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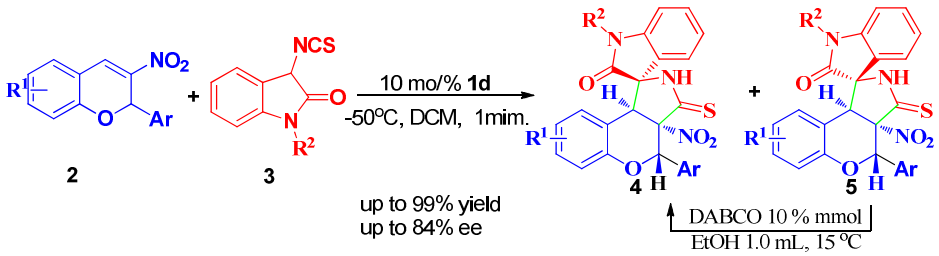

A series of chiral multi-functionalized tetracyclic spiro[chromeno[3,4-c]pyrrole-1,3'-indoline] derivatives with four vicinal chiral carbon centers including two quaternary stereocenters were successfully prepared via domino reaction of various 3-nitro-2H-chromene derivatives to 3-isothiocyanato oxindole with moderate to good enantioselectivities, employing readily available bifunctional thiourea **1d** as the organocatalyst.

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Organocatalytic Domino Michael/Cyclization Reaction: Efficient Synthesis of Multi-functionalized Tetracyclic Spirooxindoles with Multiple Stereocenters

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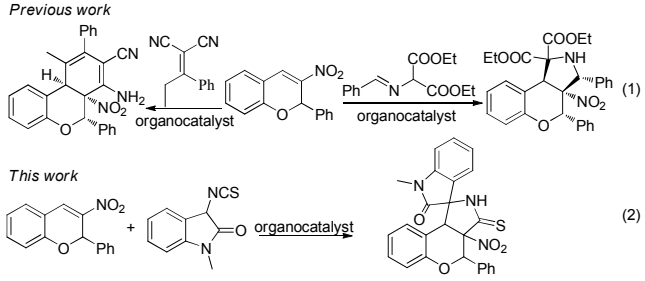
The asymmetric domino reaction of various 3-nitro-2*H*-chromene derivatives **2** to 3-isothiocyanato oxindole **3** with moderate to good enantioselectivities, employing readily available bifunctional thiourea **1d** as the organocatalyst, was described. A series of chiral multi-functionalized tetracyclic spiro[chromeno[3,4-*c*] pyrrole-1,3'-indoline] derivatives with four vicinal chiral carbon centers including two quaternary stereocenters were successfully prepared. Notably, the products **5** could be cleanly converted to the compounds **4** in ethanol under mild conditions.

Introduction

Spirocyclic compounds are recognized as important precursors for the easy access of a variety of cyclic products by rearrangement reaction due to their steric strain associated with the quaternary carbon.[1] Development of novel synthetic methods for the construction of new spirocyclic compounds represents a major challenge in synthetic organic and medicinal chemistry.[2] Recently, the highly functionalized spirocyclic oxindoles have drawn tremendous interest of researchers[3] in the area of synthetic organic chemistry as well as medicinal chemistry worldwide because they occur in many natural products and have been reported to have various types of bioactivity.[4] Due to their significant and varied biological activities design and development of novel methods for the construction of functionalized spirooxindoles have drawn remarkable interest from the synthetic, organic as well as medicinal chemists.[5] Recently, 3-isothiocyanato oxindoles emerged as the most attractive reactants in organocatalytic cascade Aldol/cyclization reactions,[6] Michael/cyclization reactions,[7] Manich/cyclization reactions[8] and [3+2] cyclization[9] for the synthesis of the highly functionalized spirocyclic oxindoles. From the literature we realized that benzopyran scaffolds exhibit a wide range of biological activities such as anti-cancer, diuretic, anticoagulant, and anti-anaphylactic activity.[10-12]. Recently, chiral multi-functionalized tetracyclic benzopyran derivatives have been prepared from 3-nitro-2*H*-chromenes in our group (Eq. 1, Scheme 1).[13] To the best of our knowledge there is no method reported for the asymmetric synthesis of chiral multi-functionalized tetracyclic spiro[chromeno[3,4- c]pyrrole-1,3'-indoline] derivatives from the cascade reaction of 3-isothiocyanato oxindoles and 3-nitro-2*H*-chromenes. In continuation of our efforts towards the development of functionalized heterocycles using domino reactions, we envisioned that chiral multi-functionalized tetracyclic spiro[chromeno[3,4-c]pyrrole-1,3'-indoline] derivatives with four vicinal chiral carbon centers including two quaternary stereocenters could be synthesized by domino reaction of 3-isothiocyanato oxindoles and 3-nitro-2*H*-chromenes in the presence of organocatalyst (Eq. 2, Scheme 1).

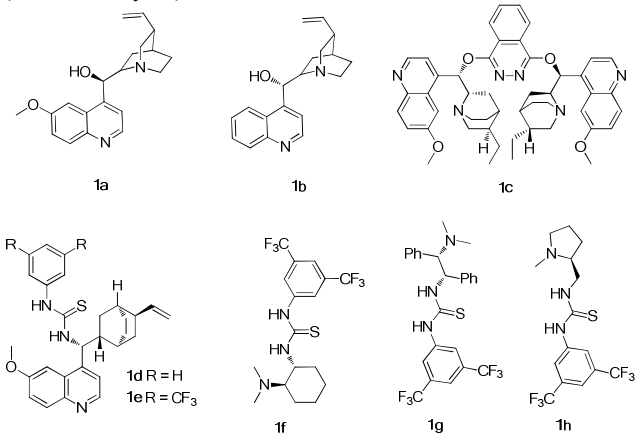


Scheme 1. General strategy for the synthesis of tetracyclic spirooxindoles

Results and discussion

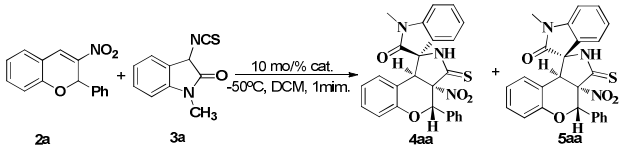
Organocatalytic asymmetric reactions have been used as a powerful tool for the synthesis of enantiopure molecules with multiple stereocenters by employing either a single catalyst or a combination of catalysts under mild, environmentally benign conditions over the past decades.[14] To evaluate this hypothesis, 3-nitro-2*H*-chromene **2a** and 3-isothiocyanato oxindole **3a** were first applied. A few representative results are shown in Table 1. To our surprise, the domino reaction was completed *within one minute* when the reaction was carried out in the presence of the organocatalysts in DCM at -50 ^{o}C, while the diastereoselectivity was poor. To our delight, the chiral multi-functionalized tetracyclic spiro[chromeno[3,4-*c*]pyrrole-1,3'-indoline]

derivatives **4aa** and **5aa** were easily isolated by column chromatography. Both cinchona alkaloids and bifunctional thioureas have appeared to be efficient organocatalysts in asymmetric transformations since the basic tertiary nitrogen of cinchona alkaloids could activate nucleophiles by deprotonation, whereas the secondary hydroxyl group or thiourea moiety would serve as hydrogen-bonding donor in the activation of electrophiles such as *α,β*-unsaturated carbonyl compounds or nitroalkenes. As such, quinine **1a** and cinchonine **1b** were firstly screened, high yields were obtained while the ees were poor to moderate (Table 1, entries 1-2). Similar results were obtained when the domino reaction was catalyzed by **1c** (Table 1, entry 3). Subsequently, the bifunctional thioureas 1d-1h which have appeared to be efficient organocatalysts for asymmetric additions,[15] exhibited a higher catalytic activity when the domino reaction was carried out at -50 °C ***within one minute*** (Table 1, entries 4-8). To our surprise, organocatalyst **1d**, derived from quinine, was proved to be superior to 1e in this domino reaction, and products were obtained with up to 78% ee (Table 1, entry 4). High yields were obtained when the domino reaction was catalyzed by other thiourea-tertiary amines **1f-1h** while the enantioselectivities were somewhat low. The effect of catalyst loading on reaction efficiency has been evaluated (Table 1, entries 9-11). While 10 mol % of thiourea-tertiary amine **1d** was routinely employed in this investigation, it appears that catalyst loadings as low as 5 mol % provide better enantioselectivity (Table 1, entry 10).



Scheme 2. Organocatalysts **1a**-**1h**

Table 1. Catalyst Screening**.** [a].

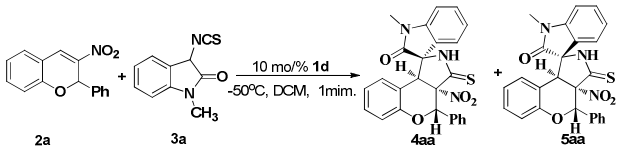


Entry	Cat.	Time	Yield%[b]/Ee[c](4aa)	Yield%[b]/Ee[c](5aa)
1	**1a**	1min.	48/61	39/-32
2	**1b**	1min.	45/30	36/05
3	**1c**	1min.	57/37	37/04
4	**1d**	**1min**.	**49/-78**	**43/72**
5	**1e**	1min.	47/75	39/60
6	**1f**	1min.	52/70	40/50
7	**1g**	1min.	53/-36	36/13
8	**1h**	1min.	47/60	41/10
9[d]	**1d**	1min.	40/76	31/69
10[e]	**1d**	1min.	49/80	43/70
11[f]	**1d**	1min.	51/78	43/72

[a] Reaction conditions: 0.24 mmol of **2a**, 0.10 mmol of **3a**, 10 mol% of cat in 1 mL DCM at -50 °C for 1 min.. [b] Isolated yield; [c] Determined by chiral HPLC analysis. [d] 1 mol% of **1d** was added. [e] 5 mol% **1d** of was added. [f] 15mol% of **1d** was added.

