Advanced Synthesis & Catalysis

Accepted Article

Title: Enantioselective Sulfa-Michael Addition of Aromatic Thiols to β-Substituted Nitroalkenes Promoted by a Chiral Multi-functional Catalyst

Authors: Qi Wei, Wenduan Hou, Na Liao, and Yungui Peng

To be cited as: *Adv. Synth. Catal.* 10.1002/adsc.201700109

Link to VoR: http://dx.doi.org/10.1002/adsc.201700109

COMMUNICATION

DOI: 10.1002/adsc.201((will be filled in by the editorial staff))

Enantioselective Sulfa-Michael Addition of Aromatic Thiols to β-Substituted Nitroalkenes Promoted by a Chiral Multifunctional Catalyst

Qi Wei,[a] Wenduan Hou,[a] Na Liao[a] and Yungui Peng[a,*]

[a] Key Laboratory of Applied Chemistry of Chongqing Municipality, School of Chemistry and Chemical Engineering, Southwest University, Chongqing 400715, P.R. China.
Fax: (+86)-023-68253157; e-mail: pengyungui@hotmail.com or pyg@swu.edu.cn

Received: ((will be filled in by the editorial staff))

Supporting information for this article is available on the WWW under http://dx.doi.org/10.1002/adsc.201######.((Please delete if not appropriate))

Abstract: An efficient enantioselective Michael addition of a series of aromatic thiols acting as nucleophiles for β-monosubstituted, α,β- and β,β-disubstituted nitroalkenes promoted by a multi-functional chiral catalyst has been developed. The methodology accommodates a wide variety of aryl thiols and nitroalkene substrates, and affords the 2-nitro-1-arylethyl sulfides in excellent yields (up to 99%) and enantioselectivities (up to 99% *ee*). This reaction could be scaled up to gram even with a dramatically reduced catalyst loading of 0.05 mol %.

Keywords: enantioselective; Michael addition; aromatic thiol; nitroalkene; multi-functional catalyst

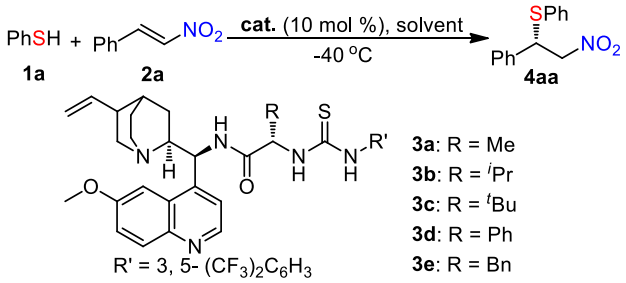
Chiral sulfur-containing motifs are widespread in biologically active natural products and pharmaceutical agents.[1] As one of the most efficient methodologies for accessing optically active chiral sulfur compounds, the catalytic enantioselective Michael addition of sulfur-centered nucleophiles to α,β-unsaturated compounds has attracted the attention of many groups, and great achievements have been made in recent decades.[2] Various types of electron-deficient olefins, including α,β-unsaturated aldehydes,[3] ketones,[4] esters,[5] nitroalkenes[6] and others,[7] have been shown to be applicable as the sulfur-centered Michael acceptor in this transformation. In particular, the use of β-substituted nitroalkenes in the enantioselective sulfa-Michael addition (SMA) represents an appealing approach to the synthesis of chiral 2-nitroethyl sulfide analogues, which are potential intermediates in the synthesis of bioactive compounds.[8] The use of thioacetic acid[9] and benzyl mercaptan[10] as sulfur donors was highly successful and gave the corresponding adducts in good yields and enantioselectivties. However, there is only one report of satisfactory results when aromatic thiols were employed as nucleophiles for β-substituted nitroalkenes, and this success was limited to compounds with Michael-donor-bearing electron-donating substituents on the aromatic ring, such as 3,4-dimethoxythiophenol.[11] Other reports have mentioned that the enantioselective SMA of aromatic thiols with β-substituted nitroalkenes gave very low enantioselectivities;[12] this can probably be ascribed to the reversibility of the reaction under the basic catalytic conditions.[2a,13] In view of the commercial availability of a wide variety of aromatic thiols and the synthetic value of the resulting chiral sulfides, the development of efficient methods for the enantioselective SMA of aromatic thiols with β-substituted nitroalkenes is an important challenge for organic chemists.

