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# Catalyst Control over S(IV)-stereogenicity via Carbene-derived Sulfinyl Azolium Intermediates

Benpeng Li,[▽] Junyuan Hu,[▽] Minghong Liao, Qin Xiong, Yaqi Zhang, Yonggui Robin Chi, Xinglong Zhang,* and Xingxing Wu*

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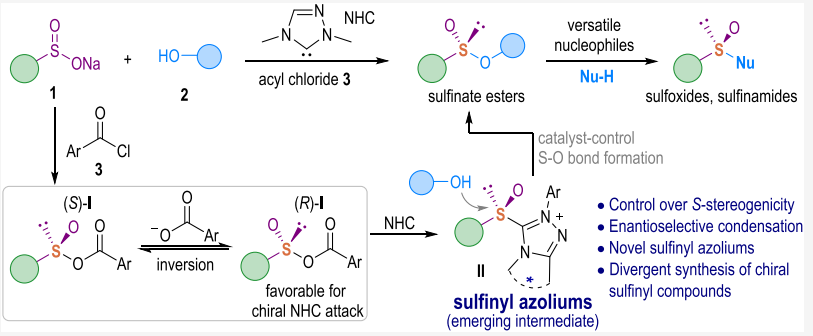


**ABSTRACT:** Stereoselective synthesis utilizing small-molecule catalysts, particularly N-heterocyclic carbene (NHC), has facilitated swift access to enantioenriched molecules through diverse activation modes and NHC-bound reactive intermediates. While carbonyl derivatives, imines, and "activated" alkenes have been extensively investigated, the exploration of heteroatom-centered analogues of NHC-bound intermediates has long been neglected, despite the significant potential for novel chemical transformations they offer once recognized. Herein, we disclose a carbene-catalyzed new activation mode by generating unique sulfinyl azolium intermediates from carbene nucleophilic addition to in situ-generated mixed sulfinic anhydride intermediates. Combined experimental and computational mechanistic investigations pinpoint the chiral NHC-catalyzed formation of sulfinyl azolium intermediate as the enantio-determining step. The novel "S"-based carbene reactive intermediate imparts high efficiency for the catalytic construction of sulfur-stereogenic compounds, giving rise to sulfinate esters with high yields and enantioselectivities under mild conditions. Notably, distinct from most of the NHC-catalyzed enantioselective transformations focusing on the "C" central chiral products, our study realizes a unique carbene-catalyst control over chiral "S" stereocenters via direct asymmetric S−O bond formation for the first time. Furthermore, these sulfinyl-containing products could serve as versatile synthetic platforms for enantioenriched *S*-stereogenic functional molecules and exhibit remarkable antibacterial activities against rice plant pathogens, which is valuable for the development of novel agrochemical agents.



## INTRODUCTION

Stereoselective synthesis by means of small-molecule catalysts has developed tremendously as a privileged synthetic platform capable of delivering scaffolds with high levels of chemo- and enantioselectivity over the past decades.[1−3] N-heterocyclic carbene (NHC) has proven to be one of the most broadly investigated organocatalysts in this context, allowing for rapid access to functional molecules with remarkable stereocontrol.[4−10] Up to now, a diverse array of activation modes and NHC-bound reactive intermediates have been extensively studied, leading to numerous novel chemical transformations (Figure 1A).[4−14] For instance, the classical Breslow and homoenolate intermediates have enabled benzoin reaction, Stetter reaction, as well as other processes involving C−C/heteroatom bond formations (Figure 1A(i)).[15−19] Additionally, acyl azoliums and their derived azolium intermediates (e.g., azolium enolate and unsaturated acyl azolium species) have also found broad applications in acyl transfer reactions, cascade annulations, etc.[20−24] It is worth noting that most of these elegant applications have focused on the selective activation of carbonyl moieties to generate various classical carbene-bound reactive intermediates. Considerable efforts have also been directed toward exploring the activation of noncarbonyl substrates for elegant synthesis. Independent research by Fu,[25] Glorius,[26] Lupton,[27,28] Matsuoka,[29,30] and

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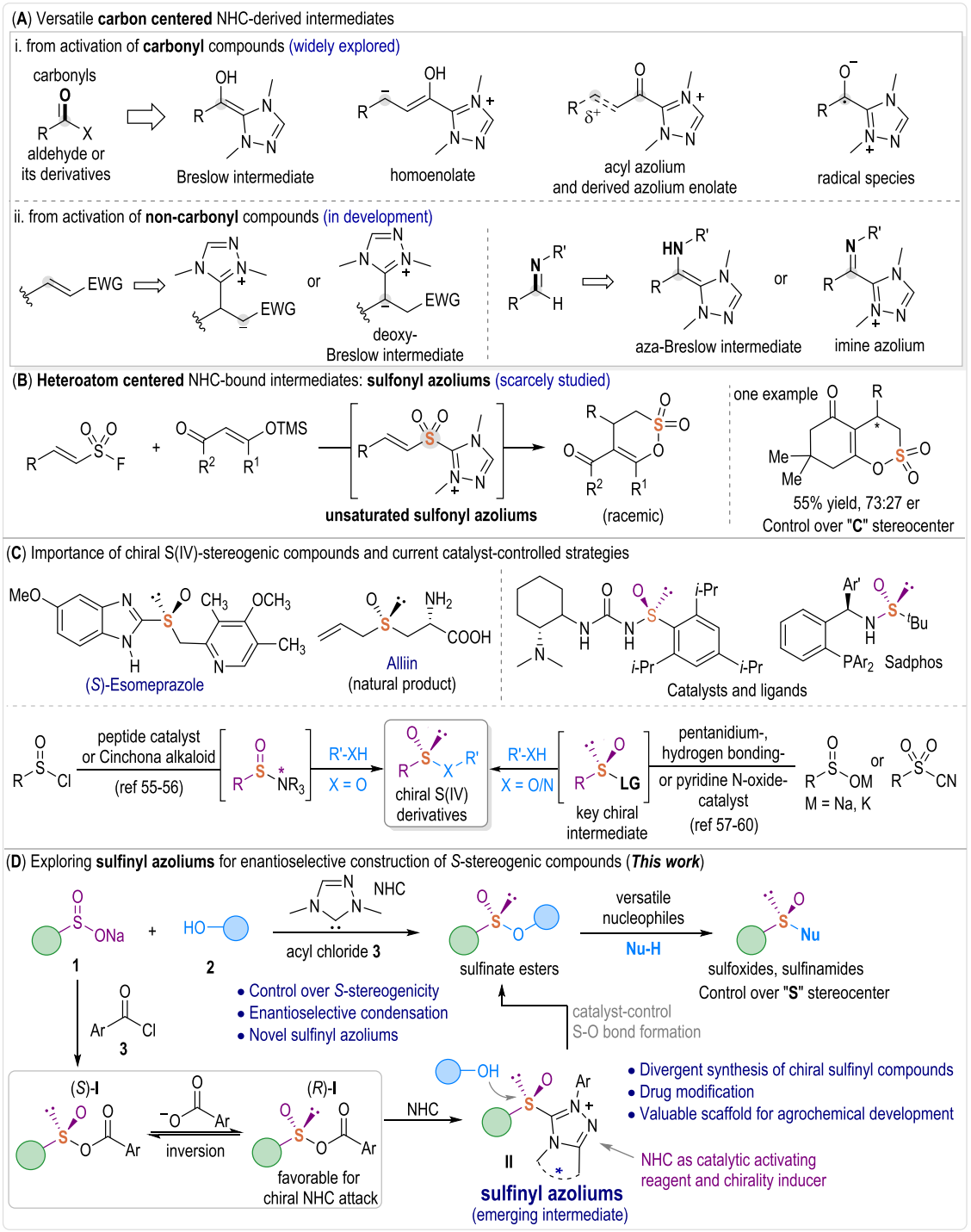


