Tetrahedron xxx (2015) 1–8

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

Diastereoselectivity in the triethylamine-catalyzed sulfa-Michael addition of thiols to nitroalkenes: kinetic and thermodynamic control

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ARTICLE INFO

Article history:
Received 16 February 2015
Received in revised form 14 April 2015
Accepted 18 April 2015
Available online xxx

Keywords:
Diastereoselectivity
Sulfa-Michael addition
Nitroalkenes
Thiophenol
Kinetic control
Thermodynamic control

ABSTRACT

The diastereoselectivity in the triethylamine-catalyzed sulfa-Michael addition of nitroalkenes and thiols was investigated. The sulfa-Michael addition is kinetic control at the beginning and thermodynamic control at the end for less bulky reactants. Thus, kinetic and thermodynamic-controlled adducts can be obtained as major products by controlling the reaction time in those cases. Linear nitroalkenes generally produce *anti*-adducts as major kinetic products due to favorable steric and stereoelectronic effects, but the diastereoselectivity decreases obviously with steric increase of the substituent located in the vicinal olefinic carbon to the nitro group, even leading to *syn*-adducts as major kinetic products. 1-Nitrocyclohexene gives rise stereospecifically to kinetic *cis*-adduct, which epimerizes into more stable *trans*-adduct as major product through the thermodynamic equilibrium. However, the Michael additions involving bulky reactants are generally slow, resulting in the direct generation of thermodynamic adducts.

1. Introduction

Sulfa-Michael additions have a profound importance in the construction of the sulfur–carbon bond in both synthetic and medicinal chemistry.[1] Conjugated nitroolefins serve as excellent Michael acceptors ascribing to the strong electron-withdrawing capacity of the nitro group.[2] Meanwhile, the nitro group can be easily converted into various useful function groups, such as ketone, nitrile, nitrile oxide, and amino groups.[3] The diastereoselective sulfa-Michael addition of α,β-disubstituted nitroolefins and thiols has been studied for many years. Although good diastereo- and even enantioselective sulfa-Michael additions of nitroolefins with thiols and thiolacetic acid were devoted under the catalysis of various organic chiral catalysts such as thiourea catalysts in recent years,[4] the diastereoselective control in the sulfa-Michael addition is still one of important issues and not clear completely. In 1990, Kamimura et al. reported the synthesis of *anti*-β-nitro sulfides from the corresponding nitroalkenes with thiolate anion followed by a harsh protonation conditions at −78 °C.[5] In their report, very lower diastereoselectivities were obtained under the catalysis of triethylamine at room temperature. Several reports have been published later until recent years for discussing the various diastereoselectivity under different catalytic systems.[6] In most cases, however, the diastereoselectivity was pretty low in the absence of chiral catalysts. In our recent study, we found that tertiary amine can catalyze the sulfa-Michael addition of α,β-disubstituted nitroolefins and thiolacetic acid in perfect yields with moderate to good diastereoselectivities.[7] Consequently, we are still interested in controlling the diastereoselectivity in the sulfa-Michael reaction of nitroolefins and thiols. Herein, we report the kinetic and thermodynamic control in the sulfa-Michael addition of thiols to α,β-disubstituted nitroalkenes under the catalysis of triethylamine.

2. Results and discussion

We initially commenced the reaction of (*E*)-2-nitro-2-butene (**1a**), the simplest 1,2-disubstituted nitroalkene, with thiophenol under the catalysis of triethylamine (10 mol%) (Table 1). The substrate was conducted on 1 mmol scale in all reactions. Very poor diastereoselectivity (*anti*:*syn*=40:60) was obtained when the reaction was conducted in acetonitrile (Table 1, entry 5), which was similar with the reported result.[5] Subsequently, we hoped to optimize the reaction conditions by carefully tracing the reaction

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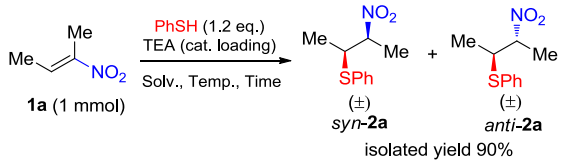
http://dx.doi.org/10.1016/j.tet.2015.04.053
0040-4020/

Table 1
Diastereoselective sulfa-Michael addition of thiolphenol to (*E*)-2-nitro-2-butene (**1a**)



Entry	Reaction conditions				Dr[b] (*anti*/*syn*)
	Solv.	Cat.[a] (mol %)	Temp(°C)	Time	
1	CH_3CN	10	rt	10 s	93:7
2		10	rt	5 min	87:13
3		10	rt	10 min	69:31
4		10	rt	30 min	51:49
5		10	rt	1 h	40:60
6		10	rt	20 h	40:60
7	THF	10	rt	10 s	91:9
8		10	rt	1 h	90:10
9		10	rt	20 h	66:34
10	Et_2O	10	rt	10 s	91:9
11		10	rt	1 h	90:10
12		10	rt	20 h	76:24
13	PhH	10	rt	10 s	91:9
14		10	rt	1 h	91:9
15		10	rt	20 h	50:50
16	EtOH	10	rt	10 s	85:15
17		10	rt	1 h	78:22
18		10	rt	20 h	42:58
19	DCM	10	rt	10 s	93:7
20		10	rt	10 min	80:20
21		10	rt	30 min	75:25
22		10	rt	1 h	71:29
23		10	rt	20 h	60:40
24		10	rt	48 h	43:57
25	DCM	1	rt	10 s	90:10[c]
26		1	rt	10 min	91:9
27		1	rt	1 h	89:11
28	DCM	5	rt	10 s	90:10[d]
29		5	rt	10 min	88:12
30		5	rt	1 h	84:16
31	DCM	20	rt	10 s	87:13
32		20	rt	10 min	76:24
33		20	rt	1 h	66:34
34	DCM	10	−78	10 s	93:7
35		10	−78	1 h	89:11
36	DCM	10	−30	10 s	92:8
37		10	−30	1 h	86:14
38	DCM	10	0	10 s	90:10
39		10	0	1 h	76:24
40	DCM	10	35	10 s	86:14
41		10	35	1 h	64:36

[a] The molar percentage amount of catalyst.
[b] Dr values were determined by ^1H NMR.
[c] The isolated yield is 36%.
[d] The isolated yield 54%.

progress with ^1H NMR analysis. After the addition of Et_3N and stirring for 10 s (s for short), excess AcOH was added to quench the reaction. Gratifyingly, nitroalkene **1a** was consumed completely and adducts **2a** were obtained in 90% isolated yield with an *anti*/*syn* ratio of 93:7. Further prolonging the reaction time clearly showed the tendency that the proportion of *anti*-**2a** was gradually decreased (Table 1, entries 1–6). Eventually, the reaction was accomplished to the thermodynamic equilibrium after 1 h with the *anti*/*syn* ratio at 40:60, because the dr ratio (diastereoselective ratio) did not change any more even extending the time to 20 h (Table 1, entry 6). The results indicate that the diastereoselectivity in the current sulfa-Michael addition is a kinetic control at the beginning and thermodynamic control at the end. The epimerization occurred in the presence of base triethylamine during reaction process. Thus, the reaction time is the key factor to control the diastereoselectivity. Moreover, considering that the epimerization process was too fast, other solvents, like tetrahydrofuran (THF), diethyl ether (Et_2O), benzene (PhH), ethanol (EtOH), and dichloromethane (DCM), were further investigated (Table 1, entries 7–24). The epimerization rate decreased with the change of solvents. However, only CH_2Cl_2 kept the dr value (Table 1, entry 19–24). Extending the time to 48 h in CH_2Cl_2 (Table 1, entry 24), the reaction also reached to the thermodynamic equilibrium as the similar ratio in CH_3CN at 1 h (Table 1, entry 5). Hence, dichloromethane was chosen as the model solvent for the further research. Detailed tendency of diastereoselectivity with the increase of reaction time in the reaction of (*E*)-2-nitro-2-butene (**1a**) and thiophenol is shown in Fig. 1. We next studied the effect of the amount of the catalyst loading (Table 1, entries 25–33). High dr values were kept when 1 mol % amount of Et_3N was investigated, but the yield is only 36% after purifying from column chromatography. Only extending to 5 min could the nitroolefin **1a** be totally transferred according to the trace of thin-layer chromatography (TLC). Moreover, the epimerization was extremely slow even prolonging to 1 h (Table 1, entry 27). Similar result was obtained with 5 mol % amount of Et_3N (Table 1, entries 28–30). In addition, increasing the amount of Et_3N to 20 mol % did not have the obvious change (Table 1, entry 33). Therefore, to obtain the both kinetic and thermodynamic stable products, 10 mol % of catalyst loading is more suitable to control. Finally, different temperature were attempted from −78 °C to 35 °C (Table 1, entries 34–41), but all results did not have obvious improvement in the dr value.

