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Pyridine-*N*-oxide catalyzed asymmetric *N*-acylative desymmetrization of sulfonimidamides†Cui-Mei Guo,^a Fang-Yuan Zhang,^a Yin Tian,^{id}*^b Ming-Sheng Xie^{id}*^a and Hai-Ming Guo^{id}*^a

A highly efficient enantioselective *N*-acylative desymmetrization of sulfonimidamides with chloroformates was reported using chiral 4-arylpyridine-*N*-oxide as the catalyst, affording *N*-acylative sulfonimidamides with sulfur(vi)-stereocenters in high yields and excellent enantioselectivities. Experiments and DFT calculations support an acyl transfer mechanism, and the nucleophilic substitution of sulfonimidamide by the *O*-acyloxypyridinium cation intermediate is the enantio-determining step of the reaction. The reaction features variability for acyloxy groups and compatibility with moisture.

Introduction

Sulfonimidamides are bioisosteres of sulfonamides, in which the sulfur(vi)-bonded oxygen atom is replaced by a nitrogen atom (Fig. 1). This modification brings significant changes, because the achiral sulfur(vi) center becomes a stereogenic S(vi) center, and chemical space on S(vi) expands to three dimensions. Meanwhile, the structure of the substituent group on the newly introduced nitrogen atom is tunable, allowing for adjusting physicochemical properties.^{1,2} When sulfonamide **LY181984**,^{3–5} which exhibits good antitumor activity, becomes its bioisostere sulfonimidamide, the activity of (–)-isomer **I** significantly increases, while the activity of (+)-isomer **II** obviously decreases, indicating that the absolute configuration of the S(vi) center for sulfonimidamide has a vital impact on bioactivity. Representative bioactive molecules are carboxypeptidase A (CP-A) inhibitor,⁶ BACE 1 inhibitor,⁷ and NLRP3 antagonist⁸ (Fig. 1). Thus, developing an efficient method to construct chiral sulfonimidamides is highly desirable.

For the construction of optically active sulfonimidamides, the traditional approach mainly relied on a chiral substrate strategy, through the nucleophilic substitution reaction of chiral sulfonimidoyl halides with different amines.^{9–14} In 2021, Willis and co-workers reported that *para*-methoxybenzyl (PMB)

protected *N,N'*-sulfonimidamides are prone to rapid tautomerization under a variety of conditions, such as in toluene, upon treatment with KOH, or upon addition of trifluoroacetic acid, creating opportunities for asymmetric catalysis. Using bis-quaternized cinchona alkaloid **Cat. 1** as the phase-transfer catalyst, Willis and co-workers developed the first catalytic enantioselective desymmetrization of sulfonimidamides *via* an asymmetric alkylation reaction, generating enantiomerically enriched sulfonimidamides in excellent yields and enantioselectivities (Scheme 1a).¹⁵ In 2024, Laconsay, Di Maso, Shaw, and co-workers reported a desymmetrization of cyclic sulfonimidamides by palladium-catalyzed asymmetric allylation using a Trost-type ligand.¹⁶ In addition to catalytic asymmetric alkylation and allylation reactions, the reported strategies mainly focused on constructing enantioenriched *N*-acylated sulfonimidamides.

As for nitrogen nucleophiles, direct catalytic enantioselective *N*-acylation reaction is challenging,^{17–22} mainly due to the strong nucleophilicity of amines leading to strong background reactions. In 2023, Lim, Toste, Sigman, and co-workers reported a palladium-catalyzed enantioselective aryl-carbonylation of sulfonimidamides with aryl and heteroaryl iodides, affording diverse

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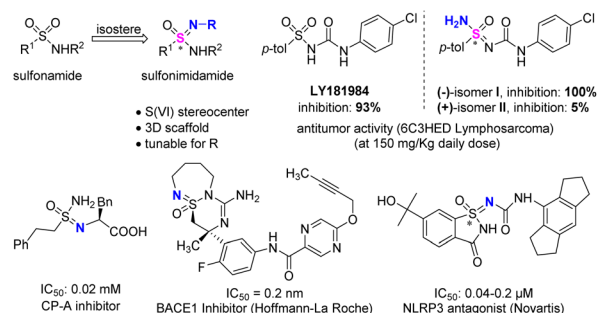
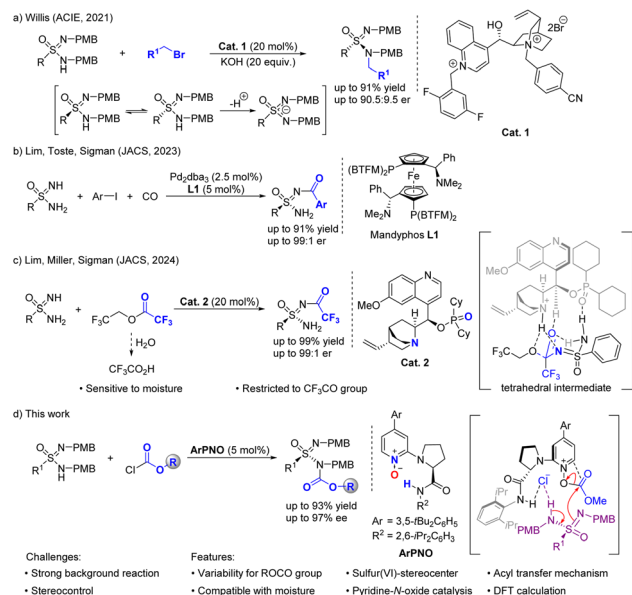


Fig. 1 Representative sulfonimidamides possessing bioactivity.