**Figure 1.** (A) Representative carbon-centered NHC-bound reactive intermediates. (B) Pioneering study on the carbene-derived sulfonyl azolium intermediate. (C) Importance of *S*-chiral compounds and current catalytic synthetic approaches. (D) Our proposed approach for preparation of various *S*-stereogenic compounds enabled by unprecedent sulfinyl azoliums by carbene activation of mixed sulfinic anhydrides.

others[31−33] have revealed nucleophilic activation to the electron-deficient double bonds, such as acrylates, to trigger various transformations via deoxy-Breslow or other activated intermediates (Figure 1A(ii), left). Recently, the groups of Lupton,[34] Biju,[35−37] Fu,[38,39] and Suresh[40,41] have explored a distinct aza-Breslow intermediate and its derived imine azolium intermediates to achieve the preparation of various N-containing heterocycles.[42] In stark contrast to these advancements relying on carbon-atom-based NHC-bound intermediates, limited attention has been given to generating heteroatom-centered analogues (e.g., sulfur, phosphorus, etc.) of NHC-bound intermediates, which, once realized, would stimulate significant opportunities for the design of numerous chemical transformations for (enantioselective) C-heteroatom bond formations. To the best of our knowledge, there is only one example, investigated by Lupton et al.,[43] which involves a novel sulfonyl analogue of $\alpha$, $\beta$-unsaturated acyl azoliums, namely, $\alpha,\beta$-unsaturated sulfonyl azoliums, resulting in the preparation of $\delta$-sultones through reaction with enolates via NHC organocatalysis (Figure 1B). In addition, the pioneering


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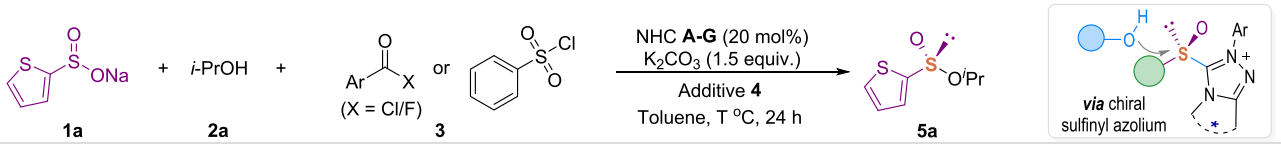
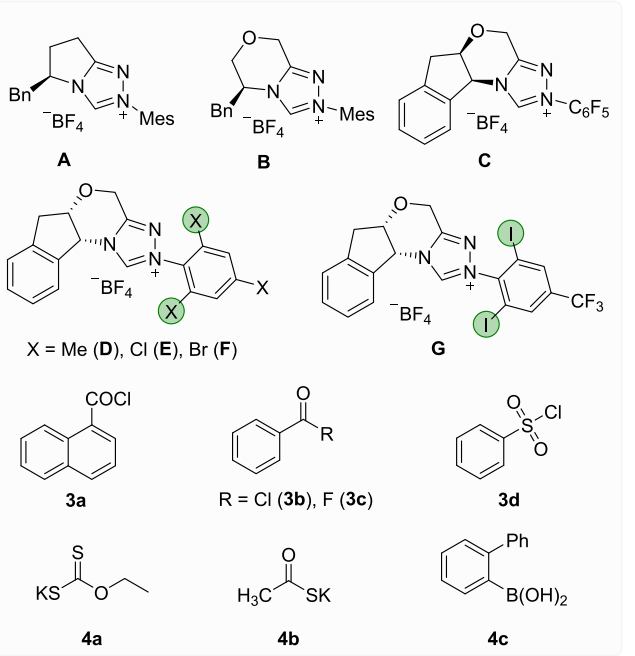
**Scheme 1. Optimization of the Carbene-catalyzed Enantioselective Condensation of Sulfinate 1a and Alcohol 2a[a]**




| Entry | NHC | 3 | Add. | T (°C) | Yield (%) | E.r. |
|---|---|---|---|---|---|---|
| 1 | None | **3a** | None | -20 | 21 | 50:50 |
| 2 | **A** | **3a** | None | -20 | 93 | 41:59 |
| 3 | **B** | **3a** | None | -20 | 91 | 45:55 |
| 4 | **C** | **3a** | None | -20 | 77 | 41:59 |
| 5 | **D** | **3a** | None | -20 | 89 | 68:32 |
| 6 | **E** | **3a** | None | -20 | 96 | 71:29 |
| 7 | **F** | **3a** | None | -20 | 95 | 78:22 |
| 8 | **G** | **3a** | None | -20 | 98 | 82:18 |
| 9 | **G** | **3b** | None | -20 | 87 | 80:20 |
| 10 | **G** | **3c** | None | -20 | 19 | 80:20 |
| 11 | **G** | **3d** | None | -20 | 61 | 63:37 |
| 12 | **G** | **3a** | None | -40 | 97 | 88:12 |
| 13 | **G** | **3a** | None | -60 | 81 | 92:8 |
| 14 | **G** | **3a** | **4a** | -60 | 30 | 95:5 |
| 15 | **G** | **3a** | **4b** | -60 | 36 | 95:5 |
| 16 | **G** | **3a** | **4c** | -60 | 96 | 95:5 |




