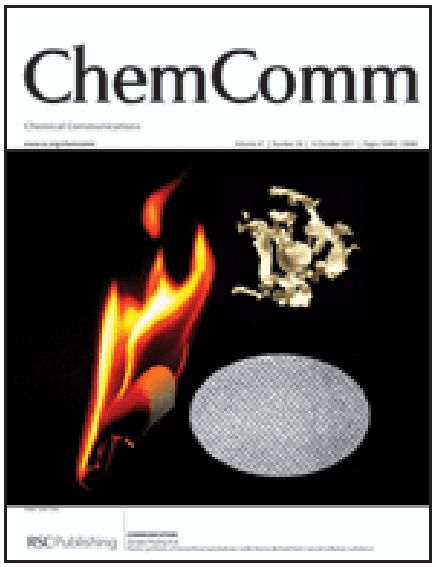
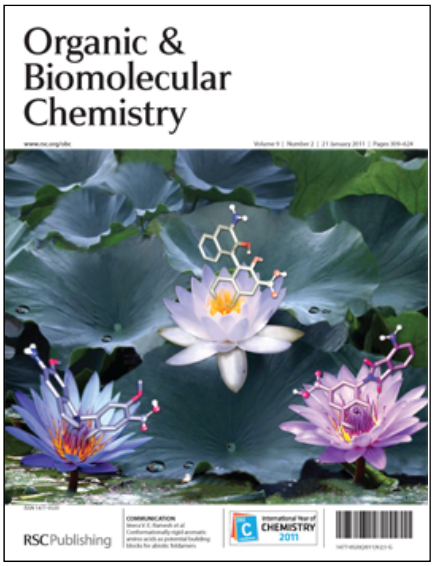




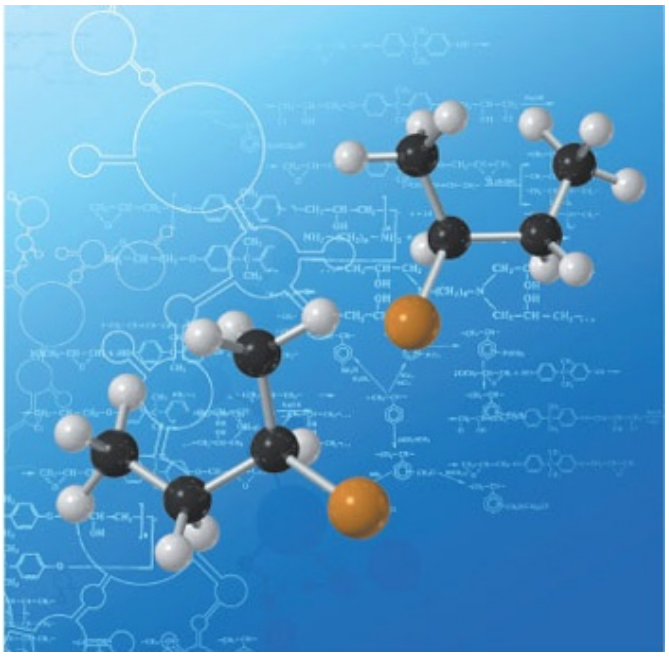
This article is part of the

Organocatalysis

web themed issue

Guest editors: Professors Keiji Maruoka, Hisashi Yamamoto, Liu-Zhu Gong and Benjamin List

All articles in this issue will be gathered together online at www.rsc.org/organocatalysis



Organic & Biomolecular Chemistry

Dynamic Article Links

Cite this: *Org. Biomol. Chem.*, 2012, **10**, 6876

www.rsc.org/obc

PAPER

Squaramide-catalysed enantio- and diastereoselective sulfa-Michael addition of thioacetic acid to α,β-disubstituted nitroalkenes†

Wen Yang and Da-Ming Du*

Received 4th June 2012, Accepted 4th July 2012
DOI: 10.1039/c2ob26068a

A highly enantio- and diastereoselective sulfa-Michael addition of thioacetic acid to α,β-disubstituted nitroalkenes catalysed by a chiral squaramide organocatalyst has been described. This organocatalytic reaction at an extremely low catalyst loading (0.2 mol%) furnished synthetically useful β-nitro sulfides in excellent yields with good diastereoselectivities and high enantioselectivities (up to 94 : 6 dr, 95% ee). In addition, the catalytic reaction can be performed on a 10 gram scale, and facile transformation into taurine derivative is also presented.

Introduction

The asymmetric sulfa-Michael addition is one of the fundamental carbon–sulfur bond forming reactions in organic synthesis, and plays a key role in the synthesis of biologically active sulfur-containing compounds.[1] In recent years, considerable efforts have been devoted, and various approaches for asymmetric sulfa-Michael additions have been reported.[2,3] To date, these reports have mainly focused on alkyl or aryl thiols as Michael donors. However, studies on the asymmetric sulfa-Michael addition employing thioacetic acid are currently limited.[4,5] Among them, the asymmetric sulfa-Michael addition of thioacetic acid to nitroalkenes is extremely attractive because it can provide an easy access to synthetically useful 1,2-aminothiol or taurine derivatives. To the best of our knowledge, only three reports have been described.[5] Wang first reported the asymmetric sulfa-Michael addition of thioacetic acid to *trans*-β-nitrostyrenes catalysed by Takemoto's thiourea, but unsatisfactory enantioselectivities (20–70% ee) were achieved.[5a] Subsequently, Ellman and co-workers developed a sulfinyl urea organocatalyst to promote this reaction with high enantioselectivities, however, harsh reaction condition (−78 °C) was required.[5b] Very recently, Ellman and co-workers extended the substrate scope to an array of cyclic α,β-disubstituted nitroalkenes.[5c] In view of these limited successes, the development of other new efficient catalytic systems for high enantioselectivity, low catalyst loading, and mild reaction conditions is in great demand. As a new class of good hydrogen-bonding organocatalyst, chiral squaramide is increasingly utilized in organocatalysis.[6] After the pioneering work reported by Rawal, various asymmetric reactions catalysed by squaramide organocatalysts have been developed.[3f,7]

In recent years, our group has also done some related research in this field.[8] As a continuation of the research on squaramide-catalysed asymmetric reactions, in this paper, we wish to describe the asymmetric sulfa-Michael addition of thioacetic acid to α,β-disubstituted nitroalkenes catalysed by chiral squaramide organocatalysts.

Results and discussion

Initially, we started our investigation with the sulfa-Michael addition of thioacetic acid **2** to *trans*-β-methyl-β-nitrostyrene **1a** as a model reaction. To our delight, when the model reaction was performed in the presence of 5 mol% catalyst **I** in CH_2Cl_2 at room temperature for 2 h, the desired adduct **3a** was obtained in 97% yield with 75 : 25 dr and 70% ee. With the promising result, a series of squaramide catalysts (Fig. 1) was readily prepared and their catalytic capacity to promote the addition was evaluated. The catalyst screening results are shown in Table 1. Squaramides **II–IV** derived from chiral 1,2-diaminocyclohexane were examined, and squaramide **III** was found to give a better result (80 : 20 dr, 84% ee) than squaramide **I** (entries 1–4). Cinchona-based squaramides **V** and **VI** afforded the corresponding adducts only with moderate diastereoselectivities and enantioselectivities (entries 5 and 6). When C_2-symmetric squaramides **VII** and **VIII** were tested, the adducts with very low enantioselectivities (18% ee and 17% ee, respectively) were obtained (entries 7 and 8). For investigation on the effect of steric hindrance, structural variations **IX** and **X** bearing a piperidinyl group as squaramide **III** were screened, but no better results were observed (entries 9–10). In contrast, common

School of Chemical Engineering and Environment, Beijing Institute of Technology, Beijing 100081, People's Republic of China.
E-mail: dudm@bit.edu.cn; Tel: +86 10 68914985

†Electronic supplementary information (ESI) available: Copies of ^1H and ^{13}C NMR spectra of new compounds, X-ray crystal structure cif file of **3e** and HPLC chromatograms. CCDC 886084. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2ob26068a

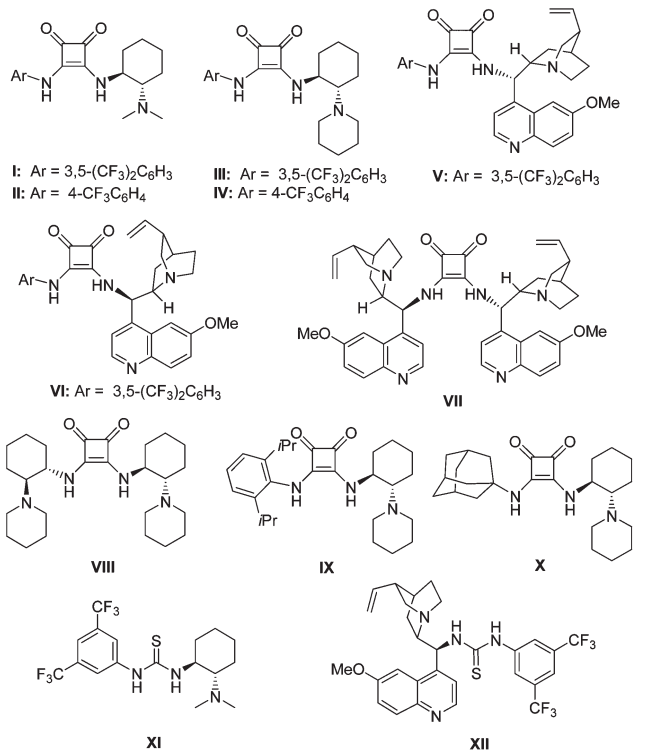
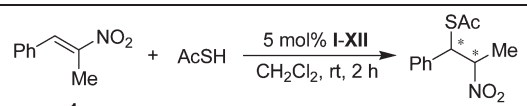


Fig. 1 Screened organocatalysts.

