A Journal of the Gesellschaft Deutscher Chemiker

Angewandte International Edition

GDCh

Chemie

www.angewandte.org

Accepted Article

Title: Diversity-oriented Desulfonylative Functionalization of Alkyl Allyl Sulfones

Authors: Yong Xia and Armido Studer

To be cited as: *Angew. Chem. Int. Ed.* 10.1002/anie.201903668
Angew. Chem. 10.1002/ange.201903668

Link to VoR: http://dx.doi.org/10.1002/anie.201903668
http://dx.doi.org/10.1002/ange.201903668

WILEY-VCH

10.1002/anie.201903668

WILEY-VCH

COMMUNICATION

Diversity-oriented Desulfonylative Functionalization of Alkyl Allyl Sulfones

Yong Xia and Armido Studer*

Abstract: The diversity-oriented desulfonylative functionalization of alkyl allyl sulfones with various sulfone-type reagents *via* radical chemistry has been developed. The readily installed allylsulfonyl moiety acts as a C-radical precursor, which is substituted by various functionalities using sulfur-based radical trapping reagents. The generality of this approach is documented by the successful desulfonylative alkynylation, azidation, trifluoromethylthiolation, sulfenylation, trifluoromethylselenylation, halogenation, and deuteration. The method is compatible with a wide range of functional groups. Considering the deuteration, products are obtained in good yields with a high level of deuterium incorporation.

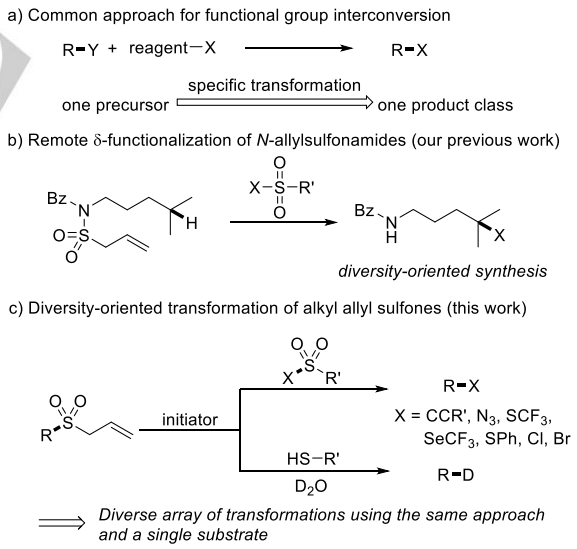
Radical chemistry is highly valuable for the construction and late-stage functionalization of complex compounds.[1] C-centered radicals can be generated from various precursors and different C-radical trapping reagents are available, offering a large portfolio of methods for functional group interconversion. For example, the decarboxylative alkylation, borylation and halogenation of aliphatic carboxylic acids;[2] deiodinative borylation, deuteration and trifluoromethylation of iodides,[3] and the direct C–H functionalization[4] among other transformations[1] have been achieved. However, the current methods generally allow the transformation of one radical precursor into one product class (Scheme 1a). In view of diversity-oriented synthesis,[5,6] development of efficient and practical methods enabling diversity-oriented functionalization where a single radical precursor allows accessing various compound classes by using derivatives of a single reagent-type would be important. Notably, staying with the same radical trapping reagent-type, the chemistry and mechanism are unaltered and hence similar protocols can be used.

Our previous efforts led to the development of diversity-oriented remote site-selective functionalization of unactivated aliphatic C–H bonds in amides with sulfone-type reagents.[7] In these transformations, the N-allylsulfonamide[8] moiety was used as a stable N-radical precursor. The C-radical, formed *via* 1,5-hydrogen atom transfer to the N-radical, is trapped with various sulfone-type reagents to enable C–N, C–X (halo), C–S and C–C bond construction (Scheme 1b).[7] Motivated by the reliability of these S-based reagents, we decided to apply them to diversity-oriented radical desulfonylative functionalization of allyl sulfones.

[a] Dr. Y. Xia and Prof. Dr. A. Studer
Organisch-Chemisches Institut, Westfälische Wilhelms-Universität
Corrensstrasse 40, 48149 Münster (Germany)
E-mail: studer@uni-muenster.de

Supporting information for this article is given via a link at the end of the document.

