

Supporting Information

Ag(I)/ (S,S)-ip-FOXAP catalyzed diastereo- and enantioselective 1,3-dipolar cycloaddition of azomethine ylides with benzosultam-3-ylidenes

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General

All the reagents were purchased from TCI chemicals and local suppliers and used without purification. The starting materials (**1a-h**) were prepared following our previous paper.¹ All reactions were monitored by TLC. Chromatography refers to open column chromatography on silica gel (100-200 mesh).

¹H NMR spectra were recorded on 500 MHz and ¹³C NMR spectra were recorded on 125 MHz by using a Bruker Avance 500M spectrometer. Chemical shifts were reported in parts per million (δ) relative to tetramethylsilane (TMS). Mass spectra were performed on an Ultima Global spectrometer with an ESI source. The X-ray single-crystal diffraction was performed on Saturn 724+ instrument. Chiral HPLC analysis was performed using a Shimadzu LC-20 HPLC.

General procedure for the preparation of spiropyrrolidinyl-benzoisothiazolines 3

After a suspension of the ip-FOXAP (0.0077 mmol, 3.7mg) and AgOAc (0.007 mol, 1.1mg) in toluene (0.2 mL) was stirred for 1h at room temperature, a solution of the imine **2** (0.12 mmol) in toluene (0.1 mL) was added. After being stirred at -25 °C for 10 mins, DABCO (0.12 mmol, 12.9mg) and a solution of the dipolarophile **1** (0.1mmol) in toluene (0.1 mL) was added and the resulting solution was stirred at -25 °C for 2h. After that, saturated aqueous NH₄Cl (0.2 mL) was added and the organic layer was separated and evaporated to remove solvent under reduced pressure. The residue was subjected to column chromatography on silica gel (100-200 mesh) using petroleum/ethyl acetate as eluent to afford spiropyrrolidinyl-benzoisothiazolines **3**.

(2'S,3S,4'R,5'S)-1-methyl-2'-phenyl-4'-(*o*-tolyl)-5'-methoxycarbonyl-1*H*-spiro[benzo[c]isothiazole-3,3'-pyrrolidine]-2,2-dioxide (3ea) (CCDC 2041776)

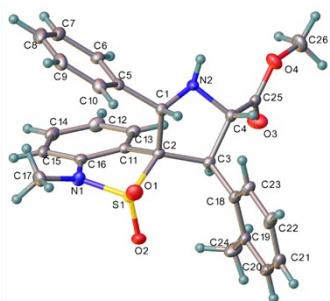
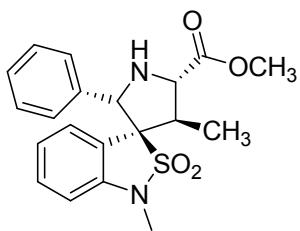


Fig 2. X-ray crystallography of compound **3ea**.

¹ G. Cao, F. Long, Y. Zhao, Y. Wang, L. Huang and D. Teng, Tetrahedron, 2014, 70, 9359.

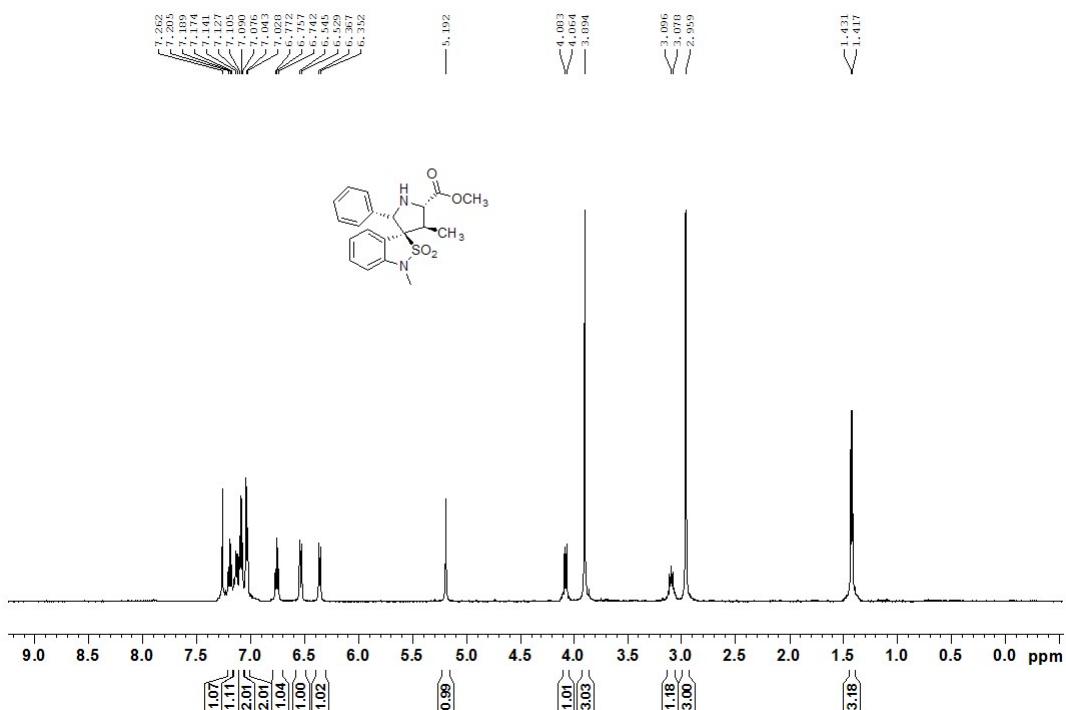
Characterization data and spectra of compound 3aa-5bc



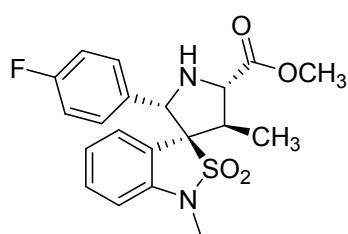
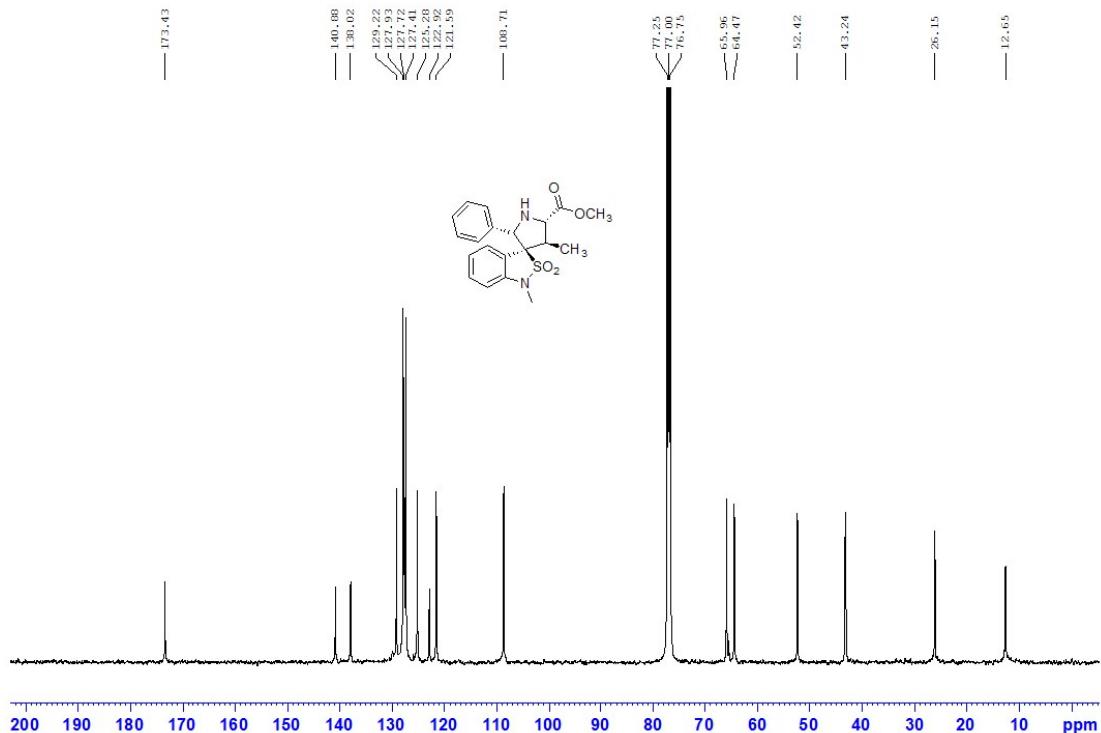
(2'S,3S,4'R,5'S)-1,4'-dimethyl-2'-phenyl-5'-methoxycarbonyl-1*H*-spiro[benzo[*c*]isothiazole-3,3'-pyrrolidine]-2,2-dioxide (**3aa**)

¹H NMR (500 MHz, CDCl₃): δ 7.19 (t, 1H, *J* = 7.8 Hz), 7.15-7.03 (m, 5H), 6.76 (t, 1H, *J* = 7.7 Hz), 6.53 (d, 1H, *J* = 7.8 Hz), 6.36 (d, 1H, *J* = 7.6 Hz), 5.19 (s, 1H), 4.07 (d, 1H, *J* = 9.4 Hz), 3.89 (s, 3H), 3.12-3.06 (m, 1H), 2.96 (s, 3H), 1.43 (d, 3H, *J* = 7.1 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 173.4, 140.9, 138.0, 129.2, 127.9, 127.7, 127.4, 125.3, 122.9, 121.6, 108.7, 66.0, 64.5, 52.4, 43.2, 26.1, 12.6.; HRMS (ESI-TOF⁺): m/z Calcd. for C₂₀H₂₃N₂O₄S [(M+H)⁺]: 387.1379. Found: 387.1375. Chiral HPLC (Daicel Chiraldapak AD-H, 30% IPA/hexanes, 1 mL/min, λ = 254 nm) *t*_R(major) = 13.958 min, *t*_R(minor) = 9.765 min; [α]²⁵_D = -54.2° (c = 0.25, CH₂Cl₂).

¹H NMR Spectrum of 3aa



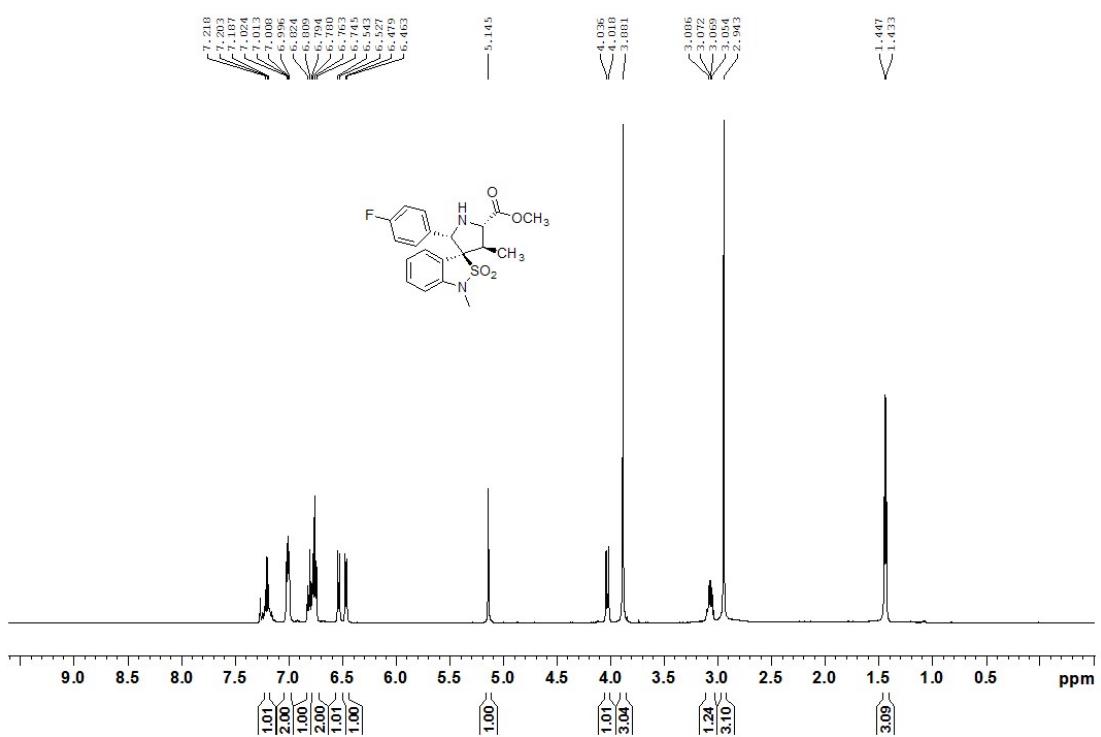
¹³C NMR Spectrum of 3aa



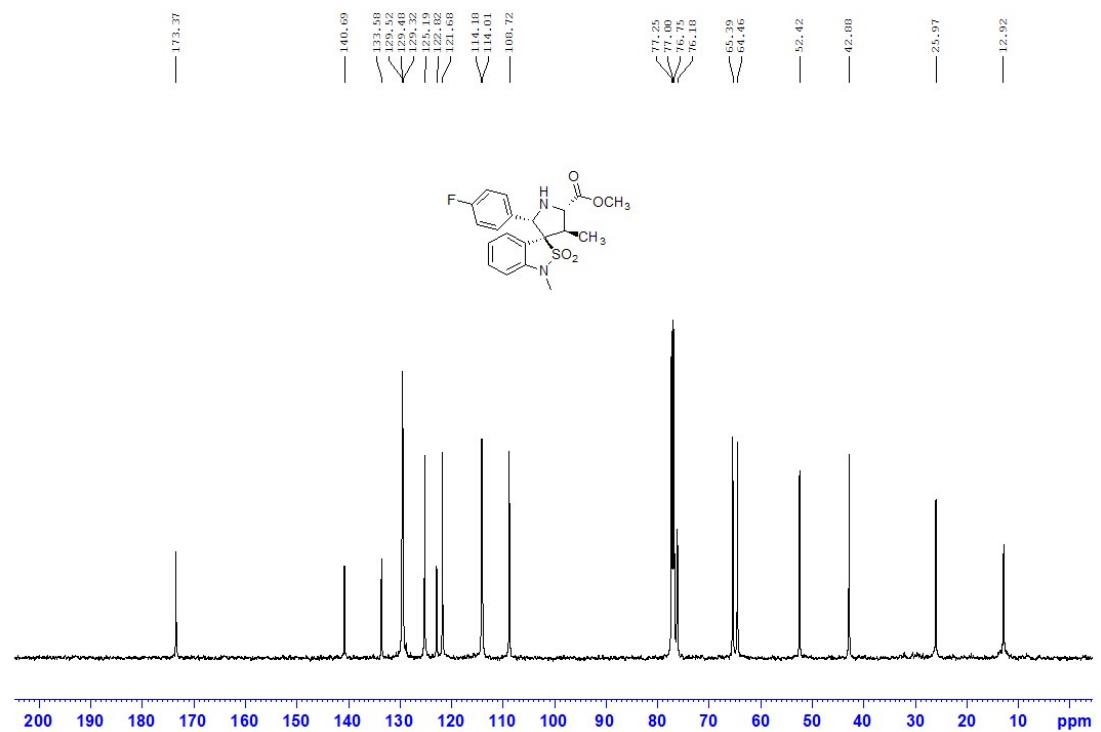
(2'S,3S,4'R,5'S)-1,4'-dimethyl-2'-(4-fluorophenyl)-5'-methoxycarbonyl-1*H*-spiro[benzo[*c*]isothiazole-3,3'-pyrrolidine]-2,2-dioxide (**3ab**)

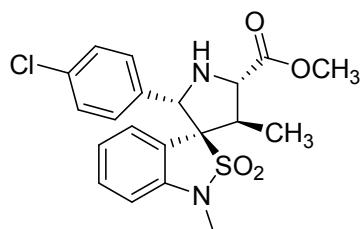
¹H NMR (500 MHz, CDCl₃): δ 7.20 (t, 1H, *J* = 7.7 Hz), 7.02-7.00 (m, 2H), 6.80 (t, 1H, *J* = 7.6 Hz), 6.76 (t, 2H, *J* = 8.7 Hz), 6.54 (d, 1H, *J* = 8.0 Hz), 6.47 (d, 1H, *J* = 7.4 Hz), 5.14 (s, 1H), 4.02 (d, 1H, *J* = 9.2 Hz), 3.88 (s, 3H), 3.09-3.05 (m, 1H), 2.94 (s, 3H), 1.44 (d, 3H, *J* = 7.1 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 173.4, 140.7, 133.6, 129.5, 129.4, 129.3, 125.2, 122.8, 121.7, 114.2, 114.0, 108.7, 76.2, 65.4, 64.5, 52.4, 42.9, 26.0, 12.9.; HRMS (ESI-TOF⁺): m/z Calcd. for C₂₀H₂₂FN₂O₄S [(M+H)⁺]: 405.1284. Found: 405.1284. Chiral HPLC (Daicel Chiraldpak AD-H, 30% IPA/hexanes, 1 mL/min, λ = 254 nm) *t*_R(major) = 11.057 min, *t*_R(minor) = 8.536 min; [α]²⁵_D = -28.3° (c = 0.25, CH₂Cl₂).

¹H NMR Spectrum of 3ab



^{13}C NMR Spectrum of 3ab

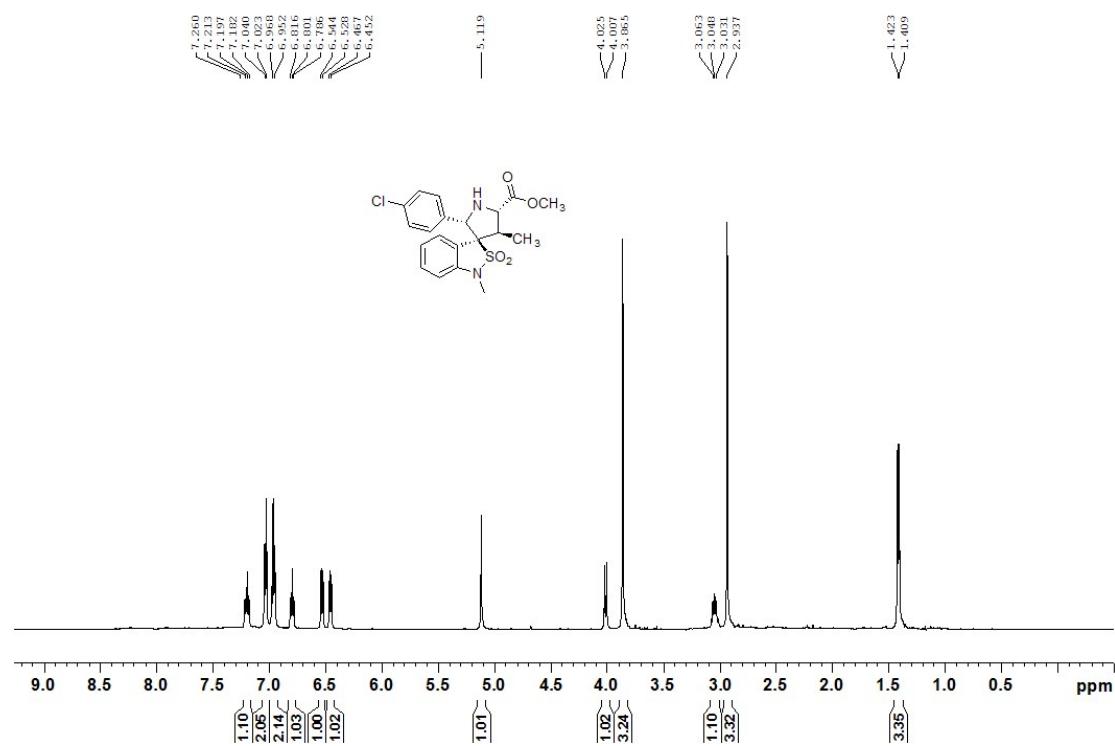




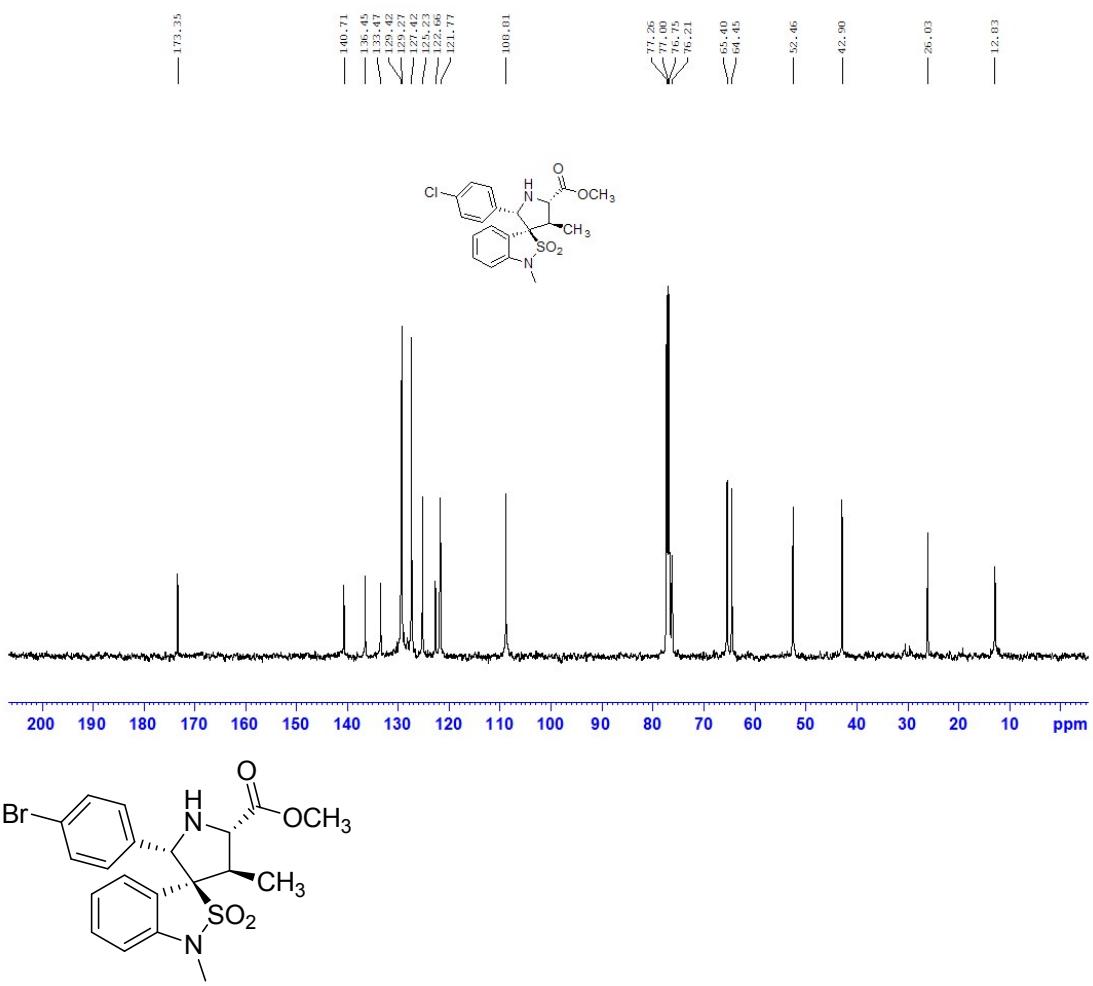
(*2'S,3S,4'R,5'S*)-1,4'-dimethyl-2'-(4-chlorophenyl)-5'-methoxycarbonyl-1*H*-spiro[benzo[*c*]isothiazole-3,3'-pyrrolidine]-2,2-dioxide (**3ac**)

¹H NMR (500 MHz, CDCl₃): δ 7.19 (t, 1H, *J* = 7.7 Hz), 7.04-6.95 (m, 4H), 6.80 (t, 1H, *J* = 7.6 Hz), 6.54 (d, 1H, *J* = 7.9 Hz), 6.46 (d, 1H, *J* = 7.6 Hz), 5.12 (s, 1H), 4.01 (d, 1H, *J* = 9.3 Hz), 3.87 (s, 3H), 3.08-3.02 (m, 1H), 2.94 (s, 3H), 1.41 (d, 3H, *J* = 7.0 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 173.4, 140.7, 136.5, 133.5, 129.4, 129.3, 127.4, 125.2, 122.7, 121.8, 108.8, 76.2, 65.4, 64.5, 52.5, 42.9, 26.0, 12.8.; HRMS (ESI-TOF⁺): m/z Calcd. for C₂₀H₂₂ClN₂O₄S [(M+H)⁺]: 421.0989. Found: 421.0988. Chiral HPLC (Daicel Chiraldak AD-H, 30% IPA/hexanes, 1 mL/min, λ = 254 nm) *t*_R(major) = 11.143 min, *t*_R(minor) = 8.749 min; $[\alpha]^{25}_D$ = -40.7° (c = 0.28, CH₂Cl₂).

