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Stereoselective Construction of Nitrile-Substituted Cyclopropanes from 2-Substituted Ethenesulfonyl Fluorides *via* Carbon-Sulfur Bond Cleavage

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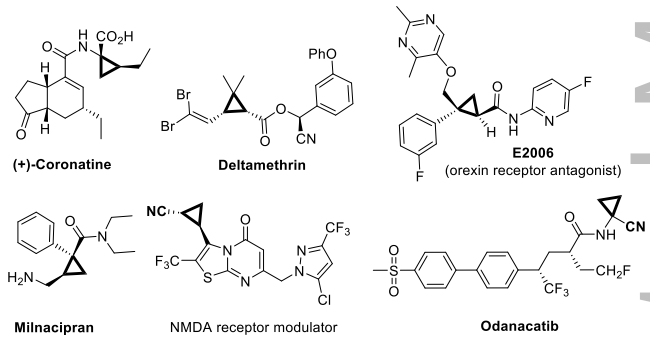
Abstract The intermolecular cyclopropanation of 2-aryl and 2-styryl substituted ethenesulfonyl fluorides with active cyano-containing methylene compounds was described. This reaction proceeds *via* carbon-sulfur bond cleavage under metal-free conditions in up to 99% yield, affording a variety of nitrile-substituted cyclopropanes with high diastereoselectivity.

Keywords: Cyclopropanation; Ethenesulfonyl fluorides; Diastereoselectivity; Nitrile-substituted;

Cyclopropyl group, the smallest cyclic alky group, is an indispensable building block of a lot of natural products and bioactive synthetic compounds (Scheme 1) for its special benefits including enhancing potency, reducing off-target effect, increasing metabolic stability, and increasing brain permeability, etc.[1] Cyano group, which possesses special biological activities and can be easily converted into a variety of functional groups, has been extensively introduced into certain molecules to endow them with unique properties. [2,3] In this regard, it was hypothesized that the synergistic effect of combining a cyano and a cyclopropyl group into one entity may grant some target pharmacologically active molecules fascinating properties. For instance, Odanacatib, a FDA-approved drug derived from cyano-substituted cyclopropanes, has been extensively utilized for osteoporosis and bone metastasis.[4]



Scheme 1. Structures of natural and bioactive synthetic cyclopropanes

However, in spite of the excellent properties of cyano-substituted cyclopropanes, the construction of its derivatives under mild conditions is quite challenging. Currently, three major strategies have been reported: cyclopropanation of alkyene and malononitrile analogs with catalytic amount of molecular iodine and a stoichiometric oxidant[5] (Scheme 2a); cyclopropanation of olefins by Ru-porphyrins,[6] iron,[7] Rh_2(S-PTAD)$_4$,[8] engineered myoglobin[9] catalysed decomposition of diazo acetonitrile (Scheme 2b); Michael-initiated ring-closure reaction[10](Scheme 2c). Besides, as the potential approaches to build cyano-substituted cyclopropanes, vinyl selenones[11]/vinyl sulfonium salts[12]-mediated cyclopropanation reactions were also reported. Each of them has shown some unique

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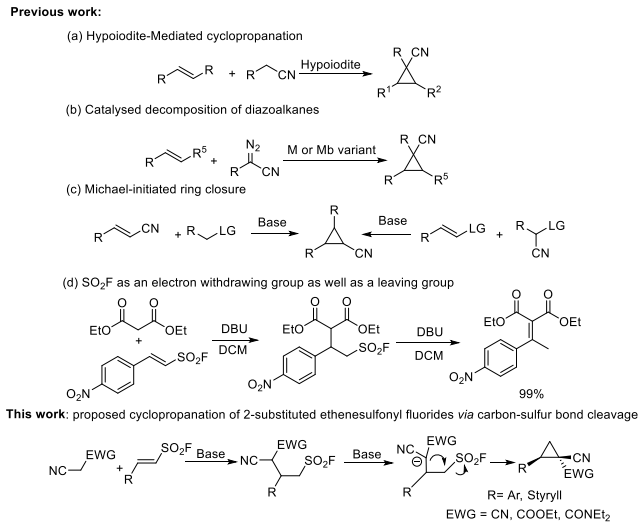
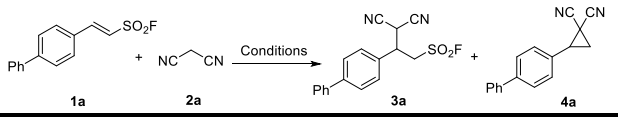
advantages but also inevitably has some non-negligible defects.