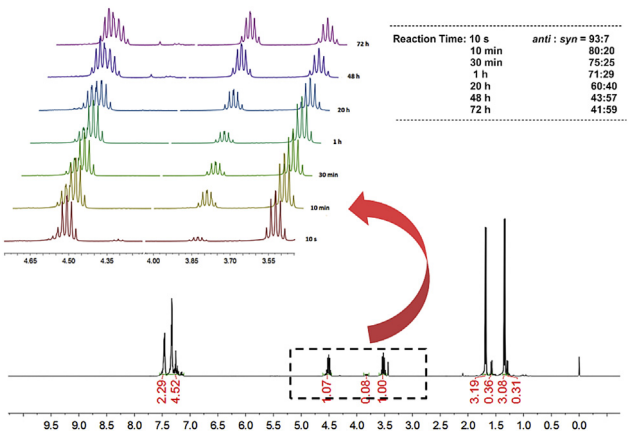
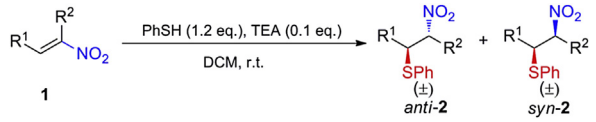
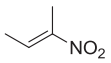
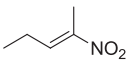
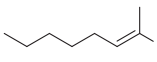
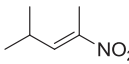
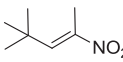
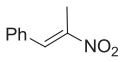
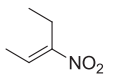
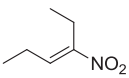
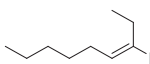
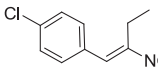
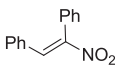


Fig. 1. Tendency of diastereoselectivity with the increase of reaction time in the reaction of (*E*)-2-nitro-2-butene (**1a**) and thiophenol.

Inspired by the above results, the substrate scope of various nitroolefins **1** was examined with thiophenol on the 1 mmol scale in CH_2Cl_2 in the presence of Et_3N (10 mol %). The results are listed in Table 2. Gratifyingly, all addition reactions showed high conversion and moderate to good diastereoselectivities (except for **1e** with low diastereoselectivity) when the reactions were quenched in 10 s. 2-Nitro-2-alkenes **1a**–**f** decrease generally the diastereoselectivity along with the increasing steric hindrance on the vicinal carbon to the nitro group (Table 2, entries 1–6). Nitroolefins **1g**–**i** with geminal ethyl and vicinal alkyl groups to the nitro group show similar diastereoselectivity (Table 2, entries 7–9). For aryl substituted nitroolefins **1f**, **j**, **k**, 1,2-diphenylnitroethene (**1k**) shows the highest diastereoselectivity (Table 2, entry 11), while 1-aryl-2-nitro-1-butene (**1j**) displays higher diastereoselectivity than 2-nitro-1-phenyl-1-propene (**1f**) (Table 2, entries 6 and 10). The results indicate that the steric hindrance of the vicinal substituents to the nitro group in 2-nitro-2-alkenes **1a**–**f** shows obvious influence on the diastereoselectivity. The thermodynamically stable ratios of the diastereomeric products **2** are also provided herein (Table 2,

Table 2
Diastereoselective sulfa-Michael addition of various nitroolefins and thiophenol



Entry	Nitroolefins	Dr (*anti*/*syn*)[a]		Yield (%)[b]
		(After 10 s)	(After 20 h)	
1	 **1a**	93:7	40:60	90
2	 **1b**	85:15	66:34[c]	86
3	 **1c**	89:11	65:35	83
4	 **1d**	75:25	68:32	83[d]
5	 **1e**	45:55	55:45	86[d]
6	 **1f**	72:28	42:58	82
7	 **1g**	87:13	86:14[c]	92
8	 **1h**	88:12	87:13	90
9	 **1i**	90:10	89:11	87
10	 **1j**	80:20	75:25	85
11	 **1k**	93:7	91:9	80

[a] Dr values were determined by both ^{1}H NMR and ^{13}C NMR.
[b] Isolated yield for 20 h by column chromatography.
[c] The thermodynamic stable dr ratios of **2b** and **2g** are 48:52 and 37:63, respectively, in Kamimura's report.[5]
[d] The conversions of **1d** and **1e** were 92% and 95% by ^{1}H NMR after 10 s.

column 4). Comparing with the nitroolefins **1b, c, f** with the geminal methyl group (Table 2, entries 2–6), the corresponding nitroolefins **1h**–**j** with the geminal ethyl group show much higher *anti*-diastereoselectivities (Table 2, entries 8–11). The results indicate that the geminal substitutent (R^2) of nitroolefins would retard the epimerization with the increase of its steric hindrance.

The configurations of the *syn*- and *anti*-products **2** were determined by the ^{13}C NMR spectra via the γ-*gauche* effect or the ^{1}H NMR coupling constants of the vicinal protons (see Electronic Supplementary data), and some of the known products were confirmed by the reported data in the literature.[5,8] The γ-*gauche* effect demonstrates that the chemical shifts of the ^{13}C atoms in the methylene (or methyl) group in the *syn*-products *syn*-**2** are in the slightly higher field than those in the corresponding *anti*-ones (Fig. 2 and Table 3).[9] The major γ-*gauche* effect affects the terminal carbons (C_3) when the C_1 atom is in the bulky substituents like isopropyl (**2d**) and *tert*-butyl (**2e**) groups (Table 3, entries 3 and 4).

Parenthetically, an interesting fragmentation in the HRMS (high-resolution mass spectroscopy) is worth to mention herein. When all of new β-nitro phenylsulfides **2** were subjected to HRMS determination under the electrospray ionization (ESI), the intensities of their protonated molecular ion peaks $[M+H]^+$ are very low and hardly detected with the relative abundance less than 1%. The major ion peaks (most of base peaks) are the $[M+H-47u]^+$, which demonstrated that a molecule of nitrous acid (HONO) is lost from the protonated molecular ions through an intramolecular nucleophilic substitution by the vicinal sulfur atom in the thioether group. Hence, the major peaks are the corresponding *S*-phenylthiiranium fragments (Table 4). Though Ono and Kamimura reported that β-nitro thioethers could lose the nitro group in the presence of Lewis acid catalyst,[8b] this fragmentation under ESI conditions is first reported herein.

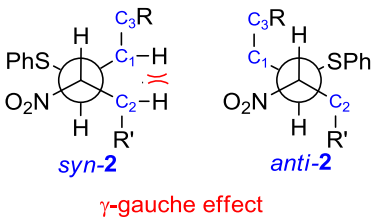


Fig. 2. γ-*Gauche* effects in *anti*- and *syn*-products **2**.

