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Enantioselective Cascade Reactions of Stable Sulfur Ylides and Nitroolefins through an Axial-to-Central Chirality Transfer Strategy

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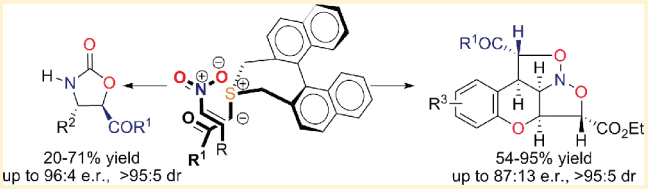
Supporting Information

ABSTRACT: An enantioselective [4 + 1] annulation/rearrangement cascade of stable sulfur ylides and nitroolefins has been developed through an efficient axial-to-central chirality transfer with the use of a chiral BINOL-derived sulfide as a reliable stereocontroller. It can provide pharmaceutically and synthetically important oxazolidinones in high stereoselectivities (up to 96:4 e.r. and >95:5 d.r.). Moreover, this strategy was also successfully applied to the asymmetric [4 + 1]/[3 + 2] cycloaddition cascade of sulfur ylides with alkene-tethered nitroolefins, and the corresponding enantioenriched fused heterocycles (up to 87:13 e.r. and >95:5 d.r.) were obtained in good to excellent yields (54−95% yields).



INTRODUCTION

Cascade reactions have been established as a powerful strategy for the rapid construction of complex functional molecules.[1] In this context, sulfur ylides have provided excellent opportunities for developing new cascade transformations.[2,3] Impressively, remarkable advances have been achieved with respect to asymmetric cascade reactions involving sulfur ylides over the past decade. For instance, elegant works from Borhan,[4] Aggarwal,[5] Tang,[6] and many other groups[7] have successfully developed sulfoxonium ylides, vinyl sulfonium salts, and crotonate-derived sulfonium salts as versatile reagents to construct highly complex and optically active heterocyclic compounds. Despite advances, cascade reactions employing stable sulfur ylides as the reactant still remain a continuing challenge due to their relatively low activity.[8] In this regard, our group has developed two types of cascade reactions of stable sulfur ylides with highly electrophilic nitroolefins,[9] which provided a powerful platform for the rapid and efficient assembly of cheap and readily available starting materials into biologically and synthetically significant oxazolidinones[10] (Scheme 1, A) and chroman-incorporated fused heterocycles[11] (Scheme 1, B). In view of their importance, considerable research efforts have been directed toward the development of efficient methods for their enantioselective synthesis.[12]

Sulfur ylide-participated asymmetric transformations mostly involve the chiral sulfur ylide dictating the chirality of the products, in which stereochemical information is transferred from the chiral sulfide to the resulting chiral product.[2,3b] Such a process is common in the asymmetric epoxidation, aziridination, and cyclopropanation,[2] as well as other cascade reactions to construct chiral dihydrofurans,[13a] cyclohexenes,[6] and nitronates.[13b] To the best of our knowledge, most of the enantiopure sulfides are derived from natural centrally chiral sources, such as camphor,[14] amino acids,[15] and sugars.[16] On the other hand, over the past decades, another strategy, "axial-to-central chirality transfer", has proven to be another important protocol for promoting the evolvement of asymmetric synthesis.[17] Nevertheless, it still remains a limited application in the transformation of sulfur ylides. To the best of our knowledge, there are only two reports primarily disclosed by Seki et al[18a] and Uemura et al[18b] before our work, wherein axial chiral sulfides **1** and **2**[19] (Scheme 2) were applied to the asymmetric epoxidation reaction of aromatic aldehydes (eqs 1 and 2, Scheme 2). Though they did not unequivocally demonstrate the idea that axial-to-central chirality transfer can indeed efficiently promote the asymmetric epoxidation of semistable sulfur ylides with excellent enantioselectivities, these achievements paved the way for the development of formal [4 + 1] annulations of stable sulfur ylides with conjugated systems, which would provide an efficient approach to highly enantiomerically enriched five-membered heterocycles.

Recently, we first applied the axial-to-central chirality transfer strategy to the asymmetric [4 + 1] pyrroline annulation of unsaturated imines with stable sulfur ylides, and excellent asymmetric induction was observed (eq 3, Scheme 2, up to 99:1 e.r.).[20] Inspired by this success, we envisaged that the axially chiral sulfide **2** might be further utilized in other enantioselective reactions. Herein, we describe two types of asymmetric cascade reactions of stable sulfur ylides with nitroolefins, giving optically active oxazolidinones and structurally complex fused heterocycles in a concise fashion with moderate to good chemo- and stereoselectivities (up to 71% yield, 96:4 e.r., and >95:5 d.r.; up to 95% yield, 87:13 e.r., and >95:5 d.r.), respectively.

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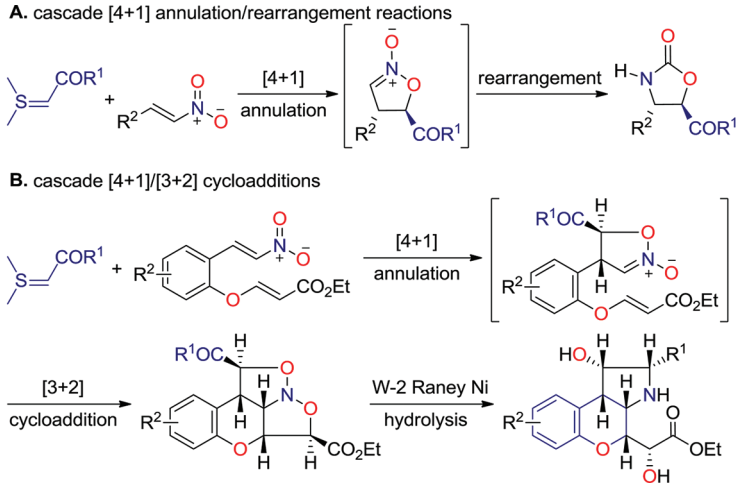
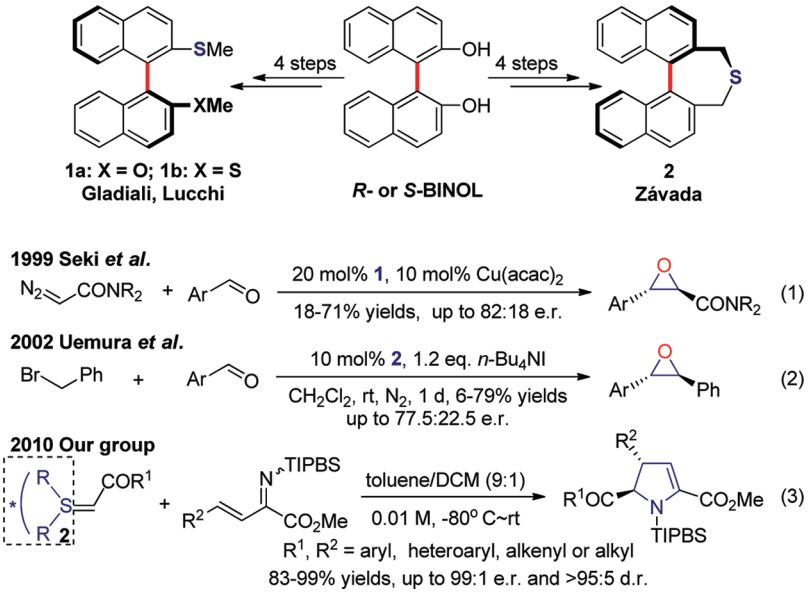
Scheme 1. Our Previous Works on the Cascade Reactions of Stable Sulfur Ylides with Nitroolefins



Scheme 2. Axially Chiral Sulfides



RESULTS AND DISCUSSION

Despite the success of the enantioselective [4 + 1] pyrroline annulation of α,β-unsaturated imines with chiral sulfur ylides **3**, there still exist two major challenges for the development of an enantioselective [4 + 1] annulation/rearrangement cascade of stable sulfur ylides and nitroolefins through an axial-to-central chirality transfer strategy (Scheme 3): (1) in the cascade reaction for oxazolidinone synthesis, the requisite combination of multiple catalysts, such as thiourea and DMAP, together with the following rearrangements made this asymmetric cascade process formidable in terms of chemo- and enantioselectivity; (2) unlike the asymmetric [4 + 1] annulation of unsaturated imines where the protecting group on nitrogen functions as a stereotunable effect, there is not a similar steric effect on the nitroolefin to improve the stereodiscrimination.

