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Asymmetric Michael addition of 4*H*-thiopyran-4-one to nitroolefins catalyzed by diamine mono-*N*-sulfonamide and its application to concise synthesis of enantiopure multiring heterocycles

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ABSTRACT

A new series of mono-*N*-sulfonamides of C_2-symmetrical 2′-bipyrrolidine have been designed, synthesized, and successfully applied as the organocatalysts to the enantio- and diastereoselective Michael addition of 4*H*-thiopyran-4-one to a variety of nitroolefins. Catalyst **10** was identified in the examinations to exhibit more superior catalytic ability than the traditional chiral pyrrolidine catalysts, giving high chemical yields, excellent diastereo- and enantioselectivities (up to 99:1 dr and 98% ee). The *tert*-butyl sulfonamide functionality of catalyst **10** is speculated to play crucial roles in the transition state as both bulky group and hydrogen-bond acceptor. Application of a representative Michael adduct has been also studied and proven to be useful for the diversity-oriented synthesis of enantiopure multiring heterocycles through a unique common bicyclic nitrone intermediate.

1. Introduction

Recent rapid development of the chemical reactions catalyzed by small organic molecules has made it to be a hot area of organic chemistry.[1] Because of their advantages of environmental friendliness, high efficiency, and excellent selectivity,[2] great attentions have been directed toward the design and application of various organocatalysts,[3] including the frequently used enamine and imine catalysis,[4,5] hydrogen-bond activation,[6] carbene catalysis,[7] and phase-transfer catalysis[8] as well. Asymmetric Michael addition is one of the most important and frequently used carbon–carbon and carbon–heteroatom forming methods.[9] Many highly efficient and enantioselective catalytic systems have been developed for the Michael addition of ketone to nitroolefins after the pioneering works by List[10a] and Barbas.[10b,10c] Several representative catalysts include Wang's pyrrolidine sulfonamides[11h] and thiourea-dehydroabietic amine,[12k] Barbas' diamines,[11i] Tang's thiourea-secondary amines,[11j] Tsogoeva's[12g,12h] and Jacobsen's primary amine-thioureas,[12i] Takemoto's thiourea-tertiary amine,[12l] and Chen's pyrrolidinyl-camphor derivatives.[12t] A series of chiral 2,2′-bipyrrolidine-type diamine catalysts were also developed by Alexakis' group for the asymmetric Michael addition of ketone to nitroolefins (Fig. 1).[10g,11a,11e]

Based on our recent synthesis of 2-(((*S*)-2-((*S*)-1-(pyridin-2-ylmethyl)pyrrolidin-2-yl)pyrrolidin-1-yl)methyl)pyridine (abbreviated as (*S*,*S*)-PDP, a chiral ligand for Fe(III)),[13] we further explored the organocatalytic application of the mono-*N*-sulfonamide

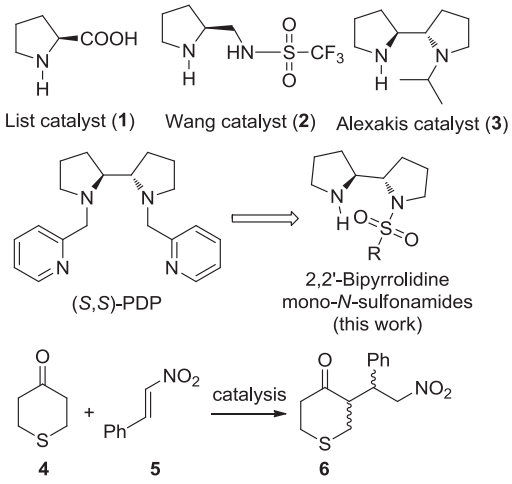

Fig. 1. Design of chiral 2,2′-bipyrrolidine mono-*N*-sulfonamides.

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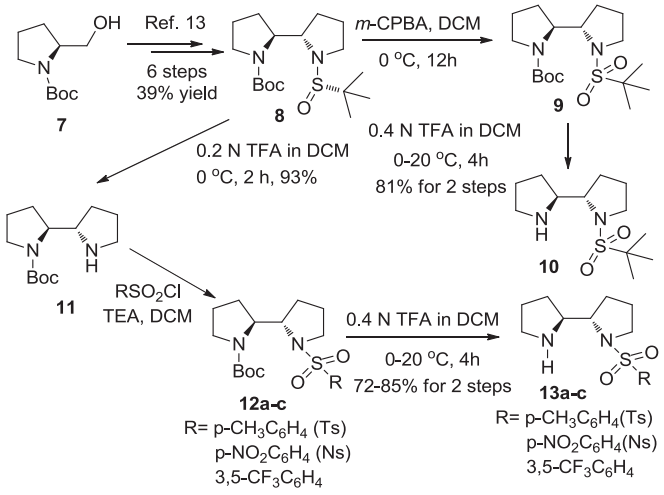
derivatives of such a C_2-symmytrical 2,2′-bipyrrolidine scaffold (Fig. 1). It was initially speculated that multiple nitrogen and oxygen atoms of the newly introduced sulfonamide functionality might be able to serve as the electron-donating elements in the catalytic processes. Herein, we wish to report the highly enantio- and diastereoselective Michael addition of 4*H*-thiopyran-4-one to nitrostyrene catalyzed by these newly prepared diamine mono-*N*-sulfonamides, and its application to the concise synthesis of enantiopure multiring heterocycles.

2. Results and discussion

The new catalysts containing a C_2-symmetrical 2,2′-bipyrrolidine core were conveniently prepared from an intermediate **8** in our previous synthesis of (*S*,*S*)-PDP.[13] Starting from *tert*-butylsulfonimide **8**, we could easily obtain the corresponding *tert*-butyl sulfonamide **9** through *m*-CPBA oxidation in 90% yield. Selective deprotection of the *N*-Boc group of **9** was achieved by treatment with 0.4 N TFA in CH_2Cl_2 at 0–20 °C, affording catalyst **10** in 92% yield. In the other parallel reaction, selective removal of the *N*-*tert*-butylsulfonimide group of **8** was accomplished with 0.2 N TFA in CH_2Cl_2 at 0 °C, affording mono-*N*-Boc-2,2′-bipyrrolidine **11** in 93% yield. Amine **11** could react in parallel with several selected sulfonyl chlorides in the presence of triethylamine to provide compounds **12a**–**c**, respectively. Finally, catalysts **13a**–**c** were prepared after removal of the *N*-Boc protecting group (Scheme 1).

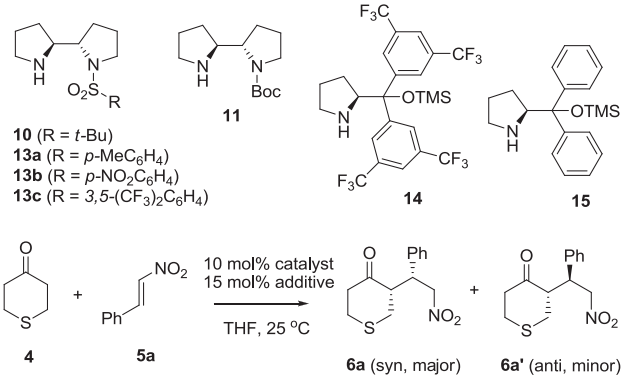


Scheme 1. Synthesis of new chiral pyrrolidine catalysts **10**, **11**, and **13a**–**13c**.

Michael addition of 4*H*-thiopyran-4-one (**4**, a commercially available and frequently used building block in organic synthesis) to *trans*-β-nitrostyrene **5a** was chosen as the benchmark reaction to examine the catalytic ability of the above newly synthesized catalysts. In the presence of catalytic amount of PhCOOH (15 mol %) as the additive, all these catalysts **10**, **11**, **13a**–**c** (10 mol %) could efficiently catalyze this reaction to the completion in THF. For comparison, two known and frequently used catalysts **14** and **15** were also applied, and both of them afforded only trace amount of products. Since catalyst **10** showed the best performance (50:1 dr and 90% ee) in the preliminary assessment (Table 1), it was selected as the catalyst for our further investigations.

A variety of solvents were then examined for an optimal set of reaction conditions. All the reactions in DMF, toluene, and EtOH were carried out with better results (Table 2, entries 1, 2, and 11), and EtOH was selected as the optimal solvent for the next step with consideration of easy operation and less toxicity. Other solvents such as DCM, DCE, and CH_3CN afforded the products in relatively lower enantioselectivity and diastereoselectivity. It is noteworthy here that this reaction also could be carried out well in MeOH and $CHCl_3$ in longer reaction times (5 days, entries 5 and 10). Under the optimal conditions, catalyst loading was also examined (entries 12 and 13). It was found that decreasing the catalyst loading would slow down the reaction rate but shows little effects on the enantio- and diastereoselectivity and chemical yield of the product. Therefore, a combination of 10 mol % of catalyst **10** and 15 mol % of additive ($PhCO_2H$) in EtOH was finally chosen as the standard conditions for the further study.