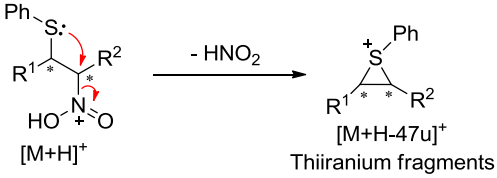
Table 3
Partial ^{13}C chemical shifts in the *syn*- and *anti*-products **2**

Entry	Products	C_1 (or C_3) (ppm)		C_2 (ppm)	
		anti-**2**	*syn*-**2**	*anti*-**2**	*syn*-**2**
1	**2b**	16.6	13.9	25.3	22.2
2	**2c**	32.1	31.3	31.2	28.7
3	**2d**	21.3 (17.7, 17.5)[a]	21.7 (17.5, 17.1)[a]	30.3	29.1
4	**2e**	36.8 (17.6)[a]	36.7 (16.5)[a]	28.4	28.3
5	**2g**	18.2	16.7	25.5	22.6
6	**2h**	24.5	22.8	25.2	22.9
7	**2i**	31.2	31.3	31.2	29.5

[a] The major γ-*gauche* effect affects the terminal carbons (C_3) when C_1 is in the bulky substituents isopropyl (**2d**) and *tert*-butyl (**2e**).

Some alkanethiols, including primary, secondary, and tertiary thiols, were also screened with the nitroalkene **1a** (Table 5, entries 1–14). Benzyl thiol (BnSH) produced the desired adducts **2l** in good yield (95%) at 10 s with the dr value of 78:22 (Table 5, entry 1).

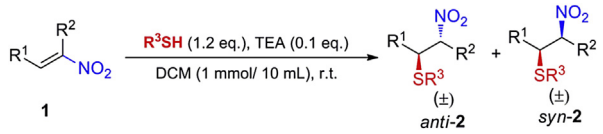
Table 4
Fragmentation of 2-nitroalkyl phenylthioethers **2** under HRMS-ESI conditions

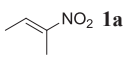
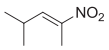


Comp.	*m*/*z*: $[M+H]^+$	*m*/*z*: Thiiranium
	Found (calcd)	Found (calcd)
2c	268.1355 (268.1366)	221.1355 (221.1358)
2e	254.1204 (254.1209)	207.1198 (207.1202)
2h	240.1052 (240.1053)	193.1044 (193.1045)
2i	282.1518 (282.1522)	235.1512 (235.1515)
2j	322.0655 (322.0663)	275.0652 (275.0656)
2k	336.1049 (336.1053)	289.1041 (289.1045)

Please cite this article in press as: Wang, J.; et al., Tetrahedron (2015), http://dx.doi.org/10.1016/j.tet.2015.04.053

Table 5
Diastereoselective sulfa-Michael addition of nitroolefins **1** and alkanethiols



Entry	Nitroolefin	Thiols	Time (h)	2	Dr[a] (*anti*/*syn*)	Yield[b] (%)
1		BnSH	10 s	**2l**	78:22	95[c]
2		BnSH	1	**2l**	47:53	100[c]
3		BnSH	20	**2l**	45:55	98
4		*n*-BuSH	10 s	**2m**	76:24	55[c]
5		*n*-BuSH	1	**2m**	66:34	96[c]
6	 **1a**	*n*-BuSH	20	**2m**	59:41	75
7		*i*-PrSH	10 s	**2n**	—	—
8		*i*-PrSH	1	**2n**	66:34	68[c]
9		*i*-PrSH	20	**2n**	56:44	86[c]
10		*i*-PrSH	48	**2n**	42:58	89
11		*t*-BuSH	10 s	**2o**	—	—
12		*t*-BuSH	1	**2o**	75:25	41[c]
13		*t*-BuSH	48	**2o**	40:60	70
14		*i*-PrSH	10 s	**2p**	—	—
15	 **1d**	*i*-PrSH	1	**2p**	65:35	80[c]
16		*i*-PrSH	48	**2p**	60:40	83
17		*t*-BuSH	10 s	**2q**	—	—
18		*t*-BuSH	1	**2q**	—	—
19		*t*-BuSH	48	**2q**	65:35	31

[a] Dr values were determined by both ^{1}H NMR and ^{13}C NMR.
[b] Isolated yield for 20 h by column chromatography.
[c] The conversion was determined by ^{1}H NMR spectrum of the reaction mixture at the time indicated in Table 5.

Similar to thiophenol, the *anti*/*syn* value decrease with prolonging the reaction time (Table 5, entries 1–3). Finally, *syn*-adduct *syn*-**2l** was obtained as major thermodynamic product (Table 5, entry 3). Primary *n*-butanethiol gave rise to the corresponding adducts **2m** in 55% yield at 10 s with the dr value of 76:24 (Table 5, entry 4). Similarly the dr value decreased extending the reaction time (Table 5, entries 4–6). However, both secondary isopropylthiol and tertiary *tert*-butylthiol showed lower reactivity with nitroalkene **1a** due to their steric hindrance (Table 5, entries 7–13). No corresponding adducts **2n** and **2o** was observed at 10 s in each of cases (Table 5, entries 7 and 11). They yielded adducts **2n** and **2o** in 68% and 41% yields, respectively, at 1 h with low diastereoselectivity (Table 5, entries 8 and 12). When they reacted with more bulky nitroolefin **1d**, isopropylthiol can give the desired adducts **2p** in 80% yield at 1 h with 65:35 *anti*/*syn*-ratio (Table 5, entry 15). However, no reaction was observed for *tert*-butylthiol at 1 h. The results indicate that the steric hindrance plays a crucial role on the reaction rate.

Finally, cyclic 1-nitrocyclohexene (**1r**) was also conducted with thiophenol. ^{1}H NMR tracing experiments during specific time intervals inclined to show the process for thermodynamic equilibrium clearly (Fig. 3). The reaction completed at 10 s in 85% isolated yield with *cis*-**2r** as sole adduct. The configuration was assigned by the vicinal H–H coupling constant. Subsequent prolonging the reaction time, thermodynamically stable *anti*-**2r** appeared and increased rapidly. The thermodynamic equilibrium achieved at 1 h with an 88:12 *trans*-/*cis*-**2r** ratio (Fig. 3).[5] It should be mentioned that CH_3CN was used in the current case to instead of CH_2Cl_2 as solvent because the epimerization was too low in CH_2Cl_2.

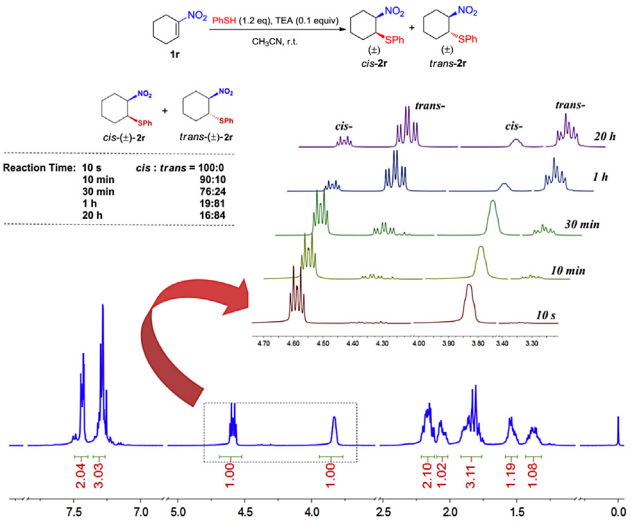


Fig. 3. Tendency of diastereoselectivity with the increase of reaction time in the reaction of 1-nitrocyclohexene and thiophenol in acetonitrile.

