

Supporting Information for

**Efficient [4+3] Cycloaddition Reaction of aza-*o*-
Quinodimethanes with *C,N*-cyclic Azomethine Imines:
Stereoselective Synthesis of 1,2,4-Triazepines**

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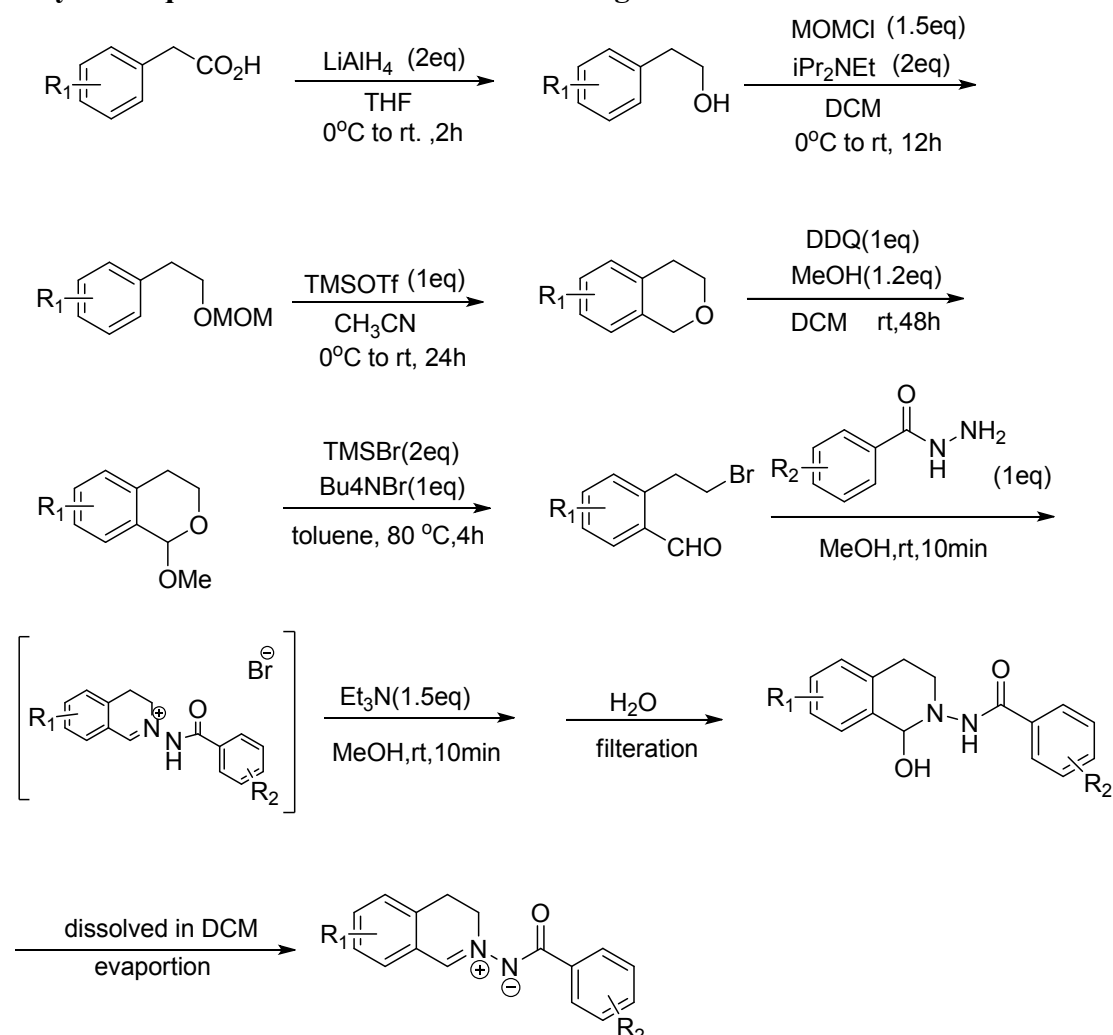
A: General Information:

Unless otherwise noted, sulfonaminobenzyl chlorides were prepared from the known procedure^[1]. All N-benzoylimino-3,4-dihydroisoquinolinium betaine and its analogs were prepared according to the known literatures.^[2] Dichloromethane(DCM) was freshly distilled from calcium hydride , tetrahydrofuran (THF) and toluene were distilled from sodium/ benzophenone . Other solvents were also purified before using. Reactions were monitored by thin layer chromatography (TLC), Chromatograms were visualized by fluorescence quenching under UV light at 254 nm. Flash column chromatography was performed using Qingdao Haiyang flash silica gel (200–300mesh).

¹H NMR spectra were recorded on a Bruker 400 MHz spectrometer. Solvent for NMR is CDCl₃, unless the otherwise noted. Chemical shifts are reported in ppm from the solvent resonance as the internal standard (CDCl₃: 7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = single, d = doublet, t = triplet, m = multiplet, dd = doublet of doublets), coupling constants (Hz) and integration; ¹³C NMR spectra were on recorded on 400 (101MHz) with complete proton decoupling. Chemical shifts are reported in ppm relative to the central line of the heptalet at 77.16 ppm for CDCl₃. Melting point was measured with melting point instrument. All high resolution mass spectra were obtained on a Finnigan/MAT 95XL-T mass spectrometer.

B: Preparation of substrates:

General procedure for the synthesis of N-benzoylimino-3,4-dihydroisoquinolinium betaine and its analogs^[2]



To a solution of substituted Phenylacetic acid (10 mmol) in dry THF (10mL) was added dropwise a solution of LiAlH₄ in THF (1M, 20 mL) while the temperature was maintained at 0 °C. The resulting mixture was allowed to warm to room temperature and was stirred for 2 h. The mixture was then hydrolyzed by addition of water (1.0mL) and 5% NaOH (2.0 mL). The resulting suspension was filtered, and the precipitate was washed with ethyl acetate. Then the combined organic collection was evaporated to give a crude material of phenyl ethanol which was used without further purification^[3].

After the dilution of this residue in CH₂Cl₂ (10 mL), *i*Pr₂NEt (3.45 mL, 20 mmol) and MOMCl (1.18 mL, 15 mmol) were added to this solution at 0 °C. The reaction solution was then allowed to warm to room temperature and stirred for 12 h. The mixture was poured into 1N HCl and extracted with ethyl acetate. The combined organic layers were dried over Na₂SO₄ and concentrated in vacuo to give phenyl ethyl methoxymethyl ether.

This crude material was diluted in CH₃CN (10 mL), and TMSOTf (1.80 mL, 10 mmol)

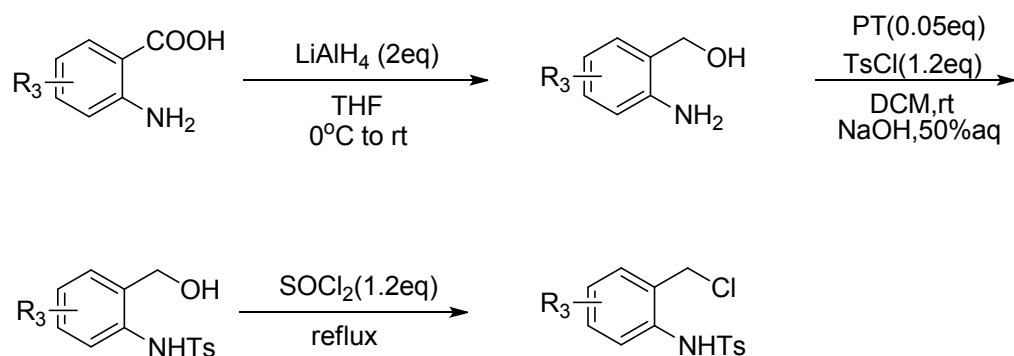
then added to this mixture at 0 °C. The reaction solution was then allowed to warm to room temperature and stirred for 24h. The mixture was then treated with NaHCO₃ aq and evaporated in vacuo to remove CH₃CN. The residue was extracted with ethyl acetate, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 20:1) to give isochroman (colorless oil).

To a solution of thus-obtained isochroman (5 mmol) in CH₂Cl₂ were added methanol (6 mmol) and DDQ (5 mmol) at room temperature. After stirring for 48 h at room temperature, the suspension was filtered off to remove the insoluble waste. The filtrate was washed with saturated NaHCO₃ (aq.), extracted with CH₂Cl₂, dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 20:1) to give 1-methoxyisochroman (colorless oil).

To a solution of the resulting 1-methoxyisochroman (2.5mmol) in toluene (2 mL) were added Bu₄NBr (2.5mmol) and TMSBr (5mmol). The reaction solution was then allowed to warm to 80°C and stirred for 4 h. The reaction solution was then treated with saturated NaHCO₃ aq., extracted with ethyl acetate. The combined organic layers were dried over Na₂SO₄ and concentrated in vacuo. The residue was purified by column chromatography on silica gel (eluting with hexane/ethyl acetate = 20:1) to give 2-(2-bromoethyl) benzaldehyde (colorless oil).

To a 0.5 M solution of the corresponding 2-(2-bromoethyl) benzaldehyde (1.05 equiv) in MeOH was added benzoylhydrazine (1equiv) at room temperature. After the immediate formation of the insoluble material, this white suspension was heated to reflux and stirred for additional 1 h to give a clear solution. After cooling to room temperature, the reaction solution was treated with Et₃N (1.5equiv), poured into water and stirred for 30 min to give a white precipitate (tentatively assigned as a methanol and/or water adduct of the corresponding N-benzoylimino-3,4-dihydroisoquinolium betaine). This solid material was washed with cold ether and then dissolved in CH₂Cl₂ to give a yellow solution. This colored solution was dried over Na₂SO₄ and evaporated in vacuo to give N-benzoylimino-3,4-dihydroisoquinolium betaine as a yellow solid.

General procedure for the synthesis of the sulfonaminobenzyl chloride compounds



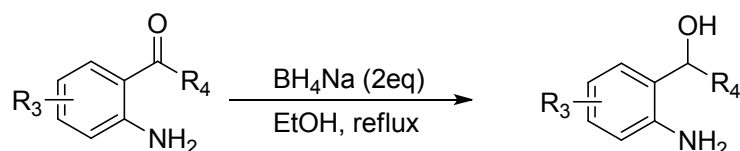
To a solution of substituted 2-amino-benzoic acid (10 mmol) in dry THF (20 mL) was

added dropwise a solution of LiAlH_4 in THF (1M, 20 mL) while the temperature was maintained at 0°C . The resulting mixture was allowed to warm to room temperature and was stirred for 2 h. The mixture was then hydrolyzed by addition of water (2 mL) and 5% NaOH (3.5 mL). The resulting suspension was filtered, and the precipitate was washed with ethyl acetate. Then the combined organic collection was evaporated. The residue was recrystallized from ethyl acetate and petroleum ether, affording the corresponding alcohols quantitatively as a white or pale yellow solid^[3].

To a round-bottom flask was added the above obtained substituted 2-aminobenzyl alcohol (10mmol), 4-Methylbenzene sulfonyl chloride (12 mmol), tetrabutylammonium hydrogen sulfate (0.5mmol) and CH_2Cl_2 (20mL) at room temperature, and NaOH (50% aq, 2mL) was added. The reaction mixture stirred at room temperature for 1-2h. After completion of the reaction as indicated by TLC, the reaction mixture was extracted with H_2O and DCM, dried with Na_2SO_4 and then concentrated. After the removal of the solvent, the residue was crystallized from CH_2Cl_2 /PE to afford the N-protected 2-aminobenzyl alcohol^[4].

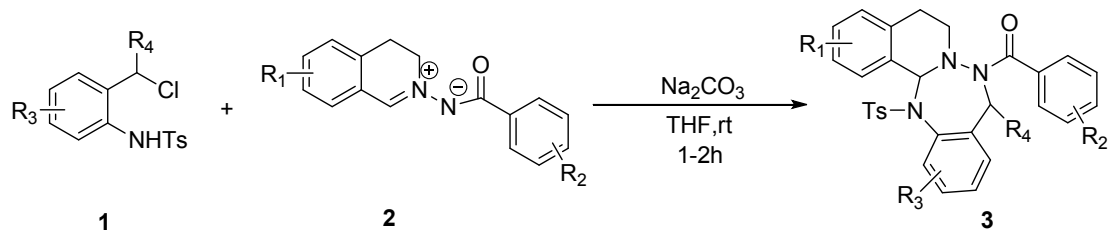
To a solution of thionyl chloride (12.0 mmol) in CHCl_3 (5.0 mL), was added a solution of benzyl alcohol (10 mmol) in CHCl_3 (40mL) over 1 min. The reaction was heated to 40°C for overnight, cooled to rt, then poured into ice water (30 mL). The layers were separated and the aqueous layer was extracted with CHCl_3 (3 x 40 mL). The combined organic layers were washed with brine (30 mL), and dried over MgSO_4 . Evaporation of the solvent under reduced pressure and recrystallization afforded sulfonaminobenzyl chloride as a solid^[1].

General procedure for the synthesis of other sulfonaminobenzyl chloride compounds



To a solution of 2-amino-phenyl ethanone (10.0 mmol) in ethanol (20.0 mL) was added NaBH_4 (20mmol). The reaction solution was then allowed to warm to 50°C and stirred for 2h. The reaction solution was then treated with saturated NaHCO_3 aq, extracted with ethyl acetate. The combined organic layers were dried over Na_2SO_4 and concentrated in vacuo to give the corresponding alcohols quantitatively.

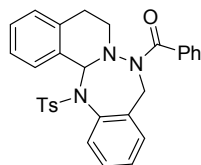
C: General procedure for the [4 + 3] annulation reactions



To a solution of THF(2.0mL) were added sulfonaminobenzyl chlorides **1**(0.10mmol), C,N-cyclic azomethine imines **2** (0.11mmol), base (Na_2CO_3 , 0.20mmol) The reaction mixture was stirred at room temperature for 1-2h and then the reaction mixture was extracted with H_2O and DCM, dried with Na_2SO_4 and then concentrated. After the removal of the solvent, the residue was purified by silica gel chromatography to yield the desired product **3**.

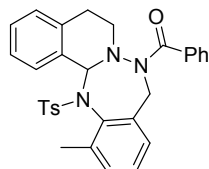
D: ¹H and ¹³C NMR spectra of all products

Phenyl(14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)methanone (3aa)



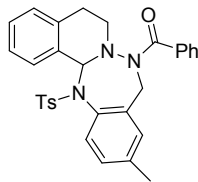
White solid, 99% yield, mp 217-219 °C. IR spectrum, ν_{\max} , cm^{-1} : 421, 526, 576, 646, 703, 712, 759, 816, 920, 988, 1070, 1160, 1240, 1260, 1350, 1400, 1440, 1500, 1650, 2840, 2910, 3050. ¹H NMR (400 MHz, CDCl₃): δ (ppm) 7.91 (d, J = 7.9 Hz, 1H), 7.62 – 7.58 (m, 2H), 7.56 (d, J = 12.2 Hz, 2H), 7.43 – 7.37 (m, 3H), 7.35– 7.31 (m, 2H), 7.28 (d, J = 1.6 Hz, 1H), 7.22 – 7.14 (m, 5H), 6.89 (d, J = 7.5 Hz, 1H), 6.45 (s, 1H), 4.25 (d, J = 16.5 Hz, 1H), 4.02 (d, J = 16.5 Hz, 1H), 2.84 – 2.77 (m, 1H), 2.49 (dd, J = 11.9, 2.0 Hz, 1H), 2.45 (s, 3H), 2.43 – 2.37 (m, 1H), 2.26 (d, J = 12.4 Hz, 1H). ¹³C NMR (100 MHz, CDCl₃): δ (ppm) 173.45, 144.14, 137.43, 136.49, 135.46, 134.93, 133.60, 133.51, 133.15, 130.03, 129.76, 129.74, 128.95, 128.16, 127.92, 127.85, 127.09, 126.84, 126.19, 74.93, 51.07, 47.31, 30.22, 21.78. HRMS (ESI): exact mass calculated for M⁺ (C₃₀H₂₆N₃O₃S) requires m/z 508.1689, found m/z 508.1695.

(13-methyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ba)



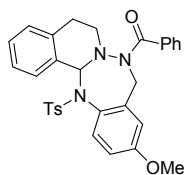
White solid, 98% yield, mp 188-190°C. IR spectrum, ν_{\max} , cm^{-1} : 461, 546, 598, 667, 733, 742, 779, 839, 933, 995, 1090, 1160, 1230, 1290, 1340, 1400, 1460, 1490, 1650, 2860, 2930, 3050. ¹H NMR (400 MHz, CDCl₃): δ (ppm) 8.11 (d, J = 7.9 Hz, 1H), 7.64 (d, J = 8.1 Hz, 2H), 7.54–7.47 (m, 2H), 7.37 – 7.28 (m, 6H), 7.22–7.14 (m, 2H), 7.11 (d, J = 7.3 Hz, 1H), 7.00 (d, J = 7.2 Hz, 1H), 6.87 (d, J = 7.5 Hz, 1H), 6.40 (s, 1H), 4.22 (d, J = 16.4 Hz, 1H), 3.81 (d, J = 16.4 Hz, 1H), 2.80 – 2.72 (m, 1H), 2.47 (s, 3H), 2.41 – 2.30 (m, 2H), 2.15 (d, J = 7.5 Hz, 1H), 1.96 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ (ppm) 172.66, 144.39, 142.61, 137.96, 136.37, 136.02, 134.44, 133.33, 132.85, 131.92, 130.64, 130.20, 129.76, 129.55, 128.25, 128.14, 127.88, 127.47, 127.29, 126.38, 126.24, 75.81, 51.88, 47.91, 29.76, 21.84, 19.61. HRMS (ESI): exact mass calculated for M⁺ (C₃₁H₂₈N₃O₃S) requires m/z 522.1846, found m/z 522.1851.

(11-methyl-14-tosyl-5,6,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ca)



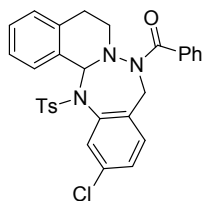
White solid, 98% yield, mp 164-166°C. IR spectrum, ν_{\max} , cm^{-1} : 484, 532, 586, 606, 663, 717, 783, 843, 930, 1040, 1090, 1160, 1230, 1330, 1400, 1450, 1490, 1600, 1640, 1810, 2860, 2930, 3050. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.88 (d, $J = 7.9$ Hz, 1H), 7.58 – 7.54 (m, 4H), 7.41 – 7.35 (m, 3H), 7.30 (t, $J = 7.6$ Hz, 1H), 7.26 (d, $J = 8.0$ Hz, 2H), 7.15 (t, $J = 6.9$ Hz, 1H), 7.02 (d, $J = 8.0$ Hz, 1H), 6.97 (d, $J = 8.2$ Hz, 1H), 6.92 (s, 1H), 6.87 (d, $J = 7.5$ Hz, 1H), 6.41 (s, 1H), 4.17 (d, $J = 16.5$ Hz, 1H), 3.97 (d, $J = 16.5$ Hz, 1H), 2.82 – 2.75 (m, 1H), 2.53 – 2.45 (m, 1H), 2.44 (s, 3H), 2.41 – 2.36 (m, 1H), 2.26 (d, $J = 19.5$ Hz, 4H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 173.46, 144.02, 139.89, 137.54, 136.63, 135.06, 134.96, 133.30, 133.26, 130.78, 130.01, 129.71, 129.66, 129.53, 128.99, 128.15, 127.86, 127.82, 127.14, 126.81, 126.20, 74.86, 51.06, 47.32, 30.27, 21.77, 21.26. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{31}\text{H}_{28}\text{N}_3\text{O}_3\text{S}$) requires m/z 522.1846, found m/z 522.1851.

(11-methoxy-14-tosyl-5,6,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3da)



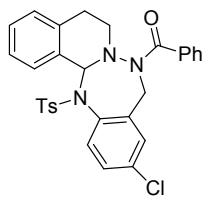
White solid, 91% yield, mp 209-211°C. IR spectrum, ν_{\max} , cm^{-1} : 463, 484, 542, 609, 617, 667, 719, 783, 841, 928, 1050, 1090, 1160, 1220, 1300, 1340, 1400, 1450, 1510, 1570, 1630, 1730, 2870, 2930, 3070. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.88 (d, $J = 7.9$ Hz, 1H), 7.56 (dd, $J = 10.5, 6.1$ Hz, 4H), 7.37 (d, $J = 4.2$ Hz, 3H), 7.30 (t, $J = 7.7$ Hz, 1H), 7.26 (d, $J = 7.9$ Hz, 2H), 7.15 (t, $J = 7.3$ Hz, 1H), 7.06 (d, $J = 8.6$ Hz, 1H), 6.88 (d, $J = 7.5$ Hz, 1H), 6.70 – 6.62 (m, 2H), 6.40 (s, 1H), 4.15 (d, $J = 16.6$ Hz, 1H), 3.94 (d, $J = 16.6$ Hz, 1H), 3.74 (s, 3H), 2.79 (dd, $J = 7.4, 2.6$ Hz, 1H), 2.52 (dd, $J = 15.7, 5.6$ Hz, 1H), 2.48 – 2.36 (m, 4H), 2.27 (d, $J = 19.1$ Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3): δ (ppm) 173.44, 160.22, 144.01, 137.37, 136.67, 136.51, 134.95, 134.61, 133.27, 129.99, 129.71, 128.92, 128.12, 127.84, 127.79, 127.10, 126.78, 126.18, 125.79, 114.56, 113.32, 74.76, 55.46, 51.11, 47.25, 30.24, 21.75. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{31}\text{H}_{28}\text{N}_3\text{O}_4\text{S}$) requires m/z 538.1795, found m/z 538.1801.

(12-chloro-14-tosyl-5,6,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ea)



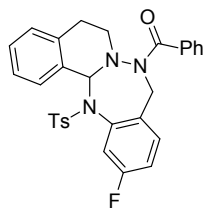
White solid, 90% yield, mp 176-178 °C . IR spectrum, ν_{\max} , cm^{-1} : 482, 540, 586, 665, 710, 783, 827, 931, 1020, 1090, 1160, 1230, 1340, 1400, 1450, 1490, 1600, 1650, 2860, 2930, 3070. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.85 (d, $J = 7.8$ Hz, 1H), 7.57 (d, $J = 8.0$ Hz, 4H), 7.40 (s, 3H), 7.35 (t, $J = 19.1$ Hz, 1H), 7.28 (d, $J = 7.1$ Hz, 2H), 7.22 – 7.16 (m, 3H), 7.09 (d, $J = 8.1$ Hz, 1H), 6.91 (d, $J = 7.3$ Hz, 1H), 6.44 (s, 1H), 4.24 (d, $J = 16.7$ Hz, 1H), 3.99 (d, $J = 16.7$ Hz, 1H), 2.88 – 2.79 (m, 1H), 2.56 – 2.49 (m, 1H), 2.44 (d, $J = 10.0$ Hz, 4H), 2.30 (d, $J = 14.7$ Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3): δ (ppm) 173.39, 144.44, 137.16, 136.22, 134.81, 134.14, 134.03, 133.51, 132.71, 130.14, 130.02, 129.90, 129.82, 128.77, 128.20, 128.14, 128.03, 127.10, 127.07, 126.21, 75.14, 50.63, 47.33, 30.19, 21.78. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{30}\text{H}_{25}\text{ClN}_3\text{O}_3\text{S}$) requires m/z 542.1300, found m/z 542.1305.