Our ongoing interest is in the development of an efficient approach to the construction of chiral sulfur-containing molecules that is triggered by sulfur nucleophiles.[14] Here, we show that the enantioselective SMA of various aromatic thiols with β-substituted nitroalkenes can be achieved in excellent yields and enantioselectivities using a multi-functional organocatalyst.

The reaction of thiophenol **1a** with β-phenyl substituted nitroalkene **2a** was chosen as a model reaction. The enantioselective variant of this reaction has been documented only with low enantioselectivities.[12] In initial screenings, quinine-derived Lu's catalyst **3a** showed good catalytic performance; an almost quantitative yield of product **4aa** was obtained with good enantioselectivity (80% *ee*) after reaction in the presence of 10 mol % **3a** at −40 °C for 1 h (Table 1, entry 1). Sulfa-Michael adducts racemize at room temperature, but this process is suppressed at low temperature to improve the enantioselectivity of the reaction.[2a,13,15] We therefore used cryogenic column chromatography to purify the product, which dramatically improved the enantioselectivity to 91% *ee* (Table 1, entry 2). Based on these results and the chiral framework of catalyst **3a**, we further synthesized catalysts **3b**–**3e**, and used them to investigate the effects of steric hindrance and the π-electron interactions of the substituents on the reaction (Table 1, entries 3–6). When the R substituent in the catalyst was changed from Me (**3a**) to ^{i}Pr (**3b**) and ^{t}Bu (**3c**), the enantioselectivity of the product increased slightly from 91% to 95% and 95%

10.1002/adsc.201700109

Table 1. Effect of catalyst substituents and reaction conditions on enantioselective sulfa-Michael additions.[a]

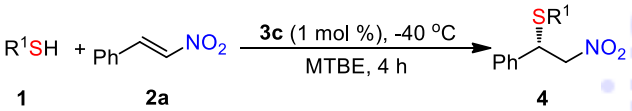


Entry	Cat.	Solvent	Time (h)	Yield [%][b]	*ee* [%][c]
1[d]	**3a**	DCM	1	99	80
2	**3a**	DCM	1	99	91
3	**3b**	DCM	1	99	95
4	**3c**	DCM	1	99	95
5	**3d**	DCM	1	99	95
6	**3e**	DCM	1	99	91
7	**3c**	THF	1	99	97
8	**3c**	2-Me-THF	1	99	86
9	**3c**	MTBE	1	99	97
10	**3c**	Et_2O	1	99	97
11	**3c**	PhF	1	99	97
12	**3c**	PhCl	1	99	96
13	**3c**	PhMe	1	99	93
14	**3c**	PhEt	1	99	92
15	**3c**	*m*-xylene	1	99	95
16[e]	**3c**	MTBE	1	99	95
17[f]	**3c**	MTBE	1	99	96
18[g]	**3c**	MTBE	2	99	95
19[h]	**3c**	MTBE	2	99	95
20[i]	**3c**	MTBE	4	99	95
21[j]	**3c**	MTBE	4	99	93

[a] Reactions were carried out with **1a** (0.12 mmol), **2a** (0.1 mmol) and the catalyst (10 mol %) in 0.5 mL of solvent at −40 °C.
[b] Isolated yield.
[c] Determined by HPLC analysis on a chiral stationary phase.
[d] Purified by column chromatography at rt.
[e] Performed at −30 °C.
[f] Performed at −50 °C.
[g] 5 mol % of **3c** was used.
[h] 2.5 mol % of **3c** was used.
[I] 1 mol % of **3c** was used.
[j] 0.5 mol % of **3c** was used.

