Supporting Information

Discovery of New Tetracyclic Tetrahydrofuran Derivatives as Potential Broad-Spectrum Psychotropic Agents.[†]

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Experimental Section

General Methods. Reaction solvents were commercially purchased from Aldrich and used without further purification. Commercial reagents were used as received. Reaction were monitored by thin-layer chromatography (TLC) on 0.25mm precoated Merck Silica Gel 60 $F_{254,}$ visualizing with ultraviolet light or phosphomolibdic acid stain. Elemental analysis are within ± 0.4% of the theoretical values. ^{1}H NMR spectra were recorded on a Bruker DPX-400 with standard pulse sequences, operating at 400 MHz. Chemical shifts (δ) are reported in parts per million (ppm) downfield from tetramethylsilane (TMS), which was used as internal standard. HPLC-MS analysis were performed with an Agilent Technologies 1100 series consisted of a quaternary pump with degasser, autosampler, column oven and DAD detector. A generic gradient: 80/10/10 of $AcONH_4$ (0.05%)/MeOH/CH_3CN to 50/50 CH_3CN/MeOH in 6min, to 100% CH_3CN in 1.5min was performed on a Zorbax XDB C-18, 30 x 4.6mm, i.d. 3.5um from Agilent Technologies. Low-resolution mass spectra (ESI/MS) were recorded on a single quadrupole Micromass Platform series II mass spectrometer with electrospray ionization (ESI). High-resolution mass spectra (HRMS) were recorded on a Micromass LCT Time of Fligh mass spectrometer with electrospray ionization and lockmass device for mass calibration. GC-EI-MS analysis were carried on an Agilent 6890 Series gas chromatograph, with split-splitless injector, directly coupled to an Agilent 5973 mass-selective detector with EI source. GC capillary column was an HP 5-MS (30 mx 0.25 mm i.d., 0,25 μm; Agilent Technologies). Flash column chromatography was performed on Merck Silica Gel 60 (230-400 mesh) using reagent grade heptane, dichloromethane and ACS-grade ethyl acetate and methanol. Preparative HPLC Normal Phase separations were carried on a Waters Delta Prep 4000 with a 5 cm i.d. Prochrom column packed with 200 gr Kromasil 60 Å/ 10um. Enantiomeric separations were performed by HPLC chromatography using a Waters Alliance 2690

instrument with chiral columns (Chiralcel OD, Chiralcel OJ, Chiralpak AD and Chiralpak AS, Daicel 10um).

Experimental procedures:

Preparation of α-allyl ketones 3a-d.

2-Fluoro-10-(2-propenyl)-dibenz[*b,f*]oxepin-11(10*H*)one (3a): Under nitrogen atmosphere, to a suspension of sodium hydride (84 mg, 3.5 mmol) in dry THF (40 mL) at 0 ºC was added dropwise the tricyclic ketone **2a** (685 mg, 3 mmol) in dry THF (20 mL). The mixture was stirred until hydrogen evolution ceased and the reaction mixture became homogeneous (ca. 2 h). Addition of allyl bromide (0.47 mL, 3.05 mmol) was followed by stirring of the reaction mixture for 12 h at room temperature. Aqueous ammonium chloride solution was added (15 mL), and the resulting mixture was extracted with diethyl ether (3 x 50 mL). The combined organic extracts were washed with water and dried over anhydrous sodium sulfate. Volatiles were evaporated in vacuo and the residue thus obtained was purified by flash column chromatography on silica gel (heptane) to give the α-allylated ketone **3a**: 683 mg, 85% yield, white solid, R_f = 0.75 (heptane); ^{1}H NMR ($CDCl_3$) δ 2.78 (m, 1 H), 3.05 (m, 1 H), 4.29 (t, 1 H, J = 7.6 Hz), 5.04 (dd, 1 H, J = 10.2, 1.0 Hz), 5.11 (dd, 1 H, J = 17.0, 1.2 Hz), 5.83 (m, 1 H), 7.26 (m, 5 H), 7.36 (dd, 1 H, J = 8.9, 4.6 Hz), 7.70 (td, 1 H, J = 10.2, 3.4 Hz); ESI/MS: 269 $(M + H)^+$