[a]The reactions were performed with sodium sulfinate **1a** (17.0 mg, 0.1 mmol, 1.0 equiv), alcohol **2a** (0.3 mmol, 3.0 equiv), NHC **A**−**G** (20 mol %), **3** (0.15 mmol, 1.5 equiv), $K_2CO_3$ (0.15 mmol, 1.5 equiv), additive **4** (0.05 mmol, 0.5 equiv), toluene (1.0 mL), 24 h. Isolated yields were reported. Er values were determined by chiral HPLC analysis. See the Supporting Information for details.

work by Lupton has demonstrated proof of concept on the enantioselective control with one example demonstrated in modest enantioselectivity for the synthesis of $\delta$-sultone product using a chiral NHC catalyst. Nevertheless, the research in this area still lags behind considerably. Further exploration of new activation modes of heteroatom-centered carbene-bound intermediates, particularly in a high enantioselective manner, is of immense interest.[43,44]

On the other hand, *S*(IV)-chiral scaffolds are ubiquitous in various natural products and bioactive compounds[45,46] and of great importance in the design of chiral catalysts/ligands for stereoselective synthesis (Figure 1C).[47−54] The catalytic construction of *S*-stereogenic compounds has thereby attracted extensive attention from chemists. In the pioneering reports by Miller/Ellman[55] and Toru/Shibata,[56] sulfinyl chlorides were utilized for the preparation of chiral sulfinate esters mediated by catalytic *N*-methylimidazole-containing peptides or stoichiometric amounts of cinchona alkaloids. To overcome the limited scope arising from the inherent highly reactive sulfinyl chlorides, very recently, Tan,[57] Yan,[58] Guo,[59] as well as we[60] have independently developed highly efficient approaches to access a broad range of chiral sulfinate esters and sulfinamides from the readily available and easily accessible sulfinates or sulfonyl cyanides.

Prompted by our extensive interest in the catalyst-controlled construction of intriguing sulfur-stereogenic compounds,[55−69] we envisioned the exploration of sulfinyl analogues of acyl azoliums to facilitate further carbene-catalyzed asymmetric bond formations for installation of a stereogenic sulfur atom. Specifically, the generation of classical acyl azoliums from stable carboxylic acids via in situ mixed anhydride formation has been well established for various reactions.[70−73] Inspired by this, we sought to employ a similar strategy to exploit their sulfur analogues, sulfinyl azoliums, through carbene nucleophilic addition to an in situ-generated mixed sulfinic anhydride intermediate (Figure 1D). Herein, we documented carbene organocatalytic control over sulfur stereogenicity by investigating a new sulfinyl azolium for asymmetric catalytic synthesis. A dynamic kinetic resolution process involving facile racemization of the mixed anhydride (**I**) under the assistance of aryl carboxylate and subsequent stereoselective formation of sulfinyl azoliums (**II**) confers high stereocontrol over the final S−O bond formation with alcohol nucleophiles. The resulting optically enriched sulfinate esters are afforded remarkably high yields and enantioselectivities under very mild conditions. It is worth noting that most of NHC-catalyzed enantioselective transformations focus on the "C" central chiral molecules. Our current study realizes a distinct carbene-catalyst control for the construction of chiral "S" stereocenters via direct asymmetric S−O bond formation for the first time. Furthermore, the obtained chiral products offer synthetic platforms for the rapid assembly of a broad range of enantioenriched *S*-stereogenic functional molecules and feature remarkable antibacterial activities against typical rice plant pathogens that are valuable for the development of novel agrochemical agents.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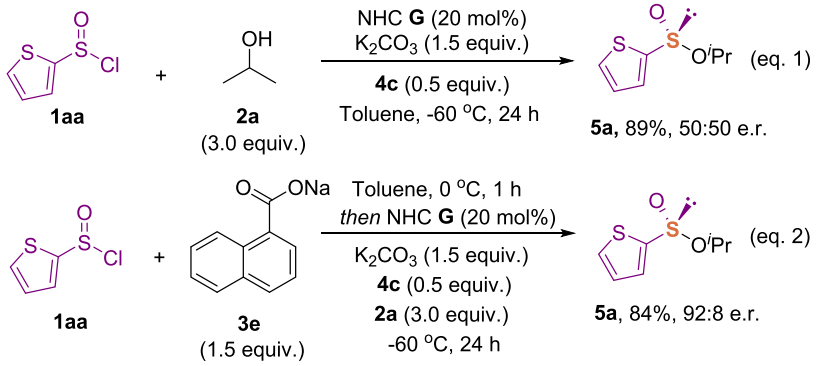
**Scheme 2. Control Experiments by Reaction with Sulfinyl Chloride 1aa**




