Supporting Information

Palladium-Catalyzed Selective Aminoamidation and Aminocyanation of Alkenes Using Isonitrile as Amide and Cyanide Sources

Hanling Gao, Bifu Liu, Wanqing Wu, Huanfeng Jiang*

School of Chemistry and Chemical Engineering, South China University of Technology, Guangzhou 510640, P. R. China

jianghf@scut.edu.cn

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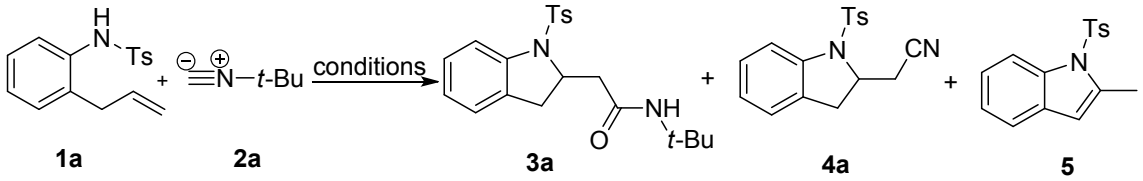
General Information

^{1}H and ^{13}C NMR spectra were recorded on BRUKER DRX/400 spectrometer using $CDCl_3$ as solvent and TMS as an internal standard. Gas chromatograph mass spectra were obtained with a SHIMADZU model GCMS/QP5000 spectrometer. IR spectra were obtained as potassium bromide pellets or as liquid films between two potassium bromide pellets with a Brucker Vector 22 spectrometer. TLC was performed using commercially prepared 100/400 mesh silica gel plates (GF254), and visualization was effected at 254 nm. High resolution exact mass measurements (HR-MS) were performed on a TOF spectrometer

Optimization Study

Table 1. Optimization of the reaction conditions.[a]

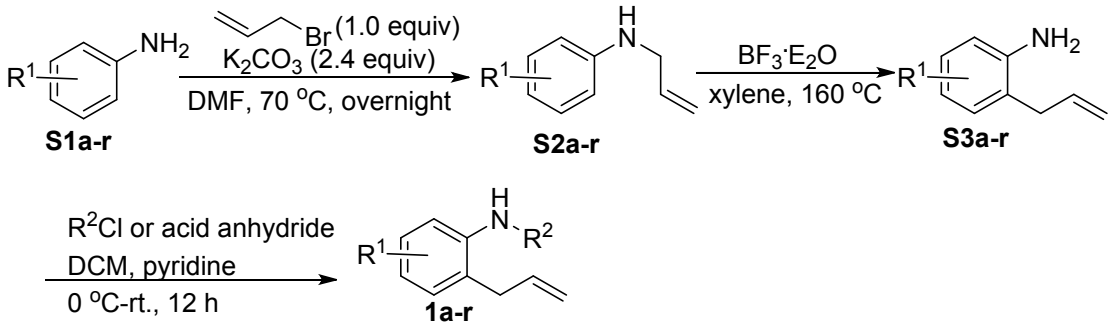


1a **2a** **3a** **4a** **5**

Entry	Catalyst	Oxidant	Solvent	Additive	Yield (%) [b]		
					3a	**4a**	**5**
1	$Pd(OAc)_2$	$Cu(OAc)_2$	DCE	$NaHCO_3$	35	—	25
2	$Pd(PPh_3)_2Cl_2$	$Cu(OAc)_2$	DCE	$NaHCO_3$	23	—	30
3	$PdCl_2$	$Cu(OAc)_2$	DCE	$NaHCO_3$	30	—	18
4	$Pd(TFA)_2$	$Cu(OAc)_2$	DCE	$NaHCO_3$	48	—	16
5	$Pd(TFA)_2$	$Cu(TFA)_2$	DCE	$NaHCO_3$	70	—	8
6	$Pd(TFA)_2$	$Cu(TFA)_2$	toluene	$NaHCO_3$	82	—	6
7	$Pd(TFA)_2$	$Cu(TFA)_2$	DMF	$NaHCO_3$	70	—	6
8	$Pd(TFA)_2$	$Cu(TFA)_2$	1,4-dioxane	$NaHCO_3$	68	—	7
9	$Pd(TFA)_2$	$Cu(TFA)_2$	toluene	KOAc	76	—	6
10	$Pd(TFA)_2$	$Cu(TFA)_2$	toluene	K_2CO_3	80	—	5
11	**$Pd(TFA)_2$**	**$Cu(TFA)_2$**	**toluene**	**DABCO**	**95(90)[c]**	—	—
12	$Pd(TFA)_2$	O_2	toluene	DABCO	46	—	30
13[d]	$Pd(TFA)_2$	$Cu(TFA)_2/O_2$	toluene	DABCO	56	—	19
14	—	$Cu(TFA)_2$	toluene	DABCO	—	—	56
15	$Pd(TFA)_2$	$Cu(TFA)_2$	toluene	—	—	16	35
16[e]	$Pd(TFA)_2$	$Cu(TFA)_2$	toluene	DABCO	90	—	—
17[f]	$Pd(TFA)_2$	$Cu(TFA)_2$	toluene	DABCO	78	—	—
18	$Pd(TFA)_2$	$Cu(TFA)_2$	toluene	PivOH	—	23	37
19	**$Pd(TFA)_2$**	**$Cu(TFA)_2$**	**toluene**	**TFA**	**—**	**70**	**10**
20	$Pd(TFA)_2$	$Cu(TFA)_2$	toluene	HOAc	—	31	23
21	$Pd(OAc)_2$	$Cu(TFA)_2$	toluene	TFA	10	15	33
22	$Pd(OAc)_2$	$Cu(OAc)_2$	toluene	TFA	18	10	36
23	$Pd(OAc)_2$	$Cu(OAc)_2$	toluene	HOAc	20	15	39
24[h]	$Pd(TFA)_2$	$Cu(TFA)_2$	toluene	TFA	—	56	21
25[i]	$Pd(TFA)_2$	$Cu(TFA)_2$	toluene	TFA	—	67	25
26[j]	$Pd(TFA)_2$	$Cu(TFA)_2$	toluene	TFA	—	68	20

Reaction conditions: unless otherwise noted, all reactions were performed with **1a** (0.3 mmol), **2a** (0.36 mmol), catalyst (10 mol %), base (0.6 mmol), and oxidant (0.3 mmol) in solvent (2.0 mL) at 100 °C for 10 h, DCE = 1,2- dichloroethane. DMF = *N*,*N*-dimethylformamide. DABCO = 1,4-diazabicyclo[2.2.2]octane. [b]Yields and conversions analyzed by GC/MS are based on **1a**. [c]isolated yield. [d]20 mol% $Cu(TFA)_2$ and O_2 balloon was used. [e] The reaction was carried out at 110 °C. [f] The reaction was carried out at 90 °C. [h] Reaction performed at 130 °C. [i] 20 mol% $Pd(TFA)_2$ was used. [j] 2 equiv isonitrile was used.

Synthesis of Starting Materials



Starting materials S2a-r: Into a flame-dried Schlenk-flask were introduced **S1** (10.0 mmol, 1.0 equiv), allylbromide (0.87 mL, 10.0 mmol, 1.0 equiv), K_2CO_3 (3.3 g, 24 mmol, 2.4 equiv) and DMF (25 mL). The flask was equipped with a stopper and the reaction mixture heated to 70 °C over night. The mixture was allowed to cool down to room temperature and washed with water (10 mL). The aqueous phase was extracted with diethyl ether (3 × 20 mL). The combined organic layers were washed with brine, dried and concentrated to provide the crude *N*-allylaniline.

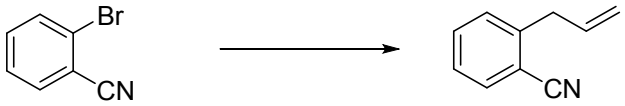
Starting materials S3a-r[1]: Into a flame-dried Schlenk-flask were introduced **S1** (8.0 mmol, 1. 0 equiv), $BF_3{\cdot}OEt_2$ (8.0 mmol, 1.0 equiv) and xylene (4 mL). The flask was

sealed and heated to 160 °C overnight. The reaction was allowed to cool down and treated with saturated aqueous K_2CO_3 solution (10 mL). The organic phase was separated and the aqueous phase was extracted with diethyl ether (3 × 20 mL). The organic layers were combined, dried over $MgSO_4$ and concentrated to provide the crude product. Purification was carried out by column chromatography (silica gel, hexanes/EtOAc, 9/1, v/v).

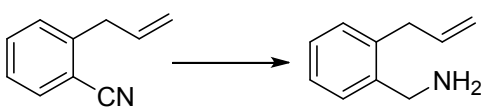
Starting materials 1a-r[2]: To an oven dried 50 mL round bottom flask containing the solution of the amine (5.0 mmol) in pyridine (10 mL), the reaction mixture was cooled to 0 °C and acyl chlorides and acid anhydrides (7.5 mmol) were added slowly. Then the mixture was stirred at room temperature for 12 h. Upon completion, the reaction mixture was washed with saturated NaCl for three times and extracted with ethyl acetate (3 × 10 mL), and the organic layers were combined, dried over anhydrous $MgSO_4$. The organic layer was then concentrated under vacuum, and the residue was separated by silica gelcolumn chromatography (hexanes/EtOAc) to give *N*-sulfonyl-2-aminobiaryls.

Starting materials 1u: The method for the synthesis of the known sulfonamide **1u** was the same as the method previously described except for replacing 3-bromoprop-1-ene with 3-bromo-2-methylprop-1-ene.

Starting materials 1s[3,4]:



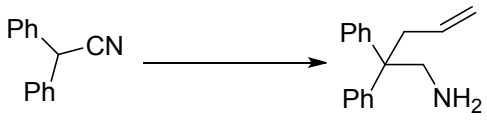
To a 100 mL round-bottomed flask was added n-BuMgBr (10 mL, 1.2 M in THF, 12 mmol) and n-BuLi (15 mL, 1.6 M in hexanes, 24 mmol) at 0 °C in THF (20 mL), and stirred for 10-15 min. The mixture was then cooled down to -78 °C and 2-bromobenzonitrile (1.82 g, 10 mmol) in THF (20 mL) was added dropwise. It was then allowed to stir at -78 °C for 1 h. Meanwhile, CuCN (269.6 mg, 3.01 mmol) and LiCl (254.3 mg, 6.00 mmol) in THF (3 mL) were added to a 15 mL round-bottomed flask and stirred at room temperature until all solids were dissolved and the mixture turned to blue color. The resulting CuCN·2LiCl solution and allyl bromide (3.5 mL, 40 mmol) were then added onto the reaction mixture at -78 °C, respectively. After 1 h stirring, the reaction mixture was then quenched with saturated aqueous NH_4Cl at room temperature. Organic materials were then extracted three times with 50 mL of Et_2O. The organic phase was washed with water and brine, and dried over $MgSO_4$. After filtration, the solvent was evaporated to give crude mixture, which was purified by Kugelrohr distillation to provide **1f** (0.93 g, 6.49 mmol) as a colorless oil for 65% yield.



A solution of 2-allylbenzonitrile (2.92 g, 0.020 mol, 1 equiv) in diethyl ether (10 mL)

was transferred via cannula over 2 mins to a Schlenk containing a lithium aluminum hydride (2.50 g, 0.063 mol, 3.2 equiv) suspension in diethyl ether (90 mL) at 0 ºC, allowing for venting of the formed gas. After stirring for 1 h at 0 ºC, the reaction mixture was carefully quenched via the dropwise addition of water (6 mL), 2M KOH (6 mL), and water (6 mL) at 0 ºC. Upon quench, the resulting suspension was brought to ambient temperature, then filtered through a Whatman filter paper and rinsed with diethyl ether (700 mL). The resulting filtrate was concentrated and the crude product thus obtained was purified by silica gel flash column chromatography (2/2/96 methanol/triethylamine/dichloromethane) to provide the desired amine as a pink oil after concentration under high vacuum (< 1 Torr) for 1 h (2.67 g, 0.018 mol, 91%). R_f = 0.42 (2/2/96 methanol/triethylamine/dichloromethane).

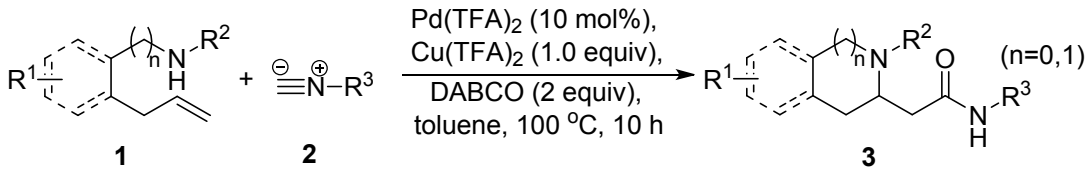
Starting materials 1t[5]:



***N*-(2,2-Diphenylpent-4-enyl)-4-methylbenzamide**. Sodium hydride (0.630 g, 21.00 mmol) was suspended in 20 mL of DMF and diphenylacetonitrile (3.86 g, 20.00 mmol) (dissolved in 6 mL of DMF) was added. The reaction was allowed to stir for 1 h. The reaction mixture was cooled to 0 °C and allyl bromide (1.861 mL, 22.00 mmol) was added. The reaction mixture was allowed to stir overnight. The reaction mixture was poured over an ice/water mixture (100 mL). The aqueous layer was extracted with benzene (3 × 50 mL). Then the combined organic layer was washed with water, dried over $MgSO_4$, and concentrated under reduced pressure. The reaction mixture

was carried on without further purification. LAH (1.594 g, mmol) was suspended in 50 mL of Et_2O and the crude product from the pervious step was added. The reaction was allowed to stir for two hours and then quenched with 50 mL of 1M NaOH. reaction mixture was filtered through celite and the celite was rinsed with Et_2O (2 × 10 mL). Reaction mixture was concentrated under reduced pressure and 2,2-diphenylpent-4-en-1-amine was carried on without further purification.

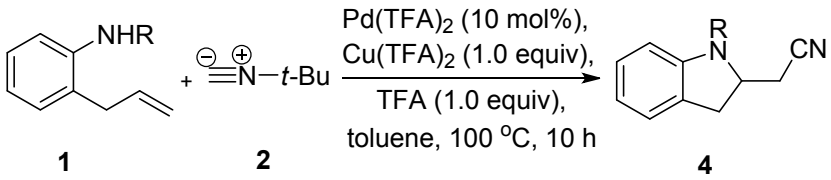
Experimental Procedures for 3a-3z:



1 **2** **3**

To the mixture of **1** (0.3 mmol), $Pd(TFA)_2$ (10 mol %) and $Cu(TFA)_2$ (1.0 equiv) in toluene (2.0 mL) solvent, TFA (2.0 equiv) were added successively. After stirred for 5 min at room temperature, isocyanide **2** (1.2 equiv) was added, and then the mixture was stirred at 100 °C for 10 h. After cooling to room temperature, the mixture was extracted by ethyl acetate (3 × 10 mL). The organic layer was washed with brine, and dried with anhydrous $MgSO_4$, filtered and concentrated under reduced pressure, and the residue was isolated by silica gel column chromatography, eluted with petroleum ether/ethyl acetate to give the pure product **3**.

Experimental Procedures for 4a-4e:



1 **2** **4**

To the mixture of **1** (0.3 mmol), $Pd(TFA)_2$ (10 mol %) and $Cu(TFA)_2$ (1.0 equiv) in toluene (2.0 mL) solvent was added TFA (1.0 equiv) dropwise. After stirred for 5 min at room temperature, isocyanide **2** (1.2 equiv) was added, and then the mixture was stirred at 100 °C for 10 h. After cooling to room temperature, the mixture was extracted by ethyl acetate (3 × 10 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ solution, and dried over anhydrous $MgSO_4$, filtered and concentrated under reduced pressure. The residue was isolated by silica gel column chromatography, eluted with petroleum ether/ethyl acetate to give the pure product **4**.

1. (a) Correa, A. Tellitu, I. Dominguez, E. SanMartin, R. *J. Org. Chem.*, 2006, **71**, 8316; (b) K. C. Nicolaou, A. J. Roecker, J. A. Pfefferkorn, G.-Q. Cao, *J. Am. Chem. Soc.*, 2000, **122**, 2966.

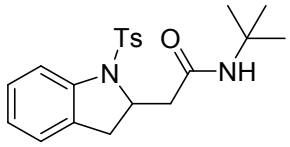
2. P. H. Fuller, J.-W. Kim, S. R. Chemler, *J. Am. Chem. Soc.*, 2008, **130**, 17638.

3. S. Sanjaya, S. Chiba, *Tetrahedron*, 2011, **67**, 590.

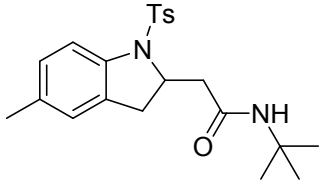
4. D. A. Ryan, D. Y. Gin, *J. Am. Chem. Soc.*, 2008, **130**, 15228.

5. P. A. Sibbald, F. E. Michael, *Org. Lett.*, 2009, **11**, 1147.

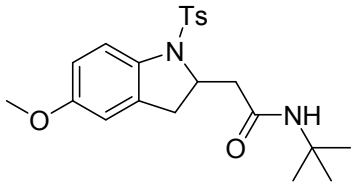
Analysis Data for Compounds 3a-3zd, 4a-4e, 5-7



***N*-(*tert*-butyl)-2-(1-tosylindolin-2-yl)acetamide (3a):** Grey solid; mp 89-91 °C. IR (KBr): 3690, 3308, 2898, 1673, 1530, 1463,1323, 1124, 816, 742; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.0 Hz, 1H), 7.52 (d, J = 7.6 Hz, 2H), 7.19-7.13 (m, 3H), 7.01-6.97 (m, 2H), 5.56 (br. s, 1H), 4.68-4.30 (m, 1H), 2.91-2.84 (m, 1H), 2.80-2.75 (m, 1H), 2.71-2.66 (m, 1H), 2.55-2.49 (m, 1H), 2.32 (s, 1H), 1.22 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 144.1, 141.2, 134.4, 131.9, 129.7, 127.7, 127.2, 125.4, 124.9, 117.1, 59.5, 51.4, 44.1, 34.0, 28.6, 21.5. HRMS (ESI) m/z: calcd for $C_{21}H_{27}N_2O_3S^+$, 387.1737; found, 387.1741.

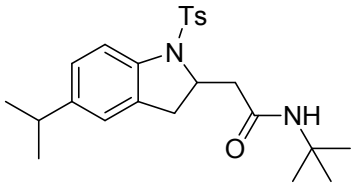


***N*-(*tert*-butyl)-2-(5-methyl-1-tosylindolin-2-yl)acetamide (3b):** Yellow solid; mp 94-96 °C. IR (KBr): 3697, 3312, 2970, 1663, 1541, 1488,1351, 1164, 816, 752; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, J = 7.2 Hz, 3H), 7.13 (d, J = 7.6 Hz, 2H), 6.97 (d, J = 8.0 Hz, 1H), 6.81 (s, 1H), 5.58 (br. s, 1H), 4.50-4.45 (m, 1H), 2.83-2.77 (m, 1H), 2.70-2.63 (m, 2H), 2.51-2.46 (m, 1H), 2.32 (s, 3H), 2.23 (s, 3H), 1.23 (s, 9H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 138.8, 134.7, 134.3, 132.0, 129.6, 128.3, 127.2, 125.9, 117.0, 59.6, 51.3, 44.0, 34.0, 28.6, 21.5, 20.9. HRMS (ESI) m/z: calcd for $C_{22}H_{29}N_2O_3S^+$, 401.1893; found, 401.1901.

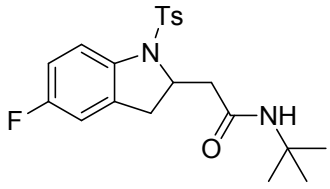


***N*-(*tert*-butyl)-2-(5-methoxy-1-tosylindolin-2-yl)acetamide (3c):**

Yellow solid; mp 102-104 °C. IR (KBr): 3667, 3319, 2968, 1662, 1538, 1486, 1352, 1164, 1032, 813, 741; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47-7.42 (m, 3H), 7.09 (d, J = 8.0 Hz, 1H), 6.67 (d, J = 8.4 Hz, 1H), 6.51 (s, 1H), 5.80 (br. s, 1H), 4.46-4.45 (m, 1H), 3.67 (s, 3H), 2.72-2.56 (m, 3H), 2.46-2.40 (m, 1H), 2.28 (s, 3H), 1.21 (s, 9H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 157.6, 144.0, 134.4, 134.1, 133.9, 129.6, 127.2, 118.4, 113.1, 110.8, 59.8, 55.5, 51.3, 43.8, 34.3, 28.6, 21.5. HRMS (ESI) m/z: calcd for $C_{22}H_{29}N_2O_4S^+$, 417.1843; found, 417.1849.

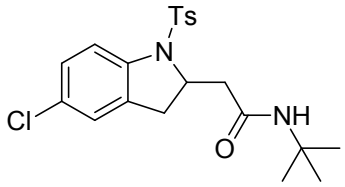


***N*-(*tert*-butyl)-2-(5-isopropyl-1-tosylindolin-2-yl)acetamide (3d):** Yellow solid; mp 140-142 °C. IR (KBr): 3683, 3317, 2964, 1661, 1541, 1353, 1164, 819, 750; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, J = 8.0 Hz, 3H), 7.08 (d, J = 8.0 Hz, 2H), 6.97 (d, J = 8.4 Hz, 1H), 6.82 (s, 1H), 5.77 (br. s, 1H), 4.48-4.44 (m, 1H), 2.82-2.72 (m, 2H), 2.68-2.60 (m, 2H), 2.49-2.44 (m, 1H), 2.27 (s, 3H), 1.17 (s, 9H), 1.11 (d, J = 6.8 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 145.8, 144.0, 139.0, 134.4, 131.9, 129.6, 127.1, 125.8, 123.3, 116.8, 59.6, 51.2, 44.0, 34.0, 33.6, 28.5, 24.1, 24.0, 21.5. HRMS (ESI) m/z: calcd for $C_{24}H_{33}N_2O_3S^+$, 429.2206; found, 429.2214.

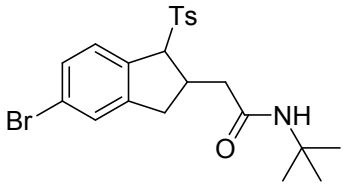


***N*-(*tert*-butyl)-2-(5-fluoro-1-tosylindolin-2-yl)acetamide (3e):** Yellow oil. IR (KBr): 3695, 3309, 3080, 2974, 1730, 1548, 1481, 1356, 1166, 816, 668; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56-7.47 (m, 3H), 7.19-7.13 (m, 2H), 6.85 (t, J = 8.0 Hz, 1H), 6.69 (d, J =

7.6 Hz, 1H), 5.64 (br. s, 1H), 4.51 (s, 1H), 2.80-2.64 (m, 3H), 2.50-2.45 (m, 1H), 2.32 (s, 3H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 160.3 (d, J = 221.1 Hz), 144.3, 137.2 (d, J = 1.7 Hz), 134.3 (d, J = 8.8 Hz), 134.0, 129.7, 127.2, 118.2 (d, J = 8.6 Hz), 114.4 (d, J = 23.2 Hz), 112.5 (d, J = 23.6 Hz), 60.0, 51.4, 43.8, 34.1, 28.6, 21.5. HRMS (ESI) m/z: calcd for $C_{21}H_{25}FN_2NaO_3S^+$, 427.1462; found, 427.1469.