Table 1 Screening of organocatalysts for the asymmetric sulfa-Michael addition of thioacetic acid to *trans*-β-methyl-β-nitrostyrene[a]



Entry	Catalyst	Yield[b] (%)	dr[c] (*anti*/*syn*)	ee[c,d] (%)
1	**I**	98	75 : 25	70
2	**II**	96	64 : 36	54
3	**III**	98	80 : 20	84
4	**IV**	98	66 : 34	57
5	**V**	89	71 : 29	52
6	**VI**	84	67 : 33	−47
7	**VII**	94	66 : 34	18
8	**VIII**	92	64 : 36	17
9	**IX**	94	67 : 33	50
10	**X**	98	68 : 32	73
11	**XI**	97	70 : 30	45
12	**XII**	97	68 : 32	40

[a] Reactions were carried out with *trans*-β-methyl-β-nitrostyrene **1a** (0.2 mmol) and thioacetic acid **2** (0.2 mmol) in CH_2Cl_2 (0.5 mL). [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] Enantiomeric excess of the major *anti* diastereomer.

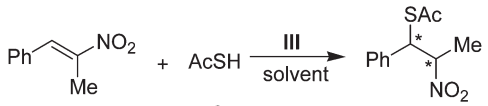
thiourea catalysts **XI** and **XII** gave lower enantioselectivities than the corresponding squaramides **I** and **V** (entries 11 and 12).

With squaramide **III** as the optimal catalyst, several reaction parameters, such as solvent, temperature, catalyst loading, and concentration were successively investigated for the optimal reaction conditions. The results are summarized in Table 2. The solvent optimization disclosed that various common solvents were well tolerated and CH_2Cl_2 was the best reaction medium (entries 1–7). It is noteworthy that the reaction proceeded smoothly in brine to achieve comparable good diastereoselectivity and enantioselectivity (entry 8). When the reaction was performed at 0 °C, an increase on the stereoselectivity (85 : 15 dr, 90% ee) was observed (entry 9). Unfortunately, further lowering the temperature did not improve the enantioselectivity (entries 10 and 11). Subsequently, the effect of catalyst loading was investigated. Interestingly, increasing the catalyst loading (10 mol%) led to a slight decrease in the stereoselectivity, while good diastereoselectivity and high enantioselectivity were maintained with a reduced catalyst loading (1 or 0.2 mol%) (entries 12–14). Further reducing the catalyst loading to 0.1 mol % decreased the enantioselectivity slightly (entry 15). Additionally, the amount of solvent was simply examined, and only a small impact was observed (entries 16 and 17).

Having established the optimal reaction conditions, we explored the scope of the asymmetric sulfa-Michael addition of thioacetic acid to α,β-disubstituted nitroalkenes. The results are presented in Table 3. An array of aromatic α,β-disubstituted nitroalkenes **1a–k** bearing electron-neutral, electron-withdrawing or electron-donating substitutions reacted smoothly with thioacetic acid **2** to afford the corresponding adducts in excellent yields with good diastereoselectivities and high enantioselectivities (87–95% ee) (entries 1–11). The position of the substitution at the aromatic ring had an effect on the enantioselectivity. Steric hindrance benefits the enantioselectivity. These nitroalkenes with *ortho* groups on the aromatic ring gave relatively higher enantioselectivities. Heteroaromatic nitroalkene **1l** derived from furfural worked well to furnish the corresponding adduct with good yield and diastereoselectivity albeit with lower enantioselectivity (entry 12). Aliphatic nitroalkenes **1m–o** were also viable substrates, despite lower reactivity (entries 13–15). The α,β-unsaturated nitroalkene **1m** afforded the product **3m** with comparable diastereoselectivity but moderate enantioselectivity (69% ee). Aliphatic nitroalkene **1n** gave product **3n** with comparable result at room temperature, and aliphatic nitroalkene **1o** proceeded with 2 mol% **III** to furnish the adduct **3o** in 76% yield with 70 : 30 dr and 78% ee. Unfortunately, aromatic nitroalkenes **1p** and **1q** with larger substituted groups at the α-position gave unsatisfactory enantioselectivities (77% ee and 75% ee, respectively) (entries 16 and 17). The addition of thioacetic acid **2** to nitroalkene **1p** was selected as a model reaction, and reaction conditions involving solvent, temperature, and catalyst loading were simply reoptimized. But no satisfactory enantioselectivity was observed. The β-nitrostyrene **1r** was also evaluated, but only moderate enantioselectivity (51% ee) was obtained (entry 18). The absolute configuration of enantiopure *anti* diastereomer of **3e** was determined to be (1*S*,2*R*) by X-ray analysis (Fig. 2).[9]

On the basis of the absolute configuration of the *anti*-**3e**, we propose a possible reaction mechanism for this Michael addition (Fig. 3). The squaramide **III** may act in a bifunctional fashion. In the transition state **A**, the squaramide moiety activates nitroalkene **1e** through double hydrogen bonding, and thioacetic acid **2** is deprotonated by the basic nitrogen atom of the tertiary amine. The thioacetic acid anion attacks the activated nitroalkene

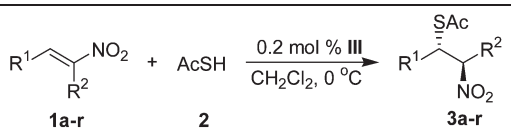
Table 2 Optimization of reaction conditions for the asymmetric sulfa-Michael addition of thioacetic acid to *trans*-β-methyl-β-nitrostyrene[a]



Entry	Solvent	Loading (mol%)	*T* (°C)	*t*(h)	Yield[b] (%)	dr[c] (*syn*/ *anti*)	ee[c,d] (%)
1	CH_2Cl_2	5	rt	2	98	80 : 20	84
2	CH_2ClCH_2Cl	5	rt	2	99	79 : 21	79
3	$CHCl_3$	5	rt	2	98	80 : 20	80
4	THF	5	rt	2	93	73 : 27	63
5	Et_2O	5	rt	2	94	77 : 23	82
6	PhMe	5	rt	2	98	72 : 28	72
7	iPrOH	5	rt	2	90	81 : 19	79
8	Brine	5	rt	2	83	77 : 23	78
9	CH_2Cl_2	5	0	3	98	85 : 15	90
10	CH_2Cl_2	5	−20	5	95	86 : 14	89
11	CH_2Cl_2	5	−40	9	92	89 : 11	88
12	CH_2Cl_2	10	0	3	94	83 : 17	87
13	CH_2Cl_2	1	0	3	94	86 : 14	90
14	CH_2Cl_2	0.2	0	6	92	85 : 15	90
15	CH_2Cl_2	0.1	0	10	95	85 : 15	88
16[e]	CH_2Cl_2	0.2	0	6	96	86 : 14	90
17[f]	CH_2Cl_2	0.2	0	10	96	85 : 15	88

[a] Unless noted otherwise, reactions were carried out with *trans*-β-methyl-β-nitrostyrene **1a** (0.2 mmol) and thioacetic acid **2** (0.2 mmol) in the solvent (0.5 mL). [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] Enantiomeric excess of the major *anti* diastereomer. [e] 0.25 mL of CH_2Cl_2 was used. [f] 1.0 mL of CH_2Cl_2 was used.