(11-chloro-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3fa)



White solid, 89% yield, mp 212-214 °C. IR spectrum, ν_{\max} , cm^{-1} : 490, 544, 590, 667, 731, 814, 935, 1030, 1090, 1160, 1290, 1340, 1400, 1450, 1500, 1600, 1650, 2860, 2930, 3060. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.85 (d, $J = 7.9$ Hz, 1H), 7.57 (dd, $J = 11.5, 6.0$ Hz, 4H), 7.43 – 7.36 (m, 3H), 7.28 (d, $J = 8.2$ Hz, 2H), 7.19 – 7.08 (m, 5H), 6.90 (d, $J = 7.5$ Hz, 1H), 6.42 (s, 1H), 4.18 (d, $J = 16.7$ Hz, 1H), 4.00 (d, $J = 16.7$ Hz, 1H), 2.85 – 2.78 (m, 1H), 2.56 – 2.48 (m, 1H), 2.43 (d, $J = 15.8$ Hz, 4H), 2.30 (d, $J = 19.9$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 173.38, 144.40, 137.30, 137.16, 136.18, 135.53, 134.87, 132.82, 132.20, 130.17, 129.91, 129.11, 128.90, 128.81, 128.20, 128.07, 127.95, 127.07, 126.94, 126.24, 74.95, 50.68, 47.28, 30.17, 21.78. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{30}\text{H}_{25}\text{ClN}_3\text{O}_3\text{S}$) requires m/z 542.1300, found m/z 542.1305.

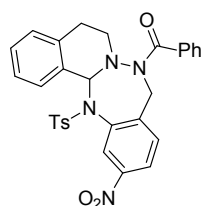
(12-fluoro-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ga)



White solid, 89% yield, mp 118-120 °C. IR spectrum, ν_{\max} , cm^{-1} : 469, 549, 567, 590, 687, 738, 829, 939, 1030, 1090, 1140, 1250, 1360, 1400, 1480, 1500, 1610, 1680, 2870, 2960, 3040. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.84 (d, $J = 7.9$

Hz, 1H), 7.57 (d, $J = 7.6$ Hz, 4H), 7.38 (d, $J = 4.6$ Hz, 3H), 7.34 – 7.29 (m, 1H), 7.30 – 7.26 (s, 1H), 7.17 (t, $J = 7.5$ Hz, 2H), 7.14 – 7.08 (m, 1H), 6.98 (dd, $J = 11.3, 5.0$ Hz, 1H), 6.91 (dd, $J = 10.9, 4.5$ Hz, 2H), 6.42 (s, 1H), 4.24 (d, $J = 16.4$ Hz, 1H), 3.98 (d, $J = 16.4$ Hz, 1H), 2.84 – 2.77 (m, 1H), 2.50 (d, $J = 9.9$ Hz, 1H), 2.42 (d, $J = 13.3$ Hz, 5H), 2.28 (d, $J = 19.2$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 173.35, 163.27, 160.79, 144.41, 137.26, 136.34, 135.15, 135.04, 134.88, 132.78, 131.44, 131.40, 130.13, 130.01, 129.92, 129.84, 128.75, 128.18, 128.12, 127.99, 127.08, 127.01, 126.19, 120.89, 120.68, 117.07, 116.86, 75.19, 50.51, 47.43, 30.18, 21.76. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{30}\text{H}_{25}\text{FN}_3\text{O}_3\text{S}$) requires m/z 526.1595, found m/z 526.1601.

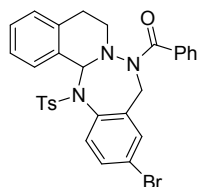
(12-nitro-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ha)



White solid, 81% yield, mp 145-147 °C. IR spectrum, ν_{max} , cm^{-1} :

540, 586, 665, 708, 785, 831, 933, 1030, 1090, 1160, 1220, 1350, 1410, 1530, 1650, 2860, 2930. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 8.13 (dd, $J = 8.4, 2.0$ Hz, 1H), 7.96 (d, $J = 3.9$ Hz, 1H), 7.81 (d, $J = 7.9$ Hz, 1H), 7.60 (dd, $J = 7.0, 2.0$ Hz, 2H), 7.56 (d, $J = 8.1$ Hz, 2H), 7.44 – 7.39 (m, 3H), 7.29 (d, $J = 8.1$ Hz, 2H), 7.19 (dd, $J = 12.4, 7.6$ Hz, 2H), 6.90 (d, $J = 7.5$ Hz, 1H), 6.48 (s, 1H), 4.40 (d, $J = 17.4$ Hz, 1H), 4.26 (d, $J = 17.4$ Hz, 1H), 2.85 (m, 1H), 2.53 – 2.47 (m, 1H), 2.45 (d, $J = 7.9$ Hz, 4H), 2.31 (d, $J = 19.8$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 173.47, 147.99, 144.86, 143.39, 136.96, 135.79, 135.18, 134.71, 132.20, 130.35, 130.20, 129.69, 129.59, 128.66, 128.46, 128.31, 128.26, 128.17, 127.61, 127.42, 127.15, 126.42, 124.56, 75.16, 50.96, 47.23, 30.16, 21.83. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{30}\text{H}_{25}\text{N}_4\text{O}_5\text{S}$) requires m/z 553.1540, found m/z 553.1546.

(11-bromo-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ia)

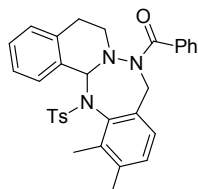


White solid, 88% yield, mp 206-208 °C. IR spectrum, ν_{max} , cm^{-1} :

444, 484, 540, 582, 663, 737, 781, 930, 1040, 1090, 1160, 1230, 1290, 1340, 1400, 1450, 1490, 1590, 1640, 2850, 2930, 3070. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.84 (d, $J = 7.8$ Hz, 1H), 7.56 (t, $J = 8.2$ Hz, 4H), 7.38 (d, $J = 3.5$ Hz, 3H), 7.29 (t, $J = 8.0$ Hz, 5H), 7.16 (t, $J = 7.3$ Hz, 2H), 7.03 (d, $J = 8.0$ Hz, 1H), 6.90 (d, $J = 7.5$ Hz, 1H), 6.41 (s, 1H), 4.17 (d, $J = 16.7$ Hz, 1H), 4.00 (d, $J = 16.7$ Hz, 1H), 2.81 (dd, $J = 7.4, 2.6$ Hz, 1H), 2.55 – 2.49 (m, 1H), 2.43 (d, $J = 15.9$ Hz, 5H), 2.30 (d, $J = 19.9$ Hz, 1H).

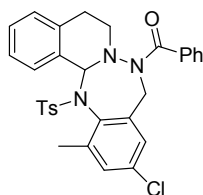
^{13}C NMR (100 MHz, CDCl_3): $\delta(\text{ppm})$ 173.37, 144.42, 137.61, 137.17, 136.18, 135.14, 134.89, 132.81, 132.77, 132.15, 131.84, 130.19, 129.93, 128.82, 128.21, 128.09, 127.97, 127.08, 126.95, 126.26, 123.68, 74.95, 50.59, 47.32, 30.19, 21.80. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{30}\text{H}_{25}\text{BrN}_3\text{O}_3\text{S}$) requires m/z 586.0795, found m/z 586.0800.

(12,13-dimethyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ja)



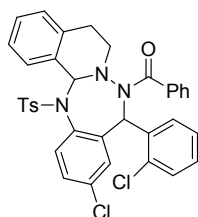
White solid, 96% yield, mp 205-207 °C. IR spectrum, ν_{max} , cm^{-1} : 451, 538, 600, 669, 708, 750, 835, 931, 995, 1100, 1160, 1230, 1290, 1360, 1440, 1570, 1630, 2940, 3050. ^1H NMR (400 MHz, CDCl_3): $\delta(\text{ppm})$ 8.11 (d, $J = 7.8$ Hz, 1H), 7.63 (d, $J = 8.0$ Hz, 2H), 7.53 – 7.48 (m, 2H), 7.32 (dd, $J = 14.9, 6.0$ Hz, 5H), 7.16 (t, $J = 7.3$ Hz, 1H), 7.07 (s, 1H), 6.88 (dd, $J = 16.3, 7.6$ Hz, 2H), 6.41 (s, 1H), 4.20 (d, $J = 16.2$ Hz, 1H), 3.78 (d, $J = 16.2$ Hz, 1H), 2.78 – 2.72 (m, 1H), 2.46 (s, 3H), 2.43 – 2.29 (m, 2H), 2.13 (d, $J = 10.8$ Hz, 4H), 1.83 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3): $\delta(\text{ppm})$ 172.57, 144.28, 141.17, 139.11, 138.06, 136.47, 134.47, 133.12, 133.05, 132.63, 130.95, 130.58, 130.13, 129.68, 128.13, 128.09, 127.88, 127.27, 126.72, 126.28, 126.23, 75.84, 51.84, 47.95, 29.70, 21.81, 20.76, 16.51. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{32}\text{H}_{31}\text{N}_3\text{O}_3\text{S}$) requires m/z 536.2013, found m/z 522.2008.

(11-chloro-13-methyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ka)



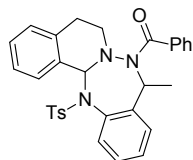
White solid, 85% yield, mp 180-182 °C. IR spectrum, ν_{max} , cm^{-1} : 472, 544, 604, 665, 698, 750, 854, 935, 997, 1090, 1160, 1230, 1290, 1350, 1400, 1450, 1490, 1580, 1650, 2250, 2930, 3010. ^1H NMR (400 MHz, CDCl_3): $\delta(\text{ppm})$ 8.07 (d, $J = 7.8$ Hz, 1H), 7.64 (d, $J = 8.0$ Hz, 2H), 7.54 – 7.47 (m, 2H), 7.33 (m, 6H), 7.18 (t, $J = 7.4$ Hz, 1H), 7.11 (s, 1H), 7.00 (s, 1H), 6.89 (d, $J = 7.5$ Hz, 1H), 6.38 (s, 1H), 4.15 (d, $J = 16.6$ Hz, 1H), 3.78 (d, $J = 16.6$ Hz, 1H), 2.83 – 2.74 (m, 1H), 2.52 – 2.34 (m, 5H), 2.21 (d, $J = 15.1$ Hz, 1H), 1.93 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3): $\delta(\text{ppm})$ 172.59, 144.64, 144.60, 137.79, 137.65, 136.05, 134.99, 134.35, 132.55, 132.07, 131.62, 130.53, 130.31, 129.91, 128.39, 128.17, 127.96, 127.29, 127.25, 126.45, 126.27, 75.82, 51.49, 47.89, 29.72, 21.83, 19.65. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{31}\text{H}_{27}\text{ClN}_3\text{O}_3\text{S}$) requires m/z 556.1456, found m/z 556.1462.

(11-chloro-9-(2-chlorophenyl)-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone (3la)



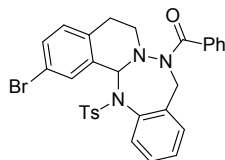
White solid, 90% yield, mp 160-162 °C. IR spectrum, ν_{\max} , cm^{-1} : 467, 546, 596, 675, 708, 742, 814, 866, 933, 1030, 1090, 1160, 1240, 1340, 1480, 1600, 1670, 2860, 2920, 3060. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.88 (d, $J = 7.9$ Hz, 1H), 7.72 (d, $J = 8.1$ Hz, 2H), 7.69 – 7.63 (m, 2H), 7.54 (d, $J = 7.7$ Hz, 1H), 7.41 – 7.32 (m, 7H), 7.29 (d, $J = 9.2$ Hz, 2H), 7.15 (s, 2H), 6.93 (d, $J = 7.5$ Hz, 1H), 6.50 (s, 1H), 6.35 (s, 1H), 6.25 (s, 1H), 3.51 – 3.44 (m, 1H), 2.76 – 2.67 (m, 1H), 2.51 – 2.43 (m, 5H), 2.35 (d, $J = 15.3$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 172.02, 144.59, 139.04, 137.95, 136.69, 136.27, 135.44, 134.78, 134.09, 133.65, 133.54, 133.15, 130.44, 130.29, 130.15, 129.59, 129.20, 129.15, 128.74, 128.19, 128.08, 127.94, 127.82, 127.60, 127.01, 126.90, 76.02, 61.19, 48.89, 30.02, 21.77. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{36}\text{H}_{28}\text{Cl}_2\text{N}_3\text{O}_3\text{S}$) requires m/z 652.1228, found m/z 652.1228.

(9-methyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ma)



White solid, 87% yield, mp 192-194 °C. IR spectrum, ν_{\max} , cm^{-1} : 571, 590, 661, 731, 775, 843, 889, 933, 1040, 1090, 1160, 1240, 1340, 1390, 1450, 1490, 1650, 2860, 2920, 3060. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.61 – 7.55 (m, 5H), 7.34 (d, $J = 8.6$ Hz, 4H), 7.29 (d, $J = 8.1$ Hz, 2H), 7.18 (dd, $J = 13.6, 6.2$ Hz, 2H), 7.14 – 7.08 (m, 2H), 6.99 (d, $J = 7.6$ Hz, 1H), 6.87 (d, $J = 7.4$ Hz, 1H), 6.05 (s, 1H), 5.19 (d, $J = 6.3$ Hz, 1H), 3.06 (s, 1H), 2.66 – 2.53 (m, 1H), 2.45 (d, $J = 11.7$ Hz, 4H), 2.29 (d, $J = 15.0$ Hz, 1H), 1.67 (d, $J = 6.5$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 171.89, 143.85, 139.80, 137.87, 137.52, 135.09, 134.25, 133.08, 132.69, 129.87, 129.67, 129.40, 128.65, 128.47, 127.89, 127.75, 127.50, 127.18, 126.61, 126.43, 74.46, 54.25, 47.58, 30.06, 21.75, 19.51. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{31}\text{H}_{28}\text{N}_3\text{O}_3\text{S}$) requires m/z 522.1846, found m/z 522.1851.

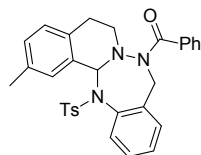
(2-bromo-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ab)



White solid, 86% yield, mp 204-206 °C. IR spectrum, ν_{\max} , cm^{-1} :

480, 536, 584, 661, 723, 781, 873, 929, 1025, 1089, 1157, 1226, 1338, 1392, 1454, 1494, 1596, 1645, 1727, 2861, 2925, 3068. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.90 (d, $J = 7.9$ Hz, 1H), 7.58 (dd, $J = 6.6, 2.9$ Hz, 2H), 7.54 (d, $J = 8.3$ Hz, 2H), 7.39 – 7.36 (m, 3H), 7.32 (t, $J = 7.7$ Hz, 1H), 7.25 (d, $J = 2.7$ Hz, 1H), 7.16 (m, 5H), 6.87 (d, $J = 7.5$ Hz, 1H), 6.44 (s, 1H), 4.24 (d, $J = 16.5$ Hz, 1H), 4.01 (d, $J = 16.5$ Hz, 1H), 2.82 – 2.76 (m, 1H), 2.47 (dd, $J = 11.8, 2.3$ Hz, 1H), 2.42 (d, $J = 12.4$ Hz, 4H), 2.25 (d, $J = 12.5$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 173.48, 144.16, 137.48, 136.53, 135.51, 134.96, 133.64, 133.57, 133.19, 130.06, 129.79, 129.75, 128.99, 128.96, 128.19, 127.94, 127.87, 127.13, 126.87, 126.23, 74.97, 51.11, 47.35, 30.26, 21.79. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{30}\text{H}_{25}\text{BrN}_3\text{O}_3\text{S}$) requires m/z 586.0795, found m/z 586.0800.

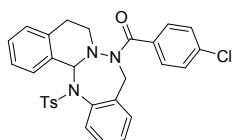
(2-methyl-14-tosyl-5,6,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ac)



White solid, 88% yield, mp 166-168 °C. IR spectrum, ν_{\max} , cm^{-1} :

499, 540, 582, 661, 714, 814, 937, 1030, 1090, 1160, 1220, 1340, 1390, 1450, 1490, 1650, 2870, 2920, 3050. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.62 – 7.54 (m, 5H), 7.37 (dd, $J = 4.1, 2.3$ Hz, 3H), 7.26 (d, $J = 8.0$ Hz, 3H), 7.19 (t, $J = 7.2$ Hz, 1H), 7.16 – 7.12 (m, 2H), 6.96 (d, $J = 7.3$ Hz, 1H), 6.76 (d, $J = 7.7$ Hz, 1H), 6.39 (s, 1H), 4.26 (d, $J = 16.5$ Hz, 1H), 4.09 (d, $J = 16.5$ Hz, 1H), 2.78 (m, 1H), 2.43 (d, $J = 10.3$ Hz, 4H), 2.37 (s, 3H), 2.19 (d, $J = 14.8$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 173.50, 144.09, 137.63, 136.59, 136.41, 135.62, 133.71, 133.53, 132.95, 131.95, 130.01, 129.71, 129.09, 128.95, 128.87, 128.14, 127.73, 127.18, 126.23, 74.96, 51.12, 47.51, 29.79, 21.76, 21.39. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{31}\text{H}_{28}\text{N}_3\text{O}_3\text{S}$) requires m/z 522.1846, found m/z 522.1851.

(4-chlorophenyl)(14-tosyl-5,6,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)methanone(3ad)

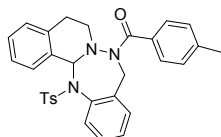


White solid, 89% yield, mp 224-226 °C. IR spectrum, ν_{\max} , cm^{-1} :

482, 538, 582, 665, 739, 783, 833, 930, 1040, 1090, 1160, 1220, 1290, 1340, 1420, 1490, 1650, 2870, 2920, 3060. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.84 (d, $J = 7.8$ Hz, 1H), 7.54 (dd, $J = 13.5, 8.2$ Hz, 4H), 7.36 (d, $J = 8.1$ Hz, 2H), 7.34 – 7.29 (m, 2H), 7.24 (s, 1H), 7.14 (m, 5H), 6.90 (d, $J = 7.4$ Hz, 1H), 6.40 (s, 1H), 4.25 (d, $J = 16.5$ Hz,

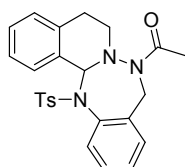
1H), 4.15 (d, $J = 16.5$ Hz, 1H), 2.80 (s, 1H), 2.52 – 2.37 (m, 5H), 2.28 (d, $J = 12.5$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): $\delta(\text{ppm})$ 172.14, 144.17, 137.42, 135.80, 135.39, 134.77, 133.54, 133.43, 132.94, 130.01, 129.80, 129.14, 129.00, 128.92, 128.87, 128.39, 128.03, 127.98, 127.93, 127.09, 126.91, 74.73, 51.05, 47.29, 30.18, 21.75. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{30}\text{H}_{25}\text{ClN}_3\text{O}_3\text{S}$) requires m/z 542.1300, found m/z 542.1305.

p-tolyl(14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)methanone(3ae)



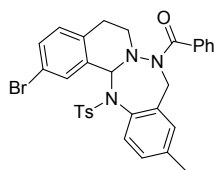
White solid, 89% yield, mp 208-210 °C. IR spectrum, ν_{max} , cm^{-1} : 482, 536, 582, 665, 727, 783, 825, 931, 1040, 1090, 1160, 1220, 1290, 1340, 1410, 1490, 1650, 1730, 2870, 2920, 3030. ^1H NMR (400 MHz, CDCl_3): $\delta(\text{ppm})$ 7.92 (d, $J = 7.9$ Hz, 1H), 7.51 (dd, $J = 10.3, 8.2$ Hz, 4H), 7.32 (t, $J = 10.1$, 1H), 7.24 (d, $J = 8.1$ Hz, 2H), 7.15 (m, 7H), 6.89 (d, $J = 7.5$ Hz, 1H), 6.45 (s, 1H), 4.22 (d, $J = 16.6$ Hz, 1H), 3.98 (d, $J = 16.6$ Hz, 1H), 2.83 – 2.75 (m, 1H), 2.50 – 2.38 (m, 5H), 2.34 (s, 3H), 2.26 (d, $J = 12.2$ Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3): $\delta(\text{ppm})$ 173.37, 144.11, 139.98, 137.46, 135.59, 134.99, 133.64, 133.54, 133.28, 130.02, 129.70, 129.04, 128.92, 128.77, 127.92, 127.86, 127.11, 126.85, 126.58, 74.99, 51.15, 47.29, 30.25, 21.77, 21.51. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{31}\text{H}_{28}\text{N}_3\text{O}_3\text{S}$) requires m/z 522.1846, found m/z 522.1851.

1-(14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)ethanone(3af)



White solid, 95% yield, mp 226-228 °C. IR spectrum, ν_{max} , cm^{-1} : 476, 540, 573, 613, 665, 735, 783, 827, 868, 930, 1010, 1090, 1160, 1220, 1340, 1390, 1450, 1490, 1680, 2870, 2930, 3060. ^1H NMR (400 MHz, CDCl_3): $\delta(\text{ppm})$ 8.00 (d, $J = 7.9$ Hz, 1H), 7.44 (d, $J = 8.3$ Hz, 2H), 7.40 – 7.34 (m, 1H), 7.25 (s, 1H), 7.22 (d, $J = 8.0$ Hz, 3H), 7.18 – 7.14 (m, 2H), 7.07 (d, $J = 7.4$ Hz, 1H), 7.00 (d, $J = 7.6$ Hz, 1H), 6.53 (s, 1H), 4.02 (d, $J = 16.5$ Hz, 1H), 3.95 (d, $J = 16.5$ Hz, 1H), 2.95-2.86 (m, 1H), 2.84 – 2.78 (m, 1H), 2.51 – 2.45 (m, 1H), 2.44 – 2.35 (m, 4H), 2.20 (s, 3H). ^{13}C NMR (100 MHz, CDCl_3): $\delta(\text{ppm})$ 173.42, 144.06, 137.44, 135.52, 134.88, 133.88, 133.47, 133.30, 130.03, 129.66, 129.25, 128.80, 128.13, 127.99, 127.04, 126.91, 74.35, 50.19, 46.90, 30.88, 21.76, 21.26. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{25}\text{H}_{24}\text{N}_3\text{O}_3\text{S}$) requires m/z 446.1533, found m/z 446.1538.

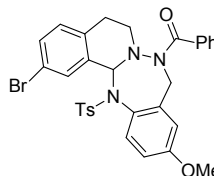
(2-bromo-11-methyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3cb)



White solid, 92% yield, mp 216-218 °C. IR spectrum, ν_{\max} , cm^{-1} :

484, 532, 586, 606, 663, 715, 783, 843, 930, 1040, 1090, 1160, 1230, 1320, 1330, 1400, 1450, 1490, 1570, 1640, 1730, 2860, 2930, 3050. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.88 (d, $J = 7.7$ Hz, 1H), 7.58 – 7.54 (m, 4H), 7.40 – 7.36 (m, 3H), 7.33 – 7.28 (m, 1H), 7.25 (d, $J = 7.7$ Hz, 1H), 7.15 (t, $J = 7.2$ Hz, 1H), 7.02 (d, $J = 7.9$ Hz, 1H), 6.97 (d, $J = 8.2$ Hz, 1H), 6.92 (s, 1H), 6.87 (d, $J = 7.5$ Hz, 1H), 6.40 (s, 1H), 4.17 (d, $J = 16.5$ Hz, 1H), 3.97 (d, $J = 16.5$ Hz, 1H), 2.77 (m, 1H), 2.52 – 2.47 (m, 1H), 2.44 (s, 3H), 2.41 – 2.36 (m, 1H), 2.26 (d, $J = 20.3$ Hz, 4H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 173.50, 144.06, 139.91, 137.56, 136.63, 135.07, 134.98, 133.29, 130.80, 130.03, 129.74, 129.69, 129.55, 129.03, 128.18, 127.88, 127.84, 127.16, 126.85, 126.23, 74.88, 51.08, 47.35, 30.29, 21.80, 21.28. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{31}\text{H}_{27}\text{BrN}_3\text{O}_3\text{S}$) requires m/z 600.0951, found m/z 600.0957.

