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Temperature-dependent annuloselectivity and stereochemistry in the reactions of methanesulfonyl sulfene with imines†

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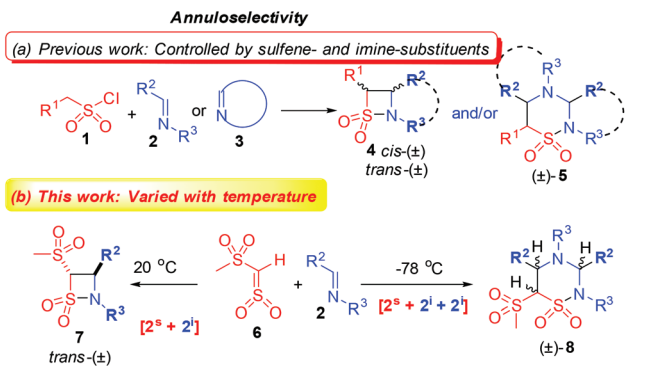
The annuloselectivity in the reactions of methanesulfonyl sulfene and imines varies with temperature. At a relatively higher temperature of 20 °C, the [$2^s + 2^i$] annulation of different *N*-alkyl imines occurs exclusively, giving four-membered *trans*-β-sultams in up to 69% yields. At a lower temperature of −78 °C, the [$2^s + 2^i + 2^i$] annulation of *N*-methyl imines takes place specifically, delivering six-membered 1,2,4-thiadiazine 1,1-dioxides, 4-aza-δ-sultams, in up to 80% yields, with diverse configurations at the C3, C5, and C6 stereocenters. The *trans*-stereochemistry involved in the [$2^s + 2^i$] annulations is attributed to the conrotatory ring closure of the thermodynamically stable 2,3-thiazabutadiene-type zwitterionic intermediates, while the diverse stereochemical outcomes in the [$2^s + 2^i + 2^i$] annulations are caused by the iminium isomerization in the stepwise nucleophilic [4 + 2] annulation between the same zwitterionic intermediates and a second molecule of *N*-methyl imines.

Introduction

The sulfa-Staudinger cycloadditions between sulfenes (or their equivalents) and imines have been developed into an efficient method to construct the β-sultam core structures,[1–3] which have witnessed wide applications in the synthetic[4] and medicinal chemistry.[5] However, the sulfa-Staudinger cycloadditions between sulfene generated from sulfonyl chlorides **1** and imines **2** or **3** proceed not only toward the [$2^s + 2^i$] annulations to yield β-sultams **4**, but also toward the [$2^s + 2^i + 2^i$] annulations to produce 1,2,4-thiadiazine 1,1-dioxides, 4-aza-δ-sultams **5** (Scheme 1a).[2b,d,3b,6] The competitive relationship of these two directions is referred to as *annuloselectivity*. Since the two kinds of annuladducts display a wide spectrum of bioactivities,[5,7] controlling the annuloselectivity becomes one of the issues of concern in this field.

Very recently, we proposed the mechanisms of the [$2^s + 2^i$] and [$2^s + 2^i + 2^i$] annulations, and also found that the annuloselectivity was controlled by the sulfene- and imine-substituents, including the ring sizes of cyclic imines (Scheme 1a).[2] In other words, the annuloselectivity is governed by the innate features of substrates. An empirical rule is also proposed to predict the annuloselective results based on the sulfene- and imine-substituents. However, from a practical synthetic viewpoint, controlling the annuloselectivity by external factors, such as temperature, additives, solvents, *etc.*, are meaningful and useful.



Scheme 1 Control of the annuloselectivity.

Although the sulfa-Staudinger cycloaddition has received much attention, the reactions between methanesulfonyl sulfene (**6**) and imines **2** have not been well explored so far.[3b] Herein, we present our studies on the temperature-dependent annuloselectivity in the reactions of methanesulfonyl sulfene (**6**), which could be generated either from the corresponding methanesulfonylmethanesulfonyl chloride (**1a**) at room temperature or by treating methanesulfonyl chloride (**1b**) at low temperature (−78 °C) with strong bases, with imines **2**

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†Electronic supplementary information (ESI) available: Copies of ^{1}H and ^{13}C NMR spectra of products **7** and **8**, NOE spectra of **8**, and the ^{1}H NMR spectra of the crude reaction mixtures. See DOI: 10.1039/c6ob01259k

(Scheme 1b), hoping to provide convenient methods to synthesize *trans*-2-methanesulfonyl-β-sultams **7** and 4-aza-6-methanesulfonyl-δ-sultams **8** from the same substrates yet under different conditions.

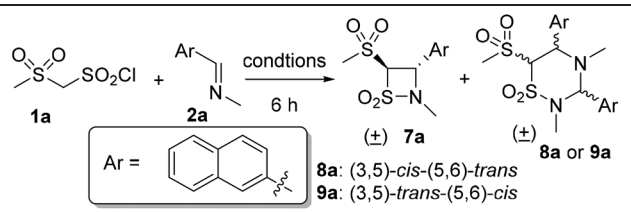
Results and discussion

The $[2^s + 2^i]$ annulation

With the model reaction between methanesulfonylmethanesulfonyl chloride (**1a**) and *N*-naphthalen-2-ylmethylene methylamine (**2a**), the condition optimization was performed. Generally, the sulfa-Staudinger cycloadditions were conducted by mixing one equiv. of sulfonyl chloride **1a** with two equiv. of imine **2a** without any other bases.[2,3] With this procedure, the solvent screening was conducted (Table 1, entries 1–7). The results revealed that dichloromethane was the best choice, with the product *trans*-sultam **7a** obtained in a relatively high 42% yield (Table 1, entry 3). In these reactions, one equiv. of imine **2a** served as the base to generate the sulfene, and the other took part in the cycloaddition. Further investigations on other bases revealed that triethylamine gave the highest yield of 51% (Table 1). Addition of bases affected not only the yield of the $[2^s + 2^i]$ annuladduct, but also the annuloselectivity. For example, in the presence of *N*,*N*-dimethylaminopyridine (DMAP) and 1,4-diazabicyclo[2.2.2]octane (DABCO), the $[2^s + 2^i + 2^i]$ annuladducts (**8a** and **9a**) were also generated in 10% and 14% yields, respectively, as a mixture of (3,5)-*cis*-(5,6)-*trans*- and (3,5)-*trans*-(5,6)-*cis*-isomers (*vide infra*).

With the optimal conditions for the $[2^s + 2^i]$ annulations, a series of structurally diverse *trans*-2-methanesulfonyl-β-sultams **7** was easily synthesized, and the results are presented in Table 2. All the crude reaction mixtures were examined using ^{1}H NMR, and no $[2^s + 2^i + 2^i]$ annuladducts were observed, indicating that the $[2^s + 2^i]$ annulations occurred annulospecifically. The *N*-methyl imines **2a–i** reacted with sulfonyl chloride **1a** to afford the corresponding $[2^s + 2^i]$ annuladducts **7a–i** in moderate yields (21–69%). The *C*-substituents of imines did not affect the $[2^s + 2^i]$ annulations so much, with most of the β-sultams obtained in 31–46% yields, except for 4-phenylphenyl (**7g**) and the sterically large *C*-substituent 9-anthracenyl (**7j**). 4-Phenylphenyl promoted the formation of the $[2^s + 2^i]$ annuladduct **7g** with a relatively high 69% yield, while 9-anthracenyl prevented the $[2^s + 2^i]$ annulation from forming **7j**, presumably due to steric hindrance. The *N*-substituents of imines did not affect the $[2^s + 2^i]$ annulations obviously, either, with most of the β-sultams obtained in 32–46% yields, except for *N*-*tert*-butyl-β-sultam (**7m**) in low yield of 4%. By conducting the reactions with one equiv. of **1a** and two equiv. of

