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Double C–N bond cleavages of *N*-alkyl 4-oxopiperidinium salts: access to unsymmetrical tertiary sulfonamides†

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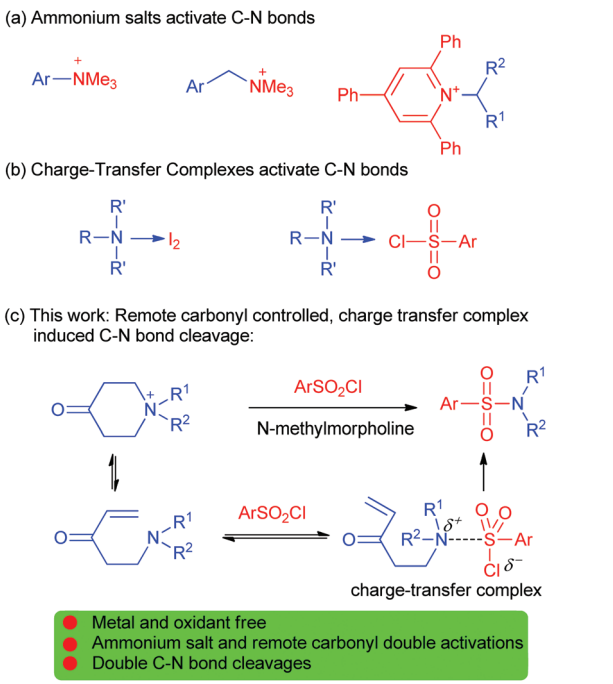
In this paper, regiospecific, double intraannular C–N bond cleavages of *N*-alkyl 4-oxopiperidinium salts are presented. The reaction sequence involves a charge-transfer complex, *in situ* formed between sulfonyl chloride and *N*-methylmorpholine, which induces S–Cl bond homolysis of sulfonyl chloride, yielding a reactive sulfonyl radical that further induces the double C–N bond cleavages of *N*-alkyl 4-oxopiperidinium salt. The secondary amine thus produced was trapped by sulfonyl chloride to yield the desired sulfonamide product. The key feature of this protocol is that two intraannular C–N bonds of the 4-oxopiperidine ring are cleaved in one step under metal- and oxidant-free conditions.

Introduction

Considering the fact that aliphatic tertiary amines are relatively stable and widely present in nature,[1] selective transformations of C(sp^3)–N bonds of simple aliphatic tertiary amines into their corresponding nitrogen-containing molecules are of substantial interest for organic synthetic chemists, especially those who are working in the area of pharmaceutical chemistry and materials sciences. However, due to thermodynamic stability and relatively high bond dissociation energies (*ca.* 80 kcal mol^{-1}), the selective cleavage of inert C(sp^3)–N bonds of tertiary amines remains a challenging task.[2] Among the various established methods for C(sp^3)–N bond activation, the conversion of electron-rich C(sp^3)–N bonds of amines into electron-deficient ammonium salts is the most efficient strategy. Since 1988, pioneered by the work of Wenkert *et al.*, aryltrimethylammonium salts,[3] *N*-alkylpyridinium salts,[4] benzylic ammonium salts,[5] propargylic ammonium salts[6] *etc.* have been extensively developed which, under transition metal catalysis, are promising C^+ equivalents and can be cross-coupled with various nucleophiles, *e.g.*, organometallics, boronic acids, alkynes, alkenes *etc.* to form C–C bonds (Scheme 1(a)). In addition, a charge-transfer complex (CTC) formed between aliphatic amines and electrophiles (I_2,[7] $ArSO_2Cl$[8]) has shown efficiency in aliphatic C–N bond activation (Scheme 1(b)). Furthermore, C–N bonds of aliphatic amines could also be activated by the neighboring functionalities. In this respect, the presence of the α-amino group in aminals,[9] the phenyl group in benzylamines[10] and the C=C double bond in allylamines[11] all have significant impacts on adjacent C–N bond



Scheme 1 Strategies for C–N bond activation.

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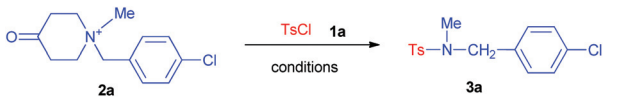
energy and thus various kinds of valuable compounds were prepared. Despite these important advances, most of the known C–N bond dissociation protocols are only effective when using expensive transition metal catalysts and commonly demand a larger excess amount of oxidants.

