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Visible light-mediated dehydrogenative β-arylsulfonylation of tertiary aliphatic amines with arylsulfonyl chlorides†

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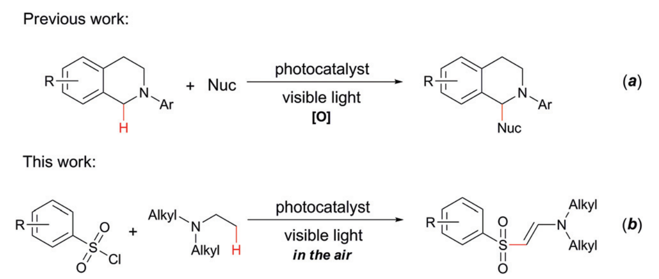
The novel synthesis of β-arylsulfonyl enamines has been achieved by visible light-mediated dehydrogenative arylsulfonylation of tertiary aliphatic amines with arylsulfonyl chlorides in moderate yield.

One of the major themes for organic chemists is to develop green and efficient synthetic methods. In this context, in the last few years visible light photoredox catalysis[1] with Ru/Ir complexes[2] or organic dyes[3] as photosensitizers seems to play a more and more important role. Many photo-catalytic reactions have been successfully developed to prepare various compounds. For example, Stephenson[4] and others[1d,5] reported that trapping iminium ions generated from tertiary amines under visible light at room temperature with various nucleophiles could give rise to α-functionalized products (Scheme 1a). Our group also found that arylsulfonyl chlorides could be reduced to arene hypochlorothioites by indoles subsequently leading to 3-(arylthio)-1*H*-indoles in visible light.[6] As indicated in some elegant work reported by Nicewicz,[7] it is crucial to match oxidants with reductants subject to the redox potential of the photocatalysts in the photocatalytic cycle. That inspired us to look for other reductive agents such as tertiary amines involved in photoredox catalysis with arylsulfonyl chlorides. In addition, compared to tertiary anilines, simple tertiary aliphatic amines that are commercially available had drawn little attention.[8]



Scheme 1 Tertiary amines involved in photoredox reactions.

On the other hand, β-functionalization of unactivated substrates is always a challenging target. With strong oxidants or transition metal catalysts, some striking reactions could be realized.[9] Recently, MacMillan fulfilled the β-arylation of ketones and aldehydes *via* merging photoredox catalysis with organocatalysis under mild conditions.[10] Herein we report the first visible light-mediated dehydrogenative β-arylsulfonylation of tertiary aliphatic amines[11] with arylsulfonyl chlorides in the air (Scheme 1b).

Our investigation started with the reaction of *p*-tolylsulfonyl chloride with 2 equivalents of triethylamine in the presence of 2.5 mol% $Ru(bpy)_3(PF_6)_2$ in an atmosphere of argon under the irradiation of 23 W fluorescent light, which afforded the partially deoxygenated product (*E*)-*N*,*N*-diethyl-1-(*p*-tolylthio)-2-tosyl-ethenamine **A** (the structure was confirmed by X-ray analysis of an analogous product starting from *N*,*N*-diisopropylethylamine, Fig. 1a) and a non-deoxygenated product (*E*)-*N*,*N*-diethyl-2-tosylethenamine **B** (Fig. 1b) (Scheme 2a). So additional oxidants were introduced to improve the yield of the latter product **B**.

The same reaction was carried out using an O_2 balloon, and sulfonamide was formed exclusively perhaps as a result of overoxidation or being sensitive to the concentration of O_2 [12] (Scheme 2b). However, once this reaction was open to air in 3 minutes, TsCl was consumed completely and the sole product β-arylsulfonyl enamine **B** was formed (Scheme 2c). Then we screened some factors such as the solvent, photocatalyst, temperature, and so on (for detailed information, see ESI†), achieving the best conditions, under which 1 equiv. of arylsulfonyl chloride and 4 equiv. of tertiary amine reacted with 1 mol% $Ru(bpy)_3(PF_6)_2$ as photocatalyst in the air between −5 and 5 °C with gentle stirring in acetone.