It is well known that nitronate anions were first generated during the addition of thiols to nitroolefins in the presence of base. The diastereoselectivity of adducts was controlled by the subsequent protonation rather than the first Michael addition step. Mohrig et al. have proved that it was the stability of the transition state, rather than that of enolate intermediates, which determined the diastereoselectivity in the protonation of the enolate anion when they investigated the Michael addition of alkyl 2-alkenoates with ethanol.[10] Similar to the enolate protonation, a Curtin-Hammett schematic diagram of the nitronate protonation is provided herein (Fig. 4). According to the Curtin-Hammett principle,[11] the conformation of the new forming chiral center, with a phenylthio group at C(1) relative to the delocalized C=N π system, was considered to determine the electrophilic direction (Fig. 4a). The kinetic control product compositions are determined by the difference in the standard Gibbs energies ($\Delta\Delta G^*$) of the respective transition states Ts-A and Ts-a (Figs. 4b and 6). In the current case, $\Delta\Delta G^*$ is approximately −1.53 kcal/mol ($\Delta\Delta G^* = -RT\ln$[*anti*-

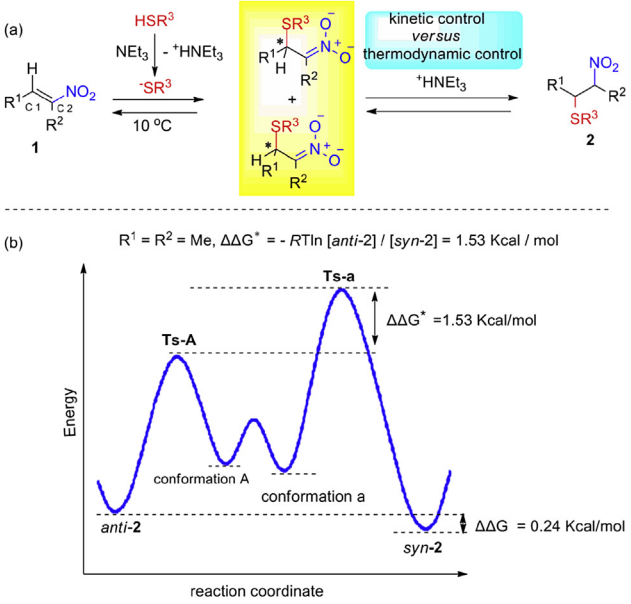


Fig. 4. Curtin-Hammett schematic diagram in the triethylamine-catalyzed sulfa-Michael addition of thiophenol to nitroalkene **1a**.

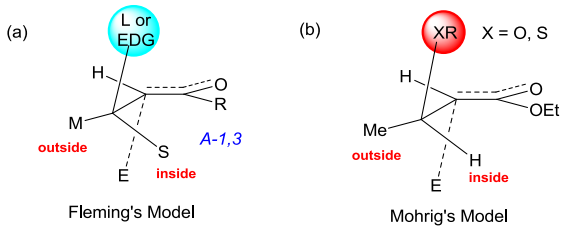


Fig. 5. Transition state models for electrophilic attack on enolate anions.

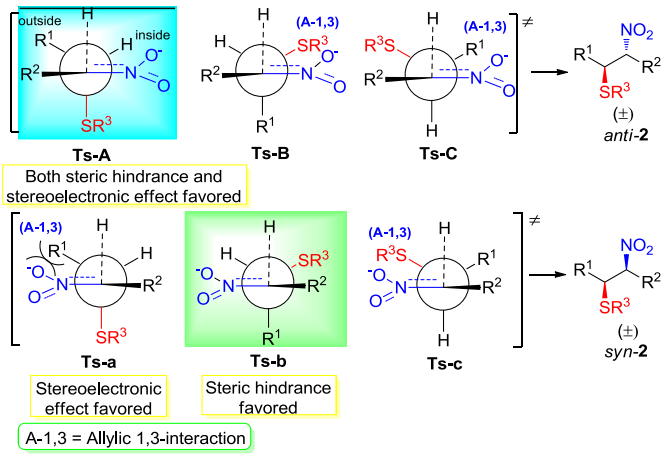


Fig. 6. Transition state models in the protonation of nitronates.

2a(10s)]/[*syn*-**2a**(10s)]=−RTln[93/7]), revealing that the transition state energy of Ts-a is at least higher than that of Ts-A 1.53 kcal/mol. Subsequently, the adducts **2a** underwent a deprotonation-protonation process, even a reverse Michael reaction, in the presence of Et_3N at room temperature, eventually achieving into the thermodynamic equilibrium (*anti*:*syn*=40:60). The *anti*:*syn* value is determined by the difference in the standard Gibbs energies (ΔΔG) of the respective products *anti*-**2a** and *syn*-**2a** (Fig. 4b). In the current case, ΔΔG is approximately 0.24 kcal/mol (ΔΔG=−RTln[*anti*-**2a**(20h)]/[*syn*-**2a**(20h)]=−RTln[40/60]). The results indicate that *syn*-**2a** is 0.24 kcal/mol more stable than *anti*-**2a**.

Similar to the nucleophilic attack on the carbonyl group, which well-known as the Cram's rule[12] and further refined by Karabatsos, Finkin, and Anh, and Cieplak,[13] the electrophilic addition to the enolate bearing an adjacent stereogenic center was also meticulously studied by Fleming[14] and Mohrig.[15] The transition state models for the electrophilic attack on the enolate anions of ketones and esters are shown in Fig. 5. Generally, in the Fleming's Model, the trajectory of the electrophile on the face of the π-bond should be opposite to the largest group (L) due to the steric hindrance or the electron-donating group due to the stereoelectronic effect with the smallest group (S) at the chiral center gauche to the π-system to avoid the allylic 1,3-interaction.[14] The further calculation evidences provided by Houk support the argument that the trajectory of electrophile would take a antiperiplanar position to the electron-donating group because of the hyperconjugative effect in the favored transition state.[16] Mohrig further applied this model in the electrophilic deuteration of the enolate anions, which were derived from the stereoselective 1,4-conjugative addition of ethanol-D to α,β-unsaturated esters.[10,16] In the current system, nitronate anions, similar to enolate analogs, should have similar results during the protonation process.

To explain the kinetic stereocontrol in the protonation of nitroate anions, six possible transition state Newman perpendicular projection models are presented in Fig. 6. The transition states **Ts-A** to **Ts-C** are responsible for the formation of *anti*-**2**, while the corresponding **Ts-a** to **Ts-c** for that of *syn*-**2**. On the basis of both stereoelectronic and steric effects, **Ts-A** is unhesitatingly the most stable transition state when R^1 and/or R^2 are/is not more steric substitutent(s), resulting in *anti*-**2** as major products kinetically. On one hand, the antiperiplanar σ* orbital of the C—S bond in **Ts-A** can stabilize the upcoming σ orbital of the forming C—H bond via the stereoelectronic interaction.[17] On the other hand, R^1 occupies at 'outside' position in the allylic chiral center to avoid destabilizing the allylic 1,3-interaction (Figs. 5 and 6).[18] **Ts-a** favors formation of *syn*-**2** stereoelectronically, but with the allylic 1,3-interaction, sterically unfavorable. **Ts-b** loses stabilizing stereoelectronic effect and possesses a gauche interaction between R^2 and R^3S groups in spite of the absence of the allylic 1,3-interaction. That is the reason why *anti*-products *anti*-**2** are kinetic products generally except for **2e**, which shows an *anti*/*syn* at 45:55 (Table 2, entry 5). However, with the steric increase of the R^1 group, such as becoming isopropyl and *tert*-butyl groups (Table 2, entries four and 5), their **Ts-A** loses the priority eventually with the competition of the corresponding **Ts-a** and **Ts-b**, especially **Ts-b**, in which less bulky R^2 group locates in the gauche position with less R^3S group, while more steric R^1 group adopts nearly perpendicular position with both R^2 and nitronate groups, resulting in increase of *syn*-products *syn*-**2**, even as major product when R^1 is the *tert*-butyl group (Table 2, entry 5).

In cyclic system (Fig. 7), the conformational restriction forces R^1 and R^2 groups, herein, both of them are the methylene group located in the gauche position, in the same side as **Ts-A**, and the protonation process is depicted in Fig. 7. In the protonation transition state, the extra stabilizing interaction is generated from the stereoelectronic effect between the σ* orbital in the C—S bond and partially formed σ-bond between the C and H atoms. Therefore, *cis*-product *cis*-**2r** was obtained kinetically as a sole product in 10 s. However, the *trans*-product *trans*-**2r** is much more thermodynamically stable. Thus, *trans*-**2r** was generated thermodynamically through the deprotonation-protonation process in the presence of triethylamine, finally reached the thermodynamic equilibrium at the *cis*/*trans* ratio of 16:84.