Subsequently, we investigated the effects of solvent on the reactivity, and most commonly used solvents are compatible with our asymmetric conditions and afforded high yields (total yields: 80-95%) with varied enantioselectivities (Table 2, entries 1-9). The reaction in a polar solvent such as THF, ethanol and ether, afforded the desired products with somewhat lower enantioselectivities (entries 3-5). After solvents were screened, chloroform turned out to be optimal to give the products in higher enantioselectivities and yields (Table 2, entry 6). In the hope of higher enantioselectivities, we decreased the reaction concentration from 1.0 to 0.5 M. As a result, a better enantiomeric excess was achieved (entry 7) within one minute. The ee was decreased when the temperature was elevated, as well as when the concentration was reduced to 0.25 M (entries 8-9). Based on the above screening, the optimal reaction conditions: 0.24 equiv of **2** and 1.0 equiv of **3a** in chloroform with 5 mol% of catalyst **1d** at -50 °C were established.

Table 2. Optimization of reaction conditions. [a].



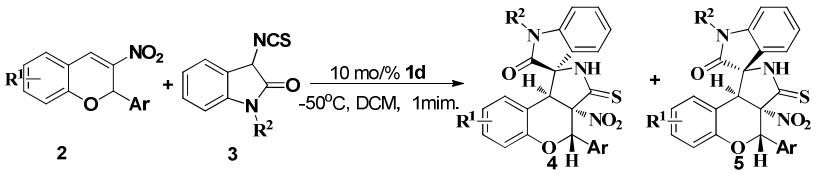
Entry	Solvent	Yield[b]/Ee[c](**4aa**)	Yield[b]/Ee[c](**5aa**)
1	DCM	49/80	43/70
2	toluene	48/65	42/48
3	THF	48/50	44/20
4	Ether	43/65	37/61
5	Ethanol	45/70	39/60
6	$CHCl_3$	52/79	43/74
7[d]	$CHCl_3$	49/81	44/77
8[e]	$CHCl_3$	50/80	45/70
9[f]	$CHCl_3$	46/82	42/70

[a] Reaction conditions: 0.24 mmol of **2a**, 0.10 mmol of **3a**, 5 mol% of **1d** in 1 mL Solvent at -50 °C. [b] Isolated yield. [c] Determined by chiral HPLC analysis. [d] 0.24 mmol of **2a**, 0.10 mmol of **3a**, in 2 mL $CHCl_3$. [e] 4 mL $CHCl_3$. [f] -60 °C.

To test the substrate scope of domino reaction, the reaction of various 3-nitro-2*H*-chromene derivatives **2** with 3-isothiocyanato oxindole **3** was studied under the optimized conditions using 5 mol% of bifunctional thiourea **1d** as the catalyst. The results are summarized in Table 3. As shown in Table 3, the domino reaction of various 3-nitro-2*H*-chromene derivatives **2** with 3-isothiocyanato oxindole **3** all gave high yields and good enantioselectivities of the desired products. Good enantioselectivities were obtained in the domino reaction of α,α-dicyanoolefins with electron-withdrawing substituent on Ar ring of 3-nitro-2*H*-chromene derivatives (Table 3, entries 2, 3, 5, 6).

In addtion, an electron-donating substituent on Ar ring of 3-nitro-2*H*-chromene derivatives tended to increase the reactivity and enantioselectivity (Table 3, entries 7-8). 3-Nitro-2*H*-chromene derivative **2d** with electron withdrawing substituents on the ortho position afford multi-functionalized tetracyclic spiro[chromeno[3,4-*c*]pyrrole-1,3'-indoline] derivative with slightly inferior enantioselectivity (Table 3, entry 4). However, it should be noted that 3-nitro-2*H*-chromene with a furanyl show no reactivity in this system, and it remains to be explored. Gratifyingly, the reaction of 3-nitro-2*H*-chromene derivatives **3** with electron withdrawing substituent or electron-donating group on the R^1 group afford the desired products with a slight effect on enantioselectivities (Table 3, entries 7-11), and the enantioselectivities were up to 84%. Further exploration of the substrate scope was focused on 3-isothiocyanato oxindole **3** bearing various substituents. Replace the substituent methyl with ethyl, 3-isothiocyanato oxindole **3b** showed good reactivity; excellent yields were obtained with high enantioselectivities (Table 3, entries 14-18).

Table 3. The substrate scope of domino reaction [a].

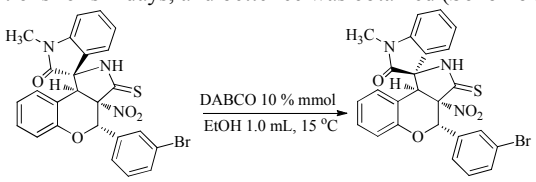


2 3

Entry	R^1	Ar	2	R^2	3	Yield[b]/e.e.%[c]4		Yield[b]/e.e.%[c]5	
1	H	Ph	**2a**	Me	**3a**	49/81	**4aa**	44/77	**5aa**
2	H	*p*-BrC_6H_4	**2b**	Me	**3a**	43/82	**4ab**	52/80	**5ab**
3	H	*m*-BrC_6H_4	**2c**	Me	**3a**	56/81	**4ac**	42/80	**5ac**
4	H	*o*-BrC_6H_4	**2d**	Me	**3a**	43/67	**4ad**	45/70	**5ad**
5	H	*p*-ClC_6H_4	**2e**	Me	**3a**	49/80	**4ae**	47/71	**5ae**
6	H	*p*-FC_6H_4	**2f**	Me	**3a**	47/82	**4af**	46/80	**5af**
7	H	*p*-$CH_3C_6H_4$	**2j**	Me	**3a**	49/83	**4ag**	40/85	**5aj**
8	H	*p*-$OCH_3C_6H_4$	**2k**	Me	**3a**	39/83	**4ah**	60/81	**5ak**
9	5-Br	Ph	**2l**	Me	**3a**	53/83	**4ai**	41/51	**5al**
10	5-Cl	Ph	**2m**	Me	**3a**	51/84	**4aj**	40/51	**5am**
11	5-Cl	*p*-$CH_3C_6H_4$	**2n**	Me	**3a**	49/82	**4ak**	37/66	**5an**
12	5-CH_3	Ph	**2o**	Me	**3a**	40/74	**4al**	47/86	**5ao**
13	4-OCH_3	Ph	**2p**	Me	**3a**	45/72	**4am**	38/76	**5ap**
14	H	Ph	**2a**	Et	**3b**	54/82	**4ba**	42/80	**5ba**
15	H	*p*-BrC_6H_4	**2b**	Et	**3b**	46/83	**4bb**	50/84	**5bb**
16	H	*p*-FC_6H_4	**2f**	Et	**3b**	46/82	**4bf**	47/82	**5bf**
17	H	*p*-$CH_3C_6H_4$	**2j**	Et	**3b**	45/83	**4bj**	48/82	**5bj**
18	H	*p*-$OCH_3C_6H_4$	**2k**	Et	**3b**	44/84	**4bk**	43/82	**5bk**

[a] Otherwise noted, reactions performed with 0.2 mmol of **2**, 0.1 mmol of **3**, 20 mol-% of **1e** in 1 ml DCM at 10 °C under N_2 for 36 h. [b] Isolated yield and yield based on **3**. [c] Determined by the chiral HPLC analysis.

Interestingly, the product **5ac** could be cleanly converted to the compound **4ac** in ethanol with quantitative yield under base conditions for six days, and better ee was obtained (**Scheme 3**).



5ac ee%=80 % **4ac** ee%= -86 %

Scheme 3 Selective transformation of domino reaction product.

To determine the absolute configuration of chiral multi-functionalized tetracyclic spiro[chromeno[3,4-c] pyrrole-1,3'-indoline] derivatives, single crystal suitable for X-ray crystallographic analysis was fortunately obtained from enantiopure **4ca** and **5ac** that bear a bromine atom. As shown in Fig. 1, it composes of (*C1R, C2S, C3S, C4S* for **4ca**; *C1S, C2S, C3S, C4S* for **5ca**) configuration.

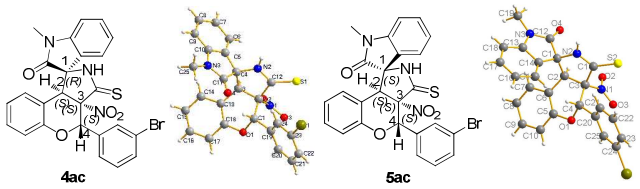


Fig. 1 The X-ray diffraction analysis of compounds **4ac** and **5ac**.