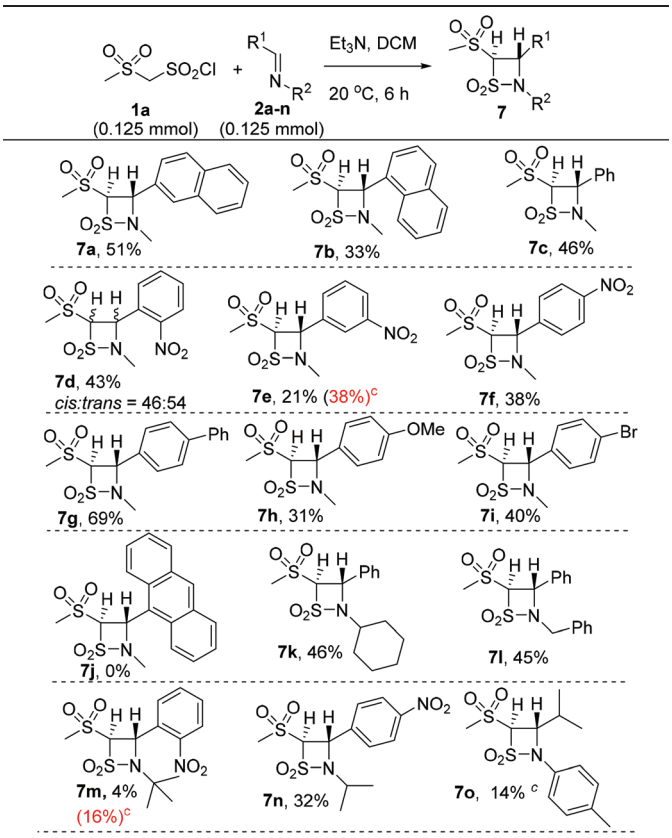
Table 1 Reaction condition optimization for the $[2^s + 2^i]$ annulation[a]



Entry	Solvent	Temp. (°C)	Base	Yield[b] (%) 7a	8a
1	THF	20	—	8	0
2	$CHCl_3$	20	—	30	0
3	CH_2Cl_2	20	—	42	0
4	DCE	20	—	11	0
5	MeCN	20	—	26	0
6	$PhCH_3$	20	—	6	0
7	DMF	20	—	Trace	0
8	**CH_2Cl_2**	**20**	**Et_3N**	**51**	**0**
9	CH_2Cl_2	20	2-ClPy	43	0
10	CH_2Cl_2	20	Py	22	0
11	CH_2Cl_2	20	DMAP	19	24[c]
12	CH_2Cl_2	20	DABCO	15	21[d]

[a] All the reactions were performed on a 0.125 mmol scale based on **1a**. In entries 1–7, 1 equiv. of **1a** and 2 equiv. of **2a** were used. In entries 8–12, 1 equiv. of **1a**, 1 equiv. of **2a**, and 1 equiv. of base were used. [b] Yields were calculated from the ^{1}H NMR spectra of the crude reaction mixtures by analyzing the ratios of imines, aldehydes, **7a**, **8a**, and/or **9a**. [c] As determined by the crude reaction mixture, **8a** : **9a** = 63 : 37. [d] As determined by the crude reaction mixture, **8a** : **9a** = 29 : 71.

Table 2 $[2^s + 2^i]$ Annulations at 20 °C[a,b]



[a] The reactions were performed under the optimal conditions in Table 1. [b] Isolated yields by column chromatography. [c] Yields were obtained by reacting 0.125 mmol of **1a** with 0.25 mmol of **2e** or **2n** in THF.

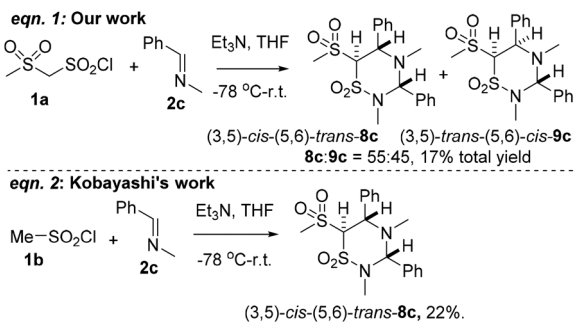
imines in tetrahydrofuran, the yields of β-sultams **7e** and **7m** were improved to 38% and 16%, respectively. Imines derived from aliphatic aldehydes, for example, *N*-2-methylpropylidene 4-methylaniline (**2o**), also reacted with methanesulfonyl sulfene (**6**) to give rise to the corresponding β-sultam **7o** in low yield (14%) due to unstable *N*-alkylidene imines. However, imines prepared from aliphatic aldehydes and aliphatic amines did not work well. For instance, the reaction of methanesulfonyl sulfene (**6**) and the imine prepared from isobutanal and benzylamine generated a complex mixture because the prepared imine *N*-2-methylpropylidene benzylamine could isomerize into *N*-benzylidene isobutanamine and both these imines are unstable.

The $[2^s + 2^i + 2^i]$ annulation

We envisioned that the $[2^s + 2^i + 2^i]$ annuloselectivity should be enhanced when the reactions between methanesulfonyl sulfene (**6**) and *N*-methyl imines were conducted at low temperature, for example, −78 °C. As predicted, the reaction between **1a** and **2b** at −78 °C yielded the $[2^s + 2^i + 2^i]$ annuladduct (3,5)-*cis*–(5,6)-*trans*-**8c** and (3,5)-*trans*–(5,6)-*cis*-**9c** in 15% total yield. As indicated by the ^{1}H NMR analysis of the crude reaction mixture, the ratio of **8c : 9c** was 55 : 45, and the $[2^s + 2^i]$ annuladduct **7c** was not observed (Scheme 2, eqn (1)).

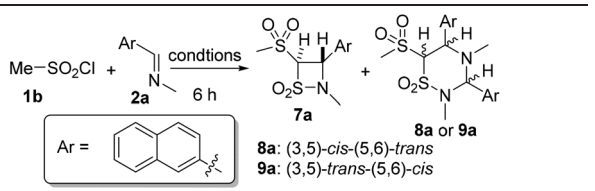
It was reported that methanesulfonyl sulfene (**6**) could be generated by treating methanesulfonyl chloride (**1b**) with triethylamine at −78 °C.[8] Thus, preparation of the $[2^s + 2^i + 2^i]$ annuladducts directly from methanesulfonyl chloride (**1b**) at −78 °C is feasible. Preliminary work by Kobayashi and co-workers disclosed that addition of methanesulfonyl chloride (**1b**) into a mixture of triethylamine and imine **2b** at −78 °C failed to give the $[2^s + 2^i]$ annuladduct **7c**; instead, $[2^s + 2^i + 2^i]$ annuladduct (3,5)-*cis*–(5,6)-*trans*-**8c** generated exclusively in 22% yield (Scheme 2, eqn (2)).[3b] It is of note that the stereochemistry in the two reactions (Scheme 2) was not completely the same, and a new diastereomer **9c** was isolated in our experiments. This indicates that the stereochemistry in the $[2^s + 2^i + 2^i]$ annulations of linear imines was not as simple as Kobayashi and co-workers reported.

With the above experimental results, the reaction condition optimization for the $[2^s + 2^i + 2^i]$ annulation was conducted by



Scheme 2 Realization of the $[2^s + 2^i + 2^i]$ annulation from different sulfene precursors.