Allylsulfones are established trapping reagents that react with C-radicals *via* addition-fragmentation to the corresponding allylated products.[9] For example, the allylation of alkyl iodides with allylsulfones was described by Zard[9l] and Ryu.[9c] Decarboxylative and deaminative allylation were reported by Li[9g] and Liu.[9d] Zard developed a radical allylation using alkyl allyl sulfones as both C-radical precursors as well as allylation reagents.[10f] Related chemistry for C–C-bond formation was later described by Kim and Ryu.[10a-e] Surprisingly, the use of allylsulfones as C-radical precursors for carbon-heteroatom bond construction has remained unexplored. Along these lines, we assumed that alkyl allyl sulfones would be ideal and readily accessed substrates for desulfonylative diversity-oriented C-functionalization and present herein first results on alkynylation, azidation, trifluoromethylthiolation, phenylsulfenylation, trifluoromethylselenylation and halogenation of alkyl allyl sulfones by applying various sulfone-type trapping reagents. Product diversity is further expanded using a deuterated thiol as the radical trapping reagent enabling the desulfonylative deuteration (Scheme 1c).



Scheme 1. Diversity-oriented transformation *via* radical reactions.

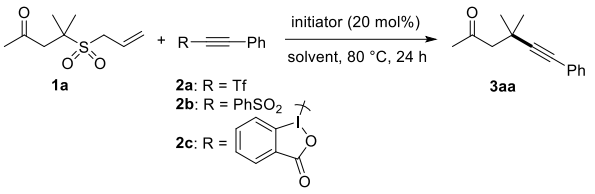
Initial studies were devoted to the radical alkynylation,[7b,11] since alkynes are versatile building blocks in synthesis and materials science.[12] The readily prepared sulfone **1a** (Table 1, for preparation of sulfones, see the Supporting Information) was used as the alkyl radical precursor. Three alkynes (**2a**-**c**) were tested as trapping reagents in combination with dilauroyl peroxide (DLP) as the radical initiator in chloroform. By using the alkynyltriflone **2a** introduced by Fuchs,[11e] C-alkynylation

10.1002/anie.201903668

COMMUNICATION

occurred and the targeted **3a** was obtained in moderate yield (50%, entry 1). With sulfone **2b** and phenylethynylbenziodoxolone **2c**, worse results were noted (entries 2,3) and **2a** was selected for further optimization. Yield was increased to 65% by replacing BPO with AIBN (entry 5). Switching to other initiators (entries 4-6) and replacing $CHCl_3$ by other solvents (entries 7-10) led to worse results. Yield further improved to 73% upon increasing the initiator loading (entry 11) and increasing reaction temperature to 85°C led to a similar result (74% yield, entry 12).

Table 1. Reaction optimization.[a]

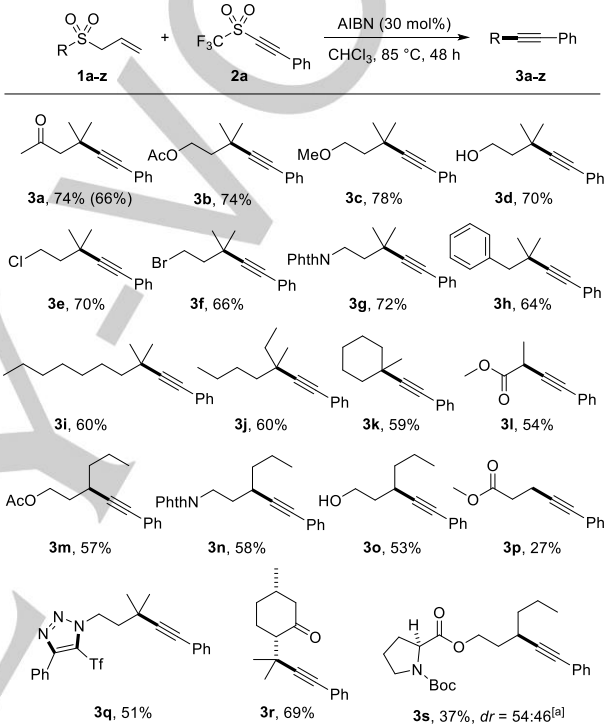


Entry	Initiator	2	Solvent	Yield (**3a**) (%)[b]
1	DLP	**2a**	$CHCl_3$	50
2	DLP	**2b**	$CHCl_3$	19
3	DLP	**2c**	$CHCl_3$	trace
4	BPO	**2a**	$CHCl_3$	49
5	AIBN	**2a**	$CHCl_3$	65
6	ACBN	**2a**	$CHCl_3$	50
7	AIBN	**2a**	CH_3CN	58
8	AIBN	**2a**	EtOAc	60
9	AIBN	**2a**	Hexane	56
10	AIBN	**2a**	Toluene	10
11[c]	AIBN	**2a**	$CHCl_3$	73
12[c,d]	AIBN	**2a**	$CHCl_3$	74

[a] Reaction conditions: **1a** (0.1 mmol), **2** (0.2 mmol, 2.0 equiv) and initiator (20 mol%) in solvent (0.4 mL) were stirred at 80 °C for 24 h. [b] NMR yield using CH_2Br_2 as an internal standard. [c] 30 mol% of AIBN was used. [d] Reaction temperature was increased to 85°C; Isolated yield at 0.2 mmol scale. DLP = dilauroyl peroxide; BPO = dibenzoyl peroxide; AIBN = α,α′-azobisisobutyronitrile; ACBN = α,α′-azobis(cyclohexanecarbonitrile).

