Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.

Supporting Information-I

Asymmetric synthesis of perhydroepoxyethanoindole cores *via* sequential [4+2]-addition/reduction/fluoroannulation reactions

Madavi S. Prasad,*[a] and Murugesan Sivaprakash [a]

Asymmetric Synthesis and Catalysis Laboratory, Department of Chemistry, Central University of Tamil Nadu, Thiruvarur, 610 005, India

shivaprasad@cutn.ac.in* and *shivacutn@gmail.com

Table of Contents

1. EXPERIMENTAL SECTION

1.1 General Experimental Procedures

Nuclear Magnetic Resonance Spectroscopy: ^{1}H NMR spectra were acquired on Bruker AVIII400 (400 MHz) spectrometer and were referenced to TMS and residual non-deuterated solvent peak in CDCl3 (δ = 7.26). Chemical shifts (δH and δC) are reported in parts per million (ppm), with signal splitting recorded as singlet (s), doublet (d), triplet (t), quartet (q), quintet (quint), and multiplet and unresolved peaks (m). Coupling constants (*J*) are mentioned in Hz and are presented as observed. ^{13}C NMR spectra were obtained on Bruker AVIII400 (100 MHz) spectrometers and were referenced to solvent peaks in CDCl3 (δ = 77.0). Where diastereomeric mixtures are formed, data is given for the major diastereomer.

Mass Spectrometry: High-resolution mass spectra (HRMS) were recorded by the Thermo Fisher spectrometer using electrospray ionization (ESI^{+}). The parent ion$[M+H]^{+}$ $[M+Na]^{+}$ is calculated to 4 decimal places from the molecular formula, and all values are within a tolerance of 5 ppm.

Specific rotations: Optical rotations were recorded on an Anton Parr MCP100 polarimeter with a path length of 1 dm (using the sodium D line, 589 nm). Specific rotations ($[\alpha]^{D}$) are reported in units of 10^{-1} deg cm^{2} g^{-1}. Concentrations are reported in g/mL. Temperatures are reported at °C (typically 25 °C).

Infrared Spectroscopy: Absorption spectra were obtained on a Shimadzu FT-IR spectrometer. Wavelengths of maximum absorbance (vmax) are quoted in wavenumbers (cm^{1}). Only selected characteristic IR absorption data are provided for each compound.

High-Performance Liquid Chromatography: Chromatograms were obtained using Shimadzu UFLC SPD-M20A with a prominence diode array detector on a selected 254nm channel.

Single Crystal XRD: Data was collected from the Sophisticated Analytical Instrumental Facility, Indian Institute of Technology Madras- Chennai.

Materials*:*

Unless otherwise stated, all reactions were carried out in oven-dried glassware using anhydrous reaction solvents. All other commercially available reagents and solvents were either used as received and/or dried and purified before use using standard procedures.

General Procedure A: *Preparation of pyrrolidine-tethered dienals*

1a-c were prepared by following the reported literature procedure.[1]

General Procedure B: *Preparation of pyrazolone enophiles*

2a-2y were synthesized using a literature report.[2]

General Procedure C: ***[4+2]-addition/reduction and fluoroannulation reaction:***

To an oven oven-dried glass vail catalyst D-DPPOTMS (0.2 equiv.), benzoic acid (0.2 equiv.) and the pyrrolidine exocyclicdienal **1** (1.2 equiv.) in toluene (0.67 M) were stirred for 10 minutes. Then the olefinic pyrazolone **2** (1.0 equiv.) was added, and the resulting mixture was stirred at ambient temperature for 5 to 12 hours; after completion of the reaction monitored by TLC, methanol (0.025 M), and $NaBH_4$ (1.5 equiv.) were added at 0° C. After the reduction (5 to 10 min), the mixture was quenched with saturated $NaHCO_3$, extracted using EtOAc, and concentrated at reduced pressure. Further, the crude product without column purification was reacted with selectfluor (2.0 equiv.) and $NaHCO_3$ in acetone (0.1 M) for 1 hour at ambient temperature. The final crude product obtained was purified by column chromatography using silica gel 100-200 mesh and ethylacetate/ hexane (4:6) as stationary and mobile faces, respectively.

General Procedure D: ***[4+2]-addition/reduction and detosylative aromatization:***

To an oven oven-dried glass vail catalyst D-DPPOTMS (0.2 equiv.), benzoic acid (0.2 equiv.) and the pyrrolidine exocyclicdienal **1** (1.2 equiv.) in toluene (0.67 M) were stirred for 10 minutes. Then the olefinic pyrazolone **2** (1.0 equiv.) was added, and the resulting mixture was stirred at ambient temperature for 5 to 12 hours; after completion of the reaction monitored by TLC, methanol (0.025 M), and $NaBH_4$ (1.5 equiv.) were added at 0° C. After the reduction (5 to 10 min), the mixture was quenched with saturated $NaHCO_3$, extracted using EtOAc, and concentrated at reduced pressure. Further, the crude product without column purification was reacted with NBS (2.0 equiv.) in acetone (0.1 M) for 15 min at 0^oC.

General Procedure E: ***[4+2]-addition/reduction and detosylative bromoannulation reaction:***

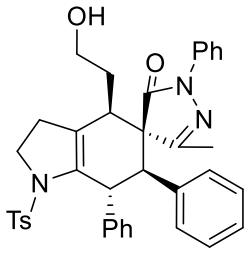
To an oven oven-dried glass vail catalyst D-DPPOTMS (0.2 equiv.), benzoic acid (0.2 equiv.) and the pyrrolidine exocyclicdienal **1** (1.2 equiv.) in toluene (0.67 M) were stirred for 10 minutes. Then the olefinic pyrazolone **2** (1.0 equiv.) was added, and the resulting mixture was stirred at ambient temperature for 5 to 12 hours; after completion of the reaction monitored by TLC, methanol (0.025 M), and $NaBH_4$ (1.5 equiv.) were added at 0° C. After the reduction (5 to 10 min), the mixture was quenched with saturated $NaHCO_3$, extracted using EtOAc, and concentrated at reduced pressure. Further, the crude product without column purification was reacted with NBS (2.0 equiv.) in acetone (0.1 M) for 5 min at ambient temperature. The final crude product obtained was purified by flash column chromatography using silica gel 100-200 mesh and ethylacetate/ hexane (3:7) as stationary and mobile faces, respectively.

temperature. The final crude product obtained was purified by flash column chromatography using silica gel 100-200 mesh and ethylacetate/hexane (3:7) as stationary and mobile faces, respectively.

References

1) a) D. C. Braddock, R. Bhuva, D. S. Millan, Y. Perez-Fuertes, C. A. Roberts, R. N. Shepperd, S. Solanki, E. S. E. Stokes, A. J. P. White, *Org. Lett.* 2007, **9**, 3, 445-448. b) V. Chintalapudi, E. A. Galvin, R. L. Greenaway, E. A. Anderson, *Chem. Commun.,* 2016, **52**, 693. c) A. Mekareeya, P. R. Walker, A. Couce-Rios, C. D. Campbell, A. Steven, R. S. Paton, E. A. Anderson, *J. Am. Chem. Soc.,* 2017, **139**, 10104−10114. d) M. S. Prasad, M. Sivaprakash, and A. Palanichamy, *Org. Biomol. Chem*., 2022, **20**, 6329–6333.
2) Y. Zhou, N. Chen, Y. Cheng, X. Cai, *J. Vis. Exp.,*2019**, 144**, 59155.

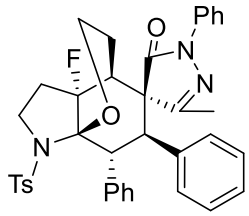
(4R,5R,6R,7R)-4-(2-hydroxyethyl)-3'-methyl-1',6,7-triphenyl-1-tosyl-1,2,3,4,6,7-hexahydrospiro[indole-5,4'-pyrazol]-5'(1'H)-one (4a):



(−)-**4a**

Prepared by following general procedure **C** intermediate, purified by column chromatography using EtOAc/hexane and isolated product **4a** in 90% yield as a white solid with **M. P.** 160-164 °C. **$[\alpha]_D^{25}$ = -140.804 ($CHCl_3$, *c* = 0.34 g/100mL)**; IR (neat) ν_{max} 3495, 2924, 1697, 1496, 1157 and 686. cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (2H, d, *J* = 8.2 Hz), 7.80 (2H, d, *J* = 7.6 Hz), 7.41 (2H, t, *J* = 7.6 Hz), 7.32 (2H, d, *J* = 8.0 Hz), 7.23-7.19 (1H, m), 7.09-6.97 (7H, m), 6.9-6.86 (3H, m), 4.82-4.80 (1H, m), 3.70-3.68 (1H, m), 3.63-3.55 (1H. m), 3.52-3.36 (2H, m), 3.24 (1H, br s), 3.07 (1H, d, *J* = 10.5 Hz), 2.46 (3H, s), 2.04-1.98 (4H, m), 1.88-1.78 (1H, m), 1.49 (1H, m), 1.30-1.22 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135) δ 172.8 (C, N-*C*=O), 161.8 (C, *C*=N), 143.5 (C), 140.7(C), 139.3 (C), 137.8 (C), 136.9 (C), 134.5 (C), 129.3 (2CH), 128.8 (8CH), 128.4(C), 128.2 (CH), 127.7 (2CH), 127.6 (CH), 126.1 (CH), 125.2 (CH), 119.2 (3CH), 61.8 (C), 60.0 (CH_2) 56.3 (CH), 49.8 (CH_2), 44.6 (CH), 36.0 (CH), 31.6 (CH_2), 30.7 (CH_2), 21.7 (CH_3), 14.0 (CH_3); HRMS (ESI) m/z: 654.2397 $[M + Na]^+$, calcd for $C_{38}H_{37}N_3O_4SNa$; Found 654.2376.

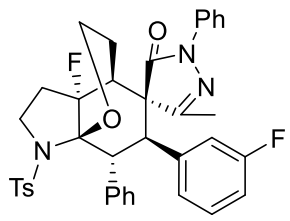
(3a'R,4S,4'S,6'R,7'R,7a'R)-3a'-fluoro-3-methyl-1,6',7'-triphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6a):



(−)-6a

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6a** in 67% yield as a white solid with **M. P**. 95 - 100 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), t_R = 19.388 min (major), t_R = 30.762 min (minor), **$[\alpha]_D^{25}$** = –129.429 ($CHCl_3$, *c* = 0.4 g/100ml for 93% ee); **IR (neat)** ν_{max} 2924, 1705, 1597, 1496, 1342 and 1159 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.27-7.26 (1H, m), 7.24-7.16 (6H, m), 7.07-6.95 (12H, m), 4.84 (1H, sept, *J* = 4 Hz), 4.59 (1H, d, *J* = 11.6 Hz), 3.84-3.76 (3H, m), 3.50 (1H, sext, *J* = 4 Hz), 2.84-2.81 (1H, m), 2.79-2.62 (1H, m), 2.34 (3H, s), 2.32 (3H, d, *J* = 5.12 Hz), 2.23-2.21 (1H, m), 2.18-2.09 (1H, m), 2.03-1.93 (1H, m); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 171.9 (C, N-*C*=O), 162.1 (C, *C*=N), 143.0 (C), 142.2 (C), 136.9 (C), 136.6 (C), 135.7 (C), 131.1 (CH), 129.9 (CH), 128.9 (2CH), 128.4 (2CH), 128.2 (2CH), 127.7 (2CH), 127.5 (CH), 127.4 (2CH), 125.8 (CH), 125.3 (CH), 120.0 (3CH), 108.4 (C, d, *J* = 187.51 Hz), 97.0 (C, d, *J* = 19.9 Hz), 62.4 (C), 59.7 (CH_2), 54.6 (CH), 51.5 (CH, d, *J* = 9.82 Hz), 47.1 (CH_2), 36.2 (CH, *C*-F, d, *J* = 17.9 Hz), 31.5 (CH_2, d, *J* = 26.4 Hz), 28.5 (CH_2, d, *J* = 7.8 Hz), 21.6 (CH_3), 14.1 (CH_3, d, *J* = 4.0 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.67; **HRMS (ESI)** m/z: 672.23028 $[M + Na]^+$, calcd. for $C_{38}H_{36}N_3O_4SFNa$; Found 672.23029.