Recently, we reported an interesting CTC promoted sulfonylation of tertiary ethylene-1,2-diamines.[8a] In these reactions, C(sp^3)–N bonds were greatly attenuated by CTC, *in situ* formed between the two reactants, *i.e.* sulfonyl chloride and tertiary 1,2-ethylenediamine. Thus, a large variety of synthetically useful *N*,*N*-disubstituted sulfonamides were easily prepared in good to high yields. In continuation of our studies on C–N bond activation and search for new synthetic procedures for pharmaceutically important *N*,*N*-disubstituted sulfonamides, our interest shifted to 4-oxopiperidinium salts as in these compounds, C–N bonds are doubly activated with ammonium cations and γ-carbonyls. We thus anticipated that under basic conditions, 4-oxopiperidinium salts could first undergo a Hoffmann type elimination to yield an unsaturated tertiary amine which could further react with sulfonyl chloride and again undergo a Hoffman type elimination, yielding an *N*,*N*-disubstituted tertiary sulfonamide (Scheme 1c). Although *N*,*N*-disubstituted sulfonamides could be easily prepared *via* cross-coupling of sulfonyl chlorides with secondary amines,[12] this protocol has clear limitations as most functionalized secondary amines are unstable in air and are not commercially available. Alternatively, *N*-substituted sulfonamides could be prepared *via* *N*-alkylation of sulfonamides with alkyl halides[13] or alcohols;[14] however, limitations such as harsh reaction conditions, requirement of expensive catalysts, narrow substrate scope *etc*. still exist. Here, we report a metal- and oxidant-free, remote carbonyl group controlled, CTC facilitated regiospecific double C–N bond cleavages of *N*-substituted 4-oxopiperidinium salts whereby *N*,*N*-disubstituted sulfonamides were conveniently prepared.

Results and discussion

In our previous studies involving reactions of sulfonyl chlorides with tertiary ethylene-1,2-diamines,[8a] Et_3N was demonstrated to be an inert amine species towards sulfonyl chlorides. Thus it was selected as a base to promote the reaction between TsCl **1a** and *N*-(4-chlorobenzyl)-*N*-methyl-4-oxopiperidin-1-ium chloride **2a**. First, when only 2 equivalents of Et_3N were introduced, this reaction proceeded in MeCN at 80 °C and sulfonamide **3a** was formed in 35% isolated yield (Table 1, entry 1). Gratifyingly, when 3 equivalents of Et_3N (1.5 mmol) were used, the yield of **3a** increased to 55%. An attempt to replace Et_3N with *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TMEDA) delivered *N*,*N*-dimethyltolylsulfonamide ($TsNMe_2$, 72% yield) as the main product (entry 3).[15] Other bases screened such as 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU), tri-*n*-butylphosphine (TBUP), K_2CO_3, Cs_2CO_3, CaH_2, and NaOMe all failed to give the desired product **3a** (Table 1, entries 4–9). The best result was obtained by using *N*-methylmorpholine (NMM) as a base,

Table 1 Optimization of the reaction conditions[a]



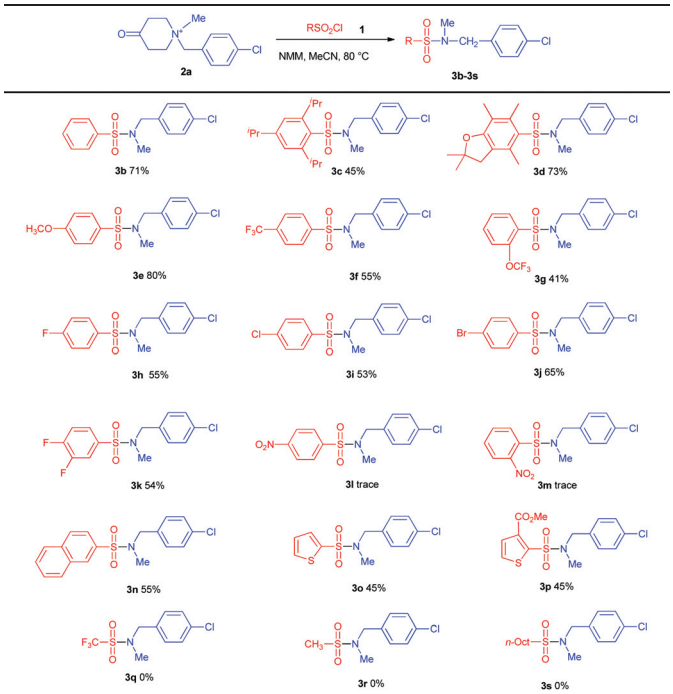
Entry	Base	Solvent	*T* (°C)	Yield[b] (%)
1	Et_3N	MeCN	80	35[c]
2	Et_3N	MeCN	80	55
3	TMEDA	MeCN	80	Trace[d]
4	DBU	MeCN	80	Trace
5	TBUP	MeCN	80	0
6	K_2CO_3	MeCN	80	0
7	Cs_2CO_3	MeCN	80	0
8	CaH_2	MeCN	80	0
9	NaOMe	MeCN	80	Trace
10	NMM	MeCN	80	76
11	NMM	CH_2Cl_2	40	n.r.[e]
12	NMM	THF	60	Trace
13	NMM	Toluene	110	30
14	NMM	DMF	80	Trace
15	NMM	MeCN	80	72[f]