Scheme 2. Previous work and proposed construction of nitrile-substituted cyclopropane through a 1,3-elimination of SO_2F

In this work, we proposed a novel strategy based on Sulfur (VI) Fluoride Exchange (SuFEx), which showed some advantages over the aforementioned conventional methods at certain aspects and might inspire future research work on the synthesis of derivatives of cyano-substituted cyclopropanes. Arylethenesulfonyl fluoride, an emerging synthon in SuFEx Chemistry[13] and a unique bis-electrophile, could be inimitably attacked by two chemoselective nucleophiles.[14a] On the basis of the pioneering work of Sharpless, Arvidsson, and our group, β-substituted vinyl sulfonyl fluorides can be easily prepared from abundant and cheap reagents (e.g., organic iodides, aryl-boronic acids and aryl-diazonium salts).[14] In our previous work[15], the Michael adduct generated from *p*-nitrophenylethenesulfonyl fluoride and diethyl malonate (DBU and $NaHCO_3$ in DCM serving as catalysis and additive, respectively) can be driven to eliminate sulfonyl fluoride, and formed an enedione when DBU approaches one equivalent, with SO_2F serving as the leaving group (Scheme 2d). Therefore, we envisioned a possible construction of cyclopropane through a 1,3-elimination of SO_2F (Scheme 2): after Michael addition and deprotonation using a suitable base, the adduct generated *in situ* would be converted into the corresponding reactive methine carbon. Afterwards, the as-prepared activated methine carbon attacked the neighbouring carbon of SO_2F and resulted in the SO_2F leaving. As a result, the corresponding cyclopropanation product was obtained.

Table 1. Screening of Reaction Conditions of Cyclopropanation of 2-Substituted Ethenesulfonyl Fluorides[a]