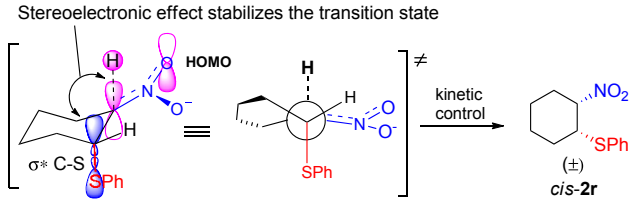


Fig. 7. Transition state model in the protonation of the cyclic nitronate.

3. Conclusions

In conclusion, the diastereoselectivity in the triethylamine-catalyzed sulfa-Michael addition between nitroalkenes and thiols was investigated. The sulfa-Michael addition involving thiophenol and primary alkanethiols is kinetic control at the beginning and thermodynamic control at the end. Thus, kinetic and thermodynamic-controlled adducts can be obtained as major products, respectively, by controlling the reaction time. Linear nitroolefins generally produce *anti*-adducts as major kinetic products due to favorable steric and stereoelectronic effects, but the diastereoselectivity decreases obviously with steric increase of the substituent located in the vicinal olefinic carbon to the nitro group, even leading to *syn*-adducts as major kinetic products. Cyclic nitrocyclohexene gives rise stereospecifically to kinetic *cis*-adduct, which epimerizes into more stable *trans*-adduct as major product through the thermodynamic equilibrium in the presence of

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triethylamine as base. However, the Michael additions of secondary and tertiary alkanethiols are apt to the formation of thermodynamic products because their reaction rates are low due to steric hindrance. The configurations of *syn*- and *anti*-adducts were determined by the H–H coupling constants of vicinal hydrogens and the ^{13}C chemical shifts via the γ-*gauche* effect. Additionally, an intramolecular fragmentation of vicinal nitrothioethers with loss of nitrous acid was also observed under the electrospray ionizations.

4. Experimental section

4.1. General

Dichloromethane was refluxed with CaH_2 and freshly distilled prior to use. Diethyl ether, THF, and benzene were refluxed over sodium with benzophenone as indicator and freshly distilled prior to use. Melting points were obtained on a Yanaco MP-500 melting point apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Bruker AV 400 (400 MHz) in $CDCl_3$ with TMS as the internal standard and the chemical shifts (δ) are reported in ppm. IR spectra were taken directly on a Nicolet AVATAR 330 FT-IR spectrometer with KBr. HRMS spectra were obtained with an Agilent LC/MSD TOF mass spectrometer. TLC analysis was performed on silica gel GF_{254} plates. Spots were visualized with UV light or iodine. Column chromatography was performed on silica gel zcx II (200–300 mesh) with a mixture of petroleum ether (PE) (60–90 °C) and ethyl acetate (EA) as an eluent with gradient elution.

4.2. General procedure for the synthesis of nitroolefins 1

Liner nitroolefins (**1a**–**1k**) were prepared by dehydration of the corresponding vicinal nitro alcohols according to literature procedure[2c] and 1-nitrocyclohexene (**1r**) was prepared by referring the Corey's method[3a] and their analytical data are identical to those reported previously.

4.3. General procedure for the synthesis of β-nitro sulfides 2

To a solution of thiophenol or alkanethiol (1.2 mmol) in 10 mL of dry dichloromethane (DCM) (or other solvents) was added triethylamine (14 μL, 10.1 mg, 0.1 mmol) and the resultant mixture continued to be stirred for 10 min at room temperature under nitrogen atmosphere. Nitroalkene **1** (1.0 mmol) was added via a syringe in one portion. For quenching the reaction, excess AcOH was added to neutralize the base in the resulting solution at the time indicated in Tables 1, 2 and 5). After removal of the solvent in vaccum, the residue was detected by ^1H NMR to provide the dr value (*anti*/*syn*). Finally, subjecting the mixture directly to purification on silica gel chromatography afforded the desired products **2**.

*4.3.1. 2-Nitro-3-phenylthiobutane (**2a**).*[5,8] Colorless oil, 202 mg, 95%, R_f=0.47 (PE:EA=20:1, *v*/*v*). *Anti*-**2a**: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.48–7.45 (m, 2H), 7.37–7.31 (m, 3H), 4.50 (dq, *J*=7.6, 6.7 Hz, 1H), 3.52 (dq, *J*=7.6, 6.9 Hz, 1H), 1.68 (d, *J*=6.7 Hz, 3H), 1.34 (d, *J*=6.9 Hz, 3H). *Syn*-**2a**: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.48–7.45 (m, 2H), 7.37–7.31 (m, 3H), 4.55 (dq, *J*=5.7, 6.7 Hz), 3.82 (dq, *J*=5.7, 7.0 Hz, 1H), 1.57 (d, *J*=6.7 Hz, 3H), 1.29 (d, *J*=7.0 Hz, 3H).

*4.3.2. 2-Nitro-3-phenylthiopentane (**2b**).*[5,8] Yellowish oil, 194 mg, 86%, R_f=0.52 (PE:EA=40:1, *v*/*v*). *Anti*-**2b**: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.48–7.42 (m, 2H), 7.36–7.28 (m, 3H), 4.60 (dq, *J*=7.5, 6.8 Hz, 1H), 3.40 (ddd, *J*=7.5, 4.4, 9.0 Hz, 1H), 1.70 (ddq, *J*=4.4, 14.7, 7.3, 1H), 1.66 (d, *J*=6.8 Hz, 3H), 1.57–1.50 (m, 1H), 1.14 (t, *J*=7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 133.4, 132.3, 129.2, 127.8, 86.2, 55.1, 25.3, 16.6, 11.5. *Syn*-**2b**: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.48–7.42 (m, 2H), 7.36–7.28 (m, 3H), 4.58 (dq, *J*=5.5, 6.8 Hz, 1H), 3.58 (ddd, *J*=3.6, 5.5, 10.1 Hz, 1H), 1.72 (ddq, *J*=10.1, 14.3, 7.3 Hz, 1H), 1.59 (d, *J*=6.8 Hz, 3H), 1.47 (ddq, *J*=3.6, 14.3, 7.3 Hz, 1H), 1.14 (t, *J*=7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 133.3, 133.1, 129.3, 128.0, 86.1, 53.7, 22.2, 13.9, 11.7.

*4.3.3. 2-Nitro-3-phenylthiooctane (**2c**).* Yellowish oil, 222 mg, 83%, R_f=0.43, 0.45 (PE:EA=40:1, v/v). *Anti*-**2c**: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.46–7.42 (m, 2H), 7.36–7.28 (m, 3H), 4.58 (dq, *J*=7.2, 6.8 Hz, 1H), 3.67 (ddd, *J*=4.4, 7.2, 8.8 Hz, 1H), 1.76–1.66 (m, 2H), 1.64 (d, *J*=6.8 Hz, 3H), 1.55–1.42 (m, 2H), 1.33–1.26 (m, 4H), 0.89 (t, *J*=6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 133.3, 133.1, 129.2, 128.0, 86.4, 53.4, 32.1, 31.2, 26.5, 22.4, 16.5, 13.9. *Syn*-**2c**: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.46–7.42 (m, 2H), 7.36–7.28 (m, 3H), 4.54 (dq, *J*=5.6, 6.8 Hz, 1H), 3.67 (ddd, *J*=3.6, 5.6 10.0 Hz, 1H), 1.63–1.56 (m, 2H), 1.59 (d, *J*=6.8 Hz, 3H), 1.55–1.42 (m, 2H), 1.33–1.26 (m, 4H), 0.88 (t, *J*=6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 133.4, 132.2, 129.3, 127.8, 85.1, 51.8, 31.3, 28.7, 26.6, 22.4, 16.5, 13.6. IR (CH_2Cl_2), *v* (cm^{-1}): 1552 (NO_2). HRMS (ESI) calcd for $C_{14}H_{22}NO_2S^+$ $[M+H]^+$ *m*/*z*: 268.1366, found 268.1355.