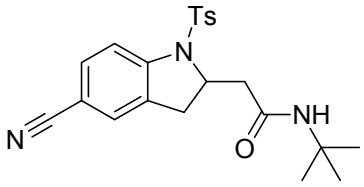


***N*-(*tert*-butyl)-2-(5-chloro-1-tosylindolin-2-yl)acetamide (3f):** Brown solid; mp 148-150 ^{o}C. IR (KBr): 3672, 3319, 2970, 1660, 1596, 1470, 1355, 1167, 816, 717; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 (d, J = 8.4 Hz, 3H), 7.13 (d, J = 8.0 Hz, 2H), 7.08 (d, J = 8.8 Hz, 1H), 6.94 (s, 1H), 5.79 (br. s, 1H), 4.51-4.49 (m, 1H), 2.86-2.79 (m,1H), 2.72-2.67 (m, 2H), 2.50-2.44 (m, 1H), 2.30 (s, 3H), 1.22 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 144.4, 139.9, 134.0, 133.8, 130.0, 129.8, 127.7, 127.1, 125.5, 117.8, 59.9, 51.5, 43.7, 34.0, 28.6, 21.5. HRMS (ESI) m/z: calcd for $C_{21}H_{26}ClN_2O_3S^+$, 421.1347; found, 421.1353.

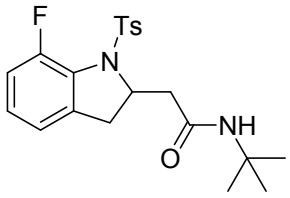


2-(5-bromo-1-tosyl-2,3-dihydro-1H-inden-2-yl)-*N*-(*tert*-butyl)acetamide (3g): Yellow solid; mp 142-144 ^{o}C. IR (KBr): 3686, 3313, 1712, 1582, 1268, 1165, 755; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58-7.45 (m, 3H), 7.29 (d, J = 5.6 Hz, 1H), 7.20-7.15 (m, 3H), 5.73 (br. s, 1H), 4.57-4.52 (m, 1H), 2.93-2.66 (m, 3H), 2.56-2.49 (m, 1H), 2.36 (s, 3H), 1.28 (s, 9H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 144.4, 134.1, 134.1, 130.7, 129.8, 128.4, 127.1, 118.2,

117.6, 59.8, 51.4, 43.8, 33.9, 28.6, 21.5. HRMS (ESI) m/z: calcd for $C_{21}H_{26}BrN_2O_3S^+$, 465.0842; found, 465.0848.

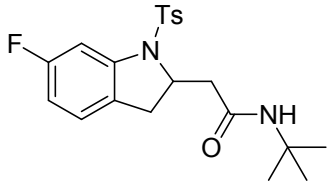


***N*-(*tert*-butyl)-2-(5-cyano-1-tosylindolin-2-yl)acetamide (3h):** Brownish solid; mp 157-159 °C. IR (KBr): 3679, 3326, 2971, 2226, 1664, 1537, 1357, 1167, 743, 667; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.4 Hz, 1H), 7.61 (d, J = 8.0 Hz, 2H), 7.48 (d, J = 8.4 Hz, 1H), 7.31 (s, 1H), 7.24 (d, J = 8.0 Hz, 2H), 5.84 (br. s, 1H), 4.67-4.60 (m, 1H), 3.10-3.04 (m, 1H), 2.97-2.92 (m, 1H), 2.87-2.83 (m, 1H), 2.60-2.54 (m, 1H), 2.37 (s, 3H), 1.29 (s, 9H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 145.4, 144.9, 134.1, 132.6, 132.5, 130.0, 129.1, 126.9, 118.8, 116.1, 107.4, 60.0, 51.4, 43.7, 33.8, 28.6, 21.5. HRMS (ESI) m/z: calcd for $C_{22}H_{25}N_3NaO_3S^+$, 434.1509; found, 434.1514.



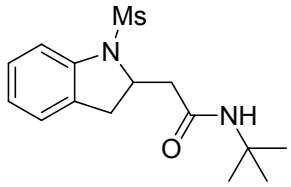
***N*-(*tert*-butyl)-2-(7-fluoro-1-tosylindolin-2-yl)acetamide (3i):** Pale yellow oil. IR (KBr): 3692, 3302, 3115, 1722, 1553, 1168, 955, 675; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, J = 7.6 Hz, 2H), 7.14 (d, J = 8.0 Hz, 2H), 7.06-7.01 (m, 1H), 6.97-6.92 (m, 1H), 6.81 (d, J = 7.2 Hz, 0H), 5.70 (br. s, 1H), 4.70-4.66 (m, 1H), 2.53-2.42 (m, 3H), 2.34 (s, 3H), 2.31-2.27 (m, 1H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 154.5 (d, J = 253.6 Hz), 144.4, 138.5 (d, J = 1.4 Hz), 134.3, 129.7, 128.2 (d, J = 10.1 Hz), 127.7 (d, J = 6.8 Hz), 127.6, 121.0 (d, J = 3.5 Hz), 115.9 (d, J = 20.2 Hz), 61.7, 51.4, 42.9,34.3, 28.6, 21.6. HRMS (ESI) m/z: calcd for

$C_{21}H_{26}FN_2O_3S^+$, 405.1643; found, 405.1651.



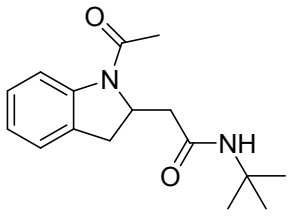
***N*-(*tert*-butyl)-2-(6-fluoro-1-tosylindolin-2-yl)acetamide (3j):**

Yellow solid; mp 98-100 °C. IR (KBr): 3695, 3301, 3114, 1725, 1546, 1493, 1356, 1165, 979, 865; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 (d, J = 8.0 Hz, 2H), 7.33 (d, J = 10.0 Hz, 1H), 7.16 (d, J = 8.0 Hz, 2H), 6.93-6.89 (m, 1H), 6.68-6.63 (m, 1H), 5.71 (br. s, 1H), 4.55-4.51 (m, 1H), 2.89-2.83 (m, 1H), 2.76-2.69 (m, 2H), 2.55-2.49 (m, 1H), 2.32 (s, 3H), 1.24 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.9, 162.5 (d, J = 242.0 Hz), 144.5, 142.5 (d, J = 11.6 Hz), 134.2, 129.8, 127.1, 126.9 (d, J = 2.6 Hz), 125.9 (d, J = 9.6 Hz), 111.4 (d, J = 22.5 Hz), 104.7 (d, J = 27.8 Hz), 60.5, 51.5, 43.9, 33.5, 28.6, 21.5. HRMS (ESI) m/z: calcd for $C_{21}H_{26}FN_2O_3S^+$, 405.1643; found, 405.1641.

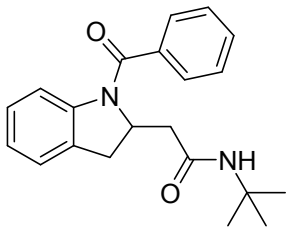


***N*-(*tert*-butyl)-2-(1-(methylsulfonyl)indolin-2-yl)acetamide (3k):**

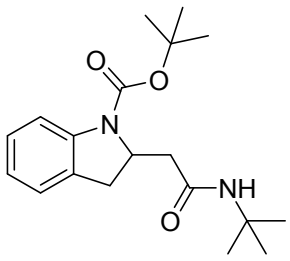
Yellow solid; mp 151-153 °C. IR (KBr): 3693, 3315, 2972, 1661, 1538, 1343, 1158, 979, 759; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, J = 8.4 Hz, 1H), 7.15-7.12 (m, 2H), 7.03-7.00 (m, 1H), 5.61 (br. s, 1H), 4.60-4.55 (m, 1H), 3.48-3.42 (m, 1H), 3.03-2.99 (m, 1H), 2.78 (s, 3H), 2.72-2.67 (m, 1H), 2.52-2.46 (m, 1H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 141.1, 131.0, 128.0, 125.6, 124.7, 115.5, 60.0, 51.3, 44.3, 35.3, 34.4, 28.6. HRMS (ESI) m/z: calcd for $C_{15}H_{22}N_2NaO_3S^+$, 333.1243; found, 333.1250.



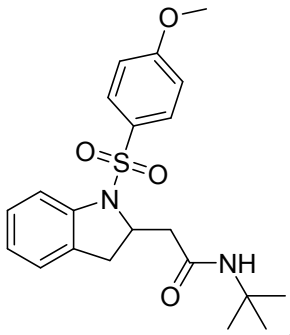
2-(1-acetylindolin-2-yl)-*N*-(*tert*-butyl)acetamide (3l): Yellow solid; mp 162-164 °C. IR (KBr): 3662, 3323, 2972, 1654, 1545, 1477, 1400, 942, 751; ^{1}H NMR (400 MHz, $(CD_3)_2C=O$) δ 8.04 (s, 1H), 7.21 (d, J = 6.8 Hz, 1H), 7.16-7.12 (m, 1H), 7.01-6.97 (m, 1H), 4.82 (br. s, 1H), 3.30 (d, J = 7.2 Hz, 1H), 2.95 (s, 1H), 2.84 (d, J = 16.0 Hz, 1H), 2.52-2.33 (m, 2H), 2.25 (s, 3H), 1.31 (s, 9H); ^{13}C NMR (100 MHz, $(CD_3)_2C=O$) δ 169.6, 168.6, 143.3, 131.7, 127.8, 125.9, 124.2, 118.2, 58.9, 51.4, 42.6, 34.9, 29.0, 23.5. HRMS (ESI) m/z: calcd for $C_{16}H_{23}N_2O_2^+$, 275.1754; found, 275.1759.



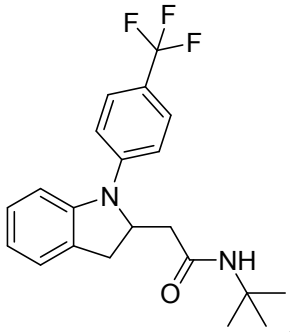
2-(1-benzoylindolin-2-yl)-*N*-(*tert*-butyl)acetamide (3m): Yellow solid; mp 172-174 °C. IR (KBr): 3693, 3323, 2971, 1646, 1480, 1393, 926, 753; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45-7.35 (m, 6H), 7.15 (d, J = 7.2 Hz, 1H), 6.92-6.89 (m, 2H), 5.72 (br. s, 1H), 4.92 (s, 1H), 3.39-3.32 (m, 1H), 2.99 (d, J = 16.4 Hz, 1H), 2.56 (s, 1H), 2.25-2.19 (m, 1H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.1, 168.7, 141.4, 136.4, 131.7, 130.6, 128.8, 127.2, 126.9, 125.7, 124.0, 116.2, 58.9, 51.2, 41.2, 33.6, 28.7. HRMS (ESI) m/z: calcd for $C_{21}H_{24}N_2NaO_2^+$, 359.1730; found, 359.1737.



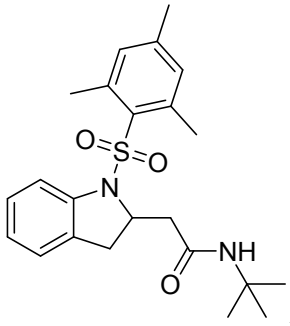
***tert*-butyl 2-(2-(tert-butylamino)-2-oxoethyl)indoline-1-carboxylate (3n):** Yellow solid; mp 129-131 °C. IR (KBr): 3662, 3323, 2975, 1754, 1645, 1477, 942, 751; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 1H), 7.14-7.10 (m, 2H), 6.91 (t, J = 7.2 Hz, 1H), 5.42 (br. s, 1H), 4.72-4.67 (m, 1H), 3.36-3.29 (m, 1H), 2.95 (d, J = 15.2 Hz, 1H), 2.66-2.62 (m, 1H), 2.27-2.22 (m, 1H), 1.55 (s, 9H), 1.26 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4,152.3, 141.7, 130.2, 127.4, 125.2, 122.8, 115.3, 81.4, 57.1, 41.9, 33.4, 28.8, 28.5. HRMS (ESI) m/z: calcd for $C_{19}H_{29}N_2O_3^+$, 333.2173; found, 333.2179.



***N*-(*tert*-butyl)-2-(1-((4-methoxyphenyl)sulfonyl)indolin-2-yl)acetamide (3o):** Yellow solid; mp 153-155 °C. IR (KBr): 3694, 3308, 2972, 1722, 1539, 1352, 1160, 1024, 835; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.0 Hz, 1H), 7.54 (d, J = 8.8 Hz, 2H), 7.15 (t, J = 7.2 Hz, 1H), 7.00-6.95 (m, 2H), 6.78 (d, J = 8.8 Hz, 2H), 5.67 (br. s, 1H), 4.51-4.46 (m, 1H), 3.75 (s, 3H), 2.90-2.82 (m, 1H), 2.74-2.65 (m, 2H), 2.52-2.46 (m, 1H), 1.21 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 163.3, 141.3, 131.9, 129.2, 128.9, 127.7, 125.4, 124.9, 117.1, 114.2, 59.5, 55.5, 51.3, 44.0, 34.1, 28.6. HRMS (ESI) m/z: calcd for $C_{21}H_{27}N_2O_4S^+$, 403.1686; found, 403.1682.

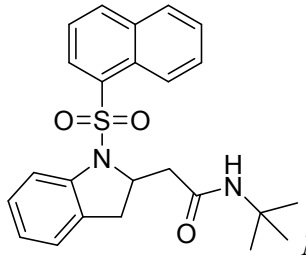


***N*-(*tert*-butyl)-2-(1-(4-(trifluoromethyl)phenyl)indolin-2-yl)acetamide (3p):** White solid; mp 137-138 °C. IR (KBr): 3661, 3322, 2972, 1662, 1537, 1324,1172, 842, 715; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.0 Hz, 2H), 7.61-7.59 (m, 3H), 7.17 (t, J = 6.8 Hz, 1H), 7.03-6.98 (m, 2H), 5.65 (br. s, 1H), 4.56-4.51 (m, 1H), 2.91-2.84 (m, 1H), 2.77-2.70 (m, 2H), 2.50-2.45 (m, 1H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 140.8, 140.5, 134.8 (q, J = 32.7 Hz), 131.7, 127.9, 127.6, 126.2 (q, J = 3.5 Hz), 125.7, 125.3, 123.1 (q, J = 271.2 Hz), 116.8, 59.8, 51.4, 43.8, 34.1, 28.6. HRMS (ESI) m/z: calcd for $C_{21}H_{24}F_3N_2O_3S^+$, 441.1454; found, 441.1457.

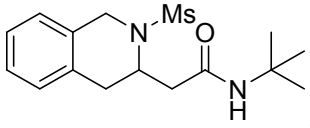


***N*-(*tert*-butyl)-2-(1-(mesitylsulfonyl)indolin-2-yl)acetamide (3q):** Yellow solid; mp 126-128 °C. IR (KBr): 3693, 3321, 2972, 1660, 1541, 1338, 1158, 1045, 750, 663; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.07 (d, J = 7.2 Hz, 1H), 7.01-6.85 (m, 5H), 5.81 (br. s, 1H), 4.60 (d, J = 1.6 Hz, 1H), 3.26-3.20 (m, 1H), 2.99 (d, J = 16.0 Hz, 1H), 2.59-2.54 (m, 1H), 2.52 (s, 6H), 2.46-2.42 (m, 1H), 2.23 (s, 3H), 1.10 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 143.1, 141.8, 140.3, 132.8, 132.3, 130.3, 127.4, 125.6, 123.4, 114.1, 59.3, 51.2, 43.2, 33.5, 28.3, 22.9,

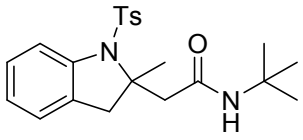
21.0. HRMS (ESI) m/z: calcd for $C_{23}H_{31}N_2O_3S^+$, 415.2050; found, 415.2048.



***N*-(*tert*-butyl)-2-(1-(naphthalen-1-ylsulfonyl)indolin-2-yl)acetamide (3r):** Yellow solid; mp 158-160 ^oC. IR (KBr): 3693, 3313, 2972, 1663, 1538, 1350, 1164, 753, 660; ^1H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 7.82 (d, J = 8.4 Hz, 1H), 7.77-7.68 (m, 3H), 7.56-7.50 (m, 3H), 7.18 (t, J = 6.8 Hz, 1H), 6.98-6.94 (m, 2H), 5.76 (br. s, 1H), 4.65-4.61 (m, 1H), 2.84-2.69 (m, 3H), 2.56-2.50 (m, 1H), 1.23 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.0, 141.1, 135.0, 134.4, 132.0, 131.8, 129.3, 128.9, 128.7, 127.8, 127.8, 127.6, 125.5, 125.0, 122.1, 117.0, 59.7, 51.4, 44.0, 34.1, 28.6. HRMS (ESI) m/z: calcd for $C_{24}H_{27}N_2O_3S^+$, 423.1737; found, 423.1745.

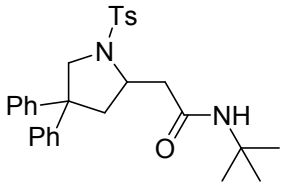


***N*-(*tert*-butyl)-2-(2-(methylsulfonyl)-1,2,3,4-tetrahydroisoquinolin-3-yl)acetamide (3s):** Yellow oil. IR (KBr): 3689, 3316, 2972, 1661, 1538, 1343, 1158, 979, 759; ^1H NMR (400 MHz, $CDCl_3$) δ 7.17-7.06 (m, 4H), 5.63 (br. s, 1H), 4.60 (d, J = 8.4 Hz, 1H), 4.38-4.34 (m, 1H), 4.25 (d, J = 16.8 Hz, 1H), 3.14-3.08 (m, 1H), 2.79-2.74 (m, 1H), 2.64 (s, 3H), 2.45-2.40 (m, 1H), 2.28-2.23 (m, 1H), 1.28 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 132.9, 132.3, 129.3, 127.6, 126.7, 125.8, 51.4, 50.3, 43.8, 41.2, 38.4, 32.9, 28.7. HRMS (ESI) m/z: calcd for $C_{16}H_{25}N_2O_3S^+$, 325.1580; found, 325.1584.



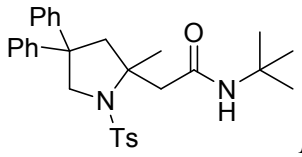
***N*-(*tert*-butyl)-2-(2-methyl-1-tosylindolin-2-yl)acetamide (3t):**

Grey solid; mp 89-91 °C. IR (KBr): 3403.9, 2960.3, 2355.7, 1661.8, 1343.0, 1013.2, 577.0; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.4 Hz, 2H), 7.31 (d, J = 7.6 Hz, 1H), 7.19 (d, J = 7.2 Hz, 2H), 7.01 (d, J = 6.8 Hz, 2H), 6.85 (t, J = 7.2 Hz, 1H), 5.89 (s, 1H), 3.78 (d, J = 16.0 Hz, 1H), 3.04 (d, J = 13.6 Hz, 1H), 2.89 (d, J = 16.4 Hz, 1H), 2.37 (d, J = 13.2 Hz, 1H), 2.32 (s, 3H), 1.60 (s, 3H), 1.18 (s, 3H), 1.05 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 143.9, 141.9, 138.4, 129.7, 128.7, 127.4, 126.8, 125.2, 123.1, 113.4, 70.9, 51.2, 49.6, 42.4, 28.2, 27.9, 21.5. HRMS (ESI) m/z: calcd for $C_{22}H_{29}N_2O_3S^+$, 401.1893; found, 401.1895.

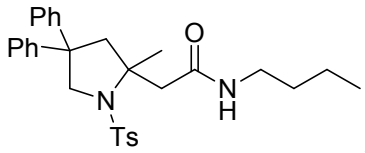


***N*-(tert-butyl)-2-(4,4-diphenyl-1-tosylpyrrolidin-2-yl)acetamide (3u):**

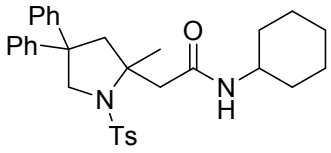
White solid; mp 99-101 °C. IR (KBr): 3387.5, 3057.0, 2968.2, 1663.4, 1532.2, 1339.4, 1159.0, 706.2, 663.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, J = 8.0 Hz, 2H), 7.19 (d, J = 4.4 Hz, 4H), 7.11-7.05 (m, 3H), 7.00 (s, 5H), 5.58 (br. s, 1H), 4.32 (d, J = 10.8 Hz, 1H), 4.05-3.97 (m, 1H), 3.73 (d, J = 10.4 Hz, 1H), 2.87-2.76 (m, 2H), 2.57-2.52 (m, 1H), 2.29 (s, 3H), 2.12-2.06 (m, 1H), 1.29 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 145.5, 144.3, 143.3, 133.6, 129.7, 128.6, 127.3, 126.7, 126.5, 126.5, 126.2, 59.0, 56.9, 52.3, 51.1, 43.2, 42.7, 28.8, 21.5. HRMS (ESI) m/z: calcd for $C_{29}H_{35}N_2O_3S^+$, 491.2363; found, 491.2369.



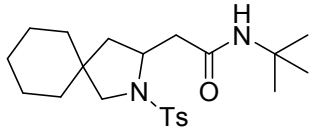
***N*-(*tert*-butyl)-2-(2-methyl-4,4-diphenyl-1-tosylpyrrolidin-2-yl)acetamide (3v):** White solid; mp 167-168 °C. IR (KBr): 3722.4, 2971.3, 2355.4, 1634.4, 1327.0, 1052.1, 663.6; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.0 Hz, 2H), 7.29 – 7.25 (m, 4H), 7.21 (t, J = 7.2 Hz, 2H), 7.14 – 7.09 (m, 4H), 7.03 (s, 2H), 5.49 (s, 1H), 4.15 (d, J = 10.0 Hz, 1H), 3.79 (d, J = 10.8 Hz, 1H), 3.59 (d, J = 13.2 Hz, 1H), 2.77 (d, J = 13.6 Hz, 1H), 2.57 (d, J = 13.2 Hz, 1H), 2.42 (s, 3H), 2.26 (d, J = 10.0 Hz, 1H), 1.35 (s, 3H), 1.30 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 145.2, 143.2, 137.6, 129.6, 128.6, 128.4, 127.6, 126.9, 126.5, 126.4, 66.9, 56.8, 51.4, 51.2, 49.7, 48.7, 28.6, 27.0, 21.5. HRMS (ESI) m/z: calcd for $C_{30}H_{37}N_2O_3S^+$, 505.2519; found, 505.2519.



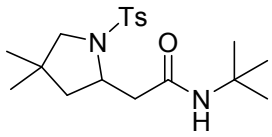
***N*-butyl-2-(2-methyl-4,4-diphenyl-1-tosylpyrrolidin-2-yl)acetamide (3w):** White solid; mp 122-124 °C. IR (KBr): 3382.4, 2930.5, 2356.4, 1645.1, 1329.2, 1154.2, 664.0; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.6 Hz, 2H), 7.30 – 7.26 (m, 4H), 7.22 (t, J = 7.2 Hz, 2H), 7.12 (d, J = 5.6 Hz, 4H), 7.05 (d, J = 6.8 Hz, 2H), 5.68 (d, J = 4.4 Hz, 1H), 4.19 (d, J = 10.4 Hz, 1H), 3.74 (d, J = 10.0 Hz, 1H), 3.59 (d, J = 13.2 Hz, 1H), 3.22 – 3.06 (m, 2H), 2.88 (d, J = 14.0 Hz, 1H), 2.57 (d, J = 13.2 Hz, 1H), 2.43 (s, 3H), 2.27 (d, J = 13.6 Hz, 1H), 1.45 – 1.40 (m, 2H), 1.36 (s, 3H), 1.34 – 1.23 (m, 3H), 0.89 (t, J = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.1, 145.3, 145.1, 143.3, 137.4, 129.6, 128.6, 128.5, 127.6, 126.9, 126.5, 126.4, 126.4, 66.7, 56.6, 51.4, 49.9, 47.6, 39.1, 31.5, 26.9, 21.5, 20.1, 13.8. HRMS (ESI) m/z: calcd for $C_{30}H_{37}N_2O_3S^+$, 505.2519; found, 505.2517.