α-allyl ketones **3b**-**d** were prepared from allyl bromide and the appropriate tricyclic ketone **2b**-**d** according to the procedure described above for compound **3a**:

2-Chloro-10-(2-propenyl)-dibenz[*b,f*]oxepin-11(10*H*)one (3b): 657 mg, 77% yield, yellow oil, R_f = 0.77 (heptane); ^{1}H NMR ($CDCl_3$) δ 2.77 (m, 1 H), 3.04 (m, 1 H), 4.26 (t, 1 H, J = 7.5 Hz), 5.04 (dq,

1 H, J = 9.0, 1.5 Hz), 5.11 (dq, 1 H, J = 17.0, 1.5 Hz), 5.82 (m, 1 H), 7.15-7.30 (m, 5 H) 7.48 (dd, 1 H, J = 8.7, 2.9 Hz), 7.98 (d, 1 H, J = 2.8 Hz); HRMS calcd for $C_{17}H_{14}ClO_2$ 285.0682, found 285.0677.

2-Bromo-10-(2-propenyl)-dibenz[*b,f*]oxepin-11(10*H*)one (3c): 395 mg, 40% yield, colorless oil, R_f = 0.75 (heptane); ^{1}H NMR ($CDCl_3$) δ 2.76 (m, 1 H), 3.03 (m, 1 H), 4.25 (t, 1 H, J = 7.5 Hz), 5.04 (dd, 1 H, J = 9.9, 0.9 Hz), 5.10 (dd, 1 H, J = 17.3, 0.9 Hz), 5.82 (m, 1 H), 7.25 (m, 5 H), 7.61 (ddd, 1 H, J = 8.7, 2.7, 0.4 Hz), 8.12 (d, 1 H, J = 2.5 Hz); HRMS calcd for $C_{17}H_{14}BrO_2$ 330.0255, found 330.0257.

2-Fluoro-10-(2-propenyl)-dibenzo[*b,f*]tiepin-11(10*H*)one (3d): 768 mg, 90% yield, yellow oil, R_f = 0.68 (heptane); ^{1}H NMR ($CDCl_3$) δ 2.85 (m, 1 H), 3.27 (m, 1 H), 4.93 (dd, 1 H, J = 8.1, 6.6 Hz), 5.04 (dd, 1 H, J = 10.2, 1.3 Hz), 5.14 (dd, 1 H, J = 17.2, 1.7 Hz), 5.84 (m, 1 H), 7.17 (m, 2 H), 7.38 (d, 1 H, J = 7.0 Hz), 7.44 (ddd, 1 H, J = 8.3, 7.8, 1.0 Hz), 7.58 (dd, 1 H, J = 8.7, 5.1 Hz), 7.67 (d, 1 H, J = 7.6 Hz), 7.87 (dd, 1 H, J = 9.9, 3.0 Hz); HRMS calcd for $C_{17}H_{14}FOS$ 285.0749, found 285.0744.

Preparation of *cis*-β-allylic alcohols 4a-d.

***cis*-10,11-Dihydro-2-fluoro-10-(2-propenyl)-dibenz[*b,f*]oxepin-11-ol (4a):** To a THF (30 mL) solution of the α-allyl ketone **3a** (537 mg, 2 mmol), cooled at –30 ºC, L-selectride (2 ml of 1.0 M solution in THF, 2 mmol) was added dropwise. The resulting mixture was further stirred and allowed to slowly warm to room temperature for 6 h. Then 2N HCl (10 mL) was added, and the organic materials were extracted with ethyl acetate (2 x 50 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), concentrated, and purified by flash column chromatography on silica gel (heptane/ethyl acetate, 4:1) to give *cis*-β-allyl alcohol **4a**: 497 mg, 92% yield, colorless oil, R_f = 0.75 (heptane); ^{1}H NMR ($CDCl_3$) δ 1.59 (d, 1 H, J = 9.8 Hz), 2.57 (m, 1 H), 2.71 (m, 1 H), 3.69 (ddd, 1 H, J