[a] Reaction conditions: **1a** (0.5 mmol), base (1.5 mmol), **2a** (0.6 mmol), solvent (2.0 mL), air, 4 h. [b] Isolated yield. [c] 1.0 mmol Et_3N was employed. [d] $TsNMe_2$ (yield: 72%) was isolated as the sole product. [e] n.r. = no reaction. [f] Experiment was performed with **1a** (5 mmol, 1.19 g) and **2a** (6 mmol, 1.14 g) yielded 1.11 g of **3a** (72%).

delivering **3a** in 76% yield (Table 1, entry 10). Further screening of the solvents and temperature indicated that MeCN and 80 °C were the optimal reaction conditions (Table 1, entries 10–14). Consequently, the best reaction conditions were selected as indicated in entry 10. A gram-scale synthesis performed under these conditions gave a 72% isolated yield of **3a** (Table 1, entry 15).

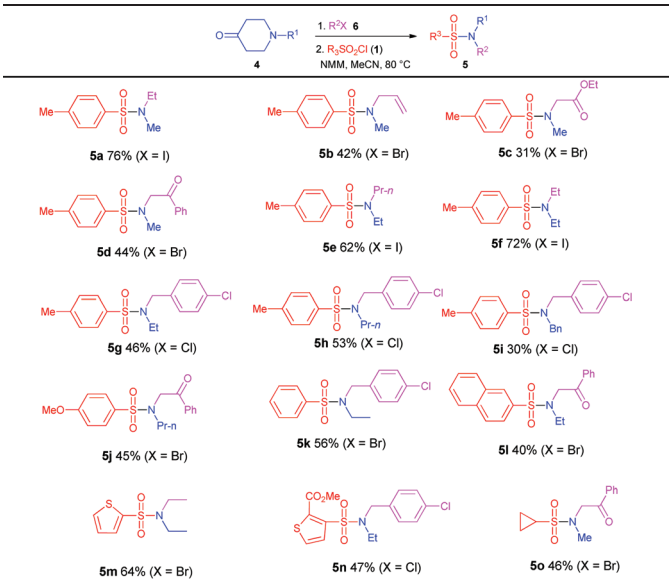
With the optimized reaction conditions in hand, the scope of this cascade reaction of double C–N bond cleavage methodology was evaluated over a wide array of sulfonyl chlorides using **2a** as a standard substrate (Table 2). First, benzenesulfonyl chlorides bearing a variety of substituents were screened to evaluate the general applicability of this transformation (**3a–m**). In this respect, functionalities such as alkyl (**3c** & **3d**), alkoxyl (**3d** & **3e**), CF_3 (**3f**) and halogens (**3h–k**) were tolerant to these optimized reaction conditions, delivering the corresponding sulfonamides in 41–80% yields. Remarkably, the highly sterically constrained 2,4,6-triisopropylbenzenesulfonyl chloride (**3c**) and 2,2,4,6,7-pentamethyl-2,3-dihydrobenzofuran-5-sulfonyl chloride (**3d**) were compatible with this reaction system, indicating the broad feasibility of this approach. Generally, benzenesulfonyl chlorides bearing an electron-donating group exhibit better efficiency than those with electron-withdrawing groups and the highest yield of sulfonamide was obtained from 4-methoxybenzenesulfonyl chloride (**3e**, 80%). When 2-trifluoromethoxybenzenesulfonyl chloride was employed, a relatively low yield of **3g** (41%) was obtained, partially due to the steric effect of 2-OCF_3. Notably, in this cascade three-bond transformation reaction, an overall 41% yield is comparable to a 74% yield of a single-bond transformation reaction; thus it is also a satisfactory result.

Table 2 Scope of sulfonyl chlorides[a,b]



[a] Reaction conditions: **1** (0.5 mmol), **2a** (0.6 mmol), NMM (1.5 mmol), CH_3CN (2 mL), 80 °C, 4 h. [b] Isolated yield.