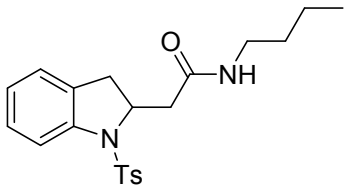
***N*-cyclohexyl-2-(2-methyl-4,4-diphenyl-1-tosylpyrrolidin-2-yl)acetamide (3x):** Brown solid; mp 156-158 ^{o}C. IR (KBr): 3709.9, 2929.5, 2355.58, 1672.3, 1150.9, 1052.6, 697.6; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.6 Hz, 2H), 7.31 – 7.21 (m, 6H), 7.16 – 7.12 (m, 4H), 7.04 (d, J = 6.4 Hz, 2H), 5.44 (d, J = 7.6 Hz, 1H), 4.20 (d, J = 10.0 Hz, 1H), 3.73 (d, J = 10.0 Hz, 1H), 3.57 (d, J = 13.2 Hz, 1H), 2.82 (d, J = 14.0 Hz, 1H), 2.55 (d, J = 13.2 Hz, 1H), 2.44 (s, 3H), 2.24 (d, J = 13.6 Hz, 1H), 1.85 (s, 3H), 1.67 – 1.57 (m, 3H), 1.35 (s, 3H), 1.28 (d, J = 15.6 Hz, 2H), 1.18 – 1.05 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.2, 145.3, 145.1, 143.3, 137.5, 129.6, 128.6, 128.5, 127.6, 126.9, 126.5, 126.4, 66.7, 56.7, 51.3, 49.7, 48.3, 47.8, 33.0, 32.9, 27.0, 25.5, 24.9, 24.9, 21.5. HRMS (ESI) m/z: calcd for $C_{32}H_{38}N_2NaO_3S^+$, 553.2495; found, 553.2504.



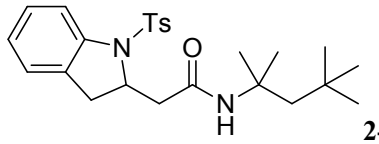
***N*-(*tert*-butyl)-2-(2-tosyl-2-azaspiro[4.5]decan-3-yl)acetamide (3y):** Yellow oil; IR (KBr): 3381.6, 2927.3, 1654.8, 1540.5, 1157.1, 661.9; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.6 Hz, 1H), 7.33 (d, J = 7.6 Hz, 1H), 6.12 (s, 0H), 3.73 (d, J = 7.6 Hz, 0H), 3.28 (d, J = 10.8 Hz, 1H), 3.09 (d, J = 10.8 Hz, 1H), 2.74 (d, J = 14.0 Hz, 1H), 2.65 – 2.60 (m, 1H), 2.42 (s, 3H), 1.88 – 1.83 (m, 1H), 1.76 – 1.71 (m, 1H), 1.37 (s, 9H), 1.27 – 1.15 (m, 8H), 0.69 – 0.64 (m, 1H), 0.49 – 0.46 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.9, 143.6, 133.7, 129.6, 127.5, 56.6, 51.0, 43.2, 40.7, 36.3, 33.6, 28.7, 25.7, 23.6, 22.6, 21.5. HRMS (ESI) m/z: calcd for $C_{22}H_{35}N_2O_3S^+$, 407.2363; found, 407.2361.



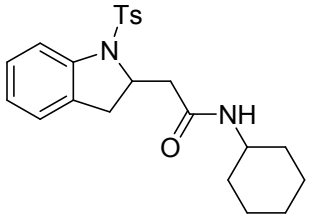
***N*-(*tert*-butyl)-2-(4,4-dimethyl-1-tosylpyrrolidin-2-yl)acetamide (3z):** Light yellow solid; mp 118-120 °C. IR (KBr): 3133.0, 2964.5, 2355.6, 1667.7, 1399.9, 1046.3, 661.4; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 7.6 Hz, 2H), 7.33 (d, J = 8.0 Hz, 2H), 6.04 (s, 1H), 3.79 (q, J = 7.5 Hz, 1H), 3.16 (d, J = 10.4 Hz, 1H), 3.08 (d, J = 10.4 Hz, 1H), 2.74 (d, J = 14.0 Hz, 1H), 2.66 – 2.60 (m, 1H),, 2.43 (s, 3H), 1.86 – 1.74 (m, 2H), 1.37 (s, 9H), 1.00 (s, 3H), 0.37 (s, 3H).. ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.8, 143.6, 133.9, 129.7, 127.6, 61.9, 57.42 (s, 3H), 51.1, 45.7, 43.2, 36.8, 28.7, 26.2, 25.5, 21.5. HRMS (ESI) m/z: calcd for $C_{19}H_{31}N_2O_3S^+$, 367.2050; found, 367.2045.



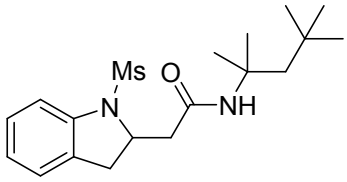
***N*-butyl-2-(1-tosylindolin-2-yl)acetamide (3za):** Yellow solid; mp 106-108 °C. IR (KBr): 3690, 3304, 2953, 1722, 1551, 1351, 1164, 966, 756, 576; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 8.0 Hz, 2H), 7.17-7.11 (m, 3H), 7.09-6.95 (m, 2H), 5.98 (br. s, 1H), 4.55-4.48 (m, 1H), 3.22-3.07 (m, 2H), 2.88-2.69 (m, 3H), 2.54-2.48 (m, 1H), 2.30 (s, 3H), 1.42-1.35 (m, 2H), 1.31-1.20 (m, 2H), 0.86 (t, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.7, 144.2, 141.1, 134.3, 131.8, 129.7, 127.7, 127.1, 125.3, 124.9, 117.2, 59.5, 43.2, 39.3, 34.3, 31.5, 21.5, 20.1, 13.7. HRMS (ESI) m/z: calcd for $C_{21}H_{26}N_2NaO_3S^+$, 409.1556; found, 409.1565.



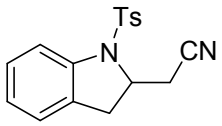
2-(1-tosylindolin-2-yl)-*N*-(2,4,4-trimethylpentan-2-yl)acetamide (3zb): Green solid; mp 130-132 °C. IR (KBr): 3694, 3311, 2956, 1665, 1540, 1353, 1164, 754, 665; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.0 Hz, 1H), 7.50 (d, J = 8.0 Hz, 2H), 7.17-6.11 (m, 3H), 6.99-6.95 (m, 2H), 5.63 (br. s, 1H), 4.52-4.48 (m, 1H), 2.89-2.83 (m, 1H), 2.74-2.68 (m, 2H), 2.50-2.44 (m, 1H), 2.30 (s, 3H), 1.71 (d, J = 14.8 Hz, 1H), 1.57 (d, J = 14.8 Hz, 1H), 1.27 (d, J = 5.6 Hz, 6H), 0.96 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.8, 144.1, 141.2, 134.3, 131.9, 129.7, 127.7, 127.1, 125.4, 124.9, 117.1, 59.5, 55.3, 51.6, 44.3, 34.2, 31.6, 31.5, 29.1, 28.9, 21.5. HRMS (ESI) m/z: calcd for $C_{25}H_{35}N_2O_3S^+$, 443.2363; found, 443.2371.



***N*-cyclohexyl-2-(1-tosylindolin-2-yl)acetamide (3zc):** Yellow solid; mp 173-175 °C. IR (KBr): 3692, 3299, 2931, 2855, 1544, 1351, 1165, 1096, 754; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, J = 8.0 Hz, 1H), 7.49 (d, J = 7.6 Hz, 2H), 7.15-7.10 (m, 3H), 6.97-6.94 (m, 2H), 5.88 (br. s, 1H), 4.52-4.48 (m, 1H), 3.69-3.61 (m, 1H), 2.87-2.80 (m, 1H), 2.75-2.69 (m, 2H), 2.53-2.47 (m, 1H), 2.29 (s, 3H), 1.86 (d, J = 8.8 Hz, 1H), 1.67-1.51 (m, 4H), 1.32-1.21 (m, 2H), 1.13-0.90 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 144.2, 141.1, 134.3, 131.8, 129.7, 127.7, 127.1, 125.3, 124.9, 117.2, 59.5, 48.3, 43.3, 34.2, 32.9, 25.5, 24.9, 21.5. HRMS (ESI) m/z: calcd for $C_{23}H_{28}N_2NaO_3S^+$, 435.1713; found, 435.1722.

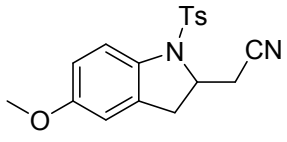


2-(1-(methylsulfonyl)indolin-2-yl)-*N*-(2,4,4-trimethylpentan-2-yl)acetamide (3zd): Yellow solid; mp 99-101 °C. IR (KBr): 3684, 3328, 2955, 1661, 1538, 1346, 1159, 979, 758; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, J = 8.0 Hz, 1H), 7.12 (t, J = 7.2 Hz, 2H), 7.00 (t, J = 7.6 Hz, 1H), 5.62 (br. s, 1H), 4.59-4.53 (m, 1H), 2.99-2.94 (m, 1H), 2.76 (s, 2H), 2.74-2.69 (m, 1H), 2.49-2.43 (m, 1H), 1.62 (q, $J_1 = J_2$ = 14.8 Hz, 2H), 1.25 (d, J = 6.4 Hz, 6H), 0.93 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 141.1, 131.0, 128.0, 125.6, 124.7, 115.5, 59.9, 55.3, 51.5, 44.5, 35.3, 34.6, 31.6, 31.4, 29.1, 28.9. HRMS (ESI) m/z: calcd for $C_{19}H_{31}N_2O_3S^+$, 367.2050; found, 367.2058.



2-(1-tosylindolin-2-yl)acetonitrile (4a):

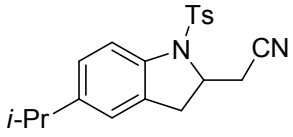
Yellow oil. IR (KBr): 2923.8, 2249.7, 1472.1, 1353.3, 1165.8, 1097.5, 756.1, 666.6; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, J = 8.4 Hz, 1H), 7.56 (d, J = 7.6 Hz, 2H), 7.26 (s, 1H), 7.20 (d, J = 8.0 Hz, 2H), 7.09-7.06 (m, 2H), 4.48-4.44 (m, 1H), 3.07-2.97 (m, 2H), 2.84-2.74 (m, 2H), 2.37 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.6, 140.5, 134.2, 129.9, 129.8, 128.4, 127.1, 125.4, 125.3, 117.0, 116.7, 58.0, 33.9, 25.5, 21.6. HRMS (ESI) m/z: calcd for $C_{17}H_{16}N_2NaO_2S^+$, 335.0825; found, 335.0830.



2-(5-methoxy-1-tosylindolin-2-yl)acetonitrile (4b):

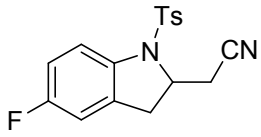
Yellow oil. IR (KBr): 2932.7, 2250.6, 1601.9, 1485.4, 1353.3, 1166.6, 1033.9, 750.3, 669.3; ^{1}H

NMR (400 MHz, $CDCl_3$) δ 7.55 (d, J = 8.8 Hz, 1H), 7.49 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 7.6 Hz, 2H), 6.77 (d, J = 8.8 Hz, 1H), 6.61 (s, 1H), 4.44-4.40 (m, 1H), 3.74 (s, 3H), 2.91-2.84 (m, 2H), 2.76-2.66 (m, 2H), 2.35 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 144.5, 133.9, 133.7, 131.9, 129.8, 127.1, 118.4, 116.7, 113.7, 110.9, 58.4, 55.6, 34.0, 25.3, 21.6. HRMS (ESI) m/z: calcd for $C_{18}H_{18}N_2NaO_3S^+$, 365.0930; found, 365.0936.



2-(5-isopropyl-1-tosylindolin-2-yl)acetonitrile (4c):

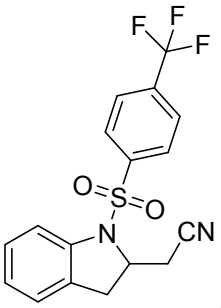
Yellow solid; mp 50-52 ^{o}C.. IR (KBr): 2959.4, 2250.7, 1486.0, 1354.1, 1165.6, 752.0, 667.4, 587.1; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.0 Hz, 3H), 7.17 (d, J = 8.0 Hz, 2H), 7.17 (d, J = 7.6 Hz, 2H), 7.07 (d, J = 8.4 Hz, 1H), 6.92 (s, 1H), 4.43-4.39 (m, 1H), 3.00-2.92 (m, 2H), 2.86-2.70 (m, 3H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 146.3, 144.5, 138.3, 134.2, 129.8, 129.8, 127.1, 126.5, 123.3, 116.8, 58.2, 34.0, 33.7, 25.4, 24.1, 24.0, 21.6. HRMS (ESI) m/z: calcd for $C_{20}H_{22}N_2NaO_2S^+$, 377.1294; found, 377.1298.



2-(5-fluoro-1-tosylindolin-2-yl)acetonitrile (4d):

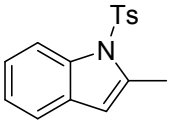
Yellow oil. IR (KBr): 2923.6, 2250.8, 1481.6, 1354.9, 1167.0, 753.0; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60-7.57 (m, 1H), 7.50 (d, J = 7.2 Hz, 2H), 7.18 (d, J = 7.6 Hz, 2H), 6.92 (d, J = 8.8 Hz, 1H), 6.76 (d, J = 8.0 Hz, 1H), 4.46-4.42 (m, 1H), 2.97-2.88 (m, 2H), 2.79-2.71 (m, 2H), 2.34 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6 (d, J = 242.9 Hz), 144.8, 136.6, 133.8, 132.2 (d, J = 8.8 Hz), 130.0, 127.1, 118.3 (d, J = 8.7 Hz), 116.5, 115.2 (d, J = 23.5 Hz), 112.6 (d, J = 24.2 Hz). HRMS (ESI) m/z:

calcd for $C_{17}H_{16}FN_2O_2S^+$, 331.0911; found, 331.0909.

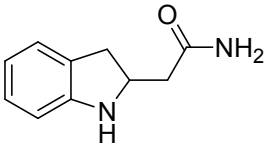


2-(1-((4-(trifluoromethyl)phenyl)sulfonyl)indolin-2-yl)acetonitrile (4e):

Yellow oil. IR (KBr): 2924.4, 2249.1, 1323.3, 1170.0, 841, 3, 752.8; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 7.6 Hz, 2H), 7.61 (d, J = 8.4 Hz, 3H), 7.23-7.19 (m, 1H), 7.05-7.00 (m, 1H), 4.40 (s, 1H), 3.02-2.88 (m, 2H), 2.80-2.70 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 140.7, 139.8, 135.2 (q, J = 33.1 Hz), 129.6, 128.7, 127.6, 126.4 (q, J = 3.4 Hz), 125.9, 125.7, 123.0 (q, J = 271.3 Hz), 116.8, 116.3, 58.2, 33.9, 25.5. HRMS (ESI) m/z: calcd for $C_{17}H_{13}F_3N_2NaO_2S^+$, 389.0542; found, 389.0543.

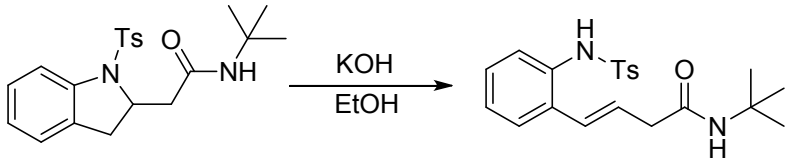


2-methyl-1-tosyl-1H-indole (5): Brown oil; IR (KBr): 2970.6, 2359.1, 1632.4, 1173.8, 1053.1, 696.2; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 7.6 Hz, 1H), 7.58 (d, J = 6.4 Hz, 2H), 7.31 (d, J = 6.0 Hz, 1H), 7.14 (d, J = 22.0 Hz, 4H), 6.25 (s, 1H), 2.52 (s, 3H), 2.25 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.7, 137.4, 136.4, 129.9, 126.3, 123.7, 123.4, 120.0, 114.5, 109.6, 21.5, 15.7. LR-MS (EI, 70 eV): m/z = 285, 207, 155, 132.



2-(indolin-2-yl)acetamide (**6**): Brown oil; IR (KBr): 3443.1, 2964.9,

2356.8, 1665.8, 1116.6, 752.8; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.05 (d, J = 7.2 Hz, 1H), 7.00 (t, J = 7.6 Hz, 1H), 6.69 (t, J = 7.2 Hz, 1H), 6.60 (d, J = 7.6 Hz, 1H), 5.85 (d, J = 56.8 Hz, 2H), 4.265 – 4.19 (m, 1H), 3.16 (dd, J = 15.6, 8.4 Hz, 1H), 2.68 (dd, J = 15.3, 7.8 Hz, 1H), 2.52 – 2.45 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 150.4, 128.2, 127.5, 124.7, 119.0, 109.6, 56.2, 41.6, 35.7. HRMS (ESI) m/z: calcd for $C_{10}H_{13}N_2O_1^+$, 177.1022; found, 177.1026.

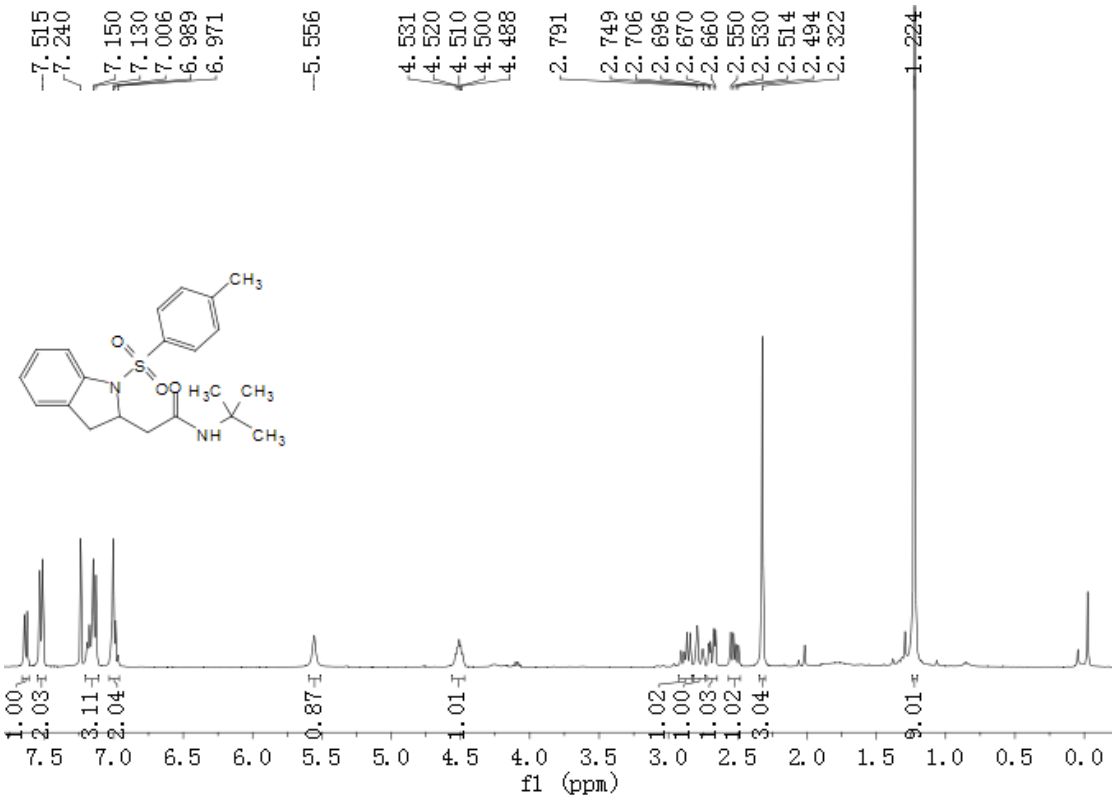


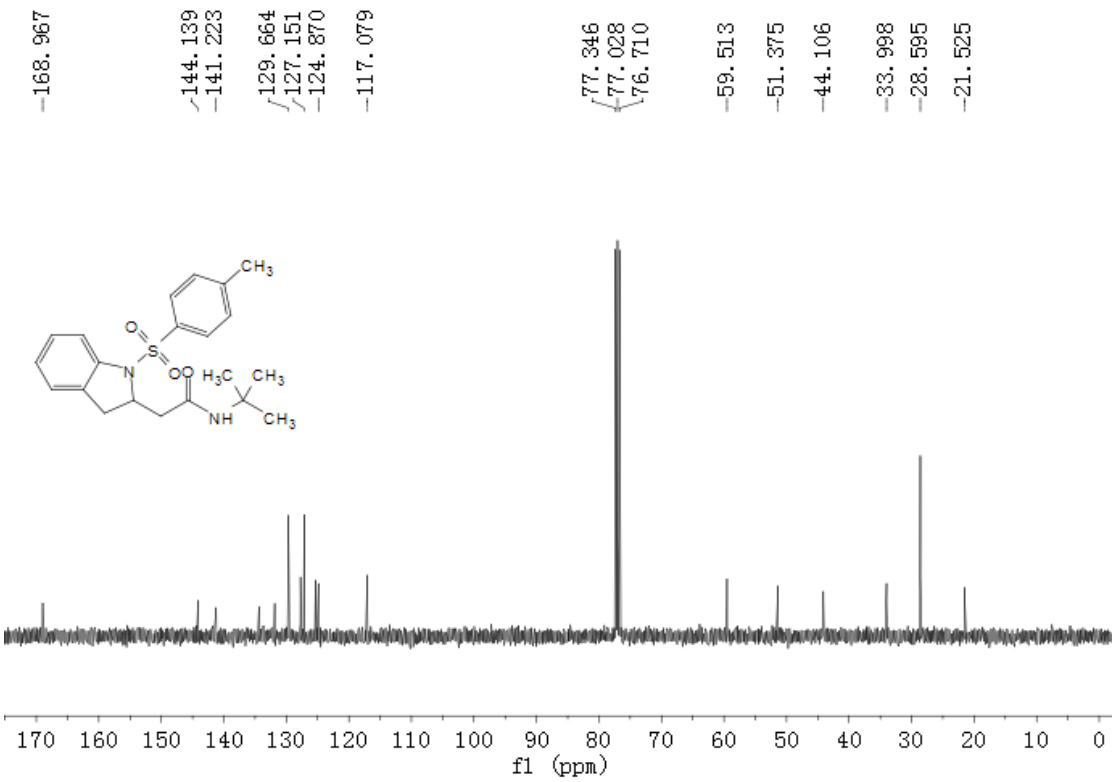
3a **7**

(E)-*N*-(tert-butyl)-4-(2-(4-methylphenylsulfonamido)phenyl)but-3-enamide (7): To a stirred solution of **3a** (38.6 mg, 0.1 mmol) in EtOH (2.0 mL) was added KOH (15.1 mg, 268.1 umol). The reaction proceeded at a reflux for 4h before EtOH was removed by rotary evaporation. The remained mixture was extracted with EtOAc, the combined organic layers were washed with H_2O and brine and dried over anhydrous Na_2SO_4, evaporated in a vacuo. The residue was purified by column chromatography on a silica gel PE/EtOAc to provide **7** in 95 % yield as a yellow oil: IR (KBr): 3133.1, 2357.5, 1649.9, 1401.2, 1051.6, 664.8; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.58 (m, 3H), 7.34 (d, J = 7.2 Hz, 1H), 7.17 (d, J = 8.0 Hz, 2H), 7.11 – 7.05 (m, 2H), 7.02 (d, J = 7.2 Hz, 1H), 6.56 (d, J = 16.0 Hz, 1H), 6.07 – 6.00 (m, 1H), 5.80 (s, 1H), 2.96 (d, J = 7.6 Hz, 2H), 2.34 (s, 3H), 1.29 (s, 9H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.3, 143.7, 136.5, 133.3, 133.2, 129.6, 129.4, 128.1, 127.3, 127.0, 126.7, 126.3, 125.6, 51.4, 42.1, 28.7, 21.5. HRMS (ESI) m/z: calcd for $C_{21}H_{27}N_2O_3S^+$, 387.1737; found, 387.1734.