Table 1
Catalyst assessment for the asymmetric Michael addition[a,b]



Entry	Cat.	Additive	Time (d)	Yield (%)	*Syn*/*anti*	ee (*syn*, %)
1	**10**	—	3	NR	—	—
2	**10**	$PhCO_2H$	2	95	50:1	90
3	**13a**	$PhCO_2H$	2.5	98	25:1	86
4	**13b**	$PhCO_2H$	1	99	27:1	85
5	**13c**	$PhCO_2H$	5	54	31:1	85
6	**11**	$PhCO_2H$	7	56	16:1	81
7	**14**	$PhCO_2H$	10	Trace	—	—
8	**15**	$PhCO_2H$	10	Trace	—	—

[a] Unless otherwise noted, the reaction was carried out with **4** (1.25 mmol), **5a** (0.25 mmol), catalyst (0.025 mmol), and additive (0.038 mmol) in THF (0.5 ml) at room temperature.
[b] *Syn*/*anti* ratio and ee values of the products were determined by chiral HPLC analysis, and absolute and relative stereochemistry of the products were judged by comparison with literature works.

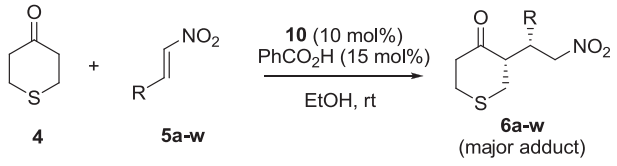
Table 2
Examination of solvents and catalyst loadings[a,b]

Entry	Solvent	$PhCO_2H$ (mol %)	Time (d)	Yield[c] (%)	*Syn*/*anti*	ee (*syn*,%)
1	DMF	15	1.5	92	65:1	91
2	PhMe	15	2	90	67:1	90
3	DCM	15	3	89	41:1	88
4	DCE	15	2	87	30:1	88
5	MeOH	15	5	71	57:1	94
6	DMSO	15	5	80	44:1	92
7	CH_3CN	15	3	87	36:1	90
8	Dioxane	15	5	81	33:1	86
9	EtOAc	15	3	78	50:1	93
10	$CHCl_3$	15	5	85	49:1	93
11	EtOH	15	3	91	59:1	95
12[d]	EtOH	7.5	7	77 (86[f])	57:1	94
13[e]	EtOH	3.75	10	69 (84[f])	55:1	94

[a] Unless otherwise noted, the reaction was carried out with **4** (1.25 mmol), **5a** (0.25 mmol), catalyst **10** (0.025 mmol), and $PhCO_2H$ (0.038 mmol) in solvent (0.5 mL) at room temperature.
[b] *Syn*/*anti* ratio and ee values of the products were determined by chiral HPLC analysis.
[c] Isolated yields of the Michael adducts.
[d] With 5 mol % loading of **10**.
[e] With 2.5 mol % loading of **10**.
[f] Yield based on recovery of the starting material.

Under the above optimal conditions, the generality of this reaction was explored with various nitroolefins **5a**–**5z** (Table 3). The results showed that all the nitroolefins (**5a**–**5w**) having a 2-aryl substituent (including variously substituted phenyls, 1- or 2-naphthyl, 2-furyl, and 2-thiophenyl) could give reasonable yields of Michael adducts with excellent diastereoselectivity (up to 99:1 dr) and enantioselectivity (up to 98% ee). Either electron-withdrawing or electron-donating groups were well tolerated at the 2-, 3-, 4- and 6-positions of the phenyl ring of the nitroolefins. Though the *syn*/*anti* ratios of Michael adducts could be varied in a wide range (7:1–99:1), enantiopurities of the major *syn* products were always excellent (ranging from 91% ee to 98% ee). Compared to the substrates having a 4-halogenated phenyl substituent (entries 2 and 3), the nitroolefins having a 2- and 3-halogenated phenyl substituent (entries 7, 8, 11, and 12) usually gave better *syn*/*anti* ratios, as well as those having two halogens (entries 15 and 18). Several aliphatic nitroolefins **5x**–**5z** were also tested (entries 24–26). Unfortunately, these three reactions gave no adducts. The poor electron-withdrawing and charge-stabilizing capacity of the aliphatic group is speculated to be associated with the disappointing results.

Table 3
Asymmetric Michael addition of **4** with various nitroolefins[a,b]



Entry	6	Time (d)	Yield (%)	*Syn*/*anti*	ee (*syn*, %)
1	**6a** (R=C_6H_5)	3	88	59:1	95
2	**6b** (R=4-ClC_6H_4)	2	87	18:1	93
3	**6c** (R=4-BrC_6H_4)	1.5	83	35:1	95
4	**6d** (R=4-$CF_3C_6H_4$)	2	84	22:1	91
5	**6e** (R=4-$MeOC_6H_4$)	5	75	18:1	93
6	**6f** (R=4-MeC_6H_4)	4	83	52:1	97
7	**6g** (R=2-ClC_6H_4)	3	98	41:1	96
8	**6h** (R=2-BrC_6H_4)	2	99	99:1	96
9	**6i** (R=2-$MeOC_6H_4$)	5	73	99:1	94
10	**6j** (R=2-$CF_3C_6H_4$)	4	81	52:1	97
11	**6k** (R=3-ClC_6H_4)	3	84	99:1	98
12	**6l** (R=3-BrC_6H_4)	5	86	78:1	98
13	**6m** (R=3-$MeOC_6H_4$)	4	76	7:1	84
14	**6n** (R=3-$CF_3C_6H_4$)	4	79	32:1	97
15	**6o** (R=2,4-$Cl_2C_6H_3$)	3	98	66:1	97
16	**6p** (R=2,4-$(MeO)_2C_6H_3$)	3	99	55:1	96
17	**6q** (R=2-Br,4-FC_6H_3)	2	96	32:1	97
18	**6r** (R=2-Cl,6-FC_6H_3)	1.5	96	99:1	96
19	**6s** (R=piperonyl)	4	81	15:1	97
20	**6t** (R=1-naphthyl)	4	83	99:1	98
21	**6u** (R=2-naphthyl)	4	85	28:1	90
22	**6v** (R=2-furyl)	4	80	25:1	95
23	**6w** (R=2-thiophenyl)	2	75	12:1	94
24	**6x** (R=2-propyl)	10	NR	—	—
25	**6y** (R=*tert*-butyl)	10	NR	—	—
26	**6z** (R=cyclohexyl)	10	NR	—	—

[a] Unless otherwise noted, the reaction was carried out with **4** (1.25 mmol), **5** (0.25 mmol), catalyst **10** (0.025 mmol), and $PhCO_2H$ (0.038 mmol) in EtOH (0.5 mL) at room temperature.
[b] *Syn*/*anti* ratios and ee values of the *syn*-diastereomers were determined by chiral HPLC analysis.

In order to explain the observed stereoselectivity, a possible catalytic mode is proposed (Fig. 2) based on our experimental results. Because the two structurally similar known proline-derived catalysts **14** and **15** didn't work in our examination (Table 1, entries 7 and 8), formation of an extensive hydrogen-bonding network is speculated to take place between the nitro group of the olefin substrate and the sulfonamide of the catalyst in the transition

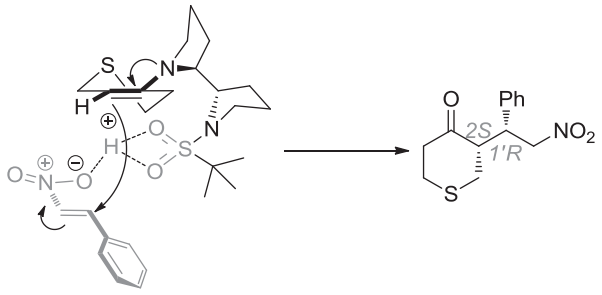
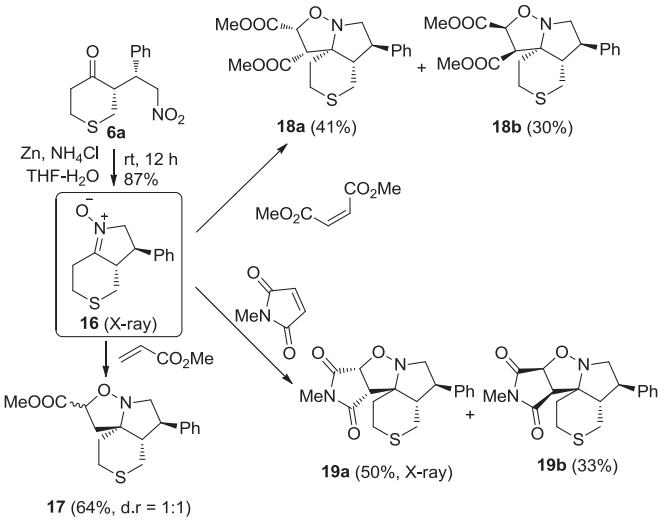


Fig. 2. A proposed catalytic mode.

state with the aid of an acidic additive.[11i,14] Such hydrogen-bonding effect caused by the *N*-sulfonamide is also thought to be stronger than that of the *N*-Boc amide (Table 1, entry 6, catalyst **11**). Therefore, the complete catalytic process could be explained as follows. The pyrrolidine moiety of catalyst **10** firstly activates the cycloketone by aid of $PhCO_2H$ through the commonly known mechanism to form an enamine intermediate, which will serve as the Michael donor in the next addition. In the transition state, the *tert*-butyl sulfonamide group of catalyst **10** might serve as both a bulky group and a hydrogen-bond acceptor. These two factors are thought to direct the favorable orientation of nitrostyrene to receive the enamine addition from *re*-face.

These newly synthesized Michael adducts are convenient precursors for nitrones, which enable quick formation of various five-membered heterocycles through 1,3-dipolar cycloadditions with the corresponding dipolarophiles.[15] Representatively, treatment of the Michael adduct **6a** with Zn/NH_4Cl in THF and water at room temperature resulted in the formation of a unique bicyclic nitrone **16** as single diastereomer, whose absolute structure was confirmed by X-ray single crystal analysis. Parallel reactions of nitrone **16** with methyl acrylate, dimethyl maleate, *N*-methylmaleimide smoothly afforded corresponding tricyclic heterocycles **17**–**19**, respectively (Scheme 2).



