Supporting Information for

Diversity through phosphine catalysis identifies octahydro-1,6-naphthyridin-4-ones as activators of endothelium-driven immunity

Daniel Cruz[a,1], *Zhiming Wang*[b,c,1], *Jon Kibbie*[a], Robert L Modlin[d], *and Ohyun Kwon*[b,2]

[a] Department of Medicine, Division of Cardiology, University of California, Los Angeles, A2-237 Center for Health Sciences, Los Angeles, CA 90095-1679

[b] Department of Chemistry and Biochemistry, University of California, Los Angeles, 607 Charles E. Young Drive East, Los Angeles, CA 90095-1569

[c] Current Address: School of Chemical Engineering, Changzhou University, Changzhou 213164, Jiangsu, People's Republic of China

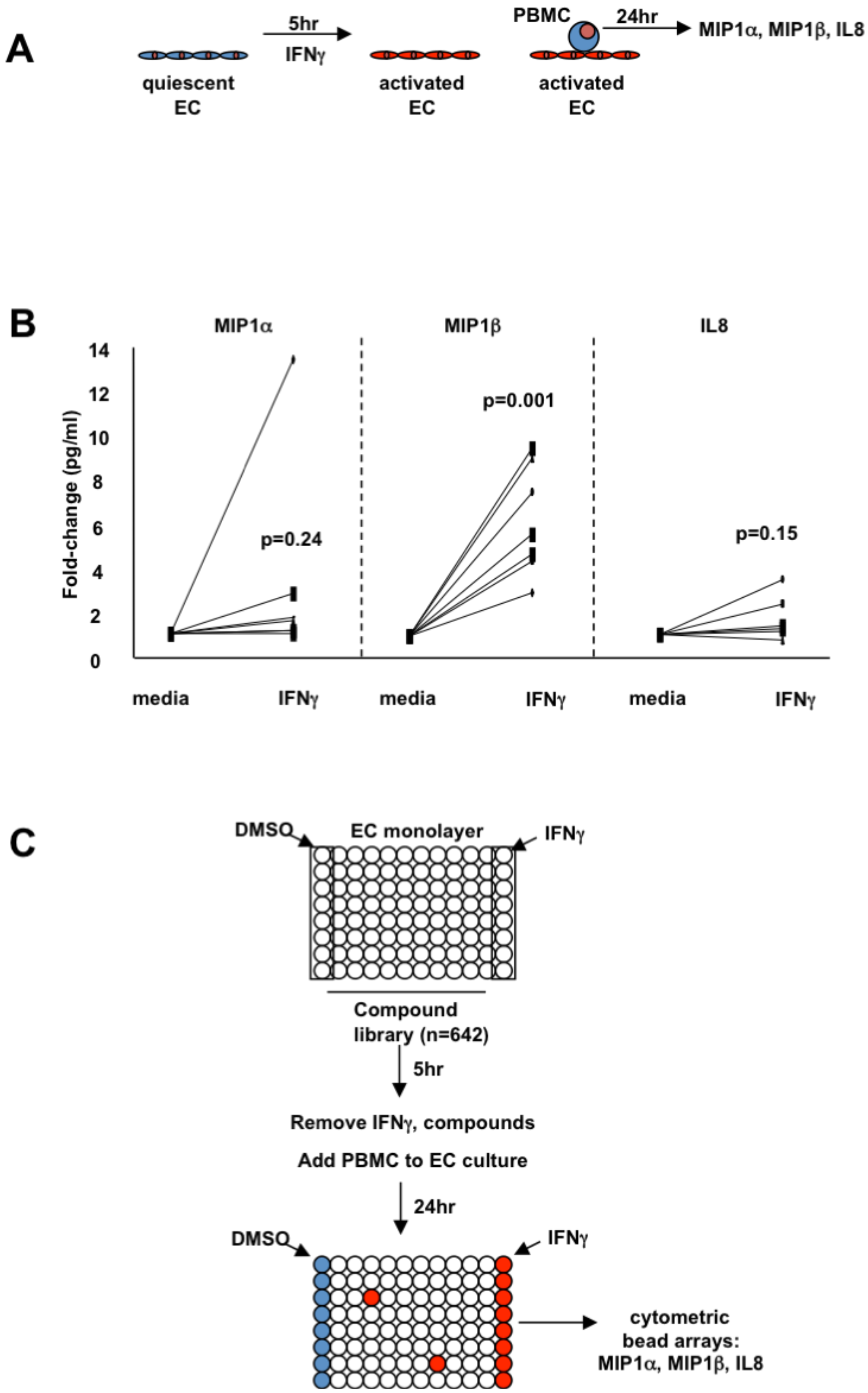
[d] Department of Medicine, Division of Dermatology, University of California, Los Angeles, 10833 Le Conte Ave, 52-121 CHS Building, Los Angeles, CA 90095

[1] These authors contributed equally.

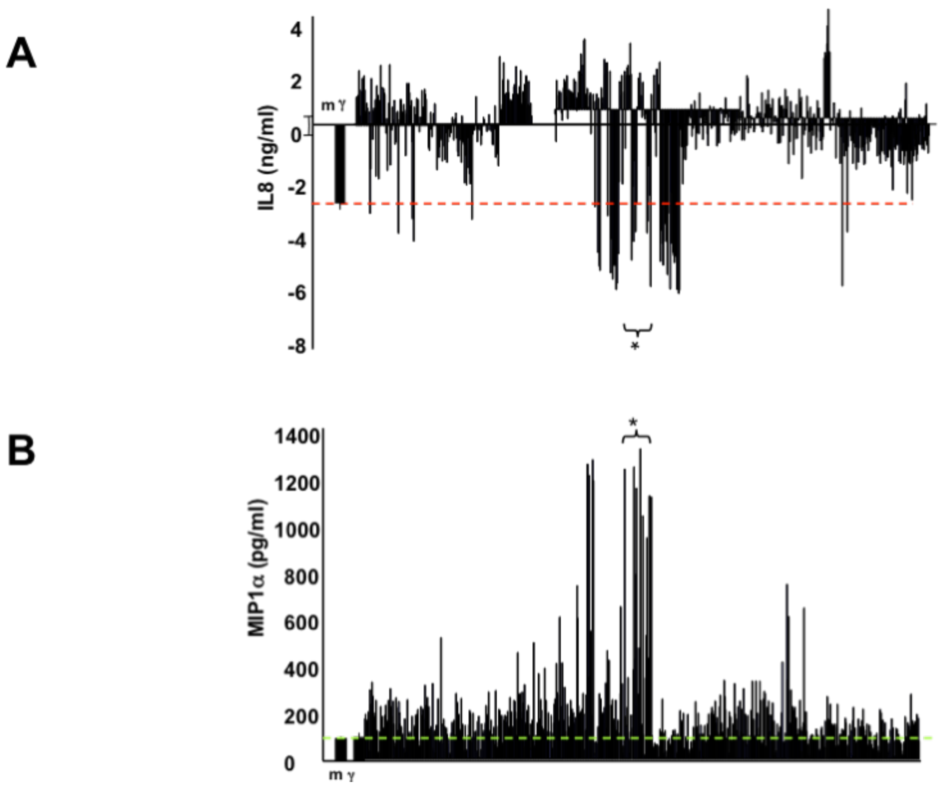
[2] Corresponding author: University of California, Los Angeles, Department of Chemistry and Biochemistry, 607 Charles E. Young Drive East, Los Angeles, CA 90095-1569. Phone number: (310) 267-4954. Fax number: (310) 206-3722. Email address: ohyun@chem.ucla.edu

Contents

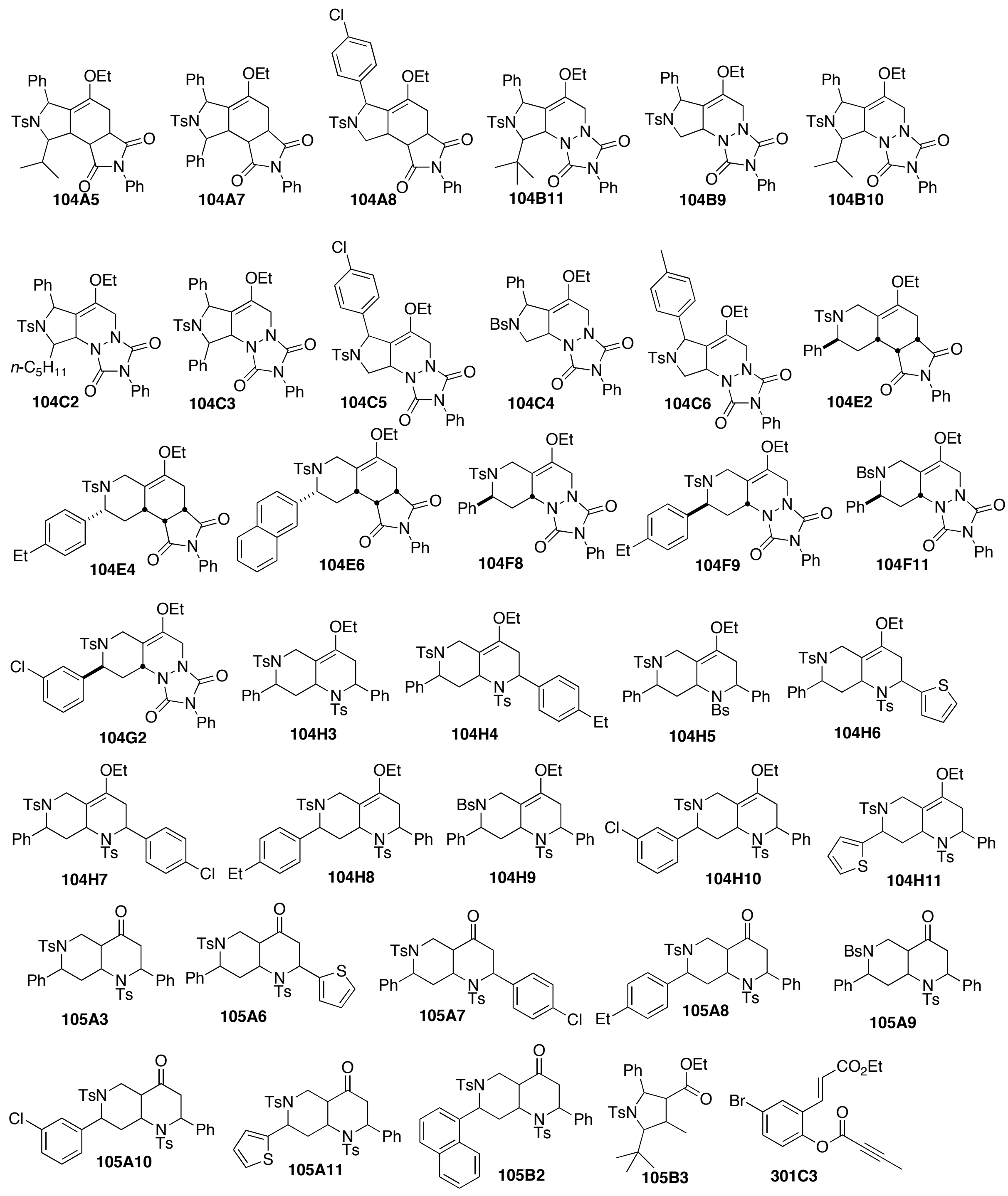
Supplemental Figures



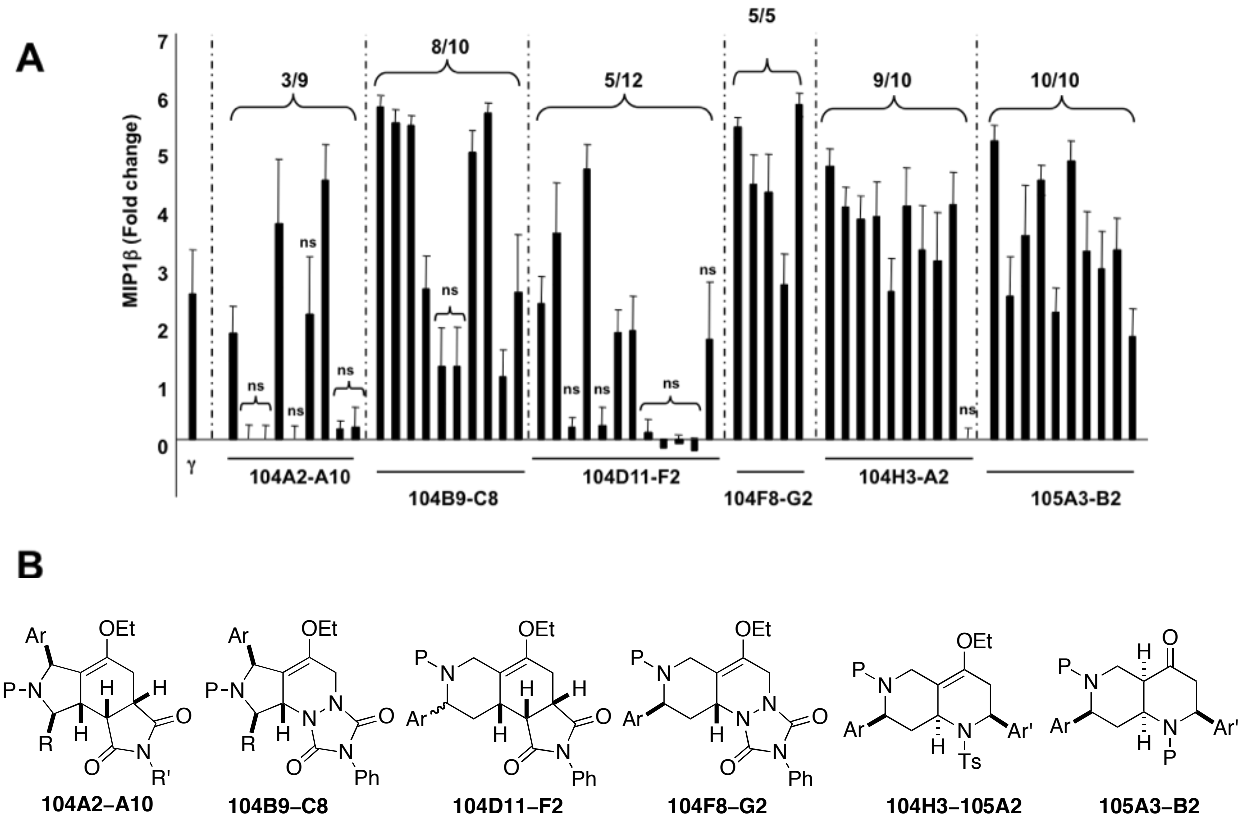
Supplemental Figure 1: A biological platform for the detection of activated endothelium. (**A**) Primary endothelial cells were seeded to confluence in a 96 well format and activated by IFNγ (10 ng/ml). After 5 hours, IFNγ was removed, wells were washed, and then primary human peripheral blood mononuclear cells (PBMC) were added at a ratio of 3:1 (PBMC:EC). 20-24 hours later, supernatants were removed and chemokines were quantified by cytometric bead arrays. (**B**) MIP1β production, but not MIP1α or IL8 levels, reliably detects endothelium activated by IFNγ. Chemokines produced in co-culture conditions with quiescent vs. activated EC; data represent the results from n=7 (MIP1α and MIP1β) and n=6 (IL8) independent experiments. (**C**) Chemical library screen for compounds that activate human endothelium. A 642 compound library was added following the same method as in A and B. Controls included DMSO and IFNγ on each plate. Supernatants were measured for chemokines by cytometric bead arrays.



Supplemental Figure 2: Identification of small molecules that activate human endothelial cells. IFNγ (10 ng/ml) and DMSO controls (n=60 total replicates) and 642 compounds (10μM) were tested for their ability to promote (**A**) IL8 and (**B**) MIP1α production. For IL8, data is expressed as change in expression in comparison to DMSO. Red dashed line represents the level for IFNγ-treated EC-PBMC co-culture. For MIP1α, DMSO and IFNγ-treated EC triggered comparable levels.



Supplemental Figure 3: Structure of 37 hits (out of 642 compounds) and their IDs (e.g., 104A5). Structure of 91 compounds (104A2–105B2) in the 642 compound library that are derived from the sequence of reactions, phosphine catalysis, Tebbe methylenation, Diels–Alder reaction, and sometime hydrolysis, are provided on pages 11–13.



Ar = phenyl, 4-MeC_6H_4, 4-EtC_6H_4, 4-ClC_6H_4, 3-ClC_6H_4, 2-thiophenyl, 1-naphthyl

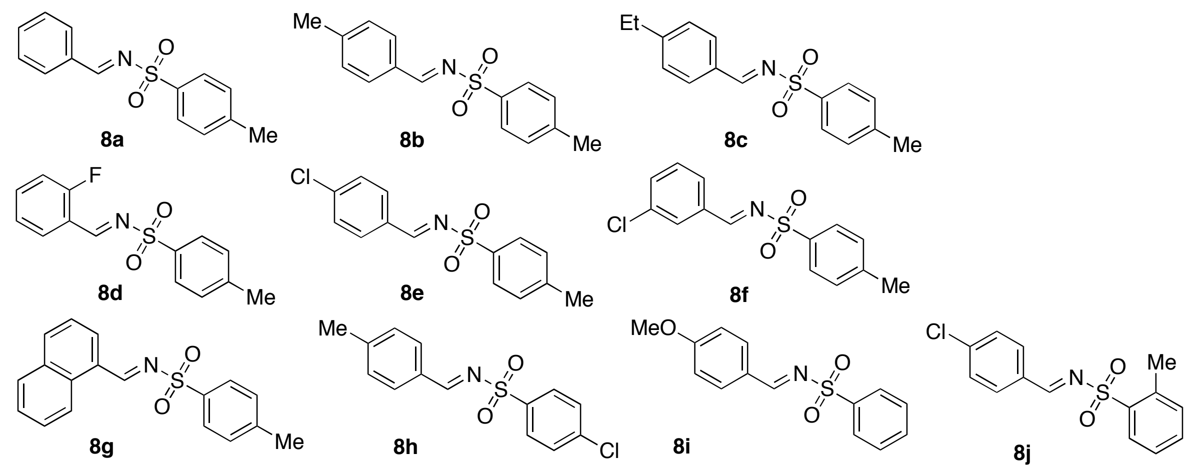
P = tosyl, benzenesulfonyl

R = H, isopropyl, *n*-pentyl, *t*-butyl, phenyl

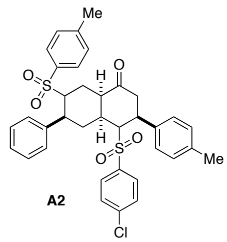
R' = phenyl, ethyl, benzyl

Ar' = phenyl, 4-EtC_6H_4, 4-ClC_6H_4, 2-thiophenyl

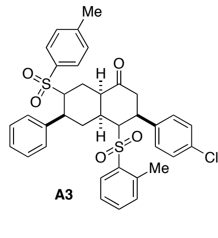
Supplemental Figure 4: Validation of the seven scaffolds accounting for the majority of EC activating compounds. (**A**) After the initial screen, the six subfamilies (hits and non-hits) were repeated in two independent experiments. Data represents mean± s.e.m. for MIP1β fold-induction over DMSO control for all three experiments. To account for experimental variability, all individual data points were log base 2 transformed. Number of family members which were significantly induced over DMSO ($p<0.05$) is shown above each family of compounds. (**B**) The general structures of the seven families of EC-activating compounds.



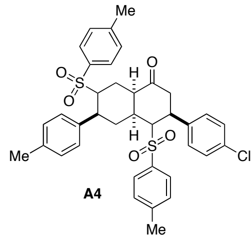
Supplemental Figure 5: Ten *N*-sulfonylimine building blocks for the solid-phase octahydro-1,6-naphthyridin-4-one library.