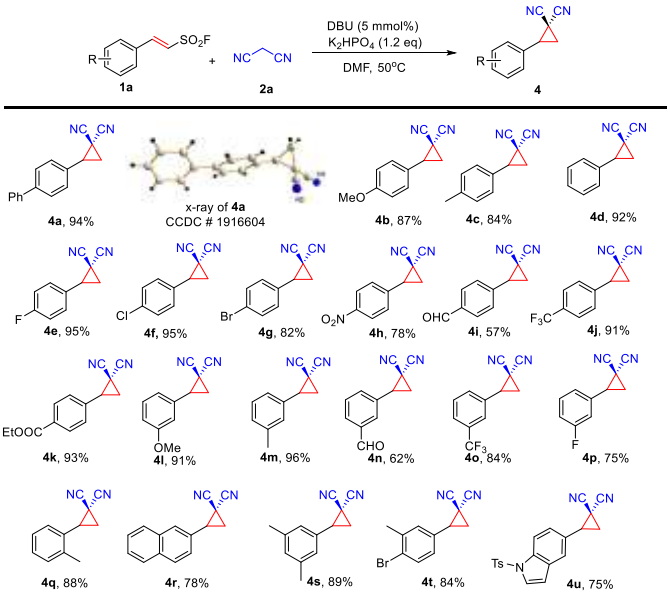
1a 2a 3a 4a

Entry	Solvent	DBU Loading (X mol%)	Reaction Temperature (°C)	Additive (Y eq.)	Yield (**3a**, %)	Yield (**4a**, %)
1	DMF	5	10-15	/	76 (75)	trace
2	DMF	50	10-15	/	28	65
3	DMF	5	10-15	$NaHCO_3$ (2.0)	0	50
4	DMF	5	10-15	Na_3PO_4 (2.0)	0	26
5	DMF	5	10-15	K_2HPO_4 (2.0)	0	68
6	DMF	5	30	K_2HPO_4 (2.0)	0	86
7	DMF	5	50	K_2HPO_4 (2.0)	0	94
8	DMF	5	70	K_2HPO_4 (2.0)	0	80
9	DCM	5	50	K_2HPO_4 (2.0)	0	trace
10[b]	**DMF**	**5**	**50**	**K_2HPO_4 (1.2)**	**0**	**95 (94)**

[a]Reaction conditions: (E)-2-([1,1'-biphenyl]-4-yl) ethene-1-sulfonyl fluoride (**1a**, 26 mg, 0.1 mmol), Malononitrile (**2a**, 0.3 mmol), solvent (1.0 mL), additive and DBU were added to a reaction tube (20 mL) and reacted for 12 h. The yields were determined by HPLC using **1a**, **3a**, **4a** as the external standard (t_{1a} = 6.223 min, λ_{max} = 308 nm; t_{3a} = 3.348 min, λ_{max} = 332 nm; t_{4a} = 4.08 min, λ_{max} = 258 nm, CH_3CN / water = 70 : 30 (v / v)). Isolated yields on a 0.5 mmol scale are reported in parentheses. [b]Malononitrile (**2a**, 0.12 mmol, 1.2 eq.) was used.

Initially, (E)-2-([1,1'-biphenyl]-4-yl) ethene-1-sulfonyl fluoride **1a** and malononitrile **2a** were selected as model substrates to optimize the direct cyclopropanation reaction (Table 1 and supporting information). When 5% DBU was added as the sole base for this reaction, only Michal adduct product **3a** was obtained with 76% yield (entry 1, Table 1). After screening of DBU loading (see supporting information for details), we observed the dicyanocyclopropanation product **4a** in 65% yield but with a certain amount of **3a** by using 50% DBU as the base. Extensive screening of additive (entry 3-5), reaction temperature (entry 6-8), solvent (entry 9), reaction ratio of **1a** and **2a** (entry 10) revealed that K_2HPO_4 (1.2 eq.) and 5 mol% DBU in DMF at 50 °C for 12 h were required to afford the optimized isolated yield of 94% of **4a** (entry 10).

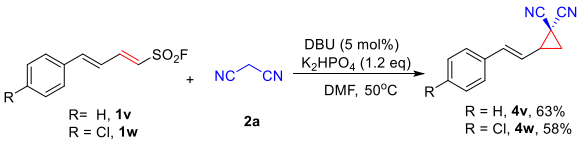
Table 2. DBU-Catalyzed Cyclopropanation of 2-Substituted Ethenesulfonyl Fluorides (**1**) and Malononitrile (**2a**)[a]



[a]Reaction conditions: 2-substituted ethenesulfonyl fluorides (**1**, 0.5 mmol), malononitrile (**2a**, 0.6 mmol), DMF (1.0 mL), K_2HPO_4 (1.2 eq.) and DBU (5 mol%) were added to a reaction tube (20 mL) and the mixture was stirred at 50 °C for 12 h. Isolated yields were shown.

Next, we set out to evaluate functional group tolerance and scope of the reaction of substituted (hetero)arylethenesulfonyl fluorides **1** and malononitrile **2a** with the optimized reaction conditions. As shown in Table 2, a broad scope of (hetero)arylethenesulfonyl fluorides substrates were examined for the cyclopropanation process. The substrates functionalized with both electron-withdrawing groups(e.g., Nitro (**1h**), acyl (**2i** and **2k**), trifluoromethyl (**2j**) and halogens (**2e**-**2g**)) and electron-donating groups (e.g., alkyl (**2i** and **2j**), aryl (**2a**), and ethers (**2b**)) were well tolerated under the reaction conditions in good to quantitative yields (from 57 to 96%). The X-ray crystal structure of **4a** demonstrated that the phenyl connected to the cyclopropane was approximately perpendicular to the cyclopropane ring (with the torsion angle of 67.477° between the two planes)[16].