= 8.5, 8.3, 1.8 Hz), 5.02 (dd, 1 H, *J* = 9.8, 1.8 Hz), 5.11 (d, 1 H, *J* = 10.2 Hz), 5.16 (dd, 1 H, *J* = 17.3, 1.4 Hz), 5.88 (m, 1 H), 6.94 (ddd, 1 H, *J* = 8.9, 7.4, 3.0 Hz), 7.13-7.29 (m, 6 H); HRMS calcd for $C_{17}H_{16}FO_2$ 271.1134, found 271.1129.

cis-β-allylic alcohols **4b**-**d** were prepared from the appropriate α-allyl ketone ketone **3b**-**d** according to the procedure described above for compound **4a**:

***cis*-10,11-Dihydro-2-chloro-10-(2-propenyl)-dibenz[*b*,*f*]oxepin-11-ol (4b):** 516 mg, 90% yield, colorless oil, R_f = 0.75 (heptane); ^{1}H NMR ($CDCl_3$) δ 1.57 (d, 1 H, *J* = 10.8 Hz), 2.59 (m, 1 H), 2.71 (m, 1 H), 3.67 (t, 1 H, *J* = 6.8 Hz), 4.99 (d, 1 H, *J* = 9.5 Hz), 5.11 (d, 1 H, *J* = 10.3 Hz), 5.16 (dd, 1 H, *J* = 17.2, 1.3 Hz), 5.87 (m, 1 H), 7.2 (m, 6 H), 7.44 (d, 1 H, *J* = 2.1 Hz); HRMS calcd for $C_{17}H_{16}ClO_2$ 287.0839, found 287.0833.

***cis*-10,11-Dihydro-2-bromo-10-(2-propenyl)-dibenz[*b*,*f*]oxepin-11-ol (4c):** 636 mg, 96% yield, colorless oil, R_f = 0.75 (heptane); ^{1}H NMR ($CDCl_3$) δ 1.56 (d, 1 H, *J* = 9.8 Hz), 2.60 (m, 1 H), 2.71 (m, 1 H), 3.67 (m, 1 H), 4.99 (dd, 1 H, *J* = 9.8, 1.7 Hz), 5.11 (broad d, 1 H, *J* = 10.8 Hz), 5.17 (broad d, 1 H, *J* = 17.0 Hz), 5.86 (m, 1 H), 7.09 (d, 1 H, *J* = 8.5 Hz), 7.15-7.30 (m, 4 H), 7.35 (dd, 1 H, *J* = 8.7, 2.3 Hz), 7.60 (d, 1 H, *J* = 2.4 Hz); HRMS calcd for $C_{17}H_{16}BrO_2$ 331.0334, found 331.0328.

***cis*-10,11-Dihydro-2-fluoro-10-(2-propenyl)-dibenzo[*b*,*f*]tiepin-11-ol (4d):** 556 mg, 97% yield, colorless oil, R_f = 0.75 (heptane); ^{1}H NMR ($CDCl_3$) δ 2.00 (m, 1 H), 2.45 (m, 1 H), 3.65 (ddd, 1 H, *J* = 7.5, 6.4, 1.1 Hz), 4.85 (dd, 1 H, *J* = 17.0, 1.9 Hz), 4.88 (d, 1 H, *J* = 9.7 Hz), 5.31 (d, 1 H, *J* = 4.6 Hz), 5.65 (m, 1 H), 5.87 (d, 1 H, *J* = 5.0 Hz), 7.08 (td, 1 H, *J* = 8.3, 2.9 Hz), 7.2 (m, 3 H), 7.34 (dd, 1 H, *J* = 10.3, 2.9 Hz), 7.40 (dd, 1 H, *J* = 7.7, 1.0 Hz), 7.50 (dd, 1 H, *J* = 8.5, 5.6 Hz); HRMS calcd for $C_{17}H_{16}FOS$ 287.0906, found 287.0900.

Preparation of *trans*-β-allylic alcohols 5a-d.