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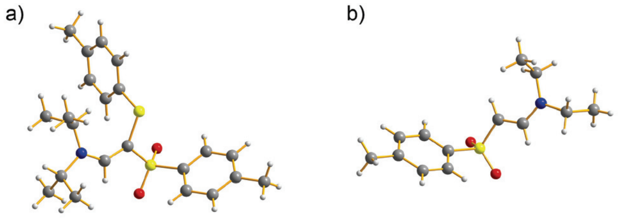
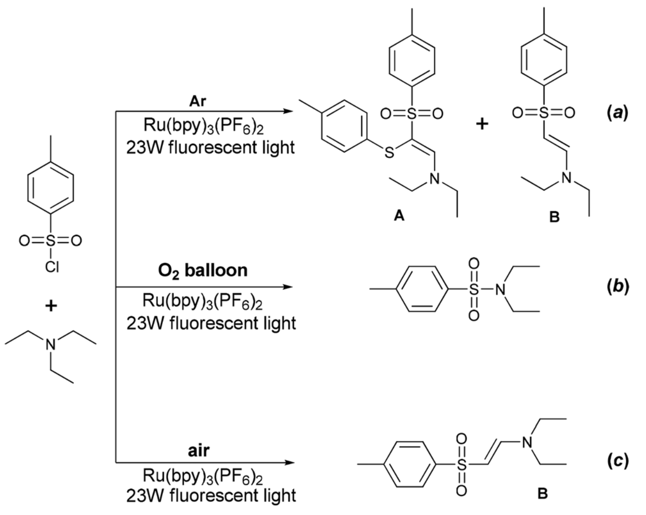


Fig. 1 The crystal structures of (*E*)-*N*-isopropyl-*N*-(2-(*p*-tolylthio)-2-tosylvinyl)propan-2-amine (a) and (*E*)-*N*,*N*-diethyl-2-tosylethenamine (**3a**, b) (C: gray; H: white; N: blue; O: red; S: yellow).

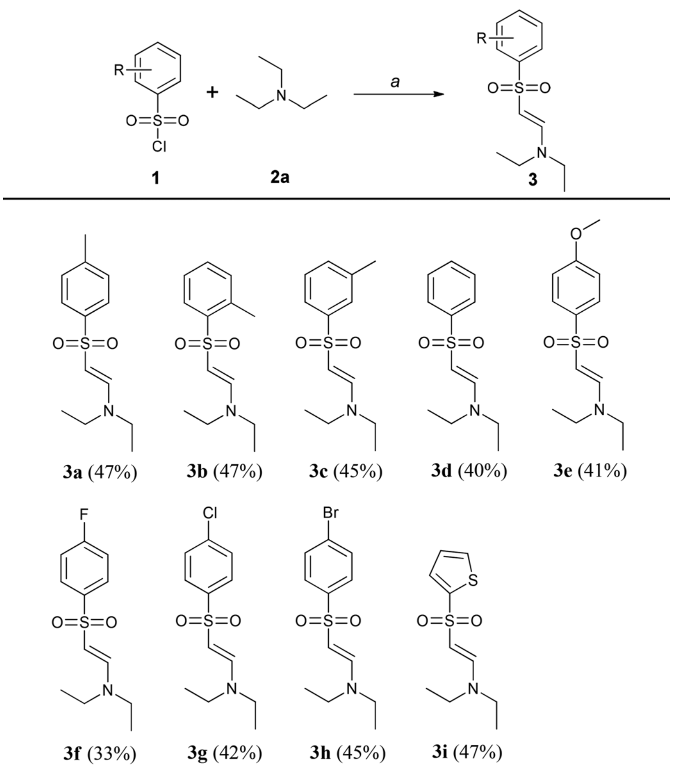


Scheme 2

With the standard conditions in hand, we investigated a range of commercially available arylsulfonyl chlorides. The products are *E*-form exclusively.[13] Besides *p*-tolylsulfonyl chloride, *o*- and *m*-methyl substituted benzene sulfonyl chlorides gave almost the same yield of products regardless of hindrance of the *o*-methyl group (Table 1, **3a–3c**). Benzene sulfonyl chloride without any substituents produced the corresponding products in a little lower yield (Table 1, **3d**), which was the same as that of the electron-donating derivative (Table 1, **3e**). The yields varied with the electron-withdrawing properties, and the reactions involving *p*-Br and *p*-Cl benzene sulfonyl chloride were in higher yield than that of *p*-F benzene sulfonyl chloride (Table 1, **3f–3h**). The hetero-arylsulfonyl chloride proceeded well too (Table 1, **3i**).