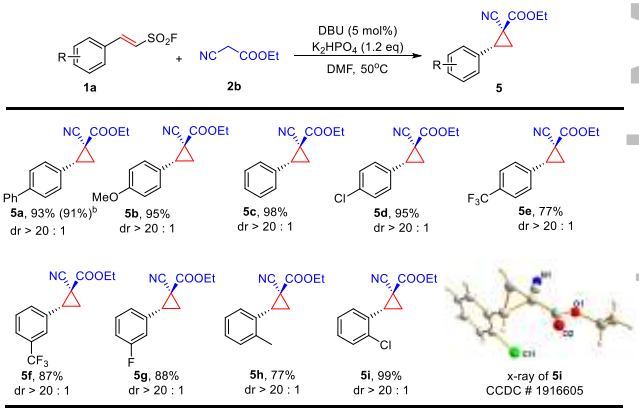
When 1,3-dienylsulfonyl fluorides **1v** and **1w** were chosen as the substrates, the corresponding alkenylcyclopropanes **4v** and **4w** were afforded readily with good yields (Scheme 3). The addition position is consistent with our previous work.[15a] As expected, the cyclopropanation reaction failed when 2-alky substituted ethenesulfonyl fluoride (**1x**) was selected as the electrophile[17].



Scheme 3. Cyclopropanation of 1,3-dienylsulfonyl fluorides and malononitrile **2a**

Then, with ethyl cyanoacetate (**2b**) as the nucleophile, the optimized reaction conditions are proven to be suitable for its cyclopropanation reaction with different arylethenesulfonyl fluorides to afford the corresponding ethyl-1-cyano-2-phenylcyclopropane-1-carboxylate **5** in good to excellent yields (Table 3). The exclusively *trans* configuration was confirmed by the X-ray crystal structure of **5i** with a slightly reduced torsion angle between the phenyl and cyclopropane planes (from 67.477° to 61.301°)[16], owing to the larger steric hindrance from the ester group compared to the cyano group. Remarkably, the efficiency of cyclopropanation reaction did not deteriorate when the reaction was performed on a 8 mmol (**1a**, 2.1 g) scale, furnishing the corresponding product **5a** in 91% isolated yield and excellent diastereoselectivity.

Table 3. DBU-Catalyzed Cyclopropanations of 2-Substituted Ethenesulfonyl Fluorides (**1**) and Ethyl cyanoacetate (**2b**)[a]

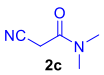
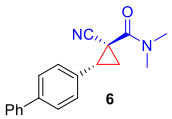
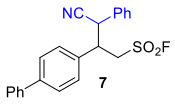
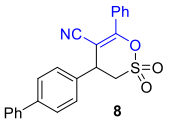
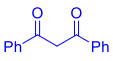
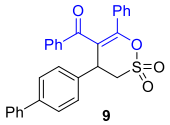
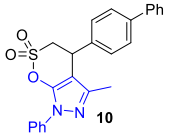
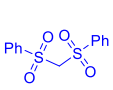
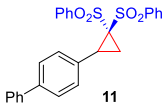


[a]Reaction conditions: 2-substituted ethenesulfonyl fluorides (**1**, 0.5 mmol), ethyl cyanoacetate (**2b**, 0.6 mmol), DMF (1.0 mL), K_2HPO_4 (1.2 eq.) and DBU (5 mol%) were added to a reaction tube (20 mL) and the mixture was stirred at 50 °C for 12 h. Isolated yields shown. Isolated yields referred to the *trans* product after column chromatography; the dr was determined from the crude reaction mixture by ^{1}H-NMR.[b]The reaction was conducted on a 8 mmol scale (**1a**, 2.1 g).