Table 3 Reaction condition optimization for the $[2^s + 2^i + 2^i]$ annulation[a]



Entry	Solvent	Temp. (°C)	Base	Yield[b] (%) 7a	8a and 9a
1	**CH_2Cl_2**	**−78**	**DABCO**	**0**[c]	**51**[d]
2	CH_2Cl_2	−78	Et_3N	0	10[e]
3	THF	−78	DABCO	0	0
4	THF	−78	Et_3N	0	0
5	THF	−78	DMAP	0	0

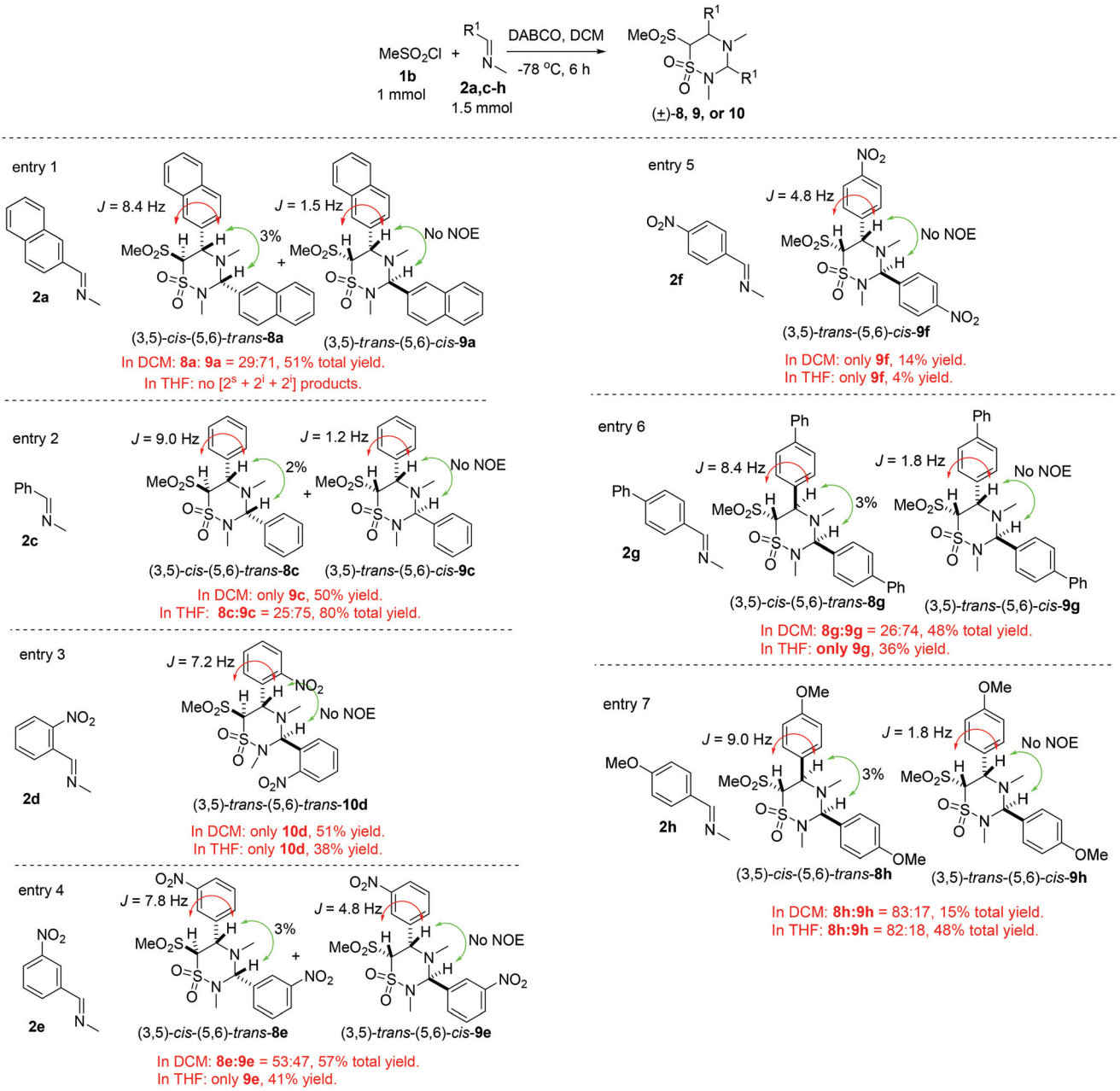
[a] All the reactions were performed on a 0.5 mmol scale based on methanesulfonyl sulfene (**6**); that is, 1 mmol of **1b**, 1 mmol of base, and 1.5 mmol of imine **2a** were used. [b] Yields were calculated from the ^{1}H NMR spectra of the crude reaction mixtures by analyzing the ratios of imines, aldehydes, **7a**, **8a**, and/or **9a**. [c] No product was observed by the ^{1}H NMR spectra of the crude reaction mixtures. [d] **8a : 9a** = 29 : 71. [e] **8a : 9a** = 15 : 85.

reacting methanesulfonyl chloride (**1b**) with *N*-naphthalen-2-ylmethylene methylamine (**2a**) at −78 °C. The results are summarized in Table 3. When dichloromethane was used as the solvent, strong bases DABCO and triethylamine promoted the reactions toward the $[2^s + 2^i + 2^i]$ pathway, delivering 4-aza-δ-sultams **8a** and **9a** in 51% and 10% total yields, respectively (Table 3, entries 1 and 2). Further stereochemical studies by NOE analyses showed that **8a** exhibited a (3,5)-*cis*–(5,6)-*trans*-configuration, while **9a** exhibited (3,5)-*trans*–(5,6)-*cis* (for detail, see Table 4, entry 1). The ratio of the two diastereomeric products **8a : 9a** was closely affected by the bases added. For example, DABCO delivered 29 : 71 ratio, while triethylamine 15 : 85 ratio. In tetrahydrofuran solvent no $[2^s + 2^i + 2^i]$ annulations were observed with any of the bases.

Studies on the $[2^s + 2^i + 2^i]$ annulations were performed, by reacting different *N*-methyl imines **2a,c–h** with methanesulfonyl chloride (**1b**) in the presence of DABCO in dichloromethane and tetrahydrofuran at −78 °C. The results are presented in Table 4. The $[2^s + 2^i + 2^i]$ annulations gave structurally diverse 4-aza-δ-sultams **8** and **9**. The stereochemistry of the C3 and C5 positions was determined by their NOE analysis. As demonstrated by our previous work, an observed NOE value between the protons at C3 and C5 positions indicated the (3,5)-*cis*-configuration; otherwise, the (3,5)-*trans*-configuration should be assigned. The stereochemistry of the C5 and C6 was assigned on the basis of the coupling constants between the protons at these positions. Generally, for the (5,6)-*cis*-configuration, J = 0 − 5 Hz; for the (5,6)-*trans*-configuration, J = 7–14 Hz.[2b,d]

The *C*-aryl substituents of imines **2a,c–h** affected not only the yields, but also the stereochemistry, of the $[2^s + 2^i + 2^i]$ annuladducts 4-aza-δ-sultams **8, 9** and **10.** Taking the reactions

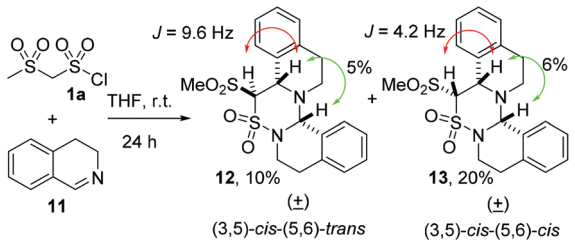
Table 4 $[2^s + 2^i + 2^i]$ Annulations at −78 °C[a,b,c]



[a] The reactions were performed under the optimal conditions in Table 3, with DCM or THF as solvents. [b] Yields for the reactions in DCM were obtained by column chromatography, while yields for reactions in THF were obtained by the ^{1}H NMR spectra of the crude reaction mixtures by analyzing the ratios of imines, aldehydes, $[2^s + 2^i + 2^i]$ annuladducts **8**, **9**, and/or **10**. [c] The ratios of **8** : **9** were determined by the ^{1}H NMR spectra of the crude reaction mixtures.

in dichloromethane as examples, the reactions of imines **2a**, **2c**, **2d**, **2e**, and **2g** afforded the corresponding 4-aza-δ-sultams in 51%, 50%, 51%, 80%, and 48% total yields (Table 4, entries 1–4, 6), respectively, while the reactions of imines **2f** and **2h** gave products in lower 14% and 15% total yields (Table 4, entries 5 and 7), respectively. In the reactions of imines **2a**, **2e**, **2g**, and **2h** in dichloromethane, both (3,5)-*cis*–(5,6)-*trans*-products (**8a,e,g,h**) and (3,5)-*trans*–(5,6)-*cis*-products (**9a,e,g,h**) generated, and the corresponding **8** : **9** ratios were 29 : 71, 53 : 47, 26 : 74, and 83 : 17 (Table 4, entries 1, 4, 6, and 7), respectively. Contrastingly, the reactions of **2c**, **2d**, and **2f** in dichloromethane stereospecifically gave rise to (3,5)-*trans*–(5,6)-*cis*-**9c**, (3,5)-*trans*–(5,6)-*trans*-**10d**, and (3,5)-*trans*–(5,6)-*cis*-**9f** (Table 4, entries 2, 3, and 5), respectively.