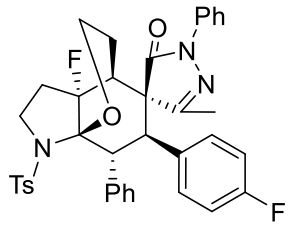
(3a'R,4S,4'S,6'R,7'R,7a'R)-3a'-fluoro-6'-(3-fluorophenyl)-3-methyl-1,7'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6b):



(–)-6b

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6b** in 65% yield as a white solid with **M. P.** 135 - 138 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 13.630 min (major), t_R = 17.696 min (minor), $[\alpha]_D^{25}$ = –73.538 ($CHCl_3$, *c* = 0.7 g/100ml for 93% ee); **IR (neat)** ν_{max} 2924, 1705, 1589, 1496, 1157 and 663 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.35 – 7.33 (3H, m), 7.24 – 7.22 (2H, m), 7.18 - 7.16 (2H, m), 7.09 - 7.08 (7H, m), 6.95 - 6.87 (3H, m), 6.75 – 6.66 (1H, m), 4.82 – 4.75 (1H, m), 4.53 (1H, d, *J* = 11.5 Hz), 3.84 - 3.73 (3H, m), 3.53 – 3.47 (1H, m), 2.84 – 2.60 (2H, m), 2.34 (3H, s), 2.30 (3H, d, *J* = 4.8 Hz), 2.25 – 2.10 (2H, m), 2.03 - 1.95 (1H, m); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 171.8 (C, N-*C*=O), 162.0 (C-F, d, J = 244 Hz), 161.9 (C, C=N), 143.1 (C), 141.9 (C), 138.5 (C, d, *J* = 6 Hz), 136.9 (C), 136.6 (C), 131.1 (CH), 129.1 (CH, d, *J* = 8 Hz), 128.9 (2CH), 128.6 (3CH), 128.2 (2CH), 127.6 (2CH), 126.0 (CH), 125.6 (CH), 125.4 (CH), 119.7 (2CH),116.8 (CH, d, *J* = 21 Hz), 114.5 (CH, d, *J* = 21 Hz), 104.4 (C),102.6 (C), 96.9 (C, d, *J* = 19 Hz), 62.3 (C), 59.6 (CH_2), 54.9 (CH), 51.2 (CH, d, *J* = 10 Hz), 47.2 (CH_2), 36.3 (CH, d, *J* = 18 Hz), 31.5 (CH_2, d, *J* = 26 Hz), 28.5 (CH_2, d, *J* = 7 Hz), 21.5 (CH_3), 15.3 (CH_3, d, *J* = 9 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -113.41, -146.50 ; **HRMS (ESI)** m/z: 668.23891 $[M + H]^+$, calcd. for $C_{38}H_{36}N_3O_4SF_2$; Found 668.23885.

(3a'R,4S,4'S,6'R,7'R,7a'R)-3a'-fluoro-6'-(4-fluorophenyl)-3-methyl-1,7'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6c):

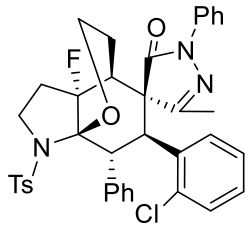


(–)-6c

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6c** in 63% yield as a white solid with **M. P.** 121 - 124 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 13.540 min (major), t_R = 17.999 min (minor), $[\alpha]_D^{25}$ = –105.826 ($CHCl_3$, *c* = 0.17 g/100ml for 91% ee); **IR (neat)** ν_{max} 2924, 1705, 1365, 1157, 756 and 663 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32 (2H, d, *J* = 8 Hz), 7.23 (2H, d, *J* = 8.4 Hz), 7.17-7.15 (3H, m), 7.11-7.08 (8H, m), 6.91-6.67 (3H, m), 4.81 (1H, sept, *J* = 4.8 Hz), 4.52 (1H, d, *J* = 11.6 Hz), 3.89-3.71 (3H, m), 3.50 (1H, sext, *J* = 6.4 Hz), 2.83 (1H, br m), 2.72 (1H, dq, *J* = 10.4, 10.4 Hz), 2.35 (3H, s), 2.31 (3H, d, *J* = 4.8 Hz), 2.14 (1H, t, *J* = 4.8 Hz), 2.05-1.95 (2H, m); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 171.9 (C, N-*C*=O), 162.0 (C, *C*=N), 161.9 (C, d, *J* = 245 Hz), 143.1 (C), 142.0 (C), 136.9 (C), 136.6 (C), 131.5 (C, d, *J* = 8 Hz), 131.1 (CH), 128.9 (3CH), 128.6 (3CH), 128.2 (2CH), 127.6 (2CH), 125.7 (2CH, d, *J* = 44 Hz), 119.7 (3CH), 114.6 (2CH, d, *J* = 21 Hz), 103.4 (C, d, *J* = 186 Hz), 96.9 (C, d, *J* = 19 Hz), 62.4 (C), 59.6 (CH_2), 55.0

(CH), 50.8 (CH, d, *J* = 10 Hz), 47.2 (CH_2), 36.2 (CH, d, *J* = 18 Hz), 31.5 (CH_2, d, *J* = 26 Hz), 28.5 (CH_2, d, *J* = 8 Hz), 21.5 (CH_3), 15.3 (CH_3, d, *J* = 9 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -114.67, -146.56 ; **HRMS (ESI)** m/z: 690.2209 $[M + Na]^+$, calcd. for $C_{38}H_{35}N_3O_4SF_2Na$; Found 690.2221.

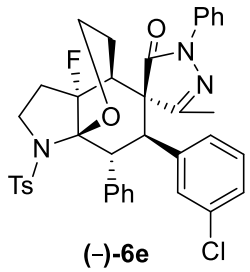
(3a'R,4S,4'S,6'S,7'R,7a'R)-6'-(2-chlorophenyl)-3a'-fluoro-3-methyl-1,7'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6d):



(–)-6d

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6d** in 58% yield as a yellow solid with **M. P**. 135 - 138 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 13.755 min (major), t_R = 17.346 min (minor), **$[\alpha]_D^{25}$** = -101.445 ($CHCl_3$, *c* = 0.33 g/100ml for 88% ee); **IR (neat)** ν_{max} 2924, 1705, 1342, 1157, 1033 and 748 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.99 (1H, d, *J* = 8 Hz), 7.33 (1H, d, *J* = 8 Hz), 7.22 (3H, t, *J* = 7.8 Hz), 7.12 – 7.00 (10H, m), 6.95 – 6.90 (2H, m), 4.94 – 4.87 (1H, m), 4.61 (1H, dd, *J* =4.9, 11.4 Hz), 4.40 (1H, d, *J* = 11.4 Hz), 3.89-3.82 (2H, m), 3.53 – 3.47 (1H, m), 2.88-2.69 (2H, m), 2.36 (3H, d, *J* = 5.8 Hz), 2.34 (3H, s), 2.26 - 2.11 (2H, m), 2.04 – 1.96 (1H, m); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 171.9 (C, N-*C*=O), 162.9 (C, *C*=N), 143.0 (C), 141.1 (C), 136.9 (C), 136.6 (C), 135.1 (C), 134.6 (C), 132.5 (CH), 131.3 (CH), 128.9 (2CH), 128.7 (CH), 128.6 (CH), 128.5 (3CH), 128.2 (2CH), 127.3 (2CH), 126.1 (CH), 125.9 (CH), 125.4 (CH), 119.8 (2CH), 102.9 (*C*-F, d, *J* = 187 Hz), 96.7 (*C*-O, d, *J* = 20 Hz), 61.5 (C), 60.0 (CH_2), 56.6 (CH), 47.2 (CH_2), 45.8 (CH, d, *J* = 10 Hz), 36.5 (CH, d, *J* = 10 Hz), 31.5 (CH_2, d, *J* = 25 Hz), 28.2 (CH_2, d, *J* = 8 Hz), 21.5 (CH_3), 16.8 (CH_3, d, *J* = 11 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -147.53; **HRMS (ESI)** m/z: 706.19130 $[M + Na]^+$, calcd. for $C_{38}H_{35}N_3O_4ClSFNa$; Found 706.19236.

(3a'R,4S,4'S,6'R,7'R,7a'R)-6'-(3-chlorophenyl)-3a'-fluoro-3-methyl-1,7'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6e):

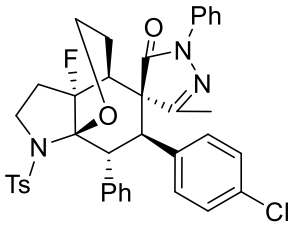


(–)-6e

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6e** in 67% yield as a yellow solid with **M. P**. 111 - 114 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 13.734 min (major), t_R = 18.601 min (minor), **$[\alpha]_D^{25}$** =-102.835 ($CHCl_3$, *c* = 0.24 g/100ml for 92% ee); **IR (neat)** ν_{max} 2916, 1705, 1458, 1157, 1087 and 756 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.30 – 7.27 (3H, m), 7.25 – 7.23 (2H, m), 7.16 – 7.03 (13H, m), 4.82 – 4.75 (1H, m), 4.51 (1H, d, *J* = 11.6 Hz), 3.84 – 3.75 (3H, m), 3.53 - 3.46 (1H, m), 2.84 – 2.82 (1H, m), 2.78 - 2.61 (1H, m), 2.34 (3H, s), 2.30 (3H, d, *J* = 4.9 Hz), 2.24 - 2.21 (1H, m), 2.19 – 2.09 (1H, m), 2.03 – 1.96 (1H, m); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 171.9 (C, N-*C*=O), 161.9 (C, *C*=N), 143.1 (C), 141.9 (C), 136.9 (C), 136.6 (C), 134.6 (C), 133.3 (C), 131.2 (2CH), 131.0 (CH), 128.9 (2CH), 128.6 (2CH), 128.2 (2CH), 127.9 (2CH), 127.7 (2CH),

126.0 (CH), 125.6 (CH), 119.9 (3CH), 103.5 (*C*-F, d, *J* = 186 Hz), 96.9 (*C*-O, d, *J* = 20 Hz), 62.4 (C), 59.6 (CH_2), 54.8 (CH), 50.9 (CH, d, *J* = 10 Hz), 47.2 (CH_2), 36.3 (CH_2, d, *J* = 18 Hz), 31.5 (CH_2, d, *J* = 26 Hz), 28.6 (CH_2, d, *J* = 8 Hz), 21.5 (CH_3), 15.3 (CH_3, d, *J* = 9 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.52; **HRMS (ESI)** m/z: 706.19130 $[M + Na]^+$, calcd. for $C_{38}H_{35}N_3O_4ClSFNa$; Found 706.19245.