Scheme 1 Asymmetric synthesis of sulfonimidamides using different strategies and catalysts.

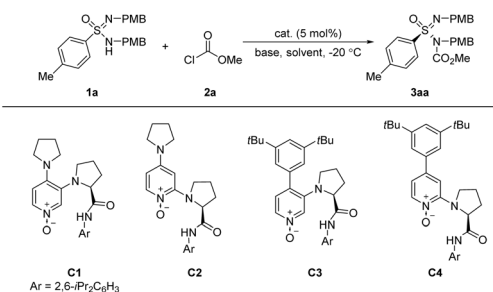
enantioenriched mono-acylated sulfonimidamides in excellent yields and enantioselectivities (Scheme 1b).²³ With unprotected sulfonimidamides as the reactants, a small amount of undesired bis-acylation products was generated. In 2024, Lim, Miller, Sigman, and co-workers developed the desymmetrization of unprotected sulfonimidamides *via* asymmetric acylation with a cinchona-phosphinate catalyst **Cat. 2**, delivering enantioenriched mono-acylation sulfonimidamides in excellent results with no observed bis-acylation products (Scheme 1c).²⁴ In the cinchona-phosphinate catalyst, the quinuclidine nitrogen and the phosphinate oxygen served as hydrogen-bond acceptors to anchor the sulfonimidamide substrate, promoting the nucleophilic addition of sulfonimidamide to 2,2,2-trifluoroethyl trifluoroacetate for the formation of a tetrahedral intermediate. Obviously, the proposed mechanism is different from the widely accepted acyl transfer mechanism.^{25–29} The electrophile was limited to 2,2,2-trifluoroethyl trifluoroacetate, resulting in the introduction of only trifluoroacetyl groups into the products, which restricted the structural diversity of the products. Meanwhile, trace moisture may hydrolyze 2,2,2-trifluoroethyl trifluoroacetate to generate trifluoroacetic acid, leading to a decrease in conversion and enantioselectivity. Thus, the catalytic system was sensitive to moisture. Considering that *N*-acyl sulfonimidamides are potential carboxylic acid bioisosteres with tunable properties,³⁰ developing a new and effective asymmetric acylative desymmetrization of sulfonimidamides for the construction of sulfur(vi)-stereocenters remains a worthy endeavor.

Chiral pyridine-*N*-oxides,^{31–36} with oxygen atoms as nucleophilic sites, have been developed as efficient nucleophilic organocatalysts since the pioneering study by Spivey and co-workers in 2017, in which an atropisomeric 4-dimethylamino-pyridine (DMAP)-*N*-oxide was applied to the kinetic resolution of 2-substituted indolines by *N*-sulfonylation.³⁷ Afterwards, our

group developed *L*-prolinamide derived chiral DMAP-*N*-oxides and 4-aryl-pyridine-*N*-oxides (ArPNO) as acyl transfer catalysts, and applied them in asymmetric *C*-acylation, *O*-acylation, and sulfinylation reactions.^{38–44} As far as we know, chiral pyridine-*N*-oxide has never been used in the asymmetric *N*-acylation reaction. For the asymmetric *N*-acylation desymmetrization of sulfonimidamides with chloroformates, stereocontrol is challenging due to their strong background reaction.²⁴ Therefore, we assume that an asymmetric acyl transfer reaction using an *L*-prolinamide derived chiral pyridine-*N*-oxide as a nucleophilic catalyst could be used to address the aforementioned challenge, where pyridine-*N*-oxide attacks the chloroformate to give the *O*-acyloxypyridinium cation, and N-H in the prolinamide moiety forms an H-bond interaction with sulfonimidamide, resulting in a synergistic effect (Scheme 1d). Herein, with chloroformates as the acylation reagent, we report a highly enantioselective *N*-acylation desymmetrization of sulfonimidamides using chiral ArPNO as the bifunctional catalyst, allowing efficient construction of sulfur(vi)-stereocenters in excellent yields and enantioselectivities. The reaction follows an acyl transfer mechanism, with variability for acyloxy groups and compatibility with moisture.