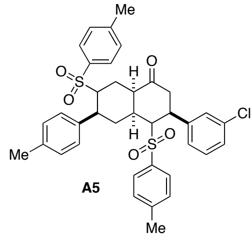
A2



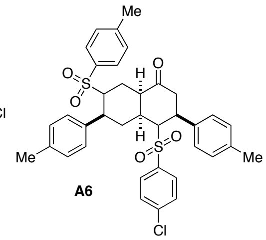
A3



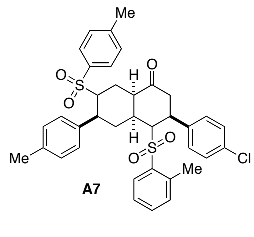
A4



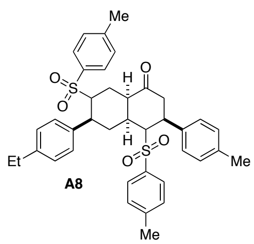
A5



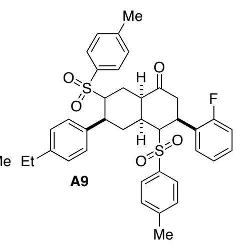
A6



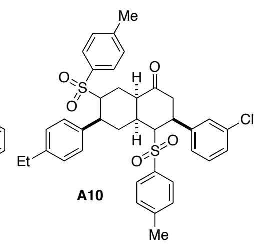
A7



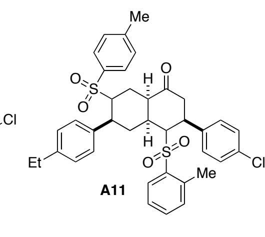
A8



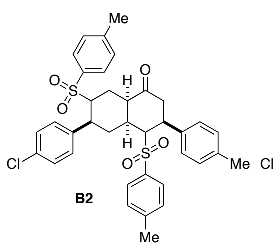
A9



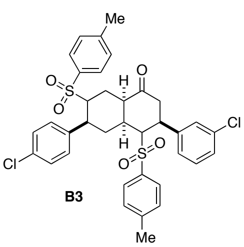
A10



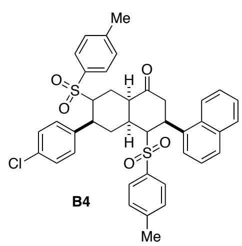
A11



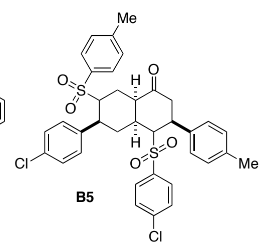
B2



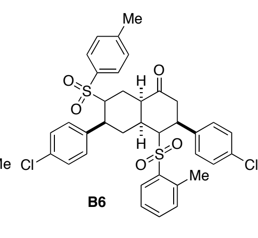
B3



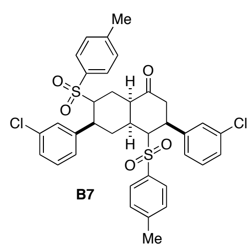
B4



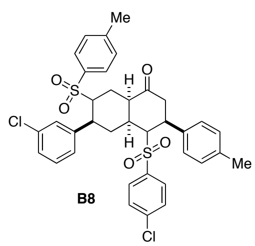
B5



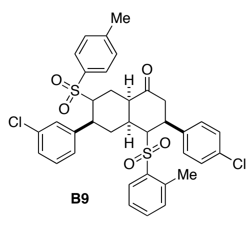
B6



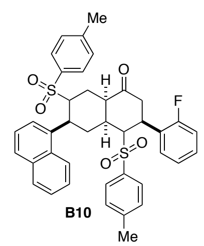
B7



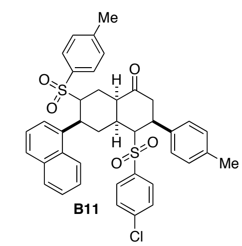
B8



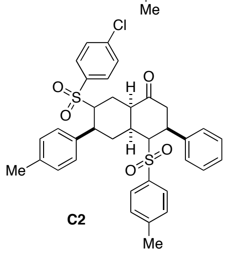
B9



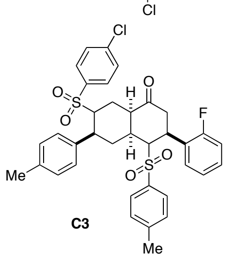
B10



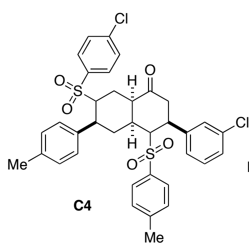
B11



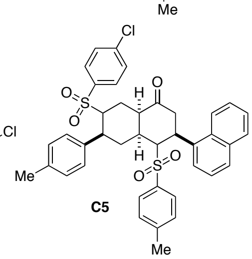
C2



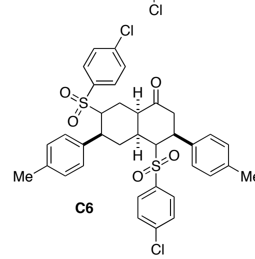
C3



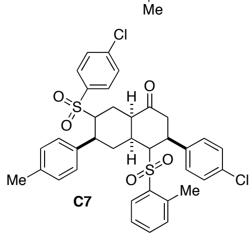
C4



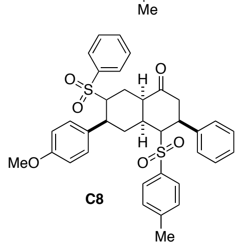
C5



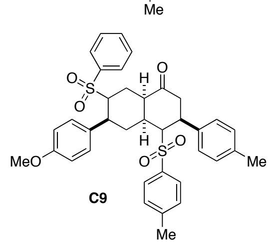
C6



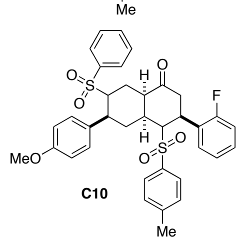
C7



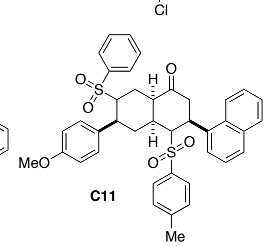
C8



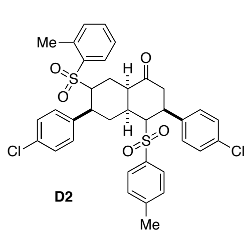
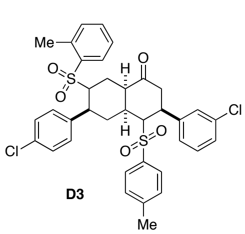
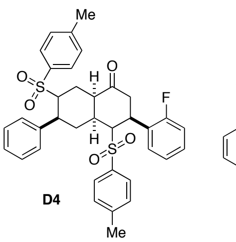
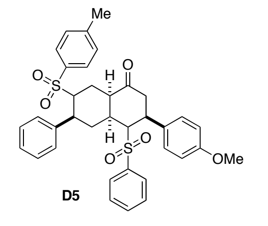
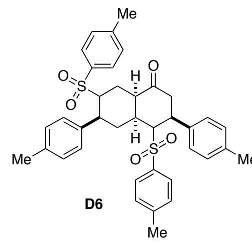
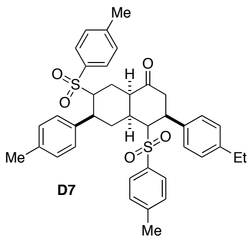
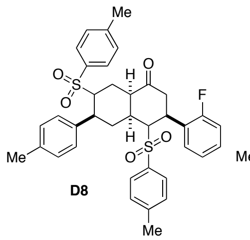
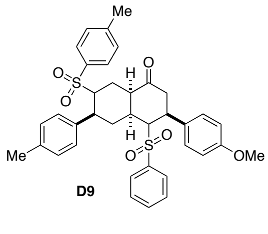
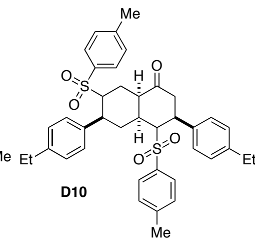
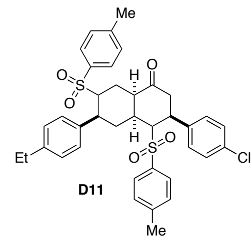
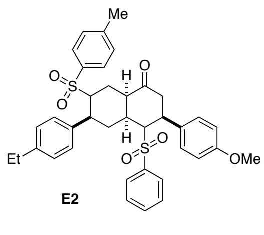
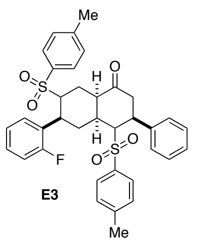
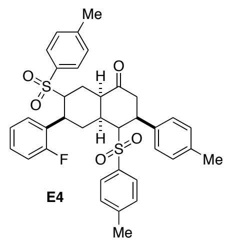
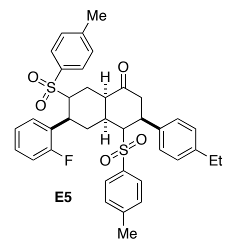
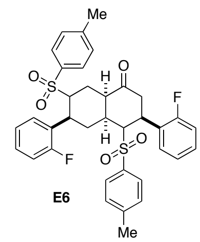
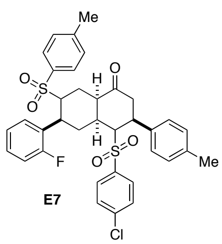
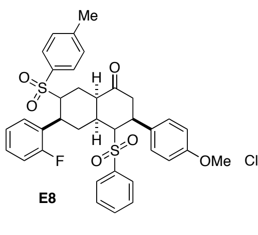
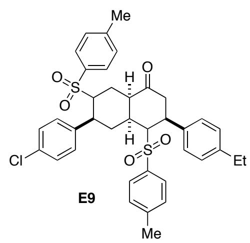
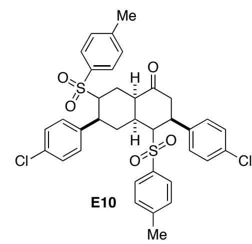
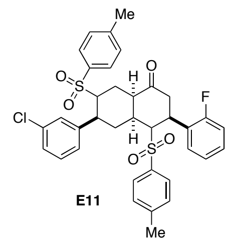
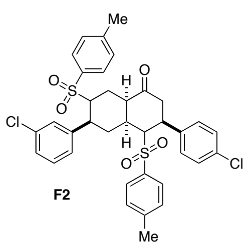
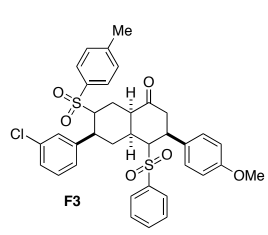
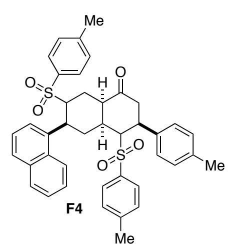
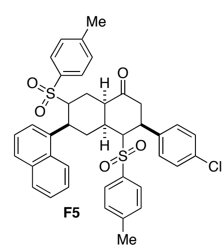
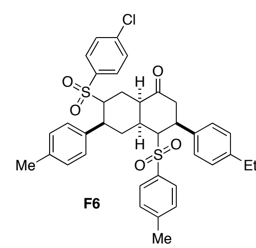
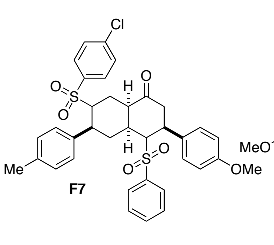
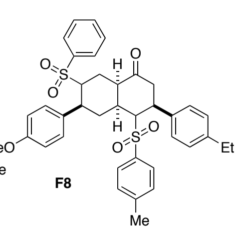
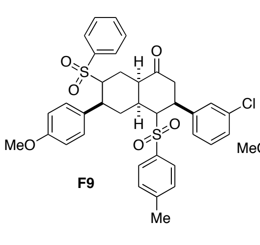
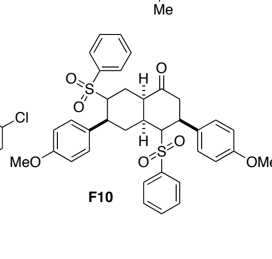
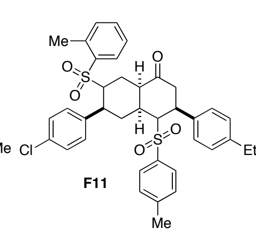
C9

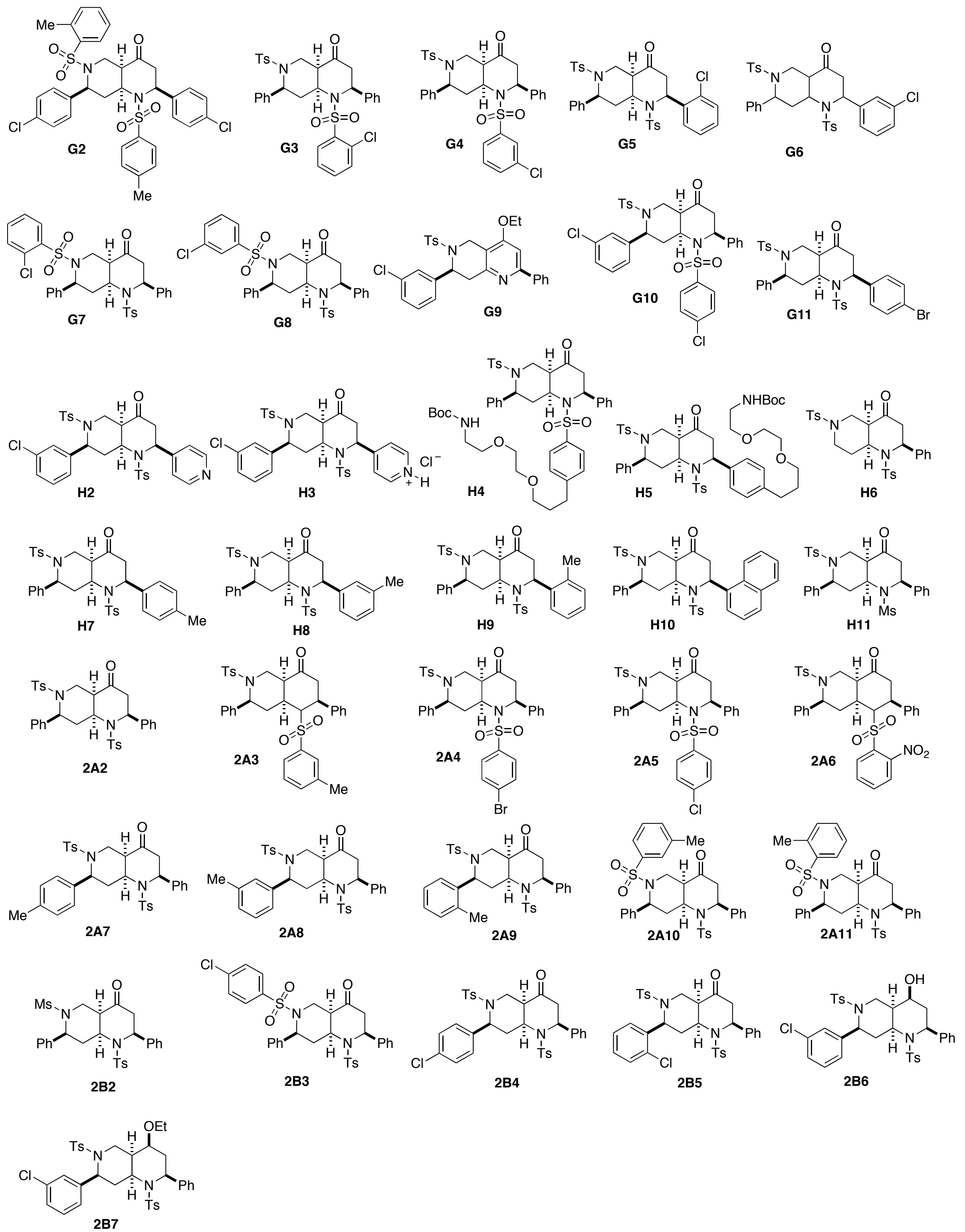


C10



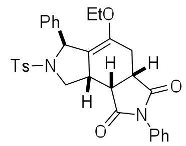
C11

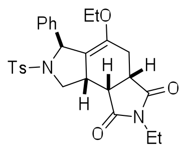

D2

D3

D4

D5

D6

D7

D8

D9

D10

D11

E2

E3

E4

E5

E6

E7

E8

E9

E10

E11

F2

F3

F4

F5

F6

F7

F8

F9

F10

F11

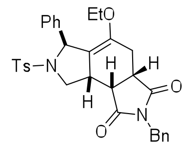


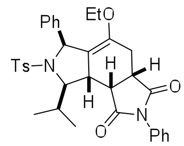
Supplemental Figure 6: Structure of 96 naphthyridinone analogs and their IDs (A02–2B07).

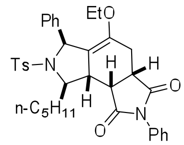
Structures of 91 compounds from the phosphine catalysis/Tebbe/Diels–Alder(/hydrolysis)

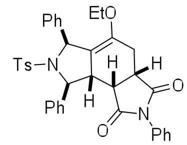

104A02

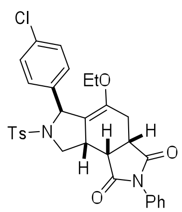

104A03

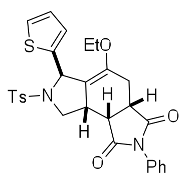

104A04

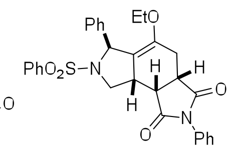

104A05

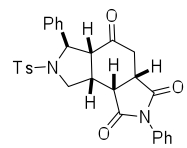

104A06

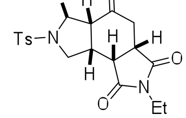

104A07

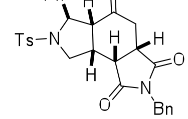

104A08

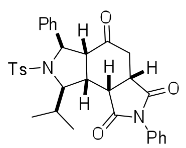

104A09

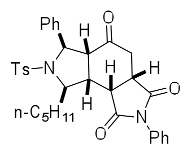

104A10

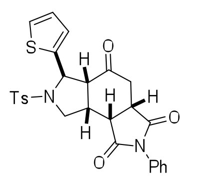

104A11

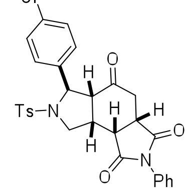

104B02

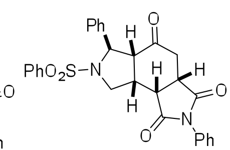

104B03

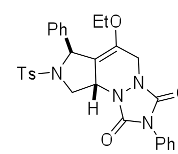

104B04

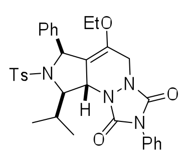

104B05

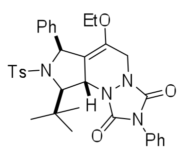

104B06

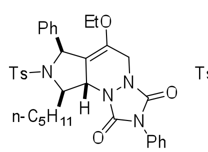

104B07

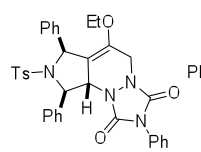

104B08

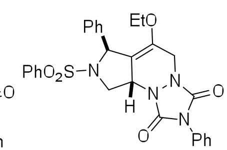

104B09

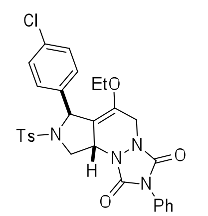

104B10

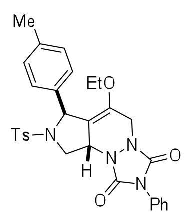

104B11

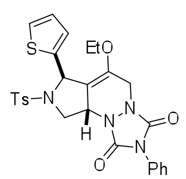

104C02

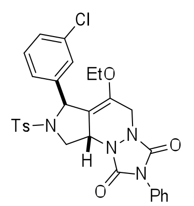

104C03

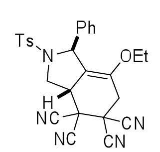

104C04

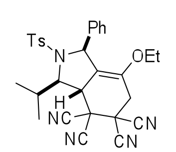

104C05

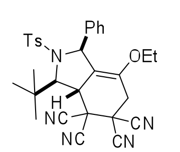

104C06

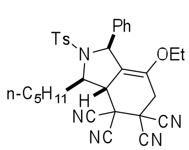

104C07

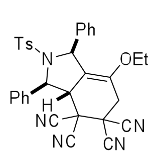

104C08

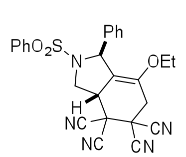

104C09

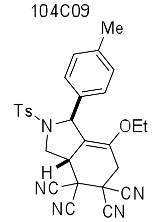

104C10

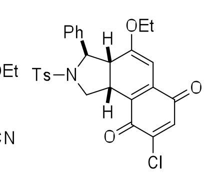

104C11

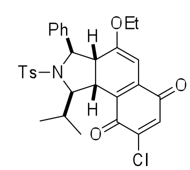

104D02

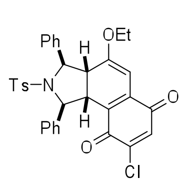

104D03

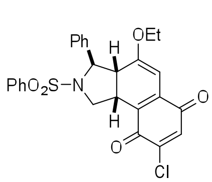

104D04

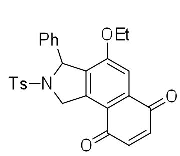

104D05

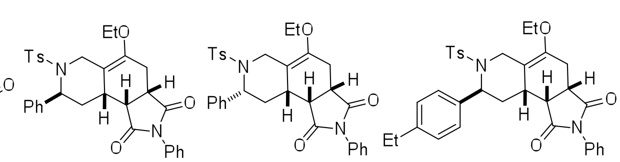

104D06

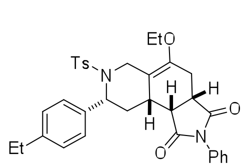

104D07


104D08

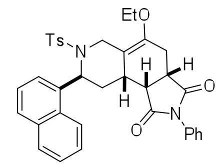

104D09


104D10

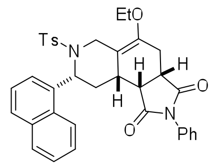

104D11 104E02 104E03



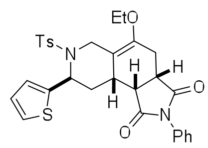
104E04



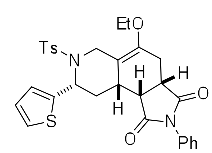
104E05



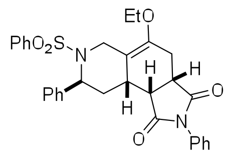
104E06



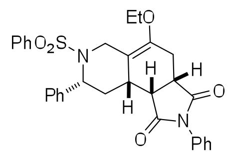
104E07



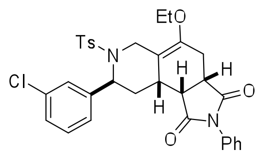
104E08



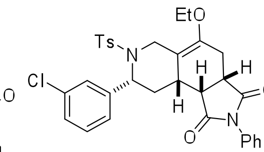
104E09



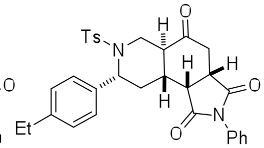
104E10



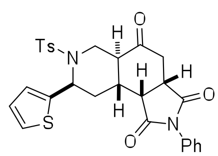
104E11



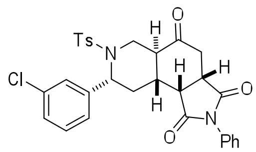
104F02



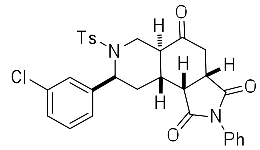
104F03



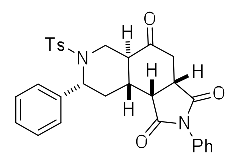
104F04



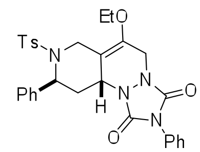
104F05



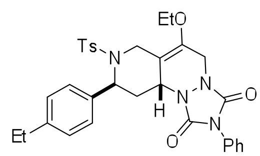
104F06



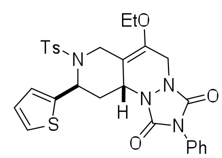
104F07



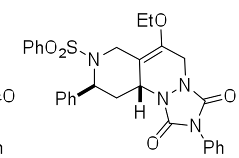
104F08



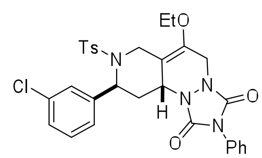
104F09



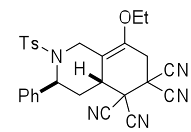
104F10



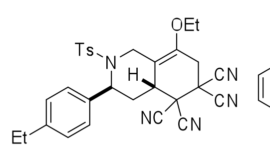
104F11



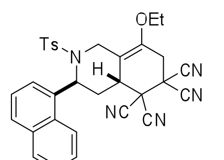
104G02



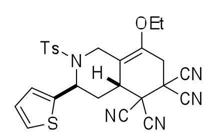
104G03



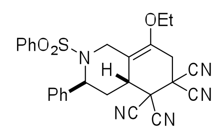
104G04



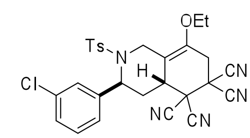
104G05



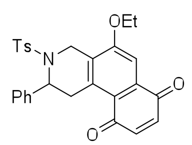
104G06



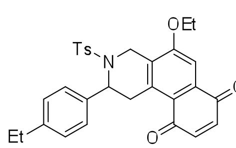
104G07



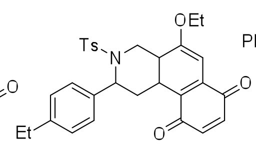
104G08



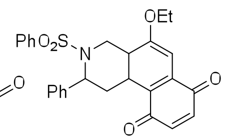
104G09



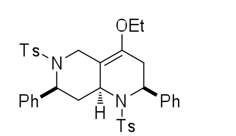
104G10



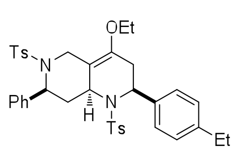
104G11



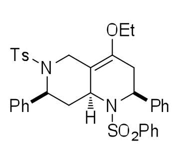
104H02



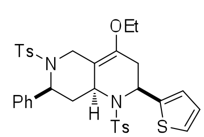
104H03



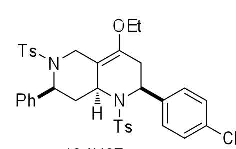
104H04



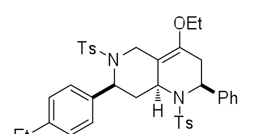
104H05



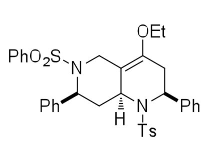
104H06



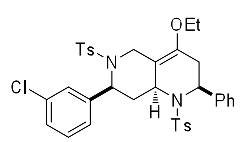
104H07



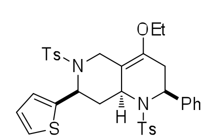
104H08



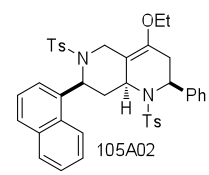
104H09



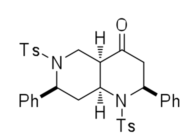
104H10



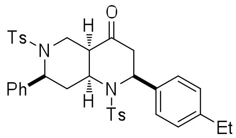
104H11



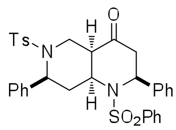
105A02



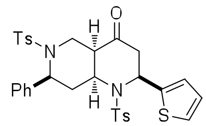
105A03



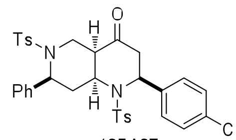
105A04



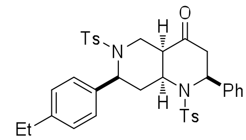
105A05



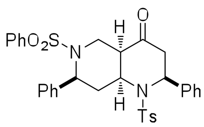
105A06



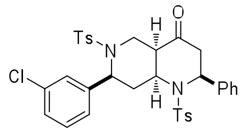
105A07



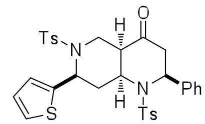
105A08



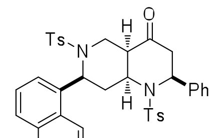
105A09



105A10



105A11



105B02

Materials and methods for biology

Cells and reagents: Human umbilical endothelial cells (HUVEC) were purchased from (Lonza) and were used between passage 5 and 8. Peripheral blood mononuclear cells were isolated from healthy donors (UCLA Institutional Review Board # 92-10-591-31) using Hypaque Ficoll (GE Healthcare). IFNγ (Peprotech) was used at 10 ng/ml in all experiments. Antibodies used: ICAM1 (Abd Serotec), E-selectin (R&D systems), CD14 (Becton Dickinson) and MIP1β (Becton Dickinson). Cytokine bead arrays for IL8, MIP1α, and MIP1β were obtained from (Becton Dickinson).

Co-culture assays: HUVEC were grown to 80-90% confluency in T150 flasks (Corning). On the day of experiments, HUVEC were harvested and plated at a confluent density in 96 well plates; these were either half or full volume plates, requiring 2.5-5 $x10^4$ EC per well, respectively, in complete EBM-2 media (Lonza). After adherence for 2-3 hours, IFNγ (10ng/ml), DMSO, or compound library (final concentration, 10 mM) was added in incomplete EBM-2 media (Lonza). After 5 hours, stimuli were removed and cells were gently washed twice with RPMI (Invitrogen), followed by addition of $7.5\text{-}10x10^4$ human PBMC in 10% FCS. For cytokine analysis, 50 ml was removed at 24 hours for CBA analysis. The biological effects observed were not attributable to either LPS contamination, nor to cellular toxicity, as determined by flow cytometric analysis and 3-(4,5-dimethythiazol-2-yl)-2,5-diphenyl tetrazolium bromide (MTT) assay.

Cytometric Bead Arrays (CBA): 50 ml of supernatant from EC alone, PBMC alone, or co-culture conditions was collected for CBA analysis for IL8, MIP1α, and MIP1β. CBA was performed as per the manufacturer's recommendations (Becton Dickinson). Standard curves and all samples were acquired on a FacsCalibur flow cytometer and data was analyzed using FloJo software.

Flow cytometry: HUVEC were stimulated with IFNγ, DMSO, or compounds of interest (10 μM) for 5 hours. Stimuli were removed and cells were gently washed and media was replaced with 10% FCS for 24 hours. Cells were stained with anti-ICAM1 and anti-E-selectin, or appropriate isotype antibodies. For intracellular chemokine staining, stimulations of HUVEC were carried out as mentioned above with IFNγ, DMSO and compound of interest. After 8 hours of PBMC and HUVEC co-culture incubation, Golgi Plug(Becton Dickinson) was added to the culture and incubation carried out for an additional 16 hours. After the incubation cells were fixed, permeabilized and stained with anti-CD14 and anti-MIP1b or appropriate isotype controls. Samples were then analyzed with a FacsCalibur flow cytometer and subsequent data analysis was performed using FloJo software.

Microarrays: HUVEC were grown as described above, and then plated at 1 x 10^6 in 6 well plates in complete EBM-2. Triplicate wells were treated with DMSO, active analogue (D10) and inactive analogue (E2)- all at equal volumes and concentration a final concentration of 10 μM in incomplete EBM-2. After 5 hours, media was removed and RNA was extracted using Trizol (Invitrogen), followed by RNeasy Minelut Cleanup Kit (Qiagen). RNA was taken to the UCLA Microarray Core Center where it was processed using the Human Genome Affymetrix U133 Plus 2.0 Array. Microarray data was analyzed using dChip software (version 11/18/07) from the Cheng Li Lab at http://biosun1.harvard.edu/complab/dchip. For statistical analysis using dChip software, only gene probes that were minimally present in two of the three replicates were used, and parameters for significance were set at fold change >1.25, p-value <0.05. Total number of probes present for active analogue (D10): 30,228. Total number of probes present for inactive analogue (E2): 30,000. Unsupervised dendrograms were created using dChip software (Fig. 5D). Genes with known function in immune regulation were selected based on published databases and gene functions identified by Gene Ontology or OMIM; dendrogram was created using dChip software (Fig. 5E).

Statistical analysis: Experimental results were compared using student t-tests; results were considered significant if *p*-value was <0.05. Canonical network analysis for all expressed probes in D10 and E2 datasets was performed by using Ingenuity Pathway Analysis software (version 6.0; Ingenuity Systems).