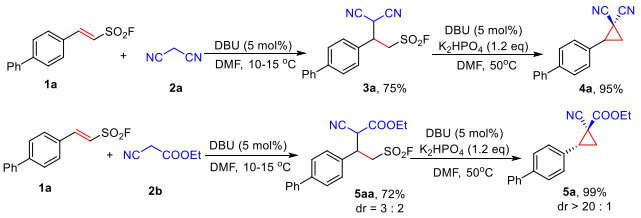
Besides, 2-cyano-N, N-dimethylacetamide (**2c**) was a suitable substrate for the reaction, affording the corresponding 1-cyano-N, N-dimethylcyclopropane-1-carboxamide (**6**) in 54% yield with excellent diastereoselectivity (entry1, table 4). However, when the nitrile group of malononitrile was replaced with a non-electron withdrawing phenyl group, only an addition product (**7**) was obtained in 75% yield (entry

2, table 4). When it was replaced with an enolizable carbonyl compound, δ-Sulton products were obtained by direct annulative SuFEx Click reaction under this reaction condition (entry 3-5, table 4). Interestingly, with bis-sulfonyl nucleophile (**2h**) being utilized as reaction partner, the corresponding cyclopropanation product **11** was afforded with good yield and excellent diastereoselectivity (entry 6, table 4). Thus, these cyclopropanation reactions need methylene compounds with relatively strong bis-electron withdrawing groups which can't be enolized under basic conditions. If single substituted or enolized methylene compounds were employed under these reaction conditions, the corresponding Michael addition products or δ-sulton products were afforded respectively.

Table 4. DBU-Catalyzed Cyclopropanations of (E)-2-([1,1'-Biphenyl]-4-yl) ethene-1-sulfonyl fluoride (**1a**) and Active Methylene Compounds (**2**)[a]

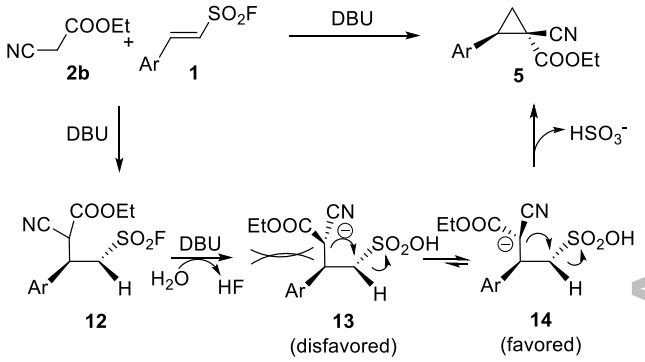
No	Substrate	Product	Yield
1	 **2c**	 **6**	54%[b] dr > 20 : 1
2	 **2d**	 **7**	75%
3	 **2e**	 **8**	77%
4	 **2f**	 **9**	69%
5	 **2g**	 **10**	87%
6	 **2h**	 **11**	43%

[a]Reaction conditions: (E)-2-([1,1'-biphenyl]-4-yl) ethene-1-sulfonyl fluoride 1a (**1a**, 0.5 mmol), active methylene compounds (**2**, 0.6 mmol), DMF (1.0 mL), K_2HPO_4 (1.2 eq.) and DBU (5 mol%) were added to a reaction tube (20 mL) and the mixture was stirred at 50 °C for 12 h. Isolated yields. [b]Isolated yields referred to the *trans* product after column chromatography; the dr was determined from the crude reaction mixture by ^{1}H-NMR.



