Supporting Information

Bicyclic diazepinones as dual ligands of the α2δ-1 subunit of voltage-gated calcium channels and the norepinephrine transporter.

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[1]ESTEVE Pharmaceuticals, Torre Esteve, Passeig de la Zona Franca, 109, 08038 Barcelona, Spain. Current affiliation: WELAB, Parc Científic Barcelona, C/ Baldiri Reixac 4-8, 08028 Barcelona, Spain.

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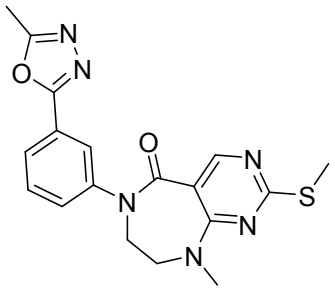
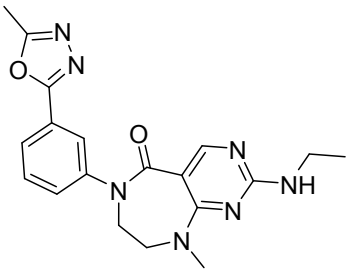
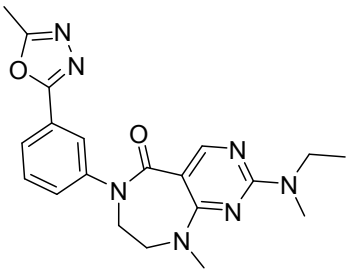
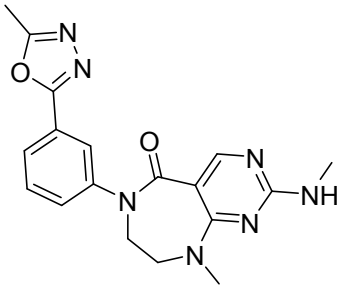
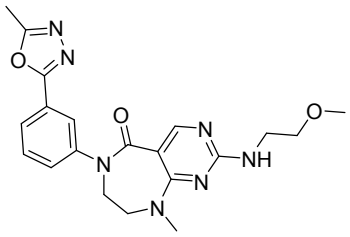
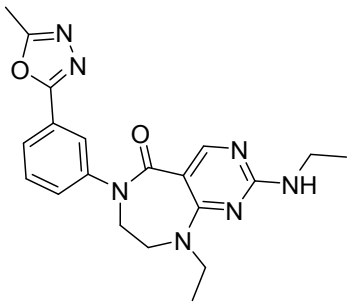
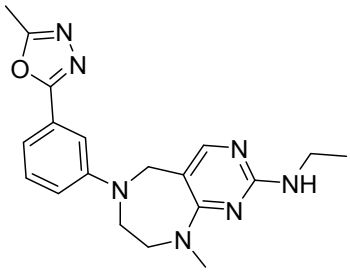
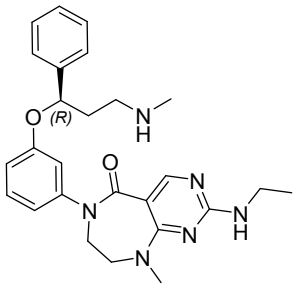
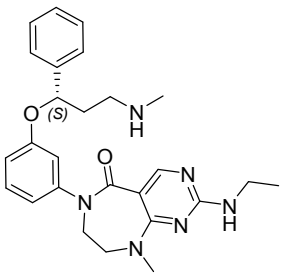
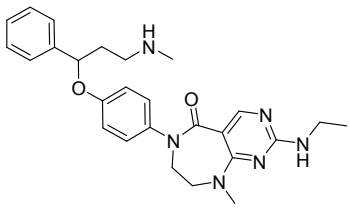
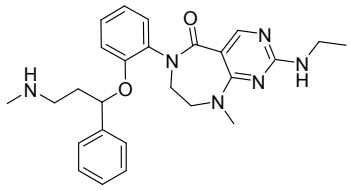
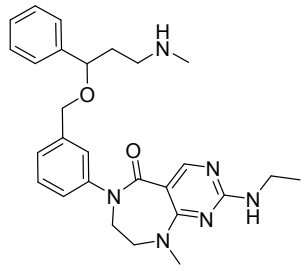
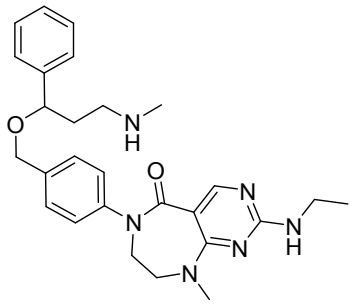
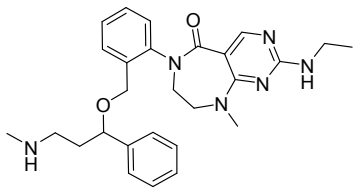
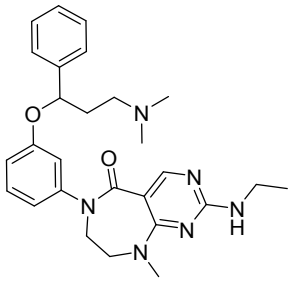
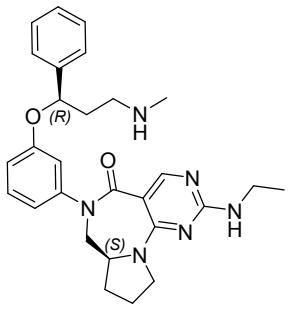
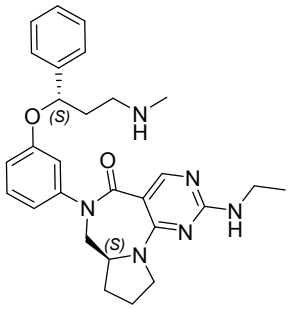
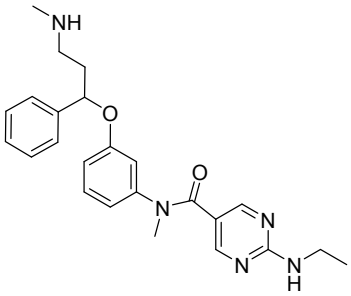
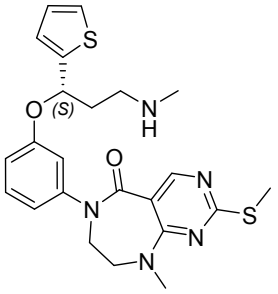
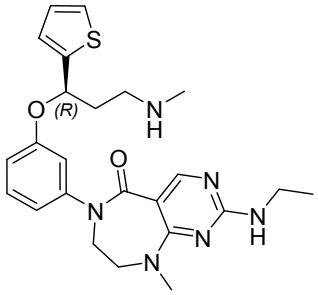
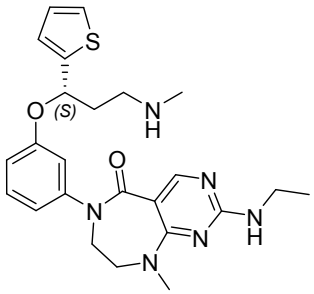
Analytical data of final compounds: purity, ^{1}H NMR, HRMS.

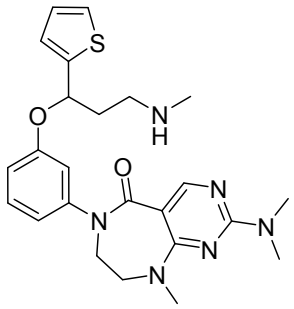
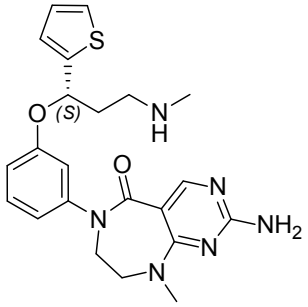
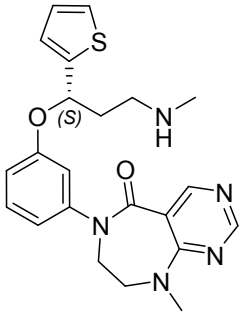
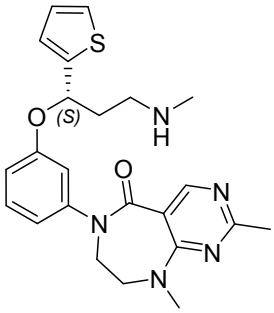
Comp.	Structure	Purity (%)	^{1}H NMR	HRMS
15-1		98.0	^{1}H NMR (500 MHz, $CDCl_3$) δ 8.82 (bs, 1H), 7.97 (t, J = 1.5 H, 1H), 7.92 (dt, J = 1.5, 7.7 Hz, 1H), 7.58 (t, J = 7.7 Hz, 1H), 7.53-7.51 (m, 1H), 4.09-4.07 (m, 2H), 3.87-3.85 (m, 2H), 3.35 (s, 3H), 2.64 (s, 3H), 2.59 (s, 3H).	383.1275 $[M+H]^+$
16a		98.4	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (bs, 1H), 7.95 (t, J = 1.5 Hz, 1H), 7.90 (dt, J = 1.7, 7.0 Hz, 1H), 7.47-7.54 (m, 2H), 5.78 (bs, 1H), 4.04-4.02 (m, 2H), 3.78-3.75 (m, 2H), 3.47 (m, 2H), 3.23 (s, 3H), 2.60 (s, 3H), 1.24 (t, J = 7.2 Hz, 3H).	380.1831 $[M+H]^+$
16b		97.4	^{1}H NMR (500 MHz, $CDCl_3$) δ 8.82 (bs, 1H), 7.97 (m, 1H), 7.91 (dt, J = 1.5, 7.3 Hz, 1H), 7.56-7.51 (m, 2H), 4.06-4.04 (m, 2H), 3.78-3.77 (m, 2H), 3.74-3.70 (m, 2H), 3.24 (s, 3H), 3.19 (s, 3H), 2.63 (s, 3H), 1.21 (t, J = 7.0 Hz, 3H).	394.1985 $[M+H]^+$
16c		99.2	^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (bs, 1H), 7.96 (t, J = 1.5 H, 1H), 7.91 (dt, J = 1.5, 7.5 Hz, 1H), 7.55-7.49 (m, 2H), 5.66 (bs, 1H), 4.05-4.03 (m, 2H), 3.79-3.78 (m, 2H), 3.27 (s, 3H), 3.02 (d, J = 4.8 Hz, 3H), 2.62 (s, 3H).	366.1689 $[M+H]^+$

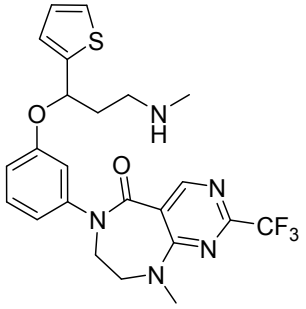
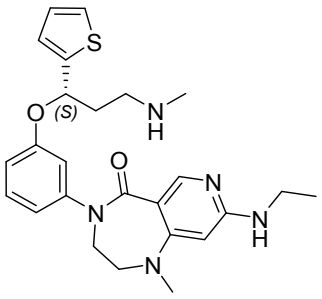
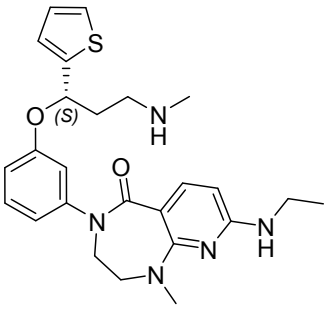
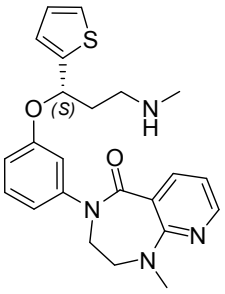
16d		95.4	^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (bs, 1H), 7.97 (t, J = 1.5 H, 1H), 7.92 (dt, J = 1.5, 7.5 Hz, 1H), 7.56-7.49 (m, 2H), 5.70 (bs, 1H), 4.06-4.04 (m, 2H), 3.79-3.78 (m, 2H), 3.59 (t, J = 5.2 Hz, 2H), 3.41 (s, 3H), 3.24 (s, 3H), 2.62 (s, 3H).	410.1942 $[M+H]^+$
17		99.0	^{1}H NMR (300 MHz, $CDCl_3$) δ 8.78 (bs, 1H), 7.94 (t, J = 1.5 Hz, 1H), 7.90 (dt, J = 1.5, 7.2 Hz, 1H), 7.56-7.46 (m, 2H), 5.56 (bs, 1H), 4.03-4.00 (m, 2H), 3.80-3.73 (m, 4H), 3.50-3.41 (m, 2H), 2.61 (s, 3H), 1.25 (t, J = 7.2 Hz, 3H), 1.23 (t, J = 7.2 Hz, 3H).	394.1995 $[M+H]^+$
23		95.1	^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (bs, 1H), 7.39 (m, 1H), 7.34-7.29 (m, 2H), 6.88-6.85 (m, 1H), 5.14 (bs, 1H), 4.48 (s, 2H), 3.80-3.76 (m, 4H), 3.42-3.35 (m, 2H), 3.12 (s, 3H), 2.62 (s, 3H), 1.20 (t, J = 7.2 Hz, 3H).	366.2031 $[M+H]^+$
31aR		97.2	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (bs, 1H), 7.48-7.46 (m, 2H), 7.42-7.38 (m, 2H), 7.34-7.26 (m, 2H), 6.92-6.91 (m, 1H), 6.89-6.85 (m, 2H), 5.42 (dd, J = 4.8, 8.0 Hz, 1H), 3.94-3.92 (m, 2H), 3.77-3.76 (m, 2H), 3.52-3.47 (m, 2H), 3.29 (s, 3H), 2.85-2.73 (m, 2H), 2.44 (s, 3H), 2.31-2.20 (m, 1H), 2.14-2.06 (m, 1H), 1.29 (t, J = 7.2 Hz, 3H).	461.2670 $[M+H]^+$
31aS		95.9	^{1}H NMR (400 MHz, CD_3OD) δ 8.58 (bs, 1H), 7.48-7.46 (m, 2H), 7.42-7.38 (m, 2H), 7.34-7.26 (m, 2H), 6.92-6.91 (m, 1H), 6.89-6.85 (m, 2H), 5.42 (dd, J = 4.8, 8.0 Hz, 1H), 3.94-3.92 (m, 2H), 3.77-3.76 (m, 2H), 3.52-3.47 (m, 2H), 3.29 (s, 3H), 2.85-2.73 (m, 2H), 2.44 (s, 3H), 2.31-2.20 (m, 1H), 2.14-2.06 (m, 1H), 1.29 (t, J = 7.2 Hz, 3H).	461.2670 $[M+H]^+$

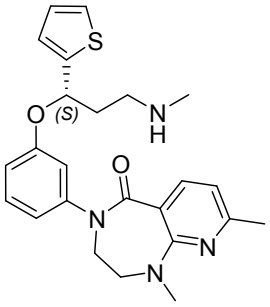
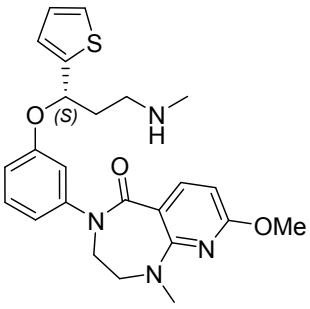
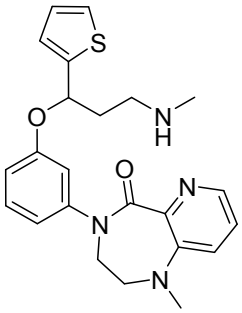
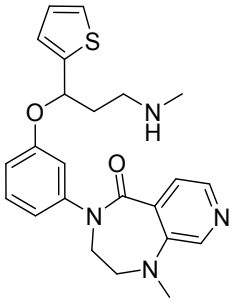
31b		97.2	^{1}H NMR (400 MHz, CD_3OD) δ 8.56 (bs, 1H), 7.47-7.45 (m, 2H), 7.41-7.37 (m, 2H), 7.33-7.29 (m, 1H), 7.14 (d, J = 8.9 Hz, 2H), 6.99 (d, J= 8.9 Hz, 2 H), 5.41 (dd, J = 4.7, 8.1 Hz, 1H), 3.92-3.90 (m, 2H), 3.78-3.76 (m, 2H), 3.51-3.46 (m, 2H), 3.28 (s, 3H), 2.86-2.73 (m, 2H), 2.44 (s, 3H), 2.31-2.20 (m, 1H), 2.14-2.05 (m, 1H), 1.28 (t, J = 7.2 Hz, 3H).	461.2663 $[M+H]^+$
31c		99.1	^{1}H NMR (400 MHz, CD_3OD) δ 8.62 (bs, 1H), 7.47-7.33 (m, 5H), 7.41-7.37 (m, 2H), 7.33-7.29 (m, 1H), 7.14 (d, J = 8.9 Hz, 2H), 6.99 (d, J = 8.9 Hz, 2 H), 5.41 (dd, J = 4.7, 8.1 Hz, 1H), 3.92-3.90 (m, 2H), 3.78-3.76 (m, 2H), 3.51-3.46 (m, 2H), 3.28 (s, 3H), 2.86-2.73 (m, 2H), 2.44 (s, 3H), 2.31-2.20 (m, 1H), 2.14-2.05 (m, 1H), 1.28 (t, J= 7.2 Hz, 3H).	461.2654 $[M+H]^+$
31d		99.5	^{1}H NMR (500 MHz, CD_3OD) δ 8.62 (bs, 1H), 7.51-7.43 (m, 5H), 7.26 (dd, J = 1.6, 7.8 Hz, 1 H), 7.18 (t, J = 7.3 Hz, 1H), 7.17 (t, J= 7.3 Hz, 1H), 6.90 (d, J = 8.2 Hz, 1H), 5.44 (bs, 1H), 4.00 (m, 4H), 3.55-3.50 (m, 2H), 3.36 (s, 3H), 2.70 (t, J= 6.7 Hz, 2H), 2.33 (s, 3H), 2.24-2.15 (m, 1H), 2.10-2.09 (m, 1H), 1.31 (t, J = 7.2 Hz, 3H).	475.2806 $[M+H]^+$
31e		100	^{1}H NMR (400 MHz, CD_3OD) δ 8.54 (s, 1H), 7.39-7.33 (m, 5H), 7.31-7.28 (m, 1H), 7.26-7.24 (m, 3H), 4.47 (dd, J = 5.1, 8.2 Hz, 1H), 4.40 (d, J = 12.0 Hz, 1H), 4.28 (d, J = 12.1 Hz, 1H), 3.95-3.94 (m, 2H), 3.77-3.75 (m, 2H), 3.44-3.40 (m, 2H), 3.23 (s, 3H), 2.68-2.64 (m, 1H), 2.60-2.55 (m, 1H), 2.32 (s, 3H), 2.06-1.99 (m, 1H), 1.89-1.82 (m, 1H), 1.22 (t, J = 7.2 Hz, 3H).	475.2718 $[M+H]^+$