The solvent effect was also an important factor in the $[2^s + 2^i + 2^i]$ annulations. In most cases, higher yields of the



Scheme 3 The $[2^s + 2^i + 2^i]$ annulations between 3,4-dihydroisoquinoline and methanesulfonyl sulfene.

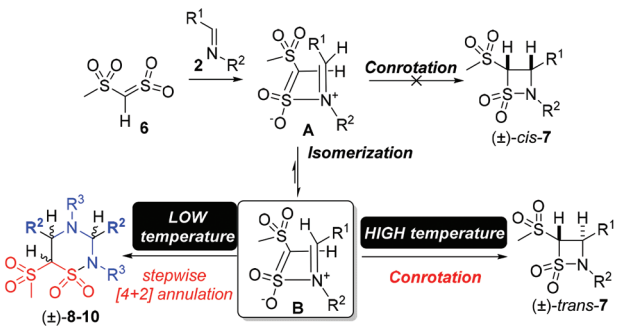
$[2^s + 2^i + 2^i]$ annuladducts were obtained in dichloromethane than those in tetrahydrofuran (Table 4, entries 1, and 3–5). However, in the reactions of imines **2c** and **2h**, a converse solvent effect was observed, that is, the yields in tetrahydrofuran were much higher than those in dichloromethane (Table 4, entries 2 and 7). In addition, the stereochemical ratios in tetrahydrofuran also differed from those in dichloromethane, as shown by the different **8 : 9** ratios obtained in the two solvents (Table 4, entries 2, 4, and 6).

The $[2^s + 2^i + 2^i]$ annulation between sulfonyl chloride **1a** and cyclic imine 3,4-dihydroisoquinoline (**11**) was also observed, giving two stereochemically different products (3,5)-*cis*–(5,6)-*trans*-**12** and (3,5)-*cis*–(5,6)-*cis*-**13** in 10% and 20% yields (Scheme 3), respectively. The detailed mechanism of the stereochemistry has been rationalized in previous reports on the cyclic imine-participated sulfa-Staudinger cycloadditions.[2b,d]

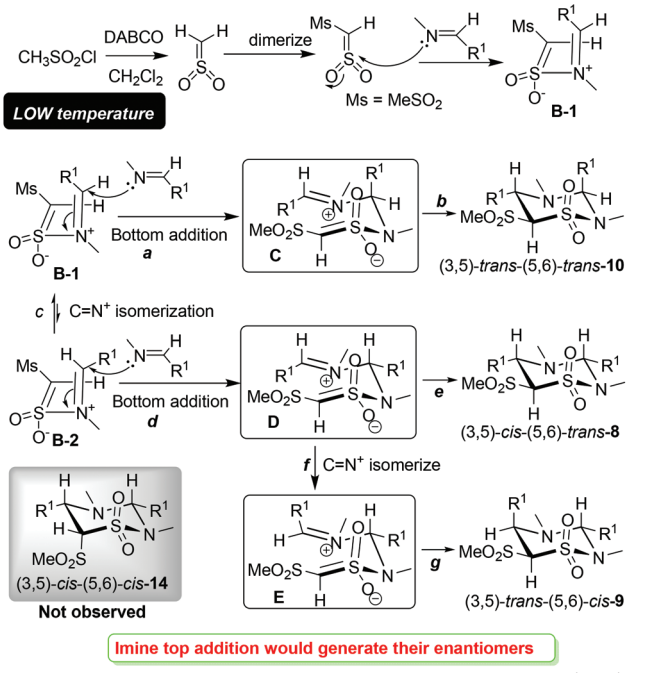
Mechanistic rationalization

The temperature-controlled $[2^s + 2^i]$ and $[2^s + 2^i + 2^i]$ annuloselectivity and the related stereochemistry can be explained well.[2] As shown in Scheme 4, the methanesulfonyl sulfene (**6**), generated either by direct elimination of HCl from methanesulfonylmethanesulfonyl chloride (**1a**) under weakly or strongly basic conditions or by the dimerization of sulfene derived from methanesulfonyl chloride (**1b**) in the presence of strong bases at −78 °C,[8] is *exo* attacked by the nitrogen atom in imines **2**, giving rise to 2,3-thiazabutadiene-type zwitterionic intermediates **A**. According to our previous theories,[2a,c] intermediates **A** are not stable, because of the large steric hindrance between the methanesulfonyl group ($MeSO_2$) and the R^2 group. On one hand, **A** will isomerize fast into the thermodynamically stable intermediates **B** by means of the C=N$^+$ bond isomerization. On the other hand, the direct conrotation of intermediates **A** was also drastically decreased by the repulsion between $MeSO_2$ and R^2, and the electron-withdrawing methanesulfonyl group. As a result, in both $[2^s + 2^i]$ and $[2^s + 2^i + 2^i]$ annulations, intermediates **B** act as the predominant reactive intermediates to evolve toward the four-membered β-sultams **7** and six-membered 4-aza-δ-sultams **8–10**. In the $[2^s + 2^i]$ annulations at room temperature, only intermediates **B** undergo the conrotatory ring closure to form *trans*-β-sultams **7**. This is the reason why most β-sultams (except for **7d**) in Table 2 show an exclusive *trans*-configuration. The results also reveal that the energy barrier of the $[2^s + 2^i]$ annulation is higher than that of the $[2^s + 2^i + 2^i]$ one because $[2^s + 2^i]$ annulation requires a relatively higher temperature.

Our previous mechanistic studies also pointed out that the conrotatory ring closure of intermediates **B** are affected by temperature.[2c] The lower the temperature, the slower the conrotation. Thus, at −78 °C, the conrotation of intermediates **B** is significantly inhibited. This provided opportunities for intermolecularly nucleophilic addition with another molecule of more strongly nucleophilic *N*-methyl imines[9] to the iminium moiety in the corresponding intermediates **B-1** (Scheme 5). The direct nucleophilic addition of *N*-methyl imines to intermediates **B-1** from the bottom side generates intermediates **C**, of which the further intramolecular nucleophilic addition affords (3,5)-*trans*–(5,6)-*trans*-**10**, as represented by **10d** in



Scheme 4 Proposed mechanisms in the temperature-controlled annuloselectivity.



Scheme 5 Proposed stepwise mechanisms for the $[2^s + 2^i + 2^i]$ annulations.

Table 4. Because the strongly electron-withdrawing *ortho*-nitrophenyl accelerates both direct intermolecular nucleophilic addition (step a) and intramolecular nucleophilic addition (step b), both C=N$^+$ bonds in intermediates **B-1** and **C** have no opportunity to isomerize at low temperature (−78 °C).

The generation of *cis*-sultam *cis*-**7d** supports that the iminium moiety in intermediate **Bd**/**B-1d** (where R^1 = 2-$O_2NC_6H_4$) shows more strong electrophilicity, favoring direct conrotatory ring closure at a relatively higher temperature of 20 °C (Table 1, **7d**)[2c] and intermolecularly nucleophilic attack with a secondary imine molecule at a lower temperature of −78 °C. In the case, isomerization of the iminium is decreased. In addition, because intermediates **C** with a strong electron-withdrawing R^1 group are thermodynamically most stable and favorable in the intramolecularly nucleophilic cyclization, no isomerization of their C=N$^+$ moieties can occur. Thus, no (3,5)-*cis*–(5,6)-*cis*-products **14** could be observed.