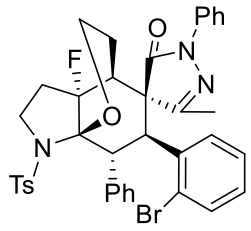
(3a'R,4S,4'S,6'R,7'R,7a'R)-6'-(4-chlorophenyl)-3a'-fluoro-3-methyl-1,7'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6f):



(–)-6f

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6f** in 63% yield as a white solid with **M. P.** 134 - 137 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 13.598 min (major), t_R = 18.270 min (minor), **$[\alpha]_D^{25}$** = -86.136 ($CHCl_3$, *c* = 0.27 g/100ml for 95% ee); **IR (neat)** ν_{max} 2924, 1705, 1496, 1157, 1087 and 756 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.30-7.28 (3H, m), 7.16-6.97 (15H, m), 4.82-4.75 (1H, m), 4.51 (1H, d, *J* = 11.6 Hz), 3.86 – 3.75 (3H, m), 3.53-3.46 (1H, m), 2.83-2.82 (1H, m), 2.78-2.61 (1H, m), 2.34 (3H, s), 2.30 (3H, d, J=4.9Hz), 2.25-2.21 (1H, m), 2.15-2.13 (1H, m), 2.04 – 1.99 (1H,m).**^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 171.8 (C, N-*C*=O), 161.9 (C, *C*=N), 143.1 (C), 141.9 (C), 136.9 (C), 136.6 (C), 134.5 (C), 133.3 (C), 131.2 (2CH), 131.0 (CH), 128.9 (2CH), 128.6 (3CH), 128.2 (2CH), 127.9 (2CH), 127.7 (2CH), 126.0 (CH), 125.6 (CH), 119.9 (2CH), 103.5 (*C*-F, d, *J* =187Hz), 96.9 (*C*-O, d, *J* =20Hz), 62.4 (C), 59.6 (CH_2), 54.8 (CH), 50.9 (CH, d, *J* =10Hz), 47.2 (CH_2), 36.3 (CH_2, d, J=26Hz), 28.6 (CH_2, d, J=8 Hz), 21.5 (CH_3), 15.3 (CH_3, d, J= 9Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.53 ; **HRMS (ESI)** m/z: 706.19130 $[M + Na]^+$, calcd. for $C_{38}H_{35}O_4N_3ClFNaS$; Found 706.19334.

(3a'R,4S,4'S,6'S,7'R,7a'R)-6'-(2-bromophenyl)-3a'-fluoro-3-methyl-1,7'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6g):

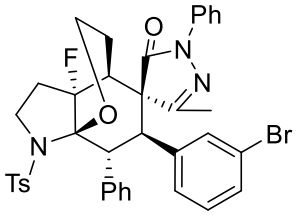


(–)-6g

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6g** in 54% yield as a yellow solid with **M. P**. 225 - 227 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 13.997 min (major), t_R = 17.623 min (minor), **$[\alpha]_D^{25}$** = -140.994 ($CHCl_3$, *c* = 0.25 g/100ml for 92% ee); **IR (neat)** ν_{max} 2924, 1705, 1342, 1157, 1087 and 748 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.0 (1H, d, *J* = 7.8 Hz), 7.33 (2H, d, *J* = 8.1 Hz), 7.24 – 7.20 (3H, m), 7.12 – 7.05 (1H, m), 6.85 (1H, t, *J* = 7.3 Hz), 4.91 – 4.84 (1H, m), 4.53 (1H, dd, *J* = 5.1, 11.3 Hz), 4.37 (1H, d, *J* = 11.2 Hz), 3.87 - 3.82 (2H, m), 3.54 – 3.48 (1H, m), 2.85 - 2.68 (2H, m), 2.41 (3H, d, *J* = 5.8 Hz), 2.34 (4H, s), 2.21 - 2.11 (1H, m), 2.02 – 1.98 (1H, m); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 171.9 (C, N-*C*=O), 162.8 (C, *C*=N), 143.0 (C),

140.9 (C), 136.9 (C), 136.6 (C), 136.5 (C), 132.8 (CH), 132.2 (CH), 131.4 (CH), 128.9 (CH), 128.9 (2CH), 128.5 (3CH), 128.2 (2CH), 127.3 (2CH), 126.7 (CH), 126.3 (C), 126.0 (CH), 125.3 (CH), 119.8 (2CH), 102.3 (*C*-F, d, *J* = 187 Hz), 96.7 (*C*-O, d, *J* = 20 Hz), 61.4 (C), 60.0 (CH_2), 57.3 (CH), 48.5 (CH, d, *J* = 10 Hz), 47.2 (CH_2), 36.4 (CH, d, *J* = 17 Hz), 31.5 (CH_2, d, *J* = 26 Hz), 28.1 (CH, d, *J* = 8 Hz), 21.5 (CH_3), 17.5 (CH_3, d, *J* = 11 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -147.49; **HRMS (ESI)** m/z: 750.14079 $[M + Na]^+$, calcd. for $C_{38}H_{35}N_3O_4BrSFNa$; Found 750.14014.

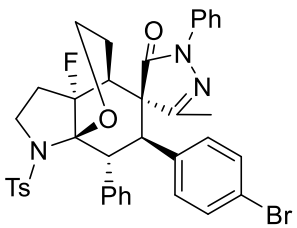
(3a'R,4S,4'S,6'R,7'R,7a'R)-6'-(3-bromophenyl)-3a'-fluoro-3-methyl-1,7'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6h):



(–)-6h

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6h** in 66% yield as a yellow solid with **M. P.** 201 - 204 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 13.637 min (major), t_R = 17.746 min (minor), **$[\alpha]_D^{25}$** = –86.972 ($CHCl_3$, *c* = 0.29 g/100ml for 91% ee); **IR (neat)** ν_{max} 2924, 1705, 1496, 1342, 1157 and 748 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.35 (2H, d, *J* = 7.9 Hz), 7.27 (1H, s), 7.25 - 7.23 (3H, m), 7.17 – 7.07 (11H, m), 6.91 – 6.87 (1H, m), 4.79 – 4.72 (1H, m), 4.52 (1H, d, *J* = 11.5 Hz), 3.83 - 3.72 (3H, m), 3.54 – 3.48 (1H, m), 2.84 - 2.82 (1H, m), 2.79 – 2.59 (1H, m), 2.35 (3H, s), 2.30 (3H, d, *J* = 4.7 Hz), 2.26 - 2.23 (1H, m), 2.19 – 2.10 (1H, m), 2.02 – 1.94 (1H, m).**^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 171.7 (C, N-*C*=O), 161.7 (C, *C*=N), 143.1 (C), 141.7 (C), 138.4 (C), 136.9 (C), 136.6 (C), 132.8 (C), 131.0 (CH), 130.7 (CH), 129.2 (CH), 128.9 (2CH), 128.5 (4CH), 128.2 (2CH), 127.7 (2CH), 126.1 (CH), 125.5 (CH), 119.7 (3CH), 103.6 (C-F, d, *J* = 187 Hz), 96.9 (C-O, d, *J* = 19 Hz), 62.3 (C), 59.5 (CH_2), 54.9 (CH), 51.2 (CH, d, *J* = 10 Hz), 47.1 (CH_2), 36.2 (CH, d, *J* = 18 Hz), 31.5 (CH_2, d, *J* = 27 Hz), 28.4 (CH_2, d, *J* = 7 Hz), 21.5 (CH_3), 15.3 (CH_3, d, *J* = 9Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.28 ; **HRMS (ESI)** m/z: 750.14079 $[M + Na]^+$, calcd. for $C_{38}H_{35}O_4N_3BrFNaS$; Found 750.14083.

(3a'R,4S,4'S,6'R,7'R,7a'R)-6'-(4-bromophenyl)-3a'-fluoro-3-methyl-1,7'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6i):

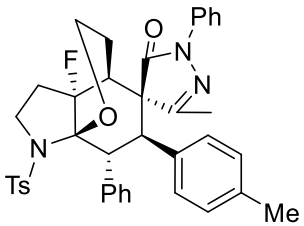


(–)-6i

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6i** in 62% yield as a white solid with **M. P.** 204 - 207 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 70:30, flow rate 0.5 mL/min, λ = 254 nm), t_R = 18.073 min (major), t_R = 29.955 min (minor), **$[\alpha]_D^{25}$** = –138.142 ($CHCl_3$, *c* = 1.2 g/100ml for 96% ee); **IR (neat)** ν_{max} 2926, 1701, 1597, 1454, 1278 and 1159 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.29-7.25 (5H, m), 7.19-7.15 (4H, m), 7.13-7.04 (8H, m), 6.98 (1H, br s), 4.78 (1H, sept, *J* = 3.2

Hz), 4.51 (1H, d, *J* = 11.6 Hz), 3.84-3.73 (3H, m), 3.50 (1H, sext, J=6.56 Hz), 2.85-2.80 (1H, m), 2.70 (1H, dq, J=13.2, 13.2 Hz), 2.34 (3H, s), 2.30 (3H, d, J=4.88Hz), 2.25-2.09 (2H, m), 2.02-1.93 (1H, m).**^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 171.9 (C, N-*C*=O), 161.9 (C, *C*=N), 143.1 (C), 141.9 (C), 136.9 (C), 136.6 (C), 135.1 (C), 131.5 (CH), 131.1 (CH), 130.9 (2CH), 129.0 (2CH), 128.6 (3CH), 128.2 (2CH), 127.7 (2CH), 126.0 (CH), 125.6 (CH), 121.6 (C), 120.0 (3CH), 103.5 (C, d, J=186.4Hz), 96.9 (C, d, J=19.6Hz), 62.3 (C), 59.6 (CH_2), 51.0 (CH, d, J=10Hz), 47.2 (CH_2), 36.3 (CH, d, J=18Hz), 31.5 (CH_2, d, J=26.3 Hz), 28.5 (CH_2, d, J=7.7 Hz), 21.5 (CH_3), 15.3 (CH_3, d, J= 8.7Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.48 ; **HRMS (ESI)** m/z: 750.1408 $[M + Na]^+$, calcd. for $C_{38}H_{35}O_4N_3BrFNaS$; Found 750.1409.

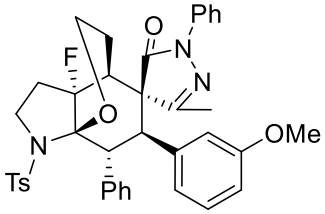
(3a'R,4S,4'S,6'R,7'R,7a'R)-3a'-fluoro-3-methyl-1,7'-diphenyl-6'-(p-tolyl)-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6j):



(–)-6j

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6j** in 59% yield as a white solid with **M. P.** 127 - 130 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 14.454 min (major), t_R = 20.768 min (minor), **$[\alpha]_D^{25}$** = -97.591 ($CHCl_3$, *c* = 0.18 g/100ml for 95% ee); **IR (neat)** ν_{max} 2924, 1705, 1597, 1365, 1157 and 756 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.81 – 7.58 (1H, m), 7.33 – 7.30 (1H, m), 7.23 - 7.17 (5H, m), 7.07 - 6.91 (9H, m), 6.85 – 6.83 (2H, m), 4.85 – 4.79 (1H, m), 4.56 (1H, d, *J* = 11.5 Hz), 3.83 - 3.73 (3H, m), 3.53 – 3.46 (1H, m), 2.81 - 2.61 (2H, m), 2.34 (3H, s), 2.30 (3H, d, *J* = 5 Hz), 2.24 - 2.21 (1H, m), 2.17 - 2.11 (1H, m), 2.08 (3H, m), 2.00- 1.92 (1H, m).**^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 172.1 (C, N-*C*=O), 162.2 (C, *C*=N), 142.9 (C), 142.4 (C), 137.0 (2C), 136.7 (C), 132.6 (C), 131.0 (CH), 129.6 (2CH), 128.9 (2CH), 128.4 (4CH), 128.2 (2CH), 127.4 (2CH), 125.7 (CH), 125.4 (CH), 120.1 (3CH), 103.4 (C-F, d, *J* =186 Hz), 97.1 (C-O, d, *J* = 19 Hz), 62.5 (C), 59.7 (CH_2), 54.6 (CH), 51.2 (CH, d, *J* = 10 Hz), 47.2 (CH_2), 36.2 (CH, d, J=18 Hz), 31.5 (CH_2, d, *J* = 26 Hz), 28.5 (CH_2, d, *J* = 8 Hz), 21.5 (CH_3), 20.9 (CH_3),15.4 (CH_3, d, J= 9 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.74; **HRMS (ESI)** m/z: 686.24593 $[M + Na]^+$, calcd. for $C_{39}H_{38}O_4N_3FNaS$; Found 686.24556.

