Accepted Manuscript

Insights into the diastereoselective control in the sulfa-Michael addition of thiols to nitroalkenes: Stereoelectronic effect in the cyclic chelated transition state

Jiandong Wang, Pingfan Li, Zhanhui Yang, Ning Chen, Jiaxi Xu

PII: S0040-4020(15)30215-5

DOI: 10.1016/j.tet.2015.11.030

Reference: TET 27287

To appear in: *Tetrahedron*

Received Date: 22 August 2015

Revised Date: 7 November 2015

Accepted Date: 16 November 2015

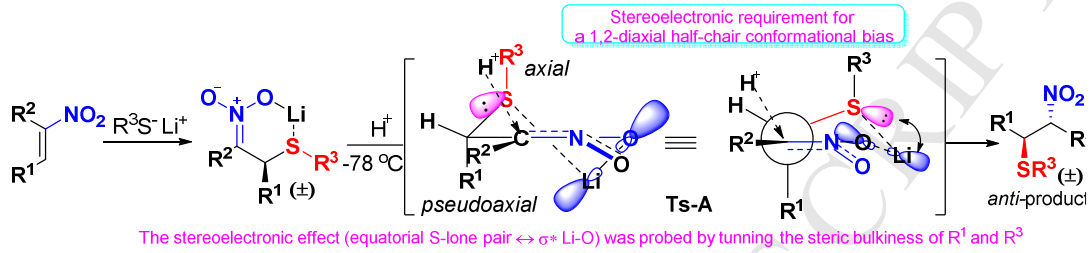
Please cite this article as: Wang J, Li P, Yang Z, Chen N, Xu J, Insights into the diastereoselective control in the sulfa-Michael addition of thiols to nitroalkenes: Stereoelectronic effect in the cyclic chelated transition state, *Tetrahedron* (2015), doi: 10.1016/j.tet.2015.11.030.

Graphical Abstract

To create your abstract, type over the instructions in the template box below.
Fonts or abstract dimensions should not be changed or altered.

Insights into the diastereoselective control in the sulfa-Micheal addition of thiols to nitroalkenes: Stereo-electronic effect in the cyclic chelated transition state

Jiandong Wang, Pingfan Li, Zhanhui Yang, Ning Chen, Jiaxi Xu*



ELSEVIER

Tetrahedron

journal homepage: www.elsevier.com

Insights into the diastereoselective control in the sulfa-Michael addition of thiols to nitroalkenes: Stereoelectronic effect in the cyclic chelated transition state

Jiandong Wang, PingfanLi, Zhanhui Yang, Ning Chen, and Jiaxi Xu*

State Key Laboratory of Chemical Resource Engineering, Department of Organic Chemistry, Faculty of Science, Beijing University of Chemical Technology, Beijing 100029, China

ARTICLE INFO

Article history:
Received
Received in revised form
Accepted
Available online

Keywords:
Diastereoselectivity
Sulfa-Michael addition
Nitroalkene
Thiol
Stereoelectronic effect
Cyclic chelated transition state
Half-chair conformation

ABSTRACT

The diastereoselective control in the sulfa-Michael addition of nitroalkenes and lithium thiolates followed by protonation was investigated. Lithium thiolates first added to nitroalkenes to afford cyclic lithium-chelated nitronates. The subsequent kinetic protonation of nitronates was proved to be the stereochemical determinant through the chelate-controlled six-membered half-chair transition state bearing two approximately 1,2-diaxial substituents due to stereoelectronic effect control. The stereoelectronic effect in the cyclic chelated transition state was probed and verified by tuning the steric bulkiness of the corresponding substituents. The reaction involving 1-nitrocyclohexene provided perfect support for the proposed diastereoselective control model. The current investigation provided not only comprehensive insights into the diastereoselective control in the sulfa-Michael addition of nitroalkenes and thiolates, but also an important role of the stereoelectronic effect in certain organic reactions involving cyclic chelate transition states.

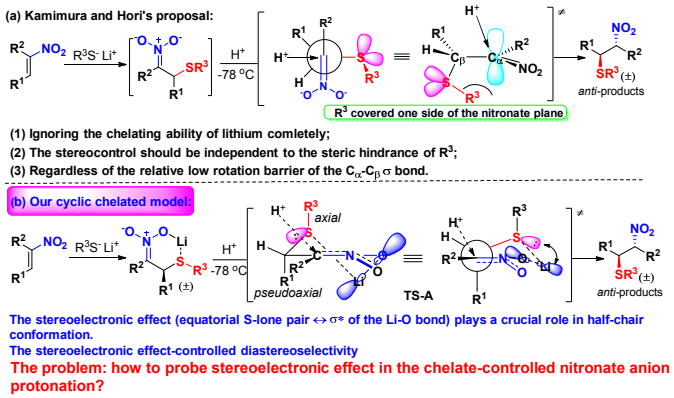
1. Introduction

The sulfa-Michael addition (SMA), which is considered as the reaction of a sulfur nucleophile and carbon-carbon multiple bond electrophile activated by an conjugated electron-deficient group, has proven to be one of the most powerful strategies in constructing the sulfur-carbon bond,[1] and always plays a crucial role in the formation of key structural motifs of biologically active sulfur-containing compounds.[2] Meanwhile, when appropriately disubstituted activated π-systems serve as Michael acceptors, the SMA has the potential to introduce two vicinal stereogenic centers via only one transformation. Thus, extensive and intensive studies have been directed toward the development of the diastereoselective control of this transformation for quite a long time.[3] As we all know, conjugated nitroalkenes act as excellent Michael acceptors ascribing to their strongly electron-withdrawing capacity of the nitro group.[4] Furthermore, the nitro group is usually considered as masked functionality to be further converted to various useful functional groups, such as ketone, nitrile, nitrile oxide, and amino groups.[5] Additionally, the SMA adducts β-nitro sulfides are particularly versatile in synthetic chemistry since they can undergo a series of attractive transformations to provide diverse functionality.[6] Therefore, the diastereoselective sulfa-Michael addition of α,β-disubstituted nitroalkenes and thiols has been studied for many years. Although impressive advances have been made in organocatalyzed asymmetric SMA of nitroalkenes with thiols and thiolacetic acid in recent years,[1b,7] the diastereoselective control in the sulfa-Michael addition is still one of important issues and not clear completely.

In our recent study on the preparation of various disubstituted taurines, moderate to good diastereoselectivities were observed in the tertiary amine-catalyzed SMA of thiolacetic acid to α,β-disubstituted nitroalkenes with perfect yields.[8] Subsequently, we found that controlling the reaction time exerted remarkable impact on the diastereoselectivity in the triethylamine-catalyzed SMA between nitroalkenes and thiols. The SMA involving thiophenol and primary alkanethiols has been proven to be kinetic control at the beginning and thermodynamic control at the end and linear nitroalkenes generally produce *anti*-adducts as major kinetic products due to favorable steric and stereoelectronic effects.[9] In our continuous interest on the diastereoselective control in the SMA of nitroalkenes without any chiral auxiliary or catalysts, we have investigated the diastereoselective formation of *anti*-β-nitro sulfides in reactions of nitroalkenes with sulfur nucleophiles, lithium thiolates R^3S Li, followed by protonation at -78 ^oC according to literature report due to their synthetic applicability.[10] Although Hori *et al* assumed a concept of "the *endo* alkoxy effect" which insisted that the substituent R^3 on the sulfur atom should take the *cis* position to the nitro fragment to cover one side of the nitronate plane to minimize the repulsion between S-lone electron pairs and the anion orbital in terms of computational consideration, their arguments were proposed on the basis of certain unconvincing hypothesis involving regardless of the chelating ability of lithium and the steric impact of substituent group R^3 on the sulfur atom (Scheme 1).[11] Furthermore, Apeloig *et al* reported that low rotation barriers for adjacent σ-bonds in carbanions stabilized by the nitro group via ab initio calculations.[12] Thus, interconversion of the conformations at the stereogenic center of carbanions in nitronate anion intermediates could take place by rotating about

* Corresponding author. Tel.: +8610-6443-5565; fax: +8610-6443-5565; e-mail: jxxu@mail.buct.edu.cn

the C_α-C_β σ-bond of the nitronate anion intermediates. Therefore, the origin of the stereocontrol in the conjugate addition reactions of sulfur nucleophiles R^3SLi to α,β-unsaturated acyclic nitroalkenes followed by protonation at -78 is still a riddle.



Scheme 1. Proposed transition state models for diastereoselective sulfa-Michael additions of lithium thiolates and nitroalkenes followed by protonation.