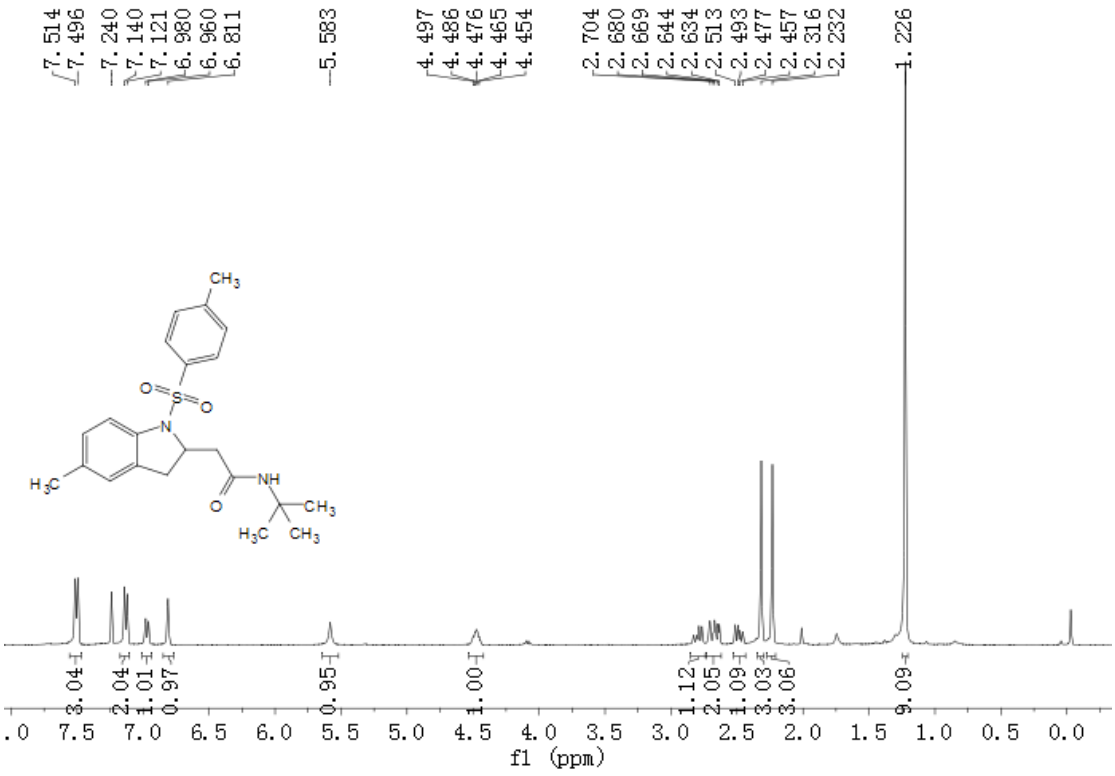
NMR Spectra for Compounds 3a-3zd, 4a-4e, 5-7

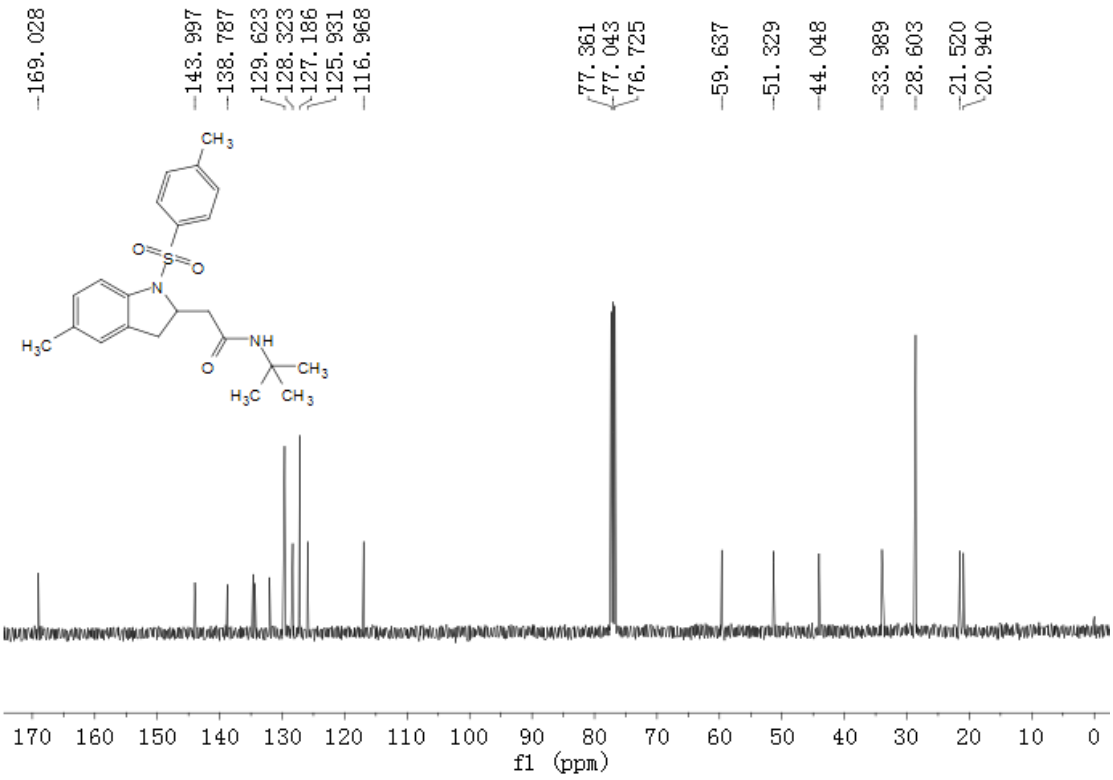
***N*-(*tert*-butyl)-2-(1-tosylindolin-2-yl)acetamide (3a)**



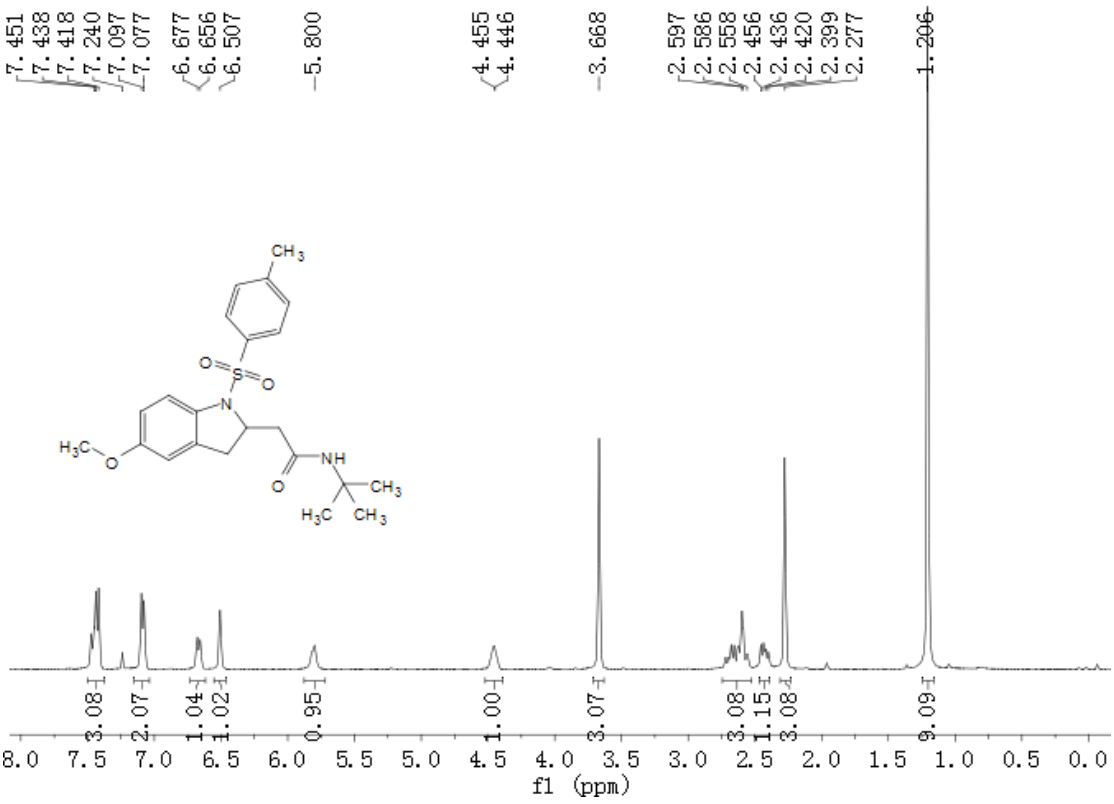


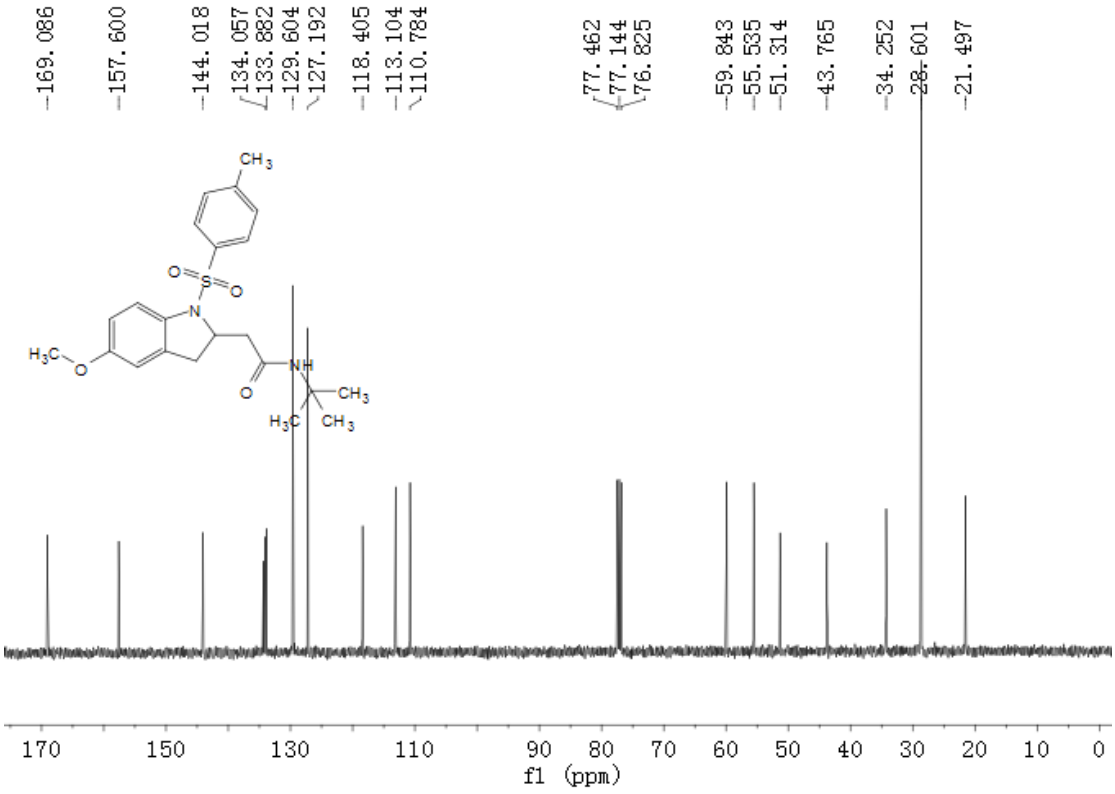
***N*-(*tert*-butyl)-2-(5-methyl-1-tosylindolin-2-yl)acetamide (3b)**



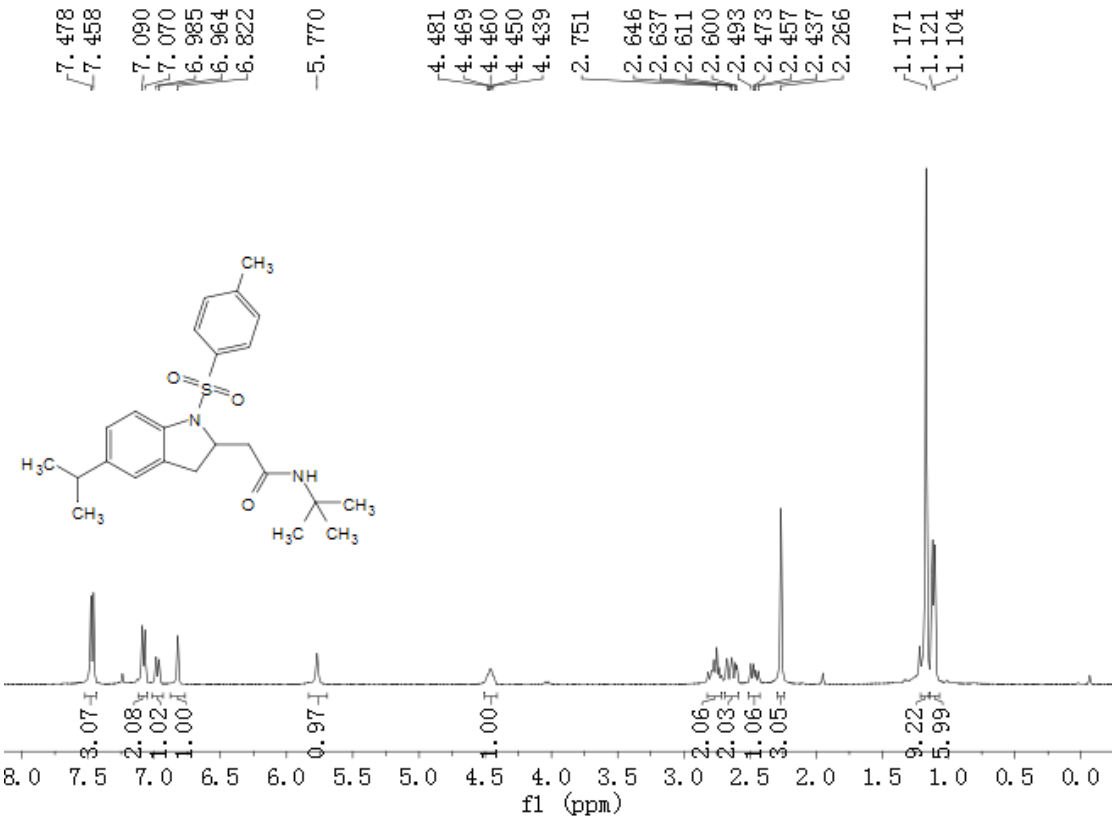


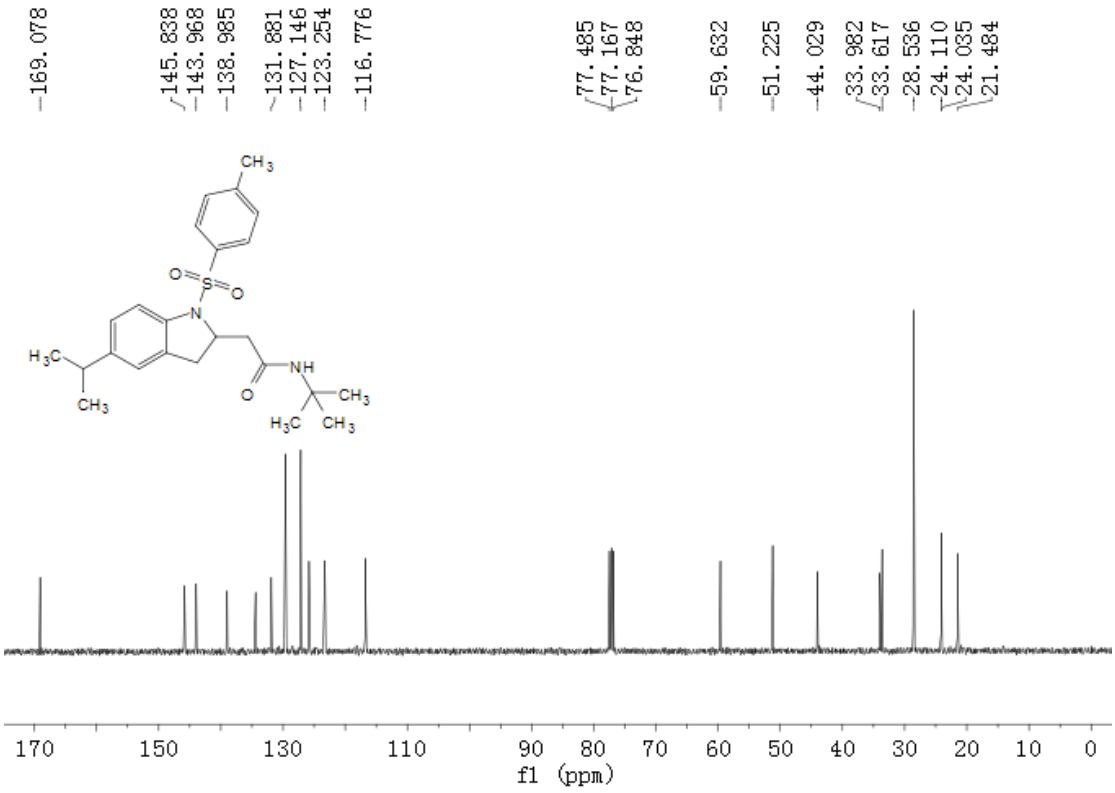
***N*-(*tert*-butyl)-2-(5-methoxy-1-tosylindolin-2-yl)acetamide (3c)**



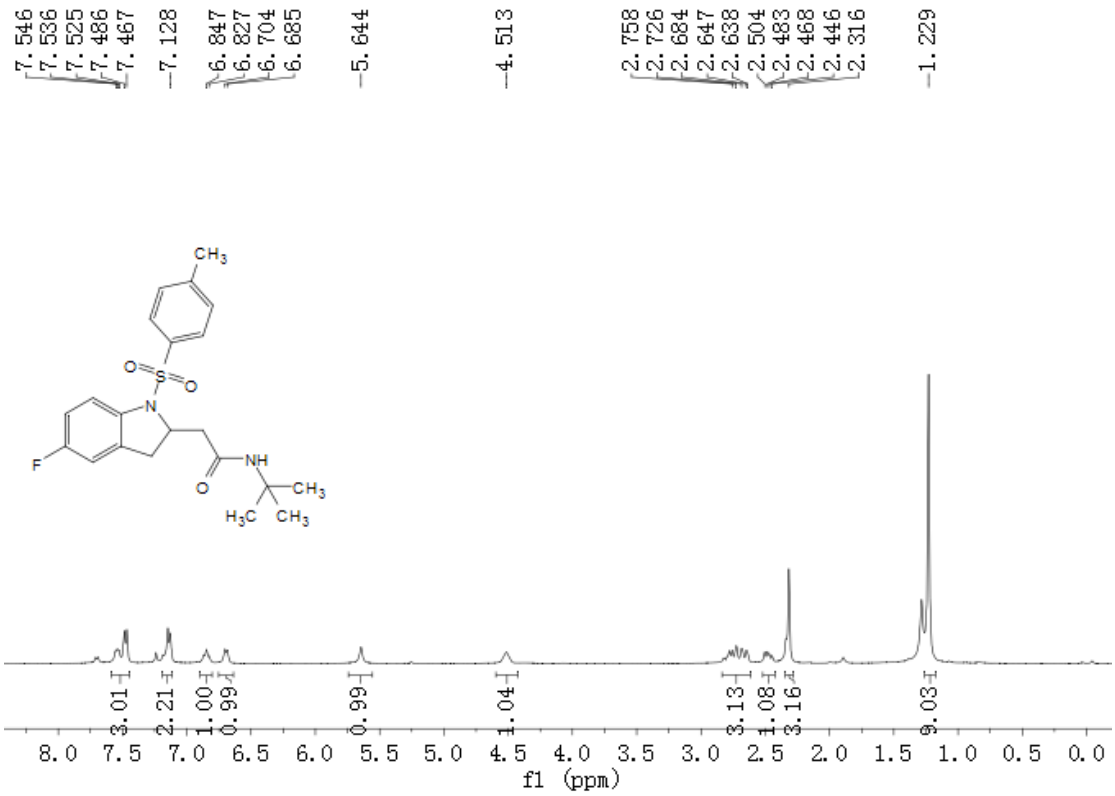


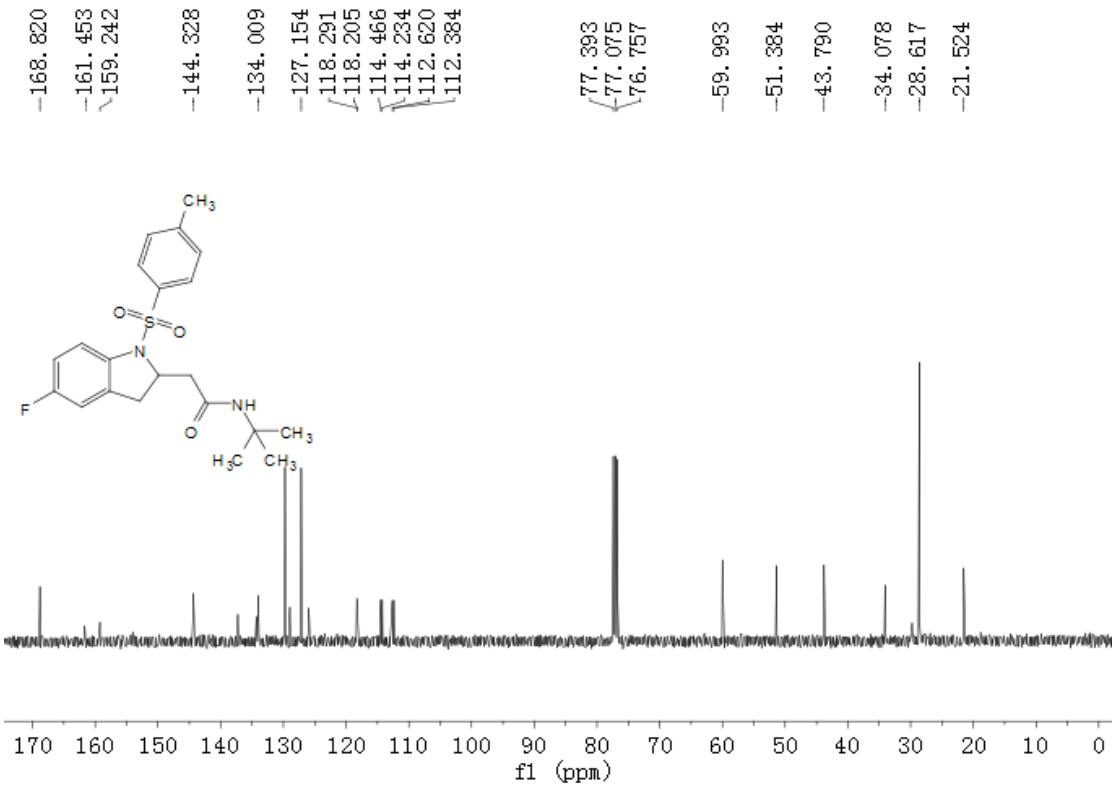
***N*-(*tert*-butyl)-2-(5-isopropyl-1-tosylindolin-2-yl)acetamide (3d)**