Under optimized conditions, substrate scope varying the alkyl allyl sulfone was investigated (Scheme 2). Alkynylation proceeded smoothly for tertiary as well as secondary alkyl sulfones, and the alkynylated products **3a**−**3o** were obtained in good yields (53-78%). As compared to tertiary alkyl sulfones, secondary alkyl congeners provided slightly lower yields. This is not surprising since the SO_2-fragmentation generating the alkyl radical is less efficient for the secondary alkyl sulfonyl radicals (see mechanistic discussion below). Along these lines, the alkynylation of the primary alkyl sulfone **1y** was possible, albeit in lower yield (**3p**, 27%). The process shows broad functional group tolerance and ketone (**3a**), ester (**3b**, **3m**, **3l**), ether (**3c**), alcohol (**3d**, **3o**), halo (**3e**,**3f**), phthalimide (**3g**, **3n**) moieties are tolerated. Nonfunctionalized sulfones including acyclic and cyclic systems also engage in this transformation (**3i**-**3k**). In the case of the azidylalkylsulfone **1q**, the triazole **3q** was obtained through radical alkynylation with concomitant regioselective [3+2] alkyne azide cycloaddition with reagent **2a**. When the reaction was performed on larger scale (1 mmol), a slight decrease of the yield was noted (**3a**, 66%).

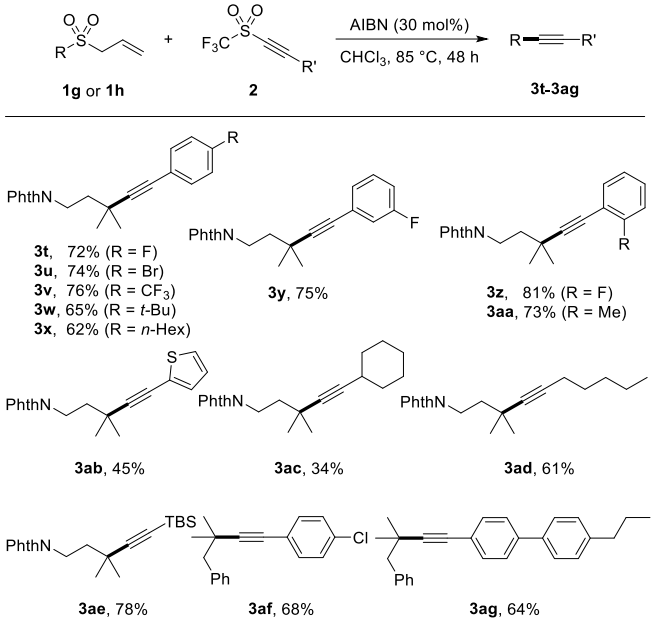
The potential of the method was further documented by alkynylation of more complex bioactive relevant compounds. 8-Mercaptomenthone, which was used as a blackcurrant flavor, could be alkynylated to give **3r** in 69% yield. Alkyne **3s** was obtained in 37% yield as a 54:46 mixture of the two diastereoisomers from the corresponding Boc-protected proline derivative.



Scheme 2. Variation of alkyl allyl sulfone (reaction conditions: **1** (0.2 mmol), **2a** (0.4mmol, 2.0 equiv) and AIBN (30 mol%) in $CHCl_3$ (0.4 mL) were stirred at 85 °C for 48 h. Yields given correspond to isolated yields. Yield in parentheses for 1.0 mmol scale experiment). a) Determined by GC-analysis.

Next, the scope of the triflone component was probed with allyl sulfone **1f** as the radical precursor (Scheme 3). Electronic effects exerted by the aryl moiety in the arylalkynyl triflones are weak and triflones bearing electron-donating and electron-withdrawing substituents at the *para*, *meta*, and *ortho*-position of the aryl group provided similar yields (**3t**−**3aa**, 62−76%). The 2-thienylalkynyl triflone also engaged in the alkynylation (**3ab**, 45%). We were pleased to find that less activated alkylalkynyl triflones are eligible reagents, as documented by the preparation of **3ac** and **3ad**. A good yield was obtained for the silylalkynylation of **1f** (**3ae**, 78%). Reaction of allyl sulfone **1h** with a chlorophenyl- and a biphenylalkynyl triflone occurred smoothly and the corresponding products were obtained in good yields (**3af**, 68%; **3ag**, 64%).