Table 3 Scope of 4-oxopiperidinium salts[a,b]

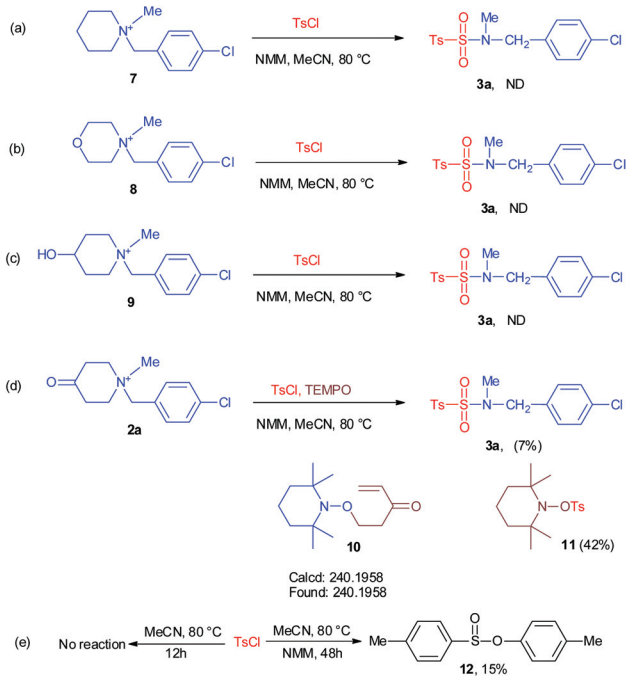


[a] Reaction conditions: (1). **4** (0.6 mmol), **6** (0.6 mmol), MeCN (2 mL), 50 °C, overnight and (2) **1** (0.5 mmol), NMM (1.5 mmol), CH_3CN (2 mL), 80 °C, 4 h. [b] Isolated yield.

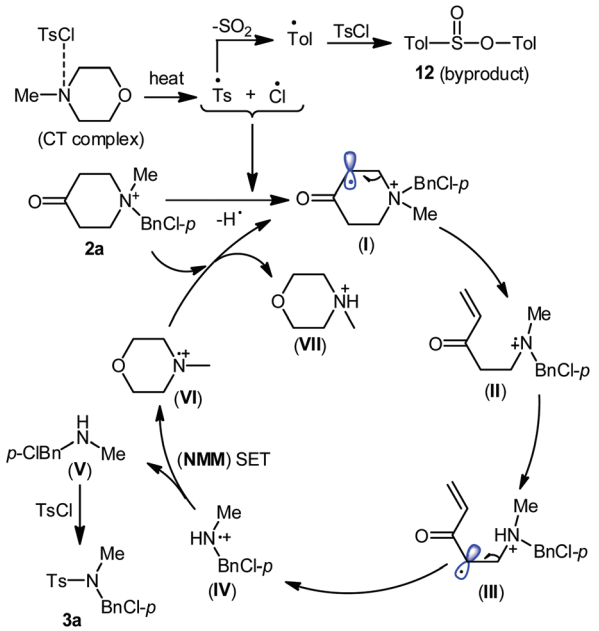
Unexpectedly, when a strong electro-withdrawing NO_2 group was installed on benzenesulfonyl chloride at either the *para* or *ortho* position, only trace amounts of the desired sulfonamide products could be observed (**3l** & **3m**). Both of the nitrobenzene sulfonyl chlorides decomposed quickly under this reaction system. As expected, reactions involving quinoline-3-sulfonyl chloride and 2-thiophenesulfonyl chlorides proceeded quite well, delivering the corresponding products **3n–p** in moderate yields. Aliphatic sulfonyl chlorides screened, *e.g.* trifluoromethylsulfonyl chloride, methanesulfonyl chloride and *n*-octyl sulfonyl chloride, could not participate in these reactions, possibly because of the instability of these alkylsulfonyl chlorides under the basic reaction conditions.[16]

To test the versatility of this double C–N bond cleavage protocol, a two-step one-pot procedure was then carried out (Table 3). At first, *N*-methyl-4-piperidone was converted by EtI (1.2 equiv.) into its ammonium salt. Then TsCl (1.2 equiv.) and NMM (3.0 equiv.) were added and after stirring the mixture at 80 °C for 4 h, sulfonamide **5a** was obtained in 76% isolated yield. Encouraged by this achievement, *N*-methyl, *N*-ethyl, *N*-propyl, and *N*-benzyl 4-piperidones (**4**) were first treated respectively with aliphatic halides **6**, *i.e.* allyl bromide, ethyl bromoacetate and 2-bromoacetophenone *etc*. to convert them into their corresponding ammonium salts. Then, TsCl (**1a**) was introduced and the reactions were performed under the optimized conditions to obtain the desired sulfonamides (**5b–5i**) in 30–76% isolated yields. Without any hesitation, 4-methoxybenzenesulfonyl chloride (**1b**), benzenesulfonyl chloride (**1c**), 2-naphthalenesulfonyl chloride (**1d**) and methyl 3-(chlorosulfonyl)thiophene-2-carboxylate (**1e**) were then screened and they all participated in this transformation smoothly to give the desired compounds in moderate yields (**5j–5n**). Unexpectedly, aliphatic cyclopropanesulfonyl chloride was able to react with *N*-methyl-4-oxo-1-(2-oxo-2-phenylethyl) piperidinium bromide, *in situ* formed *via* the reaction of *N*-methylpiperidinone and 2-bromoacetophenone, to yield sulfonamide **5o** in 46% isolated yield.