¹H NMR Spectrum of 3ac



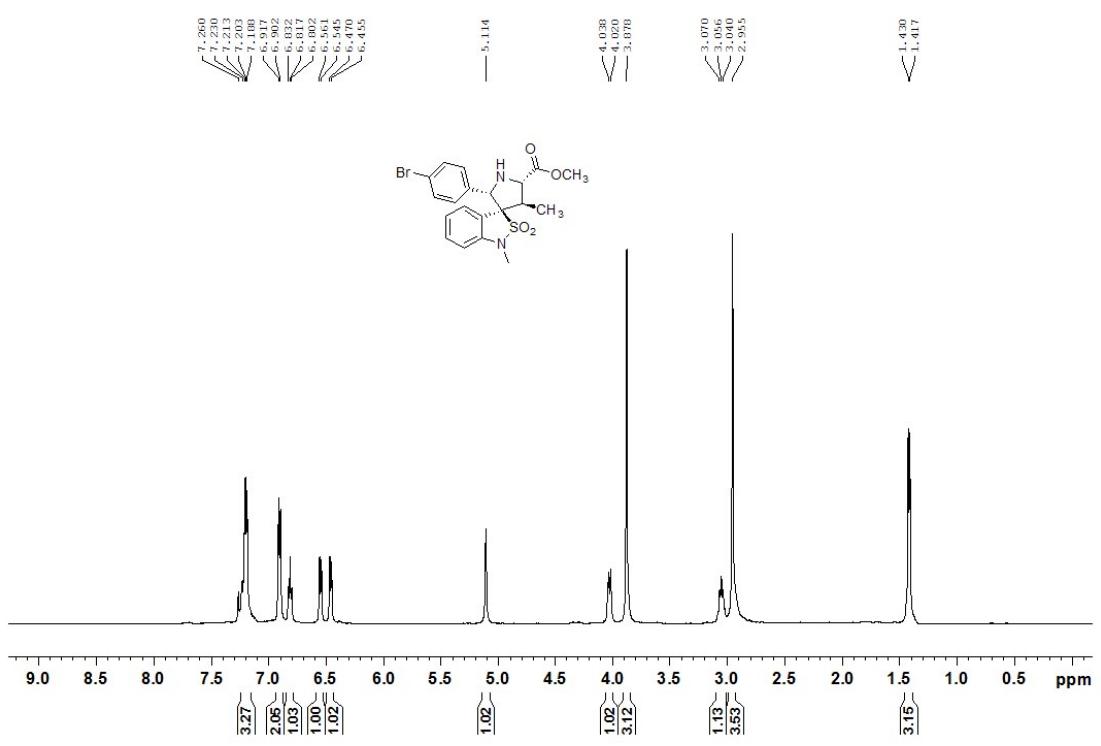
¹³C NMR Spectrum of 3ac



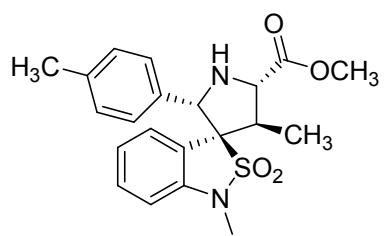
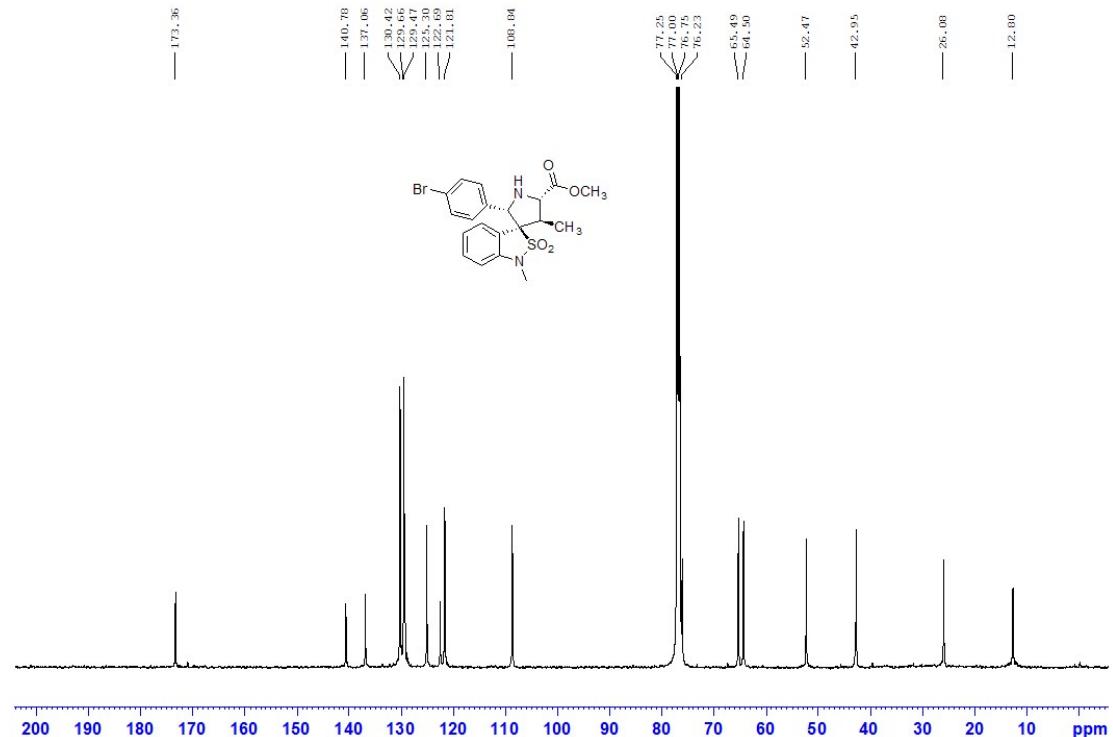
(2'S,3S,4'R,5'S)-1,4'-dimethyl-2'-(4-bromophenyl)-5'-methoxycarbonyl-1*H*-spiro[benzo[c]isothiazole-3,3'-pyrrolidine]-2,2-dioxide (3ad)

¹H NMR (500 MHz, CDCl₃): δ 7.26-7.19 (m, 3H), 6.91 (d, 2H, *J* = 7.7 Hz), 6.82 (t, 1H, *J* = 7.5 Hz), 6.55 (d, 1H, *J* = 7.9 Hz), 6.46 (d, 1H, *J* = 7.5 Hz), 5.11 (s, 1H), 4.03 (d, 1H, *J* = 8.9 Hz), 3.88 (s, 3H), 3.08-3.02 (m, 1H), 2.96 (s, 3H), 1.42 (d, 3H, *J* = 6.8 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 173.4, 140.8, 137.1, 130.4, 129.7, 129.5, 125.3, 122.7, 121.8, 108.8, 76.2, 65.5, 64.5, 52.5, 42.9, 26.1, 12.8.; HRMS (ESI-TOF⁺): m/z Calcd. for C₂₀H₂₂BrN₂O₄S [(M+H)⁺]: 465.0484. Found: 465.0481. Chiral HPLC (Daicel Chiraldak AD-H, 30% IPA/hexanes, 1 mL/min, λ = 254 nm) *t*_R(major) = 12.087 min, *t*_R(minor) = 9.789 min; $[\alpha]^{25}_D$ = -43.4° (c = 0.42, CH₂Cl₂).

¹H NMR Spectrum of 3ad



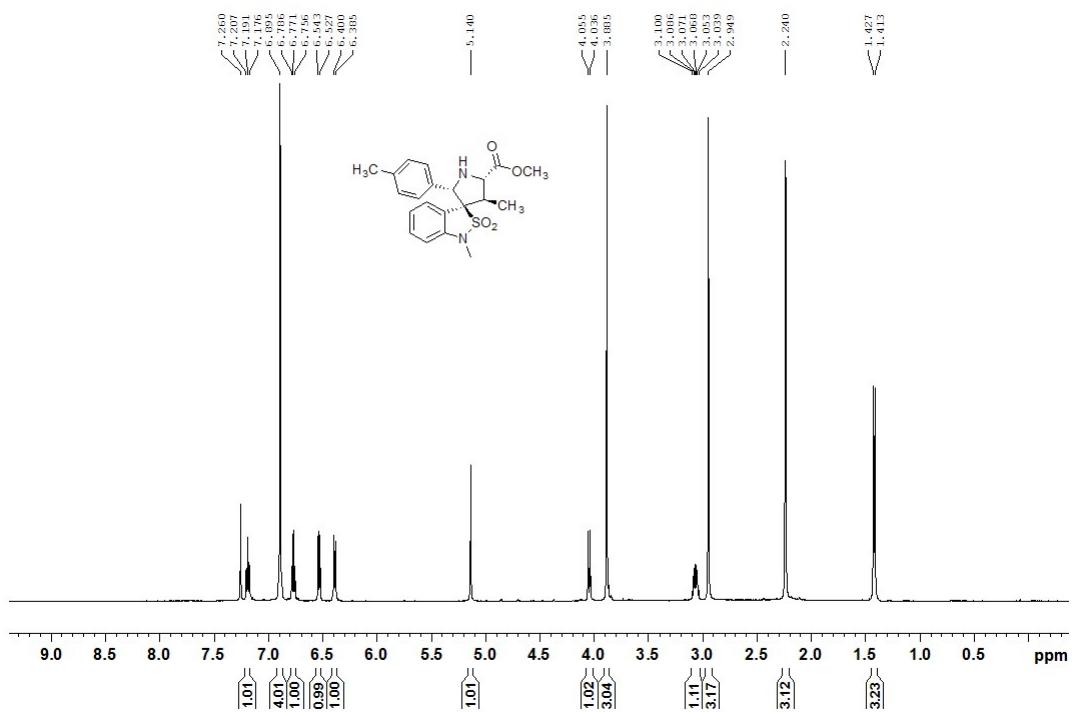
¹³C NMR Spectrum of 3ad



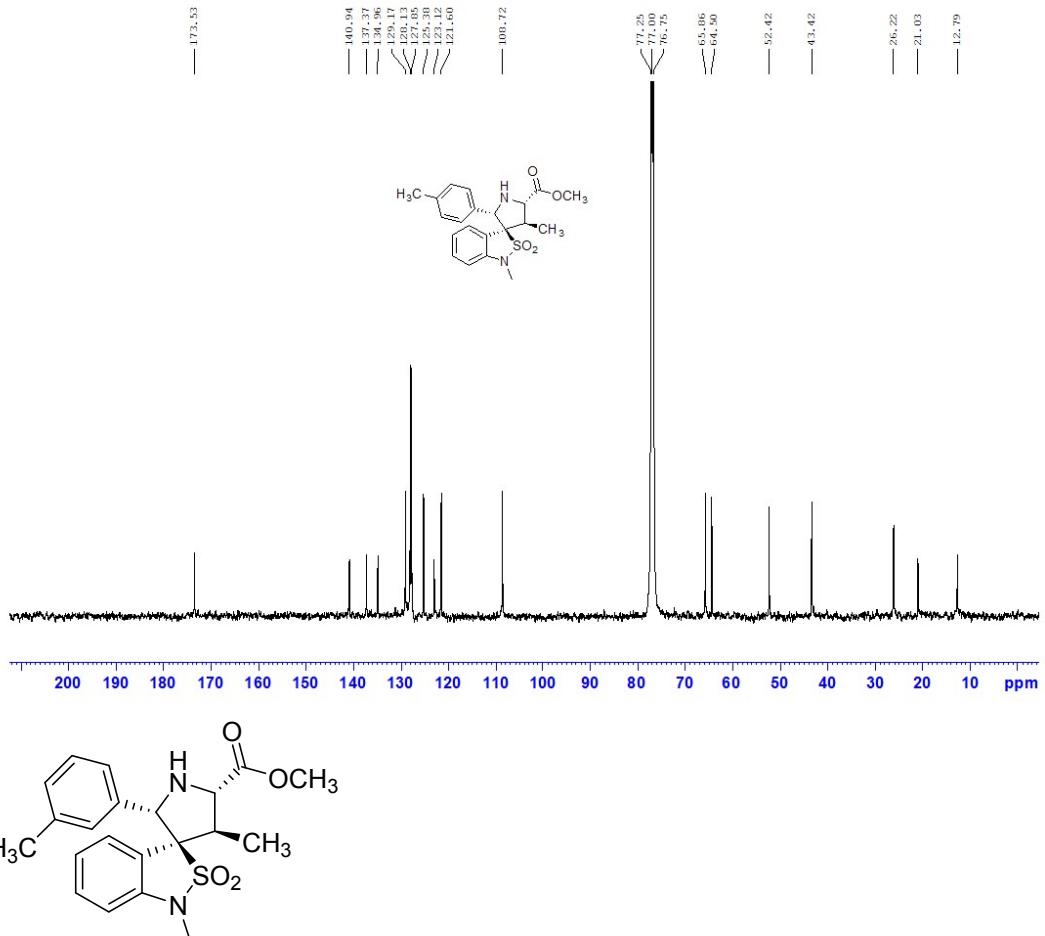
(2'S,3S,4'R,5'S)-1,4'-dimethyl-2'-(*p*-tolyl)-5'-methoxycarbonyl-1*H*-spiro[benzo[*c*]isothiazole-3,3'-pyrrolidine]-2,2-dioxide (**3ae**)

¹H NMR (500 MHz, CDCl₃): δ 7.19 (t, 1H, *J* = 7.8 Hz), 6.90 (s, 4H), 6.77 (t, 1H, *J* = 7.6 Hz), 6.53 (d, 1H, *J* = 7.9 Hz), 6.39 (d, 1H, *J* = 7.7 Hz), 5.14 (s, 1H), 4.04 (d, 1H, *J* = 9.3 Hz), 3.88 (s, 3H), 3.09-3.05 (m, 1H), 2.95 (s, 3H), 2.24 (s, 3H), 1.42 (d, 3H, *J* = 7.0 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 173.5, 140.9, 137.3, 134.9, 129.1, 128.1, 127.8, 125.3, 123.1, 121.5, 108.7, 65.8, 64.4, 52.4, 43.4, 26.2, 21.0, 12.7.; HRMS (ESI-TOF⁺): m/z Calcd. for C₂₁H₂₅N₂O₄S [(M+H)⁺]: 401.1535. Found: 401.1544. Chiral HPLC (Daicel Chiralpak AD-H, 30% IPA/hexanes, 1 mL/min, λ = 254 nm) *t*_R(major) = 12.582 min, *t*_R(minor) = 9.020 min; [α]²⁵_D = -45.3° (c = 0.36, CH₂Cl₂).

¹H NMR Spectrum of **3ae**



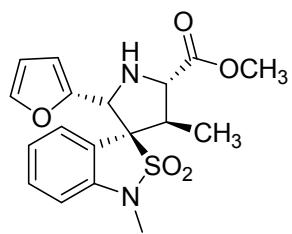
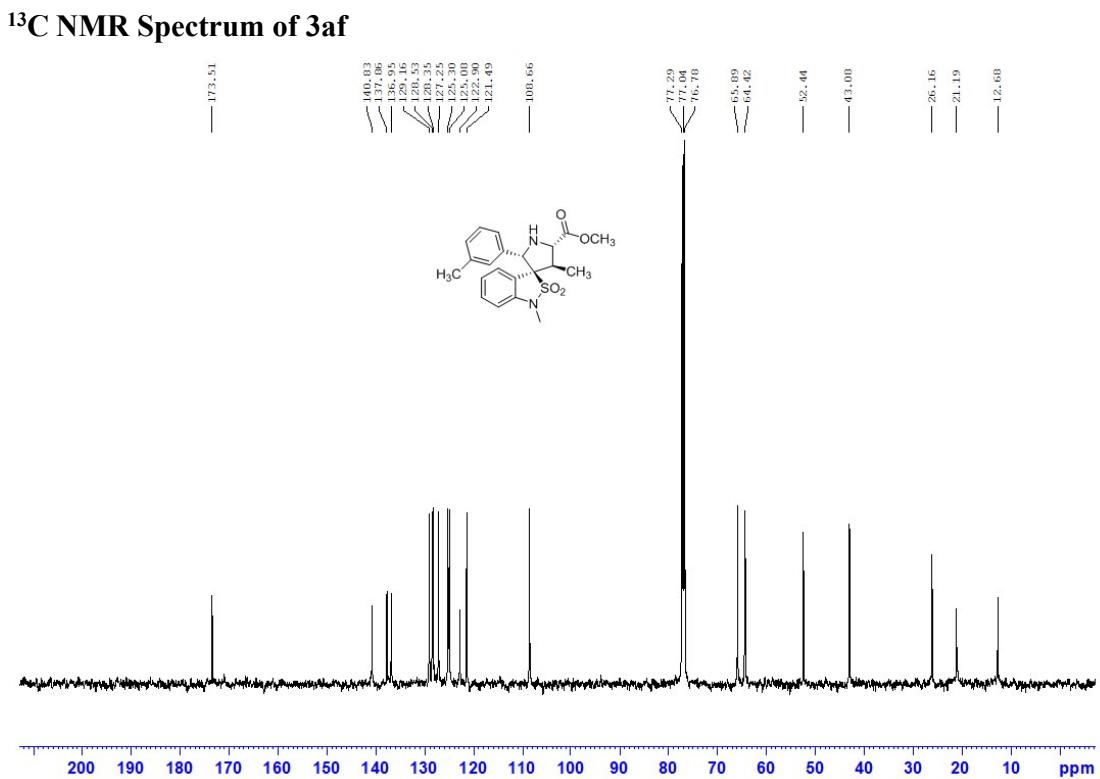
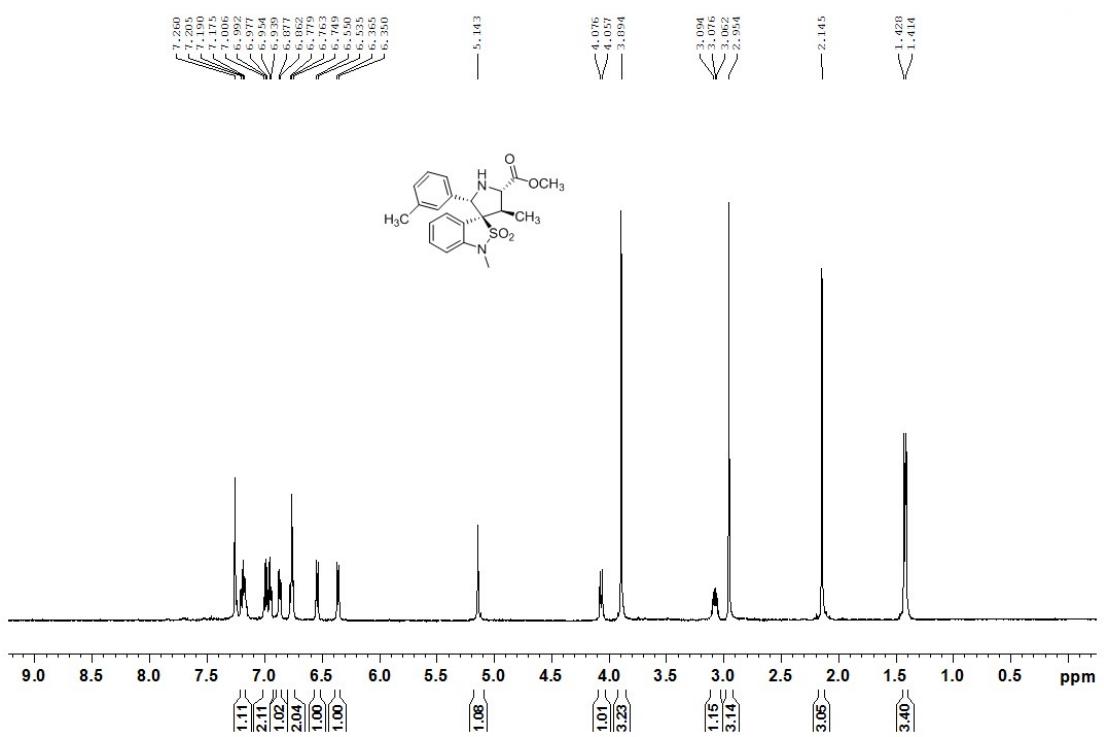
¹³C NMR Spectrum of **3ae**



(*2'S,3S,4'R,5'S*)-1,4'-dimethyl-2'-(*m*-tolyl)-5'-methoxycarbonyl-1*H*-spiro[benzo[*c*]isothiazole-3,3'-pyrrolidine]-2,2-dioxide (**3af**)

¹H NMR (500 MHz, CDCl₃): δ 7.19 (t, 1H, *J* = 7.3 Hz), 7.01-6.94 (m, 2H), 6.87 (d, 1H, *J* = 7.5 Hz), 6.78-6.75 (m, 2H), 6.54 (d, 1H, *J* = 7.9 Hz), 6.35 (d, 1H, *J* = 7.7 Hz), 5.14 (s, 1H), 4.06 (d, 1H, *J* = 9.4 Hz), 3.89 (s, 3H), 3.11-3.05 (m, 1H), 2.96 (s, 3H), 2.14 (s, 3H), 1.42 (d, 3H, *J* = 7.0 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 173.5, 140.8, 137.9, 136.9, 129.2, 128.5, 128.3, 127.3, 125.3, 125.1, 122.9, 121.5, 108.7, 65.9, 64.4, 52.4, 43.1, 26.2, 21.2, 12.7; HRMS (ESI-TOF⁺): m/z Calcd. for C₂₁H₂₅N₂O₄S [(M+H)⁺]: 401.1538. Found: 401.1534. Chiral HPLC (Daicel Chiralpak AD-H, 10% IPA/hexanes, 1 mL/min, λ = 254 nm) *t*_R(major) = 20.100 min, *t*_R(minor) = 7.738 min; [α]²⁵_D = -30.4° (c = 0.28, CH₂Cl₂).

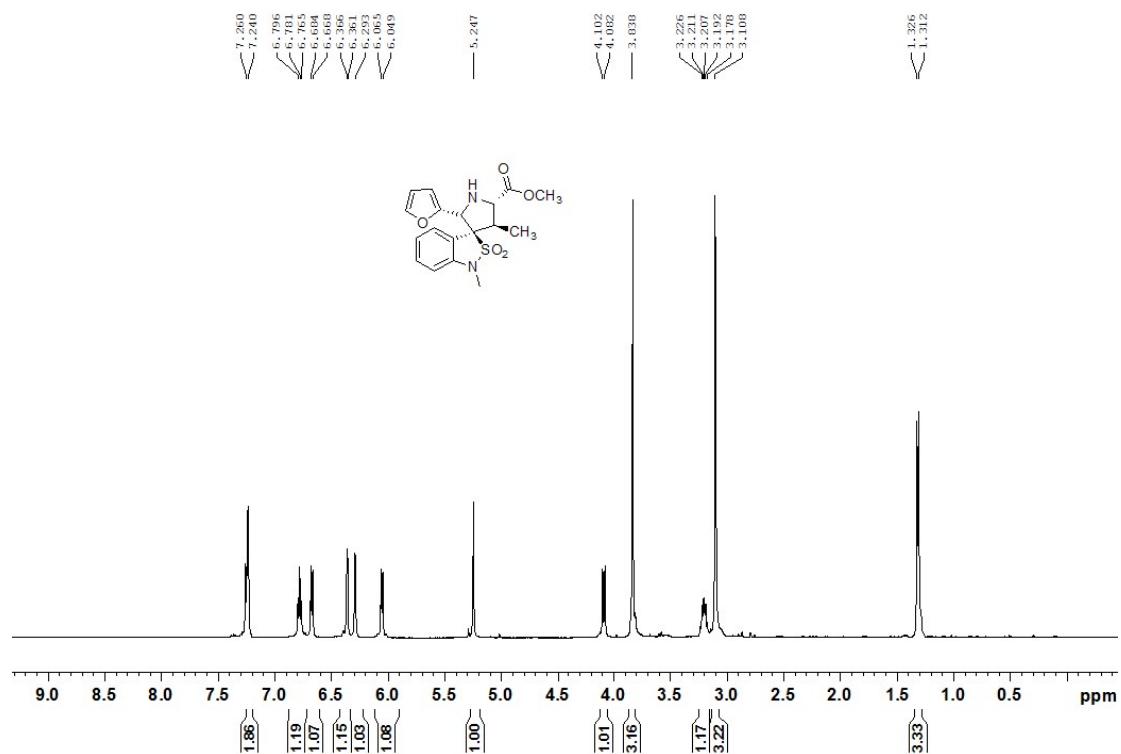
¹H NMR Spectrum of 3af



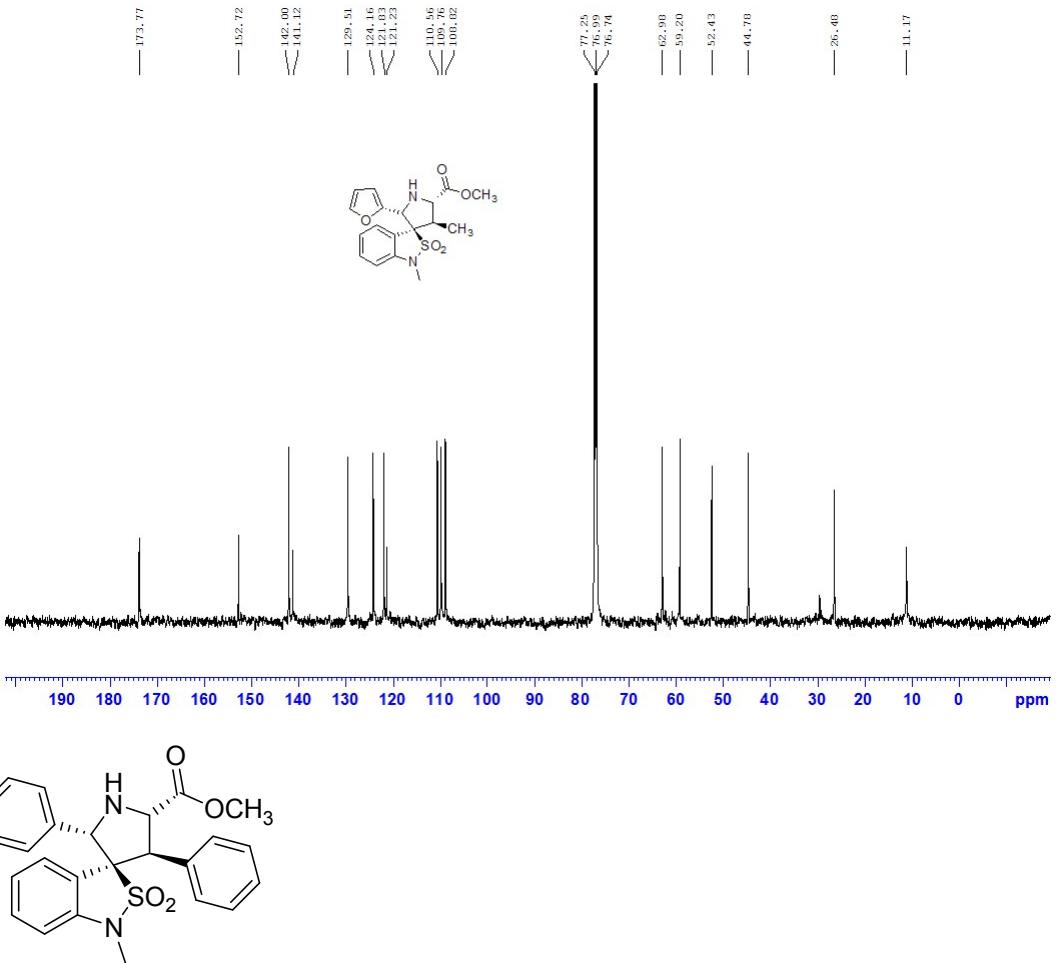
(2'S,3S,4'R,5'S)-1,4'-dimethyl-2'-(furan-2-yl)-5'-methoxycarbonyl-1*H*-spiro[benzo[*c*]isothiazole-3,3'-pyrrolidine]-2,2-dioxide (**3ag**)

¹H NMR (500 MHz, CDCl₃): δ 7.26-7.24 (m, 2H), 6.78 (t, 1H, *J* = 7.6 Hz), 6.67 (d, 1H, *J* = 7.9 Hz), 6.36 (d, 1H, *J* = 2.5 Hz), 6.29 (s, 1H), 6.05 (d, 1H, *J* = 7.7 Hz), 5.25 (s, 1H), 4.09 (d, 1H, *J* = 10.0 Hz), 3.84 (s, 3H), 3.23-3.18 (m, 1H), 3.11 (s, 3H), 1.31 (d, 3H, *J* = 7.1 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 173.8, 152.7, 142.0, 141.1, 129.5, 124.2, 121.8, 121.2, 110.6, 109.8, 108.8, 63.0, 59.2, 52.4, 44.8, 26.5, 11.2.; HRMS (ESI-TOF⁺): m/z Calcd. for C₁₈H₂₁N₂O₅S [(M+H)⁺]: 377.1171. Found: 377.1172. Chiral HPLC (Daicel Chiraldpak AD-H, 20% IPA/hexanes, 0.8 mL/min, λ = 254 nm) *t*_R(major) = 25.329 min, *t*_R(minor) = 23.234 min; [α]_D²⁵ = -42.6° (c = 0.32, CH₂Cl₂).