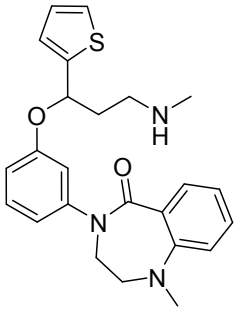
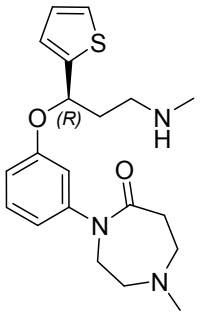
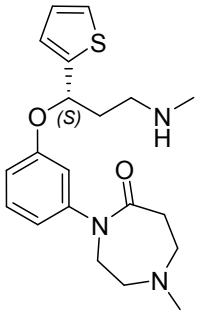
31f		97.0	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.68 and 8.65 (bs, 1H), 7.55 and 7.43 (bs, 1H), 7.36-7.21 (m, 7H), 7.13-7.09 (m, 1H), 4.42-4.17 (m, 3H), 3.87-3.42 (m, 6H), 3.16 and 3.12 (s, 3H), 2.66-2.55 (m, 2H), 2.36 (s, 3H), 2.07-1.91 (m, 1H), 1.87-1.80 (m, 1H), 1.23 (t, J = 7.2 Hz, 3H).	475.2819 $[M+H]^+$
32		96.1	^{1}H NMR (400 MHz, CD_3OD) δ 8.50 (bs, 1H), 7.40-7.38 (m, 2H), 7.34-7.30 (m, 2H), 7.26-7.18 (m, 2H), 6.84-6.83 (m, 1H), 6.81-6.76 (m, 2H), 5.31 (dd, J = 4.7, 7.9 Hz, 1H), 3.85-3.84 (m, 2H), 3.69-3.67 (m, 2H), 3.42 (q, J = 7.1, 16.0 Hz, 2H), 3.21 (s, 3H), 2.59-2.41 (m, 2H), 2.24 (s, 6H), 2.21-2.13 (m, 1H), 2.05-1.96 (m, 1H), 1.21 (t, J = 7.1 Hz, 3H).	475.2817 $[M+H]^+$
33R		97.9	^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (s, 1H), 7.36-7.30 (m, 4H), 7.26-7.23 (m, 1H), 7.16 (t, J = 8.0 Hz, 1H), 6.77-6.71 (m, 3H), 5.24 (dd, J =4.7, 8.0 Hz, 1H), 4.67 (s, 1H), 3.78-3.63 (m, 5H), 3.48-3.43 (m, 2H), 2.74 (bs, 2H), 2.42 (s, 3H), 2.20-2.13 (m, 1H), 2.06-1.96 (m, 3), 1.88-1.78 (m, 1H), 1.58-1.49 (m, 1H), 1.23 (t, J = 7.2 Hz, 3H).	487.2810 $[M+H]^+$
33S		98.2	^{1}H NMR (500 MHz, $CDCl_3$) δ 8.77 (s, 1H), 7.35-7.30 (m, 4H), 7.26-7.23 (m, 1H), 7.15 (t, J = 8.0 Hz, 1H), 6.79-6.76 (m, 2H), 6.68 (dd, J = 8.3, 1.9 Hz, 1H), 5.24 (dd, J = 8.0, 4.7 Hz, 1H), 4.67 (s, 1H), 3.88-3.83 (m, 1H), 3.80-3.71 (m, 2H), 2.69-2.62 (m, 2H), 3.48-3.42 (m, 2H), 2.74 (bs, 2H), 2.42 (s, 3H), 2.22-2.10 (m, 1H), 2.03-1.97 (m, 2H), 1.89-1.79 (m, 1H), 1.61-1.52 (m, 1H), 1.23 (t, J = 7.2 Hz, 3H).	487.2809 $[M+H]^+$

34		97.5	^{1}H NMR (400 MHz, CD_3OD) δ 8.65 (s, 2H), 7.38-7.36 (m, 2H), 7.33-7.30 (m, 2H), 7.25-7.22 (m, 2H), 6.86-6.84 (m, 1H), 6.75-6.74 (m, 2H), 5.31 (dd, J = 4.7, 8.0 Hz, 1H), 3.99-3.88 (m, 2H), 2.88 (s, 3H), 2.75-2.66 (m, 2H), 2.36 (s, 3H), 2.22-2.15 (m, 1H), 2.06-1.99 (m, 1H), 1.08 (t, J = 7.2 Hz, 3H).	420.2380 $[M+H]^+$
43S		100%	^{1}H NMR (400 MHz, CD_3OD) δ 8.56 (s, 1H), 7.32 (dd, J = 1.1 Hz, J = 5.2 Hz, 1H), 7.25 (t, 1H), 7.10 (dd, J = 0.9, 3.5 Hz, 1H), 6.95-6.89 (m, 3H), 6.84 (ddd, J = 0.8, 1.9, 7.9 Hz, 1H), 5.67 (dd, J = 5.7, 7.6, 1H), 3.93-3.91 (m, 2H), 3.81-3.79 (m, 2H), 3.30 (s, 3H), 2.75-2.62 (m, 2H), 2.54 (s, 3H), 2.36 (s, 3H) 2.33-2.23 (m, 1H), 2.14-2.06 (m, 1H).	470.1687 $[M+H]^+$
45aR		99.6%	^{1}H NMR (400 MHz, CD_3OD) δ 8.52 (s, 1H), 7.32 (dd, J = 1.1, 5.2 Hz, 1H), 7.24 (t, J = 8.2 Hz, 1H), 7.10 (dd, J = 0.7, 3.5 Hz, 1H), 6.95 (dd, J = 3.5, 5.1 Hz, 1H), 6.92-6.88 (m, 2H), 6.83 (ddd, J = 0.7, 1.7, 8.2 Hz, 1H), 5.67 (dd, J = 5.7, 7.5 Hz, 1H), 3.89-3.87 (m, 2H), 3.73-3.71 (m, 2H), 3.45-3.40 (m, 2H), 3.22 (s, 3H), 2.72-2.66 (m, 2H), 2.36 (s, 3H), 2.36-2.25 (m, 1H), 2.14-2.06 (m, 1H), 1.22 (t, J = 7.2 Hz, 3H).	467.2234 $[M+H]^+$
45aS		99.3%	^{1}H NMR (400 MHz, CD_3OD) δ 8.52 (s, 1H), 7.32 (dd, J = 1.1, 5.2 Hz, 1H), 7.24 (t, J = 8.2 Hz, 1H), 7.10 (dd, J = 0.7, 3.5 Hz, 1H), 6.95 (dd, J = 3.5, 5.1 Hz, 1H), 6.92-6.88 (m, 2H), 6.83 (ddd, J = 0.7, 1.7, 8.2 Hz, 1H), 5.67 (dd, J = 5.7, 7.5 Hz, 1H), 3.89-3.87 (m, 2H), 3.73-3.71 (m, 2H), 3.45-3.40 (m, 2H), 3.22 (s, 3H), 2.72-2.66 (m, 2H), 2.36 (s, 3H), 2.36-2.25 (m, 1H), 2.14-2.06 (m, 1H), 1.22 (t, J = 7.2 Hz, 3H).	467.2233 $[M+H]^+$

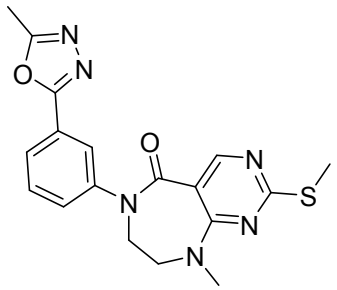
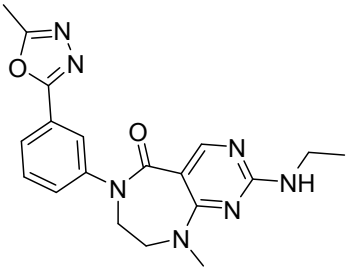
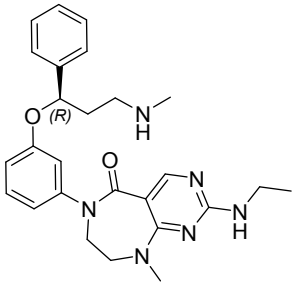
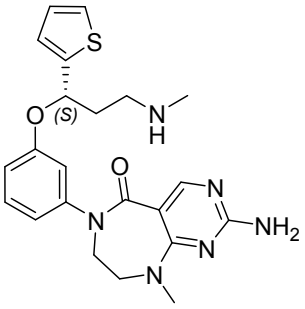
45b		100%	^{1}H NMR (400 MHz, CD_3OD) δ 8.58 (s, 1H), 7.32 (dd, J = 1.2 5.1 Hz, 1H), 7.24 (t, 1H), 7.10 (dd, J = 1.1, 3.3 Hz, 1H), 6.95 (dd, J = 3.6, 5.1 Hz, 1H), 6.92-6.88 (m, 2H), 6.83 (ddd, J = 0.7, 1.9, 8.0 Hz, 1H), 5.68 (dd, J = 5.4, 7.5, 1H), 3.88-3.86 (m, 2H), 3.72-3.70 (m, 2H), 3.21 (s, 3H), 3.18 (s, 6H), 2.85-2.72 (m, 2H), 2.41 (s, 3H), 2.35-2.27 (m, 1H), 2.17-2.10 (m, 1H).	467.2230 $[M+H]^+$
45cS		100%	^{1}H NMR (400 MHz, CD_3OD) δ 8.52 (s, 1H), 7.30 (d, J = 4.9 Hz, 1H), 7.23 (t, 1H), 7.09 (d, J = 3.6 Hz, 1H), 6.94-6.87 (m, 3H), 6.81 (d, J = 7.9 Hz, 1H), 5.66 (dd, J = 5.8, 7.7, 1H), 3.85-3.83 (m, 2H), 3.68-3.66 (m, 2H), 3.17 (s, 3H), 2.75-2.62 (m, 2H), 2.35 (s, 3H), 2.33-2.24 (m, 1H), 2.14-2.06 (m, 1H).	439.1902 $[M+H]^+$
46S		99.2%	^{1}H NMR (400 MHz, CD_3OD) δ 8.72 (s, 1H), 8.56 (s, 1H), 7.32 (dd, J = 0.9, 4.9 Hz, 1H), 7.27 (t, 1H), 7.10 (d, J = 3.3 Hz, 1H), 6.96-6.91 (m, 3H), 6.87 (d, J = 8.0 Hz, 1H), 5.68 (dd, J = 5.7, 7.7 Hz, 1H), 3.95-3.93 (m, 2H), 3.84-3.82 (m, 2H), 3.28 (s, 3H), 2.76-2.63 (m, 2H), 2.36 (s, 3H), 2.34-2.24 (m, 1H), 2.15-2.06 (m, 1H).	424.1808 $[M+H]^+$
47S		96.1%	^{1}H NMR (400 MHz, CD_3OD) δ 8.74 (s, 1H), 7.40 (dd, J = 1.1, 5.0 Hz, 1H), 7.34 (t, 1H), 7.18 (dd, J = 1.1, 3.5 Hz, 1H), 7.04-6.98 (m, 3H), 6.94 (ddd, J = 0.8, 1.9, 7.9 Hz, 1H), 5.76 (dd, J = 5.7, 7.5, 1H), 4.01-3.99 (m, 2H), 3.90-3.88 (m, 2H), 3.36 (s, 3H), 2.84-2.71 (m, 2H), 2.58 (s, 3H), 2.44 (s, 3H), 2.42-2.31 (m, 1H), 2.21-2.14 (m, 1H).	438.1959 $[M+H]^+$

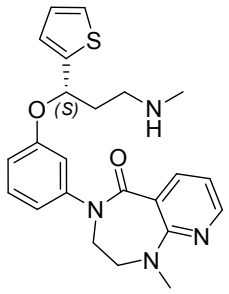
48		97.7%	^{1}H NMR (400 MHz, $CDCl_3$) δ 9.01 (s, 1H), 7.28 (d, J = 8.1 Hz, 1H), 7.24 (dd, J = 1.2, 5.1 Hz, 1H), 7.04 (d, J = 3.4 Hz, 1H), 6.95 (dd, J = 3.6 Hz, 5.2 Hz, 1H), 6.90-6.85 (m, 3H), 5.60 (dd, J = 5.6, 7.7 Hz, 1H), 3.97-3.95 (m, 2H), 3.82-3.80 (m, 2H), 3.33 (s, 3H), 2.80-2.71 (m, 2H), 2.44 (s, 3H), 2.34-2.27 (m, 1H), 2.14-2.08 (m, 1H), 1.89 (br, 1H).	492.1665 $[M+H]^+$
56S		100%	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 7.27-7.20 (m, 3H), 7.03-7.01 (m, 1H), 6.95-6.91 (m, 3H), 6.83-6.80 (m, 1H), 5.57-5.54 (m, 2H), 4.76 (br, 1H), 3.88-3.84 (m, 2H), 3.50-3.46 (m, 2H), 3.31-3.26 (m, 2H), 2.91 (s, 3H), 2.76-2.71 (m, 2H), 2.42 (s, 3H), 2.31-2.25 (m, 1H), 2.12-2.05 (m, 1H), 1.30-1.25 (m, 3H).	466.2274 $[M+H]^+$
57S		96.0%	^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 8.5 Hz, 1H), 7.22-7.18 (m, 2H), 7.01 (d, J = 3.4 Hz, 1H), 6.94-6.87 (m, 3H), 6.79 (dd, J = 2.3, 8.4 Hz, 1H), 5.86 (d, J = 8.5 Hz, 1H), 5.55 (dd, J = 5.6, 7.6 Hz, 1H), 4.59 (br, 1H), 3.89-3.87 (m, 2H), 3.58-3.56 (m, 2H), 3.39-3.32 (m, 2H), 3.07 (s, 3H), 2.77-2.67 (m, 2H), 2.41 (s, 3H), 2.32-2.21 (m, 1H), 2.12-2.04 (m, 1H), 1.24 (t, 3H).	466.2276 $[M+H]^+$
59S		97.6%	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (dd, J = 2.1, 4.8Hz, 1H), 8.04 (dd, J = 2.1, 7.6 Hz, 1H), 7.27-7.22 (m, 2H), 7.02 (d, J = 3.1 Hz, 1 H), 6.96-6.91 (m, 3H), 6.85 (dd, J = 2.3, 8.2 Hz, 1H), 6.80 (dd, J = 4.8, 7.8 Hz, 1H), 5.57 (dd, J = 5.4, 7.7 Hz, 1H), 3.90-3.87 (m, 2H), 3.61-3.58 (m, 2H), 3.08 (s, 3H), 2.77-2.67 (m, 2H), 2.42 (s, 3H), 2.35-2.20 (m, 1H), 2.14-2.03 (m, 1H).	423.1849 $[M+H]^+$

61S		95.0%	^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 7.6 Hz, 1H), 7.26-7.21 (m, 2H), 7.02 (d, J = 3.4 Hz, 1 H), 6.95-6.89 (m, 3H), 6.85 (ddd, J = 0.9, 2.4 Hz, 8.4 Hz, 1H), 6.64 (d, J = 7.7 Hz, 1H), 5.57 (dd, J = 5.3, 7.5 Hz, 1H), 3.89-3.86 (m, 2H), 3.60-3.57 (m, 2H), 3.09 (s, 3H), 2.77-2.69 (m, 2H), 2.44 (s, 3H), 2.42 (s, 3H), 2.34-2.21 (m, 1H), 2.14-2.03 (m, 1H).	437.2010 $[M+H]^+$
63S		99.5%	^{1}H NMR (400 MHz, $CDCl_3$) δ 7.95 (d, J = 8.5 Hz, 1H), 7.33 (dd, J = 1.0, 5.0 Hz, 1H), 7.26 (t, J = 7.9 Hz, 1 H), 7.12 (d, J = 3.4 Hz, 1H), 6.96-6.94 (m, H), 6.91 (dd, J = 2.8 Hz, J = 8.2 Hz, 1H), 6.86 (dd, J = 1.0 Hz, J = 7.9 Hz, 1H), 6.13 (d, J = 8.4 Hz, 1H), 5.71 (dd, J = 5.3, 7.6 Hz, 1H), 3.92 (s, 3H), 3.89-3.87 (m, 2H), 3.68-3.66 (m, 2H), 3.16 (s, 3H), 2.94-2.79 (m, 2H), 2.47 (s, 3H), 2.42 (s, 3H), 2.39-2.30 (m, 1H), 2.21-2.13 (m, 1H).	453.1948 $[M+H]^+$
65		96.6%	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, J = 3.9 Hz, 1H), 7.33-7.20 (m, 4H), 7.05-6.98 (m, 3H), 6.93 (dd, J = 3.5, 5.1 Hz, 1H), 6.85 (dd, J = 1.9, 8.2 Hz, 1H), 5.57 (dd, J = 5.6, 7.6 Hz, 1H), 3.78-3.74 (m, 2H), 3.33-3.29 (m, 2H), 2.86 (s, 3H), 2.75-2.70 (m, 2H), 2.41 (s, 3H), 2.35-2.20 (m, 1H), 2.14-2.03 (m, 1H).	423.1863 $[M+H]^+$
67		99.1%	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.31 (s, 1H), 8.29 (d, J = 4.8 Hz, 1H), 7.55 (d, J = 4.9 Hz, 1H), 7.29-7.25 (m, 2H), 7.05 (d, J = 3.2 Hz, 1 H), 7.00 (t, J = 2.0 Hz, 1H), 6.98-6.95 (m, 2H), 6.89 (dd, J = 2.1, 8.4 Hz, 1H), 5.60 (dd, J = 5.4, 7.6 Hz, 1H), 3.81-3.79 (m, 2H), 3.45-3.40 (m, 2H), 3.00 (s, 3H), 2.81-2.72 (m, 2H), 2.45 (s, 3H), 2.35-2.28 (m, 1H), 2.15-2.09 (m, 1H).	423.1856 $[M+H]^+$