(3a'R,4S,4'S,6'R,7'R,7a'R)-3a'-fluoro-6'-(3-methoxyphenyl)-3-methyl-1,7'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6k):

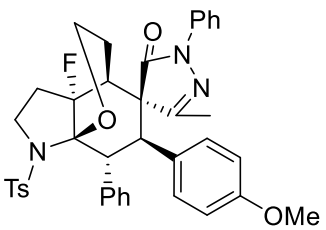


(–)-6k

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6k** in 68% yield as a white solid with **M. P.** 100 - 102 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 14.714 min (major), t_R = 19.747 min (minor), **$[\alpha]_D^{25}$** = –95.716 ($CHCl_3$, *c* =

0.26 g/100ml for 93% ee); **IR (neat)** ν_{max} 2916, 1705, 1597, 1597, 1458 and 1157 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32 (2H, d, *J* = 7.9 Hz), 7.24 – 7.18 (4H, m), 7.08 - 7.07 (8H, m), 6.95 - 6.91 (1H, m), 6.69 – 6.50 (3H, m), 4.85 – 4.78 (1H, m), 4.56 (1H, d, *J* = 11.6 Hz), 3.84 - 3.75 (3H, m), 3.64 (3H, s), 3.53 – 3.46 (1H, m), 2.82 - 2.79 (1H, m), 2.79 – 2.61 (1H, m), 2.34 (3H, s), 2.30 (3H, d, *J* = 4.8 Hz), 2.26 - 2.22 (1H, m), 2.18 - 2.09 (1H, m), 2.00 - 1.95 (1H, m).**^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 171.9 (C, N-*C*=O), 162.1 (C, *C*=N), 158.8 (C), 143.0 (C), 142.1 (C), 137.3 (C), 137.1 (C), 136.6 (C), 131.0 (CH), 128.9 (3CH), 128.5 (CH), 128.4 (3CH), 128.2 (2CH), 127.5 (2CH), 125.8 (CH), 125.3 (CH), 122.4 (CH), 119.9 (3CH), 103.5 (C, d, J=187 Hz), 97.1 (C, d, *J* = 20 Hz), 62.3 (C), 59.6 (CH_2), 55.2 (CH_3), 54.8 (CH), 51.5 (CH, d, *J* = 10 Hz), 47.2 (CH_2), 36.3 (CH, d, J=17 Hz), 31.5 (CH_2, d, *J* = 26 Hz), 28.5 (CH_2, d, *J* = 8 Hz), 21.5 (CH_3), 15.3 (CH_3, d, *J* = 8 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.15; **HRMS (ESI)** m/z: 702.24084 [M + Na]$^+$, calcd. for $C_{39}H_{38}O_5N_3FNaS$; Found 702.24185.

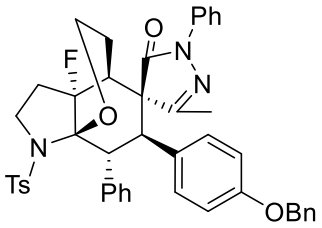
(3a'R,4S,4'S,6'R,7'R,7a'R)-3a'-fluoro-6'-(4-methoxyphenyl)-3-methyl-1,7'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6l):



(–)-6l

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6l** in 63% yield as a white solid with **M. P.** 173 - 175 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 16.279 min (major), t_R = 21.988 min (minor), **$[\alpha]_D^{25}$** = –119.672 ($CHCl_3$, *c* = 1.4 g/100ml for 97% ee); **IR (neat)** ν_{max} 2924, 1701, 1597, 1498, 1249 and 1159 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.31 (2H, d, J=8.4 Hz), 7.22 (2H, d, J=8.4 Hz), 7.19-7.16 (2H, m), 7.12-6.90 (10H, m), 6.57 (2H, br s), 4.81 (1H, sept, *J* = 3.2 Hz), 4.52 (1H, d, J=11.6Hz), 3.83-3.72 (3H, m), 3.59 (1H, s), 3.50 (1H, sext, *J* = 6.8 Hz), 2.83-2.79 (1H, m), 2.69 (1H, dq, J=13.2, 13.2 Hz), 2.34 (3H, s), 2.30 (3H, d, J=4.96 Hz), 2.24-2.21 (1H, m), 2.11-2.08 (1H, m), 2.03-1.92 (1H, m).**^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 172.2 (C, N-*C*=O), 162.2 (C, *C*=N), 158.7 (C), 143.0 (C), 142.4 (C), 137.1 (C), 136.7 (C), 131.1 (CH), 130.9 (C), 128.9 (2CH), 128.5 (3CH), 128.2 (2CH), 127.9(CH), 127.5 (3CH), 125.8 (CH), 125.3 (CH), 120.0 (3CH), 113.1 (CH), 103.5 (C, d, J=186.6 Hz), 97.1 (C, d, J=19.7Hz), 62.6 (C), 59.6 (CH_2), 55.1 (CH_3), 55.0 (CH), 50.8 (CH, d, J=9.7 Hz), 47.2 (CH_2), 36.2 (CH, d, J=19.7 Hz), 31.5 (CH_2, d, J=26.4 Hz), 28.5 (CH_2, d, J=7.8 Hz), 21.5 (CH_3), 15.4 (CH_3, d, J= 9 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.58; **HRMS (ESI)** m/z: 702.2408 [M + Na]$^+$, calcd. for $C_{39}H_{38}O_5N_3FNaS$; Found 702.2410.

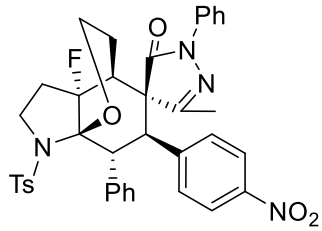
(3a'R,4S,4'S,6'R,7'R,7a'R)-6'-(4-(benzyloxy)phenyl)-3a'-fluoro-3-methyl-1,7'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6m):



(–)-6m

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6m** in 55% yield as a white solid with **M. P.** 108 - 111 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 15.029 min (major), t_R = 20.162 min (minor), $[\alpha]_D^{25}$ = -84.277 ($CHCl_3$, *c* = 0.29 g/100ml for 92% ee); **IR (neat)** ν_{max} 2924, 1705, 1597, 1458, 1157 and 756 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.32 – 7.28 (8H, m), 7.24 – 7.16 (2H, m), 7.10-7.08 (8H, m), 6.66-6.64 (2H, m), 4.86 – 4.79 (3H, m), 4.53 (1H, d, *J* = 11.5 Hz), 3.84 - 3.71 (3H, m), 3.53 – 3.47 (1H, m), 2.82-2.78 (1H, m), 2.78 – 2.61 (1H, m), 2.34 (3H, s), 2.30 (3H, d, *J* = 4.9 Hz), 2.25 - 2.22 (1H, m), 2.16 - 2.12 (1H, m), 1.99 - 1.94 (1H, m). **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 172.1 (C, N-*C*=O), 162.2 (C, *C*=N), 157.9 (C), 142.9 (C), 142.4 (C), 137.1 (C), 136.9 (C), 136.7 (C), 131.1 (CH), 128.9 (2CH), 128.5 (CH), 128.2 (2CH), 127.8 (6CH), 127.5 (2CH), 127.4 (3CH), 125.8 (CH), 125.3 (CH),119.9 (3CH), 114.1 (CH), 103.4 (C-F, d, *J* = 187 Hz), 97.1 (C-O, d, *J* = 19 Hz), 69.8 (CH_2), 62.6 (C), 59.6 (CH_2), 54.9 (CH), 50.8 (CH, d, J=9 Hz), 47.1 (CH_2), 36.2 (CH, d, J=18 Hz), 31.5 (CH_2, d, J=26 Hz), 28.5 (CH_2, d, J=8 Hz), 21.5 (CH_3), 15.4 (CH_3, d, J= 9 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.62; **HRMS (ESI)** m/z: 778.27214 [M + Na]$^+$, calcd. for $C_{45}H_{42}O_5N_3FNaS$; Found 778.27433.

(3a'R,4S,4'S,6'R,7'R,7a'R)-3a'-fluoro-3-methyl-6'-(4-nitrophenyl)-1,7'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6n):

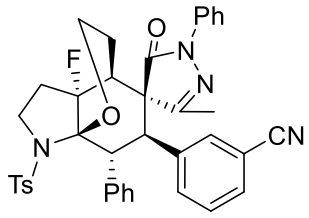


(–)-6n

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6n** in 46% yield as a white solid with **M. P**. 131 - 134 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 20.041 min (major), t_R = 25.652 min (minor), $[\alpha]_D^{25}$ = -92.779 ($CHCl_3$, *c* = 0.21 g/100ml for 95% ee); **IR (neat)** ν_{max} 2924, 1705, 1597, 1342, 1157 and 748 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.91 (2H, d, *J* = 8.4 Hz), 7.42 – 7.30 (4H, m), 7.22 (2H, t, *J* = 7.7 Hz), 7.15 – 7.14 (3H, m), 7.09 – 7.07 (7H, m), 4.83 – 4.76 (1H, m), 4.57 (1H, d, *J* = 11.5 Hz), 3.93 (1H, dd, *J* = 4.6, 11.5 Hz), 3.85 - 3.78 (2H, m), 3.55 – 3.48 (1H, m), 2.87 - 2.86 (1H, m), 2.82 – 2.62 (1H, m), 2.35 (3H, s), 2.33 (3H, d, *J* = 4.8 Hz), 2.22 – 2.20 (1H, m), 2.17 – 2.12 (1H, m), 2.05 – 1.99 (1H, m); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 171.5 (C, N-*C*=O), 161.6 (C, *C*=N), 147.0 (C), 143.9 (C), 143.2 (C), 141.4 (C), 136.7 (C), 136.5 (C), 130.9 (2CH), 128.9 (2CH), 128.7 (3CH), 128.2 (2CH), 127.9 (2CH), 126.3 (CH), 125.7 (CH), 122.9 (2CH), 119.3 (3CH), 103.6 (*C*-F, d, *J* = 187 Hz), 96.7 (*C*-O, d, *J* = 20 Hz),

62.4 (C), 59.5 (CH_2), 54.8 (CH), 51.3 (CH, d, *J* = 10 Hz), 47.2 (CH_2), 36.4 (CH, d, *J* = 19 Hz), 31.5 (CH_2, d, *J* = 26 Hz), 28.6 (CH_2, d, *J* = 8 Hz), 21.5 (CH_3), 15.3 (CH_3, d, *J* = 9 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -147.49; **HRMS (ESI)** m/z: 717.21535 $[M + Na]^+$, calcd. for $C_{38}H_{35}N_4O_6SFNa$; Found 717.41696.

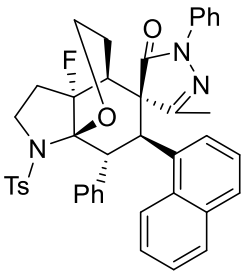
3-((3a'R,4S,4'S,6'R,7'R,7a'R)-3a'-fluoro-3-methyl-5-oxo-1,7'-diphenyl-1'-tosyl-1,2',3',3a',4',5,6',7'-octahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-6'-yl)benzonitrile (6o):



(–)-6o

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6o** in 53% yield as a yellow solid with **M. P**. 180 - 182 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 20.041 min (major), t_R = 25.652 min (minor), **$[\alpha]_D^{25}$** = –73.684 ($CHCl_3$, *c* = 0.4 g/100ml for 64% ee); **IR (neat)** ν_{max} 2924, 1697, 1496, 1327, 1157 and 756 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.36 (2H, d, *J* = 8 Hz), 7.29 – 7.26 (3H, m), 7.25 – 7.18 (3H, m), 7.14 – 7.08 (10H, m), 4.81 – 4.75 (1H, m), 4.53 (1H, d, *J* = 11.6 Hz), 3.85 - 3.76 (3H, m), 3.51 (1H, sext, *J* = 6.8 Hz), 2.86 - 2.61 (2H, m), 2.35 (3H, s), 2.32 (3H, d, *J* = 4.4 Hz), 2.29 – 2.12 (2H, m), 2.04 – 1.97 (1H, m); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 171.6 (C, N-*C*=O), 161.6 (C, *C*=N), 143.2 (C), 141.4 (C), 136.8 (C), 136.5 (C), 134.5 (C), 133.5 (C), 131.4 (CH), 130.9 (CH), 129.0 (3CH), 128.6 (4CH), 128.2 (2CH), 127.8 (2CH), 126.3 (CH), 125.5 (CH), 119.3 (3CH), 103.6 (*C*-F, d, *J* = 186 Hz), 96.8 (*C*-O, d, *J* = 20 Hz), 62.4 (C), 59.5 (CH_2), 54.9 (CH), 51.2 (CH, d, *J* = 11 Hz), 47.2 (CH_2), 36.3 (CH, d, *J* = 18 Hz), 31.5 (CH_2, d, *J* = 27 Hz), 28.5 (CH_2, d, *J* = 8 Hz), 21.5 (CH_3), 15.3 (CH_3, d, *J* = 9 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.36; **HRMS (ESI)** m/z: 697.22553 $[M + Na]^+$, calcd. for $C_{39}H_{35}N_4O_4SFNa$; Found 697.22481.