ee. The yields were excellent in all three cases (up to 99%) (Table 1, entries 2–4). Good catalytic performance was also observed with R = Ph (**3d**) and Bn (**3e**) (Table 1, entries 5 and 6). Other bifunctional and multifunctional catalysts were also screened in this reaction, no better catalytic performance was observed than that of **3c** (see ESI). From these results, we concluded that **3c** was the best catalyst for promoting the enantioselective SMA of thiophenol with β-substituted nitroalkenes. With the best catalyst in hand, we next investigated the reaction conditions. First, a series of solvents, DCM, THF, 2-Me-THF, MTBE, Et_2O, PhF, PhCl, PhMe, PhEt and *m*-xylene, were screened. All of these solvents were suitable for the reaction, but the best results in terms of both yield and enantioselectivity were achieved in MTBE (Table 1, entries 4, 7–15). Changing the reaction temperature from −40 °C to −30 °C and −50 °C caused the enantioselectivity to decrease slightly from 97% *ee* to 95% *ee* and 96% *ee* (Table 1, entries 9, 16 and 17). The effect of catalyst loading on the reaction was also optimized, and these experiments revealed that satisfactory results could be obtained with 1 mol % catalyst (Table 1, entries 9 and 18–21).

Table 2. Enantioselective sulfa-Michael reaction of various thiophenols **1** in the presence of catalyst **3c**.[a]



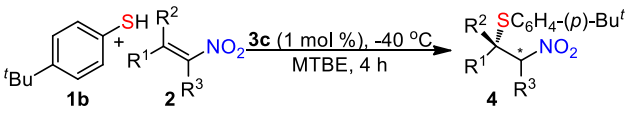
Entry	R^1	Yield [%][b]	*ee* [%][c]
1	*p*-^{t}BuC$_6$H$_4$	**4ba**, 97	97
2	*o*-MeC$_6$H$_4$	**4ca**, 95	96
3	*m*-MeC$_6$H$_4$	**4da**, 95	96
4	*p*-MeC$_6$H$_4$	**4ea**, 99	95
5	*p*-MeOC$_6$H$_4$	**4fa**, 98	97
6	*o*-FC$_6$H$_4$	**4ga**, 83	89
7	*m*-FC$_6$H$_4$	**4ha**, 91	78
8	*p*-FC$_6$H$_4$	**4ia**, 92	89
9	*o*-ClC$_6$H$_4$	**4ja**, 96	87
10	*o*-BrC$_6$H$_4$	**4ka**, 96	77
11	1-Naphthyl	**4la**, 99	92
12	2-Naphthyl	**4ma**, 88	96
13	*p*-ClC$_6$H$_4$CH$_2$	**4na**, 72	99
14	*p*-^{t}BuC$_6$H$_4$CH$_2$	**4oa**, 91	97
15	C$_6$H$_4$CH$_2$	**4pa**, 86	99
16[d]	Bu	**4qa**, 89	76
17[e]	^{t}Bu	**4ra**, 77	70

[a] Reactions were carried out with **1** (0.12 mmol), **2a** (0.1 mmol) and **3c** (1 mol %) in 0.5 mL MTBE at −40 °C for 4 h.
[b] Isolated yield.
[c] Determined by HPLC analysis on a chiral stationary phase.
[d] Reaction time was 10 h.
[e] Performed at 0 °C for 24 h.

After establishing the optimized reaction conditions, we turned our attention to the applicability of this reaction to various substrates. First, various aromatic thiols were used in the enantioselective SMA with β-phenylnitroalkene **2a**; the results are summarized in Table 2. Aromatic thiols bearing electron-donating and electron-withdrawing substituents on the aromatic ring were suitable for this reaction and gave the corresponding products in good to excellent yields and enantioselectivities (Table 2, entries 1–10). However, aromatic thiols containing electron-donating groups resulted in comparatively better yields and enantioselectivities than those with electron-withdrawing groups (Table 2, entries 1–5 *vs* 6–10). The substituent pattern had little influence on the reaction (Table 2, entries 2–4 and 6–8), and 1-

naphthyl and 2-naphthyl thiols furnished products **4la** (99% yield, 92% *ee*) and **4ma** (88% yield, 96% *ee*). Pleasingly, benzyl mercaptans also displayed good reactivity and provided chiral adducts **4na**–**4pa** in good yields and excellent enantioselectivities (Table 2, entries 13–15). Alkanethiols were applicable for the reaction and led good yields and enantioselectivities (Table 2, entries 16, 17).