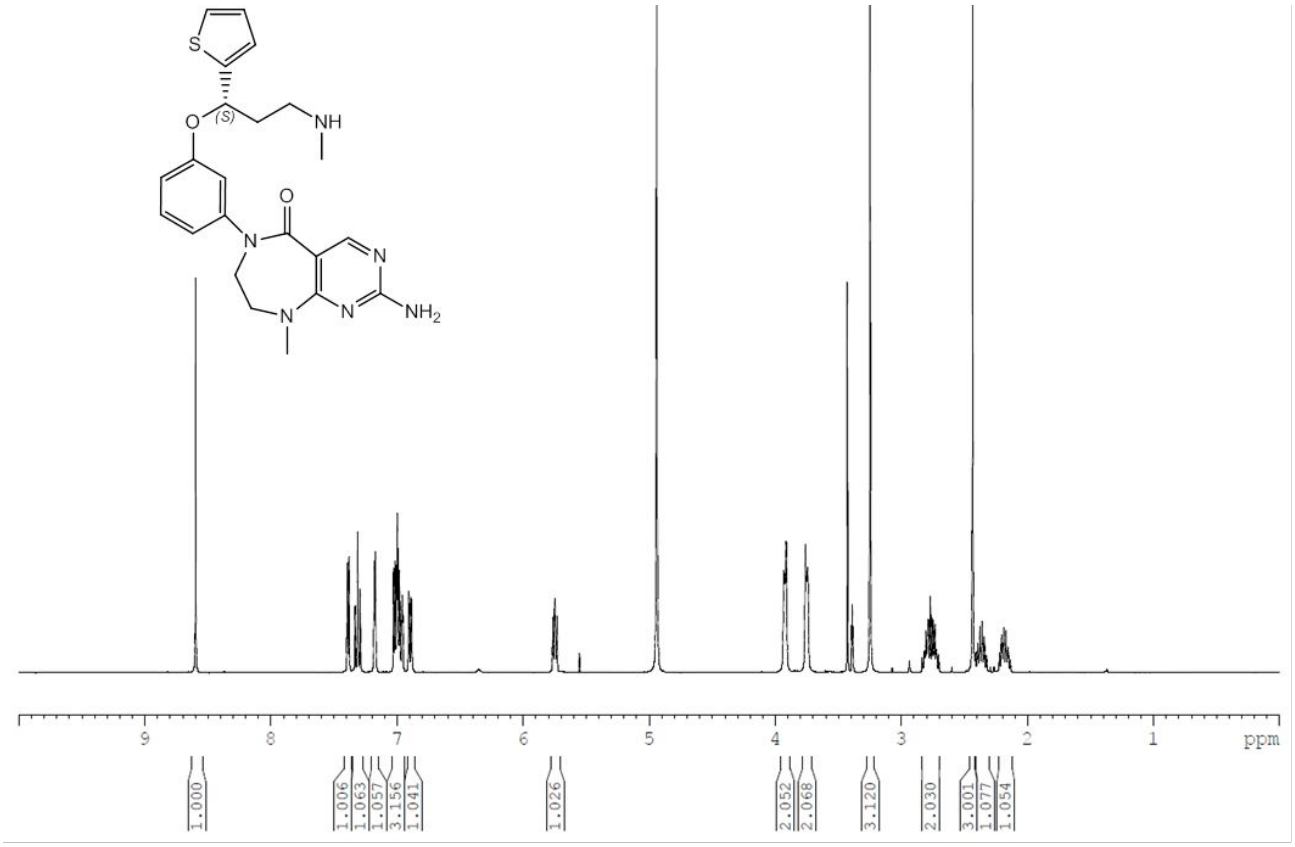
69		97.0%	^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (dd, J = 1.6, 7.6 Hz, 1H), 7.41 (td, J = 1.8, 7.7 Hz, 1H), 7.23-7.19 (m, 2H), 7.10 (d, J = 3.4 Hz, 1H), 7.03-6.90 (m, 5H), 6.83 (dd, J = 2.0, 8.2 Hz, 1H), 5.75 (dd, J = 5.1, 8.4 Hz, 1H), 3.76-3.73 (m, 2H), 3.31-3.29 (m, 2H), 3.13-3.03 (m, 2H), 2.87 (s, 3H), 2.57 (s, 3H), 2.54-2.45 (m, 1H), 2.38-2.27 (m, 1H).	422.1909 $[M+H]^+$
71R		96.6%	^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21-7.14 (m, 2H), 7.99 (dd, J = 3.2, 5.1 Hz, 1H), 6.78-6.74 (m, 3H), 5.52 (dd, J = 5.4, 7.8 Hz, 1H), 3.75 (d, J = 6.2 Hz, 2H), 3.31-3.29 (m, 2H), 2.82-2.79 (m, 2H), 2.75-2.62 (m, 6H), 2.39 (s, 3H), 2.39 (s,3H), 2.30-2.21 (m, 1H), 2.10-2.01 (m, 1H).	374.1908 $[M+H]^+$
71S		98.7%	^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21-7.14 (m, 2H), 7.99 (dd, J = 3.2 Hz, J = 5.1 Hz, 1H), 6.78-6.74 (m, 3H), 5.52 (dd, J = 5.4, 7.8 Hz, 1H), 3.75 (d, J = 6.2 Hz, 2H), 3.31-3.29 (m, 2H), 2.82-2.79 (m, 2H), 2.75-2.62 (m, 6H), 2.39 (s, 3H), 2.39 (s,3H), 2.30-2.21 (m, 1H), 2.10-2.01 (m, 1H).	374.1895 $[M+H]^+$

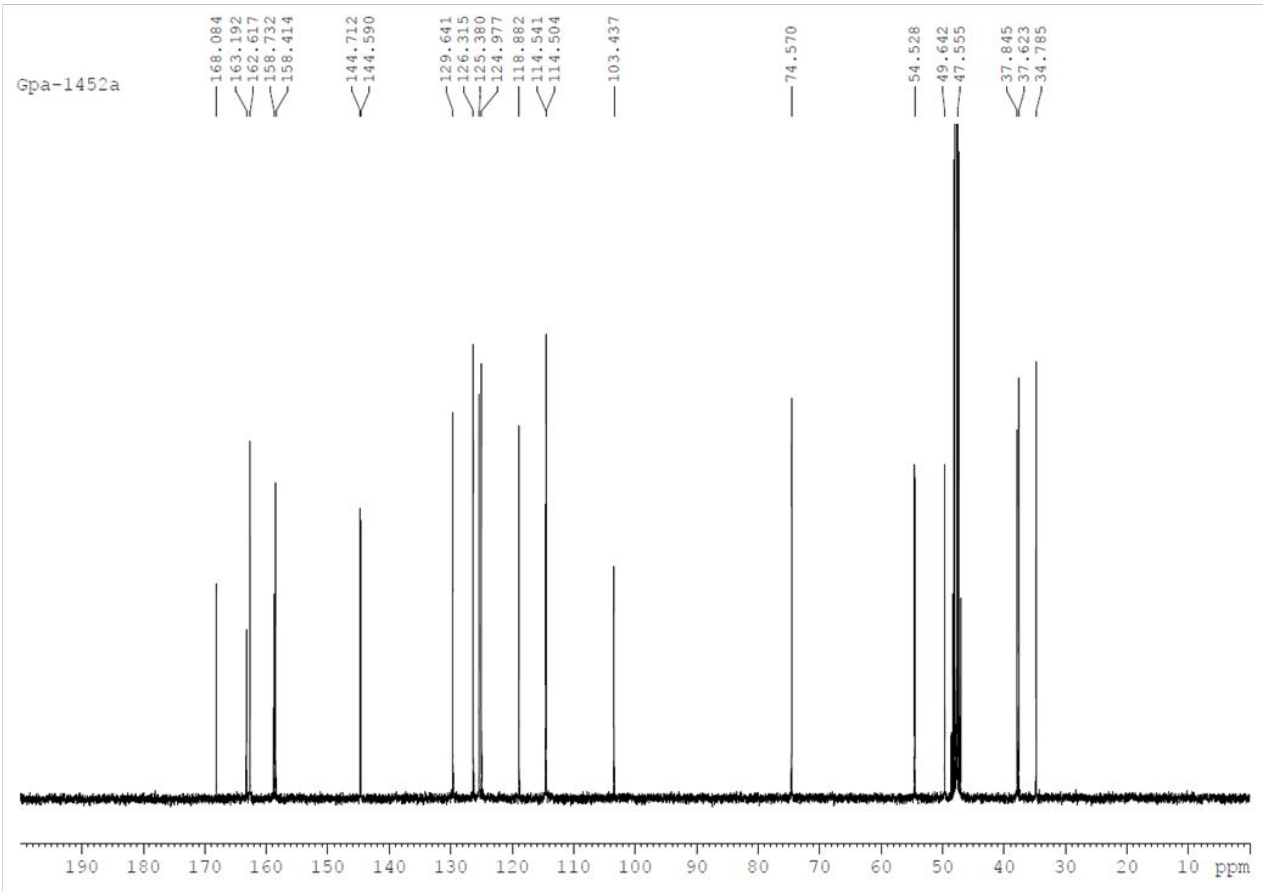
^{13}C NMR data for selected final compounds.

Comp.	Structure	^{13}C NMR
15-1		^{13}C NMR (100 MHz, $CDCl_3$) δ 174.39, 166.99, 164.18, 161.72, 156.81, 143.90, 130.04, 129.26, 125.16, 125.00, 123.94, 108.18, 55.23, 48.99, 38.69, 14.14, 11.11.
16a		^{13}C NMR (100 MHz, $CDCl_3$) δ 167.62, 164.25, 163.74, 163.67, 162.07, 158.50, 144.34, 129.81, 129.33, 124.86, 124.49, 124.05, 54.92, 49.17, 38.41, 36.19, 14.81, 11.02.
31aR		^{13}C NMR (100 MHz, CD_3OD) δ 168.37, 162.44, 158.68, 158.49, 144.73, 141.47, 129.56, 128.37, 127.49, 125.89, 118.42, 114.28, 114.23, 78.27, 54.43, 49.71, 47.50, 37.64, 37.48, 35.72, 34.70, 13.74.
45cS		^{13}C NMR (100 MHz, CD_3OD) δ 168.08, 163.19, 162.62, 158.73, 158.41, 144.71, 144.59, 129.64, 126.31, 125.38, 124.98, 118.88, 114.54, 114.50, 103.44, 74.57, 54.53, 49.64, 47.55, 37.84, 37.62, 34.78.

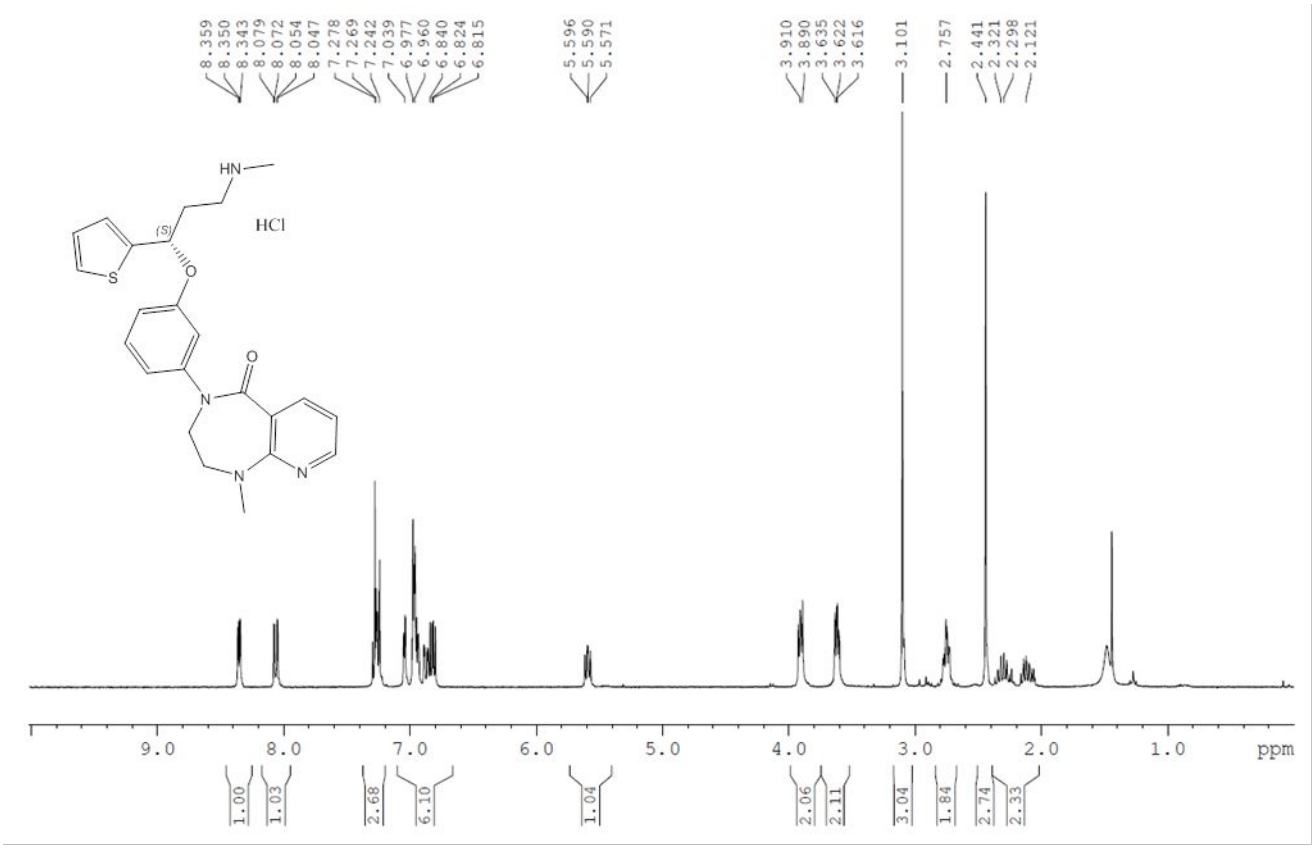
59S		^{13}C NMR (100 MHz, $CDCl_3$) δ 168.78, 158.63, 155.56, 151.22, 144.97, 143.72, 140.87, 129.85, 126.59, 124.89, 124.83, 119.64, 118.90, 114.68, 114.51, 114.34, 74.99, 56.81, 49.17, 4817, 38.76, 36.53.

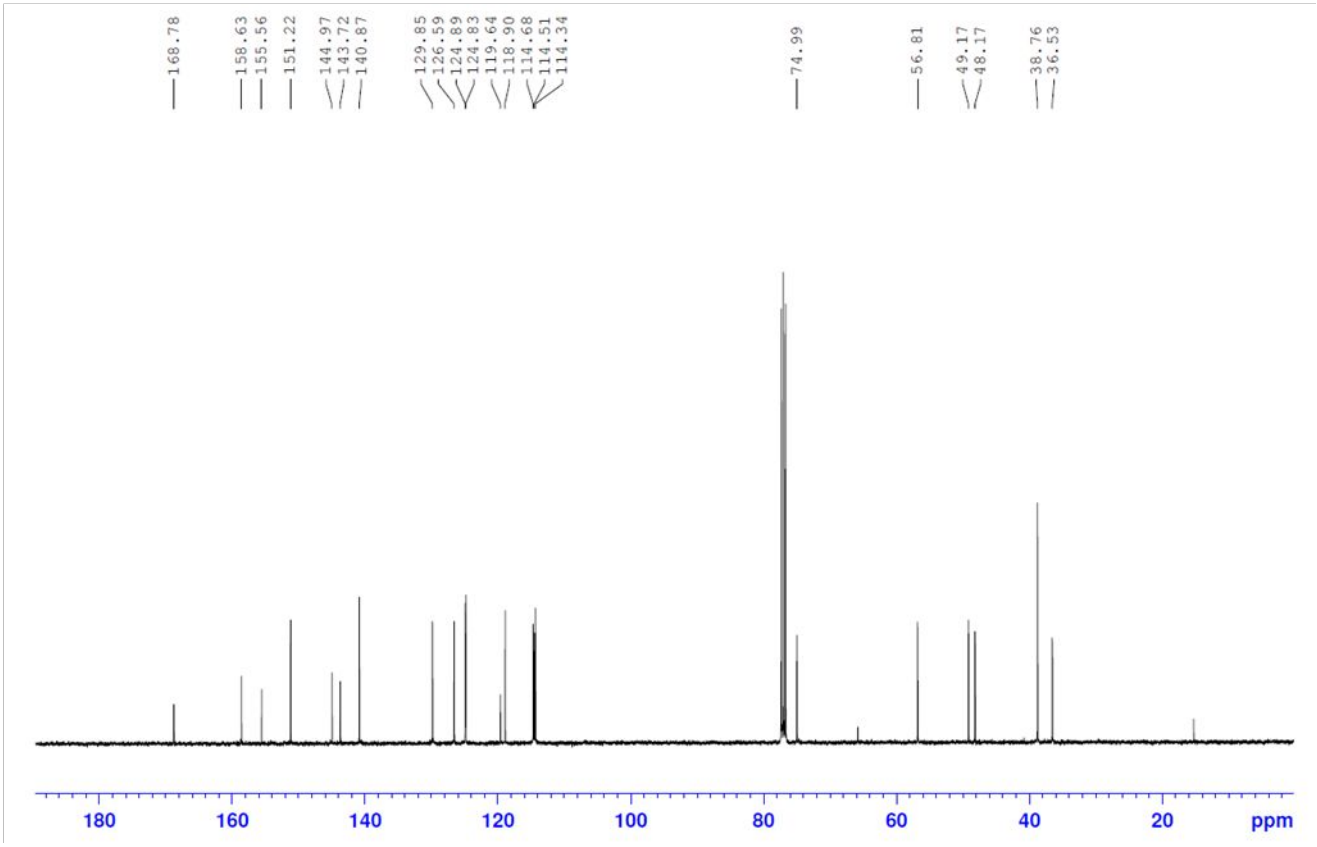
^{1}H NMR and ^{13}C NMR spectra figures of compounds 45cS and 59S.





^{1}H-NMR and ^{13}C-NMR of the free base of compound **45cS**





^{1}H-NMR and ^{13}C-NMR of compound **59S**.