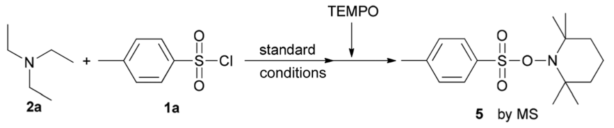
Next, the scope of tertiary amines was investigated. We were delighted to find that the sulfonyl chloride reacted with *N*,*N*-diisopropylethylamine (DIPEA) at the terminal of ethyl rather than isopropyl exclusively (Table 2, **4a**). When tri-*n*-propylamine and tri-*n*-butylamine were applied, *E*- without any *Z*-products were obtained (Table 2, **4b–c**, for NOESY experiments see ESI†). Cycloamines were examined (Table 2, **4d–e**) from which both regio-isomeric products were obtained. Interestingly, the isomers with *endo*-double bond were obtained in higher yield than those with the *exo*-double bond. Moreover, the selectivity was excellent when the acycloamines were used albeit in lower yield (Table 2, **4f**). Tertiary amine with hindrance, *N*-cyclohexyl-*N*-propyl-cyclohexanamine, reacting with sulfonyl chloride afforded the corresponding β-arylsulfonyl enamines in acceptable yield (Table 2, **4g**).

Table 1 Scope of arylsulfonyl chlorides



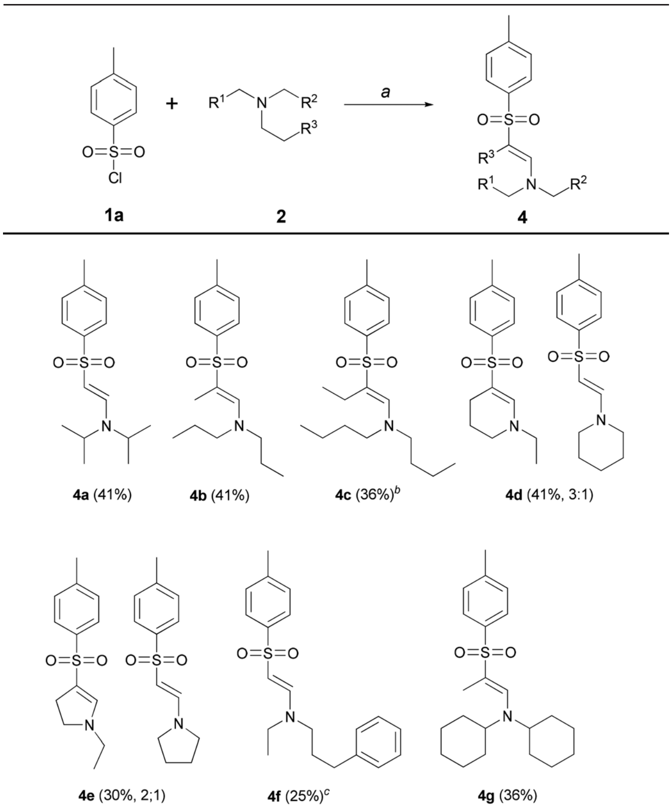
[a] Unless otherwise specified, all reactions were carried out with **1** (1 mmol), **2a** (4 mmol), photocatalyst (1 mol%) in acetone, under 23 W fluorescent light between −5 and 5 °C open to air for 3–10 min, and the yield is the isolated yield.

To probe the intermediary radical species, we added a radical trapping agent TEMPO to the model reaction of **1a** and **2a**. The reaction was quenched, and **5** could be detected by LC-MS (eqn (1)). Thus, the sulfonyl radical may be an intermediate radical. It is worth mentioning that when most of the above reactions were conducted under vigorous stirring in the air, a small amount of sulfonamides was generated concomitant with the corresponding β-arylsulfonyl enamines. The side product sulfonamides were presumably formed by the reactions of arylsulfonyl chlorides with secondary amines which may be produced from tertiary amines. Actually, in 2010, Loh[14] reported the process of copper-catalyzed tertiary amine oxidative conversion to secondary amine or enamine *via* an intermediate iminium ion. And

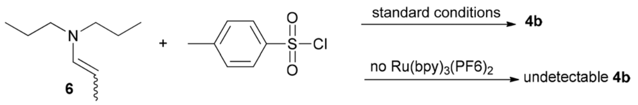


(1)

Table 2 Scope of tertiary amines



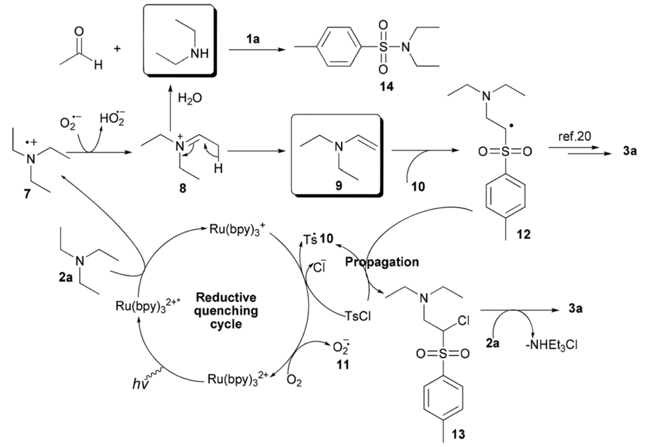
[a] Unless otherwise specified, all reactions were carried out with **1a** (1 mmol), **2** (4 mmol), photocatalyst (1 mol%) in acetone, under 23 W fluorescent light between −5 and 5 °C open to air for 3–10 min, and the yield is the isolated yield. [b] 40 min. [c] Room temperature, 40 min.