Table 3. Enantioselective sulfa-Michael reactions of various nitroalkenes **2** in the presence of catalyst **3c**.[a]

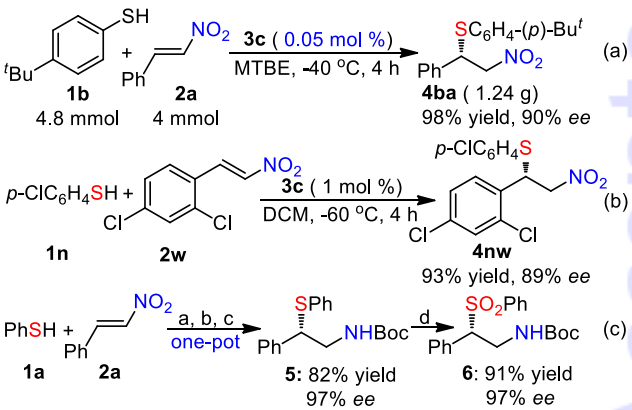


Entry	R^1	R^2, R^3	Yield [%][b]	*ee* [%][c]
1	*o*-MeC_6H_4	H, H	**4bb**, 92	96
2	*m*-MeC_6H_4	H, H	**4bc**, 99	97
3	*p*-MeC_6H_4	H, H	**4bd**, 99	96
4	*o*-FC_6H_4	H, H	**4be**, 98	96
5	*m*-FC_6H_4	H, H	**4bf**, 99	95
6	*p*-FC_6H_4	H, H	**4bg**, 97	96
7	*m*-ClC_6H_4	H, H	**4bh**, 98	93
8	*m*-BrC_6H_4	H, H	**4bi**, 96	94
9	*m*-$MeOC_6H_4$	H, H	**4bj**, 96	97
10	*p*-ClC_6H_4	H, H	**4bk**, 99	95
11	*p*-BrC_6H_4	H, H	**4bl**, 99	94
12	*p*-$MeOC_6H_4$	H, H	**4bm**, 98	96
13	2-Naphthyl	H, H	**4bn**, 99	94
14	2-Furyl	H, H	**4bo**, 92	90
15	2-Thienyl	H, H	**4bp**, 98	93
16	Pr	H, H	**4bq**, 94	96
17	^{i}Bu	H, H	**4br**, 91	95
18	Ph	Me, H	**4bs**, 88	98
19	Ph	CF_3, H	**4bt**, 61	65
20[d]	Ph	H, Ph	**4bu**, 98	83
21[e]	1-Cyclohexenyl		**4bv**, 96	82

[a] Reactions were carried out with **1b** (0.12 mmol), **2** (0.1 mmol) and **3c** (1 mol %) in 0.5 mL MTBE at −40 °C for 4 h.
[b] Isolated yield.
[c] Determined by HPLC analysis on a chiral stationary phase.
[d] The *dr* value was determined by HPLC and up to 91:9.
[e] The *dr* value was determined by HPLC and up to >99:1.