General information for chemical synthesis and compound characterization

All reactions were performed under Ar atmospheres in oven-dried glassware with dry solvents and anhydrous conditions. Unless otherwise stated, all reagents were purchased from commercial suppliers and used without further purification. Toluene, dichloromethane (DCM), and methanol were freshly distilled from CaH_2. THF was distilled from sodium benzophenone ketyl prior to use. Organic solutions were concentrated under reduced pressure on a rotary evaporator or an oil pump. Synphase lanterns (A-series lantern; capacity: 75 μmol/lantern), spindles, and cogs were purchased from Mimotopes Pty. Ltd., Clayton, Australia. Prior to their first use, the lanterns were washed (3×) with the reaction solvent. Each washing was left to settle for at least 5 min, unless otherwise stated. The solid phase washings were performed using PA-grade solvents. Tebbe reagent (ca. 1.0 M in toluene) was synthesized according to the procedure reported by Grubbs.[1] Reactions were monitored using thin layer chromatography (TLC) on silica gel–precoated glass plates (0.25 mm thickness, SiliCycle silica gel). Chromatograms were visualized through fluorescence quenching with UV light at 254 nm. Flash column chromatography was performed using SiliCycle Silica-P Flash silica gel (60 Å pore size, 40–63 μm). Infrared spectra were recorded using a Perkin–Elmer Spectrum One FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra were recorded in $CDCl_3$ on Bruker Avance 500, ARX-500, or ARX-400 spectrometers, as indicated. Chemical shifts (δ ppm) are provided relative to tetramethylsilane (TMS), with the resonance of the undeuterated solvent or TMS as the internal standard. ^{1}H NMR spectral data are reported as follows: chemical shift, multiplicity (s = singlet; d = doublet; t = triplet; q = quartet; m = multiplet), coupling constant(s) (Hz), integration. ^{13}C NMR spectral data are reported in terms of chemical shift. MALDI mass spectra were obtained using an AB/PerSpective DE-STR TOF instrument, with samples dissolved in CH_3CN and using 2,5-dihydroxybenzoic acid or 1,8,9-anthracenetriol as the matrix. X-ray crystallographic data were collected using a Bruker SMART CCD-based diffractometer equipped with a low-temperature apparatus operated at 100 K. LCMS data were obtained on an Agilent 1200 HPLC using a Acquity BEH C-18, Acquity

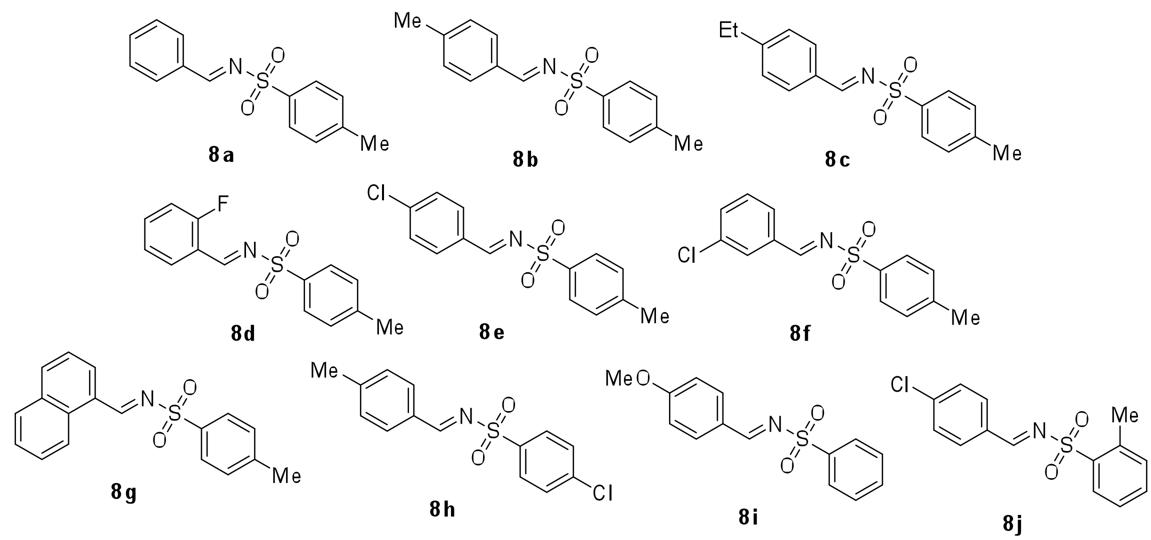
[1] L. F. Cannizzo, R. H. Grubbs, *J. Org. Chem*. **1985**, *50*, 2386.

BEH Phenyl, Acquity BEH Shield C-18, or Acquity BEH HILIC 2.1x50mm column, an Agilent 6224 TOF mass spectrometer in Waters ZQ Quadrupole /ESCI mode, and water/acetonitrile, water/methanol, methanol/THF as the eluent.

Synthetic procedures and characterization of compounds for solid-phase chemistry

Synthesis of builiding blocks 2-methyl-2,3-butadienoic acid (2) and *N*-sulfonylimines (8)

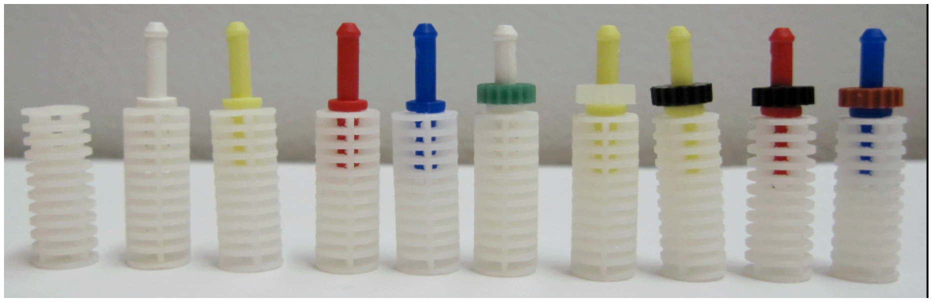
2-methyl-2,3-butadienoic acid (**2**) was synthesized following a literature procedure.[2] All *N*-sulfonylimines (**8**) were synthesized through the condensation of the corresponding aldehydes with the sulfonamides catalyzed by BF_3/OEt_2 with azeotropic water removal (Dean–Stark), according to the literature procedure.[3]



Tagging of the building Blocks

The individual lanterns were tagged with colored spindles and cogs to encode the building blocks used for each lantern. The colors of the spindles and cogs used to encode the imine building blocks of [4 + 2] annalation or Tebbe reaction were summaried and showed below. Because the Diels-Alder reaction was the last step of the synthesis, tagging for the imine building blocks of Diels-Alder reaction was not necessary.

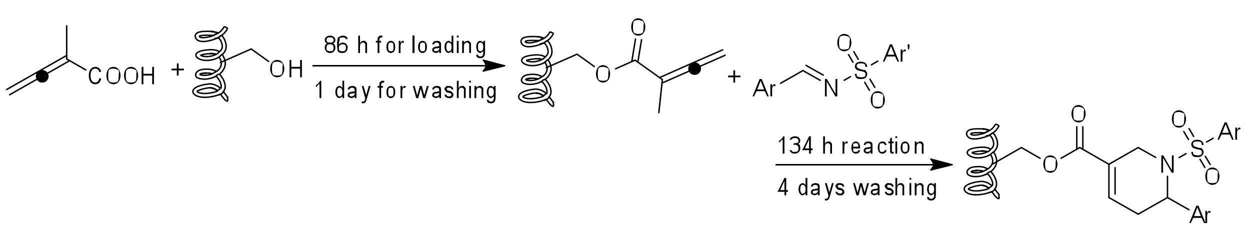
[2] Harvey, G. R.; Ratts, K. W. *J. Org. Chem.* **1966**, *31*, 3907.
[3] McKay, W. R.; Proctor, G. R. *J. Chem. Soc., Perkin Trans. 1* **1981**, 2435.



entry	*N*-sulfonylimine	spindle	cog
1	**8a**	none	none
2	**8b**	white	none
3	**8c**	yellow	none
4	**8d**	red	none
5	**8e**	blue	none
6	**8f**	white	green
7	**8g**	yellow	natural
8	**8h**	yellow	black
9	**8i**	red	black
10	**8j**	blue	brown

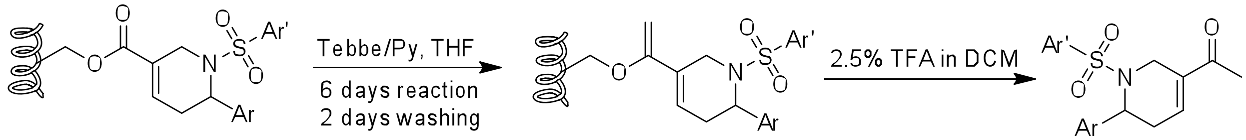
Resin loading with 2-methyl-2,3-butadienoic acid (2) and solid phase [4+2] annulations with N-sulfonylimines (8)

The resin loading with 2-methyl-2,3-butadienoic acid (**2**) and solid phase [4 + 2] annulations with N-sulfonylimines (**8**) were finished following the procedures reported previously from our group.[4] Longer reaction times were needed because A-series lantern (capacity: 75 µmol/lantern) was used instead of L-series lantern (capacity: 15 µmol/lantern).



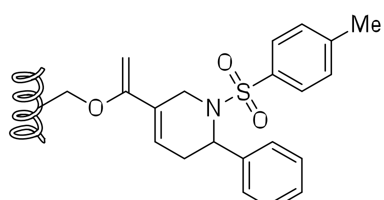
[4] Fiji, H. D. G.; Kinderman, S. S.; Watanabe, M.; de Leon, P.; Tamanoi, F.; Kwon, O. *J. Am. Chem. Soc.* **2007**, *129*, 5843.

Solid Phase Tebbe reaction of the lantern-bond α,β-unsaturated esters

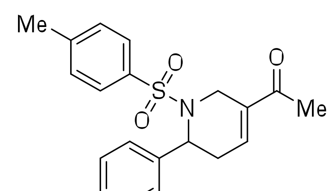


The lantern-bound α,β-unsaturated esters were placed in oven-dried 250 mL flasks and charged with Ar. The lanterns were washed two times with freshly distilled DCM, five times with freshly distilled THF, and then soaked in freshly distilled THF (3 mL/lantern). The anhydrous pyridine (1.3 eq.) and 1.0 M Tebbe reagent in toluene (13.3 eq.) were added at room temperature. After 2 days, another 13.3 eq. Tebbe reagent was added. After another 4 days, the reaction was complete. The lanterns were washed as follows: THF (5 × 40 mL), 40 mL THF + 2 mL 15% NaOH for 15 h, 50% H_2O in THF (3 × 40 mL), THF (3 × 40 mL), 50 mL THF overnight, THF (2 × 40 mL), DCM (3 × 40 mL). (Note: Lanterns were soaked for at least 15 min before changing the solvents. Before the reaction setting, two times with freshly distilled DCM (at least 50 mL DCM for 22 lanterns is required) and five times with freshly distill THF (at least 50 mL DCM for 22 lanterns is required) are very important for the reaction yield. Otherwise the reaction yield will be very low.) The Tebbe products were cleaved by treatment with TFA/DCM 2.5% (7 mL /lantern) to yield the crude α,β-unsaturated ketone products.

The spectroscopic data of the representative α,β-unsaturated ketone products are listed below.



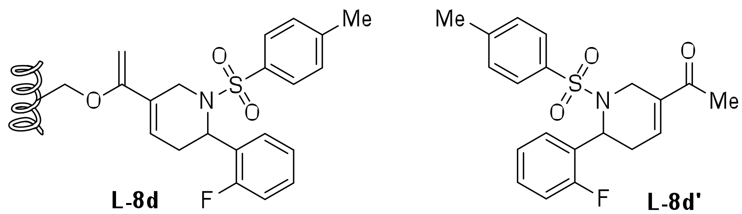
L-8a (6)



L-8a' (6')

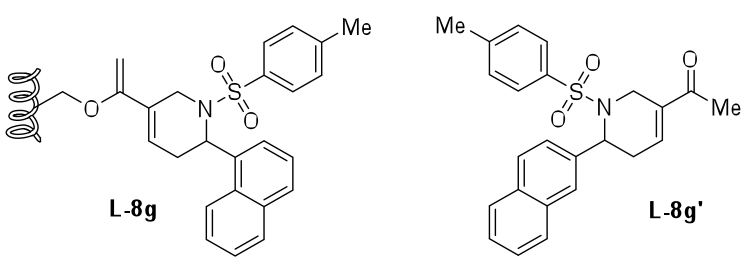
The lantern **L-8a (6)** was treated with 2.5% TFA in DCM (7 mL) to yield a crude product, which was purified by flash column chromatography on the silica gel using 20% ethyl acetate in hexanes to afford compound **L-8a' (6')** as yellow solid in 53% yield, over 4 steps; IR (film) ν_{max} 3062, 2920, 1666, 1160 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.64 (d, *J* = 8.2 Hz, 2H), 7.27-7.19 (m, 7H), 6.92 (br, 1H), 5.38 (d, *J* = 5.4 Hz, 1H), 4.46 (d, *J* = 18.4 Hz, 1H), 3.38 (ddd, *J*

= 18.4, 5.6, 3.3 Hz, 1H), 2.70-2.67 (m, 2H), 2.38 (s, 3H), 2.22 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 196.4, 143.3, 138.2, 137.1, 136.9, 136.2, 129.5, 128.5, 127.7, 127.0, 126.9, 52.1, 38.9, 27.6, 24.9, 21.4; HRMS (m/z): $[M+H]^+$ calcd. for $C_{20}H_{21}NO_3SH$, 356.1315; found, 356.1299.



L-8d **L-8d'**

The lantern **L-8d** was treated with 2.5% TFA in DCM (7 mL) to yield a crude product, which was purified by flash column chromatography on the silica gel using 20% ethyl acetate in hexanes to afford compound **L-8d'** as yellow solid in 39% yield, over 4 steps; IR (film) ν_{max} 3064, 2917, 1667, 1162 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 (d, *J* = 8.3 Hz, 2H), 7.24-7.17 (m, 3H), 7.02-6.92 (m, 4H), 5.72 (d, *J* = 7.2 Hz, 1H), 4.42 (d, *J* = 18.3 Hz, 1H), 3.59-3.52 (m, 1H), 2.93-2.84 (m, 1H), 2.64-2.57 (m, 1H), 2.37 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 196.5, 161.4, 158.9, 143.4, 137.2, 136.5, 136.3, 129.4, 127.8, 127.3, 126.7, 126.6, 124.0, 116.0, 115.8, 46.7, 39.4, 29.3, 25.0, 21.5; HRMS (m/z): $[M+Na]^+$ calcd. for $C_{20}H_{20}FNO_3SNa$, 396.1040; found, 396.1031.

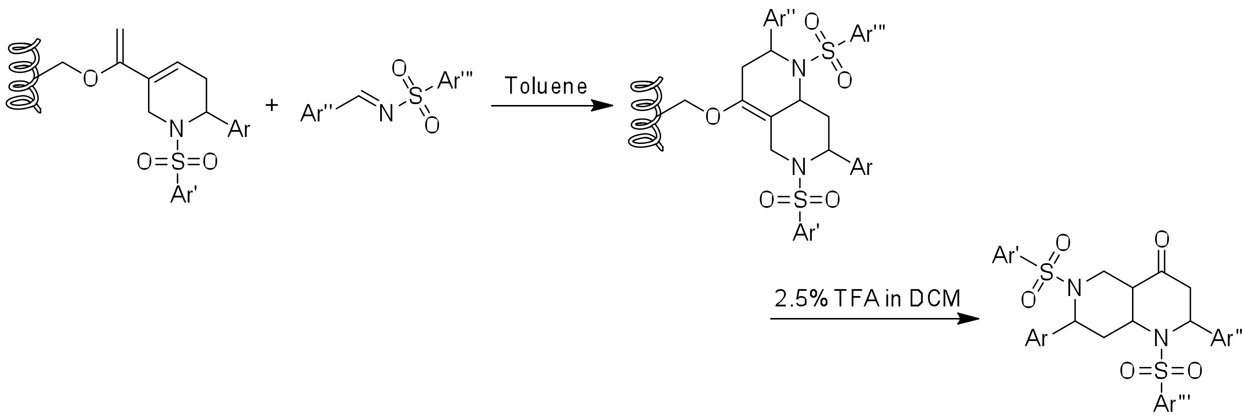


L-8g **L-8g'**

The lantern **L-8g** was treated with 2.5% TFA in DCM (7 mL) to yield a crude product, which was purified by flash column chromatography on the silica gel using 20% ethyl acetate in hexanes to afford compound **L-8g'** as yellow solid in 43% yield, over 4 steps; IR (film) ν_{max} 2979, 2917, 1709, 1166 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.59 (d, *J* = 8.5 Hz, 1H), 7.85 (d, *J* = 8.1 Hz, 1H), 7.78 (d, *J* = 8.1 Hz, 1H), 7.68 (d, *J* = 8.2 Hz, 2H), 7.62 (t, *J* = 7.3 Hz, 1H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.28 (t, *J* = 7.7 Hz, 1H), 7.18-7.16 (m, 3H), 6.96 (t, *J* = 2.3 Hz, 1H), 6.22 (d, *J* = 7.2 Hz, 1H), 4.34 (d, *J* = 18.8 Hz, 1H), 3.22 (dd, *J* = 18.8, 2.6 Hz, 1H), 2.96 (dd, *J* = 20.0, 3.0 Hz, 1H), 2.75 (ddd, *J* = 20.0, 4.8, 2.3 Hz, 1H), 2.36 (s, 3H), 2.23 (s, 3H); ^{13}C NMR (125 MHz,

$CDCl_3$): δ 196.9, 143.6, 137.8, 136.4, 136.1, 134.0, 133.4, 133.3, 129.4, 129.2, 128.7, 127.5, 126.8, 125.9, 124.5, 124.0, 123.9, 49.0, 38.8, 27.9, 24.9, 21.4; HRMS (m/z): $[M+H]^+$ calcd. for $C_{24}H_{23}NO_3SH$, 406.1471; found, 406.1458.

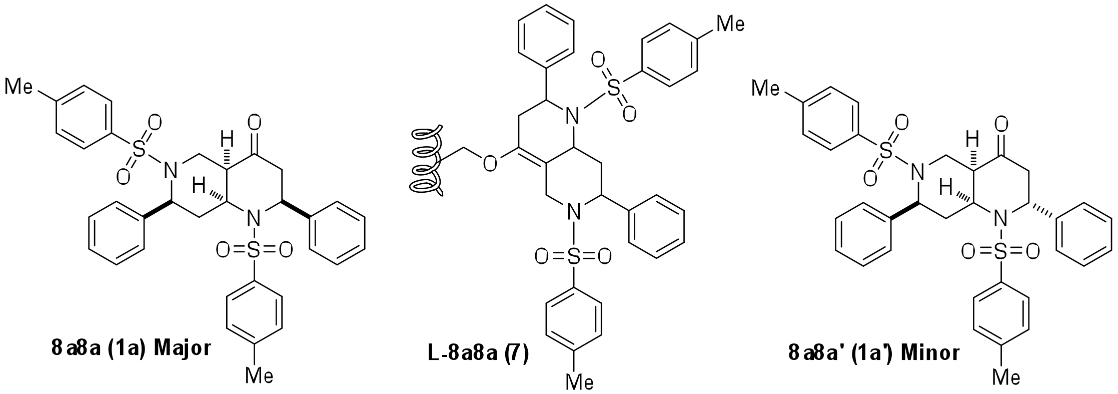
Solid Phase Diels–Alder reaction of the lantern-bound Tebbe Dienes



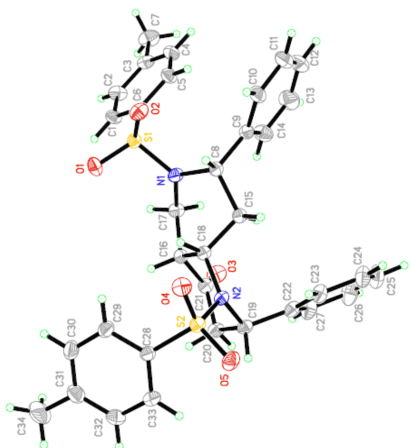
The lanterns from Tebbe reaction was place in an oven-dried 250 mL flasks and charged with Ar. The lanterns were washed three times with freshly distilled toluene (2.5 mL/lantern). The imine (26.0 eq.) was added, charged with Ar, and then the freshly distilled toluene (3 mL/lantern) was added at room temperature. The flask was removed from the Ar line, capped, and then placed aside for 6 days at 80 °C. After the reaction was complete, the lanterns were washed as follows: Toluene (×5), THF (×3), DMF (×3), DMF overnight, DMF (×3), THF (×3), Toluene (×3), THF (×3), DMF overnight, DMF (×3), THF (×3), THF/2.5 M NH_4Cl (1:1) for 1h, THF/H_2O (1:1) (×2), THF (×3), DCM (×5). After washing, the product was cleaved from the lantern by adding a solution of 2.5% TFA in DCM (7 mL). (Note: Lanterns were soaked for at least 15 min before changing the solvents.)

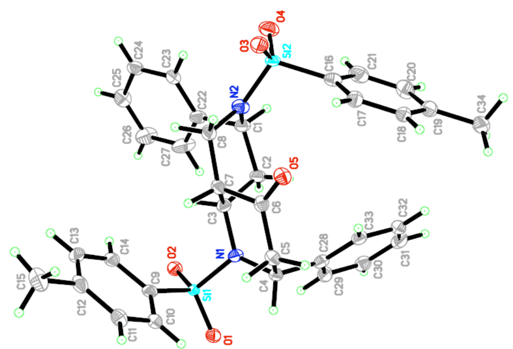
The spectroscopic data of the representative α,β-unsaturated ketone products are listed below.

Crystallographic data for **1a** and **1a´** have been deposited with the Cambridge Crystallographic Data Centre as supplementary numbers CCDC 767112 and CCDC 802608. These data can be obtained online free of charge [or from the Cambridge Crystallographic Data Center, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk].

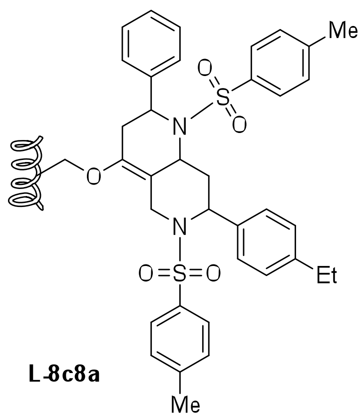


8a8a (1a) Major L-8a8a (7) 8a8a' (1a') Minor

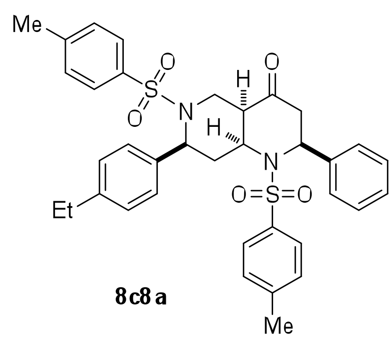




The lantern **L-8a8a (7)** was treated with 2.5% TFA in DCM (7 mL) to yield a crude product, which was purified by flash column chromatography on the silica gel using 20% ethyl acetate in hexanes to afford compounds **8a8a (1a)** and **8a8a' (1a')** as white solid in 38% yield (dr = 97:3), over 5 steps; **8a8a (1a):** IR (film) ν_{max} 3062, 2921, 1714, 1347, 1161, 659 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.3 Hz, 2H), 7.44 (d, *J* = 8.3 Hz, 2H), 7.40-7.37 (m, 4H), 7.23 (t, *J* = 7.5 Hz, 2H), 7.18-7.16 (m, 3H), 7.12-7.07 (m, 3H), 6.84-6.83 (m, 2H), 5.72 (d, *J* = 6.7 Hz, 1H), 4.92 (dd, *J* = 11.2, 7.1 Hz, 1H), 4.63-4.58 (m, 1H), 3.81 (dd, *J* = 15.3, 8.0 Hz, 1H), 3.43 (dd, *J* = 15.3, 9.2 Hz, 1H), 2.95 (dd, *J* = 14.8, 2.0 Hz, 1H), 2.68 (dd, *J* = 17.5, 8.9 Hz, 1H), 2.49 (s, 3H), 2.38 (s, 3H), 2.23 (dd, *J* = 14.1, 7.2 Hz, 1H), 1.76 (ddd, *J* = 13.6, 7.0, 2.0 Hz, 1H), 0.95 (td, *J* = 13.5, 11.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.6, 144.2, 143.2, 140.2, 139.4, 137.4, 137.0, 130.3, 129.4, 128.5, 128.2, 128.0, 127.3, 127.0, 126.7, 125.8, 58.5, 55.1, 53.3, 45.4, 41.4, 40.5, 36.3, 21.6, 21.4; HRMS (m/z): calculated for $C_{34}H_{35}N_2O_5S_2N$ $[M + H]^+$ 615.1902, found 615.1975. **8a8a' (1a'):** IR (film) ν_{max} cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.5 Hz, 2H), 7.64 (d, *J* = 8.5 Hz, 2H), 7.35-7.32 (m, 2H), 7.30-7.25 (m, 10H), 7.21 (d, *J* = 8.0 Hz, 2H), 5.72 (dd, J = 7.3, 3.4 Hz, 1H), 5.00 (s, 1H), 4.46 (d, J = 14.5 Hz, 1H), 4.42-4.38 (m, 1H), 2.92 (dd, J = 14.5, 4.6 Hz, 1H), 2.85 (dd, J = 15.2, 3.4 Hz, 1H), 2.50-2.49 (m, 4H), 2.44 (s, 3H), 2.15 (t, J = 5.4 Hz, 1H), 1.97-1.93 (m, 1H), 1.27-1.23 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.8, 144.1, 142.8, 141.1, 137.5, 136.6, 135.3, 130.1, 129.2, 128.9, 128.8, 128.5, 127.6, 127.5, 127.3, 127.0, 126.6, 55.5, 55.2, 51.5, 46.3, 42.1, 37.5, 32.9, 21.6, 21.5; MS (MALDI) calcd. for $[M + Na]^+$ 637.18, found 637.08.

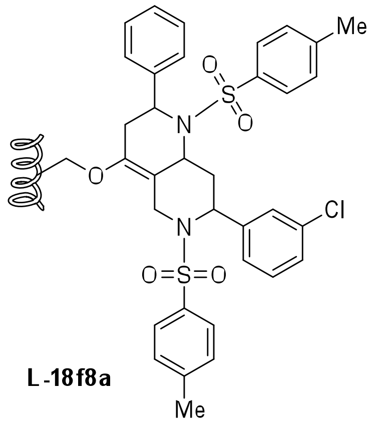


L-8c8a

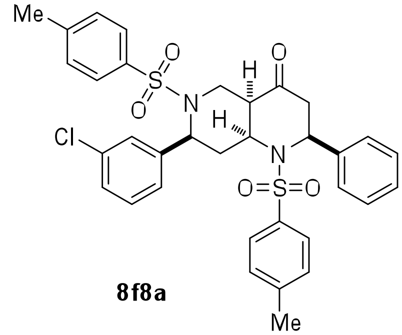


8c8a

The lantern **L-8c8a** was treated with 2.5% TFA in DCM (7 mL) to yield a crude product, which was purified by flash column chromatography on the silica gel using 20% ethyl acetate in hexanes to afford compound **8c8a** as white solid in 38% yield, over 5 steps; IR (film) ν_{max} 3057, 2964, 2921, 1716, 1347, 1162, 660 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, J = 8.1 Hz, 2H), 7.42-7.36 (m, 6H), 7.23 (d, J = 7.5 Hz, 2H), 7.18-7.14 (m, 3H), 6.90 (d, J = 8.0 Hz, 2H), 6.75 (d, J = 8.0 Hz, 2H), 5.71 (d, J = 6.4 Hz, 1H), 4.87 (dd, J = 11.1, 7.0 Hz, 1H), 4.60 (t, J = 10.5 Hz, 1H), 3.78 (dd, J = 15.3, 8.0 Hz, 1H), 3.47 (dd, J = 15.3, 9.1 Hz, 1H), 2.95 (dd, J = 15.0, 1.5 Hz, 1H), 2.68 (dd, J = 17.3, 8.7 Hz, 1H), 2.52 (q, J = 7.6 Hz, 2H), 2.47 (s, 3H), 2.36 (s, 3H), 2.24 (dd, J = 14.7, 7.1 Hz, 1H), 1.76-1.73 (m, 1H), 1.16 (t, J = 7.6 Hz, 3H), 1.01 (td, J = 12.5, 11.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.6, 144.2, 143.4, 143.0, 139.5, 137.4, 137.22, 137.21, 130.3, 129.4, 128.5, 128.0, 127.6, 127.3, 127.0, 126.6, 126.0, 58.4, 55.2, 53.4, 45.6, 41.1, 40.4, 36.3, 28.3, 21.5, 21.4, 15.4; HRMS (m/z): calculated for $C_{36}H_{39}N_2O_5S_2N$ $[M + H]^+$ 643.2215, found 643.2286.