¹H NMR Spectrum of **3ag**



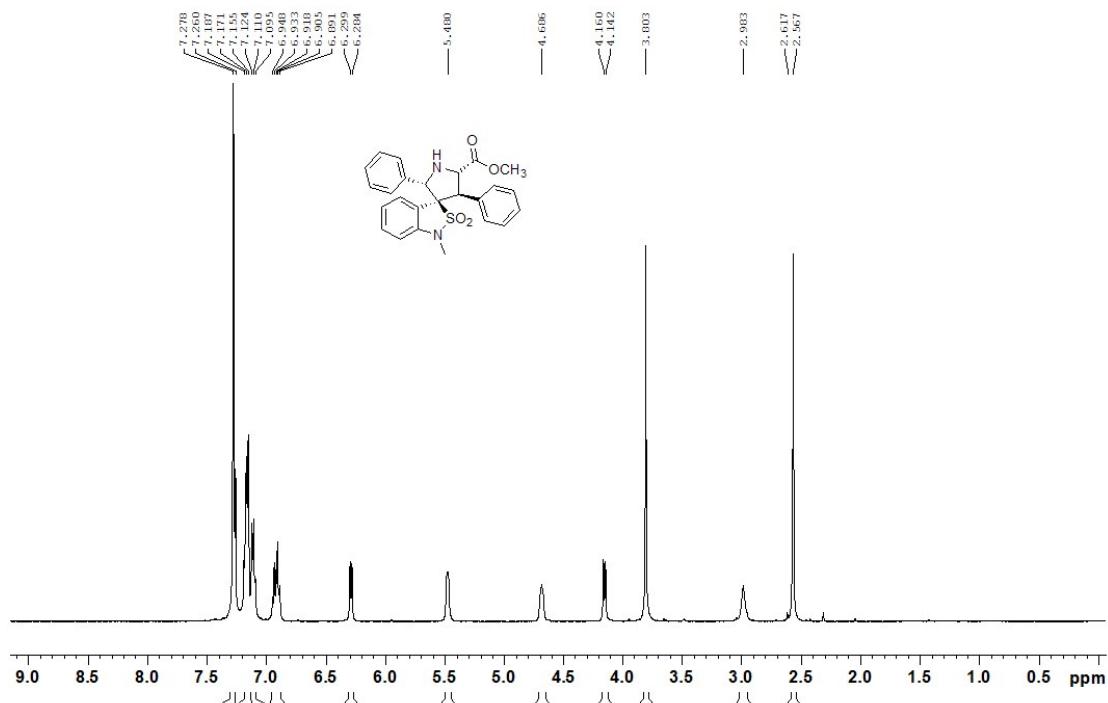
¹³C NMR Spectrum of **3ag**



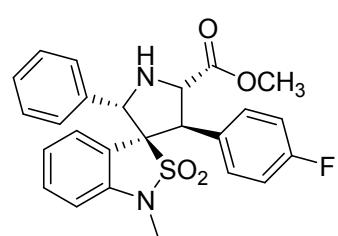
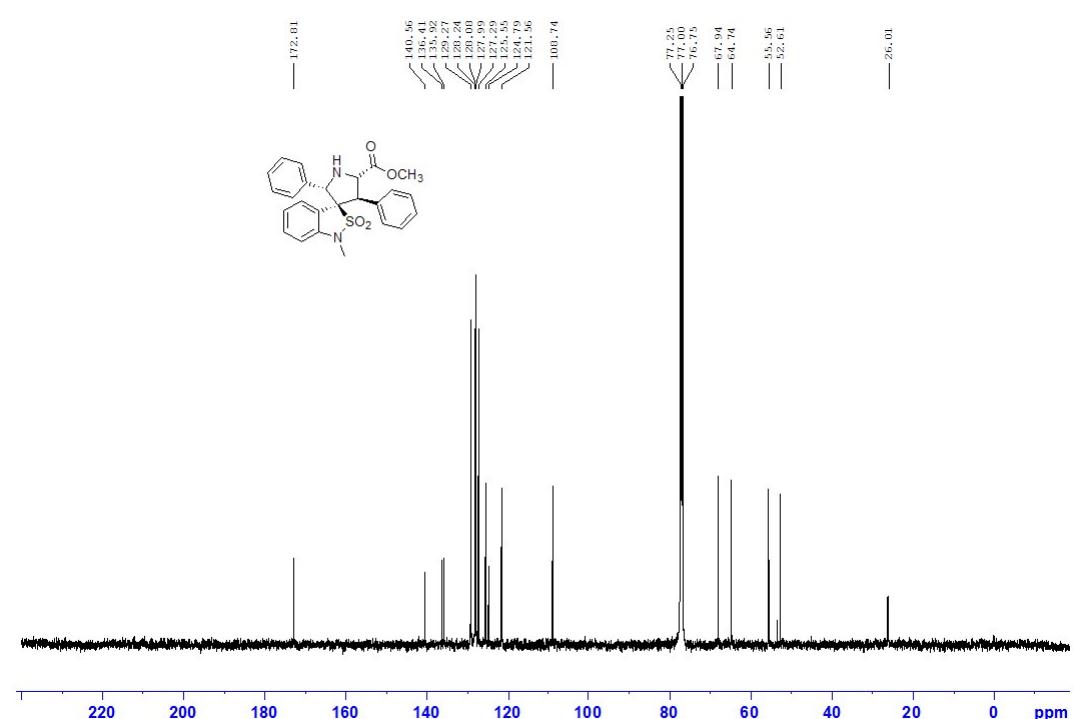
(*2'S,3S,4'R,5'S*)-1-methyl-2',4'-diphenyl-5'-methoxycarbonyl-1*H*-spiro[benzo[*c*]isothiazole-3,3'-pyrrolidine]-2,2-dioxide (**3ba**)

¹H NMR (500 MHz, CDCl₃): δ 7.28-7.26 (m, 5H), 7.19-7.10 (m, 6H), 6.95-6.89 (m, 2H), 6.29 (d, 1H, *J* = 7.9 Hz), 5.48 (s, 1H), 4.69 (s, 1H), 4.15 (d, 1H, *J* = 8.7 Hz), 3.80 (s, 3H), 2.98 (br, 1H), 2.57 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 172.8, 140.6, 136.4, 135.9, 129.3, 128.2, 128.1, 128.0, 127.3, 125.6, 124.8, 121.6, 108.7, 67.9, 64.7, 55.6, 52.6, 26.0.; HRMS (ESI-TOF⁺): m/z Calcd. for C₂₅H₂₅N₂O₄S [(M+H)⁺]: 449.1535. Found: 449.1536. Chiral HPLC (Daicel Chiraldpak AD-H, 20% IPA/hexanes, 0.8 mL/min, λ = 254 nm) *t*_R(major) = 39.815 min, *t*_R(minor) = 29.564 min; [α]_D²⁵ = -70.4° (c = 0.47, CH₂Cl₂).

¹H NMR Spectrum of **3ba**



¹³C NMR Spectrum of 3ba

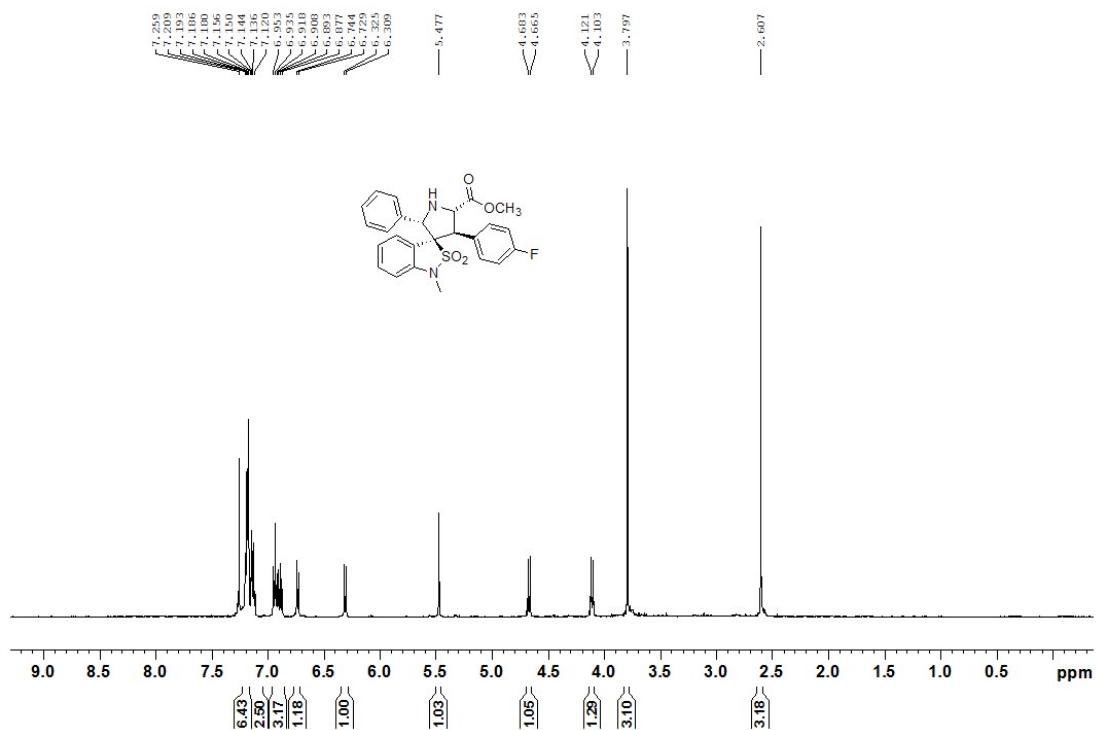


(2'S,3S,4'R,5'S)-4'-(4-fluorophenyl)-1-methyl-2'-phenyl--5'-methoxycarbonyl-1*H*-spiro[benzo[*c*]

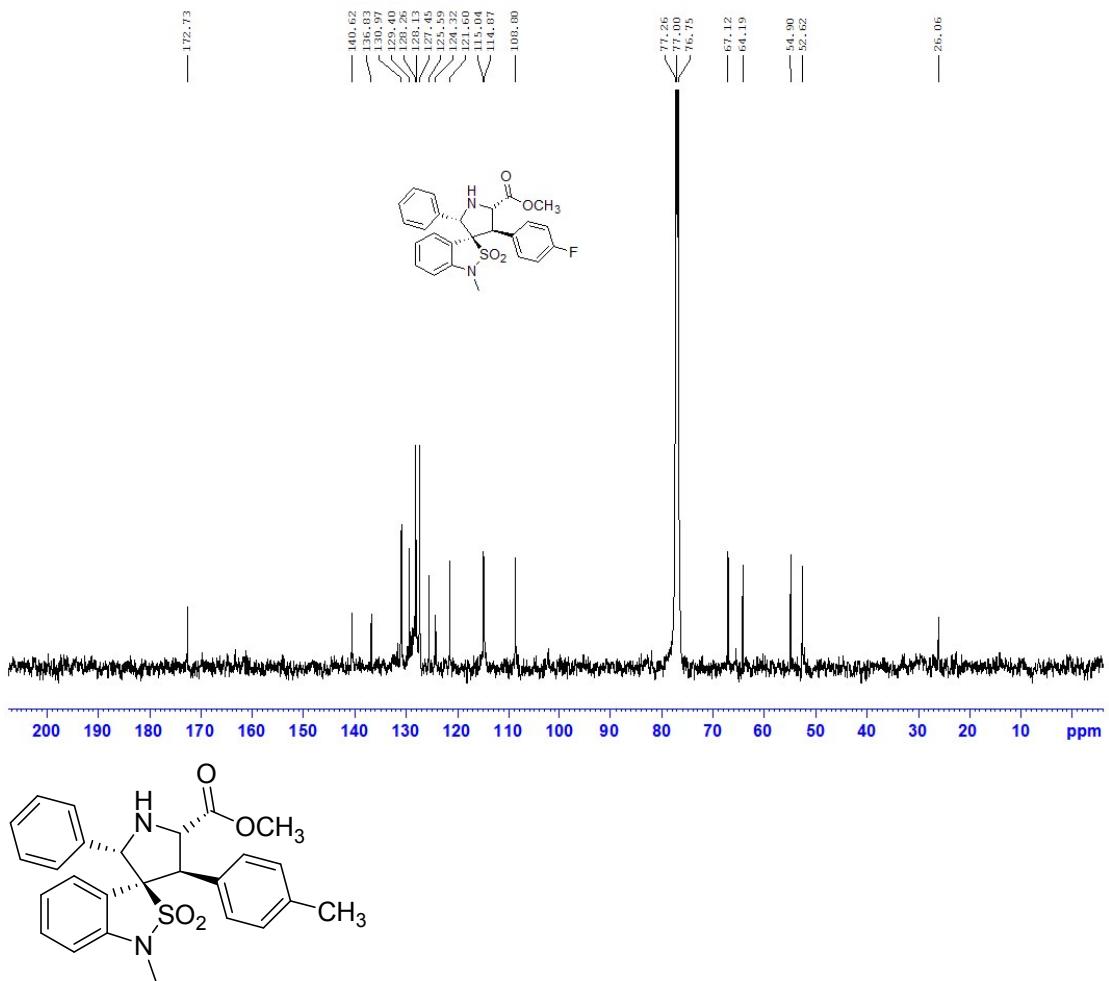
isothiazole-3,3'-pyrrolidine]-2,2-dioxide (3ca**)**

¹H NMR (500 MHz, CDCl₃): δ 7.26-7.14 (m, 8H), 6.94 (t, 2H, J = 0.87 Hz), 6.89 (t, 1H, J = 7.7 Hz), 6.73 (d, 1H, J = 7.6 Hz), 6.31 (d, 1H, J = 7.9 Hz), 5.48 (s, 1H), 4.67 (d, 1H, J = 9.0 Hz), 4.11 (d, 1H, J = 9.0 Hz), 3.80 (s, 3H), 2.61 (s, 3H). ¹³C NMR (125 MHz, CDCl₃) δ 172.7, 140.6, 136.8, 131.0, 129.4, 128.3, 128.1, 127.4, 125.6, 124.3, 121.6, 115.0, 114.9, 108.8, 67.1, 64.2, 54.9, 52.6, 26.1.; HRMS (ESI-TOF⁺): m/z Calcd. for C₂₅H₂₄FN₂O₄S [(M+H)⁺]: 467.1441. Found: 467.1446. Chiral HPLC (Daicel Chiraldpak AD-H, 30% IPA/hexanes, 0.9 mL/min, λ = 254 nm) t_R (major) = 30.036 min, t_R (minor) = 26.885 min; $[\alpha]^{25}_D$ = -20.5° (c = 0.18, CH₂Cl₂).

¹H NMR Spectrum of **3ca**



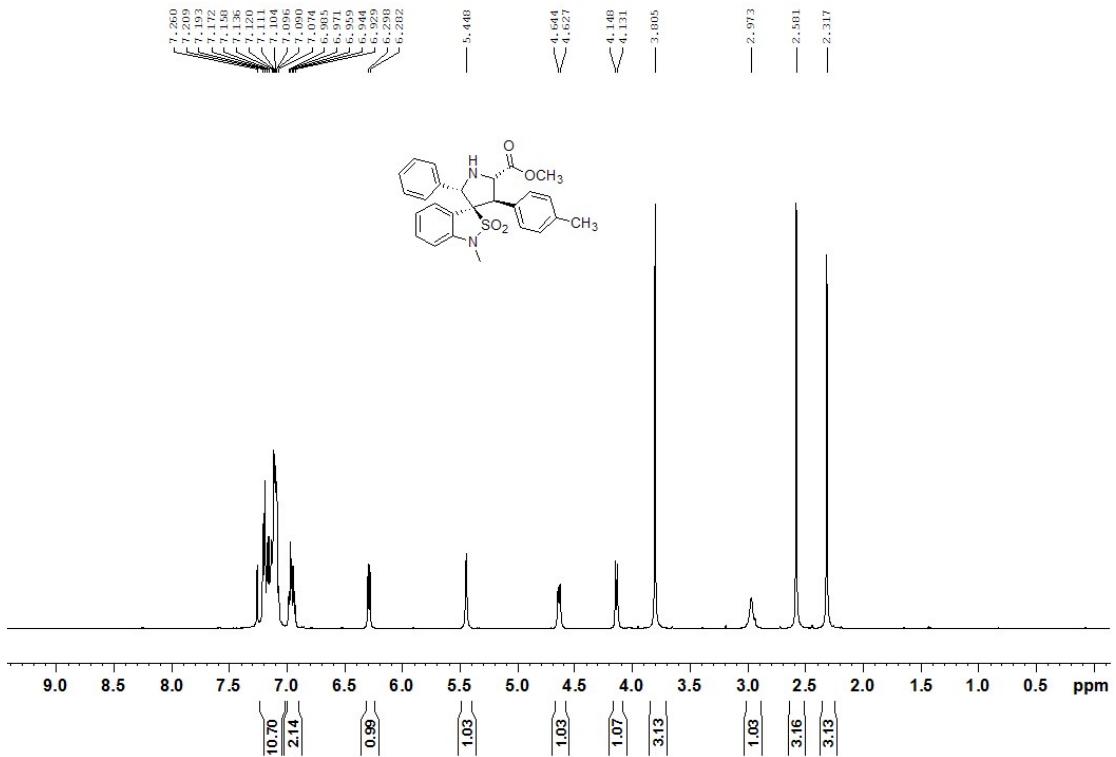
¹³C NMR Spectrum of **3ca**



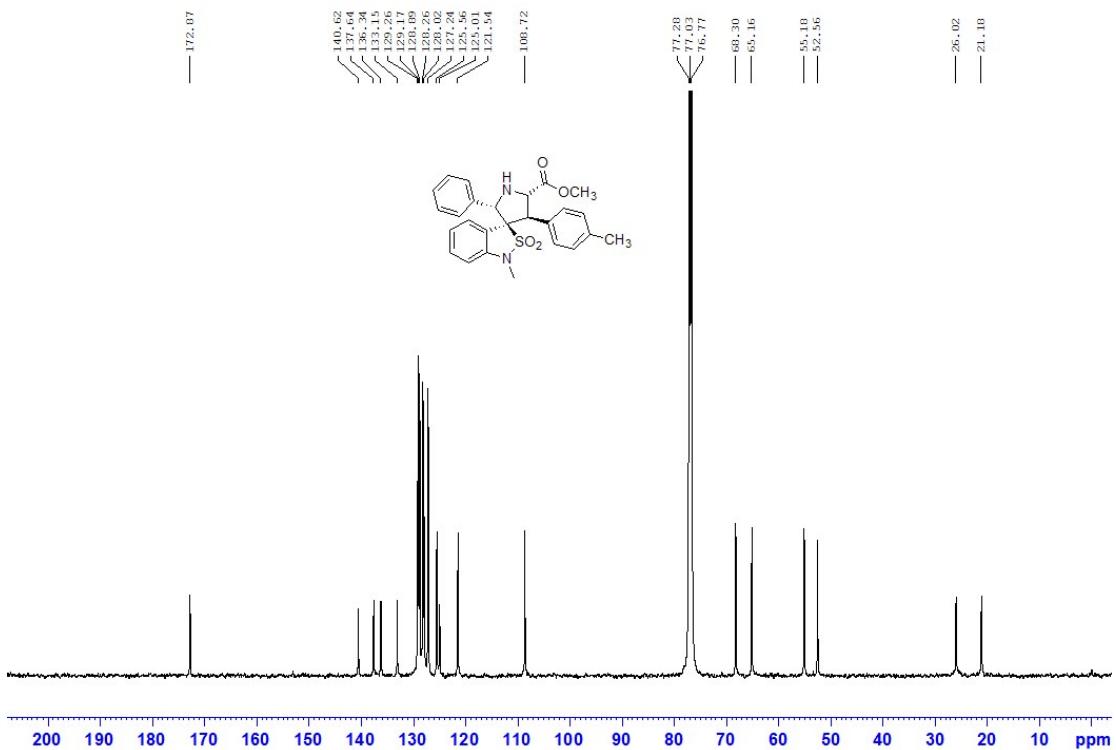
(*2'S,3S,4'R,5'S*)-1-methyl-2'-phenyl-4'-(*p*-tolyl)-5'-methoxycarbonyl-1*H*-spiro[benzo[*c*]isothiazole-3,3'-pyrrolidine]-2,2-dioxide (**3da**)

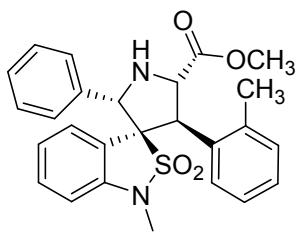
¹H NMR (500 MHz, CDCl₃): δ 7.21-7.07 (m, 10H), 6.98-6.93 (m, 2H), 6.28 (d, 1H, *J* = 7.9 Hz), 5.45 (s, 1H), 4.63 (d, 1H, *J* = 8.3 Hz), 4.13 (d, 1H, *J* = 8.5 Hz), 3.80 (s, 3H), 2.97 (br, 1H), 2.58 (s, 3H), 2.32 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 172.9, 140.6, 137.6, 136.3, 133.1, 129.3, 129.2, 128.9, 128.3, 128.0, 127.2, 125.6, 125.0, 121.5, 108.7, 68.3, 65.2, 55.2, 52.6, 26.0, 21.2.; HRMS (ESI-TOF⁺): m/z Calcd. for C₂₆H₂₈N₂O₄S [(M+H)⁺]: 463.1692. Found: 463.1688. Chiral HPLC (Daicel Chiraldpak AD-H, 20% IPA/hexanes, 0.8 mL/min, λ = 254 nm) *t*_R(major) = 43.559 min, *t*_R(minor) = 41.731 min; $[\alpha]^{25}_D$ = -90.9° (c = 0.57, CH₂Cl₂).

¹H NMR Spectrum of 3da



¹³C NMR Spectrum of 3da

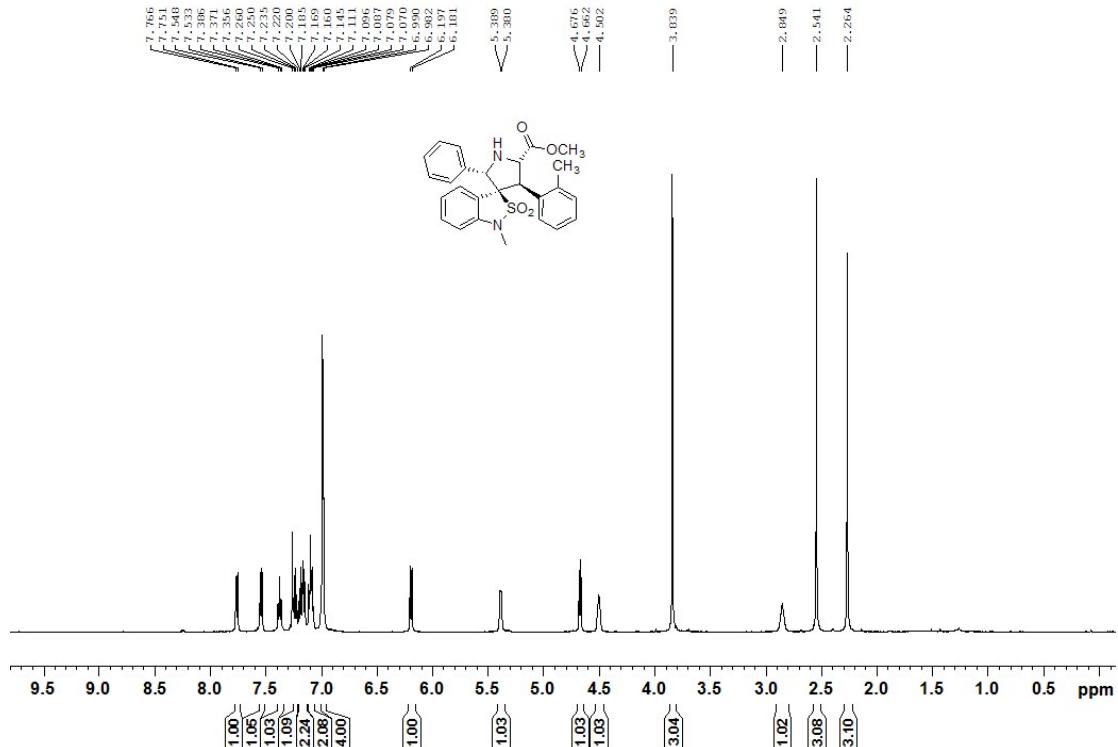




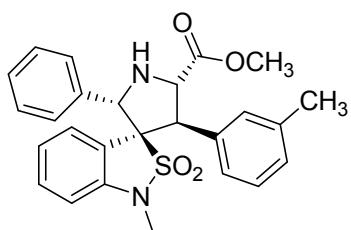
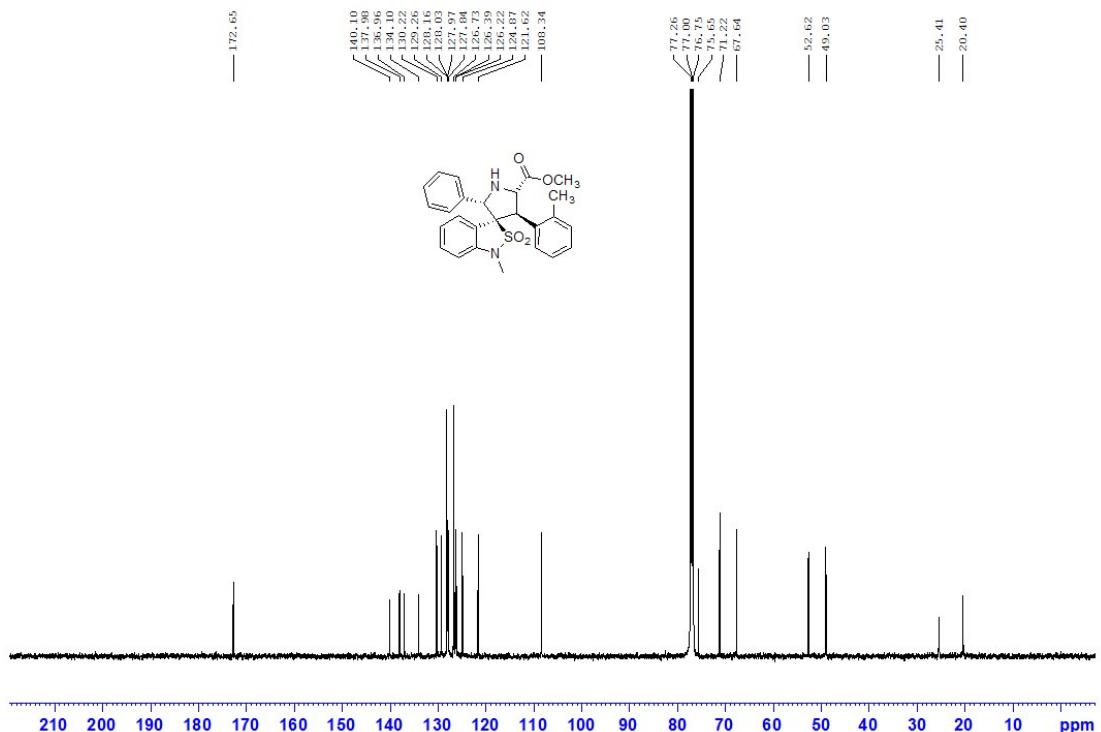
(2'S,3S,4'R,5'S)-1-methyl-2'-phenyl-4'-(*o*-tolyl)-5'-methoxycarbonyl-1*H*-spiro[benzo[*c*]isothiazole-3,3'-pyrrolidine]-2,2-dioxide (**3ea**)

¹H NMR (500 MHz, CDCl₃): δ 7.76 (d, 1H, *J* = 7.8 Hz), 7.54 (d, 1H, *J* = 7.5 Hz), 7.37 (t, 1H, *J* = 7.6 Hz), 7.23 (t, 1H, *J* = 7.5 Hz), 7.20-7.15 (m, 2H), 7.11-7.07 (m, 2H), 6.99-6.98 (m, 4H), 6.19 (d, 1H, *J* = 7.8 Hz), 5.38 (d, 1H, *J* = 4.4 Hz), 4.66 (d, 1H, *J* = 7.2 Hz), 4.50 (s, 1H), 3.84 (s, 3H), 2.85 (br, 1H), 2.54 (s, 3H), 2.26 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 172.7, 140.1, 138.0, 137.0, 134.1, 130.2, 129.3, 128.2, 128.0, 127.9, 127.8, 126.7, 126.4, 126.2, 124.9, 121.6, 108.3, 75.7, 71.2, 67.6, 52.6, 49.0, 25.4, 20.4.; HRMS (ESI-TOF⁺): m/z Calcd. for C₂₆H₂₇N₂O₄S [(M+H)⁺]: 463.1692. Found: 463.1702. Chiral HPLC (Daicel Chiraldpak AD-H, 30% IPA/hexanes, 0.9 mL/min, λ = 254 nm) *t*_R(major) = 19.522 min, *t*_R(minor) = 17.436 min; [α]₂₅D = -72.1° (c = 0.28, CH₂Cl₂).