In order to reveal the origin of the *anti*-selectivity and to find out the dominated elements in the stereocontrolled process, we proposed a cyclic transition state **TS-A** (Scheme 1) for the protonation of nitronate anions, which will be proved to be the stereochemical determinant in this transformation, incorporating with the consideration of chelation control of lithium and stereoelectronic effect control. Although **TS-A** would be expected to be stabilized by the stereoelectronic effect, stereoelectronic and steric requirements imposed an approximate 1,2-diaxial substituted half-chair conformational bias to **TS-A** (Scheme 1). Especially, one of two S-lone pair orbitals has to occupy the equatorial direction in **TS-A** to share an antiperiplanar relationship with the σ* antibonding orbital of the Li-O bond. Nevertheless, all the experimental evidences provided by literature[10,11] seem to support the prediction made by **TS-A**. However, the problem is that ***how to further probe the stereoelectronic effect in the protonation reaction of the chelate-controlled nitronate anions experimentally*?** We successfully tackled the problem by extrapolating from the diastereoselective change through tuning the steric hindrance of substituent groups R^1 and R^3. Herein, we present our results and hope that the results provide a potentially valuable guide to analyze the stereoelectronic factors that control the diastereoselectivity in chelate-controlled addition reactions.

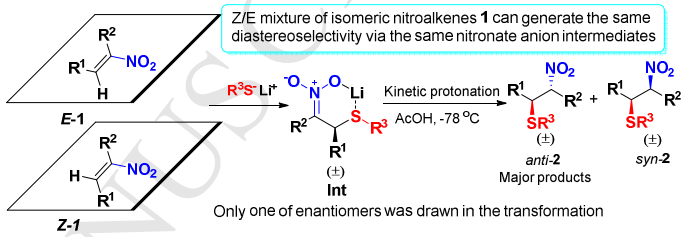
2. Results and Discussion

2.1 The stereochemical determinant step.

The original motivation of our study was to understand the diastereoselectivity of conjugate addition reactions of sulfur nucleophiles R^3SLi to α,β-unsaturated acyclic nitroalkenes. The stepwise addition reactions consisted of two processes. Initial conjugate addition of nucleophiles to Michael acceptors gave rise to nitronate anion intermediates, which were protonated or further trapped with other electrophiles. Inagaki *et al*. argued that the stereospecific conjugate addition of lithium thiophenoxides to α,β-unsaturated carboxylic acid derivatives could be achieved via rapid protonation prior to conformational change in the corresponding intermediates.[3a] However, Morig *et al* maintained that the stereoselection of enolate protonation was responsible for the diastereoselective 1,4-conjugate addition to α,β-unsaturated esters[13] and the geometry of the enolate anion intemediates should be relatively unaffcted the stereocontrol.[14]

To discern the stereochemical determinant in the sulfa-Michael addition of thiols to nitroalkenes, we should apply both (*E*)- and (*Z*)-nitroalkenes as Michael acceptors. Most of the available procedures for the synthesis of nitroalkenes, such as Henry reactions involving base mediated condensation of nitroalkanes with aldehydes followed by subsequent dehydration, are known to provide thermodynamically more stable *E* isomers, independently of the nitro compound precursors.[15] However, *Z* isomers can be prepared indirectly from the corresponding *E* derivatives. Treatment of (*E*)-2-nitro-2-butene (**1a**) and (*E*)-2-nitro-3-phenyl-2-propene (**1b**) with sodium benzeneselenolate followed by kinetically protonation with acetic acid afforded *anti*-nitroselenides. After H_2O_2-promoted *syn*-elimination of benzeneselenenic acid, *E*-**1a** and *E*-**1b** were converted into Z/E mixtures (4:1) and (2:3) of isomeric nitroalkenes, respectively.[4c,16]

Table 1 Diastereoselective sulfa-Michael addition of thiophenol to nitroalkenes **1a,b**



Entry	1	R^1	R^2	R^3	*Z*/*E*	2	Dr [a] (*anti*:*syn*)	Yield [b] (%)
1	*E*-**1a**	Me	Me	Ph	0/1	**2a**	91:9 [c]	75
2	*Z*/*E*-**1a**	Me	Me	Ph	4/1	**2a**	92:8	67 [d]
3	*E*-**1b**	Ph	Me	Ph	0/1	**2b**	75:25 [c]	70
4	*Z*/*E*-**1b**	Ph	Me	Ph	2/3	**2b**	76:24	77 [d]

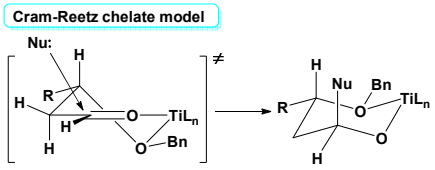
[a] Dr values were determined by ^1H NMR. [b] Isolated yield by column chromatography. [c] The dr ratios were completely in accord with Kamimura's report [ref 10]. [d] 0.22 mmol scale for the starting nitroalkenes in 2 mL dry THF.

Subsequently, the sulfa-Michael additions were performed with (*E*)-isomers and Z/E mixtures of nitroalkenes **1a** and **1b** as substrates. Not surprisingly, the *E*/*Z* mixtures provided almost the same diastereoselectivities comparing with their corresponding pure *E* isomers (Table 1, entries 1 *vs* 2, 3 *vs* 4). The experimental evidences clearly indicated that the same nitronate anion intermediates should be generated as a pair of enantiomers in each of reactions. The subsequent protonation is responsible for the generation of the diastereoselectivity. In other words, kinetic protonation of nitronate anions is the stereochemical determinant in the Michael addition of thiolates R^3SLi to α,β-disubstituted nitroalkenes. That is, the diastereoselectivity is controlled by the subsequent protonation process rather than the first Michael addition step.

2.2 Cyclic chelated TS models for kinetic protonation

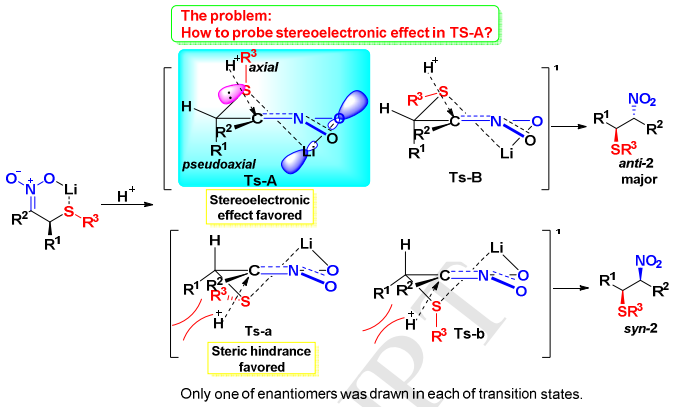
It is noteworthy that we are not considering about the stability of nitronate anions themselves but instead of the corresponding transition states for kinetic protonation process, which is quite consistent with the Curtin-Hammett principle.[17] On one hand, an asymmetric center including a heteroatom-containing substituent is introduced into the substrates in the first conjugate addition step; on the other hand, an effective transfer of the chiral information of this stereogenic center to the diastereoface may be

achieved by chelation control in the presence of equal amount of lithium. In contrast, the conjugate addition of alkyl groups to simple nitroalkenes proceeds in a nonstereoselective way.[10] In other words, the general poor magnitudes of diastereofacial selectivities in nitronate anions devoid of additional heteroatoms suggest that the potential chelation control in the 1,2-stereochemical control for protonation of β-sulfur substituted nitronate anions. Additionally, even catalytic amounts of Lewis acids such as $LiClO_4$ have been demonstrated to induce excellent degree of chelation control in the Adol reaction of an enolsilane and an α-alkoxy aldehyde.[18] However, incorporating chelation control factor for rationalizing the diastereoselectivity in the conjugate addition reactions of sulfur nucleophiles R^3SLi to α,β-unsaturated acyclic nitroalkenes has not been investigated. Furthermore, the diastereoselection investigation into the chelated-controlled reaction might not be attributed solely to steric elements, stereoelectronic consideration also cannot be ignored. Thus, the survey of literature for chelation adition reactions is necessary and the chelation control in protonation process of nitronate anions could be extrapolated from the diastereoselectively nucleophilic addition of β-alkoxy carbonyl ketones or aldehydes through six-membered-ring chelated transition states.

