


 Cite this: *RSC Adv.*, 2015, 5, 66723

 Received 8th June 2015
Accepted 28th July 2015

DOI: 10.1039/c5ra10896a

www.rsc.org/advances

With water as the reaction medium, a green and efficient method has been developed for the synthesis of (*E*)-vinyl sulfones via I₂-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 pharmaceutical 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 thiols¹² 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

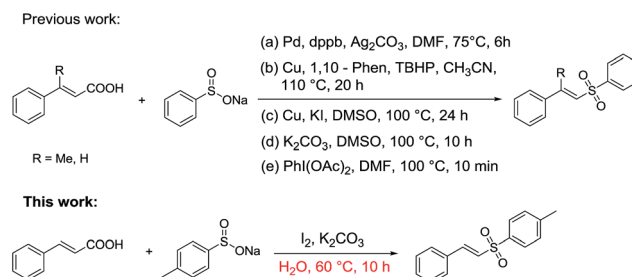
Iodine-mediated synthesis of (*E*)-vinyl sulfones from sodium sulfinates and cinnamic acids in aqueous medium†

Jian Gao, Junyi Lai and Gaoqing Yuan*

and efficient Pd- or Cu-catalyzed decarboxylative 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).

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 I₂-mediated decarboxylative 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 I₂ in the absence of a base at room temperature for 5 h (entry 1). In the presence of base K₂CO₃ (1.0 equiv.), (*E*)-1-methyl-4-(styrylsulfonyl)benzene (**3a**) could be obtained with 10% yield (entry 2). We attempted



Scheme 1 Methods for synthesis of vinyl sulfones.

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

† Electronic supplementary information (ESI) available: Detailed experimental procedures, characterization of products, and NMR spectral charts. See DOI: 10.1039/c5ra10896a

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 °C, the yield of **3a** was drastically increased to 72% (entry 4). Higher temperatures (50 °C, 60 °C and 70 °C, entries 5–7) were further tested, and a best yield was obtained (91%, entry 6). When 0.5 equiv. of I₂ or 0.5 equiv. of K₂CO₃ 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 K₂CO₃ (2.0 equiv.) was used (entry 10). At last, various bases (Cs₂CO₃, NaOAc, KOH, CH₃ONa and Et₃N) and solvents (CH₃CN, DMF, EtOAc, CH₃OH and DMSO) were screened, respectively. These results showed that K₂CO₃ was an optimal base and water was the most suitable solvent in this process (entries 11–20).

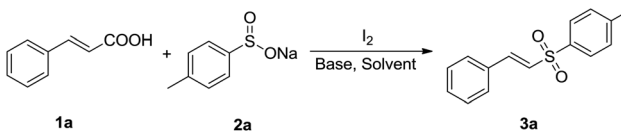
With the optimal reaction conditions in hand, the scope of substrates was investigated and the results are summarized in Table 2. On one hand, we examined the reaction of sodium 4-methyl benzenesulfinate (**2a**) with cinnamic acid derivatives in the standard reaction conditions. Some cinnamic acids which have electron-withdrawing substituents on the phenyl ring (4-CN, 4-F, 4-Cl, 4-Br, 4-CF₃ 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 sulfonylvinyl) benzene (**3t**) was obtained with 45% yield.

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

Table 1 Optimization of reaction conditions^a



| Entry | I ₂ (equiv.) | Base (equiv.) | Solvent | Time (h) | Temp. (°C) | Yield ^b (%) |
|-----------------|-------------------------|---------------------------------------|--------------------|----------|------------|------------------------|
| 1 | 1.0 | No | H ₂ O | 5 | rt | Trace |
| 2 | 1.0 | K ₂ CO ₃ (1.0) | H ₂ O | 5 | rt | 10 |
| 3 | 1.0 | K ₂ CO ₃ (1.0) | H ₂ O | 10 | rt | 23 |
| 4 | 1.0 | K ₂ CO ₃ (1.0) | H ₂ O | 10 | 40 | 72 |
| 5 | 1.0 | K ₂ CO ₃ (1.0) | H ₂ O | 10 | 50 | 80 |
| 6 | 1.0 | K ₂ CO ₃ (1.0) | H ₂ O | 10 | 60 | 91 |
| 7 | 1.0 | K ₂ CO ₃ (1.0) | H ₂ O | 10 | 70 | 84 |
| 8 | 0.5 | K ₂ CO ₃ (1.0) | H ₂ O | 10 | 60 | 40 |
| 9 | 1.0 | K ₂ CO ₃ (0.5) | H ₂ O | 10 | 60 | 41 |
| 10 | 1.0 | K ₂ CO ₃ (2.0) | H ₂ O | 10 | 60 | 80 |
| 11 | 1.0 | Cs ₂ CO ₃ (1.0) | H ₂ O | 10 | 60 | 90 |
| 12 | 1.0 | NaOAc (1.0) | H ₂ O | 10 | 60 | 14 |
| 13 | 1.0 | KOH (1.0) | H ₂ O | 10 | 60 | 30 |
| 14 | 1.0 | CH ₃ ONa (1.0) | H ₂ O | 10 | 60 | 35 |
| 15 | 1.0 | Et ₃ N (1.0) | H ₂ O | 10 | 60 | 22 |
| 16 | 1.0 | K ₂ CO ₃ (1.0) | CH ₃ CN | 10 | 60 | 7 |
| 17 | 1.0 | K ₂ CO ₃ (1.0) | DMF | 10 | 60 | 5 |
| 18 | 1.0 | K ₂ CO ₃ (1.0) | EtOAc | 10 | 60 | 3 |
| 19 | 1.0 | K ₂ CO ₃ (1.0) | CH ₃ OH | 10 | 60 | 52 |
| 20 | 1.0 | K ₂ CO ₃ (1.0) | DMSO | 10 | 60 | 5 |
| 21 ^c | 1.0 | K ₂ CO ₃ (1.0) | H ₂ O | 10 | 60 | 87 |