## RESULTS AND DISCUSSION

We commenced our study to explore the direct asymmetric condensation of sodium sulfinate **1a** and alcohol **2a** under the catalysis of various NHCs. Acyl chloride **3a** was employed to activate readily stable sulfinate **1a** by the formation of the key sulfinyl mixed anhydride intermediate. A background reaction test conducted without the addition of a catalyst readily gave rise to the racemic sulfinate ester product **5a**, albeit in poor yield, implicating the generation of the crucial anhydride species. Subsequently, we investigated the feasibility of the formation of a new NHC-bound sulfinyl azolium intermediate and its capability in stereocontrol for the preparation of novel *S*-stereogenic compounds. Encouragingly, the use of chiral NHC precatalyst **A** effectively facilitated the coupling reaction to give the product **5a** in high yield and with a promising enantioselectivity of 41:59 er, as proof of our envisioned concept on the S-heteroatom-based azolium for asymmetric catalysis. Various NHC catalysts **B**−**F** were then examined (entries 3−7, also see Tables S1−S4 for more details) to develop a more efficient system for addressing the challenge of the stereoselective control. We were pleased to find that the indanol-based catalysts **D**−**F** were superior to access the desired product **5a** in relatively high selectivity (entries 5−7). We anticipated that the rational increase of the steric bulk of the X group on the N-aromatic moiety of NHC would enhance enantioselectivity based on the results obtained with NHCs **D**−**F**. Catalyst **G** with 2,6-diiodide substituents was therefore prepared and subjected to the catalytic reaction that further improved the er value to 82:18 and with an almost quantitative yield (entry 8). Notably, considering the tunable structure of the formed mixed sulfinyl anhydrides, we also engaged our efforts to screen a diverse set of acyl or sulfonyl halides **3b**−**3d** (also see the Supporting Information for more details), while we failed to find a more effective activating reagent (entries 9−11). Remarkably, the catalytic conditions show a high efficiency on the S−O bond formation, allowing us to demonstrate the viability of the catalytic reaction at a rather low temperature (−60 °C) to deliver product **5a** in 81% yield and an increased 92:8 enantioselectivity (entry 13). However, it is worth mentioning that a trace amount of product **5a** (less than 3% yield) could still be observed when the reaction was performed in the absence of catalyst NHC **G** at −60 °C for 24 h. Last, by evaluating the effects of a variety of additives (see Table S4 for more details), we were satisfied to obtain an optimal system involving boronic acid **4c** at −60 °C, enabling the preparation of chiral product **5a** in excellent yield (96%) and high enantioselectivity (95:5 er). The use of boronic acid **4c** notably accelerated the reaction and resulted in improved enantioselectivity from the kinetic study (see Figure S10 for more details), which might owe to the formation of noncovalent bond interaction with the mixed sulfinyl anhydride to facilitate the nucleophilic attack of NHC to anhydride species.[74−78]

Prompted by Miller/Ellman[55] and Toru/Shibata's[56] pioneering work, we embarked on a study to investigate the catalytic generation of sulfinyl azolium intermediate for stereocontrol of the sulfur-stereogenic center through carbene addition to sulfinyl chloride **1aa**. Under similar conditions as explored in Scheme 1, entry 16, the reaction gave rise to the desired product **5a** in 89% yield, while no enantioselectivity was observed (Scheme 2, eq 1). Intriguingly, the precombination of sodium 1-naphthoate (**3e**) and **1aa** for 1 h significantly enhanced the selectivity of the sulfinate ester **5a** with 92:8 er and good yield. This enhancement suggests the pivotal role of the formed sulfinyl mixed anhydride in the catalytic asymmetric synthesis, presumably by suppressing the uncatalyzed sulfinylations from the direct addition of alcohol nucleophile **2a** to substrate **1aa** (Scheme 2, eq 2, also see the Supporting Information for more details).

With the optimal reaction conditions in hand, we next studied the generality of the carbene-catalyzed synthesis of *S*-chiral products via sulfinyl azolium intermediates (Scheme 3). First, we were able to carry out a gram-scale reaction between **1a** and **2a** to afford the desired product **5a** in 90% yield (1.0 g) and without erosion of enantioselectivity. Then, a variety of substituents on the thienyl moiety were examined for the preparation of chiral sulfinate esters **5a**−**5e** (Scheme 3). For instance, substrates with methyl and phenyl groups were readily transformed to desired products **5b** and **5c** in high yield and enantioselectivity under optimal conditions. Thienyl sulfinate bearing an additional transferable Cl or Br group was also compatible in this reaction, delivering the corresponding products **5d** and **5e** with 80% yield, 95:5 er and 94% yield, 95:5 er, respectively. Reactions with benzothienyl or benzofuran sulfinates proceeded smoothly as well to furnish sulfinate esters **5f** and **5g** in good yields and optical purities. Moreover, phenyl-derived sulfinate analogues with a diverse set of substitutions could also afford the corresponding chiral sulfinate products **5h**−**5u** under optimal conditions. For instance, substrates bearing alkyl units (e.g., Me, Et, *i*Pr, *t*Bu) and phenyl or halogen moieties (F, Cl, Br, I) at the *para* position of the phenyl moiety were well tolerated, yielding the chiral *S*-stereogenic products **5h**−**5q** with 76−95% yields and high enantioselectivities. Moreover, *meta*-substituted analogues (**5r**−**5t**) and 2-naphthyl sulfinates (**5u**) could also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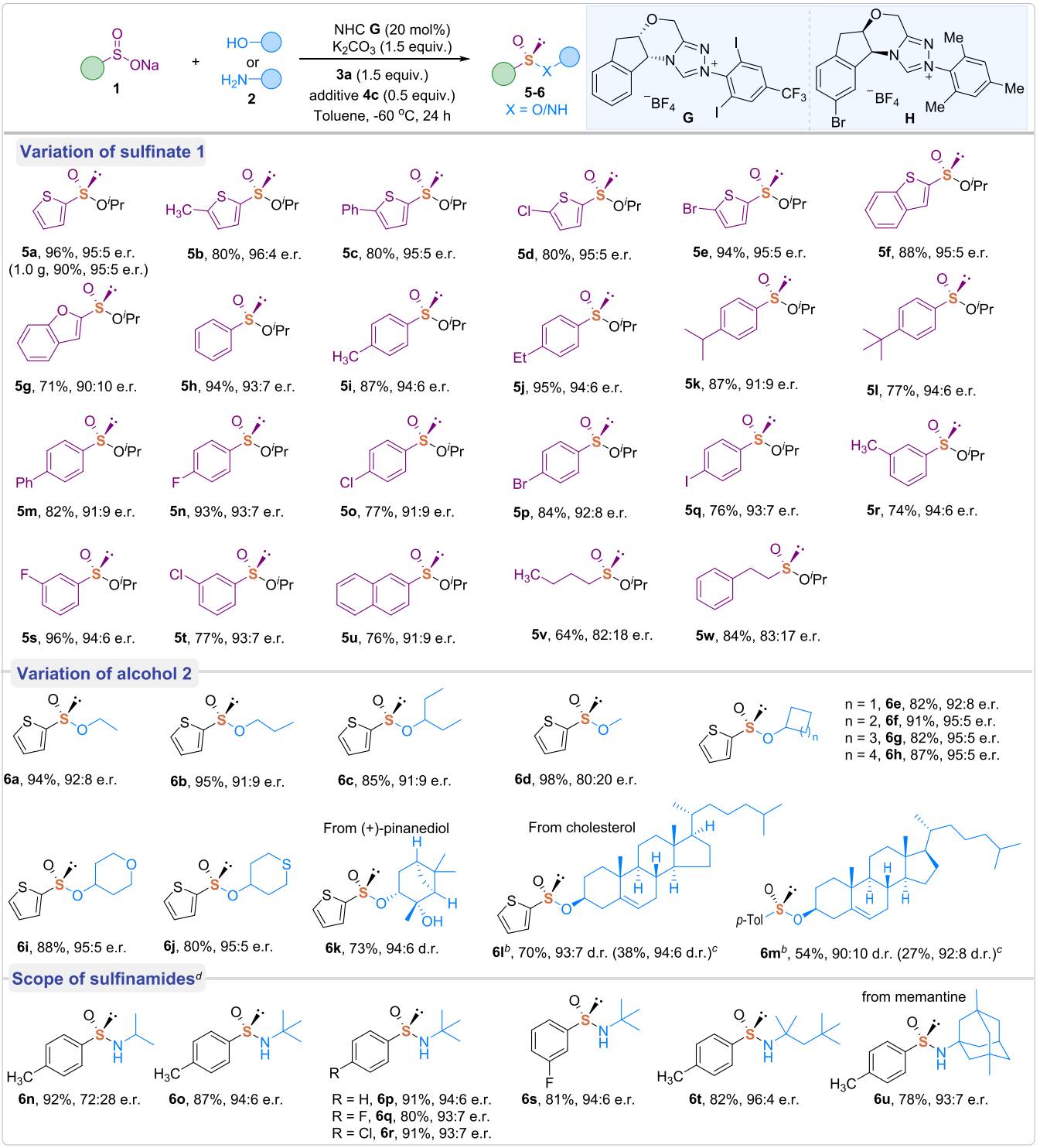
**Scheme 3. Substrate Scope of the Enantioselective Synthesis of *S*-chiral Sulfinate Esters and Sulfinamides**[a]