Results and discussion

Initially, the reaction of sulfonimidamide **1a** and methyl chloroformate **2a** was selected as the exemplary reaction (Table 1). In the absence of catalyst, the *N*-acylation reaction could occur and gave *N*-acylation product **3aa** in 19% yield at -20°C for 48 h, indicating that the background reaction was relatively strong (entry 1). When *L*-prolinamide derived 3-substituted 4-pyrrolidinopyridine (PPY)-*N*-oxide **C1** was used as the catalyst, desired sulfonimidamide **3aa** was obtained in 30% yield and 26% ee (entry 2). Then, the position of the *L*-prolinamide moiety and the electronegativity of the substituent at the C4 position for the pyridine-*N*-oxides (**C2–C4**) were evaluated (entries 3–5), and 2-substituted 4-arylpyridine-*N*-oxide (ArPNO) **C4** could afford product **3aa** with better results in 40% yield and 74% ee (entry 5). Changing the solvent from DCM to CHCl_3 improved the enantioselectivity of sulfonimidamide **3aa** with 82% ee (entry 6). Afterwards, different bases were added (entries 7–9), and Cs_2CO_3 could deliver product **3aa** with better results in 94% yield and 84% ee (entry 8). Upon lowering the reaction temperature to -50°C and prolonging the reaction time to 96 h, the enantioselectivity of **3aa** reached 92% ee, although the yield decreased to 51% (entry 10). When 4 Å MS was used as the additive, the *N*-acylative desymmetrization reaction proceeded well, affording the corresponding sulfonimidamide **3aa** in 90% yield and 92% ee (entry 11). When 5 μL of H_2O was added, the yield and enantioselectivity of the reaction were maintained (entry 12). Even with the addition of 15 μL of H_2O , a similar good result could still be obtained (entry 13), indicating that this reaction is compatible with moisture. When 25 μL of H_2O was added, the yield of product **3aa** was reduced from 89% to 75% (entry 13 vs. 14). However, upon further addition of 4 Å MS to 50 mg, the yield of product **3aa** increased from 75% to 88% (entry 14 vs. 15). The experimental results suggested that the

Table 1 Optimization of the reaction conditions^a


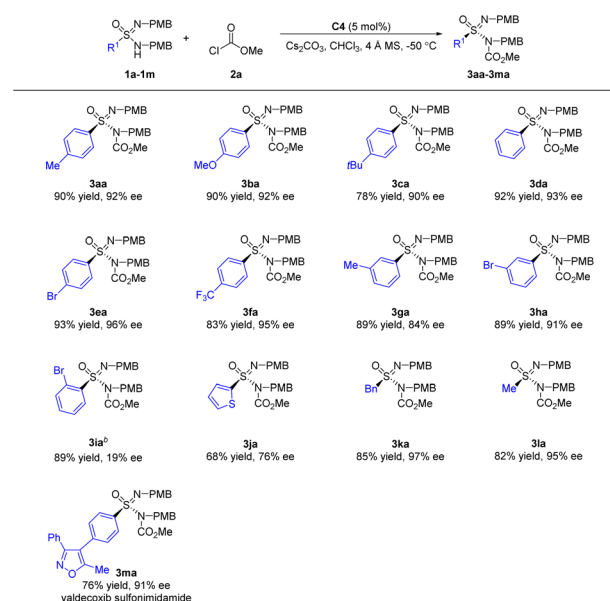
Entry	Cat.	Solvent	Base	Yield ^b (%)	ee ^c (%)
1	—	DCM	—	19	0
2	C1	DCM	—	30	26
3	C2	DCM	—	25	50
4	C3	DCM	—	43	—17
5	C4	DCM	—	40	74
6	C4	CHCl ₃	—	51	82
7	C4	CHCl ₃	KOH	71	55
8	C4	CHCl ₃	Cs ₂ CO ₃	94	84
9	C4	CHCl ₃	Et ₃ N	38	79
10 ^d	C4	CHCl ₃	Cs ₂ CO ₃	51	92
11 ^{d,e}	C4	CHCl ₃	Cs ₂ CO ₃	90	92
12 ^{d,e,f}	C4	CHCl ₃	Cs ₂ CO ₃	90	92
13 ^{d,e,g}	C4	CHCl ₃	Cs ₂ CO ₃	89	92
14 ^{d,e,h}	C4	CHCl ₃	Cs ₂ CO ₃	75	92
15 ^{d,h,i}	C4	CHCl ₃	Cs ₂ CO ₃	88	92

^a Unless otherwise noted, reaction conditions were as follows: **1a** (0.05 mmol), **2a** (0.075 mmol), **Cat.** (5 mol%), base (1.0 equiv.) in solvent (0.5 mL) at $-20\text{ }^{\circ}\text{C}$ for 48 h. ^b The yields were determined by ¹H NMR analysis of the crude reaction mixture using 1,3,5-trimethoxybenzene as the internal standard. ^c The ee values were determined by chiral HPLC analysis. ^d At $-50\text{ }^{\circ}\text{C}$ for 96 h. ^e 4 Å MS (25 mg) was added. ^f PMB = *p*-methoxybenzyl. ^g 5 μL H₂O was added. ^h 15 μL H₂O was added. ⁱ 25 μL H₂O was added. ^j 4 Å MS (50 mg) was added.

major function of 4 Å MS is to sequester the water of the catalyst system.