In other cases (Scheme 5), *N*-methyl imines nucleophilically attack thermodynamically C=N$^+$-isomerized intermediates **B-2** from their bottom side to yield intermediates **D** (step d), in which the C=N$^+$ would isomerize to form intermediates **E** (step f). Both intermediates **D** and **E** undergo intramolecularly nucleophilic addition to give rise to [2^s + 2^i + 2^i] annuladducts (3,5)-*cis*–(5,6)-*trans*-**8**, for examples, **8a**, **8c**, **8e**, **8g**, and **8h** in Table 4 (step e), and (3,5)-*trans*–(5,6)-*cis*-products **9**, as represented by **9a**, **9c**, **9e**, **9f**, **9g**, and **9h** in Table 4 (step g), respectively.

Similarly, *N*-methyl imines can also attack intermediates **B-1** and **B-2** from their top side followed by the subsequent processes, affording the enantiomers of the [2^s + 2^i + 2^i] annuladducts generated from the bottom-side attack.

The stereochemical results in Table 4 indicated that not only the intermolecularly nucleophilic addition of *N*-methyl imines to **B-1** (step a), and isomerization of **B-1** to **B-2** (step c), but also the C=N$^+$ isomerizations and intramolecular addition inside intermediates **D** (step e and f) are in competition. The competitions are sensitively affected by the steric hindrance or electronic properties of the *C*-aryl substituents in the *N*-methyl imines **2**, and consequently give [2^s + 2^i + 2^i] annuladducts in different stereochemistry. The inter/intramolecular nucleophilic additions and C=N$^+$ isomerizations are the stereodetermining steps, deciding the C3, C5, and C6 stereochemistry in different cases.

Staudinger intermediates *vs.* sulfa-Staudinger intermediates

In the Staudinger cycloadditions, similar [2^k + 2^i + 2^i] annulations between one ketene molecule and two imine molecules are also frequently observed.[10] The key intermediates involved are 2-aza-butadiene-type zwitterionic intermediates **16**,[11] structurally similar to the sulfa-Staudinger intermediates **15** (Fig. 1). Even though both **15** and **16** can directly undergo conrotatory ring closure to form β-sultams and β-lactams, respectively, the mechanisms of the corresponding [2^s + 2^i + 2^i] and [2^k + 2^i + 2^i] annulations differ distinctly. In the [2^s + 2^i + 2^i] annulations, the sulfa-Staudinger intermediates **15** react with a second imine molecule followed by a stepwise mechanism,

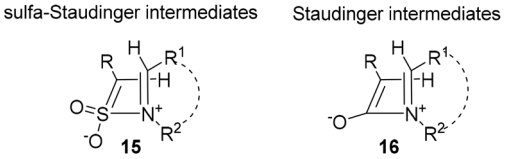


Fig. 1 The intermediates in sulfa-Staudinger and Staudinger cycloadditions.

as depicted in Scheme 5, delivering stereochemically diverse annuladducts. Contrastingly, in most [2^k + 2^i + 2^i] annulations, the Staudinger intermediates **16** follow a concerted hetero-Diels–Alder cycloaddition mechanism, with an *endo*- or *exo*-selectivity, to react with a second imine molecule, giving stereochemically predictable annuladducts.[12]

Conclusions

The annuloselectivity in the reactions of methanesulfonyl sulfene and imines varies with temperature. At a relatively higher temperature of 20 °C with methanesulfonylmethanesulfonyl chloride as the sulfene precursor, the [2^s + 2^i] annulation of different *N*-alkyl imines occur exclusively, giving four-membered *trans*-β-sultams in up to 69% yields. At a lower temperature of −78 °C with methanesulfonyl chloride as the sulfene precursor, the [2^s + 2^i + 2^i] annulations of *N*-methyl imines take place specifically, delivering six-membered 4-aza-δ-sultams in up to 80% yields, with diverse configurations at the C3, C5, and C6 stereocenters. The *trans*-stereochemistry involved in the [2^s + 2^i] annulations is attributed to the conrotatory ring closure of the thermodynamically 2,3-thiazabutadiene-type zwitterionic intermediates **B**. The diverse stereochemistry in the [2^s + 2^i + 2^i] annulations is explained well by the stepwise [4 + 2] annulation between intermediates **B** and *N*-methyl imines, with the inter/intramolecular nucleophilic additions and iminium isomerization as stereodetermining steps. The current study provides convenient methods to synthesize *trans*-β-sultams and 4-aza-δ-sultams selectively from imines and methanesulfonyl chloride.

Experimental

General information

Tetrahydrofuran and toluene were refluxed over sodium with diphenyl ketone as an indicator, while acetonitrile, dichloromethane, and 1,2-dichloroethane were refluxed over calcium hydride. All the solvents were 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 400 MHz or 600 MHz spectrometer in $CDCl_3$ with TMS as an internal standard and the chemical shifts (δ) are reported in parts per million (ppm). The one-dimensional selected NOE experiments were conducted on a Bruker 600 MHz spectrometer. The IR spectra (KBr pellets,

ν [cm^{-1}]) were obtained on a Nicolet 370 FTIR spectrometer. HRMS measurements were carried out on an Agilent LC/MS TOF mass spectrometer. TLC analyses were performed on silica gel G plates, and the plates were visualized with UV light. PE is the abbreviation for petroleum ether (60–90 °C), and EA for ethyl acetate.

Sulfonyl chlorides **1a** and **1b** were used directly as commercially received. Imines **2a–o** were prepared in quantitative yields by refluxing the corresponding aldehydes (1 equiv.) and amines (1 equiv.) in dichloromethane for several hours with $MgSO_4$ (1.5 equiv.) as drying agents.[2b,c]

General procedure for the [2^s + 2^i] annulation

To a 10 mL reaction tube charged with a solution of an imine **2** (0.125 mmol) and triethylamine (13 mg, 0.125 mmol) in dry dichloromethane (1 mL) was added (methanesulfonyl)methanesulfonyl chloride (**1a**) (24 mg, 0.125 mmol). The tube was quickly sealed, immersed into a 20 °C oil bath and stirred for 6 h. After adding dichloromethane (5 mL), washing with brine (5 mL), drying over $MgSO_4$, and concentrating at reduced pressure, the residue was purified by column chromatography on silica gel with PE and EA (3 : 1, v/v) as the eluent to afford β-sultam.

***trans*-2-Methyl-4-(methanesulfonyl)-3-(naphthalen-2-yl)-1,2-thiazetidine 1,1-dioxide (7a).** White solid, mp 45–47 °C. Yield: 21 mg, 51%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98–7.85 (m, 4H), 7.65–7.44 (m, 3H), 5.31 (d, J = 5.4 Hz, 1H), 4.83 (d, J = 5.4 Hz, 1H), 3.24 (s, 3H), 2.86 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.9, 133.1, 130.9, 129.9, 128.2, 127.9, 127.3, 127.1, 127.1, 123.3, 90.1, 53.8, 41.6, 30.7. IR (film) ν cm^{-1} 2921, 1334, 1180, 1142, 1123, 971. HRMS (ESI) calcd for $C_{14}H_{16}NO_4S_2$ (M + H^+) m/z 326.0515, found 326.0512.

***trans*-2-Methyl-4-(methanesulfonyl)-3-(naphthalen-1-yl)-1,2-thiazetidine 1,1-dioxide (7b).** White solid, mp 180–182 °C. Yield: 13 mg, 33%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 8.5 Hz, 1H), 7.97–7.90 (m, 3H), 7.67–7.61 (m, 1H), 7.60–7.52 (m, 2H), 5.46 (d, J = 5.5 Hz, 1H), 5.30 (d, J = 5.5 Hz, 1H), 3.18 (s, 3H), 2.88 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.0, 130.8, 130.6, 129.2, 129.0, 127.4, 126.6, 125.5, 124.8, 122.2, 90.3, 50.7, 42.1, 31.0. IR (film) ν cm^{-1} 2922, 1458, 1333, 1174, 1146, 960. HRMS (ESI) calcd for $C_{14}H_{16}NO_4S_2$ (M + H^+) m/z 326.0515, found 326.0515.