[a]Reaction conditions: sodium sulfinate **1** (0.1 mmol, 1.0 equiv), NHC **G** (13.94 mg, 20 mol %), alcohol **2** (0.3 mmol, 3.0 equiv), **3a** (28.6 mg, 0.15 mmol, 1.5 equiv), $K_2CO_3$ (20.7 mg, 0.15 mmol, 1.5 equiv), additive **4c** (9.9 mg, 0.05 mmol, 0.5 equiv), toluene (1.0 mL), 24 h at −60 °C. [b]Reactions were performed with the conditions as in Scheme 2, entry 2. [c]Reaction results in parentheses under optimal conditions. [d]These reactions were conducted with sodium sulfinate **1** (0.1 mmol, 1.0 equiv), NHC **H** (20 mol %), amine **2** (0.2 mmol, 2.0 equiv), **3b** (0.15 mmol, 1.5 equiv), $K_2CO_3$ (0.15 mmol, 1.5 equiv), toluene (1.0 mL), 2 h at −20 °C. See the Supporting Information for details.

deliver the *S*-chiral products with enantioselectivities ranging from 91:9 to 94:6 er. Notably, our protocol was also feasible for alkyl sulfinate substrates, as illustrated by the preparation of sulfinate esters **5v** and **5w**, albeit with modest enantioselectivity.

The generality of alcohol **2** was further explored with sulfinate **1a** utilized as the model substrate. EtOH, *n*-PrOH, and 3-pentanol were readily converted to the desired sulfinyl coupling products **6a**−**6c** in 85−95% yield and high enantioselectivity. Reaction with MeOH afforded the product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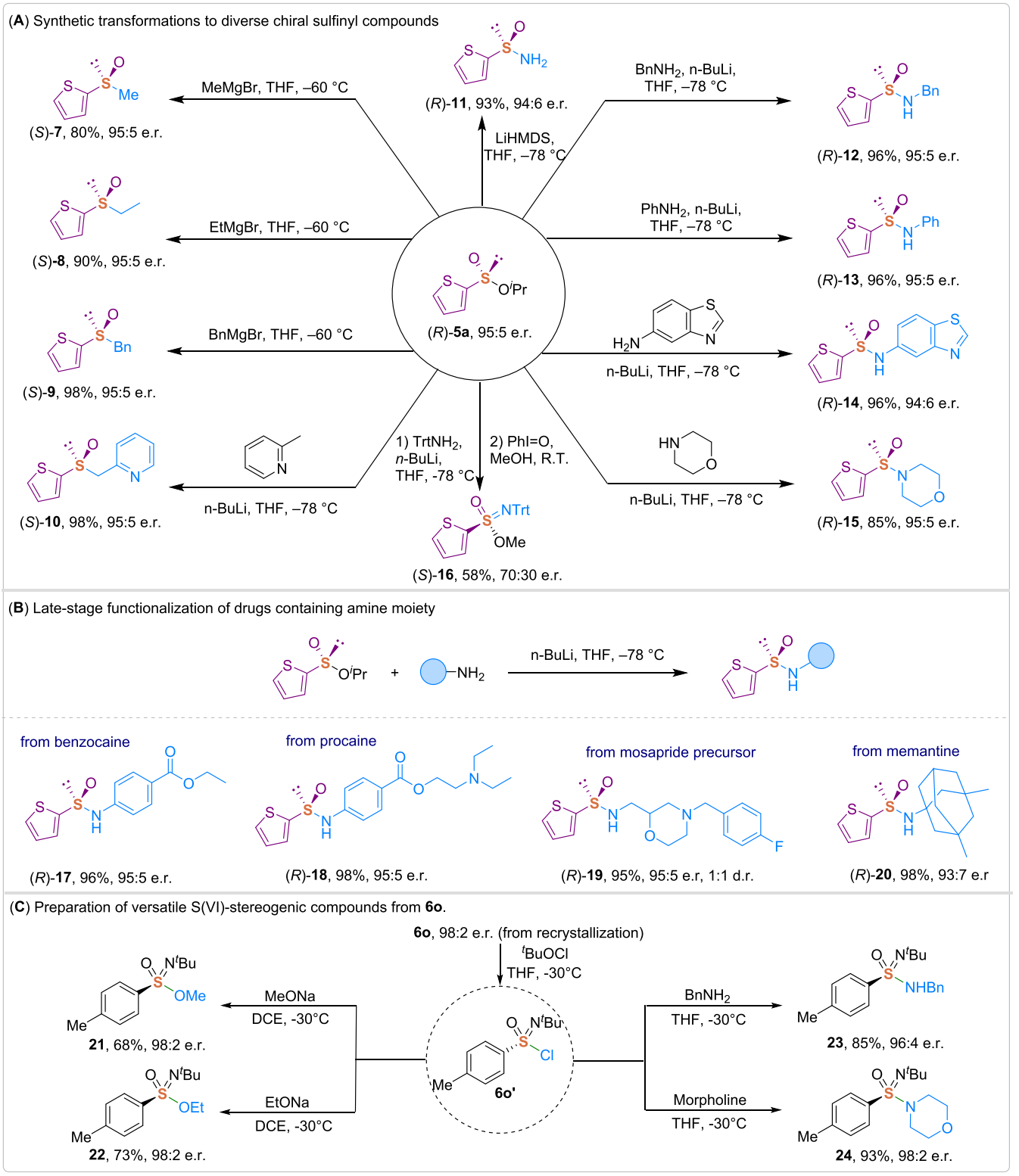
**Scheme 4. Synthetic Transformations of the Catalytically Obtained Chiral Sulfinate Esters and Sulfinamides**