¹H NMR Spectrum of **3ea**



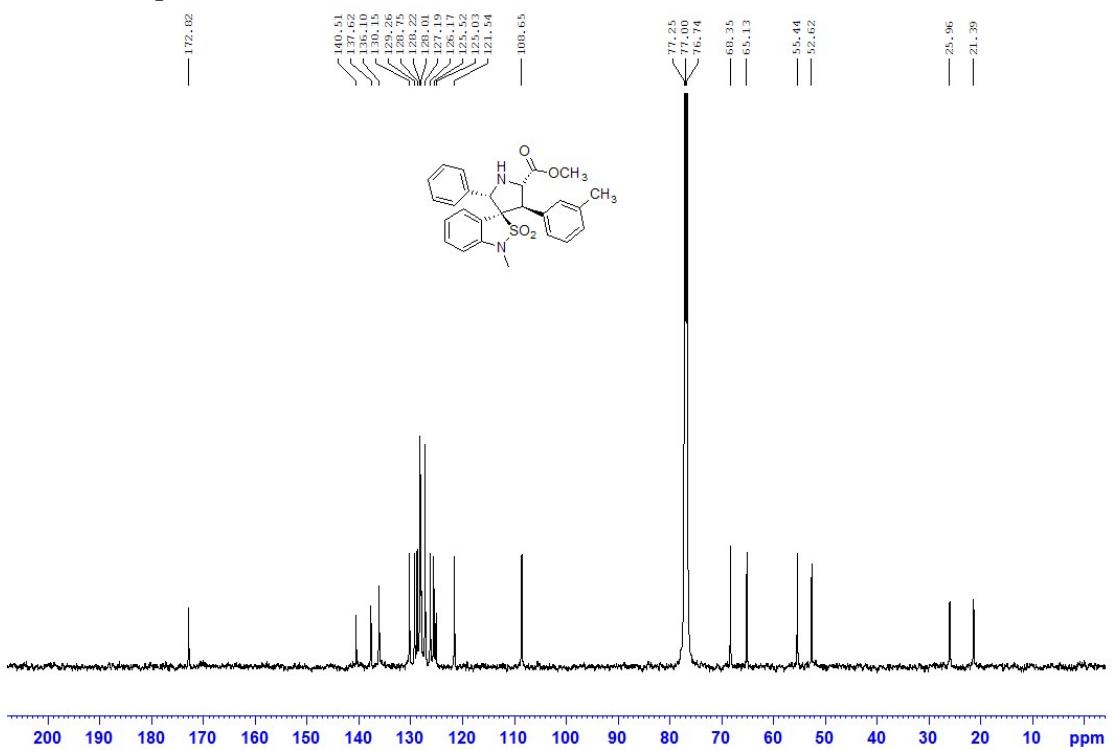
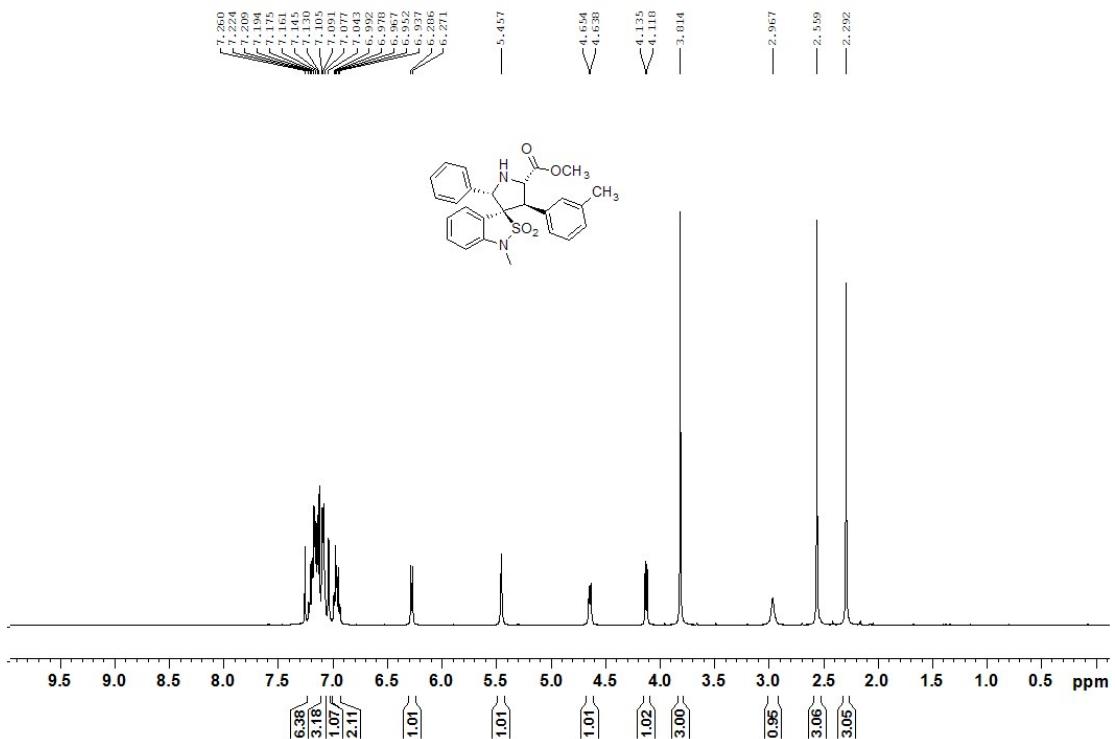
¹³C NMR Spectrum of **3ea**



(2'S,3S,4'R,5'S)-1-methyl-2'-phenyl-4'-(m-tolyl)-5'-methoxycarbonyl-1H-spiro[benzo[c]isothiazole-3,3'-pyrrolidine]-2,2-dioxide (**3fa**)

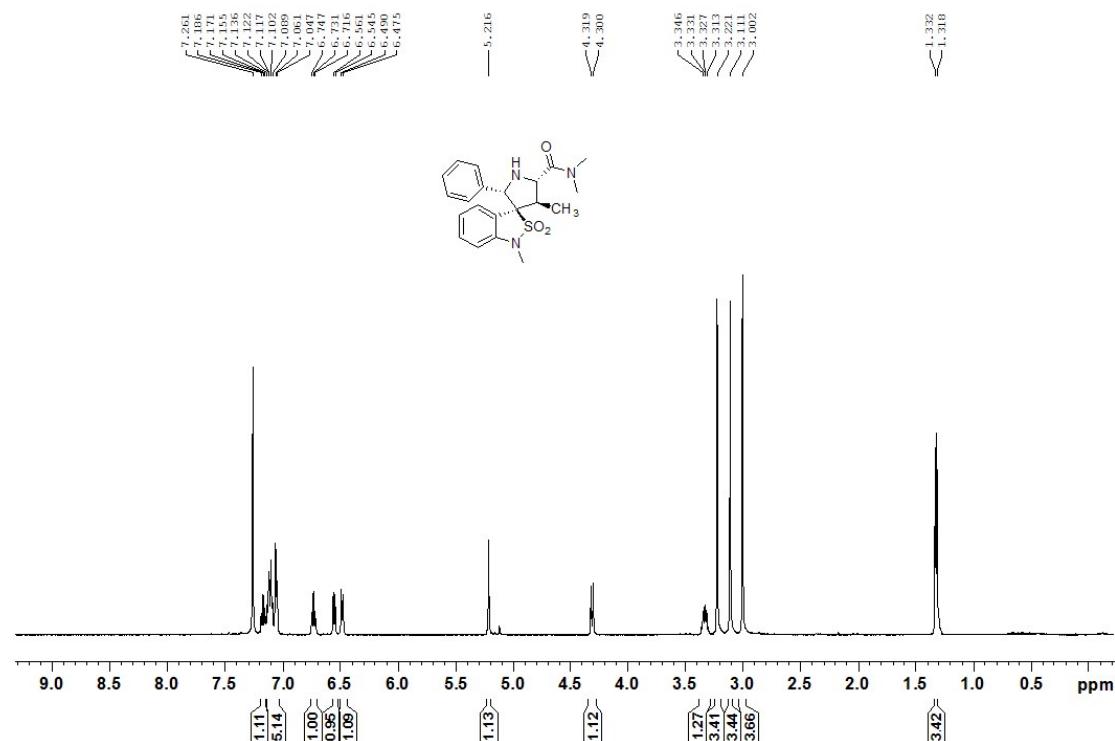
¹H NMR (500 MHz, CDCl₃): δ 7.22-7.08 (m, 9H), 7.04 (s, 1H), 6.99-6.94 (m, 2H), 6.28 (d, 1H, J = 7.9 Hz), 5.46 (s, 1H), 4.64 (d, 1H, J = 8.4 Hz), 4.12 (d, 1H, J = 8.5 Hz), 3.81 (s, 3H), 2.97 (br, 1H), 2.56 (s, 3H), 2.29 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 172.8, 140.5, 137.6, 136.1, 130.2, 129.3, 128.8, 128.2, 128.0, 127.2, 126.2, 125.5, 125.0, 121.5, 108.6, 68.3, 65.1, 55.4, 52.6, 26.0, 21.4.; HRMS (ESI-TOF⁺): m/z Calcd. for C₂₆H₂₇N₂O₄S [(M+H)⁺]: 463.1692. Found: 463.1696. Chiral HPLC (Daicel Chiralpak AD-H, 30% IPA/hexanes, 0.9 mL/min, λ = 254 nm) t_R(major) = 17.139 min, t_R(minor) = 11.212 min; [α]²⁵D = -68.6° (c = 0.37, CH₂Cl₂).

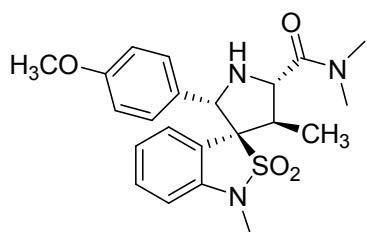
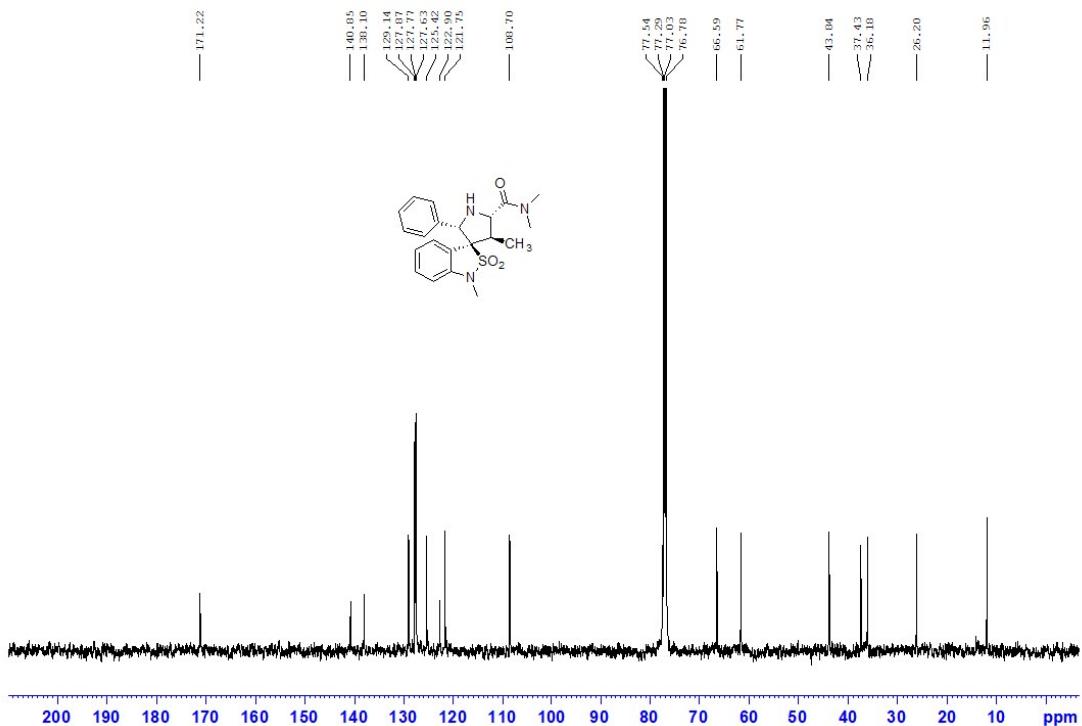
¹H NMR Spectrum of 3fa



isothiazole-3,3'-pyrrolidine]-2,2-dioxide (5aa)

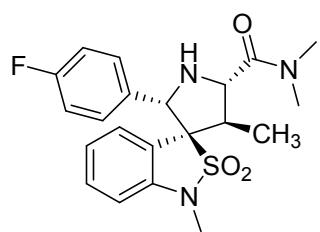
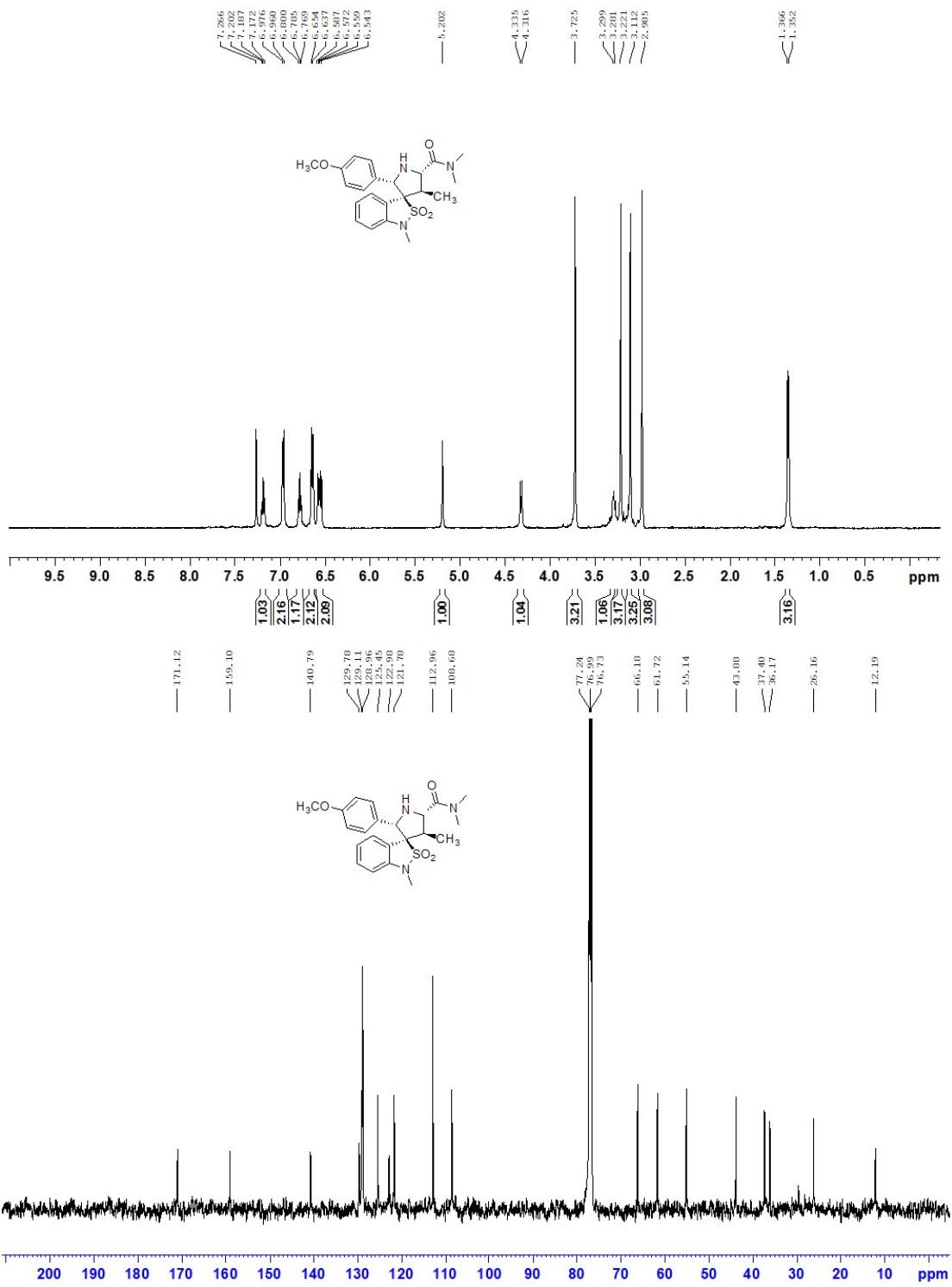
¹H NMR (500 MHz, CDCl₃) δ 7.17 (t, 1H, J = 7.5 Hz), 7.14-7.05 (m, 5H), 6.73 (t, 1H, J = 7.6 Hz), 6.55 (d, 1H, J = 7.9 Hz), 6.48 (d, 1H, J = 7.6 Hz), 5.21 (s, 1H), 4.30 (d, 1H, J = 9.5 Hz), 3.36-3.30 (m, 1H), 3.22 (s, 3H), 3.11 (s, 3H), 3.00 (s, 3H), 1.32 (d, 3H, J = 7.1 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 171.2, 140.9, 138.1, 129.1, 127.9, 127.8, 127.6, 125.4, 122.9, 121.7, 108.7, 77.5, 66.6, 61.8, 43.8, 37.4, 36.2, 26.2, 12.0.; HRMS (ESI-TOF⁺): m/z Calcd. for C₂₁H₂₅N₃O₃S [(M+H)⁺]: 400.1695. Found: 400.1691. Chiral HPLC (Daicel Chiraldpak AD-H, 25% IPA/hexanes, 0.8 mL/min, λ = 254 nm) *t*_R(major) = 46.160 min, *t*_R(minor) = 18.956 min; [α]²⁵_D = -76.3° (c = 0.38, CH₂Cl₂).





(2'S,3S,4'R,5'S)-1-methyl-2'-*p*-methoxyphenyl-4'-methyl-5'-*N,N*-dimethylaminocarbonyl-1*H*-spiro[benzo[*c*] isothiazole-3,3'-pyrrolidine]-2,2-dioxide (5ab)

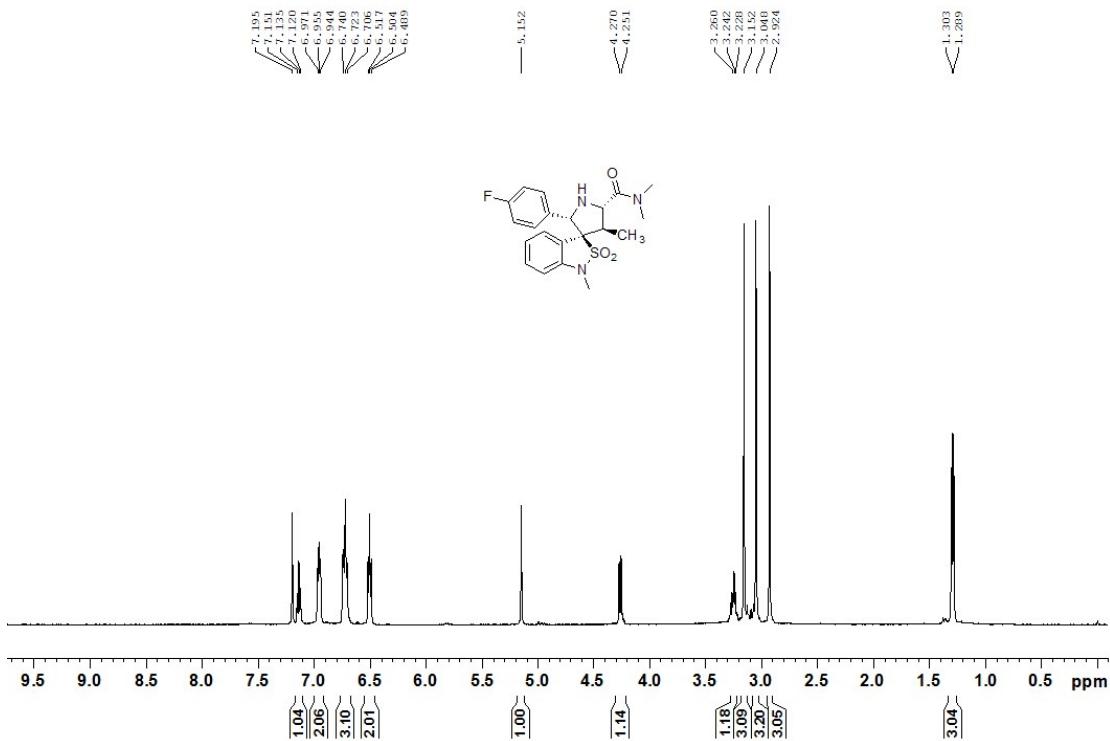
¹H NMR (500 MHz, CDCl₃): δ 7.19 (t, 1H, J = 7.7 Hz), 6.97 (d, 2H, J = 8.4 Hz), 6.78 (t, 1H, J = 7.6 Hz), 6.64 (d, 2H, J = 8.5 Hz), 6.58 (d, 1H, J = 7.7 Hz), 6.55 (d, 1H, J = 8.0 Hz), 5.20 (s, 1H), 4.32 (d, 1H, J = 9.2 Hz), 3.73 (s, 3H), 3.30-3.28 (m, 1H), 3.22 (s, 3H), 3.11 (s, 3H), 2.98 (s, 3H), 1.36 (d, 3H, J = 7.1 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 171.1, 159.1, 140.8, 129.8, 129.1, 129.0, 125.5, 123.0, 121.8, 113.0, 108.7, 66.2, 61.7, 55.1, 43.9, 37.4, 36.2, 26.2, 12.2. HRMS (ESI-TOF⁺): m/z Calcd. for C₂₂H₂₇N₃O₄S [(M+H)⁺]: 430.1801. Found: 430.1808. Chiral HPLC (Daicel Chiralpak AD-H, 25% IPA/hexanes, 0.8 mL/min, λ = 254 nm) *t*_R(major) = 33.434 min, *t*_R(minor) = 18.395 min; [α]_D²⁵ = -56.3° (c = 0.32, CH₂Cl₂).

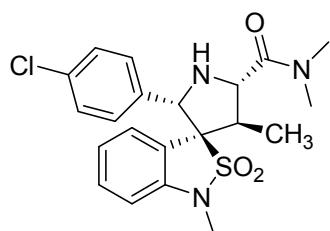
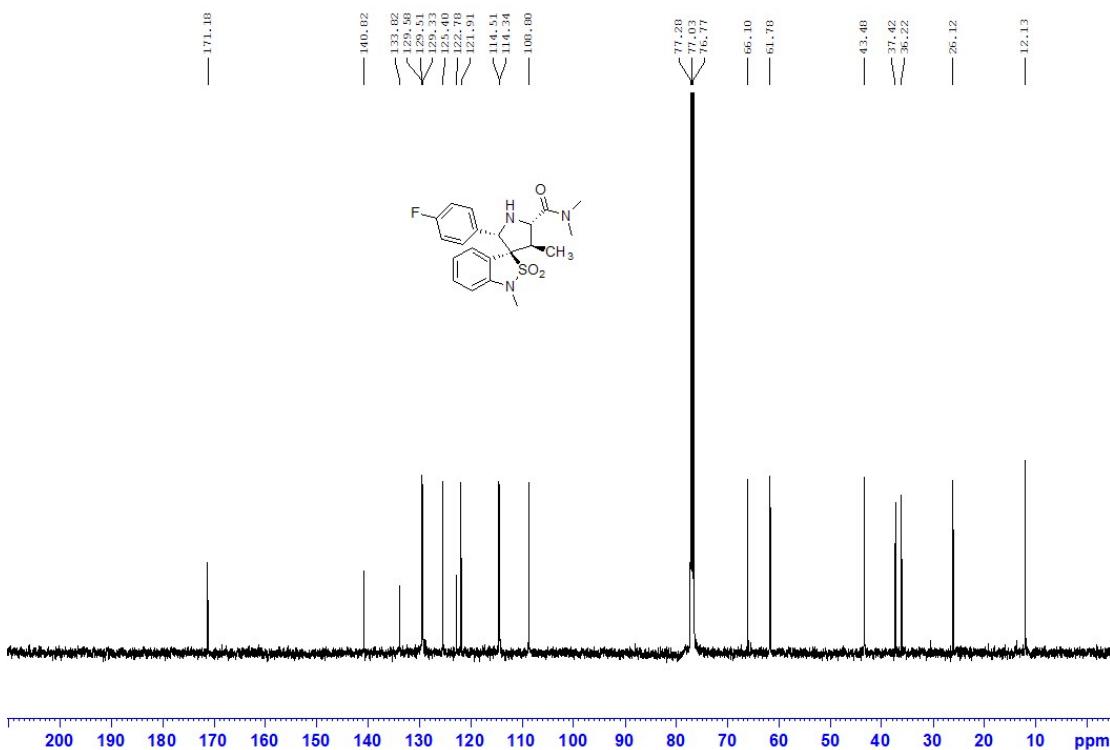


(2'S,3S,4'R,5'S)-1-methyl-2'-*p*-flourophenyl-4'-methyl-5'-*N,N*-dimethylaminocarbonyl-1*H*-spiro

[benzo[*c*]isothiazole-3,3'-pyrrolidine]-2,2-dioxide (5ac)

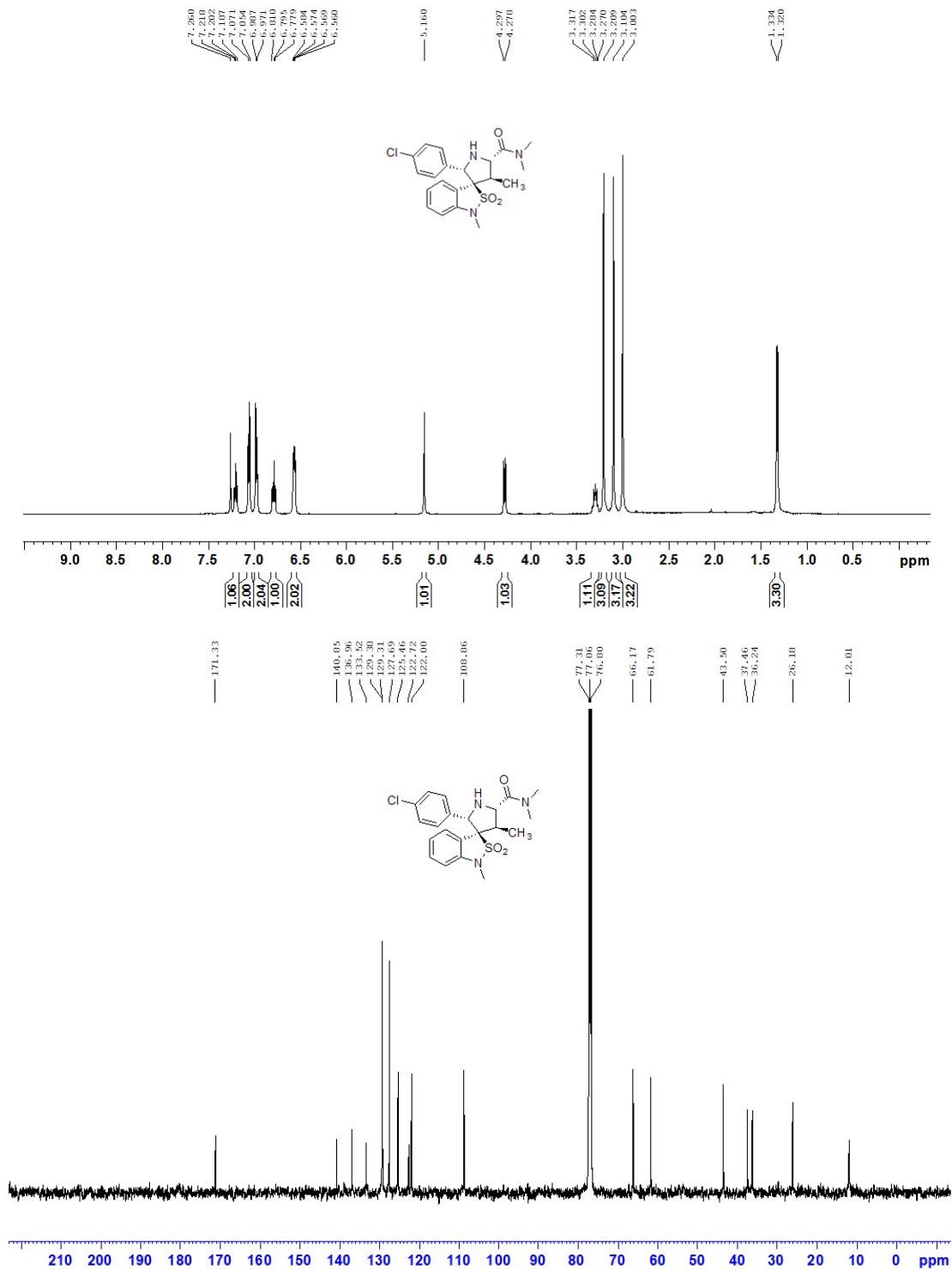
¹H NMR (500 MHz, CDCl₃): δ 7.14 (t, 1H, *J* = 7.7 Hz), 6.97-6.94 (m, 2H), 6.74-6.71 (m, 3H), 6.52-6.49 (m, 2H), 5.15 (s, 1H), 4.26 (d, 1H, *J* = 9.2 Hz), 3.26-3.23 (m, 1H), 3.15 (s, 3H), 3.05 (s, 3H), 2.92 (s, 3H), 1.29 (d, 3H, *J* = 7.1 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 171.2, 140.8, 133.8, 129.6, 129.5, 129.3, 125.4, 122.8, 121.9, 114.5, 114.3, 108.8, 66.1, 61.8, 43.5, 37.4, 36.2, 26.1, 12.1, HRMS (ESI-TOF⁺): m/z Calcd. for C₂₁H₂₄FN₃O₃S [(M+H)⁺]: 418.1601. Found: 418.1607. Chiral HPLC (Daicel Chiraldpak AD-H, 25% IPA/hexanes, 0.8 mL/min, λ = 254 nm) *t*_R(major) = 34.346 min, *t*_R(minor) = 19.098 min; $[\alpha]^{25}_D$ = -62.4° (c = 0.26, CH₂Cl₂)