To elucidate the selectivity dependence of ring-opening pathways on the structure of the aza rings, some control experiments were conducted (Scheme 2). First, when *N*-(4-chlorobenzyl)-*N*-methylpiperidinium chloride **7**, instead of **2a**, was added to the standard reaction systems to react with TsCl for the synthesis of **3a**, no coupling reaction took place, and as a result, the formation of **3a** was not detected. Other attempts to replace the 4-oxopiperidine ring in **2a** with morpholine (**8**) and 4-hydroxypiperidine (**9**) also failed to give **3a** (Scheme 2(a)–(c)), implying that the presence of the 4-oxo moiety on the piperidine ring was indispensable. Furthermore, when two equivalents of 2,2,6,6-tetramethylpiperidinooxy (TEMPO) as a radical scavenger were added to the standard reaction systems for the synthesis of **3a**, the yield dramatically decreased to 7%, indicating that these reactions should follow a radical pathway. HRMS studies of the reaction mixture showed that compounds **10** and **11** (42% isolated yield) were formed, indicating that a pent-1-en-3-one-5-yl radical and a sulfonyl radical were formed during the formation of **3a**, possibly because of the radical homolysis of the S–Cl bond in sulfonyl chloride[17] (Scheme 2(d)). This assumption was further confirmed by the control reactions listed in Scheme 3(e) where



Scheme 2 Control experiments.



Scheme 3 Proposed mechanism for the formation of 3a.

TsCl alone was stable at 80 °C and gradually decomposed to *p*-tolyl 4-methylbenzenesulfinate **12** in the presence of NMM, demonstrating the key role of tertiary amines in the pyrolysis of sulfonyl chloride and the presence of both *p*-tolylsulfonyl and *p*-tolyl radicals in the reaction system.[18]

To understand the reason why a tertiary amine could activate the S–Cl bond in sulfonyl chloride, a UV test was performed. When NMM in MeCN (0.01 M) was added to a solution of TsCl (**1a**) in MeCN (0.01 M) at room temperature, the color immediately changed from colorless to brownish (Fig. 1A). Furthermore, the UV-Vis absorption spectra of **1a** (0.1 M), ammonium salt **2a** and NMM (0.1 M) were measured separately and combined (Fig. 1B). When **1a** (0.1 M) and NMM (0.1 M) were mixed, a new band ranging from 350 to 450 nm appeared (Fig. 1B), which is attributed to the charge transfer complex arising from the charge transfer from NMM to **1a**.

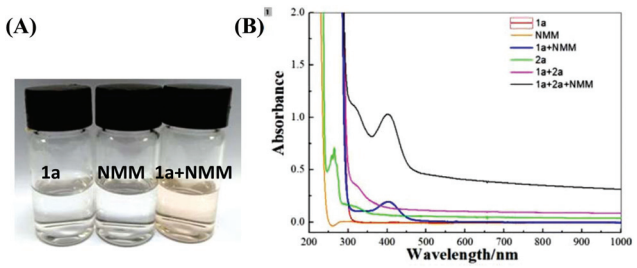


Fig. 1 (A) Photographs of **1a** (TsCl), NMM, and **1a** + NMM in MeCN (0.01 M). (B) UV-Vis absorption spectra of **1a** (0.01 M), NMM (0.01 M), **2a** (0.01 M) and their mixtures: **1a** + NMM (0.01 M), **1a** + **2a** (0.01 M), and **1a** + **2a** + NMM (0.01 M) in MeCN.