We then employed 4-(*tert*-butyl)phenylthiol **1b** as a nucleophile in reactions with various nitrostyrenes (Table 3). High yields (92%–99%) with excellent enantioselectivities (93%–97% *ee*) were achieved irrespective of whether the substituent on the phenyl ring of the β-nitroalkene was electron donating or withdrawing (Table 3, entries 1–12). The substituent pattern had almost no effect on the reactivity and stereocontrol results (Table 3, entries 1–6). Reactions of nitrostyrenes with a β-naphthyl or heteroaromatic ring also proceeded smoothly to furnish the corresponding products in 92%–99% yields and 90%–94% *ee* (Table 3, entries 13–15). Less reactive aliphatic nitroalkenes also reacted well and gave the products in good yields (91%–94%) and enantioselectivities (95%–96% *ee*) (Table 3, entries 16 and 17). β,β-Disubstituted nitroalkenes were also suitable for the reaction (Table 3, entries 18 and 19). However, when one of the β substituents was CF_3, the product was obtained in only 61% yield and 65% *ee* (Table 3, entry 19). α,β-Disubstituted nitroalkenes were amenable to the reaction and afforded the corresponding products with excellent yields, good diastereoselectivities and enantioselectivities (Table 3, entries 20 and 21).

To evaluate the potential utility of this methodology in organic synthesis, reactions with a dramatically reduced catalyst loading (0.05 mol %) were investigated on a gram scale. The reaction was successful and gave the product in 98% yield with slightly lower enantioselectivity (90% *ee*) (Scheme 1a). The product of the SMA reaction of 4-chlorobenzyl thiol (**1n**) with 2,4-dichloro-1-(2-nitrovinyl)benzene (**2u**) is an intermediate in the synthesis of the antifungal agent sulconazole.[10a,16] We thus aimed to promote the enantioselective version of this reaction using our catalytic system and obtained the product **4nw** in 93% yield with 89% *ee* (Scheme 1b). To demonstrate the synthetic utility of available products **4**, we further transformed them into chiral amino sulfone derivatives. A one-pot strategy has been exploited for this reaction to avoid the possible racemization of **4aa** at room temperature. Treatment of the final reaction mixture of **1a** and **2a** with Zn/MeOH/HCl, followed by protection of the resulting amine with Boc_2O gave intermediate **5** in 82% yield and did not affect the enantiopurity of the product (97% *ee*). Subsequent oxidation of the sulfide with *m*-CPBA afforded sulfone **6** in 91% yield and 97% *ee* (Scheme 1c).



Scheme 1. Gram-scale sulfa-Michael addition and subsequent derivatization

The absolute configuration of product **4oa** was determined as *S* by comparing its specific rotation $[\alpha]_D^{20}$ = + 187° (c = 0.5, DCM, 97% *ee*) with literature data $[\alpha]_D^{20}$ = + 177° (c = 0.428, DCM, 93% *ee*),[12b] and the configuration of the other products was deduced according to this. A transition-state model that accounts for the stereochemical outcome is

proposed in Figure 1. The protons of the thiourea interact with the nitro group through two hydrogen bonds; this activates the nitroalkene. The thiophenol is deprotonated by the tertiary amine moiety of the catalyst and the resulting thiolate anion forms hydrogen bonds with the amide group. This orientation allows the sulfa-Michael addition to proceed from the *Si*-face of the nitrostyrene, which results in the observed product.

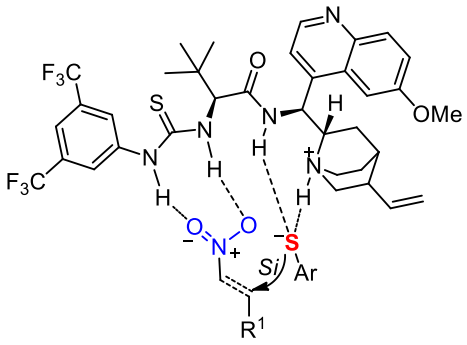


Figure 1. Proposed transition-state model

In summary, an efficient enantioselective sulfa-Michael reaction of aromatic thiols with β-nitroalkenes has been established in the presence of a multifunctional chiral organocatalyst. This reaction accommodates an unprecedented range of sulfur-containing nucleophiles; aromatic and alkyl thiols reacted smoothly and afforded the corresponding products in excellent yields and enantioselectivities**.** The catalyst loading could be dramatically reduced to 0.05 mol %, and also exhibited good catalytic performance when the reaction was performed on the gram scale.