(3a'R,4S,4'S,6'R,7'R,7a'R)-3a'-fluoro-3-methyl-6'-(naphthalen-1-yl)-1,7'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6p):

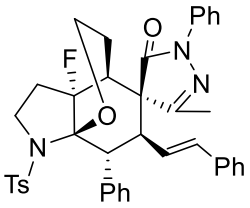


(–)-6p

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6p** in 41% yield as a white solid with **M. P.** 109 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 14.945 min (major), t_R = 21.654 min (minor), **$[\alpha]_D^{25}$** = –84.000 ($CHCl_3$, *c* = 0.10 g/100ml for 92% ee); **IR (neat)** ν_{max} 2854, 1705, 1597, 1458, 1157 and 756 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.17 (1H, d, *J* = 7.4 Hz), 7.56 – 7.38 (6H, m), 7.16 - 7.12 (5H, m), 7.09 – 7.07 (6H, m), 6.93 – 6.86 (3H, m), 4.91 – 4.84 (2H, m), 4.67 (1H, d, *J* = 11.2 Hz), 4.00 - 3.83 (3H, m), 3.60 – 3.53 (1H, m), 2.88 - 2.85 (1H, m), 2.76 – 2.68 (1H, m), 2.34 – 2.33 (6H, m), 2.26 – 2.17 (1H, m), 2.04 – 1.96 (1H, m). **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 172.2 (C, N-*C*=O), 162.0 (C, *C*=N), 143.0 (C), 141.7 (C), 136.8 (C), 136.6 (C), 133.1 (C), 133.0 (C), 132.5 (C), 130.9 (CH),128.9 (2CH), 128.8 (CH), 128.6 (CH), 128.3 (3CH), 128.2

(2CH), 128.1 (CH), 127.3 (2CH), 125.8 (CH), 125.2 (CH), 125.2 (CH), 124.8 (CH), 124.6 (CH), 121.7 (CH), 119.8 (2CH), 103.7 (C-F, d, *J* = 187 Hz), 97.0 (C-O, d, *J* = 20 Hz), 62.1 (C), 59.8 (CH_2), 57.8 (CH), 47.2 (CH_2), 43.8 (CH, d, *J* = 10 Hz), 36.5 (CH, d, J=18 Hz), 31.6 (CH_2, d, *J* = 26 Hz), 28.4 (CH_2, d, *J* = 8 Hz), 21.5 (CH_3), 16.2 (CH_3, d, *J* = 10 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.17; **HRMS (ESI)** m/z: 772.24593 $[M + Na]^+$, calcd. for $C_{42}H_{38}O_4N_3FNaS$; Found 722.24455.

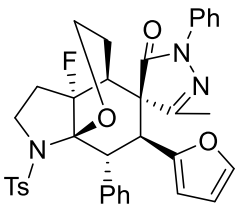
(3a'R,4S,4'S,6'S,7'R,7a'R)-3a'-fluoro-3-methyl-1,7'-diphenyl-6'-((E)-styryl)-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6q):



(–)-6q

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6q** in 53% yield as a white solid with **M. P.** 171 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 15.088 min (major), t_R = 17.582 min (minor), **$[\alpha]_D^{25}$** = –57.304 ($CHCl_3$, *c* = 0.19 g/100ml for 95% ee); **IR (neat)** ν_{max} 2924, 1705, 1597, 1496, 1157 and 663 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.64 (2H, d, *J* = 7.9 Hz), 7.30 – 7.20 (4H, m), 7.20 - 7.19 (3H, m), 7.14 – 7.07 (8H, m), 6.95 – 6.93 (2H, m), 5.98 – 5.91 (1H, m), 5.63 (1H, d, *J* = 15.6 Hz), 4.90 – 4.83 (1H, m), 4.04 (1H, d, *J* = 10.7 Hz), 3.85 - 3.80 (2H, m), 3.53 – 3.46 (1H, m), 3.21 – 3.14 (1H, m), 2.80 – 2.63 (2H, m), 2.35 (3H, s), 2.21 (3H, d, *J* = 5.2 Hz), 2.13 – 2.00 (3H, m). **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 172.5 (C, N-*C*=O), 162.8 (C, *C*=N), 142.9 (C), 142.6 (C), 137.4 (C), 136.7 (C), 136.5 (C), 134.2 (CH), 131.1 (CH), 128.9 (2CH), 128.7 (3CH), 128.3 (2CH), 128.2 (2CH), 127.8 (2CH), 127.4 (CH), 127.2 (CH), 126.4 (2CH), 126.0 (CH), 125.5 (CH), 119.9 (2CH), 102.9 (C-F, d, *J* = 186 Hz), 96.5 (C-O, d, *J* = 20 Hz), 61.5 (C), 59.7 (CH_2), 54.0 (CH), 49.0 (CH, d, *J* = 10 Hz), 47.2 (CH_2), 36.6 (CH, d, *J* = 18 Hz), 31.3 (CH_2, d, *J* = 25 Hz), 28.7 (CH_2, d, *J* = 8 Hz), 21.5 (CH_3), 15.3 (CH_3, d, *J* = 10 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -147.88; **HRMS (ESI)** m/z: 698.24593 $[M + Na]^+$, calcd. for $C_{40}H_{38}O_4N_3FNaS$; Found 698.24741.

(3a'R,4S,4'S,6'S,7'R,7a'R)-3a'-fluoro-6'-(furan-2-yl)-3-methyl-1,7'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6r):

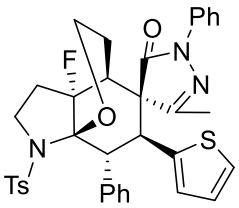


(–)-6r

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6r** in 61% yield as a white solid with **M. P.** 118 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 15.638 min (major), t_R = 27.233 min (minor), **$[\alpha]_D^{25}$** = –53.830 ($CHCl_3$, *c* = 0.14 g/100ml for 95% ee); **IR (neat)** ν_{max} 2924, 1712, 1597, 1357, 1157 and 756 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.47 (2H, d, J=7.6 Hz), 7.28-7.26 (2H, m), 7.24 - 7.23 (2H, m), 7.13 - 7.07 (8H, m), 6.89 (2H, d, *J* = 4.4 Hz), 6.70 (1H, t, *J* = 4.3 Hz), 4.80 – 4.73 (1H, m), 4.47 (1H, d, *J* = 11.5 Hz), 4.09 (1H, dd, *J* = 4.5, 11.4 Hz), 3.81 - 3.67 (2H, m), 3.51 – 3.44 (1H, m),

2.84 - 2.80 (1H, m), 2.77 – 2.57 (1H, m), 2.34 (3H, s), 2.28 (3H, d, *J* = 4.6 Hz), 2.25 - 2.08 (2H, m), 2.01 - 1.93 (1H, m);**^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 171.7 (C, N-*C*=O), 162.6 (C, *C*=N), 150.6 (C), 143.0 (C), 142.0 (C), 141.7 (CH), 137.4 (C), 136.6 (C), 130.9 (CH), 128.9 (2CH), 128.6 (3CH), 128.3 (2CH), 127.6 (2CH), 126.2 (CH), 125.2 (CH), 119.7 (2CH), 110.2 (CH), 109.0 (CH), 103.4 (C-F, d, *J* = 187 Hz), 96.5 (C-O, d, *J* = 19 Hz), 61.2 (C), 59.3 (CH_2), 53.3 (CH), 47.1 (CH_2), 45.2 (CH, d, *J* = 10 Hz), 36.3 (CH, d, *J* = 18 Hz), 31.3 (CH_2, d, *J* = 27 Hz), 28.5 (CH_2, d, *J* = 7 Hz), 21.5 (CH_3), 14.9 (CH_3, d, *J* = 8 Hz), **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.29; **HRMS (ESI)** m/z: 662.20954 $[M + Na]^+$, calcd. for $C_{36}H_{34}O_5N_3FNaS$; Found 662.211049.

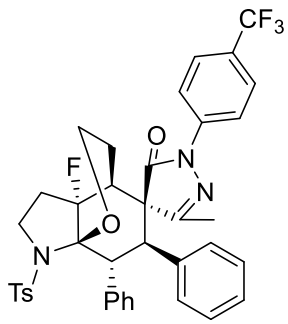
(3a'R,4R,4'S,6'S,7'R,7a'R)-3a'-fluoro-3-methyl-1,7'-diphenyl-6'-(thiophen-2-yl)-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6s):



(–)-6s

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6s** in 52% yield as a white solid with **M. P.** 192 - 200 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 15.609 min (major), t_R = 29.384 min (minor), **$[\alpha]_D^{25}$** = –122.286 ($CHCl_3$, *c* = 1.1 g/100ml for 97% ee); **IR (neat)** ν_{max} 2924, 1705, 1597, 1498, 1278 and 1159 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.47 (2H, d, J=7.64 Hz), 7.29-7.27 (2H, m), 7.25-7.24 (2H, m), 7.13-7.07 (8H, m), 6.90 (2H, d, J=4.44 Hz), 6.71 (1H, t, J=4.4 Hz), 4.77 (1H, sept, *J* = 3.2 Hz), 4.48 (1H, d, *J* = 11.5 Hz), 4.10 (1H, dd, *J* = 13.2, 13.2 Hz), 3.82-3.67 (2H, m), 3.48 (sext, 1H, *J* = 6.5 Hz), 2.84-2.81 (1H, m), 2.67 (1H, dq, *J* = 13.2 13.2 Hz), 2.34 (3H, s), 2.28 (3H, d, *J* = 4.6 Hz), 2.25-2.08 (2H, m), 2.02-1.93 (1H, s).**^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 171.9 (C, N-*C*=O), 162.4 (C, *C*=N), 143.1 (C), 141.9 (C), 138.9 (C), 137.3 (C), 136.6 (C), 131.2 (CH), 128.9 (2CH), 128.6 (3CH), 128.2 (2CH), 127.5 (2CH), 127.2 (CH), 126.5(CH), 126.0 (CH), 125.4 (CH), 124.3 (CH), 119.9 (3CH), 103.5 (C, d, *J* = 186.4 Hz), 96.9 (C, d, *J* = 19.7 Hz), 62.5 (C), 59.5 (CH_2), 56.9 (CH), 47.2 (CH_2), 46.3 (CH, d, *J* = 10.9 Hz), 36.4 (CH, d, *J* = 18 Hz), 31.5 (CH_2, d, *J* = 26.4 Hz), 28.7 (CH_2, d, *J* = 7.8 Hz), 21.5 (CH_3), 15.0 (CH_3, d, *J* = 26.4 Hz), **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.3; **HRMS (ESI)** m/z: 678.1867 $[M + Na]^+$, calcd. for $C_{36}H_{34}O_4N_3FNaS_2$; Found 678.1866.