Table 3 Scope of the asymmetric sulfa-Michael addition of thioacetic acid to α,β-disubstituted nitroalkenes[a]



Entry	R^1	R^2	*t*(h)	Product	Yield[b] (%)	dr[c] (*anti*/*syn*)	ee[c,d] (%)
1	C_6H_5	Me	6	**3a**	96	86 : 14	90
2	4-FC_6H_4	Me	6	**3b**	97	86 : 14	90
3	4-ClC_6H_4	Me	6	**3c**	97	87 : 13	90
4	2-ClC_6H_4	Me	6	**3d**	96	89 : 11	95
5[e]	4-BrC_6H_4	Me	6	**3e**	98	86 : 14	90
6	2-BrC_6H_4	Me	6	**3f**	93	86 : 14	94
7	4-MeC_6H_4	Me	6	**3g**	95	88 : 12	88
8	2-MeC_6H_4	Me	6	**3h**	98	92 : 8	95
9	4-$MeOC_6H_4$	Me	6	**3i**	97	86 : 14	87
10	2-$MeOC_6H_4$	Me	6	**3j**	97	89 : 11	90
11	1-Naphthyl	Me	12	**3k**	92	80 : 20	94
12	2-Furanyl	Me	12	**3l**	85	92 : 8	78
13	Cinnamyl	Me	12	**3m**	77	85 : 15	69
14[f]	iPr	Me	12	**3n**	91	72 : 28	84
15[g]	Cyclohexyl	Me	24	**3o**	76	70 : 30	78
16	C_6H_5	Et	6	**3p**	95	94 : 6	77
17	C_6H_5	Ph	6	**3q**	94	86 : 14	75
18	C_6H_5	H	2	**3r**	94	—	51

[a] Unless noted otherwise, reactions were carried out with α,β-disubstituted nitroalkenes **1** (0.2 mmol) and thioacetic acid **2** (0.2 mmol) in CH_2Cl_2 (0.25 mL). [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] Enantiomeric excess of the major *anti* diastereomer. [e] The absolute configuration of **3e** was determined by X-ray analysis. [f] Reaction was performed at room temperature. [g] 2 mol% **III** was used at room temperature.

1e from the *Si*-face to afford the intermediate **C**. Since the steric hindrance of methyl is greater than the planar nitro group, the proposed Newman projection in the box is favored. Then the intermediate **C** abstracts a proton from ammonium *via* the transition state **B** to form the desired *anti*-**3e** with the release of catalyst **III**. The steric hindrance of phenyl group is greater than that of AcS group, so the protonation occurs favorably from the less steric AcS side leading to (1*S*,2*R*)-configuration.

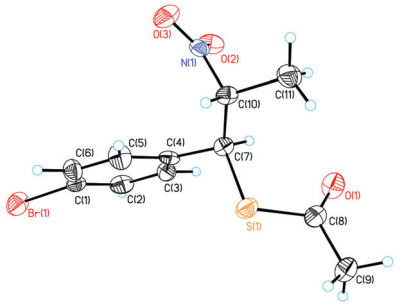


Fig. 2 X-ray crystal structure of the enantiopure *anti* diastereomer of **3e**.

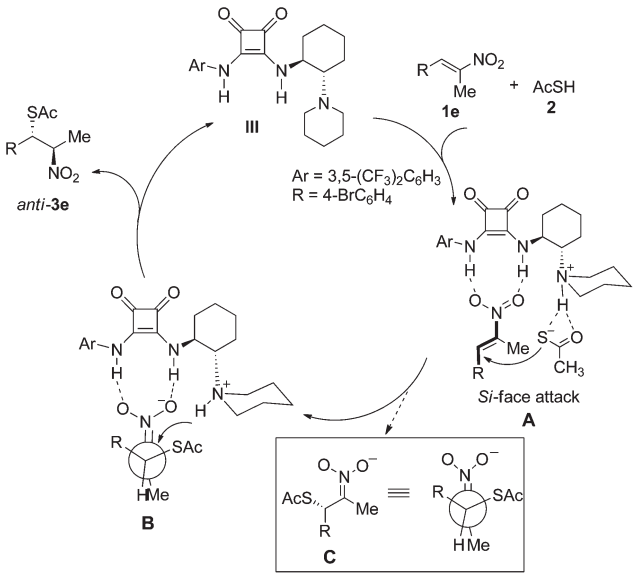
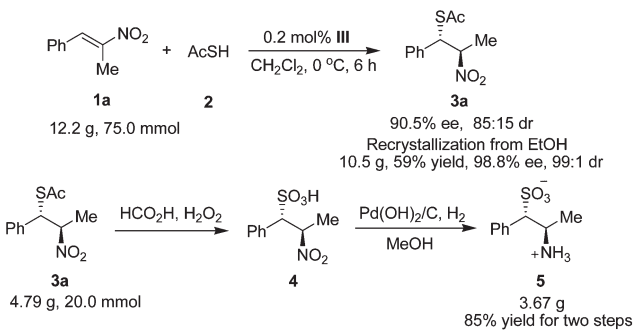


Fig. 3 Proposed mechanism for the Michael addition.



Scheme 1 The gram-scale preparation and transformation of **3a**.

To further evaluate the synthetic potential of this catalytic system, the gram-scale preparation and transformation of **3a** were conducted. As shown in Scheme 1, the catalytic reaction on a 10 gram scale was performed well without any loss of yield and stereoselectivity, and almost optically pure adduct **3a** was easily obtained by a simple recrystallization from EtOH. According to the recently reported method,[10] β-nitro sulfide **3a** was readily transformed to taurine derivative **5** in good yield through successive oxidation and hydrogenation.

Conclusions

In conclusion, we have developed a squaramide-catalysed highly asymmetric sulfa-Michael addition of thioacetic acid to α,β-disubstituted nitroalkenes. The reactions proceeded well with 0.2 mol% catalyst, and the desired adducts were obtained in excellent yields with good diastereoselectivities and high enantioselectivities. This process provides an easy access to optically active β-nitro sulfides, which can be readily transformed into taurine derivatives. Moreover, this catalytic reaction can be performed on a 10 gram scale. Further studies on squaramide-catalysed asymmetric reactions are underway in our laboratory.

Experimental

General methods

Commercially available compounds were used without further purification, unless otherwise stated. Column chromatography was carried out with silica gel (200–300 mesh). Melting points were measured with a XT-4 melting point apparatus without correction. ^{1}H NMR spectra were recorded with a Varian Mercury-plus 400 MHz spectrometer. Chemical shifts were reported in ppm with the internal TMS signal at 0.0 ppm as a standard. ^{13}C NMR spectra were recorded at 100 MHz. The high resolution MS spectra were obtained with ESI ionization using a Bruker APEX IV FTMS. Optical rotations were measured with a Krüss P8000 polarimeter at the indicated concentration with units g/100 mL. The enantiomeric excesses were determined by chiral HPLC using an Agilent 1200 LC instrument with Daicel Chiralpak IA, AS-H or Chiralcel OJ-H column.

Materials

α,β-Disubstituted nitroalkenes were prepared according to the literature procedures.[11] The squaramide catalysts **I–VI**,[7b,8a,b] **VII**,[12] **VIII**,[8e] and thiourea catalysts **XI**[13] and **XII**[14] were prepared following the reported procedures, respectively.

Preparation of squaramide catalyst IX

To a solution of 3,4-dimethoxycyclobut-3-ene-1,2-dione (1.42 g, 10.0 mmol) in MeOH (15 mL) was added 2,6-diisopropylbenzenamine (1.77 g, 10.0 mmol). After stirring for 48 h at room temperature, the reaction mixture was concentrated and directly purified by silica gel column chromatography to afford the mono-squaramide **6** as a pale yellow solid (1.40 g, 49% yield). M.p. 152–154 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.06 (s, 1H, NH), 7.35 (t, J = 7.8 Hz, 1H, ArH), 7.18 (d, J = 7.6 Hz, 2H, ArH), 4.18 (s, 3H, OCH_3), 3.12–3.05 (m, 2H, CH), 1.19 (d, J = 6.8 Hz, 12 H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.4, 184.0, 179.2, 172.1, 146.1, 131.0, 129.2, 123.6, 60.4, 28.6, 23.5; IR (KBr): ν 3207, 3028, 2966, 2869, 1813, 1707, 1611, 1584, 1521, 1457, 1369, 1358, 1031, 937, 813, 757 cm^{-1}; HRMS (ESI): m/z calcd for $C_{17}H_{22}NO_3$ $[M + H]^+$ 288.15942, found 288.15957.