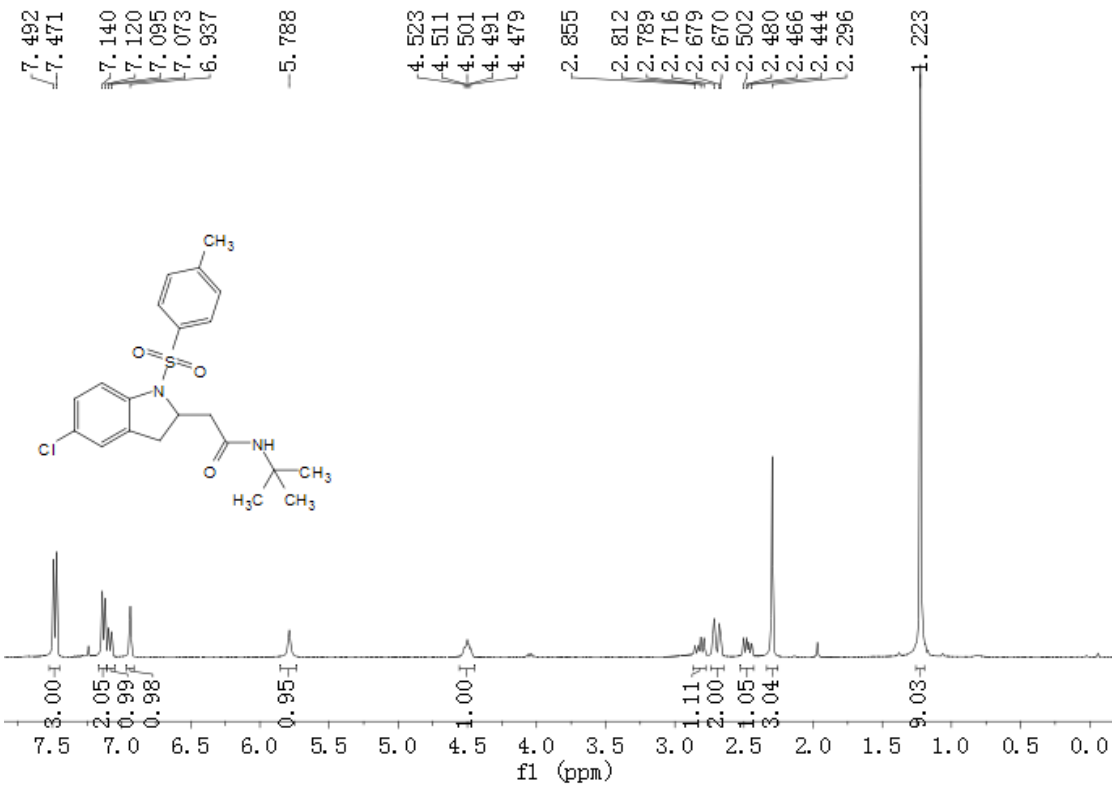


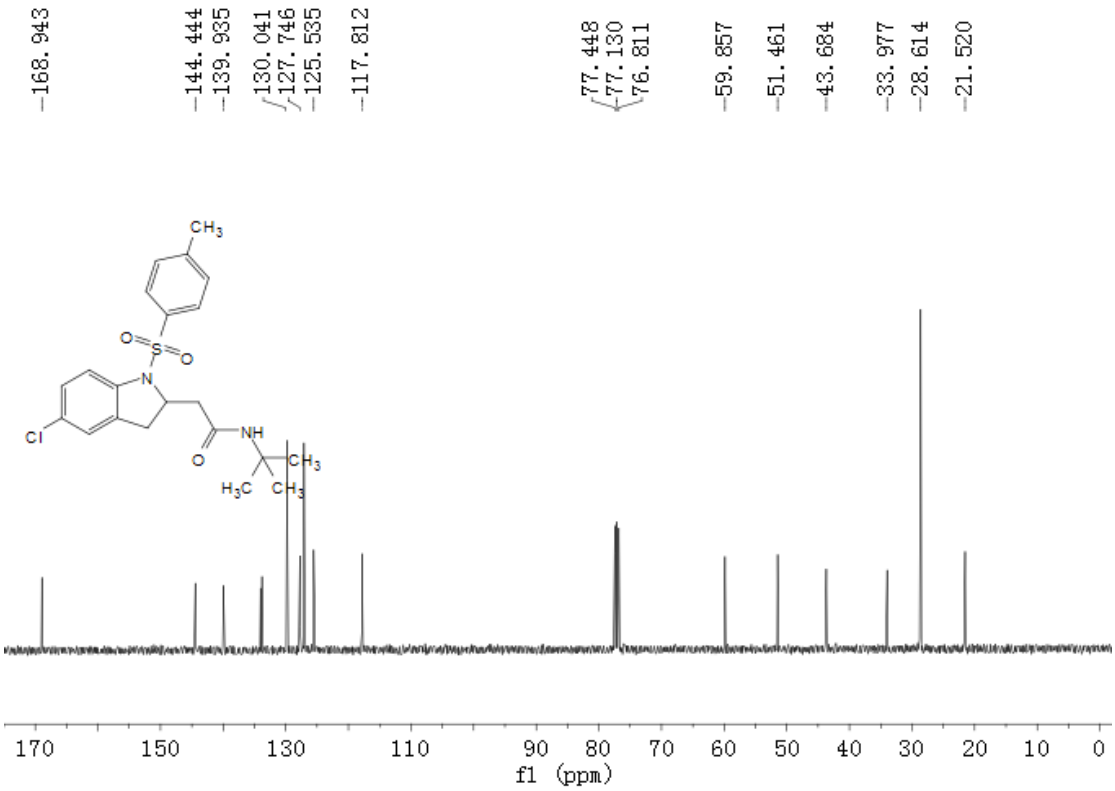
***N*-(*tert*-butyl)-2-(5-fluoro-1-tosylindolin-2-yl)acetamide (3e)**



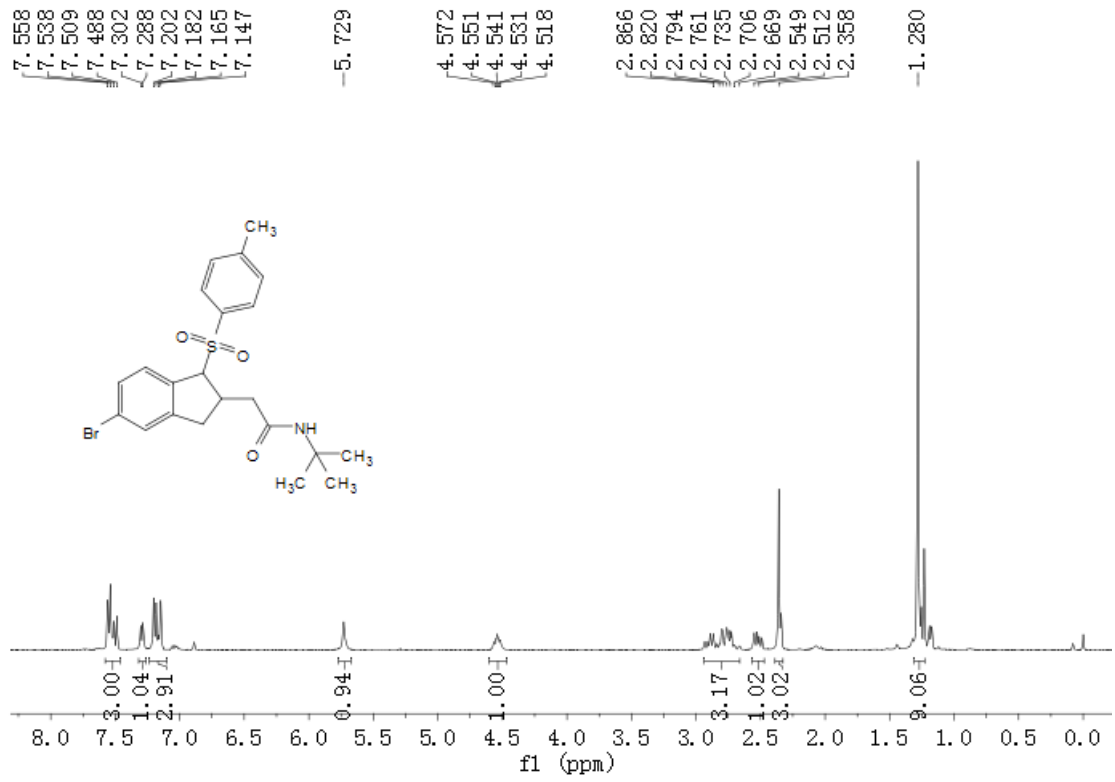


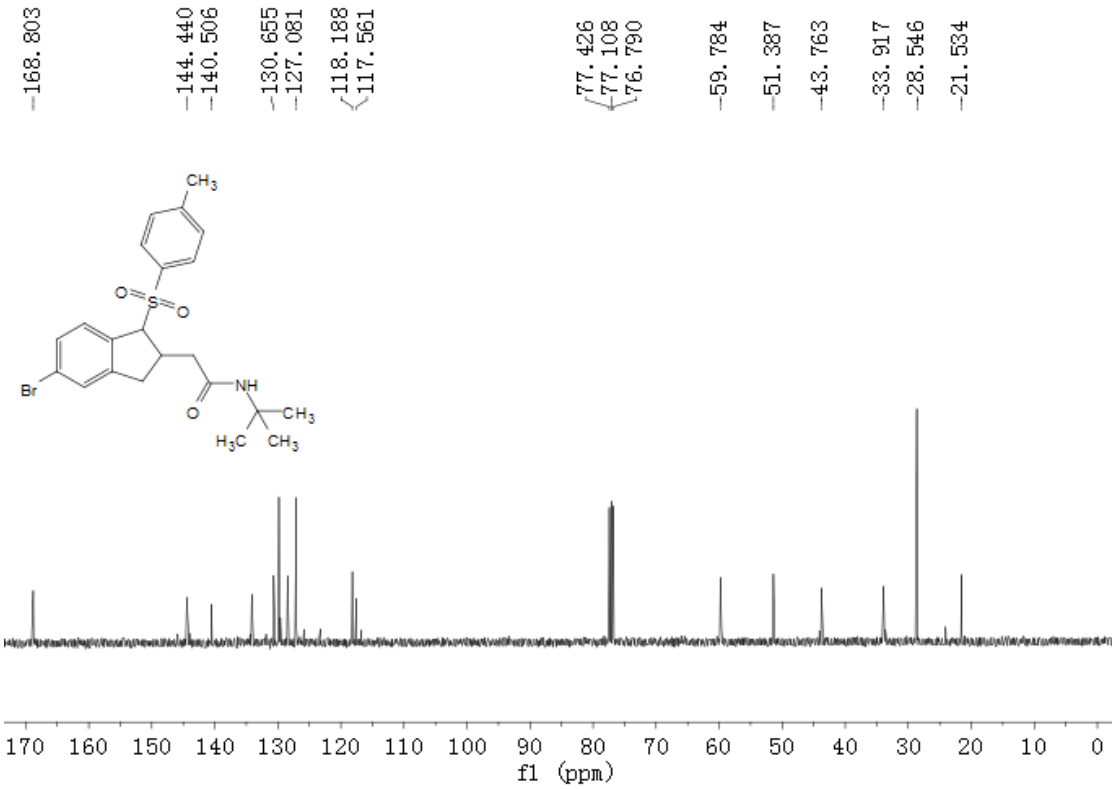
***N*-(*tert*-butyl)-2-(5-chloro-1-tosylindolin-2-yl)acetamide (3f)**



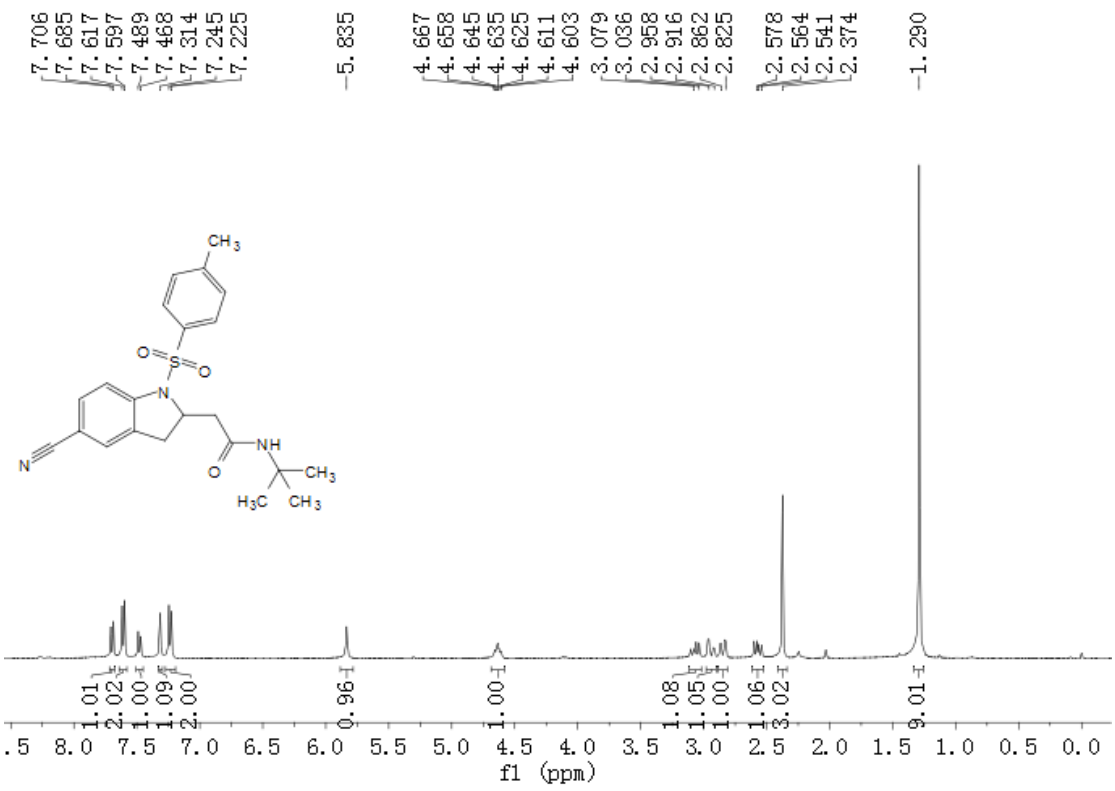


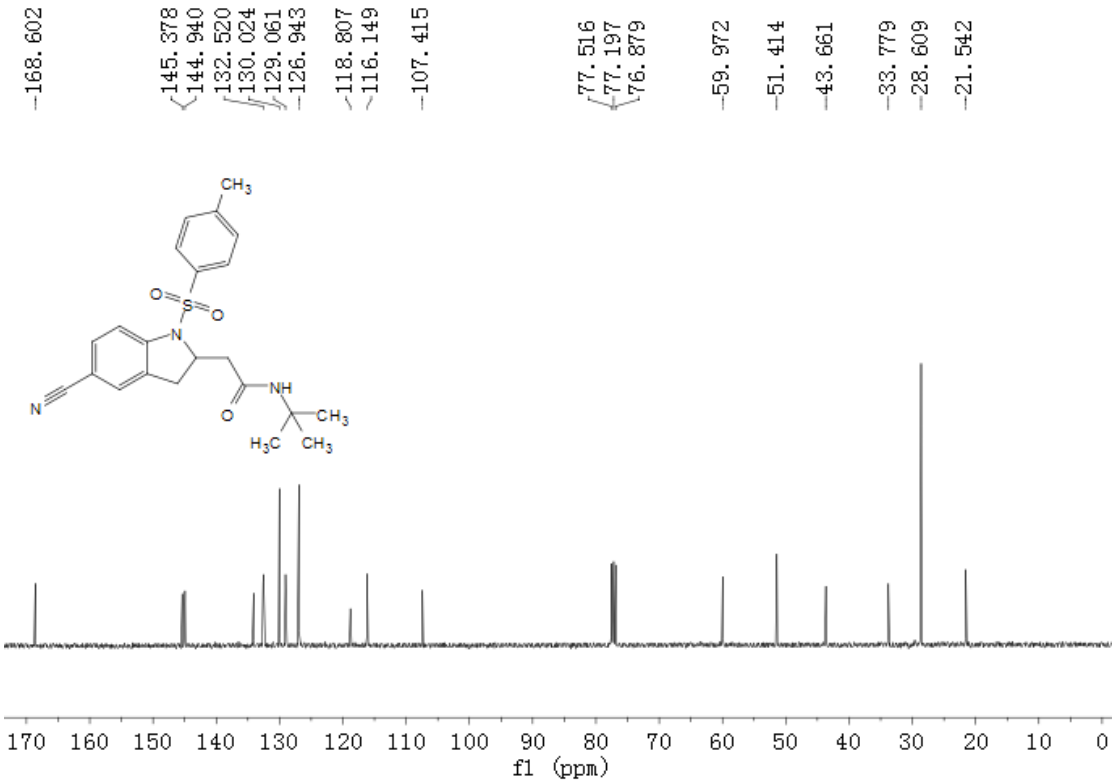
2-(5-bromo-1-tosyl-2,3-dihydro-1H-inden-2-yl)-*N*-(*tert*-butyl)acetamide (3g)



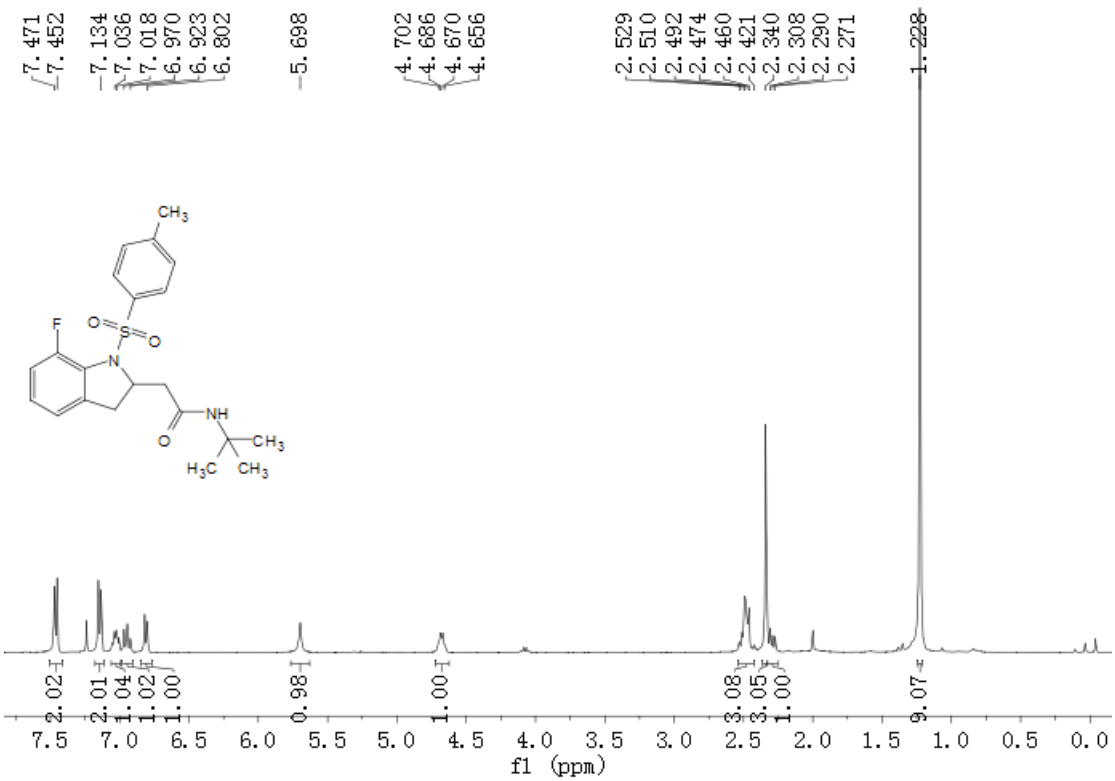


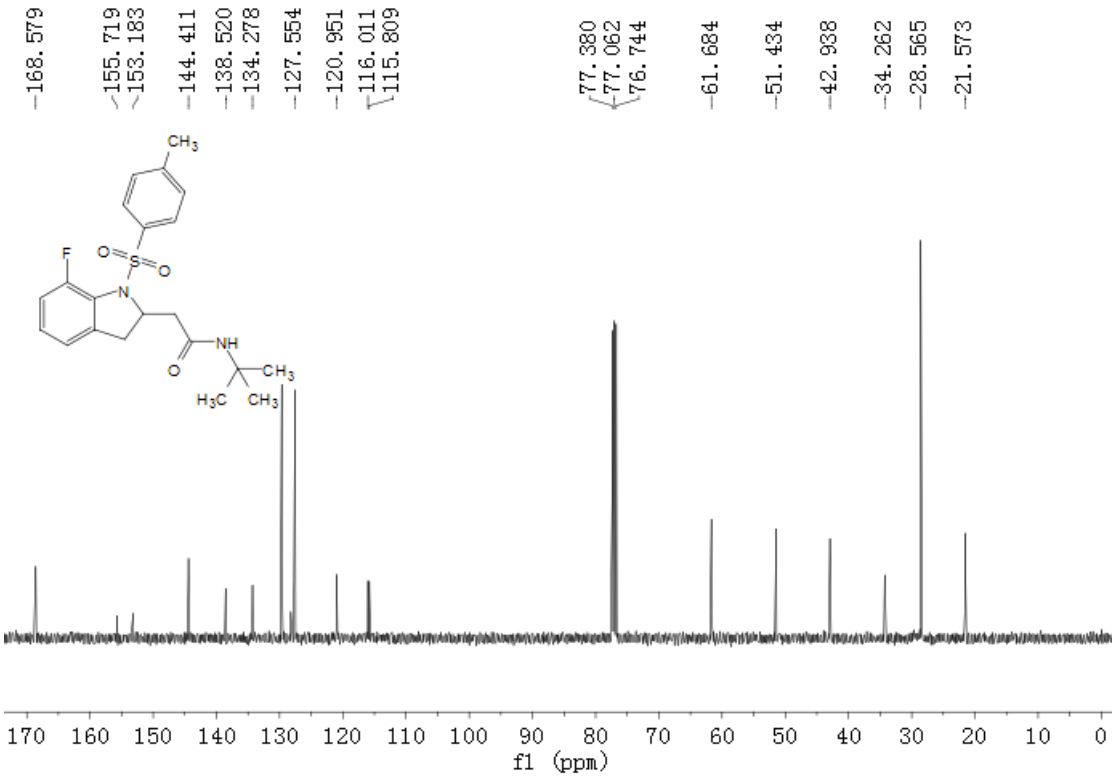
***N*-(*tert*-butyl)-2-(5-cyano-1-tosylindolin-2-yl)acetamide (3h)**