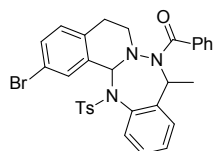
(2-bromo-11-methoxy-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3gb)



White solid, 89% yield, mp 197-199 °C. IR spectrum, ν_{\max} , cm^{-1} :

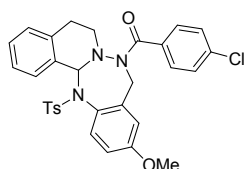
542, 609, 667, 719, 783, 841, 930, 1050, 1090, 1160, 1220, 1290, 1340, 1400, 1450, 1500, 1630, 2870, 2930. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.88 (d, $J = 7.9$ Hz, 1H), 7.59 – 7.52 (m, 4H), 7.40 – 7.35 (m, 3H), 7.31 (t, $J = 7.8$ Hz, 1H), 7.26 (d, $J = 8.0$ Hz, 2H), 7.16 (t, $J = 7.1$ Hz, 1H), 7.06 (d, $J = 8.6$ Hz, 1H), 6.88 (d, $J = 7.5$ Hz, 1H), 6.67 (dd, $J = 8.7, 2.7$ Hz, 1H), 6.63 (d, $J = 2.5$ Hz, 1H), 6.40 (s, 1H), 4.15 (d, $J = 16.6$ Hz, 1H), 3.93 (d, $J = 16.6$ Hz, 1H), 3.75 (s, 3H), 2.82 – 2.76 (m, 1H), 2.56 – 2.49 (m, 1H), 2.44 (s, 3H), 2.40 (dd, $J = 12.0, 4.6$ Hz, 1H), 2.27 (d, $J = 15.2$ Hz, 1H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 173.54, 160.28, 144.08, 137.43, 136.73, 136.55, 135.00, 134.69, 133.35, 130.05, 129.78, 129.01, 128.19, 127.89, 127.83, 127.17, 126.86, 126.25, 125.89, 114.62, 113.39, 74.83, 55.52, 51.19, 47.33, 30.31, 21.81. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{31}\text{H}_{27}\text{BrN}_3\text{O}_4\text{S}$) requires m/z 616.0900, found m/z 616.0906.

(2-bromo-9-methyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3mb)



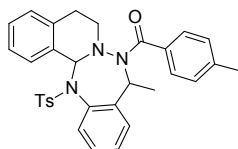
White solid, 87% yield, mp 188-190 °C. IR spectrum, ν_{\max} , cm^{-1} : 540, 590, 640, 661, 731, 781, 843, 889, 933, 1040, 1090, 1160, 1240, 1340, 1390, 1450, 1490, 1650, 1730, 2860, 2920, 3060. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.58 (d, $J = 7.4$ Hz, 5H), 7.35 (d, $J = 5.5$ Hz, 4H), 7.28 (d, $J = 8.1$ Hz, 2H), 7.20 (t, $J = 7.4$ Hz, 1H), 7.11 (m, 2H), 7.00 (d, $J = 7.6$ Hz, 1H), 6.87 (d, $J = 7.4$ Hz, 1H), 6.05 (s, 1H), 5.15 (d, $J = 6.3$ Hz, 1H), 3.06 (s, 1H), 2.65 – 2.53 (m, 1H), 2.45 (d, $J = 7.1$ Hz, 4H), 2.28 (d, $J = 15.0$ Hz, 1H), 1.66 (d, $J = 6.5$ Hz, 3H). ^{13}C NMR (100 MHz, CDCl_3): δ (ppm) 171.90, 143.88, 139.86, 137.91, 137.58, 135.13, 134.31, 133.17, 132.80, 129.91, 129.68, 129.44, 128.70, 128.58, 127.95, 127.79, 127.56, 127.20, 126.68, 126.47, 74.51, 54.28, 47.65, 30.13, 21.80, 19.57. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{31}\text{H}_{27}\text{BrN}_3\text{O}_3\text{S}$) requires m/z 600.0951, found m/z 600.0957.

(4-chlorophenyl)(11-methoxy-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)methanone(3gd)



White solid, 95% yield, mp 217-219 °C. IR spectrum, ν_{\max} , cm^{-1} : 482, 542, 607, 665, 748, 847, 930, 1050, 1090, 1160, 1220, 1290, 1340, 1410, 1450, 1500, 1610, 1640, 2870, 2930. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.83 (d, $J = 7.9$ Hz, 1H), 7.53 (t, $J = 8.8$ Hz, 4H), 7.35 (d, $J = 8.4$ Hz, 2H), 7.30 (t, $J = 7.6$ Hz, 1H), 7.24 (s, 1H), 7.17 (t, $J = 7.3$ Hz, 2H), 7.02 (d, $J = 8.5$ Hz, 1H), 6.90 (d, $J = 7.5$ Hz, 1H), 6.72 – 6.61 (m, 2H), 6.36 (s, 1H), 4.16 (d, $J = 16.6$ Hz, 1H), 4.06 (d, $J = 16.6$ Hz, 1H), 3.74 (s, 3H), 2.82 – 2.75 (m, 1H), 2.53 (m, 2H), 2.44 (s, 3H), 2.31 (d, $J = 14.8$ Hz, 1H). ^{13}C NMR (101 MHz, CDCl_3): δ (ppm) 172.21, 160.30, 144.08, 137.37, 136.60, 135.80, 134.81, 134.78, 134.51, 133.10, 130.00, 128.89, 128.39, 127.99, 127.89, 127.13, 126.89, 125.81, 114.58, 113.41, 74.60, 55.49, 51.13, 47.27, 30.23, 21.76. HRMS (ESI): exact mass calculated for M^+ ($\text{C}_{31}\text{H}_{27}\text{ClN}_3\text{O}_4\text{S}$) requires m/z 572.1405, found m/z 572.1411.

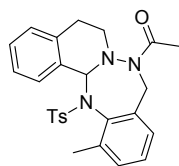
(9-methyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(p-tolyl)methanone(3me)



White solid, 90% yield, mp 201-203 °C. IR spectrum, ν_{\max} , cm^{-1} : 434, 563, 584, 665, 725, 773, 825, 893, 935, 1030, 1090, 1160, 1240, 1340, 1450, 1490, 1650, 2860, 2920, 3030. ^1H NMR (400 MHz, CDCl_3): δ (ppm) 7.62 (d, $J = 7.7$ Hz, 1H), 7.57 (d, $J = 7.9$ Hz, 2H), 7.50 (d, $J = 7.7$ Hz, 2H), 7.32 (d, $J = 7.2$ Hz, 1H), 7.28 (d, $J = 8.2$ Hz, 2H), 7.23 – 7.18 (m, 1H), 7.17 – 7.09 (m, 5H), 7.01 (d, $J = 7.5$ Hz,

1H), 6.89 (d, J = 7.4 Hz, 1H), 6.04 (s, 1H), 5.13 (d, J = 6.1 Hz, 1H), 3.07 (s, 1H), 2.72 – 2.62 (m, 1H), 2.43 (d, J = 8.7 Hz, 4H), 2.31 (d, J = 19.4 Hz, 4H), 1.64 (d, J = 6.6 Hz, 3H). ¹³C NMR (100 MHz, CDCl₃): δ(ppm) 171.77, 143.82, 139.92, 139.52, 137.92, 135.17, 134.35, 133.31, 132.81, 129.88, 129.63, 128.64, 128.55, 127.91, 127.75, 127.56, 127.18, 126.79, 126.67, 77.48, 77.16, 76.84, 74.49, 54.22, 47.64, 30.11, 21.79, 21.53, 19.59. HRMS (ESI): exact mass calculated for M⁺ (C₃₂H₃₀N₃O₃S) requires m/z 536.2002, found m/z 536.2008.

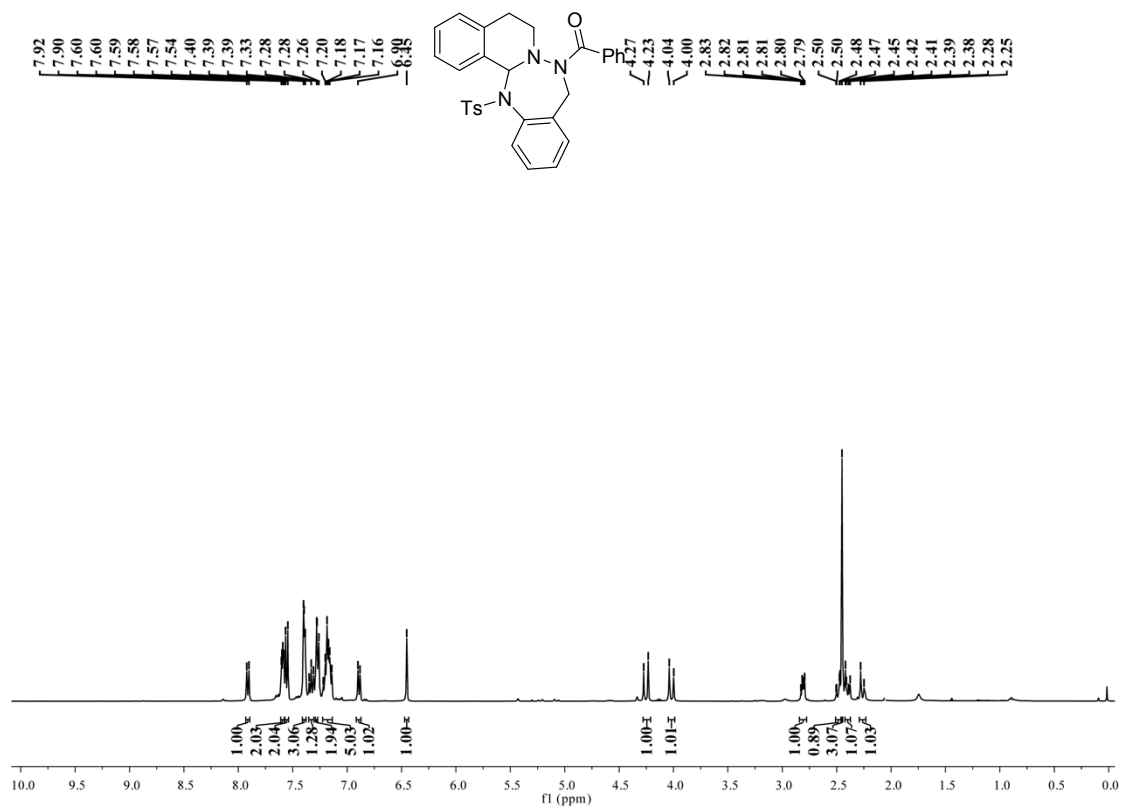
1-(13-methyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)ethanone(3bf)

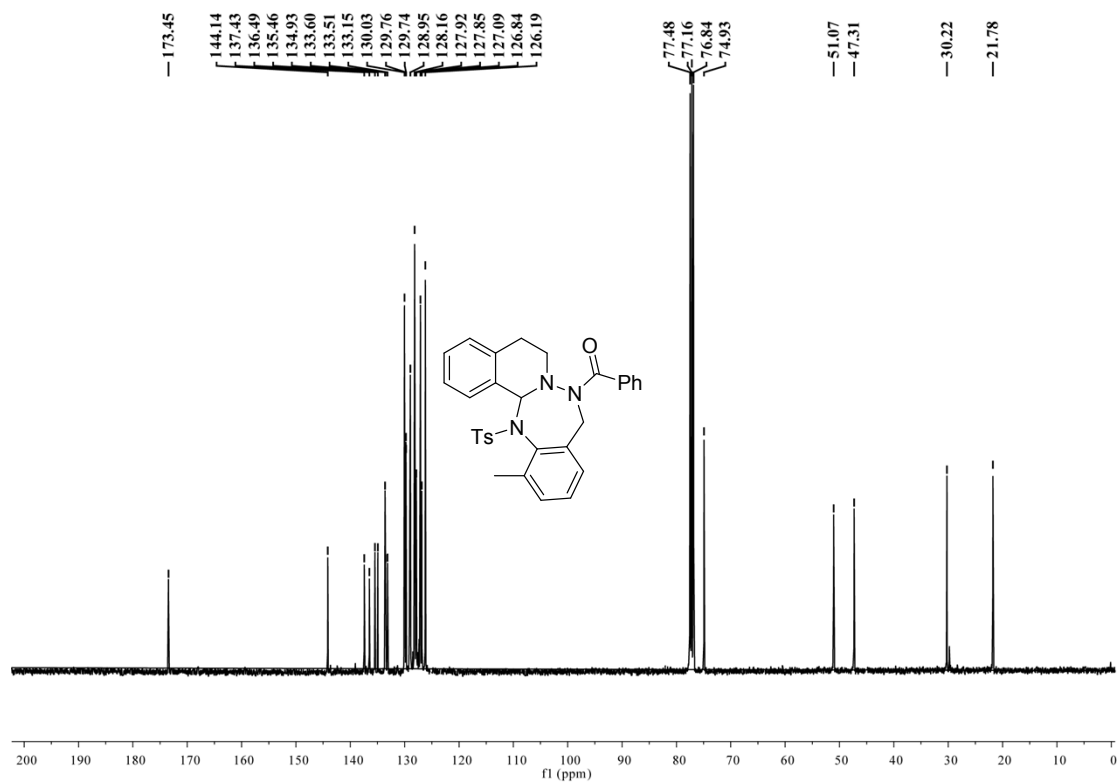


White solid, 89% yield, mp 212-214 °C. IR spectrum, ν_{\max} , cm⁻¹:

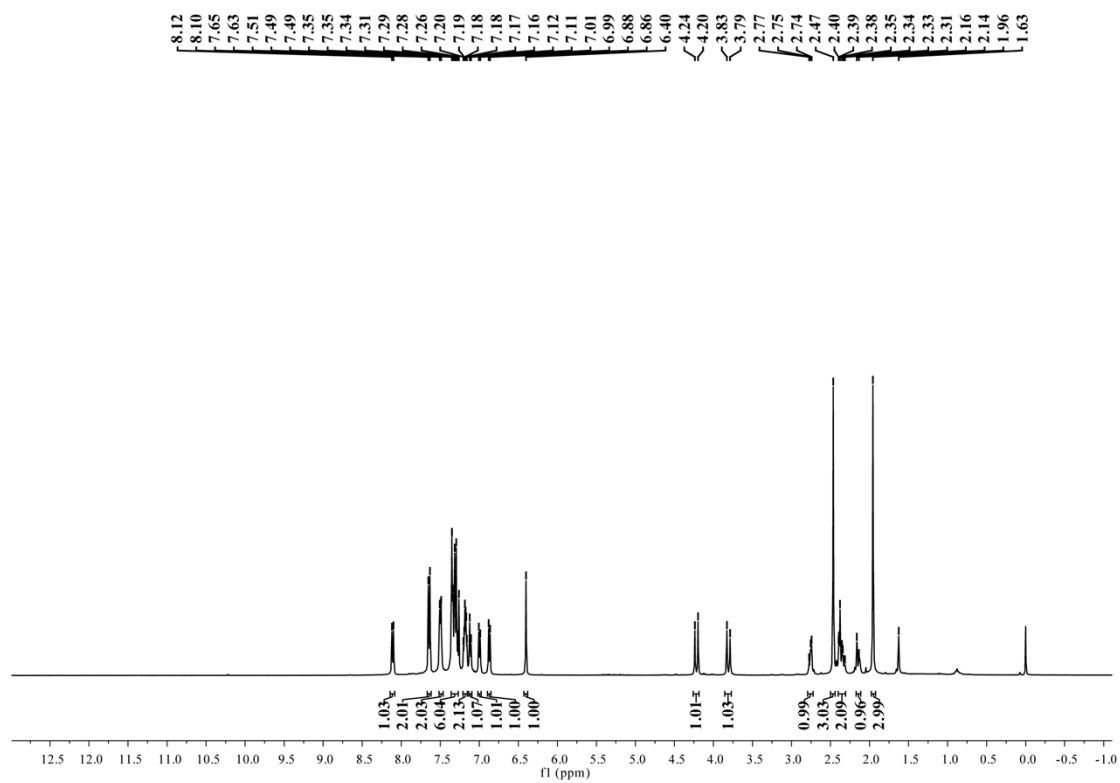
469, 540, 598, 665, 675, 771, 814, 933, 1000, 1090, 1160, 1230, 1290, 1350, 1390, 1460, 1600, 1670, 2860, 2920. ¹H NMR (400 MHz, CDCl₃): δ(ppm) 8.23 (d, J = 7.8 Hz, 1H), 7.55 (d, J = 8.2 Hz, 2H), 7.36 (t, J = 7.5 Hz, 1H), 7.27 (s, 1H), 7.24 (d, J = 5.8 Hz, 2H), 7.16 (t, J = 7.5 Hz, 1H), 7.10 (d, J = 7.3 Hz, 1H), 7.00 (d, J = 7.6 Hz, 1H), 6.93 (d, J = 7.2 Hz, 1H), 6.47 (s, 1H), 4.01 (d, J = 16.3 Hz, 1H), 3.78 (d, J = 16.3 Hz, 1H), 2.87–2.77 (m, 2H), 2.45 (s, 3H), 2.44–2.30 (m, 2H), 2.12 (s, 3H), 2.00 (s, 3H). ¹³C NMR (100 MHz, CDCl₃): δ(ppm) 172.98, 144.27, 142.69, 137.85, 135.98, 134.46, 133.25, 133.00, 131.62, 130.70, 130.11, 129.45, 128.42, 128.02, 127.22, 127.06, 126.56, 77.48, 77.16, 76.84, 75.01, 51.03, 47.35, 30.38, 21.77, 21.14, 19.62. HRMS (ESI): exact mass calculated for M⁺ (C₂₆H₂₆N₃O₃S) requires m/z 460.1689, found m/z 460.1695.

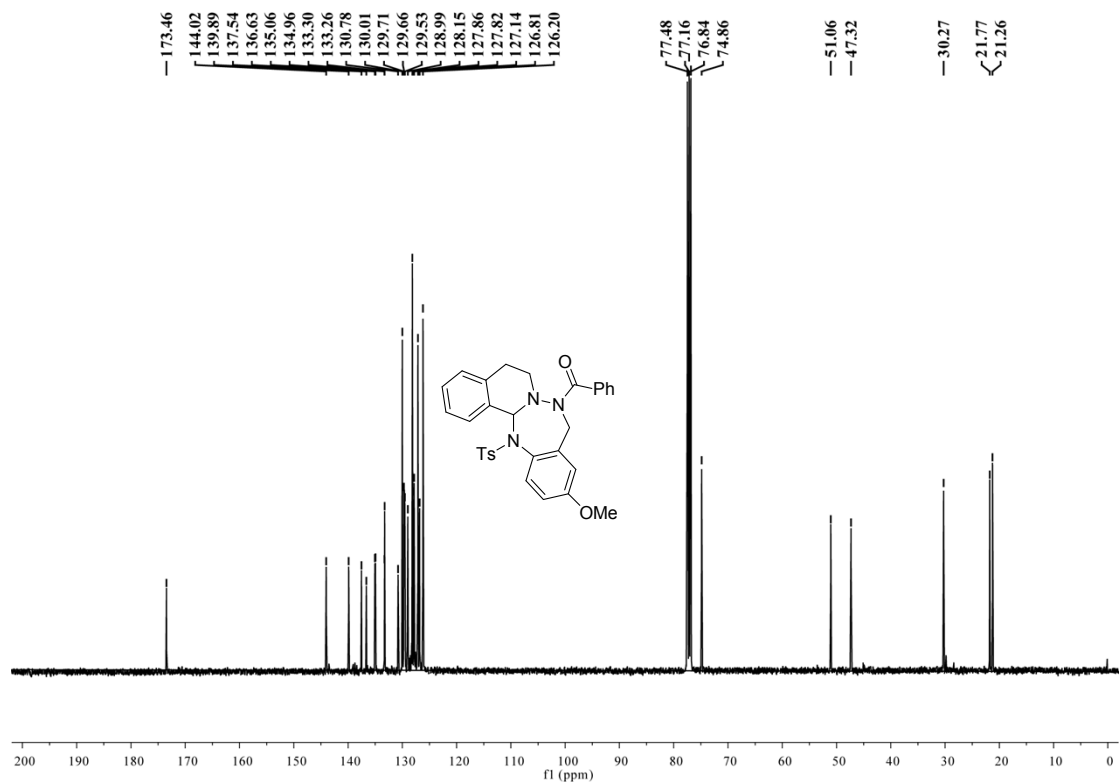
Phenyl(14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)methanone(3aa)