Scheme 4. "Two-step" cyclopropanation reaction

To gain some insight into the reaction mechanism, two-step cyclopropanation reactions were designed (Scheme 4). Michael adduct product **3a** was first synthesized in 75% isolated yield without the additvie (K_2HPO_4). Then the cyclopropanation reaction was also conducted smoothly with excellent yield. When ethyl cyanoacetate (**2b**) was employed for this "two-step" reaction, the Michael adduct product **5aa** was observed as diastereomeric mixture (dr = 3 : 2), which was transformed into the corresponding cyclopropanation product (**5a**) with excellent diastereoselectivity (dr > 20 : 1). The control experiments is consistent with our initial conception. Based on our mechanism study and recent research[18], a plausible mechanism is illustrated in Scheme 5. Initially, the intermediate **12** was afforded after Michael addition. The hydrolysis of sulfonyl fluoride under DBU catalysis generated the sulfonic acid intermediates **13** and **14**. Fluoride ion (F^-) generated from this step was obviously observed from the reaction ^{19}F-NMR spectra (see the mechanism study in supporting information). With an intramolecular attack by the activated methine carbon and leaving of sulfite (HSO_3^-), intermediate **14** is favored over intermediate **13** due to steric effects, affording the *trans* diastereomer **5**. However, the details still remain unclear.



Scheme 5. A plausible mechanism for the stereoselective construction of nitrile-substituted arylcyclopropanes

In conclusion, a mild and practical method for construction of nitrile-substituted cyclopropanes from 2-aryl and 2-styryl substituted ethenesulfonyl fluorides *via* Carbon-Sulfur bond cleavage was developed. The reaction proceeded without any metal catalysts, exhibiting excellent compatibility to a large

variety of functional groups (over 34 examples), resulting in good to quantitative yields and excellent diastereoselectivity.

Experimental Section

General Procedures for Cyclopropanation

An oven-dried reaction tube (20 mL) was charged with arylethenesulfonyl fluoride (**1**, 0.5 mmol), active methylene compounds (**2**, 0.6 mmol, 1.2 eq.), DBU (5 mol%) and K_2HPO_4 (0.6 mmol, 1.2 eq.). The resulting mixture was stirred at 50 °C for 12 h. When the arylethenesulfonyl fluoride had been consumed (monitored by TLC), the reaction mixture was poured into water (30 mL), extracted with ethyl acetate (3 × 25 mL). The combined organic layers were then washed with water (3 ×25 mL) and dried over anhydrous sodium sulfate. The crude products were purified by column chromatography on silica gel to give the title compounds.

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Reference

[1] For selected reviews on cyclopropanes, see: a) S. Patai, Z. Rappoport, *The Chemistry of the Cyclopropyl Group*, Wiley & Sons, New York, **1987**; b). M. Rubin, M. Rubina, V. Gevorgyan, *Chem. Rev*. **2007**, *107*, 3117-3179; c) M. A. Cavitt, L. H. Phun, S. France, *Chem. Soc. Rev*. **2014**, *43*, 804-818; d) H.-U. Reissig, R. Zimmer, *Chem. Rev*. **2003**, *103*, 1151-1196; e) D. Y.-K. Chen, R. H. Pouwer, J.-A. Richard, *Chem. Soc. Rev*. **2012**, *41*, 4631-4642; f) L. A. Wessjohann, W. Brandt, T. Thiemann, *Chem. Rev*. **2003**, *103*, 1625-1648; g) R. Faust, *Angew. Chem., Int. Ed*. **2001**, *40*, 2251-2253; h) T. T. Talele, *J. Med. Chem*. **2016**, *59*, 8712-8756; i) H. Lebel, J.-F. Marcoux, C. Molinaro, A. B. Charette, *Chem. Rev*. **2003**, *103*, 977-1050.

[2] For selected reviews on Nitriles biological activities, see: a) F. F. Fleming, *Nat. Prod. Rep*. **1999**, *16*, 597-606; b) F. F. Fleming, L. Yao, P. C. Ravikumar, L. Funk, B. C. Shook, *J. Med. Chem*. **2010**, *53*, 7902-7917; c) M. Frizler, F. Lohr, N. Furtmann, J. Kläs, M. Gütschow, *J. Med. Chem*. **2011**, *54*, 396-400.