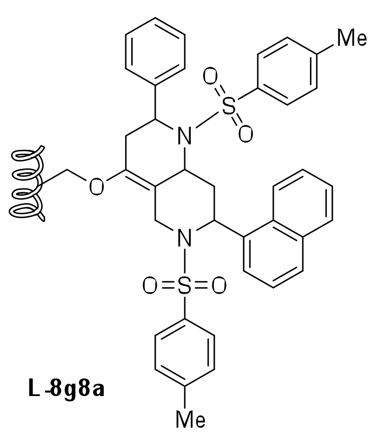


L-18f8a

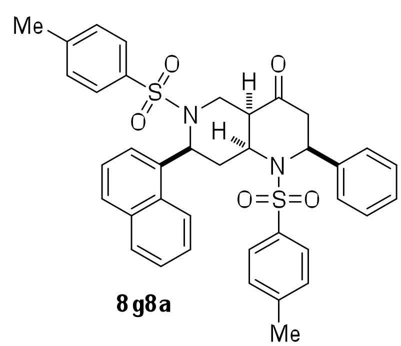


8f8a

The lantern **L-8f8a** was treated with 2.5% TFA in DCM (7 mL) to yield a crude product, which was purified by flash column chromatography on the silica gel using 20% ethyl acetate in hexanes to afford compound **8f8a** as white solid in 25% yield, over 5 steps; IR (film) ν_{max} 3063, 2920, 1714, 1348, 1162, 660 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 8.3 Hz, 2H), 7.39-7.37 (m, 4H), 7.25-7.16 (m, 5H), 7.07-7.01 (m, 2H), 6.75 (d, *J* = 7.4 Hz, 1H), 6.63 (s, 1H), 5.72 (d, *J* = 6.7 Hz, 1H), 4.80 (dd, *J* = 11.3, 6.8 Hz, 1H), 4.59-4.54 (m, 1H), 3.79 (dd, *J* = 15.2, 7.8 Hz, 1H), 3.46 (dd, *J* = 15.3, 8.9 Hz, 1H), 2.96 (dd, *J* = 14.8, 1.9 Hz, 1H), 2.66 (dd, *J* = 17.1, 8.6 Hz, 1H), 2.47 (s, 3H), 2.38 (s, 3H), 2.24 (dd, *J* = 14.7, 7.1 Hz, 1H), 1.71 (ddd, *J* = 13.6, 6.8, 2.3 Hz, 1H), 0.87 (td, *J* = 13.4, 11.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.3, 144.2, 143.6, 142.0, 139.4, 137.3, 136.9, 134.0, 130.3, 129.6, 129.5, 128.6, 128.1, 127.5, 127.3, 127.0, 126.6, 126.0, 124.3, 58.0, 55.1, 53.2, 45.4, 41.4, 40.7, 36.4, 21.6, 21.4; HRMS (m/z): calculated for $C_{34}H_{34}ClN_2O_5S_2$ $[M + H]^+$ 649.1516, found 649.1590.



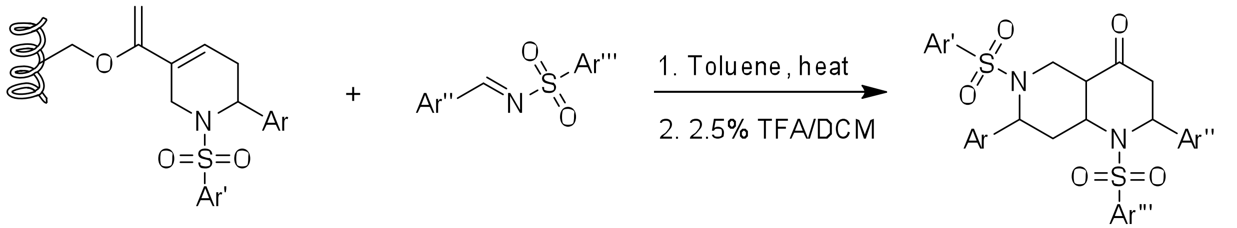
L-8g8a



8g8a

The lantern **L-8g8a** was treated with 2.5% TFA in DCM (7 mL) to yield a crude product, which was purified by flash column chromatography on the silica gel using 20% ethyl acetate in hexanes to afford compound **8g8a** as white solid in 25% yield, over 5 steps; IR (film) ν_{max} 3062, 2914, 1715, 1348, 1162, 660 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (d, *J* = 8.2 Hz, 3H), 7.75 (d, *J* = 7.5 Hz, 1H), 7.61 (d, *J* = 8.1 Hz, 1H), 7.52-7.37 (m, 6H), 7.32 (d, *J* = 7.8 Hz, 2H), 7.16-7.06 (m, 5H), 7.00 (t, *J* = 7.8 Hz, 2H), 5.71 (d, *J* = 5.9 Hz, 1H), 5.63 (dd, *J* = 11.6, 6.3 Hz, 1H), 4.77-4.71 (m, 1H), 4.02 (dd, *J* = 15.4, 7.8 Hz, 1H), 3.67 (dd, *J* = 15.4, 9.2 Hz, 1H), 2.97 (dd, *J* = 14.8, 2.3 Hz, 1H), 2.81 (dd, *J* = 17.3, 8.8 Hz, 1H), 2.51 (s, 3H), 2.32 (s, 3H), 2.32-2.27 (m, 1H), 1.98 (ddd, *J* = 13.8, 6.2, 2.3 Hz, 1H), 1.03 (td, *J* = 13.5, 11.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.7, 144.3, 143.3, 139.2, 137.5, 136.8, 136.3, 133.6, 130.4, 129.8, 129.3, 128.7, 128.6, 128.1, 128.0, 127.3, 127.2, 126.8, 126.4, 125.6, 125.1, 122.8, 122.5, 56.0, 55.3, 53.9, 46.0, 41.7, 41.6, 37.1, 21.7, 21.5; HRMS (m/z): calculated for $C_{38}H_{36}N_2O_5S_2Na$ [M + Na]$^+$ 687.1959, found 687.1953.

LCMS Data of the solid phase naphthyridinone library



	product					LCMS					
	Ar	Ar'	Ar''	Ar'''	No.	[M][a]	RT[b] (min)	[M+H][c]	Purity[d] %[e]	Purity[d] %[f]	Yield[g] (%)
1	Ph	4-MeC$_6$H$_4$	Ph	4-MeC$_6$H$_4$	**8a8a**	614.1909	3.70	615.1975	97	78	20
2	Ph	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	**8a8b**	628.2066	3.79	629.2133	91	65	4
3	Ph	4-MeC$_6$H$_4$	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	**8a8c**	642.2222	3.89	643.2287	93	54	14
4	Ph	4-MeC$_6$H$_4$	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	**8a8d**	632.1815	3.62	633.1880	96	69	18
5	Ph	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8a8e**	648.1519	3.81	649.1586	95	66	16
6	Ph	4-MeC$_6$H$_4$	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8a8f**	648.1519	3.77	649.1589	93	72	29
7	Ph	4-MeC$_6$H$_4$	1-Naphthyl	4-MeC$_6$H$_4$	**8a8g**	664.2066	3.81	665.2132	84	60	21
8	Ph	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	**8a8h**	648.1519	3.83	649.1586	96	72	28
9	Ph	4-MeC$_6$H$_4$	4-MeOC$_6$H$_4$	Ph	**8a8i**	630.1858	3.59	631.1926	91	45	11
10	Ph	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	**8a8j**	648.1519	3.82	649.1584	92	69	29
11	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	Ph	4-MeC$_6$H$_4$	**8b8a**	628.2066	3.78	629.2127	97	82	21
12	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	**8b8b**	642.2222	3.87	643.2290	98	72	16

13	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	**8b8c**	656.2379	3.97	657.2450	91	63	12
14	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	**8b8d**	646.1971	3.73	647.2037	91	70	20
15	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8b8e**	662.1676	3.89	663.1744	95	65	20
16	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8b8f**	662.1676	3.86	663.1741	96	77	37
17	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	1-Naphthyl	4-MeC$_6$H$_4$	**8b8g**	678.2222	3.88	679.2292	83	64	27
18	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	**8b8h**	662.1676	3.91	663.1737	96	79	36
19	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeOC$_6$H$_4$	Ph	**8b8i**	644.2015	3.64	645.2083	92	51	13
20	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	**8b8j**	662.1676	3.92	663.1746	93	72	28
21	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	Ph	4-MeC$_6$H$_4$	**8c8a**	642.2222	3.88	643.2286	97	84	30
22	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	**8c8b**	656.2379	3.96	657.2445	98	75	30
23	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	**8c8c**	670.2535	4.07	671.2604	92	62	15
24	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	**8c8d**	660.2128	3.81	661.2195	91	68	21
25	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8c8e**	676.1832	3.97	677.1900	94	69	17
26	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8c8f**	676.1832	3.97	677.1896	96	81	35
27	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	1-Naphthyl	4-MeC$_6$H$_4$	**8c8g**	692.2379	3.98	693.2445	75	66	30
28	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	**8c8h**	676.1832	4.00	677.1900	85	87	36
29	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeOC$_6$H$_4$	Ph	**8c8i**	658.2171	3.73	659.2241	91	56	13
30	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	**8c8j**	676.1832	4.00	677.1900	90	78	28
31	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	Ph	4-MeC$_6$H$_4$	**8d8a**	632.1815	3.71	633.1880	92	85	14
32	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	**8d8b**	646.1971	3.78	647.2042	95	56	10
33	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	**8d8c**	660.2128	3.88	661.2193	96	51	10
34	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	**8d8d**	650.1721	3.61	651.1786	91	57	14
35	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8d8e**	666.1425	3.76	667.1491	84	58	7
36	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8d8f**	666.1425	3.77	667.1489	84	56	10
37	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	1-Naphthyl	4-MeC$_6$H$_4$	**8d8g**	682.1971	3.80	683.2039	81	68	17
38	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	**8d8h**	666.1425	3.82	667.1490	92	71	17
39	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeOC$_6$H$_4$	Ph	**8d8i**	648.1764	3.59	649.1829	94	49	6
40	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	**8d8j**	666.1425	3.81	667.1497	84	67	12
41	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	Ph	4-MeC$_6$H$_4$	**8e8a**	648.1519	3.82	649.1586	92	80	24
42	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	**8e8b**	662.1676	3.92	663.1739	96	63	24
43	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	**8e8c**	676.1832	4.01	677.1902	96	56	14
44	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	**8e8d**	666.1425	3.75	667.1494	85	64	17
45	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8e8e**	682.1130	3.92	683.1199	94	57	16
46	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8e8f**	682.1130	3.90	683.1194	96	68	30
47	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	1-Naphthyl	4-MeC$_6$H$_4$	**8e8g**	698.1676	3.93	699.1739	94	76	23

48	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	**8e8h**	682.1130	3.95	683.1190	94	73	30
49	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeOC$_6$H$_4$	Ph	**8e8i**	664.1469	3.67	665.1533	80	45	18
50	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	**8e8j**	682.1130	3.90	683.1191	95	67	25
51	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	Ph	4-MeC$_6$H$_4$	**8f8a**	648.1519	3.76	649.1590	95	78	24
52	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	**8f8b**	662.1676	3.86	663.1737	83	52	6
53	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	**8f8c**	676.1832	3.96	677.1891	84	44	2
54	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	**8f8d**	666.1425	3.70	667.1492	98	59	14
55	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8f8e**	682.1130	3.86	683.1193	97	53	16
56	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8f8f**	682.1130	3.83	683.1195	99	63	26
57	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	1-Naphthyl	4-MeC$_6$H$_4$	**8f8g**	698.1676	3.86	699.1736	81	60	23
58	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	**8f8h**	682.1130	3.90	683.1191	93	70	29
59	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeOC$_6$H$_4$	Ph	**8f8i**	664.1469	3.64	665.1538	99	46	18
60	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	**8f8j**	682.1130	3.90	683.1195	94	65	25
61	1-Naphthyl	4-MeC$_6$H$_4$	Ph	4-MeC$_6$H$_4$	**8g8a**	664.2066	3.75	665.2134	93	81	19
62	1-Naphthyl	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	**8g8b**	678.2222	3.85	679.2283	93	53	17
63	1-Naphthyl	4-MeC$_6$H$_4$	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	**8g8c**	692.2379	3.94	693.2439	88	32	3
64	1-Naphthyl	4-MeC$_6$H$_4$	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	**8g8d**	682.1971	3.72	683.2041	100	69	22
65	1-Naphthyl	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8g8e**	698.1676	3.87	699.1736	92	55	14
66	1-Naphthyl	4-MeC$_6$H$_4$	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8g8f**	698.1676	3.83	699.1742	72	58	39
67	1-Naphthyl	4-MeC$_6$H$_4$	1-Naphthyl	4-MeC$_6$H$_4$	**8g8g**	714.2222	3.86	715.2278	87	64	7
68	1-Naphthyl	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	**8g8h**	698.1676	3.88	699.1742	90	64	24
69	1-Naphthyl	4-MeC$_6$H$_4$	4-MeOC$_6$H$_4$	Ph	**8g8i**	680.2015	3.63	681.2081	89	41	8
70	1-Naphthyl	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	**8g8j**	698.1676	3.87	699.1739	88	62	24
71	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	Ph	4-MeC$_6$H$_4$	**8h8a**	648.1519	3.82	649.1585	94	81	21
72	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	**8h8b**	662.1676	3.90	663.1742	90	48	19
73	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	**8h8c**	676.1832	4.02	677.1891	100	62	16
74	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	**8h8d**	666.1425	3.77	667.1485	95	62	20
75	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8h8e**	682.1130	3.80	683.1196	76	43	11
76	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8h8f**	682.1130	3.89	683.1190	99	71	29
77	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	1-Naphthyl	4-MeC$_6$H$_4$	**8h8g**	698.1676	3.93	699.1738	92	71	21
78	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	**8h8h**	682.1130	3.44	683.1190	97	71	24
79	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	4-MeOC$_6$H$_4$	Ph	**8h8i**	664.1469	3.70	665.1531	95	43	12
80	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	**8h8j**	682.1130	3.94	683.1191	96	70	25
81	4-MeOC$_6$H$_4$	Ph	Ph	4-MeC$_6$H$_4$	**8i8a**	630.1858	3.56	631.1912	95	85	26
82	4-MeOC$_6$H$_4$	Ph	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	**8i8b**	644.2015	3.65	645.2066	93	58	22

83	4-MeOC$_6$H$_4$	Ph	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	**8i8c**	658.2171	3.75	659.2224	98	56	13
84	4-MeOC$_6$H$_4$	Ph	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	**8i8d**	648.1764	3.53	649.1819	92	42	21
85	4-MeOC$_6$H$_4$	Ph	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8i8e**	664.1469	3.68	665.1517	46	26	18
86	4-MeOC$_6$H$_4$	Ph	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8i8f**	664.1469	3.64	665.1525	95	68	11
87	4-MeOC$_6$H$_4$	Ph	1-Naphthyl	4-MeC$_6$H$_4$	**8i8g**	680.2015	3.68	681.2071	98	80	23
88	4-MeOC$_6$H$_4$	Ph	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	**8i8h**	664.1469	3.71	682.1800	89	65	26
89	4-MeOC$_6$H$_4$	Ph	4-MeOC$_6$H$_4$	Ph	**8i8i**	646.1807	3.47	647.1871	96	48	12
90	4-MeOC$_6$H$_4$	Ph	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	**8i8j**	664.1469	3.56	682.1789	88	37	8
91	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	Ph	4-MeC$_6$H$_4$	**8j8a**	648.1519	3.84	649.1579	89	84	16
92	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-MeC$_6$H$_4$	**8j8b**	662.1676	3.94	663.1741	93	64	24
93	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	4-EtC$_6$H$_4$	4-MeC$_6$H$_4$	**8j8c**	676.1832	4.04	677.1889	94	37	11
94	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	2-FC$_6$H$_4$	4-MeC$_6$H$_4$	**8j8d**	666.1425	3.77	667.1490	80	62	23
95	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	4-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8j8e**	682.1130	3.94	683.1182	94	56	14
96	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	3-ClC$_6$H$_4$	4-MeC$_6$H$_4$	**8j8f**	682.1130	3.92	683.1188	92	71	25
97	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	1-Naphthyl	4-MeC$_6$H$_4$	**8j8g**	698.1676	3.97	699.1747	84	69	24
98	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	4-MeC$_6$H$_4$	4-ClC$_6$H$_4$	**8j8h**	682.1130	4.00	683.1172	74	76	19
99	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	4-MeOC$_6$H$_4$	Ph	**8j8i**	664.1469	3.75	665.1538	88	45	12
100	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	4-ClC$_6$H$_4$	2-MeC$_6$H$_4$	**8j8j**	682.1130	4.01	683.1190	82	54	15

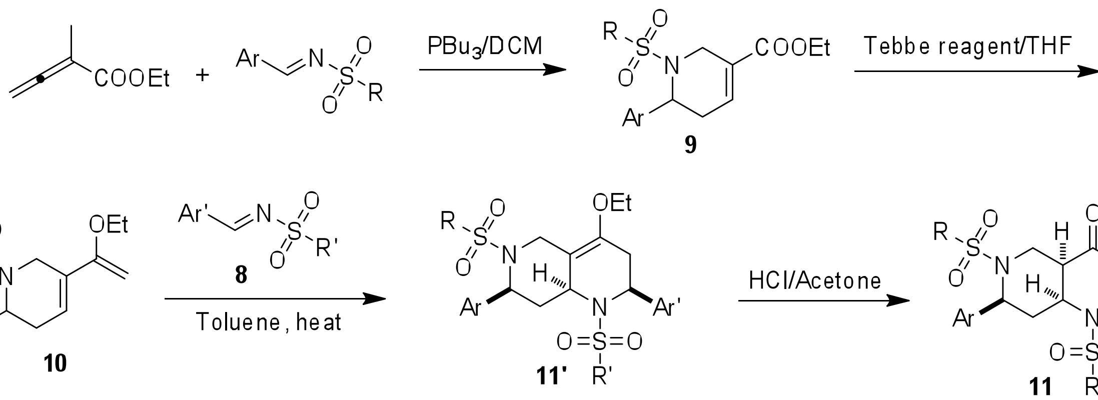
[a] Calculated exact mass. [b] Retention time. [c] High resolution mass found. [d] UV area percent. [e] Final purity after prep HPLC purification. [f] Crude purity after TFA cleaving. [g] Final isolated yield based on the lantern capacity after prep HPLC isolation.

Solution phase medicinal chemistry and characterization of compounds

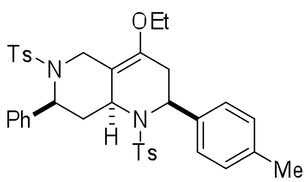
Synthesis of naphthyridine enol ethers 11' and naphthyridinones 11

All dienes (**9**), naphthyridine enol ethers (**11'**), and naphthyridinones (**11**) were synthesized according to procedures reported previously.[5]

[5] Wang Z, et al. (2010) Diversity Through a Branched Reaction Pathway: Generation of Multicyclic Scaffolds and Identification of Antimigratory Agents. *Chem Eur J* Published online on Nov 9; DOI: 10.1002/chem.201002195.

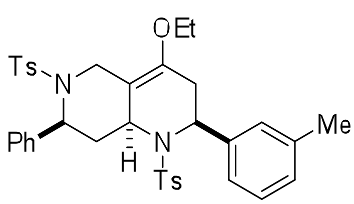


Reaction Sequence for Naphthyridinone Library Synthesis



11'a

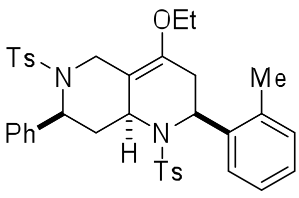
71% yield; white solid; IR (film) ν_{max} 3030, 2978, 2923, 1701, 1346, 1162, 668 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.2 Hz, 2H), 7.51 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.1 Hz, 2H), 7.22 (d, *J* = 8.0 Hz, 4H), 7.14-7.11 (m, 3H), 7.05 (d, *J* = 8.0 Hz, 2H), 6.93-6.92 (m, 2H), 5.15 (d, *J* = 5.8 Hz, 1H), 4.80 (t, *J* = 8.7 Hz, 1H), 4.26 (d, *J* = 16.4 Hz, 1H), 4.14-4.08 (m, 2H), 3.80 (dq, *J* = 9.8, 7.1 Hz, 1H), 3.64 (dq, *J* = 9.8, 7.1 Hz, 1H), 2.51 (d, *J* = 16.5 Hz, 1H), 2.45 (s, 3H), 2.39 (s, 3H), 2.26-2.20 (m, 4H), 1.93-1.88 (m, 1H), 1.23-1.15 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.4, 142.9, 142.6, 140.8, 137.5, 137.1, 136.6, 136.5, 129.7, 129.3, 128.9, 127.9, 127.3, 127.2, 127.1, 126.7, 126.6, 110.6, 63.3, 58.3, 52.4, 51.7, 42.7, 38.5, 25.6, 21.5, 21.4, 20.8, 15.1; MS (MALDI) calcd. for $C_{37}H_{40}N_2O_5S_2Na$ $[M + Na]^+$ 679.23, found 679.68.



11'b

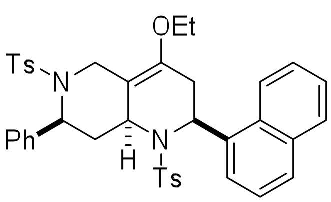
78% yield; white solid; IR (film) ν_{max} 3030, 2978, 2917, 1702, 1346, 1161, 656 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.2 Hz, 2H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.28 (d, *J* = 8.0 Hz, 2H), 7.22 (d, *J* = 8.1 Hz, 4H), 7.18 (s, 1H), 7.14-7.13 (m, 5H), 7.00-6.94 (m, 3H), 5.15 (d, *J* = 6.3 Hz, 1H), 4.85 (t, *J* = 8.7 Hz, 1H), 4.28 (d, *J* = 16.7 Hz, 1H), 4.18-4.12 (m, 2H), 3.80 (dq, *J* = 9.8, 7.1

Hz, 1H), 3.64 (dq, J = 9.8, 7.1 Hz, 1H), 2.51 (d, J = 16.5 Hz, 1H), 2.44 (s, 3H), 2.38 (s, 3H), 2.30-2.25 (m, 4H), 1.92-1.87 (m, 1H), 1.28 (td, J = 12.7, 10.0 Hz, 1H), 1.15 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.5, 143.0, 142.7, 140.8, 139.7, 137.8, 137.4, 136.7, 129.8, 129.4, 128.4, 128.2, 128.1, 128.0, 127.1, 126.7, 126.6, 124.2, 110.5, 63.3, 58.2, 52.6, 51.7, 42.7, 38.4, 25.4, 21.5, 21.45, 21.42, 15.1; MS (MALDI) calcd. for $C_{37}H_{40}N_2O_5S_2Na$ $[M + Na]^+$ 679.23, found 679.66.



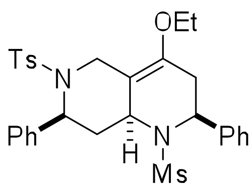
11'c

68% yield; white solid; IR (film) ν_{max} 3030, 2979, 2925, 1702, 1348, 1162, 654 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, J = 8.2 Hz, 2H), 7.45 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 7.18 (d, J = 8.1 Hz, 2H), 7.13-7.06 (m, 7H), 6.87 (dd, J = 7.8, 1.1 Hz, 2H), 5.47 (d, J = 6.1 Hz, 1H), 4.71 (dd, J = 9.6, 7.6 Hz, 1H), 4.25-4.19 (m, 2H), 4.13 (d, J = 17.1 Hz, 1H), 3.64 (dq, J = 10.0, 7.1 Hz, 1H), 3.46 (dq, J = 10.0, 7.1 Hz, 1H), 2.49 (s, 3H), 2.42 (s, 3H), 2.39-2.36 (m, 4H), 2.26-2.21 (m, 1H), 2.10-2.04 (m, 1H), 1.27-1.16 (m, 1H), 1.01 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 143.2, 142.9, 140.4, 137.8, 137.4, 136.8, 136.6, 131.3, 129.6, 129.2, 127.9, 127.8, 127.4, 127.2, 127.1, 126.9, 126.8, 125.4, 110.7, 63.2, 58.6, 52.0, 51.3, 42.9, 36.6, 27.0, 21.4, 20.2, 14.9; MS (MALDI) calcd. for $C_{37}H_{40}N_2O_5S_2Na$ $[M + Na]^+$ 679.23, found 679.50.



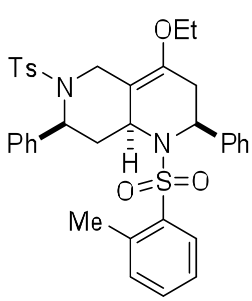
11'd

67% yield; white solid; IR (film) ν_{max} 3053, 2978, 2921, 1702, 1346, 1161, 658 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.68 (d, J = 8.7 Hz, 1H), 7.78 (d, J = 8.2 Hz, 1H), 7.72 (d, J = 7.9 Hz, 1H), 7.66 (d, J = 8.1 Hz, 2H), 7.59 (t, J = 7.6 Hz, 1H), 7.48-7.45 (m, 3H), 7.36-7.30 (m, 2H), 7.27-7.26 (m, 2H), 7.20 (d, J = 8.0 Hz, 2H), 7.12-7.07 (m, 3H), 6.81 (d, J = 6.5 Hz, 2H), 6.12 (d, J = 6.2 Hz, 1H), 4.58 (t, J = 8.6 Hz, 1H), 4.24 (s, 2H), 4.14 (d, J = 12.0 Hz, 1H), 3.67 (dq, J = 9.9, 7.1 Hz, 1H), 3.52 (dq, *J* = 9.9, 7.1 Hz, 1H), 2.60 (d, *J* = 16.6 Hz, 1H), 2.48-2.42 (m, 4H), 2.39 (s, 3H), 1.76-1.72 (m, 1H), 1.08-1.01 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 143.5, 136.6, 135.0, 133.8, 129.6, 129.3, 128.9, 128.7, 127.9, 127.6, 127.1, 126.8, 126.4, 125.7, 125.1, 124.6, 124.4, 124.0, 110.2, 63.3, 58.5, 52.0, 50.4, 42.9, 36.3, 27.8, 21.4, 15.0; MS (MALDI) calcd. for $C_{40}H_{40}N_2O_5S_2Na$ $[M + Na]^+$ 715.23, found 715.54.