Scheme 2. 1,3-Dipolar cycloadditions of representative nitrone **16** prepared from Michael adduct **6a**.

3. Conclusion

In summary, a new series of 2,2′-bipyrrolidine mono-*N*-sulfonamide organocatalysts have been designed and synthesized.

Catalyst **10** was identified to exhibit outstanding catalytic ability under mild conditions, by comparison with two known chiral pyrrolidine catalysts, in the enantio- and diastereoselective Michael addition of 4*H*-thiopyran-4-one to nitroolefins. Introduction of the *tert*-butyl sulfonamide group into the catalyst as both a bulky group and a hydrogen-bond acceptor was proven to be a successful protocol to direct the favorable orientation of nitrostyrene for the addition of enamine. The developed catalytic reactions resulted in high yield of the products with excellent diastereoselectivity (up to 99:1 dr) and enantioselectivity (up to 98% ee). One of the Michael adducts was successfully converted into a unique bicyclic nitrone and further applied in the diverse synthesis of enantiopure multiring heterocycles.

4. Experimental section

4.1. General

All reactions were conducted using oven-dried glassware. Tetrahydrofuran was dried over Na with benzophenone as indicator. Toluene, dichloromethane, petroleum ether, and ethyl acetate were obtained from commercial suppliers and used without further distillation. ^{1}H NMR spectra were recorded at 300 and 400 MHz, and ^{13}C NMR spectra were recorded at corresponding instruments in $CDCl_3$ using TMS as internal standard. IR spectra were recorded on a Bruker Vector 22 FTIR instrument. All new compounds were further characterized by HRMS (high resolution mass spectra) or elemental analysis. Enantiomeric excesses (ees) were determined by chiral HPLC analysis on an Agilent HP 1200 instrument. Optical rotations were measured on a Rudolph Autopol III automaticpolarimeter.

4.2. Synthesis of catalysts 9–13c

The common intermediate **8** was prepared according to the literature.[13] $[\alpha]_D^{30}$ −68.7 (*c* 1.50, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): δ 1.16 (s, 9H), 1.37–1.56 (m, 9H), 1.63–2.05 (m, 8H), 3.18–3.76 (m, 4H), 3.76–4.19 (m, 2H). MS (ESI, *m*/*z*): 367.3 $[M+Na]^+$.

*4.2.1. (2S,2′S)-1-(tert-Butylsulfonyl)-2,2′-bipyrrolidine (**10**).* To a dried flask was added *m*-CPBA (70–75%, 1.2 g, 4.8 mmol) and CH_2Cl_2 (15 mL) under N_2 atmosphere. The mixture was cooled down to 0 °C, and then **8** (550 mg, 1.6 mmol) in CH_2Cl_2 (15 mL) was added slowly via a syringe. The reaction mixture was stirred overnight at 0 °C and quenched with saturated aqueous $Na_2S_2O_3$. The mixture was extracted with CH_2Cl_2 for three times. After being washed with saturated aqueous $NaHCO_3$ and brine, the combined organic layers were dried over Na_2SO_4 and concentrated.

Without further purification, crude **9** from above was added to a dried flask with CH_2Cl_2 (15 mL) under N_2 atmosphere. The mixture was cooled to 0 °C and then TFA (0.45 mL, 6.0 mmol) was added slowly. The reaction mixture was stirred at 0 °C for 30 min and warmed to room temperature. After being stirred for 4 h at room temperature, the reaction mixture was concentrated directly to remove excess TFA. The residue was purified by silica gel chromatography (CH_2Cl_2/MeOH/NH_3=30:1:1) to give **10** (337 mg, 81% for two steps) as a white solid. Mp 153–154 °C. $[\alpha]_D^{28}$ −40.8 (*c* 1.03, $CHCl_3$). IR (KBr, ν_{max}): 2980, 2773, 1419, 1396, 1315, 1198, 1168, 1122 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.22–4.14 (m, 1H), 4.05–3.97 (m, 1H), 3.67–3.51 (m, 2H), 3.39–3.31 (m, 1H), 3.24–3.15 (m, 1H), 2.29–2.17 (m, 2H), 2.11–1.89 (m, 4H), 1.75–1.63 (m, 2H), 1.46 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.3, 24.9, 25.4, 28.5, 29.6, 45.3, 50.8, 61.7, 62.5, 77.1. HRMS (MALDI-TOF, *m*/*z*) calcd for $C_{12}H_{25}N_2O_2S$ $([M+H]^+)$ 261.1631; found 261.1655.

*4.2.2. (2S,2′S)-tert-Butyl [2,2′-bipyrrolidine]-1-carboxylate (**11**).* To a dried flask was added **8** (840 mg, 2.4 mmol) and CH_2Cl_2 (25 mL) under N_2 atmosphere. After being cooled to 0 °C, TFA (0.37 mL, 5.0 mmol) was added slowly. The reaction mixture was stirred at 0 °C for 2 h, and concentrated directly to remove excess TFA. The residue was purified by silica gel chromatography (CH_2Cl_2/MeOH/NH_3=30:1:1) to give **11** (544 mg, 93%) as a yellow solid. Mp 104–105 °C. $[\alpha]_D^{30}$ −57.9 (*c* 0.50, $CHCl_3$). IR (KBr, ν_{max}): 2979, 1689, 1404, 1200, 1171, 1134 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 3.97–3.89 (m, 2H), 3.57–3.52 (m, 1H), 3.42 (dd, *J*=5.2, 8.0 Hz, 2H), 3.23–3.16 (m, 1H), 2.28–2.20 (m, 1H), 2.14–1.84 (m, 5H), 1.74–1.62 (m, 2H), 1.47 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.4, 24.6, 28.2, 29.1, 29.2, 45.1, 47.5, 60.0, 64.1, 82.4, 158.8. HRMS (MALDI-TOF, *m*/*z*) calcd for $C_{17}H_{32}N_2NaO_3S$ $([M+H]^+)$ 241.1911; found 241.1887.

*4.2.3. Synthesis of the chiral catalysts **13a–13c**. General procedure* (**13a** as an example): To a solution of **11** (210 mg, 0.88 mmol) in CH_2Cl_2 (5 mL) was added anhydrous triethylamine (0.49 mL, 3.5 mmol) slowly at 0 °C under N_2 atmosphere. Then a solution of TsCl (334 mg, 1.76 mmol) in CH_2Cl_2 (5 mL) was added to the reaction, and the mixture was stirred at 0 °C for 2 h. The mixture was then quenched with aqueous saturated $NaHCO_3$ at 0 °C. The aqueous phase was extracted with CH_2Cl_2 for three times. The combined organic layers were washed with brine and dried over Na_2SO_4. Concentration of the solution gave the crude **12a**.

Without further purification, the above crude product was added to a dried flask with CH_2Cl_2 (7 mL) under N_2 atmosphere. The mixture was cooled to 0 °C and then TFA (0.21 mL, 2.8 mmol) was added slowly. The reaction mixture was stirred at 0 °C for 30 min and then warmed to room temperature. After being stirred for 4 h, the mixture was concentrated directly to remove excess TFA. The residue was purified on silica gel chromatography (CH_2Cl_2/MeOH/NH_3=25:1:1) to give **13a** (200 mg, 81% for two steps) as a yellow oil.

The procedure for the synthesis of **13b** and **13c** was analogous.

*4.2.3.1. (2S,2′S)-N^1-Tosyl-2,2′-bipyrrolidine (**13a**).* Yellow oil. $[\alpha]_D^{30}$ −101.4 (*c* 1.01, $CHCl_3$). IR (neat, ν_{max}): 2960, 2877, 1690, 1597, 1458, 1341, 1199, 1158, 1091 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74 (d, *J*=8.0 Hz, 2H), 7.32 (d, *J*=8.0 Hz, 2H), 3.67 (dt, *J*=3.6, 8.0 Hz, 1H), 3.45 (s, 1H), 3.40–3.31 (m, 2H), 3.20 (dd, *J*=6.8, 15.0 Hz, 1H), 3.13–3.09 (m, 1H), 2.97–2.91 (m, 1H), 2.43 (s, 3H), 1.93–1.71 (m, 4H), 1.60–1.37 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.5, 24.2, 24.9, 28.2, 28.6, 45.8, 49.2, 61.9, 63.8, 127.6, 129.8, 134.8, 143.6. HRMS (MALDI-TOF, *m*/*z*) calcd for $C_{15}H_{23}N_2O_2S$ $([M+H]^+)$ 295.1475; found 295.1486.

*4.2.3.2. (2S,2′S)-N^1-((4-Nitrophenyl)sulfonyl)-2,2′-bipyrrolidine (**13b**).* Yellow oil. $[\alpha]_D^{30}$ −100.2 (*c* 0.13, $CHCl_3$). IR (neat, ν_{max}): 2964, 1685, 1597, 1510, 1306, 1197 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07 (d, *J*=9.6 Hz, 2H), 6.76 (d, *J*=9.6 Hz, 2H), 3.99–3.95 (m, 1H), 3.59–3.54 (m, 1H), 3.30 (dd, *J*=9.6, 17.6 Hz, 1H), 3.21 (dd, *J*=8.0, 14.8 Hz, 1H), 3.04–2.99 (m, 1H), 2.82 (dd, *J*=7.6, 17.2 Hz, 1H), 2.18–2.01 (m, 2H), 1.98–1.88 (m, 2H), 1.86–1.67 (m, 4H), 1.49–1.40 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.4, 24.8, 28.5, 46.5, 49.1, 62.2, 63.4, 111.6, 125.9, 136.8, 153.1. HRMS (MALDI-TOF, *m*/*z*) calcd for $C_{14}H_{20}N_3O_4S$ $([M+H]^+)$ 326.1169; found 326.1154.