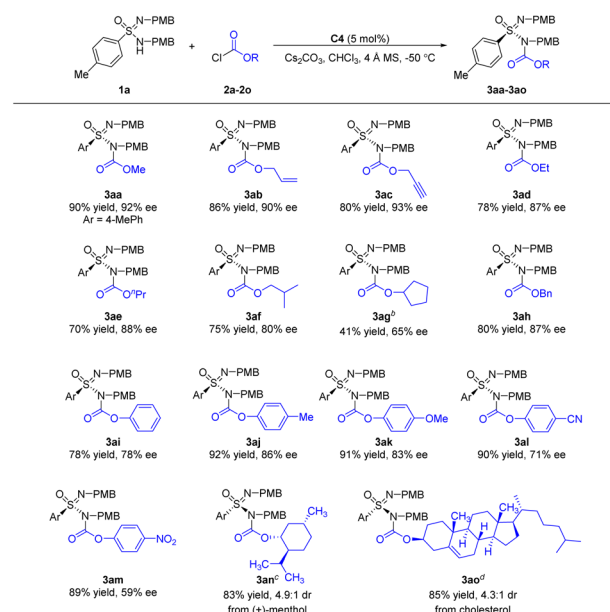
Under the optimized reaction conditions (Table 1, entry 11), the scope of sulfonimidamides was explored (Scheme 2). For the exemplary reaction, the desired *N*-acylative sulfonimidamide **3aa** was isolated in 90% yield and 92% ee. For sulfonimidamides **1b–f** bearing electron-donating or electron-withdrawing substituents at the *para*-position of the aryl moieties, the adducts **3ba–3fa** were obtained in 78–93% yields and 90–96% ee. 3-Bromophenyl derived sulfonimidamide **1h** exhibited better enantioselectivity than 3-methylphenyl derived sulfonimidamide **1g**. 2-Bromophenyl derived sulfonimidamide **1i** afforded product **3ia** in good yield, albeit with low enantioselectivity. In the case of 2-thienyl derived sulfonimidamide **1j**, the *N*-acylative desymmetrization reaction proceeded well to deliver adduct **3ja**. When aliphatic benzyl and methyl derived sulfonimidamides **1k** and **1l** were used, the corresponding adducts **3ka** and **3la** were obtained in 82–85% yields and 95–97% ee. Complex sulfonimidamide **1m** was also a suitable reactant, affording valdecoxib analogue **3ma** in good results with 91% ee.

Subsequently, the scope of chloroformates was evaluated (Scheme 3). Allyl chloroformate **2b** and propargyl chloroformate

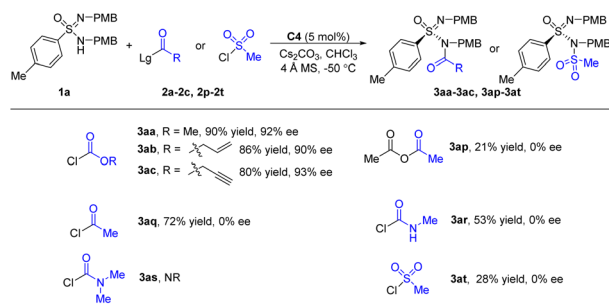


Scheme 2 Substrate scope of sulfonimidamides^a. ^aReaction conditions: **1** (0.1 mmol), **2a** (0.15 mmol), **C4** (5 mol%), Cs₂CO₃ (0.1 mmol) and 4 Å MS (50 mg) in CHCl₃ (1 mL) at $-50\text{ }^{\circ}\text{C}$ for 96 h. Isolated yields are reported. The ee values were determined by chiral HPLC analysis. ^bAt r.t. for 48 h.

2c reacted smoothly in the *N*-acylative desymmetrization reactions, generating adducts **3ab** and **3ac** in 80–86% yields and 90–93% ee. Straight chain alkane derived chloroformates **2d–e** could give adducts **3ad–3ae** in 87–88% ee. In the case of



Scheme 3 Substrate scope of chloroformates^a. ^aReaction conditions: **1a** (0.1 mmol), **2** (0.15 mmol), **C4** (5 mol%), Cs₂CO₃ (0.1 mmol) and 4 Å MS (50 mg) in CHCl₃ (1 mL) at $-50\text{ }^{\circ}\text{C}$ for 96 h. Isolated yields are reported. The ee values were determined by chiral HPLC analysis. ^bAt $-20\text{ }^{\circ}\text{C}$. ^c*ent*-**C4** (5 mol%) at r.t. for 72 h. ^d*ent*-**C4** (5 mol%) at $0\text{ }^{\circ}\text{C}$ for 72 h.