To a solution of (1*S*,2*S*)-2-(1-piperidinyl)-cyclohexanamine (547 mg, 3.0 mmol) in CH_2Cl_2 (5 mL) was added **6** (575 mg, 2.0 mmol). After stirring for 24 h at room temperature, the

reaction mixture was concentrated and directly purified by silica gel column chromatography to afford the squaramide catalyst **IX** as a pale yellow solid (485 mg, 55% yield). M.p. > 310 °C (Decomp.); $[\alpha]_D^{25}$ +35.5 (*c* 0.31, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.82 (s, 1H, NH), 7.34 (t, *J* = 7.6 Hz, 1H, ArH), 7.20 (t, *J* = 7.6 Hz, 2H, ArH), 4.96 (s, 1H, NH), 3.51 (t, *J* = 9.6 Hz, 1H, CH), 3.32–3.26 (m, 1H, CH), 3.14–3.08 (m, 1H, CH), 2.54 (d, *J* = 9.6 Hz, 1H, CH_2), 2.41 (d, *J* = 10.0 Hz, 2H, CH_2), 1.98 (t, *J* = 7.6 Hz, 2H, CH_2), 1.74–1.72 (m, 3H, CH_2), 1.61 (d, *J* = 12.8 Hz, 1H, CH_2), 1.27–0.94 (m, 22H, CH_3 + CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 183.5, 182.6, 169.5, 166.5, 146.8, 131.5, 129.3, 123.7, 123.2, 68.8, 53.5, 49.2, 34.8, 28.8, 28.4, 26.0, 25.4, 24.6, 24.5, 24.3, 23.7, 23.3, 22.5, 22.2 ppm; IR (KBr): ν 3145, 2932, 2854, 1800, 1650, 1572, 1537, 1449, 1362, 1333, 1144, 871, 800, 732 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{27}H_{40}N_3O_2$ $[M + H]^+$ 438.31150, found 438.31065.

Preparation of squaramide catalyst X

To a solution of 3,4-dimethoxycyclobut-3-ene-1,2-dione (1.42 g, 10.0 mmol) in MeOH (10 mL) was added adamantanamine (1.50 g, 10.0 mmol). The reaction mixture was stirred for 48 h at room temperature and the white precipitation formed. The mono-squaramide **7** was obtained by filtration as a white solid (2.20 g, 84% yield).

To a solution of (1*S*,2*S*)-2-(1-Piperidinyl)-cyclohexanamine (547 mg, 3.0 mmol) in CH_2Cl_2 (5 mL) was added mono-squaramide **7** (523 mg, 2.0 mmol). After stirring for 24 h at room temperature, the reaction mixture was concentrated and directly purified by silica gel column chromatography to afford the squaramide catalyst **X** as a white solid (294 mg, 36% yield). M.p. > 280 °C (Decomp.); $[\alpha]_D^{25}$ +36.8 (*c* 0.25, DMSO); ^{1}H NMR (400 MHz, d^6-DMSO): δ 7.44 (s, 1H, NH), 7.20 (d, *J* = 8.8 Hz, 1H, NH), 3.86–3.79 (m, 1H, CH), 2.60 (t, *J* = 7.6 Hz, 2H, CH_2), 2.27–2.16 (m, 3H, CH + CH_2), 2.08 (s, 3H, CH), 2.03–1.82 (m, 8H, CH_2), 1.72–1.63 (m, 8H, CH_2), 1.37–1.18 (m, 10H, CH_2) ppm; ^{13}C NMR (100 MHz, d^6-DMSO): δ 182.2, 180.4, 169.1, 167.2, 68.5, 53.8, 51.8, 49.2, 42.6, 35.3, 34.3, 28.9, 26.2, 24.7, 24.5, 24.4, 23.4; IR (KBr): ν 3243, 2909, 2852, 2791, 1790, 1663, 1574, 1526, 1453, 1438, 1359, 1308, 1127, 1105, 1021, 870, 660 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{25}H_{38}N_3O_2$ $[M + H]^+$ 412.29585, found 412.29547.

General procedure for the asymmetric sulfa-Michael addition of thioacetic acid to α,β-disubstituted nitroalkenes

7.8 mg of organocatalyst **III** was added to dichloromethane to afford 10 mL of catalyst solution (*c* 1.6 mmol L^{-1}). A mixture of α,β-disubstituted nitroalkene **1** (0.2 mmol) and 0.25 mL of the above catalyst solution (0.0004 mmol, 0.2 mol%) was stirred at 0 °C for 30 min. Then thioacetic acid **2** (0.2 mmol) was added in one portion. After stirring at 0 °C for 6–12 h, the reaction mixture was concentrated and directly purified by silica gel column chromatography to afford the desired adduct **3**.

(1*S*,2*R*)-2-Nitro-1-phenylpropyl ethanethioate (3a). The title compound **3a** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure (45.7 mg, 96% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (86 : 14 dr, 90% ee for the major *anti* diastereomer) by HPLC (IA and AS-H columns in series, *n*-hexane-2-propanol 95 : 5, flow rate 0.5 mL min^{-1}, detection at 254 nm): *anti* diastereomer: t_{major} = 33.9 min, t_{minor} = 36.4 min; *syn* diastereomer: t_R = 37.6, 42.0 min. The *anti* diastereomer was obtained by recrystallization from ethyl acetate/petroleum ether as a colorless solid, m.p. 91–93 °C; $[\alpha]_D^{22}$ +302.0 (*c* 1.38, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.26 (m, 5H, ArH), 5.14 (d, *J* = 9.2 Hz, 1H, CH), 5.01–4.93 (m, 1H, CH), 2.36 (s, 3H, $COCH_3$), 1.68 (d, *J* = 6.4 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.3, 136.9, 128.9, 128.5, 127.9, 86.6, 50.3, 30.4, 17.5 ppm; IR (KBr): ν 2995, 2942, 1695, 1552, 1451, 1388, 1356, 1288, 1127, 1100, 949, 865, 743, 700, 659, 630 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{11}H_{13}NNaO_3S$ $[M + Na]^+$ 262.05084, found 262.05060.

(1*S*,2*R*)-1-(4-Fluorophenyl)-2-nitropropyl ethanethioate (3b). The title compound **3b** (the mixture of the *syn* and *anti* diastereomer) was obtained as a colorless solid according to the general procedure (50.2 mg, 97% yield), m.p. 60–62 °C. It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (86 : 14 dr, 90% ee for the major *anti* diastereomer) by HPLC (AS-H column, *n*-hexane-2-propanol 95 : 5, flow rate 1.0 mL min^{-1}, detection at 254 nm): *anti* diastereomer: t_{major} = 11.7 min, t_{minor} = 13.4 min; *syn* diastereomer: t_R = 16.2, 19.2 min. $[\alpha]_D^{22}$ +205.5 (*c* 0.94, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.24 (m, 2H, ArH), 7.00 (t, *J* = 8.4 Hz, 2H, ArH), 5.10 (d, *J* = 9.2 Hz, 1H, CH), 4.97–4.90 (m, 1H, CH), 2.36 (s, 3H, $COCH_3$), 1.67 (d, *J* = 6.8 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.1, 162.4 (d, $^1J_{C\text{-}F}$ = 246.8 Hz), 132.8 (d, $^4J_{C\text{-}F}$ = 3.2 Hz), 129.8 (d, $^3J_{C\text{-}F}$ = 8.2 Hz), 115.8 (d, $^2J_{C\text{-}F}$ = 21.9 Hz), 86.5, 49.6, 30.4, 17.6 ppm; IR (KBr): ν 2987, 2940, 1702, 1603, 1556, 1511, 1452, 1389, 1359, 1301, 1231, 1127, 1101, 957, 842, 801, 661, 622 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{11}H_{12}FNNaO_3S$ $[M + Na]^+$ 280.04141, found 280.04139.

(1*S*,2*R*)-1-(4-Chlorophenyl)-2-nitropropyl ethanethioate (3c). The title compound **3c** (the mixture of the *syn* and *anti* diastereomer) was obtained as a colorless solid according to the general procedure (53.0 mg, 97% yield), m.p. 59–61 °C. It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (87 : 13 dr, 90% ee for the major *anti* diastereomer) by HPLC (AS-H column, *n*-hexane-2-propanol 95 : 5, flow rate 1.0 mL min^{-1}, detection at 254 nm): *anti* diastereomer: t_{major} = 11.0 min, t_{minor} = 13.7 min; *syn* diastereomer: t_R = 16.6, 19.9 min. $[\alpha]_D^{22}$ +237.8 (*c* 0.98, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.29 (d, *J* = 8.0 Hz, 2H, ArH), 7.22 (d, *J* = 8.4 Hz, 2H, ArH), 5.08 (d, *J* = 9.2 Hz, 1H, CH), 4.97–4.90 (m, 1H, CH), 2.36 (s, 3H, $COCH_3$), 1.67 (d, *J* = 6.4 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.0, 135.5, 134.4, 129.3, 129.1, 86.3, 49.6, 30.4, 17.6 ppm; IR (KBr): ν 2993, 2941, 1704, 1556, 1493, 1452, 1411, 1388, 1358, 1291, 1127, 1093, 1015, 956, 866, 826, 657, 622 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{11}H_{12}ClNNaO_3S$ $[M + Na]^+$ 296.01186, found 296.01186.