(3a'R,4S,4'S,6'R,7'R,7a'R)-3a'-fluoro-3-methyl-6'-(4-nitrophenyl)-1,7'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6t):

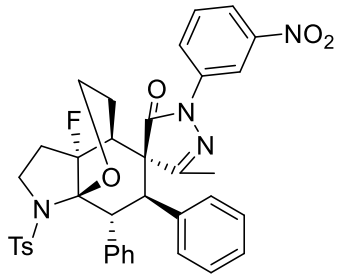


(–)-6t

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6t** in 57% yield as a white solid with **M. P**. 120 - 124 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 11.375 min (major), t_R = 13.771 min (minor), **$[\alpha]_D^{25}$** = -110.024 ($CHCl_3$, *c* =

0.16 g/100ml for 93% ee); **IR (neat)** ν_{max} 2924, 1712, 1612, 1458, 1319 and 1118 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.54 (2H, d, *J* = 8.5 Hz), 7.45 (2H, d, *J* = 8.7 Hz), 7.35 – 7.30 (1H, m), 7.18 – 7.16 (3H, m), 7.08 – 7.02 (10H, m), 4.78 – 4.72 (1H, m), 4.60 (1H, d, *J* = 11.5 Hz), 3.85 – 3.72 (3H, m), 3.54 - 3.47 (1H, m), 2.85 - 2.82 (1H, m), 2.80 – 2.35 (3H, s), 2.33 (3H, d, *J* = 4.7 Hz), 2.20 – 2.19 (1H, m), 2.17 – 2.11 (1H, m), 2.01 – 1.96 (1H, m); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 172.3 (C, N-*C*=O), 162.7 (C, *C*=N), 143.1 (C), 142.0 (C), 139.8 (C), 136.6 (C), 135.5 (C), 131.1 (CH), 129.7 (CH), 128.9 (3CH), 128.2 (2CH), 127.7 (2CH), 127.6 (CH), 127.5 (2CH), 126.5 (*C*, q, *J* = 33 Hz), 125.9 (CH), 125.6 (2CH, q, *J* = 33 Hz), 124.0 (C-F_3, q, *J* = 270 Hz), 118.7 (3CH), 103.5 (C-F, d, *J* = 187 Hz), 97.0 (*C*-O, d, *J* = 19 Hz), 62.8 (C), 59.4 (CH_2), 54.9 (CH), 51.7 (CH, d, *J* = 10 Hz), 47.1 (CH_2), 36.2 (CH, d, *J* = 18 Hz), 31.5 (CH_2, d, *J* = 26 Hz), 28.5 (CH_2, d, *J* = 8 Hz), 21.5 (CH_3), 15.4 (CH_3, d, *J* = 9 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -62.21,-146.19; **HRMS (ESI)** m/z: 740.21766 $[M + Na]^+$, calcd. for $C_{39}H_{35}N_3O_4SF_4Na$; Found 740.21847.

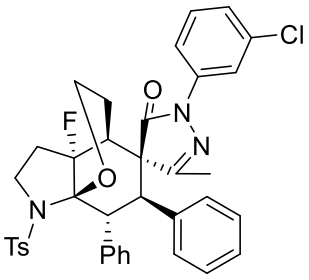
(3a'R,4S,4'S,6'R,7'R,7a'R)-3a'-fluoro-3-methyl-1-(3-nitrophenyl)-6',7'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6u):



(–)-6u

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6u** in 44% yield as a white solid with **M. P**. 213 - 215 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 17.935 min (major), t_R = 26.464 min (minor), **$[\alpha]_D^{25}$** = -82.945 ($CHCl_3$, *c* = 0.24 g/100ml for 85% ee); **IR (neat)** ν_{max} 2916, 1705, 1527, 1342, 1157 and 663 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.25 (1H, s), 7.89 (1H, d, *J* = 8.2 Hz), 7.80 (1H, d, *J* = 8.3 Hz), 7.36 (1H, t, *J* = 8.2 Hz), 7.31 – 7.29 (1H, m), 7.18 - 7.03 (12H, m), 6.94 – 6.90 (1H, m), 4.76 – 4.69 (1H, m), 4.60 (1H, d, *J* = 11.4 Hz), 3.85 – 3.73 (3H, m), 3.54 - 3.48 (1H, m), 2.86 - 2.84 (1H, m), 2.80 – 2.60 (1H, m), 2.35 (6H, s), 2.26 – 2.12 (2H, m), 2.04 – 1.97 (1H, m); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 172.3 (C, N-*C*=O), 162.9 (C, *C*=N), 148.2 (C), 143.1 (C), 141.8 (C), 138.0 (C), 136.6 (C), 135.4 (C), 131.1 (CH), 129.8 (CH), 129.3 (3CH), 128.9 (3CH), 128.2 (2CH), 127.7 (2CH), 127.7 (CH), 127.6 (2CH), 125.9 (CH), 124.4 (CH), 119.4 (CH), 113.9 (2CH), 103.5 (C-F, d, *J* = 187 Hz), 97.1 (*C*-O, d, *J* = 20 Hz), 62.9 (C), 59.3 (C), 55.0 (CH), 51.8 (CH, d, *J* = 9 Hz), 47.1 (CH_2), 36.1 (CH, d, *J* = 18 Hz), 31.5 (CH_2, d, *J* = 26 Hz), 28.5 (CH_2, d, *J* = 8 Hz), 21.5 (CH_3), 15.3 (CH_3, d, *J* = 9 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.07; **HRMS (ESI)** m/z: 717.21535 $[M + Na]^+$, calcd. for $C_{38}H_{35}N_4O_6SFNa$; Found 717.21638.

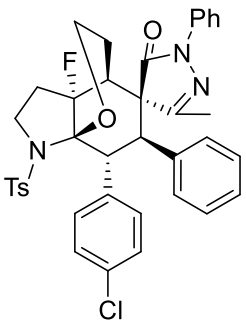
(3a'R,4S,4'S,6'S,7'R,7a'R)-1-(3-chlorophenyl)-3a'-fluoro-3,6'-dimethyl-7'-phenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6v):



(–)-6v

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6v** in 62% yield as a white solid with **M. P.** 209 - 213 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 13.189 min (major), t_R = 17.593 min (minor), **$[\alpha]_D^{25}$** = -107.622 ($CHCl_3$, *c* = 0.17 g/100ml for 93% ee); **IR (neat)** ν_{max} 2924, 1705, 1597, 1473, 1157 and 671 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.37 (1H, br s), 7.32 – 7.28 (1H, m), 7.18 – 7.14 (3H, m), 7.12 – 6.98 (13H, m), 4.80 - 4.73 (1H, m), 4.59 (1H, d, *J* = 11.5 Hz), 3.84 – 3.69 (3H, m), 3.54 - 3.47 (1H, m), 2.83 - 2.81 (1H, m), 2.77 - 2.60 (1H, m), 2.35 (3H, s), 2.32 (3H, d, *J* = 4.8 Hz), 2.19 - 2.18 (1H, m), 2.16 - 2.10 (1H, m), 2.02 – 1.95 (1H,m).**^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 172.1 (C, N-*C*=O), 162.4 (C, *C*=N), 143.1 (C), 142.1 (C), 138.1 (C), 136.6 (C), 135.6 (C), 134.1 (C), 131.0 (CH), 129.8 (CH), 129.5 (CH), 128.9 (2CH), 128.2 (2CH), 127.7 (2CH), 127.6 (CH), 127.5 (2CH), 125.9 (CH), 125.1 (CH), 119.6 (2CH), 117.4 (2CH), 103.5 (*C*-F, d, *J* =186 Hz), 97.0 (*C*-O, d, *J* =20Hz), 62.7 (C), 59.5 (CH_2), 54.8 (CH), 51.6 (CH, d, *J* =10Hz), 47.2 (CH_2), 36.2 (CH, d, *J* = 18 Hz), 31.1 (CH_2, d, *J* = 26 Hz), 28.4 (CH_2, d, *J* = 7 Hz), 21.5 (CH_3), 15.4 (CH_3, d, J= 9Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.35 ; **HRMS (ESI)** m/z: 706.19130 $[M + Na]^+$, calcd. for $C_{38}H_{35}O_4N_3ClFNaS$; Found 706.19226.

(3a'R,4S,4'S,6'R,7'R,7a'R)-7'-(4-chlorophenyl)-3a'-fluoro-3-methyl-1,6'-diphenyl-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6w):

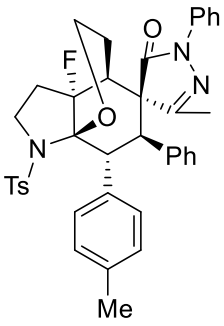


(–)-6w

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6w** in 51% yield as a yellow solid with **M. P.** 205 - 207 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 11.065 min (major), t_R = 16.470 min (minor), **$[\alpha]_D^{25}$** = -123.754 ($CHCl_3$, *c* = 0.29 g/100ml for 90% ee); **IR (neat)** ν_{max} 2924, 1697, 1496, 1342, 1157 and 1087 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.24 – 7.19 (4H, m), 7.13 – 6.99 (14H, m), 4.84 – 4.78 (1H, m), 4.57 (1H, d, *J* = 11.6 Hz), 3.90 – 3.84 (1H, m), 3.74 – 3.67 (2H, m), 3.57 – 3.51 (1H, m), 2.83 – 2.62 (2H, m), 2.37 (3H, s), 2.30 (3H, d, *J* = 5 Hz), 2.20 – 2.07 (2H, m), 2.03 – 1.95 (1H, m).**^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 171.9 (C, N-*C*=O), 161.9 (C, *C*=N), 143.2 (C), 140.8 (C), 136.9 (C), 136.6 (C), 135.4 (C), 132.4 (CH), 131.8 (C), 129.8 (CH), 128.9 (2CH), 128.5 (3CH), 127.9 (2CH), 127.9 (2CH), 127.7 (CH), 127.6 (2CH), 125.5 (CH), 119.9 (3CH), 103.6 (*C*-F, d, *J* =187 Hz), 96.8 (*C*-O, d, *J* = 19 Hz), 62.3 (C), 59.8 (CH_2), 54.0 (CH), 51.5 (CH, d, *J* =10Hz), 47.3 (CH_2), 36.2 (CH, d, *J* = 18 Hz), 31.5 (CH_2, d,

J = 27 Hz), 28.5 (CH_2, d, *J* = 8 Hz), 21.5 (CH_3), 15.4 (CH_3, d, J= 9Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.73 ; **HRMS (ESI)** m/z: 706.19130 $[M + Na]^+$, calcd. for $C_{38}H_{35}O_4N_3ClFNaS$; Found 706.19294.