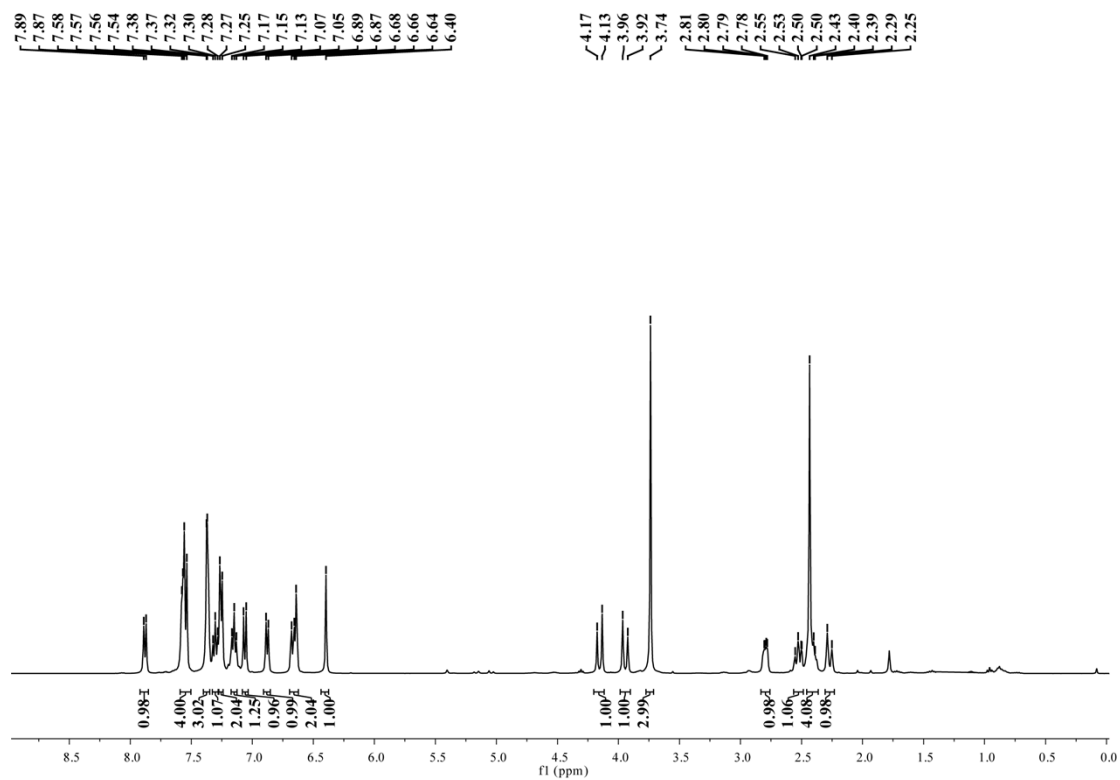


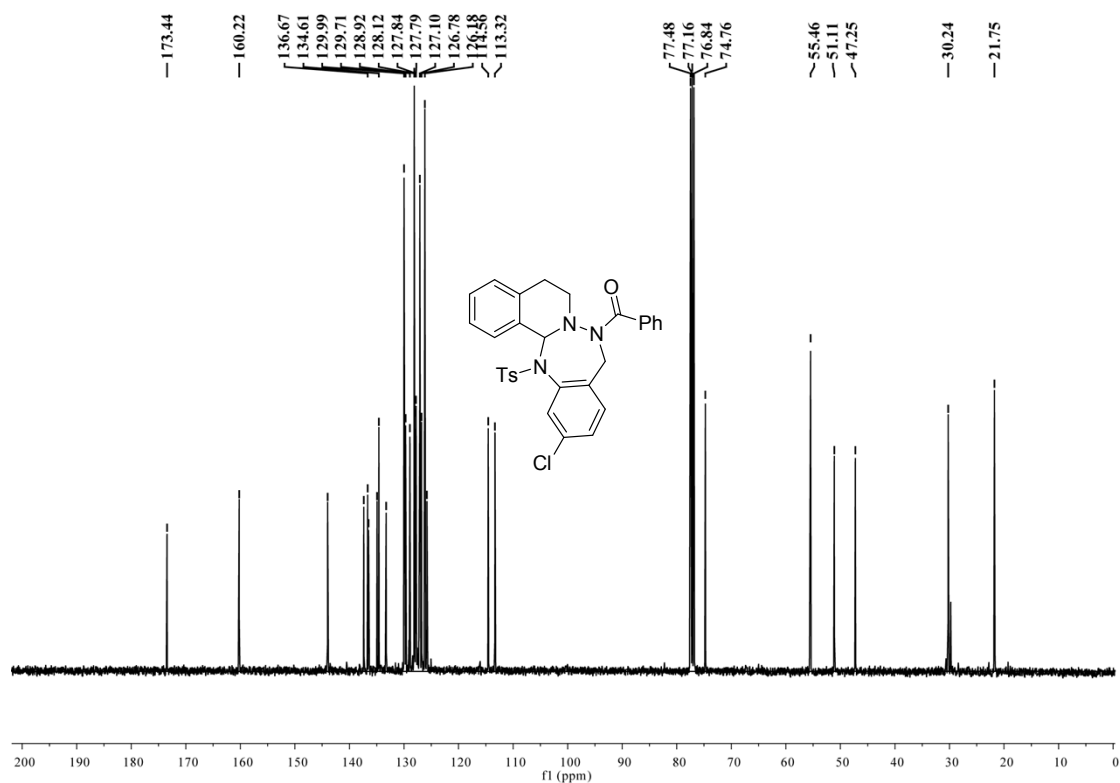
(13-methyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ba)



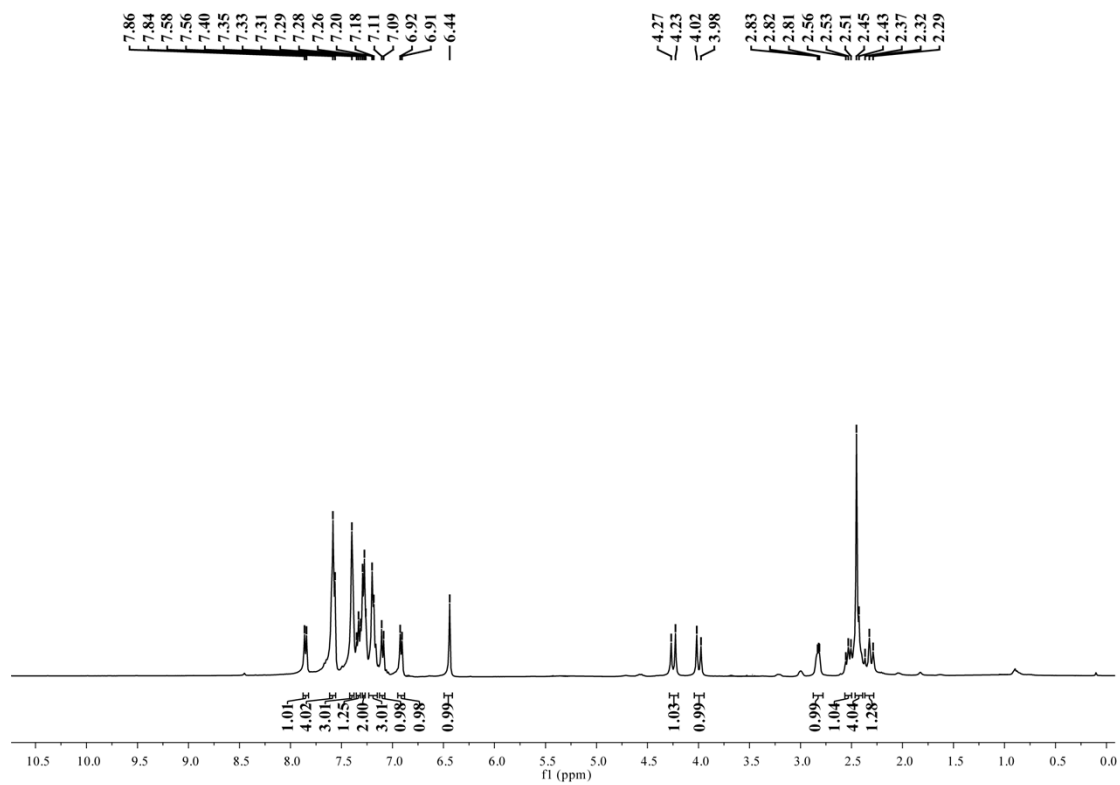


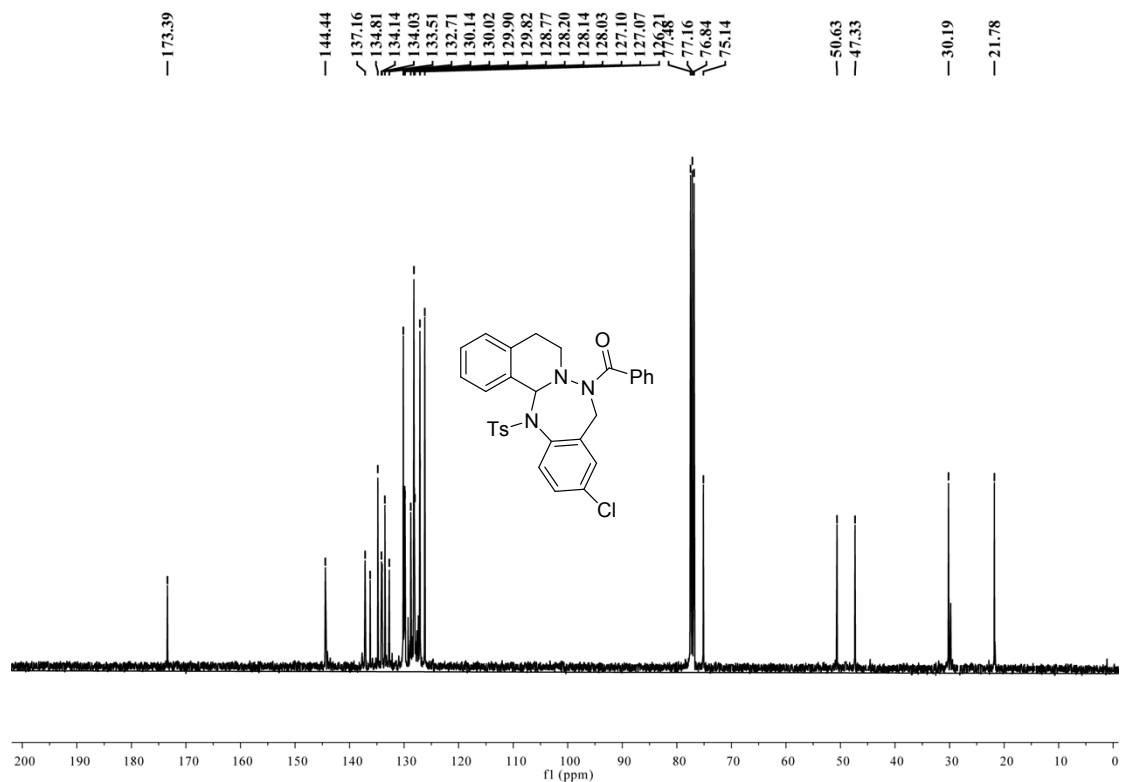
(11-methoxy-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3da)



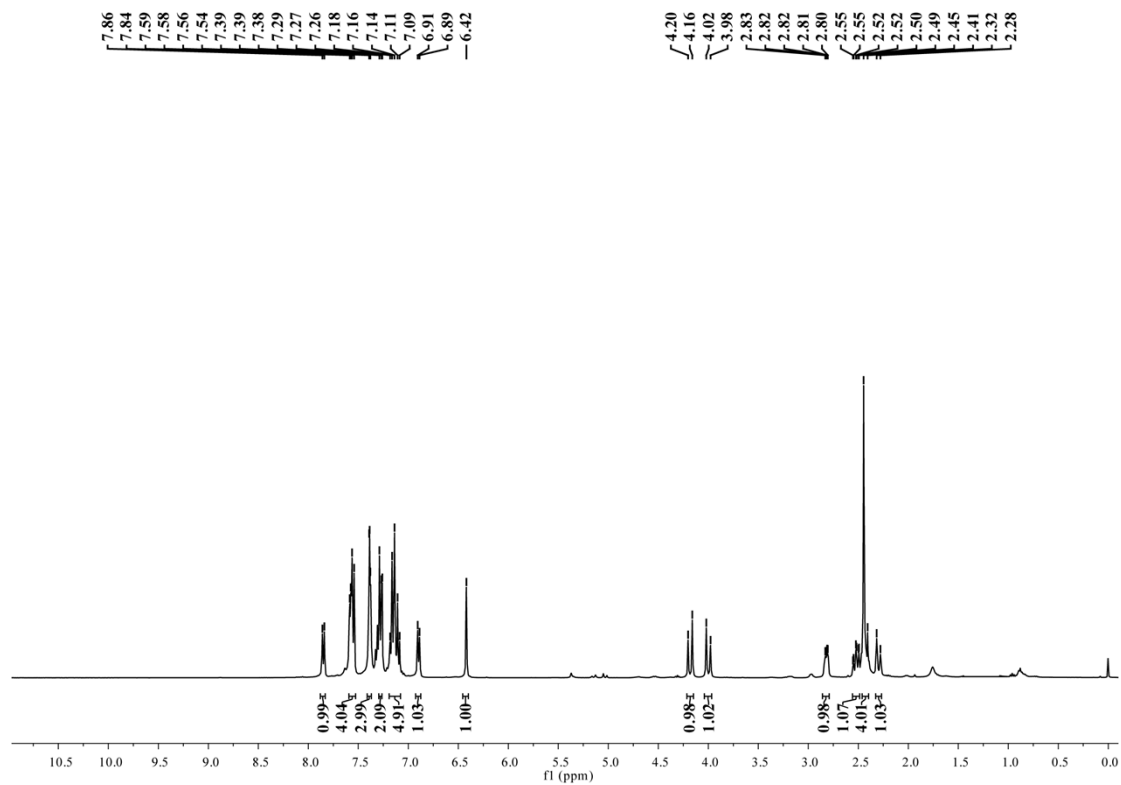


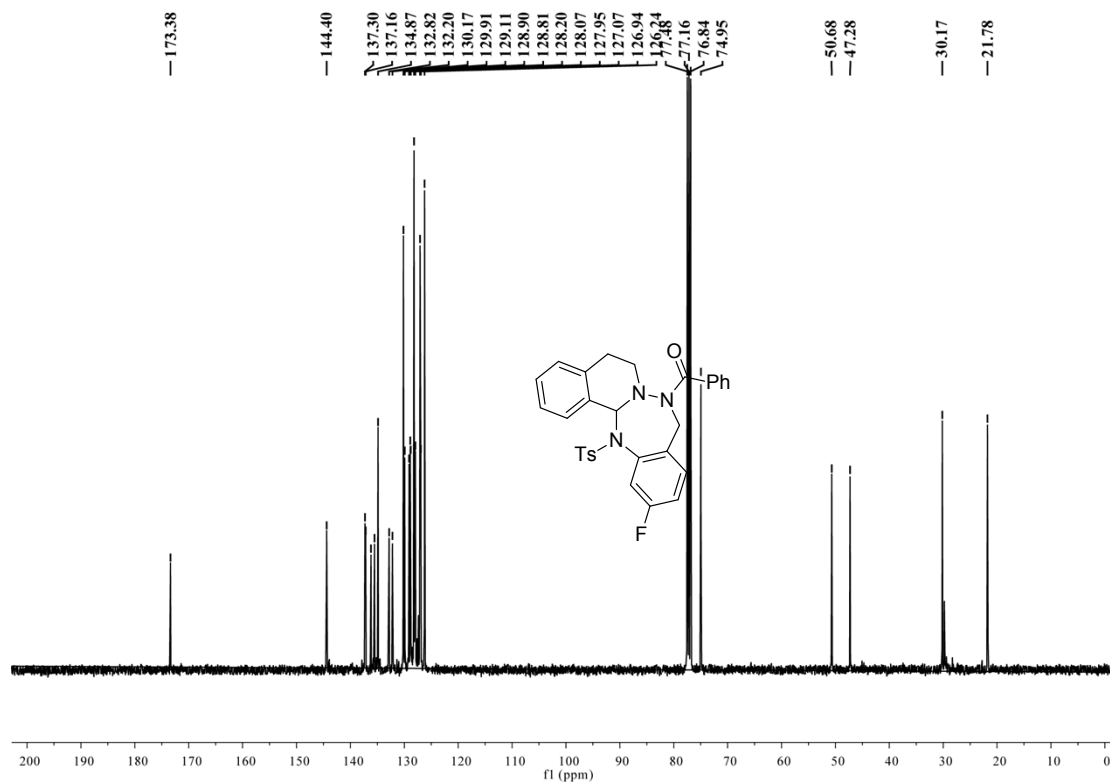
(12-chloro-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ea)



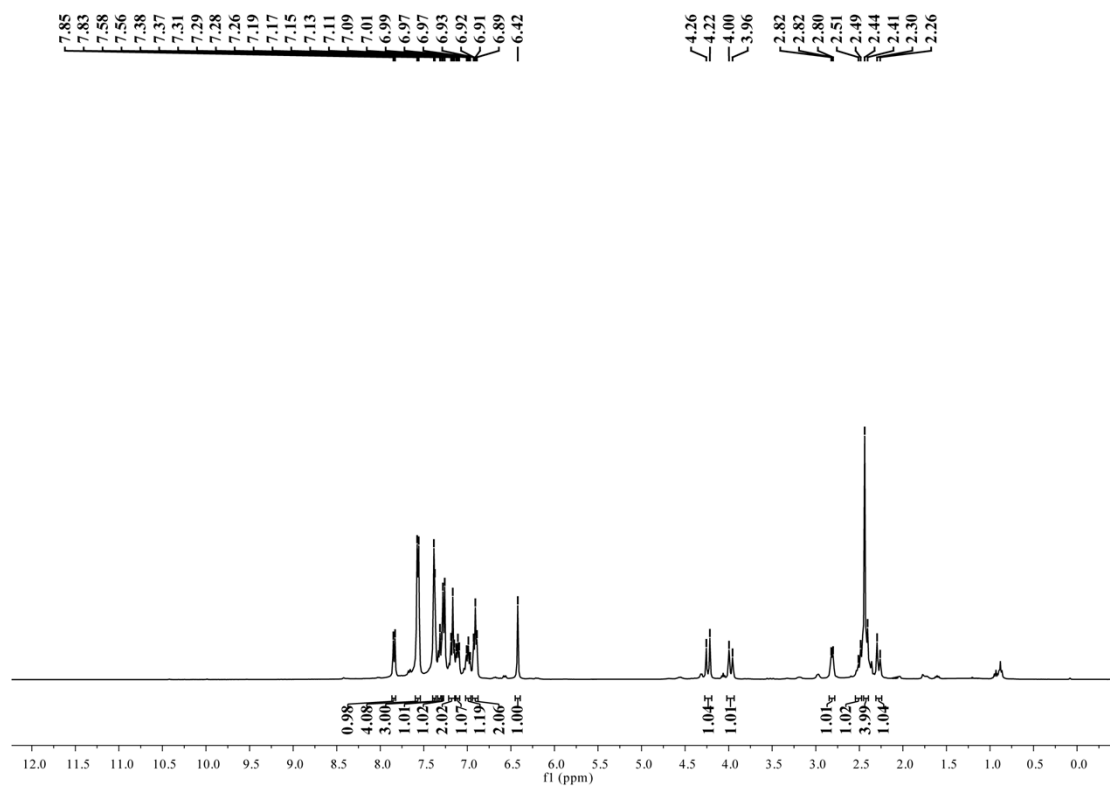


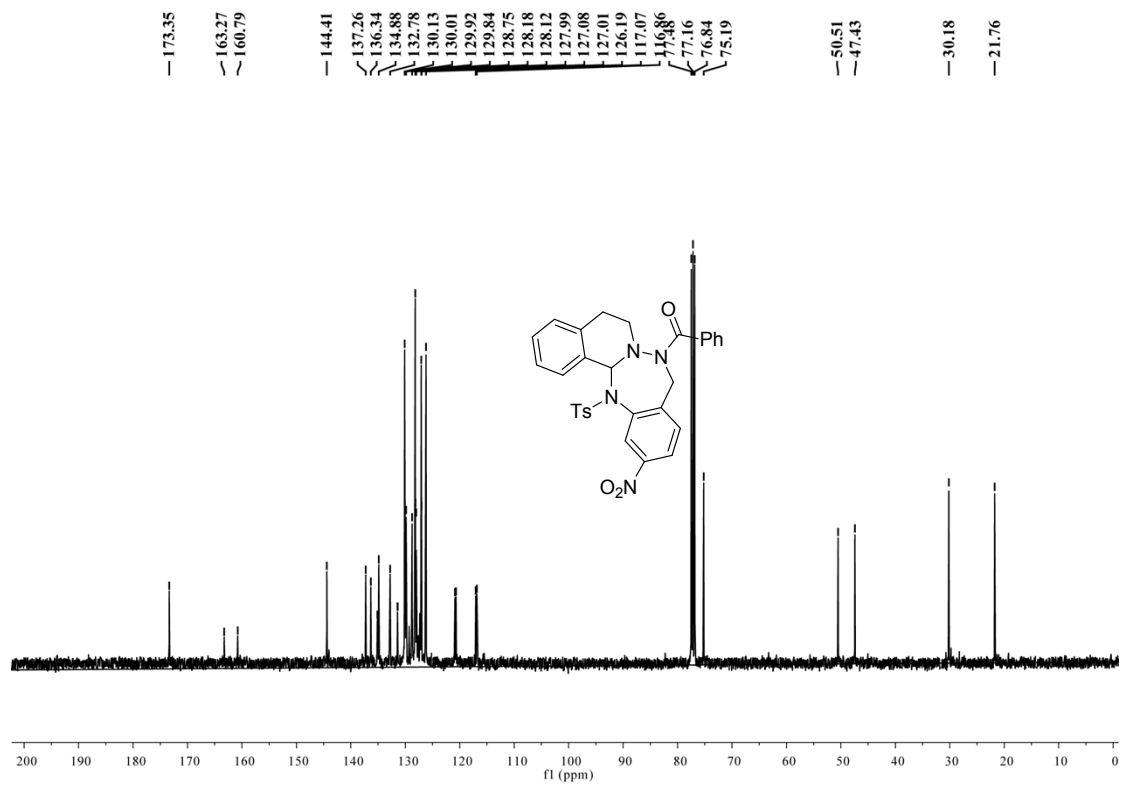
(11-chloro-14-tosyl-5,6,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3fa)