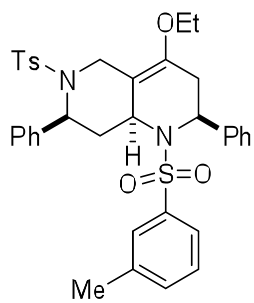
11'e

60% yield; white solid; IR (film) ν_{max} 3030, 2979, 2929, 1673, 1336, 1157, 664 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.2 Hz, 2H), 7.33(d, *J* = 7.7 Hz, 2H), 7.26-7.21 (m, 4H), 7.19-7.14 (m, 4H), 7.02-7.00 (m, 2H), 5.24 (d, *J* = 5.7 Hz, 1H), 4.81 (dd, *J* = 10.1, 7.8 Hz, 1H), 4.55 (d, *J* = 17.4 Hz, 1H), 4.05 (d, *J* = 17.6 Hz, 1H), 3.96 (dq, *J* = 9.6, 7.1 Hz, 1H), 3.84 (dq, *J* = 9.6, 7.1 Hz, 1H), 3.55 (d, *J* = 12.4 Hz, 1H), 2.83 (d, *J* = 16.6 Hz, 1H), 2.63 (s, 3H), 2.56-2.51 (m, 1H), 2.38 (s, 3H), 2.30-2.28 (m, 1H), 1.32 (t, *J* = 7.1 Hz, 1H), 1.15 (td, *J* = 12.8, 10.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.0, 142.7, 140.8, 139.6, 136.7, 129.4, 128.9, 128.3, 128.1, 127.5, 127.2, 127.1, 126.2, 110.7, 63.5, 58.0, 52.6, 51.3, 42.5, 38.0, 37.9, 27.0, 21.4, 15.5; MS (MALDI) calcd. for $C_{30}H_{34}N_2O_5S_2Na$ $[M + Na]^+$ 589.18, found 589.32.



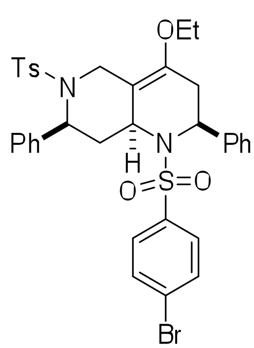
11'f

80% yield; white solid; IR (film) ν_{max} 3062, 2978, 2925, 1674, 1311, 1161, 664 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 7.8 Hz, 1H), 7.49-7.46 (m, 3H), 7.37-7.30 (m, 4H), 7.24 (d, *J* = 7.8 Hz, 2H), 7.20-7.11 (m, 6H), 6.94-6.92 (m, 2H), 5.06 (d, *J* = 5.8 Hz, 1H), 4.68 (dd, *J* = 9.7, 7.5 Hz, 1H), 4.29 (s, 2H), 4.18 (d, *J* = 12.2 Hz, 1H), 3.91 (dq, *J* = 9.7, 7.1 Hz, 1H), 3.78 (dq, *J* = 9.7, 7.1 Hz, 1H), 2.63 (d, *J* = 16.0 Hz, 1H), 2.56 (s, 3H), 2.33-2.29 (m, 4H), 2.17-2.12 (m, 1H), 1.28-1.19 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.1, 143.0, 140.7, 139.6, 138.0, 137.5, 136.3, 132.9, 132.8, 129.4, 129.2, 128.3, 128.0, 127.6, 127.2, 127.0, 126.7, 126.2, 110.7, 63.5, 58.6, 52.2, 51.5, 43.2, 38.1, 26.4, 21.4, 20.6, 15.3; MS (MALDI) calcd. for $C_{36}H_{38}N_2O_5S_2Na$ [M + Na]$^+$ 665.21, found 665.48.



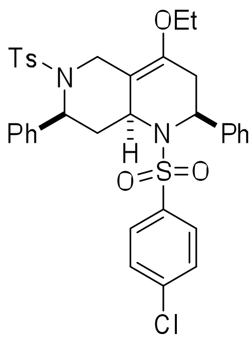
11’g

61% yield; white solid; IR (film) ν_{max} 3060, 2977, 2921, 1699, 1344, 1160, 663 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (s, 1H), 7.47 (d, *J* = 8.0 Hz, 2H), 7.42-7.35 (m, 5H), 7.25-7.23 (m, 2H), 7.19-7.16 (m, 3H), 7.11-7.09 (m, 3H), 6.89 (d, *J* = 6.9 Hz, 2H), 4.82 (t, *J* = 8.7 Hz, 1H), 4.28-4.22 (m, 2H), 4.11 (d, *J* = 17.3 Hz, 1H), 3.81 (dq, *J* = 9.9, 7.5 Hz, 1H), 3.64 (dq, *J* = 9.9, 7.5 Hz, 1H), 2.54 (d, *J* = 16.5 Hz, 1H), 2.44 (s, 3H), 2.36 (s, 3H), 2.27-2.22 (m, 1H), 1.96-1.92 (m, 1H), 1.88-1.14 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.9, 142.5, 140.6, 140.1, 139.6, 139.4, 136.6, 133.5, 129.3, 129.0, 128.3, 128.0, 127.4, 127.3, 127.1, 126.7, 123.6, 110.9, 63.4, 58.3, 52.6, 51.8, 42.7, 38.5, 25.5, 21.4, 21.3, 15.1; MS (MALDI) calcd. for $C_{36}H_{38}N_2O_5S_2Na$ [M + Na]$^+$ 665.21, found 665.45.



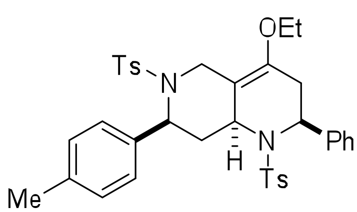
11’h

75% yield; white solid; IR (film) ν_{max} 3060, 2977, 1699, 1346, 1162, 664 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8.5 Hz, 2H), 7.56 (d, *J* = 8.5 Hz, 2H), 7.49 (d, *J* = 8.2 Hz, 2H), 7.35 (d, *J* = 7.7 Hz, 2H), 7.28-7.25 (m, 2H), 7.21-7.18 (m, 3H), 7.13-7.09 (m, 3H), 6.90 (dd, *J* = 7.5, 1.6 Hz, 2H), 5.21 (d, J = 5.8 Hz, 1H), 4.84 (dd, J = 9.6, 8.0 Hz, 1H), 4.28 (d, J = 17.0 Hz, 1H), 4.17 (d, J = 12.4 Hz, 1H), 4.08 (d, J = 17.0 Hz, 1H), 3.83 (dq, J = 9.8, 7.1 Hz, 1H), 3.67 (dq, J = 9.8, 7.1 Hz, 1H), 2.59 (d, J = 16.5 Hz, 1H), 2.38 (s, 3H), 2.28-2.23 (m, 1H), 1.98-1.93 (m, 1H), 1.23-1.14 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.0, 142.4, 140.5, 139.4, 139.3, 136.7, 132.5, 129.3, 128.4, 128.2, 128.0, 127.63, 127.62, 127.4, 127.2, 127.1, 126.6, 110.7, 63.4, 58.1, 52.7, 52.0, 42.6, 38.3, 25.6, 21.4, 15.1; MS (MALDI) calcd. for $C_{35}H_{35}BrN_2O_5S_2Na$ $[M + Na]^+$ 731.10, found 731.40.



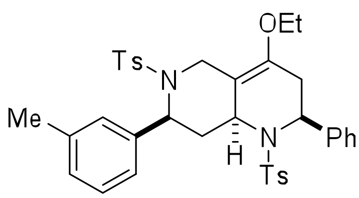
11’i

76% yield; white solid; IR (film) ν_{max} 3062, 2979, 2925, 1699, 1346, 1163, 665 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, J = 8.6 Hz, 2H), 7.49-7.47 (m, 4H), 7.35 (d, J = 7.7 Hz, 2H), 7.27-7.24 (m, 2H), 7.20-7.18 (m, 3H), 7.14-7.09 (m, 3H), 6.89 (dd, J = 7.6, 1.6 Hz, 2H), 5.21 (d, J = 5.8 Hz, 1H), 4.84 (dd, J = 9.6, 8.0 Hz, 1H), 4.28 (d, J = 16.7 Hz, 1H), 4.17 (d, J = 12.4 Hz, 1H), 4.08 (d, J = 17.0 Hz, 1H), 3.83 (dq, J = 9.8, 7.1 Hz, 1H), 3.66 (dq, J = 9.8, 7.1 Hz, 1H), 2.59 (d, J = 16.5 Hz, 1H), 2.38 (s, 3H), 2.28-2.23 (m, 1H), 1.98-1.92 (m, 1H), 1.21-1.13 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 142.9, 142.4, 140.5, 139.3, 139.2, 138.9, 136.7, 129.5, 129.3, 128.4, 128.1, 128.0, 127.6, 127.4, 127.2, 127.1, 126.6, 110.7, 63.4, 58.1, 52.7, 51.9, 42.6, 38.3, 25.6, 21.4, 15.1; MS (MALDI) calcd. for $C_{35}H_{35}ClN_2O_5S_2Na$ $[M + Na]^+$ 685.16, found 685.48.



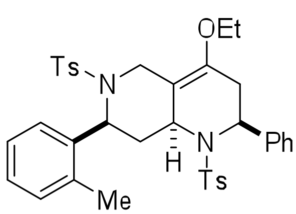
11’j

81% yield; white solid; IR (film) ν_{max} 3027, 2978, 2917, 1700, 1344, 1162, 655 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, J = 8.3 Hz, 2H), 7.50 (d, J = 8.3 Hz, 2H), 7.36 (d, J = 7.5 Hz, 2H), 7.30-7.18 (m, 7H), 6.92 (d, J = 7.9 Hz, 2H), 6.81 (d, J = 8.0 Hz, 2H), 5.19 (d, J = 5.7 Hz, 1H), 4.77 (dd, J = 9.7, 7.7 Hz, 1H), 4.26 (d, J = 16.6 Hz, 1H), 4.17-4.09 (m, 2H), 3.81 (dq, J = 9.8, 7.0 Hz, 1H), 3.65 (dq, J = 9.8, 7.0 Hz, 1H), 2.53 (d, J = 16.5 Hz, 1H), 2.44 (s, 3H), 2.38 (s, 3H), 2.26-2.19 (m, 4H), 1.95-1.88 (m, 1H), 1.22-1.15 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 143.0, 142.6, 139.8, 137.8, 137.6, 136.9, 136.8, 129.9, 129.4, 128.9, 128.4, 127.6, 127.3, 126.9, 126.7, 111.0, 63.5, 58.4, 52.7, 52.0, 42.8, 38.7, 25.6, 21.6, 21.0, 15.2; MS (MALDI) calcd. for $C_{37}H_{40}N_2O_5S_2Na$ $[M + Na]^+$ 679.23, found 679.55.



11’k

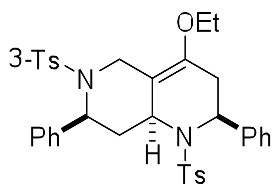
85% yield; white solid; IR (film) ν_{max} 3029, 2978, 2913, 1702, 1345, 1162, 656 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, J = 7.6 Hz, 2H), 7.47 (d, J = 7.7 Hz, 2H), 7.36 (d, J = 7.6 Hz, 2H), 7.29 (d, J = 8.0 Hz, 2H), 7.24 (d, J = 7.6 Hz, 2H), 7.19-7.16 (m, 3H), 7.01 (t, J = 7.5 Hz, 1H), 6.92 (d, J = 7.4 Hz, 1H), 6.74 (d, J = 7.5 Hz, 1H), 6.63 (s, 1H), 5.19 (d, J = 5.7 Hz, 1H), 4.76 (dd, J = 9.8, 7.6 Hz, 1H), 4.29 (d, J = 16.7 Hz, 1H), 4.18-4.11 (m, 2H), 3.82 (dq, J = 9.5, 6.9 Hz, 1H), 3.65 (dq, J = 9.5, 6.9 Hz, 1H), 2.54 (d, J = 16.4 Hz, 1H), 2.45 (s, 3H), 2.37 (s, 3H), 2.24-2.19 (m, 1H), 2.16 (s, 3H), 1.95-1.91 (m, 1H), 1.20-1.16 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.5, 142.8, 142.5, 140.5, 139.7, 137.5, 137.4, 136.9, 129.8, 129.2, 128.2, 127.9, 127.8, 127.4, 127.37, 127.35, 127.1, 126.8, 123.8, 111.0, 63.4, 58.5, 52.6, 51.9, 42.8, 38.7, 25.6, 21.5, 21.4, 21.2, 15.1; MS (MALDI) calcd. for $C_{37}H_{40}N_2O_5S_2Na$ $[M + Na]^+$ 679.23, found 679.73.



11’l

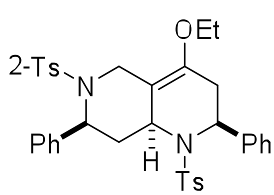
83 yield; white solid; IR (film) ν_{max} 3063, 2978, 2921, 1699, 1345, 1162, 656 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, J = 8.1 Hz, 2H), 7.38-7.30 (m, 6H), 7.28-7.23 (m, 2H), 7.17 (t, J = 7.2 Hz, 1H), 7.11 (d, J = 8.1 Hz, 2H), 7.00 (t, J = 7.4 Hz, 1H), 6.92 (d, J = 7.4 Hz, 1H), 6.87 (t, J = 7.4 Hz, 1H), 6.78 (d, J = 7.7 Hz, 1H), 5.23 (d, J = 5.8 Hz, 1H), 4.79 (dd, J = 11.3, 5.7 Hz, 1H),

4.43 (d, J = 16.3 Hz, 1H), 4.26-4.20 (m, 2H), 3.86 (dq, J = 9.6, 7.0 Hz, 1H), 3.70 (dq, J = 9.6, 7.0 Hz, 1H), 2.59 (d, J = 16.5 Hz, 1H), 2.45 (s, 3H), 2.36 (s, 3H), 2.18 (s, 3H), 2.14-2.10 (m, 1H), 2.02-1.97 (m, 1H), 1.28-1.20 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.5, 142.7, 142.6, 139.7, 138.9, 137.4, 136.7, 134.9, 130.1, 129.8, 129.0, 128.3, 127.4, 127.3, 127.0, 126.9, 126.8, 126.5, 125.7, 111.2, 63.5, 56.9, 52.8, 43.9, 38.5, 25.9, 21.5, 21.3, 19.0, 15.2; MS (MALDI) calcd. for $C_{37}H_{40}N_2O_5S_2Na$ $[M + Na]^+$ 679.23, found 679.37.



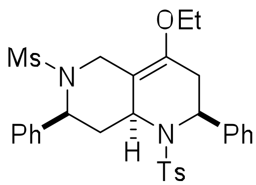
11'm

87% yield; white solid; IR (film) ν_{max} 3057, 2978, 2914, 1699, 1301, 1161, 657 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, J = 8.0 Hz, 2H), 7.45-7.44 (m, 1H), 7.36-7.23 (m, 9H), 7.17 (t, J = 7.2 Hz, 1H), 7.12-7.09 (m, 3H), 6.92-6.91 (m, 2H), 5.18 (d, J = 5.7 Hz, 1H), 4.85 (dd, J = 10.4, 7.1 Hz, 1H), 4.35 (d, J = 16.8 Hz, 1H), 4.15 (d, J = 12.3 Hz, 1H), 4.09 (d, J = 16.8 Hz, 1H), 3.81 (dq, J = 9.7, 7.0 Hz, 1H), 3.65 (dq, J = 9.7, 7.0 Hz, 1H), 2.54 (d, J = 16.5 Hz, 1H), 2.45 (s, 3H), 2.31-2.24 (m, 4H), 1.94-1.89 (m, 1H), 1.23-1.16 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.4, 142.5, 140.6, 139.7, 139.6, 139.0, 137.4, 132.9, 129.8, 128.5, 128.2, 128.0, 127.5, 127.4, 127.3, 127.1, 126.8, 126.6, 124.2, 111.0, 63.4, 58.4, 52.6, 51.8, 42.6, 38.5, 25.6, 21.4, 21.2, 15.1; MS (MALDI) calcd. for $C_{36}H_{38}N_2O_5S_2Na$ $[M + Na]^+$ 665.21, found 665.62.



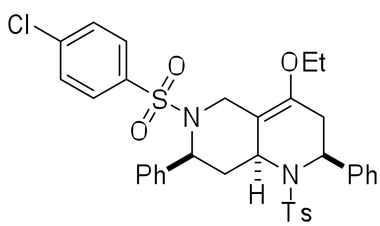
11'n

86% yield; white solid; IR (film) ν_{max} 3060, 2978, 2924, 1703, 1338, 1158, 656 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, J = 8.2 Hz, 2H), 7.44 (d, J = 7.6 Hz, 2H), 7.34-7.20 (m, 8H), 7.12 (t, J = 7.8 Hz, 1H), 6.97-6.90 (m, 2H), 6.83 (t, J = 7.7 Hz, 2H), 6.56 (t, J = 7.3 Hz, 2H), 5.35 (d, J = 6.1 Hz, 1H), 4.66 (d, J = 15.3 Hz, 1H), 4.53 (dd, J = 10.6, 5.7 Hz, 1H), 4.42 (d, J = 12.0 Hz, 1H), 3.88-3.82 (m, 2H), 3.68 (dq, J = 9.6, 7.0 Hz, 1H), 2.60 (d, J = 16.6 Hz, 1H), 2.48 (s, 3H), 2.45 (s, 3H), 2.13-2.09 (m, 1H), 2.04-2.00 (m, 1H), 1.19-1.06 (m, 4H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 143.5, 143.3, 140.0, 138.7, 137.5, 137.0, 131.9, 131.7, 129.9, 129.3, 128.2, 127.8, 127.7, 127.5, 127.4, 127.3, 126.7, 125.6, 110.9, 63.6, 60.0, 52.6, 42.5, 39.0, 25.3, 21.4, 19.8, 15.0; MS (MALDI) calcd. for $C_{36}H_{38}N_2O_5S_2Na$ $[M + Na]^+$ 665.21, found 665.60.



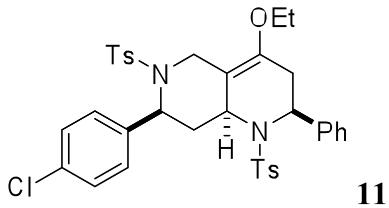
11’o

81% yield; white solid; IR (film) ν_{max} 3031, 2979, 2930, 1701, 1341, 1164, 657 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.79 (d, J = 8.2 Hz, 2H), 7.43 (d, J = 7.7 Hz, 2H), 7.34 (d, J = 8.2 Hz, 2H), 7.30-7.26 (m, 2H), 7.24-7.18 (m, 4H), 7.03-7.02 (m, 2H), 5.37 (d, J = 5.8 Hz, 1H), 4.88 (dd, J = 9.7, 8.0 Hz, 1H), 4.53 (d, J = 12.2 Hz, 1H), 4.26 (d, J = 16.2 Hz, 1H), 4.07 (d, J = 16.4 Hz, 1H), 3.85 (dq, J = 9.6, 7.1 Hz, 1H), 3.64 (dq, J = 9.6, 7.1 Hz, 1H), 2.64 (d, J = 16.5 Hz, 1H), 2.43 (s, 3H), 2.35-2.30 (m, 1H), 2.28 (s, 3H), 2.14-2.09 (m, 1H), 1.26 (td, J = 12.7, 10.2 Hz, 1H), 1.15 (t, J = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 143.7, 142.7, 139.9, 139.8, 137.3, 130.0, 128.5, 128.3, 127.9, 127.6, 127.5, 127.3, 126.7, 110.4, 63.4, 58.4, 52.6, 51.7, 42.4, 39.4, 37.9, 25.5, 21.5, 15.1; MS (MALDI) calcd. for $C_{30}H_{34}N_2O_5S_2Na$ $[M + Na]^+$ 589.18, found 589.33.



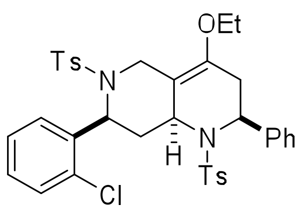
11’p

82% yield; white solid; IR (film) ν_{max} 3062, 2979, 2925, 1699, 1349, 1163, 657 cm^{-1}; ^{1}H NMR (500 MHz, CDCl$_3$) δ 7.61 (d, J = 8.2 Hz, 2H), 7.47 (d, J = 8.6 Hz, 2H), 7.37 (d, J = 7.6 Hz, 2H), 7.34-7.31 (m, 4H), 7.26-7.24 (m, 2H), 7.19-7.15 (m, 1H), 7.13-7.08 (m, 3H), 6.90 (d, J = 6.7 Hz, 2H), 5.23 (d, J = 5.7 Hz, 1H), 4.83 (dd, J = 10.2, 7.4 Hz, 1H), 4.33 (d, J = 16.7 Hz, 1H), 4.19-4.11 (m, 2H), 3.82 (dq, J = 9.7, 7.0 Hz, 1H), 3.65 (dq, J = 9.7, 7.0 Hz, 1H), 2.57 (d, J = 16.4 Hz, 1H), 2.44 (s, 3H), 2.33-2.28 (m, 1H), 1.96-1.91 (m, 1H), 1.23 (td, J = 12.7, 10.7 Hz, 1H), 1.16 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 143.7, 142.9, 140.2, 139.7, 138.5, 138.4, 137.2, 130.0, 128.9, 128.5, 128.3, 128.1, 127.5, 127.39, 127.37, 126.7, 126.6, 110.2, 63.3, 58.8, 52.7, 51.9, 42.8, 38.7, 25.6, 21.5, 15.2; MS (MALDI) calcd. for $C_{35}H_{35}ClN_2O_5S_2Na$ $[M + Na]^+$ 685.16, found 685.24.



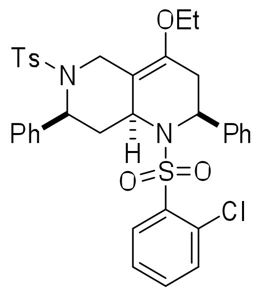
11'q

85% yield; white solid; IR (film) ν_{max} 3062, 2978, 2917, 1702, 1346, 1162, 655 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.2 Hz, 2H), 7.49 (d, *J* = 8.6 Hz, 2H), 7.35 (d, *J* = 7.6 Hz, 2H), 7.28-7.16 (m, 6H), 7.06 (d, *J* = 8.5 Hz, 2H), 6.82 (d, *J* = 8.4 Hz, 2H), 5.17 (d, *J* = 5.7 Hz, 1H), 4.71 (dd, *J* = 9.8, 7.4 Hz, 1H), 4.21-4.10 (m, 3H), 3.80 (dq, *J* = 9.7, 7.0 Hz, 1H), 3.63 (dq, *J* = 9.7, 7.0 Hz, 1H), 2.52 (d, *J* = 16.6 Hz, 1H), 2.42 (s, 3H), 2.38 (s, 3H), 2.21-2.14 (m, 1H), 1.92-1.87 (m, 1H), 1.16-1.06 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 143.2, 142.9, 139.6, 139.3, 137.4, 136.4, 132.9, 129.8, 129.4, 128.3, 128.1, 128.0, 127.48, 127.47, 127.1, 126.7, 110.2, 63.4, 57.9, 52.5, 51.7, 42.9, 38.7, 25.3, 21.5, 15.1; MS (MALDI) calcd. for $C_{36}H_{37}ClN_2O_5S_2Na$ $[M + Na]^+$ 699.17, found 699.41.



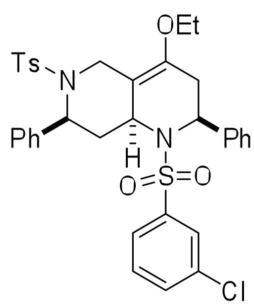
11'r

85% yield; white solid; IR (film) ν_{max} 3062, 2978, 2917, 1698, 1348, 1163, 656 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.58 (d, *J* = 8.2 Hz, 2H), 7.53 (d, *J* = 8.2 Hz, 2H), 7.33-7.28 (m, 4H), 7.24-7.21 (m, 4H), 7.17-7.13 (m, 2H), 7.08-7.04 (m, 4H), 5.22 (d, *J* = 5.7 Hz, 1H), 4.94 (dd, *J* = 12.3, 6.9 Hz, 1H), 4.39-4.32 (m, 2H), 4.02 (d, *J* = 12.2 Hz, 1H), 3.85 (dq, *J* = 9.7, 7.1 Hz, 1H), 3.70 (dq, *J* = 9.7, 7.1 Hz, 1H), 2.57 (d, *J* = 16.4 Hz, 1H), 2.44 (s, 3H), 2.40 (s, 3H), 2.26-2.22 (m, 1H), 2.01-1.96 (m, 1H), 1.21 (t, *J* = 7.1 Hz, 3H), 1.08 (td, *J* = 12.6, 12.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 143.1, 142.9, 139.7, 138.8, 137.3, 135.9, 131.6, 129.8, 129.3, 129.2, 128.3, 128.2, 128.0, 127.4, 127.3, 127.2, 126.9, 126.6, 110.8, 63.5, 56.8, 52.7, 52.4, 43.9, 37.6, 26.0, 21.5, 15.2; MS (MALDI) calcd. for $C_{36}H_{37}ClN_2O_5S_2Na$ $[M + Na]^+$ 699.17, found 699.38.



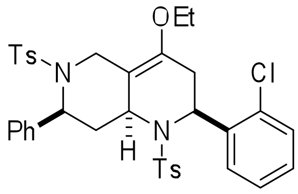
11’s

81% yield; white solid; IR (film) ν_{max} 3063, 2979, 1700, 1346, 1162, 700 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, *J* = 8.0 Hz, 1H), 7.53-7.38 (m, 7H), 7.27-7.24 (m, 2H), 7.20-7.10 (m, 6H), 6.93-6.91 (m, 2H), 5.08 (d, *J* = 5.7 Hz, 1H), 4.71 (t, *J* = 8.5 Hz, 1H), 4.30 (d, *J* = 16.4 Hz, 1H), 4.16 (d, *J* = 16.4 Hz, 1H), 3.92-3.86 (m, 1H), 3.79-3.73 (m, 1H), 2.60 (d, *J* = 16.5 Hz, 1H), 2.36 (s, 3H), 2.29-2.25 (m, 2H), 1.31-1.24 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.1, 143.0, 140.8, 139.4, 137.2, 136.3, 133.9, 132.4, 132.1, 131.7, 129.4, 128.3, 128.0, 127.6, 127.3, 127.2, 127.1, 126.8, 110.8, 63.6, 58.8, 52.6, 52.2, 43.2, 38.6, 26.5, 21.4, 15.3; MS (MALDI) calcd. for $C_{35}H_{35}ClN_2O_5S_2Na$ $[M + Na]^+$ 685.16, found 685.68.



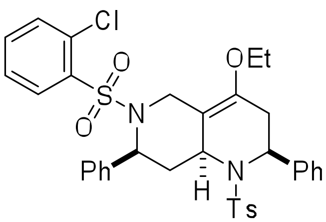
11’t

70% yield; white solid; IR (film) ν_{max} 3063, 2979, 1672, 1345, 1164, 668 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (t, *J* = 1.7 Hz, 1H), 7.58-7.55 (m, 2H), 7.51 (d, *J* = 8.3 Hz, 2H), 7.45 (d, *J* = 7.9 Hz, 1H), 7.37 (d, *J* = 7.7 Hz, 2H), 7.27-7.24 (m, 2H), 7.22-7.18 (m, 3H), 7.14-7.10 (m, 3H), 6.91-6.89 (m, 2H), 5.20 (d, *J* = 5.9 Hz, 1H), 4.84 (t, *J* = 8.7 Hz, 1H), 4.28 (d, *J* = 16.6 Hz, 1H), 4.17-4.12 (m, 2H), 3.83 (dq, *J* = 9.8, 7.1 Hz, 1H), 3.67 (dq, *J* = 9.8, 7.1 Hz, 1H), 2.58 (d, *J* = 16.6 Hz, 1H), 2.35 (s, 3H), 2.26-2.21 (m, 1H), 2.00-1.95 (m, 1H), 1.23-1.17 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.1, 142.6, 142.1, 140.5, 139.2, 136.6, 135.3, 132.8, 130.6, 129.5, 128.4, 128.0, 127.6, 127.4, 127.2, 127.1, 126.6, 124.8, 110.6, 63.5, 58.1, 52.7, 52.0, 42.7, 38.2, 25.6, 21.4, 15.2; MS (MALDI) calcd. for $C_{35}H_{35}ClN_2O_5S_2Li$ $[M + Li]^+$ 669.18, found 669.26.