**6d** an almost quantitative yield, with a dropped enantioselectivity, presumably owing to its relatively strong nucleophilicity. We next examined an array of cyclic alcohols, ranging from 4 to 7 membered rings, and were delighted to find that the corresponding products **6e**–**6h** were afforded with 82–91% yields and up to 95:5 er values. Alcohols featuring oxygen- or sulfur-containing heterocycles were also amenable to this reaction, yielding the products **6i**–**6j** with 88% yield, 95:5 er and 80% yield, 95:5 er, respectively. Considering the intriguing biological activity of the sulfinate scaffold, we demonstrated the catalytic asymmetric condensation for the late-stage functionalization of natural products, such as (+)-pinanediol (**6k**) and cholesterol (**6l**–**6m**). As a technical note, the optimal conditions delivered the corresponding products **6l**–**6m** in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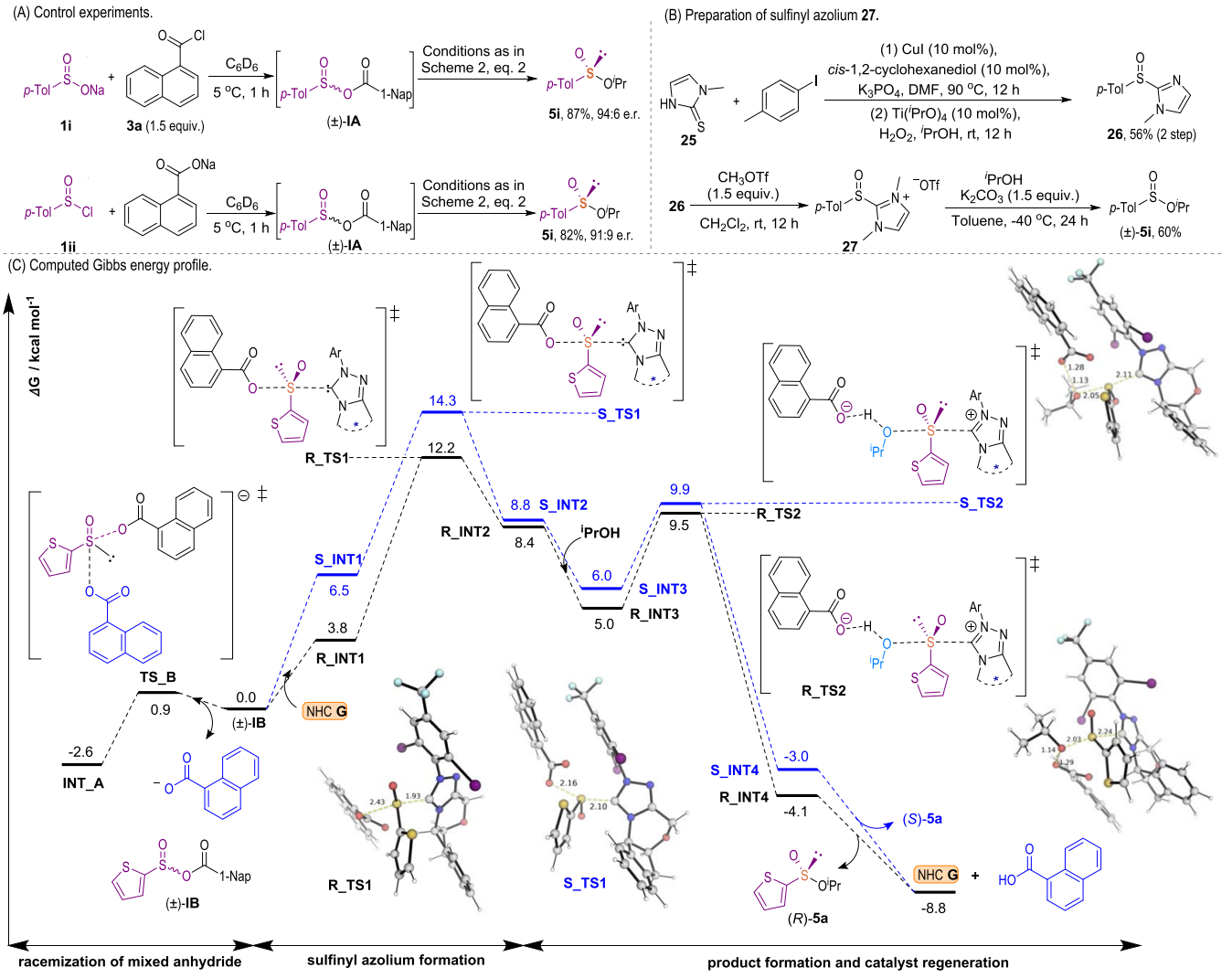
**Scheme 5. (A) Control Experiments, (B) Preparation of Sulfinyl Azolium, and (C) Computed Gibbs Energy Profile; INT_A Is the Complex Formed between Mixed Anhydride IB and 1-Naphthoate; See Figures S16 and S19 for All DFT-optimized Structures**




27−38% yields. In these cases, a modified sulfination method employing sulfinyl chloride and sodium 1-naphthoate (**3e**) (as shown in Scheme 2, eq 2) was performed to achieve satisfactory results.