***trans*-2-Methyl-4-(methanesulfonyl)-3-phenyl-1,2-thiazetidine 1,1-dioxide (7c).** Colorless oil. Yield: 17 mg, 46%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54–7.51 (m, 2H), 7.48–7.43 (m, 3H), 5.23 (d, J = 5.2 Hz, 1H), 4.66 (d, J = 5.2 Hz, 1H), 3.22 (s, 3H), 2.82 (s, 3H). ^{13}C NMR (400 MHz, $CDCl_3$) δ 133.7, 129.9, 129.5, 126.9, 90.0, 53.4, 41.5, 30.6. IR (film) ν cm^{-1} 2960, 1577, 1497, 1457, 1332, 1182, 1147, 1005, 963, 763, 727, 698. HRMS (ESI) calcd for $C_{10}H_{13}NNaO_4S_2$ (M + H^+) m/z 298.0178, found 298.0177.

***cis*- and *trans*-2-Methyl-4-(methanesulfonyl)-3-(2-nitrophenyl)-1,2-thiazetidine 1,1-dioxide (7d).** Yellowish solid, mp 48–50 °C. Yield: 17 mg, 43%.

***cis*-Isomer:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30–7.25 (m, 4H), 5.81 (d, J = 8.0 Hz, 1H), 5.30 (d, J = 8.0 Hz, 1H), 2.89 (s, 3H), 2.77 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.4, 134.7, 130.9, 129.6, 128.3, 125.9, 91.1, 54.4, 42.6, 32.1.

***trans*-Isomer:** ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30–7.25 (m, 4H), 5.44 (d, J = 6.0 Hz, 1H), 5.16 (d, J = 6.1 Hz, 1H), 3.26 (s, 3H), 2.82 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.8, 134.4, 130.7, 128.4, 126.2, 125.1, 86.9, 50.2, 40.1, 31.2.

IR (film) ν cm^{-1} 2930, 1528, 1497, 1342, 1193, 1166, 1144, 965. HRMS (ESI) calcd for $C_{10}H_{13}N_2O_6S_2$ (M + H^+) m/z 321.0210, found 321.0207.

IR (film) ν cm^{-1} 2930, 1528, 1497, 1342, 1193, 1166, 1144, 965. HRMS (ESI) calcd for $C_{10}H_{13}N_2O_6S_2$ (M + H^+) m/z 321.0210, found 321.0207.

***trans*-2-Methyl-4-(methanesulfonyl)-3-(3-nitrophenyl)-1,2-thiazetidine 1,1-dioxide (7e).** White solid, mp 160–162 °C. Yield: 9 mg, 21%. ^{1}H NMR (400 MHz, $CDCl_3$) 8.44 (dd, J = 1.8, 1.8 Hz, 1H), 8.33 (dd, J = 8.2, 1.2 Hz, 1H), 7.91 (d, J = 7.7 Hz, 1H), 7.70 (dd, J = 8.0, 8.0 Hz, 1H), 5.23 (d, J = 5.6 Hz, 1H), 4.75 (d, J = 5.6 Hz, 1H), 3.28 (s, 3H), 2.90 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.0, 136.4, 132.9, 130.8, 124.8, 121.7, 89.8, 52.3, 41.6, 31.5. ESI-HRMS: 321.0207. IR (film) ν cm^{-1} 2921, 1348, 1181, 1143, 963. HRMS (ESI) calcd for $C_{10}H_{13}N_2O_6S_2$ (M + H^+) m/z 321.0210, found 321.0207.

***trans*-2-Methyl-4-(methanesulfonyl)-3-(4-nitrophenyl)-1,2-thiazetidine 1,1-dioxide (7f).** White solid, mp 122–123 °C. White solid. R_f = 0.2 (PE : EA = 3 : 1). Yield: 15 mg, 38%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, J = 8.8 Hz, 2H), 7.74 (d, J = 8.7 Hz, 2H), 5.20 (d, J = 5.5 Hz, 1H), 4.75 (d, J = 5.5 Hz, 1H), 3.28 (s, 3H), 2.90 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.8, 141.0, 127.8, 124.7, 89.8, 52.2, 41.7, 31.5. IR (film) ν cm^{-1} 2919, 1523, 1348, 1181, 1143, 963. HRMS (ESI) calcd for $C_{10}H_{13}N_2O_6S_2$ (M + H^+) m/z 321.0210, found 321.0205.

***trans*-3-([1,1′-Biphenyl]-4-yl)-2-methyl-4-(methanesulfonyl)-1,2-thiazetidine 1,1-dioxide (7g).** White solid, mp 38–40 °C. Yield: 30 mg, 69%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.3 Hz, 2H), 7.59 (d, J = 8.4 Hz, 2H), 7.59–7.45 (m, 5H), 5.26 (d, J = 5.4 Hz, 1H), 4.71 (d, J = 5.4 Hz, 1H), 3.24 (s, 3H), 2.85 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.0, 139.9, 132.5, 128.9, 128.2, 127.9, 127.4, 127.1, 90.1, 53.3, 41.5, 30.6. IR (film) ν cm^{-1} 2921, 1487, 1452, 1331, 1185, 1147, 962. HRMS (ESI) calcd for $C_{16}H_{18}NO_4S_2$ (M + H^+) m/z 352.0672, found 352.0666.

***trans*-3-(4-Methoxyphenyl)-2-methyl-4-(methanesulfonyl)-1,2-thiazetidine 1,1-dioxide (7h).** Yellowish oil. Yield: 12 mg, 31%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (d, J = 8.7 Hz, 2H), 6.96 (d, J = 8.7 Hz, 2H), 5.18 (d, J = 5.3 Hz, 1H), 4.62 (d, J = 5.3 Hz, 1H), 3.83 (s, 3H), 3.22 (s, 3H), 2.78 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 160.9, 128.4, 125.3, 114.9, 90.2, 55.4, 53.3, 41.4, 30.3. IR (film) ν cm^{-1} 2921, 1330, 1171, 1147, 964. HRMS (ESI) calcd for $C_{11}H_{16}NO_5S_2$ (M + H^+) m/z 306.0464, found 306.0466.

***trans*-3-(4-Bromophenyl)-2-methyl-4-(methanesulfonyl)-1,2-thiazetidine 1,1-dioxide (7i).** Yellowish oil. Yield: 18 mg, 40%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.5 Hz, 2H), 7.41 (d, J = 8.4 Hz, 2H), 5.18 (d, J = 5.4 Hz, 1H), 4.62 (d, J = 5.4 Hz, 1H), 3.23 (s, 3H), 2.82 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.9, 132.7, 128.5, 124.2, 89.9, 52.8, 41.5, 30.8. IR (film) ν cm^{-1} 2920, 1329, 1147, 1120, 963. HRMS (ESI) calcd for $C_{10}H_{13}BrNO_4S_2$ (M + H^+) m/z 353.9464, found 353.9460.

***trans*-2-Cyclohexyl-4-(methanesulfonyl)-3-phenyl-1,2-thiazetidine 1,1-dioxide (7k).** White solid, mp 82–83 °C. Yield: 20 mg, 46%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58–5.56 (m, 2H), 7.46–7.38 (m, 3H), 5.07 (d, J = 5.0 Hz, 1H), 4.82 (d, J = 5.0 Hz, 1H), 3.39–3.28 (m, 1H), 3.20 (s, 3H), 2.04–1.16 (m, 10H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.1, 129.6, 129.4, 126.7, 89.4, 57.0, 50.2, 41.5, 31.6, 30.3, 25.2, 24.3, 24.0. IR (film) ν cm^{-1} 2924, 1453, 1383, 1331, 1175, 1144, 962. HRMS (ESI) calcd for $C_{15}H_{22}NO_4S_2$ (M + H$^+$) m/z 344.0985, found 344.0984.

***trans*-2-Benzyl-4-(methanesulfonyl)-3-phenyl-1,2-thiazetidine 1,1-dioxide (7l).** Yellowish solid, mp 107–108 °C. Yield: 20 mg, 45%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47–7.44 (m, 2H), 7.41–7.39 (m, 3H), 7.31–7.26 (m, 5H), 5.20 (d, J = 5.0 Hz, 1H), 4.69 (d, J = 5.0 Hz, 1H), 4.36 (d, J = 14.5 Hz, 1H), 4.25 (d, J = 14.5 Hz, 1H), 3.19 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.0, 133.1, 129.8, 129.4, 128.9, 128.8, 128.5, 127.0, 89.9, 51.8, 49.0, 41.3. IR (film) ν cm^{-1} 2920, 1496, 1457, 1332, 1178, 1148, 961. HRMS (ESI) calcd for $C_{16}H_{18}NO_4S_2$ (M + H$^+$) m/z 352.0672, found 352.0671.