On the basis of the above results, especially due to the fact that these reactions occurred only when pyrolysis of sulfonyl chlorides began, that is, when compound **12** was detected, a plausible mechanism accounting for the formation of **3a** is proposed (Scheme 3). Initially, a charge-transfer complex involving TsCl and NMM (*N*-methylmorpholine) was formed. Under heating and activation by a CT-complex, slight pyrolysis of the S–Cl bond in TsCl occurred, delivering a chlorine radical (Cl$^{\bullet}$) and a tosyl radical (Ts$^{\bullet}$).[19] Radical Ts$^{\bullet}$ is not stable which, after SO_2 extrusion, delivers a tolyl radical (Tol$^{\bullet}$) and reacts with TsCl to yield the byproduct **12**. The main reaction was initiated *via* radical abstraction of a hydrogen atom from **2a** with a chlorine radical or a tosyl radical (Cl$^{\bullet}$ or Ts$^{\bullet}$). The yielded carbon radical ammonium **I** initiated the first C–N bond cleavage to produce the tertiary amine radical cation **II**. Intramolecular hydrogen transfer in **II** gave the carbon radical ammonium (**III**). Again, C–N bond cleavage in **III** occurred and a secondary amine cation radical **IV** was generated. Single electron transfer (SET) between NMM and **IV** produced the secondary amine **V** and the *N*-methylmorpholine radical cation **VI** which then abstracted a hydrogen atom from **2a** to regenerate radical **I**, completing the full reaction cycle. Finally, amine **V**, a key reaction intermediate, was captured and reacted with TsCl to form sulfonamide **3a**.

Conclusions

We have established an efficient method to realize regiospecific double C–N bond cleavages in unstrained *N*-substituted 4-oxopiperidium salts *via* a self-promoted radical pathway. From these reactions, synthetically useful sulfonamides were conveniently prepared. In general, these novel oxidant- and metal-free transformations, accomplished under mild con-

ditions and showing good tolerance toward a variety of functional groups, are promising complements to previously reported synthetic strategies, especially to those for which secondary amines are not easily available. Further studies on the utility of this reaction protocol in synthetic chemistry and its detailed mechanism are currently underway in our laboratory.

Experimental

General procedure for the synthesis of sulfonamides 3

A 10 mL test tube was charged with sulfonyl chloride **1** (0.5 mmol), *N*-(4-chlorobenzyl)-*N*-methyl-4-oxopiperidin-1-ium chloride (165 mg, 0.6 mmol), *N*-methylmorpholine (165 mg, 1.5 mmol) and acetonitrile (2.0 mL). The reaction mixture was heated to 80 °C under air for 4 h. Upon completion (TLC) and after cooling to ambient temperature, the reaction mixture was dissolved in ethyl acetate (10 mL) and washed successively with water (2 × 10 mL) and then brine (10 mL). The aqueous phase was further extracted with ethyl acetate (10 mL) and washed as described previously. The organic phase was combined, dried over Na_2SO_4 and concentrated. Purification by silica gel column chromatography gave the desired sulfonamide products.

General procedure for the synthesis of sulfonamides 5

A 10 mL test tube was charged with *N*-substituted 4-piperidinone **4** (0.6 mmol), organohalide **6** (0.6 mmol) and MeCN (2 mL). The reaction mixture was stirred at 50 °C for 24 h. Upon completion (TLC), *N*-methylmorpholine (165 mg, 1.5 mmol) and sulfonyl chloride (0.5 mmol) were added and the reaction mixture was heated to 80 °C under air for 4 h. After cooling to ambient temperature, the reaction mixture was dissolved in ethyl acetate (10 mL) and washed successively with water (2 × 10 mL) and then brine (10 mL). The aqueous phase was further extracted with ethyl acetate (10 mL) and washed as described previously. The organic phase was combined, dried over Na_2SO_4 and concentrated. Purification by silica gel column chromatography gave the desired sulfonamide products.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

1 (*a*) L. M. Blair and J. Sperry, *Nat. Prod.*, 2013, **76**, 794; (*b*) A. T. Balaban, D. C. Oniciu and A. R. Katritzky, *Chem. Rev.*, 2004, **104**, 2777; (*c*) G. Song, F. Wang and X. Li, *Chem. Soc. Rev.*, 2012, **41**, 3651; (*d*) S. H. Cho, J. Y. Kim, J. Kwak and S. Chang, *Chem. Soc. Rev.*, 2011, **40**, 5068; (*e*) J.-R. Chen, X.-Q. Hu, L.-Q. Lu and W.-J. Xiao, *Chem. Soc. Rev.*, 2016, **45**, 2044.

2 (*a*) Y.-R. Luo, *Handbook of Bond Dissociation Energies in Organic Compounds*, CRS Press, Boca Raton, FL, 2002; (*b*) Q. Wang, Y. Su, L. Li and H. Huang, *Chem. Soc. Rev.*, 2016, **45**, 1257; (*c*) K. Ouyang, W. Hao, W.-X. Zhang and Z. Xi, *Chem. Rev.*, 2015, **115**, 12045; (*d*) A. N. Desnoyer and J. A. Love, *Chem. Soc. Rev.*, 2017, **46**, 197; (*e*) M. D. Kärkäs, *Chem. Soc. Rev.*, 2018, **47**, 5786.