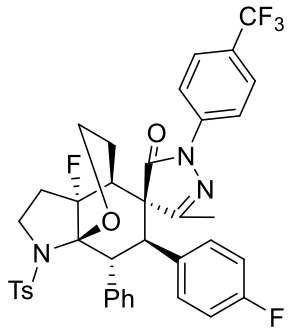
(3a'R,4S,4'S,6'R,7'R,7a'R)-3a'-fluoro-3-methyl-1,6'-diphenyl-7'-(p-tolyl)-1'-tosyl-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6x):



(–)-6x

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6x** in 48% yield as a white solid with **M. P.** 191 - 194 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 13.657 min (major), t_R = 22.293 min (minor), **$[\alpha]_D^{25}$** = -104.332 ($CHCl_3$, *c* = 0.44 g/100ml for 92% ee); **IR (neat)** ν_{max} 2924, 1697, 1597, 1496, 1157 and 663 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.34 – 7.30 (1H, m), 7.23 – 7.18 (4H, m), 7.15 – 6.96 (11H, m), 6.86 (2H, d, *J* = 7.9 Hz), 4.83 – 4.76 (1H, m), 4.56 (1H, d, *J* = 11.4 Hz), 3.85 - 3.72 (3H, m), 3.54 – 3.47 (1H, m), 2.83 - 2.60 (2H, m), 2.35 (3H, s), 2.31 (3H, d, *J* = 5 Hz), 2.26 - 2.20 (4H, m), 2.17 - 2.08 (1H, m), 2.01- 1.92 (1H, m).**^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 172.0 (C, N-*C*=O), 162.1 (C, *C*=N), 142.9 (C), 139.1 (C), 136.9 (C), 136.8 (C), 135.9 (C), 135.2 (C), 130.9 (CH), 129.9 (2CH), 128.8 (2CH), 128.4 (3CH), 128.2 (3CH), 127.7 (2CH), 127.5 (CH), 125.4 (CH), 120.0 (3CH), 103.5 (C-F, d, *J* =187 Hz), 97.1 (C-O, d, *J* = 20 Hz), 62.5 (C), 59.6 (CH_2), 54.3 (CH), 51.5 (CH, d, *J* = 9 Hz), 47.2 (CH_2), 36.3 (CH, d, *J* = 18 Hz), 31.5 (CH_2, d, *J* = 26 Hz), 28.5 (CH_2, d, *J* = 7 Hz), 21.5 (CH_3), 21.1 (CH_3),15.4 (CH_3, d, *J* = 9 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -146.67; **HRMS (ESI)** m/z: 686.24593 $[M + Na]^+$, calcd. for $C_{39}H_{38}O_4N_3FNaS$; Found 686.24442.

(3a'R,4S,4'S,6'R,7'R,7a'R)-3a'-fluoro-6'-(4-fluorophenyl)-3-methyl-7'-phenyl-1'-tosyl-1-(4-(trifluoromethyl)phenyl)-2',3',3a',4',6',7'-hexahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (6y):

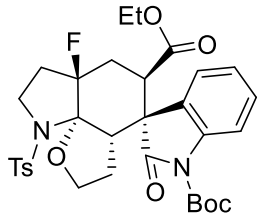


(–)-6y

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6y** in 53% yield as a white solid with **M. P**. 185 - 188 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 65:35, flow rate 0.5 mL/min, λ = 254 nm), t_R = 10.851 min (major), t_R = 12.158 min (minor), **$[\alpha]_D^{25}$** = -148.585 ($CHCl_3$, *c* = 0.89 g/100ml for 96% ee); **IR (neat)** ν_{max} 2924, 1712, 1612, 1159 and 754 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.61 (2H, d, *J* = 8.6 Hz), 7.49 (2H, d, *J* = 8.7 Hz), 7.16 – 7.82 (11H, m), 6.73 (2H, t, *J* = 7.7 Hz), 4.70 (1H, quint, *J* = 6.6 Hz), 4.52 (1H, d, *J* = 11.5 Hz), 3.84 – 3.70 (3H, m), 3.50 (1H, sext, *J* = 6.6 Hz), 2.85 - 2.82 (1H, m), 2.68 (1H, dq, *J* = 13.3 Hz), 2.35 (3H, s), 2.32 – 2.31 (3H, d, *J* = 4.5 Hz), 2.23 – 2.11 (2H, m), 2.03 – 1.94 (1H, m); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 172.2 (C, N-*C*=O), 162.6 (C, *C*=N), 161.9 (C-F, d, *J* = 245.2

Hz), 143.2 (C), 141.7 (C), 139.8 (C), 136.6 (C), 131.6 (C), 131.4 (CH, d, *J* = 8 Hz), 131.0 (CH, d, *J* = 5.6 Hz), 129.0 (3CH), 128.2 (2CH), 127.7 (2CH), 126.7 (*C*, q, *J* = 32.4 Hz), 126.1 (CH), 125.8 (2CH, q, *J* = 3.8 Hz), 124.0 (C-F_3, q, *J* = 270 Hz), 118.6 (3CH), 114.7 (2CH, d, *J* = 21.2 Hz), 103.6 (C-F, d, *J* = 186.8 Hz), 97.0 (*C*-O, d, *J* = 20 Hz), 62.8 (C), 59.3 (CH_2), 55.5 (CH), 50.9 (CH, d, *J* = 10 Hz), 47.1 (CH_2), 36.2 (CH, d, *J* = 18 Hz), 31.5 (CH_2, d, *J* = 26.5 Hz), 28.5 (CH_2, d, *J* = 7.8 Hz), 21.5 (CH_3), 15.3 (CH_3, d, *J* = 8.4 Hz); **^{19}F NMR (376MHz, $CDCl_3$)** δ -62.2, -114.3, -146.19; **HRMS (ESI)** m/z: 758.20824 $[M + Na]^+$, calcd. for $C_{39}H_{34}N_3O_4SF_5Na$; Found 758.20765.

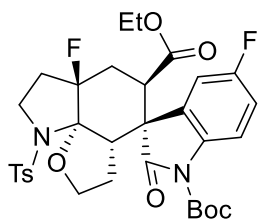
1'-(tert-butyl) 5-ethyl (3aS,4R,5R,6aR,9aS)-6a-fluoro-2'-oxo-9-tosyl-3,3a,5,6,6a,7,8,9-octahydro-2H-spiro[furo[3,2-h]indole-4,3'-indoline]-1',5-dicarboxylate (6'a):



(–)-6'a

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6'a** in 69% yield as a white solid with **M. P**. 110 – 113 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IC column (hexane/EtOAc = 75:25, flow rate 0.5 mL/min, λ = 254 nm), t_R = 11.761 min (major), t_R = 19.739 min (minor), **$[\alpha]_D^{25}$** = –27.450 ($CHCl_3$, *c* = 0.99 g/100ml for 99.9% ee); **IR (neat)** ν_{max} 2978, 1766, 1728, 1477, 1149 and 667 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.84 (1H, d, *J* = 7.2 Hz), 7.72 (2H, d, *J* = 8.4 Hz), 7.49 (1H, d, *J* = 7.2 Hz), 7.33 (1H, ddd, *J* = 1.2, 1.2, 1.2 Hz), 7.28-7.25 (2H, m), 7.18 (1H, ddd, *J* = 1.2, 1.2, 1.2 Hz), 3.99-3.95 (2H, m), 3.86-3.66 (4H, m), 3.46-3.39 (2H, m), 2.80-2.67 (1H, m), 2.61-2.48 (2H, m), 2.41 (3H, s), 2.29-2.21 (1H, m), 2.03-1.90 (2H, m), 1.67 (9H, s), 0.89 (3H, t, *J* = 7.2 Hz); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 176.0 (C, *C*=O), 170.9 (C, *C*=*O*), 149.2 (C, *C*=*O*), 143.9 (C), 138.8 (C), 135.5 (C), 129.6 (C), 129.3 (2CH), 128.7 (CH), 128.6 (2CH), 125.6 (CH), 124.3 (CH), 114.6 (CH), 97.4 (C, d, *J* = 194 Hz), 97.3 (C, d, *J* = 21 Hz), 84.4 (C), 66.3 (CH_2), 61.3 (CH_2), 50.3 (C), 44.6 (CH, d, *J* = 7 Hz), 43.2 (CH), 38.6 (CH), 31.0 (CH_2, d, *J* = 8 Hz), 30.8 (CH_2, d, *J* = 5 Hz), 28.8 (CH_2, d, *J* = 4 Hz), 28.2 ($3CH_3$), 21.6 (CH_3), 13.3 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -159.76; **HRMS (ESI)** m/z: 651.2147 $[M + Na]^+$, calcd. for $C_{32}H_{37}N_2O_8SFNa$; Found 651.2127.

1'-(tert-butyl) 5-ethyl (3aS,4R,5R,6aR,9aS)-5',6a-difluoro-2'-oxo-9-tosyl-3,3a,5,6,6a,7,8,9-octahydro-2H-spiro[furo[3,2-h]indole-4,3'-indoline]-1',5-dicarboxylate (6'b):

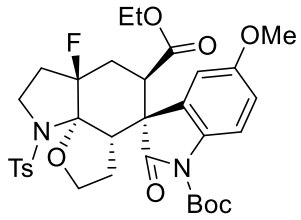


(–)-6'b

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6'b** in 44% yield as a white solid with **M. P**. 111 – 114 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IA column (hexane/EtOAc = 75:25, flow rate 0.5 mL/min, λ = 254 nm), t_R = 11.804 min (minor), t_R = 13.065 min (major), **$[\alpha]_D^{25}$** = –26.560 ($CHCl_3$, *c* = 0.64 g/100ml for 98% ee); **IR (neat)** ν_{max} 2924, 1766, 1728, 1477, 1145 and 667 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ

7.85 (1H, dd, *J* = 4.8, 4.8 Hz), 7.74 (2H, d, *J* = 8.4 Hz), 7.27 (2H, d, *J* = 7.6 Hz), 7.22 (1H, dd, *J* = 2.8, 2.8 Hz), 7.05 (1H, ddd, *J* = 2.8, 2.8, 2.8 Hz), 4.01-3.97 (2H, m), 3.91-3.81 (2H, m), 3.77 (1H, dd, *J* = 7.6, 7.6 Hz), 3.70 (1H, dd, *J* = 4.4, 4.4 Hz), 3.47-3.35 (2H, m), 2.78-2.68 (1H, m), 2.60 (1H, dtd, *J* = 4.4, 4.4, 4.4 Hz), 2.41 (3H, s), 2.39-2.20 (2H, m), 2.02-1.91 (2H, m), 1.66 (9H, s), 0.93 (3H, t, *J* = 7.2 Hz); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 175.6 (C, *C*=O), 170.7 (C, *C*=*O*), 159.2 (C-F, d, *J* = 242 Hz), 149.1 (C, *C*=*O*), 144.0 (C), 135.1 (C), 134.9 (C, d, *J* = 2 Hz), 131.2 (C, d, *J* = 8 Hz), 129.3 (2CH), 128.7 (2CH), 115.7 (CH, d, *J* = 8 Hz), 115.1 (CH, d, *J* = 22 Hz), 113.7 (CH, d, *J* = 25 Hz), 97.3 (C, d, *J* = 194 Hz), 97.2 (C, d, *J* = 21 Hz), 84.6 (C), 66.4 (CH_2), 61.4 (CH_2), 50.5 (C), 44.5 (CH_2, d, *J* = 7 Hz), 43.0 (CH), 38.5 (CH), 30.9 (CH_2, d, *J* = 25 Hz), 30.8 (CH_2, d, *J* = 22 Hz), 28.7 (CH_2, d, *J* = 3 Hz), 28.1 ($3CH_3$), 21.6 (CH_3), 13.4 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -117.41, -159.75; **HRMS (ESI)** m/z: 669.2053 $[M + Na]^+$, calcd. for $C_{32}H_{36}N_2O_8SF_2Na$; Found 669.2062.