Condition Optimization for the Enantioselective [4 + 1] Annulation/Rearrangement Cascade. With these thoughts in mind, initial attempts for experimental validation of the hypothesis were implemented using axially chiral sulfur ylides to provide enantioenriched oxazolidinones (Table 1). To our delight, the reaction of axially chiral sulfur ylide **3a** with nitroolefin **4a** afforded the corresponding oxazolidinone **5aa** in good yield (69%) with good enantioselectivity (85:15 e.r.) upon treatment with 10 mol % 2-chlorophenyl thioures (2-CTU) and 4-(dimethylamino)pyridine (DMAP) in dichloromethane at room temperature for 16 h (Table 1, entry 1). Further examination of reaction media showed that this asymmetric cascade reaction was remarkably influenced by the polarity of solvents (Table 1, entries 1−8). The weak polar solvents, such as toluene, have positively affected the enantioselectivity (Table 1, entry 8, 35% yield and 90:10 e.r.), and the moderately polar dichloromethane was the best solvent of choice in terms of reaction efficiency (Table 1, entry 1, 69% yield and 85:15 e.r.). Interestingly, we found that a mixture of toluene and CH_2Cl_2 in a 4:1 ratio provided the satisfactory results with 63% yield and 90:10 e.r. (Table 1, entry 9).[21] Further optimization of reaction parameters, such as the ratio of reagents (**3a**/**4a**), concentration, and temperature, resulted in a higher yield and enantiomeric ratio of the desired chiral oxazolidinone (Table 1, entry 13, 71% yield and 95:5 er). When the reaction was conducted at −40 °C, the enantiomeric

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Scheme 3. Proposal and Challenge

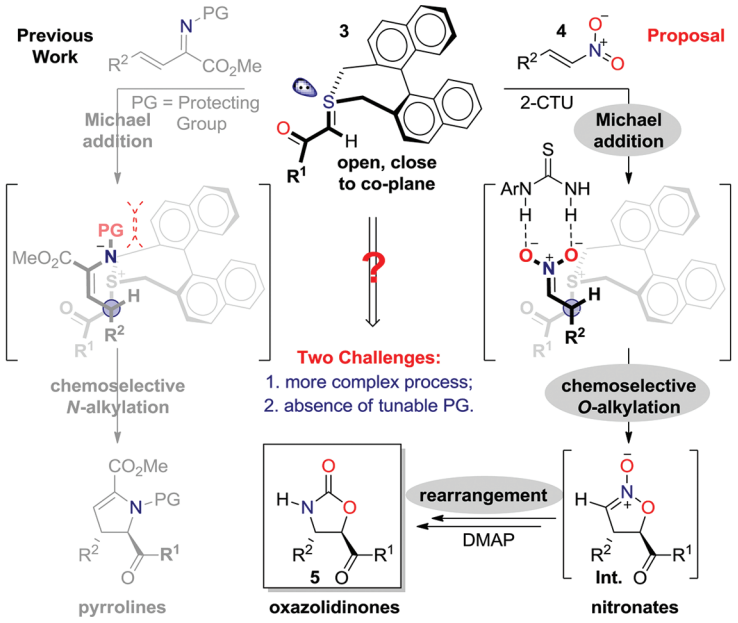
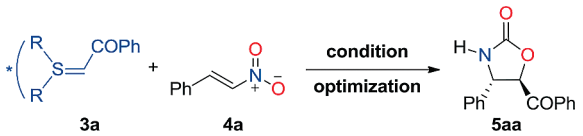


Table 1. Condition Optimization for the Enantioselective Cascade [4 + 1] Annulation/Rearrangement Reaction[a]



entry	solvent	concn (M)	time (h)	yield[b] (%)	e.r.[c] (%)
1	CH_2Cl_2	0.08	16	69	85:15
2	$CHCl_3$	0.08	48	47	87:13
3	Et_2O	0.08	48	25	82:18
4	THF	0.08	60	45	85:15
5	DMF	0.08	48	trace	n.d.[d]
6	CH_3CN	0.08	35	43	64:36
7	CH_3OH	0.08	40	53	46:54
8	toluene	0.08	48	35	90:10
9[e]	toluene/CH_2Cl_2	0.08	48	63	90:10
10[e,f]	toluene/CH_2Cl_2	0.08	65	59	90:10
11[e,g]	toluene/CH_2Cl_2	0.08	65	68	92:8
12[e,g]	toluene/CH_2Cl_2	0.01	48	52	95:5
13[e,h]	toluene/CH_2Cl_2	0.01	26	71	95:5
14[e,h,i]	toluene/CH_2Cl_2	0.01	72	41	97:3

[a]The reactions were carried out on a 0.2 mmol scale of **4a** with 1.1 equiv of **3a** at room temperature in the corresponding solvent. [b]Isolated yield. [c]e.r. was determined by chiral stationary phase HPLC analysis. [d]n.d. = not determined. [e]The ratio of toluene and DCM is 4:1. [f]The ratio of **3a**/**4a** was changed to 1:1. [g]The ratio of **3a**/**4a** was changed to 1:1.5. [h]The ratio of **3a**/**4a** was changed to 1.25:1. [i]The reaction was carried out at −40 °C.

ratio could be improved to 97:3, albeit with a lowered yield (Table 1, entry 14).

Scope of the Enantioselective [4 + 1] Annulation/Rearrangement Cascade. Under the optimal conditions, experiments to probe the scope of the nitroolefin component have been implemented. As highlighted in Scheme 4, reactions with a wide range of nitroolefins with varying electronic/steric functional groups on the benzene ring all proceed well. For instance, the electron-rich, electron-neutral, and electron-deficient *β*-nitrostyrenes could give the corresponding products in good results with 56−71% yields, >95:5 d.r., and up to 95:5 e.r. (Scheme 4, **5aa**−**5af**). Moreover, variation of the substitute position proved to be feasible. For example, when *meta*-bromo sustituted nitrostyrene was applied, good yields and excellent enantiomeric ratios are obtained (Scheme 4, **5ag**: 68% yield, >95:5 d.r., and 95:5 e.r.). In the cases of 2-methoxyl-*β*-nitrostyrene and *α*-naphthyl nitroolefin, the asymmetric cascade reactions also gave corresponding products, though the decrease in enantiomeric excess was observed because of the possible steric repulsion (Scheme 4, **5ah**: 65% yield, >95:5 d.r., 88:12 e.r.; **5ai**: 58% yield, >95:5 d.r., 92:8 e.r.). Notably, multiple substituted 3,4-difluoro-*β*-nitrostyrene was also successfully utilized to prepare chiral oxazolidinone conveniently in moderate yield with good stereoselectivity (Scheme 4, **5aj**: 50% yield, >95:5 d.r., 92:8 e.r.), which is an important intermediate to access a potential alpha adrenergic receptor antagonist.[22] Finally, aliphatic nitroolefins, such as isopropyl nitroolefin, were tried, but only limited success was achieved