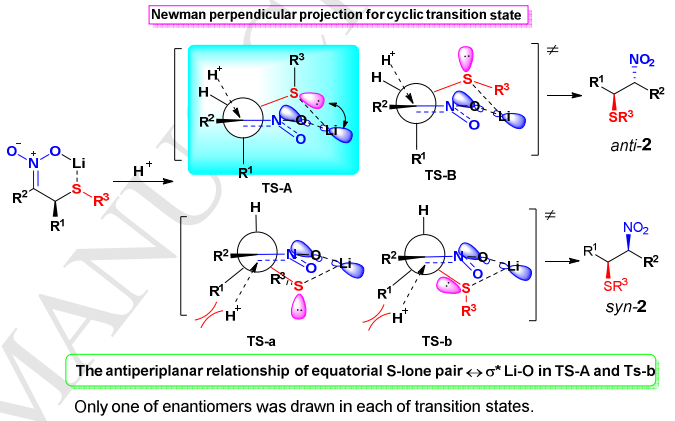


Scheme 2. Cram-Reetz Chelate model

The analysis of chelation control in the nucleophilic attack on the carbonyl group is of particular interest since Cram's seminal research on the diastereoselective addition of organometallic reagents to acyclic carbonyl substrates bearing heteroatom-containing substituents.[19] The chelation controlled transition state model of α-chelation (the five-membered chelate ring) was proposed to rationalize the carbonyl π-facial diastereoselectivity (1,2-stereochemical control) via reacting selectively from the sterically less hindered π-face.[20] For 1,3-stereochemical control of β-chelation (the six-membered chelate ring), Narasaka reported the synthesis of *syn*-1,3-diols from β-hydroxyketones by the treatment with tributylborane and the successive reduction with hydride through chelated pseudo boat or chelated pseudo chair conformation.[21] Still and Schneider firstly reported that β-alkoxy aldehydes reacted with Gilman reagents via β-chelation to provide the chelation controlled products with high levels of stereocontrol.[22] Thus, a conformationally constrained six-membered ring bearing sterically differentiated diastereofaces could be conceivable via metal ion chelation between the carbonyl group and the corresponding β-heteroatom substituents. In 1983, Reetz and Jung reported the reaction of chiral β-alkoxy aldehydes, unsubstituted at the α-position, with the very Lewis acidic compound CH_3TiCl_3 to form Cram-type chelates, which then converted to chelation-controlled products.[23] Then Reetz proposed a half-chair chelated transition state model (Cram-Reetz chelate model), which would lead to a chair-like intermediate, to account for the diastereoselectivity (Scheme 2).[24] Keck and Castellino provided spectroscopic evidence that the favored $TiCl_4$ chelate half-chair conformation positions β-alkyl substituent in the pseudoequatorial position when the *O*-substituent was sterically more demanding than the methyl group due to disfavored gauche interaction.[25] Additionally, stereoelectronic factors can be extrapolated from nucleophilic addition to heteroatom-substituted six-membered ring oxocarbenium ion which exhibits a pseudoaxial conformation bias for the nucleophilic attack.[26]



Scheme 3. Transition state models in the protonation of nitronates



Scheme 4. Newman projections for transition state models in the protonation of nitronates

Inspired by the understanding of the chelation control in diastereoselective nucleophilic attack at the carbonyl compounds, especially Cram-Reetz chelate model which exhibits a half chair conformation from an experimental viewpoint, four possible cyclic chelated transition states which would convert to the corresponding chair-like intermediates have been presented in scheme 3 in order to explain the diastereofacial differentiation in the protonation of nitroate anions. Meanwhile, four possible transition state Newman perpendicular projection models are also presented in Scheme 4. Presumably, the observed diastereoselectivity of the sulfa-Michael addition is determined by the competing four transition states, in which heteroatoms in nitronate anions linked together through chelation to lithium. The half-chair chelated transition states **Ts-A** and **Ts-B** are responsible for the formation of *anti*-**2**, while the corresponding **Ts-a** to **Ts-b** for that of *syn*-**2**. On the basis of the principle of least conformational change,[27] the optimal trajectory for electrophilic attack of proton is considered as on the upper surface relative to the delocalized C=N π system in **Ts-A**/**Ts-B** and on the lower surface of the same π plane in **Ts-a**/**Ts-b** because the opposite attack can give rise to the corresponding intermediates bearing a twist-boat conformation, which is too high in energy in kinetic control process. Although **Ts-A** is almost 1,2-diaxially substituted, it is still considered as the favored even most stable transition state for nitronate anion protonation under chelation control of lithium due to strong stereoelectronic effect, resulting in *anti*-**2** as major products kinetically. In the six-membered chelation **TS-A**, the substituted group R^3 occupies axial direction and R^1 locates pseudoaxial

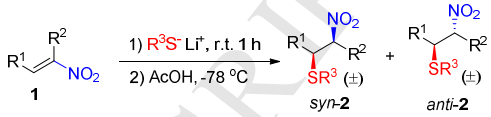
orientation of the half-chair conformation. In spite of unfavorably steric elements, the stereoelectronic effect, which provides the stabilization for the diaxial conformer and overrides the inherent steric bias of the axial substituent R^1 and R^3, may serve as a critical factor in determining the *anti*-selective stereocontrol. When substituent R^3 takes the axial orientation, the sulfur lone pair orbital would stay in the equatorial position in **TS-A**, leading to the antiperiplanar relationship between S-lone pair orbital and lithium-oxygen σ^* acceptor orbital. Subsequently the donor-acceptor interaction (the effective orbital overlap between S-lone pair and antibonding σ* Li-O) will decrease the energy of **TS-A** and compensate for destabilized energy causing by the steric bias. Meanwhile **TS-A** could convert to **TS-a** via ring flipping. To avoid a large swing to final tetrahedral geometry, the approach angle for protonation is expected to be abuse. Although **TS-a** seems to be more stable from the viewpoint of steric effect because of the equatorial substituent R^3 and pseudoequatorial R^1, on the other hand, R^1 and R^3 are in *gauche* position in **TS-a** rather than *anti* in **TS-A**, the steric hindrance of pseudoequatorial R^1 would obstruct the approaching of proton, resulting in the increasing repulsive energy to destabilize **TS-a**. Meanwhile, **TS-b** also bears the same disfavored repulsive interaction. Therefore, the priority for **TS-A** could ascribe to two factors: 1). stereoelectronic effect; 2). devoid of repulsive interaction between the pseudo-equatorial R^1 and upcoming attack of proton.

Thus, the proposed stereoelectronic effect appears to exhibit significant role in determining diastereofacial selectivity in the sulfa-Michael addition to nitroalkenes followed protonation at -78 °C. However, the problem provided above is that ***how to probe the stereoelectronic effect in this chelation control protonation reaction from experimental investigations***? The stereoelectronic effect which exerts a conformational bias, 1,2-diaxial substituted half-chair conformation, for protonation process of nitronate anions can be extrapolated from the change of diastereomeric ratio triggering by tuning the steric hindrance in both nitroalkenes and thiols. Especially, we have to provide experimental evidence to prove that the substituent R^3 was constrained to occupy the axial position in the half-chair chelated **TS-A** to meet the requirements for orbital overlap consideration of the equatorial S-lone pair orbital and σ*Li-O. Thus, the *anti*-selectivity would be expected to decrease along with the increase the size of axial substituent R^3. Meanwhile, the diastereoselectivity affected by the increasing of steric bulkiness of R^3 can also rule out the open-chain non-chelation transition state model in which R^3 was regarded as irrelevant factor.[10,11] Additionally, the destabilized energy would be also increased along with the increase steric hindrance of pseudoaxial substituent R^1, resulting in the dr value decrease as well. Thus, the competitive relationship between steric effect and stereoelectronic effect would be demonstrated by the decreasing *anti*-selectivity caused by the increasing steric effect of R^1. The poorly diastereoselective outcome, ultimately, would suggest that the stereoelectronic effect and steric effect are closely balanced. Herein, we shall present our results and hope that the results provide an important guide to the understanding stereoelectronic elements in controlling the diastereoselectivity in the sulfa-Michal addition of thiols to nitroalkenes under chelation conditions and to discern the relative importance of stereoelectronic effect and steric effect.

2.3 To probe the stereoelectronic effect in TS-A

In the most stable chelated transition state model **TS-A** (Schemes 3 and 4) which incorporates the stereoelectronic effect to control the stereochemistry, substituent R^2, which locates in the delocalized C=N π plane and is nearly vertical to C_β-R^1 σ bond, seeming to play a minimal role in stereocontrol of kinetic protonation for nitronates. And the experimental evidences from literature[10] have supported this assumption. In Table 2, when keeping vicinal alkyl group (R^1) to nitro group and the substituent (R^3) on sulfur unchanged, the appropriate substituents in the R^2 position, such as methyl, ethyl, 1-cyclohexenyl, 1-cycloheptenyl, and phenyl groups, show similar diastereoselectivities (*anti*:*syn* = 91:9 in average) except for isopropyl (which possibly followed both half-chair and twist-boat conformations as shown in Schemes 3 and 5 due to its bulkiness, *vida post*). However, the importance of R^1 and R^3, especially the substituent group R^3, in **TS-A** has not been systematically investigated.

Table 2 Relationship between substituent R^2 and the diastereoselectivity[a]



Entry	R^1	R^2	R^3	Yield (%)	Dr (*anti*:*syn*)
1	Me	Me	Ph	75	91:9
2	Me	Et	Ph	63	91:9
3	Me	1-cyclohexenyl	Ph	67	96:4
4	Me	1-cycloheptenyl	Ph	58	92:8
5	Me	*i*-Pr	Ph	56	57:43
6	Me	Ph	Ph	79	90:10

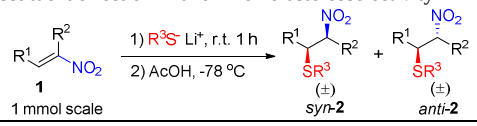
[a] Cited from Kamimura's paper [10].