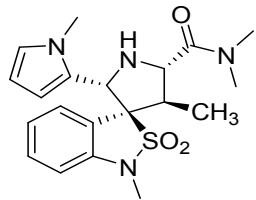




(2'S,3S,4'R,5'S)-1-methyl-2'-p-chlorophenyl-4'-methyl-5'-N,N-dimethylaminocarbonyl-1H-spiro[benzo[c]isothiazole-3,3'-pyrrolidine]-2,2-dioxide (5ad)

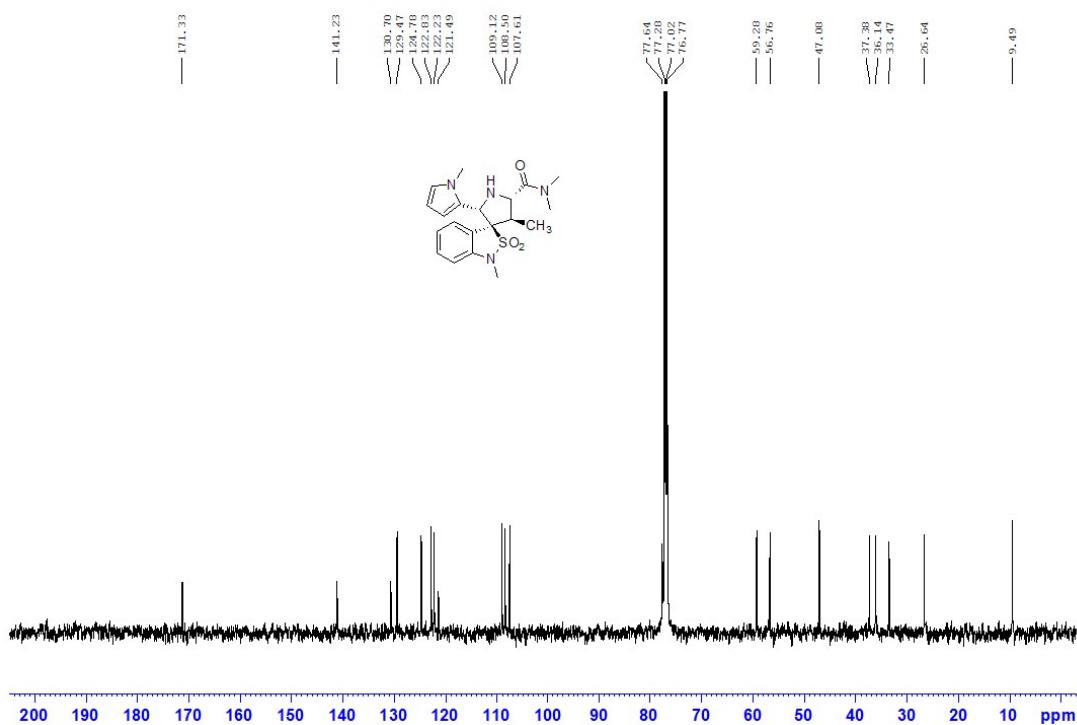
¹H NMR (500 MHz, CDCl₃) δ 7.20 (t, 1H, J = 7.8 Hz), 7.07-6.97 (m, 4H), 6.79 (t, 1H, J = 7.6 Hz), 6.58-6.56 (m, 2H), 5.16 (s, 1H), 4.28 (d, 1H, J = 9.4 Hz), 3.32-3.27 (m, 1H), 3.21 (s, 3H), 3.10 (s, 3H), 3.00 (s, 3H), 1.32 (d, 3H, J = 7.0 Hz). ¹³C NMR (125 MHz, CDCl₃) δ 171.3, 140.9, 137.0, 133.5, 129.4, 129.3, 127.7, 125.5, 122.7, 122.0, 108.9, 66.2, 61.8, 43.5, 37.5, 36.2, 26.2, 12.0; HRMS (ESI-TOF⁺): m/z Calcd. for C₂₁H₂₄ClN₃O₃S [(M+H)⁺]: 434.1305. Found: 434.1307. Chiral HPLC (Daicel Chiraldpak AD-H, 25% IPA/hexanes, 0.8 mL/min, λ = 254 nm) t_R(major) = 30.552 min, t_R(minor) = 18.571 min; [α]²⁵_D = -42.1° (c = 0.25, CH₂Cl₂)

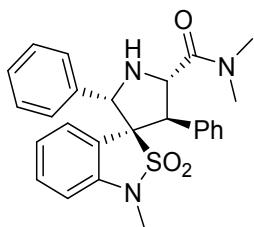
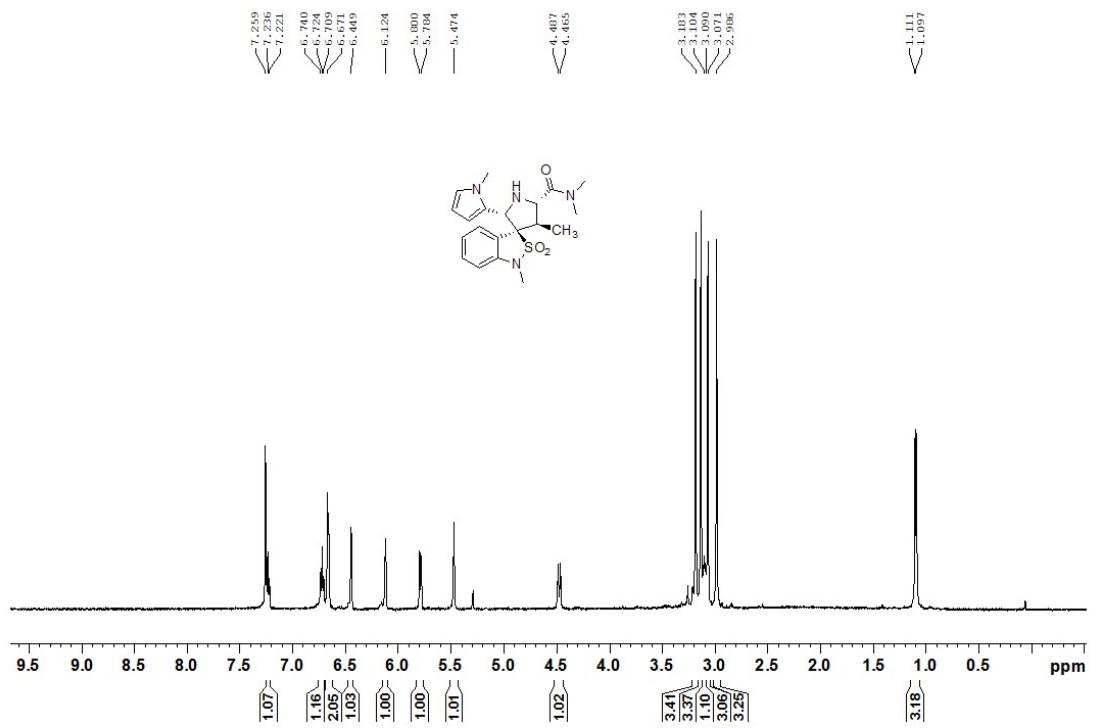




(2'S,3S,4'R,5'S)-N,N,1,4'-tetramethyl-2'-(1-methyl-1H-pyrrol-2-yl)-1H-spiro[benzo[c]isothiazole-3,3'-pyrrolidine]-5'-carboxamide 2,2-dioxide(5ae)

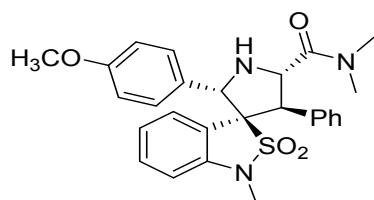
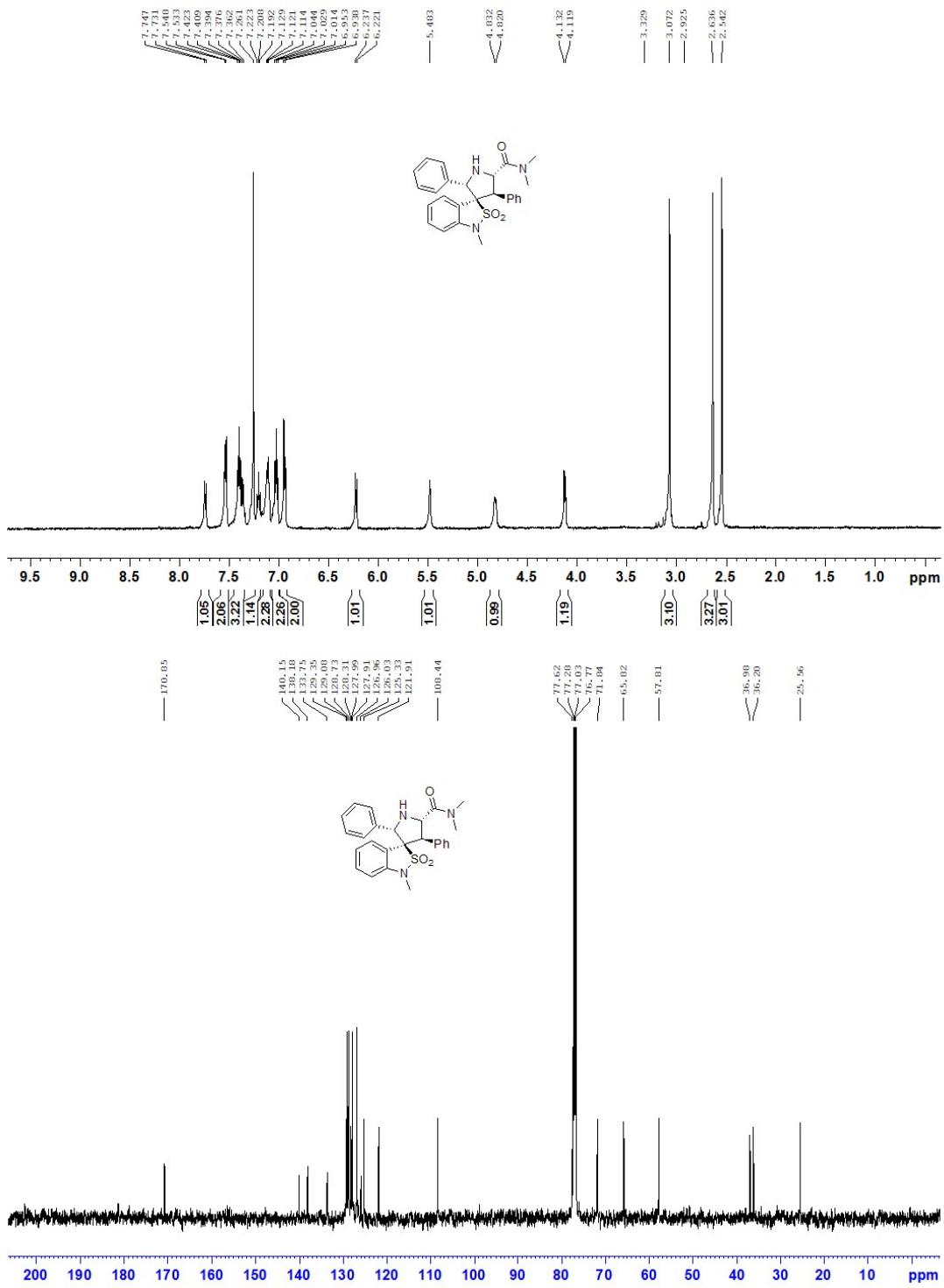
¹H NMR (500 MHz, CDCl₃): δ 7.24 (t, 1H, J = 7.9 Hz), 6.72 (t, 1H, J = 7.6 Hz), 6.67-6.66 (m, 2H), 6.45 (s, 1H), 6.12 (s, 1H), 5.79 (d, 1H, J = 7.7 Hz), 5.47 (s, 1H), 4.47 (d, 1H, J = 10.8 Hz), 3.18 (s, 3H), 3.13 (s, 3H), 3.12-3.10 (m, 1H), 3.07 (s, 3H), 2.99 (s, 3H), 1.10 (d, 3H, J = 7.1 Hz). ¹³C NMR (125 MHz, CDCl₃): δ 171.3, 141.2, 130.7, 129.5, 124.8, 122.8, 122.2, 121.5, 109.1, 108.5, 107.6, 77.6, 59.3, 56.8, 47.1, 37.4, 36.1, 33.5, 26.6, 9.5. HRMS (ESI-TOF⁺): m/z Calcd. for C₂₀H₂₆N₄O₃S [(M+H)⁺]: 403.1804. Found: 403.1804. Chiral HPLC (Daicel Chiraldpak AD-H, 25% IPA/hexanes, 0.8 mL/min, λ = 254 nm) t_R(major) = 35.043 min, t_R(minor) = 22.527 min; [α]²⁵_D = -56.4° (c = 0.31, CH₂Cl₂)





(2'S,3S,4'R,5'S)-N,N,1-trimethyl-2',4'-diphenyl-1H-spiro[benzo[c]isothiazole-3,3'-pyrrolidine]-5'-carboxamide 2,2-dioxide(5ba)

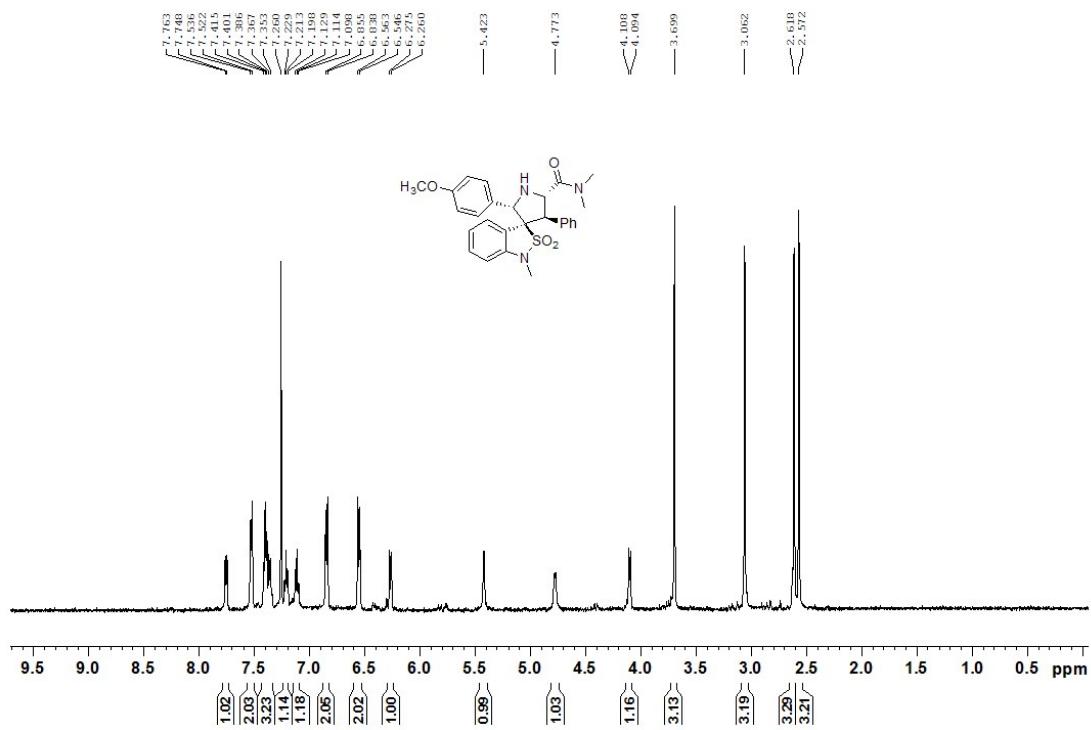
¹H NMR (500 MHz, CDCl₃): δ 7.74 (d, 1H, J = 7.5 Hz), 7.54 (d, 2H, J = 7.4 Hz), 7.42-7.36 (m, 3H), 7.21 (t, 1H, J = 7.6 Hz), 7.13-7.11 (m, 2H), 7.04-7.01 (m, 2H), 6.94 (d, 2H, J = 7.7 Hz), 6.22 (d, 1H, J = 7.8 Hz), 5.48 (s, 1H), 4.83 (d, 1H, J = 5.9 Hz), 4.12 (d, 1H, J = 6.9 Hz), 3.07 (s, 3H), 2.64 (s, 3H), 2.54 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 170.9, 140.2, 138.2, 133.7, 129.4, 129.1, 128.7, 128.3, 128.0, 127.9, 127.0, 126.0, 125.3, 121.9, 108.4, 77.6, 71.8, 65.8, 57.8, 37.0, 36.2, 25.6. HRMS (ESI-TOF⁺): m/z Calcd. for C₂₆H₂₈N₃O₃S [(M+H)⁺]: 462.1851. Found: 462.1853. Chiral HPLC (Daicel Chiralpak AD-H, 19% IPA/hexanes, 0.6 mL/min, λ = 254 nm) *t*_R(major) = 84.636 min, *t*_R(minor) = 52.818 min; [α]_D²⁵ = -52.3° (c = 0.28, CH₂Cl₂)

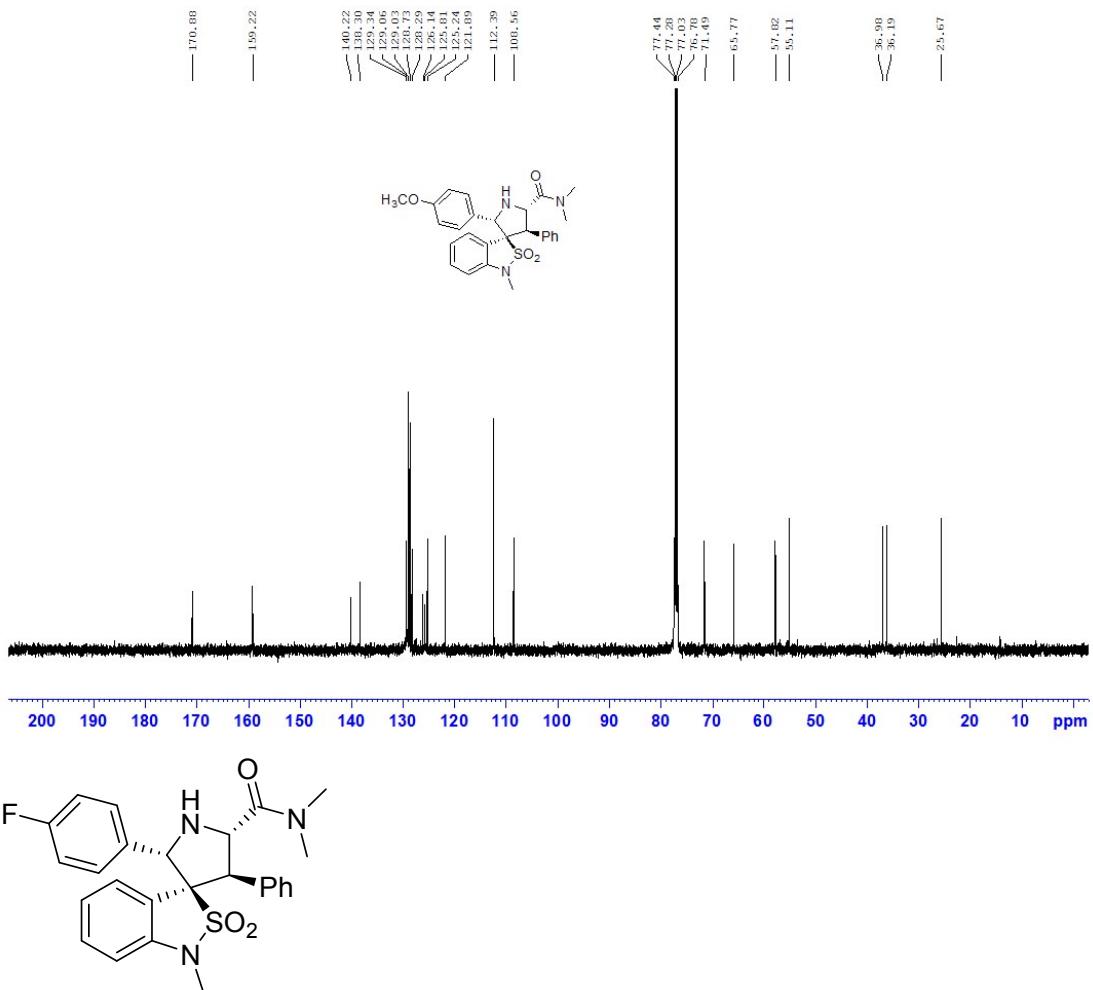


(2'S,3S,4'R,5'S)-2'-(4-methoxyphenyl)-N,N,1-trimethyl-4'-phenyl-1H-spiro[benzo[c]isothiazole-

3,3'-pyrrolidine]-5'-carboxamide 2,2-dioxide(5bb)

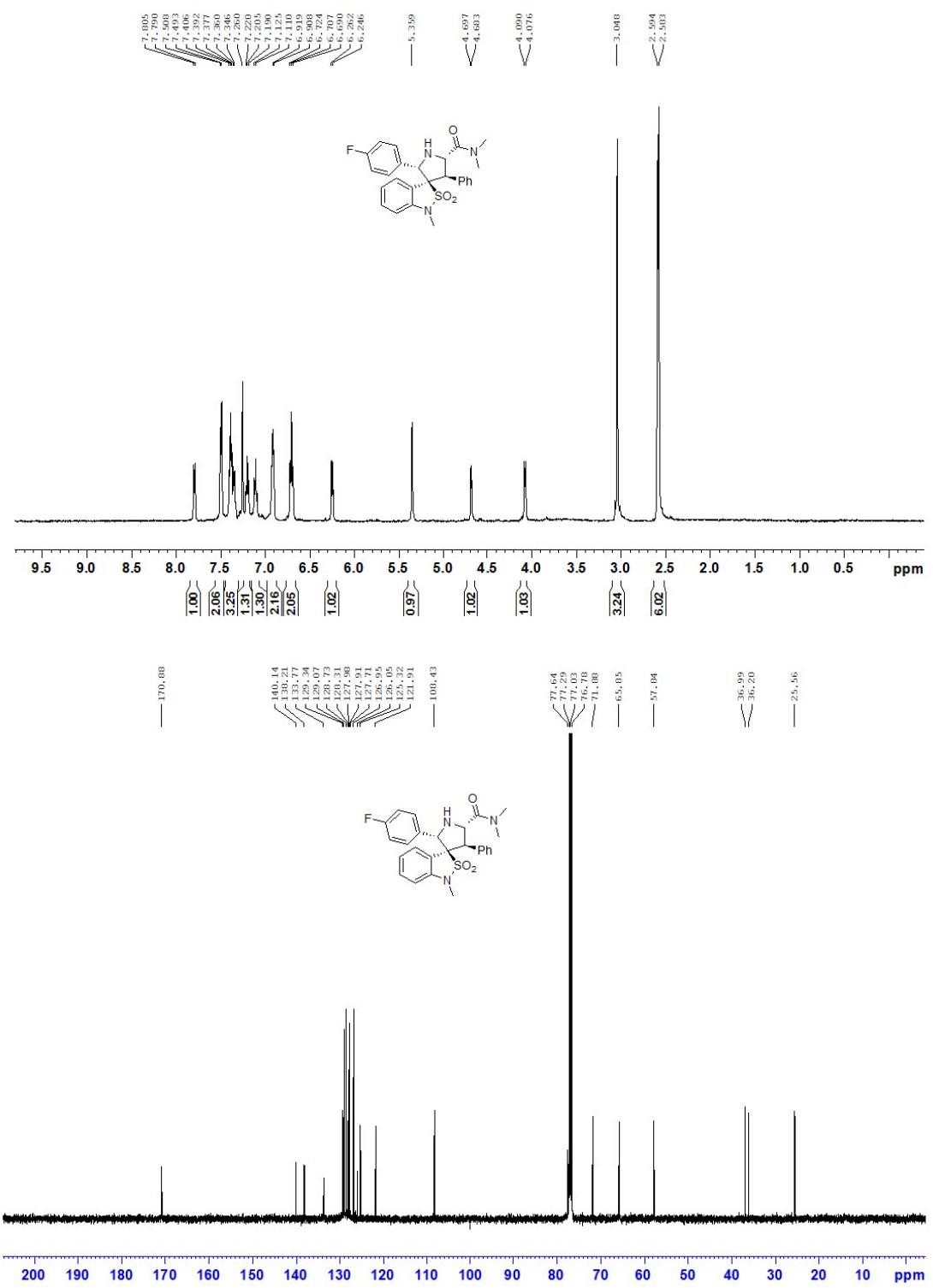
¹H NMR (500 MHz, CDCl₃): δ 7.76 (d, 1H, J = 7.6 Hz), 7.53 (d, 2H, J = 7.3 Hz), 7.42-7.35 (m, 3H), 7.21 (t, 1H, J = 7.6 Hz), 7.11 (t, 1H, J = 7.6 Hz), 6.84 (d, 2H, J = 8.5 Hz), 6.55 (d, 2H, J = 8.4 Hz), 6.27 (d, 1H, J = 7.9 Hz), 5.42 (s, 1H), 4.78 (d, 1H, 5.5 Hz), 4.10 (d, 1H, J = 7.0 Hz), 3.70 (s, 3H), 3.06 (s, 3H), 2.62 (s, 3H), 2.57 (s, 3H). ¹³C NMR (125 MHz, CDCl₃): δ 170.9, 159.2, 140.2, 138.3, 129.3, 129.1, 129.0, 128.7, 128.3, 126.1, 125.8, 125.2, 121.9, 112.4, 108.6, 77.4, 71.5, 65.8, 57.8, 55.1, 37.0, 36.2, 25.7. HRMS (ESI-TOF⁺): m/z Calcd. for C₂₇H₂₉N₃O₄S [(M+H)⁺]: 492.1957. Found: 492.1953. Chiral HPLC (Daicel Chiraldpak AD-H, 19% IPA/hexanes, 0.6 mL/min, λ = 254 nm) *t*_R(major) = 103.481 min, *t*_R(minor) = 60.855 min; [α]²⁵_D = -48.7° (c = 0.31, CH₂Cl₂)

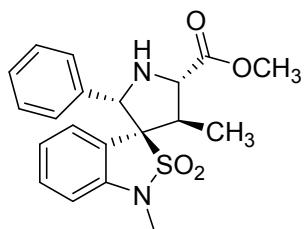




(2'S,3S,4'R,5'S)-2'-(4-fluorophenyl)-N,N,1-trimethyl-4'-phenyl-1H-spiro[benzo[c]isothiazole-3,3'-pyrrolidine]-5'-carboxamide 2,2-dioxide(5bc)