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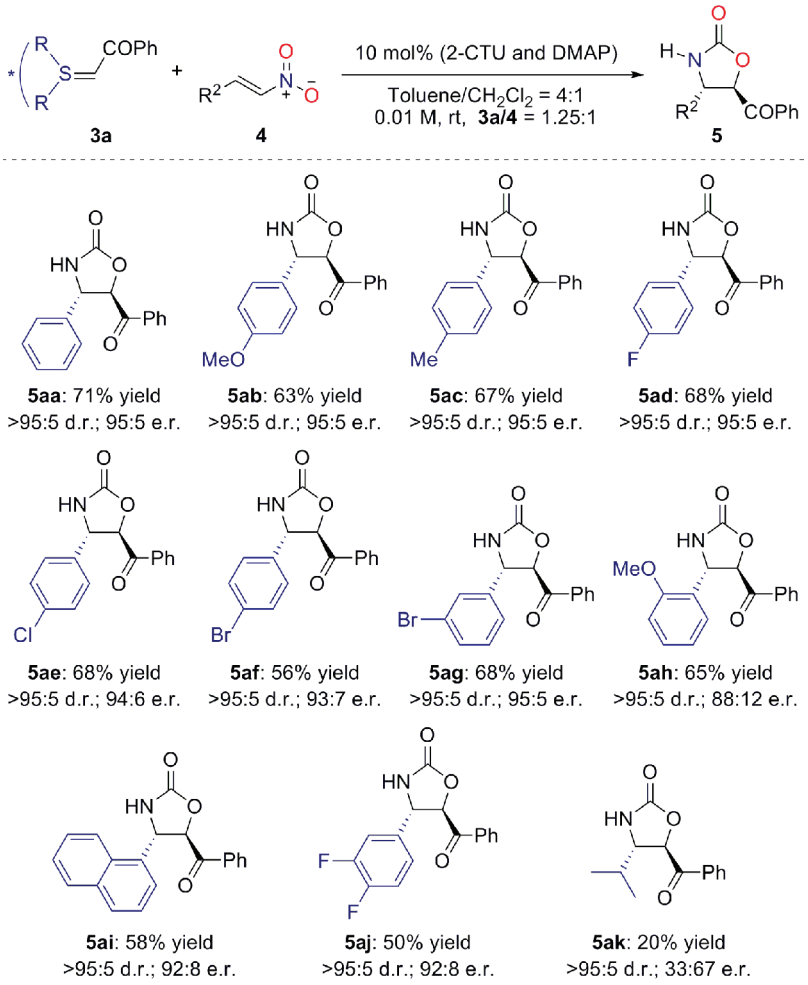
Scheme 4. Scope of Nitroolefins for the Enantioselective Cascade [4 + 1] Annulation/Rearrangement Reaction



(Scheme 4, **5ak**, 20% yield, >95:5 d.r., and 33:67 e.r.), and the work to further improve these results is currently ongoing in our laboratory.

This asymmetric cascade reaction to access chiral oxazolidinones is also general with respect to stable sulfur ylides, as revealed in Scheme 5. When aromatic sulfur ylides were utilized, variation of electronic contribution of substituents on the benzene ring is possible without obvious loss in stereoselectivity (Scheme 5, **5aa**−**5fa**: 44−71% yields, >95:5 d.r., and 94:6−96:4 e.r.). A bulky *meta*-substituted substrate was also efficient in this transformation, such as *meta*-bromo sulfur ylide, giving the desired product **5ga** in 50% yield, >95:5 d.r., and 91:9 e.r. It was noted that halogenated chiral oxazolidin-2-ones should be valuable precursors for many further transformations.[23] Moreover, the scope of sulfur ylides could be significantly extended to heteroaryl and alkylacyl ylides. For example, when a 2-thiophenyl incorporated substrate was applied, the enantioenriched oxazolidinone, including the heteroarene architecture, could be obtained in moderated yield and excellent stereoselectivities (Scheme 5, **5ha**: 58% yield, >95:5 d.r., and 95:5 e.r.). In addition, the (2-phenylpropyl)acyl ylide can also react with nitroolefin **4i** to afford the desired product in moderate yield and with excellent stereoselectivities (Scheme 5, **5ii**: 46% yield, 78:22 e.r., and >95:5 d.r.).

The absolute configuration of oxazolidinone **5fa** was unambiguously confirmed to be (*4S,5R*) by X-ray crystallographic analysis (see the Supporting Information),[24] and other oxazolidinone products could be tentatively assigned according to an analogous enantioinduction. It is worth noting that these experimental results confirmed the rationality of our proposed stereochemically controlled mechanism, as depicted in Scheme 3.

Enantioselective [4 + 1]/[3 + 2] Cycloaddition Cascade. On the basis of the above success, we further evaluated the axial-to-central chirality transfer strategy in the asymmetric [4 + 1]/[3 + 2] cylcoaddition cascade. For example, with mixed fluorobenzene/$CHCl_3$ (1:4) as the solvent,[21] axially chiral sulfur ylide **3a** reacted with acrylate-tethered nitrostyrene **6a** and enantioenriched fused heterocycle **7aa** was delivered in high chemoselectivity and diastereoselectivity, though in moderate enantioselectivity (95% yield, >95:5 d.r., 81:19 e.r.). As highlighted in Scheme 6, a range of acrylate-tethered nitroolefins, including electron-neutral, electron-rich, and electron-deficient substituents, at the *para* position of the oxygen atom could be well tolerated, leading to desired fused heterocycles in high yields and moderate enantioselectivities (Scheme 6, **7aa**−**7ad**: 75−95% yields, 77:23−81:19 e.r.). Variation of the electronic properties on sulfur ylides proved to be feasible, and moderate to good yields with good enantioselectivities were achieved (Scheme 6, **7aa**−**7ca**: 54−95% yields, >95:5 d.r., and 81:19−87:13 e.r.). Note that the axially chiral sulfide **2** as an efficient stereocontroller could induce the generation of five sequential stereocenters.