When keeping vicinal substituent R^1 and germinal alkyl R^2 relative to nitro group unchanged, the dr (*anti*/*syn*) value generally decrease with increasing the steric bulkiness of R^3 (Table 3). For instance, when R^1= R^2 = Me, the dr values (*anti*/*syn*) decrease from 92:8 to 86:14 to 84:16 along with increasing R^3 from phenyl to isopropyl to *tert*-butyl substituents (Table 3, entries 1–3). Subsequently when changing R^1 and R^2 to the ethyl group, the same phenomenon was observed. The dr value reduced gradually from 85:15 to 78:22 along with increasing R^3 from phenyl to *tert*-butyl substituents (Table 3, entries 4–6). Furthermore, the obvious decreased tendency in the dr value from 73:27 to 55:45 along with increasing R^3 from phenyl to isopropyl substituent was exhibited (Table 3, entries 8 and 9) when keeping R^1 = *i*-Pr and R^2 = Me. For aryl substituted nitroalkenes, the paradigm between the dr value change and the steric hindrance of R^3 was still obvious. For instance**,** 1,2-diphenylnitroethene (**1l**) showed the highest diastereoselectivity (dr 89:11) (Table 3, entry 11) when it reacted with thiophenol, while the reaction of 1-methyl-2-phenylnitroethene (**1b**) and thiophenol displays much higher diastereoselectivity than the reaction of **1b** and isopropanethiol (Table 2, entries 12 and 13, dr 76:24 *vs* 65:35). The results clearly indicate that the steric hindrances of R^3 show obvious influence on the diastereoselectivity. Consequently, the hypothesis above about the R^3 group preferring to occupying the axial position of **TS-A** had been proved by the experimental results in Table 3 (entries 1 *vs* 2 and 3, 4 *vs* 5 and 6, 8 *vs* 9, 12 *vs* 13). In other words, the importance of the stereoelectronic effect seems inescapable in the diastereoselective chelation control addition reaction.

Additionally, the steric bulkiness of R^1 could also exert significant influence on the stereochemistry because R^1 takes the pseudo-axial position in **TS-A** as well (Schemes 3 and 4). Keeping geminal methyl or ethyl (R^2) unchanged, the diastereoselectivity in the sulfa-Michael addition of thiophenol to

nitroalkenes obviously decreased along with the increasing steric hindrance of R^1 on the vicinal carbon to the nitro group. For instance, the *dr* values (*anti*:*syn*) were generally in the range of 92:8 to 85:15 when R^1 is methyl, ethyl, or other primary straight chain alkyl group (Table 3, entries 1, 4, and 7). However, when isopropyl and phenyl occupied the position of R^1, the diastereoselective ratio falled to 73:27 (Table 3, entry 8) and 76:24 (Table 3, entry 12), respectively. With the continuous steric increase of the R^1 group, such as becoming *tert*-butyl substituent, the diastereoselectivity dramatically decrease to 53:47 (Table 3, entry 10). Subsequently, the sulfa-Michael addition of isopropanethiol to various α,β-disubstituted nitroalkenes also exhibited the same tendency (Table 3, entries 2, 5, 9, and 13), the dr value decrease from 86:14 when R^1 is the methyl group to 55:45 when R^1 is the isopropyl group. These poor diastereoselective outcomes (Table 3, entries 9 and 10) indicate that the stabilized energy provided by the stereoelectronic effect and the destabilized energy generated by steric factors are closely balanced. Thus, the experimental results are strongly in favor of our argument about the stereoelectronic effect in **TS-A** and we can probe the stereoelectronic effect from the dr value change by tuning steric effect.

Table 3 Substituent effect of R^3 and R^1 on diastereoselectivity



Entry	**1**	R^1	R^2	R^3	Product	Yield, (%)	Dr, [b] *anti*:*syn*
1	**1a**	Me [c]	Me [c]	Ph	**2a**	77	92:8
2	**1a**	Me	Me	*i*-Pr	**2c**	27	86:14
3	**1a**	Me	Me	*t*-Bu	**2d**	12	84:16
4	**1c**	Et	Et	Ph	**2e**	50	85:15
5	**1c**	Et	Et	*i*-Pr	**2f**	66	77:23
6	**1c**	Et	Et	*t*-Bu	**2g**	54	78:22
7	**1d**	*n*-hex	Et	Ph	**2h**	41	85:15
8	**1e**	*i*-Pr	Me	Ph	**2i**	37	73:27
9	**1e**	*i*-Pr	Me	*i*-Pr	**2j**	7	55:45
10	**1f**	*t*-Bu	Me	Ph	**2k**	10	53:47
11	**1g**	Ph	Ph	Ph	**2l**	78	89:11
12	**1b**	Ph [c]	Me [c]	Ph	**2b**	77	76:24
13	**1b**	Ph	Me	*i*-Pr	**2m**	70	65:35
14	**1a**	Me	Me	4-MeOC_6H_5	**2n**	67	88:12
15	**1a**	Me	Me	4-$O_2NC_6H_5$	**2o**	31	95:5

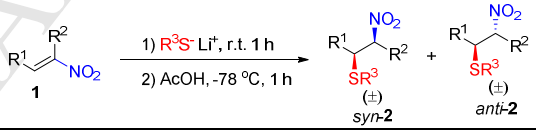
[a] Dr values were determined by both ^{1}H NMR and ^{13}C NMR. [b] Isolated yield by column chromatography. [c] Z/E = 4:1 for 2-nitro-2-butene (**1a**) and Z/E = 2:3 for 2-nitro-3-phenyl-2-propene (**1b**)

It would be interesting to look into influence of different substituents on the aromatic ring in ArSLi on the diastereoselectivity. Arenethiols with *para* electron-donating MeO and electron- withdrawing NO_2 groups were evaluated with (*E*)-2-nitro-2-butene (**1a**) (Table 3, entries 14 and 15). The results reveal that the electron-deficient 4-nitrothiophenol shows better diastereoselectivity than the electron-rich 4-methoxythiophenol possibly because the sulfur atom in 4-nitrothiophenol is harder acid than that in 4-methoxythiophenol, favorably coordinating with hard base lithium cation. The electronic effect of substituents on the aromatic ring of thiophenols do affect the stereocontrol, attributing to the stereoelectronic interaction between S-lone pair orbital and lithium-oxygen σ^* acceptor orbital in the proposed cyclic transition state because the electronic effect reinforces or weakens the cyclic transition state.

The configurations of the *syn*- and *anti*-products **2** were determined by the coupling constants of the vicinal protons and the ^{13}C NMR spectra *via* the γ-gauche effect and some of the known products were confirmed by the reported data in the literature.[8-10] 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.[9,28]

We wonder whether *syn*-**2** could serve as major products, while inherent steric hindrance overrides the stereoelectronic effect. When R^1 and R^3 still remained steric increasing, the steric effect may be dominated the stereocontrol process and 1,2-diaxial substituted **TS-A** may incline to flip to steric favored **Ts-a** (Schemes 3 and 4), which were expected to offer reversal stereoselectivity. Thus, several special nitroalkenes bearing a bulky group on R^1 position were screened to react with bulky secondary or tertiary thiols in order to verify our assumption. However, the turnover in diastereoselectivity had not been observed. And it is really puzzled that the similar moderate dr value (approximately *anti*:*syn* = 80:20) had been provided when very bulky substituents occupy the positions of R^1 and R^3 (Table 4, entries 1–3). Additionally, in the sulfa-Michael addition of *tert*-butanethiol to *tert*-butyl substituted nitroalkene, (*E*)-4,4-dimethyl-2-nitropent-2-ene (**1f**), no desired product could be monitored by the analysis of TLC and ^{1}H-NMR from really complex reaction mixture. And how to rationalize the interesting results in these bulky steric cases?

Table 4 Bulky substituent effect of R^3 and R^1 on the diastereoselectivity

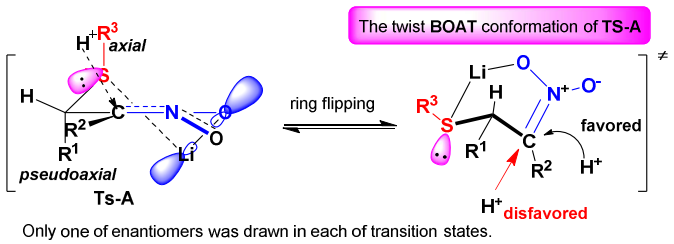


Entry	**1**	R^1	R^2	R^3	Product	Yield,[a] (%)	*Dr* [b] *anti*:*syn*
1	**1e**	*i*-Pr	Me	*t*-Bu	**2p**	10	80:20
2	**1f**	*t*-Bu	Me	*i*-Pr	**2q**	11	77:23
3	**1b**	Ph	Me	*t*-Bu	**2r**	69	79:21
4	**1f**	*t*-Bu	Me	*t*-Bu	**2s**	---	N.D. [c]

[a] Dr values were determined by both ^{1}H NMR and ^{13}C NMR.
[b] Isolated yield by column chromatography. [c] Not detected.