*4.2.3.3. (2S,2′S)-N^1-((3,5-Bis(trifluoromethyl)phenyl)sulfonyl)-2,2′-bipyrrolidine (**13c**).* Yellow oil. $[\alpha]_D^{30}$ −45.2 (*c* 0.25, $CHCl_3$). IR (neat, ν_{max}): 2964, 1685, 1597, 1510, 1306, 1197 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.40 (s, 2H), 8.08 (s, 1H), 3.80 (dt, *J*=3.2, 7.8 Hz, 1H), 3.44–3.35 (m, 2H), 3.17 (dd, *J*=6.8, 14.8 Hz, 1H), 3.08–3.02 (m, 1H), 2.91–2.85 (m, 1H), 2.22 (s, H), 1.92–1.57 (m, 7H), 1.44–1.35 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.4, 25.2, 28.4, 28.7, 46.2, 49.0, 62.1, 64.9, 121.2, 123.9, 126.0 (m, *J*=3.6 Hz), 127.8 (d, *J*=2.7 Hz), 132.7 (q, *J*=4.3 Hz), 144.8. HRMS (MALDI-TOF, *m*/*z*) calcd for $C_{16}H_{19}F_6N_2O_2S$ $([M+H]^+)$ 417.1066; found 417.1066.

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4.3. Synthesis of the Michael adducts 6a–6w

General procedure (**6a** as an example): To a solution of catalyst **10** (6.5 mg, 0.025 mmol) in CH_2Cl_2 (0.5 mL) was added PhCOOH (4.5 mg, 0.038 mmol) and 4*H*-thiopyran-4-one (145 mg, 1.25 mmol) successively at room temperature. Nitroolefin (37 mg, 0.25 mmol) was then added, and the reaction mixture was stirred for 72 h. The reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with ethyl acetate for three times. The combined organic layers were washed with saturated aqueous $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated. Purification on silica gel chromatography (petroleum ether/ethyl acetate=6:1–4:1) gave **6a** (59 mg, 91%) as a white solid.

*4.3.1. (S)-3-((R)-2-Nitro-1-phenylethyl)dihydro-thiopyran-4-one (**6a**).* White solid. Mp 162–163 °C. $[\alpha]_D^{30}$ −36.5 (*c* 0.50, $CHCl_3$). 95% ee (Chiralpak AS-H; *i*-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 25.0 min, t_R (major) 26.3 min). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.38–7.28 (m, 3H), 7.21–7.19 (m, 2H), 4.74 (dd, *J*=4.8, 12.6 Hz, 1H), 4.63 (dd, *J*=10.0, 12.6 Hz, 1H), 3.98 (dt, *J*=4.4, 10.4 Hz, 1H), 3.05 (dt, *J*=4.4, 9.6 Hz, 1H), 3.00–2.96 (m, 2H), 2.90–2.78 (m, 2H), 2.65–2.60 (m, 1H), 2.46 (dd, *J*=9.2, 13.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.6, 35.1, 43.5, 44.5, 55.0, 78.6, 128.2, 128.3, 136.5, 209.5. HRMS (MALDI-TOF, *m*/*z*) calcd for $C_{13}H_{16}NO_3S$ ($[M+H]^+$) 266.0845; found 266.0845. Anal. Calcd for $C_{13}H_{15}NO_3S$ (%): C 58.85, H 5.70, N 5.28; found: C 51.78, H 6.17, N 5.23.

*4.3.2. (S)-3-((R)-1-(4-Chlorophenyl)-2-nitroethyl)dihydro-thiopyran-4-one (**6b**).* White solid. Mp 163–164 °C. $[\alpha]_D^{30}$ −31.7 (*c* 0.50, $CHCl_3$). 93% ee (Chiralpak OD-H; *i*-PrOH/hexane=20:80, 1.0 mL/min; 210 nm, t_R (minor) 16.51 min, t_R (major) 19.50 min). IR (KBr, ν_{max}): 3032, 2907, 1704, 1546, 1487, 1428, 1380, 1197 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36–7.32 (m, 2H), 7.17–7.14 (m, 2H), 4.73 (dd, *J*=4.8, 12.6 Hz, 1H), 4.60 (dd, *J*=10.0, 12.6 Hz, 1H), 3.98 (dt, *J*=4.4, 10.4 Hz, 1H), 3.05–2.96 (m, 3H), 2.89–2.76 (m, 2H), 2.64–2.60 (m, 1H), 2.45 (dd, *J*=9.2, 13.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.6, 35.0, 43.0, 44.5, 54.9, 78.4, 129.5, 129.6, 134.3, 135.0, 209.1. HRMS (MALDI-TOF, *m*/*z*): calcd for $C_{13}H_{15}Cl_1N_1O_3S_1$ $[M+H]^+$ 300.0456; found 300.0480. Anal. Calcd for $C_{13}H_{14}NO_3SCl$ (%): C 52.09, H 4.71, N 4.67; found: C 52.18, H 4.69, N 4.57.

*4.3.3. (S)-3-((R)-1-(4-Bromophenyl)-2-nitroethyl)dihydro-thiopyran-4-one (**6c**).* White solid. Mp 179–180 °C. $[\alpha]_D^{30}$ −25.6 (*c* 0.50, $CHCl_3$). 95% ee (Chiralpak OD-H; *i*-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 35.45 min, t_R (major) 38.57 min). IR (KBr, ν_{max}): 2921, 1706, 1548, 1428, 1380, 1196 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.51–7.47 (m, 2H), 7.11–7.08 (m, 2H), 4.73 (dd, *J*=4.4, 12.8 Hz, 1H), 4.60 (dd, *J*=10.0, 12.8 Hz, 1H), 3.96 (dt, *J*=4.4, 10.4 Hz, 1H), 3.04–2.96 (m, 3H), 2.88–2.78 (m, 2H), 2.63–2.58 (m, 1H), 2.45 (dd, *J*=9.6, 14.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.5, 35.0, 43.0, 44.5, 54.8, 78.3, 122.4, 129.9, 132.5, 135.6, 209.1. HRMS (MALDI-TOF, *m*/*z*) calcd for $C_{13}H_{15}BrNO_3SNa$ ($[M+Na]^+$) 365.9770; found 365.9780. Anal. Calcd for $C_{13}H_{14}NO_3SBr$ (%): C 45.36, H 4.10, N 4.07; found: C 45.46; H 4.16, N 3.98.

*4.3.4. (S)-3-((R)-2-Nitro-1-(4-(trifluoromethyl)phenyl)ethyl)dihydro-thiopyran-4-one (**6d**).* White solid. Mp 191–192 °C. $[\alpha]_D^{30}$ −30.6 (*c* 0.50, $CHCl_3$). 91% ee (Chiralpak OD-H; *i*-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 14.84 min, t_R (major) 22.98 min). IR (KBr, ν_{max}): 2922, 1707, 1551, 1380, 1330, 1219, 1120, 772 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.63 (d, *J*=8.4 Hz, 1H), 7.36 (d, *J*=8.0 Hz, 1H), 4.78 (dd, *J*=4.4, 13.0 Hz, 1H), 4.66 (dd, *J*=10.0, 13.0 Hz, 1H), 4.08 (dt, *J*=4.8, 10.2 Hz, 1H), 3.11–2.97 (m, 3H), 2.90–2.80 (m, 2H), 2.61–2.56 (m, 1H), 2.46 (dd, *J*=9.6, 14.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.6, 35.0, 43.3, 44.6, 54.8, 78.1, 122.4, 125.1, 126.3 (dd, *J*=3.6, 8.2 Hz), 130.5 (q, *J*=2.5 Hz), 130.8, 140.8, 208.8. HRMS (MALDI-TOF, *m*/*z*) calcd for $C_{14}H_{14}NF_3O_3SNa$ ($[M+Na]^+$) 356.0539; found 356.0534. Anal. Calcd for $C_{14}H_{14}F_3NO_3S$ (%): C 50.45, H 4.23, N 4.20; found: C 50.34, H 4.19, N 4.21.

*4.3.5. (S)-3-((R)-1-(4-Methoxyphenyl)-2-nitroethyl)dihydro-thiopyran-4-one (**6e**).* White solid. Mp 127–129 °C. $[\alpha]_D^{30}$ −39.0 (*c* 0.50, $CHCl_3$). 93% ee (Chiralpak AD-H; *i*-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 14.26 min, t_R (major) 39.88 min). IR (KBr, ν_{max}): 2958, 2924, 1703, 1611, 1583, 1548, 1513, 1430, 1380, 1248, 1177 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42 (d, *J*=2.1 Hz, 1H), 7.27–7.17 (m, 2H), 4.86–4.72 (m, 2H), 4.37 (dt, *J*=4.5, 10.2 Hz, 1H), 3.30–3.21 (m, 1H), 3.01–2.91 (m, 2H), 2.84–2.72 (m, 2H), 2.61–2.50 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 31.4, 35.0, 42.7, 44.4, 55.0, 55.1, 78.7, 114.6, 128.1, 129.1, 159.3, 209.5. HRMS (MALDI-TOF, *m*/*z*) calcd for $C_{14}H_{17}N_1O_4SNa$ ($[M+H]^+$) 318.0770; found 318.0792. Anal. Calcd for $C_{14}H_{17}NO_4S$ (%): C 56.93, H 5.80, N 4.74; found: C 56.91, H 5.89, N 4.64.