***trans*-10,11-Dihydro-2-fluoro-10-(2-propenyl)-dibenz[*b,f*]oxepin-11-ol (5a):** To solution of the *cis*-β-allyl alcohol **4a** (541 mg, 2 mmol) and triphenylphosphine (1.31 g, 10 mmol) in 30 ml of THF, cooled at 0 ºC, a diisopropyl azodicarboxylate (DIAD, 2.02 g, 10 mmol) was added portionwise. The mixture was stirred until a precipitate was formed. A solution of *p*-nitrobenzoic acid (735 mg, 4.4 mmol) in THF (50 mL) was dropwise added and the resulting mixture was further stirred at room temperature for 12 h. The solvent was evaporated under vacuum and the residue thus obtained was filtered through silica gel. The residue thus obtained was taken up in dioxane/water (1:1, 30 mL) and LiOH (53 mg, 2.2 mmol) was portionwise added. The reaction mixture was stirred at room temperature for 12 h. Aqueous ammonium chloride solution was added (10 mL), and the resulting mixture was extracted with ethyl acetate (3 x 50 mL). The combined organic extracts were washed with brine, dried (Na_2SO_4), concentrated, and purified by flash column chromatography on silica gel (heptane/ethyl acetate, 4:1) to give the *trans*-β-allyl alcohol **5a**: 448 mg, 83% yield, colorless oil, R_f = 0.75 (heptane); ^{1}H NMR ($CDCl_3$) δ 1.99 (d, 1 H, J = 8.7 Hz), 2.41 (m, 1 H), 2.58 (m, 1 H), 3.29 (m, 1 H), 4.91 (dd, 1 H, J = 8.8, 5.5 Hz), 4.98 (m, 2 H), 5.75 (m, 1 H), 6.97 (ddd, 1 H, J = 8.9, 7.7, 3.1 Hz), 7.05-7.25 (m, 6 H); HRMS calcd for $C_{17}H_{16}FO_2$ 271.1134, found 271.1133.

trans-β-allylic alcohols **5b-d** were prepared from the appropriate *cis*-β-allylic alcohols **4b-d** according to the procedure described above for compound **5a**:

***trans*-10,11-Dihydro-2-chloro-10-(2-propenyl)-dibenz[*b,f*]oxepin-11-ol (5b):** 401 mg, 70% yield, colorless oil, R_f = 0.75 (heptane); ^{1}H NMR ($CDCl_3$) δ 1.89 (d, 1 H, J = 5.8 Hz), 2.38 (m, 1 H), 2.54 (m, 1 H), 3.28 (m, 1 H), 4.95 (m, 3 H), 5.73 (m, 1 H), 7.05-7.28 (m, 6 H), 7.34 (d, 1 H, J = 2.7 Hz); HRMS calcd for $C_{17}H_{16}ClO_2$ 287.0839, found 287.0835.

***trans*-10,11-Dihydro-2-bromo-10-(2-propenyl)-dibenz[*b*,*f*]oxepin-11-ol (5c):** 503 mg, 76% yield, colorless oil, R_f = 0.75 (heptane); ^{1}H NMR ($CDCl_3$) δ 1.92 (d, 1 H, *J* = 6.0 Hz), 2.39 (m, 1 H), 2.56 (m, 1 H), 3.29 (m, 1 H), 4.96 (m, 3 H), 5.74 (m, 1 H), 7.06-7.28 (m, 6 H), 7.44 (d, 1 H, *J* = 2.7 Hz). HRMS calcd for $C_{17}H_{16}BrO_2$ 331.0334, found 331.0330.

***trans*-10,11-Dihydro-2-fluoro-10-(2-propenyl)-dibenzo[*b*,*f*]tiepin-11-ol (5d):** 412 mg, 72% yield, colorless oil, R_f = 0.75 (heptane); ^{1}H NMR ($CDCl_3$) δ 2.46 (d, 1 H, *J* = 5.4 Hz), 2.69 (m, 1 H), 2.79 (m, 1 H), 3.25 (m, 1 H), 5.07 (m, 2 H), 5.65 (dd, 1 H, *J* = 9.1, 5.4 Hz), 5.84 (m, 1 H), 6.81 (td, 1 H, *J* = 8.3, 2.5 Hz), 7.03-7.20 (m, 3 H), 7.03-7.20 (m, 3 H), 7.31 (dd, 1 H, *J* = 9.8, 2.3 Hz), 7.43 (dd, 1 H, *J* = 8.5, 5.6 Hz), 7.46 (d, 1 H, *J* = 8.1 Hz); HRMS calcd for $C_{17}H_{16}FOS$ 287.0906, found 287.0901.