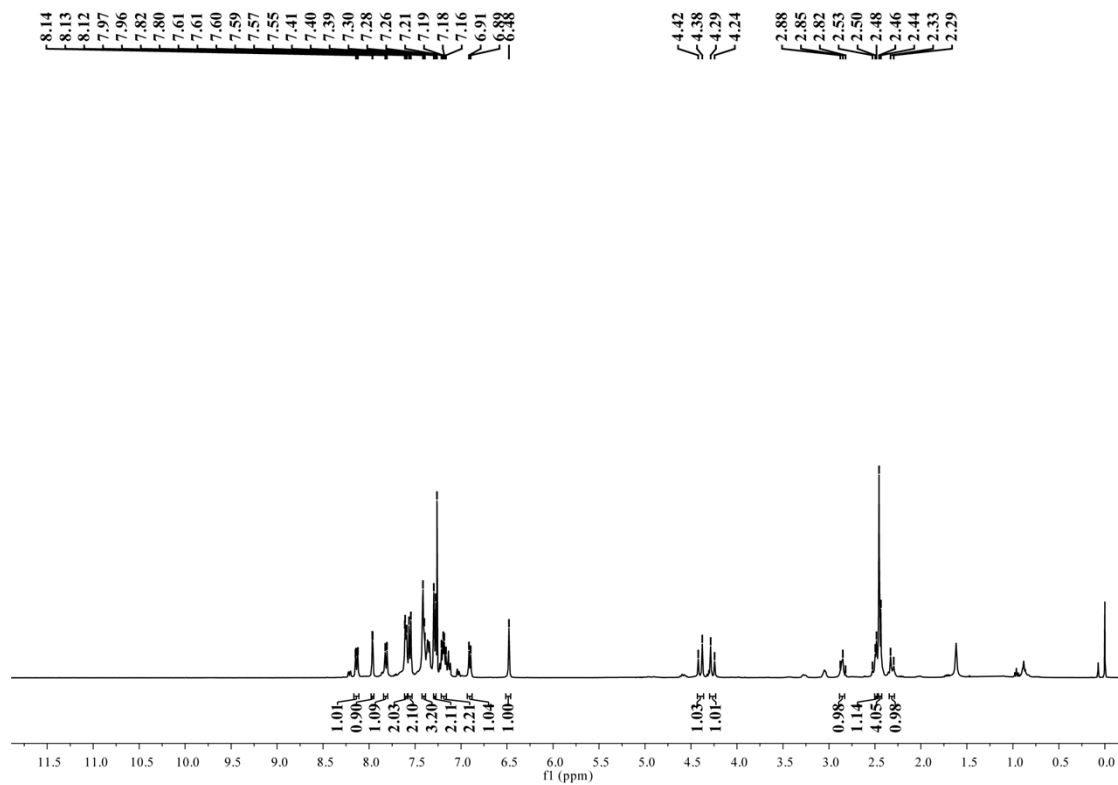


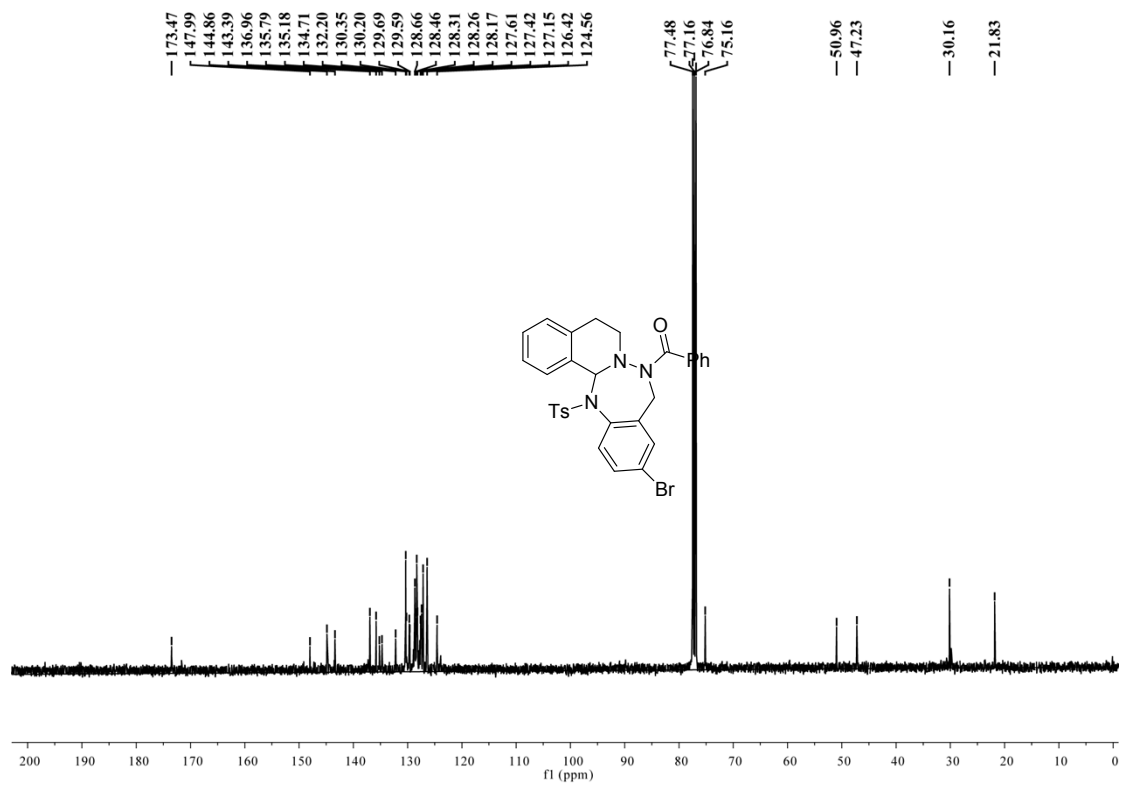
(12-fluoro-14-tosyl-5,6,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ga)



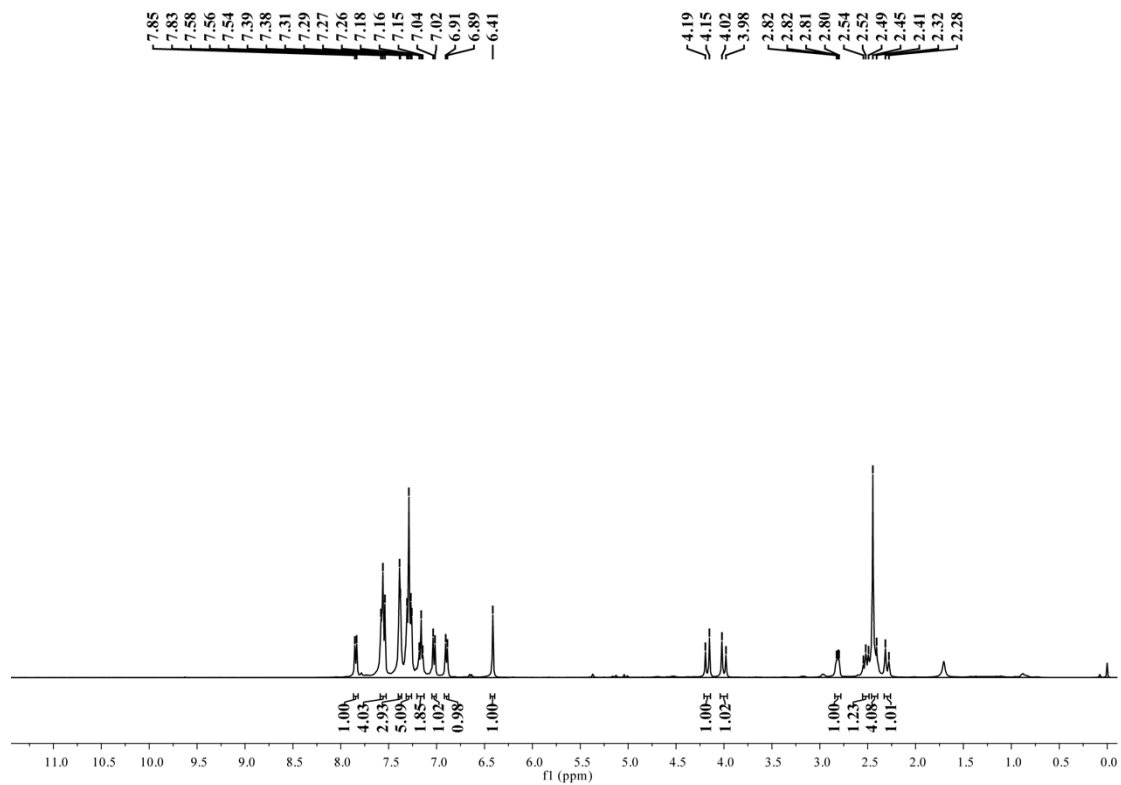


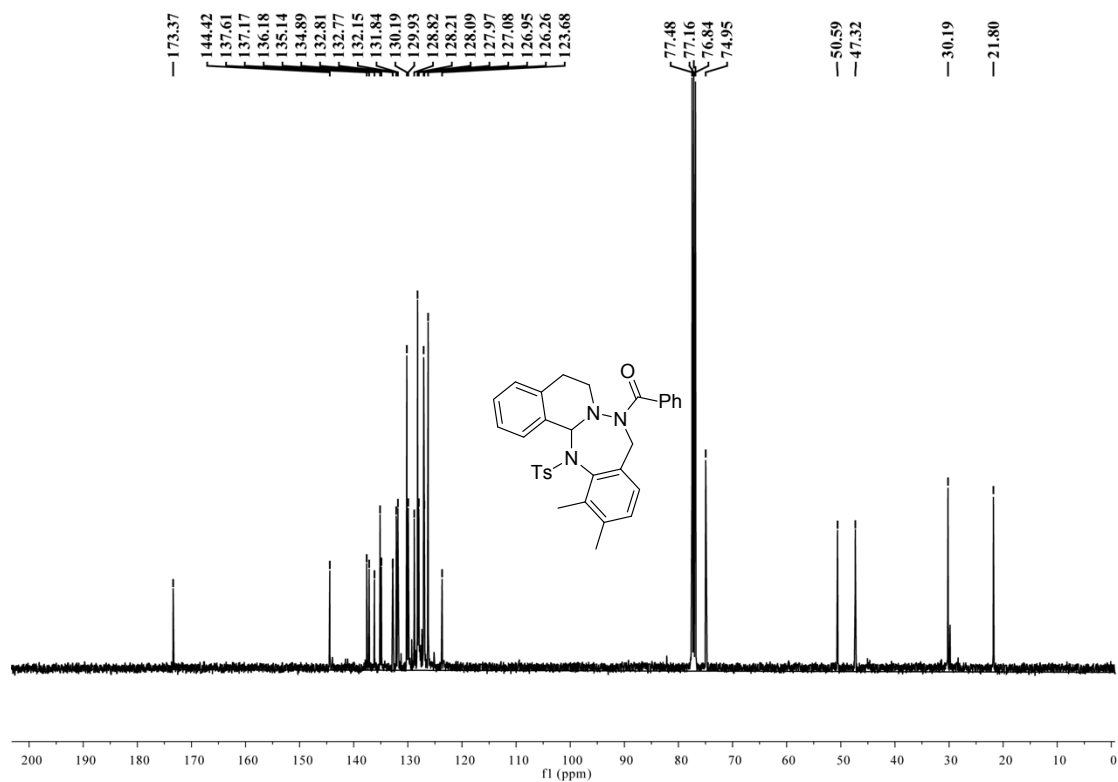
(12-nitro-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ha)



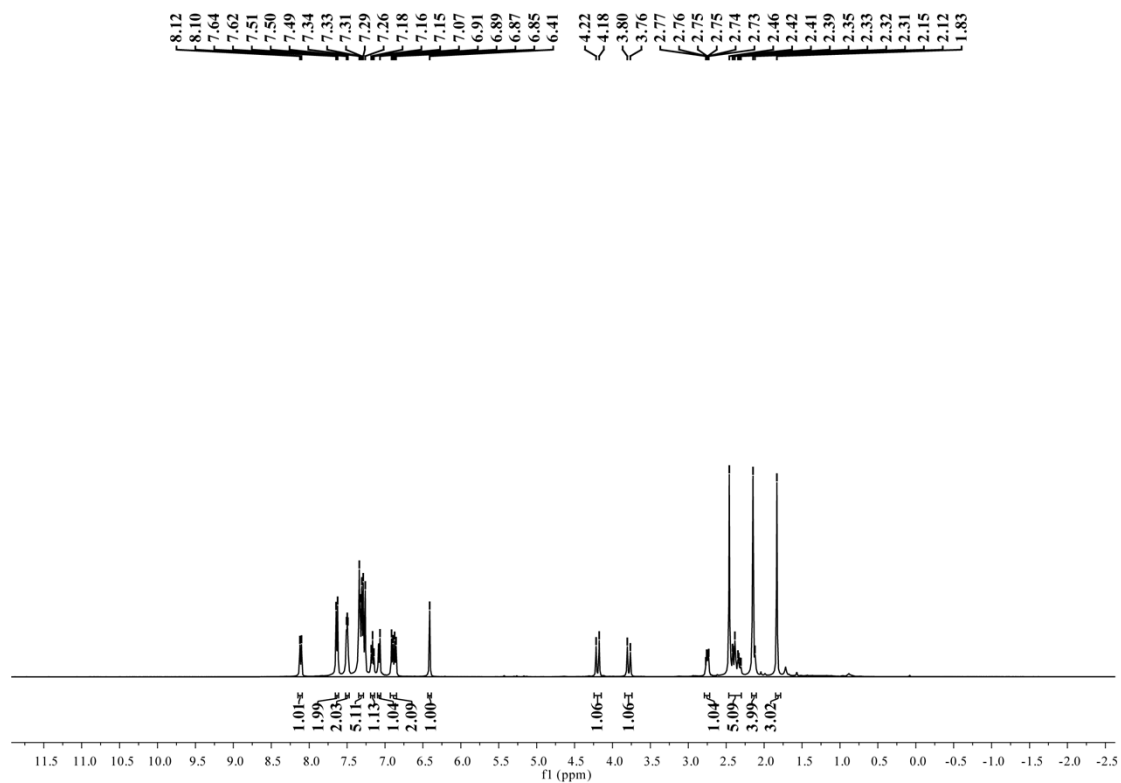


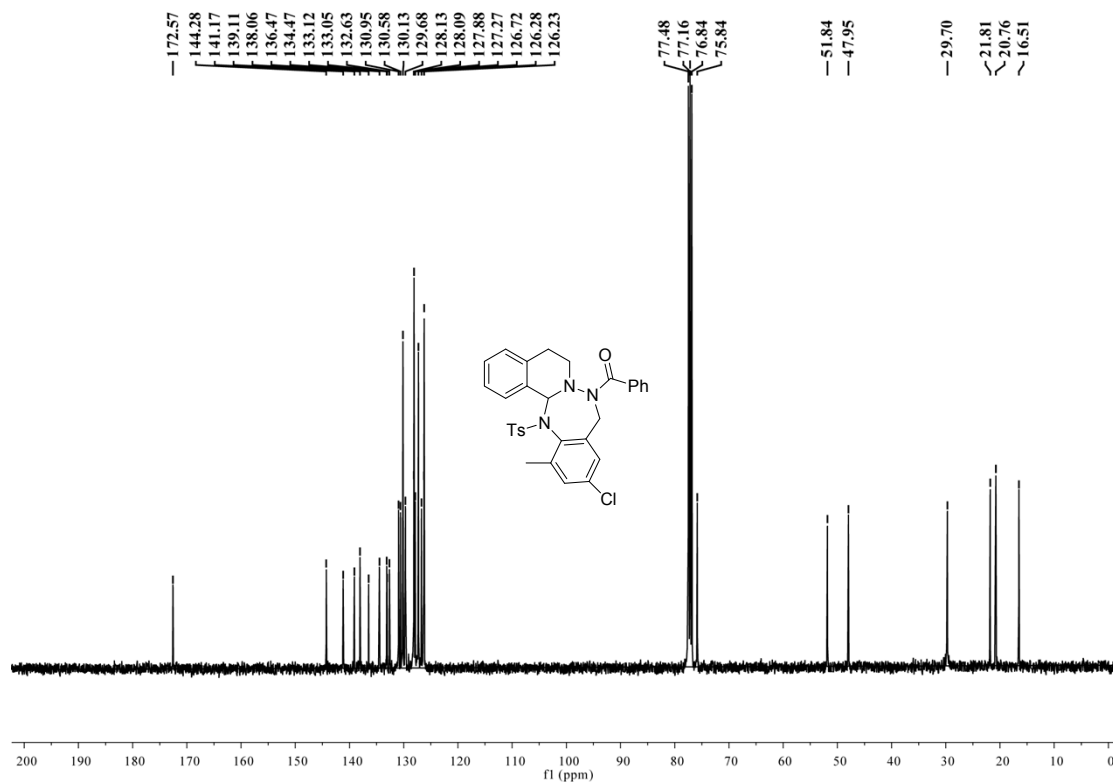
(11-bromo-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ia)



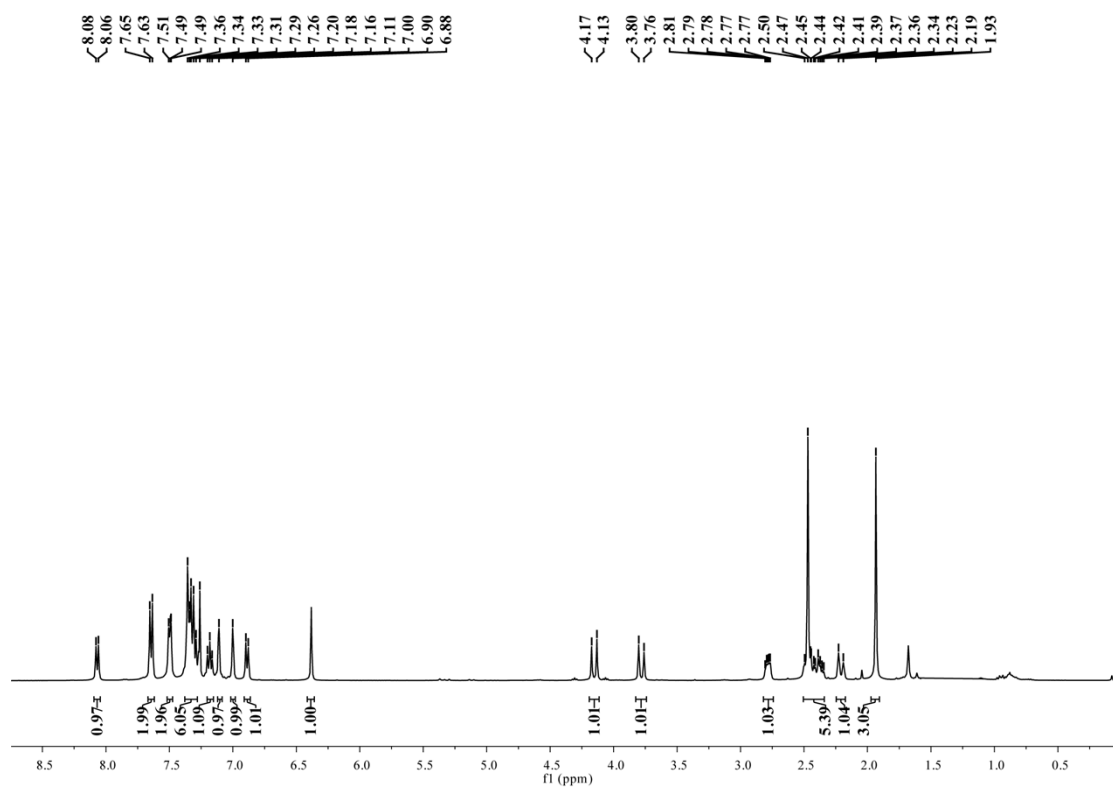


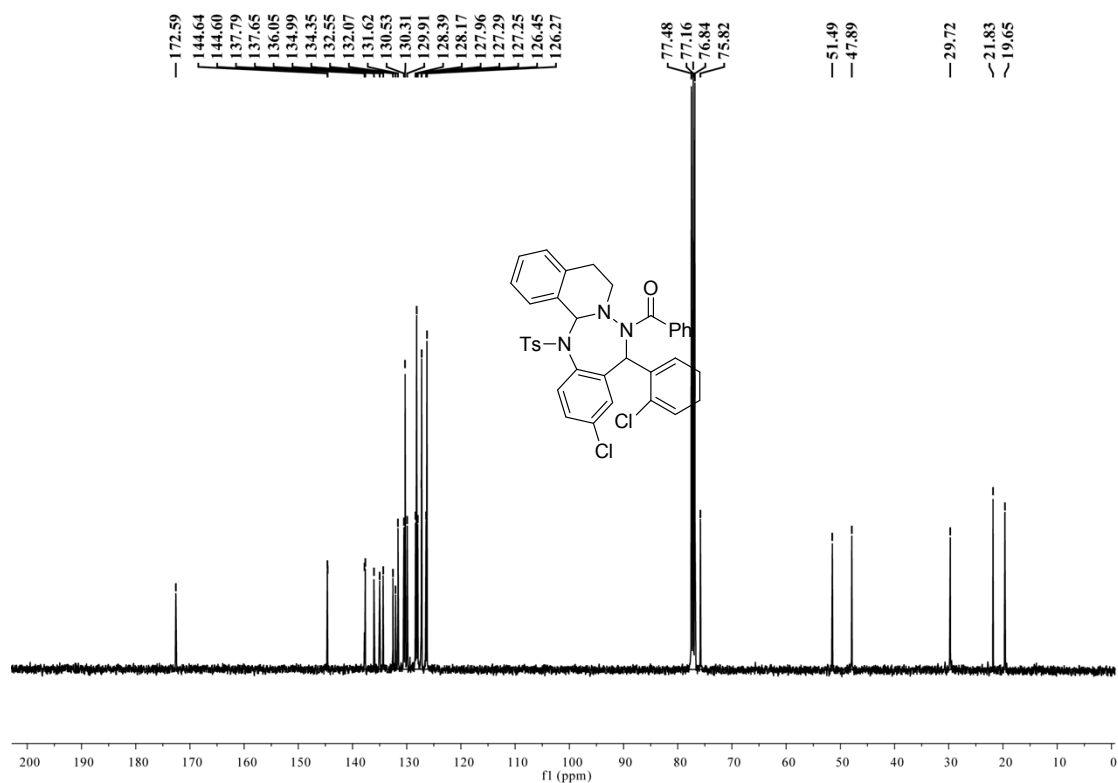
(12,13-dimethyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ja)



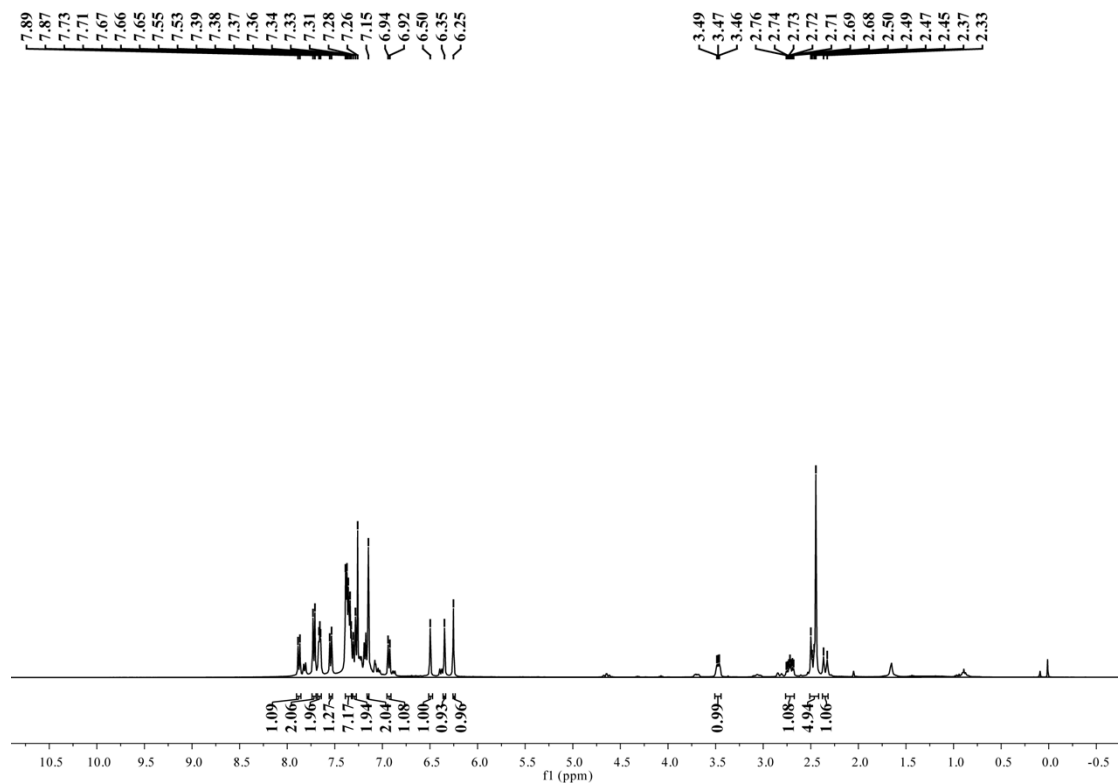


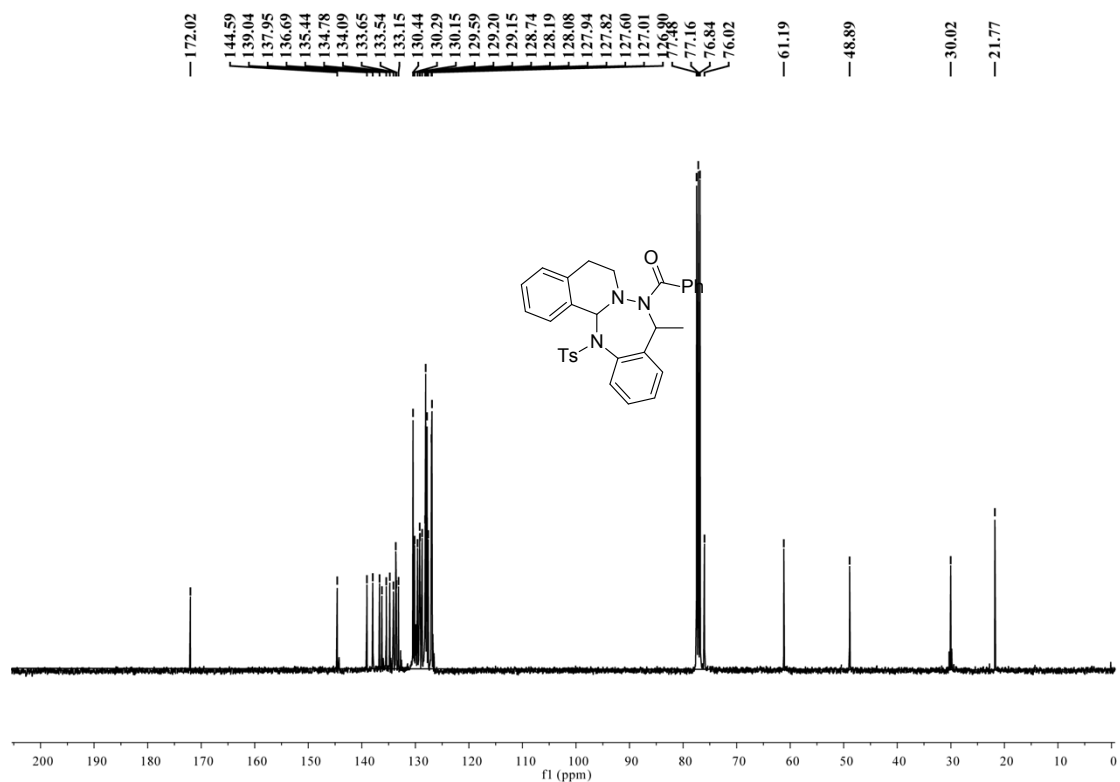
(11-chloro-13-methyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ka)