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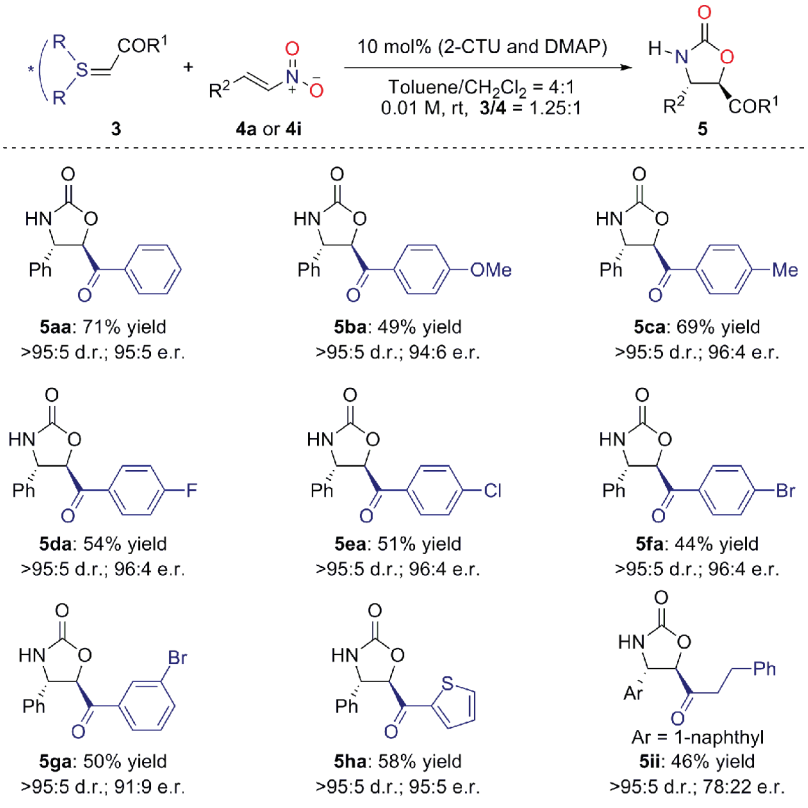
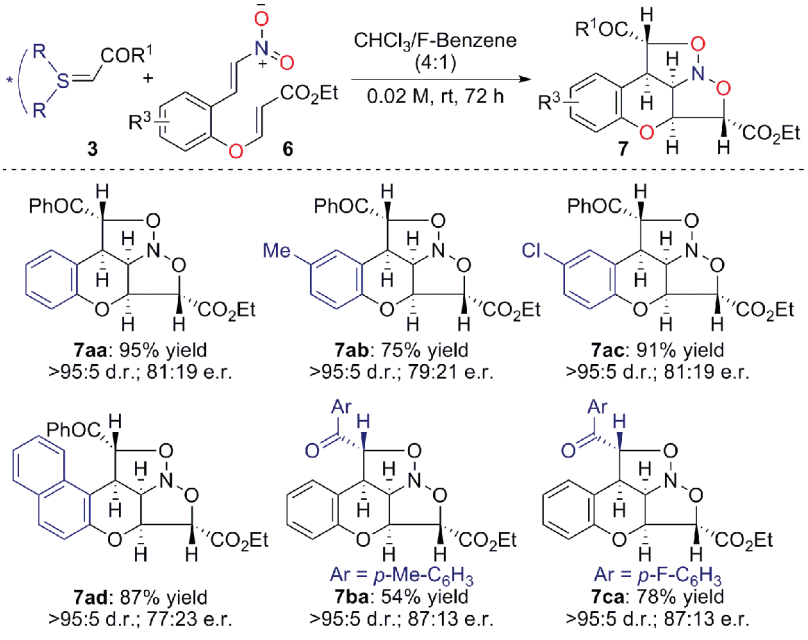
Scheme 5. Scope of Stable Sulfur Ylides for the Enantioselective Cascade [4 + 1] Annulation/Rearrangement Reaction



Scheme 6. Representative Results of Enantioselective [4 + 1]/[3 + 2] Cascade Reactions



CONCLUSION

In summary, we have described two types of enantioselective cascade reactions of stable sulfur ylides and nitroolefins by virtue of the efficient axial-to-central chirality transfer strategy. The formal [4 + 1] annulation/rearrangement cascade delivered optically active oxazolidinones in a concise way with excellent stereoselectivities. In addition, the same strategy has been further extended to asymmetric [4 + 1]/[3 + 2] cycloaddition cascades of sulfur ylides and acrylate-tethered β-nitrostyrene, efficiently affording enantioenriched fused heterocycles in excellent yields and high stereoselectivities. Other related asymmetric transformations based on this protocol will be reported in due course.

EXPERIMENTAL SECTION

Representative Procedure for the Enantioselective [4 + 1] Annulation/Rearrangement Cascade. To a 50 mL flask equipped with a magnetic stir bar was added nitroolefin **4** (0.2 mmol, 1.0 equiv),

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1-(2-chlorophenyl)thiourea (2-CTU, 0.02 mmol, 3.73 mg, 0.1 equiv), *N*,*N*-dimethylaminopyridine (DMAP, 0.02 mmol, 2.44 mg, 0.1 equiv), and toluene/CH_2Cl_2 (4:1, 20 mL). This solution was stirred at ambient temperature for 0.5 h, and then chiral sulfur ylide **3** (0.25 mmol, 1.25 equiv) was introduced and continued to stir for 24−48 h at the same temperature. Upon the completion of the reaction monitored by TLC, the solvent was removed under reduced pressure. The crude product was purified by flash chromatography on silica gel (silica, 200−300; eluant, petroleum ether/dichloromethane/ethyl acetate (5:1:1−3:1:1)) to provide pure product **5**. The absolute configuration of oxazolidinone **5** was assigned by the X-ray crystallographic analysis of **5fa** according to an analogous enantioinduction. The diastereomer ratio was determined by ^{1}H NMR of the reaction mixture. The enantiomeric ratio was determined by chiral HPLC at 25 °C using a UV detector tuned for 254 nm.

(4S,5R)-5-Benzoyl-4-phenyloxazolidin-2-one (***5aa***): 71% yield; white solid; diastereomeric ratio, >95:5; enantiomeric ratio, 95:5. Daicel Chirapak OD-H, hexane/isopropanol = 80/20, flow rate = 0.7 mL/min, t_R = 21.32 min (major), t_R = 26.63 min (minor). $[\alpha]_D^{27}$ = −82 (*c* = 2.0, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.94 (d, *J* = 8.0 Hz, 2H), 7.62 (t, *J* = 7.2 Hz, 1H), 7.47 (t, *J* = 6.4 Hz, 2H), 7.44−7.34 (m, 5H), 6.30 (s, 1H), 5.46 (d, *J* = 5.2 Hz, 1H), 5.32 (d, *J* = 5.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 192.3, 157.7, 139.0, 134.4, 133.6, 129.4, 129.3, 129.0, 128.8, 126.3, 83.3, 57.0. MS: *m*/*z* = 268.4. Anal. Calcd for ($C_{16}H_{13}NO_3$): C, 71.90; H, 4.90; N, 5.24. Found: C, 72.13; H, 5.14; N, 5.58.

(4S,5R)-5-Benzoyl-4-(4-methoxyphenyl)oxazolidin-2-one (***5ab***): 63% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 95:5. Daicel Chirapak OD-H, hexane/isopropanol = 80/20, flow rate = 0.7 mL/min, t_R = 37.26 min (major), t_R = 49.28 min (minor). $[\alpha]_D^{27}$ = −103 (*c* = 2.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.94 (d, *J* = 7.6 Hz, 2H), 7.62 (t, *J* = 7.6 Hz, 2H), 7.47 (t, *J* = 7.6 Hz, 2H), 7.33 (d, *J* = 8.0 Hz, 2H), 6.93 (d, *J* = 8.4 Hz, 2H), 5.88 (s, 1H), 5.45 (d, *J* = 5.6 Hz, 1H), 5.24 (d, *J* = 5.6 Hz, 1H), 3.82 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6 (9:1)): δ (ppm) 191.9, 158.3, 156.2, 132.8, 132.2, 130.5, 127.6, 127.4, 126.3, 112.9, 81.0, 55.7, 53.8. MS: *m*/*z* = 297.3. Anal. Calcd for ($C_{17}H_{15}NO_4$): C, 68.68; H, 5.09; N, 4.71. Found: C, 68.83; H, 5.30; N, 4.59.