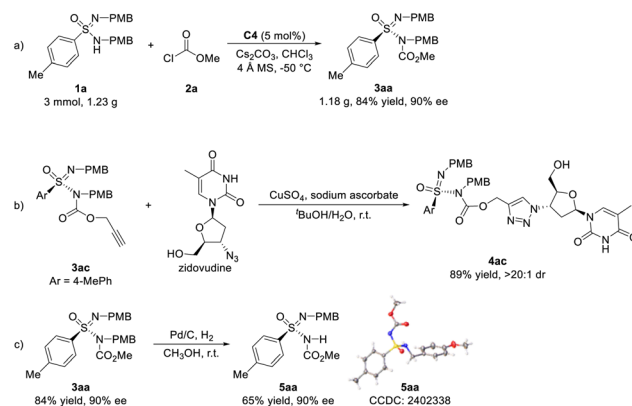


Scheme 4 Substrate scope of electrophiles^a. ^aReaction conditions: **1a** (0.1 mmol), **2** (0.15 mmol), **C4** (5 mol%), Cs_2CO_3 (0.1 mmol) and 4 Å MS (50.0 mg) in CHCl_3 (1 mL) at -50°C for 96 h. Isolated yields are reported. The ee values were determined by chiral HPLC analysis.

branched alkene derived chloroformate **2f**, the corresponding adduct **3af** was generated with a slight decrease in enantioselectivity. As for cyclic alkane derived chloroformate **2g**, the desired *N*-acylative product **3ag** was obtained in moderate enantioselectivity. Benzyl chloroformate **2h** was a suitable electrophile. When phenyl chloroformate **2i** was employed, the desired adduct **3ai** was afforded in 78% yield and 78% ee. As for aryl chloroformates **2j–m**, the enantioselectivity of chloroformates with electron-rich aromatic groups (**2j–k**) was superior to that of electron-deficient aromatic groups (**2l–m**). With *ent*-**C4** as the catalyst, complex chloroformates **2n** and **2o**, which were derived from (+)-menthol and cholesterol, were also suitable electrophiles, affording the corresponding *N*-acylative adducts **3an** and **3ao** in good results.

Different electrophiles including acid anhydrides, acyl chlorides, carbamic chlorides, and sulfonyl chlorides were also evaluated in the *N*-acylative desymmetrization reactions (Scheme 4). With acetic anhydride **2p** as the electrophile, the corresponding adduct **3ap** was obtained in low yield as a racemic mixture. The reactivity of acyl chloride was higher than that of the acid anhydride, and a racemic product was still formed. When methylcarbamic chloride **2r** was used, the desired product **3ar** was obtained in 53% yield and 0% ee. In the case of dimethylcarbamic chloride **2s**, the reaction did not occur. The above comparative experiments among **2p**, **2q**, **2r**, and **2s** indicated that the oxygen atom in the O–Me moiety of methyl chloroformate **2a** plays a vital role. Sulfonyl chloride **2t** also afforded the corresponding adducts **3at** without stereocontrol. As a result, the desymmetrization reactions have high structural requirements for electrophilic reagents, and chloroformates with variability for ester groups can achieve satisfactory stereocontrol.

To further evaluate the synthetic utility of this catalytic system, gram-scale synthesis of sulfonimide **3aa** was performed. Using 5 mol% of catalyst **C4**, 3 mmol of sulfonimide **1a** reacted with methyl chloroformate **2a** for an extended time of 8 days, affording the corresponding *N*-acylative product **3aa** in 1.18 g (84% yield) with 90% ee (Scheme 5a). Considering that *N*-acylative product **3ac** has a terminal alkyne group, a Cu(I)-catalyzed click reaction with drug molecule zidovudine was carried out, affording the corresponding ligation product

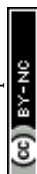


Scheme 5 (a) Gram-scale synthesis of **3aa** (b and c) further synthetic transformations. Reaction conditions: (a) **1a** (3 mmol), **2a** (4.5 mmol), **C4** (5 mol%), Cs_2CO_3 (3 mmol) and 4 Å MS (1.5 g) in CHCl_3 (30 mL) at -50°C for 8 days. (b) **3ac** (0.1 mmol), zidovudine (0.15 mmol), CuSO_4 (20 mol%) and sodium ascorbate (60 mol%) in $t\text{-BuOH}/\text{H}_2\text{O}$ (1 : 1, v/v, 1 mL) at r.t. for 12 h. (c) **3aa** (0.1 mmol), Pd/C (0.3 mmol) and H_2 (1 atm) in CH_3OH (1 mL) at r.t. for 48 h.