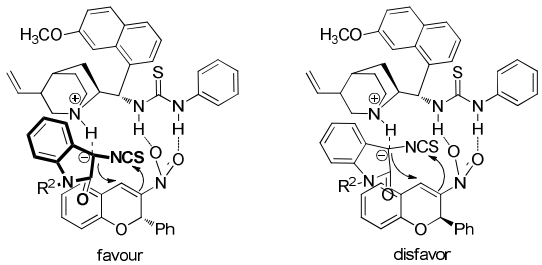


Fig. 2 Proposed transition states.

According to the above experimental results and previously reported dual activation model,[13b] both the substrates involved in the transition state are activated by bifunctional thiourea **1d** as proposed in **Fig. 2**. The Michael acceptor is assumed to be activated and oriented by the hydrogen bonds of the bifunctional thiourea, while the tertiary amine of the catalyst would provide suitable basicity to enhance the nucleophilicity of the 3-isothiocyanato oxindole. The well-defined orientation facilitates the *Re* attack on the activated 3-nitro-2*H*-chromene derivative, which favors the formation of the *C2S* stereocenter. Subsequent intramolecular cyclization through the attack the isothiocyanato group afforded the major *C3S* configured product.

Conclusions

In conclusion, we have successfully demonstrated the domino reaction of various 3-nitro-2*H*-chromene derivatives **2** to 3-isothiocyanato oxindole **3** with moderate to good enantioselectivities, employing readily available bifunctional thiourea **1d** as the organocatalyst, which shows to be more effective catalyst than the ditrifluoromethylated one. After simple synthetic transformations, chiral multi-functionalized tetracyclic spiro[chromeno[3,4-*c*]pyrrole-1,3'-indoline] derivatives with four vicinal chiral carbon centers including two quaternary stereocenters were successfully prepared. Notably, the products **5** could be cleanly converted to the compounds **4** in DCM under mild conditions. Further application of this reaction to other substrates and to the preparation of biologically relevant compound are currently underway.

Experimental Section

General Methods

Column chromatography was performed using silica gel (200-300 mesh) eluting with ethyl acetate and petroleum ether. ^{1}H NMR and ^{13}C NMR spectra were recorded on Bruker DRX 400 spectrometer at room temperature in $CDCl_3$ as solvent. Chemical shifts for protons are reported using residual $CHCl_3$ as internal reference (=7.26 ppm). Carbon spectra were referenced to the shift of the ^{13}C signal of $CDCl_3$ (=77.0 ppm). Coupling constants (*J*) are given in Hz. IR spectra were recorded using a Perkin-Elmer 1600 Series FTIR. ESI-HRMS spectrometer was measured with a Finnigan LCQ^{DECA} ion trap mass spectrometer. Optical rotations were measured at 589 nm at 25 °C in a 1 dm cell and specific rotations are given in 10^{-1} deg cm^2 g^{-1}. Enantiomeric excess were determined by HPLC analysis using Daicel Chiralpak AD column (4.6 mm* 250 mm, 5μm) Commercial grade solvents were dried and purified by standard procedures as specified in Purification of Laboratory Chemicals, 4th Ed (Armarego, W. L. F.; Perrin, D. D. Butterworth Heinemann: 1997).

General procedure for the synthesis of chiral multi-functionalized tetracyclic spiro[chromeno[3,4- c]pyrrole- ,3'-indoline] derivatives:

A mixture of **2a** (25.3 mg, 0.10 mmol), **3a** (20.4 mg, 0.10 mmol) and 5 mol% of **1d** was stirred in $CHCl_3$ (1 mL) at -50 °C for 1 minute, then flash chromatography on silica gel (20% ethyl acetate/petroleum ether) gave product **4aa** and **5aa** as yellow solid.

4aa Yellow solid, mp 204.8–206.1°C; 22.4 mg, yield 49 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.60 (d, *J* = 7.4 Hz, 1H), 7.57 – 7.49 (m, 3H), 7.41 – 7.34 (m, 3H), 7.30 – 7.24 (m, 1H), 7.16 (t, *J* = 7.8 Hz, 1H), 6.99 (d, *J* = 8.3 Hz, 1H), 6.94 (d, *J* = 7.8 Hz, 1H), 6.74 (t, *J* = 7.5 Hz, 1H), 6.44 (s, 1H), 6.28 (d, *J* = 7.8 Hz, 1H), 5.05 (s, 1H), 2.99 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.9, 172.7, 154.4, 143.5, 133.6, 131.9, 129.7, 129.6, 128.9, 127.0, 126.9, 126.3, 124.7, 124.5, 122.2, 118.1, 115.8, 109.4, 97.2, 79.7, 71.6, 53.0, 26.7.ESI-HRMS: calcd. for $C_{25}H_{19}N_3O_4S$+Na 480.0988, found 480.0983; $[\alpha]^{20}_D$ = –155.3 (*c* 0.47, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (25% 2-propanol/hexane, 1.0 mL/min), -81% ee, t_{minor} = 6.61 min, t_{major} = 15.71 min.

5aa Yellow solid, mp 188.4–190.2 °C; 20.1 mg, yield 44 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.75 (s, 1H), 7.26 – 7.23 (m, 2H), 7.18 – 7.15 (m, 4H), 7.02 – 6.97 (m, 1H), 6.84 (d, *J*= 7.8 Hz, 1H), 6.78 – 6.70 (m, 2H), 6.64 – 6.59 (m, 1H), 6.39 (dd, *J*= 18.5, 6.7 Hz, 3H), 5.46 (s, 1H), 3.30 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.1, 174.8, 152.4, 143.6, 133.5, 131.1, 129.6, 129.4, 129.3, 128.9, 128.1, 126.4, 123.7, 123.2, 122.6, 120.5, 118.8, 108.9, 98.4, 81.6, 72.8, 47.3, 27.3.ESI-HRMS: calcd. for $C_{25}H_{19}N_3O_4S$+Na 480.0988, found 480.0989; $[\alpha]^{20}_D$ = –103.8 (*c* 0.35, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (25% 2-propanol/hexane, 1.0 mL/min), 77% ee, t_{major} = 5.87 min, t_{minor} = 10.61 min.

4ab Yellow solid, mp 208.2–209.6°C; 23.0 mg, yield 43 %;^{1}H NMR (600 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.61 (d, *J* = 7.3 Hz, 1H), 7.53 (t, *J* = 7.7 Hz, 1H), 7.48 (d, *J* = 8.5 Hz, 2H), 7.43 (d, *J* = 8.6 Hz, 2H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.16 (dd, *J* = 11.4, 4.2 Hz, 1H), 6.99 (d, *J* = 8.2 Hz, 1H), 6.94 (d, *J* = 7.9 Hz, 1H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.42 (s, 1H), 6.27 (d, *J* = 7.7 Hz, 1H), 5.07 (s, 1H), 2.99 (s, 1H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.8, 172.7, 165.6, 154.3, 143.5, 132.8, 132.1, 131.5, 130.1, 129.8, 126.8, 126.4, 124.8, 124.5, 123.1, 122.5, 118.1, 115.6, 109.5, 97.3, 79.2, 71.7, 53.0, 26.8. ESI-HRMS: calcd. for $C_{25}H_{18}BrN_3O_4S$+Na 560.0079, found 560.0074; $[\alpha]^{20}_D$ = –125.6 (*c* 0.39, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), -82% ee, t_{minor} = 5.28 min, t_{major} = 11.24 min.

5ab Yellow solid, mp 198.5–200°C; 27.8 mg, yield 52 %;^{1}H NMR (600 MHz, DMSO) δ 11.68 (s, 1H), 7.48 (d, *J* = 8.5 Hz, 2H), 7.28 (dd, *J* = 7.5, 4.8 Hz, 3H), 7.09 (d, *J* = 7.8 Hz, 1H), 7.05 – 7.02 (m, 1H), 6.80 (d, *J* = 8.1 Hz, 1H), 6.75 (t, *J* = 7.5 Hz, 1H), 6.66 (dd, *J* = 11.5, 4.3 Hz, 1H), 6.60 (d, *J* = 7.4 Hz, 2H), 6.08 (s, 1H), 5.42 (s, 1H), 3.29 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 193.0, 174.3, 152.2, 144.2, 133.4, 131.8, 131.1, 131.0, 129.9, 129.8, 126.1, 124.4, 123.2, 123.0, 120.1, 118.1, 109.7, 99.2, 80.0, 73.2, 55.3, 47.7, 27.4. $[\alpha]^{20}_D$ = –87.7 (*c* 0.22, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), 80% ee, t_{major} = 5.09 min, t_{minor} = 9.81 min.

4ac Yellow solid, mp 154.4–155.3°C; 29.9 mg, yield 56 %;^{1}H NMR (400 MHz, $CDCl_3$) δ 8.46 (s, 1H), 7.73 (s, 1H), 7.62 (d, *J* = 7.4 Hz, 1H), 7.55 – 7.45 (m, 3H), 7.31 – 7.13 (m, 3H), 7.00 (d, *J* = 8.3 Hz, 1H), 6.95 (d, *J* = 7.8 Hz, 1H), 6.76 (t, *J* = 7.5 Hz, 1H), 6.42 (s, 1H), 6.28 (d, *J* = 7.7 Hz, 1H), 5.09 (s, 1H), 3.01 (s, 3H).