*4.3.4. 4-Methyl-2-nitro-3-phenylthiopentane (**2d**).*[5,8] Colorless oil, 205 mg, 83%, R_f=0.23, 0.28. *Anti*-**2d**: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.45–7.42 (m, 2H), 7.36–7.27 (m, 2H), 7.27–7.20 (m, 1H), 4.80 (dq, *J*=9.6, 6.8 Hz, 1H), 3.46 (dd, *J*=4.4, 9.6 Hz, 1H), 1.91 (dhept, *J*=4.4, 6.8 Hz, 1H), 1.63 (d, *J*=6.8 Hz, 3H), 1.16 (d, *J*=6.8 Hz, 3H), 1.04 (d, *J*=6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 135.8, 131.3, 129.2, 127.3, 86.14, 61.2, 30.3, 21.3, 17.7, 17.5. *Syn*-**2d**: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.45–7.42 (m, 2H), 7.36–7.27 (m, 2H), 7.27–7.20 (m, 1H), 4.70 (dq, *J*=8.4, 6.8 Hz, 1H), 3.48 (dd, *J*=4.4, 8.4, 1H), 2.13 (dhept, *J*=4.4, 6.8 Hz, 1H), 1.16 (d, *J*=6.8 Hz, 3H), 1.11 (d, *J*=6.8 Hz, 3H), 0.99 (d, *J*=6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 135.5, 131.1, 129.0, 127.4, 86.7, 59.9, 29.1, 21.7, 17.5, 17.1.

*4.3.5. 4,4-Dimethyl-2-nitro-3-phenylthiopentane (**2e**).* Colorless oil, 218 mg, 86%, R_f=0.23 (PE:EA=40:1, *v*/*v*). *Anti*-**2e**: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.41–7.38 (m, 2H), 7.33–7.21 (m, 3H), 4.87 (dq, *J*=3.8, 6.7 Hz, 1H), 3.83 (d, *J*=3.8 Hz, 1H), 1.70 (d, *J*=6.7 Hz, 3H), 1.14 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 136.2, 131.3, 129.1, 127.2, 83.8, 64.7, 36.7, 28.4, 17.6. *Syn*-**2e**: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.48–7.45 (m, 2H), 7.33–7.21 (m, 3H), 4.91 (dq, *J*=3.3, 6.8 Hz, 1H), 3.4 (d, *J*=3.3 Hz, 1H), 1.74 (d, *J*=6.8 Hz, 3H), 1.21 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 136.9, 130.9, 129.3, 127.0, 83.7, 63.6, 36.8, 28.3, 16.5. IR (CH_2Cl_2), *v* (cm^{-1}): 1549 (NO_2). HRMS (ESI) calcd for $C_{13}H_{20}NO_2S^+$ $[M+H^+]$ *m*/*z*: 254.1209, found 254.1204.

*4.3.6. 2-Nitro-3-phenyl-3-phenylthiopropane (**2f**).*[5,8] Yellowish oil, 222 mg, 81%, R_f=0.48, 0.50 (PE:EA=20:1, v/v). *Anti*-**2f**: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.29–7.10 (m, 8H), 7.19–7.08 (m, 2H), 4.95 (dq, *J*=9.39, 6.6 Hz, 1H), 4.56 (d, *J*=9.39 Hz, 1H), 1.82 (d, *J*=6.6 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 136.5, 133.7, 132.4, 129.0, 126.6, 128.4, 128.2, 128.1, 86.9, 57.3, 18.1. *Syn*-**2f**: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.29–7.10 (m, 8H), 7.19–7.08 (m, 2H), 4.95 (dq, *J*=9.38, 6.7 Hz, 1H), 4.57 (d, *J*=9.38 Hz, 1H), 1.41 (d, *J*=6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 136.5, 134.0, 132.1, 129.0, 128.7, 128.5, 128.3, 127.9, 86.3, 56.7, 17.5.

*4.3.7. 3-Nitro-2-phenylthiopentane (**2g**).*[5,8] Yellowish oil, 208 mg, 92%, R_f=0.37, 0.39 (PE:EA=40:1, v/v). *Anti*-**2g**: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.47–7.44 (m, 2H), 7.34–7.30 (m, 3H), 4.31 (ddd, *J*=3.2, 8.6, 10.6 Hz, 1H), 3.42 (dq, *J*=8.6, 6.9 Hz, 1H), 2.23 (ddq, *J*=3.2, 14.7, 7.3 Hz, 1H), 2.02 (ddq, *J*=10.6, 14.7, 7.3 Hz, 1H), 1.32 (d, *J*=6.9 Hz, 3H), 0.95 (t, *J*=7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 133.8, 132.1, 129.2, 128.4, 94.3, 45.6, 25.5, 18.2, 10.4. *Syn*-**2g**: ^1H NMR (400 MHz, $CDCl_3$) δ: 7.47–7.44 (m, 2H), 7.34–7.30 (m, 3H), 4.36 (ddd, *J*=3.6, 7.0,

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10.4 Hz, 1H), 3.60 (dq, *J*=7.0, 7.0 Hz, 1H), 2.23 (ddq, *J*=3.6, 14.7, 7.3 Hz, 1H), 2.02–1.91 (m, 1H), 1.31 (d, *J*=7.0 Hz, 3H), 0.96 (t, *J*=7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 133.6, 132.1, 129.2, 128.3, 92.9, 45.5, 22.6, 16.7, 10.6.

*4.3.8. 3-Nitro-4-phenylthiohexane (**2h**).* Colorless oil, 217 mg, 90%, R_f=0.40, 0.40 (PE:EA=40:1, *v*/*v*). *Anti*-**2h**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.45–7.42 (m, 2H), 7.35–7.29 (m, 3H), 4.39 (ddd, *J*=3.2, 9.2, 10.8 Hz, 1H), 3.28 (ddd, *J*=3.6, 9.2, 9.2 Hz, 1H), 2.27 (ddq, *J*=3.2, 14.4, 7.2 Hz, 1H), 1.99 (ddq, *J*=10.8, 14.4, 7.2 Hz, 1H), 1.68 (ddq, *J*=3.6, 14.6, 7.2 Hz, 1H), 1.49 (ddq, *J*=9.2, 14.6, 7.2 Hz, 1H), 1.15 (t, *J*=7.2 Hz, 3H), 0.93 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 133.2, 133.0, 129.2, 128.0, 93.7, 53.8, 25.2, 24.5, 11.2, 10.4. *Syn*-**2h**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.45–7.42 (m, 2H), 7.35–7.29 (m, 3H), 4.45 (ddd, *J*=4.0, 7.2, 10.8 Hz, 1H), 3.39 (ddd, *J*=3.6, 7.2, 10.0 Hz, 1H), 2.13–2.02 (m, 1H), 1.68 (ddq, *J*=3.6, 14.0, 7.2 Hz, 1H), 1.89–1.71 (m, 2H), 1.12 (t, *J*=7.2 Hz, 3H), 0.96 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 133.2, 132.8, 129.2, 127.9, 92.5, 53.7, 22.9, 22.8, 11.5, 10.8. IR (CH_2Cl_2), *ν* (cm^{-1}): 1549 (NO_2). HRMS (ESI) calcd for $C_{12}H_{18}NO_2S^+$ $[M+H]^+$ *m*/*z*: 240.1053, found 240.1052.