*4.3.6. (S)-3-((R)-2-Nitro-1-(p-tolyl)ethyl)dihydro-thiopyran-4-one (**6f**).* White solid. Mp 101–102 °C. $[\alpha]_D^{30}$ −36.5 (*c* 0.50, $CHCl_3$). 97% ee (Chiralpak AD-H; *i*-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 9.58 min, t_R (major) 24.58 min). IR (KBr, ν_{max}): 2922, 1713, 1550, 1431, 1384, 1296, 1193, 1109 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.14 (d, *J*=8.0 Hz, 2H), 7.08 (d, *J*=8.0 Hz, 2H), 4.72 (dd, *J*=4.4, 12.4 Hz, 1H), 4.60 (dd, *J*=9.6, 12.6 Hz, 1H), 3.94 (dt, *J*=4.8, 10.4 Hz, 1H), 3.05–2.93 (m, 3H), 2.86–2.75 (m, 2H), 2.64–2.59 (m, 1H), 2.44 (dd, *J*=9.2, 13.8 Hz, 1H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1, 31.6, 35.1, 43.2, 44.5, 55.0, 78.8, 128.0, 130.0, 133.4, 138.0, 209.6. HRMS (MALDI-TOF, *m*/*z*) calcd for $C_{14}H_{18}NO_3S$ ($[M+H]^+$) 280.1002; found 280.0964. Anal. Calcd for $C_{14}H_{17}NO_3S$ (%): C 60.19, H 6.13, N 5.01; found: C 60.18, H 6.14, N 5.04.

*4.3.7. (S)-3-((R)-1-(2-Chlorophenyl)-2-nitroethyl)dihydro-thiopyran-4-one (**6g**).* White solid. Mp 118–119 °C. $[\alpha]_D^{30}$ −36.2 (*c* 0.50, $CHCl_3$). 96% ee (Chiralpak OD-H; *i*-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 11.32 min, t_R (major) 13.07 min). IR (KBr, ν_{max}): 2918, 1701, 1545, 1476, 1425, 1375, 1219, 1113, 1036 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.42–7.40 (m, 1H), 7.30–7.22 (m, 3H), 4.86 (dd, *J*=9.2, 13.0 Hz, 1H), 4.77 (dd, *J*=4.4, 12.8 Hz, 1H), 4.42 (dt, *J*=4.4, 9.8 Hz, 1H), 3.36–3.30 (m, 1H), 3.05–2.93 (m, 2H), 2.88–2.78 (m, 2H), 2.58–2.53 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.8, 35.1, 40.5, 45.2, 54.2, 77.3, 127.7, 129.4, 130.7, 134.3, 134.6, 209.1. HRMS (MALDI-TOF, *m*/*z*) calcd for $C_{13}H_{14}ClNO_3SNa$ ($[M+Na]^+$) 322.0275; found 322.0256. Anal. Calcd for $C_{13}H_{14}NO_3SCl$ (%): C 52.09, H 4.71, N 4.67; found: C 51.85, H 4.79, N 4.48.

*4.3.8. (S)-3-((R)-1-(2-Bromophenyl)-2-nitroethyl)dihydro-thiopyran-4-one (**6h**).* White solid. Mp 129–131 °C. $[\alpha]_D^{30}$ −38.4 (*c* 0.50, $CHCl_3$). 96% ee (Chiralpak OD-H; *i*-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 13.52 min, t_R (major) 15.43 min). IR (KBr, ν_{max}): 2916, 1694, 1551, 1473, 1437, 1378, 1293, 1112, 1023 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (dd, *J*=1.6, 8.2 Hz, 1H), 7.32 (dt, *J*=1.2, 7.4 Hz, 1H), 7.22 (dd, *J*=1.6, 8.0 Hz, 1H), 7.16 (dt, *J*=1.6, 7.6 Hz, 1H), 4.86–4.76 (m, 2H), 4.48–4.45 (m, 1H), 3.32 (s, 1H), 3.06–2.94 (m, 2H), 2.86–2.81 (m, 2H), 2.66–2.52 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.8, 35.1, 42.4, 45.3, 54.6, 77.2, 128.4, 129.6, 134.0, 136.1, 209.1. HRMS (MALDI-TOF, *m*/*z*) calcd for $C_{13}H_{15}BrNO_3SNa$ ($[M+Na]^+$) 365.9770; found 365.9799. Anal. Calcd for $C_{13}H_{14}NO_3SBr$ (%): C 45.36, H 4.10, N 4.07; found: C 45.47, H 4.16, N 4.01.

*4.3.9. (S)-3-((R)-1-(2-Methoxyphenyl)-2-nitroethyl)dihydro-thiopyran-4-one (**6i**).* White solid. Mp 78–80 °C. $[\alpha]_D^{30}$ −41.0 (*c* 0.50, $CHCl_3$). 94% ee (Chiralpak OD-H; *i*-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 9.69 min, t_R (major) 10.64 min). IR (KBr, ν_{max}): 2922, 1701, 1546, 1491, 1376, 1220, 1108, 1019 cm^{-1}. ^{1}H NMR

(400 MHz, $CDCl_3$): δ 7.26 (dt, J=1.2, 8 Hz, 1H), 7.42–7.40 (d, J=6.8 Hz, 1H), 6.90 (t, J=7.2 Hz, 2H), 4.84 (dd, J=9.6, 12.4 Hz, 1H), 4.67 (dd, J=4.4, 12.4 Hz, 1H), 4.12 (dt, J=4.4, 10.4 Hz, 1H), 3.85 (s, 3H), 3.37 (dt, J=4.4, 10.2 Hz, 1H), 2.94–2.90 (m, 2H), 2.87–2.76 (m, 2H), 2.58–2.53 (m, 1H), 2.44 (dd, J=9.6, 13.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.6, 35.3, 41.2, 44.7, 53.0, 55.4, 77.1, 111.3, 121.1, 124.1, 129.5, 131.4, 157.6, 210.0. HRMS (MALDI-TOF, m/z) calcd for $C_{14}H_{17}N_1O_4SNa$ ($[M+H]^+$) 318.0770; found 318.0796. Anal. Calcd for $C_{14}H_{17}NO_4S$ (%): C 56.93, H 5.80, N 4.74; found: C 56.79, H 5.65, N 4.66.

*4.3.10. (S)-3-((R)-2-Nitro-1-(2-(trifluoromethyl)phenyl)ethyl)dihydro-thiopyran-4-one (**6j**).* White solid. Mp 147–149 °C. $[\alpha]_D^{25}$ −11.3 (c 0.20, $CHCl_3$). 97% ee (Chiralpak OD-H; i-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 8.72 min, t_R (major) 9.78 min). IR (KBr, ν_{max}): 2922, 1701, 1551, 1427, 1309, 1111, 1035, 770 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (d, J=8.0 Hz, 1H), 7.59 (t, J=7.6 Hz, 1H), 7.44 (t, J=7.6 Hz, 1H), 7.37 (d, J=8.0 Hz, 1H), 4.93 (dd, J=7.2, 12.0 Hz, 1H), 4.69 (dd, J=4.4, 11.8 Hz, 1H), 4.20–4.15 (m, 1H), 3.46 (dt, J=4.4, 11.0 Hz, 1H), 3.08–2.83 (m, 4H), 2.60–2.54 (m, 1H), 2.44–2.39 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 32.1, 35.7, 38.6, 45.6, 55.2, 78.3, 122.7, 125.4, 126.9 (q, J=5.5 Hz), 128.1, 128.3, 129.5 (q, J=29.8 Hz), 132.9, 136.0, 209.1. HRMS (MALDI-TOF, m/z) calcd for $C_{14}H_{15}NF_3O_3S$ ($[M+H]^+$) 334.0719, found 334.0733. Anal. Calcd for $C_{14}H_{14}F_3NO_3S$ (%): C 50.45, H 4.23, N 4.20; found: C 50.37, H 4.39, N 4.18.

*4.3.11. (S)-3-((R)-1-(3-Chlorophenyl)-2-nitroethyl)dihydro-thiopyran-4-one (**6k**).* White solid. Mp 74–75 °C. $[\alpha]_D^{30}$ −33.8 (c 0.50, $CHCl_3$). 98% ee (Chiralpak OD-H; i-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 17.40 min, t_R (major) 18.58 min). IR (KBr, ν_{max}): 2922, 2853, 1707, 1553, 1433, 1378, 1306, 1117, 797 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33–7.26 (m, 2H), 7.21 (m, 1H), 7.14–7.07 (m, 1H), 4.74 (dd, J=4.5, 12.6 Hz, 1H), 4.60 (dd, J=9.9, 12.8 Hz, 1H), 3.97 (dt, J=4.5, 10.2 Hz, 1H), 3.07–2.94 (m, 3H), 2.90–2.74 (m, 2H), 2.64–2.58 (m, 1H), 2.47 (dd, J=9.3, 13.8 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 31.6, 35.1, 43.2, 44.6, 54.8, 78.2, 126.4, 128.4, 128.6, 130.6, 135.2, 138.7, 209.0. HRMS (MALDI-TOF, m/z) calcd for $C_{13}H_{15}ClNO_3S$ ($[M+H]^+$) 300.0456; found 300.0464. Anal. Calcd for $C_{13}H_{14}NO_3SCl$ (%): C 52.09, H 4.71, N 4.67; found: C 51.85, H 5.07, N 4.36.