[3] a) A. J. Fatiadi, *Preparation and Synthetic Applications of Cyano Compounds* (Eds: S. Patai, Z. Rappaport), Wiley, New York, **1983**; b) R. C. Larcok, *Comprehensive Organic Transformations: A Guide to Functional Group Preparations*, VCH, New York, **1989**.

[4] M. Volgraf, B. D. Sellers, Y. Jiang, G. Wu, C. Q. Ly, E. Villemure, R. M. Pastor, P.-W. Yuen, A. Lu, X. Luo, M. Liu, S. Zhang, L. Sun, Y. Fu, P. J. Lupardus, H. J. A. Wallweber, B. M. Liederer, G. Deshmukh, E. Plise, S. Tay, P. Reynen, J. Herrington, A. Gustafson, Y. Liu, A. Dirksen, M. G. A. Dietz, Y. Liu, T.-M. Wang, J. E. Hanson, D. Hackos, K. Scearce-Levie, J. B. Schwarz, *J. Med. Chem*. **2016**, *59*, 2760-2779.

[5] a) A. Yoshimura, T. N. Jones, M. S. Yusubov, V. V. Zhdankina, *Adv. Synth. Catal*. **2014**, *356*, 3336-3340; b) A. Yoshimura, S. R. Koski, B. J. Kastern, J. M. Fuchs, T. N. Jones, R. Y. Yusubova, V. N. Nemykin, V. V. Zhdankin, *Chem. Eur. J*. **2014**, *20*, 5895-5898; c) S. Lin, M. Li, Z. Dong, F. Liang, J. Zhang, *Org. Biomol. Chem*. **2014**, *12*, 1341-1350; d) K. Usami, Y. Nagasawa, E. Yamaguchi, N. Tada, A. Itoh, *Org. Lett*. **2016**, *18*, 8-11.

[6] Y. Ferrand, P. Le Maux, G. Simonneaux, *Tetrahedron: Asymmetry* **2005**, *16*, 3829-3836.

[7] K. J. Hock, R. Spitzner, R. M. Koenigs, *Green Chem*. **2017**, *19*, 2118-2122.

[8] a) J. R. Denton, K. Cheng, H. M. L. Davies, *Chem. Commun*. **2008**, 1238-1240; b) D. Marcoux, S. Azzi, A. B. Charette, *J. Am. Chem. Soc*. **2009**, *131*, 6970-6792.

[9] A. L. Chandgude, R. Fasan, *Angew. Chem. Int. Ed*. **2018**, *57*, 15852-15856.

[10] a) L. S. Aitken, L. E. Hammond, R. Sundaram, K. Shankland, G. D. Brown, A. J. A. Cobb, *Chem. Commun*. **2015**, *51*, 13558-13561; b) F. Marini, S. Sternativo, F. Del Verme, L. Testaferri, M. Tieccoa, *Adv. Synth. Catal*. **2009**, *351*, 1801-1806.

[11] a) M. Palomba, L. Rossi, L. Sancineto, E. Tramontano, A. Corona, L. Bagnoli, C. Santi, C. Pannecouque, O. Tabarrinia, F. Marini, *Org. Biom. Chem*. **2016**, *14*, 2015-2024; b) L. Bagnoli, C. Scarponi, L. Testaferri, M. Tiecco, *Tetrahedron: Asymm*. **2009**, *20*, 1506-1514; c) R. Ando, T. Sugawara, M. Shimizu, I. Kuwajima, *Bull. Chem. Soc. Jpn*. **1984**, *57*, 2897-2904.