^{13}C NMR (100 MHz, $CDCl_3$) δ 192.7, 172.7, 154.2, 143.5, 135.9, 132.7, 132.1, 131.9, 129.8, 128.5, 128.3, 126.8, 126.4, 124.8, 124.5, 122.5, 121.0, 118.1, 115.6, 109.5, 97.3, 78.8, 71.7, 53.0, 26.8. ESI-HRMS: calcd. for $C_{25}H_{18}BrN_3O_4S$+Na 560.0079, found 560.0058; $[\alpha]^{20}_D$ = –251.9 (*c* 0.35, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (25% 2-propanol/hexane, 1.0 mL/min), -81% ee, t_{minor}= 6.34 min, t_{major}= 7.56 min.

5ac Yellow solid, mp 216.2–218.1°C; 22.5 mg, yield 42 %; ^{1}H NMR (400 MHz, DMSO) δ 11.68 (s, 1H), 7.56– 7.53 (m, 2H), 7.28 (ddd, *J* = 18.8, 14.2, 7.8 Hz, 3H), 7.07 (dd, *J* = 18.6, 7.6 Hz, 2H), 6.84 (d, *J* = 8.1 Hz, 1H), 6.76 (t, *J* = 7.5 Hz, 1H), 6.68 (t, *J* = 7.0 Hz, 2H), 6.62 (d, *J* = 7.3 Hz, 1H), 6.04 (s, 1H), 5.40 (s, 1H), 3.29 (s, 3H). ^{13}C NMR (100 MHz, DMSO) δ 192.8, 174.3, 152.2, 147.4, 144.2, 136.5, 132.5, 131.0, 130.0, 129.8, 128.6, 126.2, 124.4, 123.2, 123.1, 121.1, 119.8, 118.0, 109.7, 99.1, 79.7, 73.1, 55.3, 47.8, 27.4. $[\alpha]^{20}_D$ = –37.9 (*c* 0.29, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (25% 2-propanol/hexane, 1.0 mL/min), 80% ee, t_{major} = 5.40 min, t_{minor} = 7.25 min.

4ad Yellow solid, mp 196.3–198.1°C; 23.0 mg, yield 43 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.59 (d, *J*= 7.6 Hz, 2H), 7.54 – 7.51 (m, 2H), 7.38 (t, *J*= 7.4 Hz, 1H), 7.27 (d, *J*= 7.6 Hz, 1H), 7.26 – 7.23 (m, 1H), 7.18 (t, *J*= 7.7 Hz, 1H), 6.99 – 6.96 (m, 2H), 6.95 (s, 1H), 6.78 (t, *J*= 7.5 Hz, 1H), 6.36 (d, *J*= 7.7 Hz, 1H), 4.93 (s, 1H), 3.04 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.0, 172.1, 153.9, 143.7, 134.0, 132.3, 132.0, 130.6, 129.7, 126.9, 126.7, 126.1, 124.6, 122.4, 118.3, 116.5, 109.3, 96.3, 77.9, 71.5, 26.7. ESI-HRMS: calcd. for $C_{25}H_{18}BrN_3O_4S$+Na 560.0079, found 560.0047; $[\alpha]^{20}_D$ = –122.0 (*c* 0.19, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (25% 2-propanol/hexane, 1.0 mL/min), -67% ee, t_{minor}= 8.58 min, t_{major}=10.10 min.

5ad Yellow solid, mp 118.6–119.7°C; 24.1 mg, yield 45 %; ^{1}H NMR (600 MHz, DMSO) δ 11.75 (s, 1H), 7.67 (dd, *J*= 8.0, 1.0 Hz, 1H), 7.24 (td, *J*= 7.8, 1.0 Hz, 1H), 7.19 (td, *J*= 7.8, 1.5 Hz, 1H), 7.07 (dd, *J*= 18.2, 7.9 Hz, 2H), 7.00 – 6.92 (m, 2H), 6.91 (s, 1H), 6.67 (t, *J*= 7.2 Hz, 2H), 6.63 (d, *J*= 6.6 Hz, 1H), 6.57 (dd, *J*= 11.6, 4.2 Hz, 1H), 6.32 (d, *J*= 7.5 Hz, 1H), 5.69 (s, 1H), 3.26 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 193.8, 174.1, 151.5, 143.9, 133.8, 133.2, 131.5, 130.9, 130.1, 129.7, 129.3, 127.4, 126.0, 125.4, 124.8, 123.4, 122.8, 118.2, 109.5, 100.0, 79.8, 73.8, 55.4, 49.0, 46.3, 27.3. $[\alpha]^{20}_D$ = –48.0 (*c* 0.25, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), 70% ee, t_{major} = 14.60 min, t_{minor} =22.57 min.

4ae Yellow solid, mp 174.3–175.8°C; 20.1 mg, yield 49 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.61 (d, *J* = 18.1 Hz, 1H), 7.62 (d, *J* = 7.4 Hz, 1H), 7.56 – 7.44 (m, 3H), 7.37 – 7.27 (m, 3H), 7.17 (t, *J* = 7.8 Hz, 1H), 6.99 (d, *J* = 8.1 Hz, 1H), 6.95 (d, *J* = 7.9 Hz, 1H), 6.76 (t, *J* = 7.5 Hz, 1H), 6.43 (d, *J* = 12.7 Hz, 1H), 6.28 (d, *J* = 7.7 Hz, 1H), 5.08 (s, 1H), 3.01 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.8, 172.7, 154.4, 143.5, 134.8, 132.2, 132.1, 131.2, 129.8, 127.2, 126.8, 126.4, 124.8, 124.5, 122.5, 118.2, 115.6, 109.5, 97.3, 97.3, 79.1, 71.7, 53.0, 26.7. ESI-HRMS: calcd. for $C_{25}H_{18}ClN_3O_4S$+Na 514.0059, found 514.0589; $[\alpha]^{20}_D$ = –100.0 (*c* 0.14, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), -80% ee, t_{minor} = 5.17 min, t_{major} = 10.49 min.

5ae Yellow solid, mp 119.5–121.2 °C; 23.1 mg, yield 47 %; ^{1}H NMR (600 MHz, DMSO) δ 11.63 (s, 1H), 7.29 (s, 4H), 7.23 (td, *J*= 7.7, 1.0 Hz, 1H), 7.04 (d, *J*= 7.8 Hz, 1H), 7.00 – 6.96 (m, 1H), 6.75 (d, *J*= 7.5 Hz, 1H), 6.70 (td, *J*= 7.6, 0.6 Hz, 1H), 6.63 – 6.58 (m, 1H), 6.54 (d, *J*= 7.7 Hz, 2H), 6.04 (s, 1H), 5.37 (s, 1H), 3.23 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 193.0, 174.3, 152.2, 144.2, 134.3, 133.0, 131.5, 131.0, 129.9, 129.7, 128.1, 126.1, 124.4, 123.1, 123.0, 120.2, 118.1, 109.7, 99.2, 79.9, 73.2, 47.6, 27.4. $[\alpha]^{20}_D$ = –164.3 (*c* 0.14, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), 71% ee, t_{major} = 4.97 min, t_{minor} = 8.80 min.

4af Yellow solid, mp 177.3–178.9 °C; 21.8 mg, yield 47 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.62 (d, *J* = 7.4 Hz, 1H), 7.55 – 7.52 (m, 3H), 7.30 (t, *J* = 7.6 Hz, 1H), 7.17 (t, *J* = 7.7 Hz, 1H), 7.04 (t, *J* = 8.6 Hz, 2H), 7.00 (d, *J* = 8.3 Hz, 1H), 6.95 (d, *J* = 7.9 Hz, 1H), 6.82 – 6.70 (m, 1H), 6.43 (d, *J* = 11.1 Hz, 1H), 6.28 (d, *J* = 7.7 Hz, 1H), 5.06 (s, 1H), 3.01 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.0, 172.7, 163.9, 162.3, 154.4, 143.5, 132.1, 131.6, 131.6, 129.8, 129.5, 126.9, 126.3, 124.8, 124.5, 122.4, 118.2, 115.6, 114.1, 113.9, 109.5, 97.2, 79.2, 71.7, 53.1, 26.7. ESI-HRMS: calcd. for $C_{25}H_{18}FN_3O_4S$+Na 498.0894, found 498.0871; $[\alpha]^{20}_D$ = –223.9 (*c* 0.22, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (25% 2-propanol/hexane, 1.0 mL/min), -82% ee, t_{minor} = 6.33 min, t_{major} = 15.26 min.

5af Yellow solid, mp 184.3–185.6 °C; 21.8 mg, yield 46 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.77 (s, 1H), 7.26 (dd, *J*= 9.4, 6.0 Hz, 1H), 7.17 (dd, *J*= 8.7, 5.2 Hz, 2H), 7.01 (dd, *J*= 11.2, 4.2 Hz, 1H), 6.89 – 6.83 (m, 3H), 6.79 – 6.72 (m, 2H), 6.64 (t, *J*= 7.5 Hz, 1H), 6.42 (d, *J*= 7.5 Hz, 1H), 6.38 (d, *J*= 7.6 Hz, 1H), 6.30 (s, 1H), 5.42 (s, 1H), 3.30 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.8, 174.7, 164.0, 162.3, 152.3, 143.6, 131.2, 130.9, 130.8, 129.7, 129.5, 129.3, 126.4, 123.6, 123.3, 122.8, 120.1, 118.8, 115.2, 115.1, 109.0, 98.3, 80.8, 72.7, 47.4, 31.6. $[\alpha]^{20}_D$ = –57.3 (*c* 0.23, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (25% 2-propanol/hexane, 1.0 mL/min), 80% ee, t_{major} = 5.95 min, t_{minor} = 11.33 min.