***trans*-2-(*tert*-Butyl)-4-(methanesulfonyl)-3-(2-nitrophenyl)-1,2-thiazetidine 1,1-dioxide (7m).** White solid, mp 177–178 °C. Yield: 2 mg, 4%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17 (dd, J = 8.0, 1.0 Hz, 1H), 8.00 (dd, J = 8.2, 0.9 Hz, 1H), 7.78 (dd, J = 7.7, 7.7 Hz, 1H), 7.58 (ddd, J = 8.0, 8.0, 1.3 Hz, 1H), 5.91 (d, J = 5.1 Hz, 1H), 5.01 (d, J = 5.1 Hz, 1H), 3.26 (s, 3H), 1.32 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.4, 134.3, 133.0, 130.4, 128.5, 125.4, 90.5, 58.8, 43.0, 40.7, 27.7. IR (film) ν cm^{-1} 2976, 2922, 1530, 1334, 1171, 1149, 961. HRMS (ESI) calcd for $C_{13}H_{19}N_2O_6S_2$ (M + H$^+$) m/z 363.0679, found 363.0673.

***trans*-2-Isopropyl-4-(methanesulfonyl)-3-(4-nitrophenyl)-1,2-thiazetidine 1,1-dioxide (7n).** Colorless oil. Yield: 14 mg, 32%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (d, J = 8.8 Hz, 2H), 7.79 (d, J = 8.7 Hz, 2H), 5.08 (d, J = 5.2 Hz, 1H), 4.90 (d, J = 5.2 Hz, 1H), 3.68 (hept, J = 6.4 Hz, 1H), 3.25 (s, 3H), 1.34 (d, J = 6.4 Hz, 3H), 1.14 (d, J = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.7, 143.3, 127.7, 124.7, 89.0, 50.4, 49.1, 41.7, 21.6, 20.4. IR (film) ν cm^{-1} 2925, 1526, 1348, 1185, 1145, 1111, 962. HRMS (ESI) calcd for $C_{12}H_{17}N_2O_6S_2$ (M + H$^+$) m/z 349.0523, found 349.0525.

***trans*-3-Isopropyl-4-(methanesulfonyl)-2-(4-methylphenyl)-1,2-thiazetidine 1,1-dioxide (7o).** Yellowish oil. Yield: 11 mg, 14%. ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.19 (d, J = 8.4 Hz, 2H), 7.07 (d, J = 8.4 Hz, 2H), 5.16 (d, J = 4.7 Hz, 1H), 4.32 (dd, J = 4.7, 4.7 Hz, 1H), 3.29 (s, 3H), 2.34 (s, 3H), 2.32–2.29 (m, 1H), 1.07 (d, J = 6.9 Hz, 3H), 1.05 (d, J = 6.8 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 136.4, 132.9, 130.4, 120.7, 84.2, 54.3, 41.4, 30.2, 20.9, 18.8, 16.7. IR (film) ν cm^{-1} 2922, 1655, 1514, 1328, 1220, 1047, 966. HRMS (ESI) calcd for $C_{13}H_20NO_4S_2$ (M + H$^+$) m/z 318.0828, found 318.0825.

General procedure for the [2^s + 2^i + 2^i] annulations

To a 10 mL reaction tube were added *N*-methyl imine **2** (1.5 mmol) and DABCO (112 mg, 1.0 mmol). Under a nitrogen atmosphere at −78 °C, dry dichloromethane (4 mL) was added, followed by slow addition of methanesulfonyl chloride (**1b**) (115 mg, 0.08 mL, 1 mmol). The resultant mixture was stirred at −78 °C for 6 h, and then was slowly warmed to room temperature. After adding dichloromethane (5 mL), washing with brine (10 mL), drying over $MgSO_4$, and concentrating at reduced pressure, the residue was purified by column chromatography on silica gel with PE and EA as the eluent to afford 4-aza-δ-sultam.

***rel*(3*S*,5*S*,6*S*)- and *rel*(3*R*,5*S*,6*S*)-2,4-Dimethyl-6-(methanesulfonyl)-3,5-di(naphthalen-2-yl)-1,2,4-thiadiazinane 1,1-dioxide (8a and 9a).** Inseparable mixtures. Colorless crystals, mp 105–110 °C. Total yield: 126 mg, 51%.

*rel(3S,5S,6S)-Isomer (**8a**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06–7.44 (m, 14H), 5.38 (s, 1H), 4.91 (d, J = 8.3 Hz, 1H), 4.61 (d, J = 8.3 Hz, 1H), 2.89 (s, 3H), 2.87 (s, 3H), 1.89 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.6, 133.7, 133.61, 133.4, 133.03, 132.84, 129.4, 129.1, 128.9, 128.8, 128.25, 128.15, 127.76, 127.72, 126.93, 126.8, 126.7, 126.6, 125.6, 125.2, 83.6, 79.2, 66.7, 43.9, 39.6, 32.9.

*rel(3R,5S,6S)-Isomer (**9a**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.06–7.44 (m, 14H), 5.25 (d, J = 1.9 Hz, 1H), 5.12 (d, J = 2.0 Hz, 1H), 4.42 (s, 1H), 3.48 (s, 3H), 2.84 (s, 3H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.9, 133.2, 133.01, 132.8, 132.6, 130.4, 129.3, 129.3, 129.0, 128.6, 128.3, 128.2, 128.0, 127.72, 127.68, 127.1, 127.0, 126.88, 126.5, 125.7, 84.9, 81.9, 63.9, 40.2, 40.1, 31.9.

IR and HRMS. IR (film) ν cm^{-1} 2928, 1318, 1165, 1141, 1020, 964. HRMS (ESI) calcd for $C_{26}H_{27}N_2O_4S_2$ (M + H$^+$) m/z 495.1407, found 495.1400.

***rel*(3*S*,5*S*,6*R*)- and *rel*(3*R*,5*S*,6*S*)-Dimethyl-6-(methanesulfonyl)-3,5-diphenyl-1,2,4-thiadiazinane 1,1-dioxide (8c and 9c).** Inseparable mixtures. Colorless crystals. Mp 140–144 °C. Yield: 104 mg, 50%.

*rel(3S,5S,6R)-Isomer (**8c**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, J = 7.2 Hz, 1H), 7.73–7.68 (m, 1H), 7.59 (d, J = 7.0 Hz, 2H), 7.57–7.31 (m, 6H), 5.26 (s, 1H), 4.75 (d, J = 9.0 Hz, 1H), 4.36 (d, J = 9.0 Hz, 1H), 2.83 (s, 3H), 2.81 (s, 3H), 1.85 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.8, 139.1, 135.9, 129.6, 129.1, 128.8, 128.64, 128.62, 82.8, 79.0, 67.0, 44.0, 39.4, 32.4.

*rel(3R,5S,6S)-Isomer (**9c**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57–7.44 (m, 5H), 7.40–7.31 (m, 5H), 5.06 (d, J = 1.9 Hz, 1H), 4.90 (d, J = 1.9 Hz, 1H), 4.22 (s, 1H), 3.42 (s, 3H), 2.78 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.4, 133.1, 129.6, 129.11, 129.10, 128.8, 128.64, 128.63, 84.8, 81.5, 63.9, 40.02, 39.97, 31.8.

IR and HRMS. IR (film) ν cm^{-1} 2922, 1456, 1313, 1227, 1154, 1135, 1116, 1000, 963. HRMS (ESI) calcd for $C_{18}H_{22}N_2NaO_4S_2$ (M + H$^+$) m/z 417.0913, found 417.0907.