(4S,5R)-5-Benzoyl-4-p-tolyloxazolidin-2-one (***5ac***): 67% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 95:5. Daicel Chirapak OD-H, hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, t_R = 17.30 min (major), t_R = 19.98 min (minor). $[\alpha]_D^{27}$ = −64 (*c* = 2.2, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.89 (d, *J* = 5.8 Hz, 2H), 7.58 (s, 1H), 7.43 (s, 2H), 7.24 (d, *J* = 5.5 Hz, 2H), 7.18 (s, 2H), 6.78 (s, 1H), 5.40 (s, 1H), 5.18 (s, 1H), 2.33 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 192.4, 158.0, 138.7, 136.0, 134.2, 133.6, 129.7, 129.2, 128.7, 126.1, 83.2, 57.0, 21.0. MS: *m*/*z* = 281.8. Anal. Calcd for $C_{17}H_{15}NO_3$: C, 72.58; H, 5.37; N, 4.98. Found: C, 72.49; H, 5.27; N, 4.88.

(4S,5R)-5-Benzoyl-4-(4-fluorophenyl)oxazolidin-2-one (***5ad***): 68% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 95:5. Daicel Chirapak OD-H, hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, t_R = 14.72 min (major), t_R = 19.11 min (minor). $[\alpha]_D^{27}$ = −96 (*c* = 1.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.96 (d, *J* = 8.0 Hz, 2H), 7.63 (t, *J* = 7.2 Hz, 1H), 7.49 (t, *J* = 7.6 Hz, 2H), 7.42−7.39 (m, 2H), 7.11 (t, *J* = 8.8 Hz, 2H), 5.97 (s, 1H), 5.41 (d, *J* = 5.6 Hz, 1H), 5.36 (d, *J* = 5.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6 (9:1)): δ (ppm) 192.4, 163.5, 161.0, 157.2, 135.2, 134.0, 133.3, 128.8, 128.4, 127.8, 127.8, 115.7, 115.5, 82.4, 56.3. MS: *m*/*z* = 285.9. Anal. Calcd for ($C_{16}H_{12}FNO_3$): C, 67.36; H, 4.24; N, 4.91. Found: C, 67.27; H, 4.54; N, 4.82.

(4S,5R)-5-Benzoyl-4-(4-chlorophenyl)oxazolidin-2-one (***5ae***): 68% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 94:6. Daicel Chirapak OD-H, hexane/isopropanol = 80/20, flow rate = 0.7 mL/min, t_R = 22.55 min (major), t_R = 30.42 min (minor). $[\alpha]_D^{27}$ = −66 (*c* = 1.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.94 (d, *J* = 7.6 Hz, 2H), 7.63 (t, *J* = 7.2 Hz, 1H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.38−7.32 (m, 4H), 6.62 (s, 1H), 5.39 (d, *J* = 5.6 Hz, 1H), 5.32 (d, *J* = 6.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 192.2, 157.7, 137.5, 134.9, 134.6, 133.6, 129.4, 129.4, 128.9, 127.7, 83.2, 56.6. MS: *m*/*z* = 301.3. Anal. Calcd for ($C_{16}H_{12}ClNO_3$): C, 63.69; H, 4.01; N, 4.64. Found: C, 63.75; H, 3.65; N, 4.48.

(4S,5R)-5-Benzoyl-4-(4-bromophenyl)oxazolidin-2-one (***5af***): 56% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 93:7. Daicel Chirapak OD-H, hexane/isopropanol = 85/15, flow rate = 1.0 mL/min, t_R = 27.29 min (major), t_R = 42.08 min (minor). $[\alpha]_D^{27}$ = −50 (*c* = 2.2, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.97 (d, *J* = 7.6 Hz, 2H), 7.64 (t, *J* = 7.4 Hz, 1H), 7.56 (d, *J* = 8.3 Hz, 2H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.31 (d, *J* = 8.3 Hz, 2H), 5.79 (s, 1H), 5.39 (d, *J* = 5.9 Hz, 1H), 5.36 (d, *J* = 5.7 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$ + DMSO-d_6 (9:1)): δ (ppm) 191.8, 156.4, 138.1, 133.3, 132.6, 131.0, 128.1, 127.8, 127.2, 121.2, 81.1, 55.7. MS: *m*/*z* $[M + 2]^+$ = 347.6. Anal. Calcd for $C_{16}H_{12}BrNO_3$: C, 55.51; H, 3.49; N, 4.05. Found: C, 55.40; H, 3.38; N, 3.98.

(4S,5R)-5-Benzoyl-4-(3-bromophenyl)oxazolidin-2-one (***5ag***): 68% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 95:5. Daicel Chirapak OD-H, hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, t_R = 18.45 min (major), t_R = 24.37 min (minor). $[\alpha]_D^{27}$ = −89 (*c* = 2.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.93 (d, *J* = 7.2 Hz, 2H), 7.61 (t, *J* = 7.0 Hz, 1H), 7.48−7.44 (m, 2H), 7.32−7.28 (m, 1H), 6.96−6.87 (m, 3H), 6.53 (d, *J* = 6.0 Hz, 1H), 5.26 (d, *J* = 4.8 Hz, 1H), 3.79 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 192.3, 160.2, 157.8, 140.6, 134.4, 133.6, 130.4, 129.3, 128.8, 118.3, 114.5, 111.6, 83.1, 57.0, 55.3. MS: *m*/*z* = 345.7 (M + 2 = 347.8). Anal. Calcd for ($C_{16}H_{12}BrNO_3$): C, 55.51; H, 3.49; N, 4.05. Found: C, 55.64; H, 3.19; N, 4.01.

(4S,5R)-5-Benzoyl-4-(2-methoxyphenyl)oxazolidin-2-one (***5ah***): 65% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 88:12. Daicel Chirapak OD-H, hexane/isopropanol = 80/20, flow rate = 0.7 mL/min, t_R = 18.77 min (major), t_R = 24.82 min (minor). $[\alpha]_D^{27}$ = −50 (*c* = 1.7, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.98 (d, *J* = 7.5 Hz, 2H), 7.62 (t, *J* = 7.4 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 2H), 7.42−7.29 (m, 2H), 7.04 (t, *J* = 7.4 Hz, 1H), 6.89 (d, *J* = 8.2 Hz, 1H), 5.59 (d, *J* = 4.5 Hz, 1H), 5.52 (d, *J* = 4.3 Hz, 2H), 3.64 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6 (9:1)): δ (ppm) 192.6, 157.7, 155.4, 133.6, 133.4, 128.9, 128.3, 128.1, 127.1, 125.7, 120.1, 109.9, 79.8, 54.2, 52.5. MS: *m*/*z* = 297.6. Anal. Calcd for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09; N, 4.71. Found: C, 68.57; H, 5.02; N, 4.62.

(4S,5R)-5-Benzoyl-4-(naphthalen-1-yl)oxazolidin-2-one (***5ai***): 71% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 92:8. Daicel Chirapak OD-H, hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, t_R = 23.07 min (minor), t_R = 38.55 min (major). $[\alpha]_D^{27}$ = 74 (*c* = 1.3, CH_2Cl_2). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.01 (d, *J* = 8.0 Hz, 2H), 7.95−7.88 (m, 3H), 7.71 (d, *J* = 7.2 Hz, 1H), 7.63−7.44 (m, 6H), 6.34 (d, *J* = 3.6 Hz, 1H), 5.83 (s, 1H), 5.51 (d, *J* = 3.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6 (9:1)): δ (ppm) 192.9, 157.4, 135.1, 133.9, 133.5, 133.5, 129.5, 129.2, 128.7, 128.3, 126.5, 125.7, 125.1, 123.1, 121.8, 113.9, 81.9, 52.7. MS: *m*/*z* = 317.2. Anal. Calcd for ($C_{20}H_{15}NO_3$): C, 75.70; H, 4.76; N, 4.41. Found: C, 75.79; H, 4.96; N, 4.41.