^a Reaction conditions: **1a** (0.5 mmol), **2a** (0.6 mmol), base (1.0 equiv.), I₂ (1.0 equiv.), H₂O (2 mL) at 60 °C for 10 h. ^b Determined by GC-MS using dodecane as the internal standard. ^c Under N₂ atmosphere.

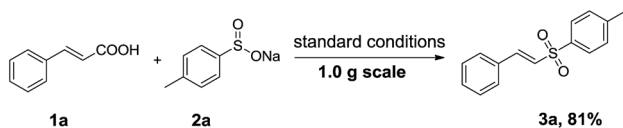
Table 2 Synthesis of (*E*)-vinyl sulfones^{a,b}

| 1 | 2 | 3 |
|--|---|---|
| | | |
| $\xrightarrow[\text{H}_2\text{O}, 60\text{ }^\circ\text{C}, 10\text{ h}]{\text{I}_2, \text{K}_2\text{CO}_3}$ | | |
| | | |
| | | |
| | | |
| | | |
| | | |
| | | |
| | | |

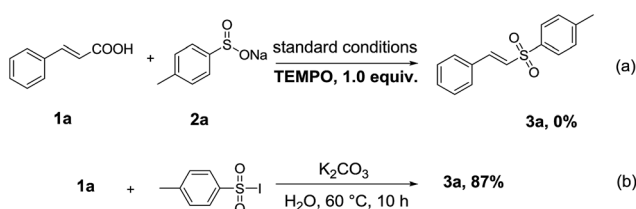
R = H, **3a**, 81%
 R = Me, **3b**, 79%
 R = OMe, **3c**, 80%
 R = CN, **3d**, 63%
 R = F, **3e**, 84%
 R = Cl, **3f**, 84%
 R = Br, **3g**, 81%
 R = CF₃, **3h**, 80%
 R = t-Bu, **3i**, 69%

 R' = H, **3p**, 78%
 R' = F, **3q**, 79%
 R' = Cl, **3r**, 83%
 R' = Br, **3s**, 81%
 R' = t-Bu, **3t**, 45%

^a Reaction conditions: **1** (0.5 mmol), **2** (0.6 mmol), I₂ (1.0 equiv.), K₂CO₃ (1.0 equiv.), H₂O (2 mL) at 60 °C for 10 h. ^b Isolated yields.



Scheme 2 Reaction on a 1.0 gram scale.



Scheme 3 Control experiments.

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 ESI.† In addition, it should be pointed out that I₂ is almost converted to iodine anions after the reaction in two steps (*i.e.*, the reaction of ArSO₂Na with I₂, and the reaction of ArSO₂I with cinnamic acid) in the present standard conditions, which is confirmed by iodometric 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



Scheme 4 Possible reaction mechanism.

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}

In conclusion, we have developed a green and efficient method for the synthesis of vinyl sulfones *via* I₂-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

- 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.
- 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 Adv.*, 2013, **3**, 11957; (d) C. L. Sun and Z. J. Shi, *Chem. Rev.*, 2014, **114**, 9219; (e) S. Roscales and A. G. Csáký, *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 Adv.*, 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. 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 Adv.*, 2015, **5**, 37013; (e) N. Taniguchi, *Tetrahedron*, 2014, **70**, 1984; (f) N. Taniguchi, *Synlett*, 2012, **23**, 1245; (g) P. Katur, 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. Hlekhilai, 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. Rev.*, 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.