Preparation of 2-iodomethyl derivatives 6a-d.

[(2*SR*,3a*RS*,12b*SR*)+(2*SR*,3a*RS*,12b*SR*)]-11-Fluoro-2-iodomethyl-2,3,3a,12b-tetrahydrodibenzo[*b*,*f*]furo[2,3-*d*]oxepin (6a): To a stirred solution of the *trans*-β-allyl alcohol **5a** (540.6 mg, 2 mmol) in dry dichloromethane (20 mL) at room temperature, IPy_2BF_4 (bis(pyridine)iodonium(I) tetrafluoroborate, 919 mg, 2.2 mmol) was added at once. The resulting mixture was stirred at room temperature for 10 min. Dichloromethane (100 mL) was added and the resulting solution was successively washed with an aqueous $Na_2S_2O_4$ saturated solution, brine and water. The organic phase was dried (Na_2SO_4) and vacuum evaporated, affording a residue that was purified by HPLC chromatography (heptane) to give the 2-iodomethyl derivative **6a** as a 1:1 mixture of diastereoisomers: 729 mg, 93% yield, white solid, R_f = 0.75 (heptane); ^{1}H NMR ($CDCl_3$) δ 1.98 (td, 1 H, *J* = 12.2, 10.1 Hz), 2.29 (m, 1 H), 2.43 (m, 1 H), 2.76 (ddd, 1 H, *J* = 12.2, 7.1, 5.2 Hz), 3.21 (dd, 1 H, *J* = 9.7, 7.8 Hz), 3.38 (m, 2 H), 3.41 (dd, 1 H, *J* = 9.8, 5.3 Hz), 3.93 (m, 2 H), 4.35 (m, 2 H), 5.60

(d, 1 H, J = 8.5 Hz), 5.67 (d, 1 H, J = 8.3 Hz), 6.90 (m, 2 H), 7.07-7-24 (m, 12 H); GC-EI-MS: 396 (M^+).

2-iodomethyl derivatives **6b**-**d** were prepared by iodocyclization with IPy_2BF_4 from the appropriate *trans*-β-allylic alcohol **5b**-**d** according to the procedure described above for compound **6a**:

(2*SR*,3a*RS*,12b*SR*)-11-Chloro-2-iodomethyl-2,3,3a,12b-tetrahydrodibenzo[*b*,*f*]furo[2,3-*d*]oxepin (6b): 776 mg, 94% yield, white solid, R_f = 0.75 (heptane); ^{1}H NMR ($CDCl_3$) δ 2.01 (m, 1 H), 2.24 (m, 1 H), 2.41 (m, 1 H), 2.73 (m, 1 H), 3.22 (dd, 1 H, J = 9.6, 7.5 Hz), 3.51 (m, 3 H), 4.11 (m, 2 H), 4.47 (m, 2 H), 5.64 (d, 1 H, J = 8.3 Hz), 5.58 (d, 1 H, J = 7.5 Hz), 6.93 (m, 2 H), 7.12-7-35 (m, 12 H); GC-EI-MS: 412 (M^+).

[(2*SR*,3a*RS*,12b*SR*)+(2*SR*,3a*RS*,12b*SR*)]-11-Bromo-2-iodomethyl-2,3,3a,12b-tetrahydrodibenzo[*b*,*f*]furo[2,3-*d*]oxepin (6c): 777 mg, 85% yield, white solid, R_f = 0.75 (heptane); ^{1}H NMR ($CDCl_3$) δ 1.98 (m, 1 H), 2.28 (m, 1 H), 2.45 (m, 1 H), 2.74 (m, 1 H), 3.20 (dd, 1 H, J = 9.7, 7.7 Hz), 3.42 (m, 2 H), 3.44 (dd, 1 H, J = 10.1, 5.1 Hz), 4.01 (m, 2 H), 4.37 (m, 2 H), 5.69 (d, 1 H, J = 8.3 Hz), 5.58 (d, 1 H, J = 7.5 Hz), 6.93 (m, 2 H), 7.02-7-29 (m, 12 H); GC-EI-MS: 456 (M^+).