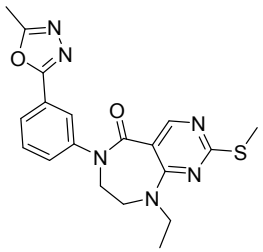
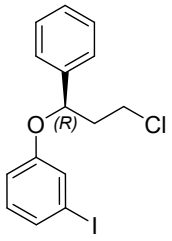
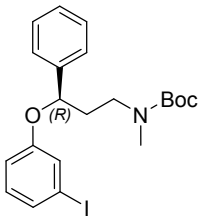
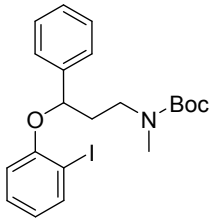
Enantiomeric excess by chiral HPLC and optical rotation of enantiopure compounds.

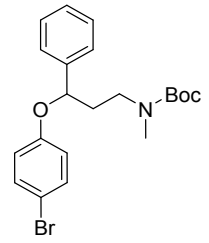
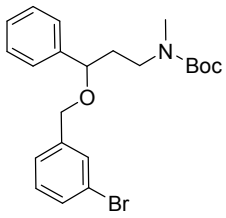
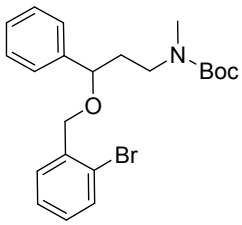
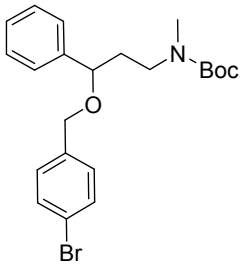
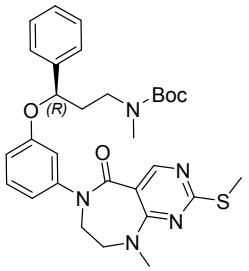
Comp.	ee (%)	Chiral Chromatographic conditions	Optical rotation [α]20D
31aR	100	Method 3	+8.3 (c, 0.18, MeOH)
31aS	100	Method 3	-3.9 (c, 0.07, MeOH)
33R	(ed) 100	Method 5	+41.8 (c, 0.17, MeOH)
33S	(ed) 100	Method 5	+66.3 (c, 0.12, MeOH)
43S	99.4	Method 4	-43.8 (c, 0.19, MeOH)
45aR	100	Method 4	+42.29 (c, 0.17, MeOH)
45aS	98.0	Method 4	-41.9 (c, 0.20, MeOH)
45cS	99.1	Method 3	-44.4 (c, 0.17, MeOH)
46S	99.5	Method 5	-38.8 (c, 0.18, MeOH)
47S	100	Method 5	-30.5 (c, 0.19, MeOH)
56S	98.9	Method 3	-46.9 (c, 0.17, MeOH)
57S	100	Method 5	-35.1 (c, 0.17, MeOH)

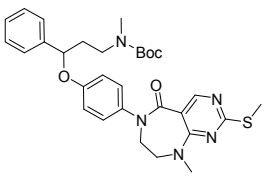
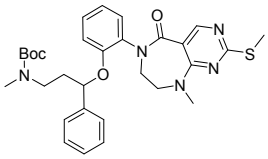
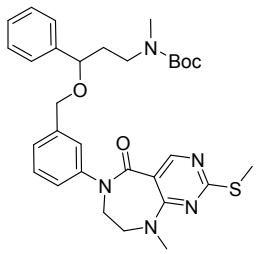
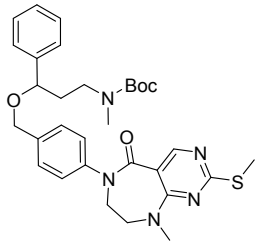
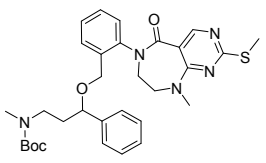
59S	100	Method 5	-32.1 (c, 0.17, MeOH)
61S	100	Method 5	-36.3 (c, 0.04, MeOH)
63S	99.2	Method 4	-35.1 (c, 0.17, MeOH)
71R	95.8	Method 4	+48.2 (c, 0.21, MeOH)
71S	96.3	Method 4	-47.1 (c, 0.48, MeOH)

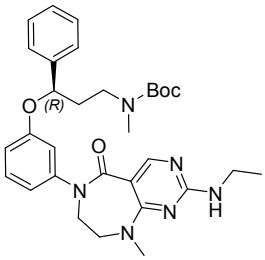
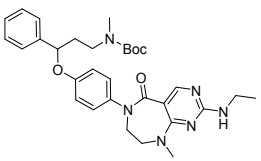
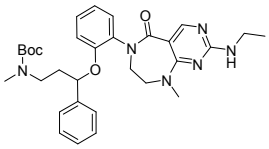
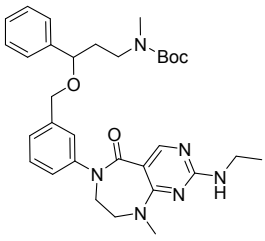
Methods described in the experimental part

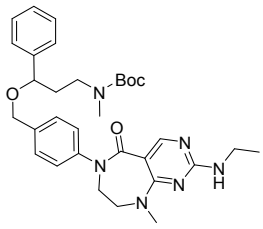
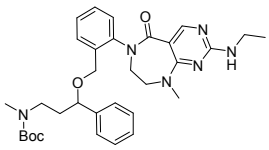
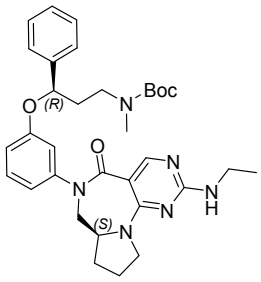
Chemical characterization of intermediates.

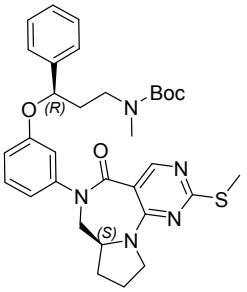
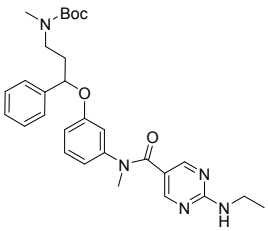
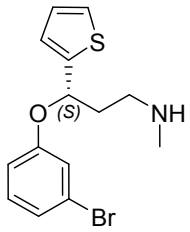
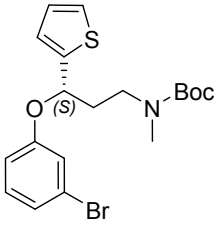
Intermediate	Structure	Chemical Name	NMR
15-2		9-Ethyl-6-(3-(5-methyl-1,3,4-oxadiazol-2-yl)phenyl)-2-(methylthio)-6,7,8,9-tetrahydro-5H-pyrimido[4,5-e][1,4]diazepin-5-one	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 7.94 (t, J= 1.5 Hz, 1H), 7.91 (dt, J= 1.5, 7.7 Hz, 1H), 7.53 (t, J = 8 Hz, 1H), 7.47 (m, 1H), 4.03 (m, 2H), 3.83 (m, 4H), 3.81 (q, J = 7.1 Hz, 2H), 2.60 (s, 3H), 2.53 (s, 3H), 1.25 (t, J = 7.1 Hz, 3H).
26R-meta		(*R*)-1-(3-Chloro-1-phenylpropoxy)-3-iodobenzene	^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41-7.36 (m, 4H), 7.32 (m, 1H), 7.29 (m, 1H), 7.25 (m, 1H), 6.91 (t, J = 8.5 Hz, 1H), 6.82 (m, 1H), 5.37 (m, 1H), 3.84-3.77 (m, 1H), 3.65-3.58 (m, 1H), 2.53-2.43 (m, 1H), 2.28-2.18 (m, 1H).
27-1R-meta		*tert*-Butyl (*R*)-(3-(3-iodophenoxy)-3-phenylpropyl)(methyl)carbamate	^{1}H NMR (300 MHz, $CDCl_3$) δ 7.41-7.26 (m, 5H), 7.25 (m, 1H), 7.21 (m, 1H), 6.88 (t, J = 8.5 Hz, 1H), 6.77 (m, 1H), 5.10 (m, 1H), 3.56-3.26 (m, 2H), 2.87 (s, 3H), 2.28-2.01 (m, 2H), 1.52-1.33 (bs, 9H).
27-1-ortho		*tert*-Butyl (3-(2-iodophenoxy)-3-phenylpropyl)(methyl)carbamate	^{1}H NMR (300 MHz, $CDCl_3$) δ 7.74 (dd, J = 1.6, 7.8 Hz, 1H), 7.34-7.22 (m, 5H), 7.07 (td, J = 1.6, 7.8 Hz, 1H), 6.61 (td, J = 1.2, 7.6 Hz, 1H), 6.55 (d, J = 8.2 Hz, 1H), 5.21-5.17 (m, 1H), 3.63-3.28 (m, 2H), 2.86 (s, 3H), 2.27-2.01 (m, 2H), 1.38 (s, 9H).

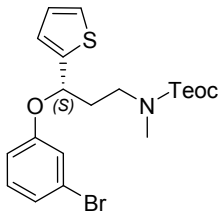
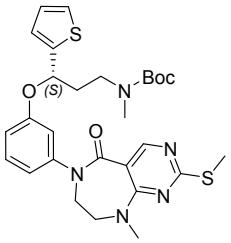
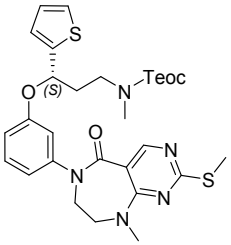
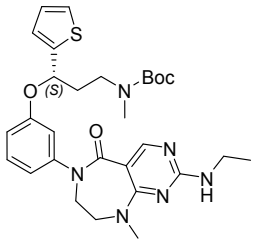
27-1-para		*tert*-Butyl (3-(4-bromophenoxy)-3-phenylpropyl)(methyl)carbamate	^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.24 (m, 5H), 6.69 (d, J = 8.9 Hz, 2H), 5.07-5.04 (m, 1H), 3.49-3.27 (m, 2H), 2.84 (s, 3H), 2.20-2.01 (m, 2H), 1.39 (bs, 9H).
27-2-meta		*tert*-Butyl (3-((3-bromobenzyl)oxy)-3-phenylpropyl)(methyl)carbamate	^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (s, 1H), 7.44-7.37 (m, 3H), 7.37-7.30 (m, 3H), 7.26-7.19 (m, 2H), 4.40 (d, J = 12.1 Hz, 1H), 4.34 (m, 1H), 4.25 (d, J = 12.1 Hz, 1H), 3.41-3.22 (m, 2H), 2.85 (s, 3H), 2.07 (m, 1H), 1.94 (m, 1H), 1.45 (s, 9H).
27-2-ortho		*tert*-Butyl (3-((2-bromobenzyl)oxy)-3-phenylpropyl)(methyl)carbamate	^{1}H NMR (500 MHz, $CDCl_3$) δ 7.51 (d, J = 7.9 Hz, 2H), 7.38-7.29 (m, 5H), 7.14 (td, , J = 1.4, 7.6 Hz, 1H), 4.46-4.33 (m, 3H), 3.40-3.20 (m, 2H), 2.82 (s, 3H), 2.17-1.91 (m, 2H), 1.41 (s, 9H).
27-2-para		*tert*-Butyl (3-((4-bromobenzyl)oxy)-3-phenylpropyl)(methyl)carbamate	^{1}H NMR (500 MHz, $CDCl_3$) δ 7.45 (d, J = 8.3 Hz, 2H), 7.37-7.28 (m, 5H), 7.17 (d, , J = 8.3 Hz, 2H), 4.36 (d, J = 11.9 Hz, 1H), 4.32 (dd, J = 4.8, 8.3 Hz, 1H), 4.21 (d, J = 12.1 Hz, 1H), 3.39-3.21 (m, 2H), 2.82 (s, 3H), 2.08-2.01 (m, 1H), 1.94-1.87 (m, 1H), 1.43 (s, 9H).
30-1a		*tert*-Butyl (*R*)-methyl(3-(3-(9-methyl-2-(methylthio)-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)phenoxy)-3-phenylpropyl)carbamate	^{1}H NMR (500 MHz, $CDCl_3$) δ 8.78 (s, 1H), 7.35 (m, 4H), 7.28 (m, 1H), 7.20 (m, 1H), 6.82 (m, 2H), 6.72 (m, 1H), 5.13 (m, 1H), 3.90 (m, 2H), 3.71 (m, 2H), 3.41 (m, 2H), 3.28 (s, 3H), 2.86 (s, 3H), 2.57 (s, 3H), 2.14 (m,2 H), 1.42 (s, 9H).

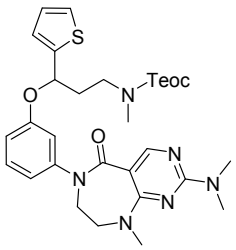
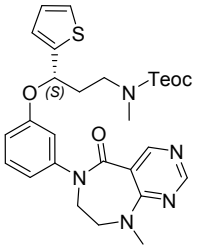
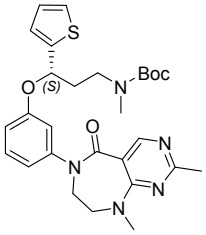
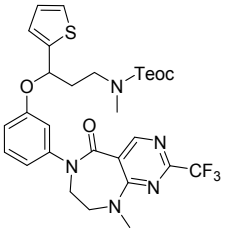
30-1b		*tert*-Butyl methyl(3-(4-(9-methyl-2-(methylthio)-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)phenoxy)-3-phenylpropyl)carbamate	^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.32 (m, 4H), 7.26 (m, 1H), 7.06 (d, J = 9 Hz, 2H), 6.84 (d, J = 9 Hz, 2H), 5.10 (m, 1H), 3.87 (m, 2H), 3.71 (m, 2H), 3.40 (m, 2H), 3.24 (s, 3H), 2.85 (s, 3H), 2.52 (s, 3H), 2.21-2-02 (m, 2H), 1.41 (s, 9H).
30-1c		*tert*-Butyl methyl(3-(2-(9-methyl-2-(methylthio)-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)phenoxy)-3-phenylpropyl)carbamate	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.88 (s, 1H), 7.38-7.25 (m, 5H), 7.21 (dd, J = 1.4, 7.7 Hz, 1H), 7.11 (t, J = 7.8 Hz, 1H), 6.94 (t, J = 7.8 Hz, 2H), 6.76 (d, J = 8.5 Hz, 1H), 5.19 (m, 1H), 3.95 (m, 2H), 3.87 (m, 2H), 3.32 (s, 3H), 3.28 (m, 2H), 2.74 (s, 3H), 2.58 (s, 3H), 2.10 (m, 2H), 1.39 (bs, 9H).
30-2d		*tert*-Butyl methyl(3-((3-(9-methyl-2-(methylthio)-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)benzyl)oxy)-3-phenylpropyl)carbamate	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 7.36 (m, 6H), 7.22 (m, 3H), 4.42 (m, 1H), 4.35 (m, 1H), 4.29 (m, 1H), 4.00 (m, 2H), 3.80 (m, 2H), 3.35 (m, 2H), 3.29 (s, 3H), 2.82 (s, 3H), 2.56 (s, 3H), 2.06 (m, 1H), 1.92 (m, 1H), 1.43 (s, 9H).
30-2e		*tert*-Butyl methyl(3-((4-(9-methyl-2-(methylthio)-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)benzyl)oxy)-3-phenylpropyl)carbamate	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 7.39-7.23 (m, 9H), 4.41 (d, J= 11.8 Hz, 1H), 4.35 (dd, J= 4.8, 8.4 Hz, 1 H), 4.26 (d, J = 11.8 Hz, 1 H), 3.99-3.97 (m, 2H), 3.80-3.78 (m, 2H), 3.34 (bs, 2H), 3.28 (s, 3H), 2.82 (s, 3H), 2.54 (s, 3H), 2.09-2.00 (m, 1H), 1.92-1.87 (bs, 1H), 1.42 (s, 9H).
30-2f		*tert*-Butyl methyl(3-((2-(9-methyl-2-(methylthio)-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72-8.66 (m, 1H), 7.57-7.43 (m, 1H), 7.32-7.25 (m, 7H), 7.10-7.09 (m, 1H), 4.31-4.27 (m,

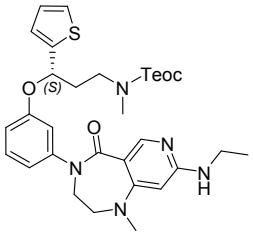
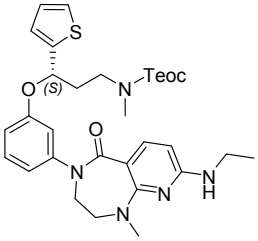
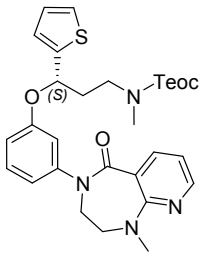
		yl)benzyl)oxy)-3-phenylpropyl)carbamate	3H), 3.84-3.51 (m, 4H), 3.23-3.17 (m, 5H), 2.77 (bs, 3H), 2.53 (s, 3H), 2.14-1.89 (m, 2H), 1.40 (s, 9H).
BOC intermediate for 31aR		*tert*-Butyl (*R*)-(3-(3-(2-(ethylamino)-9-methyl-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)phenoxy)-3-phenylpropyl)(methyl)carbamate	^{1}H NMR (500 MHz, $CDCl_3$) δ 8.71 (s, 1H), 7.35 (m, 4H), 7.26 (m, 1H), 7.17 (m, 1H), 6.83 (m, 2H), 6.68 (m, 1H), 5.11 (m, 1H), 3.87 (m, 2H), 3.63 (m, 2H), 3.48 (m, 2H), 3.40 (m, 2H), 3.20 (s, 3H), 2.85 (s, 3H), 2.16 (m, 1H), 2.09 (m, 1H), 1.42 (s, 9H), 1.25 (t, J = 7 Hz, 3H).
BOC intermediate for 31b		*tert*-Butyl (3-(4-(2-(ethylamino)-9-methyl-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)phenoxy)-3-phenylpropyl)(methyl)carbamate	^{1}H NMR (500 MHz, $CDCl_3$) δ 8.70 (s, 1H), 7.35 (m, 4H), 7.26 (m, 1H), 7.07 (d, J = 9 Hz, 2H), 6.84 (d, J = 9 Hz, 2H), 5.10 (m, 1H), 3.87 (m, 2H), 3.67 (m, 2H), 3.46 (m, 2H), 3.41 (m, 2H), 3.20 (s, 3H), 2.86 (s, 3H), 2.16 (m, 1H), 2.08 (m, 1H), 1.44 (s, 9H), 1.24 (t, J = 7.1 Hz, 3H).
BOC intermediate for 31c		*tert*-Butyl (3-(2-(2-(ethylamino)-9-methyl-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)phenoxy)-3-phenylpropyl)(methyl)carbamate	^{1}H NMR (300 MHz, $CDCl_3$) δ 8.80 (s, 1H), 7.37-7.22 (m, 5H), 7.20 (dd, J = 1.4, 7.7 Hz, 1H), 7.07 (m, 1H), 6.91 (t, J = 7.7 Hz, 2H), 6.72 (d, J = 8 Hz, 1H), 5.17 (m, 1H), 3.91 (m, 2H), 3.81 (m, 2H), 3.48 (m, 2H), 3.29 (m, 2H), 3.24 (s, 3H), 2.72 (s, 3H), 2.09 (m, 2H), 1.37 (bs, 9H), 1.25 (t, J = 7.4 Hz, 3H).
BOC intermediate for 31d		*tert*-Butyl (3-((3-(2-(ethylamino)-9-methyl-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)benzyl)oxy)-3-phenylpropyl)(methyl)carbamate	^{1}H NMR (300 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.35 (m, 6H), 7.21 (m, 3H), 5.26 (bs, 1H), 4.35 (m, 3H), 3.98 (m, 2H), 3.73 (m, 2H), 3.48 (m, 2H), 3.33 (m, 2H), 3.23 (s, 3H), 2.82 (s, 3H), 2.05 (m, 1H), 1.92 (m, 1H), 1.43 (s, 9H), 1.25 (t, J = 7 Hz,