3 (*a*) E. Wenkert, A.-L. Han and C.-J. Jenny, *J. Chem. Soc., Chem. Commun.*, 1988, 975; (*b*) H. Ogawa, Z.-K. Yang, H. Minami, K. Kojima, T. Saito, C. Wang and M. Uchiyama, *ACS Catal.*, 2017, **7**, 3988; (*c*) F. He and Z.-X. Wang, *Tetrahedron*, 2017, **73**, 4450; (*d*) Z.-K. Yang, D.-Y. Wang, H. Minami, H. Ogawa, T. Ozaki, T. Saito, K. Miyamoto, C. Wang and M. Uchiyama, *Chem. – Eur. J.*, 2016, **22**, 15693; (*e*) D. Wu, J.-L. Tao and Z.-X. Wang, *Org. Chem. Front.*, 2015, **2**, 265; (*f*) X.-Q. Zhang and Z.-X. Wang, *Org. Biomol. Chem.*, 2014, **12**, 1448; (*g*) W.-J. Guo and Z.-X. Wang, *Tetrahedron*, 2013, **69**, 9580; (*h*) W.-C. Dai and Z.-X. Wang, *Chem. – Asian. J.*, 2017, **12**, 3005; (*i*) J. T. Reeves, D. R. Fandrick, Z. Tan, J. J. Song, H. Lee, N. K. Yee and C. H. Senanayake, *Org. Lett.*, 2010, **12**, 4388; (*j*) S. B. Blakey and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2003, **125**, 6046; (*k*) Q. Chen, F. Gao, H. Tang, M. Yao, Q. Zhao, Y. Shi, Y. Dang and C. Cao, *ACS Catal.*, 2019, **9**, 3730; (*l*) B. Yang and Z.-X. Wang, *J. Org. Chem.*, 2019, **84**, 1500; (*m*) T. Uemura, M. Yamaguchi and N. Chatani, *Angew. Chem., Int. Ed.*, 2016, **55**, 3162.

4 (*a*) S. Plunkett, C. H. Basch, S. O. Santana and M. P. Watson, *J. Am. Chem. Soc.*, 2019, **141**, 2257; (*b*) M. Ociepa, J. Turkowska and D. Gryko, *ACS Catal.*, 2018, **8**, 11362; (*c*) F. J. R. Klauck, H. Yoon, M. J. James, M. Lautens and F. Glorius, *ACS Catal.*, 2019, **9**, 236; (*d*) Z.-K. Yang, N.-X. Xu, C. Wang and M. Uchiyama, *Chem. – Eur. J.*, 2019, **25**, 5433; (*e*) J. Wu, P. S. Grant, X. Li, A. Noble and V. K. Aggarwal, *Angew. Chem., Int. Ed.*, 2019, **58**, 5697; (*f*) J. Liao, W. Guan, B. P. Boscoe, J. W. Tucker, J. W. Tomlin, M. R. Garnsey and M. P. Watson, *Org. Lett.*, 2018, **20**, 3030; (*g*) C. H. Basch, J. Liao, J. Xu, J. J. Piane and M. P. Watson, *J. Am. Chem. Soc.*, 2017, **139**, 5313; (*h*) K. R. Buszek and N. Brown, *Org. Lett.*, 2007, **9**, 707; (*i*) D.-Y. Wang, M. Kawahata, Z.-K. Yang, K. Miyamoto, S. Komagawa, K. Yamaguchi, C. Wang and M. Uchiyama, *Nat. Commun.*, 2016, **7**, 12937.

5 (*a*) P. Maity, D. M. Shacklady-McAtee, G. P. A. Yap, E. R. Sirianni and M. P. Watson, *J. Am. Chem. Soc.*, 2013, **135**, 280; (*b*) Z. Zhang, H. Wang, N. Qiu, Y. Kong, W. Zeng, Y. Zhang and J. Zhao, *J. Org. Chem.*, 2018, **83**, 8710; (*c*) T. Wang, S. Yang, S. Xu, C. Han, G. Guo and J. Zhao, *RSC Adv.*, 2017, **7**, 15805; (*d*) W. Jiang, N. Li, L. Zhou and Q. Zeng, *ACS Catal.*, 2018, **8**, 9899.

6 M. Guisán-Ceinos, V. Martín-Heras and M. Tortosa, *J. Am. Chem. Soc.*, 2017, **139**, 8448.

7 (*a*) H. Yu, B. Hu and H. Huang, *J. Org. Chem.*, 2018, **83**, 13922; (*b*) H. Yu, B. Hu and H. Huang, *Chem. – Eur. J.*, 2018, **24**, 7114; (*c*) H. Yu, B. Gao, B. Hu and H. Huang, *Org. Lett.*, 2017, **19**, 3520; (*d*) J. Wu, L. He, A. Noble and V. K. Aggarwal, *J. Am. Chem. Soc.*, 2018, **140**, 10700.