*4.3.12. (S)-3-((R)-1-(3-Bromophenyl)-2-nitroethyl)dihydro-thiopyran-4-one (**6l**).* White solid. Mp 70–71 °C. $[\alpha]_D^{30}$ −35.4 (c 0.50, $CHCl_3$). 98% ee (Chiralpak OD-H; i-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 14.98 min, t_R (major) 16.12 min). IR (KBr, ν_{max}): 2921, 2853, 1704, 1549, 1478, 1432, 1219, 1083 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30–7.29 (m, 2H), 7.22–7.21 (m, 1H), 7.12–7.09 (m, 1H), 4.74 (dd, J=4.5, 12.6 Hz, 1H), 4.60 (dd, J=9.9, 12.8 Hz, 1H), 3.97 (dt, J=4.5, 10.2 Hz, 1H), 3.07–2.97 (m, 3H), 2.90–2.74 (m, 2H), 2.64–2.58 (m, 1H), 2.47 (dd, J=9.6, 14.0 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.6, 35.1, 43.2, 44.6, 54.8, 78.2, 126.4, 128.4, 128.6, 130.6, 135.2, 138.7, 209.0. HRMS (MALDI-TOF, m/z) calcd for $C_{13}H_{15}BrNO_3SNa$ ($[M+Na]^+$) 365.9770; found 365.9793. Anal. Calcd for $C_{13}H_{14}NO_3SBr$ (%): C 45.36, H 4.10, N 4.07; found: C 45.74, H 4.42, N 4.34.

*4.3.13. (S)-3-((R)-1-(3-Methoxyphenyl)-2-nitroethyl)dihydro-thiopyran-4-one (**6m**).* White solid. Mp 129–130 °C. $[\alpha]_D^{30}$ −31.1 (c 0.50, $CHCl_3$). 84% ee (Chiralpak AD-H; i-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 12.47 min, t_R (major) 18.49 min). IR (KBr, ν_{max}): 2922, 2852, 1699, 1601, 1489, 1379, 1250, 1051 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28–7.24 (m, 1H), 6.84–6.74 (m, 3H), 4.73 (dd, J=4.4, 12.6 Hz, 1H), 4.62 (dd, J=9.6, 12.8 Hz, 1H), 3.94 (dt, J=4.4, 10.4 Hz, 1H), 3.79 (s, 3H), 3.05–2.93 (m, 3H), 2.88–2.75 (m, 2H), 2.66–2.62 (m, 1H), 2.47 (dd, J=9.6, 13.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.6, 35.1, 43.5, 44.5, 55.0, 55.2, 78.5, 113.2, 114.5, 120.2, 130.4, 138.1, 160.1, 209.5. HRMS (MALDI-TOF, m/z) calcd for $C_{14}H_{17}N_1O_4SNa$ ($[M+H]^+$) 318.0770; found 318.0783. Anal. Calcd for $C_{14}H_{17}NO_4S$ (%): C 56.93, H 5.80, N 4.74; found: C 56.73, H 5.87, N 4.75.

*4.3.14. (S)-3-((R)-2-Nitro-1-(3-(trifluoromethyl)phenyl)ethyl)dihydro-thiopyran-4-one (**6n**).* White solid. Mp 77–78 °C. $[\alpha]_D^{30}$ −32.3 (c 0.50, $CHCl_3$). 97% ee (Chiralpak OD-H; i-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 13.39 min, t_R (major) 14.19 min). IR (KBr, ν_{max}): 2923, 1708, 1551, 1427, 1329, 1163, 1120, 1075 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.58 (d, J=7.6 Hz, 1H), 7.52–7.48 (m, 2H), 7.43 (d, J=8.0 Hz, 1H), 4.78 (dd, J=4.4, 12.8 Hz, 1H), 4.66 (dd, J=10.0, 13.0 Hz, 1H), 4.08 (dt, J=4.4, 10.4 Hz, 1H), 3.11–2.97 (m, 3H), 2.90–2.78 (m, 2H), 2.60–2.56 (m, 1H), 2.46 (dd, J=9.6, 13.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.5, 35.0, 43.4, 44.6, 54.8, 78.1, 122.4, 125.0 (dd, J=4.6, 8.2 Hz), 125.3 (q, J=3.6 Hz), 129.9, 131.5, 131.6, 131.8 (q, J=32.5 Hz), 137.8, 208.8. HRMS (MALDI-TOF, m/z) calcd for $C_{14}H_{15}NF_3O_3S$ ($[M+H]^+$) 334.0719, found 334.0735. Anal. Calcd for $C_{14}H_{14}F_3NO_3S$ (%): C 50.45, H 4.23, N 4.20; found: C 50.32, H 4.44, N 4.18.

*4.3.15. (S)-3-((R)-1-(2,4-Dichlorophenyl)-2-nitroethyl)dihydro-thiopyran-4-one (**6o**).* White solid. Mp 97–98 °C. $[\alpha]_D^{30}$ −33.7 (c 0.50, $CHCl_3$). 97% ee (Chiralpak OD-H; i-PrOH/hexane=7:93, 1.0 mL/min; 254 nm; t_R (minor) 28.52 min, t_R (major) 36.72 min). IR (KBr, ν_{max}): 2919, 1708, 1552, 1475, 1426, 1377, 1106, 816 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.44 (d, J=2.0 Hz, 1H), 7.27 (dd, J=2.0, 8.4 Hz, 1H), 7.19 (d, J=8.4 Hz, 1H), 4.84 (dd, J=9.2, 12.8 Hz, 1H), 4.76 (dd, J=4.4, 12.8 Hz, 1H), 4.38 (dt, J=4.0, 10.0 Hz, 1H), 3.05–2.95 (m, 2H), 2.87–2.78 (m, 2H), 2.62–2.54 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.8, 35.1, 40.2, 45.2, 54.1, 77.2, 128.1, 130.5, 133.0, 134.7, 135.3, 208.8. HRMS (MALDI-TOF, m/z) calcd for $C_{13}H_{14}Cl_2NO_3S$ ($[M+H]^+$) 334.0066; found 334.0088. Anal. Calcd for $C_{13}H_{13}Cl_2NO_3S$ (%): C 55.34, H 4.64, N 3.40; found: C 55.12, H 4.62, N 3.63.

*4.3.16. (S)-3-((R)-1-(2,4-Dimethoxyphenyl)-2-nitroethyl)dihydro-thiopyran-4-one (**6p**).* Yellow solid. Mp 88–89 °C. $[\alpha]_D^{30}$ −39.0 (c 0.50, $CHCl_3$). 96% ee (Chiralpak AD-H; i-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 10.93 min, t_R (major) 14.48 min). IR (KBr, ν_{max}): 2922, 2837, 1706, 1611, 1551, 1437, 1288, 1209, 1158, 1031, 771 cm^{-1}. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.00 (d, J=8.4 Hz, 1H), 6.44–6.38 (m, 2H), 4.79 (dd, J=9.6, 12.3 Hz, 1H), 4.62 (dd, J=4.5, 12.3 Hz, 1H), 4.02 (dt, J=4.5, 10.5 Hz, 1H), 3.80 (s, 3H), 3.75 (s, 3H), 3.30 (dt, J=4.5, 10.2 Hz, 1H), 2.96–2.71 (m, 4H), 2.60–2.54 (m, 1H), 2.42 (dd, J=9.9, 13.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$): δ 31.4, 35.2, 40.7, 44.5, 52.9, 55.2, 55.3, 77.2, 99.2, 104.6, 116.1, 131.8, 158.4, 160.7, 210.0. HRMS (MALDI-TOF, m/z) calcd for $C_{15}H_{20}NO_5S$ ($[M+H]^+$) 326.1057; found 326.1062.

*4.3.17. (S)-3-((R)-1-(2-Bromo-4-fluorophenyl)-2-nitroethyl)dihydro-thiopyran-4-one (**6q**).* White solid. Mp 117–119 °C. $[\alpha]_D^{25}$ −36.1 (c 0.20, $CHCl_3$). 97% ee (Chiralpak OD-H; i-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 12.96 min, t_R (major) 15.15 min). IR (KBr, ν_{max}): 2920, 2850, 1702, 1597, 1547, 1486, 1375, 1219, 858, 772 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.36 (dd, J=2.4, 8.2 Hz, 1H), 7.23 (dd, J=6.0, 8.8 Hz, 1H), 7.07 (dt, J=2.8, 7.8 Hz, 1H), 4.86–4.75 (m, 2H), 4.45–4.39 (m, 1H), 3.26 (s, 1H), 3.06–2.93 (m, 2H), 2.86–2.76 (m, 2H), 2.65–2.52 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.8, 35.0, 41.4, 41.8, 45.2, 54.7, 77.2, 115.6 (d, J=20.7 Hz), 121.1 (d, J=24.3 Hz), 125.6, 129.8, 132.2, 160.3, 162.8, 208.9. HRMS (MALDI-TOF, m/z): calcd for $C_{13}H_{14}BrFNO_3S$ ($[M+H]^+$) 361.9856; found 361.9850. Anal. Calcd for $C_{13}H_{13}BrFNO_3S$ (%): C 43.11, H 3.62, N 3.87; found: C 43.13, H 3.63, N 3.83.