(4S,5R)-5-Benzoyl-4-(3,4-difluorophenyl)oxazolidin-2-one (***5aj***): 50% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 92:8. Daicel Chirapak OD-H, hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, t_R = 13.49 min (major), t_R = 16.20 min (minor). $[\alpha]_D^{27}$ = −25 (*c* = 2.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.97 (d, *J* = 8.1 Hz, 2H), 7.65 (t, *J* = 7.4 Hz, 1H), 7.50 (t, *J* = 7.8 Hz, 2H), 7.35−7.24 (m, 1H), 7.25−7.11 (m, 2H), 6.58 (s, 1H), 5.38 (s, 2H). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 193.1, 157.8, 155.6, 133.8, 133.5, 129.1, 128.6, 128.3, 127.4, 125.9, 120.3, 110.1, 79.9, 54.4, 52.6. MS: *m*/*z* = 303.0. Anal. Calcd for $C_{16}H_{11}F_2NO_3$: C, 63.37; H, 3.66; N, 4.62. Found: C, 63.27; H, 3.55; N, 4.53.

(4S,5R)-5-Benzoyl-4-isopropyloxazolidin-2-one (***5ak***): 20% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 67:33. Daicel Chirapak AD-H, hexane/isopropanol = 85/15, flow rate = 1.0 mL/min, t_R = 9.59 min (major), t_R = 22.75 min (minor). $[\alpha]_D^{27}$ = −35 (*c* = 0.53, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.03 (d, *J* = 7.6 Hz, 2H), 7.63 (t, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 2H), 6.29 (s, 1H), 5.33 (d, *J* = 4.4 Hz, 1H), 4.10 (t, *J* = 5.2 Hz, 1H), 1.94−1.86 (m, 1H), 1.03 (d, *J* = 6.8 Hz, 3H), 0.96 (d, *J* = 6.8 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 193.5, 158.4, 134.1, 129.3, 128.8, 79.3, 59.0,

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32.4, 18.0, 17.3. MS: m/z = 234.1. Anal. Calcd for ($C_{13}H_{15}NO_3$): C, 66.94; H, 6.48; N, 6.00. Found: C, 66.58; H, 6.28; N, 5.90.

(4S,5R)-5-(4-Methoxybenzoyl)-4-phenyloxazolidin-2-one (**5ba**): 49% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 94:6. Daicel Chirapak OD-H, hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, t_R = 22.83 min (major), t_R = 32.52 min (minor). $[\alpha]_D^{27}$ = −154 (c = 1.6, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.95 (d, J = 8.8 Hz, 2H), 7.42 (d, J = 3.8 Hz, 4H), 7.40−7.34 (m, 1H), 6.94 (d, J = 8.8 Hz, 2H), 5.82 (s, 1H), 5.42 (d, J = 5.7 Hz, 1H), 5.36 (d, J = 5.3 Hz, 1H), 3.88 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$+ DMSO-d_6 (9:1)): δ (ppm) 190.9, 164.3, 158.0, 139.6, 131.6, 129.0, 128.6, 126.3, 114.0, 82.6, 57.4, 55.5. MS: m/z = 297.6. Anal. Calcd for ($C_{17}H_{15}NO_4$): C, 68.68; H, 5.09; N, 4.71. Found: C, 68.57; H, 5.37; N, 4.71.

(4S,5R)-5-(4-Methylbenzoyl)-4-phenyloxazolidin-2-one (**5ca**): 69% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 96:4. Daicel Chirapak OD-H, hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, t_R = 14.34 min (major), t_R = 22.12 min (minor). $[\alpha]_D^{27}$ = −97 (c = 1.8, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.83 (d, J = 5.2 Hz, 1H), 7.36−7.41 (m, 5H), 7.26 (d, J = 5.2 Hz, 2H), 6.63 (s, 1H), 5.44 (d, J = 3.6 Hz, 1H), 5.28 (d, J = 3.2 Hz, 1H), 2.42 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.8, 158.0, 145.5, 139.1, 131.1, 129.5, 129.4, 129.3, 128.9, 126.3, 83.2, 57.2, 21.7. MS: m/z = 282.2. Anal. Calcd for ($C_{17}H_{15}NO_3$): C, 72.58; H, 5.37; N, 4.98. Found: C, 72.35; H, 5.54; N, 4.75.

(4S,5R)-5-(4-Fluorobenzoyl)-4-phenyloxazolidin-2-one (**5da**): 54% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 96:4. Daicel Chirapak OD-H, hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, t_R = 17.10 min (major), t_R = 20.97 min (minor). $[\alpha]_D^{27}$ = −94 (c = 1.4, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.80 (s, 1H), 8.48 (d, J = 8.2 Hz, 1H), 8.34 (d, J = 7.8 Hz, 1H), 7.73 (t, J = 8.0 Hz, 1H), 7.58−7.32 (m, 5H), 6.03 (s, 1H), 5.49−5.44 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6 (9:1)): δ (ppm) 191.0, 156.7, 147.7, 138.9, 134.6, 129.8, 128.7, 128.4, 127.8, 125.8, 123.7, 82.5, 56.4. MS: m/z = 285.5. Anal. Calcd for $C_{16}H_{12}FNO_3$: C, 67.36; H, 4.24; N, 4.91. Found: C, 67.23; H, 4.15; N, 4.82.

(4S,5R)-5-(4-Chlorobenzoyl)-4-phenyloxazolidin-2-one (**5ea**): 51% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 96:4. Daicel Chirapak OD-H, hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, t_R = 18.02 min (major), t_R = 21.97 min (minor). $[\alpha]_D^{27}$ = −103 (c = 1.2, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.93 (d, J = 8.4 Hz, 2H), 7.41−7.47 (m, 7H), 5.57 (s, 1H), 5.39 (s, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 191.2, 157.4, 141.1, 138.8, 132.0, 130.8, 129.3, 129.2, 129.1, 126.3, 83.4, 56.9. MS: m/z = 302.0. Anal. Calcd for ($C_{16}H_{12}ClNO_3$): C, 63.69; H, 4.01; N, 4.64. Found: C, 63.85; H, 4.29; N, 4.57.

(4S,5R)-5-(4-Bromobenzoyl)-4-phenyloxazolidin-2-one (**5fa**): 44% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 96:4. Daicel Chirapak OD-H, hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, t_R = 20.10 min (major), t_R = 24.01 min (minor). $[\alpha]_D^{27}$ = −69 (c = 3.6, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 7.84 (d, J = 8.5 Hz, 2H), 7.63 (d, J = 8.5 Hz, 2H), 7.46−7.37 (m, 5H), 5.87 (s, 1H), 5.41−5.37 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$ + DMSO-d_6 (9:1)): δ (ppm) 191.2, 156.4, 138.7, 131.4, 131.0, 129.7, 128.3, 128.0, 127.6, 125.3, 81.3, 56.1. MS: m/z [M + 1]$^+$ = 347.7. Anal. Calcd for $C_{16}H_{12}BrNO_3$: C, 55.51; H, 3.49; N, 4.05. Found: C, 55.38; H, 3.34; N, 3.99.

(4S,5R)-5-(3-Bromobenzoyl)-4-phenyloxazolidin-2-one (**5ga**): 50% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 91:9. Daicel Chirapak AD-H, hexane/isopropanol = 70/30, flow rate = 1.0 mL/min, t_R = 22.63 min (major), t_R = 11.60 min (minor). $[\alpha]_D^{27}$ = −60 (c = 1.6, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$): δ 8.07 (s, 1H), 7.87 (d, J = 7.6 Hz, 1H), 7.74 (d, J = 7.7 Hz, 1H), 7.44−7.34 (m, 6H), 6.34 (s, 1H), 5.39 (d, J = 5.6 Hz, 1H), 5.34 (d, J = 5.6 Hz, 1H). ^{13}C NMR (150 MHz,$CDCl_3$): δ 191.1, 157.5, 138.7, 137.3, 135.3, 132.3, 130.4, 129.4, 129.1, 128.0, 126.3, 123.1, 83.3, 56.9. HRMS (ESI) Calcd for $C_{16}H_{12}BrNO_3$ [M + Na$^+$]: 367.9898. Found: 367.9897.