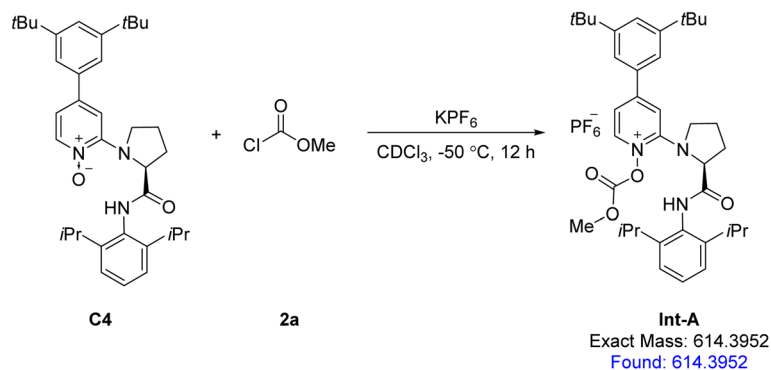
triazole **4ac** in 89% yield and >20 : 1 dr (Scheme 5b). By treatment with Pd/C, the hydrogenation of sulfonimide **3aa** could proceed to remove a PMB protecting group, giving sulfonimide **5aa** in 65% yield with no loss of enantiomeric purity (Scheme 5c). The absolute configuration of the sulfonimide **5aa** was determined to be the *R* configuration via single-crystal X-ray diffraction, which also proved that the absolute configuration of chiral sulfonimide **3aa** was *R*-configuration.

To probe the mechanism of the *N*-acylative desymmetrization reaction, the reaction of catalyst **C4** and methyl chloroformate **2a** was analyzed by HRMS, where the peak at m/z 614.3952 corresponded to the possible formation of *O*-acyloxypyridinium cation **Int-A** (Fig. 2a). Afterwards, the kinetic order of each reaction component was established by studying the initial rates of reaction (Fig. 2b). Catalyst **C4** and sulfonimide **1a** exhibited approximately first-order rate dependence, suggesting that they were involved in the rate-determining step and nucleophilic attack of sulfonimide **1a** to *O*-acyloxypyridinium cation **Int-A** may be the rate-determining step of the reaction. In the case of methyl chloroformate **2a**, the rate showed an approximately zero-order kinetic effect in the reaction, indicating that the formation of *O*-acyloxypyridinium cation **Int-A** between methyl chloroformate **2a** and catalyst **C4** was not involved in the rate-determining step. Furthermore, Cs_2CO_3 exhibited approximately first-order rate dependence, which suggested that the addition of Cs_2CO_3 was beneficial for binding HCl. In addition, examination of the ^1H NMR spectrum of sulfonimide **1a** in CDCl_3 at room temperature showed that the two PMB groups appeared to be chemically and magnetically equivalent, which suggests that sulfonimide **1a** is prone to rapid tautomerization in CDCl_3 (see Fig. S1 in the ESI† for details).

To gain insight into the reaction mechanism catalyzed by chiral 4-aryl-pyridine-*N*-oxide **C4**, density functional theory



a) HRMS experiment



b) Kinetic order of each reaction component

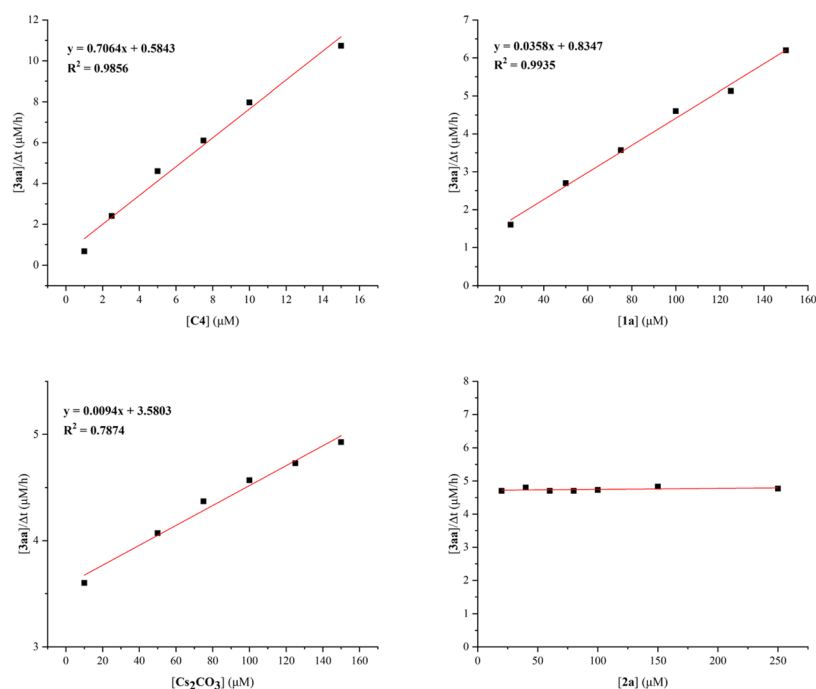


Fig. 2 (a) HRMS experiment shows the formation of intermediate **Int-A**. (b) Kinetic orders of **C4**, **1a**, Cs_2CO_3 and **2a**.