*4.3.18. (S)-3-((R)-1-(2-Chloro-6-fluorophenyl)-2-nitroethyl)dihydro-thiopyran-4-one (**6r**).* White solid. Mp 131–133 °C. $[\alpha]_D^{25}$ −64.4 (c 0.10, $CHCl_3$). 96% ee (Chiralpak OD-H; i-PrOH/hexane=10:90, 1.0 mL/min; 254 nm; t_R (minor) 14.53 min, t_R (major) 17.69 min). IR

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(KBr, ν_{max}): 2957, 2923, 2853, 1709, 1552, 1454, 1378, 1245, 1115, 881, 780 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.28–7.22 (m, 2H), 7.06–7.01 (m, 1H), 4.86–4.72 (m, 3H), 3.32 (s, 1H), 3.05–2.89 (m, 2H), 2.88–2.77 (m, 2H), 2.63–2.57 (m, 1H), 2.49–2.44 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.6, 34.9, 37.8, 45.2, 53.0, 76.3, 115.1 (d, J=23.6 Hz), 122.8 (d, J=10.0 Hz), 126.5, 130.1, 136.8, 160.6, 163.1, 208.6. HRMS (MALDI-TOF, m/z): calcd for $C_{13}H_{14}ClFNO_3S$ ($[M+H]^+$) 318.0361; found 318.0335. Anal. Calcd for $C_{13}H_{13}ClFNO_3S$ (%): C 49.14, H 4.12, N 4.41; found: C 49.25, H 4.25, N 4.31.

*4.3.19. (S)-3-((R)-1-(Benzo[d][1,3]dioxol-5-yl)-2-nitroethyl)dihydro-thiopyran-4-one (**6s**).* White solid. Mp 149–150 °C. $[\alpha]_D^{30}$ −29.6 (c 0.50, $CHCl_3$). 97% ee (Chiralpak OD-H; i-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 25.80 min, t_R (major) 26.64 min). IR (KBr, ν_{max}): 3278, 3626, 2922, 2852, 1701, 1547, 1484, 1375, 1242, 1034 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 6.76 (d, J=8.1 Hz, 1H), 6.67–6.64 (m, 2H), 5.96 (s, 2H), 4.70 (dd, J=4.5, 12.6 Hz, 1H), 4.54 (dd, J=9.9, 12.4 Hz, 1H), 3.90 (dt, J=4.5, 10.2 Hz, 1H), 3.00–2.65 (m, 6H), 2.48 (dd, J=9.0, 13.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.6, 35.1, 43.3, 44.5, 55.1, 78.7, 101.4, 108.0, 108.9, 121.8, 129.9, 147.6, 148.4, 209.5. HRMS (MALDI-TOF, m/z) calcd for $C_{14}H_{16}NO_5S$ ($[M+H]^+$) 310.0744; found 310.0718. Anal. Calcd for $C_{14}H_{15}NO_5S$ (%): C 54.36, H 4.89, N 4.53; found: C 54.16, H 5.02, N 4.42.

*4.3.20. (S)-3-((R)-1-(Naphthalen-1-yl)-2-nitroethyl)dihydro-thiopyran-4-one (**6t**).* White solid. Mp 126–128 °C. $[\alpha]_D^{30}$ −79.6 (c 0.50, $CHCl_3$). 98% ee (Chiralpak AS-H; i-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 22.09 min, t_R (major) 29.22 min). IR (KBr, ν_{max}): 3052, 2917, 1698, 1548, 1427, 1376, 1304, 1117, 787 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$) δ 8.23 (d, J=6.9 Hz, 1H), 7.84 (dd, J=8.1, 20.6 Hz, 2H), 7.60–7.40 (m, 4H), 4.97–4.85 (m, 3H), 3.24 (s, 1H), 2.97–2.78 (m, 4H), 2.45 (dd, J=7.2 Hz, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 31.7, 35.1, 36.3, 44.8, 56.3, 78.6, 122.7, 123.8, 125.5, 125.8, 126.0, 126.8, 128.6, 129.1, 132.3, 133.5, 134.0, 209.7. HRMS (MALDI-TOF, m/z) calcd for $C_{17}H_{18}NO_3S$ ($[M+H]^+$) 316.1002; found 316.1020. Anal. Calcd for $C_{17}H_{17}NO_3S$ (%): C 64.74, H 5.43, N 4.44; found: C 64.65, H 5.48, N 4.42.

*4.3.21. (S)-3-((R)-1-(Naphthalen-2-yl)-2-nitroethyl)dihydro-thiopyran-4-one (**6u**).* White solid. Mp 144–146 °C. $[\alpha]_D^{30}$ −30.4 (c 0.50, $CHCl_3$). 90% ee (Chiralpak OD-H; i-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 24.72 min, t_R (major) 54.15 min). IR (KBr, ν_{max}): 3058, 2921, 1704, 1552, 1431, 1379, 1307, 1224, 1114 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.85–7.78 (m, 3H), 7.67 (s, 1H), 7.52–7.46 (m, 2H), 7.30 (dd, J=1.5, 8.4 Hz, 1H), 4.81 (dd, J=4.4, 12.8 Hz, 1H), 4.72 (dd, J=10.0, 12.6 Hz, 1H), 4.16 (dt, J=4.4, 10.2 Hz, 1H), 3.13 (dt, J=4.4, 9.4 Hz, 1H), 3.00–2.75 (m, 4H), 2.62–2.57 (m, 1H), 2.46 (dd, J=9.2, 13.8 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.5, 35.2, 43.7, 44.6, 54.9, 78.6, 124.8, 126.5, 126.7, 127.7, 127.9, 128.1, 129.4, 133.0, 133.4, 133.8, 209.4. HRMS (MALDI-TOF, m/z) calcd for $C_{17}H_{18}NO_3S$ ($[M+H]^+$) 316.1002; found 316.1015. Anal. Calcd for $C_{17}H_{17}NO_3S$ (%): C 64.74, H 5.43, N 4.44; found: C 64.53, H 5.52, N 4.24.

*4.3.22. (S)-3-((S)-1-(Furan-2-yl)-2-nitroethyl)dihydro-thiopyran-4-one (**6v**).* White solid. Mp 105–107 °C. $[\alpha]_D^{30}$ −17.3 (c 0.50, $CHCl_3$). 95% ee (Chiralpak OD-H; i-PrOH/hexane=10:90, 1.0 mL/min; 254 nm; t_R (minor) 18.24 min, t_R (major) 19.19 min). IR (KBr, ν_{max}): 2923, 1707, 1553, 1383, 1190, 1116, 915 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.37 (d, J=1.2 Hz, 1H), 6.31–6.24 (m, 2H), 4.68–4.64 (m, 2H), 4.16–4.08 (m, 1H), 3.12 (dt, J=4.8, 9.9 Hz, 1H), 2.99–2.94 (m, 2H), 2.85–2.74 (m, 2H), 2.64–2.48 (m, 2H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 31.2, 34.5, 37.2, 44.6, 53.4, 76.2, 109.7, 110.4, 142.8, 149.5, 208.4. HRMS (MALDI-TOF, m/z) calcd for $C_{11}H_{13}NNaO_4S$ ($[M+Na]^+$) 278.0457; found 278.0449. Anal. Calcd for $C_{11}H_{13}NO_4S$ (%): C 51.75, H 5.13, N 5.49; found: C 51.71, H 5.17, N 5.29.

*4.3.23. (S)-3-((S)-2-Nitro-1-(thiophen-2-yl)ethyl)dihydro-thiopyran-4-one (**6w**).* Yellow solid. Mp 109–110 °C. $[\alpha]_D^{30}$ −34.3 (c 0.50, $CHCl_3$). 94% ee (Chiralpak OD-H; i-PrOH/hexane=20:80, 1.0 mL/min; 254 nm; t_R (minor) 15.68 min, t_R (major) 18.36 min). IR (KBr, ν_{max}): 2923, 1701, 1546, 1425, 1376, 1219, 771, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.26 (d, J=5.6 Hz, 1H), 6.97–6.93 (m, 2H), 4.74 (dd, J=4.4, 12.6 Hz, 1H), 4.64 (dd, J=9.6, 12.6 Hz, 1H), 4.32 (dt, J=4.4, 9.4 Hz, 1H), 3.08–2.96 (m, 3H), 2.86–2.74 (m, 3H), 2.56 (dd, J=10.0, 13.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.5, 34.9, 39.0, 44.6, 55.8, 79.0, 125.6, 127.2, 127.3, 139.1, 208.9. HRMS (MALDI-TOF, m/z) calcd for $C_{11}H_{13}NNaO_3S_2$ ($[M+Na]^+$) 294.0229; found 294.0230. Anal. Calcd for $C_{11}H_{13}NO_3S_2$ (%): C 48.69, H 4.83, N 5.16; found: C 48.71, H 4.87, N 5.11.