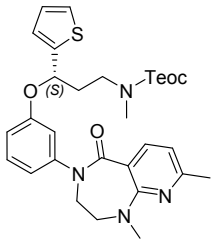
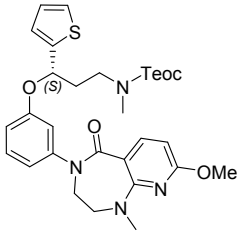
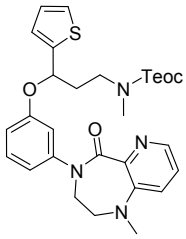
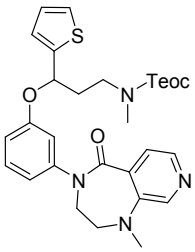
			3H).
BOC intermediate for 31e		*tert*-Butyl (3-((4-(2-(ethylamino)-9-methyl-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)benzyl)oxy)-3-phenylpropyl)(methyl)carbamate	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.73 (s, 1H), 7.40-7.30 (m, 7H), 7.27-7.23 (m, 2H), 4.41 (d, J= 11.7 Hz, 1H), 4.34 (dd, J= 4.8, 8.3 Hz, 1 H), 4.25 (d, J= 11.7 Hz, 1 H), 3.98-3.95 (m, 2H), 3.73-3.70 (m, 2H), 3.51-3.42 (m, 2H), 3.31 (bs, 2H), 3.22 (s, 3H), 2.82 (s, 3H), 2.07-1.98 (m, 1H), 1.93-1.87 (m, 1H), 1.42 (s, 9H), 1.24 (t, J = 7.2 Hz, 3H).
BOC intermediate for 31f		*tert*-Butyl (3-((2-(2-(ethylamino)-9-methyl-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)benzyl)oxy)-3-phenylpropyl)(methyl)carbamate	^{1}H NMR (300 MHz, $CDCl_3$) δ 8.65 (s, 1H), 7.59-7.10 (m, 9H), 5.80 (bs, 1H), 4.34-4.18 (m, 3H), 3.82-3.50 (m, 4H), 3.48-3.14 (m, 2H), 3.28 (m, 2H), 3.14 (s, 3H), 2.78 (s, 3H), 2.04-2.00 (m, 1H), 1.89 (m, 1H), 1.41 (s, 9H), 1.24 (t, J = 7.2 Hz, 3H).
BOC intermediate for 33		*tert*-Butyl ((*R*)-3-(3-((S)-2-(ethylamino)-5-oxo-7a,8,9,10-tetrahydro-5H-pyrimido[5,4-f]pyrrolo[1,2-a][1,4]diazepin-6(7H)-yl)phenoxy)-3-phenylpropyl)(methyl)carbamate	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.78 (s, 1H), 7.35-7.32 (m, 4H), 7.29-7.24 (m, 1H), 7.18 (t, J = 8.0 Hz, 1H), 6.79 (m, 1H), 6.74 (m, 1H), 6.70 (m, 1H), 5.32 (bs, 1H), 5.12 (dd, J = 4.1, 8.4 Hz, 1H), 3.80 (m, 3 H), 3.70-3.65 (m, 2H), 3.50-3.39 (m, 4H), 2.86 (s, 3H), 2.18-2.00 (m, 4H), 1.91-1.78 (m, 1H), 1.61-.1.50 (m, 1H), 1.42 (s, 9H), 1.24 (t, J = 7.2 Hz, 3H).

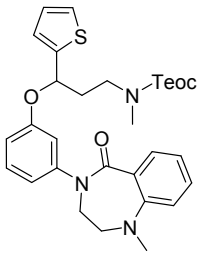
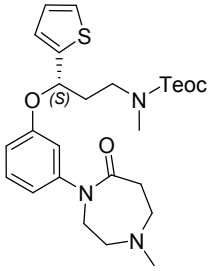
BOC and SMe intermediate for 33		*tert*-Butyl methyl((*R*)-3-(3-((*S*)-2-(methylthio)-5-oxo-7a,8,9,10-tetrahydro-5H-pyrimido[5,4-f]pyrrolo[1,2-a][1,4]diazepin-6(7H)-yl)phenoxy)-3-phenylpropyl)carbamate	^{1}H NMR (500 MHz, $CDCl_3$) δ 8.83 (s, 1H), 7.37-7.34 (m, 4H), 7.29-7.24 (m, 1H), 7.20 (t, J = 8.4 Hz, 1H), 6.80-6.78 (m, 1H), 6.75-6.73 (m, 2H), 5.13 (dd, J = 3.9, 8.3 Hz, 1H), 3.85-3.80 (m, 3H), 3.73-3.70 (m, 2H), 3.41 (m, 2H), 2.86 (s, 3H), 2.56 (s, 3H), 2.19-2.17 (m, 1H), 2.12-2.04 (m, 5H), 1.94-1.84 (m, 1H), 1.63-1.54 (m, 1H), 1.51 (s, 9H).
BOC intermediate for 34		*tert*-Butyl (3-(3-(2-(ethylamino)-N-methylpyrimidine-5-carboxamido)phenoxy)-3-phenylpropyl)(methyl)carbamate	^{1}H NMR (300 MHz, $CDCl_3$) δ 8.65 (s, 2H), 7.34-7.19 (m, 5H), 6.81-6.74 (m, 2 H), 6.72 (m, 1H), 6.13 (m, 1H), 5.10 (dd, J= 4.2, 8.1 Hz, 1H), 3.97-3.83 (m, 2H), 3.47-3.35 (m, 2H), 2.97 (d, J = 4.8 Hz, 3H), 2.84 (s, 3H), 2.23-2.02 (m, 2H), 1.40 (s, 9H), 1.12 (t, J= 7.2 Hz, 3H).
40S		(*S*)-3-(3-Bromophenoxy)-N-methyl-3-(thiophen-2-yl)propan-1-amine	^{1}H (400 MHz, $CDCl_3$) δ 7.25 (dd, J = 1.2, 5.1 Hz, 1H), 7.13 (m, 1H), 7.10-7.06 (m, 2H), 7.03 (m, 1H), 6.96 (dd, J = 3.4, 5.0 Hz, 1H), 6.87 (dt, J = 2.2, 7.2 Hz, 1H), 5.57 (dd, J = 5.2, 7.5 Hz, 1H), 2.78 (m, 2H), 2.47 (s, 3H), 2.32 (m, 1H), 2.24 (bs, 1H), 2.13 (m, 1H).
41-1S		*tert*-Butyl (*S*)-(3-(3-bromophenoxy)-3-(thiophen-2-yl)propyl)(methyl)carbamate	^{1}H NMR (300 MHz, $CDCl_3$) δ 7.25 (d, J = 5 Hz, 1H), 7.10 (m, 1H), 7.06 (m, 2H), 7.02 (m, 1H), 6,96 (m, 1H), 6.85 (td, J = 2.5, 7.0 Hz, 1H), 5.41 (m, 1H), 3.43 (m, 2H), 2.87 (s, 3H), 2.31 (m, 1H), 2.18 (m, 1H), 1.42 (s, 9H).

41-2S		2-(Trimethylsilyl)ethyl (*S*)-(3-(3-bromophenoxy)-3-(thiophen-2-yl)propyl)(methyl)carbamate	^{1}H NMR (400 MHz, $CDCl_3$) δ 7.21 (m, 1H), 7.11-7.05 (m, 3H), 7.03 (m, 1H), 6.92 (m, 1H), 6.83 (m, 1H), 5.42 (m, 1H), 4.19-3.93 (m, 2H), 3.57 (m, 1H), 3.37 (m, 1H), 2.89 (m, 3H), 2.29 (m, 1H), 2.16 (m, 1H), 0.99 (m, 1H), 0.81 (m, 1H), 0.03 s, 9H).
42-1S		*tert*-Butyl (*S*)-methyl(3-(3-(9-methyl-2-(methylthio)-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)phenoxy)-3-(thiophen-2-yl)propyl)carbamate	^{1}H NMR (300 MHz, $CDCl_3$) δ 8.78 (s,1H), 7.25 (m, 2H), 7.03 (m, 1H), 6.95 (m, 1H), 6.87 (m, 2H), 6.82 (m, 1H), 5.43 (m, 1H), 3.93 (m, 2H), 3.75 (m, 2H), 3.39 (m, 2H), 3.29 (s, 3H), 2.86 (s, 3H), 2.56 (s, 3H), 2.25 (m, 2H), 1.42 (s, 9H).
42-2S		2-(Trimethylsilyl)ethyl (*S*)-methyl(3-(3-(9-methyl-2-(methylthio)-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)phenoxy)-3-(thiophen-2-yl)propyl)carbamate	^{1}H NMR (500 MHz, $CDCl_3$) δ 8.78 (s, 1H), 7.26 (m, 2H), 7.04 (m, 1H), 6.96 (m, 1H), 6.88 (m, 2H), 6.84 (m, 1H), 5.45 (m, 1H), 4.15 (m, 2H), 3,95 (m, 2H), 3.76 (m, 2H), 3.45 (m, 2H), 3.30 (s, 3H), 2.91 (s, 3H), 2.57 (s, 3H), 2-33 (m, 1H), 2-19 (m, 1H), 1.00 (m, 1H), 0.93 (m, 1H), 0.05 (s, 9H).
BOC intermediate for 45a		*tert*-Butyl (*S*)-(3-(3-(2-(ethylamino)-9-methyl-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)phenoxy)-3-(thiophen-2-yl)propyl)(methyl)carbamate	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.70 (s, 1H), 7.23-7.19 (m, 2H), 7.01 (d, J = 3.0 Hz, 1H), 6.93 (dd, J = 3.6, 5.0 Hz, 1H), 6.87-6.85 (m, 2H), 6.78 (ddd, J = 0.8, 2.2, 8.2 Hz, 1H), 5.41 (dd, J = 5.2, 7.8, 1H), 5.16 (bs, 1H), 3.90-3.88 (m, 2H), 3.67-3.65 (m, 2H), 3.50-3.43 (m, 2H), 3.41-3.33 (m, 2H), 3.20 (s, 3H), 2.84 (s, 3H), 2.32-2.26 (m, 1H), 2.20-2.11 (m, 1H), 1.41 (s, 9H), 1.23 (t, J = 7.3 Hz, 3H).

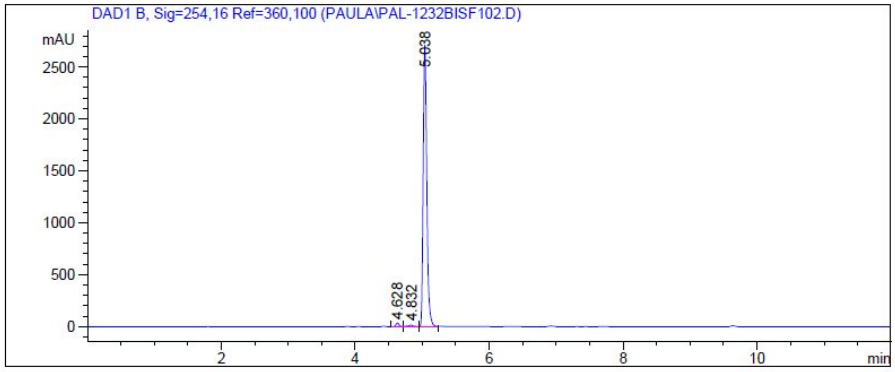
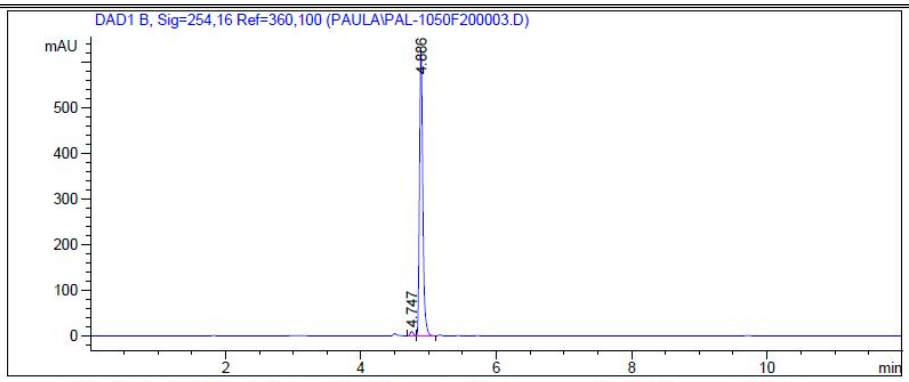
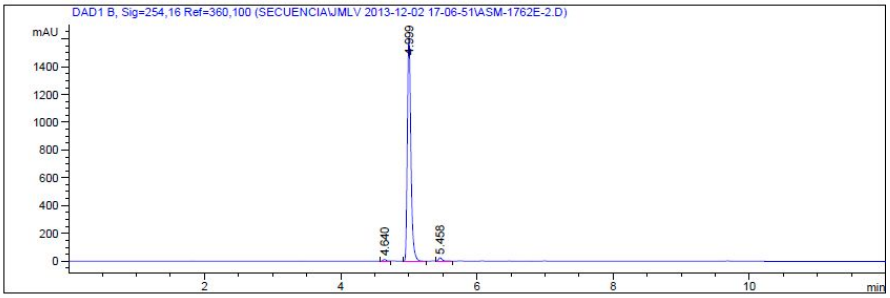
Teoc intermediate for 45b		2-(Trimethylsilyl)ethyl (3-(3-(2-(dimethylamino)-9-methyl-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)phenoxy)-3-(thiophen-2-yl)propyl)(methyl)carbamate	^{1}H NMR (500 MHz, $CDCl_3$) δ 8.75 (s, 1H), 7.21-7.17 (m, 2H), 7.03-6.68 (m, 1H), 6.93-6.91 (m, 1H), 6.86-6.84 (m, 2H), 6.78-6.74 (m, 1H), 5.44-5.39 (m, 1H), 4.17-4.03 (m, 2H), 3.88-3.86 (m, 2H), 3.65-3.63 (m, 2H), 3.50-3.34 (m, 2H), 3.19 (s, 6H), 3.18 (s, 3H), 2.87 (s, 3H), 2.34-2.24 (m, 1H), 2.21-2.11 (m, 1H), 1.00-0.87 (m, 2H), 0.01 (s, 9H) .
Teoc intermediate for 46		2-(Trimethylsilyl)ethyl (*S*)-methyl(3-(3-(9-methyl-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)phenoxy)-3-(thiophen-2-yl)propyl)carbamate	^{1}H NMR (500 MHz, $CDCl_3$) δ 8.91 (s, 1H), 8.69 (s, 1H), 7.27-7.23 (m, 2H), 7.04 (m, 1H), 6.95 (m, 1H), 6.88 (m, 2H), 6.84 (m, 1H), 5.45 (m, 1H), 4.20-4.05 (m, 2H), 3.94 (m, 2H), 3.77 (m, 2H), 3.51-3.39 (m, 2H), 3.28 (s, 3H), 2.90 (s, 3H), 2.32 (m, 1H), 2.19 (m, 1H), 0.99 (m, 1H), 0.92 (m, 1H), 0.037 (s, 9H).
BOC intermediate for 47		*tert*-Butyl (*S*)-(3-(3-(2,9-dimethyl-5-oxo-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)phenoxy)-3-(thiophen-2-yl)propyl)(methyl)carbamate	^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (s,1H), 7.23 (m, 2H), 7.03 (m, 1H), 6.94 (m, 1H), 6.87 (m, 2H), 6.82 (m, 1H), 5.43 (m, 1H), 3.91 (m, 2H), 3.73 (m, 2H), 3.38 (m, 2H), 3.27 (s, 3H), 2.85 (s, 3H), 2.57 (s, 3H), 2.30 (m, 1H), 2-18 (m, 1H), 1.42 (s, 9H).
Teoc intermediate for 48		2-(Trimethylsilyl)ethyl methyl(3-(3-(9-methyl-5-oxo-2-(trifluoromethyl)-5,7,8,9-tetrahydro-6H-pyrimido[4,5-e][1,4]diazepin-6-yl)phenoxy)-3-(thiophen-2-yl)propyl)carbamate	^{1}H NMR (300 MHz, $CDCl_3$) δ 8.99 (s, 1H), 7.27-7.20 (m, 2H), 7.03-6.83 (m, 5H), 5.45-5.35 (m, 1H), 4.17-4.02 (m, 2H), 3.95-3.92 (m, 2H), 3.80-3.77 (m, 2H), 3.49-3.38 (m, 2H), 3.30 (s, 3H), 2.88 (s, 3H), 2.37-2.09 (m, 2H), 0.97-0.83 (m, 2H), 0.01 (s, 9H).