Scheme 3 Enamine involved in reactions.

Stephenson[15] also verified the feasibility of the iminium ion to enamine with the photocatalyst. We deduced that the pivotal intermediate enamine was generated in our system. Therefore, additional experiments were conducted. When enamine **6**[16] was treated with TsCl under our optimised conditions, **4b** was obtained. While without a photocatalyst within 30 minutes, **4b** was undetectable in the mixture of the reaction (Scheme 3).

Based on the above results and the matched reductive potential[1d] of tertiary amines with that of $Ru(bpy)_3^{2+}*$/$Ru(bpy)_3^{+}$, a possible mechanism is postulated in Scheme 4. The photosensitizer $Ru(bpy)_3^{2+}$ is excited by visible light to form $Ru(bpy)_3^{2+}*$, which is trapped by triethylamine[17] *via* a reductive quenching path[18] producing $Ru(bpy)_3^{+}$ and radical cation **7**. The highly reducing Ru(I) can regenerate $Ru(bpy)_3^{2+}$ by transferring one electron to TsCl or O_2,[19] affording radical **10** or **11**, respectively. On the other hand, after the hydrogen atom being abstracted by **11**, **7** gives an iminium ion **8**, which lead to two distinct destinies. One is that **8** hydrolyses to propionaldehyde and diethylamine being converted into sulfonamide **13**, the other is forming enamine **9**. Subsequently, **9** may be attacked by **10**, followed by being oxidized and losing a proton, providing the final product **3a**.[20] However, the path of **12** reacting with TsCl giving **13** and subsequent E2 elimination of HCl could not be excluded now, although **13** was not detected even by MS.[21]



Scheme 4 Proposed mechanism.

Conclusions

In conclusion, we herein report a novel synthesis method of β-arylsulfonyl enamines by photoredox catalysis. This reaction was carried out in non-pretreated acetone open to air, and most of them completed within 10 minutes without any additives. Importantly, all of the products are in *E*-form.

Acknowledgements

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Notes and references

1 For some recent reviews, see: (*a*) J. W. Tucker and C. R. J. Stephenson, *J. Org. Chem.*, 2012, **77**, 1617; (*b*) K. Zeitler, *Angew. Chem., Int. Ed.*, 2009, **48**, 9785; (*c*) J. Xuan and W.-J. Xiao, *Angew. Chem., Int. Ed.*, 2012, **51**, 6828; (*d*) C. K. Prier, D. a. Rankic and D. W. C. MacMillan, *Chem. Rev.*, 2013, **113**, 5322; (*e*) L. Shi and W. Xia, *Chem. Soc. Rev.*, 2012, **41**, 7687; (*f*) Y. Xi, H. Yi and A. Lei, *Org. Biomol. Chem.*, 2013, **11**, 2387; (*g*) T. P. Yoon, M. a. Ischay and J. Du, *Nat. Chem.*, 2010, **2**, 527.

2 For some recent reviews, see: S. Campagna, P. Francesco, G. Bergamini, V. Balzani, C. Inorganica and C. Analitica, *Top. Curr. Chem.*, 2007, **280**, 117.

3 For some examples, see: (*a*) M. Neumann, S. Füldner, B. König and K. Zeitler, *Angew. Chem., Int. Ed.*, 2011, **50**, 951; (*b*) Y. C. Teo, Y. Pan and C. H. Tan, *ChemCatChem*, 2013, **5**, 235; (*c*) M. Majek and A. J. von Wangelin, *Chem. Commun.*, 2013, **49**, 5507.

4 For selected examples, see: (*a*) A. G. Condie, J. C. González-Gómez and C. R. J. Stephenson, *J. Am. Chem. Soc.*, 2010, **132**, 1464; (*b*) D. B. Freeman, L. Furst, A. G. Condie and C. R. J. Stephenson, *Org. Lett.*, 2012, **14**, 94.

5 For one of the elegant work, see: Y.-Q. Zou, L.-Q. Lu, L. Fu, N.-J. Chang, J. Rong, J.-R. Chen and W.-J. Xiao, *Angew. Chem., Int. Ed.*, 2011, **50**, 7171.