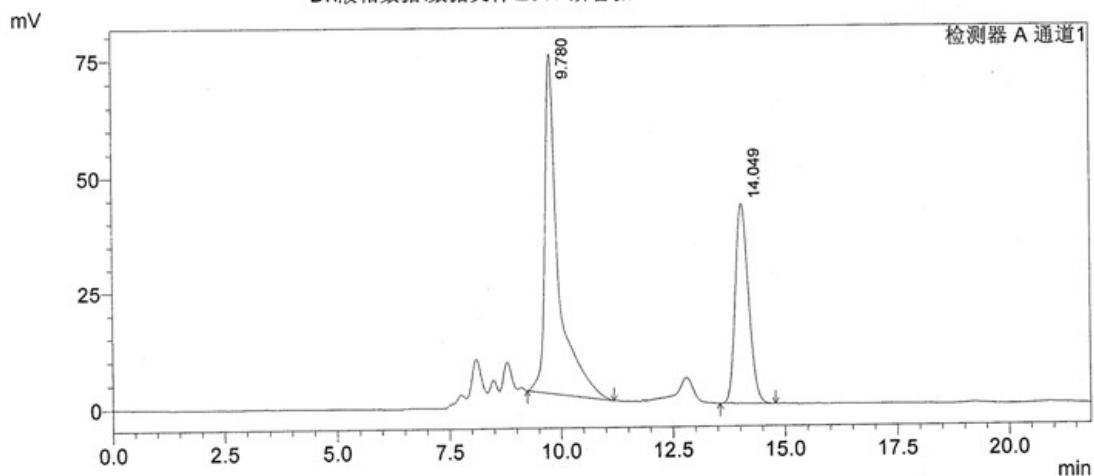
^1H NMR (500 MHz, CDCl_3): δ 7.80 (d, 1H, $J = 7.5$ Hz), 7.51-7.49 (m, 2H), 7.40-7.34 (m, 3H), 7.20 (t, 1H, $J = 7.4$ Hz), 7.11 (t, 1H, $J = 7.5$ Hz), 6.93-6.91 (m, 2H), 6.70 (t, 2H, $J = 8.5$ Hz), 6.25 (d, 1H, $J = 7.8$ Hz), 5.36 (s, 1H), 4.68 (d, 1H, $J = 7.1$ Hz), 4.08 (d, 1H, $J = 7.1$ Hz), 3.24 (s, 3H), 2.59 (s, 3H), 2.58 (s, 3H). ^{13}C NMR (125 MHz, CDCl_3): δ 170.9, 140.1, 138.2, 133.8, 129.3, 129.1, 128.7, 128.3, 128.0, 127.9, 127.7, 126.9, 126.0, 125.3, 121.9, 108.4, 77.6, 71.9, 65.9, 57.8, 37.0, 36.2, 25.6. HRMS (ESI-TOF $^+$): m/z Calcd. for $\text{C}_{26}\text{H}_{26}\text{PN}_3\text{O}_3\text{S}$ [(M+H) $^+$]: 480.1757. Found: 480.1756. Chiral HPLC (Daicel Chiraldak AD-H, 11% IPA/hexanes, 0.7 mL/min, $\lambda = 254$ nm) t_{R} (major) = 105.849 min, t_{R} (minor) = 79.699 min; $[\alpha]^{25}_{\text{D}} = -62.1^\circ$ ($c = 0.26$, CH_2Cl_2)





HPLC Conditions: Daicel Chiralpak AD-H, 30% IPA/hexanes, 1 mL/min

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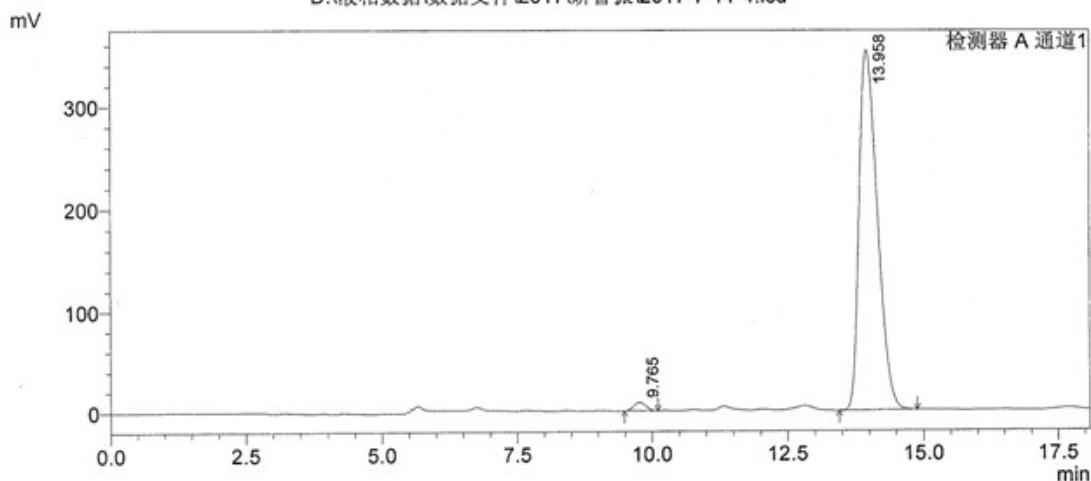


1 检测器 A 通道1/254nm

峰表

检测器 A Ch1 254nm		面积	高度	面积 %	高度 %
峰#	保留时间				
1	9.780	1538811	73352	63.438	62.801
2	14.049	886867	43449	36.562	37.199
总计		2425678	116802	100.000	100.000

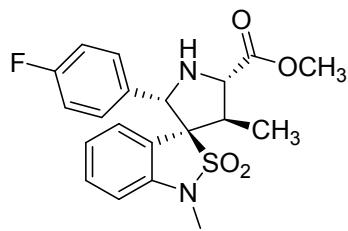
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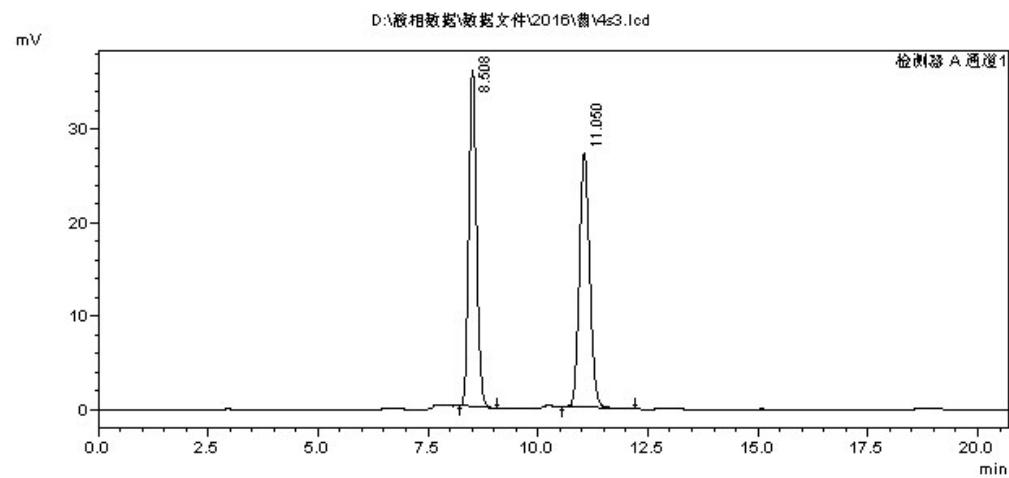
1 检测器 A 通道1/254nm

峰表

检测器 A Ch1 254nm		面积	高度	面积 %	高度 %
峰#	保留时间				
1	9.765	129557	8534	1.533	2.348
2	13.958	8324066	354962	98.467	97.652
总计		8453623	363496	100.000	100.000



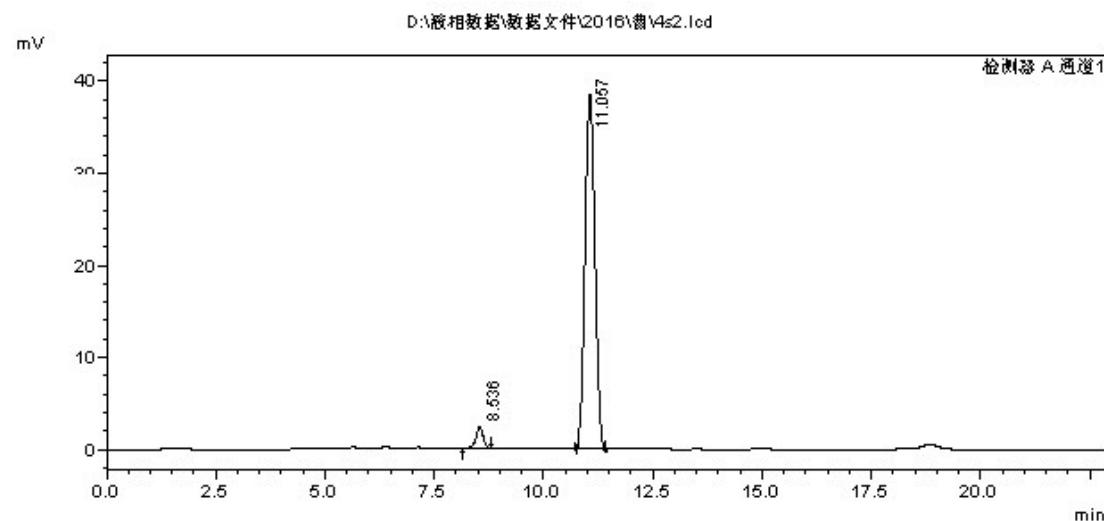
HPLC Conditions: Daicel Chiralpak AD-H, 30% IPA/hexanes, 1 mL/min



1 检测器 A 通道1/254nm

峰表
检测器 A Ch1 254nm

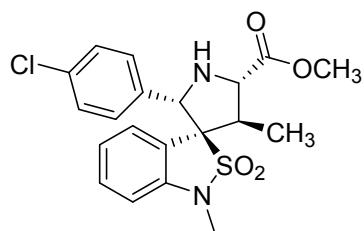
峰#	保留时间	面积	高度	面积 %	高度 %
1	8.508	441415	35925	49.855	56.974
2	11.050	443980	27130	50.145	43.026
总计		885395	63055	100.000	100.000



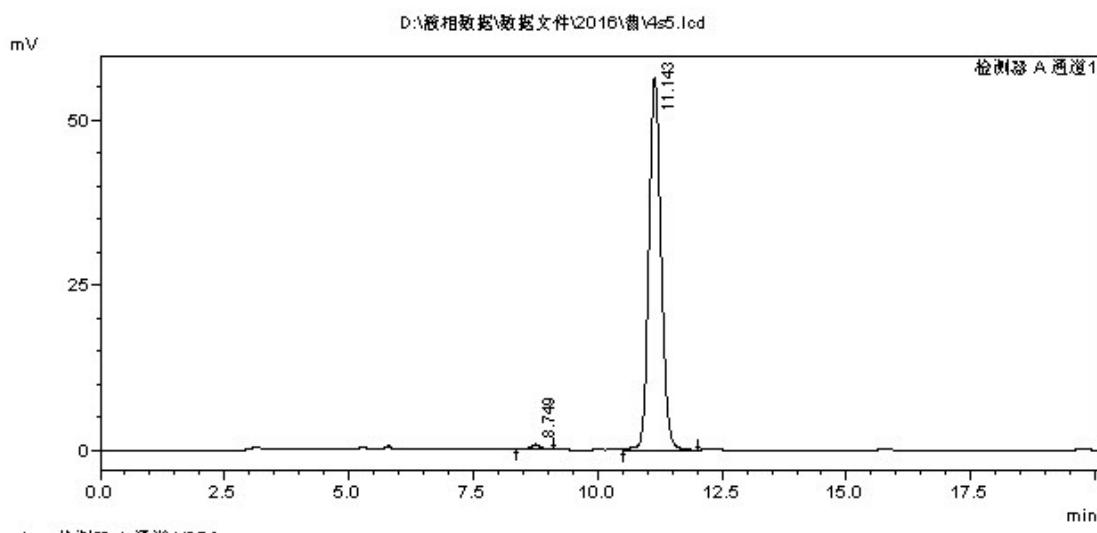
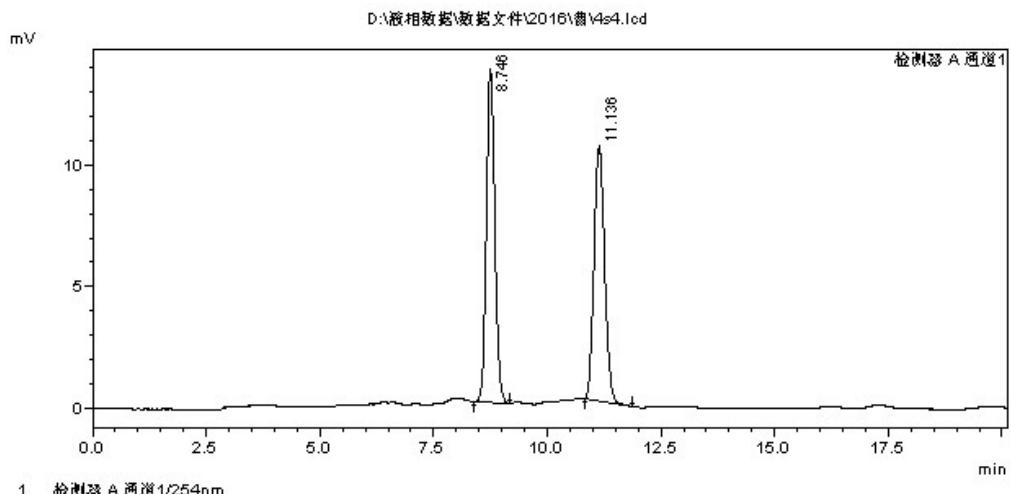
1 检测器 A 通道1/254nm

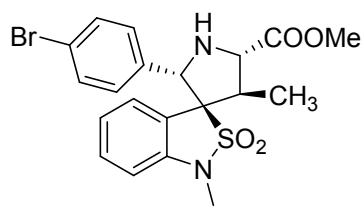
峰表
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	8.536	25918	2276	4.366	5.737
2	11.057	567742	37397	95.634	94.263
总计		593660	39674	100.000	100.000

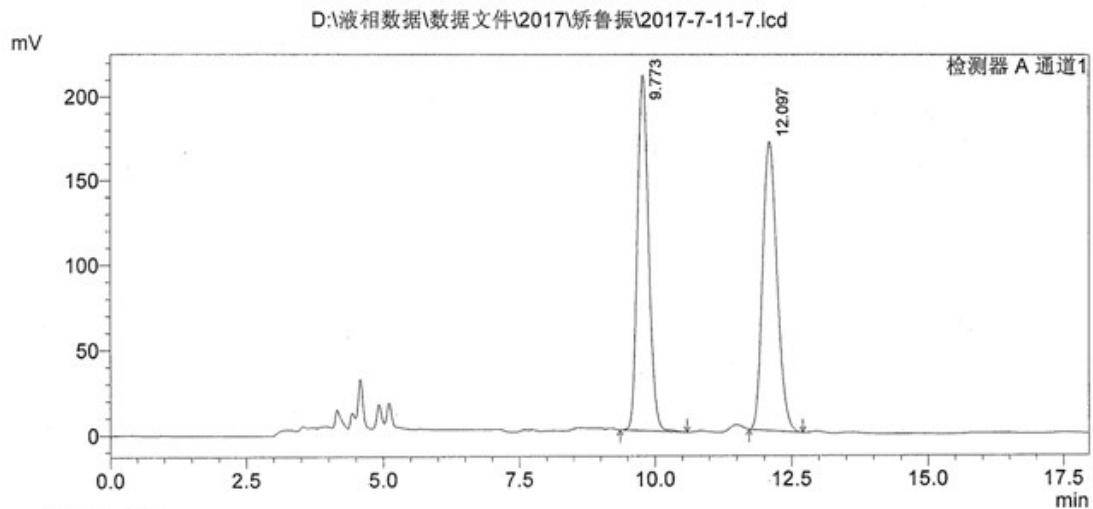


HPLC Conditions: Daicel Chiralpak AD-H, 30% IPA/hexanes, 1 mL/min



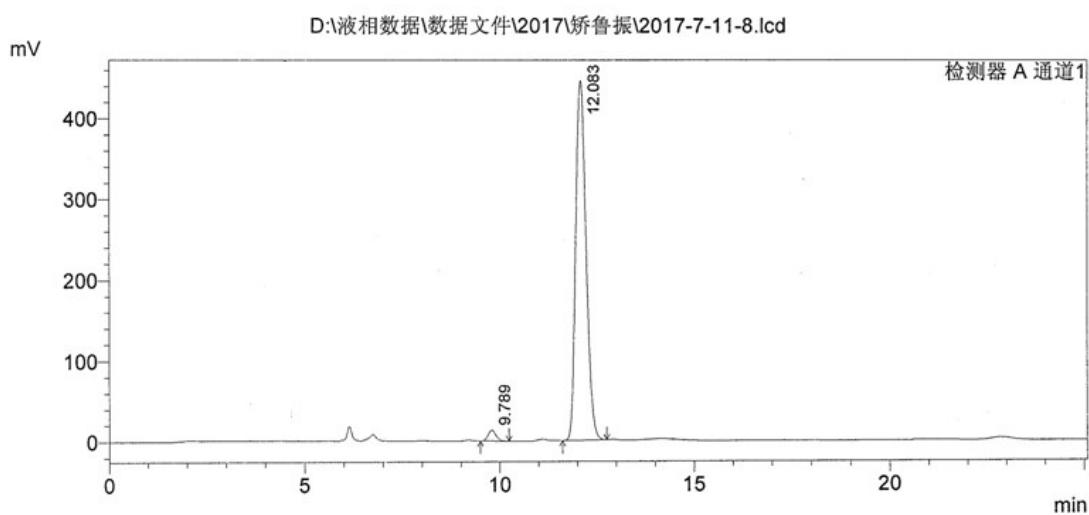


HPLC Conditions: Daicel Chiralpak AD-H, 30% IPA/hexanes, 1 mL/min



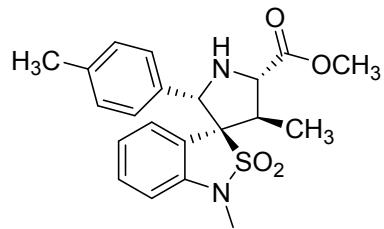
峰表

检测器 A Ch1 254nm					
峰#	保留时间	面积	高度	面积 %	高度 %
1	9.773	3037592	211163	49.250	55.239
2	12.097	3130084	171109	50.750	44.761
总计		6167676	382272	100.000	100.000

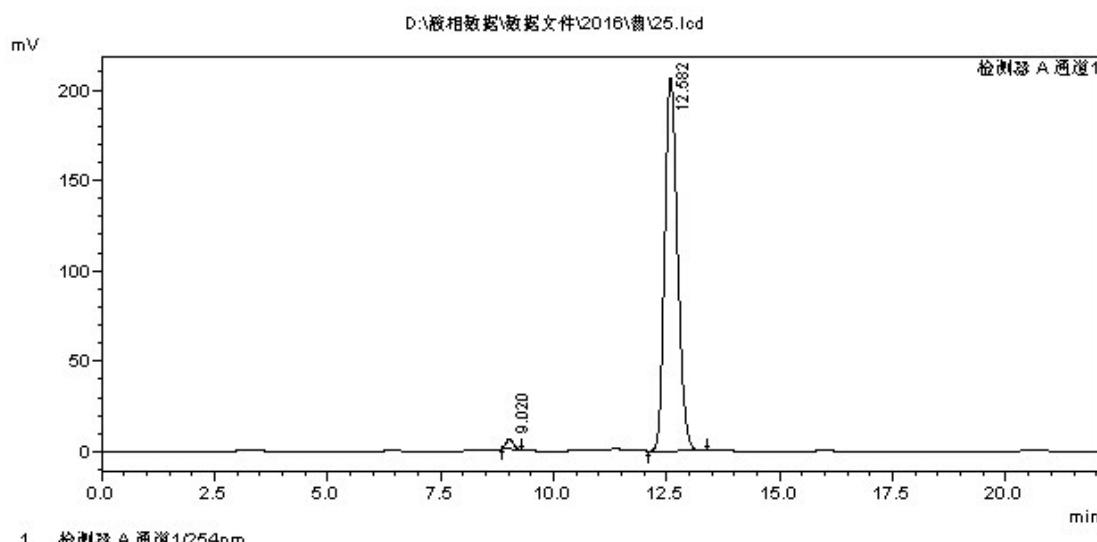
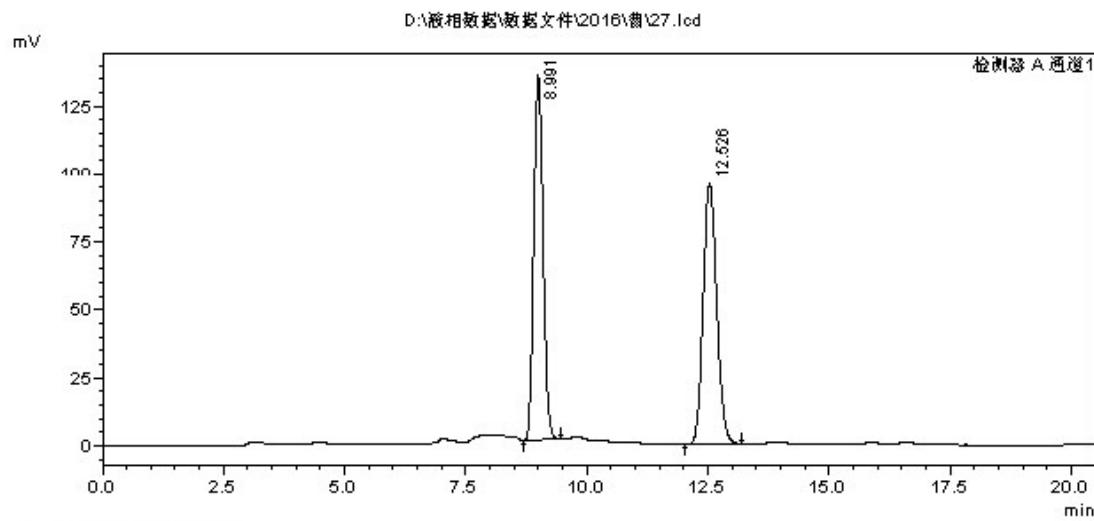


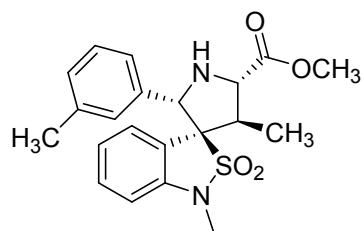
峰表

检测器 A Ch1 254nm					
峰#	保留时间	面积	高度	面积 %	高度 %
1	9.789	189577	13662	2.244	2.968
2	12.083	8258808	446576	97.756	97.032
总计		8448385	460238	100.000	100.000



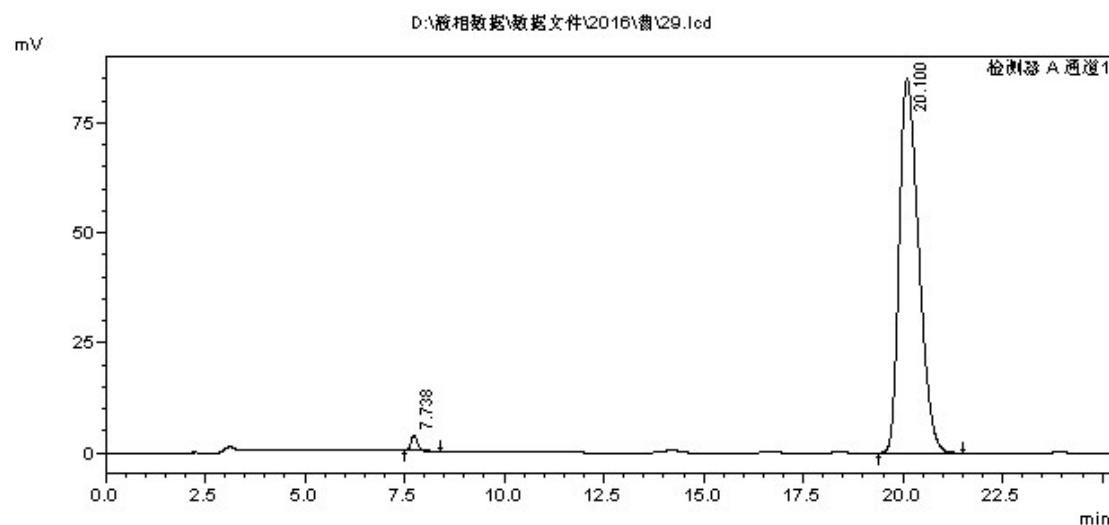
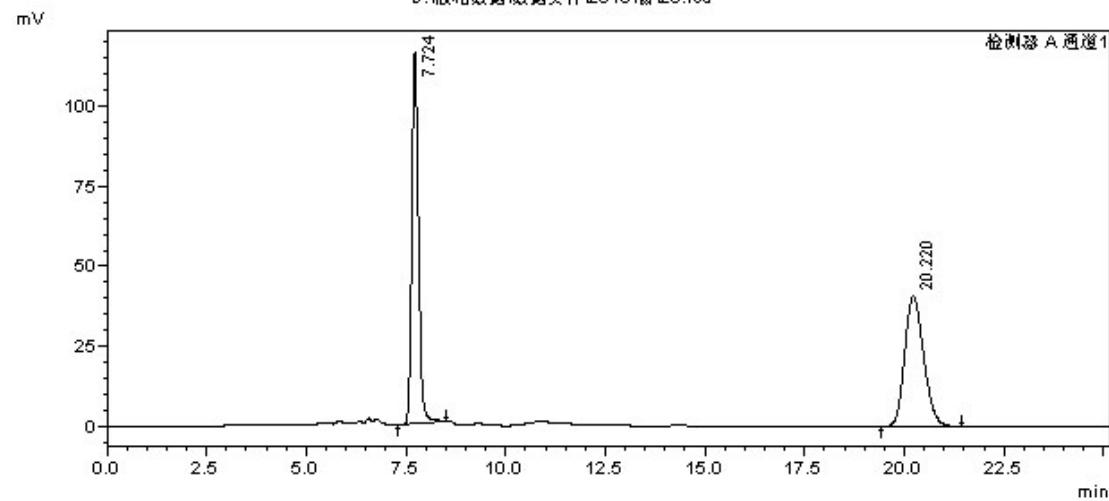
HPLC Conditions: Daicel Chiralpak AD-H, 30% IPA/hexanes, 1 mL/min

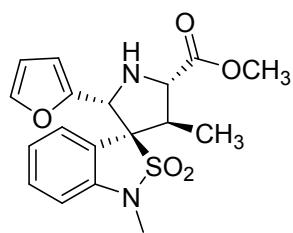




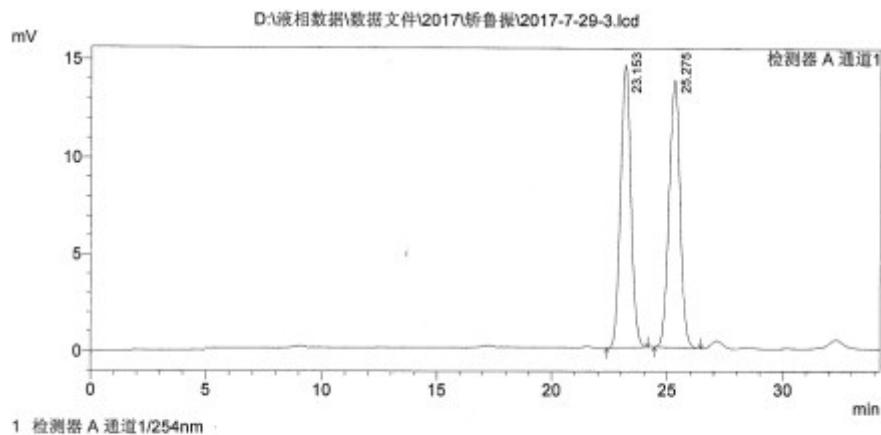
HPLC Conditions: Daicel Chiralpak AD-H, 10% IPA/hexanes, 1 mL/min

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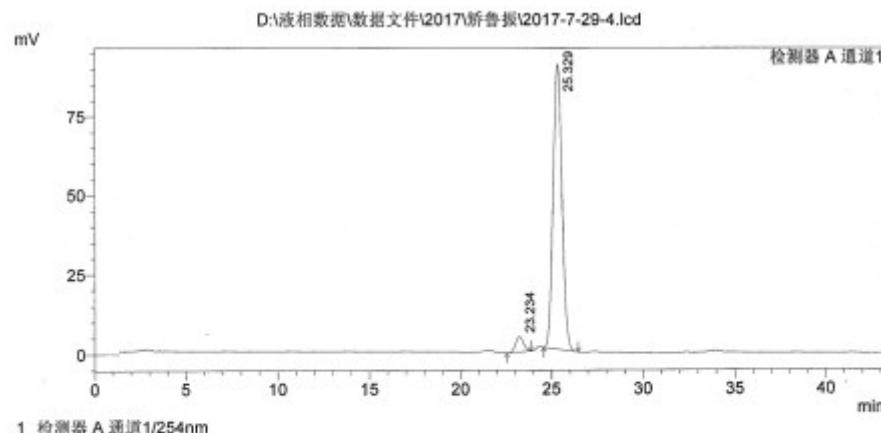
HPLC Conditions: Daicel Chiralpak AD-H, 20% IPA/hexanes, 0.8 mL/min