4ag Yellow solid, mp 144.7–145.9 °C; 23.1 mg, yield 49 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.51 (s, 1H), 7.60 (d, *J* = 7.4 Hz, 1H), 7.51 (t, *J* = 7.8 Hz, 1H), 7.42 (d, *J* = 8.1 Hz, 2H), 7.27 (t, *J* = 7.6 Hz, 1H), 7.15 (dd, *J* = 14.4, 4.6 Hz, 3H), 6.98 – 6.97 (m, 1H), 6.93 (d, *J* = 7.9 Hz, 1H), 6.73 (td, *J* = 7.7, 1.0 Hz, 1H), 6.39 (s, 1H), 6.28 (d, *J* = 7.7 Hz, 1H), 5.03 (s, 1H), 2.99 (s, 3H), 2.37 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.1, 172.8, 154.5, 143.6, 138.8, 131.9, 130.7, 129.7, 129.6, 127.9, 127.1, 126.3, 124.7, 124.5, 122.2, 118.2, 115.9, 109.4, 97.2, 79.8, 71.6, 53.0, 26.7, 21.5. ESI-HRMS: calcd. for $C_{26}H_{21}N_3O_4S$+Na 494.1145, found 494.1117; $[\alpha]^{20}_D$ = –119.1 (*c* 0.23, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), -83% ee, t_{minor} = 6.96 min, t_{major} = 11.49 min.

5ag Yellow solid, mp 166.1–167.4 °C; 18.8 mg, yield 40 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.66 (s, 1H), 7.26 – 7.23 (m, 1H), 7.03 (dd, *J* = 8.3, 1.8 Hz, 2H), 6.99 (td, *J* = 8.2, 1.5 Hz, 1H), 6.96 (d, *J* = 8.0 Hz, 2H), 6.83 (d, *J* = 7.8 Hz, 1H), 6.77 – 6.73 (m, 1H),

6.72 (td, *J* = 7.6, 0.8 Hz, 1H), 6.61 (td, *J* = 7.6, 1.1 Hz, 1H), 6.37 (dt, *J* = 6.6, 2.3 Hz, 3H), 5.47 (s, 1H), 3.30 (s, 3H), 2.23 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.3, 174.7, 152.4, 143.5, 139.3, 131.0, 130.4, 129.5, 129.3, 128.8, 128.7, 126.4, 123.6, 123.1, 122.5, 120.6, 118.8, 108.8, 98.4, 81.5, 72.6, 47.1, 27.2, 21.1. $[\alpha]^{20}_D$ = –316.2 (*c* 0.12, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), 85% ee, t_{major} = 4.56 min, t_{minor} = 9.23 min.

4ah Yellow solid, mp 182.4–183.5 °C; 18.9 mg, yield 39 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.49 (s, 1H), 7.61 (d, *J* = 7.4 Hz, 1H), 7.52 (td, *J* = 7.8, 1.0 Hz, 1H), 7.45 (d, *J* = 8.7 Hz, 2H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.17 – 7.14 (m, 1H), 6.98 (d, *J* = 8.2 Hz, 1H), 6.94 (d, *J* = 7.8 Hz, 1H), 6.87 (d, *J* = 8.8 Hz, 2H), 6.75 – 6.72 (m, 1H), 6.38 (s, 1H), 6.28 (d, *J* = 7.6 Hz, 1H), 5.02 (s, 1H), 3.82 (s, 3H), 2.99 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.2, 172.8, 160.0, 154.5, 143.6, 132.0, 131.0, 129.7, 127.0, 126.3, 125.8, 124.7, 124.5, 122.2, 118.2, 115.8, 112.5, 109.4, 97.1, 79.6, 71.6, 55.3, 53.1, 26.7. ESI-HRMS: calcd. for $C_{26}H_{21}N_3O_5S$+Na 510.1049, found 510.1055; $[\alpha]^{20}_D$ = –90.6 (*c* 0.18, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), -83% ee, t_{minor} = 6.99 min, t_{major} = 16.59 min.

5ah Yellow solid, mp 166.3–167.5 °C; 29.2 mg, yield 60 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.70 (s, 1H), 7.26 – 7.23 (m, 1H), 7.06 (d, *J* = 8.7 Hz, 2H), 7.00 (t, *J* = 7.7 Hz, 1H), 6.84 (t, *J* = 7.7 Hz, 1H), 6.76 (d, *J* = 8.1 Hz, 1H), 6.72 (t, *J* = 7.6 Hz, 1H), 6.65 – 6.60 (m, 3H), 6.36 (d, *J* = 8.5 Hz, 3H), 5.46 (s, 1H), 3.69 (s, 3H), 3.28 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.3, 174.7, 160.1, 152.5, 143.6, 131.1, 130.3, 129.6, 129.5, 126.5, 125.6, 123.7, 123.2, 122.5, 120.7, 118.9, 113.5, 108.9, 98.5, 81.4, 72.7, 55.2, 47.1, 27.2. $[\alpha]^{20}_D$ = –187.5 (*c* 0.11, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), 81% ee, t_{major} = 4.91 min, t_{minor} = 10.33 min.

4ai Yellow solid, mp 208.4–209.5 °C; 28.4 mg, yield 53 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.61 (d, *J*= 7.3 Hz, 1H), 7.56 (t, *J*= 7.8 Hz, 1H), 7.50 (d, *J*= 7.1 Hz, 2H), 7.40 – 7.34 (m, 3H), 7.31 (t, *J*= 7.5 Hz, 1H), 7.27 (dd, *J*= 8.8, 2.3 Hz, 1H), 6.99 (d, *J*= 7.9 Hz, 1H), 6.89 (d, *J*= 8.8 Hz, 1H), 6.41 (d, *J*= 2.2 Hz, 1H), 6.39 (s, 1H), 4.98 (s, 1H), 3.04 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.4, 172.6, 153.6, 143.4, 133.2, 132.7, 132.3, 129.7, 129.2, 129.0, 127.1, 126.6, 125.0, 124.5, 120.0, 118.2, 114.3, 109.5, 96.5, 80.1, 71.5, 31.7, 26.8. ESI-HRMS: calcd. for $C_{25}H_{18}BrN_3O_4S$+Na 560.0079, found 560.0034; $[\alpha]^{20}_D$ = –171.4 (*c* 0.16, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), -83% ee, t_{minor} = 5.16 min, t_{major} = 18.83 min.

5ai Yellow solid, mp 189.1–190.7 °C; 21.9 mg, yield 41 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.83 (s, 1H), 7.33 – 7.30(m, 1H), 7.28 – 7.24 (m, 1H), 7.19 (t, *J*= 7.7 Hz, 2H), 7.16 – 7.12 (m, 2H), 7.11 – 7.09 (m, 1H), 6.89 (d, *J*= 7.8 Hz, 1H), 6.81 (t, *J*= 7.6 Hz, 1H), 6.65 (dd, *J*= 8.6, 4.3 Hz, 1H), 6.41 (dd, *J*= 9.6, 4.3 Hz, 2H), 6.37 (t, *J*= 6.5 Hz, 1H), 5.38 (s, 1H), 3.29 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.8, 174.6, 151.6, 143.5, 133.1, 132.5, 132.3, 131.6, 129.6, 128.8, 128.3, 126.3, 123.3, 123.1, 122.4, 120.5, 114.6, 109.2, 97.7, 81.5, 72.7, 46.8.$[\alpha]^{20}_D$ = –82.2 (*c* 0.24, $CHCl_3$); T he enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), 51% ee, t_{major} = 5.60 min, t_{minor} = 10.99 min.

4aj Yellow solid, mp 200.4–201.2 °C; 25.0 mg, yield 51 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.40 (s, 1H), 7.61 (d, *J*= 7.3 Hz, 1H), 7.56 (t, *J*= 7.8 Hz, 1H), 7.51 (d, *J*= 7.1 Hz, 2H), 7.42 – 7.34 (m, 3H), 7.31 (t, *J*= 7.6 Hz, 1H), 7.18 – 7.11 (m, 1H), 6.97 (dd, *J*= 21.8, 8.3 Hz, 2H), 6.40 (s, 1H), 6.26 (d, *J*= 2.3 Hz, 1H), 4.99 (s, 1H), 3.05 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.4, 172.6, 153.1, 143.4, 133.2, 132.3, 129.8, 129.7, 129.2, 128.0, 127.1, 127.1, 126.6, 126.0, 125.0, 124.5, 119.6, 117.6, 109.6, 100.0, 96.6, 80.1, 71.4, 52.7, 26.8. ESI-HRMS: calcd. for $C_{25}H_{18}ClN_3O_4S$+Na 514.0599, found 514.0552; $[\alpha]^{20}_D$ = –114.9 (*c* 0.16, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), -84% ee, t_{minor} = 5.17 min, t_{major} = 18.67 min.