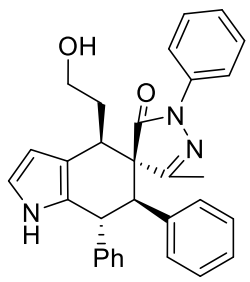
1'-(tert-butyl) 5-ethyl (3aS,4R,5R,6aR,9aS)-6a-fluoro-5'-methoxy-2'-oxo-9-tosyl-3,3a,5,6,6a,7,8,9-octahydro-2H-spiro[furo[3,2-h]indole-4,3'-indoline]-1',5-dicarboxylate (6'c):



(–)-6'c

Prepared by following general procedure **C** purified by column chromatography using EtOAc/hexane and isolated product **6'c** in 45% yield as a white solid with **M. P**. 114 – 117 °C. The enantiomeric excess (*ee*) was determined by chiral stationary phase **HPLC** using a Daicel Chiralpak IA column (hexane/EtOAc = 75:25, flow rate 0.5 mL/min, λ = 254 nm), t_R = 14.047 min (minor), t_R = 15.433 min (major), **$[\alpha]_D^{25}$** = –24.102 ($CHCl_3$, *c* = 0.67 g/100ml for 93% ee); **IR (neat)** ν_{max} 2978, 1766, 1728, 1485, 1153 and 667 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.77 (1H, d, *J* = 9.2 Hz), 7.73 (2H, d, *J* = 8.4 Hz), 7.27 (2H, d, *J* = 8 Hz), 7.04 (1H, d, *J* = 2.4 Hz), 6.86 (1H, dd, *J* = 2.4, 2.4 Hz), 4.0-3.95 (2H, m), 3.87 (3H, s), 3.85-3.75 (3H, m), 3.66 (1H, dd, *J* = 4.4, 4.4 Hz), 3.44 (2H, dd, *J* = 3.2, 3.2 Hz), 2.80-2.67 (1H, m), 2.61-2.43 (2H, m), 2.41 (3H, s), 2.28-2.21 (1H, m), 2.02-1.91 (2H, m), 1.66 (9H, s), 0.91 (3H, t, *J* = 7.2 Hz); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 176.0 (C, *C*=O), 170.8 (C, *C*=*O*), 156.2 (C), 149.2 (C, *C*=*O*), 143.9 (C), 135.5 (C), 132.2 (C), 130.7 (C), 129.3 (2CH), 128.7 (2CH), 115.4 (CH), 113.9 (CH), 111.7 (CH), 97.3 (C, d, *J* = 194 Hz), 97.3 (C, d, *J* = 22 Hz), 84.1 (C), 66.4 (CH_2), 61.3 (CH_2), 55.5 (CH_3), 50.6 (C), 44.7 (CH_2, d, *J* = 7 Hz), 43.2 (CH), 38.6 (CH), 31.1 (CH_2, d, *J* = 4 Hz), 30.8 (CH_2), 28.9 (CH_2, d, *J* = 4 Hz), 28.2 ($3CH_3$), 21.6 (CH_3), 13.3 (CH_3); **^{19}F NMR (376MHz, $CDCl_3$)** δ -159.66; **HRMS (ESI)** m/z: 681.2253 $[M + Na]^+$, calcd. for $C_{33}H_{39}N_2O_9SFNa$; Found 681.2234.

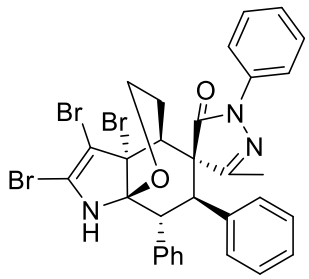
(4R,5R,6R,7R)-4-(2-hydroxyethyl)-3'-methyl-1',6,7-triphenyl-1,4,6,7-tetrahydrospiro[indole-5,4'-pyrazol]-5'(1'H)-one :



(–)-7a

Prepared by following general procedure **D** purified by column chromatography using EtOAc/hexane and isolated product **7a** in 30% yield as a white solid with **M. P**. 95 - 98 °C. **$[\alpha]_D^{25}$** = –250.000 ($CHCl_3$, *c* = 0.1 g/100ml); **IR (neat)** ν_{max} 3332, 2920, 1685, 1492, 1365, 1292 and 698 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.75 (2H, d, *J* = 7.6 Hz), 7.57 (1H, s), 7.36 (2H, t, *J* = 8.4 Hz), 7.19 – 6.81 (12H, m), 6.69 (1H, t, *J* = 2 Hz), 6.17 (1H, t, *J* = 2.8 Hz), 4.86 (1H, d, *J* 10.8Hz), 3.95 (2H, q, *J* = 7.2 Hz), 3.66 (1H, d, *J* = 8.4 Hz), 2.08 (3H, s), 2.01 – 1.96 (2H, m); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 173.1 (C, *C*=O), 162.0 (C, *C*=N), 141.0 (C), 137.8 (C), 137.4 (C), 129.0 (2CH), 128.8 (C), 128.7 (3CH), 128.3 (4CH), 127.5 (CH), 126.9 (CH), 125.0 (CH), 119.2 (3CH), 117.7 (CH), 116.7 (C), 105.6 (CH), 62.7 (C), 61.4 (CH_2), 55.2 (CH), 43.2 (CH), 35.7 (CH), 34.6 (CH_2), 14.2 (CH_3); **HRMS (ESI)** m/z: 498.21520 $[M + Na]^+$, calcd. for $C_{31}H_{29}O_2N_3Na$; Found 498.21195.

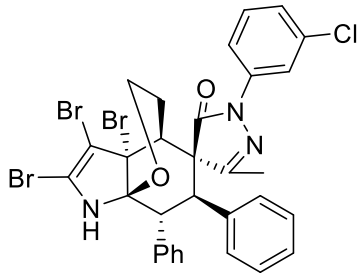
(3a'R,4S,4'S,6'R,7'R,7a'R)-2',3',3a'-tribromo-3-methyl-1,6',7'-triphenyl-3a',4',6',7'-tetrahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one :



(–)-8a

Prepared by following general procedure **E** purified by column chromatography using EtOAc/hexane and isolated product **8a** in 25% yield as a white solid with **M. P**. 111 - 114 °C. **$[\alpha]_D^{25}$** = –80.000 ($CHCl_3$, *c* = 0.1 g/100ml); **IR (neat)** ν_{max} 3267, 2920, 1681, 1597, 1049, and 694 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 8.18 (1H, s), 7.61 (2H, d, *J* = 8 Hz), 7.35 (2H, t, *J* = 7.6 Hz), 7.20 – 6.62 (12H, m), 4.91 (1H, d, *J* = 11.2 Hz), 3.90 – 3.84 (1H, m), 3.76 - 3.70 (1H, m), 3.64 (1H, br s), 3.30 (1H, d, *J* = 10.8 Hz), 2.54 - 2.46 (1H, m), 2.10 (3H, s), 1.81 (1H, sext, *J* = 8.8 Hz); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 173.3 (C, *C*=O), 162.4 (C, *C*=N), 139.7 (C), 137.4 (C), 136.2 (C), 131.0 (C), 129.2 (CH), 128.8 (4CH), 128.5 (2CH), 128.3 (CH), 127.8 (CH), 127.4 (2CH), 125.4 (CH), 119.4 (3CH), 116.3 (C), 100.7 (C), 96.7 (C), 62.6 (C), 61.4 (CH_2), 54.9 (CH), 42.4 (CH), 35.7 (CH), 32.5 (CH_2), 14.4 (CH_3); **HRMS (ESI)** m/z: 656.0342 $[M - Br + Na]^+$, calcd. for $C_{31}H_{27}N_3O_2Br\ ^{81}BrNa$; Found 656.0321.

(3a'R,4S,4'S,6'R,7'R,7a'R)-2',3',3a'-tribromo-1-(3-chlorophenyl)-3-methyl-6',7'-diphenyl-3a',4',6',7'-tetrahydro-1'H-spiro[pyrazole-4,5'-[7a,4](epoxyethano)indol]-5(1H)-one (8b):

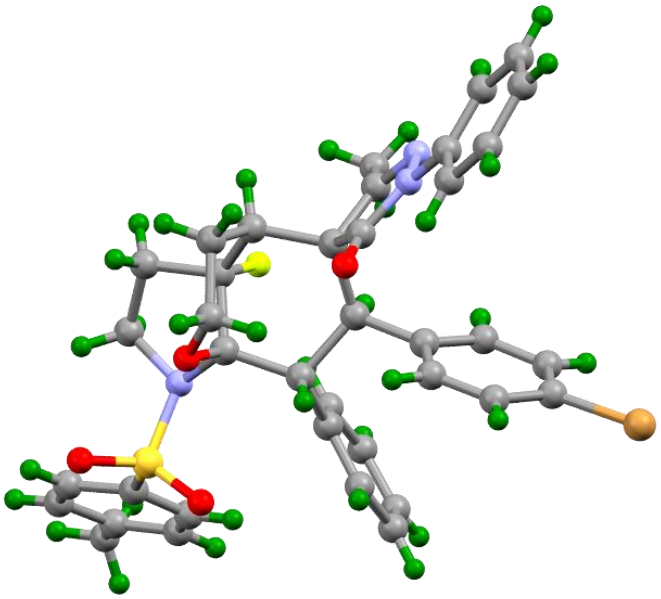


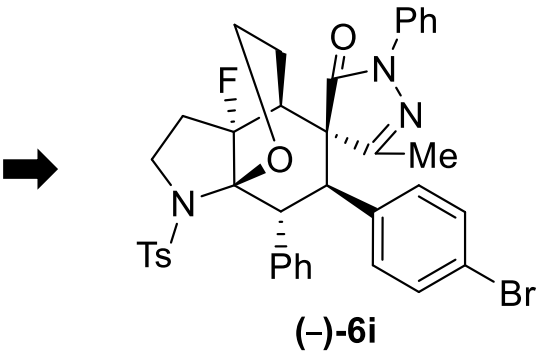
(–)-8b

Prepared by following general procedure **E** purified by column chromatography using EtOAc/hexane and isolated product **8b** in 37% yield as a white solid with **M. P**. 120 - 123 °C. **$[\alpha]_D^{25}$** = –92.647 ($CHCl_3$, *c* = 0.136 g/100ml); **IR (neat)** ν_{max} 3271, 2924, 1689, 1593, 1481 and 698 cm^{-1}; **^{1}H NMR (400 MHz, $CDCl_3$)** δ 7.82 (1H, s), 7.76 (1H, s), 7.66 (1H, d, *J* =*8* Hz), 7.29 (1H, t, *J* =*8* Hz), 7.16 – 7.13 (4H, m), 7.07-6.97 (4H,

m), 4.90 (1H, d, *J* = 11.2 Hz), 3.87 (1H, sept, *J* = 6 Hz), 3.75 - 3.65 (2H, m), 3.34 (1H, d, *J* = 10.8 Hz), 2.50 - 2.40 (1H, m), 2.12 (3H, s), 1.82 (1H, sept, *J* = 9.2 Hz); **^{13}C NMR (100 MHz, $CDCl_3$, DEPT-135)** δ 173.5 (C, *C*=O), 162.7 (C, *C*=N), 139.3 (C), 138.5 (C), 136.0 (C), 134.6 (C), 131.2 (C), 129.9 (2CH), 129.1 (CH), 128.6 (2CH), 128.4 (CH), 127.9 (CH), 127.5 (CH), 125.2 (2CH), 119.1 (2CH), 116.9 (2CH), 116.3 (C), 100.6 (C), 96.9 (C), 62.8 (C), 61.3 (CH_2), 54.7 (CH), 42.3 (CH), 35.8 (CH), 32.4 (CH_2), 14.4 (CH_3); **HRMS (ESI)** m/z: 689.9952 $[M - Br + Na]^+$, calcd. for $C_{31}H_{26}N_3O_2Br^{81}BrClNa$; Found 689.9930.

Single Crystal X-ray data for the product (–)-**6i**





(–)-6i

Identification code	shelx
Empirical formula	C38 H35 Br F N3 O4 S
Formula weight	728.66
Temperature	297(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P 21
Unit cell dimensions	a = 11.2594(6) A alpha = 90 deg. b = 17.7861(11) A beta = 92.839(2) deg. c = 17.1349(10) A gamma = 90 deg.
Volume	3427.2(3) A^3
Z, Calculated density	4, 1.412 Mg/m^3
Absorption coefficient	1.311 mm^-1
F(000)	1504
Crystal size	0.495 x 0.295 x 0.013 mm

Theta range for data collection	3.304 to 25.999 deg.
Limiting indices	-13<=h<=13, -21<=k<=21, -21<=l<=21
Reflections collected / unique	103711 / 13400 [R(int) = 0.1115]
Completeness to theta	= 25.242 99.7 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.738 and 0.663
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	13400 / 1 / 870
Goodness-of-fit on F^2	1.007
Final R indices [I>2sigma(I)]	R1 = 0.0463, wR2 = 0.0849
R indices (all data)	R1 = 0.0718, wR2 = 0.0942
Absolute structure parameter	0.026(8)
Extinction coefficient	n/a
Largest diff. peak and hole	0.255 and -0.399 e.A^-3