Experimental Section

General Experimental Procedure for the Sulfa-Michael Reactions

Nitrostyrenes **2** (0.1 mmol, 1.0 equiv.) and **3c** (1 mol %) were dissolved in 0.5 mL of THF at –40 °C and stirred for 5 min. Thiophenols **1** (0.12 mmol, 1.2 equiv.) was added at –40 °C and stir for 4 h, monitored by TLC until the nitrostyrenes **2** have been completely consumed. The reaction was then treated with CH_3CO_2H, which was added in a dropwise manner to quench the catalyst. The mixture was then purified directly by flash chromatography over silica gel (0.5–2% EtOAc/PE) to give the product **4**.

Acknowledgements

We are grateful to the National Natural Science Foundation of China (21172180 and 21472151)

References

[1] a) A. Nudelman, *The Chemistry of Optically Active Sulfur Compounds*; Gordon and Breach: New York, **1984**; b) L. A. Damani, *Sulphur-Containing Drugs and Related Organic Compounds*; Wiley: New York, **1989**; c) J. R. F. da Silva, R. J. P. Williams, *The Biological Chemistry of the Elements*; Oxford University Press: New York, **2001**.

[2] a) D. Enders, K. Lüttgen, A. A. Narine, *Synthesis* **2007**, *7*, 959–980; b) P. Chauhan, S. Mahajan, D. Enders, *Chem. Rev*. **2014**, *114*, 8807–8864.

[3] a) C. Palomo, A. Mielgo, *Angew. Chem*. **2006**, *118*, 8042–8046; *Angew. Chem. Int. Ed*. **2006**, *45*, 7876–7880; b) W. Wang, H. Li, J. Wang, L. S. Zu, *J. Am. Chem. Soc*. **2006**, *128*, 10354–10355; c) S. Brandau, E. Maerten, K. A. Jørgensen, *J. Am. Chem. Soc*. **2006**, *128*, 14986–14991; d) R. Rios, H. Sundén, I. Ibrahem, G. L. Zhao, L. Eriksson, A. Córdova, *Tetrahedron Lett*. **2006**, *47*, 8547–8551.

[4] a) P. McDaid, Y. G. Chen, L. Deng, *Angew. Chem*. **2002**, *114*, 348–3450; *Angew. Chem. Int. Ed*. **2002**, *41*, 338–340; b) P. Ricci, A. Carlone, G. Bartoli, M. Bosco, L. Sambri, P. Melchiorre, *Adv. Synth. Catal*. **2008**, *350*, 49–53; c) N. K. Rana, S. Selvakumar, V. K. Singh, *J. Org. Chem*. **2010**, *75*, 2089–2091; d) M. Yoshida, Y. Ohno, S. Hara, *Tetrahedron Lett*. **2010**, *51*, 5134–5136; e) L. Dai, S. X. Wang, F. E. Chen, *Adv. Synth. Catal*. **2010**, *352*, 2137–2141; f) Y. H. Hui, J. Jiang, W. T. Wang, W. L. Chen, Y. F. Cai, L. L. Lin, X. H. Liu, X. M. Feng, *Angew. Chem*. **2010**, *122*, 4386–4389; *Angew. Chem. Int. Ed*. **2010**, *49*, 4290–4293; g) M. Moccia, F. Fini, M. Scagnetti, M. F. A. Adamo, *Angew. Chem*. **2011**, *123*, 7025–7027; *Angew. Chem. Int. Ed*. **2011**, *50*, 6893–6895; h) X. Tian, C. Cassani, Y. K. Liu, A. Moran, A. Urakawa, P. Galzerano, E. Arceo, P. Melchiorre, *J. Am. Chem. Soc*. **2011**, *133*, 17934–17941; i) S. Bonollo, D. Lanari, F. Pizzo, L. Vaccaro, *Org. Lett*. **2011**, *13*, 2150–2152; j) F. L. Zhao, W. Zhang, Y. Y. Yang, Y. H. Pan, W. C. Chen, H. J. Liu, L. Yan, C. H. Tan, Z. Y. Jiang, *Adv. Synth. Catal*. **2011**, *353*, 2624–2630; k) N. K. Rana, R. Unhale, V. K. Singh, *Tetrahedron Lett*. **2012**, *53*, 2121–2124; l) L. Yao, K. Liu, H. Y. Tao, G. F. Qiu, X. Zhou, C. J. Wang, *Chem. Commun*. **2013**, 49, 6078–6080; m) J. D. White, S. Shaw, *Chem. Sci*. **2014**, *5*, 2200–2204; n) N. K. Fu, L. Zhang, S. Z. Luo, J. P. Cheng, *Org. Lett*. **2014**, *16*, 4626–4629; o) M. Fernández, U. Uria, L. Orbe, J. L. Vicario, E. Reyes, L. Carrillo, *J. Org. Chem*. **2014**, *79*, 441–445; p) R. Kowalczyk, P. J. Boratyński, A. J. Wierzba, J. Bąkowicz, *RSC Adv*. **2015**, *5*, 66681–66686.