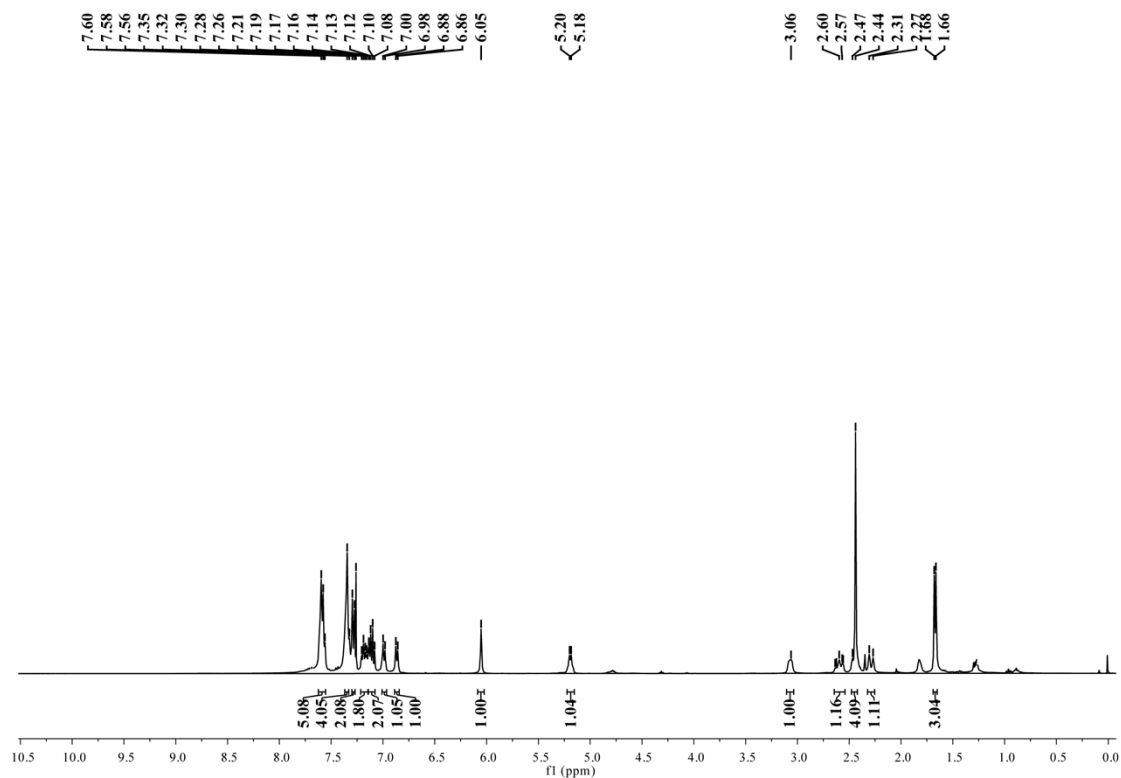


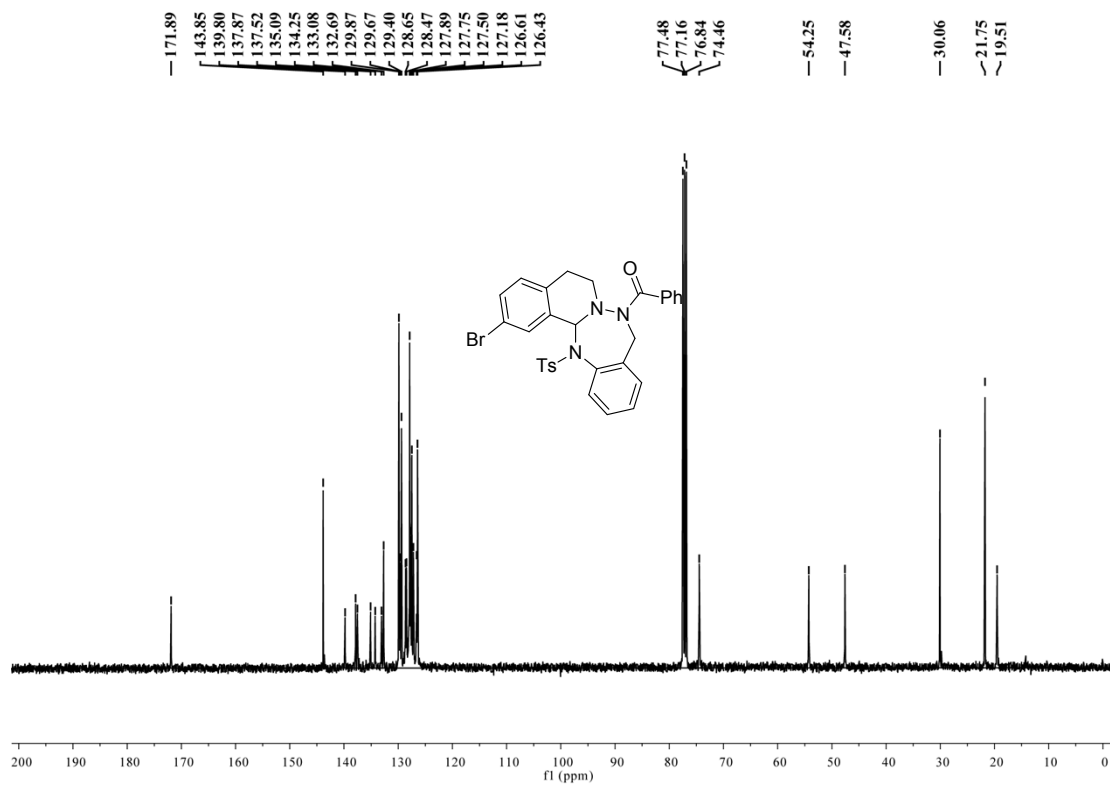
(11-chloro-9-(2-chlorophenyl)-14-tosyl-5,6,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone (3la)



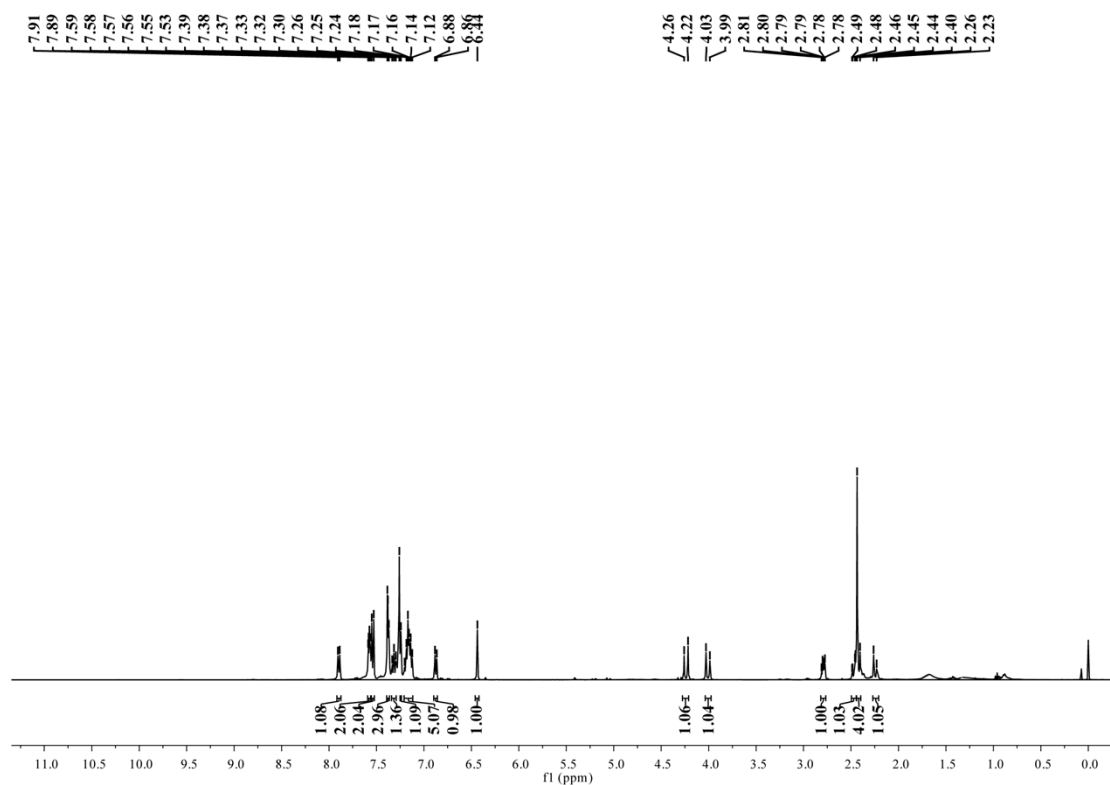


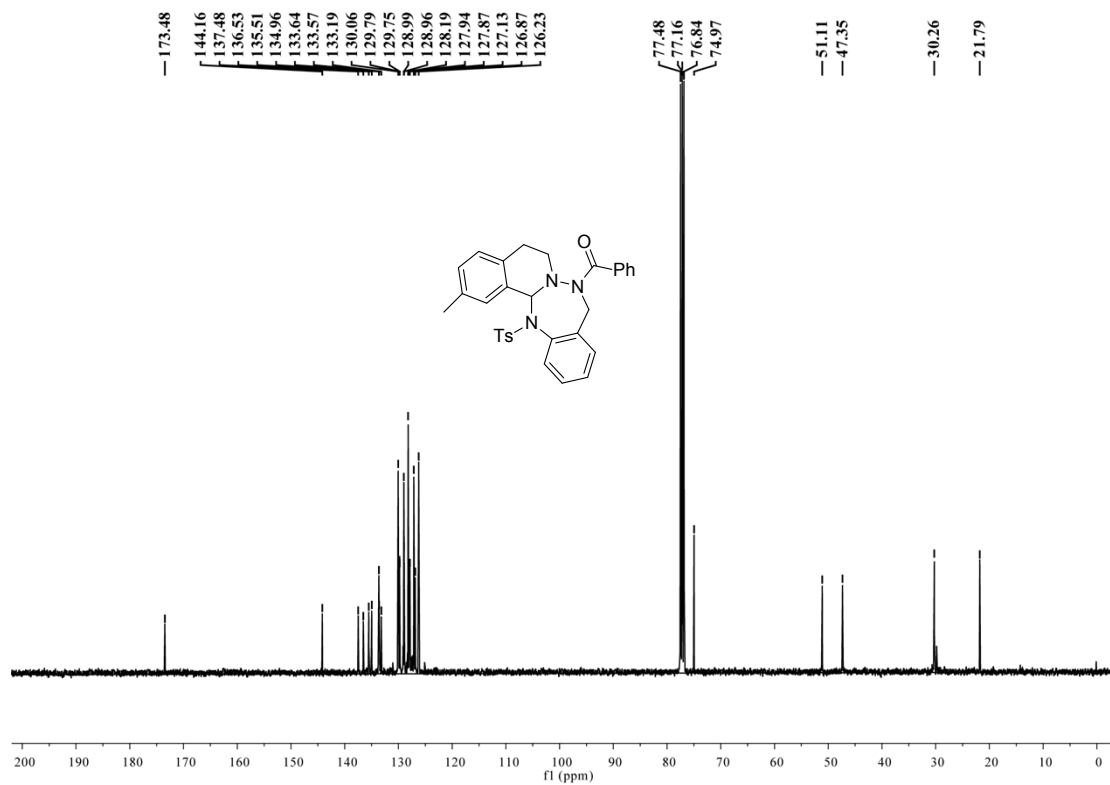
(9-methyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ma)



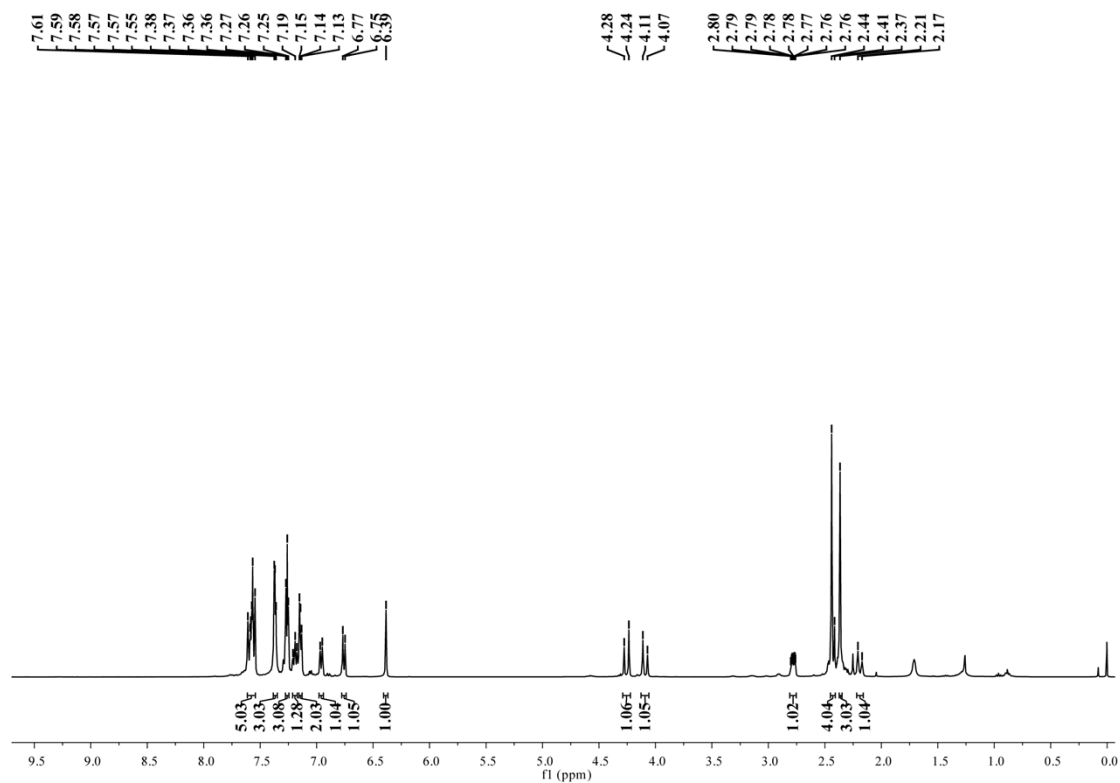


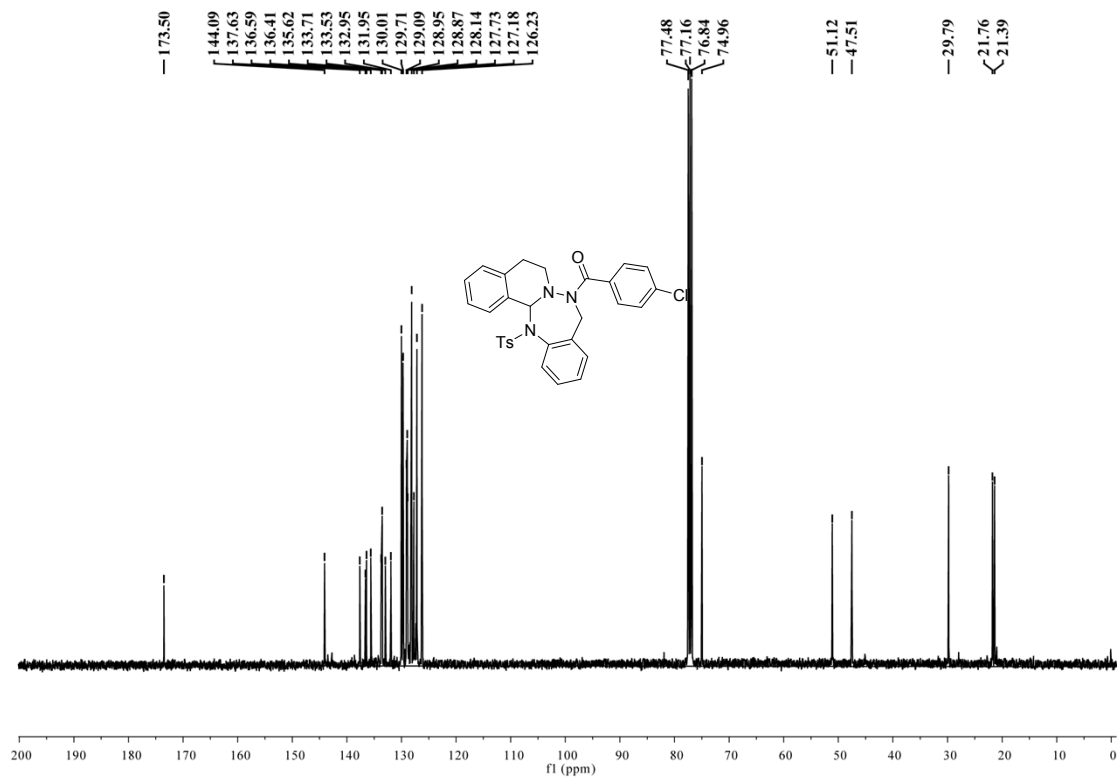
(2-bromo-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ab)



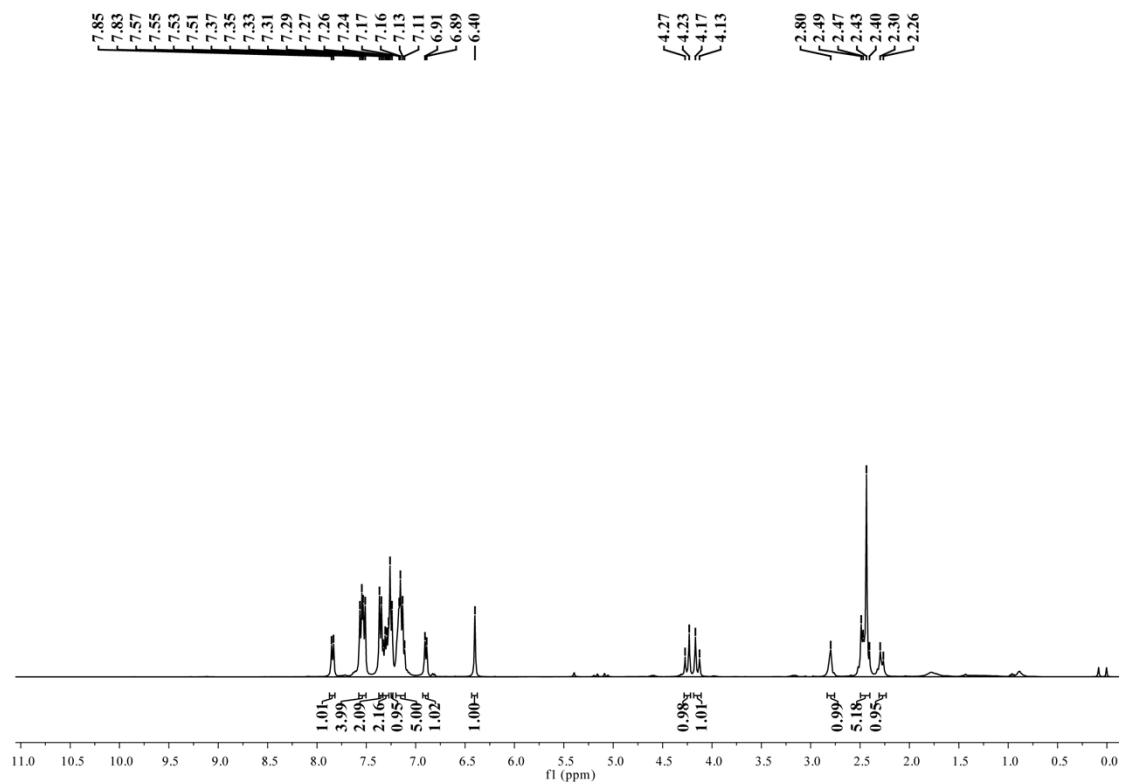


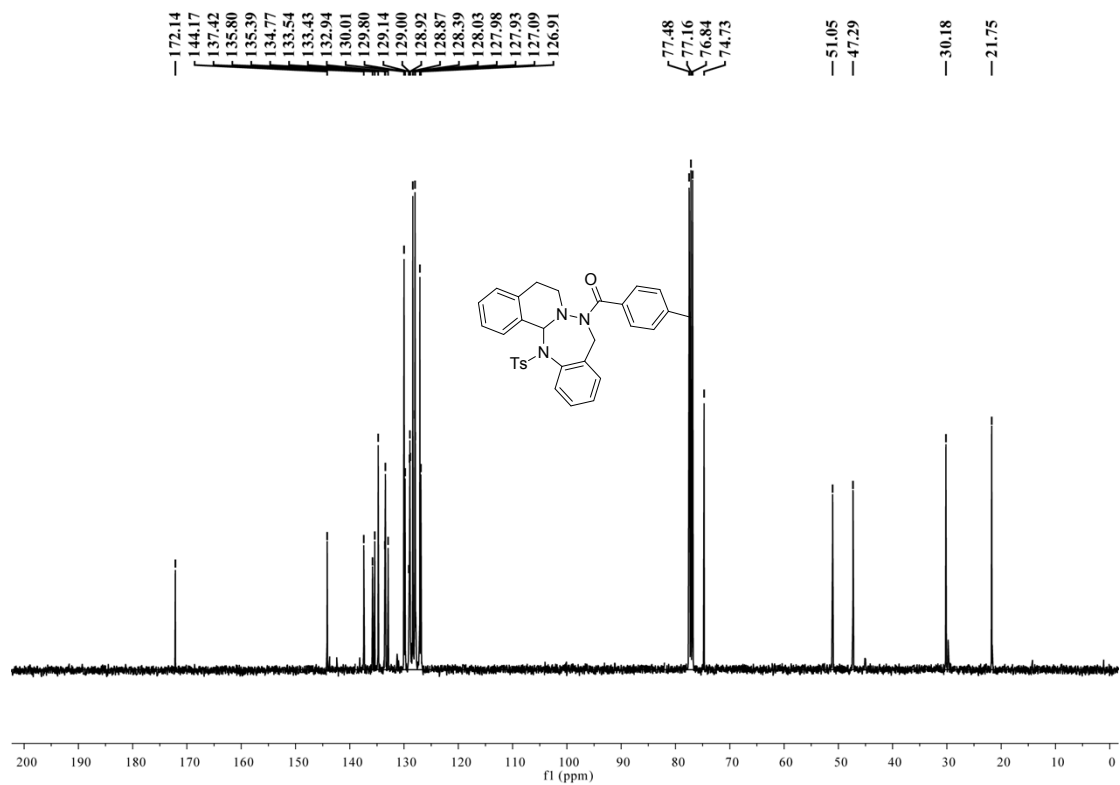
(2-methyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3ac)