(1*S*,2*R*)-1-(2-Chlorophenyl)-2-nitropropyl ethanethioate (3d). The title compound **3d** (the mixture of the *syn* and *anti* diastereomer) was obtained as colorless oil according to the general

procedure (52.7 mg, 96% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (89 : 11 dr, 95% ee for the major *anti* diastereomer) by HPLC (OJ-H column, *n*-hexane-2-propanol 95 : 5, flow rate 0.5 mL min^{-1}, detection at 254 nm): *anti* diastereomer: t_{major} = 41.4 min, t_{minor} = 28.7 min; *syn* diastereomer: t_R = 20.0, 24.8 min. $[\alpha]_D^{22}$ +216.1 (*c* 1.18, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.39–7.37 (m, 1H, ArH), 7.33–7.30 (m, 1H, ArH), 7.26–7.21 (m, 2H, ArH), 5.59 (d, J = 9.2 Hz, 1H, CH), 5.28–5.21 (m, 1H, CH), 2.37 (s, 3H, $COCH_3$), 1.67 (d, J = 6.8 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.2, 134.2, 133.5, 130.4, 130.1, 129.7, 127.2, 84.6, 47.8, 30.2, 17.2 ppm; IR (KBr): ν 3064, 2993, 2941, 2899, 1705, 1554, 1475, 1447, 1388, 1358, 1289, 1128, 1038, 955, 865, 754, 657, 623 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{11}H_{12}ClNNaO_3S$ $[M + Na]^+$ 296.01186, found 296.01210.

(1*S*,2*R*)-1-(4-Bromophenyl)-2-nitropropyl ethanethioate (3e). The title compound **3e** (the mixture of the *syn* and *anti* diastereomer) was obtained as a colorless solid according to the general procedure (62.1 mg, 98% yield), m.p. 66–68 °C. It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (86 : 14 dr, 90% ee for the major *anti* diastereomer) by HPLC (AS-H column, *n*-hexane-2-propanol 95 : 5, flow rate 1.0 mL min^{-1}, detection at 254 nm): *anti* diastereomer: t_{major} = 10.9 min, t_{minor} = 13.2 min; *syn* diastereomer: t_R = 15.3, 18.6 min. $[\alpha]_D^{22}$ +253.7 (*c* 1.43, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.48–7.42 (m, 2H, ArH), 7.18–7.12 (m, 2H, ArH), 5.07 (d, J = 9.6 Hz, 1H, CH), 4.97–4.90 (m, 1H, CH), 2.36 (s, 3H, $COCH_3$), 1.67 (d, J = 6.4 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.0, 136.0, 132.0, 129.6, 122.5, 86.2, 49.6, 30.4, 17.6 ppm; IR (KBr): ν 2992, 2940, 1704, 1555, 1489, 1451, 1407, 1388, 1357, 1292, 1127, 1074, 1012, 956, 866, 822, 660, 621 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{11}H_{12}BrNNaO_3S$ $[M + Na]^+$ 339.96135, found 339.96121.

(1*S*,2*R*)-1-(2-Bromophenyl)-2-nitropropyl ethanethioate (3f). The title compound **3f** (the mixture of the *syn* and *anti* diastereomer) was obtained as colorless oil according to the general procedure (59.1 mg, 93% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (86 : 14 dr, 94% ee for the major *anti* diastereomer) by HPLC (OJ-H column, *n*-hexane-2-propanol 90 : 10, flow rate 1.0 mL min^{-1}, detection at 254 nm): *anti* diastereomer: t_{major} = 41.2 min, t_{minor} = 28.6 min; *syn* diastereomer: t_R = 18.4, 25.9 min. $[\alpha]_D^{22}$ +142.2 (*c* 1.44, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.57 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H, ArH), 7.33–7.25 (m, 2H, ArH), 7.17–7.12 (m, 1H, ArH), 5.64 (d, J = 8.0 Hz, 1H, CH), 5.26–5.23 (m, 1H, CH), 2.37 (s, 3H, $COCH_3$), 1.67 (d, J = 6.4 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.1, 135.8, 133.7, 129.9, 127.8, 84.6, 49.7, 30.2, 16.9; IR (KBr): ν 3060, 2989, 2939, 1702, 1553, 1472, 1441, 1387, 1357, 1286, 1127, 1026, 954, 865, 751, 656, 621 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{11}H_{12}BrNNaO_3S$ $[M + Na]^+$ 339.96135, found 339.96121.

(1*S*,2*R*)-1-(4-Methylphenyl)-2-nitropropyl ethanethioate (3g). The title compound **3g** (the mixture of the *syn* and *anti* diastereomer) was obtained as a colorless solid according to the general procedure (48.1 mg, 95% yield), m.p. 44–46 °C. It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (88 : 12 dr, 88% ee for the major *anti* diastereomer) by HPLC (AS-H column, *n*-hexane-2-propanol = 98 : 2, flow rate 0.4 mL min^{-1}, detection at 254 nm): *anti* diastereomer: t_{major} = 24.8 min, t_{minor} = 28.0 min; *syn* diastereomer: t_R = 29.6, 35.3 min. $[\alpha]_D^{22}$ +262.4 (*c* 1.01, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.15 (d, J = 8.0 Hz, 2H, ArH), 7.11 (d, J = 8.0 Hz, 2H, ArH), 5.10 (d, J = 9.2 Hz, 1H, CH), 4.99–4.92 (m, 1H, CH), 2.34 (s, 3H, $COCH_3$), 2.30 (s, 3H, CH_3), 1.66 (d, J = 6.8 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.4, 138.3, 133.8, 129.5, 127.8, 86.6, 50.0, 30.3, 21.1, 17.5 ppm; IR (KBr): ν 2989, 2941, 1698, 1558, 1516, 1446, 1391, 1358, 1294, 1126, 1040, 967, 869, 828, 784, 662, 623 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{12}H_{15}NNaO_3S$ $[M + Na]^+$ 276.06649, found 276.06648.

(1*S*,2*R*)-1-(2-Methylphenyl)-2-nitropropyl ethanethioate (3h). The title compound **3h** (the mixture of the *syn* and *anti* diastereomer) was obtained as colorless oil according to the general procedure (53.4 mg, 98% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (92 : 8 dr, 95% ee for the major *anti* diastereomer) by HPLC (OJ-H column, *n*-hexane-2-propanol 95 : 5, flow rate 0.5 mL min^{-1}, detection at 254 nm): *anti* diastereomer: t_{major} = 49.6 min, t_{minor} = 68.5 min; *syn* diastereomer: t_R = 39.2, 47.9 min. $[\alpha]_D^{22}$ +289.2 (*c* 1.18, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.20–7.14 (m, 4H, ArH), 5.47 (d, J = 9.6 Hz, 1H, CH), 5.07–4.99 (m, 1H, CH), 2.43 (s, 3H, CH_3), 2.35 (s, 3H, $COCH_3$), 1.70 (d, J = 6.8 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.6, 136.1, 135.2, 131.1, 128.3, 127.0, 126.5, 86.0, 46.1, 30.2, 19.4, 17.4 ppm; IR (KBr): ν 3067, 3021, 2970, 2941, 1701, 1555, 1491, 1452, 1387, 1358, 1288, 1127, 1103, 1037, 955, 865, 751, 723, 658, 625 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{12}H_{15}NNaO_3S$ $[M + Na]^+$ 276.06649, found 276.06649.

(1*S*,2*R*)-1-(4-Methoxyphenyl)-2-nitropropyl ethanethioate (3i). The title compound **3i** (the mixture of the *syn* and *anti* diastereomer) was obtained as a colorless solid according to the general procedure (52.1 mg, 97% yield), m.p. 57–59 °C. It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (86 : 14 dr, 87% ee for the major *anti* diastereomer) by HPLC (AS-H column, *n*-hexane-2-propanol = 99 : 1, flow rate 0.4 mL min^{-1}, detection at 254 nm): *anti* diastereomer: t_{major} = 64.9 min, t_{minor} = 81.2 min; *syn* diastereomer: t_R = 70.2, 107.2 min. $[\alpha]_D^{22}$ +233.7 (*c* 1.27, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.19 (d, J = 8.4 Hz, 2H, ArH), 6.83 (d, J = 8.8 Hz, 2H, ArH), 5.08 (d, J = 9.2 Hz, 1H, CH), 4.98–4.90 (m, 1H, CH), 3.76 (s, 3H, OCH_3), 2.35 (s, 3H, $COCH_3$), 1.66 (d, J = 6.8 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.4, 159.4, 129.1, 128.7, 114.2, 86.7, 55.2, 49.8, 30.4, 17.5 ppm; IR (KBr): ν 2945, 1692, 1611, 1556, 1516, 1460, 1391, 1356, 1253, 1183, 1127, 1032, 960, 842, 816, 767, 657, 635, 625 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{12}H_{15}NNaO_4S$ $[M + Na]^+$ 292.06140, found 292.06150.