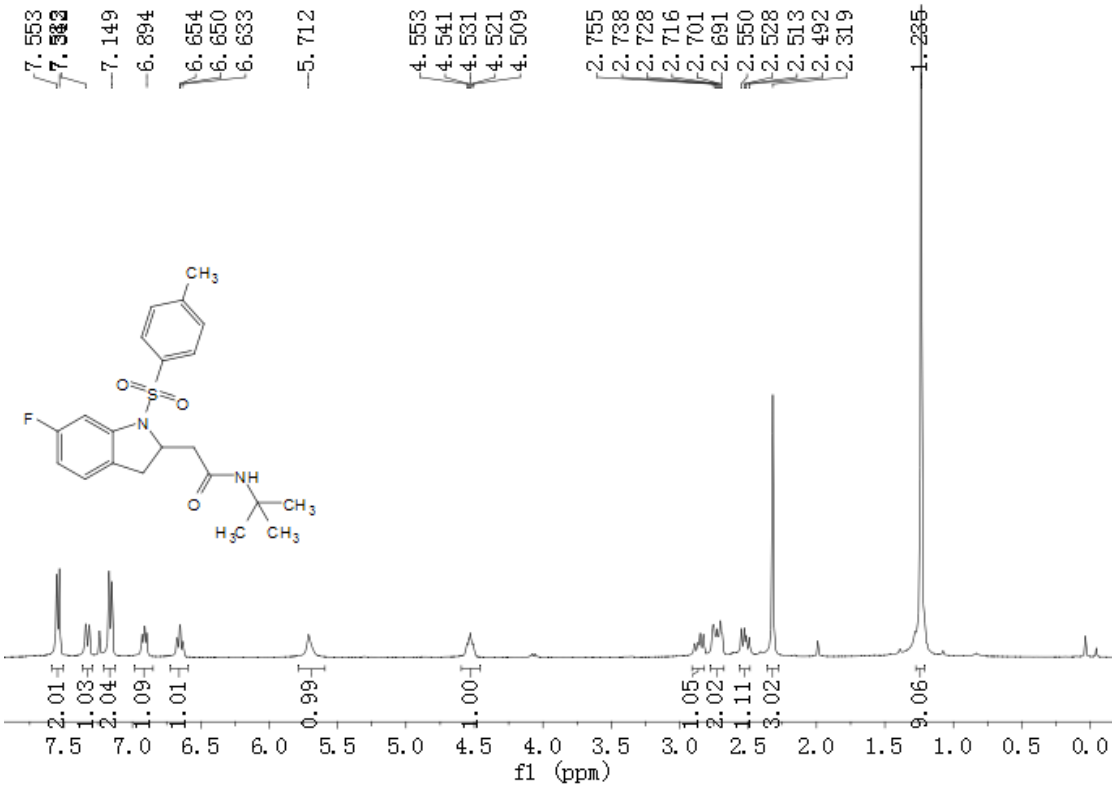


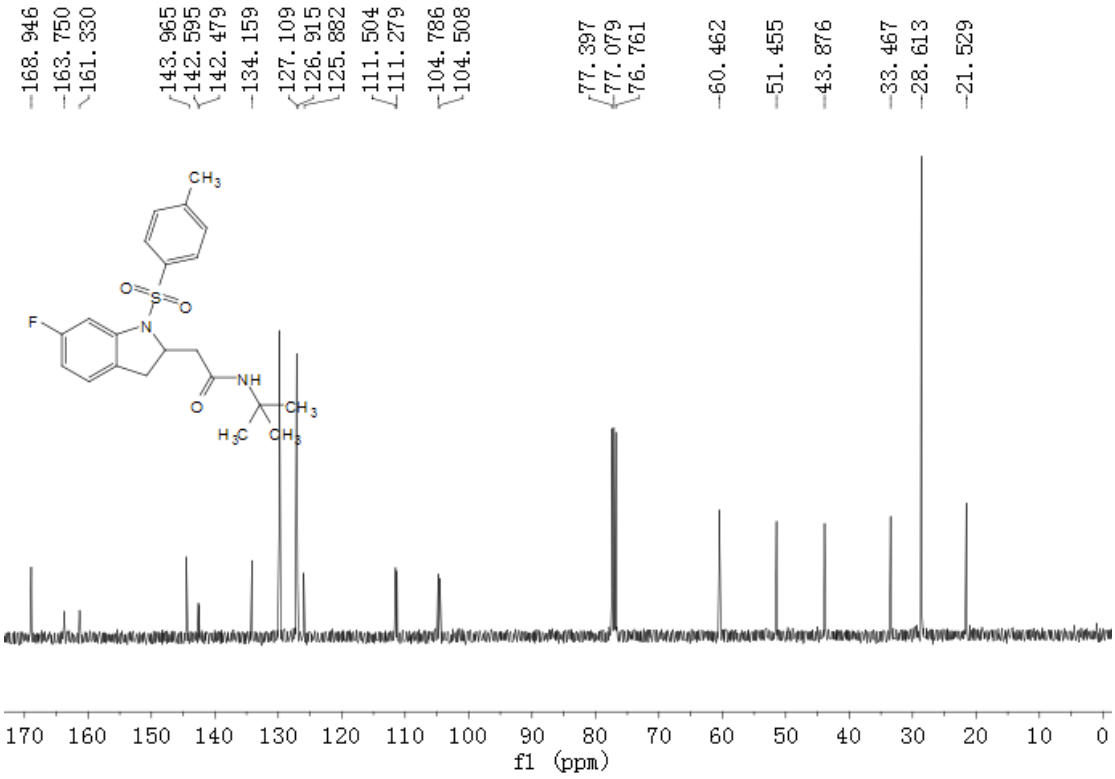
_N_-(_tert_-butyl)-2-(7-fluoro-1-tosylindolin-2-yl)acetamide (3i)



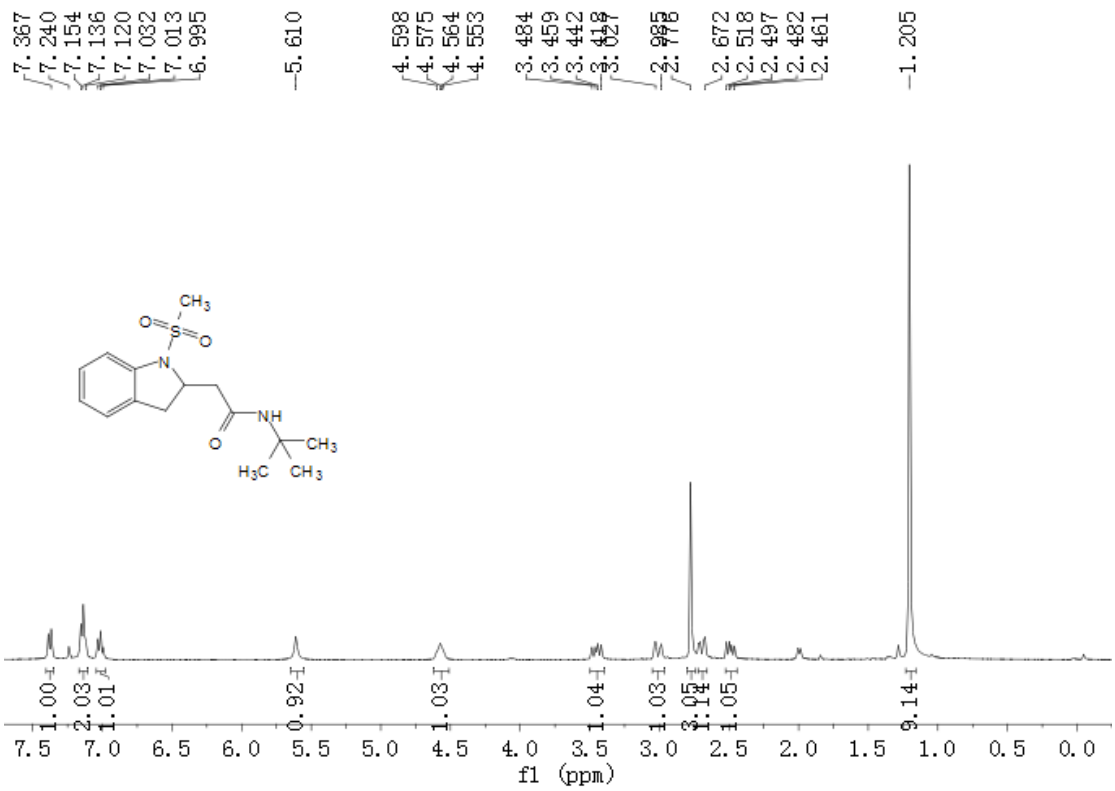


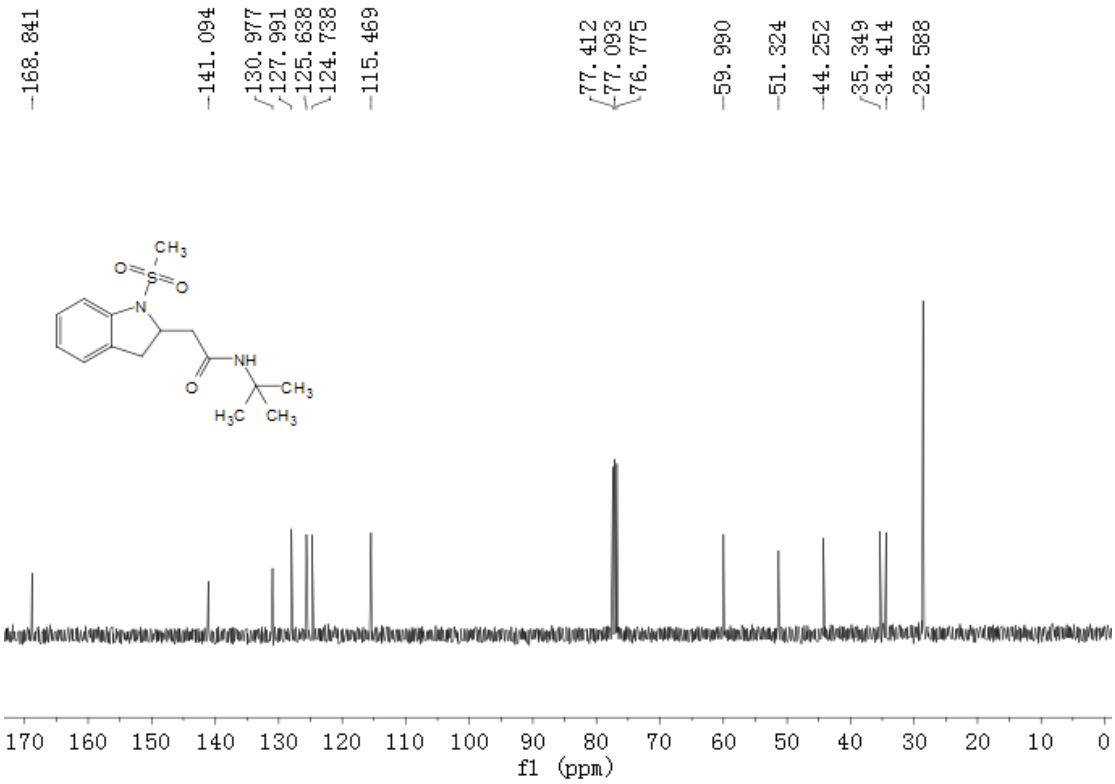
_N_-(_tert_-butyl)-2-(6-fluoro-1-tosylindolin-2-yl)acetamide (3j)



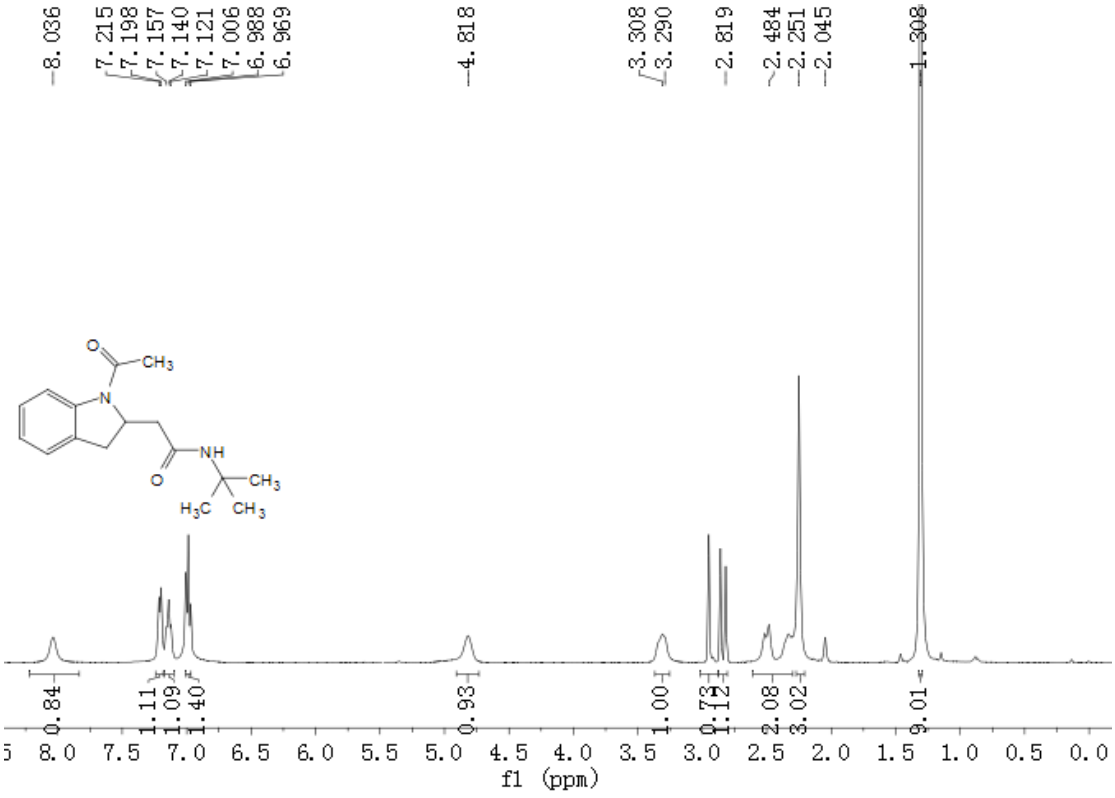


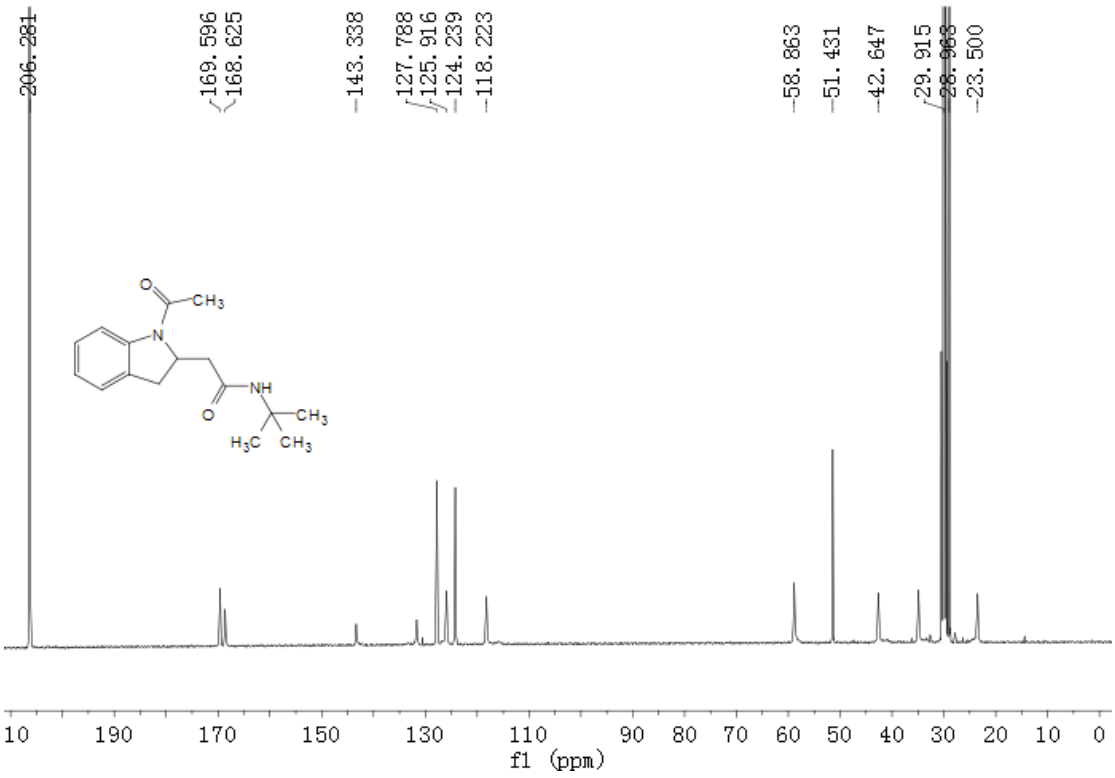
***N*-(*tert*-butyl)-2-(1-(methylsulfonyl)indolin-2-yl)acetamide (3k)**



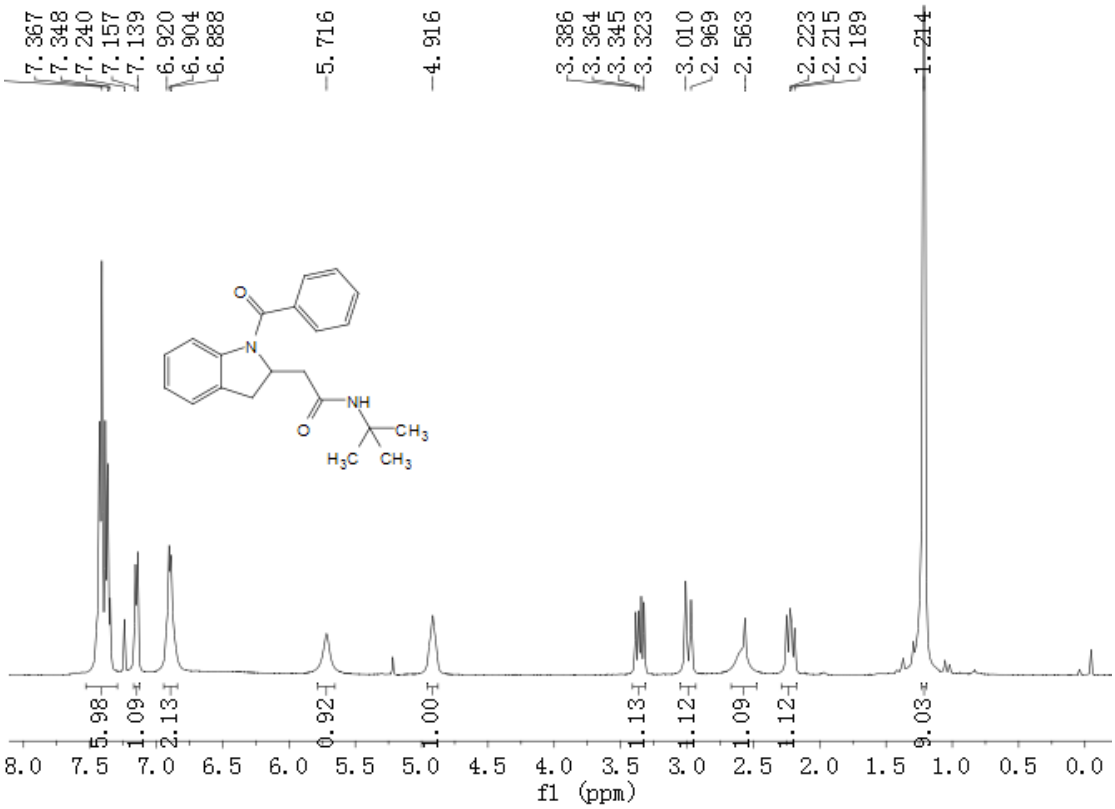


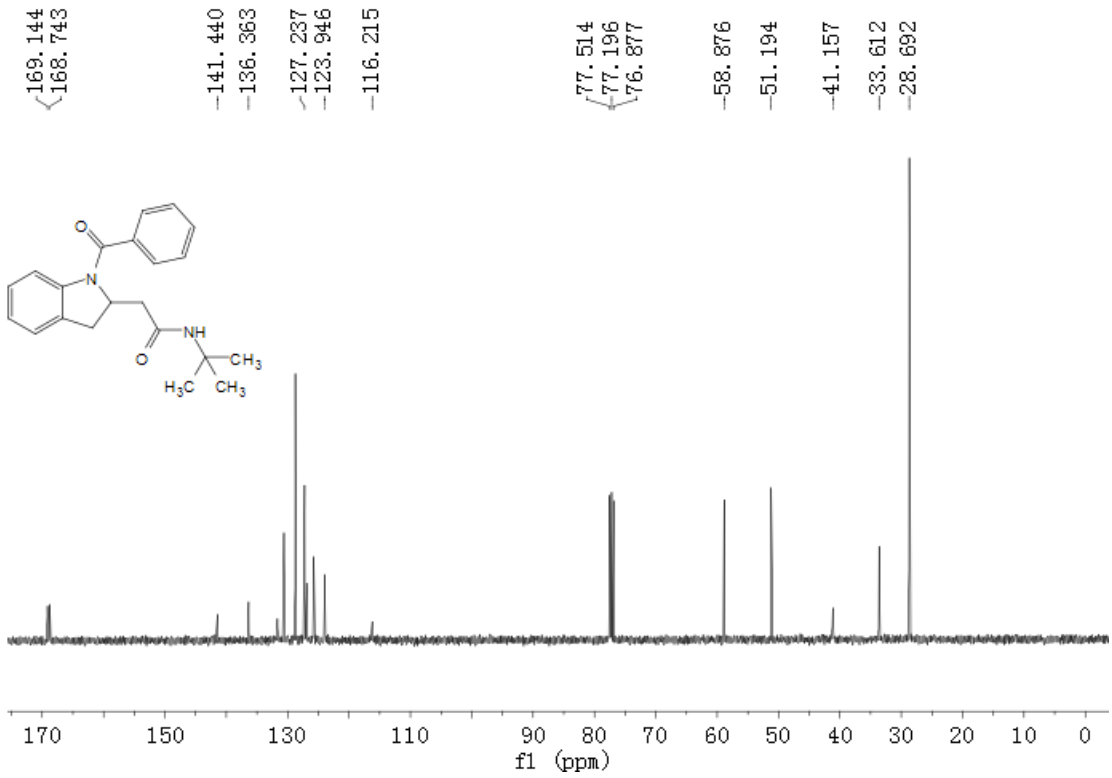
2-(1-acetylindolin-2-yl)-*N*-(*tert*-butyl)acetamide (3l)