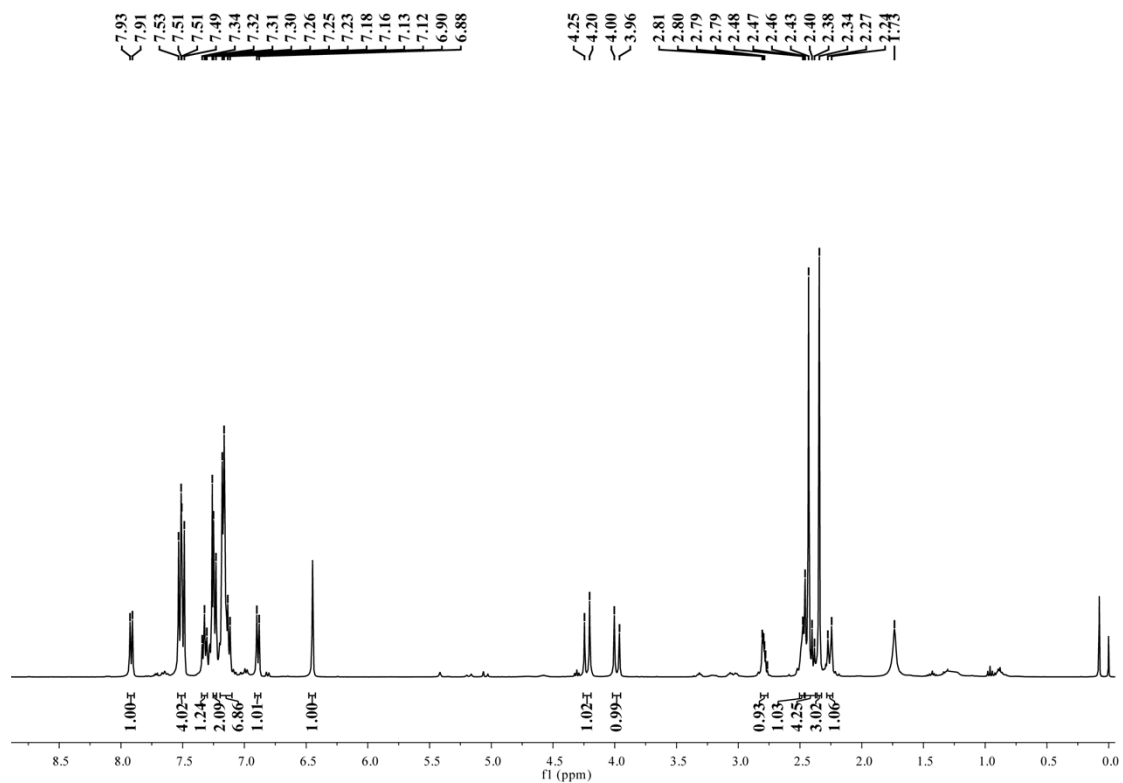


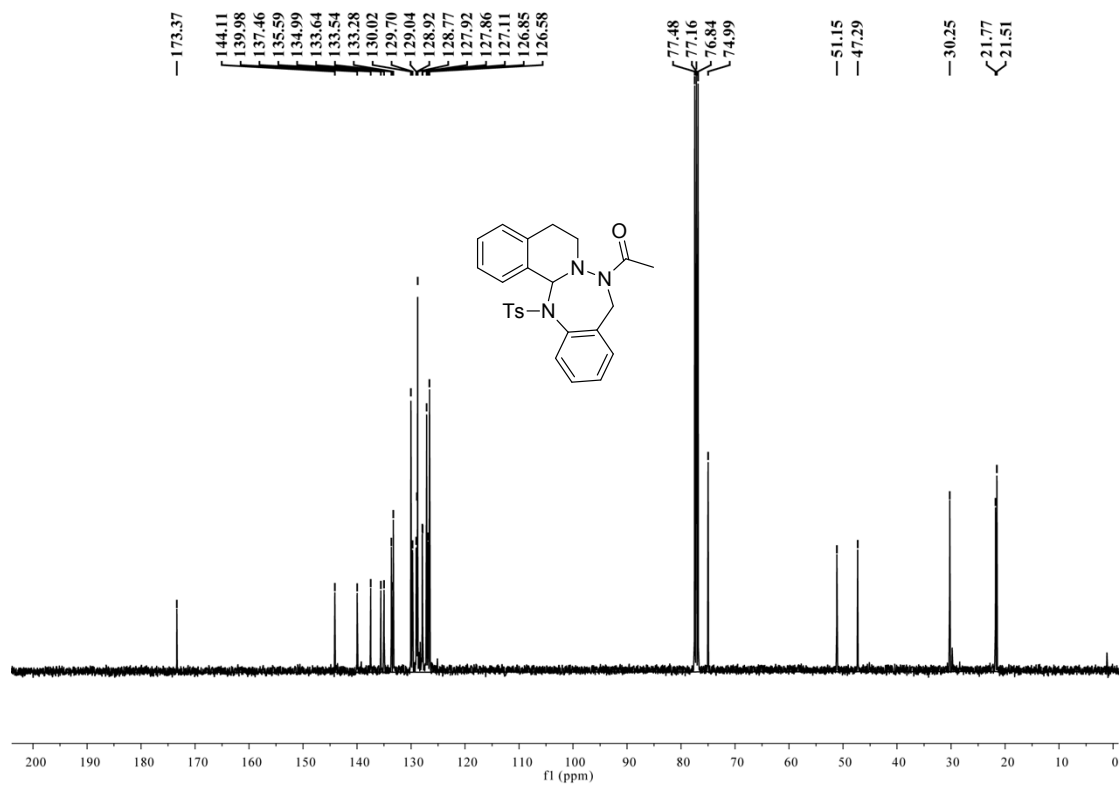
(4-chlorophenyl)(14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)methanone(3ad)



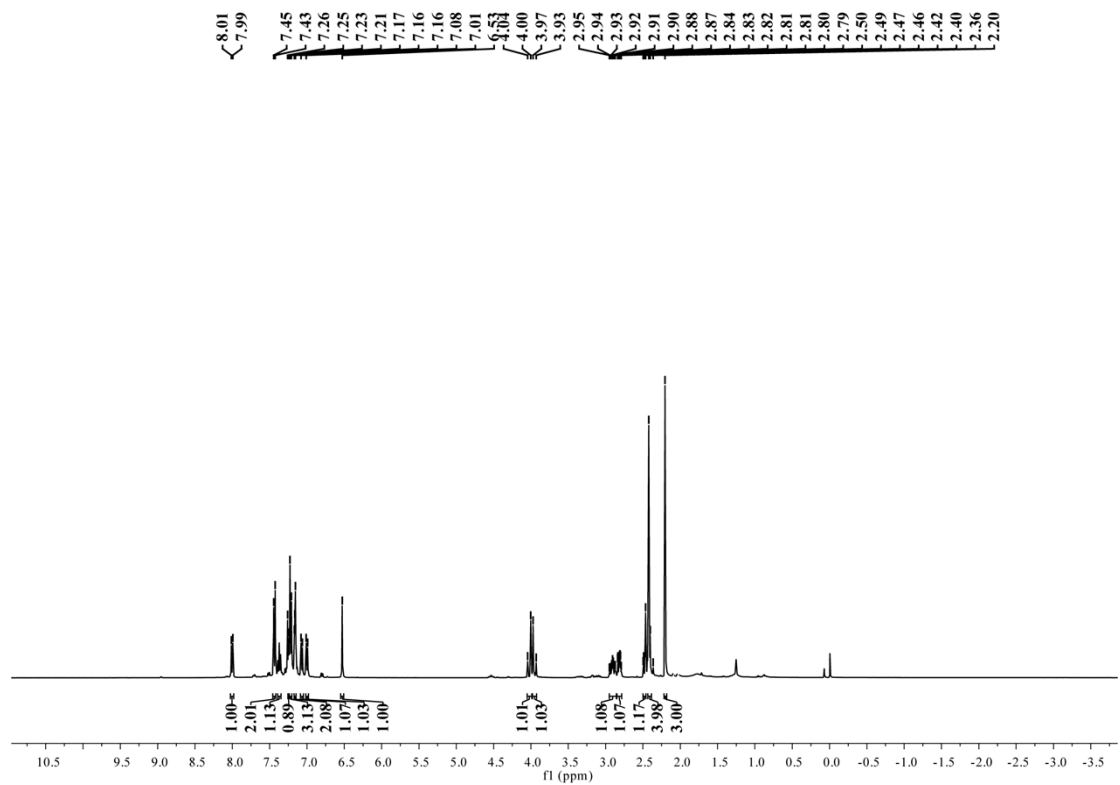


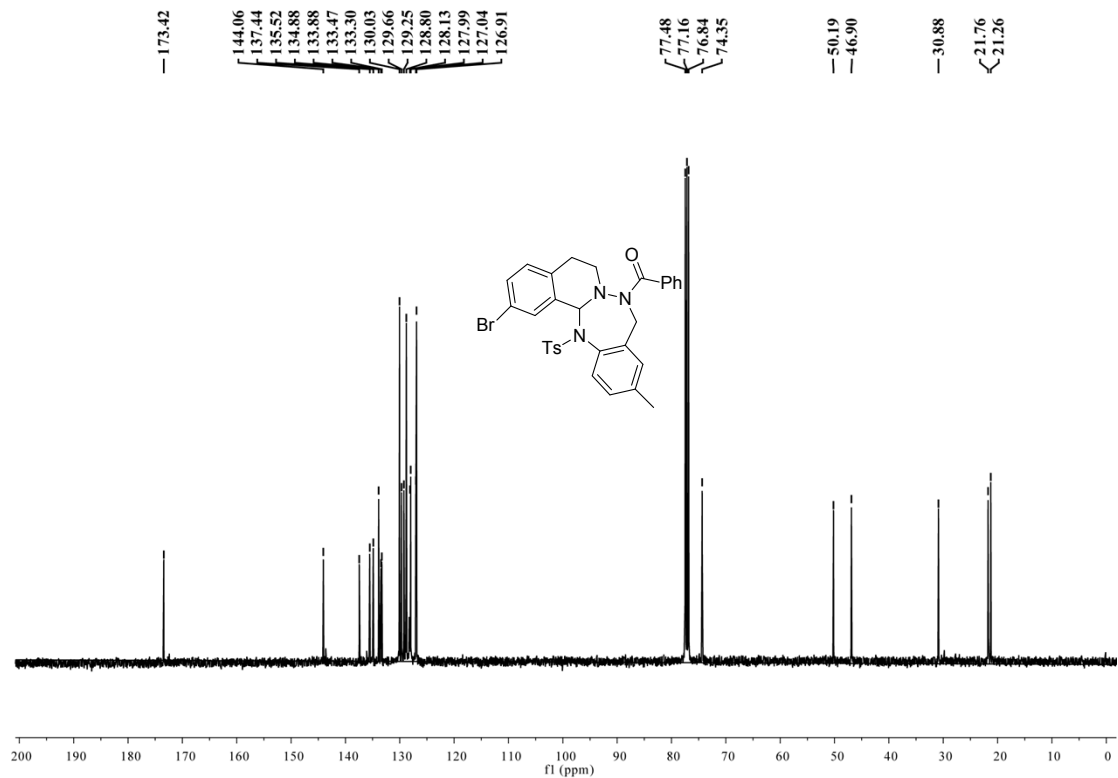
p-tolyl(14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)methanone(3ae)



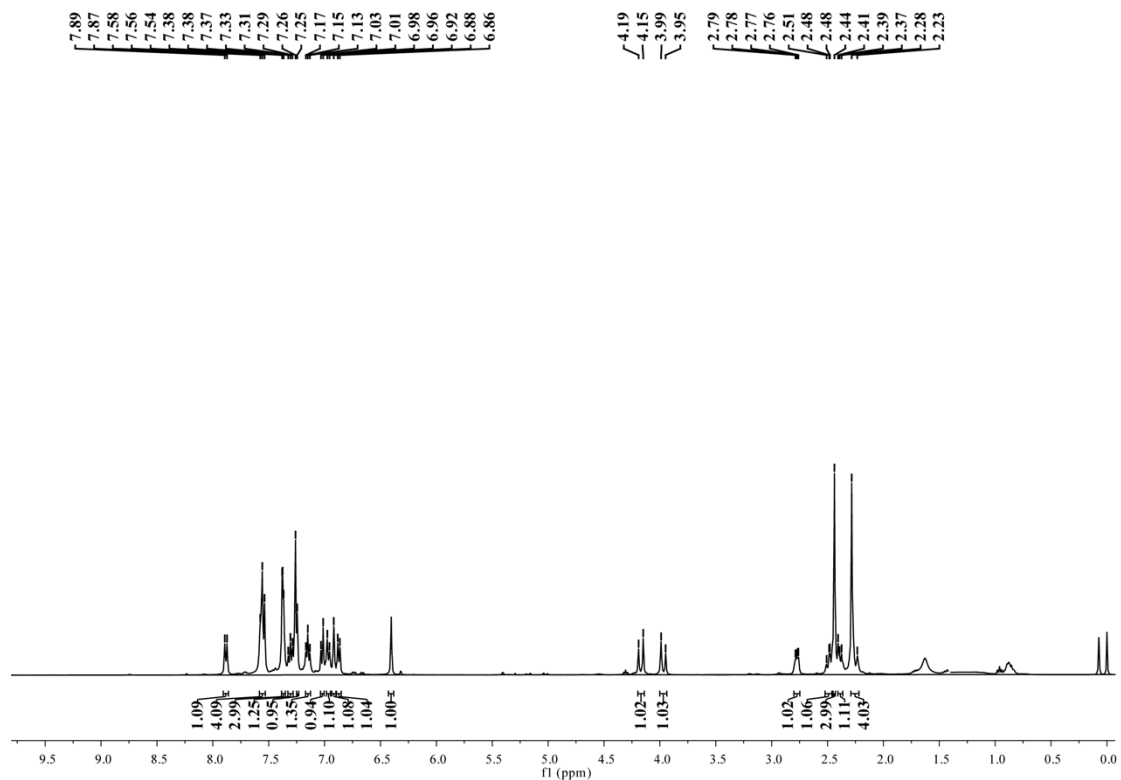


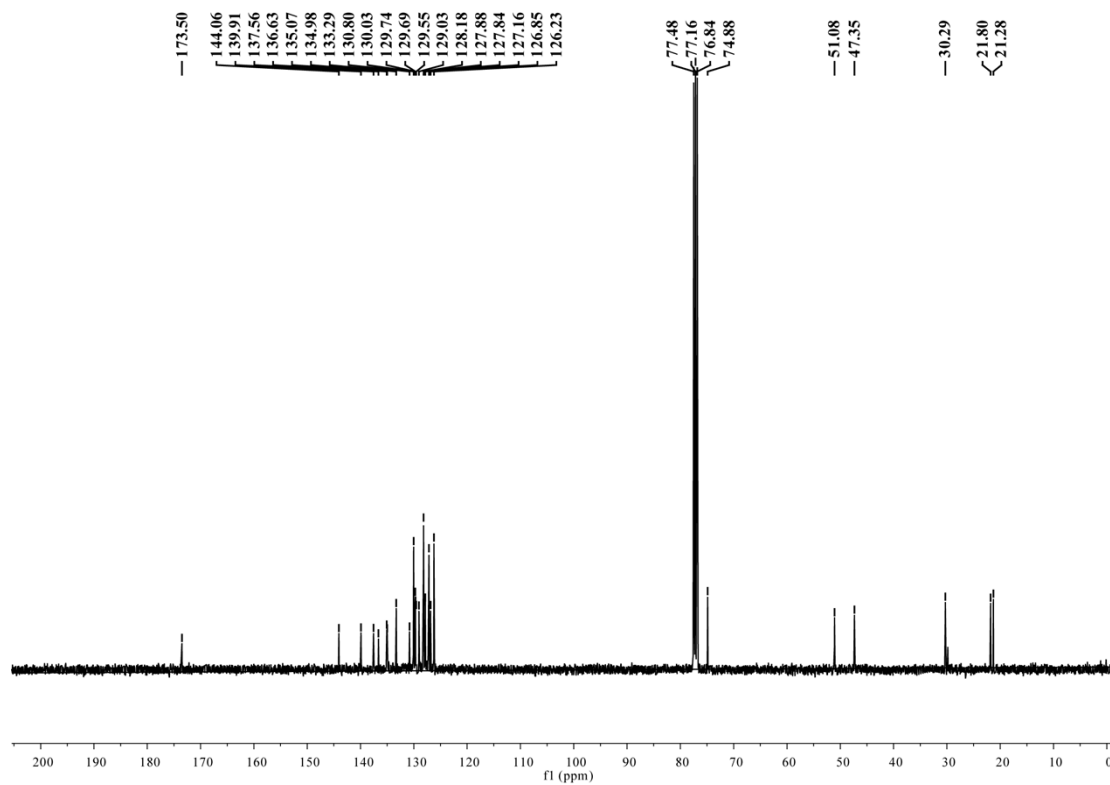
1-(14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)ethanone(3af)



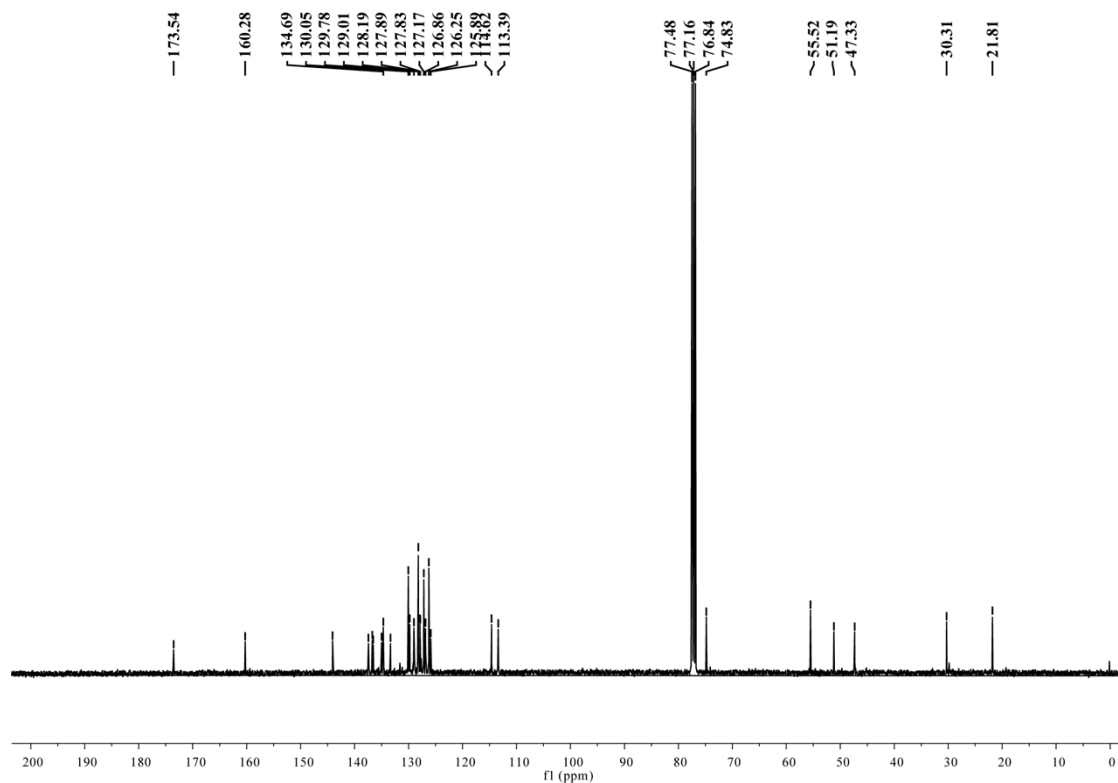
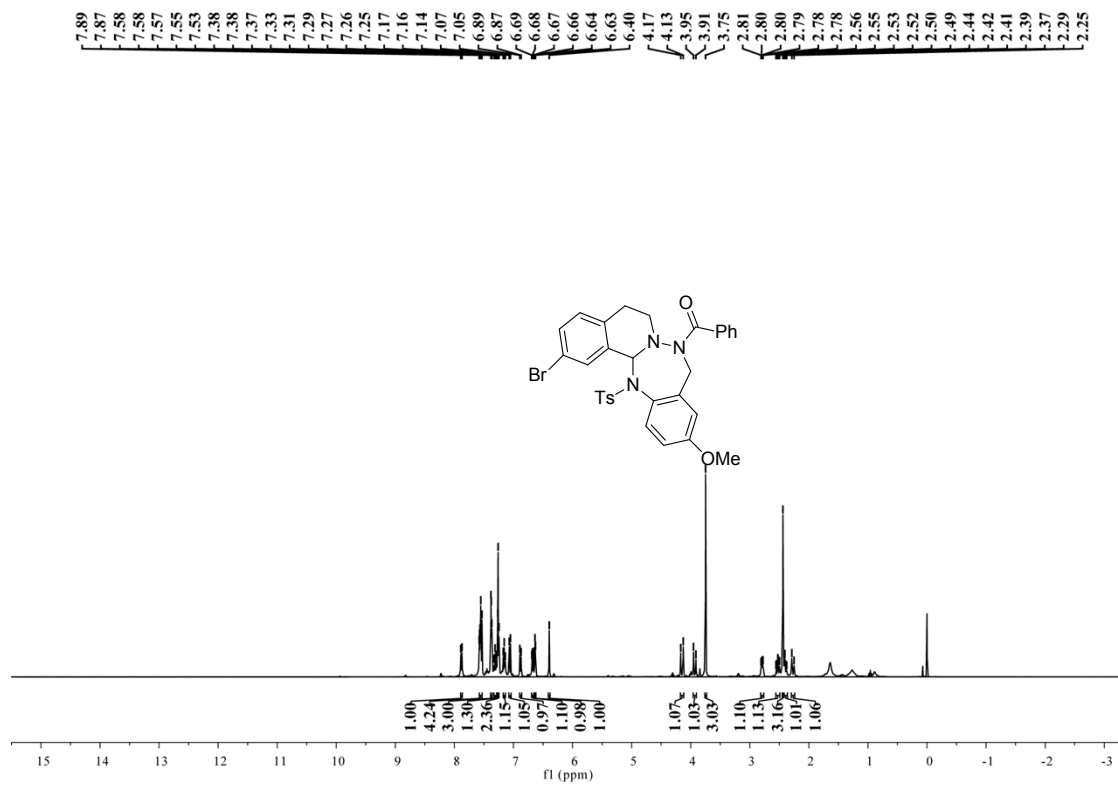