(1*S*,2*R*)-1-(2-Methoxyphenyl)-2-nitropropyl ethanethioate (3j). The title compound **3j** (the mixture of the *syn* and *anti* diastereomer) was obtained as colorless oil according to the general procedure (52.2 mg, 97% yield). It was analyzed to determine the

diastereoselectivity and enantioselectivity of the reaction (89 : 11 dr, 90% ee for the major *anti* diastereomer) by HPLC (IA and AS-H columns in series, *n*-hexane-2-propanol = 95 : 5, flow rate 0.5 mL min^{-1}, detection at 254 nm): *anti* diastereomer: t_{major} = 29.8 min, t_{minor} = 31.8 min; *syn* diastereomer: t_R = 35.8 min. $[\alpha]_D^{22}$ +262.3 (*c* 1.13, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.28–7.18 (m, 2H, ArH), 6.89–6.84 (m, 2H, ArH), 5.29–5.23 (m, 2H, CH), 3.88 (s, 3H, OCH_3), 2.34 (s, 3H, $COCH_3$), 1.64 (d, *J* = 6.4 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.6, 156.9, 130.2, 129.9, 124.6, 120.8, 111.1, 85.0, 55.5, 47.4, 30.2, 17.6 ppm; IR (KBr): *v* 2939, 2835, 1698, 1600, 1553, 1494, 1452, 1387, 1358, 1292, 1250, 1127, 1050, 1023, 954, 865, 755, 626 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{12}H_{15}NNaO_4S$ $[M + Na]^+$ 292.06140, found 292.06149.

(1*S*,2*R*)-1-(1-Naphthyl)-2-nitropropyl ethanethioate (3k). The title compound **3k** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure (53.6 mg, 92% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (80 : 20 dr, 94% ee for the major *anti* diastereomer) by HPLC (AS-H column, *n*-hexane-2-propanol = 98 : 2, flow rate 0.5 mL min^{-1}, detection at 254 nm): *anti* diastereomer: t_{major} = 28.3 min, t_{minor} = 32.8 min; *syn* diastereomer: t_R = 35.5, 44.4 min. The *anti* diastereomer was obtained as a colorless solid by silica gel column chromatography, m.p. 55–57 °C. $[\alpha]_D^{22}$ +300.2 (*c* 1.19, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 8.18 (br s, 1H, ArH), 7.85 (d, *J* = 8.0 Hz, 1H, ArH), 7.78 (d, *J* = 8.0 Hz, 1H, ArH), 7.61 (t, *J* = 7.6 Hz, 1H, ArH), 7.51 (t, *J* = 7.2 Hz, 1H, ArH), 7.46 (d, *J* = 7.2 Hz, 1H, ArH), 7.39 (t, *J* = 7.6 Hz, 1H, ArH), 6.16 (br s, 1H, CH), 5.28–5.24 (m, 1H, CH), 2.36 (s, 3H, $COCH_3$), 1.72 (d, *J* = 6.8 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.7, 134.0, 132.8, 130.4, 129.3, 129.1, 127.1, 126.2, 125.1, 122.6, 85.5, 30.2, 19.1, 17.1 ppm; IR (KBr): *v* 3051, 2989, 2940, 1698, 1553, 1552, 1452, 1387, 1357, 1278, 1127, 954, 866, 791, 775, 619 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{15}H_{15}NNaO_3S$ $[M + Na]^+$ 312.06649, found 312.06630.

(1*R*,2*R*)-1-(2-Furyl)-2-nitropropyl ethanethioate (3l). The title compound **3l** (the mixture of the *syn* and *anti* diastereomer) was obtained as pale yellow oil according to the general procedure (39.1 mg, 85% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (92 : 8 dr, 78% ee for the major *anti* diastereomer) by HPLC (OJ-H column, *n*-hexane-2-propanol 95 : 5, flow rate 0.5 mL min^{-1}, detection at 254 nm): *anti* diastereomer: t_{major} = 30.9 min, t_{minor} = 37.4 min; *syn* diastereomer: t_R = 24.4, 26.6 min. $[\alpha]_D^{22}$ +199.7 (*c* 1.18, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.35 (s, 1H, ArH), 6.33–6.29 (m, 2H, ArH), 5.35 (d, *J* = 8.0 Hz, 1H, CH), 5.09–4.99 (m, 1H, CH), 2.39 (s, 3H, $COCH_3$), 1.66 (d, *J* = 6.8 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.2, 149.0, 143.0, 110.6, 108.9, 84.2, 43.5, 30.3, 17.0 ppm; IR (KBr): *v* 2988, 2940, 1704, 1555, 1452, 1388, 1358, 1291, 1128, 1013, 956, 864, 748, 622 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_9H_{11}NNaO_4S$ $[M + Na]^+$ 252.03010, found 252.03005.

(*E*,3*S*,4*R*)-4-Nitro-1-phenylpent-1-en-3-yl ethanethioate (3m). The title compound **3m** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure (40.8 mg, 77% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (85 : 15 dr, 69% ee for the major *anti* diastereomer) by HPLC (AS-H column, *n*-hexane-2-propanol 98 : 2, flow rate 0.4 mL min^{-1}, detection at 254 nm): *anti* diastereomer: t_{major} = 35.6 min, t_{minor} = 33.6 min; *syn* diastereomer: t_R = 39.1, 41.5 min. The *anti* diastereomer was obtained by recrystallization from ethyl acetate/petroleum ether as a white solid, m.p. 77–79 °C; $[\alpha]_D^{22}$ +301.3 (*c* 0.79, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 7.37–7.28 (m, 5H, ArH), 6.68 (d, *J* = 15.6 Hz, 1H,=CH), 6.15 (dd, J_1 = 15.6 Hz, J_2 = 9.6 Hz, 1H,=CH), 4.87–4.80 (m, 1H, CH), 4.64 (dd, J_1 = 15.6 Hz, J_2 = 9.6 Hz, 1H, CH), 2.38 (s, 3H, $COCH_3$), 1.65 (d, *J* = 6.8 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.0, 135.6, 135.2, 128.6, 128.4, 126.7, 122.3, 85.4, 49.0, 30.7, 17.4 ppm; IR (KBr): *v* 2999, 2982, 1693, 1553, 1447, 1387, 1354, 1288, 1120, 968, 950, 866, 742, 690, 658, 628 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_{13}H_{15}NNaO_3S$ $[M + Na]^+$ 288.06649, found 288.06616.

(3*S*,4*R*)-2-Methyl-4-nitropentan-3-yl ethanethioate (3n). A mixture of α,β-disubstituted nitroalkene **1n** (0.4 mmol, 51.6 mg) and 0.5 mL of the above catalyst solution (0.2 mol%) was stirred at room temperature for 30 min. Then thioacetic acid **2** (0.4 mmol) was added in one portion. After stirring for 12 h, the reaction mixture was concentrated and directly purified by silica gel column chromatography to afford the desired adduct **3n** (the mixture of the *syn* and *anti* diastereomer, 74.4 mg, 91% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (72 : 28 dr, 84% ee for the major *anti* diastereomer) by HPLC (AS-H column, *n*-hexane-2-propanol 99 : 1, flow rate 0.5 mL min^{-1}, detection at 210 nm): *anti* diastereomer: t_{major} = 12.9 min, t_{minor} = 11.6 min; *syn* diastereomer: t_R = 16.3, 17.6 min. The *anti* diastereomer was obtained as colorless oil by silica gel column chromatography. $[\alpha]_D^{22}$ +66.4 (*c* 1.59, CH_2Cl_2); ^1H NMR (400 MHz, $CDCl_3$): δ 4.76–4.68 (m, 1H, CH), 4.08 (dd, J_1 = 9.6 Hz, J_2 = 4.0 Hz, 1H, CH), 2.41 (s, 3H, $COCH_3$), 1.92–1.85 (m, 1H, CH), 1.58 (d, *J* = 6.4 Hz, 3H, CH_3), 0.97 (d, *J* = 6.8 Hz, 3H, CH_3), 0.93 (d, *J* = 6.8 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.3, 84.6, 53.1, 30.7, 28.9, 20.6, 17.8, 17.3 ppm; IR (KBr): *v* 2968, 2934, 2877, 1703, 1553, 1454, 1388, 1358, 1293, 1129, 952, 863, 658, 627 cm^{-1}; HRMS (ESI): *m*/*z* calcd for $C_8H_{15}NNaO_3S$ $[M + Na]^+$ 228.06649, found 228.06647.