([(2*SR*,3a*RS*,12b*SR*)+(2*SR*,3a*RS*,12b*SR*)]-11-Fluoro-2-iodomethyl-2,3,3a,12b-tetrahydrodibenzo[*b*,*f*]furo[2,3-*d*]tiepin (6d): 775 mg, 94% yield, pale yellow solid, R_f = 0.75 (heptane); ^{1}H NMR ($CDCl_3$) δ 2.05 (m, 1 H), 2.38 (m, 1 H), 2.55 (m, 1 H), 2.82 (m, 1 H), 3.25-3.55 (m, 6 H), 4.26 (m, 1 H), 4.33 (m, 1 H), 5.64 (d, 1 H, J = 10.8 Hz), 5.66 (d, 1 H, J = 10.6 Hz), 6.79 (m, 2 H), 7.05 (m, 4 H), 7.20 (m, 2 H), 7.35 (m, 4 H), 8.52 (d, 1 H, J = 4.1 Hz), 8.65 (d, 1 H, J = 5.2 Hz); GC-EI-MS: 412 (M^+).

Preparation of 2-N,N-dimethylamino detivatives 7a-d and 8a-d.

(2*SR*,3a*RS*,12b*SR*)-2-N,N-Dimethylaminomethyl-11-fluoro-2,3,3a,12b-tetrahydrodibenzo[*b*,*f*]furo[2,3-*d*]oxepin (7a) and (2*RS*,3a*RS*,12b*SR*)-2-N,N-Dimethylamino methyl-11-fluoro-2,3,3a,12b-tetrahydrodibenzo[*b*,*f*]furo[2,3-*d*]oxepin (8a): To a solution of the corresponding 2-iodomethyl derivative **6a** (594 mg, 1.5 mmol) in 20 mL of THF, CaO (841 mg, 15 mmol) and 4 mL of a 2 M solution of dimethyamine in THF were added at room temperature. The resulting reaction mixture was heated at 120 ºC (oil bath temperature) into a pressure reactor vessel for 12 h. After cooling to rt the solids were filtered off and the organic solution was evaporated. The resudue thus obtained was taken up with dichloromethane (50 mL) and was successively washed with an aqueous Na_2CO_3 saturated solution and water. The organic extract was dried (Na_2SO_4) and vacuum concentrated affording a residue that was purified by HPLC chromatography on silica gel (CH_2Cl_2/MeOH(NH_3), 98:2) yielding the corresponding diastereoisomers **7a** and **8a**. **7a**: 140 mg, 30% yield, colorless oil, R_f = 0.32 (CH_2Cl_2/MeOH(NH_3) 95:5); ^{1}H NMR ($CDCl_3$) δ 1.94 (m, 1 H), 2.23 (s, 6 H), 2.50 (m, 2 H), 2.70 (m, 1 H), 3.31 (m, 1 H), 4.42 (m, 1 H), 4.92 (d, 1 H, *J* = 10.8 Hz), 7.05-7.30 (m, 7 H); HRMS calcd for $C_{19}H_{21}FNO_2$ 314.1556, found 314.1558. **8a:** 164 mg, 35% yield, colorless oil, R_f = 0.25 (CH_2Cl_2/MeOH(NH_3), 95:5); ^{1}H NMR ($CDCl_3$) δ 2.24 (s, 6 H), 2.35 (m, 1 H), 2.42 (m, 1 H), 2.43 (m, 2 H), 3.27 (m, 1 H), 4.38 (m, 1 H), 4.87 (d, 1 H, *J* = 10.8 Hz), 7.10 (m, 3 H), 7.18 (dd, 1 H, *J* = 8.3, 1.3 Hz), 7.24 (m, 3 H); HRMS calcd for $C_{19}H_{21}FNO_2$ 314.1556, found 314.1559.