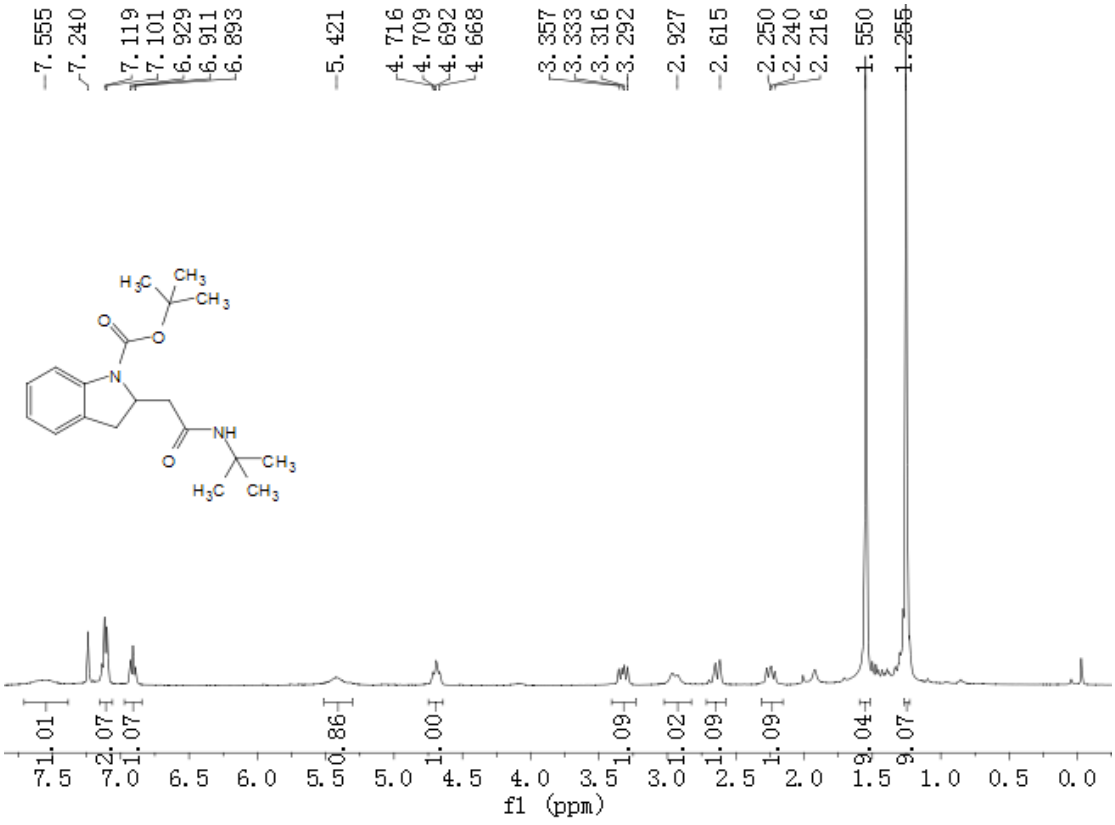


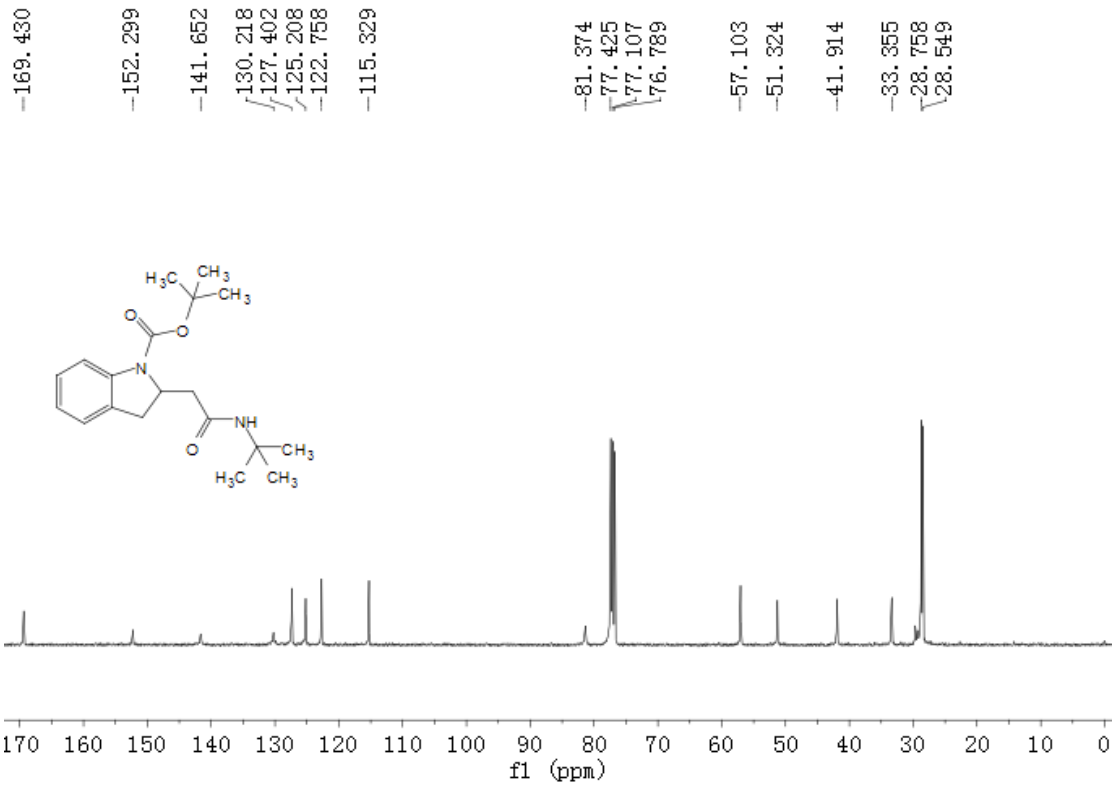
2-(1-benzoylindolin-2-yl)-*N*-(*tert*-butyl)acetamide (3m)



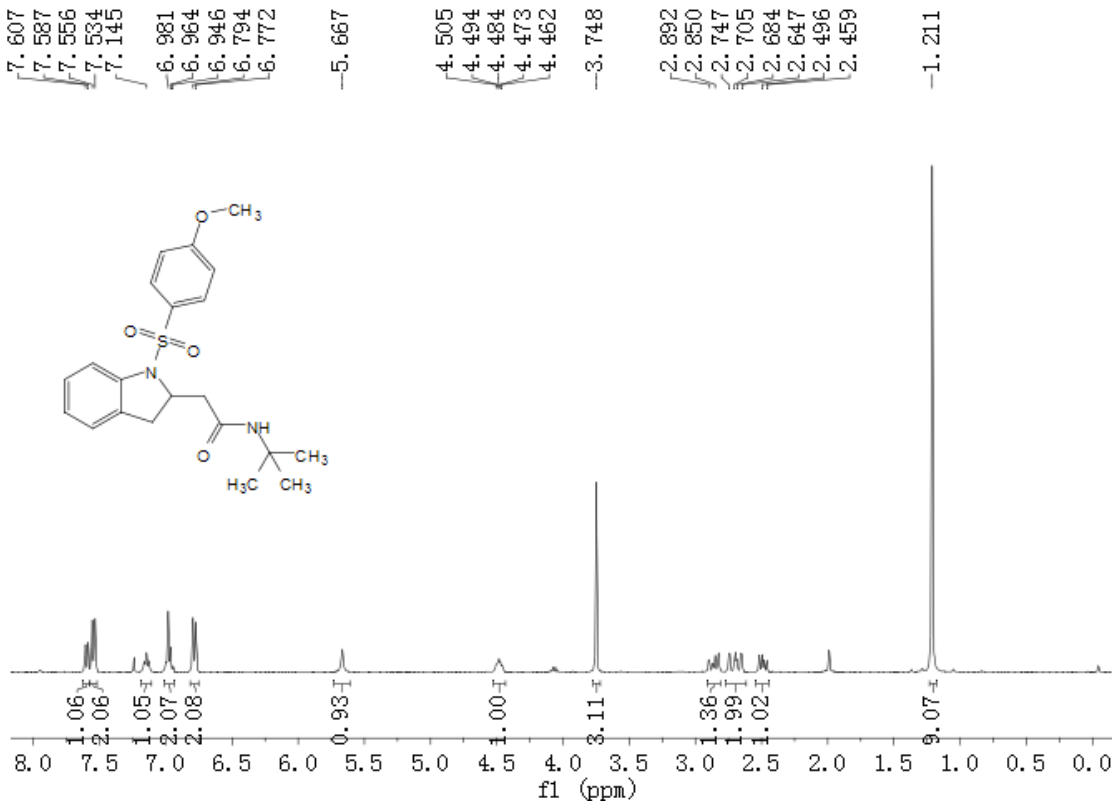


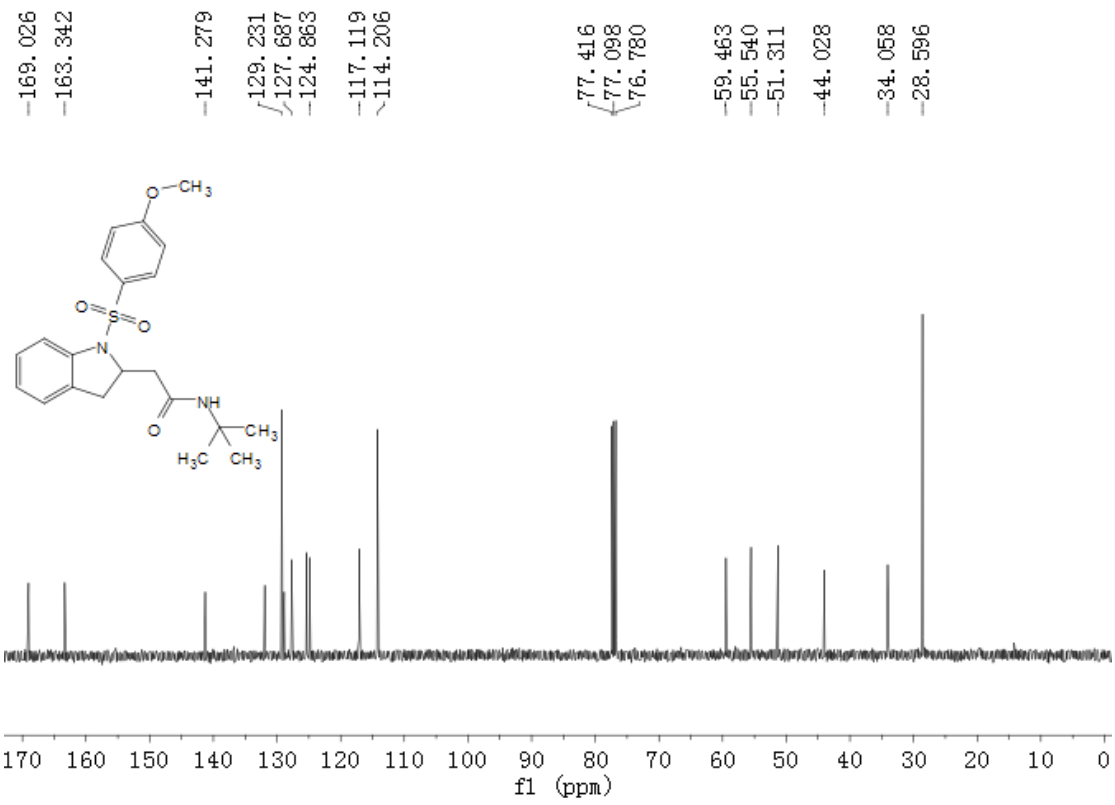
tert-butyl 2-(2-(tert-butylamino)-2-oxoethyl)indoline-1-carboxylate (3n)



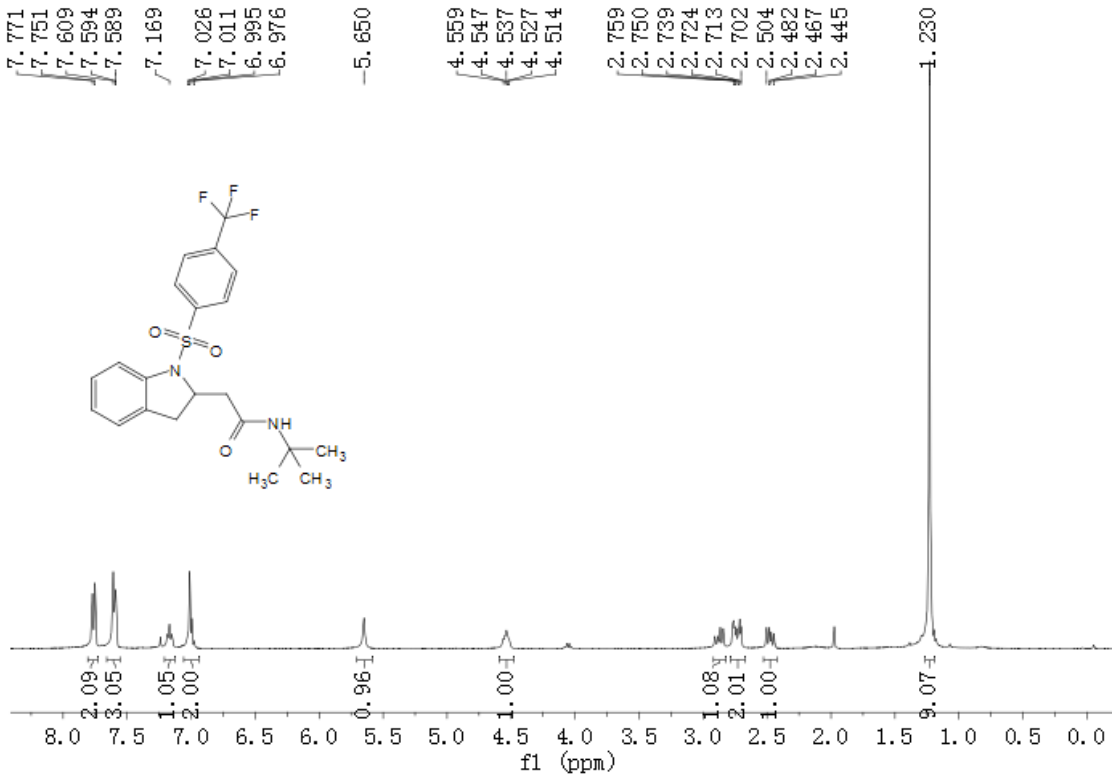


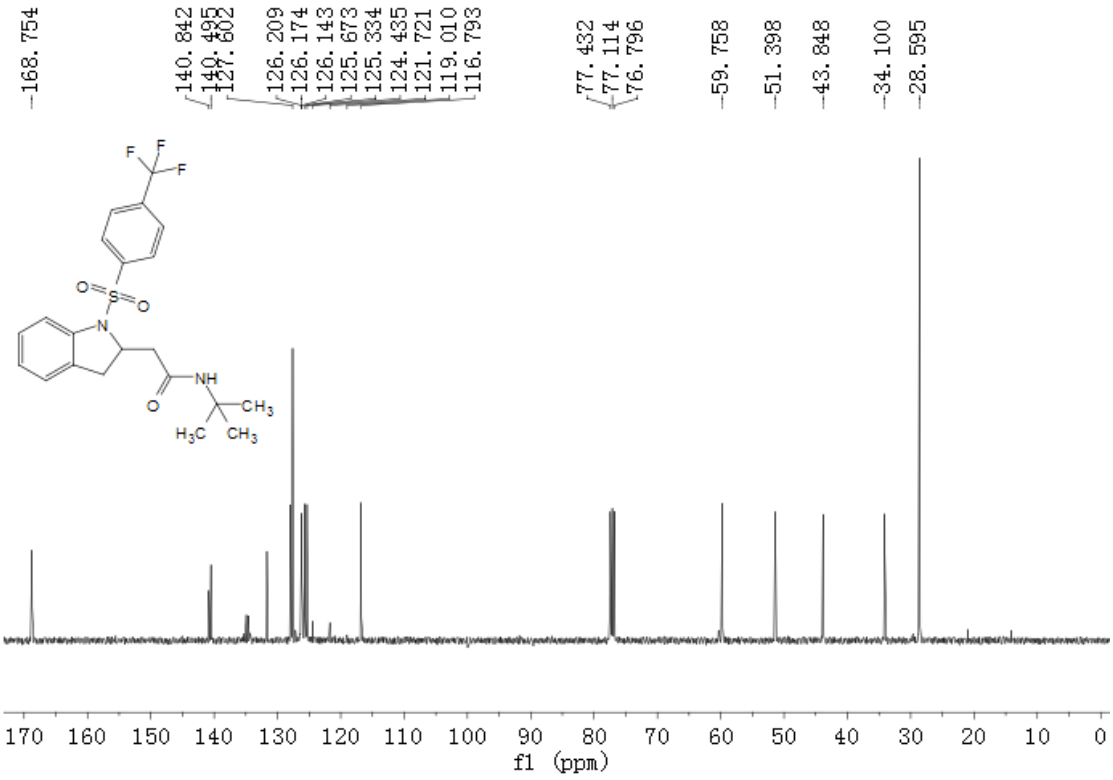
***N*-(*tert*-butyl)-2-(1-((4-methoxyphenyl)sulfonyl)indolin-2-yl)acetamide (3o)**

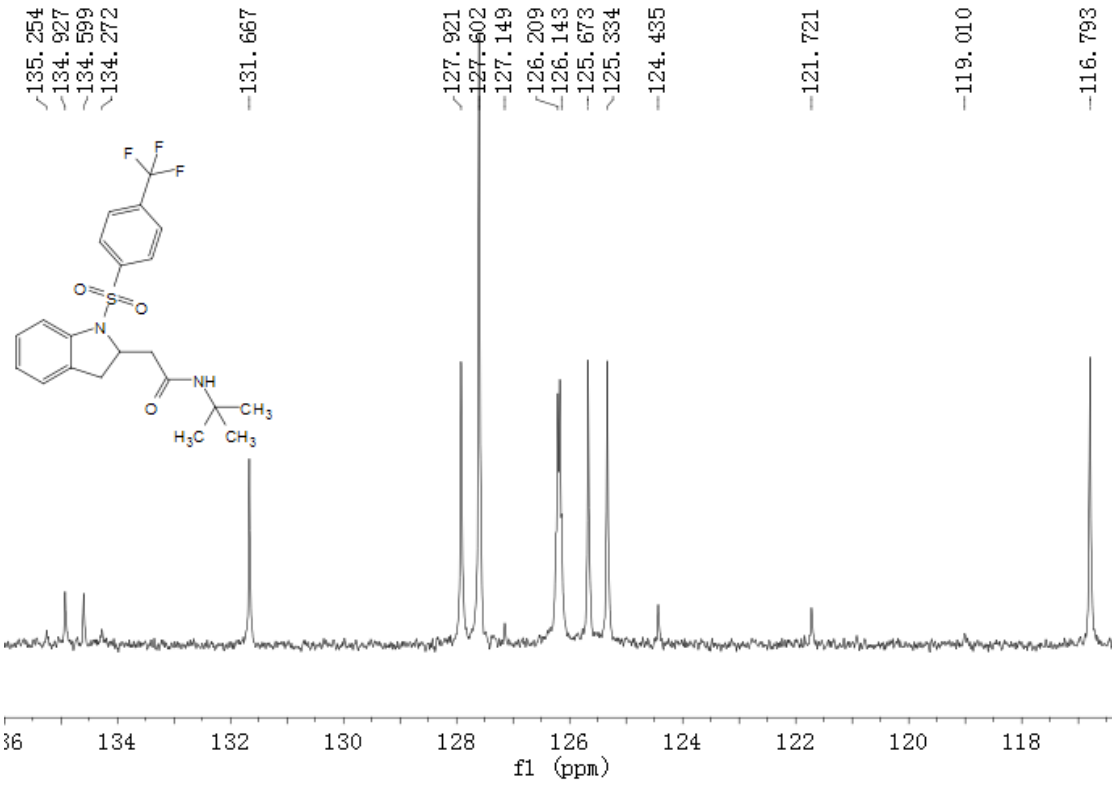




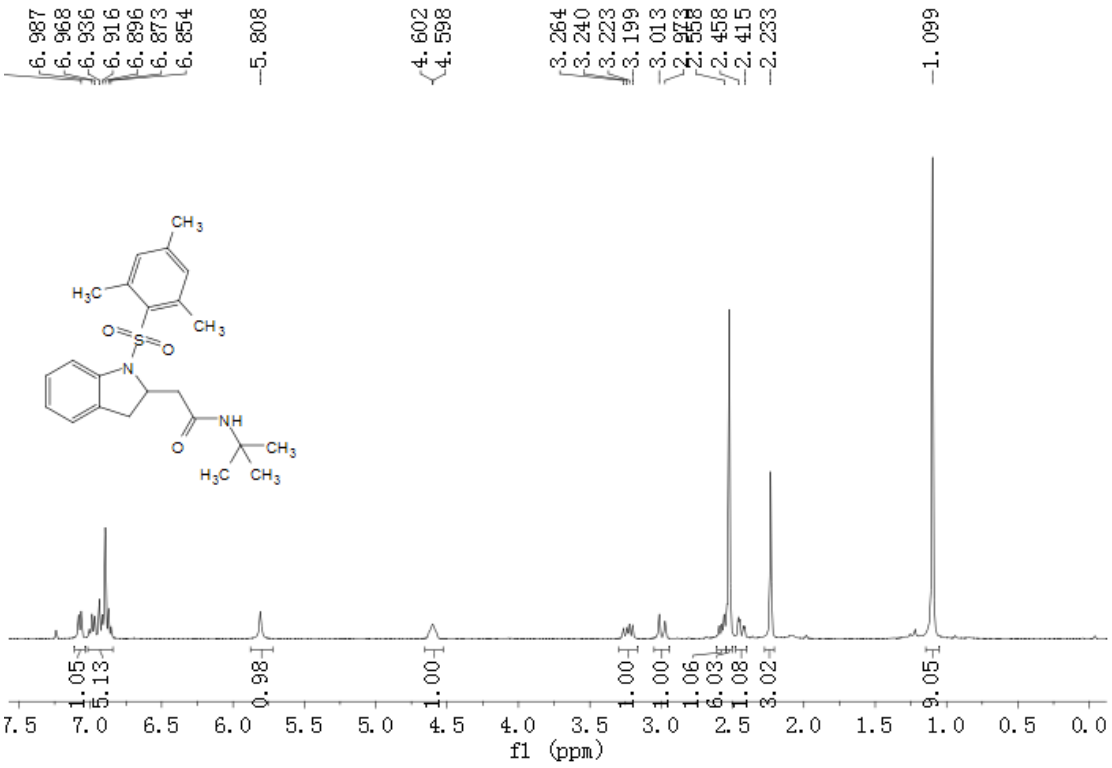
***N*-(*tert*-butyl)-2-(1-(4-(trifluoromethyl)phenyl)indolin-2-yl)acetamide (3p)**