[12] a) M. Zhou, K. En, Y. Hu, Y. Xu, H. C. Shen, X. Qian, *RSC Adv*. **2017**, *7*, 3741-3745; b) T. Ishikawa, N. Kasai, Y. Yamada, T. Hanamoto, *Tetrahedron*, **2015**, *71*, 1254-1260; c) Z. Mao, H. Qu, Y. Zhao, X. Lin, *Chem. Commun*. **2012**, *48*, 9927-9929.

[13] a) J. Dong, L. Krasnova, M. G. Finn, K. B. Sharpless, *Angew. Chem., Int. Ed*. **2014**, *53*, 9430-9448; b) Q. Chen, P. Mayerand, H. Mayr, *Angew. Chem., Int. Ed*. **2016**, *55*, 12664-12667; c) A. Ungureanu, A. Levens, L. Candish, D. W. Lupton, *Angew. Chem., Int. Ed*. **2015**, *54*, 11780-11784.

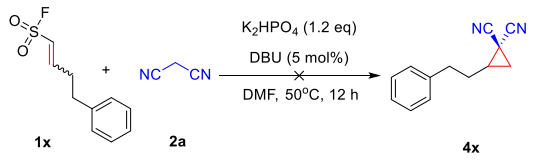
[14] a) H.-L. Qin, Q. Zheng, G. A. L. Bare, P. Wu, K. B. Sharpless, *Angew. Chem., Int. Ed*. **2016**, *55*, 14155-14158; b) G.-F. Zha, Q.Z heng, J. Leng, P. Wu, H.-L. Qin, K. B. Sharpless, *Angew. Chem., Int. Ed*. **2017**, *56*, 4849-4852; c) G.-F. Zha, G. A. L. Bare, J. Leng, Z.-P. Shang, Z. Luo, H.-L. Qin, *Adv. Synth. Catal*. **2017**, *359*, 3237-3242; d) P. K. Chinthakindi, K. B. Govender, A. S. Kumar, H. G. Kruger, T. Govender, T. Naicker, P. I. Arvidsson, *Org. Lett*. **2017**, *19*, 480-483; e) C. Li, S.-M. Wang, H.-L. Qin, *Org. Lett*. **2018**, *20*,

4699-4703; f) S.-M. Wang, C. Li, J. Leng, S. N. A. Bukhari, H.-L. Qin, *Org. Chem. Front*. **2018**, *5*, 1411-1415; g) S.-M. Wang, B. Moku, J. Leng, H.-L. Qin, *Eur. J. Org. Chem*. **2018**, *32*, 4407-4410; h) G. Ncube, M. P. Huestis, *Organometallics* **2019**, *38*, 76-80; i) X.-Y. Chen, Y. Wu, J. Zhou, P. Wang, J.-Q. Yu, *Org. Lett*. **2019**, *21*, 1426-1429.

[15] a) X. Chen, G.-F. Zha, G. A. L. Bare, J. Leng, S.-M. Wang, H.-L. Qin, *Adv. Synth. Catal*. **2017**, *359*, 3254-3260; b) X. Chen, G.-F. Zha, W.-Y. Fang, K. P. Rakesh, H.-L. Qin, *Chem. Commun*. **2018**, *54*, 9011-9014.

[16] CCDC 1916604 and CCDC 1916605 contain the data of compounds **4a** and **5i,** respectively. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.can.ac.uk/data_request/cif.

[17] 4-phenylbut-1-ene-1-sulfonyl fluoride (**1x**, 0.2 mmol) malononitrile (**2a**, 0.24 mmol), DMF (0.5 mL), K_2HPO_4 (1.2 eq.) and DBU (5 mol%) were added to a reaction tube (20 mL) and the mixture was stirred at 50 °C for 12 h. No new spots were detected (TLC).



[18] a) C. Li, H.-L. Qin, *Org. Lett*. **2019**, *21*, 4495-4499; b) S. K. Arupula, S. K. Gudimella, S. Guin, S. M. Mobin, S. Samanta, *Org. Biomol. Chem*. **2019**, *17*, 3451-3461.

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UPDATE

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