*4.3.9. 3-Nitro-4-phenylthiononane (**2i**).* Yellowish oil, 248 mg, 87%, R_f=0.56, 0.58 (PE:EA=40:1, v/v). *Anti*-**2i**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.44–7.42 (m, 2H), 7.32–7.31 (m, 3H), 4.37 (ddd, *J*=3.2, 9.2, 10.8 Hz, 1H), 3.31 (ddd, *J*=3.6, 7.2, 9.2 Hz, 1H), 2.24 (ddq, *J*=3.2, 14.8, 7.2 Hz, 1H), 1.98 (ddq, *J*=10.8, 14.4, 7.2 Hz, 1H), 1.77–1.68 (m, 1H), 1.60–1.57 (m, 1H), 1.53–1.44 (m, 2H), 1.34–1.25 (m, 4H), 0.93 (t, *J*=7.2 Hz, 3H), 0.89 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 133.3, 133.1, 129.2, 128.4, 93.6, 52.2, 31.3, 31.2, 26.3, 25.2, 22.4, 13.9, 10.5. *Syn*-**2i**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.46–7.42 (m, 2H), 7.35–7.27 (m, 3H), 4.43 (ddd, *J*=4.0, 6.8, 10.0 Hz, 1H), 3.46 (ddd, *J*=3.2, 6.8, 10.4 Hz, 1H), 2.12–1.80 (m, 2H), 1.77–1.68 (m, 1H), 1.60–1.57 (m, 1H), 1.53–1.44 (m, 2H), 1.34–1.25 (m, 4H), 0.95 (t, *J*=7.2 Hz, 3H), 0.90 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 133.1, 132.8, 128.9, 127.9, 92.6, 51.9, 31.3, 29.5, 26.4, 25.2, 22.6, 13.8, 10.8. IR (CH_2Cl_2), *ν* (cm^{-1}): 1549 (NO_2). HRMS (ESI) calcd for $C_{15}H_{24}NO_2S^+$ $[M+H]^+$ *m*/*z*: 282.1522, found 282.1518.

*4.3.10. 4-(4-Chlorophenyl)-3-nitro-4-phenylthiobutane (**2j**).* Yellowish oil, 273 mg, 85%, R_f=0.28 (PE:EA=40:1, *v*/*v*). *Anti*-**2j**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.28–7.17 (m, 7H), 7.05–7.02 (d, *J*=8.4 Hz, 2H), 4.78 (ddd, *J*=3.0, 10.5, 10.5 Hz, 1H), 4.42 (d, *J*=10.5 Hz, 1H), 2.51 (ddq, *J*=3.0, 14.8, 7.2 Hz, 1H), 2.12 (ddq, *J*=10.5, 14.8, 7.2 Hz, 1H), 1.04 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 136.0, 134.6, 134.0, 131.5, 129.2, 129.1, 128.8, 128.7, 93.15, 55.4, 26.1, 10.2. *Syn*-**2j**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.28–7.17 (m, 7H), 7.05–7.02 (d, *J*=8.4 Hz, 2H), 4.73 (ddd, *J*=3.1, 10.3, 10.3 Hz, 1H), 4.41 (d, *J*=10.3 Hz, 1H), 1.77 (ddq, *J*=10.3, 14.5, 7.2 Hz, 1H), 1.56 (ddq, *J*=3.1, 14.5, 7.2 Hz, 1H), 0.88 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 135.7, 134.2, 133.9, 131.4, 129.7, 129.5, 128.9, 128.6, 92.8, 55.7, 25.7, 10.3. IR (CH_2Cl_2), *ν* (cm^{-1}): 1551 (NO_2). HRMS (ESI) calcd for $C_{16}H_{17}ClNO_2S^+$ $[M+H]^+$ *m*/*z*: 322.0663, found 322.0665.

*4.3.11. 1-Nitro-1,2-diphenyl-2-phenylthioethane (**2k**).* Colorless crystals, 269 mg, 80%, m.p. (for *anti*-**2k**) 160–162 °C, R_f=0.24, 0.26 (PE:EA=40:1, *v*/*v*). *Anti*-**2k**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.62–7.60 (d, *J*=6.8 Hz, 2H), 7.44–7.36 (m, 3H), 7.28–7.25 (m, 5H), 7.17 (t, *J*=7.2 Hz, 1H), 7.10–7.07 (t, *J*=7.2 Hz, 2H), 6.99–6.97 (d, *J*=7.2 Hz, 2H), 5.89 (d, *J*=11.7 Hz, 1H), 5.03 (d, *J*=11.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 137.4, 134.4, 132.3, 132.1, 130.4, 128.9, 128.7, 128.6, 128.3, 128.2, 127.8, 94.7, 56.4. *Syn*-**2k**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.49 (d, *J*=6.8 Hz, 2H), 7.44–7.35 (m, 3H), 7.30–7.23 (m, 5H), 7.17–6.97 (m, 5H), 5.86 (d, *J*=12.2 Hz, 1H), 5.03 (d, *J*=12.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 137.3, 135.2, 131.1, 130.5, 129.8, 129.1, 128.9, 128.6, 128.3, 128.2, 127.6, 94.2, 56.2. IR (CH_2Cl_2), *ν* (cm^{-1}): 1549 (NO_2). HRMS (ESI) calcd for $C_{20}H_{18}NO_2S^+$ $[M+H]^+$ *m*/*z*: 336.1053, found 336.1049.

*4.3.12. 3-Benzylthio-2-nitrobutane (**2l**).* Colorless oil, 220 mg, 98%, R_f=0.25 (PE:diethyl ether=40:1, *v*/*v*). *Anti*-**2l**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.35–7.25 (m, 5H), 4.46 (dq, *J*=7.1, 6.7 Hz, 1H), 3.76 (s, 2H), 3.14 (dq, *J*=7.1, 7.0 Hz, 1H), 1.58 (d, *J*=6.7 Hz, 3H), 1.29 (d, *J*=7.0 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 137.4, 128.9, 128.6, 127.4, 87.1, 42.9, 35.6, 18.9, 16.4. *Syn*-**2l**, ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.38–7.25 (m, 5H), 4.55 (dq, *J*=5.8, 6.8 Hz, 1H), 3.79 (d, *J*=14.0 Hz, 1H), 3.75 (d, *J*=14.0 Hz, 1H), 3.26 (dq, *J*=5.8, 7.1 Hz, 1H), 1.52 (d, *J*=6.8 Hz, 3H), 1.21 (d, *J*=7.1 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 137.4, 128.8, 128.7, 127.4, 86.1, 42.1, 36.2, 16.1, 14.1. IR (CH_2Cl_2), *ν* (cm^{-1}): 1552 (NO_2). HRMS (ESI) calcd for $C_{11}H_{15}NNaO_2S^+$, $[M+Na]^+$ *m*/*z*: 248.0716, found 248.0718.

*4.3.13. 3-Butylthio-2-nitrobutane (**2m**).* Colorless oil, 144 mg, 75%, R_f=0.30 (PE:diethyl ether=40:1, *v*/*v*). *Anti*-**2m**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.63 (dq, *J*=6.2, 6.7 Hz, 1H), 3.36 (dq, *J*=6.2, 7.0 Hz, 1H), 2.63–2.52 (m, 2H), 1.62–1.52 (m, 2H), 1.57 (d, *J*=6.7 Hz, 3H), 1.46–1.36 (m, 2H), 1.28 (d, *J*=7.0 Hz, 3H), 0.92 (t, *J*=7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 86.4, 42.8, 31.5, 31.3, 21.9, 16.2, 14.1, 13.6. *Syn*-**2m**, ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.55 (dq, *J*=7.5, 6.6 Hz, 1H), 3.21 (dq, *J*=7.4, 7.0 Hz, 1H), 2.63–2.52 (m, 2H), 1.66 (d, *J*=6.7 Hz, 3H), 1.62–1.52 (m, 2H), 1.46–1.36 (m, 2H), 1.35 (d, *J*=7.0 Hz, 3H), 0.91 (t, *J*=7.3 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 87.6, 43.6, 31.7, 30.9, 21.9, 19.2, 16.7, 13.6. IR (CH_2Cl_2), *ν* (cm^{-1}): 1550 (NO_2). HRMS (ESI) calcd for $C_8H_{17}NNaO_2S^+$, $[M+Na]^+$ *m*/*z*: 214.0872, found 214.0878.