***rel*(3*R*,5*S*,6*R*)-2,4-Dimethyl-6-(methanesulfonyl)-3,5-bis-(2-nitrophenyl)-1,2,4-thiadiazinane 1,1-dioxide (10d).** Yellow oil. Yield: 124 mg, 51%. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.23 (d, J = 7.9 Hz, 1H), 7.93 (dd, J = 8.0, 8.0 Hz, 2H), 7.80 (dd, J = 7.7, 7.7 Hz, 1H), 7.75 (dd, J = 7.6, 7.6 Hz, 1H), 7.65 (d, J = 7.7 Hz, 1H), 7.60 (dd, J = 7.7, 7.7 Hz, 2H), 6.10 (d, J = 7.0 Hz, 1H), 5.88 (s, 1H), 5.02 (d, J = 7.0 Hz, 1H), 3.28 (s, 3H), 3.02 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.1, 149.5, 133.5, 132.8, 130.18, 130.06, 129.75, 129.69, 129.5, 129.2, 125.6, 125.1, 79.8, 54.2, 42.6, 38.99, 38.92, 34.7.

IR (film) ν cm^{-1} 2928, 1529, 1345, 1318, 1165, 1142, 967. HRMS (ESI) calcd for $C_{18}H_{21}N_4O_8S_2$ (M + H^+) *m*/*z* 485.0795, found 485.0790.

***rel*(3*S*,5*S*,6*R*)-2,4-Dimethyl-6-(methanesulfonyl)-3,5-bis(3-nitrophenyl)-1,2,4-thiadiazinane 1,1-dioxide (8e).** A trace amount was isolated as a yellow oil, therefore, only the ^{1}H NMR is provided. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45 (s, 1H), 8.38 (s, 1H), 8.30 (d, *J* = 10.4 Hz, 1H), 8.26 (d, *J* = 8.4 Hz, 1H), 7.98 (t, *J* = 7.5 Hz, 2H), 7.69 (dd, *J* = 7.9, 7.9 Hz, 1H), 7.63 (d, *J* = 8.0, 8.0 Hz, 1H), 5.25 (s, 1H), 4.71 (d, *J* = 7.7 Hz, 1H), 4.61 (d, *J* = 7.7 Hz, 1H), 3.23 (s, 3H), 2.85 (s, 3H), 1.88 (s, 3H).

***rel*(3*R*,5*S*,6*S*)-2,4-Dimethyl-6-(methanesulfonyl)-3,5-bis(3-nitrophenyl)-1,2,4-thiadiazinane 1,1-dioxide (9e).** Colorless crystals. Mp 110–120 °C. Yield: 99 mg, 41%, isolated from the reaction in THF. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.49 (s, 1H), 8.39–8.31 (m, 2H), 8.26 (dd, *J* = 8.2, 2.3 Hz, 1H), 8.09 (d, *J* = 7.7 Hz, 1H), 7.92 (d, *J* = 7.7 Hz, 1H), 7.82 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.74 (dd, *J* = 8.0, 8.0 Hz, 1H), 6.17 (d, *J* = 3.8 Hz, 1H), 5.21 (d, *J* = 3.8 Hz, 1H), 4.85 (s, 1H), 3.34 (s, 3H), 2.91 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.9, 147.7, 138.6, 136.4, 134.86, 134.81, 130.1, 129.9, 124.4, 123.9, 123.5, 123.2, 80.3, 79.7, 61.2, 39.7, 38.4, 33.4. IR (film) ν cm^{-1} 2927, 1530, 1349, 1315, 1229, 1154, 1139, 968. HRMS (ESI) calcd for $C_{18}H_{21}N_4O_8S_2$ (M + H^+) *m*/*z* 485.0795, found 485.0782.

***rel*(3*R*,5*S*,6*S*)-2,4-Dimethyl-6-(methanesulfonyl)-3,5-bis(4-nitrophenyl)-1,2,4-thiadiazinane 1,1-dioxide (9f).** Colorless crystals. Mp 197–199 °C. Yield: 34 mg, 14%. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.36 (d, *J* = 8.5 Hz, 2H), 8.29 (d, *J* = 8.5 Hz, 2H), 7.87 (d, *J* = 8.6 Hz, 2H), 7.78 (d, *J* = 8.5 Hz, 2H), 6.11 (d, *J* = 4.6 Hz, 1H), 5.17 (d, *J* = 4.6 Hz, 1H), 4.98 (s, 1H), 3.32 (s, 3H), 2.93 (s, 3H), 2.33 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.7, 147.4, 143.6, 140.7, 131.0, 129.5, 123.6, 123.4, 80.0, 61.1, 40.4, 38.4, 34.3, 31.5. IR (film) ν cm^{-1} 2922, 1314, 1144, 1035, 1006. HRMS (ESI) calcd for $C_{18}H_{21}N_4O_8S_2$ (M + H^+) *m*/*z* 485.0795, found 485.0796.

***rel*(3*R*,5*R*,6*S*)- and *rel*(3*R*,5*S*,6*S*)-3,5-Di([1,1′-biphenyl]-4-yl)-2,4-dimethyl-6-(methanesulfonyl)-1,2,4-thiadiazinane 1,1-dioxide (8g and 9g).** Inseparable mixtures. White solid. Mp 158–160 °C. Yield: 131 mg, 48%.

*rel(3R,5R,6S)-Isomer (**8g**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78–7.36 (m, 18H), 5.34 (s, 1H), 4.86 (d, *J* = 8.8 Hz, 1H), 4.47 (d, *J* = 8.9 Hz, 2H), 2.92 (s, 3H), 2.90 (s, 4H), 1.97 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 82.8, 79.1, 66.7, 44.0, 39.5, 32.6 (only for aliphatic carbons).

*rel(3R,5S,6S)-Isomer (**9g**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78–7.36 (m, 18H), 5.14 (d, *J* = 1.8 Hz, 1H), 5.00 (d, *J* = 1.9 Hz, 1H), 4.37 (s, 1H), 3.47 (s, 3H), 2.97 (s, 3H), 2.36 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 84.7, 81.3, 63.7, 40.1, 38.9, 31.9 (only for aliphatic carbons).

IR and HRMS. IR (film) ν cm^{-1} 2922, 1486, 1367, 1317, 1167, 1141, 968. HRMS (ESI) calcd for $C_{30}H_{31}N_2O_4S_2$ (M + H^+) *m*/*z* 547.1720, found 547.1702.

***rel*(3*R*,5*R*,6*S*)- and *rel*(3*R*,5*S*,6*S*)-3,5-Bis(4-methoxyphenyl)-2,4-dimethyl-6-(methanesulfonyl)-1,2,4-thiadiazinane 1,1-dioxide (8h and 9h).** Inseparable mixtures. Yellowish oil. Yield: 36 mg, 15%.

*rel(3R,5R,6S)-Isomer (**8h**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.39 (m, 4H), 6.96–6.89 (m, 4H), 5.21 (s, 1H), 4.69 (d, *J* = 9.2 Hz, 1H), 4.28 (d, *J* = 9.2 Hz, 1H), 3.83 (s, 3H), 3.82 (s, 3H), 2.82 (s, 3H), 2.80 (s, 3H), 1.83 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 82.0, 78.9, 66.8, 55.3, 55.2, 44.1, 39.1, 32.0 (only for aliphatic carbons).

*rel(3R,5S,6S)-Isomer (**9h**).* ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49–7.39 (m, 4H), 6.96–6.89 (m, 4H), 5.00 (d, *J* = 1.9 Hz, 1H), 4.81 (d, *J* = 1.9 Hz, 1H), 4.10 (s, 1H), 3.86 (s, 3H), 3.81 (s, 3H), 3.40 (s, 3H), 2.74 (s, 3H), 2.19 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 85.4, 81.2, 63.4, 55.5, 55.4, 42.0, 39.9, 31.5 (only for aliphatic carbons).

IR and HRMS. IR (film) ν cm^{-1} 2922, 1512, 1384, 1317, 1306, 1258, 1152, 1144, 974. HRMS (ESI) calcd for $C_{20}H_{26}N_2NaO_6S_2$ (M + H^+) *m*/*z* 477.1124, found 477.1114.

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