8 (*a*) Y. Fu, Q.-S. Xu, C.-Z. Shi, Z. Du and C. Xiao, *Adv. Synth. Catal.*, 2018, **360**, 3502; (*b*) Y. Fu, Q.-S. Xu, Q.-Z. Li, M.-P. Li, C.-Z. Shi and Z. Du, *ChemistryOpen*, 2019, **8**, 127; (*c*) Y. Fu, X. Zhao and B. Hou, *Chin. J. Org. Chem.*, 2016, **36**, 1184.

9 (*a*) P. Liu, S. Zou, B. Yu, L. Li and H. Huang, *Org. Lett.*, 2018, **20**, 3601; (*b*) L. Li, P. Liu, Y. Su and H. Huang, *Org. Lett.*, 2016, **18**, 5736; (*c*) Y. Zhang, B. Yu, B. Gao, T. Zhang and H. Huang, *Org. Lett.*, 2019, **21**, 535; (*d*) G. Qin, L. Li, J. Li and H. Huang, *J. Am. Chem. Soc.*, 2015, **137**, 12490; (*e*) Y. Liu, Y. Xie, H. Wang and H. Huang, *J. Am. Chem. Soc.*, 2016, **138**, 4314; (*f*) L. Li, X. Zhou, B. Yu and H. Huang, *Org. Lett.*, 2017, **19**, 4600.

10 S. Song, D. M. Golden, R. K. Hanson and C. T. Bowman, *J. Phys. Chem. A*, 2002, **106**, 6094.

11 C. Fan, X.-Y. Lv, L.-J. Xiao, J.-H. Xie and Q.-L. Zhou, *J. Am. Chem. Soc.*, 2019, **141**, 2889.

12 E. L. Eliel and K. W. Nelson, *J. Org. Chem.*, 1955, **20**, 1657.

13 (*a*) Y. Hu, H. Kang, H. Li and P. Wei, *Chin. J. Appl. Chem.*, 2007, **24**, 474–476; (*b*) T. Gajda and A. Zwierzak, *Synthesis*, 1981, 1005; (*c*) J. Alvarez-Builla, J. J. Vaquero, J. L. G. Navio, J. F. Cabello, C. Sunkel, M. F. de Casa-Juana, F. Dorrego and L. Santos, *Tetrahedron*, 1990, **46**, 967.

14 (*a*) Y. Ai, P. Liu, R. Liang, Y. Liu and F. Li, *New J. Chem.*, 2019, **43**, 10755; (*b*) X. Cui, F. Shi, M. K. Tse, D. Gördes, K. Thurow, M. Beller and Y. Deng, *Adv. Synth. Catal.*, 2009, **351**, 2949; (*c*) X. Yu, C. Liu, L. Jiang and Q. Xu, *Org. Lett.*, 2011, **13**, 6184; (*d*) S. L. Feng, C. Z. Liu, Q. Li, X. C. Yu and Q. Xu, *Chin. Chem. Lett.*, 2011, **22**, 1021.

15 TMEDA reacted with sulfonyl chlorides more quickly than tertiary monoamines, see ref. 8*a*.

16 In the presence of tertiary amines, aliphatic sulfonyl chlorides are prone to undergo an elimination process to produce sulfenes. For details, see: J. F. King, R. P. Beatson and J. M. Buchshriber, *Can. J. Chem.*, 1977, **55**, 2323. CF_3SO_2Cl chloride is an unstable substrate and decomposes easily under these reaction conditions. In addition, CF_3SO_2Cl is frequently employed as CF_3 radical equivalent in organic synthesis; see: T. Rawner, M. Knorn, E. Lutsker, A. Hossain and O. Reiser, *J. Org. Chem.*, 2016, **81**, 7139–7147.

17 (*a*) M. P. Bertrand and C. Ferreri, in *Radicals in Organic Synthesis*, ed. P. Renaud and M. Sibi, Wiley-VCH, Weinheim, 2001, vol. 2, pp. 485–504; (*b*) X.-Q. Pan, J.-P. Zou, W.-B. Yi and W. Zhang, *Tetrahedron*, 2015, **71**, 7481.

18 A plausible explanation for the formation of compound **13** might be the attack of the *p*-tolyl radical, generated *via* decomposition of the *p*-tosyl radical, on *p*-tosyl chloride.

19 A. V. Navrotskii, G. V. Stepanov, S. A. Safronov, A. N. Gaidadin, A. A. Seleznev, V. A. Navrotskii and A. Novakov, *Dokl. Chem.*, 2018, **480**, 93.