Encouraged by the broad scope of our carbene catalytic approach, we turned to achieve the stereoselective preparation of sulfinamide analogues. As demonstrated in Scheme 3, with slightly modified reaction conditions, an array of sulfinamide products **6o**−**6u** were produced in excellent yield and high stereoselectivity. Our method is a notable progress for the challenging selective amine sulfinylations[57−60] despite the current condition relying on the use of sterically congested amine nucleophiles (**6o** vs **6n**) to suppress the noncatalytic background reaction.

The catalytically prepared optically enriched sulfinate ester products could readily undergo versatile synthetic transformations (Scheme 4). For instance, nucleophilic addition with various Grignard reagents provided the sulfoxide products (*S*)-**7**−**9** in 80−98% yields and without erosion of enantioselectivity. Moreover, product (*S*)-**10**, containing a pyridine unit that could serve as a bidentate ligand for enantioselective catalysis, was quantitatively produced upon reaction with lithium 2-methylpyridine. The importance of the obtained chiral sulfinate esters was further demonstrated to access a broad range of enantioenriched sulfinamides, which is another representative class of *S*-chiral scaffolds with wide applications. Simple treatment of (*R*)-**5a** with the corresponding in situ-formed lithium amines readily afforded products **11**−**13** with inverted sulfur stereocenters. Additionally, the heterocyclic amines were also compatible with this transformation, allowing for the rapid preparation of (*R*)-**14** and (*R*)-**15** of potential biological interest. A two-step sequence, involving sulfinamide formation and oxidation with PhI = O, readily furnished the sulfoximine ester (*S*)-**16** with an attractive scaffold for drug discovery,[79] albeit in modest enantioselectivity after the transformation. Furthermore, the chiral sulfinate ester products provided a strategy for drug modification by the installment of chiral sulfinyl moieties. In this context, a variety of amine-containing commercially available drugs, such as benzocaine, procaine, mosapride precursor, and memantine, were successfully functionalized with the thienyl sulfinyl fragment to give products **17**−**20** with high efficiency (Scheme 4). On the other hand, the prepared sulfinamide **6o** is also viable to access a diverse set of *S*-chiral compounds. Oxidation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with *t*BuOCl readily provided chloride **6o'** without further purification, which is a privileged chiral scaffold to prepare an array of S(VI)-stereogenic compounds. For instance, sulfonimidate **21**−**22** and sulfonimidamide **23**−**24** could be easily obtained by nucleophilic displacement with various nucleophiles, which are highly attractive frameworks for potential drug discovery.

**Mechanistic Studies.** Control experiments were performed to shed insight into the carbene catalytic process. As illustrated in Scheme 5A, a stepwise reaction procedure was performed to ensure the initial generation of mixed sulfinyl anhydride intermediate **IA** (see Schemes S31−S33 and Figures S1−S3 for details). Under the catalytic conditions as in Scheme 2, eq 2, reactions by utilization of either sulfinate **1i** or sulfinyl chloride **1ii** resulted in the formation of the desired product **5i** in good enantioselectivity, which is comparable to the results of that obtained under the catalytic optimal conditions (87%, 94:6 er, Scheme 3).

Next, to discern the viability of the sulfinyl azolium species to afford the sulfinate ester, a simplified sulfinyl azolium species **27** was prepared. As depicted in Scheme 5B, a sequence involving S arylation of **25** and $H_2O_2$ oxidation readily afforded sulfoxide **26**.[80] Based on previously reported procedure,[43,81−83] *N*-methylation of **26** would give the corresponding sulfinyl azolium **27** ($^1H/^{13}C$ NMR and HRMS confirmed). Reaction of azolium salt **27** with isopropanol at −40 °C provided the sulfinate ester (±)-**5i** in a modest 60% yield likely due to its poor solubility in toluene, implying the general structure and reactivity of the sulfinyl azoliums. Further evidence to verify the intermediacy of sulfinyl azolium in the catalytic asymmetric reaction was elucidated from the HRMS detection of the versatile azolium intermediates derived from various NHC catalysts (Figures S4−S6).

To understand the full catalytic cycle, density functional theory (DFT) studies were carried out (see Sections S3.1 and S3.2 for computational details). The computed Gibbs energy profile is shown in Scheme 5C. We found that the mixed anhydride (±)-**IB** can racemize rapidly under the assistance of 1-naphthoate, with a barrier of only 3.5 kcal/mol (Section S3.4 and Figure S14).[84,85] Chiral NHC **G** then undergoes a stereoselective attack on the mixed anhydride, with **R_TS1** (attack on (*R*)-**IB**) having a barrier of 12.2 kcal/mol and **S_TS1** (attack on (*S*)-**IB**) 14.3 kcal/mol (Scheme 5C and Section S3.5), to yield the sulfinyl azolium intermediates, which are difficult to racemize under the reaction conditions (Section S3.6). Subsequent 1-naphthoate facilitates the nucleophilic attack of the sulfinyl azolium intermediate by isopropanol, thereby furnishing the final product **5a**. The formation of the product via **TS2** is exergonic and irreversible. From the Gibbs energy profile, the resting state/turnover frequency-determining intermediate (TDI) is the complex formed between mixed anhydride **IB** and 1-naphthoate, **INT_A**, while the turnover frequency-determining transition state (TDTS) is the formation of sulfinyl azolium intermediate, **TS1**. As TDTS involves the carbene catalyst and the mixed anhydride but not isopropanol, we predict a first-order rate dependence on each of the concentrations of NHC **G**, acyl chloride **3a**, and sodium sulfinate **1a** (precursors for the mixed anhydride) and zero-order rate dependence on the concentration of isopropanol. This is well corroborated with experimental kinetic studies (Section S2.6(e) and Figure S11). The overall Gibbs energy profile gives the energetic span as 14.8 kcal/mol for the formation of the major product (from **INT_A** to **R_TS1**), consistent with reactivity at −60 °C. The Gibbs energy difference of 2.1 kcal/mol between **R_TS1** and **S_TS1** suggests that product (*R*)-**5a** will be formed more favorably to (*S*)-**5a**, giving a predicted er ratio of 97:3, in good agreement with the observed er ratio of 92:8.