[5] a) D. Leow, S. S. Lin, S. K. Chittimalla, X. Fu, C. H. Tan, *Angew. Chem*. **2008**, *120*, 5723–5727; *Angew. Chem. Int. Ed*. **2008**, *47*, 5641–5645; b) X. Q. Dong, X. Fang, C. J. Wang, *Org. Lett*. **2011**, *13*, 4426–4429; c) H. Shen, K. F. Yang, Z. H. Shi, J. X. Jiang, G. Q. Lai, L. W. Xu, *Eur. J. Org. Chem*. **2011**, 5031–5038; d) C. Aydillo, A. Avenoza, J. H. Busto, G. Jiménez-Osés, J. M. Peregrina, M. M. Zurbano, *Org. Lett*. **2012**, *14*, 334–337; e) X. Fang, J. Li, C. J. Wang, *Org. Lett*. **2013**, *15*, 3448–3451; f) C. Aydillo, I. Compañón, A. Avenoza, J. H. Busto, F. Corzana, J. M. Peregrina, M. M. Zurbano, *J. Am. Chem. Soc*. **2014**, *136*, 789–800; g) Z. P. Hu, Z. Zhuang, W. W. Liao, *J. Org. Chem*. **2015**, *80*, 4627-4637; h) A. J. M. Farley, C. Sandford, D. J. Dixon, *J. Am. Chem. Soc*. **2015**, *137*, 15992–15995; i) J. C. Yang,

A. J. M. Farley, D. J. Dixon, *Chem. Sci*. **2017**, *8*, 606–610; j) P. F. Yuan, S. X. Meng, J. A. Chen, Y. Huang, *Synlett* **2016**, *27*, 1068–1072.

[6] a) H. H. Lu, F. G. Zhang, X. G. Meng, S. W. Duan, W. J. Xiao, *Org. Lett*. **2009**, *11*, 3946–3949; b) K. L. Kimmel, M. T. Robak, S. Thomas, M. Lee, J. A. Ellman, *Tetrahedron* **2012**, *68*, 2704–2712; c) Q. L. Pei, W. Y. Han, Z. J. Wu, X. M. Zhang, W. C. Yuan, *Tetrahedron* **2013**, *69*, 5367–5373.