5aj Yellow solid, mp 178.7–180.1 °C; 19.6 mg, yield 40 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.80 (s, 1H), 7.31 (t, *J*= 7.8 Hz, 1H), 7.26 (t, *J*= 7.3 Hz, 1H), 7.19 (t, *J*= 7.7 Hz, 2H), 7.14 (d, *J*= 7.5 Hz, 2H), 7.02 – 6.93 (m, 2H), 6.89 (d, *J*= 7.8 Hz, 1H), 6.80 (t, *J*= 7.6 Hz, 1H), 6.71– 6.49 (m, 1H), 6.43 – 6.37 (m, 2H), 6.29 (d, *J*= 2.3 Hz, 1H), 5.39 (s, 1H), 3.30 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.8, 174.6, 151.1, 143.5, 133.1, 131.6, 129.7, 129.6, 129.2, 128.8, 128.3, 127.4, 126.3, 123.3, 123.2, 122.0, 120.1, 109.2, 97.8, 81.6, 72.6, 46.9, 27.3. $[\alpha]^{20}_D$ = –191.5 (*c* 0.16, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), 51% ee, t_{major} = 5.68 min, t_{minor} = 10.67 min.

4ak Yellow solid, mp 192.3–193.7 °C; 24.7 mg, yield 49 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.61 (d, *J*= 7.3 Hz, 1H), 7.56 (t, *J*= 7.6 Hz, 1H), 7.38 (d, *J*= 7.8 Hz, 2H), 7.31 (t, *J*= 7.5 Hz, 1H), 7.20 – 7.11 (m, 3H), 6.99 (d, *J*= 7.8 Hz, 1H), 6.94 (d, *J*= 8.8 Hz, 1H), 6.35 (s, 1H), 6.26 (d, *J*= 2.1 Hz, 1H), 4.97 (s, 1H), 3.04 (s, 3H), 2.38 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.5, 172.6, 153.1, 143.5, 139.1, 132.3, 130.2, 129.8, 129.5, 128.0, 127.0, 125.9, 124.9, 124.5, 119.6, 117.7, 109.5, 96.5, 80.1, 71.4, 52.6, 26.8, 21.5. ESI-HRMS: calcd. for $C_{26}H_{20}ClN_3O_4S$+Na 528.0755, found 528.0717; $[\alpha]^{20}_D$ = –75.0 (*c* 0.13, $CHCl_3$); T he enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), -82% ee, t_{minor} = 7.71 min, t_{major} = 17.79 min.

5ak Yellow solid, mp 174.3–175.1 °C; 18.7 mg, yield 37 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.84 (s, 1H), 7.31 (t, *J*= 7.7 Hz, 1H), 7.02 (d, *J*= 8.3 Hz, 2H), 7.00 – 6.96 (m, 2H), 6.96 (d, *J*= 2.4 Hz, 1H), 6.90 (d, *J*= 7.8 Hz, 1H), 6.80 (t, *J*= 7.6 Hz, 1H), 6.70 (d, *J*= 8.7 Hz, 1H), 6.40 (s, 1H), 6.36 (d, *J*= 7.4 Hz, 1H), 6.30 (d, *J*= 2.3 Hz, 1H), 5.41 (s, 1H), 3.31 (s, 3H), 2.24 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.0, 174.6, 151.1, 143.5, 139.6, 131.5, 130.1, 129.6, 129.3, 129.0, 128.7, 127.3, 126.3, 123.2, 122.3, 120.2, 109.2, 97.9, 81.6, 72.6, 46.8, 27.3, 21.2. $[\alpha]^{20}_D$ = –80.0 (*c* 0.15, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), 66% ee, t_{major} = 5.14 min, t_{minor} = 12.27 min.

4al Yellow solid, mp 176.2–177.1 °C; 18.8 mg, yield 40 %; ^{1}H NMR (600 MHz, DMSO) δ 11.56 (s, 1H), 7.83 (d, *J*= 7.3 Hz, 1H), 7.60 (t, *J*= 7.8 Hz, 1H), 7.40 – 7.32 (m, 6H), 7.22 (d, *J*= 7.9 Hz, 1H), 7.04 – 6.99 (m, 1H), 6.87 (d, *J*= 8.3 Hz, 1H), 6.36 (s, 1H), 6.03 (s, 1H), 5.05 (s, 1H), 2.99 (s, 3H), 1.99 (s, 3H). ^{13}C NMR (150 MHz, DMSO) δ 192.1, 173.1, 151.8, 143.9, 134.4, 131.9,

131.6, 130.4, 129.8, 129.1, 127.9, 127.3, 126.7, 125.2, 124.6, 117.4, 116.9, 109.9, 97.4, 79.7, 72.1, 51.7, 26.9, 21.2. ESI-HRMS: calcd. for $C_{26}H_{21}N_3O_4S$+Na 494.1145, found 494.1114; $[\alpha]^{20}_D$ = –179.2 (*c* 0.24, $CHCl_3$); T he enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), -74% ee, t_{minor} = 4.56 min, t_{major} = 17.89 min.

5al Yellow solid, mp 190.1–191.6 °C; 22.1 mg, yield 47 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.74 (s, 1H), 7.29 – 7.22 (m, 2H), 7.19 – 7.12 (m, 4H), 6.85 (d, *J*= 7.8 Hz, 1H), 6.79 (dd, *J*= 8.3, 1.4 Hz, 1H), 6.73 (t, *J*= 7.6 Hz, 1H), 6.64 (d, *J*= 8.2 Hz, 1H), 6.40 (s, 1H), 6.32 (d, *J*= 7.4 Hz, 1H), 6.07 (s, 1H), 5.39 (s, 1H), 3.29 (s, 3H), 1.92 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.5, 174.8, 150.2, 143.6, 133.7, 131.9, 131.1, 130.2, 130.1, 129.3, 128.9, 128.2, 126.6, 123.6, 122.9, 119.9, 118.4, 108.8, 98.3, 81.5, 72.8, 47.0, 27.2, 21.1. $[\alpha]^{20}_D$ = –54.5 (*c* 0.15, $CHCl_3$); T he enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), 86% ee, t_{major} = 4.53 min, t_{minor} = 12.58 min.

4am Yellow solid, mp 148.3–149.6 °C; 21.9 mg, yield 45 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.52 (s, 1H), 7.63 (d, *J* = 7.4 Hz, 1H), 7.57 (d, *J* = 6.7 Hz, 2H), 7.53 (dd, *J* = 15.1, 7.4 Hz, 1H), 7.44 – 7.34 (m, 3H), 7.31 – 7.26 (m, 1H), 6.94 (d, *J* = 7.9 Hz, 1H), 6.53 (d, *J* = 2.4 Hz, 1H), 6.45 (d, *J* = 7.0 Hz, 1H), 6.35 (dd, *J* = 8.7, 2.5 Hz, 1H), 6.18 (d, *J* = 8.7 Hz, 1H), 4.99 (s, 1H), 3.71 (s, 3H), 3.02 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.2, 172.9, 160.5, 155.5, 143.5, 133.6, 131.9, 129.8, 129.0, 127.0, 124.7, 124.5, 110.2, 109.4, 107.5, 102.1, 97.1, 79.8, 71.8, 55.3, 53.2, 26.7. ESI-HRMS: calcd. for $C_{26}H_{21}N_3O_5S$+Na 510.1049, found 510.1056; $[\alpha]^{20}_D$ = –101.5 (*c* 0.22, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), -72% ee, t_{minor} = 6.79 min, t_{major} = 10.83 min.

5am Yellow solid, mp 138.3–139.7 °C; 18.5 mg, yield 38 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.62 (s, 1H), 7.29 – 7.24 (m, 3H), 7.18 – 7.16 (m, 3H), 6.84 – 6.83 (m, 1H), 6.78 (td, *J* = 7.6, 0.7 Hz, 1H), 6.42 (d, *J* = 7.6 Hz, 1H), 6.37 – 6.34 (m, 1H), 6.31 (t, *J* = 2.4 Hz, 1H), 6.27 – 6.18 (m, 2H), 5.37 (s, 1H), 3.62 (s, 3H), 3.27 (s, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.2, 174.8, 160.5, 153.6, 143.7, 133.5, 131.2, 130.3, 129.5, 128.9, 128.2, 126.8, 123.6, 123.2, 112.0, 109.7, 108.9, 103.3, 98.3, 81.6, 72.8, 55.4, 46.9, 27.2. $[\alpha]^{20}_D$ = –105.0 (*c* 0.13, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (35% 2-propanol/hexane, 1.0 mL/min), 76% ee, t_{major} = 5.04 min, t_{minor} = 7.99 min.

4ba Yellow solid, mp 162.1–163.6 °C; 25.4 mg, yield 54 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.45 (br, 1H), 7.54 (d, *J*= 7.3 Hz, 1H), 7.48 (d, *J*= 6.9 Hz, 2H), 7.44 (dd, *J*= 15.2, 7.5 Hz, 1H), 7.29 (ddd, *J*= 15.9, 7.7, 2.4 Hz, 3H), 7.20 (t, *J*= 7.6 Hz, 1H), 7.08 (t, *J*= 7.3 Hz, 1H), 6.92 (d, *J*= 8.1 Hz, 1H), 6.87 (d, *J*= 7.8 Hz, 1H), 6.66 (t, *J*= 7.5 Hz, 1H), 6.42 (s, 1H), 6.23 (d, *J*= 7.7 Hz, 1H), 4.97 (s, 1H), 3.54 (dt, *J*= 14.4, 7.4 Hz, 1H), 3.27-3.18 (m, 1H), 0.63-0.61 (m, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.1, 172.8, 154.5, 143.4, 133.6, 132.0, 129.8, 129.8, 129.0, 127.0, 126.6, 124.8, 124.5, 122.2, 118.2, 115.6, 109.6, 96.9, 79.8, 71.4, 53.4, 42.5, 20.7, 11.4. ESI-HRMS: calcd. for $C_{26}H_{21}N_3O_4S$+Na 494.1145, found 494.1141; $[\alpha]^{20}_D$ = –86.5 (*c* 0.17, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (30% 2-propanol/hexane, 1.0 mL/min), -82% ee, t_{minor} = 5.63 min, t_{major} = 11.55 min.