(4S,5R)-4-Phenyl-5-(thiophene-2-carbonyl)oxazolidin-2-one (**5ha**): 58% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 95:5. Daicel Chirapak OD-H, hexane/isopropanol = 80/20, flow rate = 1.0 mL/min, t_R = 16.35 min (major), t_R = 10.67 min (minor). $[\alpha]_D^{26}$ = −36 (c = 1.8, CH_2Cl_2). ^{1}H NMR (600 MHz, $CDCl_3$): δ 7.89 (d, J = 3.5 Hz, 1H), 7.78 (d, J = 4.7 Hz, 1H), 7.41 (s, 4H), 7.39−7.34 (m, 1H), 7.16 (t, J = 4.2 Hz, 1H), 6.42 (s, 1H), 5.29 (d, J = 5.4 Hz, 1H), 5.23 (d, J = 5.5 Hz, 1H). ^{13}C NMR (150 MHz, $CDCl_3$): δ 186.2, 157.7, 140.2, 139.0, 136.2, 135.1, 129.3, 129.0, 128.7, 126.2 84.3, 57.8. HRMS (ESI) Calcd for $C_{14}H_{11}NO_3S$ [M + Na$^+$]: 296.0357. Found: 296.0370.

(4S,5R)-4-(Naphthalen-1-yl)-5-(3-phenylpropanoyl)-oxazolidin-2-one (**5ii**): 46% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 78:22. Daicel Chirapak OD-H, hexane/isopropanol = 70/30, flow rate = 1.0 mL/min, t_R = 30.30 min (major), t_R = 13.73 min (minor). $[\alpha]_D^{27}$ = 30 (c = 2.9, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.13 (d, J = 8.4 Hz, 1H), 7.91 (d, J = 8.4 Hz, 1H), 7.86 (d, J = 8.4 Hz, 1H), 7.61−7.53 (m, 3H), 7.48 (t, J = 7.5 Hz, 1H), 7.28 (t, J = 7.2 Hz, 2H), 7.22−7.19 (m, 3H), 6.03 (s, 1H), 5.80 (s, 1H), 4.65 (d, J = 2.4 Hz, 1H), 3.17−2.99 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 207.0, 158.3, 140.1, 134.2, 133.9, 129.6, 129.4, 129.1, 128.5, 128.3, 127.1, 126.3, 125.3, 122.6, 122.1, 85.4, 54.8, 40.8, 28.8. HRMS (ESI) Calcd for $C_{22}H_{19}NO_3$ [M + Na$^+$]: 368.1263. Found: 368.1265.

Representative Procedure for the Enantioselective Cascade [4 + 1]/[3 + 2] Cycloaddition. To the solution of nitroolefin **6a** (0.1 mmol, 1.0 equiv, 26.3 mg) in $CHCl_3$/F-benzene ((4:1), 5 mL) was added chiral sulfur ylide **3a** (0.125 mmol, 1.25 equiv, 53.82 mg). The reaction mixture was stirred for 72 h at room temperature. Upon the completion of the reaction monitored by TLC, the solvent was removed under reduced pressure. The crude product was purified by flash chromatography on silica gel (silica, 200−300; eluant, petroleum ether/dichloromethane/acetone (10:3:1)) to provide pure product **7aa**. The diastereomer ratio was determined by ^{1}H NMR of the reaction mixture. The enantiomeric ratio was determined by chiral HPLC at 25 °C using a UV detector tuned for 254 nm.

Ethyl (1R,4S,4aS,9bR,9cR)-1-(Phenylcarbonyl)-4,4a,9b,9c-tetrahydro-1H-2,3,5-trioxa-2a-azapentaleno[1,6-ab]nap-hthalene-4-carboxylate (**7aa**): 95% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 81:19. Daicel Chirapak OD-H, hexane/isopropanol = 70/30, flow rate = 1.0 mL/min, t_R = 10.96 min (major), t_R = 13.84 min (minor). $[\alpha]_D^{27}$ = +12.3 (c = 2.1, $CHCl_3$). ^{1}H NMR (400 MHz, $CDCl_3$): δ (ppm) 8.00 (d, J = 7.6 Hz, 2H), 7.56 (t, J = 7.2 Hz, 1H), 7.42 (t, J = 7.6 Hz, 2H), 7.33 (d, J = 7.6 Hz, 1H), 7.23 (t, J = 7.6 Hz, 1H), 7.01 (d, J = 8.0 Hz, 2H), 5.41 (d, J = 8.8 Hz, 1H), 5.11 (s, 1H), 5.10 (s, 1H), 4.52 (t, J = 7.8 Hz, 1H), 4.42 (t, J = 9.0 Hz, 1H), 4.31 (q, J = 7.2 Hz, 2H), 1.34 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ (ppm) 192.4, 168.0, 153.2, 134.8, 134.1, 130.0, 129.5, 129.1,128.5, 123.6, 121.7, 117.8, 85.6, 82.7, 81.6, 73.9, 62.2, 41.7, 14.1. MS: m/z = 382.3 ([M + H]$^+$). Anal. Calcd for ($C_{21}H_{19}NO_6$): C, 66.13; H, 5.02; N, 3.67. Found: C, 65.95; H, 4.74; N, 3.53.

Ethyl (1R,4S,4aS,9bR,9cR)-8-Methyl-1-(phenylcarbonyl)-4,4a,9b,9c-tetrahydro-1H-2,3,5-trioxa-2a-azapentaleno-[1,6-ab]-naphthalene-4-carboxylate (**7ab**): 75% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 79:21. Daicel Chirapak OD-H, hexane/isopropanol = 70/30, flow rate = 1.0 mL/min, t_R = 8.62 min (major), t_R = 10.89 min (minor). $[\alpha]_D^{26}$ = +35.6 (c = 1.9, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.01 (d, J = 7.8 Hz, 2H), 7.57 (t, J = 7.2 Hz, 1H), 7.43 (t, J = 7.8 Hz, 2H), 7.12 (s, 1H), 7.03 (d, J = 8.4 Hz, 1H), 6.92 (d, J = 8.4 Hz, 1H), 5.41 (d, J = 9.0 Hz, 1H), 5.10 (d, J = 1.8 Hz, 1H), 5.07 (dd, J_1 = 2.4 Hz, J_2 = 6.6 Hz, 1H), 4.90 (dd, J_1 = 6.0 Hz, J_2 = 9.0 Hz, 1H), 4.38 (t, J = 9.0 Hz, 1H), 4.33−4.29 (m, 2H), 2.26 (s, 1H), 1.35 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 192.6, 168.1, 150.9, 134.9, 134.0, 133.1, 130.3, 129.6, 129.5, 128.5, 121.5, 117.5, 85.6, 82.8, 81.6, 74.0, 62.1, 41.8, 20.6, 14.1. MS: m/z = 396.4 ([M + H]$^+$). Anal. Calcd for ($C_{22}H_{21}NO_6$): C, 66.83; H, 5.35; N, 3.54. Found: C, 66.95; H, 5.53; N, 3.52.