(DFT) is utilized to explore and analyze the reaction process. As described in Fig. 3, the mechanism consists of a two-step process: nucleophilic attack of catalyst **C4** on methyl chloroformate **2a** to form the *O*-acyloxypyridinium cation (step 1), and nucleophilic substitution of sulfonimidamide **1a** by the *O*-acyloxypyridinium cation (step 2). In step 1, methyl chloroformate **2a** and free catalyst **C4** approach each other to form a reactant complex **RC**. With the oxygen atom as the nucleophilic site, the nucleophilic attack of catalyst **C4** on methyl chloroformate **2a** occurred along the *Si* face of methyl chloroformate **2a** *via* transition state **TS1** with the energy barrier of 5.3 kcal mol⁻¹. Simultaneously, the chloride anion generated *via* cleavage of the C–Cl bond of **2a** was trapped and stabilized by the H-bond from amide N–H on **C4**, and intermediate **IM1** was then formed.

With the addition of sulfonimidamide **1a**, the H-bond between the chloride anion and N–H of sulfonimidamide **1a** was formed, which generated the intermediate **IM2**. Then, nucleophilic substitution of sulfonimidamide **1a** by the *O*-acyloxypyridinium cation occurred *via* transition state **TS2** with the energy barrier of 6.6 kcal mol⁻¹. Simultaneously, the C–O single bond of the *O*-acyloxypyridinium cation was cleaved, and the electron of N–H in **1a** was transferred to S–N to form S=N. Finally, the product complex **PC** was generated, which then released the catalyst **C4** and (*R*)-**3aa**·HCl. With the help of Cs_2CO_3 , (*R*)-**3aa** was finally generated from (*R*)-**3aa**·HCl.

The geometry information of the enantio-determining transition states and free energy were further analyzed to understand the stereoselectivity of the reaction (Fig. 4). As described in Fig. 4a and b, the relative free energy of (*Si*,*R*)-**TS2** was 4.9 kcal mol⁻¹ ($\Delta\Delta G^\ddagger$) lower than that of (*Si*,*S*)-**TS2**, which indicated that



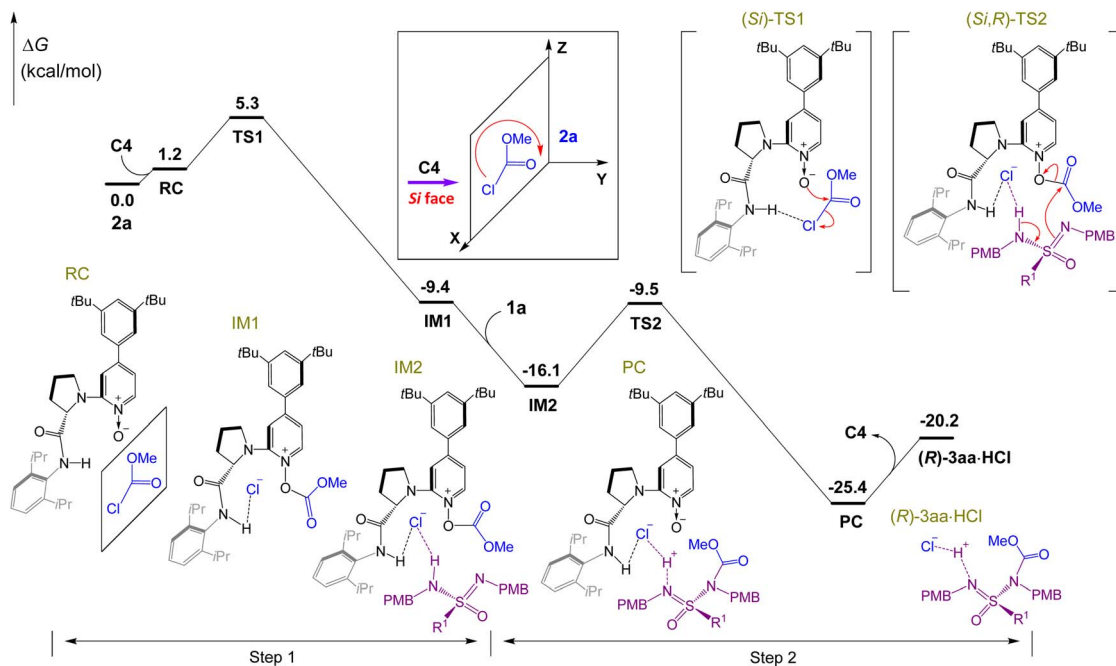


Fig. 3 DFT-computed relative energy profiles (kcal mol^{-1}) of C4 nucleophilic attack along the Si-face of the substrate **2a** plane at the M06-2X/6-31G(d,p)/SMD(trichloromethane) level. $R^1 = 4\text{-MePh}$.