2-N,N-dimethyl derivatives **7b**-**d** and **8b**-**d** were prepared from the appropriate 2-iodomethyl derivative **6b**-**d** according to the procedure described above for compounds **7a** and **8a**:

(2*SR*,3a*RS*,12b*SR*)-2-N,N-Dimethylaminomethyl-11-chloro-2,3,3a,12b-tetrahydrodibenzo[*b*,*f*]furo[2,3-*d*]oxepin (7b): 186 mg, 41% yield, colorless oil, R_f = 0.25 (CH_2Cl_2/MeOH(NH_3), 95:5); ^{1}H NMR ($CDCl_3$) δ 2.36 (m, 1 H), 2.45 (m, 1 H), 2.53 (s, 6 H), 2.79 (m, 2 H), 3.40 (m, 1 H), 4.49 (m, 1 H), 4.90 (d, 1 H, *J* = 10.4 Hz), 7.06 (d, 1 H, *J* = 8.4 Hz), 7.08 (m, 1 H),

7.20 (m, 3 H), 7.33 (dd, 1 H, J = 8.4, 2.5 Hz), 7.64 (d, 1 H, J = 2.5 Hz); HRMS calcd for $C_{19}H_{21}ClNO_2$ 330.1261, found 330.1265.

(2*SR*,3a*RS*,12b*SR*)-2-N,N-Dimethylaminomethyl-11-bromo-2,3,3a,12b-tetrahydrodibenzo[*b*,*f*]furo[2,3-*d*]oxepin (7c): 161 mg, 28% yield, colorless oil, R_f = 0.19 (CH_2Cl_2/MeOH(NH_3), 95:5); ^{1}H NMR ($CDCl_3$) δ 2.37 (m, 1 H), 2.46 (m, 1 H), 2.52 (s, 6 H), 2.80 (m, 2 H), 3.41 (m, 1 H), 4.48 (m, 1 H), 4.89 (d, 1 H, J = 10.5 Hz), 7.05 (d, 1 H, J = 8.5 Hz), 7.09 (m, 1 H), 7.18 (m, 3 H), 7.33 (dd, 1 H, J = 8.5, 2.5 Hz), 7.63 (d, 1 H, J = 2.5 Hz); HRMS calcd for $C_{19}H_{21}BrNO_2$ 374.0756, found 374.0760.

(2*SR*,3a*RS*,12b*SR*)-2-N,N-Dimethylaminomethyl-11-fluoro-2,3,3a,12b-tetrahydrodibenzo[*b*,*f*]furo[2,3-*d*]tiepin (7d): 196 mg, 40% yield, colorless oil, R_f = 0.26 (CH_2Cl_2/MeOH(NH_3), 95:5); ^{1}H NMR ($CDCl_3$) δ 2.07 (m, 1 H), 2.36 (s, 6 H), 2.53 (dd, 1 H, J = 12.6, 4.1 Hz), 2.65 (dd, 1 H, J = 12.6, 7.2 Hz), 2.77 (m, 1 H), 3.50 (m, 1 H), 4.52 (m, 1 H), 5.66 (d, 1 H, J = 10.1 Hz), 6.86 (m, 1 H), 7.16 (m, 3 H), 7.37 (m, 2 H), 7.45 (dd, 1 H, J = 8.4, 5.3 Hz); HRMS calcd for $C_{19}H_{21}FNOS$ 330.1328, found 330.1331.

(2*RS*,3a*RS*,12b*SR*)-2-N,N-Dimethylaminomethyl-11-chloro-2,3,3a,12b-tetrahydrodibenzo[*b*,*f*]furo[2,3-*d*]oxepin (8b): 142 mg, 29% yield, colorless oil, R_f = 0.22 (CH_2Cl_2/MeOH(NH_3), 95:5); ^{1}H NMR ($CDCl_3$) δ 2.44 (m, 2 H), 2.49 (dd, 1 H, J = 12.9, 6.4 Hz), 2.59 (dd, 1 H, J = 12.8, 6.3 Hz), 3.37 (m, 1 H), 4.46 (m, 1 H), 4.94 (d, 1 H, J = 10.8 Hz), 7.09 (m, 2 H), 7.18 (m, 4 H), 7.52 (dd, 1 H, J = 2.5, 0.9 Hz); HRMS calcd for $C_{19}H_{21}ClNO_2$ 330.1261, found 330.1263.