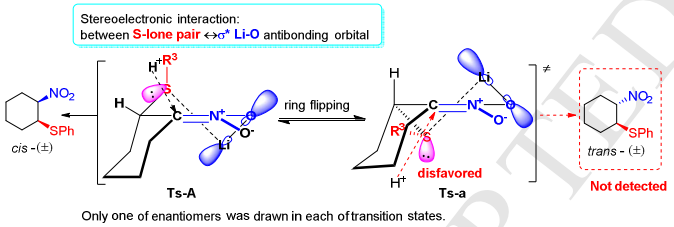
In the investigation of chelation control in Lewis acid promoted Mukaiyama aldol rections of chiral β-hydroxy aldehydes and achiral unsubstituted enolsilanes, Evans argued that boat chelates were responsible for the stereocontrol based on the semiempirical calculations (PM3).[29] Thus, it is logical to hypothesize that 1,2-diaxial **TS-A** would be potential to flip to the corresponding lower energy twist boat geometry, rather than standard boat conformation because the standard boat conformation locates in relatively higher potential energy than the twist boat one,[30] due to steric factors reinforced by bulky substituents (Scheme 5). Although the twist boat conformation of **TS-A** was deemed to be lack of the stereoelectronic effect, it is favored solely from the viewpoint of steric factor. Especially, substituents R^2 and R^3 occupied the bowsprit and stern positions in the twist-boat conformation, respectively, while hydrogen and lone-pair orbital of oxygen atom tend to take up the flagstaff positions. And proton would attack from unhindered approach (*exo* side)(as shown in Scheme 5) to afford *anti*-**2** mainly. It is reasonable to conclude that the steric factors may act as dominate element in the twist-boat chelae transition state for kinetic protonation of nitronate anions when the stereoelectronic effect could not balance the destabilizing energy provided by opposing

steric factors in the half-chair **TS-A**. When R^1 and R^3 are both *tert*-butyl group, no target β-nitro sulfide could be monitored because too much angle and torsional strain would be imposed even in twist-boat conformation and prevent the protonation process, even sulfa-Michael addition due to heavy bulkiness.



Scheme 5. Twist boat conformation of **TS-A** for protonation of nitronates with two heavily bulky substituents.

Our stereoelectronic controlled transition state model **TS-A** also could be applied to cyclic system with conformational restriction. In literature reports, exposure of 1-nitrocyclohex-1-ene to thiophenol under standard procedure resulted in the formation of *cis*-1-nitro-2-(phenylthio)cyclohexane exclusively.[10,31] However, no convincing explanation was provided for the priority of formation *cis*-product which was always considered to be less thermodynamically stable. In this case, the most stable transition state **TS-A**, which would convert to *cis*-decalin-like intermediate followed transformation to the corresponding product in *cis*-configuration, inclined to adopt a chair/half-chair conformation which is favored by the stereoelectronic effect. However, it is unfavorable enormously for protonation when **TS-A** flips to its conformer **TS-a** which would be responsible for *trans*-product because of steric hindrance (Scheme 6). The preference for approach of proton from the lower surface of C=N π plane is strongly blocked by the cyclohexane ring.



Scheme 6. Transition state model in the protonation of the cyclic nitronate.

Our stereoelectronic controlled cyclic chelate transition state model TS-A can be applied to rationalize the diastereoselectivities in sulfa-Michael additions involving both linear and cyclic nitroalkenes, even other Michael additions, in which both donors and acceptors possess coordinating atoms in appropriate positions in the presence of metal ions in the reaction system. However, the Kamimura and Hori's model completely ignored the stereoelectronic effect and chelation in the sulfa-Michael additions. They considered repellency between S-lone pair orbitals and p orbital in C=N bond only in their model. They mentioned that R^3 did not impact the diastereoselectivity on the basis of their model. In fact, R^3 does affect the diastereoselectivity according to our experimental results. Our proposed stereoelectronic controlled cyclic chelate transition state model was verified by tuning the steric bulkiness of the corresponding substituents.

3. Conclusions

The stereoelectronic effect plays an extremely important role in the diastereoselective sulfa-Michael addition between nitroalkenes and thiols under chelation conditions of lithium. Firstly, the experimental results clearly indicate that nitronate protonation serves as the stereochemical determinant in this chelation control reaction. Subsequently, half-chair six-membered chelate ring transition state bearing a nearly 1,2-diaxial substituents was proposed for nitronate protonation on the basis of the stereoelectronic effect control (the equatorial S-lone pair orbital shares an antiperiplanar relationship with the antibonding orbital of the Li-O bond). The stereoelectronic effect was verified through the change of diastereoselectivity by tuning the steric bulkiness of R^1 and R^3. Especially, R^3 occupying the axial position or S-lone pair taking the equatorial direction has been proved to be rational by the decreasing diastereoselectivity along with the steric increasing of R^3. Meanwhile, the diastereoselectivity also decreases obviously with steric increase of the substituent located in the vicinal olefinic carbon to the nitro group because it possesses a pseudoaxial position in the half-chair conformation. The poor diastereoselective outcomes indicate that the stereoelectronic effect and opposing steric effect are closely balanced. When the steric hindrance of substituent R^3 and R^1 increases continuously, **TS-A** inclines to flip to the corresponding twist boat conformation which generates moderate *anti*-selectivity dominated by steric effect exclusively. The reaction of nitrocyclohexene and thiophenol supports the proposed cyclic chelate transition state model perfectly. As a consequence, stereoelectronic control elements cannot be ignored in diastereoselective chelate-controlled addition reactions.

4. Experimental section

4.1 General

Dry tetrahydrofuran (THF) was refluxed under nitrogen with sodium wire and benzophenone as an indicator, and freshly distilled prior to use. Melting points were obtained on a Yanaco MP-500 melting point apparatus and are uncorrected. ^{1}H 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^o) and ethyl acetate (EA) as an eluent with gradient elution.

4.2 General procedure for the synthesis of nitroalkenes 1

Nitroalkenes **1** in Table 3–4 were prepared by dehydration of the corresponding vicinal nitro alcohols according to literature procedure[15] and 1-nitrohexane was prepared by referring the Corey's method[5a] and their analytical data are identical to those reported previously.

4.3 General procedure for the synthesis of β-nitro sulfides 2[10]

To a solution of thiophenol or alkanethiol (1.2 mmol) in 2.0 mL of dry THF was added *n*-butyllithium (2.4 M, 450μL, 1.1 mmol) at below 0 ^{o}C, and the resultant mixture was continued to be stirred for 30 min at the same temperature under nitrogen atmosphere. Subsequently, α,β-disubstituted nitroalkene **1** (1.0 mmol) was added via a syringe in one portion at 0 ^{o}C, and the mixture was stirred for 1 h at room temperature. For kinetic protonation process of nitronate anion intermediate, the resulting solution was required to cool at -78 ^{o}C, excess AcOH (0.3 mL) was added and the resulting solution was stirred for 1 h at -78 ^{o}C.

After warming to room temperature, the solution was poured into water (10 mL) and extracted with EA (10 mL × 3). The combined extracts were washed with brine (15 mL) and dried over Na_2SO_4 and concentrated in vacuo to afford crude β-nitro sulfide. Finally, subjecting the mixture directly to purification on silica gel chromatography (PE/EA) afforded the desired product **2**.

*4.3.1 2-Nitro-3-phenylthiobutane (**2a**)* [9,10]
Colorless oil, 163 mg, 77%, R_f = 0.47 (PE:EA = 20:1, *v*/*v*) , mixture of *anti*- and *syn*-**2a**. *Anti*-**2a**: ^{1}H 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**: ^{1}H 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-phenyl-3-phenylthiopropane (**2b**)* [9,10]
Yellowish oil, 211 mg, 77%, R_f = 0.48, 0.50 (PE:EA = 20:1, v/v), mixture of *anti*- and *syn*-**2b**. *Anti*-**2b**: ^{1}H 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*-**2b**: ^{1}H 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.

*4.3.3 3-Isopropylthio-2-nitrobutane (**2c**)* [9]
Colorless oil, 48 mg, 27%, R_f = 0.28 (PE:diethyl ether = 40:1, *v*/*v*), mixture of *anti*- and *syn*-**2c**. *Anti*-**2c**: ^{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*-**2c**: ^{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.