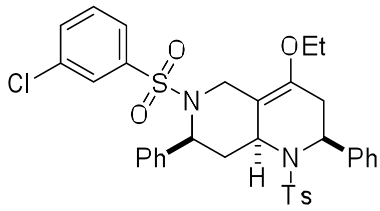
11'u

60% yield; white solid; IR (film) ν_{max} 3063, 2979, 1699, 1348, 1163, 670 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62-7.58 (m, 4H), 7.36-7.25 (m, 8H), 7.19 (d, *J* = 8.1 Hz, 2H), 7.16-7.11 (m, 3H), 5.48 (d, *J* = 4.7 Hz, 1H), 4.90 (dd, *J* = 11.3, 6.4 Hz, 1H), 4.75 (d, *J* = 16.9 Hz, 1H), 3.76 (d, *J* = 11.5 Hz, 1H), 3.45 (dq, *J* = 9.9, 7.1 Hz, 1H), 3.34 (dq, *J* = 9.9, 7.1 Hz, 1H), 2.94-2.89 (m, 1H), 2.50 (d, *J* = 16.1 Hz, 1H), 2.42 (s, 3H), 2.39 (s, 3H), 1.94-1.83 (m, 2H), 0.97 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 143.7, 143.1, 141.7, 138.4, 136.4, 135.8, 132.0, 129.7, 129.2, 128.8, 128.7, 128.4, 127.5, 127.3, 127.2, 126.5, 126.0, 110.1, 63.2, 58.2, 53.3, 52.5, 41.2, 38.6, 28.3, 21.5, 15.0; MS (MALDI) calcd. for $C_{36}H_{37}ClN_2O_5S_2Na$ $[M + Na]^+$ 699.17, found 699.38.



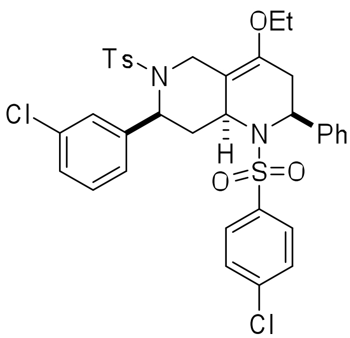
11'v

76% yield; white solid; IR (film) ν_{max} 3059, 2980, 1697, 1341, 1162, 656 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 7.8 Hz, 2H), 7.37-7.26 (m, 7H), 7.21 (t, *J* = 7.3 Hz, 1H), 7.00-6.94 (m, 2H), 6.85 (t, *J* = 7.6 Hz, 2H), 6.68 (d, *J* = 7.6 Hz, 2H), 5.35 (d, *J* = 6.0 Hz, 1H), 4.74 (d, *J* = 15.5 Hz, 1H), 4.65 (dd, *J* = 10.6, 5.9 Hz, 1H), 4.42 (d, *J* = 11.9 Hz, 1H), 4.03 (d, *J* = 15.6 Hz, 1H), 3.86 (dq, *J* = 9.7, 7.1 Hz, 1H), 3.69 (dq, *J* = 9.7, 7.1 Hz, 1H), 2.61 (d, *J* = 16.7 Hz, 1H), 2.45 (s, 3H), 2.14-2.04 (m, 2H), 1.28 (td, *J* = 12.5, 10.9 Hz, 1H), 1.16 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.5, 143.1, 139.9, 138.6, 138.4, 137.5, 132.6, 131.7, 131.1, 131.0, 129.8, 128.3, 127.8, 127.6, 127.4, 127.2, 126.7, 126.3, 110.9, 63.5, 59.8, 52.6, 52.5, 43.6, 38.8, 25.4, 21.4, 15.0; MS (MALDI) calcd. for $C_{35}H_{35}ClN_2O_5S_2Na$ $[M + Na]^+$ 685.16, found 685.67.



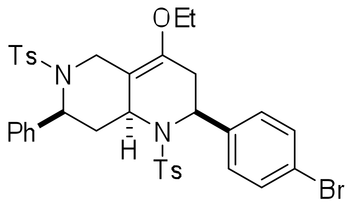
11'w

72% yield; white solid; IR (film) ν_{max} 3063, 2979, 1701, 1351, 1164, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, *J* = 8.2 Hz, 2H), 7.44-7.42 (m, 3H), 7.37-7.24 (m, 7H), 7.18 (t, *J* = 7.2 Hz, 1H), 7.13-7.08 (m, 3H), 6.88 (d, *J* = 7.1 Hz, 2H), 5.23 (d, *J* = 5.6 Hz, 1H), 4.79 (dd, *J* = 10.4, 7.3 Hz, 1H), 4.35 (d, *J* = 16.1 Hz, 1H), 4.17-4.14 (m, 2H), 3.86 (dq, *J* = 9.7, 7.1 Hz, 1H), 3.69 (dq, *J* = 9.7, 7.1 Hz, 1H), 2.59 (d, *J* = 16.5 Hz, 1H), 2.47 (s, 3H), 2.28-2.24 (m, 1H), 2.02-1.97 (m, 1H), 1.22-1.18 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.6, 143.0, 141.6, 139.8, 139.6, 137.3, 134.7, 132.1, 129.9, 128.3, 128.0, 127.5, 127.4, 127.3, 127.0, 126.8, 126.7, 125.0, 110.3, 63.4, 59.0, 52.6, 51.9, 42.9, 38.6, 25.7, 21.4, 15.2; MS (MALDI) calcd. for $C_{35}H_{35}ClN_2O_5S_2Na$ $[M + Na]^+$ 685.16, found 685.59.



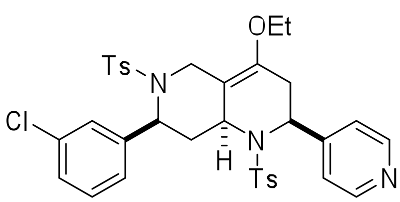
11'x

73% yield; white solid; IR (film) ν_{max} 3063, 2979, 1699, 1347, 1163, 664 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 (d, *J* = 8.6 Hz, 2H), 7.48-7.46 (m, 4H), 7.35 (d, *J* = 7.6 Hz, 2H), 7.26 (t, *J* = 7.5 Hz, 2H), 7.22-7.19 (m, 3H), 7.08-7.03 (m, 2H), 6.82 (d, *J* = 7.2 Hz, 1H), 6.74 (s, 1H), 5.22 (d, *J* = 5.8 Hz, 1H), 4.74 (dd, *J* = 9.8, 7.6 Hz, 1H), 4.22 (d, *J* = 16.0 Hz, 1H), 4.16-4.13 (m, 2H), 3.83 (dq, *J* = 9.7, 7.1 Hz, 1H), 3.67 (dq, *J* = 9.7, 7.1 Hz, 1H), 2.58 (d, *J* = 16.6 Hz, 1H), 2.37 (s, 3H), 2.22-2.17 (m, 1H), 1.99-1.94 (m, 1H), 1.18 (t, *J* = 7.1 Hz, 3H), 1.07 (td, *J* = 12.7, 10.2 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.3, 142.9, 142.5, 139.3, 139.2, 138.8, 136.4, 133.8, 129.5, 129.4, 129.3, 128.4, 128.1, 127.7, 127.4, 127.3, 127.1, 126.7, 125.0, 110.0, 63.4, 57.8, 52.7, 51.8, 42.8, 38.4, 25.6, 21.4, 15.1; MS (MALDI) calcd. for $C_{35}H_{34}Cl_2N_2O_5S_2Na$ $[M + Na]^+$ 719.12, found 719.34.



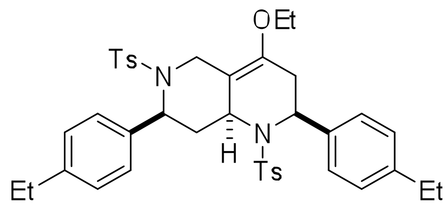
11'y

56% yield; white solid; IR (film) ν_{max} 3031, 2978, 1700, 1347, 1162, 657 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.2 Hz, 2H), 7.49 (d, *J* = 8.2 Hz, 2H), 7.37 (d, *J* = 8.5 Hz, 2H), 7.30 (d, *J* = 8.1 Hz, 2H), 7.22-7.20 (m, 4H), 7.17-7.15 (m, 3H), 6.92-6.90 (m, 2H), 5.12 (d, *J* = 5.7 Hz, 1H), 4.82 (dd, *J* = 9.8, 7.6 Hz, 1H), 4.26 (d, *J* = 16.5 Hz, 1H), 4.15 (d, *J* = 12.2 Hz, 1H), 4.09 (d, *J* = 16.8 Hz, 1H), 3.79 (dq, *J* = 9.8, 7.1 Hz, 1H), 3.63 (dq, *J* = 9.8, 7.1 Hz, 1H), 2.48-2.45 (m, 4H), 2.38 (s, 3H), 2.30-2.26 (m, 1H), 1.94-1.89 (m, 1H), 1.21-1.14 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.7, 143.0, 142.3, 140.6, 138.9, 137.1, 136.6, 131.4, 129.8, 129.4, 129.3, 128.1, 127.2, 127.1, 126.7, 126.5, 121.4, 110.9, 63.4, 58.2, 52.2, 51.8, 42.6, 38.8, 25.5, 21.5, 21.4, 15.1; MS (MALDI) calcd. for $C_{36}H_{37}BrN_2O_5S_2Na$ $[M + Na]^+$ 745.12, found 745.31.



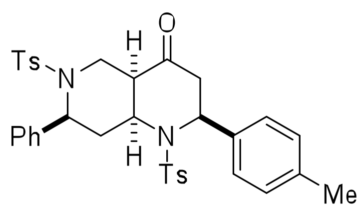
11'z

80% yield; white solid; IR (film) ν_{max} 3031, 2979, 2925, 1700, 1346, 1162, 656 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.47 (d, *J* = 5.7 Hz, 2H), 7.55 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.29 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 5.7 Hz, 2H), 7.08-7.02 (m, 2H), 6.82-6.80 (m, 2H), 5.07 (d, *J* = 5.3 Hz, 1H), 4.81 (dd, *J* = 10.5, 7.3 Hz, 1H), 4.41 (d, *J* = 17.0 Hz, 1H), 4.09 (d, *J* = 11.8 Hz, 1H), 3.98 (d, *J* = 17.2 Hz, 1H), 3.79 (dq, *J* = 9.7, 7.1 Hz, 1H), 3.62 (dq, *J* = 9.7, 7.1 Hz, 1H), 2.50 (d, *J* = 16.5 Hz, 1H), 2.42 (s, 3H), 2.38-2.35 (m, 4H), 1.88-1.84 (m, 1H), 1.17-1.10 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 149.9, 149.0, 144.0, 143.3, 142.6, 142.3, 136.6, 136.5, 134.0, 130.0, 129.6, 129.4, 127.4, 127.0, 126.8, 126.3, 124.4, 122.2, 110.7, 63.5, 57.7, 52.1, 51.9, 42.4, 39.1, 25.2, 21.5, 21.4, 15.1; MS (MALDI) calcd. for $C_{35}H_{36}ClN_3O_5S_2Na$ $[M + Na]^+$ 700.17, found 701.25.



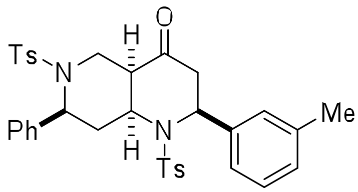
11’aa

70% yield; white solid; IR (film) ν_{max} 2965, 2925, 1702, 1346, 1162, 655 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.2 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.30-7.27 (m, 4H), 7.19 (d, *J* = 8.0 Hz, 2H), 7.09 (d, *J* = 8.2 Hz, 2H), 6.93 (d, *J* = 8.2 Hz, 2H), 6.82 (d, *J* = 8.2 Hz, 2H), 5.18 (d, *J* = 5.8 Hz, 1H), 4.76 (dd, *J* = 9.8, 7.6 Hz, 1H), 4.24-4.15 (m, 3H), 3.82 (dq, *J* = 9.8, 7.1 Hz, 1H), 3.65 (dq, *J* = 9.8, 7.1 Hz, 1H), 2.61-2.51 (m, 5H), 2.44 (s, 3H), 2.37 (s, 3H), 2.23-2.17 (m, 1H), 1.96-1.90 (m, 1H), 1.20-1.15 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.5, 143.4, 143.1, 142.8, 142.7, 137.9, 137.6, 136.9, 136.8, 129.8, 129.3, 127.7, 127.5, 127.4, 127.2, 126.8, 126.7, 110.8, 63.4, 58.4, 52.4, 51.8, 42.8, 38.5, 28.3, 25.6, 21.5, 21.4, 15.5, 15.4, 15.1; MS (MALDI) calcd. for $C_{40}H_{46}N_2O_5S_2Na$ $[M + Na]^+$ 721.27, found 721.18.



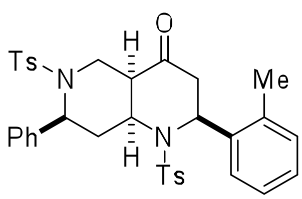
H07

89% yield; white solid; IR (film) ν_{max} 3031, 2919, 2868, 1713, 1347, 1162, 659 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 7.9 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.2 Hz, 2H), 7.18 (d, *J* = 8.1 Hz, 2H), 7.13-7.10 (m, 3H), 7.02 (d, *J* = 8.0 Hz, 2H), 6.86 (dd, *J* = 7.5, 1.0 Hz, 2H), 5.67 (d, *J* = 6.6 Hz, 1H), 4.91 (dd, *J* = 11.3, 7.0 Hz, 1H), 4.60-4.56 (m, 1H), 3.80 (dd, *J* = 15.4, 8.0 Hz, 1H), 3.43 (dd, *J* = 15.4, 9.3 Hz, 1H), 2.92 (dd, *J* = 14.8, 1.9 Hz, 1H), 2.67 (dd, *J* = 17.5, 8.8 Hz, 1H), 2.48 (s, 3H), 2.38 (s, 3H), 2.23-2.19 (m, 4H), 1.79-1.74 (m, 1H), 0.99 (td, *J* = 13.5, 11.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.7, 144.1, 143.2, 140.2, 137.8, 137.4, 137.1, 136.3, 130.3, 129.4, 129.1, 128.2, 127.3, 127.2, 127.0, 126.6, 125.9, 58.5, 54.9, 53.2, 45.4, 41.5, 40.5, 36.2, 21.5, 21.4, 20.8; MS (MALDI) calcd. for $C_{35}H_{36}N_2O_5S_2Na$ $[M + Na]^+$ 651.20, found 651.52.



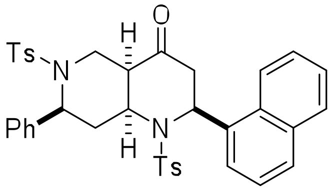
H08

92% yield; white solid; IR (film) ν_{max} 3060, 2922, 1713, 1347, 1162, 660 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.0 Hz, 2H), 7.44 (d, *J* = 8.1 Hz, 2H), 7.38 (d, *J* = 8.1 Hz, 2H), 7.20-7.08 (m, 8H), 6.96 (d, *J* = 7.2 Hz, 1H), 6.86 (d, *J* = 7.0 Hz, 2H), 5.67 (d, *J* = 6.7 Hz, 1H), 4.91 (dd, *J* = 11.3, 7.0 Hz, 1H), 4.62-4.58 (m, 1H), 3.79 (dd, *J* = 15.4, 8.0 Hz, 1H), 3.47 (dd, *J* = 15.4, 9.1 Hz, 1H), 2.93 (dd, *J* = 14.8, 1.4 Hz, 1H), 2.67 (dd, *J* = 17.5, 8.7 Hz, 1H), 2.48 (s, 3H), 2.37 (s, 3H), 2.24-2.20 (m, 4H), 1.79-1.74 (m, 1H), 1.04 (td, *J* = 12.5, 11.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.6, 144.1, 143.2, 140.2, 139.4, 138.2, 137.4, 137.1, 130.3, 129.4, 128.7, 128.3, 128.2, 128.1, 127.3, 127.0, 126.6, 125.9, 124.2, 58.5, 55.1, 53.3, 45.4, 41.4, 40.5, 36.2, 21.5, 21.4, 21.3; MS (MALDI) calcd. for $C_{35}H_{36}N_2O_5S_2Na$ [M + Na]$^+$ 651.20, found 651.57.



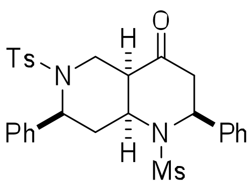
H09

83% yield; white solid; IR (film) ν_{max} 3060, 2959, 1722, 1350, 1162, 660 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.0 Hz, 2H), 7.36-7.34 (m, 4H), 7.14-7.08 (m, 7H), 7.03-7.01 (m, 2H), 6.85-6.83 (m, 2H), 5.81 (t, *J* = 5.5 Hz, 1H), 4.77 (dd, *J* = 11.4, 6.5 Hz, 1H), 4.53-4.48 (m, 1H), 3.78 (dd, *J* = 14.8, 7.5 Hz, 1H), 3.47 (dd, *J* = 14.8, 8.9 Hz, 1H), 2.88 (dd, *J* = 16.2, 4.7 Hz, 1H), 2.72-2.66 (m, 2H), 2.53 (s, 3H), 2.47 (s, 3H), 2.36 (s, 3H), 1.78-1.73 (m, 1H), 1.27 (td, *J* = 13.5, 11.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.2, 144.4, 143.2, 140.0, 138.2, 137.3, 136.7, 136.3, 131.2, 129.3, 128.2, 128.1, 127.5, 127.4, 127.1, 126.3, 126.2, 126.0, 58.9, 53.9, 52.5, 45.2, 43.5, 41.8, 36.0, 21.5, 21.4, 20.2; MS (MALDI) calcd. for $C_{35}H_{36}N_2O_5S_2Na$ [M + Na]$^+$ 651.20, found 651.78.



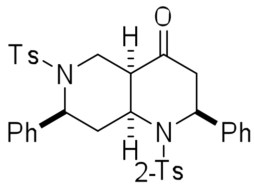
H10

85% yield; white solid; IR (film) ν_{max} 3060, 2951, 2923, 1704, 1352, 1161, 661 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71 (d, *J* = 8.6 Hz, 1H), 7.87 (d, *J* = 8.3 Hz, 2H), 7.78 (d, *J* = 7.7 Hz, 1H), 7.71 (d, *J* = 7.7 Hz, 1H), 7.65-7.62 (m, 1H), 7.51 (t, *J* = 7.5 Hz, 1H), 7.37-7.24 (m, 6H), 7.12-7.08 (m, 3H), 7.05-7.02 (m, 2H), 6.69 (d, *J* = 7.2 Hz, 2H), 6.55 (dd, *J* = 6.7, 2.5 Hz, 1H), 4.53 (dd, *J* = 11.3, 6.8 Hz, 1H), 4.33-4.28 (m, 1H), 3.90 (dd, *J* = 15.1, 7.8 Hz, 1H), 3.42 (dd, *J* = 15.1, 9.3 Hz, 1H), 3.11 (dd, *J* = 15.9, 2.9 Hz, 1H), 2.98 (dd, *J* = 16.0, 7.1 Hz, 1H), 2.48 (s, 3H), 2.37 (s, 3H), 1.17-1.13 (m, 1H), 1.03 (td, *J* = 13.5, 11.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 207.9, 144.6, 143.2, 139.9, 136.8, 136.0, 135.8, 133.8, 131.4, 130.2, 130.0, 129.3, 128.7, 128.1, 127.7, 127.4, 127.0, 126.7, 126.2, 126.0, 125.0, 124.4, 124.3, 58.5, 52.8, 52.7, 45.2, 43.8, 41.4, 34.5, 21.6, 21.4; MS (MALDI) calcd. for $C_{38}H_{36}N_2O_5S_2Na$ [M + Na]$^+$ 687.20, found 688.43.



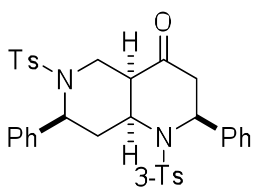
H11

80% yield; white solid; IR (film) ν_{max} 3062, 2928, 1713, 1344, 1157, 661 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, *J* = 8.0 Hz, 2H), 7.35 (d, *J* = 7.4 Hz, 2H), 7.24-7.11 (m, 8H), 6.90 (d, *J* = 6.2 Hz, 2H), 5.69 (d, *J* = 5.9 Hz, 1H), 4.83 (dd, *J* = 10.8, 7.2 Hz, 1H), 4.17 (t, *J* = 10.7 Hz, 1H), 3.95 (dd, *J* = 15.3, 7.9 Hz, 1H), 3.56 (dd, *J* = 15.3, 9.1 Hz, 1H), 3.17 (d, *J* = 15.0 Hz, 1H), 3.01 (dd, *J* = 17.1, 8.5 Hz, 1H), 2.93 (s, 3H), 2.81 (dd, *J* = 14.9, 7.0 Hz, 1H), 2.37 (s, 3H), 1.78-1.74 (m, 1H), 1.01 (td, *J* = 12.5, 11.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.2, 143.4, 140.0, 139.4, 136.9, 129.6, 128.6, 128.3, 128.1, 127.4, 127.3, 127.0, 125.8, 58.5, 55.0, 52.9, 45.9, 42.8, 40.7, 40.1, 36.1, 21.4; MS (MALDI) calcd. for $C_{28}H_{30}N_2O_5S_2Na$ [M + Na]$^+$ 561.15, found 561.52.



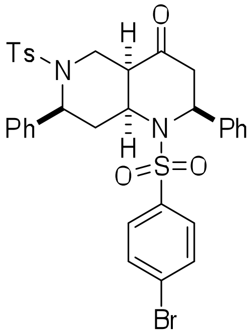
2A02

90% yield; white solid; IR (film) ν_{max} 3062, 2975, 1713, 1346, 1162, 735 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.05 (d, *J* = 7.6 Hz, 1H), 7.54 (t, *J* = 7.3 Hz, 1H), 7.42-7.36 (m, 4H), 7.26-7.24 (m, 2H), 7.19-7.16 (m, 2H), 7.14-7.06 (m, 6H), 6.83 (d, *J* = 7.2 Hz, 2H), 5.62 (d, *J* = 6.5 Hz, 1H), 4.81 (dd, *J* = 11.3, 6.8 Hz, 1H), 4.61-4.57 (m, 1H), 3.81 (dd, *J* = 15.2, 7.9 Hz, 1H), 3.55 (dd, *J* = 15.2, 8.8 Hz, 1H), 3.07 (dd, *J* = 14.9, 1.4 Hz, 1H), 2.92 (dd, *J* = 17.0, 8.5 Hz, 1H), 2.73 (s, 3H), 2.33 (s, 3H), 1.73-1.70 (m, 1H), 1.03 (td, *J* = 12.6, 11.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.8, 143.2, 140.0, 139.4, 137.2, 137.1, 136.9, 133.4, 133.2, 130.1, 129.4, 128.5, 128.2, 128.1, 127.4, 127.3, 126.9, 126.8, 126.0, 58.8, 55.0, 52.7, 46.4, 42.3, 40.8, 36.1, 21.4, 21.0; MS (MALDI) calcd. for $C_{34}H_{34}N_2O_5S_2Na$ [M + Na]$^+$ 637.18, found 637.48.



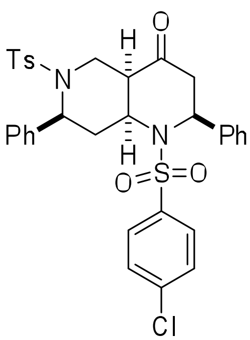
2A03

85% yield; white solid; IR (film) ν_{max} 3063, 2923, 1713, 1347, 1158, 661 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.84 (s, 1H), 7.69-7.67 (m, 1H), 7.48-7.47 (m, 2H), 7.42-7.36 (m, 4H), 7.24-7.21 (m, 2H), 7.18-7.14 (m, 3H), 7.11-7.06 (m, 3H), 6.82-6.81 (m, 2H), 5.75 (d, *J* = 6.7 Hz, 1H), 4.96 (dd, *J* = 11.2, 7.1 Hz, 1H), 4.69-4.65 (m, 1H), 3.76 (dd, *J* = 15.3, 8.0 Hz, 1H), 3.41 (dd, *J* = 15.3, 9.2 Hz, 1H), 2.97 (dd, *J* = 14.8, 1.9 Hz, 1H), 2.69 (dd, *J* = 17.5, 8.9 Hz, 1H), 2.50 (s, 3H), 2.36 (s, 3H), 2.29 (dd, *J* = 14.5, 7.2 Hz, 1H), 1.80-1.76 (m, 1H), 0.97 (td, *J* = 13.5, 11.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.6, 143.2, 140.2, 140.0, 139.4, 136.9, 134.0, 129.5, 129.4, 128.5, 128.2, 128.0, 127.3, 127.2, 127.1, 125.6, 123.5, 58.2, 55.2, 53.3, 45.6, 41.4, 40.4, 36.1, 21.4, 21.3; MS (MALDI) calcd. for $C_{34}H_{34}N_2O_5S_2Na$ [M + Na]$^+$ 637.18, found 637.64.



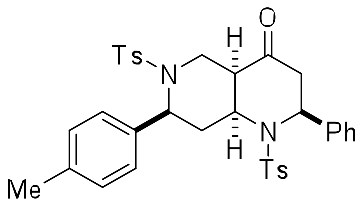
2A04

90% yield; white solid; IR (film) ν_{max} 3062, 2917, 1713, 1348, 1164, 661 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.81-7.74 (m, 4H), 7.44-7.37 (m, 4H), 7.26-7.08 (m, 8H), 6.83 (d, *J* = 6.3 Hz, 2H), 5.74 (d, *J* = 6.3 Hz, 1H), 4.96 (t, *J* = 8.8 Hz, 1H), 4.62 (t, *J* = 11.0 Hz, 1H), 3.77 (dd, *J* = 14.8, 7.5 Hz, 1H), 3.41 (dd, *J* = 13.4, 10.1 Hz, 1H), 3.01 (d, *J* = 14.9 Hz, 1H), 2.72 (dd, *J* = 15.9, 7.5 Hz, 1H), 2.37 (s, 3H), 2.28 (dd, *J* = 16.4, 10.7 Hz, 1H), 1.80-1.76 (m, 1H), 0.97 (td, *J* = 12.2, 11.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.1, 143.3, 140.0, 139.4, 139.0, 136.8, 133.0, 129.4, 128.6, 128.3, 128.2, 128.1, 127.4, 127.3, 127.1, 58.1, 55.3, 53.4, 45.6, 41.6, 40.3, 36.0, 21.4; MS (MALDI) calcd. for $C_{33}H_{31}BrN_2O_5S_2Na$ $[M + Na]^+$ 703.07, found 703.63.