峰表

检测器 A Ch1 254nm

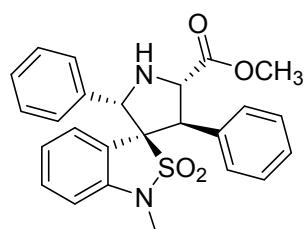
峰#	保留时间	面积	高度	面积 %	高度 %
1	23.153	457227	14576	49.973	51.343
2	25.275	457715	13813	50.027	48.657
总计		914942	28389	100.000	100.000



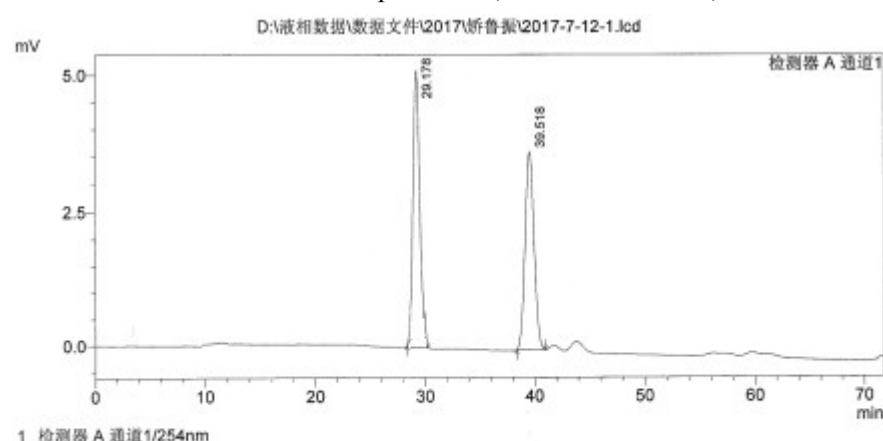
峰表

检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	23.234	141986	4730	4.478	4.986
2	25.329	3028807	90131	95.522	95.014
总计		3170793	94861	100.000	100.000



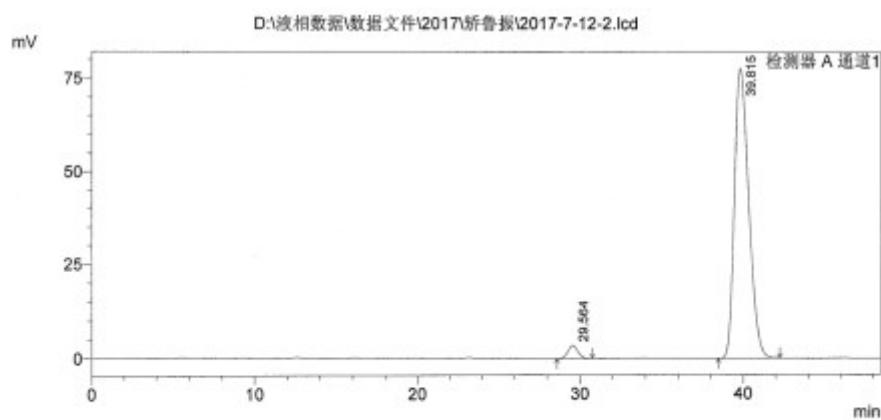
HPLC Conditions: Daicel Chiralpak AD-H, 20% IPA/hexanes, 0.8 mL/min



峰表

检测器 A Ch1 254nm

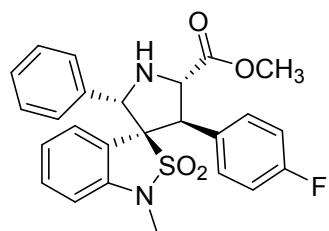
峰#	保留时间	面积	高度	面积 %	高度 %
1	29.178	191182	4778	48.623	56.511
2	39.518	210269	3677	51.377	43.489
总计		401452	8455	100.000	100.000



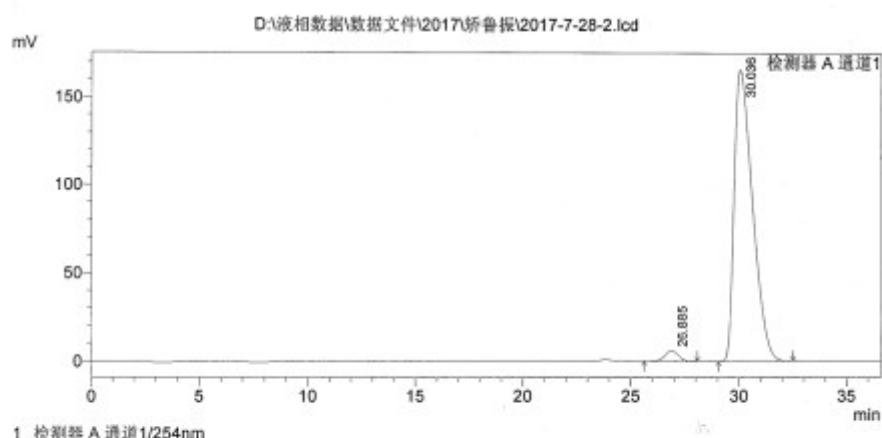
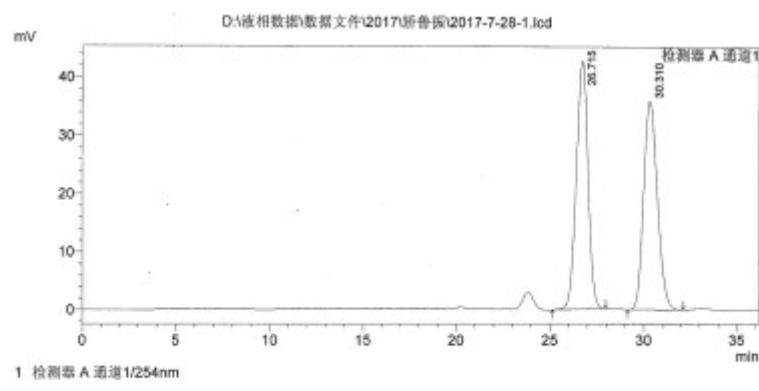
峰表

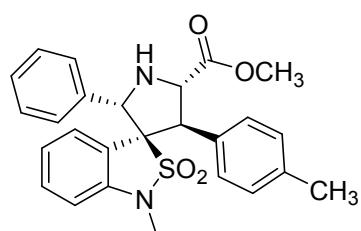
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	29.564	143344	3393	2.939	4.176
2	39.815	4733645	77856	97.061	95.824
总计		4876988	81249	100.000	100.000

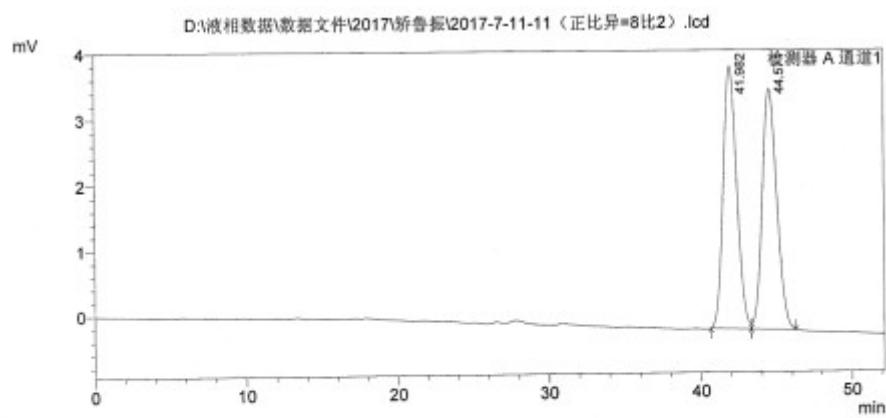


HPLC Conditions: Daicel Chiralpak AD-H, 30% IPA/hexanes, 0.9 mL/min





HPLC Conditions: Daicel Chiralpak AD-H, 20% IPA/hexanes, 0.8 mL/min



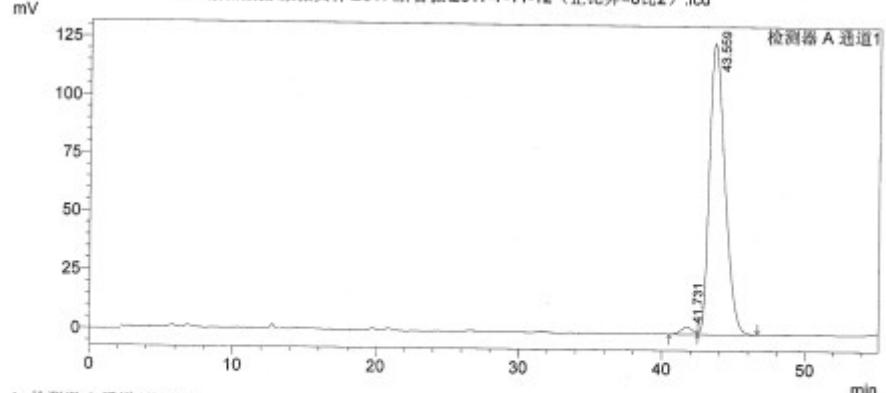
1 检测器 A 通道1/254nm

峰表

检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	41.982	249793	4028	50.216	52.145
2	44.571	247647	3696	49.784	47.855
总计		497441	7724	100.000	100.000

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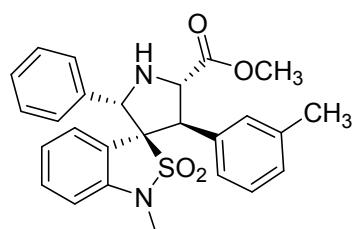


1 检测器 A 通道1/254nm

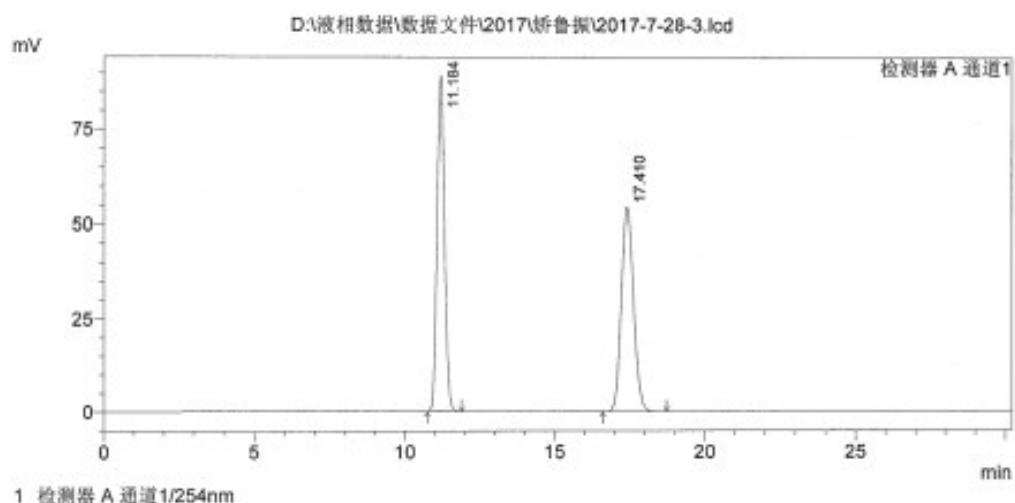
峰表

检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	41.731	169293	3008	1.788	2.348
2	43.559	9297057	125071	98.212	97.652
总计		9466349	128078	100.000	100.000



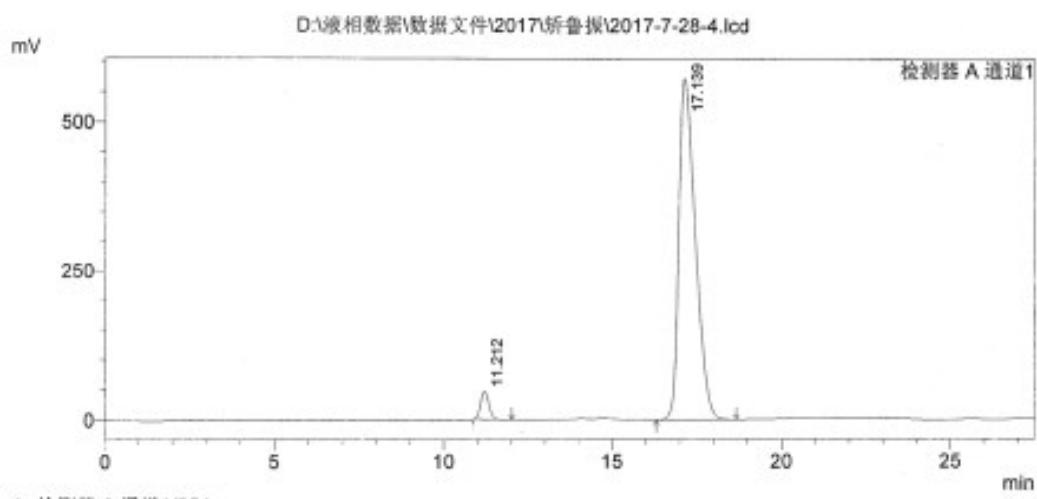
HPLC Conditions: Daicel Chiralpak AD-H, 30% IPA/hexanes, 0.9 mL/min



峰表

检测器 A Ch1 254nm

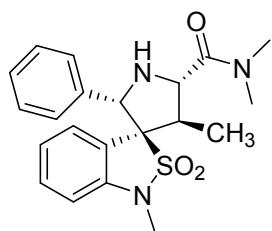
峰#	保留时间	面积	高度	面积 %	高度 %
1	11.184	1545634	89237	49.911	62.051
2	17.410	1551163	54575	50.089	37.949
总计		3096797	143812	100.000	100.000



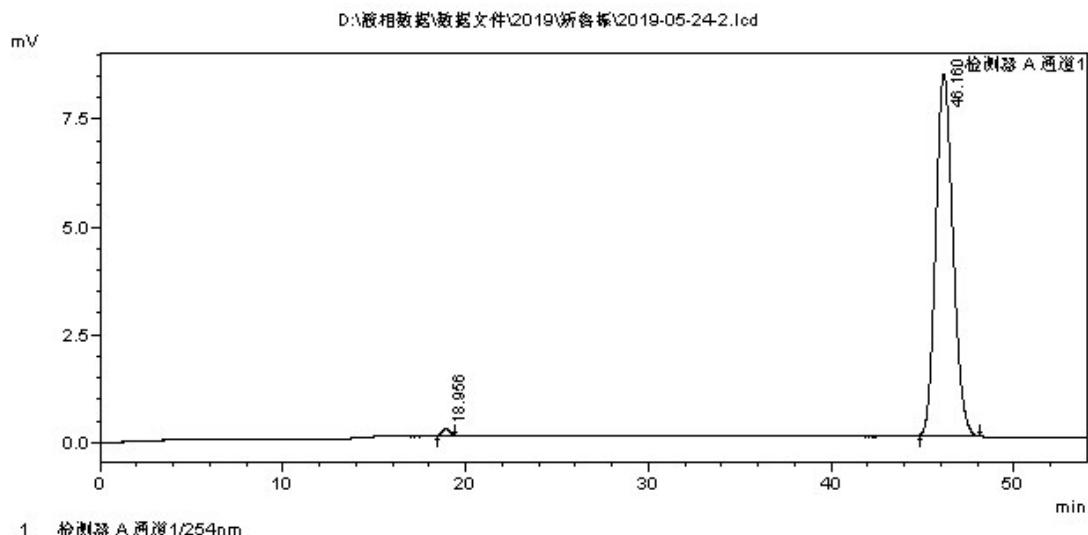
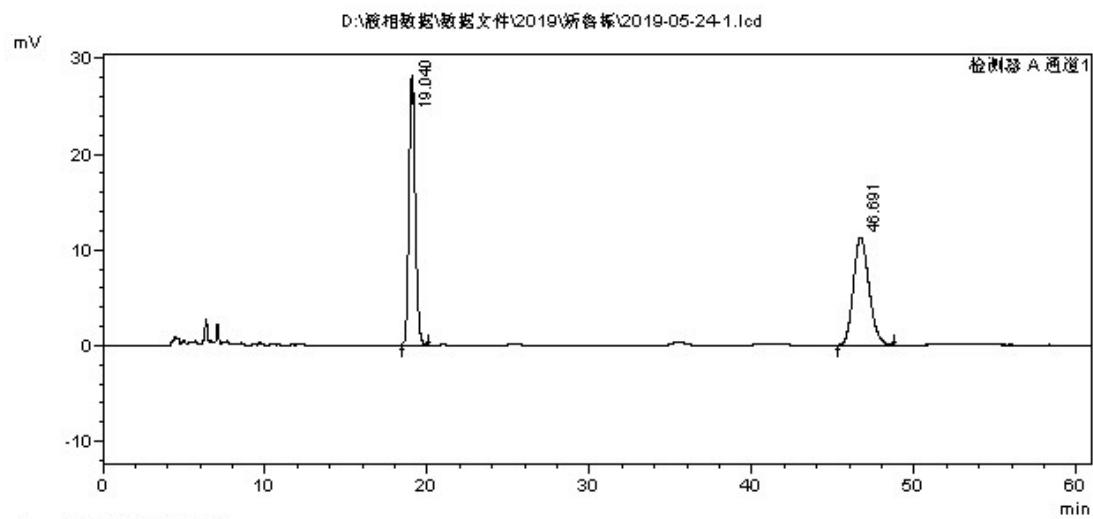
峰表

检测器 A Ch1 254nm

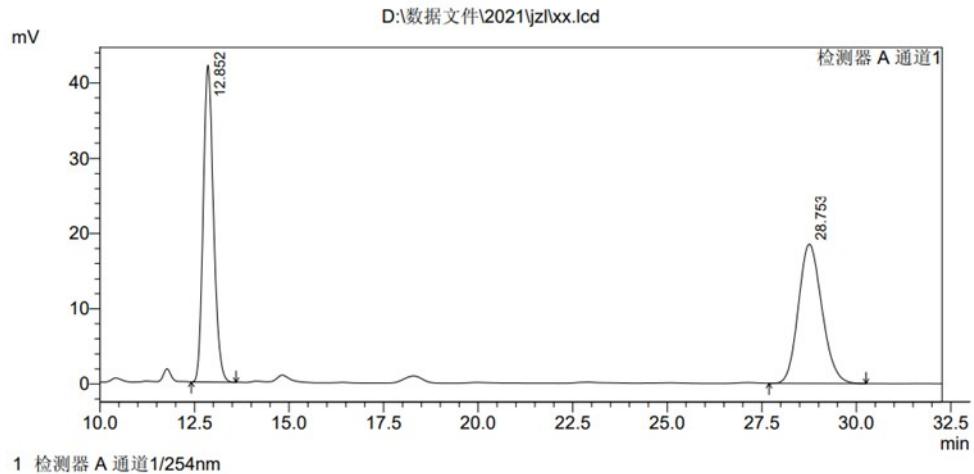
峰#	保留时间	面积	高度	面积 %	高度 %
1	11.212	798358	46785	3.944	7.546
2	17.139	19441888	573218	96.056	92.454
总计		20240246	620003	100.000	100.000



HPLC Conditions: Daicel Chiralpak AD-H, 25% IPA/hexanes, 0.8 mL/min
The experimental results of Ag-catalysis



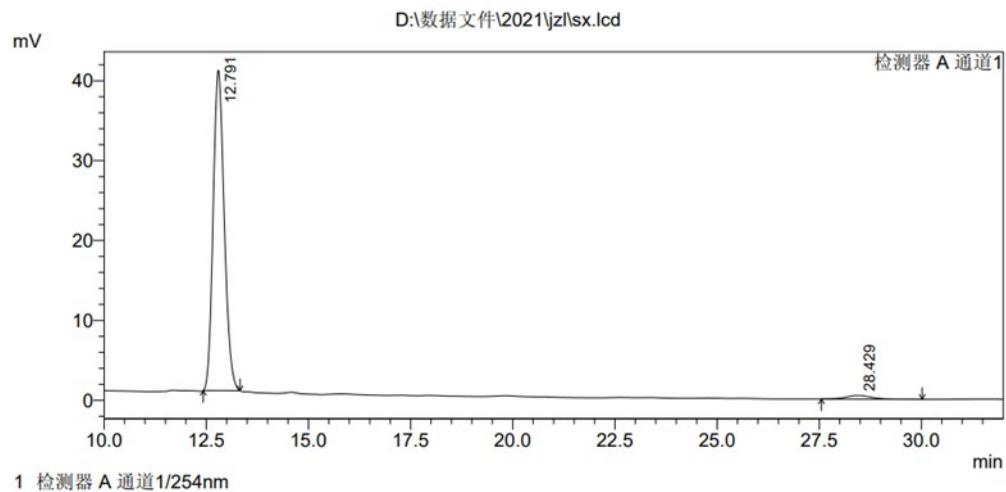
The experimental results of Cu-catalysis



峰表

检测器 A Ch1 254nm

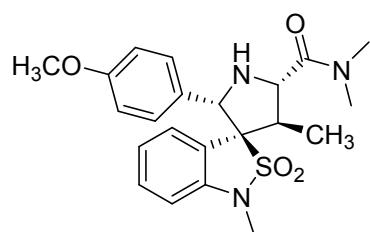
峰#	保留时间	面积	高度	面积 %	高度 %
1	12.852	797554	42096	49.902	69.462
2	28.753	800688	18507	50.098	30.538
总计		1598242	60603	100.000	100.000



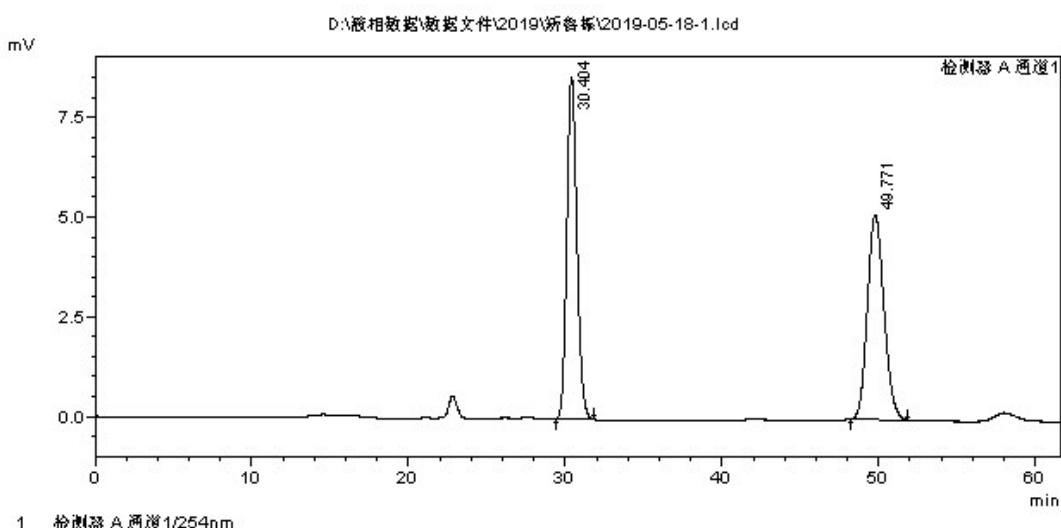
峰表

检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	12.791	755959	40097	97.608	98.901
2	28.429	18530	445	2.392	1.099
总计		774489	40543	100.000	100.000



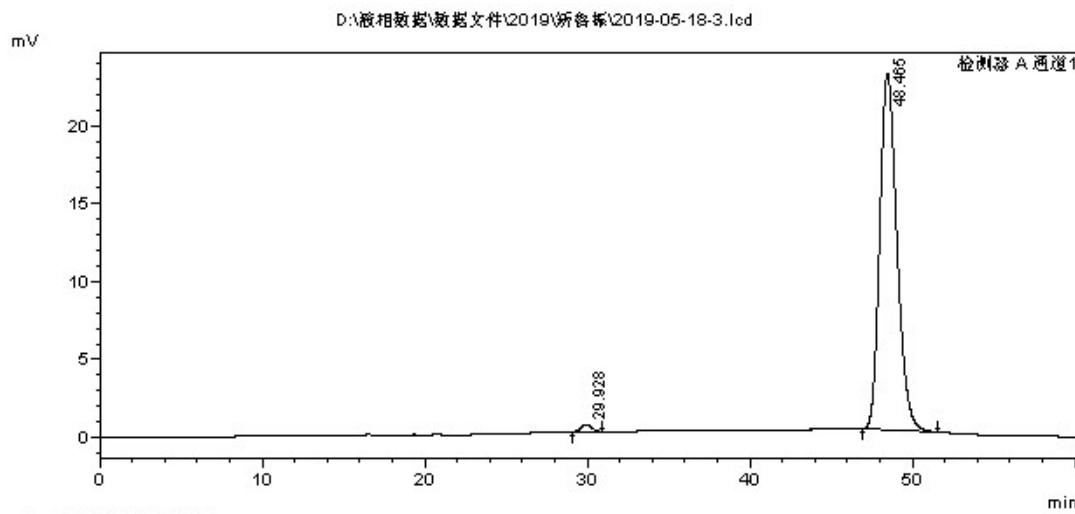
HPLC Conditions: Daicel Chiralpak AD-H, 25% IPA/hexanes, 0.8 mL/min



峰表

检测器 A Ch1 254nm

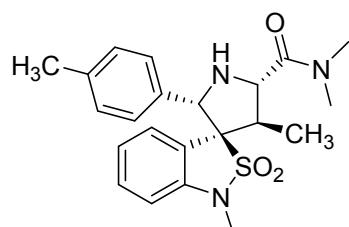
峰#	保留时间	面积	高度	面积 %	高度 %
1	30.404	381238	8561	50.211	62.481
2	49.771	378031	5141	49.789	37.519
总计		759269	13702	100.000	100.000



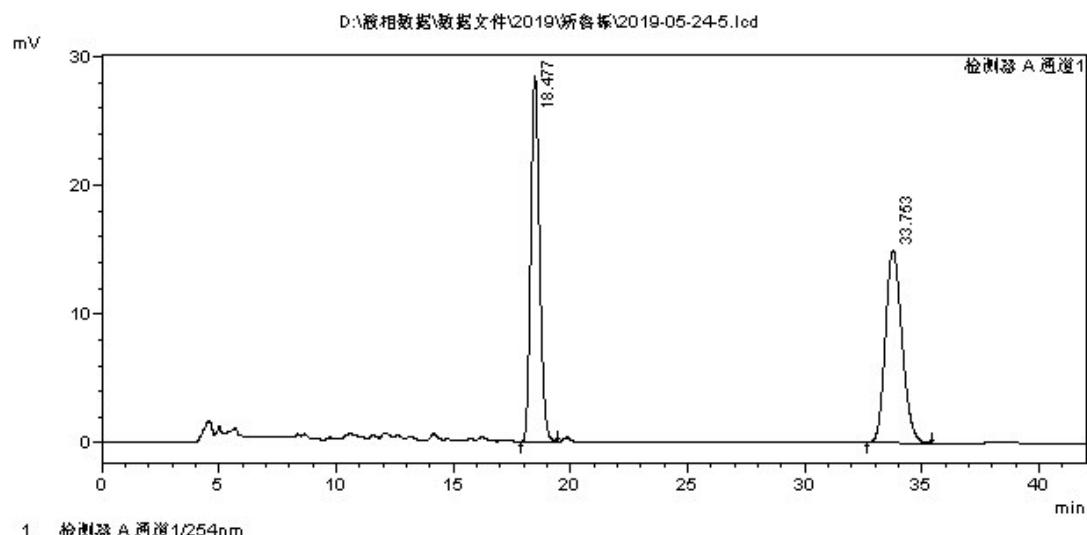
峰表

检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	29.928	21004	477	1.233	2.046
2	48.465	1682920	22833	98.767	97.954
总计		1703924	23309	100.000	100.000