10.1002/anie.201903668

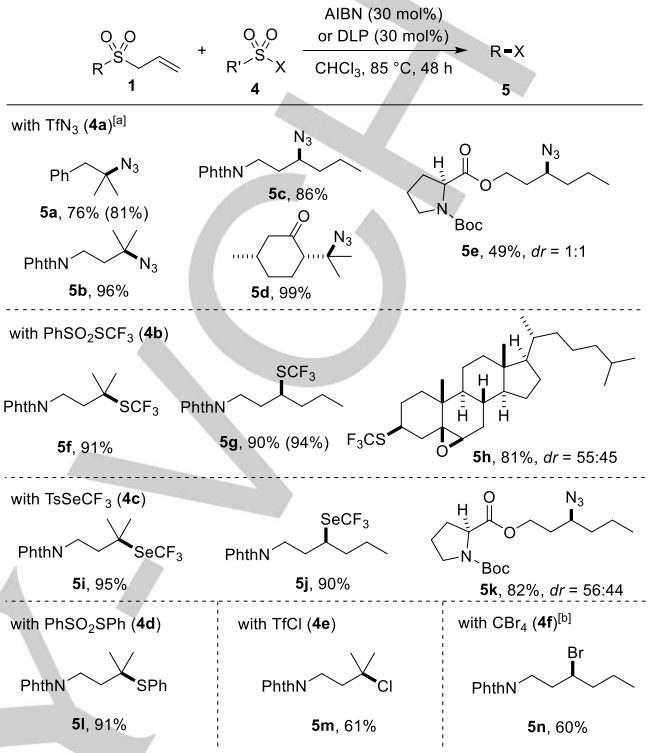


Scheme 3. Variation of the triflone reagents (reaction conditions: **1** (0.2 mmol), **2a** (0.4 mmol, 2.0 equiv) and AIBN (30 mol%) in $CHCl_3$ (0.4 mL) were stirred at 85 °C for 48 h. Yields given correspond to isolated yields.)

To document the diversity of our approach, related radical transformations varying the sulfone-type radical trapping reagent were studied and the azidation[13] was first explored (Scheme 4). Reaction of **1h** with trifluoromethanesulfonylazide (TfN_3, **4a**)[7a,13e] under the above optimized conditions afforded the azide **5a** in 48% yield. With DLP as the initiator, the yield could be increased to 76% and all following azidations were initiated with DLP. Reactions with reagent **4a** proceeded well for tertiary and secondary alkyl sulfones, delivering the corresponding azides **5a**–**5c** in good to excellent yields (76-96%). More complex allyl sulfones could also be converted to the targeted azides (**5d**, **5e**).

Because of the high lipophilicity of the SCF_3 moiety, which influences membrane permeability and bioavailability of a compound, efforts have been devoted to the development of trifluoromethylthiolation methods. The direct trifluoromethylthiolation[14] of stable alkyl allyl sulfones with commercial available *S*-(trifluoromethyl) benzenesulfonothioate ($PhSO_2SCF_3$, **4b**) would be attractive. Gratifyingly, the desulfonylative functionalization proceeded well and trifluoromethylthiolation of tertiary and secondary alkyl sulfones was achieved in excellent yields (**5f**, 91%; **5g**, 90%). A derivative of the steroid hormone thiocholesterol was also trifluoromethylthiolated to afford **5h** in 81% yield.

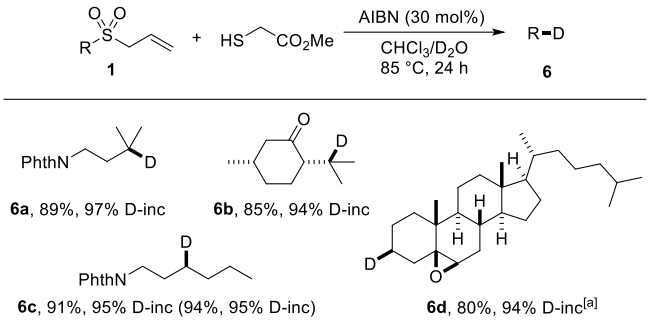
Although selenylated compounds have found various applications,[15] trifluoromethylselenylation is still not well investigated. We selected $TsSeCF_3$ (**4c**) as the radical trapping reagent[15b,c] and found that trifluoromethylselenylation occurred smoothly to give the targeted products in excellent yields (**5i**-**5k**, 82-95%). By simply switching to commercial *S*-phenyl benzenesulfonothioate ($PhSO_2SPh$, **4d**), phenylsulfenylation[16] was possible (**5l**, 91%). Moreover, chlorination was achieved by using the commercial trifluoromethanesulfonyl chloride (**4e**) as the Cl-source (**5m**, 61%) and with tetrabromomethane (**4f**) as the trapping reagent, the bromide **5n** was obtained (60%).