*4.3.4 3-tert-Butylthio-2-nitrobutane (**2d**)* [9]
Colorless oil, 24 mg, 12%, R_f = 0.36 (PE:diethyl ether = 40:1, v/v), mixture of *anti*- and *syn*-**2d**. *Anti*-**2d**: ^{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*-**2d**: ^{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.

*4.3.5 3-Nitro-4-phenylthiohexane (**2e**)* [9]
Colorless oil, 121mg, 50%, R_f = 0.40 (PE:EA = 40:1, v/v), mixture of *anti*- and *syn*-**2e**. *Anti*-**2e**: ^{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*-**2e**: ^{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.

4.3.6 *4-Isopropylthio-3-nitrohexane (**2f**)*
Colorless oil, 135mg, 66%, R_f = 0.46 (PE:EA = 40:1, v/v), mixture of *anti*- and *syn*-**2f**. *Anti*-**2f**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.37 (ddd, *J* = 2.8, 9.2, 10.8 Hz, 1H), 2.94 (ddd, *J* = 3.4, 9.2, 8.8 Hz, 1H), 2.93 (hept, *J* = 6.8 Hz, 1H), 2.25 (ddq, *J* = 14.8, 2.8, 7.3 Hz, 1H), 2.06 (ddq, *J* = 14.8, 10.8, 7.3 Hz 1H), 1.66 (ddq, *J* = 14.4, 3.4, 7.2 Hz, 1H), 1.47 (ddq, *J* = 14.4, 8.8, 7.2 Hz,1H), 1.30 (d, *J* = 6.8 Hz, 3H), 1.26 (d, *J* = 6.8 Hz, 3H), 1.06 (t, *J* = 7.3Hz, 3H), 0.97 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 94.2, 49.3, 36.3, 25.9, 24.8, 24.0, 23.5, 10.7, 10.6. *Syn*-**2f**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.47 (ddd, *J* = 10.2, 6.6, 3.3 Hz, 1H), 2.98 (ddd, *J* = 9.7, 6.6, 3.6 Hz, 1H), 2.96–2.87 (m, 1H), 2.03–1.98 (m, 1H), 1.91 (ddq, *J* = 14.8, 3.2, 7.2 Hz, 1H), 1.77 (ddq, *J* = 14.4, 3.6, 7.2 Hz, 1H), 1.52–1.40 (m, 1H), 1.30 (d, *J* = 6.8 Hz, 3H), 1.25 (d, *J* = 6.8 Hz, 3H), 1.04 (t, *J* = 7.2 Hz, 3H), 1.01 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 94.1, 49.0, 36.3, 24.1, 23.8, 23.4, 23.0, 11.0, 10.8. IR (CH_2Cl_2) *ν* (cm^{-1}): 2970, 1550, 1398, 1368. HRMS (ESI) calcd. for fragment $C_9H_{19}S^+$ $[M+H-47u]^+$ or $[M+H-HONO]^+$ *m/z*: 159.1202, found 159.1200.

4.3.7 *4-tert-Butylthio-3-nitrohexane (**2g**)*
Colorless oil, 118mg, 54%, R_f = 0.35 (PE:EA = 40:1, v/v), mixture of *anti*- and *syn*-**2g**. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.36 (ddd, *J* = 11.3, 8.8, 2.9 Hz, 1H), 2.99 (ddd, *J* = 8.8, 7.2, 4.4 Hz, 1H), 2.26 (ddq, *J* = 14.8, 2.9, 7.3 Hz, 1H), 1.98 (ddq, *J* = 14.8, 11.3, 7.3 Hz, 1H), 1.72 (ddq, *J* = 14.7, 4.4, 7.2 Hz, 1H), 1.58 (ddq, *J* = 14.7, 7.2, 7.2 Hz, 1H), 1.33 (s, 9H), 1.04 (t, *J* = 7.3 Hz, 3H), 0.96 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 93.6, 46.7, 44.1, 31.5, 27.4, 25.0, 10.8, 10.2. ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.52 (ddd, *J* = 10.6, 5.2, 3.0 Hz, 1H), 3.03–2.97 (m, 1H), 2.50 (ddq, *J* = 14.8, 10.6, 7.2 Hz, 1H), 1.89 (ddq, *J* = 14.8, 3.0, 7.2 Hz, 1H), 1.79 (ddq, *J* = 14.4, 3.6, 7.2 Hz, 1H), 1.65–1.54 (m, 1H), 1.36 (s, 9H), 1.04 (t, *J* = 7.2 Hz, 3H), 0.98 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 94.8, 47.5, 44.1, 31.2, 23.9, 21.4, 11.3, 11.2. IR (CH_2Cl_2) *ν* (cm^{-1}): 2970, 1551, 1400, 1366. HRMS (ESI) calcd. for fragment $C_{10}H_{21}S^+$ $[M+H-47u]^+$ or $[M+H-HONO]^+$ *m/z*: 173.1358, found 173.1352.

*4.3.8 3-Nitro-4-phenylthiononane (**2h**)* [9]
Yellowish oil, 117 mg, 41%, R_f = 0.56, 0.58 (PE:EA = 40:1, v/v), mixture of *anti*- and *syn*-**2h**. *Anti*-**2h**: ^{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*-**2h**: ^{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.

*4.3.9 4-Methyl-2-nitro-3-phenylthiopentane (**2i**)* [9,10]
Colorless oil, 90 mg, 37%, R_f = 0.23, 0.28, mixture of *anti*- and *syn*-**2i**. *Anti*-**2i**: ^{1}H 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*-**2i**: ^{1}H 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.

*4.3.10 3-Isopropylthio-2-methyl-4-nitropentane (**2j**)* [9]
Colorless oil, 16 mg, 7%, R_f = 0.31, 0.37 (PE: diethyl ether = 40:1, v/v), mixture of *anti*- and *syn*-**2j**. *Anti*-**2j**: ^{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*-**2j**: ^{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, 16.84.

*4.3.11 4,4-Dimethyl-2-nitro-3-phenylthiopentane (**2k**)* [9]
Colorless oil, 26 mg, 10%, R_f = 0.23 (PE:EA = 40:1, *v*/*v*), mixture of *anti*- and *syn*-**2k**. *Anti*-**2k**: ^{1}H 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*-**2k**: ^{1}H 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.

*4.3.12 1-Nitro-1,2-diphenyl-2-phenylthioethane (**2l**)* [9]
Colorless crystals, 262 mg, 78%, m.p. (for *anti*-**2l**) 160–162 °C, R_f = 0.24, 0.26 (PE:EA = 40:1, v/v), mixture of *anti*- and *syn*-**2l**. *Anti*-**2l**: ^{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* = 7.2Hz, 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*-**2l**: ^{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.

*4.3.13 2-nitro-3-isopropylthio-3-phenylpropane (**2m**)*
Colorless oil, 168 mg, 70%, R_f = 0.51 (PE:EA = 10:1, v/v), mixture of *anti*- and *syn*-**2m**. *Anti*-**2m**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.36–7.34 (m, 2H), 7.33–7.29 (m, 2H), 7.28–7.23 (m, 1H), 4.82 (dq, *J* = 9.2, 6.6 Hz, 1H), 4.36 (d, *J* = 9.2 Hz, 1H), 2.63 (hept, *J* = 6.8, 1H), 1.73 (d, *J* = 6.6 Hz, 3H), 1.24 (d, *J* = 6.8 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 138.4, 128.7, 128.4, 128.1, 87.8, 52.3, 35.3, 23.4, 22.9, 17.6. *Syn*-**2m**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.37-7.34(m, 2H), 7.32–7.29 (m, 2H), 7.28–7.23 (m, 1H), 4.82 (dq, *J* = 9.5, 6.7 Hz, 1H), 4.30 (d, *J* = 9.5 Hz, 1H), 2.71 (hept, *J* = 6.8, 1H), 1.35 (d, *J* = 6.7 Hz, 3H), 1.22 (d, *J* = 6.8 Hz, 3H), 1.14 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 137.8, 128.9, 128.2, 128.1, 87.3, 51.8, 35.7, 23.13, 23.06, 17.8. IR (CH_2Cl_2) *ν* (cm^{-1}): 2960, 2925, 1552, 1451, 1385, 1357. HRMS (ESI) calcd. for $C_{12}H_{18}NO_2S^+$ $[M+H]^+$ *m/z*: 240.1053, found 240.1054.

*4.3.14 anti-2-(4-Methoxyphenylthio)-3-nitrobutane (anti-**2n**)*
The reaction was performed on a 0.5-mmol scale. Colorless oil, 81 mg, 67%, R_f = 0.45 (PE:EA = 20:1, *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.41 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 4.45 (dq, *J* = 6.7, 6.7 Hz, 1H), 3.81 (s, 3H), 3.33 (dq, *J* = 6.9, 6.9 Hz, 1H), 1.70 (d, *J* = 6.7 Hz, 3H), 1.29 (d, *J* = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 160.3, 136.8, 132.6, 114.7, 87.2, 55.3, 47.5, 18.3, 17.4. IR (film, KBr) *ν* cm^{-1} 1549, 1493, 1388, 1286, 1248, 1173, 1030. HRMS (ESI) calcd. for fragment $C_{11}H_{15}OS$ [M+H-47u] or $[M+H-HONO]^+$ *m/z*: 195.0838, found 195.0836.