4.4. Procedure for 1,3-dipolar cycloadditions

*4.4.1. (3R,3aS)-3-Phenyl-2,3,3a,4,6,7-hexahydrothiopyrano[4,3-b] pyrrole 1-oxide (**16**).* A suspension of **6a** (265 mg, 1 mmol), zinc dust (650 mg, 10 mmol), and NH_4Cl (50 mg, 0.9 mmol) in THF (5 mL) and H_2O (2 mL) was stirred at room temperature under N_2 atmosphere for 12 h. The mixture was filtrated through a pad of Celite, and the filtration was concentrated in vacuo. The residue was purified by column chromatography on silica gel (CH_2Cl_2/MeOH/NH_3=30:1:1) to afford **16** (203 mg, 87%) as a brown solid. Mp 187–188 °C. $[\alpha]_D^{25}$ −56.6 (c 0.10, $CHCl_3$). IR (KBr, ν_{max}): 2921, 2852, 1605, 1457, 1235, 769 cm^{-1}. ^1H NMR (300 MHz, $CDCl_3$): δ 7.38–7.22 (m, 5H), 4.30–4.21 (m, 1H), 4.17–4.07 (m, 1H), 3.57–3.52 (m, 1H), 3.27–3.09 (m, 2H), 2.86–2.74 (m, 2H), 2.66 (dt, J=3.3, 12.6 Hz, 1H), 2.53 (dd, J=11.1, 13.0 Hz, 1H), 2.42–2.31 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 25.3, 26.2, 33.0, 44.5, 50.6, 66.8, 126.3, 126.8, 128.2, 137.8. HRMS (MALDI-TOF, m/z) calcd for $C_{13}H_{16}NOS$ ($[M+H]^+$) 234.0947; found 234.0964.

*4.4.2. Synthesis of the 1,3-dipolar cycloaddition adducts **17**–**20** (using **20** as an example).* A solution of **16** (23 mg, 0.1 mmol) and N-methylmaleimide (111 mg, 1 mmol) in toluene (3 mL) was stirred at room temperature under N_2 atmosphere for 15 min. The reaction mixture was then heated to reflux for 4 h. The solution was cooled down to room temperature and concentrated directly. The residue was purified by column chromatography on silica gel (petroleum ether/ethyl acetate=3:1) to afford **20a** (15 mg, 50%) and **20b** (11 mg, 33%).

*4.4.2.1. (6R,6aS,10aS)-Methyl-6-phenyloctahydrothiopyrano [4′,3′:2,3]pyrrolo[1,2-b]isoxazole-2-carboxylate (**17**).* Colorless oil (inseparable diastereomeric mixture, dr=1:1). $[\alpha]_D^{24}$ −105.6 (c 0.50, $CHCl_3$). IR (neat, ν_{max}): 2923, 2852, 1734, 1457, 1207, 1015 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.40–7.29 (m, 4H), 7.24–7.20 (m, 1H), 4.75–4.68 (m, 1H), 3.85–3.75 (m, 5H), 3.58–3.50 (m, 1H), 2.86 (dt, J=4.0, 14.0 Hz), 2.72–2.31 (m, 6H), 1.94–1.80 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 26.1, 26.2, 26.3, 26.4, 31.8, 32.0, 43.4, 43.3, 47.7, 47.8, 50.2, 50.7, 52.4, 52.7, 60.7, 60.8, 73.6, 73.9, 74.4, 75.2, 77.2, 126.7, 128.1, 128.2, 128.8, 142.4, 142.5, 171.2, 172.8. HRMS (MALDI-TOF, m/z) calcd for $C_{17}H_{22}NO_3S$ ($[M+H]^+$) 320.1315; found 320.1307.

*4.4.2.2. (1S,2R,6R,6aS,10aR)-Dimethyl-6-phenyloctahydrothiopyrano[4′,3′:2,3]pyrrolo[1,2-b]isoxazole-1,2-dicarboxylate (**18a**).* Colorless oil. $[\alpha]_D^{28}$ −63.3 (c 0.25, $CHCl_3$). IR (neat, ν_{max}): 2926, 2852, 1719, 1453, 1218, 1071 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.35–7.29 (m, 4H), 7.25–7.21 (m, 1H), 4.99 (d, J=8.8 Hz, 1H), 3.90–3.82 (m, 2H), 3.81 (s, 3H), 3.74 (s, 3H), 3.64 (td, J=5.2, 9.4 Hz, 1H), 2.97 (dd, J=3.6, 14.6 Hz, 1H), 2.72–2.65 (m, 1H), 2.59–2.49 (m, 2H), 2.36–2.32 (m, 1H), 1.91–1.76 (m, 2H). ^{13}C NMR (100 MHz,

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$CDCl_3$): δ 25.1, 26.2, 28.0, 46.4, 51.9, 52.3, 52.7, 57.9, 61.2, 75.8, 76.4, 126.9, 128.1, 128.9, 142.4, 169.7, 170.7. HRMS (MALDI-TOF) calcd for $C_{19}H_{23}NO_5SNa$ ($[M+Na]^+$) 400.1189; found 400.1173.

*4.4.2.3. (1R,2S,6R,6aS,10aR)-Dimethyl-6-phenyloctahydrothio-?tjl]pyrano[4′,3′:2,3]pyrrolo[1,2-b]isoxazole-1,2-dicarboxylate (**18b**).* Colorless oil. $[\alpha]_D^{24}$ −90.0 (*c* 0.33, $CHCl_3$). IR (neat, ν_{max}): 2923, 2852, 1736, 1458, 1208, 1074 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.35–7.32 (m, 2H), 7.27–7.24 (m, 1H), 7.21–7.19 (m, 2H), 3.88 (s, 3H), 3.87 (s, 3H), 3.60 (dd, *J*=10.0, 13.6 Hz, 1H), 3.50 (dd, *J*=9.6, 13.6 Hz, 1H), 3.29 (dd, *J*=3.6, 14.4 Hz, 1H), 3.23 (dd, *J*=2.8, 9.8 Hz, 1H), 3.01 (t, 12.4 Hz), 2.63–2.50 (m, 3H), 2.36 (dd, *J*=3.2, 13.2 Hz, 1H), 2.06 (dt, *J*=4.4, 13.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.3, 26.5, 40.2, 48.9, 51.8, 52.9, 53.0, 65.8, 77.2, 80.6, 115.5, 127.4, 127.5, 129.0, 138.9, 152.2, 165.2. HRMS (MALDI-TOF) calcd for $C_{19}H_{23}NO_5SNa$ ($[M+Na]^+$) 400.1189; found 400.1186.

*4.4.2.4. (4aS,5R,8aR,11aS,11bR)-10-Methyl-5-phenylhexahydro-1H-pyrrolo[3,4-d]thiopyrano[4′,3′:2,3]pyrrolo[1,2-b]isoxazole-9,11(2H,8aH)-dione (**19a**).* White solid. $[\alpha]_D^{24}$ −56.4 (*c* 0.33, $CHCl_3$). IR (KBr, ν_{max}): 2923, 2853, 1707, 1435, 1382, 1287, 1135 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.36–7.30 (m, 4H), 7.26–7.21 (m, 1H), 4.92 (d, *J*=7.2 Hz, 1H), 3.88 (dt, *J*=4.5, 10.4 Hz, 1H), 3.76 (dd, *J*=10.0, 15.8 Hz, 1H), 3.61 (dd, *J*=10.0, 15.6 Hz, 1H), 3.53 (d, *J*=7.2 Hz, 1H), 3.06 (s, 3H), 3.05 (dt, *J*=4.5, 9.4 Hz, 1H), 2.98 (dd, *J*=4.0, 14.6 Hz, 1H), 2.61–2.56 (m, 1H), 2.51 (td, *J*=2.4, 7.2 Hz, 1H), 2.33 (td, *J*=3.2, 10.4 Hz, 1H), 1.84–1.79 (m, 1H), 1.69 (dt, *J*=3.6, 13.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.9, 25.4, 25.9, 28.3, 47.0, 51.2, 53.8, 60.4, 75.7, 77.1, 126.9, 128.2, 128.8, 142.6, 173.6, 175.2. HRMS (MALDI-TOF, *m*/*z*) calcd for $C_{18}H_{20}N_2O_3SNa$ ($[M+Na]^+$) 367.1087; found 367.1071.

*4.4.2.5. (4aS,5R,8aS,11aR,11bR)-10-Methyl-5-phenylhexahydro-1H-pyrrolo[3,4-d]thiopyrano[4′,3′:2,3]pyrrolo[1,2-b]isoxazole-9,11(2H,8aH)-dione (**19b**).* Colorless oil. $[\alpha]_D^{28}$ −161.9 (*c* 1.1, $CHCl_3$). IR (neat, ν_{max}): 2923, 2853, 1708, 1434, 1280, 1138, 1008 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ 7.34–7.30 (m, 2H), 7.27–7.21 (m, 3H), 4.97 (d, *J*=8.0 Hz, 1H), 3.91 (dt, *J*=7.2, 10.0 Hz, 1H), 3.72 (dd, *J*=9.6, 15.2 Hz, 1H), 3.55 (d, *J*=8.0 Hz, 1H), 3.43 (dd, *J*=7.2, 15.0 Hz, 1H), 3.10 (dt, *J*=2.0, 13.0 Hz, 1H), 3.04–2.99 (m, 4H), 2.64 (dd, *J*=4.8, 8.8 Hz, 1H), 2.30–2.26 (m, 1H), 2.09–2.03 (m, 1H), 1.89 (dt, *J*=3.2, 12.6 Hz). ^{13}C NMR (100 MHz, $CDCl_3$): δ 24.3, 25.2, 26.0, 33.6, 47.5, 48.9, 59.4, 59.6, 75.7, 77.0, 127.0, 128.2, 129.0, 142.0, 172.2, 173.0. HRMS (MALDI-TOF, *m*/*z*) calcd for $C_{18}H_{20}N_2O_3SNa$ ($[M+Na]^+$) 367.1087; found 367.1082.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at http://dx.doi.org/10.1016/j.tet.2013.05.116.

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