5ba Yellow solid, mp 130.5–131.6 °C; 19.8 mg, yield 42 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.59 (s, 1H), 7.23 (t, *J*= 7.8 Hz, 2H), 7.20 – 7.14 (m, 4H), 7.00 (t, *J*= 7.2 Hz, 1H), 6.84 (d, *J*= 7.9 Hz, 1H), 6.76 (d, *J*= 8.2 Hz, 1H), 6.72 (t, *J*= 7.6 Hz, 1H), 6.62 (t, *J*= 7.4 Hz, 1H), 6.44 (d, *J*= 7.5 Hz, 1H), 6.39 (t, *J*= 7.0 Hz, 2H), 5.48 (d, *J*= 3.9 Hz, 1H), 3.83 (dt, *J*= 14.4, 7.4 Hz, 1H), 3.70 – 3.64 (m, 1H), 1.06 (t, *J*= 7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.2, 174.6, 152.5, 143.1, 133.6, 131.1, 129.6, 129.4, 129.2, 128.9, 128.2, 127.0, 126.6, 123.8, 123.0, 122.6, 120.6, 118.9, 109.2, 100.0, 98.5, 81.7, 79.8, 72.6, 47.5, 42.5. $[\alpha]^{20}_D$ = –71.4 (*c* 0.14, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (30% 2-propanol/hexane, 1.0 mL/min), 80% ee, t_{major} = 4.99 min, t_{minor} = 5.94 min.

4bb Yellow solid, mp 164.4–165.1 °C; 25.2 mg, yield 46 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.56 (s, 1H), 7.63 (d, *J*= 7.3 Hz, 1H), 7.55 – 7.43 (m, 5H), 7.29 (t, *J*= 7.5 Hz, 1H), 7.17 (t, *J*= 7.4 Hz, 1H), 6.97 (dd, *J*= 19.4, 8.0 Hz, 2H), 6.75 (t, *J*= 7.4 Hz, 1H), 6.48 (s, 1H), 6.30 (d, *J*= 7.7 Hz, 1H), 5.07 (s, 1H), 3.62 (dt, *J*= 14.5, 7.4 Hz, 1H), 3.34 – 3.27 (m, 1H), 0.71 (t, *J*= 7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 192.8, 172.7, 154.3, 143.2, 132.8, 132.1, 131.5, 130.2, 129.8, 126.8, 126.7, 124.7, 124.6, 123.2, 122.5, 118.1, 115.4, 109.7, 97.0, 79.1, 71.6, 42.5, 31.7, 11.4. $[\alpha]^{20}_D$ = –175.0 (*c* 0.12, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (30% 2-propanol/hexane, 1.0 mL/min), -83% ee, t_{minor} = 5.91 min, t_{major} = 12.47 min.

5bb Yellow solid, mp 180.5–181.9 °C; 27.4 mg, yield 50 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.76 (s, 1H), 7.32 (d, *J*= 8.5 Hz, 2H), 7.24 (t, *J*= 7.7 Hz, 1H), 7.07 (t, *J*= 7.4 Hz, 2H), 7.02 (dd, *J*= 11.3, 4.2 Hz, 1H), 6.85 (d, *J*= 7.9 Hz, 1H), 6.77 (d, *J*= 8.2 Hz, 1H), 6.73 (t, *J*= 7.6 Hz, 1H), 6.64 (t, *J*= 7.5 Hz, 1H), 6.47 (t, *J*= 8.7 Hz, 1H), 6.39 (d, *J*= 7.8 Hz, 1H), 6.25 (s, 1H), 5.41 (s, 1H), 3.82 (dt, *J*= 14.4, 7.3 Hz, 1H), 3.71 – 3.64 (m, 1H), 1.05 (t, *J*= 7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.5, 174.5, 152.2, 143.0, 132.5, 131.2, 131.1, 130.5, 130.0, 129.7, 129.0, 126.4, 123.7, 123.6, 123.0, 122.8, 120.0, 118.7, 109.2, 98.1, 80.8, 72.58 42.5, 31.6, 11.5. $[\alpha]^{20}_D$ = –55.6 (*c* 0.41, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (30% 2-propanol/hexane, 1.0 mL/min), 84% ee, t_{major} = 5.20 min, t_{minor} = 7.23 min.

4bf Yellow solid, mp 182.3–183.8 °C; 22.5 mg, yield 46 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.71 (s, 1H), 7.54 (d, *J*= 7.4 Hz, 1H), 7.50 – 7.41 (m, 3H), 7.23 – 7.17 (m, 1H), 7.09 (t, *J*= 7.7 Hz, 1H), 6.96 (dd, *J*= 12.1, 5.0 Hz, 2H), 6.91 (d, *J*= 8.2 Hz, 1H), 6.87 (d, *J*= 7.9 Hz, 1H), 6.66 (dd, *J*= 10.8, 4.2 Hz, 1H), 6.41 (d, *J*= 9.1 Hz, 1H), 6.22 (d, *J*= 7.5 Hz, 1H), 4.97 (s, 1H), 3.54 (dt, 14.0, 7.0 Hz, 1H), 3.23 (dt, *J*= 13.9, 6.9 Hz, 1H), 0.62 (t, *J*= 7.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.0, 172.7, 171.2, 162.3, 154.4, 143.2, 132.0, 131.6, 131.6, 129.8, 126.7, 124.7, 124.5, 122.4, 118.1, 115.4, 114.0, 113.9, 109.6, 97.0, 79.1, 71.6, 60.5, 42.5, 11.4. $[\alpha]^{20}_D$ = –142.4 (*c* 0.19, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (20% 2-propanol/hexane, 1.0 mL/min), -82% ee, t_{minor} = 7.78 min, t_{major} = 19.81 min.

5bf Yellow solid, mp 172.3–173.1 °C; 30.0 mg, yield 47 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.85 (s, 1H), 7.16 (t, *J*= 7.7 Hz, 1H),

7.11 (dd, *J*= 8.6, 5.3 Hz, 2H), 6.94 (t, *J*= 7.7 Hz, 1H), 6.79 (dd, *J*= 17.4, 8.5 Hz, 3H), 6.70 (d, *J*= 8.2 Hz, 1H), 6.68 – 6.63 (m, 1H), 6.56 (t, *J*= 7.5 Hz, 1H), 6.38 (d, *J*= 7.3 Hz, 1H), 6.32 (d, *J*= 7.7 Hz, 1H), 6.23 (d, *J*= 3.1 Hz, 1H), 5.35 (s, 1H), 3.74 (dt, *J*= 14.3, 7.3 Hz, 1H), 3.64 – 3.57 (m, 1H), 0.98 (t, *J*= 7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 194.7, 174.6, 164.0, 162.3, 152.4, 143.1, 131.1, 130.9, 130.8, 129.7, 129.1, 126.5, 123.1, 122.8, 120.2, 118.8, 115.2, 115.1, 109.2, 98.3, 80.8, 72.6, 42.5, 20.8, 11.5. $[\alpha]^{20}_D$ = –189.5 (*c* 0.19, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (20% 2-propanol/hexane, 1.0 mL/min), 82% ee, t_{major} = 6.50 min, t_{minor} = 9.12 min.

4bj Yellow solid, mp 134.7–135.4 °C; 21.8 mg, yield 45 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.49 (s, 1H), 7.62 (d, *J*= 7.4 Hz, 1H), 7.51 (t, *J*= 7.5 Hz, 1H), 7.43 (d, *J*= 8.0 Hz, 2H), 7.27 (dd, *J*= 12.7, 5.1 Hz, 1H), 7.16 (dd, *J*= 11.1, 8.4 Hz, 3H), 6.98 (d, *J*= 8.2 Hz, 1H), 6.94 (d, *J*= 7.9 Hz, 1H), 6.73 (t, *J*= 7.5 Hz, 1H), 6.44 (s, 1H), 6.31 (d, *J*= 7.7 Hz, 1H), 5.02 (s, 1H), 3.61 (dt, *J*= 14.5, 7.4 Hz, 1H), 3.29 (dt, *J*= 14.1, 7.1 Hz, 1H), 2.38 (s, 3H), 0.70 (t, *J*= 7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.1, 172.7, 154.5, 143.3, 138.8, 131.9, 130.7, 129.7, 129.6, 127.9, 127.0, 126.6, 124.7, 124.5, 122.2, 118.1, 115.7, 109.6, 79.7, 42.4, 21.5, 20.7, 11.4. $[\alpha]^{20}_D$ = –86.7 (*c* 0.15, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (30% 2-propanol/hexane, 1.0 mL/min), -83% ee, t_{minor} = 8.08 min, t_{major} = 12.57 min.