Teoc intermediate for 56		2-(Trimethylsilyl)ethyl (*S*)-(3-(3-(8-(ethylamino)-1-methyl-5-oxo-1,2,3,5-tetrahydro-4H-pyrido[4,3-e][1,4]diazepin-4-yl)phenoxy)-3-(thiophen-2-yl)propyl)(methyl)carbamate	^{1}H NMR (500 MHz, $CDCl_3$) δ 8.41 (s, 1H), 7.22-7.19 (m, 2H), 7.04-7.00 (m, 1H), 6.94-6.91 (m, 3H) 6.78 (d, J = 8.0 Hz, 1H), 5.45-5.41 (m, 1H), 4.94-4.91 (m, 1H), 4.16-4.05 (m, 2H), 3.87-3.85 (m, 2H), 3.51-3.45 (m, 2H), 3.45-3.35 (m, 2H), 3.31-3.26 (m, 2H), 2.92 (s, 3H), 2.88 (s, 3H), 2.34-2.26 (m, 1H), 2.22-2.12 (m, 1H), 1.28 (t, J = 7.2 Hz, 3H), 1.01-0.89 (m, 2H), 0.01 (s, 9H) .
Teoc intermediate for 57		2-(Trimethylsilyl)ethyl (*S*)-(3-(3-(8-(ethylamino)-1-methyl-5-oxo-1,2,3,5-tetrahydro-4H-pyrido[2,3-e][1,4]diazepin-4-yl)phenoxy)-3-(thiophen-2-yl)propyl)(methyl)carbamate	^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (d, J = 8.5 Hz, 1H), 7.27-7.19 (m, 2H), 7.03 (br, 1H), 6.95-6.90 (m, 3H), 6.78 (d, J = 8.0 Hz, 1H), 5.87 (d, J = 8.4 Hz, 1H), 5.46-5.42 (m, 1H), 4.63-4.59 (m, 1H), 4.17-4.10 (m, 2H), 3.91-3.88 (m, 2H), 3.60-3.57 (m, 2H), 3.45-3.31 (m, 4H), 3.09 (s, 3H), 2.90 (s, 3H), 2.35-2.28 (m, 1H), 2.22-2.12 (m, 1H), 1.26 (t, J = 7.2 Hz, 3H), 0.97 (bs, 2H), 0.04 (s, 9H).
Teoc intermediate for 59		2-(Trimethylsilyl)ethyl (*S*)-methyl(3-(3-(1-methyl-5-oxo-1,2,3,5-tetrahydro-4H-pyrido[2,3-e][1,4]diazepin-4-yl)phenoxy)-3-(thiophen-2-yl)propyl)carbamate	^{1}H NMR (300 MHz, $CDCl_3$) δ 8.35 (dd, J = 1.8 Hz, J = 4.9 Hz, 1H), 8.05 (dd, J = 1.9, 7.5 Hz, 1H), 7.28-7.23 (m, 2H), 7.05 (br, 1H), 6.96-6.94 (m, 4H), 6.85-6.79 (m, 2H), 5.46-5.42 (m, 1H), 4.16-4.10 (m, 2H), 3.92-3.89 (m, 2H), 3.63-3.60 (m, 2H), 3.46-3.31 (m, 2H), 3.09 (s, 3H), 2.90 (s, 3H), 2.36-2.29 (m, 1H), 2.22-2.12 (m, 1H), 0.97 (bs, 2H), 0.04 (s, 9H).

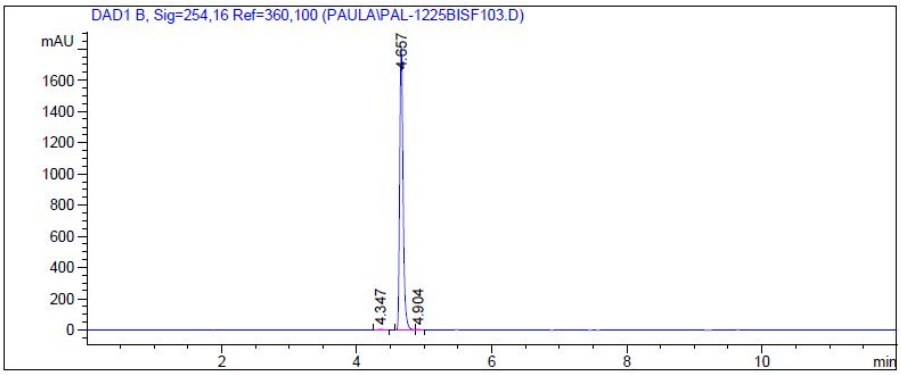
Teoc intermediate for 61		2-(Trimethylsilyl)ethyl (*S*)-(3-(3-(1,8-dimethyl-5-oxo-1,2,3,5-tetrahydro-4H-pyrido[2,3-e][1,4]diazepin-4-yl)phenoxy)-3-(thiophen-2-yl)propyl)(methyl)carbamate	^{1}H NMR (300 MHz, $CDCl_3$) δ 7.93 (d, J = 7.5 Hz, 1H), 7.27-7.27 (m, 2H), 7.05 (br, 1H), 6.97-6.92 (m, 3H), 6.82 (d, J = 8.1 Hz, 1H), 6.65 (d, J = 7,1 Hz, 1H), 5.46-5.42 (m, 1H), 4.14 (bs, 2H), 3.92-3.89 (m, 2H), 3.63-3.60 (m, 2H), 3.45 (bs, 2H), 3.11 (s, 3H), 3.09 (s, 3H), 2.90 (s, 3H), 2,46 (s, 3H), 2.37-2.29 (m, 1H), 2.22-2.12 (m, 1H), 0.96 (bs, 2H), 0.04 (s, 9H).
Teoc intermediate for 63		2-(Trimethylsilyl)ethyl (*S*)-(3-(3-(8-methoxy-1-methyl-5-oxo-1,2,3,5-tetrahydro-4H-pyrido[2,3-e][1,4]diazepin-4-yl)phenoxy)-3-(thiophen-2-yl)propyl)(methyl)carbamate	^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (d, J = 8.5 Hz, 1H), 7.27-7.21 (m, 2H), 7.05 (m, 1H), 6.95 (m, 1H), 6.93-6.89 (m, 2H), 6.81 (m, 1H), 6.19 (d, J = 8.5 Hz, 1H), 5.45 (m, 1H), 4.14 (m, 2H), 3.94 (s, 3H), 3.92 (m, 2H), 3.66 (m, 2H), 3.44 (m, 2H), 3.16 (s, 3H), 2.90 (s, 3H), 2.32 (m, 1H), 2.19 (m, 1H), 0.97 (m, 2H), 0.04 (s, 9H).
Teoc intermediate for 65		2-(Trimethylsilyl)ethyl methyl(3-(3-(1-methyl-5-oxo-1,2,3,5-tetrahydro-4H-pyrido[3,2-e][1,4]diazepin-4-yl)phenoxy)-3-(thiophen-2-yl)propyl)carbamate	^{1}H NMR (300 MHz, $CDCl_3$) δ 8.36 (dd, J = 1.5 Hz, J = 4.3 Hz, 1H), 7.35-7.23 (m, 4H), 7.07-7.02 (m, 3H), 6.96-6.94 (m, 1H), 6.84 (d, J = 8.0 Hz, 2H), 5.46-5.42 (m, 1H), 4.14 (bs, 2H), 3.81-3.77 (m, 2H), 3.44 (bs, 2H), 3.36-3.32 (m, 2H), 2.91 (s, 3H), 2.88 (s, 3H), 2.39-2.27 (m, 1H), 2.20 (bs, 1H), 0.97 (bs, 2H), 0.04 (s, 9H).
Teoc intermediate for 67		2-(Trimethylsilyl)ethyl methyl(3-(3-(1-methyl-5-oxo-1,2,3,5-tetrahydro-4H-pyrido[3,4-e][1,4]diazepin-4-yl)phenoxy)-3-(thiophen-2-yl)propyl)carbamate	^{1}H NMR (400 MHz, $CDCl_3$) δ 8.30 (bs, 2H), 7.54 (d, J = 4.8 Hz, 1H), 7.28-7.24 (m, 2H), 7.05 (br, 1H), 6.98-6.94 (m, 3H), 6.86 (d, J = 8.0 Hz, 1H), 5.46 (bs, 1H), 4.14 (bs, 2H), 3.81-3.79 (m, 2H), 3.51-

			3.38 (m, 4H), 3.00 (s, 3H), 2.90 (s, 3H), 2.33 (bs, 1H), 2.20 (bs, 1H), 0.95 (bs, 2H), 0.04 (s, 9H).
Teoc intermediate for 69		2-(Trimethylsilyl)ethyl methyl(3-(3-(1-methyl-5-oxo-1,2,3,5-tetrahydro-4H-benzo[e][1,4]diazepin-4-yl)phenoxy)-3-(thiophen-2-yl)propyl)carbamate	^{1}H NMR (300 MHz, $CDCl_3$) δ 7.43-6.70 (m, 11H), 5.46 (bs, 1H), 4.14 (bs, 2H), 3.84-3.74 (m, 4H), 3.46-3.31 (m, 2H), 2.86 (s, 3H), 2.85 (s, 3H), 2.84 (s, 3H), 2.36-2.12 (bs, 2H), 0.97 (bs, 2H), 0.04 (s, 9H).
Teoc intermediate for 71		2-(Trimethylsilyl)ethyl (*S*)-methyl(3-(3-(4-methyl-7-oxo-1,4-diazepan-1-yl)phenoxy)-3-(thiophen-2-yl)propyl)carbamate	^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22-7.15 (m, 2H), 7.01 (m, 1H), 6.93-6.91 (m, 1H), 6.78-6.76 (m, 2H), 5.41 (bs, 1H), 4.13 (bs, 2H), 3.77-3.76 (m, 2H), 3.41 (bs, 2H), 2.88 (s, 3H), 2.82-2.81 (m, 2H), 2.68-2.64 (m, 4H), 2.37 (s, 3H), 2.30 (bs, 1H), 2.17 (bs, 1H), 0.93 (bs, 2H), 0.04 (s, 9H).

HPLC traces of final compounds.

Compound	HPLC chromatogram	Purity (%)
15-1	 Peak # / RetTime [min] / Type / Width [min] / Area [mAU*s] / Height [mAU] / Area % 1 4.628 VV 0.0507 114.84566 34.66278 1.1075 2 4.832 VV 0.0775 85.88580 15.30203 0.8283 3 5.038 VV 0.0577 1.01688e4 2714.82275 98.0642	98.0
16a	 Peak # / RetTime [min] / Type / Width [min] / Area [mAU*s] / Height [mAU] / Area % 1 4.747 VV 0.0556 34.72219 9.73376 1.5998 2 4.886 VV 0.0539 2135.62793 624.27246 98.4002	98.4
16b	 Peak # / RetTime [min] / Type / Width [min] / Area [mAU*s] / Height [mAU] / Area % 1 4.640 BV 0.0581 47.71693 12.61813 0.7921 2 4.999 VB 0.0563 5872.99072 1618.42480 97.4885 3 5.458 VV 0.0603 103.58255 25.01776 1.7194	97.4

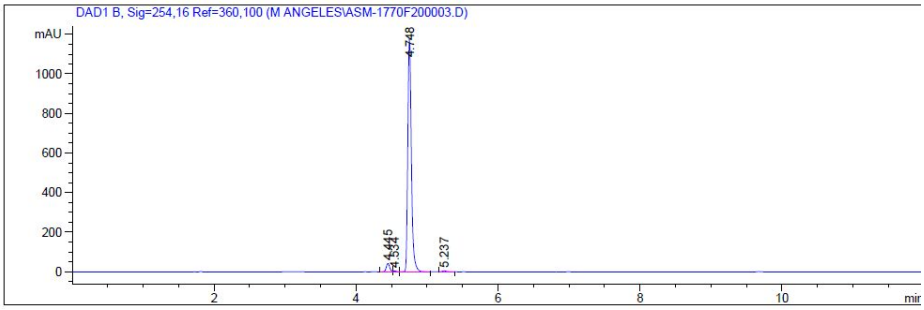
16c



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.347	BV	0.0906	29.36371	4.84918	0.4563
2	4.657	VV	0.0550	6384.50098	1818.62024	99.2212
3	4.904	VB	0.0665	20.74859	4.61241	0.3225

99.2

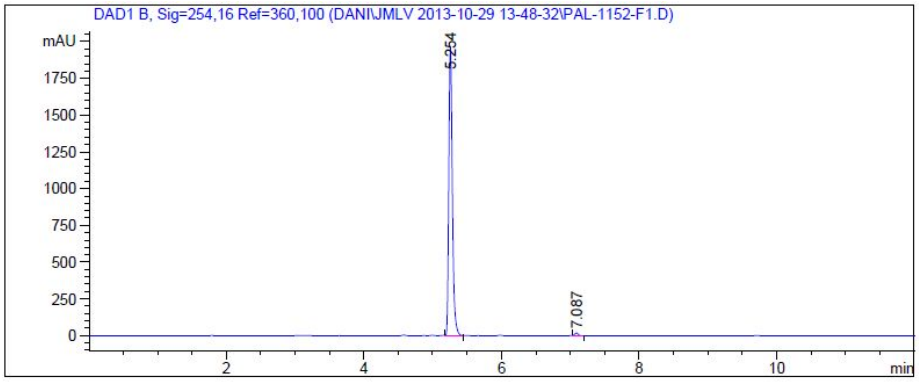
16d



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.445	VV	0.0530	151.07607	43.01703	3.4703
2	4.534	VV	0.0528	18.65908	5.08085	0.4286
3	4.748	VV	0.0550	4154.03857	1181.25354	95.4203
4	5.237	VB	0.0776	29.63881	5.61039	0.6808

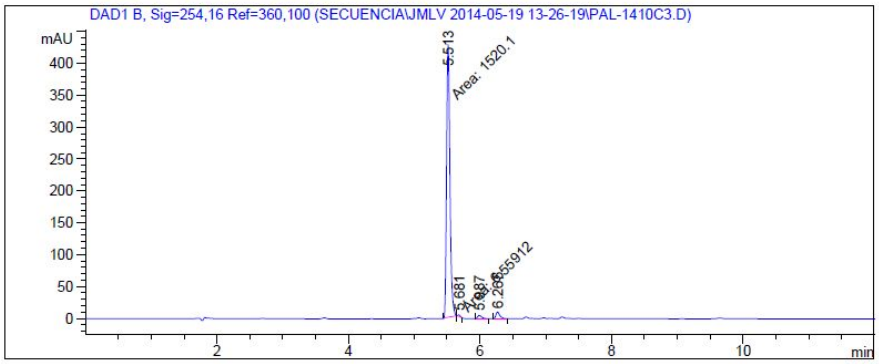
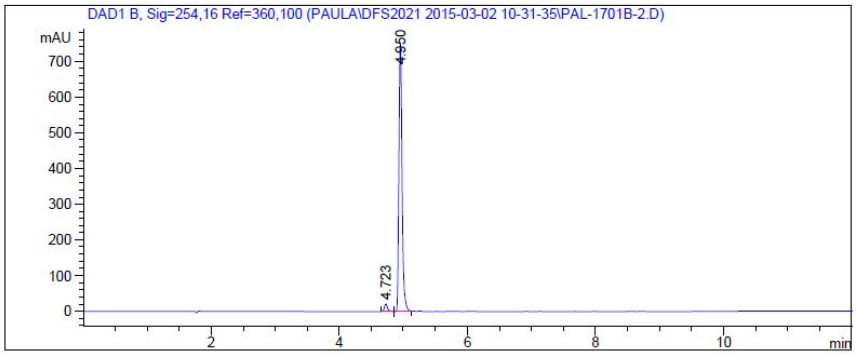
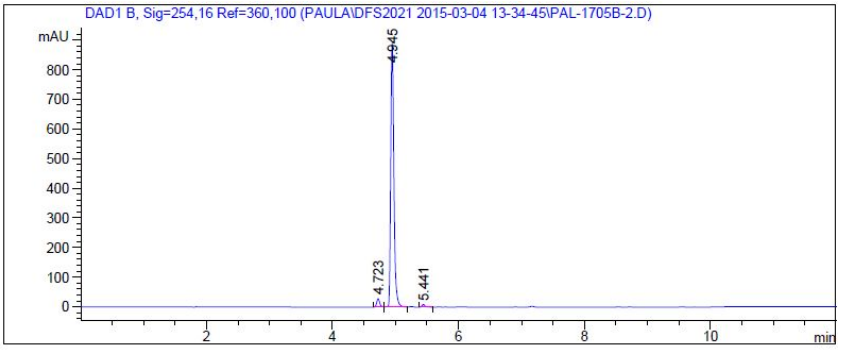
95.4

17

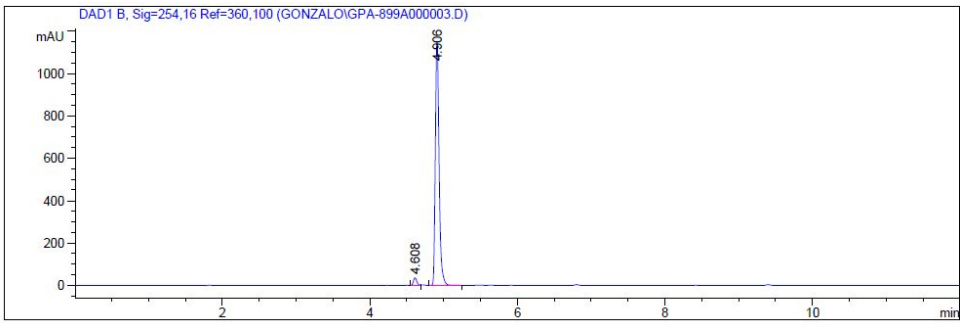


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.254	VV	0.0562	7142.85449	1975.75525	99.0550
2	7.087	VB	0.0555	68.14140	19.13602	0.9450