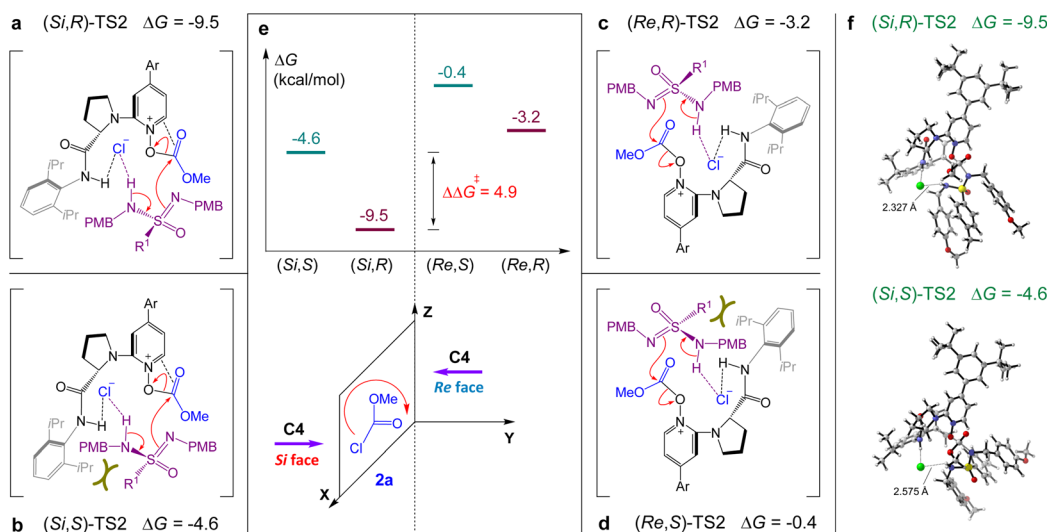


Fig. 4 DFT-computed relative free energies (ΔG , kcal mol^{-1}) of enantio-determining transition states (direction, configuration)-TS2 along C4-catalyzed pathways at the M06-2X/6-31G(d,p)/SMD(trichloromethane) level. Ar = 3,5-*t*Bu₂Ph, $R^1 = 4\text{-MePh}$.

(*R*)-**3aa** was the dominant adduct and displayed good agreement with the experimental results (Table 1, entry 11). In the case of (*Si,S*)-TS2, the observed increase of the energy barrier was mainly caused by the obvious steric repulsion between the 2,6-*i*Pr₂Ph group and R^1 group of sulfonimidamide, which also resulted in the increase of the H-bond length between the chloride anion and N-H of sulfonimidamide. When catalyst C4 attacked methyl chloroformate **2a** from the *Re* face (Fig. 4c and d), the relative free energies of transition states (*Re,R*)-TS2 and (*Re,S*)-TS2 were much higher than those of (*Si,R*)-TS2 and (*Si,S*)-TS2, resulting in the *Si* face attack as the dominant attack

pathway. Compared with (*Si,R*)-TS2 and (*Re,R*)-TS2 (Fig. 4a and c), the increase of the energy barrier was mainly caused by the lack of π - π interaction between the pyridinium cation of C4 and C=O of the *O*-acyloxypyridinium cation in (*Re,R*)-TS2, which is displayed in ESI Fig. S2.†

Conclusions

In summary, we have developed an asymmetric *N*-acylative desymmetrization of sulfonimidamides with chloroformates for the construction of sulfur(vi)-stereocenters. With 5 mol%



ArPNO as the catalyst, diverse *N*-acylative sulfonimidamides were obtained in high yields (up to 93% yield) and excellent enantioselectivities (up to 97% ee). In the presence of ArPNO, the mechanism of the reaction is an acyl transfer mechanism, which is different from Lim, Miller, and Sigman's work. Using chloroformates as the electrophiles, the structure of the ester moiety is variable, which provides an opportunity for post modification of the *N*-acylative products. Furthermore, the catalyzed reaction is compatible with moisture. Control experiments and DFT calculations revealed that the nucleophilic substitution of sulfonimidamide by the *O*-acyloxy pyridinium cation intermediate is the enantio-determining step of the reaction. The high enantioselectivity of the reaction is governed by steric factors, and the H-bonding interactions between the N–H of the amide moiety of the catalyst, chloride ion, and N–H of sulfonimidamide play a vital role.

Data availability

The exploratory investigation results, experimental procedures, computational data, and characterization data are available.

Author contributions

Methodology, M.-S. X. and H.-M. G.; investigation, C.-M. G. and F.-Y. Z.; computational studies, Y. T.; writing – original draft, M.-S. X., C.-M. G. and Y. T.; writing – review & editing, C.-M. G., M.-S. X., Y. T., and H.-M. G.; supervision, M.-S. X., Y. T., and H.-M. G.

Conflicts of interest

There are no conflicts to declare.

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