Scheme 4. Variation of radical trapping reagents (reaction conditions: **1** (0.2 mmol), **4** (0.4 mmol, 2.0 equiv) and AIBN (30 mol%) in $CHCl_3$ (0.4 mL) were stirred at 85 °C for 48 h. Yields given correspond to isolated yields. Yields in parentheses for 1.0 mmol scale experiments. Diastereoselectivity was determined by NMR (**5e**, **5k**) or GC-analysis (**5h**)); a) Using DLP (30 mol%) as the initiator. b) $CHBr_3$ was used as the solvent.

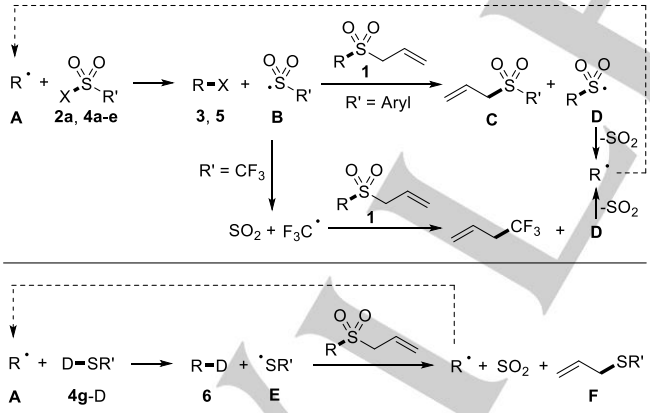
Site-specific incorporation of deuterium is important since deuterium-labeled compounds are widely applied in synthetic and medicinal chemistry (kinetic isotope effect measurements, pharmacokinetic and pharmacodynamics research).[17] Radical deuteration[3a,18] using D_2O as the D-source represents a promising approach due to the low cost of D_2O and the high functional group tolerance of radical chemistry. Recently, MacMillan[18e] and Renaud[3a] developed radical deuterations with D_2O as the formal D-donor using phenol or thiol type HAT-reagents, that readily exchange their protons with D_2O. Inspired by these works, we assumed that alkyl allyl sulfones can be deuterated with D_2O in combination with a suitable HAT reagent. Pleasingly, high level of deuterium incorporation was achieved with methyl thioglycolate in $D_2O/CHCl_3$. Both tertiary and secondary alkyl allyl sulfones were deuterated in good yields (**6a**-**6d**, 80-91%) and high deuterium incorporation (94-97%), further documenting the generality of our approach (Scheme 5).

10.1002/anie.201903668



Scheme 5. Deuteration of alkyl allyl sulfones (reaction conditions: **1** (0.2 mmol), methyl thioglycolate (0.3 mmol, 1.5 equiv) and AIBN (30 mol%) in $D_2O/CHCl_3$ (1:1 1.0 mL) were stirred at 85 °C for 24 h. Yields given correspond to isolated yields. Yield in parentheses for 1.0 mmol scale experiment). a) Diastereoselectivity could not be determined.

Mechanistically, the radical **A** generated in the initiation sequence reacts with the sulfone reagents **2a** or **4a**-**e** in an atom or group transfer to give product R–X (**3** or **5**) along with the sulfonyl radical **B** (Scheme 6). Considering the alkynylation, azidation and chlorination, **B** fragments the CF_3-radical that reacts with the substrate **1** to give allyltrifluoromethane as a byproduct and sulfonyl radical **D**, which fragments SO_2 to give **A** closing the radical chain. For reagents **4b**-**d**, sulfonyl radical **B** reacts with the substrate **1** to allylsulfone **C** (byproduct) and radical **D**. Of note is the good chemoselectivity obtained for the reaction of C-radicals **A** with the sulfone-type reagents, where direct addition of **A** to **1** did not occur. Desulfonylative deuteration works in analogy with the deuterated thiol **4g**-D as the reducing reagent to give thiyl radical **E** which reacts with **1** in an addition/elimination/SO_2-fragmentaion to radical **A**. The allylsulfide **F** is formed as the byproduct.



Scheme 6. Suggested mechanisms.

In summary, we have presented a highly practical approach for diversity-oriented desulfonylative functionalization of various alkyl allyl sulfones. The starting allyl sulfones are readily prepared and by simply varying the radical trapping reagent, different product classes can be accessed from the same substrate under identical or similar reaction conditions. Of note, some of these radical trapping reagents are commercially available. These processes feature broad substrate scope and excellent functional group compatibility. The potential of this approach is further documented by the functionalization of more complex and biologically relevant compounds.

Acknowledgements

This work was financially supported by the Deutsche Forschungsgemeinschaft (DFG).