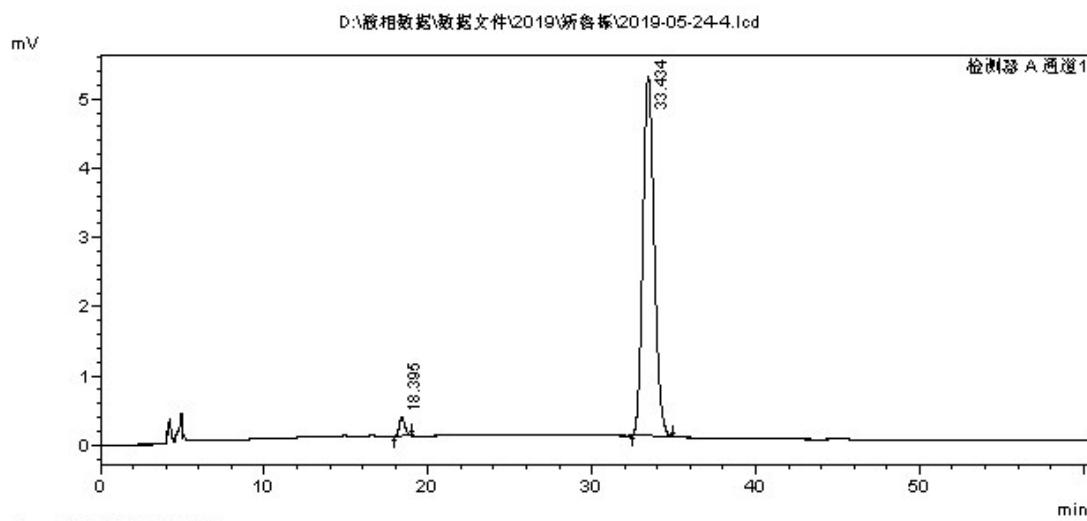
HPLC Conditions: Daicel Chiralpak AD-H, 25% IPA/hexanes, 0.8 mL/min



峰表

检测器 A Ch1 254nm

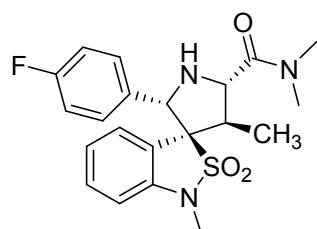
峰#	保留时间	面积	高度	面积 %	高度 %
1	18.477	741016	28390	50.154	65.480
2	33.753	736456	14967	49.846	34.520
总计		1477471	43356	100.000	100.000



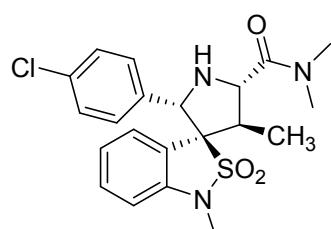
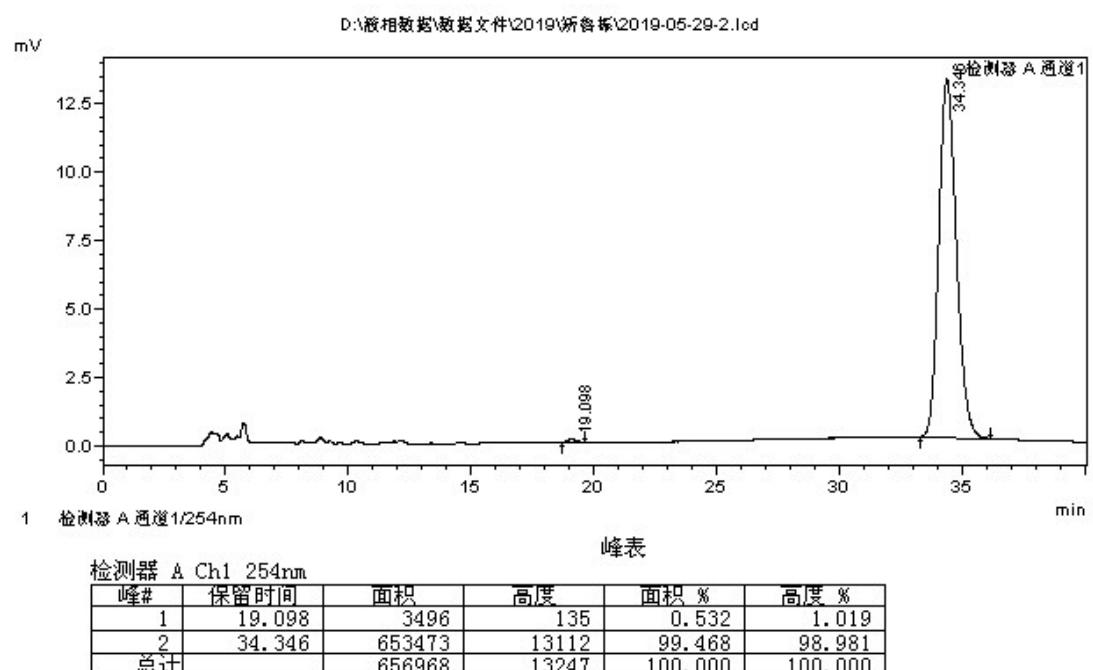
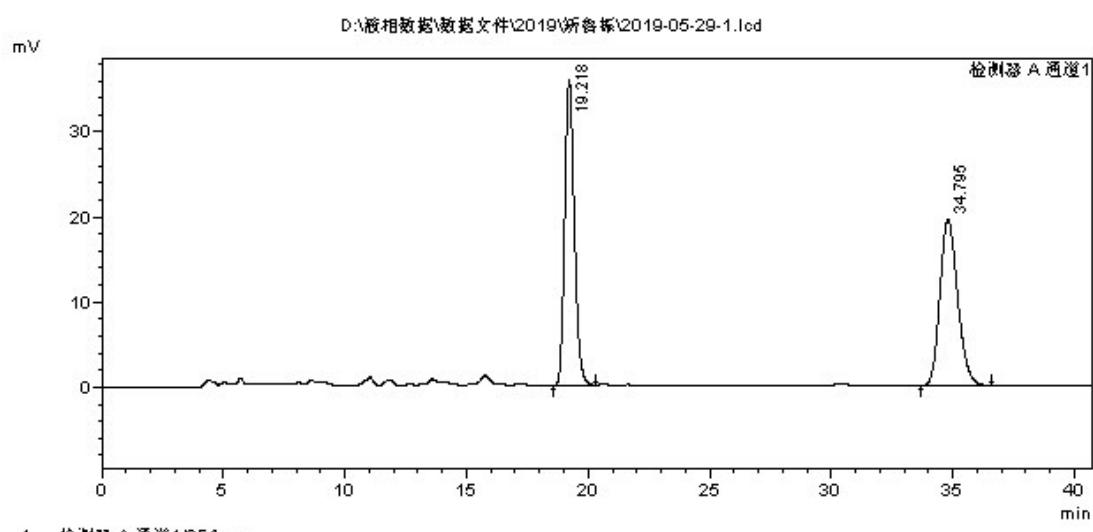
峰表

检测器 A Ch1 254nm

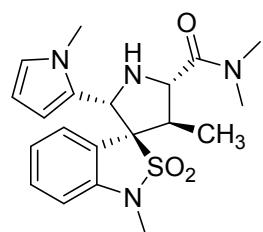
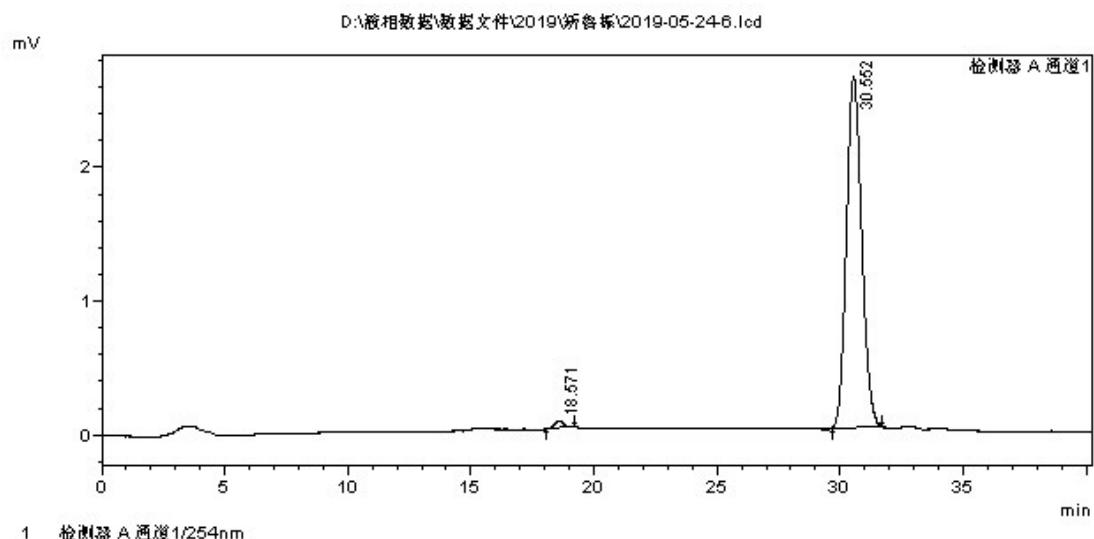
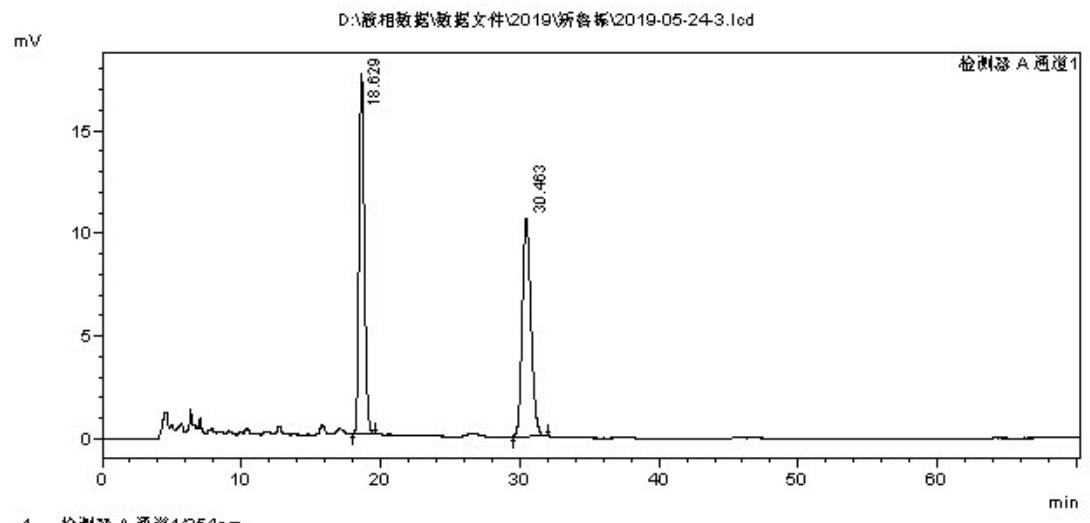
峰#	保留时间	面积	高度	面积 %	高度 %
1	18.395	6482	267	2.530	4.892
2	33.434	249718	5190	97.470	95.108
总计		256201	5456	100.000	100.000



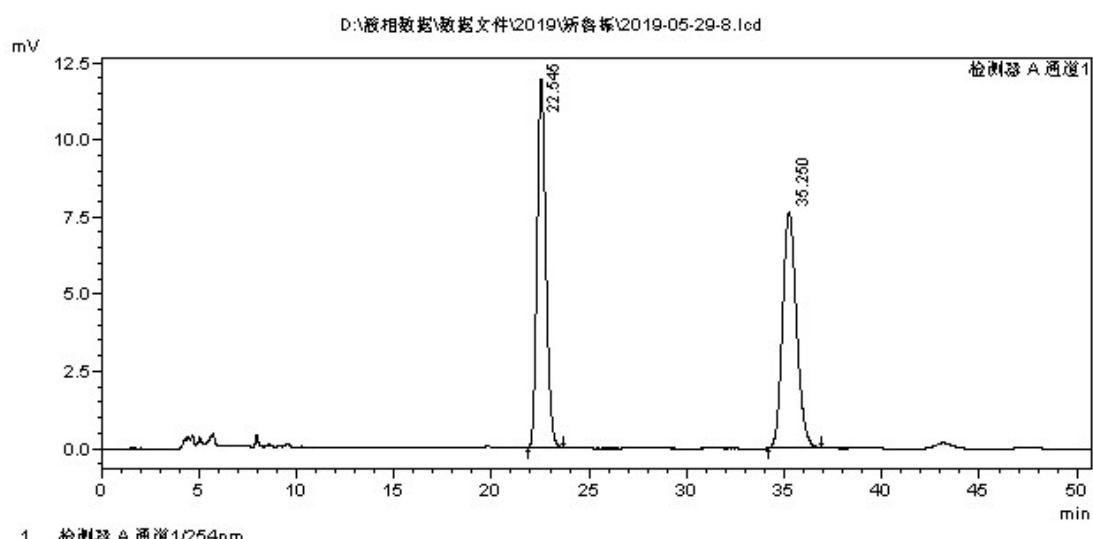
HPLC Conditions: Daicel Chiraldak AD-H, 25% IPA/hexanes, 0.8 mL/min



HPLC Conditions: Daicel Chiraldak AD-H, 25% IPA/hexanes, 0.8 mL/min

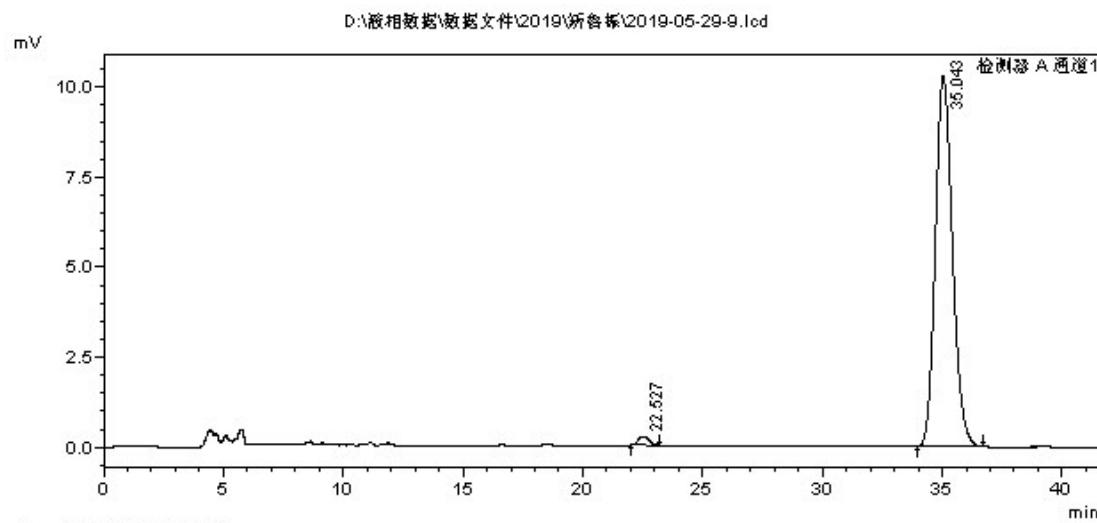


HPLC Conditions: Daicel Chiraldak AD-H, 25% IPA/hexanes, 0.8 mL/min



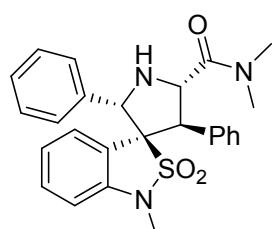
峰表
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	22.545	374352	11935	49.685	61.016
2	35.250	379099	7625	50.315	38.984
总计		753452	19560	100.000	100.000

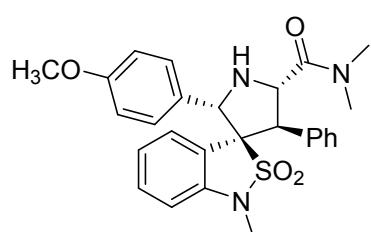
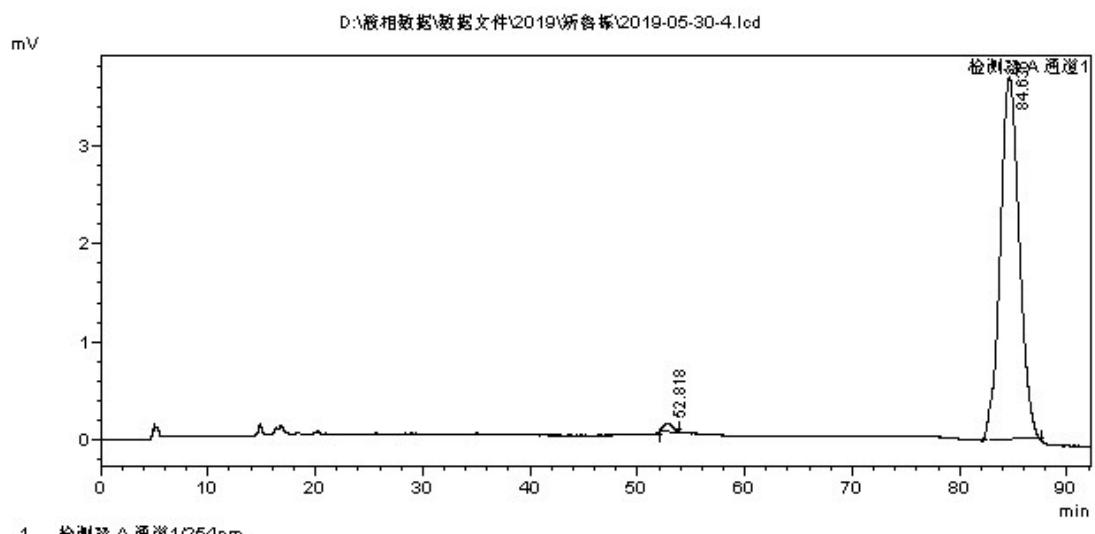
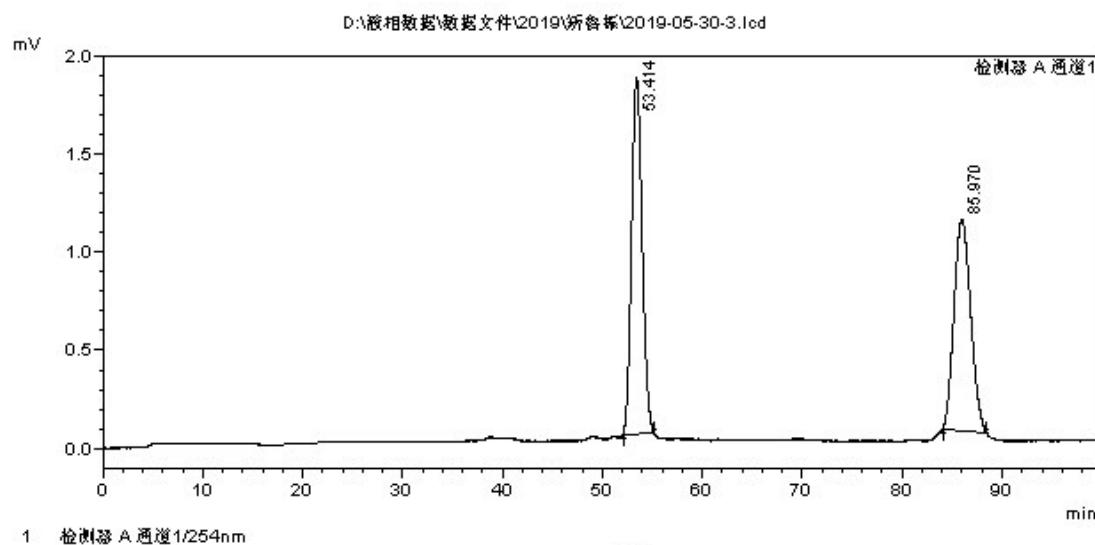


峰表
检测器 A Ch1 254nm

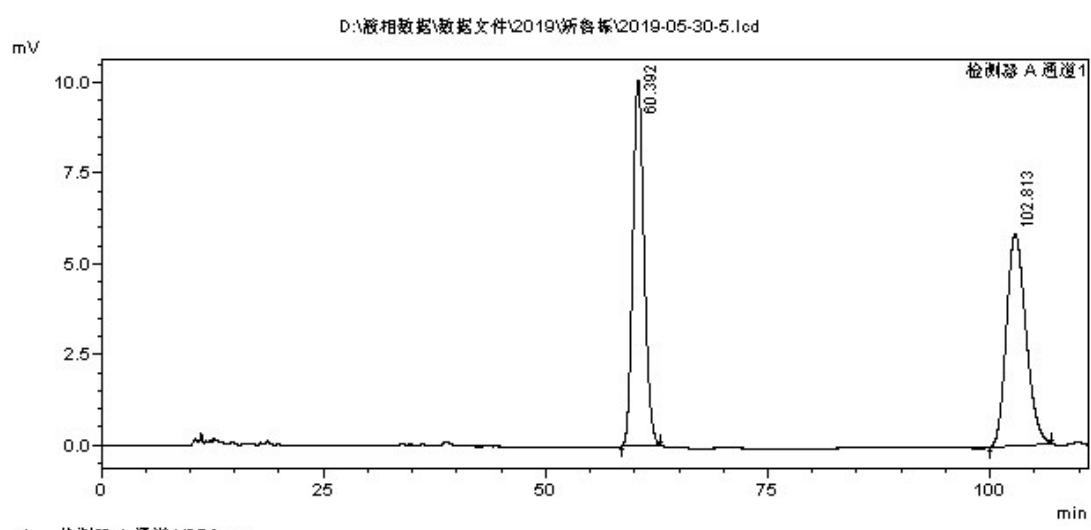
峰#	保留时间	面积	高度	面积 %	高度 %
1	22.527	7155	240	1.381	2.281
2	35.043	510921	10280	98.619	97.719
总计		518075	10520	100.000	100.000



HPLC Conditions: Daicel Chiraldak AD-H, 19% IPA/hexanes, 0.6 mL/min

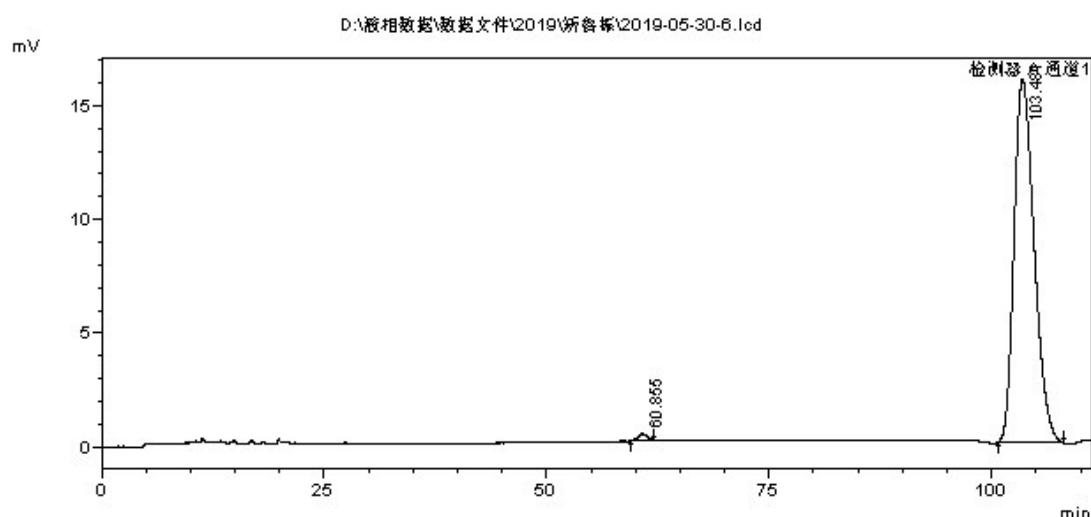


HPLC Conditions: Daicel Chiralpak AD-H, 19% IPA/hexanes, 0.6 mL/min



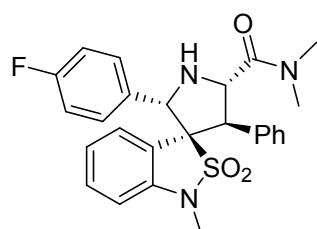
峰表
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	60.392	889680	10074	49.879	63.265
2	102.813	894015	5850	50.121	36.735
总计		1783695	15924	100.000	100.000

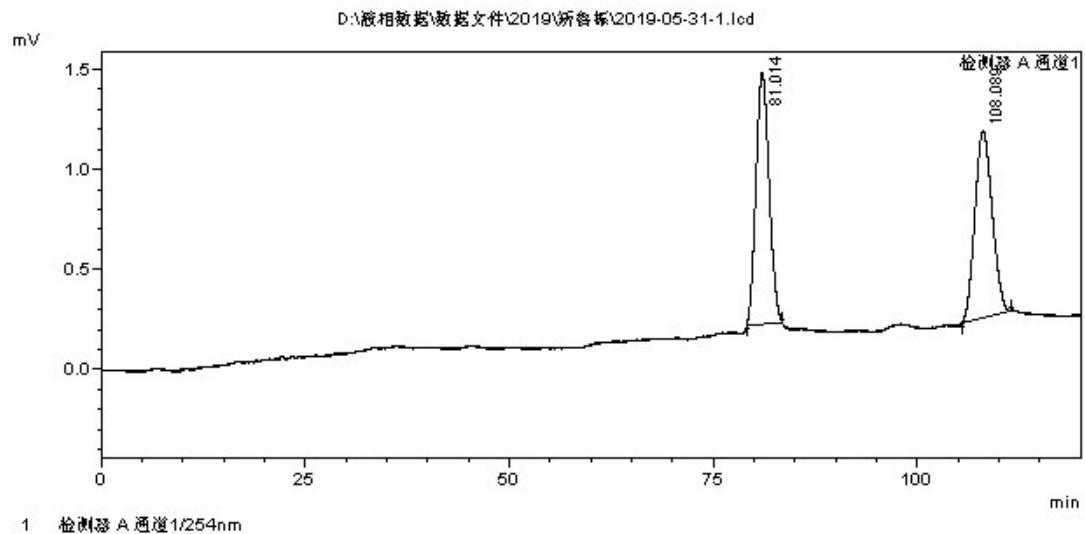


峰表
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	60.855	22537	289	0.888	1.777
2	103.481	2514687	15974	99.112	98.223
总计		2537224	16263	100.000	100.000

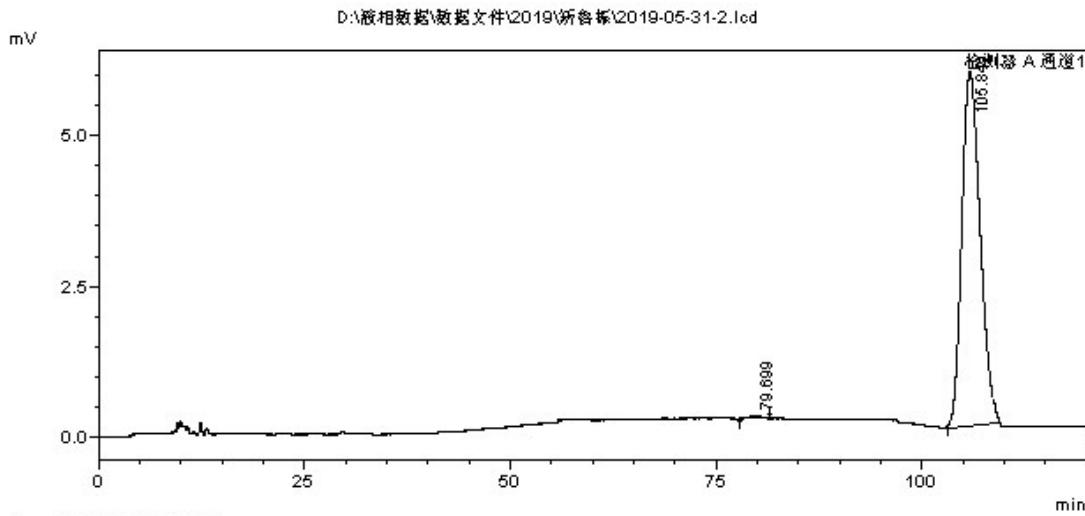


HPLC Conditions: Daicel Chiraldak AD-H, 11% IPA/hexanes, 0.7 mL/min



峰表
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	81.014	141295	1256	50.493	57.259
2	108.089	138533	938	49.507	42.741
总计		279828	2194	100.000	100.000



峰表
检测器 A Ch1 254nm

峰#	保留时间	面积	高度	面积 %	高度 %
1	79.699	4374	43	0.512	0.742
2	105.849	849572	5711	99.488	99.258
总计		853946	5754	100.000	100.000