(1*S*,2*R*)-1-Cyclohexyl-2-nitropropyl ethanethioate (3o). To a solution of α,β-disubstituted nitroalkene **1o** (0.2 mmol, 33.8 mg) and oraganocatalyst **III** (0.004 mmol, 1.9 mg) in CH_2Cl_2 (0.25 mL) was added thioacetic acid **2** (0.2 mmol, 15 μL) in one portion. After stirring at room temperature for 24 h, the reaction mixture was concentrated and directly purified by silica gel column chromatography to afford the desired adduct **3o** (the mixture of the *syn* and *anti* diastereomer, 37.2 mg, 76% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (70 : 30 dr, 78% ee for the major *anti* diastereomer) by HPLC (AS-H column, *n*-hexane-2-propanol 99 : 1, flow rate 0.5 mL min^{-1}, detection at 210 nm): *anti* diastereomer: t_{major} = 14.7 min, t_{minor} = 13.1 min; *syn* diastereomer: t_R = 16.7, 18.6 min. The *anti* diastereomer was obtained by recrystallization from ethyl acetate/petroleum ether as a white solid, m.p. 95–97 °C; $[\alpha]_D^{22}$ +52.7 (*c* 0.74, CH_2Cl_2); ^1H NMR

(400 MHz, $CDCl_3$): δ 4.80–4.73 (m, 1H, CH), 4.08 (dd, J_1 = 8.8 Hz, J_2 = 4.4 Hz, 1H, CH), 2.39 (s, 3H), 1.82–1.60 (m, 5H, CH + CH_2), 1.56 (d, J = 6.4 Hz, 3H, CH_3), 1.52–1.45 (m, 1H, CH_2), 1.29–1.09 (m, 4H, CH_2), 1.03–0.94 (m, 1H, CH_2) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.3, 83.9, 52.3, 38.9, 30.7, 30.6, 28.5, 25.9, 25.86, 25.82, 17.0 ppm; IR (KBr): ν 2927, 2854, 1694, 1552, 1450, 1388, 1358, 1299, 1134, 958, 884, 865, 632 cm^{-1}; HRMS (ESI): m/z calcd for $C_{11}H_{19}NNaO_3S$ $[M + Na]^+$ 268.09779, found 268.09753.

(1*S*,2*R*)-2-Nitro-1-phenylbutyl ethanethioate (3p). The title compound **3p** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure (45.0 mg, 89% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (94 : 6 dr, 77% ee for the major *anti* diastereomer) by HPLC (AS-H column, *n*-hexane-2-propanol 95 : 5, flow rate 0.5 mL min^{-1}, detection at 254 nm): *anti* diastereomer: t_{major} = 16.1 min, t_{minor} = 23.8 min; *syn* diastereomer: t_R = 17.9, 22.4 min. The *anti* diastereomer was obtained by recrystallization from ethyl acetate/petroleum ether as a white solid, m.p. 120–122 °C; $[\alpha]_D^{22}$ +311.5 (*c* 0.94, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.33–7.24 (m, 5H, ArH), 5.08 (d, J = 10.0 Hz, 1H, CH), 4.84–4.78 (m, 1H, CH), 2.36 (s, 3H, $COCH_3$), 2.13–2.04 (m, 2H, CH_2), 0.99 (t, J = 7.2 Hz, 3H, CH_3) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 192.3, 136.9, 128.9, 128.5, 127.9, 93.4, 49.4, 30.4, 25.2, 10.3 ppm; IR (KBr): ν 2974, 2932, 1698, 1553, 1456, 1374, 1261, 1133, 963, 956, 811, 746, 696, 651, 628 cm^{-1}; HRMS (ESI): m/z calcd for $C_{12}H_{15}NNaO_3S$ $[M + Na]^+$ 276.06649, found 276.06632.

(1*S*,2*R*)-2-Nitro-1,2-diphenylethyl ethanethioate (3q). The title compound **3q** (the mixture of the *syn* and *anti* diastereomer) was obtained according to the general procedure (56.4 mg, 94% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (86 : 14 dr, 75% ee for the major *anti* diastereomer) by HPLC (AS-H column, *n*-hexane-2-propanol 95 : 5, flow rate 0.5 mL min^{-1}, detection at 254 nm): *anti* diastereomer: t_{major} = 19.8 min, t_{minor} = 21.1 min; *syn* diastereomer: t_R = 23.2, 35.1 min. The *anti* diastereomer was obtained by recrystallization from ethyl acetate/petroleum ether as a white solid, m.p. 155–157 °C; $[\alpha]_D^{22}$ +114.5 (*c* 0.77, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (dd, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 2H, ArH), 7.44–7.28 (m, 8H, ArH), 5.91 (d, J = 12.0 Hz, 1H, CH), 5.68 (d, J = 12.0 Hz, 1H, CH), 2.11 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.3, 137.6, 132.0, 130.5, 129.0, 128.9, 128.5, 128.4, 127.9, 94.0, 49.2, 30.2; IR (KBr): ν 3035, 2951, 1694, 1554, 1497, 1456, 1360, 1266, 1128, 965, 744, 721, 702, 670, 629 cm^{-1}; HRMS (ESI): m/z calcd for $C_{16}H_{15}NNaO_3S$ $[M + Na]^+$ 324.06649, found 324.06662. (NO 1590)

(*S*)-2-Nitro-1-phenylethyl ethanethioate (3r).[5a] The title compound **3r** was obtained according to the general procedure (42.2 mg, 94% yield). It was analyzed to determine the enantioselectivity of the reaction (51% ee) by HPLC (AS-H column, *n*-hexane-2-propanol 95 : 5, flow rate 1.0 mL min^{-1}, detection at 254 nm): major enantiomer t_R = 17.1 min, minor enantiomer t_R = 22.0 min. White solid, m.p. 122–124 °C; $[\alpha]_D^{22}$ +136.4 (*c* 0.90, CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.35–7.30 (m, 5H, ArH), 5.29 (t, J = 8.0 Hz, 1H, CH), 4.84 (d, J = 8.0 Hz, 2H, CH_2), 2.36 (s, 3H, $COCH_3$) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 193.3, 135.6, 129.2, 128.8, 127.7, 77.9, 44.4, 30.3 ppm.

The 10 gram scale preparation of 3a and its transformation

A mixture of *trans*-β-Methyl-β-nitrostyrene **1a** (12.2 g, 75.0 mmol) and catalyst **III** (0.2 mol%, 73.4 mg, 0.15 mmol) in CH_2Cl_2 (100 mL) was stirred at 0 °C for 30 min. Then thioacetic acid **2** (5.7 g, 75.0 mmol) was added dropwise. After stirring at 0 °C for 6 h until completion of the reaction (monitored by TLC), the mixture was quenched by addition of saturated NH_4Cl (50 mL). The organic layer was separated, washed with saturated brine, and dried over anhydrous Na_2SO_4. The crude adduct **3a** was obtained by concentration *in vacuo* (17.7 g, 99% yield). It was analyzed to determine the diastereoselectivity and enantioselectivity of the reaction (85 : 15 dr, 90.5% ee for the major *anti* diastereomer) by HPLC. The *anti* diastereomer was obtained by a simple recrystallization from EtOH as a white solid (10.5 g, 59% yield, 98.8% ee, 99 : 1 dr).

According to the reported procedure,[10] the transformation of **3a** into **5** was performed. A mixture of formic acid (98%, 50 mL) and hydrogen peroxide (30%, 20 mL) was stirred at 0 °C for 2 h (peroxyformic acid solution was prepared *in situ*), then a solution of **3a** (4.79 g, 20.0 mmol) in THF (15 mL) was added dropwise. The reaction mixture was stirred at room temperature for 12 h until completion (monitored by TLC), and water (150 mL) was added. The mixture was washed with diethyl ether (80 mL) and dichloromethane (80 mL), respectively. The aqueous phase was concentrated to afford 2-nitroalkylsulfonic acid **4** as a yellow solid. The crude product was used directly in the subsequent hydrogenation without any further purification.