99.0

23	 Peak # / RetTime [min] / Type / Width [min] / Area [mAU*s] / Height [mAU] / Area % 1 — 5.513 — PP — 0.0588 — 1520.09839 — 430.61874 — 95.1106 2 — 5.681 — MM — 0.0397 — 6.55912 — 2.75362 — 0.4104 3 — 5.987 — BB — 0.0677 — 25.45984 — 5.52959 — 1.5930 4 — 6.265 — BB — 0.0638 — 46.12537 — 10.81389 — 2.8860	95.1
31aR	 Peak # / RetTime [min] / Type / Width [min] / Area [mAU*s] / Height [mAU] / Area % 1 — 4.723 — BV — 0.0527 — 73.72601 — 21.11136 — 2.7699 2 — 4.950 — VV — 0.0520 — 2588.00000 — 754.82886 — 97.2301	97.2
31aS	 Peak # / RetTime [min] / Type / Width [min] / Area [mAU*s] / Height [mAU] / Area % 1 — 4.723 — BV — 0.0521 — 98.36090 — 28.59948 — 3.0333 2 — 4.945 — VV — 0.0545 — 3111.38452 — 895.25073 — 95.9513 3 — 5.441 — BB — 0.0571 — 32.92675 — 8.91385 — 1.0154	95.9

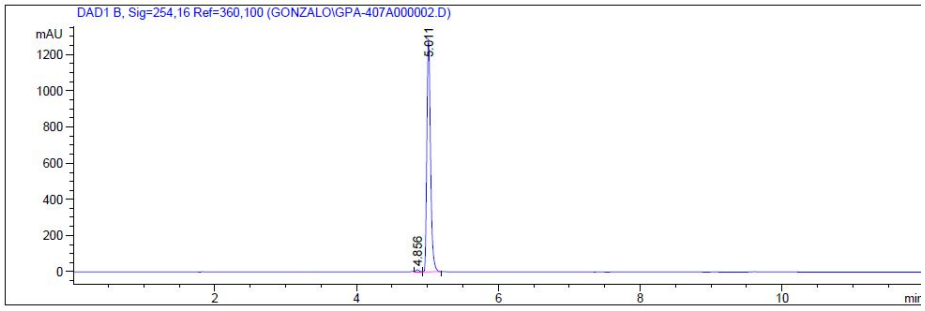
31b



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.608	VV	0.0496	115.90099	35.91969	2.7488
2	4.906	VB	0.0531	4100.55811	1164.76892	97.2512

97.2

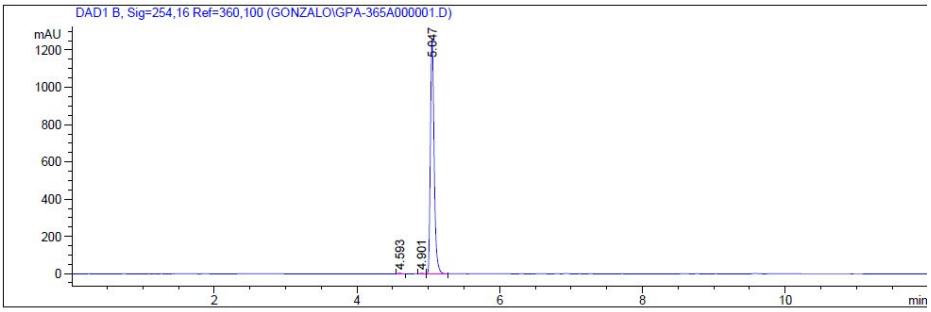
31c



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.856	VV	0.0534	41.66845	11.74383	0.8869
2	5.011	VV	0.0561	4656.73193	1291.40527	99.1131

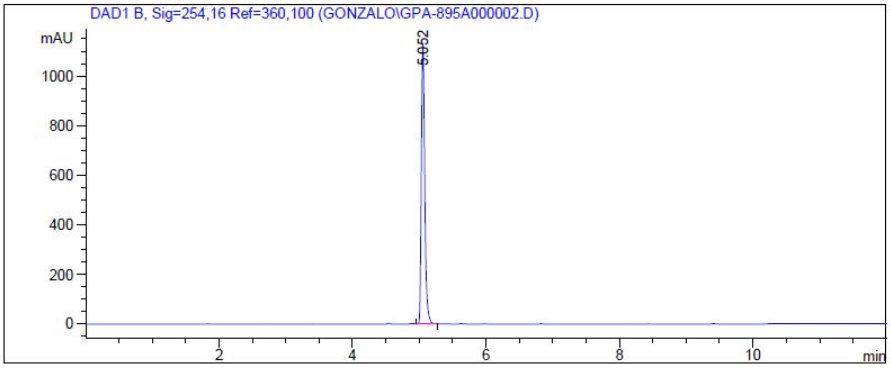
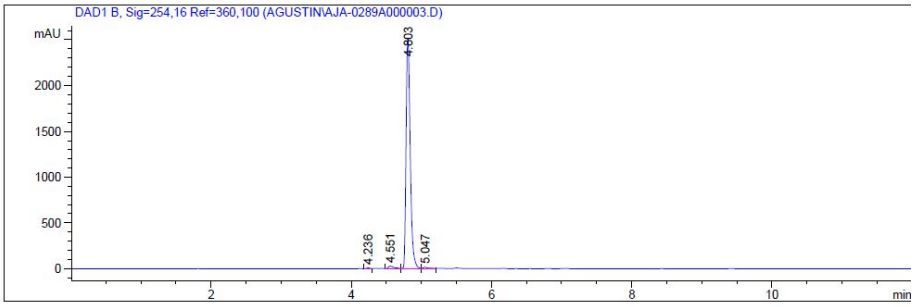
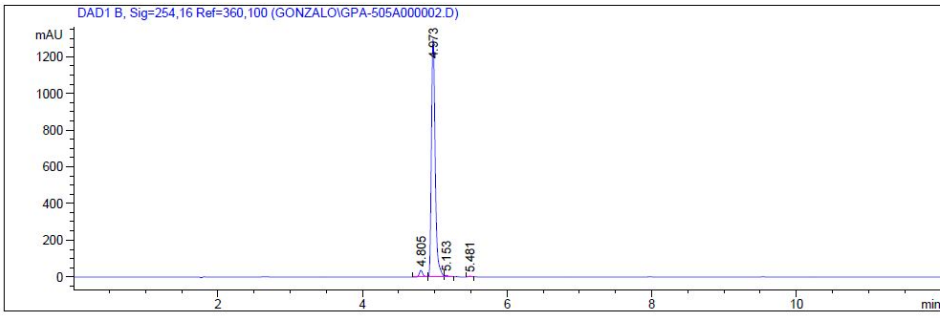
99.1

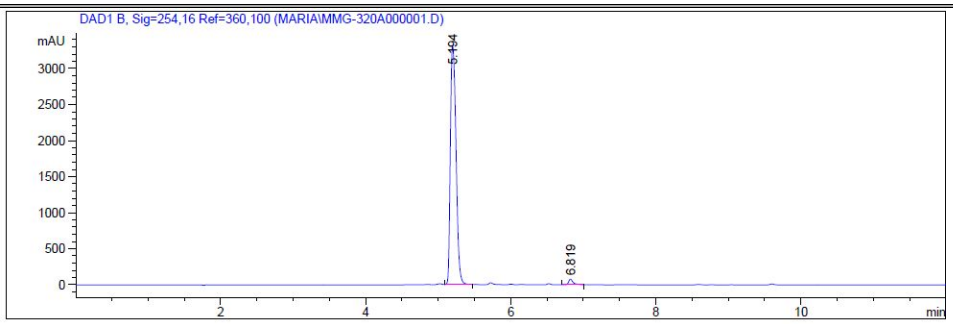
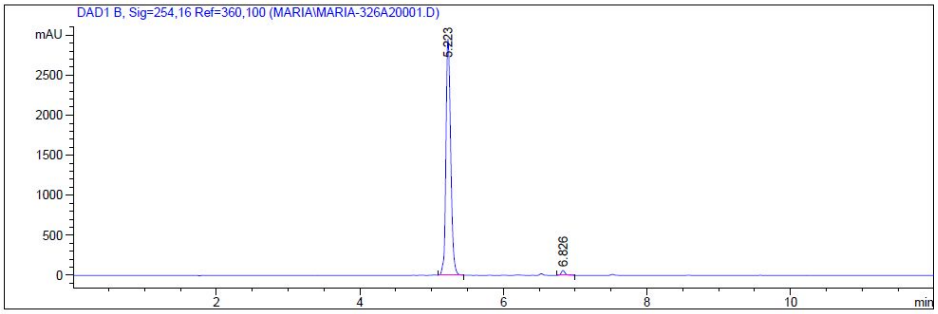
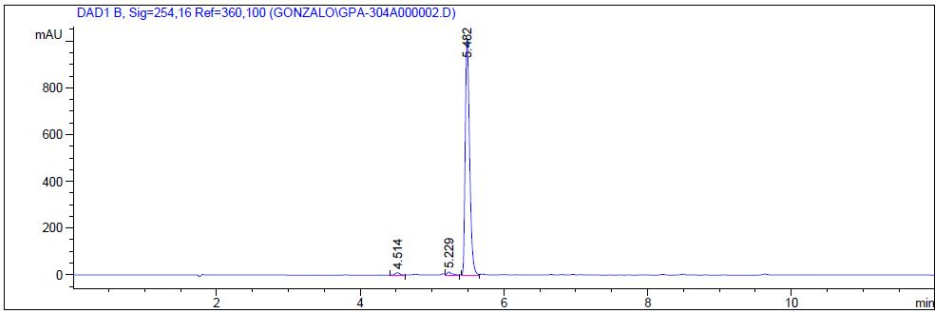
31d

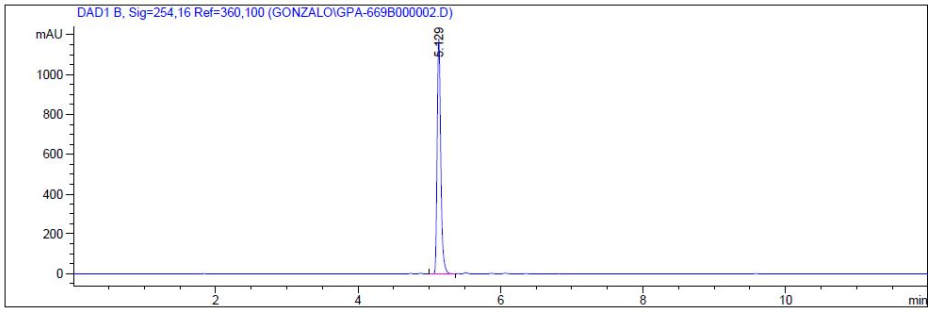
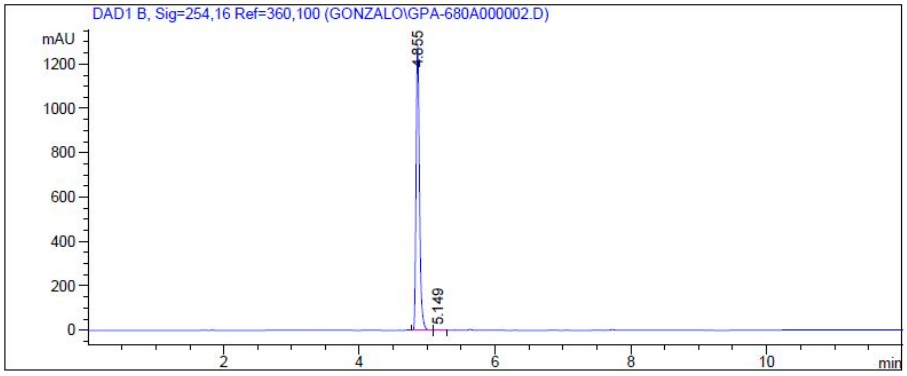
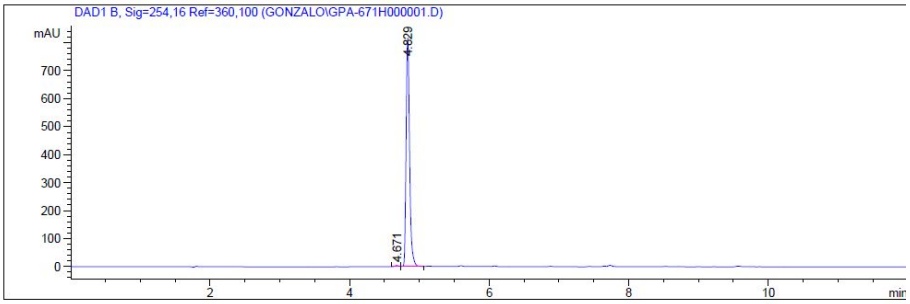


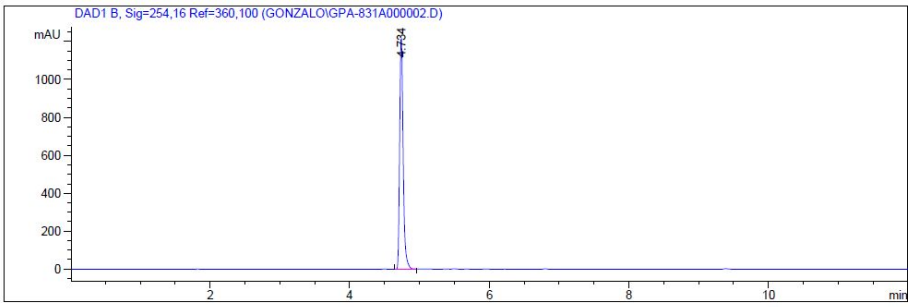
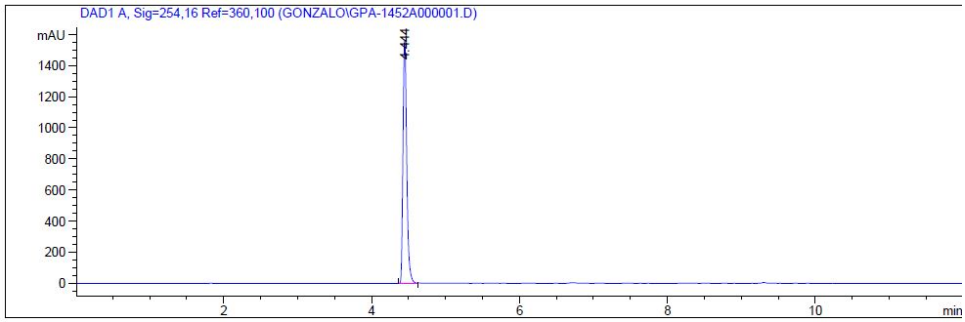
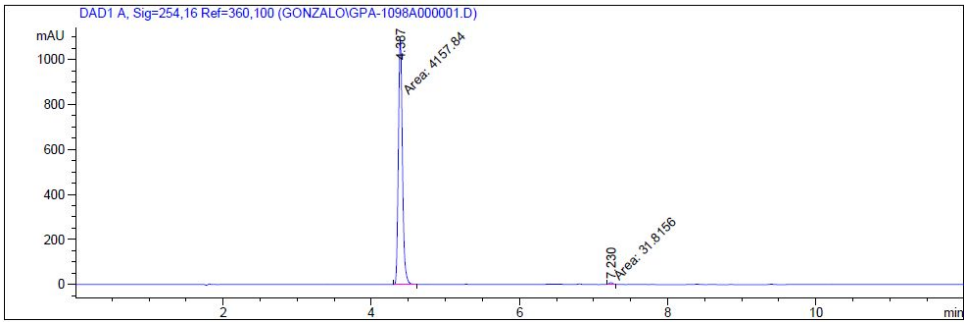
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.593	BV	0.0491	12.30676	3.87190	0.2670
2	4.901	VV	0.0515	10.42724	3.07802	0.2263
3	5.047	VB	0.0543	4585.85352	1265.97217	99.5067

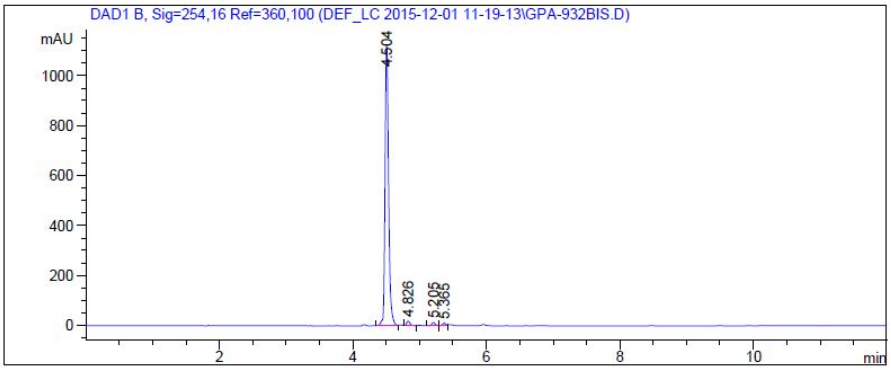
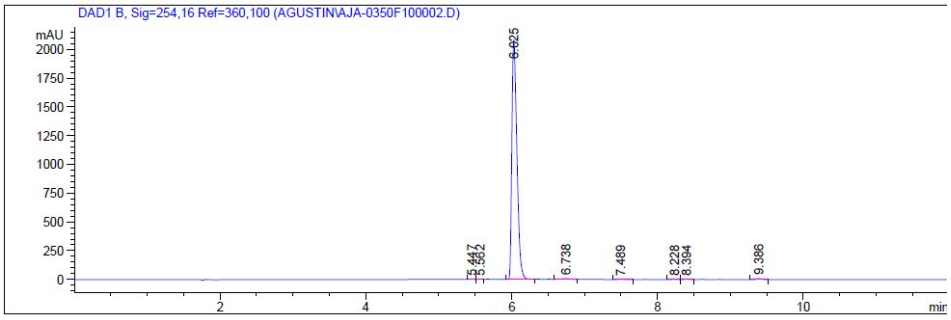
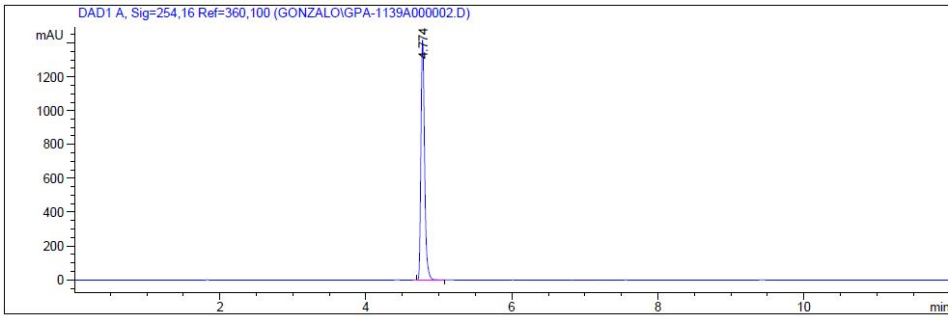
99.5