**Bioassay Studies.** Intrigued by the diverse biological activities of sulfoxide derivatives,[86,87] we conducted preliminary studies on the antibacterial activities of the obtained chiral sulfinate products to search for potent antimicrobial agrochemicals for plant protection. In vitro bioassay evaluations were performed to assess the inhibition activity against two plant pathogens, including *Xoo* (*Xanthomonas oryzae pv oryzae*) and *Xoc* (*Xanthomonas oryzae pv oryzicola*) that could lead to bacterial leaf blight and bacterial leaf streak diseases, respectively, posing a serious threat to rice plants.[88] Satisfyingly, the bioassay results demonstrate that most of these compounds show efficiency to inhibit these two bacteria (Table 1). Particularly noteworthy are compounds (*R*)-**5t** and

**Table 1. In Vitro Antibacterial Activity of the Target Compounds against *Xoo* and *Xoc* at 50 μg/mL[a]**

| compound | *Xoo* inhibition rate [%] | *Xoc* inhibition rate [%] |
|---|---|---|
| (*R*)-**5p** | 40.12 ± 2.44 | 74.94 ± 5.03 |
| (±)-**5p** | | 56.19 ± 2.65 |
| (*R*)-**5t** | **84.35 ± 1.85** | 33.65 ± 1.76 |
| (±)-**5t** | 72.59 ± 1.28 | |
| (*R*)-**6e** | 82.03 ± 1.45 | **85.25 ± 1.64** |
| (±)-**6e** | 81.36 ± 3.83 | 82.96 ± 4.18 |
| (*R*)-**6i** | 81.65 ± 2.56 | 73.43 ± 0.94 |
| (±)-**6i** | 71.55 ± 4.26 | 75.59 ± 0.45 |
| (*R*)-**6j** | **84.12 ± 0.34** | 57.61 ± 1.99 |
| (±)-**6j** | 78.53 ± 2.45 | |
| **BT**[b] | 30.79 ± 2.64 | 45.97 ± 3.97 |
| **TC**[c] | 33.13 ± 2.23 | 29.09 ± 2.58 |

[a]All data were average data of three replicates. The bold is used to highlight the notable highest inhibition rate of these compounds. [b]Commercial bactericide, BT = bismerthiazol was used as the positive control. [c]Commercial bactericide, TC = thiodiazole-copper was used as the positive control.

(*R*)-**6j** showed a significant inhibition rate of 84.35 and 84.12%, respectively, against *Xoo* at a concentration of 50 μg/mL, surpassing the positive control with the commercial bactericides, thiodiazole-copper (TC) and bismerthiazol (BT). Meanwhile, sulfinate derivative (*R*)-**6e** demonstrated a notable efficacy against *Xoc*, which is superior to that with TC (29.09%) and BT (45.97%) as the positive control. Furthermore, the racemates of the corresponding sulfinate products generally showed slightly diminished inhibitory activity, as observed with compounds **5p**, **5t**, and **6j**. These findings underscore the potential of our products as novel scaffolds for the development of potent bactericides.

## CONCLUSIONS

In summary, we have developed a carbene organocatalytic approach for enantioselective sulfinyl transfer reactions with readily stable sulfinates and alcohols by exploiting an unprecedented NHC-bound sulfinyl azolium intermediate. A wide range of *S*-chiral sulfinate esters was efficiently prepared in high yields and excellent stereoselectivities by means of carbene-catalyst control. Practical divergent synthesis of various chiral sulfinyl scaffolds, including sulfoxides and


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sulfinamides, was readily achieved through substitutions with a variety of nucleophilic components. Our method provides a synthetic chiral sulfinyl coupling platform for the late-stage modification of natural products and commercial drugs. Furthermore, the yielded sulfinyl compounds exhibit notable antimicrobial activities and hold promise as lead scaffolds for the development of potent bactericides for crop protection. New avenues for synthetic implementation driven by the exploration of novel heteroatom-centered carbene reactive intermediates to access novel chiral frameworks bearing heteroatom-stereogenicity could be anticipated. Ongoing studies in our laboratory also include development of the obtained *S*-chiral compounds for new chiral catalyst design and potent agrochemical discovery.

## ■ ASSOCIATED CONTENT

### Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.4c10486.

Full experimental details for the preparation of all new compounds and their spectroscopic and chromatographic data (PDF)

### Accession Codes

CCDC 2351664 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, U.K.; fax: +44 1223 336033.

## ■ AUTHOR INFORMATION


### Corresponding Authors

**Xinglong Zhang** − *Department of Chemistry, The Chinese University of Hong Kong, Hong Kong, China; Institute of High Performance Computing, Agency for Science, Technology and Research (A*STAR), Singapore 138632, Singapore;* orcid.org/0000-0003-1698-692X; Email: zhang_xinglong@ihpc.a-star.edu.sg

**Xingxing Wu** − *State Key Laboratory of Green Pesticide, Key Laboratory of Green Pesticide and Agricultural Bioengineering, Ministry of Education, Guizhou University, Guiyang 550025, China;* orcid.org/0000-0002-6281-243X; Email: wuxx@gzu.edu.cn

### Authors

**Benpeng Li** − *State Key Laboratory of Green Pesticide, Key Laboratory of Green Pesticide and Agricultural Bioengineering, Ministry of Education, Guizhou University, Guiyang 550025, China; School of Life and Health Science, Kaili University, Kaili 556011, China*

**Junyuan Hu** − *Institute of Advanced Synthesis, School of Chemistry and Molecular Engineering, Jiangsu National Synergetic Innovation Center for Advanced Materials, Nanjing Tech University, Nanjing 211816, China*

**Minghong Liao** − *State Key Laboratory of Green Pesticide, Key Laboratory of Green Pesticide and Agricultural Bioengineering, Ministry of Education, Guizhou University, Guiyang 550025, China*

**Qin Xiong** − *State Key Laboratory of Green Pesticide, Key Laboratory of Green Pesticide and Agricultural Bioengineering, Ministry of Education, Guizhou University, Guiyang 550025, China*

**Yaqi Zhang** − *State Key Laboratory of Green Pesticide, Key Laboratory of Green Pesticide and Agricultural Bioengineering, Ministry of Education, Guizhou University, Guiyang 550025, China*

**Yonggui Robin Chi** − *State Key Laboratory of Green Pesticide, Key Laboratory of Green Pesticide and Agricultural Bioengineering, Ministry of Education, Guizhou University, Guiyang 550025, China; School of Chemistry, Chemical Engineering, and Biotechnology, Nanyang Technological University, Singapore 637371, Singapore;* orcid.org/0000-0003-0573-257X

Complete contact information is available at: https://pubs.acs.org/10.1021/jacs.4c10486

### Author Contributions

[▽]B.L. and J.H. have equal contributions.


### Notes

The authors declare no competing financial interest.

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