[7] The sulfa-Michael addition to α,β-unsaturated amides and imides, see: a) S. J. K. Sauerland, E. Kiljunen, A. M. P. Koskinen, *Tetrahedron Lett*. **2006**, *47*, 1291–1293; b) Y. Liu, B. F. Sun, B. M. Wang, M. Wakem, L. Deng, *J. Am. Chem. Soc*. **2009**, *131*, 418–419; c) N. K. Rana, V. K. Singh, *Org. Lett*. **2011**, *13*, 6520–6523; d) L. Dai, H. J. Yang, J. Z. Niu, F. E. Chen, *Synlett* **2012**, *23*, 314–316; e) A. C. Breman, J. M. M. Smits, R. de Gelder, J. H. van Maarseveen, S. Ingemann, H. Hiemstra, *Synlett* **2012**, *23*, 2195–2200; f) X. Q. Dong, X. Fang, H. Y. Tao, X. Zhou, C. J. Wang, *Adv. Synth. Catal*. **2012**, *354*, 1141–1147; g) R. A. Unhale, N. K. Rana, V. K. Singh, *Tetrahedron Lett*. **2013**, *54*, 1911–1915; h) B. L. Zhao, D. M. Du, *Org. Biomol. Chem*. **2014**, *12*, 1585–1594; i) B. L. Zhao, D. M. Du, *RSC Adv*. **2014**, *4*, 27346–27353; j) A. C. Breman, S. E. M. Telderman, R. P. M. van Santen, J. I. Scott, J. H. van Maarseveen, S. Ingemann, H. Hiemstra, *J. Org. Chem*. **2015**, *80*, 10561–10574; Addition to α,β-unsaturated sulfonates and sulfones, see: k) D. Enders, K. Hoffman, *Eur. J. Org. Chem*. **2009**, 1665–1668; l) X. Fang, X. Q. Dong, Y. Y. Liu, C. J. Wang, *Tetrahedron Lett*. **2013**, *54*, 4509–4511.

[8] N. Ono, *The Nitro Group in Organic Synthesis*; Wiley-VCH: New York, **2001**.

[9] a) H. Li, J. Wang, L. S. Zu, W. Wang, *Tetrahedron Lett*. **2006**, *47*, 2585–2589; b) K. L. Kimmel, M. T. Robak, J. A. Ellman, *J. Am. Chem. Soc*. **2009**, *131*, 8754–8755; c) W. Yang, D. M. Du, *Org. Biomol. Chem*. **2012**, *10*, 6876–6884; d) R. C. Wang, J. Liu, J. X. Xu, *Adv. Synth. Catal*. **2015**, *357*, 159–167.

[10] a) R. Kowalczyk, A. E. Nowak, J. Skarżewski, *Tetrahedron: Asymmetry* **2013**, *24*, 505–514; b) J. A. Chen, S. X. Meng, L. M. Wang, H. M. Tang, Y. Huang, *Chem. Sci*. **2015**, *6*, 4184–4189.

[11] D. Uraguchi, N. Kinoshita, D. Nakashima, T. Ooi, *Chem. Sci*. **2012**, *3*, 3161–3164.

[12] a) C. Palacio, S. J. Connon, *Chem. Commun*. **2012**, *48*, 2849–2851; b) S. Kawazoe, K. Yoshida, Y. Shimazaki, T. Oriyama, *Tetrahedron Lett*. **2015**, *56*, 410–413.

[13] M. Marigo, T. Schulte, J. Franzén, K. A. Jørgensen, *J. Am. Chem. Soc*. **2005**, *127*, 15710–15711.

[14] a) R. Ding, B. Zheng, Y. Wang, Y. G. Peng, *Org. Lett*. **2015**, *17*, 4128–4131; b) W. D. Hou, Q. Wei, G. S. Liu, J. Chen, J. Guo, Y. G. Peng, *Org. Lett*. **2015**, *17*, 4870–4873; c) W. D. Hou, Q. Wei, Y. G. Peng, *Adv. Synth. Catal*. **2016**, *358*, 1035–1041.

[15] Racemization was observed when purified **4aa** with 80% *ee* in was stored overnight in DCM at rt.

[16] R. A. Fromtling, *Clin. Microbiol. Rev*. **1988**, *1*, 187–217.

10.1002/adsc.201700109

COMMUNICATION

Enantioselective Sulfa-Michael Addition of Aromatic Thiols to β-Substituted Nitroalkenes Promoted by a Chiral Multi-functional Catalyst

Adv. Synth. Catal. **Year**, *Volume*, Page – Page

Qi Wei, Wenduan Hou, Na Liao and Yungui Peng*