6 M. Chen, Z.-T. Huang and Q.-Y. Zheng, *Chem. Commun.*, 2012, **48**, 11686.

7 (*a*) T. M. Nguyen and D. A. Nicewicz, *J. Am. Chem. Soc.*, 2013, **135**, 9588; (*b*) M. Riener and D. A. Nicewicz, *Chem. Sci.*, 2013, **4**, 2625.

8 A. Singh, A. Arora and J. D. Weaver, *Org. Lett.*, 2013, **15**, 5390.

9 For selected examples, see: (*a*) M. Wasa, K. M. Engle and J.-Q. Yu, *J. Am. Chem. Soc.*, 2009, **131**, 9886; (*b*) A. Renaudat, L. Jean-Gérard, R. Jazzar, C. E. Kefalidis, E. Clot and O. Baudoin, *Angew. Chem., Int. Ed.*, 2010, **49**, 7261; (*c*) Y. Ano, M. Tobisu and N. Chatani, *J. Am. Chem. Soc.*, 2011, **133**, 12984; (*d*) S.-L. Zhang, H.-X. Xie, J. Zhu, H. Li, X.-S. Zhang, J. Li and W. Wang, *Nat. Commun.*, 2011, **2**, 211; (*e*) M. V. Leskinen, K.-T. Yip, A. Valkonen and P. M. Pihko, *J. Am. Chem. Soc.*, 2012, **134**, 5750.

10 M. T. Pirnot, D. A. Rankic, D. B. C. Martin and D. W. C. MacMillan, *Science*, 2013, **339**, 1593.

11 It seems similar to the Polonovski–Potier reaction generating conjugated unsaturated amines, but it is milder.

12 Y. Cheng, J. Yang, Y. Qu and P. Li, *Org. Lett.*, 2012, **14**, 98.

13 (*a*) W. E. Truce and D. G. Brady, *J. Org. Chem.*, 1966, **31**, 3543; (*b*) J. Sauer and H. Prahl, *Tetrahedron Lett.*, 1966, **7**, 2863; (*c*) S. I. Miller and R. Tanaka, *J. Org. Chem.*, 1971, **36**, 3856.

14 J.-S. Tian and T.-P. Loh, *Angew. Chem., Int. Ed.*, 2010, **49**, 8417.

15 L. Furst, B. S. Matsuura, J. M. R. Narayanam, J. W. Tucker and C. R. J. Stephenson, *Org. Lett.*, 2010, **12**, 3104.

16 The enamine **6** was prepared by the reaction of propionaldehyde with dipropylamine with K_2CO_3 as the dehydrating agent for 1.5 hours, and used without further purification.

17 J. M. R. Narayanam, J. W. Tucker and C. R. J. Stephenson, *J. Am. Chem. Soc.*, 2009, **131**, 8756.

18 The oxidative quenching path may be highly unlikely due to the relatively high reductive potential of TsCl (−1.03 V *vs.* SCE), see: A. Houmam and E. M. Hamed, *Phys. Chem. Chem. Phys.*, 2012, **14**, 113. However, in the previous work (C. J. Wallentin, J. D. Nguyen, P. Finkbeiner and C. R. J. Stephenson, *J. Am. Chem. Soc.*, 2012, 134, 8875; G.-B. Deng, Z.-Q. Wang, J.-D. Xia, P.-C. Qian, R.-J. Song, M. Hu, L.-B. Gong and J.-H. Li, *Angew. Chem. Int. Ed.*, 2013, 52, 1535), TsCl may be the only oxidant which can reduce $Ru(bpy)_3{}^{2+*}$ to $Ru(bpy)_3{}^{3+}$. So we could not preclude the oxidative quenching mechanism absolutely now.

19 J.-J. Zhong, Q.-Y. Meng, G.-X. Wang, Q. Liu, B. Chen, K. Feng, C.-H. Tung and L.-Z. Wu, *Chem. – Eur. J.*, 2013, **19**, 6443.

20 (*a*) H. Jiang, X. Chen, Y. Zhang and S. Yu, *Adv. Synth. Catal.*, 2013, **355**, 809; (*b*) H. Jiang, C. Huang, J. Guo, C. Zeng, Y. Zhang and S. Yu, *Chem. – Eur. J.*, 2012, **18**, 15158; (*c*) H. Jiang, Y. Cheng, Y. Zhang and S. Yu, *Eur. J. Org. Chem., 2013*, 2013, 5485; (*d*) N. Iqbal, S. Choi, E. Kim and E. J. Cho, *J. Org. Chem.*, 2012, **77**, 11383.

21 The model reaction of **1a** and **2a** was “paused” after light was off, and continued to react until the light was on and finished within 10 minutes.