5bj Yellow solid, mp 164.7–165.1 °C; 23.3 mg, yield 48 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.78 (s, 1H), 7.25 – 7.20 (m, 1H), 7.03 (d, *J*= 7.8 Hz, 2H), 7.01 – 6.94 (m, 3H), 6.84 (d, *J*= 7.9 Hz, 1H), 6.75 (d, *J*= 8.1 Hz, 1H), 6.70 (t, *J*= 7.6 Hz, 1H), 6.61 (t, *J*= 7.5 Hz, 1H), 6.41 (d, *J*= 7.5 Hz, 1H), 6.39 – 6.33 (m, 2H), 5.45 (s, 1H), 3.82 (dt, *J*= 14.3, 7.3 Hz, 1H), 3.69 – 3.63 (m, 1H), 2.23 (s, 3H), 1.05 (q, *J*= 7.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.3, 174.6, 152.5, 143.1, 139.3, 131.0, 129.6, 129.2, 128.9, 128.8, 126.6, 123.8, 123.0, 122.5, 118.9, 109.1, 81.6, 72.6, 42.5, 21.2, 20.8, 11.5. $[\alpha]^{20}_D$ = –113.8 (*c* 0.19, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (30% 2-propanol/hexane, 1.0 mL/min), 82% ee, t_{major} = 4.62 min, t_{minor} = 6.47 min.

4bk Yellow solid, mp 162.1–163.6 °C; 20.0 mg, yield 44 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.45 (s, 1H), 7.66 (t, *J*= 8.1 Hz, 1H), 7.52 (t, *J*= 7.7 Hz, 1H), 7.46 (t, *J*= 8.4 Hz, 2H), 7.29 (dd, *J*= 10.2, 4.9 Hz, 1H), 7.18 – 7.13 (m, 1H), 6.99 (d, *J*= 8.2 Hz, 1H), 6.95 (d, *J*= 7.9 Hz, 1H), 6.87 (dd, *J*= 8.8, 5.5 Hz, 2H), 6.73 (t, *J*= 8.0 Hz, 1H), 6.46 – 6.42 (m, 1H), 6.31 (d, *J*= 7.7 Hz, 1H), 5.02 (s, 1H), 3.83 (s, 3H), 3.65 – 3.59 (m, 1H), 3.30 (ddd, *J*= 14.1, 8.0, 6.2 Hz, 1H), 0.70 (t, *J*= 7.4 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 193.2, 172.7, 160.0, 154.5, 143.3, 131.9, 131.0, 130.3, 129.7, 127.0, 126.6, 125.8, 124.8, 124.5, 122.1, 118.1, 113.6, 112.5, 109.6, 79.5, 71.5, 55.2, 42.5, 22.7, 11.4. $[\alpha]^{20}_D$ = –100.0 (*c* 0.11, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (25% 2-propanol/hexane, 1.0 mL/min), -84% ee, t_{minor} = 11.35 min, t_{major} = 24.91 min.

5bk Yellow solid, mp 210.3–211.3 °C; 21.5 mg, yield 43 %; ^{1}H NMR (600 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.23 (t, *J*= 7.7 Hz, 1H), 7.07 (d, *J*= 8.6 Hz, 2H), 7.01 (t, *J*= 7.4 Hz, 1H), 6.84 (d, *J*= 7.8 Hz, 1H), 6.76 (d, *J*= 8.1 Hz, 1H), 6.71 (t, *J*= 7.6 Hz, 1H), 6.67 – 6.60 (m, 3H), 6.41 – 6.32 (m, 3H), 5.47 (d, *J*= 5.4 Hz, 1H), 3.81 (dt, *J*= 14.6, 7.3 Hz, 1H), 3.74 – 3.62 (m, 4H), 1.04 (t, *J*= 7.3 Hz, 3H). ^{13}C NMR (150 MHz, $CDCl_3$) δ 195.3, 174.5, 160.1, 152.5, 143.1, 131.0, 130.3, 129.6, 129.3, 126.7, 125.6, 123.7, 123.0, 122.5, 119.0, 113.5, 109.1, 98.5, 81.4, 72.6, 42.4, 20.8, 11.5. $[\alpha]^{20}_D$ = –32.7 (*c* 0.18, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (25% 2-propanol/hexane, 1.0 mL/min), 82% ee, t_{major} = 5.58 min, t_{minor} = 9.72 min.

4bc/5bc Yellow solid, 51.9 mg, yield 85 %; dr =1:1. ^{1}H NMR (600 MHz, DMSO) δ 11.80 (s, 1H), 11.68 (s, 1H), 7.80 (d, *J* = 7.3 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.26 (d, *J* = 8.5 Hz, 2H), 7.15 (t, *J* = 7.9 Hz, 1H), 6.96 – 6.92 (m, 2H), 6.87 (d, *J* = 8.0 Hz, 1H), 6.67 (t, *J* = 8.1 Hz, 2H), 6.61 (t, *J* = 7.6 Hz, 1H), 6.53 (d, *J* = 7.1 Hz, 1H), 6.45 (dd, *J* = 7.6, 0.8 Hz, 1H), 6.43 (s, 1H), 6.37 (d, *J* = 7.0 Hz, 1H), 6.13 (d, *J* = 7.4 Hz, 1H), 5.40 (s, 1H), 5.08 (s, 1H), 4.98 (d, *J* = 15.7 Hz, 1H), 4.91 (d, *J* = 15.7 Hz, 1H). ^{13}C NMR (150 MHz, DMSO) δ 193.2, 174.5, 153.7, 143.1, 136.0, 133.7, 131.9, 131.0, 130.9, 129.8, 129.1, 128.2, 128.1, 127.4, 126.3, 124.8, 124.6, 123.2, 123.1, 120.3, 118.1, 110.7, 99.3, 96.8, 80.1, 51.5, 44.0. $[\alpha]^{20}_D$= – 42.9(*c* 0.19, $CHCl_3$); The enantiomeric ratio was determined by HPLC on Chiralpak AD column (25% 2-propanol/hexane, 1.0 mL/min), -65% ee, t_{minor} = 7.52 min, t_{major} = 12.58 min;50% ee, t_{major} = 6.18 min, t_{minor} = 8.85 min.

Crystal data for 4ac (CCDC: 1001582): $C_{25}H_{18}BrN_3O_4S$ (536.39), Triclinic, space group P -1, a=9.0285(3), b=9.3506(3), c=14.1171(5) Å, *V* =1109.38(6) Å^3, Z = 10, specimen 0.237x0.143x0.124 mm^3, *T* = 296(2) K, SIEMENS P4 diffractometer, absorption coefficient 1.987 mm^{-1}, reflections collected 38048, independent reflections 5164 [R(int) = 0.0398], refinement by Full-matrix least-squares on F^2, data/restraints/parameters 5164 / 0 / 308, goodness-of-fit on F^2 = 1.022, final *R* indices [*I*>2(*I*)] *R*1 = 0.0418, *wR*2 = 0.0954 , *R* indices (all data) *R*1 = 0.0600, *wR*2 = 0.1048, largest diff. peak and hole 0.989 and -0.734 e Å^{-3}.

Crystal data for 5ac (CCDC: 1001583): $C_{25}H_{18}BrN_3O_4S$(536.39), Orthorhombic, space group P2(1)2(1)2(1), a=7.8034(10), b=9.5210(13), c=30.485(4) Å, *V* =2264.9(5) Å^3, Z = 21, specimen 0.243x0.162x0.148 mm^3, *T* = 296(2) K, SIEMENS P4 diffractometer, absorption coefficient 1.946 mm^{-1}, reflections collected 11290, independent reflections 4963 [R(int) = 0.0245], refinement by Full-matrix least-squares on F^2, data/restraints/parameters 4963 / 0 / 307, goodness-of-fit on F^2 = 1.004, final *R* indices [*I*>2(*I*)] *R*1 = 0.0372, *wR*2 = 0.0798 , *R* indices (all data) *R*1 = 0.0588, *wR*2 = 0.0736, largest diff. peak and hole 0.463 and -0.478 e Å^{-3}.

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Notes and references

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Organocatalytic Domino Michael/Cyclization Reaction: Efficient Synthesis of Multi-functionalized Tetracyclic Spirooxindoles with Multiple Stereocenters

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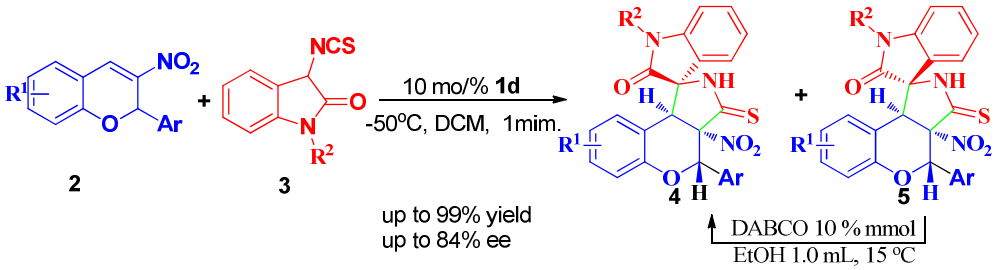

A series of chiral multi-functionalized tetracyclic spiro[chromeno[3,4-c]pyrrole- 1,3'-indoline] derivatives with four vicinal chiral carbon centers including two quaternary stereocenters were successfully prepared via domino reaction of various 3-nitro-2H-chromene derivatives to 3-isothiocyanato oxindole with moderate to good enantioselectivities, employing readily available bifunctional thiourea **1d** as the organocatalyst.