Keywords: azidation • desulfonylativealkynylation • deuteration• diversity-oriented synthesis• radical chemistry

[1] a) K. J. Romero, M. S. Galliher, D. A. Pratt, C. R. J. Stephenson, *Chem. Soc. Rev.* **2018**, *47*, 7851; b) K. Hung, X. Hu, T. J. Maimone, *Nat. Prod. Rep.* **2018**, *35*, 174; c) H. Yi, G. Zhang, H. Wang, Z. Huang, J. Wang, A. K. Singh, A. Lei, *Chem. Rev.* **2017**, *117*, 9016; d) C. Chatgilialoglu, A. Studer (Eds.), *Encyclopedia of Radicals in Chemistry, Biology and Materials*, Wiley **2012**.

[2] For selected reviews and examples: a) T. Zhang, N.-X. Wang, Y. Xing, *J. Org. Chem.* **2018**, *83*, 7559; b) C. Li, J. Wang, L. M. Barton, S. Yu, M. Tian, D. S. Peters, M. Kumar, A. W. Yu, K. A. Johnson, A. K. Chatterjee, M. Yan, P. S. Baran, *Science* **2017**, *356*, 6342; c) Y. Wei, P. Hu, M. Zhang, W. Su, *Chem. Rev.* **2017**, *117*, 8864; d) Y. Jin, H. Fu, *Asian J. Org. Chem.* **2017**, *6*, 368; e) C. P. Johnston, R. T. Smith, S. Allmendinger, D. W. C. MacMillan, *Nature.* **2016**, *536*, 322; f) H. Huang, K. Jia, Y. Chen, *ACS Catal.* **2016**, *6*, 4983; g) A. J. Borah, G. Yan, *Org. Biomol. Chem.* **2015**, *13*, 8094; h) J. Xuan, Z.-G. Zhang, W.-J. Xiao, *Angew. Chem. Int. Ed.* **2015**, *54*, 15632; *Angew. Chem.* **2015**, *127*, 15854; i)F. Yin, Z. Wang, Z. Li, C. Li, *J. Am. Chem. Soc.* **2012**, *134*, 10401.

[3] For selected recent examples: a) V. Soulard, G. Villa, D. P. Vollmar, P. Renaud, *J. Am. Chem. Soc.* **2018**, *140*, 155; b) Y. Cheng, C. Mück-Lichtenfeld, A. Studer, *Angew. Chem. Int. Ed.* **2018**, *57*, 16832; *Angew. Chem.* **2018**, *130*, 17074; c) H. Shen, Z. Liu, P. Zhang, X. Tan, Z. Zhang, C. Li, *J. Am. Chem. Soc.* **2017**, *139*, 9843.

[4] For selected reviews: a) M. C. White, J. Zhao, *J. Am. Chem. Soc.* **2018**, *140*, 13988; b) X.-Q. Chu, D. Ge, Z.-L. Shen, T.-P. Loh, *ACS Catal.* **2018**, *8*, 258; c) K. E. Kim, A. M. Adams, N. D. Chiappini, J. D. Bois, B. M. Stoltz, *J. Org. Chem.* **2018**, *83*, 3023.

[5] M. D. Burke, S. L. Schreiber, *Angew. Chem. Int. Ed.* **2004**, *43*, 46; *Angew. Chem.* **2004**, *116*, 48.

[6] a) F. Berger, M. B. Plutschack, J. Riegger, W. Yu, S. Speicher, M. Ho, N. Frank, T. Ritter, *Nature* **2019**, *567*, 223; b) K. A. Margrey, W. L. Czaplyski, D. A. Nicewicz, E. J. Alexanian, *J. Am. Chem. Soc.* **2018**, *140*, 4213; c) S. P. Morcillo, E. D. Dauncey, J. H. Kim, J. J. Douglas, N. S. Sheikh, D. Leonori, *Angew. Chem. Int. Ed.* **2018**, *57*, 12945; *Angew. Chem.* **2018**, *130*, 13127; d) J. Davies, N. S. Sheikh, D. Leonori, *Angew. Chem. Int. Ed.* **2017**, *56*, 13361; *Angew. Chem.* **2017**, *129*, 13546; e)W. L. Czaplyski, C. G. Na, E. J. Alexanian, *J. Am. Chem. Soc.* **2016**, *138*, 13854.

[7] a) Y. Xia, L. Wang, A. Studer, *Angew. Chem. Int. Ed.* **2018**, *57*, 12940; *Angew. Chem.* **2018**, *130*, 13122; b) L. Wang, Y. Xia, K. Bergander, A. Studer, *Org. Lett.* **2018**, *20*, 5817.

[8] C. Moutrille, S. Z. Zard, *Chem. Commun.* **2004**, 1848.