*4.3.15 anti-2-Nitro-3-(4-nitrophenylthio)butane (**2o**)*
The reaction was performed on a 0.5-mmol scale. Brown oil, 40 mg, 31%, R_f = 0.42 (PE:EA = 20:1, *v*/*v*). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 8.17 (d, *J* = 8.9 Hz, 2H), 7.51 (d, *J* = 8.9 Hz, 2H), 4.62 (dq, *J* = 6.8, 6.8 Hz, 1H), 3.91 (dq, *J* = 6.9, 6.9 Hz, 1H), 1.67 (d, *J* = 6.8 Hz, 3H), 1.47 (d, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ*: 146.6, 143.3, 130.3, 124.2, 86.5, 45.9, 18.7, 16.3. IR (film, KBr) *ν* cm^{-1} 1551, 1508, 1339, 1315, 1106, 1077. HRMS (ESI) calcd. for fragment $C_{10}H_{12}NO_2S$ [M+H-47u] or $[M+H-HONO]^+$ *m/z*: 210.0583, found 210.0574.

*4.3.16 3-tert-Butylthio-2-methyl-4-nitropentane (**2p**)* [9]
Colorless oil, 22 mg, 10%, R_f = 0.31 (PE: diethyl ether = 40:1, v/v), mixture of *anti*- and *syn*-**2p**. *Anti*-**2p**: ^{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*-**2n**: ^{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.

*4.3.17 anti-3-Isopropylthio-4,4-dimethyl-2-nitropentane (anti-**2q**)*
Colorless oil, 19 mg, 8.5%, R_f = 0.35 (PE: diethyl ether = 40:1, v/v). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.89 (dq, *J* = 3.6, 6.8 Hz, 1H), 2.90 (hept, *J* = 7.0 Hz 1H), 2.78 (d, *J* = 3.6 Hz, 1H), 1.71 (d, *J* = 6.8 Hz, 3H), 1.31 (d, *J* = 7.0 Hz, 3H), 1.29 (d, *J* = 7.0 Hz, 3H), 1.07 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 84.9, 58.7, 38.0, 36.4, 28.2, 23.7, 23.3, 18.3. IR (CH_2Cl_2) *ν* (cm^{-1}): 2964, 2951, 1552, 1453, 1386, 1364. HRMS (ESI) calcd. for fragment $C_{10}H_{21}S^+$ $[M+H-47u]^+$ or $[M+H-HONO]^+$ *m/z*: 173.1358, found 173.1357.

*4.3.18 syn-3-Isopropylthio-4,4-dimethyl-2-nitropentane (syn-**2q**)*
Colorless oil, 6 mg, 2.5%, R_f = 0.41 (PE: diethyl ether = 40:1, v/v). ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 4.88 (dq, *J* = 3.5, 6.6 Hz, 1H), 3.31 (d, *J* = 3.5 Hz, 1H), 2.75 (hept, *J* = 6.7 Hz 1H), 1.63 (d, *J* = 6.6 Hz, 3H), 1.25 (d, *J* = 6.6 Hz, 3H), 1.18 (d, *J* = 6.7 Hz, 3H), 1.09 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 84.0, 59.6, 37.5, 36.0, 30.9, 28.3, 23.6, 16.0. IR (CH_2Cl_2) *ν* (cm^{-1}): 2965, 2950, 1551, 1452, 1385, 1366. HRMS (ESI) calcd. for fragment $C_{10}H_{21}S^+$ $[M+H-47u]^+$ or $[M+H-HONO]^+$ *m/z*: 173.1358, found 173.1359.

*4.3.19 3-tert-Butylthio-2-nitro-3-phenylpropane (**2r**)*
Colorless oil, 175 mg, 69%, R_f = 0.43 (PE:EA = 10:1, v/v), mixture of *anti*- and *syn*-**2r**. *Anti*-**2r**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.40 (d, *J* = 7.6 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 2H), 7.27–7.20

(m, 1H), 4.71 (dq, *J* = 8.1, 6.6 Hz, 1H), 4.40 (d, *J* = 8.1 Hz, 1H), 1.67 (d, *J* = 6.6 Hz, 3H), 1.22 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 140.4, 128.6, 128.3, 127.8, 88.1, 51.1, 44.6, 31.1, 16.6. ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 140.4, 128.6, 128.3, 127.8, 88.1, 51.1, 44.6, 31.1, 16.6. *Syn*-**2r**: ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.40 (d, *J* = 7.4 Hz, 2H), 7.35–7.29 (m, 2H), 7.27–7.22 (m, 1H), 4.74 (dq, *J* = 9.3, 6.6 Hz, 1H), 4.33 (d, *J* = 9.3 Hz, 1H), 1.32 (d, *J* = 6.6 Hz, 3H), 1.21 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 139.4, 128.7, 128.6, 127.9, 87.6, 50.3, 44.8, 31.0, 17.5. IR (CH_2Cl_2) *ν* (cm^{-1}): 2960, 1552, 1494, 1452, 1386, 1357, 750, 701. HRMS (ESI) calcd. for $C_{13}H_{20}NO_2S^+$ $[M+H]^+$ *m/z*: 254.1209, found 254.1202.

*4.3.20 anti-3-tert-Butylthio-2-nitro-3-phenylpropane (**2r**)*
Colorless oil, 138 mg, 55%, R_f = 0.43 (PE:EA = 10:1, v/v) ^{1}H NMR (400 MHz, $CDCl_3$) *δ*: 7.40 (d, *J* = 7.6 Hz, 2H), 7.31 (t, *J* = 7.4 Hz, 2H), 7.27–7.20 (m, 1H), 4.71 (dq, *J* = 8.1, 6.6 Hz, 1H), 4.40 (d, *J* = 8.1 Hz, 1H), 1.67 (d, *J* = 6.6 Hz, 3H), 1.22 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 140.4, 128.6, 128.3, 127.8, 88.1, 51.1, 44.6, 31.1, 16.6. ^{13}C NMR (101 MHz, $CDCl_3$) *δ*: 140.4, 128.6, 128.3, 127.8, 88.1, 51.1, 44.6, 31.1, 16.6. IR (CH_2Cl_2) *ν* (cm^{-1}): 2961, 1553, 1495, 1451, 1387, 1359, 751, 702. HRMS (ESI) calcd. for $C_{13}H_{20}NO_2S^+$ $[M+H]^+$ *m/z*: 254.1209, found 254.1205.

Acknowledgement

This work was supported in part by the National Basic Research Program of China (No. 2013CB328905), the National Natrual Science Foundation of China (Nos. 21372025 and 21172017) and specialized Research Fund for the Doctoral Program of Higher Education, Ministry of Education of China (No. 20110010110011).

Supplementary data

The copies of ^{1}H NMR and ^{13}C NMR spectra of the unknown products and ^{1}H NMR spectra of the crude reaction mixtures in Tables 3 and 4 are included in the Supporting Information.