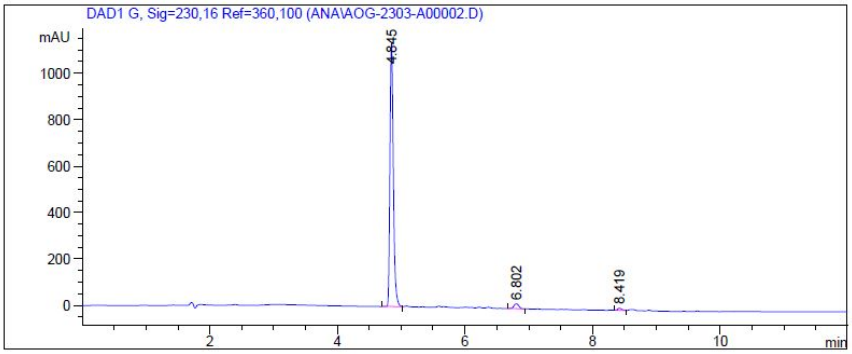
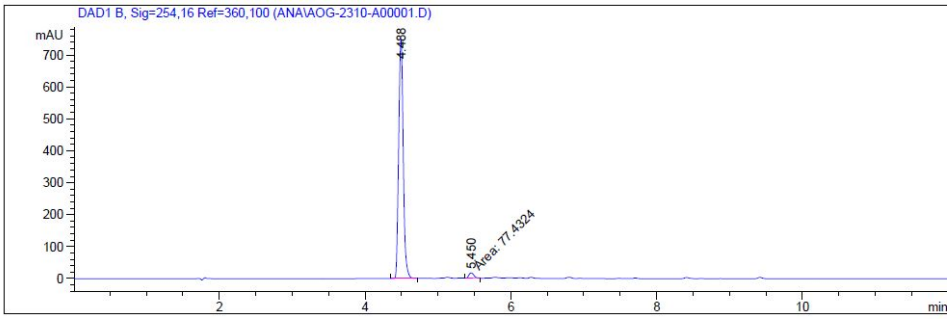
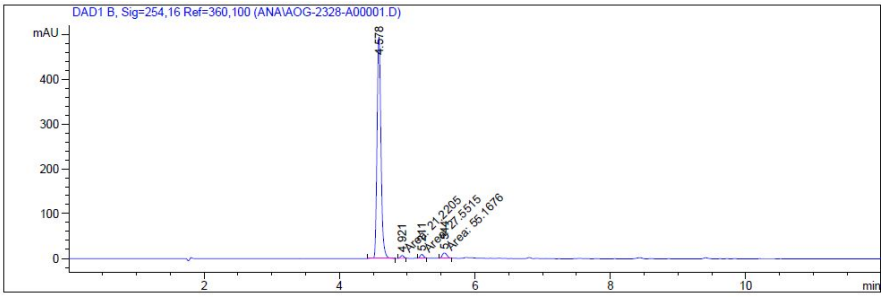
31e	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 5.052 VB 0.0555 4040.06372 1135.02100 100.0000	100
31f	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.236 VV 0.0523 33.05176 9.56052 0.3083 2 4.551 VV 0.0841 175.03912 29.13860 1.6330 3 4.803 VV 0.0638 1.04044e4 2538.28613 97.0657 4 5.047 VV 0.0878 106.43698 16.82004 0.9930	97.0
32	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.805 BV 0.0556 129.82599 36.40449 2.6380 2 4.973 VV 0.0564 4732.81006 1303.67065 96.1676 3 5.153 VV 0.0637 42.04026 9.13386 0.8542 4 5.481 BV 0.0526 16.73975 4.80938 0.3401	96.1

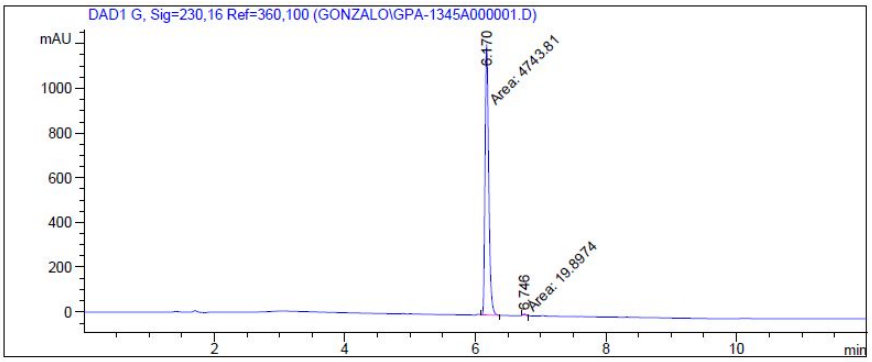
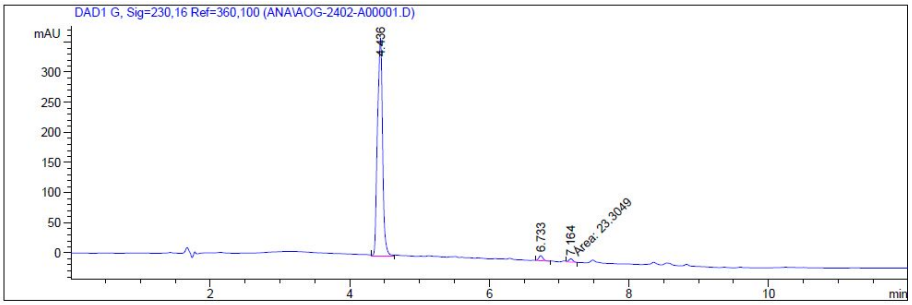
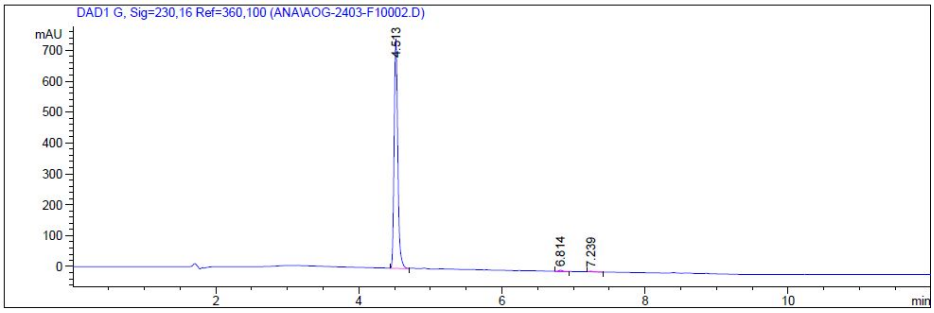
33R	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 5.194 VV 0.0876 1.81229e4 3324.86426 97.9996 2 6.819 VV 0.0683 369.92917 79.45224 2.0004	97.9
33S	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 5.223 VV 0.0742 1.37421e4 2957.79712 98.2078 2 6.826 BV 0.0610 250.77539 62.26231 1.7922	98.2
34	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.514 BV 0.0670 44.37872 10.15274 1.0127 2 5.229 VB 0.0650 60.88377 13.40350 1.3893 3 5.482 BV 0.0634 4277.02734 1009.53918 97.5980	97.5

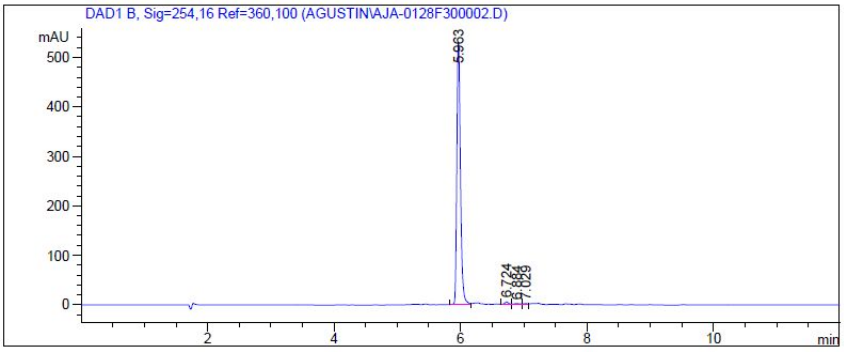
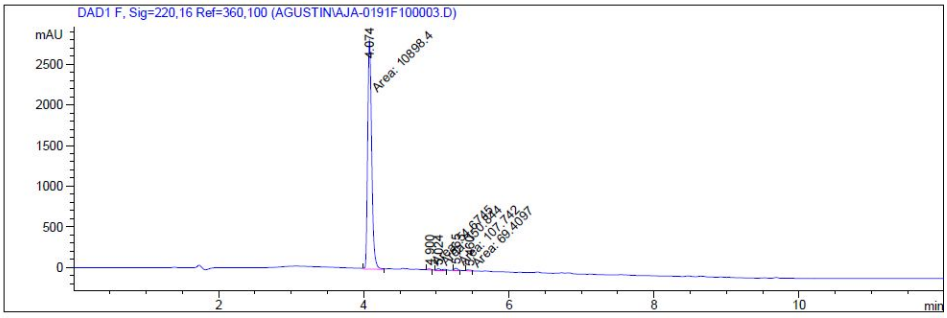
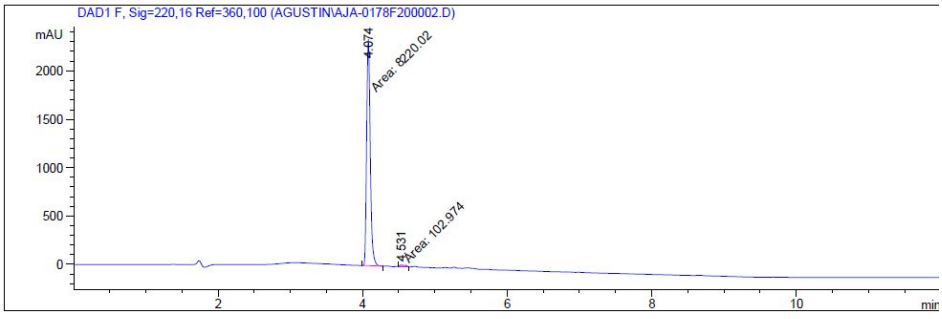
43S	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 5.129 BV 0.0553 4187.44727 1182.14050 100.0000	100
45aR	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.855 VV 0.0548 4503.70459 1288.10986 99.6447 2 5.149 VB 0.0682 16.05864 3.45446 0.3553	99.6
45aS	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.671 BV 0.0654 17.30176 4.25983 0.6055 2 4.829 VV 0.0524 2839.97925 819.81415 99.3945	99.3

45b	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.734 BV 0.0526 4274.92627 1227.45593 100.0000	100
45cS	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.444 BV 0.0532 5560.15137 1575.10413 100.0000	100
46S	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.387 MM 0.0634 4157.83740 1093.54187 99.2406 2 7.230 MM 0.0624 31.81557 8.49798 0.7594	99.2

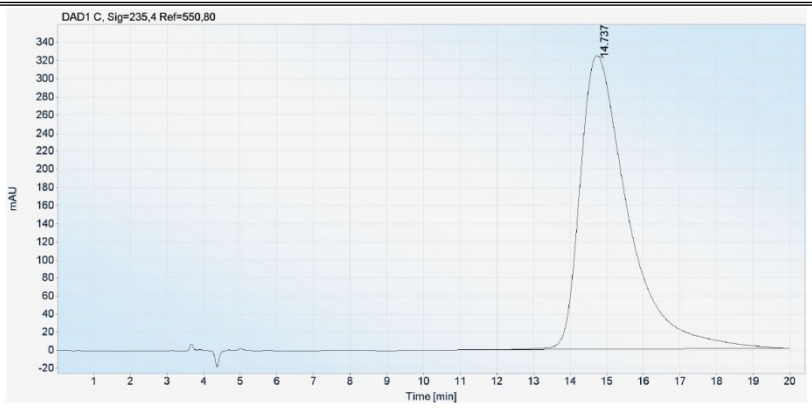
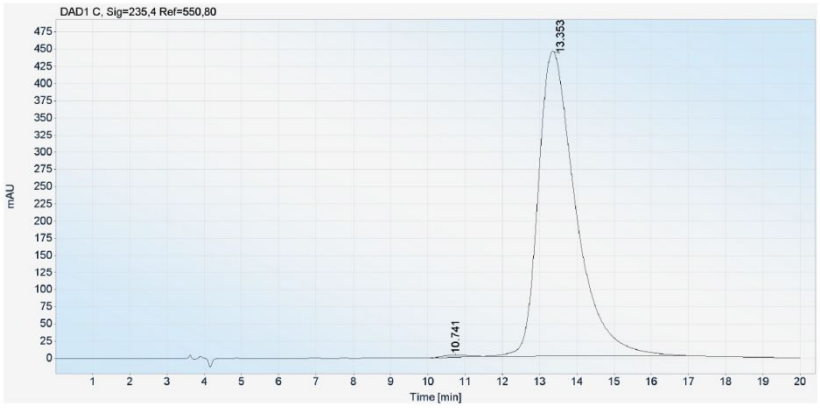
47S	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.504 VV 0.0568 4151.58154 1132.07214 96.1791 2 4.826 VV 0.0561 71.39601 18.88989 1.6540 3 5.205 VV 0.0596 53.04648 13.57049 1.2289 4 5.365 VV 0.0549 40.48840 11.02016 0.9380	96.1
48	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 5.447 VV 0.0646 18.68172 4.30705 0.1815 2 5.562 VV 0.0615 18.01847 4.42314 0.1751 3 6.025 VV 0.0742 1.00630e4 2090.45581 97.7908 4 6.738 VV 0.1360 89.79748 8.73204 0.8726 5 7.489 BV 0.1394 21.55582 2.14127 0.2095 6 8.228 VV 0.0656 15.16479 3.43096 0.1474 7 8.394 VV 0.0732 22.68702 4.47222 0.2205	97.7
56S	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.774 VV 0.0547 4963.49756 1422.85632 100.0000	100

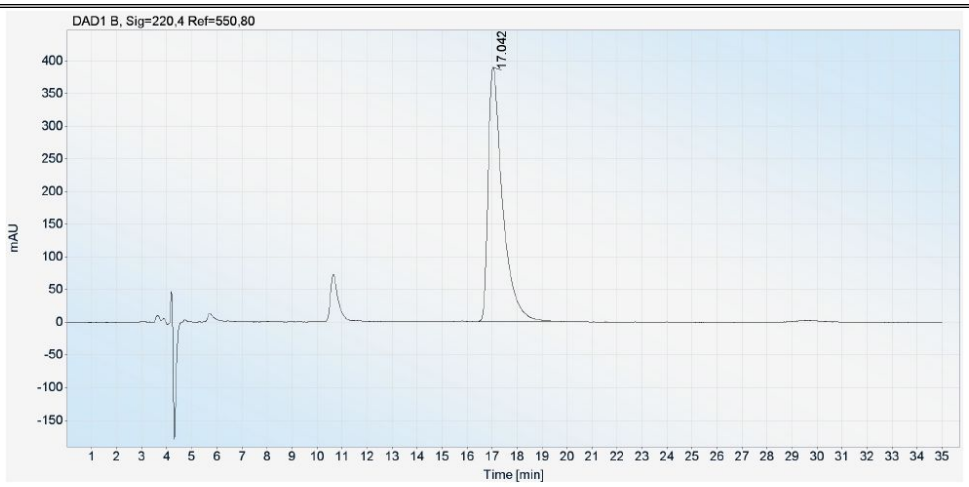
57S	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.845 BV 0.0552 4233.73975 1144.09924 96.0008 2 6.802 VV 0.0914 126.78940 21.93269 2.8750 3 8.419 BV 0.0737 49.58060 10.03123 1.1242	96.0
59S	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.488 BB 0.0690 3286.36255 751.27826 97.6981 2 5.450 MM 0.0778 77.43236 16.57967 2.3019	97.6
61S	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.578 BV 0.0627 1988.53894 496.33371 95.0327 2 4.921 MM 0.0554 21.22049 6.38736 1.0141 3 5.211 MM 0.0570 27.55152 8.05884 1.3167 4 5.544 MM 0.0781 55.16758 11.77612 2.6365	95.0

63S	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 6.170 MM 0.0650 4743.80957 1215.90295 99.5823 2 6.746 MM 0.0488 19.89736 6.79251 0.4177	99.5
65	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.436 VB 0.0714 1842.52185 361.89377 96.6993 2 6.733 VB 0.0685 39.58691 8.79190 2.0776 3 7.164 MF 0.0693 23.30486 5.60648 1.2231	96.6
67	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.513 BV 0.0556 2660.07910 745.60406 99.1739 2 6.814 BB 0.0568 13.43128 3.66542 0.5007 3 7.239 VB 0.0586 8.72716 2.28091 0.3254	99.1

69	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 5.963 BV 0.0624 2125.09033 534.33612 97.0935 2 6.724 VV 0.0695 29.16042 5.92067 1.3323 3 6.884 VV 0.0984 20.74663 2.80007 0.9479 4 7.029 VV 0.0726 13.70769 2.72959 0.6263	97.0
71R	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.074 MM 0.0640 1.08984e4 2837.42700 96.6079 2 4.900 MM 0.0602 54.67455 15.12566 0.4847 3 5.024 MM 0.1083 150.84372 23.22374 1.3371 4 5.265 MM 0.0577 107.74153 31.11305 0.9551	96.6
71S	 Peak RetTime Type Width Area Height Area # [min] [min] [mAU*s] [mAU] % 1 4.074 MM 0.0582 8220.01660 2352.34375 98.7628 2 4.531 MM 0.0910 102.97409 18.85987 1.2372	98.7

HPLC traces ee determination of final compounds

Compound	HPLC chromatogram	ee (%)
31aR	 Signal: DAD1 C, Sig=235,4 Ref=550,80 RT [min] | Type | Width [min] | Area | Height | Area% 14.737 | BBA | 1.3431 | 29355.5703 | 323.9961 | 100.0000 Sum | 29355.5703	100
45cS	 Signal: DAD1 C, Sig=235,4 Ref=550,80 RT [min] | Type | Width [min] | Area | Height | Area% 10.741 | BB | 0.5061 | 136.7411 | 3.2421 | 0.4392 13.353 | MM | 1.1639 | 30995.4453 | 443.8264 | 99.5608 Sum | 31132.1864	99.1

59S		100

Signal: DAD1 B, Sig=220,4 Ref=550,80

RT [min]	Type	Width [min]	Area	Height	Area%
17.042	VV R	0.5625	15505.0674	389.4476	100.0000
		Sum	15505.0674		