[9] For selected examples: a) K. Wu, L. Wang, S. Colón-Rodríguez, G.-U. Flechsig, T. Wang, *Angew. Chem. Int. Ed.* **2019**, *58*, 1774; *Angew. Chem.* **2019**, *131*, 1788; b) J.-F. Zhao, P. Gao, X.-H. Duan, L.-N. Guo, *Adv. Synth. Catal.* **2018**, *360*, 1775; c) S. Sumino, M. Uno, H.-J. Huang, Y.-K. Wu, I. Ryu, *Org. Lett.* **2018**, *20*, 1078; d) M.-M. Zhang, F. Liu, *Org. Chem. Front.* **2018**, *5*, 3443; e) Q.-Q. Zhao, J. Chen, D.-M. Yan, J.-R. Chen, W.-J. Xiao, *Org. Lett.* **2017**, *19*, 3620; f) J. Zhang, Y. Li, R. Xu, Y. Chen, *Angew. Chem. Int. Ed.* **2017**, *56*, 12619; *Angew. Chem.* **2017**, *129*, 12793; g) L. Cui, H. Chen, C. Liu, C. Li, *Org. Lett.* **2016**, *18*, 2188; h) N.

Charrier, S. Z. Zard, *Angew. Chem. Int. Ed.* **2008**, *47*, 9443; *Angew. Chem.* **2008**, *120*, 9585; i) S. Kim, S. Kim, *Bull. Chem. Soc. Jpn.* **2007**, *80*, 809; j) A.-P. Schaffner, P. Renaud, *Angew. Chem. Int. Ed.* **2003**, *42*, 2658; *Angew. Chem.* **2003**, *115*, 2762; k) B. Sire, S. Seguin, S. Z. Zard, *Angew. Chem. Int. Ed.* **1998**, *37*, 2864; *Angew. Chem.* **1998**, *110*, 3056; l) F. Le Guyader, B. Quiclet-Sire, S. Seguin, S. Z. Zard, *J. Am. Chem. Soc.* **1997**, *119*, 7410.

[10] a) S. Kim, K.-C. Lim, S. Kim, I. Ryu, *Adv. Synth. Catal.* **2007**, *349*, 527; b) S. Kim, K.-C. Lim, S. Kim, *Chem. Commun.* **2007**, 4507; c) S. Kim, S. Kim, N. Otsuka, I. Ryu, *Angew. Chem. Int. Ed.* **2005**, *44*, 6183; *Angew. Chem.* **2005**, *117*, 6339; d) S. Kim, C. J. Lim, *Bull. Korean Chem. Soc.* **2003**, *24*, 1219.e) S. Kim, C. J. Lim, *Angew. Chem. Int. Ed.***2002**, *41*, 3265; *Angew. Chem.* **2002**, *114*, 3399; f) B. Quiclet-Sire, S. Z. Zard, *J. Am. Chem. Soc.* **1996**, *118*, 1209.

[11] a) X. Liu, Z. Wang, X. Cheng, C. Li, *J. Am. Chem. Soc.* **2012**, *134*, 14330; b) V. Liautard, F. Robert, Y. Landais, *Org. Lett.* **2011**, *13*, 2658; c) A.-P. Schaffner, V. Darmency, P. Renaud, *Angew. Chem. Int. Ed.* **2006**, *45*, 5847; *Angew. Chem.* **2006**, *118*, 5979; d) Z. Li, C.-J. Li, *J. Am. Chem. Soc.* **2004**, *126*, 11810; e) J. Gong, P. L. Fuchs, *J. Am. Chem. Soc.* **1996**, *118*, 4486; f) G. A. Russell, P. Ngoviwatchai, H. I. Tashtoush, A. Pla-Dalmau, R. K. Khanna, *J. Am. Chem. Soc.* **1988**, *110*, 3530;

[12] F. Diederich, P. J. Stang, R. R. Tykwinski, *Acetylene Chemistry: Chemistry, Biology and Material Science*; Wiley-VCH: Weinheim, **2005**.

[13] For selected reviews and examples: a) X. Bao, Q. Wang, J. Zhu, *Nat. Commun.* **2019**, 10, 769; b) X. Huang, J. T. Groves, *ACS Catal.* **2016**, *6*, 751; c) Y. Wang, G.-X. Li, G. Yang, G. He, G. Chen, *Chem. Sci.* **2016**, *7*, 2679; d) C. Liu, X. Wang, Z. Li, L. Cui, C. Li, *J. Am. Chem. Soc.* **2015**, *137*, 9820; e) K. Weidner, P. Renaud, *Austr. J. Chem.* **2013**, *66*, 341; f) E. Lallana, R. Riguera, E. Fernandez-Megia, *Angew. Chem. Int. Ed.* **2011**, *50*, 8794; *Angew. Chem.* **2011**, *123*, 8956; g) C. I. Schilling, N. Jung, M. Biskup, U. Schepers, S. Brase, *Chem. Soc. Rev.* **2011**, *40*, 4840; h) E. M. Sletten, C. R. Bertozzi, *Acc. Chem. Res.* **2011**, *44*, 666; i) E.Nyfeler, P. Renaud, *Org. Lett.* **2008**, *10*, 985; g) S. Bräse, C. Gil, K. Knepper, V. Zimmermann, *Angew. Chem. Int. Ed.* **2005**, *44*, 5188; *Angew. Chem.* **2005**, *117*, 5320.