Ethyl (1R,4S,4aS,9bR,9cR)-1-(Phenylcarbonyl)-4,4a,9b,9c-tetrahydro-1H-2,3,5-trioxa-2a-azapen-taleno[1,6-ab]na-phthalene-4-carboxylate (**7ac**): 91% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 81:19. Daicel Chirapak OD-H, hexane/isopropanol = 70/30, flow rate = 1.0 mL/min, t_R = 10.55 min (major), t_R = 13.77 min (minor). $[\alpha]_D^{26}$ = +36.1 (c = 2.5, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.04 (d, J = 7.8 Hz, 2H), 7.60−7.58 (m, 1H), 7.45

(t, J = 7.8 Hz, 2H), 7.37 (s, 1H), 7.20 (dd, J_1 = 1.8 Hz, J_2 = 8.4 Hz,1H), 6.97 (d, J = 8.4 Hz, 1H), 5.38 (d, J = 9.0 Hz, 1H), 5.11 (d, J = 6.6 Hz, 1H), 5.09 (s, 1H), 4.50 (dd, J_1 = 6.6 Hz, J_2 = 9.6 Hz, 1H), 4.40 (t, J = 9.0 Hz, 1H), 4.33−4.30 (m, 2H), 1.35 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 192.1, 167.8, 151.7, 134.6, 134.2, 129.7, 129.5, 129.1, 128.6, 128.4, 123.4, 119.2, 85.7, 82.8, 81.4, 73.4, 62.2, 41.3, 14.0. MS: m/z = 416.2 ([M + H]$^+$). Anal. Calcd for ($C_{21}H_{18}ClNO_6$): C, 60.66; H, 4.36; N, 3.37. Found: C, 60.79; H, 4.47; N, 3.18.

*Ethyl (1R,4S,4aS,9bR,9cR)-1-(Phenylcarbonyl)-4,4a,11c,11d-tetrahydro-1H-2,3,5-trioxa-2a-azapentaleno[1,6-bc]p-henanthrene-4-carboxylate (**7ad**):* 87% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 77:23. Daicel Chirapak OD-H, hexane/isopropanol = 70/30, flow rate = 1.0 mL/min, t_R = 15.62 min (minor), t_R = 20.69 min (major). $[\alpha]_D^{27}$ = +43.5(c = 2.1, $CHCl_3$). Daicel Chirapak OD-H, hexane/isopropanol = 70/30, flow rate = 1.0 mL/min, T = 25 °C, 254 nm, t_R = 10.96 min (major), t_R = 13.84 min (minor). $[\alpha]_D^{27}$ = +12.3 (c = 2.1, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.20 (d, J = 8.4 Hz, 1H), 7.91 (dd, J_1 = 1.2 Hz, J_2 = 8.4 Hz, 2H), 7.77 (dd, J_1 = 8.4 Hz, J_2 = 13.2 Hz, 2H), 7.55−7.52 (m, 1H), 7.50−7.47 (m, 1H), 7.40 (t, J = 7.5 Hz, 1H), 7.34 (t, J = 7.8 Hz, 2H), 7.25 (d, J = 9.0 Hz, 1H), 5.39−5.33 (m, 3H), 5.02 (dd, J_1 = 1.8 Hz, J_2 = 6.0 Hz, 1H), 4.58 (dd, J_1 = 6.6 Hz, J_2 = 8.4 Hz, 1H), 4.33 (q, J = 7.2 Hz, 2H), 1.36 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 194.1, 167.8, 152.2, 134.7, 133.7, 131.5, 130.5, 129.6, 129.4, 128.5, 128.4, 127.2, 124.6, 122.3, 118.6, 116.0, 84.7, 84.5, 82.8, 75.7, 62.2, 37.6, 14.1. MS: m/z = 432.5([M + H]$^+$). Anal. Calcd for ($C_{25}H_{21}NO_6$): C, 69.60; H, 4.91; N, 3.25. Found: C, 69.48; H, 5.18; N, 3.03.

*Ethyl (1R,4S,4aS,9bR,9cR)-1-[(4-Methylphenyl)-carbon-yl]-4,4a,9b,9c-tetrahydro-1H-2,3,5-trioxa-2a-azapentaleno [1,6-ab]-naphthalene-4-carboxylate (**7ba**):* 54% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 87:13. Daicel Chirapak OD-H, hexane/isopropanol = 70/30, flow rate = 1.0 mL/min, t_R = 11.32 min (major), t_R = 16.39 min (minor). $[\alpha]_D^{27}$ = +15.7 (c = 1.4, $CHCl_3$).^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 7.91 (d, J = 7.2, 2H), 7.34 (d, J = 7.8 Hz, 1H), 7.25−7.22 (m, 3H), 7.02 (t, J = 8.1 Hz, 2H), 5.40 (d, J = 9.0 Hz, 1H), 5.11 (t, J = 6.6 Hz, 2H), 4.53−4.51 (m, 1H), 4.42 (t, J = 9.0 Hz, 1H), 4.33−4.30 (m, 2H), 2.39 (s, 1H), 1.35 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 191.9, 168.1, 153.2, 145.2, 132.5, 130.0, 129.6, 129.3, 129.1, 123.6, 121.7, 117.8, 85.7, 82.7, 81.5, 73.9, 62.2, 41.7, 21.7, 14.1. MS: m/z = 395.5 (M$^+$). Anal. Calcd for ($C_{22}H_{21}NO_6$): C, 66.83; H, 5.35; N, 3.54. Found: C, 67.04; H, 5.11; N, 3.40.

*Ethyl (1R,4S,4aS,9bR,9cR)-1-[(4-Fluorophenyl)carbon-yl]-4,4a,9b,9c-tetrahydro-1H-2,3,5-trioxa-2a-azapentaleno-[1,6-ab]-naphthalene-4-carboxylate (**7ca**):* 78% yield; white solid; diastereomer ratio, >95:5; enantiomeric ratio, 87:13. Daicel Chirapak AD-H, hexane/isopropanol = 60/40, flow rate = 1.0 mL/min, t_R = 35.82 min (major), t_R = 40.69 min (minor). $[\alpha]_D^{27}$ = +14.7 (c = 2.02, $CHCl_3$). ^{1}H NMR (600 MHz, $CDCl_3$): δ (ppm) 8.06 (dd, J_1 = 5.4 Hz, J_2 = 8.4 Hz, 2H), 7.36 (d, J = 6.6 Hz, 1H), 7.24 (d, J = 7.8 Hz, 1H), 7.10 (t, J = 8.7 Hz, 2H), 7.04 (t, J = 6.9 Hz, 2H), 5.35 (d, J = 9.0 Hz, 1H), 5.12 (s, 1H), 5.11 (d, J = 6.0 Hz, 1H), 4.52 (dd, J_1 = 6.0 Hz, J_2 = 9.0 Hz, 1H), 4.42 (t, J = 9.3 Hz, 1H), 4.34−4.29 (m, 2H), 1.36 (t, J = 7.2 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$): δ (ppm) 191.0, 168.0, 153.3, 132.41, 132.35, 131.3, 130.0, 129.2, 123.7, 121.7, 117.9, 115.9, 115.7, 85.6, 82.8, 81.7, 74.1, 62.2, 41.8, 14.1. MS: m/z = 399.3 (M$^+$). Anal. Calcd for ($C_{21}H_{18}FNO_6$): C, 63.16; H, 4.54; N, 3.51. Found: C, 63.10; H, 4.34; N, 3.48.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Experimental details, NMR spectra, HPLC spectra of all products, and X-ray crystallographic data (CIF) for **5fa**. This material is available free of charge via the Internet at http://pubs.acs.org.

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