The yellow solid **4** prepared above was dissolved in MeOH (50 mL), and 10 wt% $Pd(OH)_2/C$ (1.40 g, 5 mol%) was added. The mixture was placed under an atmosphere of H_2 in a rubber balloon and stirred at room temperature for 36 h. After filtration with celite, the filtrate was concentrated *in vacuo* to afford the crude product. The pure 2-aminoalkylsulfonic acid **5** was obtained by recrystallization from methanol/diethyl ethyl as a white solid (3.67 g, 85% yield), m.p. >310 °C (Decomp.). $[\alpha]_D^{20}$ +122.5 (*c* 1.58, H_2O); ^{1}H NMR (400 MHz, D_2O): δ 7.53 (s, 5H, ArH), 4.28 (d, J = 6.0 Hz, 1H, CH), 4.22–4.17 (m, 1H, CH), 1.52 (d, J = 6.4 Hz, 1H, CH_3); ^{13}C NMR (100 MHz, D_2O–HCO_2H): δ 132.0, 130.1, 130.0, 68.1, 49.5, 17.7 ppm.

Acknowledgements

We are grateful for financial support from the National Natural Science Foundation of China (Grant No 21072020), the Science and Technology Innovation Program of Beijing Institute of Technology (Grant No 2011CX01008) and the Development Program for Distinguished Young and Middle-aged Teachers of Beijing Institute of Technology.

Notes and references

1 P. Perlmutter, *Conjugate Addition Reactions in Organic Synthesis*, Pergamon, Oxford, 1992.
2 For a review see: D. Enders, K. Lüttgen and A. A. Narine, *Synthesis*, 2007, 959.

3 For selected recent examples of asymmetric sulfa-Michael additions: (*a*) P. Ricci, A. Carlone, G. Bartoli, M. Bosco, L. Sambri and P. Melchiorre, *Adv. Synth. Catal.*, 2008, **350**, 49; (*b*) Y. Liu, B. Sun, B. Wang, M. Wakem and L. Deng, *J. Am. Chem. Soc.*, 2009, **131**, 418; (*c*) D. Ender and K. Hoffman, *Eur. J. Org. Chem.*, 2009, 1665; (*d*) Y. Hui, J. Jiang, W. Wang, W. Chen, Y. Cai, L. Lin, X. Liu and X. Feng, *Angew. Chem., Int. Ed.*, 2010, **49**, 4290; (*e*) N. K. Rana, S. Selvakumar and V. K. Singh, *J. Org. Chem.*, 2010, **75**, 2089; (*f*) L. Dai, S.-X. Wang and F.-E. Chen, *Adv. Synth. Catal.*, 2010, **352**, 2137; (*g*) X.-F. Wang, Q.-L. Hua, Y. Cheng, X.-L. An, Q.-Q. Yang, J.-R. Chen and W.-J. Xiao, *Angew. Chem., Int. Ed.*, 2010, **49**, 8379; (*h*) F. L. Zhao, W. Zhang, Y. Y. Yang, Y. H. Pan, W. C. Chen, H. J. Liu, L. Yan, C.-H. Tan and Z. Y. Jiang, *Adv. Synth. Catal.*, 2011, **353**, 2624; (*i*) Q.-L. Pei, H.-W. Sun, Z.-J. Wu, X.-L. Du, X.-M. Zhang and W.-C. Yuan, *J. Org. Chem.*, 2011, **76**, 7849; (*j*) S. Bonollo, D. Lanari, F. Pizzo and L. Vaccaro, *Org. Lett.*, 2011, **13**, 2150; (*k*) X.-Q. Dong, X. Fang and C.-J. Wang, *Org. Lett.*, 2011, **13**, 4426; (*l*) N. K. Rana and V. K. Singh, *Org. Lett.*, 2011, **13**, 6520; (*m*) X. Tian, C. Cassani, Y. K. Liu, A. Moran, A. Urakawa, P. Galzerano, E. Arceo and P. Melchiorre, *J. Am. Chem. Soc.*, 2011, **133**, 17934; (*n*) C. Palacio and S. J. Connon, *Chem. Commun.*, 2012, **48**, 2849.

4 (*a*) F. Effenberger and H. Isak, *Chem. Ber.*, 1989, **122**, 553; (*b*) T.-C. Tseng and M.-J. Wu, *Tetrahedron: Asymmetry*, 1995, **6**, 1633; (*c*) B. H. Kim, H. B. Lee, J. K. Hwang and Y. G. Kim, *Tetrahedron: Asymmetry*, 2005, **16**, 1215; (*d*) H. Li, L. Zu, J. Wang and W. Wang, *Tetrahedron Lett.*, 2006, **47**, 3145.

5 Asymmetric sulfa-Michael addition of thioacetic acid to nitroalkenes: (*a*) H. Li, J. Wang, L. S. Zu and W. Wang, *Tetrahedron Lett.*, 2006, **47**, 2585; (*b*) K. L. Kimmel, M. T. Robak and J. A. Ellman, *J. Am. Chem. Soc.*, 2009, **131**, 8754; (*c*) K. L. Kimmel, M. T. Robak, S. Thomas, M. Lee and J. A. Ellman, *Tetrahedron*, 2012, **68**, 2704.

6 For reviews of squaramides, see: (*a*) R. I. Storer, C. Aciro and L. H. Jones, *Chem. Soc. Rev.*, 2011, **40**, 2330; (*b*) J. Alemán, A. Parra, H. Jiang and K. A. Jørgensen, *Chem.–Eur. J.*, 2011, **17**, 6890.

7 For selected examples of asymmetric reactions using squaramides, see: (*a*) J. P. Malerich, K. Hagihara and V. H. Rawal, *J. Am. Chem. Soc.*, 2008, **130**, 14416; (*b*) Y. Zhu, J. P. Malerich and V. H. Rawal, *Angew. Chem., Int. Ed.*, 2010, **49**, 153; (*c*) D. Q. Xu, Y.-F. Wang, W. Zhang, S.-P. Luo, A.-G. Zhong, A.-B. Xia and Z.-Y. Xu, *Chem.–Eur. J.*, 2010, **16**, 4177; (*d*) Y. Qian, G. Ma, A. Lv, H.-L. Zhu, J. Zhao and V. H. Rawal, *Chem. Commun.*, 2010, **46**, 3004; (*e*) H. Konishi, T. Y. Lam, J. P. Malerich and V. H. Rawal, *Org. Lett.*, 2010, **12**, 2028; (*f*) S. V. Pansare and E. K. Paul, *Chem. Commun.*, 2011, **47**, 1027; (*g*) C. Min, X. Han;, Z. Q. Liao, X. F. Wu, H.-B. Zhou and C. Dong, *Adv. Synth. Catal.*, 2011, **353**, 2715; (*h*) H. Y. Bae, S. Some, J. H. Lee, J.-Y. Kim, M. J. Song, S. Lee, Y. J. Zhang and C. E. Song, *Adv. Synth. Catal.*, 2011, **353**, 3196.

8 Asymmetric reactions using squaramides reported by our group: (*a*) W. Yang and D.-M. Du, *Org. Lett.*, 2010, **12**, 5450; (*b*) W. Yang and D.-M. Du, *Adv. Synth. Catal.*, 2011, **353**, 1241; (*c*) W. Yang and D.-M. Du, *Chem. Commun.*, 2011, **47**, 12706; (*d*) W. Yang, Y. Jia and D.-M. Du, *Org. Biomol. Chem.*, 2012, **10**, 332; (*e*) W. Yang, J. S. Wang and D.-M. Du, *Tetrahedron: Asymmetry*, 2012, DOI: 10.1016/j.tetasy.2012.06.018.

9 Crystallographic data for enantiopure *anti* diastereomer of **3e** has been provided as CIF file in ESI.†

10 N. Chen and J. Xu, *Tetrahedron*, 2012, **68**, 2513.

11 (*a*) A. Fryszkowska, K. Fisher, J. M. Gardiner and G. M. Stephens, *J. Org. Chem.*, 2008, **73**, 4295; (*b*) L. Muñoz, A. M. Rodriguez, G. Rosell, M. P. Bosch and A. Guerrero, *Org. Biomol. Chem.*, 2011, **9**, 8171.

12 J. W. Lee, T. H. Ryu, J. S. Oh, H. Y. Bae, H. B. Jang and C. E. Song, *Chem. Commun.*, 2009, **45**, 7224.

13 T. Okino, Y. Hoashi and Y. Takemoto, *J. Am. Chem. Soc.*, 2003, **125**, 12672.

14 B. Vakulya, S. Varga, A. Csampai and T. Soós, *Org. Lett.*, 2005, **7**, 1967.