(2-bromo-11-methyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl) (phenyl)methanone (3cb)

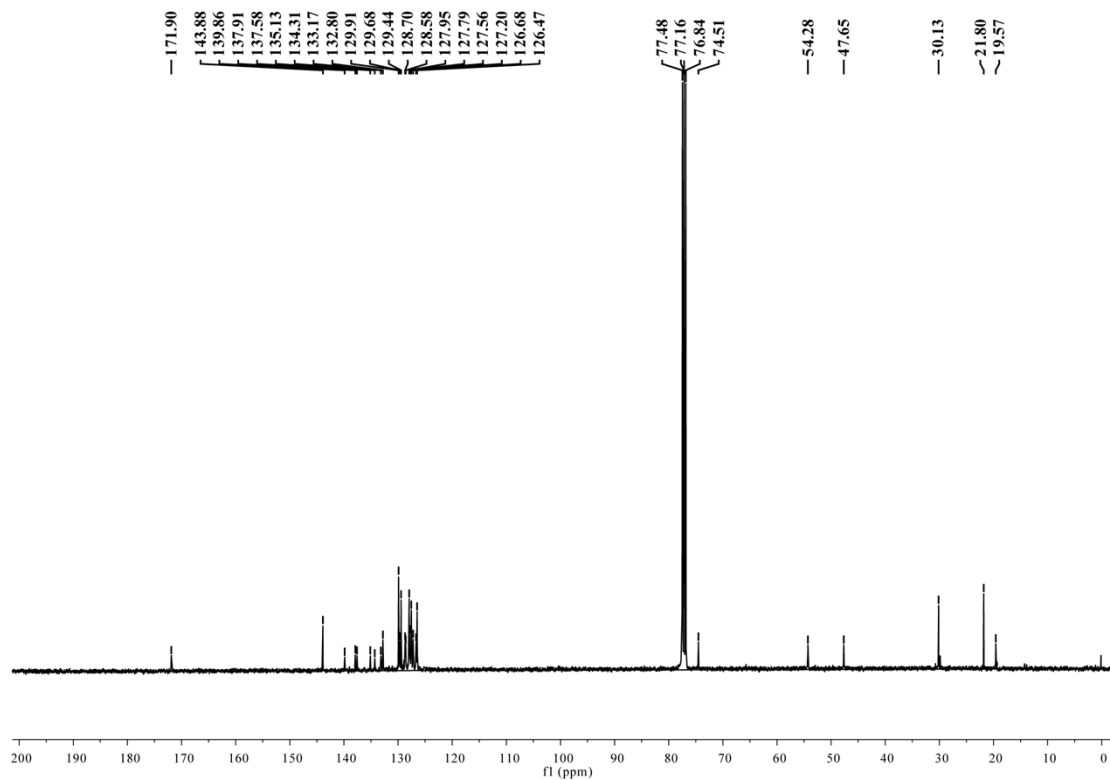
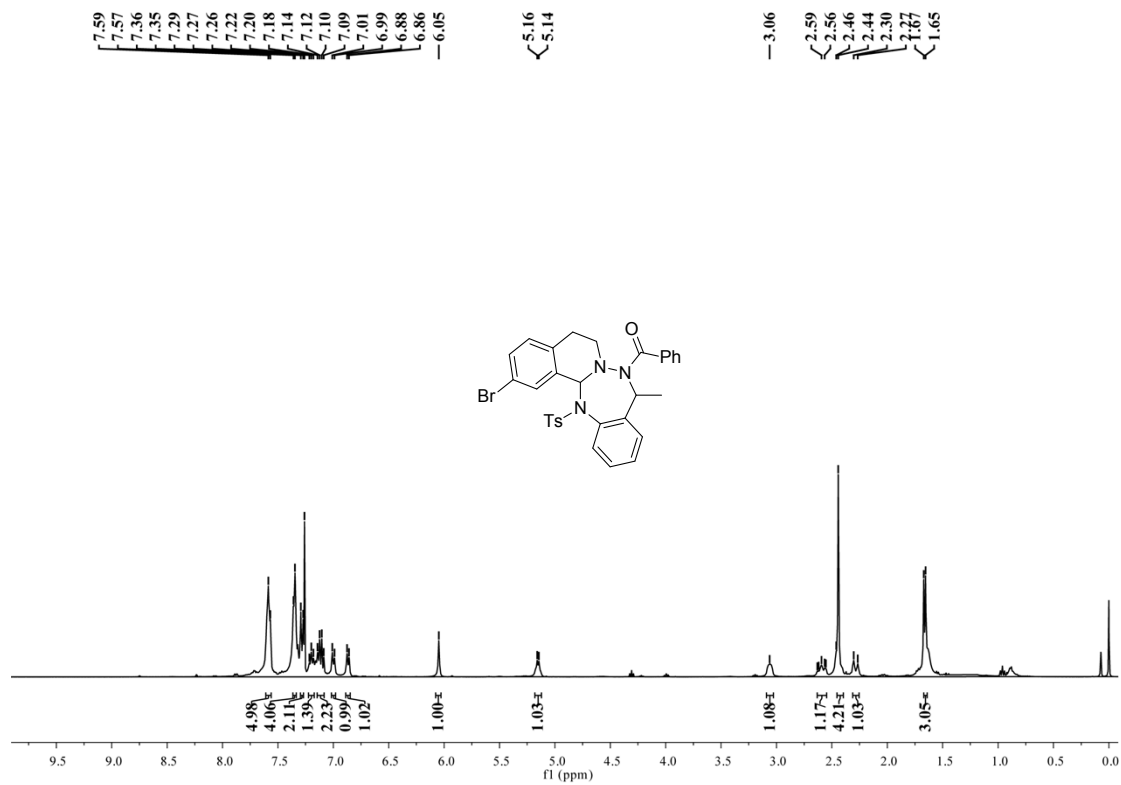




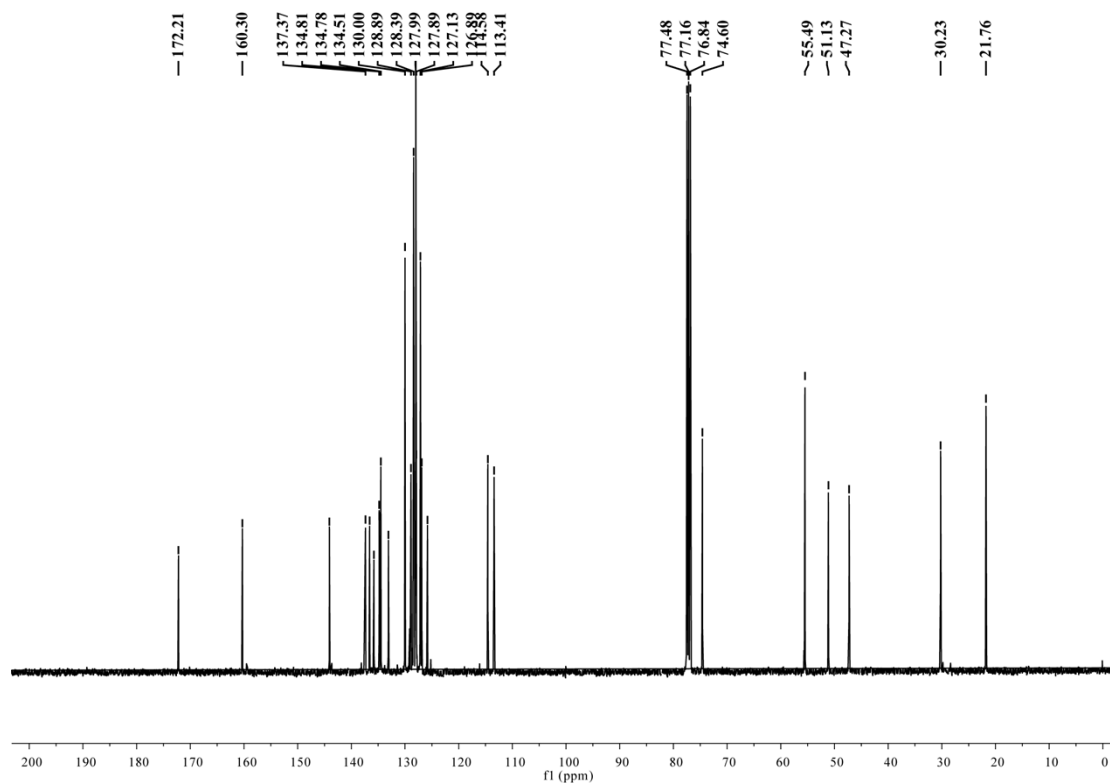
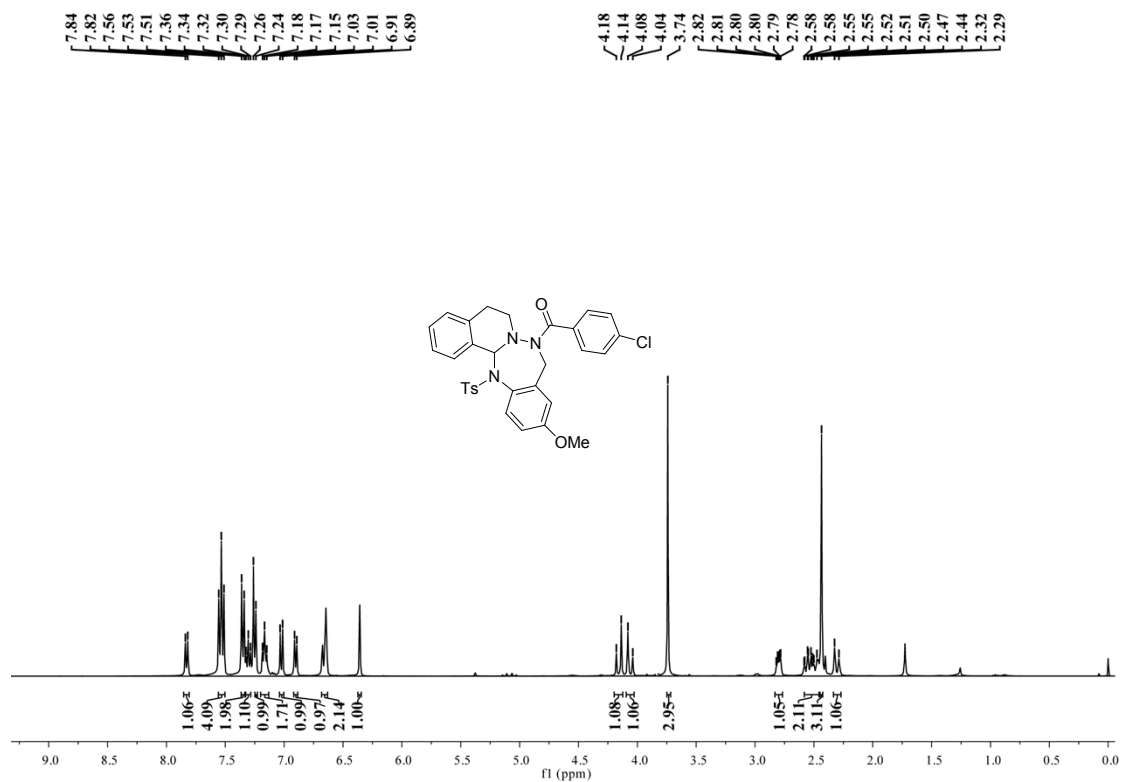
(2-bromo-11-methoxy-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3gb)



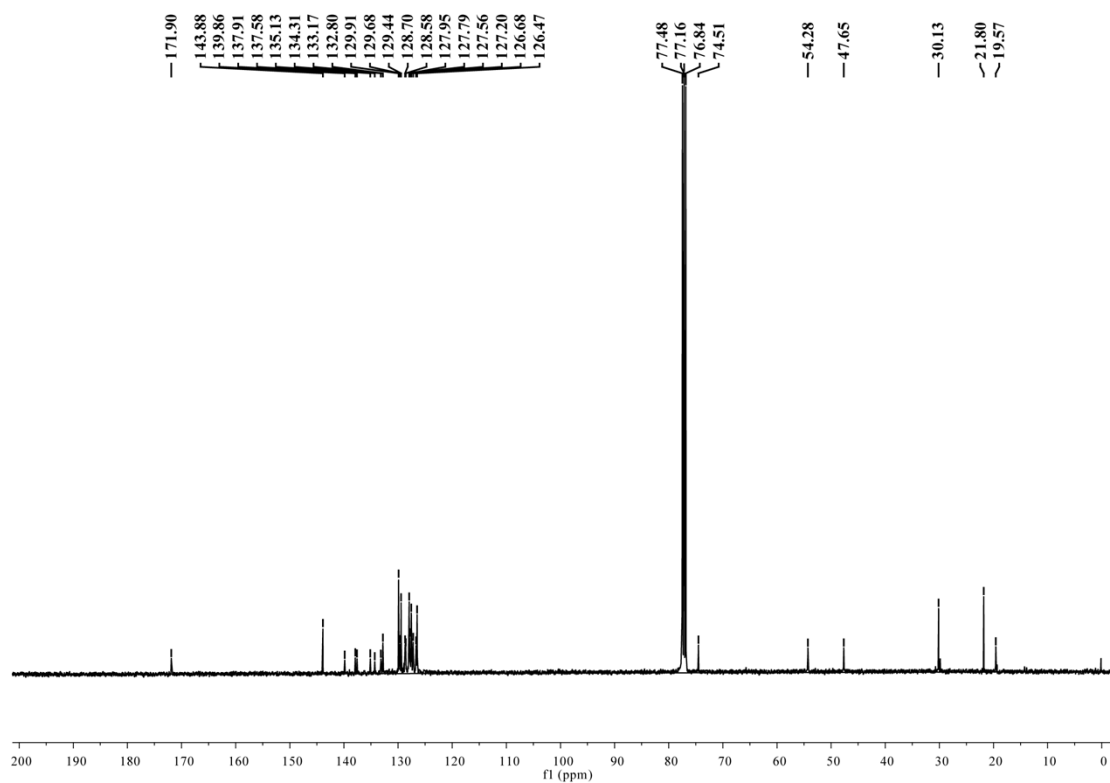
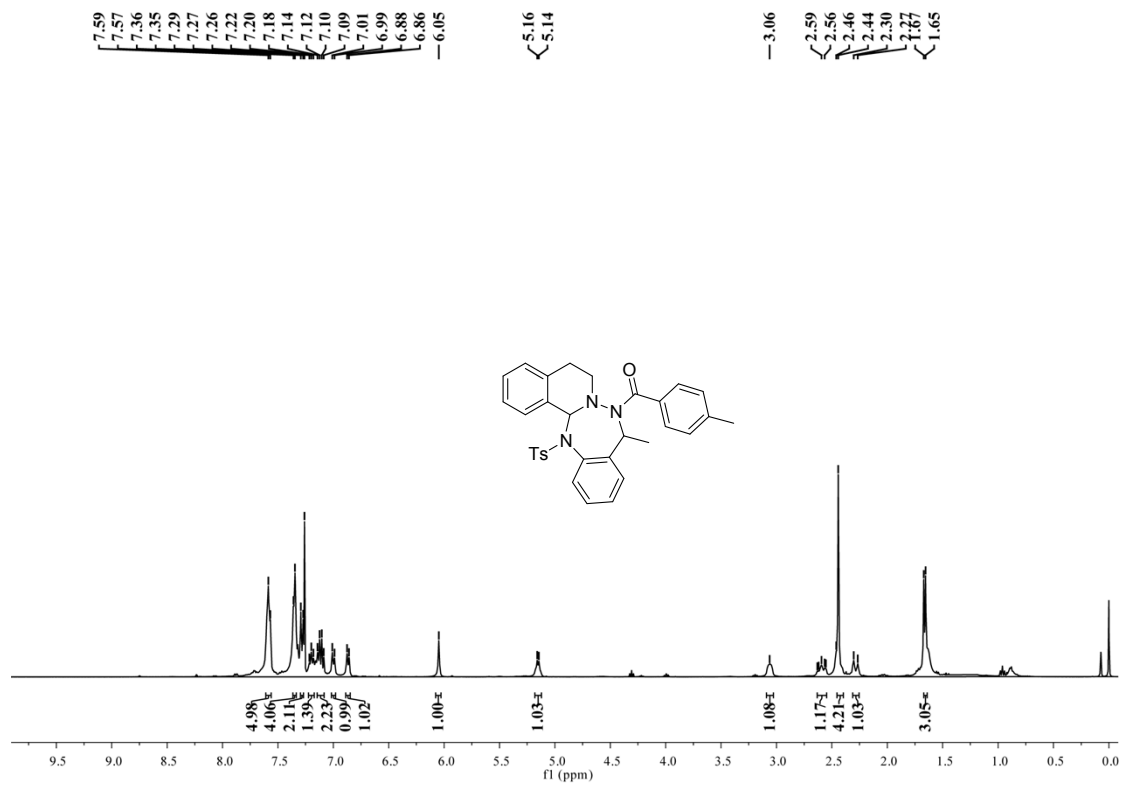
(2-bromo-9-methyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(phenyl)methanone(3mb)



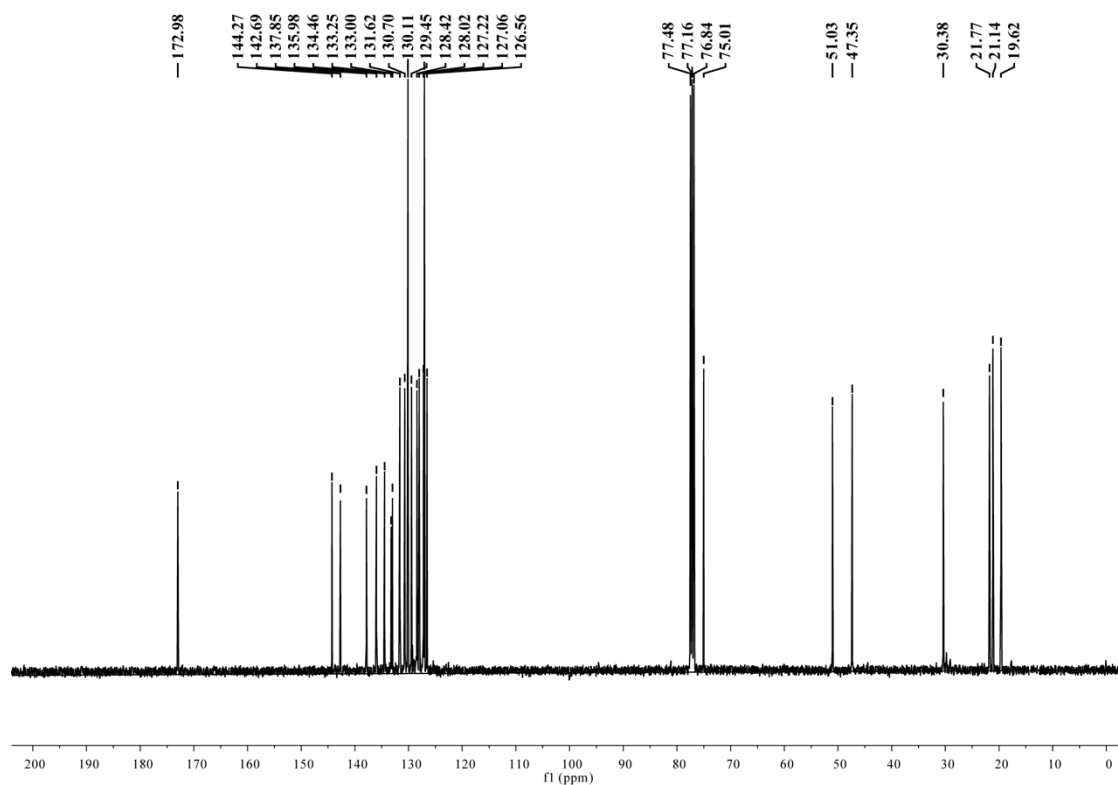
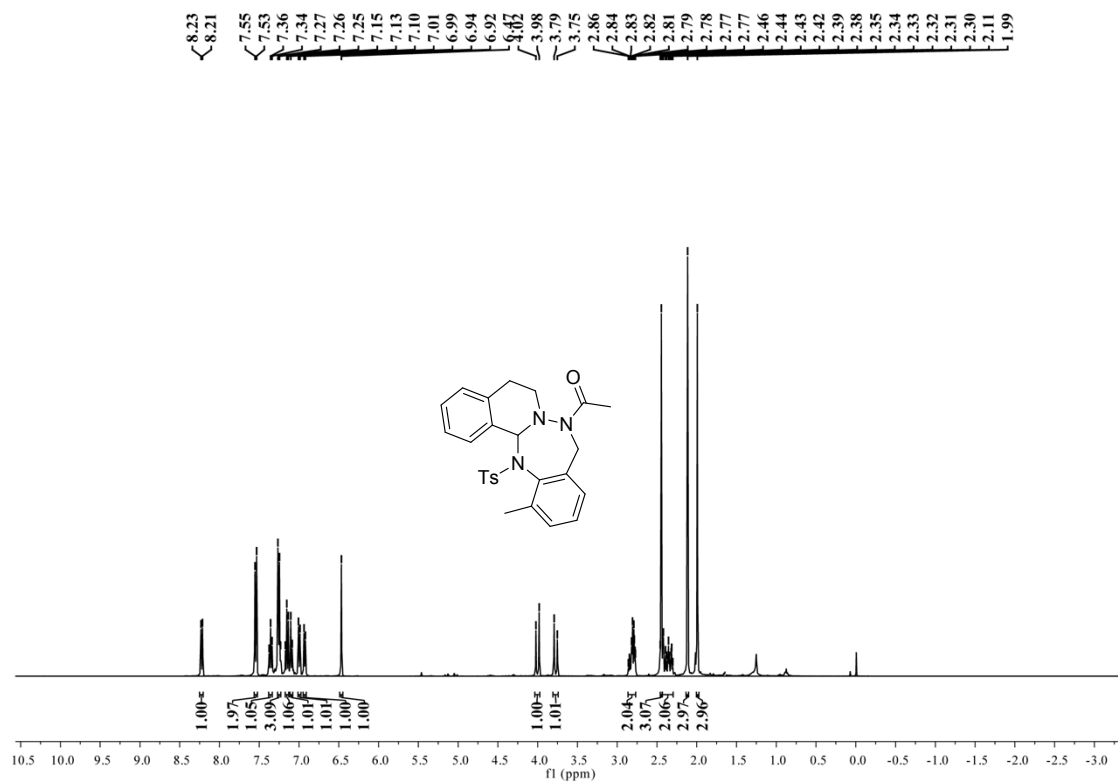
(4-chlorophenyl)(11-methoxy-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)methanone(3gd)



(9-methyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)(p-tolyl)methanone(3me)



1-(13-methyl-14-tosyl-5,6,14,14a-tetrahydrobenzo[5,6][1,2,4]triazepino[3,2-a]isoquinolin-8(9H)-yl)ethanone(3bf)



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