References and notes

1. (a) Enders, D.; Lüttgen, K.; Narine, A. A. *Synthesis* **2007,** 959–980. (b) Chauhan, P.; Mahajan, S.; Enders, D. *Chem. Rev.* **2014**, *114*, 8807–8864; (c) White, J. D.; Shaw, S. *Chem. Sci*. **2014,** *5*, 2200–2204.
2. (a) Aydillo, C.; Compañón, I.; Avenoza, A.; Busto, J. H.; Corzana, F.; Peregrina, J. M.; Zurbano, M. M. *J. Am. Chem. Soc.* **2014,** *136*, 789–800; (b) Boutureira, O.; Bernardes, G. J. L., *Chem. Rev.* **2015,** *115*, 2174–2195. (c) Yao, L.; Liu, K.; Tao, H.-Y.; Qiu, G.-F.; Zhou, X.; Wang, C.-J. *Chem. Commun.* **2013,** *49*, 6078–6080; (d) Aydillo, C.; Avenoza, A.; Busto, J. H.; Jiménez-Osés, G.; Peregrina, J. M.; Zurbano, M. M. *Org. Lett.*, **2012,** *14*, 334–337.
3. (a) Miyata, O.; Shinada, T.; Ninomiya, I.; Naito, T.; Date, T.; Okamura, K.; Inagaki, S. *J. Org. Chem* **1991**, *56*, 6556–6564; (b) Miyata, O.; Fujiwara, Y.; Ninomiya, I.; Naito, T. *J. Chem. Soc., Perkin Trans. 1* **1998**, 2167–2174. (c) Ono, M.; Nishimura, K.; Nagaoka, Y.; Tomioka, K. *Tetrahedron Lett*. **1999,** *40*, 1509–1512; (d) Kamimura, A.; Murakami, N.; Kawahara, F.; Yokota, K.; Omata, Y.; Matsuura, K.; Oishi, Y.; Morita, R.; Mitsudera, H.; Suzukawa, H.; Kakehi, A.; Shirai, M.; Okamoto, H. *Tetrahedron* **2003,** *59*, 9537–9546. (e) Shimizu, M.; Nishi, T. *Chem. Lett.* **2002**, 46–47.
4. (a) Ballini, R.; Araújo, N.; Gil, M. V.; Román, E.; Serrano, J. A. *Chem. Rev.* **2013,** *113*, 3493–3515; (b) Barrett, A. G. M.; Graboski, G. G. *Chem. Rev.* **1986,** *86*, 751–762; (c) Dumez, E.; Faure, R.; Dulcère, J.-P. *Eur. J. Org. Chem.* **2001**, 2577–2588; (d) Berner, O. M.; Tedeschi, L.; Enders, D. *Eur. J. Org. Chem.* **2002**, 1877–1894.
5. (a) Corey, E. J.; Estreicher, H. *J. Am. Chem. Soc.* **1978,** *100*, 6294–6295; (b) Capecchi, T.; de Koning, C. B.; Michael, J. P., *J. Chem. Soc., Perkin Trans. 1* **2000**, 2681–2688; (c) Mineno, T.; Miller, M. J. *J. Org. Chem* **2003,** *68*, 6591–6596; (d) Kozikowski, A. P. *Acc. Chem. Res.* **1984,** *17*, 410–416; (e) Eyer, M.; Seebach, D. *J. Am. Chem. Soc.* **1985,** *107*, 3601–3606. (f) Xu, C. X.; Xu, J. X. *Amino Acids* **2011**, *41*, 195–203.
6. (a) Ono, N.; Kamimura, A.; Sasatani, H.; Kaji, A. *J. Org. Chem.* **1987,** *52* , 4133–4135; (b) Kamimura, A.; Sasatani, H.; Hashimoto, T.; Ono, N. *J. Org. Chem.* **1989,** *54*, 4998–5003; (c) Lin, W.-W.; Jang, Y.-J.; Wang, Y.; Liu, J.-T.; Hu, S.-R.; Wang, L.-Y.; Yao, C.-F. *J. Org. Chem* **2001,** *66*, 1984–1991. (d) Ouvry, G.; Quiclet-Sire, B.; Zard, S. Z. *Org. Lett.*, **2003,** *5*, 2907–2909
7. For selected examples of the diastereo- and enantioselective sulfa-Michael additions of α,β-disubstituted nitroolefins and thiols, see: (a) Wang, X. F.; Hua, Q. L.; Chen, Y.; An, X. L.; Yang, Q. Q.; Chen, J. R.; Xiao, W. J. *Angew. Chem. Int. Ed.* **2010**, *49*, 8379–8383; (b) Wang, X. F.; Peng, L.; An, J.; Li, C.; Yang, Q. Q.; Lu, L. Q.; Gu, F. L.; Xiao, W. J. *Chem. Eur. J.* **2011**, *17*, 6484–6491; (c) Kimmel, K. L.; Robak, M. T.; Thomas, S.; Lee, M.; Ellman, J. A. *Tetrahedron* **2012**, *68*, 2704–2712; (d) Pei, Q. L.; Han, W. Y.; Wu, Z. J.; Zhang, X. M.; Yuan, W. C. *Tetrahedron* **2013**, *69*, 5367–5373; (e)Yang, W.; Yang, Y.; Du, D. M. *Org. Lett.* **2013**, *15*, 1190–1193; (f) Zhang, Y.; Vongvilai, P.; Sakulsombat, M.; Fischer, A.; Ramstrçm, O. *Adv. Synth. Catal*. **2014**, *356*, 987–992; (h) Wang, R. C.; Xu, J. X. *Helv. Chim. Acta*. **2014**, *97*, 1700–1707.
8. Chen, N.; Xu. J. X. *Tetrahedron* **2012**, *68*, 2513–2522.
9. Wang, J. D.; Chen, N.; Xu. J. X. *Tetrahedron* **2015**, *71*, 4007–4014.
10. Kamimura, A.; Sasatani, H.; Hashimoto, T.; Kawai, T.; Hori, K.; Ono, N. *J. Org. Chem.* **1990,** *55*, 2437–2442.
11. Hori, K.; Higuchi, S.; Kamimura, A. *J. Org. Chem* **1990,** *55*, 5900–5905.
12. Apeloig, Y.; Karni, M.; Rappoport, Z. *J. Am. Chem. Soc.* **1983,** *105*, 2784–2793
13. Mohrig, J. R.; Rosenberg, R. E.; Apostol, J. W.; Bastienaansen, M.; Evans, J. W. *J. Am. Chem. Soc.* **1997,** *119*, 479–486.
14. Crump, R. A. N. C.; Fleming, I.; Hill, J. H. M.; Parker, D.; Reddy, N. L.; Waterson, D. *J. Chem. Soc., Perkin Trans. 1* **1992**, 3277–3294.
15. (a) Ballini, R.; Castagnani, R.; Petrini, M. *J. Org. Chem* **1992,** *57*, 2160–2162; (b) Hübner, J.; Liebscher, J.; Pätzel, M. *Tetrahedron* **2002,** *58*, 10485–10500.
16. Ono, N.; Kamimura, A.; Kawai, T.; Kaji, A. *Chem. Commun*. **1987**, 1550–1551.
17. Seeman, J. I. *Chem. Rev*. **1983**, *83*, 83–134.
18. (a) Reetz, M. T.; Fox, D. N. A. *Tetrahedron Lett.* **1993,** *34*, 1119–1122; (b) Reetz, M. T.; Raguse, B.; Marth, C. F.; Hügel, H. M.; Bach, T.; Fox, D. N. A. *Tetrahedron* **1992,** *48*, 5731–5742.
19. (a) Cram, D. J.; Kopecky, K. R. *J. Am. Chem. Soc*. **1959**, *81*, 2748–2755. (b) Leitereg, T. J.; Cram, D. J. *J. Am. Chem. Soc*. **1968**, *90*, 4019–4026.
20. Mengel, A.; Reiser, O. *Chem. Rev*. **1999**, *99*, 1191–1223.
21. Narasaka, K.; Pai, H. C. *Chem. Lett.* **1980**, 1415–1418.
22. Clark Still, W.; Schneider, J. A. *Tetrahedron Lett.* **1980**, *21*, 1035–1038.
23. (a)Reetz, M. T.; Jung, A. *J. Am. Chem. Soc*. **1983,** *105*, 4833–4835. (b). Baldwin, S. W.; McIver, J. M. *Tetrahedron Lett.* **1991,** *32*, 1937–1940
24. Reetz, M. T. *Acc. Chem. Res.* **1993,** *26*, 462–468.
25. (a) Keck, G. E.; Castellino, S. *J. Am. Chem. Soc*. **1986,** *108*, 3847–3849. (b) Keck, G. E.; Castellino, S.; Wiley, M. R. *J. Org. Chem* **1986,** *51*, 5478–5480.
26. (a) Romero, J. A. C.; Tabacco, S. A.; Woerpel, K. A. *J. Am. Chem. Soc*. **2000,** *122*, 168–169. (b) Lewis, M. D.; Cha, J. K.; Kishi, Y. *J. Am. Chem. Soc*. **1982,** *104*, 4976–4978.
27. (a) Ye X. L. *Youji Huaxue* **1985**, (*1*), 60–70; (b) Ye X. L. *Huaxue Tongbao* **1986**, *(4)*, 1–11.
28. (a) Heathcock, C. H.; Pirrung, M. C.; Sohn, J. E. *J. Org. Chem.* **1979,** *44*, 4294–4299; (b) Hoffmann, R. W.; Froech, S. *Tetrahedron Lett.* **1985,** *26*, 1643–1646; (c) Rychnovsky, S. D.; Skalitzky, D. J. *Tetrahedron Lett.* **1990,** *31*, 945–948; (d) Peter, A.; Vaughan-Williams, G. F.; Rosser, R. M. *Tetrahedron* **1993,** *49*, 3007–3034.
29. Evans, D. A.; Allison, B. D.; Yang, M. G.; Masse, C. E. *J. Am. Chem. Soc*. **2001,** *123*, 10840–10852.
30. Xu, J. X. *Univ. Chem*. **2006**, *21(4)*, 40–44.
31. (a) Da Silva, F. M.; Jones, J. J. *J. Braz. Chem. Soc*. **2001**, *12*, 135–137; (b) Almeida, Q. A. R.; Pereira, M. L. O.; Coelho, R. B.; Carvalho, E. M.; Kaiser, C. R.; Jones, J. J.; Silva, F. M. *J. Braz. Chem. Soc*. **2008**, *19*, 894–902.