(2*RS*,3a*RS*,12b*SR*)-2-N,N-Dimethylaminomethyl-11-bromo-2,3,3a,12b-tetrahydrodibenzo[*b*,*f*]furo[2,3-*d*]oxepin (8c): 203 mg, 36% yield, colorless oil, R_f = 0.25 (CH_2Cl_2/MeOH(NH_3), 95:5); ^{1}H NMR ($CDCl_3$) δ 2.39 (s, 6 H), 2.40 (m, 2 H), 2.48 (dd, 1 H, J = 12.8,

6.3 Hz), 2.58 (dd, 1 H, *J* = 12.8, 6.4 Hz), 3.38 (m, 1 H), 4.48 (m, 1 H), 4.90 (d, 1 H, *J* = 10.7 Hz), 7.09 (d, 1 H, *J* = 8.5Hz), 7.14-7.29 (m, 4 H), 7.37 (dd, 1 H, *J* = 8.6, 2.4 Hz), 7.60 (d, 1 H, *J* = 2.4 Hz); HRMS calcd for $C_{19}H_{21}BrNO_2$ 374.0756, found 374.0752.

(2*RS*,3a*RS*,12b*SR*)-2-N,N-Dimethylaminomethyl-11-fluoro-2,3,3a,12b-tetrahydrodibenzo[*b*,*f*]furo[2,3-*d*]tiepin (8d): 161 mg, 32% yield, colorless oil, R_f = 0.23 (CH_2Cl_2/MeOH(NH_3), 95:5); ^{1}H NMR ($CDCl_3$) δ 2.38 (s, 6 H), 2.40-2.57 (m, 3 H), 2.63 (dd, 1 H, *J* = 12.5, 6.5 Hz), 3.40 (m, 1 H), 4.42 (m, 1 H), 5.61 (d, 1 H, *J* = 10.5 Hz), 6.87 (td, 1 H, *J* = 8.4, 3.0 Hz), 7.10 (m, 1 H), 7.17 (m, 2 H), 7.38 (m, 2 H), 7.45 (dd, 1 H, *J* = 8.5, 5.4 Hz); HRMS calcd for $C_{19}H_{21}FNOS$ 330.1328, found 330.1322. Anal. calcd for $C_{19}H_{20}FNOS$ C, 76.11; H, 4.88, O, 11.9, found C, 76.23; H, 4.97; O, 11.96.

Appendix. Purity determination for intermediates and target compounds: GC, HPLC, ^{1}H-NMR, combustion analysis.

Comp.	GC-purity	HPLC-purity	^{1}H-NMR	Combustion analysis	
				Calculated	Found
3a	97%	97%	OK	-	-
3b	98%	97%	OK	-	-
3c	97%	99%	OK	-	-
3d	98%	100%	OK	-	-
4a	-	98%	OK	-	-
4b	-	98%	OK	-	-
4c	-	99%	OK	-	-
4d	-	96%	OK	-	-
5a	-	99%	OK	-	-
5b	-	99%	OK	-	-
5c	-	99%	OK	-	-
5d	-	100%	OK	-	-
6a	-	97%	OK	-	-
6b	-	100%	OK	-	-

6c	-	99%	OK	-	-
6d	-	98%	OK	-	-
7a	-	98%	OK	-	-
7b	-	-	OK	69.19 % C, 6.11 % H, 4.25 % N	69.17 % C, 6.12 % H, 4.23 % N
7c	97%	99%	OK	-	-
7d	98%	98%	OK	-	-
8a	-	-	OK	72.82 % C, 6.43 % H, 4.47 % N	72.80 % C, 6.42 % H, 4.42 % N
8b	-	-	OK	69.19 % C, 6.11 % H, 4.25 % N	69.16 % C, 6.14 % H, 4.23 % N
8c	97%	99%	OK	-	-
8d	-	-	OK	69.27 % C, 6.12 % H, 4.25 % N	69.29 % C, 6.11 % H, 4.26 % N
(-)-**8d**	-	-	OK	69.27 % C, 6.12 % H, 4.25 % N	69.20 % C, 6.14 % H, 4.24 % N
(+)-**8d**	-	-	OK	69.27 % C, 6.12 % H, 4.25 % N	69.23 % C, 6.14 % H, 4.27 % N