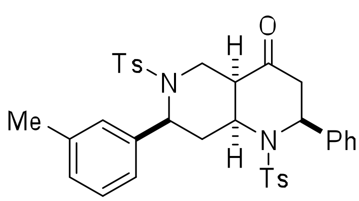
2A05

88% yield; white solid; IR (film) ν_{max} 3062, 2923, 2865, 1725, 1334, 1162, 667 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.88 (d, *J* = 8.6 Hz, 2H), 7.59 (d, *J* = 8.6 Hz, 2H), 7.44 (d, *J* = 8.3 Hz, 2H), 7.38 (d, *J* = 8.0 Hz, 2H), 7.24 (t, *J* = 8.3 Hz, 2H), 7.19-7.16 (m, 3H), 7.13-7.08 (m, 3H), 6.83-6.82 (m, 2H), 5.75 (d, *J* = 6.6 Hz, 1H), 4.96 (dd, *J* = 11.1, 7.2 Hz, 1H), 4.63 (t, *J* = 10.5 Hz, 1H), 3.77 (dd, *J* = 15.5, 8.1 Hz, 1H), 3.41 (dd, *J* = 15.5, 9.2 Hz, 1H), 3.01 (dd, *J* = 14.9, 2.0 Hz, 1H), 2.72 (dd, *J* = 17.6, 8.8 Hz, 1H), 2.37 (s, 3H), 2.31 (dd, *J* = 14.7, 7.1 Hz, 1H), 1.80-1.76 (m, 1H), 0.97 (td, *J* = 13.5, 11.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.4, 142.9, 140.8, 139.8, 138.0, 137.4, 135.3, 129.8, 129.0, 128.6, 128.5, 127.8, 127.5, 127.4, 127.0, 126.5, 55.6, 55.2, 51.6, 46.5, 42.4, 37.7, 33.0, 21.6; MS (MALDI) calcd. for $C_{33}H_{31}ClN_2O_5S_2Na$ $[M + Na]^+$ 657.12, found 657.69.



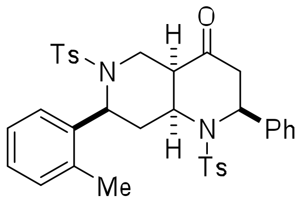
2A07

89% yield; white solid; IR (film) ν_{max} 3029, 2922, 2864, 1712, 1347, 1162, 660 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 7.39-7.37 (m, 4H), 7.24-7.21 (m, 2H), 7.18-7.15 (m, 3H), 6.89 (d, *J* = 7.8 Hz, 1H), 6.73 (d, *J* = 8.0 Hz, 2H), 5.71 (d, *J* = 6.5 Hz, 1H), 4.87 (dd, *J* = 11.1, 7.0 Hz, 1H), 4.61-4.56 (m, 1H), 3.77 (dd, *J* = 15.4, 8.0 Hz, 1H), 3.44 (dd, *J* = 15.3, 9.1 Hz, 1H), 2.94 (d, *J* = 14.8 Hz, 1H), 2.67 (dd, *J* = 17.4, 8.7 Hz, 1H), 2.48 (s, 3H), 2.38 (s, 3H), 2.25-2.21 (m, 4H), 1.76-1.72 (m, 1H), 0.98 (td, *J* = 12.5, 11.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.6, 144.2, 143.2, 139.4, 137.4, 137.2, 137.0, 130.3, 129.4, 128.8, 128.5, 128.0, 127.3, 127.0, 126.6, 125.8, 58.3, 55.2, 53.4, 45.5, 41.4, 40.4, 36.3, 21.6, 21.4, 20.9; MS (MALDI) calcd. for $C_{35}H_{36}N_2O_5S_2Na$ $[M + Na]^+$ 651.20, found 651.56.



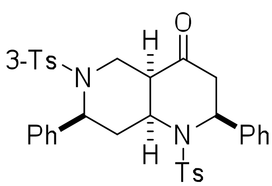
2A08

88% yield; white solid; IR (film) ν_{max} 3061, 2922, 2864, 1713, 1348, 1162, 660 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.79 (d, *J* = 7.9 Hz, 2H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.40-7.38 (m, 4H), 7.25-7.22 (m, 2H), 7.17-7.16 (m, 3H), 6.98 (t, *J* = 7.5 Hz, 1H), 6.91 (d, *J* = 7.4 Hz, 1H), 6.65 (d, *J* = 7.4 Hz, 1H), 6.51 (s, 1H), 5.73 (d, *J* = 6.5 Hz, 1H), 4.84 (dd, *J* = 11.2, 6.9 Hz, 1H), 4.63-4.58 (m, 1H), 3.79 (dd, *J* = 15.3, 7.9 Hz, 1H), 3.47 (dd, *J* = 15.2, 9.1 Hz, 1H), 2.96 (d, *J* = 14.8 Hz, 1H), 2.68 (dd, *J* = 17.4, 8.7 Hz, 1H), 2.48 (s, 3H), 2.37 (s, 3H), 2.28-2.22 (m, 1H), 2.11 (s, 3H), 1.76-1.72 (m, 1H), 0.97 (td, *J* = 13.0, 12.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.6, 144.2, 143.1, 139.9, 139.5, 137.7, 137.4, 137.2, 130.3, 129.3, 128.5, 128.1, 128.0, 127.9, 127.3, 127.0, 126.7, 126.6, 123.2, 58.6, 55.2, 53.4, 45.6, 41.4, 40.6, 36.4, 21.5, 21.4, 21.1; MS (MALDI) calcd. for $C_{35}H_{36}N_2O_5S_2Na$ $[M + Na]^+$ 651.20, found 651.84.



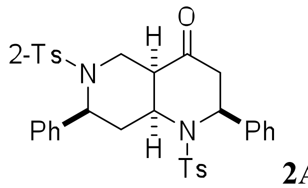
2A09

91% yield; white solid; IR (film) ν_{max} 3058, 2953, 2914, 1713, 1362, 1162, 660 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.80 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 8.0 Hz, 2H), 7.36-7.33 (m, 4H), 7.19 (t, *J* = 7.6 Hz, 2H), 7.13-7.10 (m, 3H), 7.00-6.95 (m, 2H), 6.80(t, *J* = 7.2 Hz, 1H), 6.66 (d, *J* = 7.7 Hz, 1H), 5.72 (d, *J* = 6.2 Hz, 1H), 5.01 (dd, *J* = 11.7, 6.2 Hz, 1H), 4.62-4.57 (m, 1H), 3.90 (dd, *J* = 15.2, 7.8 Hz, 1H), 3.58 (dd, *J* = 15.3, 9.2 Hz, 1H), 2.96 (dd, *J* = 14.9, 2.2 Hz, 1H), 2.76 (dd, *J* = 17.4, 8.8 Hz, 1H), 2.48 (s, 3H), 2.35 (s, 3H), 2.29 (dd, *J* = 14.7, 7.2 Hz, 1H), 2.21 (s, 3H), 1.68-1.64 (m, 1H), 0.90 (td, *J* = 12.7, 12.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.5, 144.2, 143.1, 139.3, 138.8, 137.3, 136.9, 134.3, 130.3, 130.2, 129.3, 128.5, 128.0, 127.2, 127.1, 127.0, 126.7, 125.9, 125.1, 56.0, 55.1, 53.6, 45.8, 41.6, 41.5, 36.2, 21.5, 21.4, 19.0; MS (MALDI) calcd. for $C_{35}H_{36}N_2O_5S_2Na$ $[M + Na]^+$ 651.20, found 651.84.



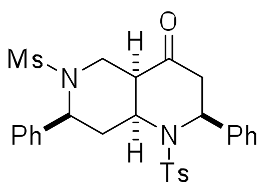
2A10

90% yield; white solid; IR (film) ν_{max} 3062, 2921, 1713, 1347, 1162, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, *J* = 8.2 Hz, 2H), 7.39-7.38 (m, 5H), 7.29-7.21 (m, 5H), 7.16 (t, *J* = 7.3 Hz, 1H), 7.11-7.06 (m, 3H), 6.84-6.82 (m, 2H), 5.73 (d, *J* = 6.7 Hz, 1H), 4.93 (dd, *J* = 11.3, 7.0 Hz, 1H), 4.65-4.60 (m, 1H), 3.82 (dd, *J* = 15.2, 8.0 Hz, 1H), 3.46 (dd, *J* = 15.3, 9.2 Hz, 1H), 2.96 (dd, *J* = 14.8, 2.0 Hz, 1H), 2.68 (dd, *J* = 17.5, 8.9 Hz, 1H), 2.49 (s, 3H), 2.28-2.23 (m, 4H), 1.79-1.74 (m, 1H), 0.98 (td, *J* = 13.5, 11.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.6, 144.2, 140.0, 139.9, 139.4, 139.1, 137.4, 133.1, 130.3, 128.6, 128.5, 128.1, 128.0, 127.40, 127.39, 127.3, 126.6, 125.9, 124.0, 58.7, 55.1, 53.3, 45.6, 41.4, 40.5, 36.4, 21.5, 21.1; MS (MALDI) calcd. for $C_{34}H_{34}N_2O_5S_2Na$ $[M + Na]^+$ 637.18, found 637.52.



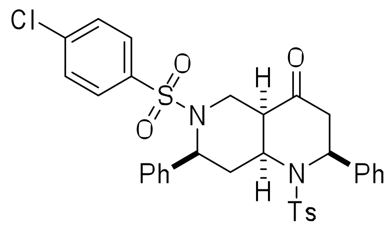
2A11

90% yield; white solid; IR (film) ν_{max} 3062, 2921, 1713, 1309, 1162, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.93 (d, *J* = 8.2 Hz, 2H), 7.66 (dd, *J* = 7.9, 0.9 Hz, 1H), 7.44-7.41 (m, 4H), 7.31-7.23 (m, 3H), 7.16 (t, *J* = 7.3 Hz, 1H), 7.10 (t, *J* = 7.6 Hz, 1H), 7.05-7.01 (m, 2H), 6.95-6.92 (m, 2H), 6.62 (d, *J* = 7.3 Hz, 2H), 5.82 (d, *J* = 6.5 Hz, 1H), 4.89-4.84 (m, 1H), 4.70 (dd, *J* = 11.2, 6.5 Hz, 1H), 3.75 (dd, *J* = 15.2, 7.5 Hz, 1H), 3.66 (dd, *J* = 15.2, 8.3 Hz, 1H), 3.02 (dd, *J* = 14.8, 2.2 Hz, 1H), 2.71 (dd, *J* = 16.4, 8.1 Hz, 1H), 2.48 (s, 3H), 2.39 (dd, *J* = 14.3, 7.2 Hz, 1H), 2.28 (s, 3H), 1.73-1.68 (m, 1H), 1.08 (td, *J* = 13.4, 11.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.5, 144.2, 139.8, 138.0, 137.3, 137.2, 132.6, 132.2, 130.4, 129.9, 128.5, 128.0, 127.9, 127.3, 126.8, 126.1, 125.8, 58.8, 55.5, 53.6, 46.0, 41.6, 40.4, 36.0, 21.5, 19.8; MS (MALDI) calcd. for $C_{34}H_{34}N_2O_5S_2Na$ $[M + Na]^+$ 637.18, found 637.50.



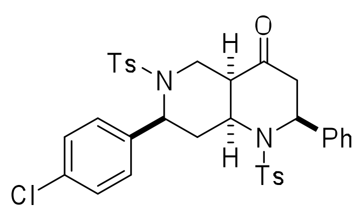
2B02

87% yield; white solid; IR (film) ν_{max} 3062, 3027, 2925, 1713, 1333, 1163, 670 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, *J* = 8.2 Hz, 2H), 7.43-7.39 (m, 4H), 7.26-7.16 (m, 6H), 7.00-6.98 (m, 2H), 5.83 (d, *J* = 6.7 Hz, 1H), 4.87 (dd, *J* = 11.2, 7.1 Hz, 1H), 4.75-4.71 (m, 1H), 3.80 (dd, *J* = 15.0, 8.2 Hz, 1H), 3.48 (dd, *J* = 14.9, 9.2 Hz, 1H), 3.03 (dd, *J* = 14.8, 1.7 Hz, 1H), 2.75 (dd, *J* = 17.6, 8.8 Hz, 1H), 2.46 (s, 3H), 2.43-2.39 (m, 4H), 1.80-1.74 (m, 1H), 1.04 (td, *J* = 13.3, 11.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.6, 144.3, 139.6, 139.5, 137.2, 130.4, 128.7, 128.5, 128.1, 128.0, 127.4, 126.7, 126.0, 58.2, 55.2, 53.2, 46.2, 41.6, 40.4, 40.3, 36.7, 21.5; MS (MALDI) calcd. for $C_{28}H_{30}N_2O_5S_2Na$ $[M + Na]^+$ 561.15, found 561.45.



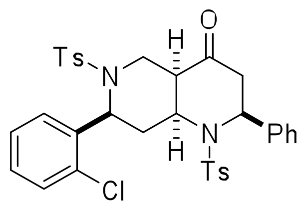
2B03

90% yield; white solid; IR (film) ν_{max} 3063, 2917, 1713, 1349, 1163, 699 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.82 (d, *J* = 8.0 Hz, 2H), 7.41-7.36 (m, 6H), 7.28-7.20 (m, 4H), 7.17-7.10 (m, 2H), 7.07-7.02 (m, 2H), 6.78 (d, *J* = 7.8 Hz, 2H), 5.75 (d, *J* = 6.5 Hz, 1H), 4.85 (dd, *J* = 11.4, 6.7 Hz, 1H), 4.65-4.60 (m, 1H), 3.78 (dd, *J* = 15.1, 7.8 Hz, 1H), 3.52 (dd, *J* = 15.1, 9.0 Hz, 1H), 2.99 (d, *J* = 14.9 Hz, 1H), 2.70 (dd, *J* = 17.1, 8.6 Hz, 1H), 2.47 (s, 3H), 2.31 (dd, *J* = 14.9, 7.1 Hz, 1H), 1.76-1.72 (m, 1H), 1.00 (td, *J* = 12.6, 11.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.3, 144.3, 139.4, 139.3, 138.7, 138.6, 137.3, 130.4, 128.9, 128.5, 128.3, 128.2, 128.0, 127.6, 127.3, 126.6, 126.1, 59.0, 55.1, 53.4, 45.6, 41.4, 40.8, 36.5, 21.5; MS (MALDI) calcd. for $C_{33}H_{31}ClN_2O_5S_2Na$ $[M + Na]^+$ 657.12, found 657.43.



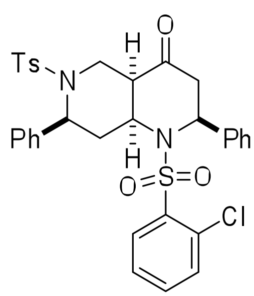
2B04

90% yield; white solid; IR (film) ν_{max} 3062, 2923, 2864, 1713, 1347, 1162, 660 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.0 Hz, 2H), 7.46 (d, *J* = 8.1 Hz, 2H), 7.37-7.36 (m, 4H), 7.23-7.14 (m, 5H), 7.03 (d, *J* = 8.4 Hz, 2H), 6.75 (d, *J* = 8.4 Hz, 2H), 5.68 (d, *J* = 6.5 Hz, 1H), 4.82 (dd, *J* = 11.2, 6.9 Hz, 1H), 4.56-4.52 (m, 1H), 3.79 (dd, *J* = 15.4, 7.9 Hz, 1H), 3.44 (dd, *J* = 15.3, 9.0 Hz, 1H), 2.93 (d, *J* = 14.8 Hz, 1H), 2.64 (dd, *J* = 17.2, 8.6 Hz, 1H), 2.45 (s, 3H), 2.38 (s, 3H), 2.20 (dd, *J* = 14.8, 7.1 Hz, 1H), 1.74-1.69 (m, 1H), 0.87 (td, *J* = 12.6, 11.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.3, 144.2, 143.5, 139.3, 138.7, 137.3, 136.9, 133.1, 130.3, 129.6, 128.5, 128.3, 128.0, 127.3, 127.2, 127.0, 126.6, 58.0, 55.1, 53.2, 45.3, 41.3, 40.5, 36.4, 21.5, 21.4; MS (MALDI) calcd. for $C_{34}H_{33}ClN_2O_5S_2Na$ $[M + Na]^+$ 671.14, found 671.33.



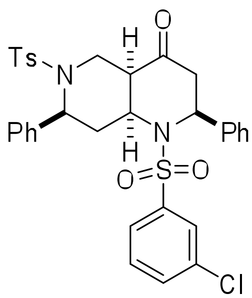
2B05

91% yield; white solid; IR (film) ν_{max} 3063, 2946, 2923, 1712, 1349, 1162, 660 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.69 (d, *J* = 8.3 Hz, 2H), 7.57 (d, *J* = 8.2 Hz, 2H), 7.37 (d, *J* = 5.3 Hz, 2H), 7.30 (d, *J* = 7.8 Hz, 2H), 7.26-7.24 (m, 2H), 7.19-7.09 (m, 4H), 7.06-6.98 (m, 2H), 6.94 (dd, *J* = 7.6, 1.6 Hz, 1H), 5.68 (d, *J* = 6.2 Hz, 1H), 5.10 (dd, *J* = 11.6, 6.3 Hz, 1H), 4.42-4.38 (m, 1H), 4.06 (dd, *J* = 15.6, 7.9 Hz, 1H), 3.55 (dd, *J* = 15.6, 9.6 Hz, 1H), 2.93 (dd, *J* = 14.9, 2.2 Hz, 1H), 2.69 (dd, *J* = 17.8, 9.1 Hz, 1H), 2.47 (s, 3H), 2.40 (s, 3H), 2.26 (dd, *J* = 14.6, 7.1 Hz, 1H), 1.86-1.82 (m, 1H), 0.74 (td, *J* = 12.6, 11.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.5, 144.2, 143.6, 139.1, 138.4, 137.3, 136.5, 131.1, 130.2, 129.6, 129.5, 128.5, 128.4, 128.2, 128.0, 127.2, 127.1, 126.9, 126.7, 56.6, 54.9, 53.2, 45.3, 41.6, 41.4, 34.8, 21.5, 21.4; MS (MALDI) calcd. for $C_{34}H_{33}ClN_2O_5S_2Na$ [M + Na]$^+$ 671.14, found 671.72.



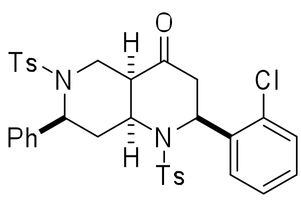
G03

88% yield; white solid; IR (film) ν_{max} 3063, 2917, 1713, 1348, 1164, 662 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (dd, *J* = 7.8, 1.4 Hz, 1H), 77.63-7.58 (m, 2H), 7.53-7.50 (m, 1H),7.40 (d, *J* = 7.7 Hz, 2H), 7.36 (d, *J* = 8.2 Hz, 2H), 7.22 (t, *J* = 7.5 Hz, 2H), 7.18-7.06 (m, 6H), 6.84 (d, *J* = 6.8 Hz, 2H), 5.72 (d, *J* = 5.4 Hz, 1H), 4.88 (dd, *J* = 11.4, 6.8 Hz, 1H), 3.84 (dd, *J* = 15.2, 7.9 Hz, 1H), 3.45 (dd, *J* = 15.3, 9.2 Hz, 1H), 3.07 (dd, *J* = 15.0, 2.0 Hz, 1H), 2.92 (dd, *J* = 17.5, 8.8 Hz, 1H), 2.76 (dd, *J* = 14.8, 7.0 Hz, 1H), 2.35 (s, 3H), 1.92-1.88 (m, 1H), 1.04 (td, *J* = 13.5, 11.8 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.8, 143.2, 140.2, 139.3, 136.9, 136.7, 134.2, 132.8, 132.3, 131.2, 129.4, 128.6, 128.2, 128.1, 127.6, 127.5, 127.3, 126.9, 125.9, 58.4, 55.2, 53.1, 46.1, 42.5, 40.8, 36.2, 21.4; MS (MALDI) calcd. for $C_{33}H_{31}ClN_2O_5S_2Na$ $[M + Na]^+$ 657.12, found 657.43.



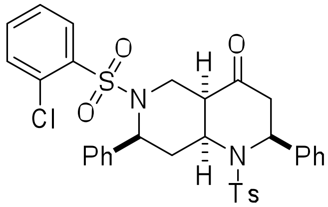
G04

85% yield; white solid; IR (film) ν_{max} 3064, 2921, 1713, 1348, 1165, 668 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.92 (t, *J* = 1.8 Hz, 1H), 7.80 (d, *J* = 8.8 Hz, 1H), 7.64-7.62 (m, 1H), 7.55 (t, *J* = 7.9 Hz, 1H), 7.46 (d, *J* = 8.2 Hz, 2H), 7.37 (d, *J* = 7.9 Hz, 2H), 7.23 (t, *J* = 7.5 Hz, 2H), 7.19-7.16 (m, 3H), 7.13-7.08 (m, 3H), 6.85-6.83 (m, 2H), 5.72 (d, *J* = 6.5 Hz, 1H), 4.93 (dd, *J* = 11.1, 7.1 Hz, 1H), 4.59 (t, *J* = 10.4 Hz, 1H), 3.80 (dd, *J* = 15.4, 8.1 Hz, 1H), 3.45 (dd, *J* = 15.5, 9.1 Hz, 1H), 3.01 (dd, *J* = 14.9, 2.0 Hz, 1H), 2.74 (dd, *J* = 17.5, 8.7 Hz, 1H), 2.36 (s, 3H), 2.31 (dd, *J* = 14.9, 7.1 Hz, 1H), 1.80-1.75 (m, 1H), 0.99 (td, *J* = 13.5, 11.7 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.0, 143.4, 142.0, 140.0, 139.0, 136.8, 135.9, 133.4, 131.0, 129.5, 128.6, 128.2, 128.1, 127.4, 127.3, 127.1, 126.6, 125.8, 124.8, 58.2, 55.4, 53.4, 45.6, 41.7, 40.4, 36.1, 21.4; MS (MALDI) calcd. for $C_{33}H_{31}ClN_2O_5S_2Na$ $[M + Na]^+$ 657.12, found 657.38.



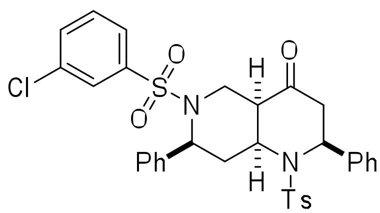
G05

80% yield; white solid; IR (film) ν_{max} 3063, 2923, 1725, 1351, 1165, 658 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.41-7.31 (m, 6H), 7.21-7.12 (m, 7H), 7.00 (d, *J* = 7.1 Hz, 2H), 5.54 (dd, *J* = 10.1, 5.7 Hz, 1H), 4.71 (dd, *J* = 11.2, 5.6 Hz, 1H), 4.51-4.46 (m, 1H), 3.85 (dd, *J* = 14.2, 7.2 Hz, 1H), 3.54 (dd, *J* = 14.1, 6.6 Hz, 1H), 2.88 (dd, *J* = 16.8, 5.7 Hz, 1H), 2.65 (dd, *J* = 16.8, 10.2 Hz, 1H), 2.53 (dd, *J* = 14.4, 7.1 Hz, 1H), 2.46 (s, 3H), 2.42-2.38 (m, 4H), 1.86 (td, *J* = 13.3, 11.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.1, 144.5, 143.3, 139.64, 139.62, 136.7, 131.7, 130.1, 129.9, 129.3, 128.8, 128.2, 127.6, 127.5, 127.4, 127.3, 127.2, 126.8, 60.0, 54.6, 53.1, 45.5, 43.8, 43.2, 39.5, 21.5, 21.4; MS (MALDI) calcd. for $C_{34}H_{33}ClN_2O_5S_2Na$ $[M + Na]^+$ 671.14, found 671.53.



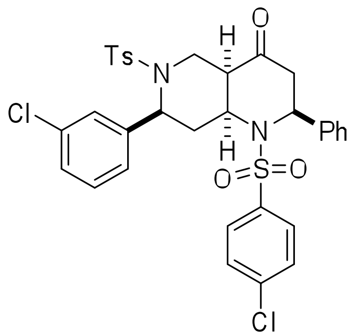
G07

87% yield; white solid; IR (film) ν_{max} 3063, 2921, 1714, 1336, 1163, 661 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.90 (d, *J* = 8.2 Hz, 2H), 7.73 (d, *J* = 7.5 Hz, 1H), 7.42-7.40 (m, 4H), 7.28-7.22 (m, 4H), 7.17-7.11 (m, 2H), 6.99-6.92 (m, 3H), 6.73 (d, *J* = 6.9 Hz, 2H), 5.80 (d, *J* = 6.5 Hz, 1H), 4.84 (dd, *J* = 11.1, 6.9 Hz, 1H), 4.80-4.75 (m, 1H), 4.17 (dd, *J* = 15.3, 8.0 Hz, 1H), 3.68 (dd, *J* = 15.4, 9.1 Hz, 1H), 3.02 (dd, *J* = 14.9, 2.1 Hz, 1H), 2.69 (dd, *J* = 17.4, 8.8 Hz, 1H), 2.48 (s, 3H), 2.38 (dd, *J* = 14.7, 7.1 Hz, 1H), 1.80-1.75 (m, 4H), 1.05 (td, *J* = 13.5, 11.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.2, 144.2, 139.6, 139.0, 137.6, 137.3, 133.2, 131.8, 131.4, 130.4, 128.5, 128.0, 127.9, 127.4, 127.3, 126.7, 126.6, 125.6, 59.0, 55.3, 53.3, 46.2, 41.6, 36.3, 21.5; MS (MALDI) calcd. for $C_{33}H_{31}ClN_2O_5S_2Na$ $[M + Na]^+$ 657.12, found 657.62.



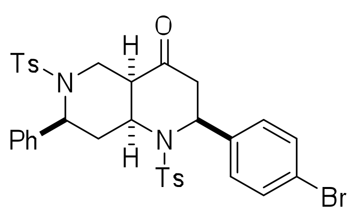
G08

84% yield; white solid; IR (film) ν_{max} 3063, 2917, 1713, 1349, 1163, 660 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.84 (d, *J* = 8.2 Hz, 2H), 7.42-7.39 (m, 5H), 7.34 (d, *J* = 7.9 Hz, 1H), 7.30 (s, 1H), 7.24-7.21 (m, 3H), 7.17-7.11 (m, 2H), 7.06 (t, *J* = 7.5 Hz, 2H), 6.78 (d, *J* = 7.4 Hz, 2H), 5.77 (d, *J* = 6.5 Hz, 1H), 4.84 (dd, *J* = 11.4, 6.7 Hz, 1H), 4.65 (t, *J* = 10.1 Hz, 1H), 3.81 (dd, *J* = 15.0, 7.8 Hz, 1H), 3.56 (dd, *J* = 15.0, 8.9 Hz, 1H), 3.01 (dd, *J* = 14.9, 1.7 Hz, 1H), 2.74 (dd, *J* = 17.1, 8.5 Hz, 1H), 2.49 (s, 3H), 2.34 (dd, *J* = 15.3, 6.5 Hz, 1H), 1.75-1.71 (m, 1H), 1.03 (td, *J* = 13.5, 11.9 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.3, 144.3, 141.8, 139.4, 139.0, 137.3, 134.8, 132.3, 130.4, 130.0, 128.5, 128.2, 128.0, 127.9, 127.3, 126.9, 126.7, 126.2, 124.8, 59.2, 55.2, 53.4, 45.8, 41.5, 40.9, 36.4, 21.5; MS (MALDI) calcd. for $C_{33}H_{31}ClN_2O_5S_2Na$ $[M + Na]^+$ 657.12, found 657.48.



