem.*, 2010, 5633.

11 (*a*) G. W. Rong, J. C. Mao, H. Yan, Y. Zheng and G. Q. Zhang, *J. Org. Chem.*, 2015, **80**, 4697; (*b*) X. W. Li, Y. L. Xu, C. Jiang, C. R. Qi and H. F. Jiang, *Chem. Eur. J.*, 2014, 20, 7911; (*c*) S. Tang, Y. Wu, W. Q. Liao, R. P. Bai, C. Liu and A. W. Lei, *Chem. Commun.*, 2014, 50, 4496.

12 Q. C. Xue, Z. J. Mao, Y. Shi, H. B. Mao, Y. X. Cheng and C. J. Zhu, *Tetrahedron Lett.*, 2012, **53**, 1851.

13 Y. J. Jiang and T. P. Loh, *Chem. Sci.*, 2014, **5**, 4939.

14 (*a*) R. Q. Guo, Q. W. Gui and D. D. Wang, *Catal. Lett.*, 2014, **144**, 1377; (*b*) B. V. Rokade and K. R. Prabhu, *J. Org. Chem.*, 2014, **79**, 8110; (*c*) Q. Jiang, B. Xu, A. Zhao, Y. R. Zhao, Y. Y. Li, N. N. He and C. C. Guo, *J. Org. Chem.*, 2014, **79**, 7372; (*d*) Y. L. Xu, X. T. Tang, W. G. Hu, W. Q. Wu and H. F. Jiang, *Green Chem.*, 2014, **16**, 3720; (*e*) P. Katrun, S. Hlekhlai, J. Meesin, M. Pohmakotr, V. Reutrakul, T. Jaipetch, D. Soorukram and C. Kuhakarn, *Org. Biomol. Chem.*, 2015, **13**, 4785; (*f*) H. S. Li and G. Liu, *J. Org. Chem.*, 2014, **79**, 509.

15 (*a*) L. Shi, Y. Y. Liu, Q. F. Liu, B. Wei and G. S. Zhang, *Green Chem.*, 2012, **14**, 1372; (*b*) M B. Gawande, A. D. B. Bonifácio, P. S. Branco and R. S. Varma, *Chem. Soc. Rev.*, 2013, **42**, 5522; (*c*) N. E. Leadbeater, *Chem. Commun.*, 2005, 2881; (*d*) H. D. Velazquez and F. Verpoort, *Chem. Soc. Rev.*, 2012, **41**, 7032; (*e*) Y. L. Gu, *Green Chem.*, 2012, **14**, 2091; (*f*) B. Li and P. H. Dixneuf, *Chem. Soc. Chem.*, 2013, **42**, 5744.

16 (*a*) W. E. Truce and G. C. Wolf, *J. Org. Chem.*, 1971, **36**, 1727; (*b*) P. Katrun, C. Mueangkaew, M. Pohmakotr, V. Reutrakul, T. Jaipetch, D. Soorukram and C. Kuhakarn, *J. Org. Chem.*, 2014, **79**, 1778; (*c*) E. Truce, D. L. Heuring and G. C. Wolf, *J. Org. Chem.*, 1980, **45**, 406; (*d*) L. M. Harwood, M. Julia and G. L. Thuiller, *Tetrahedron*, 1980, **36**, 2483; (*e*) D. C. Craig, G. L. Edwards and C. A. Muldoon, *Synlett*, 1977, 1441.

17 Q. Jiang, J. Jia, A. Zhao and C. C. Guo, *J. Org. Chem.*, 2015, **80**, 3586.

View Article Online
DOI: 10.1039/C5RA10896A

Iodine-mediated synthesis of (*E*)-vinyl sulfones from sodium sulfinates and cinnamic acids in aqueous medium

Jian Gao, Junyi Lai and Gaoqing Yuan*

School of Chemistry and Chemical Engineering, South China University of Technology, Guangzhou, China

A green and highly efficient method for the synthesis of (*E*)-vinyl sulfones promoted by iodine in water medium has been developed, without transition metal catalysts and ligands.