[14] a) X. Zhao, B. Yang, A. Wei, J. Sheng, M. Tian, Q. Li, K. Lu, *Tetrahedron Lett.* **2018**, *59,* 1719; b) H. Li, C. Shan, C.-H. Tung, Z. Xu, *Chem. Sci.* **2017**, *8*, 2610; c) G. Yin, I. Kalvet, U. Englert, F. Schoenebeck, *J. Am. Chem. Soc.* **2015**, *137*, 4164; d) X. Xu, K. Matsuzaki, N. Shibata, *Chem. Rev.* **2015**, *115*, 731; e) X. Yang, T. Wu, R. J. Phipps, F. D. Toste, *Chem. Rev.* **2015**, *115*, 826; f) C. Ni, M. Hu, J. Hu, *Chem. Rev.* **2015**, *115*, 765; g) P. Chauhan, S. Mahajan, D. Enders, *Chem. Rev.* **2014**, *114*, 8807;

[15] a) A. Tlili, E. Ismalaj, Q. Glenadel, C. Ghiazza, T. Billard, *Chem. Eur. J.* **2018***, 24,* 3659; b) C. Ghiazza, V. Debrauwer, C. Monnereau, L. Khrouz, M. Médebielle, T. Billard, A. Tlili, *Angew. Chem. Int. Ed.* **2018**, *57*, 11781; *Angew. Chem.* **2018**, *130*, 11955; c) C. Ghiazza, L. Khrouz, C. Monnereau, T. Billard, A. Tlili, *Chem. Commun.* **2018**, *54*, 9909; d) Z. Cai, *J. Chin. Chem. Soc.* **2017**, *64*, 457.

[16] a) D.-Q. Dong, S.-H. Hao, D.-S. Yang, L.-X. Li, Z.-L. Wang, *Eur. J. Org. Chem.* **2017**, 6576; b) W. Kong, H. An, Q. Song, *Chem. Commun.* **2017**, *53*, 8968; c) A.-P. Schaffner, F. Montermini, D. Pozzi, V. Darmency, E. M. Scanlan, P. Renaud, *Adv. Synth. Catal.* **2008**, *350*, 1163; d) M. Kobayashi, M. Kobayashi, M. Yoshida, *Bull. Chem. Soc. Jpn*. **1985**, *58*, 473.

[17] a) J. Atzrodt, V. Derdau, W. J. Kerr, M. Reid, *Angew. Chem. Int. Ed.* **2018**, *57*, 1758; *Angew. Chem.* **2018**, *130*, 1774; b) C. S. Elmore, R. A. Bragg, *Bioorg. Med. Chem. Lett.* **2015**, *25*, 167; c) R. D.Tung, *Future Med. Chem.* **2016**, *8*, 491.

[18] For selected examples: a) M. Zhang, X.-A. Yuan, C. Zhu, J. Xie, *Angew. Chem. Int. Ed.* **2019**, *58*, 312; *Angew. Chem.* **2019**, *131*, 318; b) T. R. Puleo, A. J. Strong, J. S. Bandar, *J. Am. Chem. Soc.* **2019**, *141*, 1467; c) J. L. Koniarczyk, D. Hesk, A. Overgard, I. W. Davies, A. McNally, *J. Am. Chem. Soc.* **2018**, *140*, 1990; d) M. Zhang, J. Xie, C. Zhu, *Nat. Commun.* **2018**, *9*, 3517; e) Y. Y. Loh, K. Nagao, A. J. Hoover, D. Hesk, N. R. Rivera, S. L. Colletti, I. W. Davies, D. W. C. MacMillan, *Science* **2017**, *358*, 1182; f) D. A. Spiegel, K. B. Wiberg, L. N. Schacherer, M. R. Medeiros, J. L. Wood, *J. Am. Chem. Soc.* **2005**, *127*, 12513.

10.1002/anie.201903668

WILEY-VCH

Entry for the Table of Contents (Please choose one layout)

Layout 2:

COMMUNICATION

Y. Xia, A. Studer

Page No. – Page No.

Diversity-oriented Desulfonylative Functionalization of Alkyl Allyl Sulfones

Diversity-oriented radical desulfonylative functionaliztion of alkyl allyl sulfones was realized with various sulfone-based trapping reagents using practical conditions.The novel approach was successfully applied to desulfonylative alkynylation, azidation, trfluoromethylthiolation, trifluoromethylselenolation, phenylthiolation, chlorination, bromination and deuteration.