*4.3.14. 3-Isopropylthio-2-nitrobutane (**2n**).* Colorless oil, 158 mg, 89%, R_f=0.28 (PE:diethyl ether=40:1, *v*/*v*). *Syn*-**2n**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.50 (dq, *J*=7.0, 6.7 Hz, 1H), 3.29 (dq, *J*=7.0, 6.9 Hz, 1H), 2.987 (hept, *J*=6.7 Hz, 1H), 1.64 (d, *J*=6.7 Hz, 3H), 1.35 (d, *J*=6.7 Hz, 3H), 1.30 (d, *J*=7.0 Hz, 3H), 1.25 (d, *J*=6.9 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 87.6, 42.5, 35.5, 23.8, 23.5, 20.1, 16.3. *Syn*-**2n**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.63 (dq, *J*=5.8, 6.7 Hz, 1H), 3.42 (dq, *J*=5.8, 7.0 Hz, 1H), 2.994 (hept, *J*=6.7 Hz 1H), 1.57 (d, *J*=6.7 Hz, 3H), 1.32 (d, *J*=6.7 Hz, 3H), 1.27 (d, *J*=7.0 Hz, 3H), 1.26 (d, *J*=6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 86.7, 41.4, 35.4, 23.6, 23.3, 16.7, 13.9. IR (CH_2Cl_2), *ν* (cm^{-1}): 1551 (NO_2). HRMS (ESI) calcd for $C_7H_{15}NNaO_2S^+$, $[M+Na]^+$ *m*/*z*: 200.0716, found 200.0719.

*4.3.15. 3-tert-Butylthio-2-nitrobutane (**2o**).* Colorless oil, 135 mg, 70%, R_f=0.36 (PE:diethyl ether=40:1, *v*/*v*). *Anti*-**2o**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.45 (dq, *J*=7.2, 7.2 Hz, 1H), 3.21 (dq, *J*=7.2, 6.8 Hz, 1H), 1.63 (d, *J*=6.8 Hz, 3H), 1.33 (s, 9H), 1.40 (d, *J*=7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 87.9, 44.0, 40.9, 31.2, 22.5, 16.4. *Syn*-**2o**, ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.66 (dq, *J*=5.2, 6.7 Hz, 1H), 3.40 (dq, *J*=5.2, 7.1 Hz, 1H), 1.54 (d, *J*=6.7 Hz, 3H), 1.36 (s, 9H), 1.28 (d, *J*=7.1 Hz, 3H) ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 87.5, 44.3, 39.9, 31.0, 18.2, 13.4. IR (CH_2Cl_2), *ν* (cm^{-1}): 1549 (NO_2). HRMS (ESI) calcd for $C_8H_{17}NaNO_2S^+$ $[M+Na]^+$ *m*/*z*: 214.0872, found 214.0882.

*4.3.16. 3-Isopropylthio-2-methyl-4-nitropentane (**2p**).* Colorless oil, 171 mg, 83%, R_f=0.31, 0.37 (PE: diethyl ether=40:1, v/v). *Anti*-**2p**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.65 (dq, *J*=9.5, 6.7 Hz, 1H), 2.98 (dd, *J*=3.4, 9.5 Hz, 1H), 2.81 (hept, *J*=6.7 Hz, 1H), 2.06 (dhept, *J*=3.4, 6.7 Hz, 1H), 1.60 (d, *J*=6.7 Hz, 3H), 1.25 (d, *J*=6.6 Hz, 3H), 1.20 (d, *J*=6.7 Hz, 3H), 1.11 (d, *J*=6.6 Hz, 3H), 0.85 (d, *J*=6.7 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 86.3, 55.8, 37.5, 30.1, 23.9, 23.6, 21.1, 17.6, 17.2. *Syn*-**2p**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.68 (dq, *J*=8.9, 6.6 Hz, 1H), 2.94 (dd, *J*=4.5, 8.9 Hz, 1H), 2.87 (hept, *J*=6.6 Hz, 1H), 1.75 (dhept, *J*=4.5, 6.6 Hz, 1H), 1.70 (d, *J*=6.6 Hz, 3H), 1.30 (d, *J*=6.6 Hz, 3H), 1.26 (d, *J*=6.8 Hz, 3H), 1.06 (d, *J*=6.6 Hz, 3H), 0.96 (d, *J*=6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 88.2, 54.5, 37.4, 28.4, 23.9, 23.4, 21.5, 17.8,

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16.84. IR (CH_2Cl_2), ν (cm^{-1}): 1551 (NO_2). HRMS (ESI) calcd for $C_9H_{20}NO_2S^+$ [M+H$^+$] m/z: 206.1209, found 206.1207.

*4.3.17. 3-tert-Butylthio-2-methyl-4-nitropentane (**2q**).* Colorless oil, 68 mg, 31%, R_f=0.31 (PE: diethyl ether=40:1, v/v). *Anti*-**2q**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.65 (dq, J=8.8, 6.8, Hz, 1H), 3.03 (dd, J=4.4, 8.8 Hz, 1H), 1.81 (dhept, J=4.4, 7.2 Hz, 1H), 1.69 (d, J=6.8 Hz, 3H), 1.32 (s, 9H), 1.05 (d, J=7.2 Hz, 3H), 0.96 (d, J=7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 86.0, 52.6, 43.6, 32.0, 30.9, 21.1, 18.0, 17.9. *Syn*-**2q**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.67 (dq, J=6.4, 6.8 Hz, 1H), 3.16 (dd, J=4.4, 6.4 Hz, 1H), 1.97 (dhept, J=4.4, 6.8 Hz, 1H), 1.62 (d, J=6.8 Hz, 3H), 1.33 (s, 9H), 1.01 (d, J=6.8 Hz, 3H), 0.95 (d, J=6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ: 88.3, 51.7, 43.7, 31.4, 28.1, 21.7, 19.0, 15.1. IR (CH_2Cl_2), ν (cm^{-1}): 1549 (NO_2). HRMS (ESI) calcd for $C_{10}H_{21}NaNO_2S^+$ [M+Na]$^+$ m/z: 242.1185, found 242.1187.

*4.3.18. 1-Nitro-2-phenylthiocyclohexane (**2r**).*[5,8] Colorless oil, 203 mg, 85%, R_f=0.43, 0.31 (PE:EA=20:1, v/v). *Cis*-**2r**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.44–7.42 (m, 2H), 7.30–7.26 (m, 3H), 4.59 (ddd, J=4.1, 4.1, 9.5 Hz, 1H), 3.82 (m, 1H), 2.21–2.12 (m, 2H), 2.09–2.02 (m, 1H), 1.92–1.86 (m, 1H), 1.83–1.75 (m, 2H), 1.57–1.49 (m, 1H), 1.42–1.31 (m, 1H). *Trans*-**2r**: ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50–7.47 (m, 2H), 7.34–7.33 (m, 3H), 4.38 (ddd, J=4.1, 10.9, 10.9 Hz, 1H), 3.34 (ddd, J=4.1, 10.9, 10.9 Hz, 1H), 2.34–2.30 (m, 1H), 2.19–2.16 (m, 1H), 1.97–1.87 (m, 1H), 1.81–1.73 (m, 2H), 1.40–1.33 (m, 2H), 1.28–1.19 (m, 1H).

Acknowledgements

This work was supported in part by the National Basic Research Program of China (No. 2013CB328905) and the National Natural Science Foundation of China (Nos. 21372025 and 21172017).

Supplementary data

Supplementary data (copies of ^{1}H and ^{13}C NMR spectra of products **2**, copies of ^{1}H NMR spectra of all reaction mixtures for determination of their diastereoselectivities, and list of the vicinal H–H coupling constants in *anti*- and *syn*-products **2a**–**2q** and *cis*- and *trans*-**2r**) associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.tet.2015.04.053. These data include MOL files and InChIKeys of the most important compounds described in this article.

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