G10

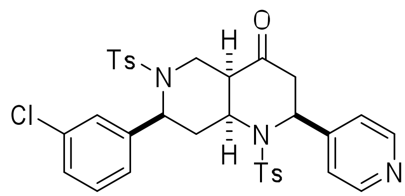
83% yield; white solid; IR (film) ν_{max} 3060, 2918, 1717, 1349, 1164, 661 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.87 (d, *J* = 8.4 Hz, 2H), 7.87 (d, *J* = 8.4 Hz, 2H), 7.58 (d, *J* = 8.4 Hz, 2H), 7.47 (d, *J* = 8.1 Hz, 2H), 7.38 (d, *J* = 7.6 Hz, 2H), 7.27-7.24 (m, 2H), 7.21-7.19 (m, 3H), 7.08-7.02 (m, 2H), 6.74 (d, *J* = 7.4 Hz, 1H), 6.63 (s, 1H), 5.75 (d, *J* = 6.6 Hz, 1H), 4.85 (dd, *J* = 11.2, 7.0 Hz, 1H), 4.59 (t, *J* = 10.2 Hz, 1H), 3.77 (dd, *J* = 15.4, 7.9 Hz, 1H), 3.43 (dd, *J* = 15.4, 8.9 Hz, 1H), 3.02 (dd, *J* = 14.9, 1.5 Hz, 1H), 2.71 (dd, *J* = 17.2, 8.6 Hz, 1H), 2.39 (s, 3H), 2.32 (dd, *J* = 14.8, 7.1 Hz, 1H), 1.76-1.71 (m, 1H), 0.89 (td, *J* = 13.4, 11.5 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.8, 143.7, 141.8, 139.8, 139.1, 138.8, 136.6, 134.1, 130.0, 129.5, 128.6, 128.2, 128.1, 127.5, 127.3, 127.1, 125.9, 124.2, 57.7, 55.3, 53.3, 45.5, 41.6, 40.5, 36.0, 21.4; MS (MALDI) calcd. for $C_{33}H_{30}Cl_2N_2O_5S_2Na$ $[M + Na]^+$ 691.09, found 691.46.



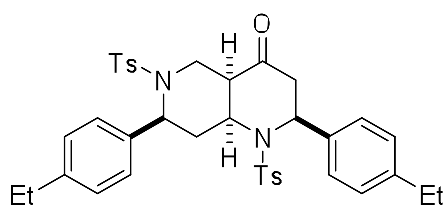
G11

85% yield; white solid; IR (film) ν_{max} 3060, 2921, 1714, 1347, 1163, 660 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.77 (d, *J* = 8.2 Hz, 2H), 7.44 (d, *J* = 8.2 Hz, 2H), 7.40-7.34 (m, 4H), 7.27 (d, *J* = 7.4 Hz, 2H), 7.18-7.11 (m, 5H), 6.86-6.85 (m, 2H), 5.64 (d, *J* = 6.6 Hz, 1H), 4.95 (dd, *J* = 11.1, 7.0 Hz, 1H), 4.64 (t, *J* = 10.3 Hz, 1H), 3.76 (dd, *J* = 15.4, 8.0 Hz, 1H), 3.46 (dd, *J* = 15.4, 9.1 Hz, 1H), 2.89 (dd, *J* = 14.7, 1.9 Hz, 1H), 2.69 (dd, *J* = 17.4, 8.6 Hz, 1H), 2.49 (s, 3H), 2.38 (s, 3H), 2.32 (dd, *J* = 14.7, 7.1 Hz, 1H), 1.83-1.79 (m, 1H), 0.99 (td, *J* = 13.5, 11.6 Hz, 1H); ^{13}C NMR

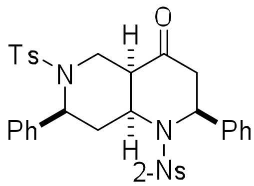
(125 MHz, $CDCl_3$) δ 206.2, 144.3, 143.3, 139.9, 138.5, 137.1, 137.0, 131.6, 130.3, 129.4, 129.0, 128.3, 127.4, 127.1, 126.6, 125.8, 122.2, 58.4, 54.9, 53.5, 45.6, 41.3, 40.3, 36.5, 21.5, 21.4; MS (MALDI) calcd. for $C_{34}H_{34}BrN_2O_5S_2Na$ $[M + Na]^+$ 695.11, found 695.44.


H02

87% yield; white solid; IR (film) ν_{max} 3061, 2923, 1715, 1349, 1162, 660 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.48 (d, J = 5.6 Hz, 2H), 7.77 (d, J = 8.2 Hz, 2H), 7.45-7.31 (m, 6H), 7.19-7.14 (m, 2H), 7.06-7.00 (m, 2H), 6.71-6.67 (m, 2H), 5.63 (d, J = 6.2 Hz, 1H), 4.87 (dd, J = 11.0, 6.9 Hz, 1H), 4.62 (t, J = 10.2 Hz, 1H), 3.77 (dd, J = 15.3, 7.9 Hz, 1H), 3.47 (dd, J = 15.3, 8.8 Hz, 1H), 2.91 (dd, J = 14.7, 2.0 Hz, 1H), 2.68 (dd, J = 16.9, 8.5 Hz, 1H), 2.46 (s, 3H), 2.36 (s, 3H), 2.29-2.24 (m, 1H), 1.84-1.81 (m, 1H), 0.87 (td, J = 13.3, 12.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 205.3, 150.2, 148.5, 143.7, 141.7, 136.7, 136.6, 134.2, 130.5, 129.7, 129.6, 127.6, 127.0, 126.6, 125.8, 123.8, 122.1, 58.0, 54.7, 53.8, 45.5, 40.7, 40.4, 36.8, 21.6, 21.4; MS (MALDI) calcd. for $C_{33}H_{32}ClN_3O_5S_2Na$ $[M + Na]^+$ 672.14, found 673.50.


D10

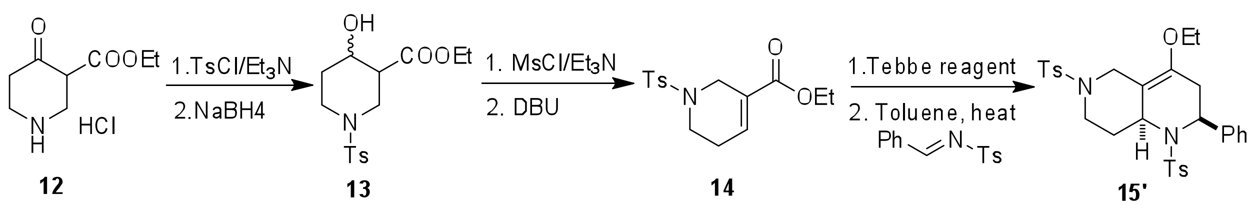
88% yiled; white solid; IR (film) ν_{max} 2965, 2930, 1713, 1347, 1162, 660 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.76 (d, J = 8.3 Hz, 2H), 7.42 (d, J = 8.3 Hz, 2H), 7.37 (d, J = 8.0 Hz, 2H), 7.27 (d, J = 8.0 Hz, 2H), 7.16 (d, J = 8.0 Hz, 2H), 7.05 (d, J = 8.2 Hz, 2H), 6.89 (d, J = 8.1 Hz, 2H), 6.73 (d, J = 8.1 Hz, 2H), 5.69 (d, J = 6.5 Hz, 1H), 4.85 (dd, J = 11.3, 6.9 Hz, 1H), 4.56 (t, J = 10.5 Hz, 1H), 3.78 (dd, J = 15.3, 8.0 Hz, 1H), 3.41 (dd, J = 15.3, 9.2 Hz, 1H), 2.93 (dd, J = 14.9, 2.0 Hz, 1H), 2.668 (dd, J = 17.5, 8.9 Hz, 1H), 2.55-2.50 (m, 4H), 2.48 (s, 3H), 2.37 (s, 3H), 2.23 (dd, J = 14.8, 7.1 Hz, 1H), 1.74-1.69 (m, 1H), 1.15 (t, J = 7.0 Hz, 3H), 1.07 (t, J = 7.0 Hz, 1H), 0.94 (td, J = 13.6, 11.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.7, 144.3, 144.1, 143.4, 143.0, 137.5, 137.3, 137.2, 136.6, 130.2, 129.4, 128.0, 127.5, 127.4, 127.0, 126.6, 126.0, 58.3, 54.9, 53.1, 45.4, 41.5, 40.5, 36.3, 28.3, 21.5, 21.4, 15.5, 15.4; MS (MALDI) calcd. for $C_{38}H_{42}N_2O_5S_2Na$ $[M + Na]^+$ 693.24, found 693.77.



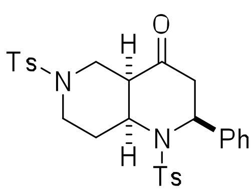
2A06

81% yield; white solid; IR (film) ν_{max} 3064, 2921, 1714, 1544, 1373, 1165, 699 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 8.30-8.28 (m, 1H), 7.84-7.79 (m, 2H), 7.77-7.74 (m, 1H), 7.41-7.37 (m, 4H), 7.24 (t, *J* = 7.5 Hz, 2H), 7.18 (t, *J* = 7.2 Hz, 1H), 7.13-7.07 (m, 5H), 6.81 (d, *J* = 7.1 Hz, 2H), 5.86 (d, *J* = 6.4 Hz, 1H), 4.99 (dd, *J* = 11.1, 7.1 Hz, 1H), 4.60 (t, *J* = 10.3 Hz, 1H), 3.79 (dd, *J* = 15.3, 8.1 Hz, 1H), 3.46 (dd, *J* = 15.4, 9.1 Hz, 1H), 3.18 (dd, *J* = 15.1, 2.0 Hz, 1H), 3.03 (dd, *J* = 15.1, 7.1 Hz, 1H), 2.93 (dd, *J* = 17.4, 8.7 Hz, 1H), 2.38 (s, 3H), 1.95-1.91 (m, 1H), 1.03 (td, *J* = 13.2, 11.3 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 206.8, 147.6, 143.4, 140.0, 139.3, 136.5, 134.2, 132.9, 132.5, 131.8, 129.4, 128.6, 128.2, 128.1, 127.4, 127.3, 127.1, 125.8, 124.5, 58.1, 55.9, 53.5, 46.2, 42.6, 40.6, 35.5, 21.4; MS (MALDI) calcd. for $C_{33}H_{31}N_3O_7S_2Na$ $[M + Na]^+$ 668.15, found 668.42.

Procedure for the synthesis of naphthyridine enol ether 15′



To a solution of ethyl 4-piperidone-3-carboxylate hydrochloride (2.0g, 9.6 mmol) in DCM (40 mL) was added dropwise at 0 °C Et_3N (5.3 mL, 4.0 eq.). After 30 mins, a solution of TsCl in DCM (20 mL) was added dropwise to the mixture. After stirring over night at room temperature, the reaction mixture was washed by 2 N HCl (3 X 30 mL), saturated $NaHCO_3$ (2 X 30 mL), and brine (2 X 30 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated. The crude residue was used for the next step without any purification. To a stirred solution of the crude residue (~9.6 mmol) in absolute ethanol (15 ml) was added dropwise at 0 °C a solution of $NaBH_4$ (363 mg, 9.6 mmol) in absolute ethanol (15 mL). Stirring was continued for an additional 13 h, during which the reaction temperature rose slowly to room temperature. A few drops of aqueous acetic acids followed by water were added to the reaction mixture which was then extracted with DCM (3 X 30 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated. The crude residue was purified by flash column chromatography on the silica gel using 33% ethyl acetate in hexanes to afford the product alcohol in 54% yield, two steps. To a stirred solution of the alcohol (1.7 g, 5.2 mmol) and Et_3N (2.2 mL, 3.0 eq.) in ether (12 mL) was added dropwise at 0 °C methanesulfonyl chloride (0.8 mL). The reaction was stirred for 3 h after which a solution of DBU (1.5 mL) in ether (6 mL) was added to it. Stirring was contined for an additional 4 h after which the reaction mixture was quenched by the addition of water, and then extracted with ether (3 X 30 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated. The crude residue was purified by flash column chromatography on the silica gel using 20% ethyl acetate in hexanes to afford the product α,β-unsaturated ester in 70% yield, two steps.[6] Naphthyridine enol ether (**15'**) was synthesized following the same procedure of naphthyridine enol ethers (**11'**) synthesis from the α,β-unsaturated ester as white solid in 53% yield, two steps. IR (film) ν_{max} 3060, 2978, 2921, 1699, 1343, 1165, 655 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.67 (d, *J* = 7.9 Hz, 2H), 7.60 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 7.6 Hz, 2H), 7.34-7.26 (m, 7H), 5.31 (d, *J* = 6.6 Hz, 1H), 4.86 (dd, *J* = 12.1, 2.0 Hz, 1H), 4.02 (d, *J* = 11.8 Hz, 1H), 3.82 (dq, *J* = 9.5, 7.1 Hz, 1H), 3.74 (dq, *J* = 9.5, 7.1 Hz, 1H), 3.53 (d, *J* = 12.0 Hz, 1H), 2.60 (d, *J* = 17.1 Hz, 1H), 2.47-2.44 (m, 4H), 2.41 (s, 3H), 2.23 (td, *J* = 12.2, 2.3 Hz, 1H), 2.09-2.04 (m, 1H), 1.67-1.63 (m, 1H), 1.19 (t, *J* = 7.1 Hz, 3H), 0.96 (ddd, *J* = 24.8, 12.4, 4.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.1, 143.5, 139.6, 137.5, 132.8, 129.8, 129.5, 128.4, 127.7, 127.6, 126.5, 110.0, 63.9, 53.9, 52.4, 46.1, 44.6, 32.7, 24.6, 21.5, 21.4, 15.0; MS (MALDI) calcd. for $C_{30}H_{34}N_2O_5S_2Na$ $[M + Na]^+$ 589.18, found 589.60.

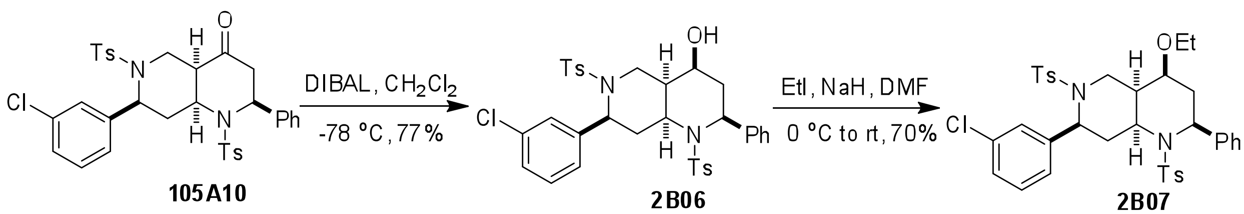


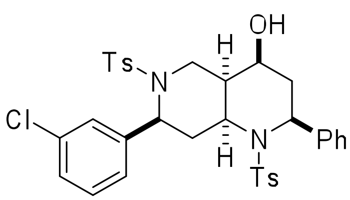
H06

[6] Kosugi, H., Yamabe, O. & Kato, M. Synthetic study of marine lobane diterpenes: efficient synthesis of (+)-fuscol. *J. Chem. Soc. Perkin Trans*. 217-221 (1998).

Naphthyridinone (**H06**) was synthesized following the same procedure of naphthyridinone (**11**) synthesis from naphthyridine enol ehter (**15'**) in 87% yield; white solid; IR (film) ν_{max} 3059, 2922, 2843, 1725, 1338, 1165, 656 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.3 Hz, 2H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.39 (d, *J* = 7.5 Hz, 2H), 7.32-7.29 (m, 6H), 7.27-7.26 (m, 1H), 5.61 (dd, *J* = 7.1, 3.9 Hz, 1H), 4.37-4.33 (m, 1H), 4.27 (d, *J* = 12.0 Hz, 1H), 3.53-3.51 (m, 1H), 3.01 (dd, *J* = 15.5, 4.0 Hz, 1H), 2.51 (dd, *J* = 15.5, 7.4 Hz, 1H), 2.43 (s, 6H), 2.29-2.26 (m, 1H), 2.13-2.08 (m, 2H), 1.49-1.47 (m, 1H), 1.32-1.24 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 202.7, 144.2, 143.6, 140.7, 137.0, 132.8, 130.2, 129.5, 128.6, 127.7, 127.6, 126.9, 126.7, 56.2, 55.6, 46.4, 45.7, 43.5, 42.2, 31.0, 21.5, 21.4; MS (MALDI) calcd. for $C_{28}H_{30}N_2O_5S_2Na$ $[M + Na]^+$ 561.15, found 561.77.

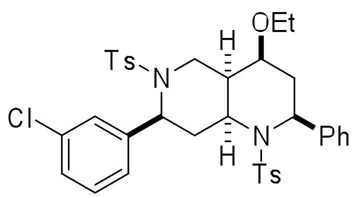
Stnthesis of compounds 2B06 and 2B07





2B06

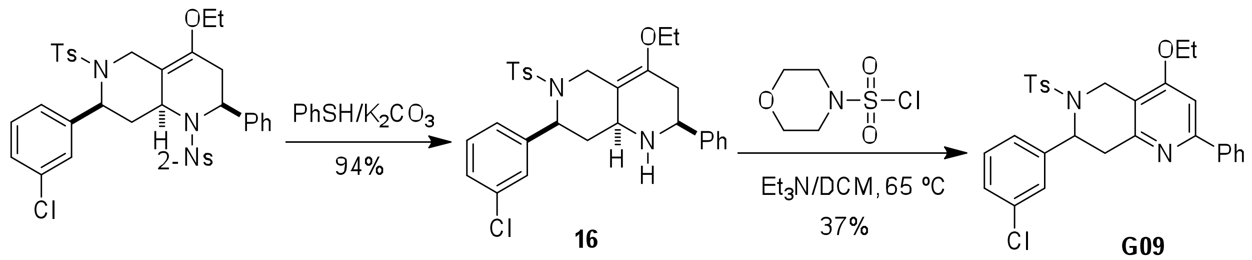
To a solution of naphthyridinone (**105A10**, 0.22 mmol) in CH_2Cl_2 (6 mL) at −78 °C, 0.55 mL diisobutylaluminium hydride (DIBAL, 1.0 M in CH_2Cl_2) was added dropwise. The reaction was finished in an hour. Water (0.03 mL) was added at −78 °C and the reaction was warmed up to room temperature. Anhydrous Na_2SO_4 (0.1 g) was added. The reaction mixture was filtered through the Celite pad and the filtrate was concentrated. The crude residue was purified by flash column chromatography on the silica gel using 33% ethyl acetate in hexanes to afford the product (**2B06**) as a white solid in 77% yield; IR (film) ν_{max} 3516, 3061, 2954, 2925, 1598, 1344, 1161, 667 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.2 Hz, 2H), 7.43 (d, *J* = 8.3 Hz, 2H), 7.36 (d, *J* = 7.8 Hz, 2H), 7.31-7.24 (m, 4H), 7.19-7.16 (m, 3H), 7.13-7.10 (m, 2H), 7.00-6.97 (m, 1H), 6.88 (s, 1H), 5.07 (t, *J* = 7.9 Hz, 1H), 4.83 (dd, *J* = 11.9, 6.0 Hz, 1H), 4.29-4.24 (m, 1H), 3.83 (dd, J = 14.7, 6.7 Hz, 1H), 3.47 (dd, J = 14.8, 10.8 Hz, 1H), 3.43-3.39 (m, 1H), 2.46 (s, 3H), 2.40 (s, 3H), 2.33-2.24 (m, 2H), 2.17-2.10 (m, 1H), 2.00-1.90 (m, 2H), 1.67 (d, J = 3.6 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.8, 143.5, 143.2, 142.5, 137.0, 136.6, 134.2, 129.9, 129.7, 129.5, 128.3, 127.5, 126.9, 126.8, 126.7, 126.0, 125.6, 124.3, 65.6, 58.6, 56.0, 50.8, 41.6, 38.8, 35.8, 33.3, 21.5, 21.4; MS (MALDI) calcd. for $C_{34}H_{35}ClN_2O_5S_2Na$ [M + Na]$^+$ 673.16, found 673.79.

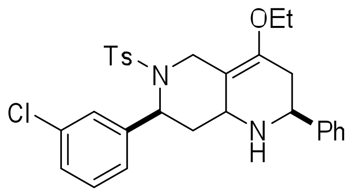


2B07

To a solution of **2B06** (0.16 mmol) and NaH (60% in minoral oil, 0.24 mmol) in anhydrous DMF (2.5 mL), ethyl iodide (0.24 mmol) was added dropwise at 0 °C and the reaction was warmed up to room temperature. The mixture was stirred at 50 °C for 5 hours. The saturated NaCl (2.0 mL) was added and the mixture was extracted by ethyl acetate (3 X 10 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated. The crude residue was purified by flash column chromatography on the silica gel using 20% ethyl acetate in hexanes to afford final product **2B07** as yellow oil in 70% yield; IR (film) ν_{max} 3061, 2971, 1598, 1345, 1161, 665 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, J = 8.2 Hz, 2H), 7.46 (d, J = 8.3 Hz, 2H), 7.34-7.30 (m, 4H), 7.27-7.24 (m, 2H), 7.21-7.15 (m, 3H), 7.00-6.97 (m, 1H), 7.12-7.10 (m, 2H), 7.01-6.98 (m, 1H), 6.93 (s, 1H), 5.01-4.93 (m, 2H), 4.32-4.27 (m, 1H), 3.81 (dd, J = 15.0, 7.0 Hz, 1H), 3.30 (dd, J = 15.0, 11.8 Hz, 1H), 3.19-3.05 (m, 2H), 2.64-2.60 (m, 1H), 2.47 (s, 3H), 2.44-2.40 (m, 4H), 2.29-2.25 (m, 1H), 2.11-2.04 (m, 1H), 1.94-1.83 (m, 2H), 0.96 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 143.7, 143.4, 143.3, 142.5, 137.5, 136.8, 134.2, 129.8, 129.7, 129.4, 128.2, 127.4, 126.8, 125.8, 125.4, 124.2, 72.3, 64.2, 58.0, 56.6, 50.7, 40.5, 38.4, 34.6, 30.4, 21.5, 21.4, 14.8; MS (MALDI) calcd. for $C_{36}H_{39}ClN_2O_5S_2Na$ [M + Na]$^+$ 701.19, found 701.75.

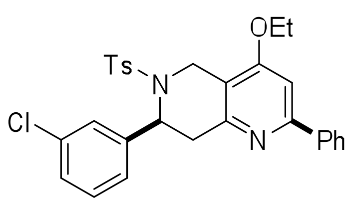
Synthesis of compound G09





16

To a mixture of naphthyridine enol ether (0.10 mmol) and K_2CO_3 (0.30 mmol) in anhydrous CH_3CN (2.5 mL), PhSH (0.12 mmol) was added dropwise at room temperature. The mixture was stirred at 50 °C for 8 hours. The saturated NaCl (2.0 mL) was added and the mixture was extracted by ethyl acetate (3 X 10 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated. The crude residue was purified by flash column chromatography on the silica gel using 1% triethylamine and 80% ethyl acetate in hexanes to afford final product **16** as white solid in 94% yield; IR (film) ν_{max} 3400, 3062, 2977, 1597, 1346, 1161, 701 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.62 (d, J = 8.3 Hz, 2H), 7.34-7.16 (m, 11H), 4.86 (dd, J = 10.8, 6.9 Hz, 1H), 4.71 (d, J = 17.2 Hz, 1H), 4.14 (dt, J = 17.2, 1.4 Hz, 1H), 3.84-3.71 (m, 2H), 3.56 (dd, J = 10.5, 4.4 Hz, 1H), 2.91 (d, J = 11.3 Hz, 1H), 2.43 (s, 3H), 2.30 (d, J = 14.8 Hz, 1H), 2.25-2.14 (m, 2H), 1.70 (td, J = 12.1, 11.5 Hz, 1H), 1.57 (br, 1H), 1.26 (t, J = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.4, 144.2, 143.3, 143.2, 136.6, 134.1, 129.6, 129.3, 128.6, 127.5, 127.3, 127.2, 126.3, 126.2, 124.4, 111.7, 62.8, 58.3, 56.9, 51.9, 41.4, 37.6, 34.0, 21.4, 15.5; MS (MALDI) calcd. for $C_{29}H_{31}ClN_2O_3SNa$ $[M + Na]^+$ 545.16, found 545.79.



G09

To a solution of **16** (0.10 mmol) and triethylamine (0.30 mmol) in anhydrous CH_2Cl_2 (2.5 mL), the sulfonyl chloride (0.12 mmol) was added dropwise at room temperature. The mixture was stirred at 65 °C for 12 hours. The saturated NaCl (2.0 mL) was added and the mixture was extracted by ethyl acetate (3 X 10 mL). The organic phase was dried over anhydrous Na_2SO_4 and concentrated. The crude residue was purified by flash column chromatography on the silica gel using 50% ethyl acetate in hexanes to afford final product **G9** as white solid in 37% yield; IR (film) ν_{max} 3061, 2982, 2932, 1589, 1346, 1160, 663 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.90-7.88 (m, 2H), 7.71 (d, *J* = 8.3 Hz, 2H), 7.46-7.43 (m, 2H), 7.41-7.37 (m, 1H), 7.26 (s, 1H), 7.21 (d, *J* = 8.0 Hz, 2H), 7.18-7.12 (m, 3H), 6.96 (s, 1H), 5.53 (d, *J* = 5.9 Hz, 1H), 4.93 (d, *J* = 18.0 Hz, 1H), 4.16-4.07 (m, 2H), 3.94 (d, *J* = 18.0 Hz, 1H), 3.34 (dd, *J* = 17.2, 0.7 Hz, 1H), 3.14 (dd, *J* = 17.3, 6.5 Hz, 1H), 2.35 (s, 3H), 1.44 (t, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.6, 157.8, 152.5, 143.5, 140.6, 139.5, 137.3, 134.4, 129.7, 128.9, 128.6, 127.7, 127.6, 126.8, 126.7, 125.3, 114.6, 101.6, 63.8, 53.7, 38.5, 33.4, 21.4, 14.4; MS (MALDI) calcd. for $C_{29}H_{27}ClN_2O_3SNa$ $[M + Na]^+$ 541.13, found 542.64.