_N_-(_tert_-butyl)-2-(1-(mesitylsulfonyl)indolin-2-yl)acetamide (3q)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6.936
6.916
6.896
6.873
6.854
5.808
4.602
4.598
3.264
3.240
3.223
3.199
3.013
2.973
2.558
2.458
2.415
2.233
1.099
1.05
5.13
0.98
1.00
1.00
1.00
1.06
6.03
1.08
3.02
9.05
7.5
7.0
6.5
6.0
5.5
5.0
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2.5
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1.0
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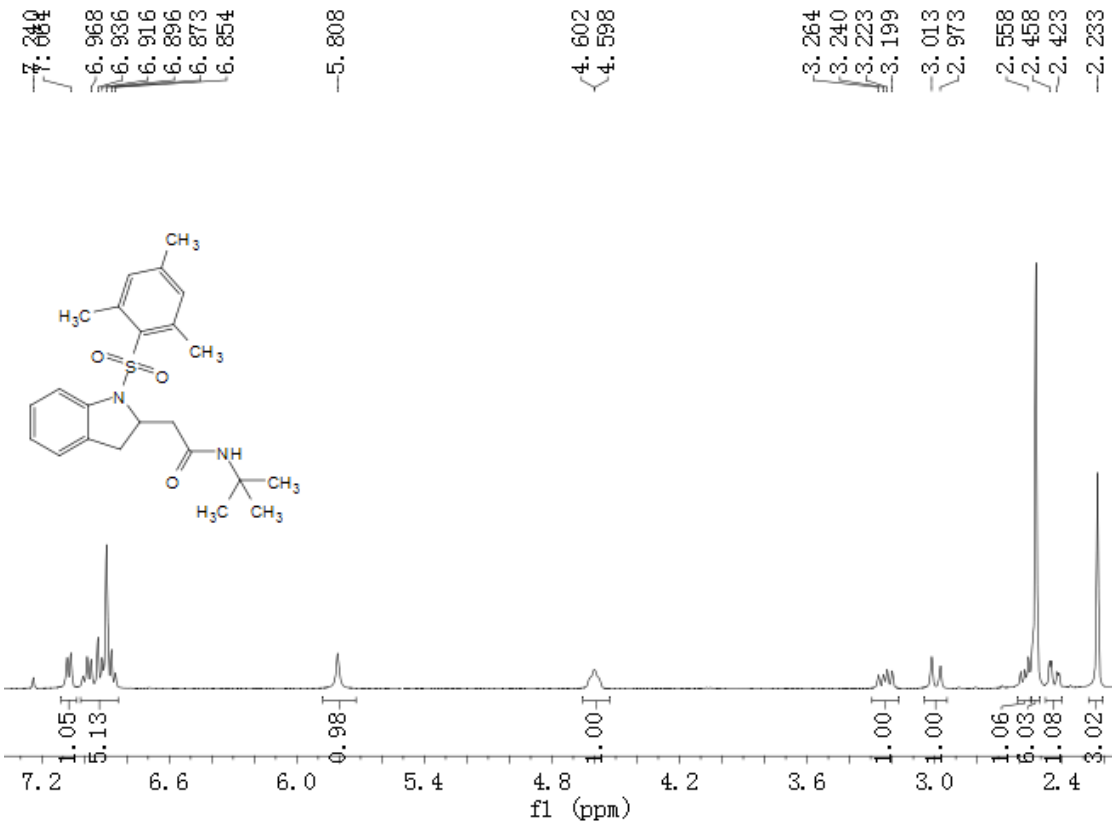
0.0
f1 (ppm)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3.223
3.199
3.013
2.973
2.558
2.458
2.423
2.233
1.05
5.13
0.98
1.00
1.00
1.06
6.03
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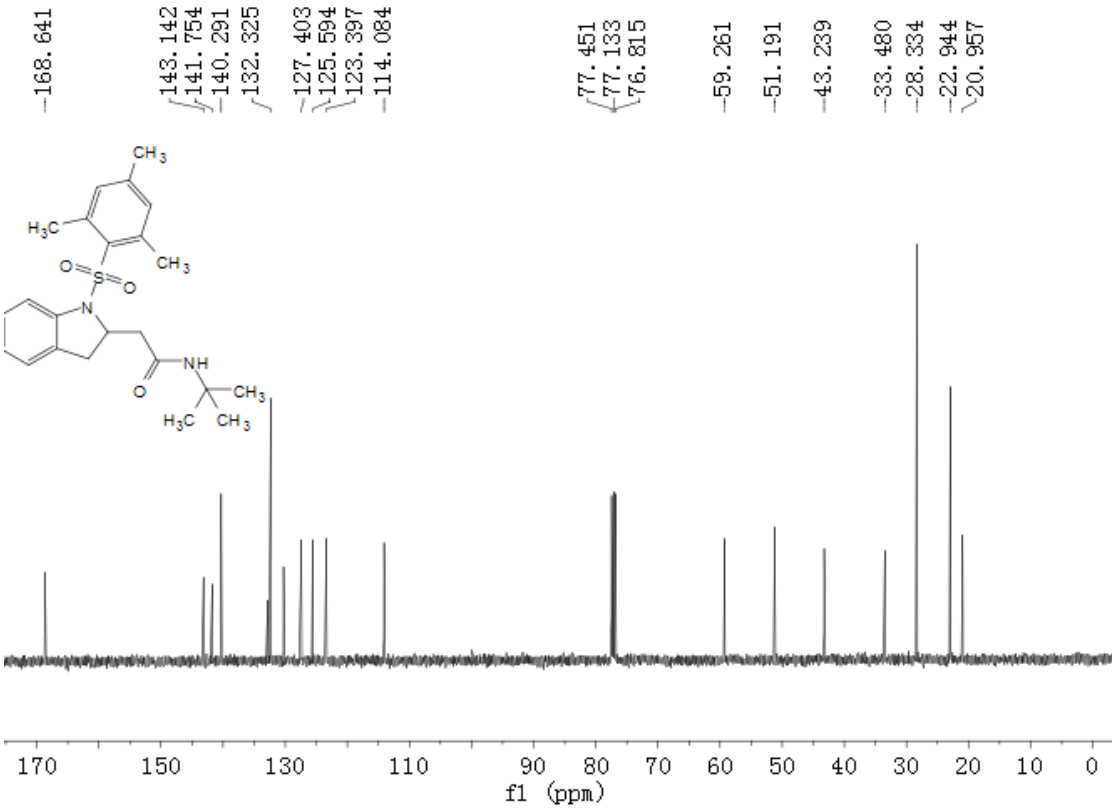
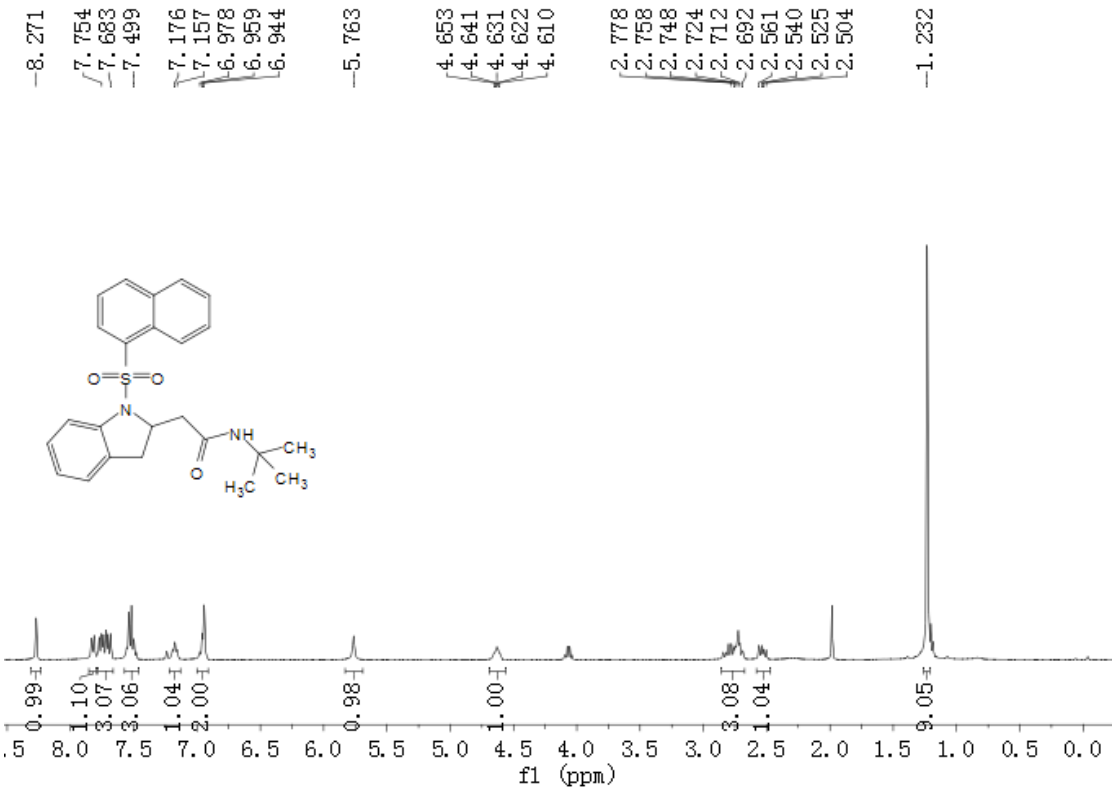
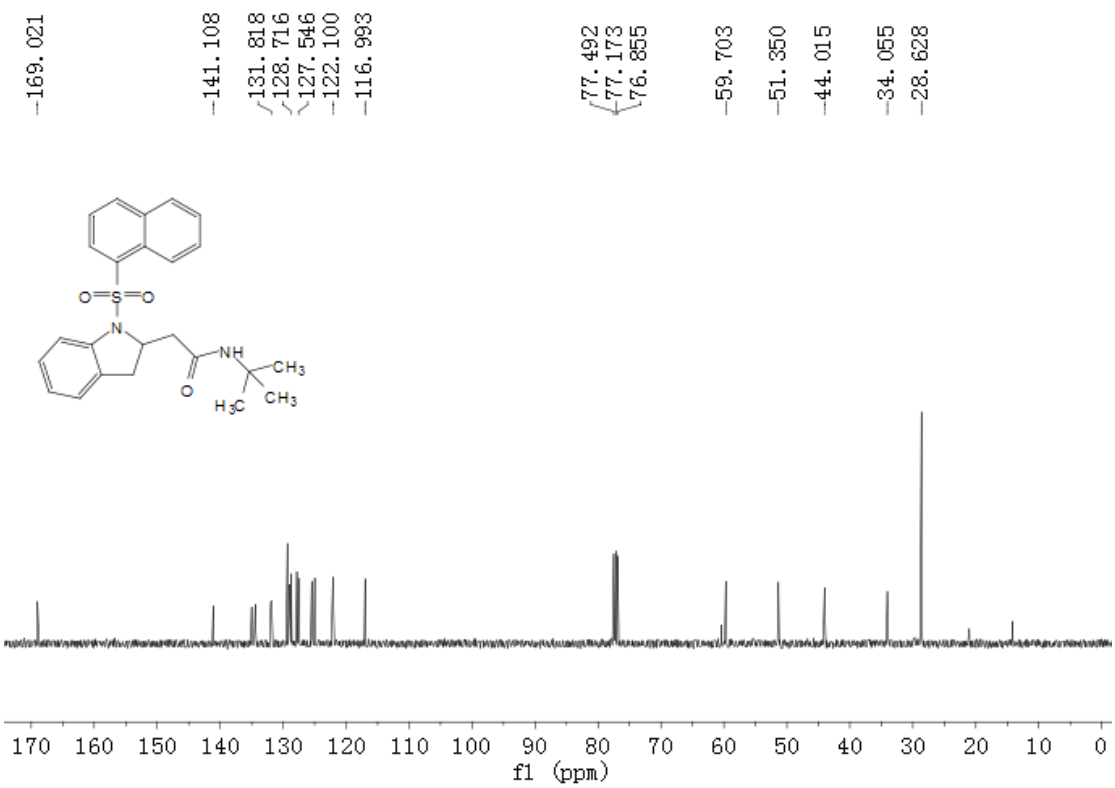
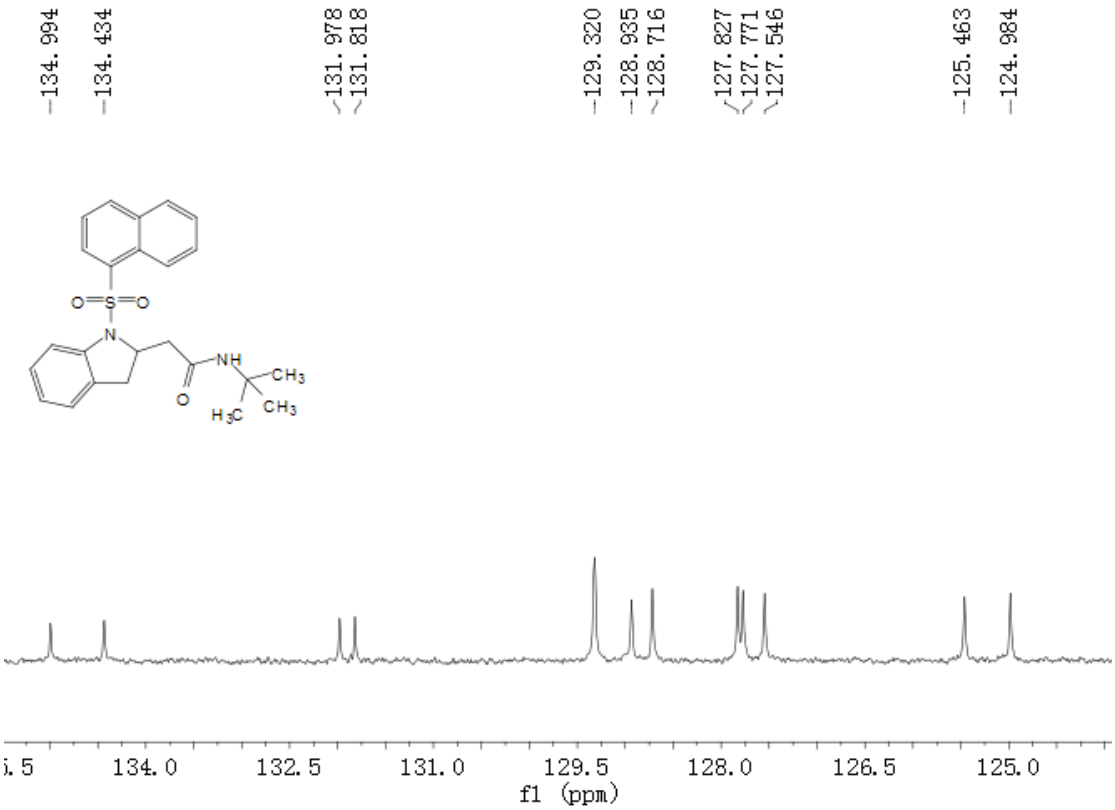
f1 (ppm)



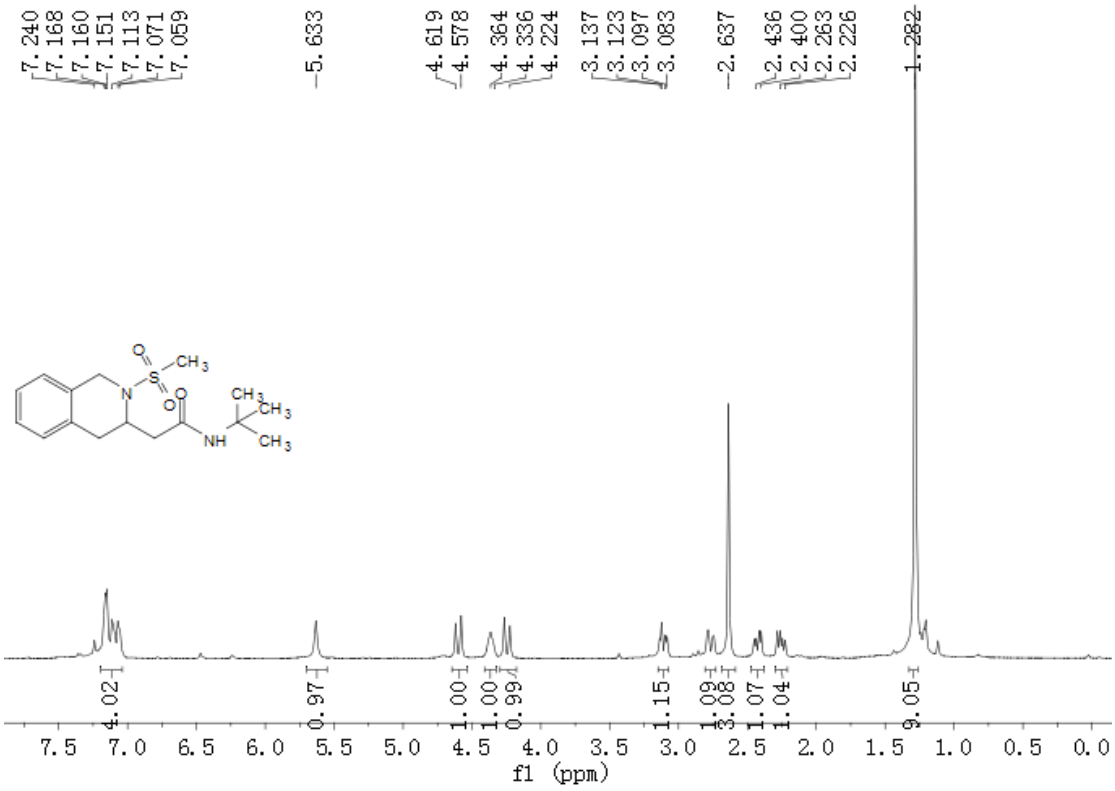
***N*-(*tert*-butyl)-2-(1-(naphthalen-1-ylsulfonyl)indolin-2-yl)acetamide (3r)**

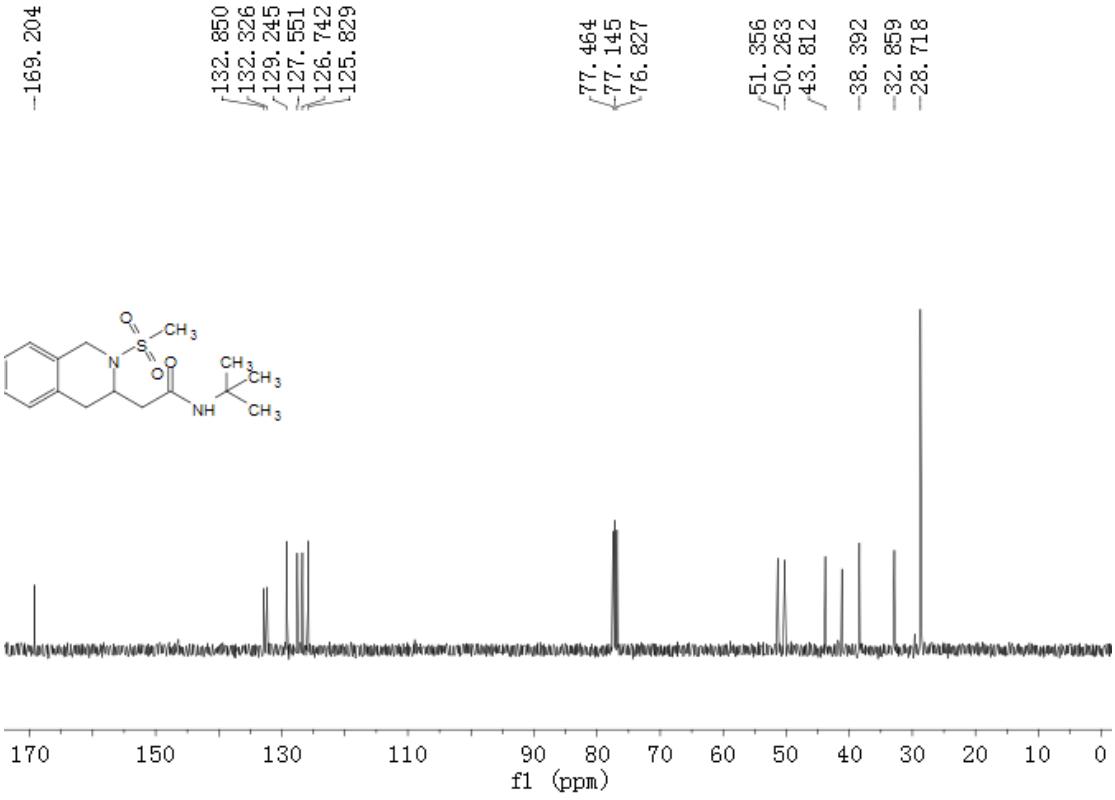




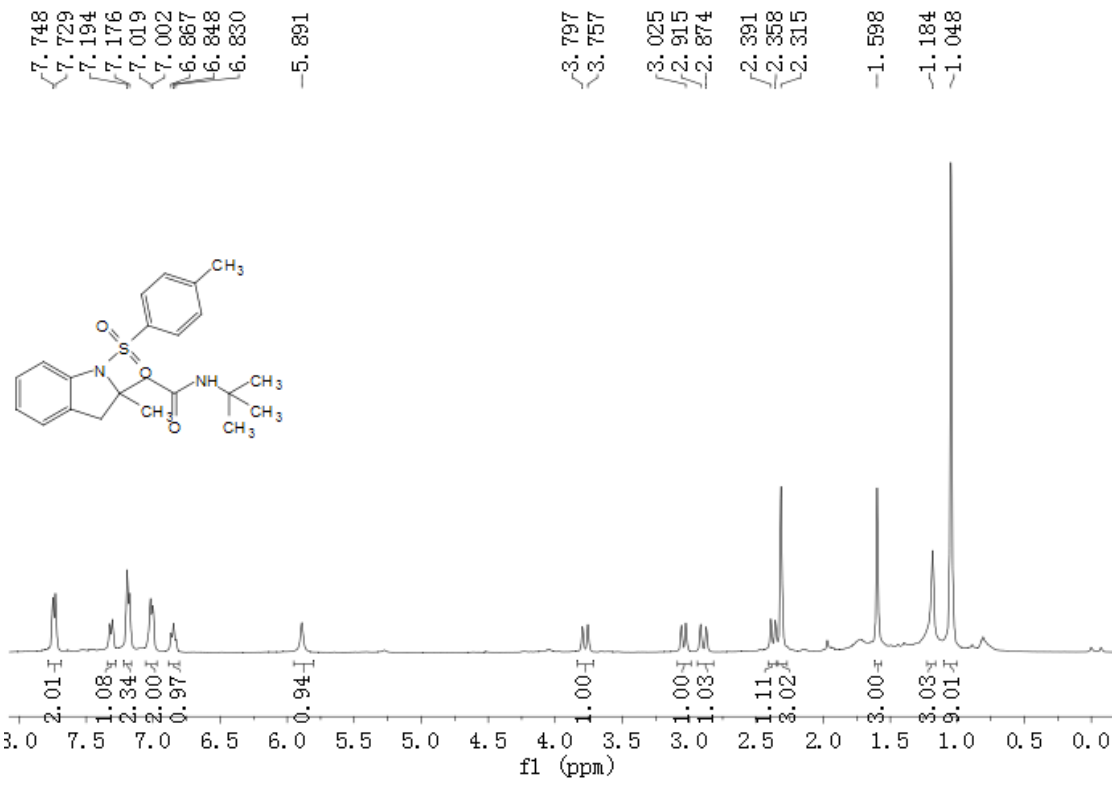


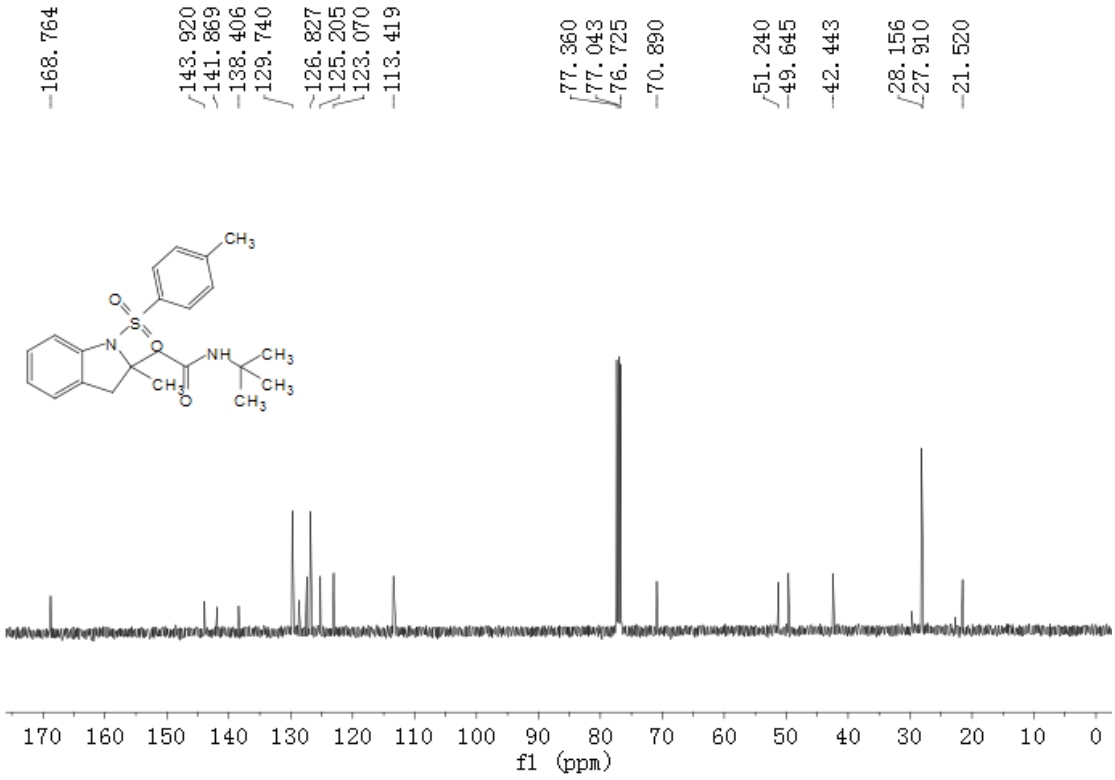
_N_-(_tert_-butyl)-2-(2-(methylsulfonyl)-1,2,3,4-tetrahydroisoquinolin-3-yl)acetamide (3s)



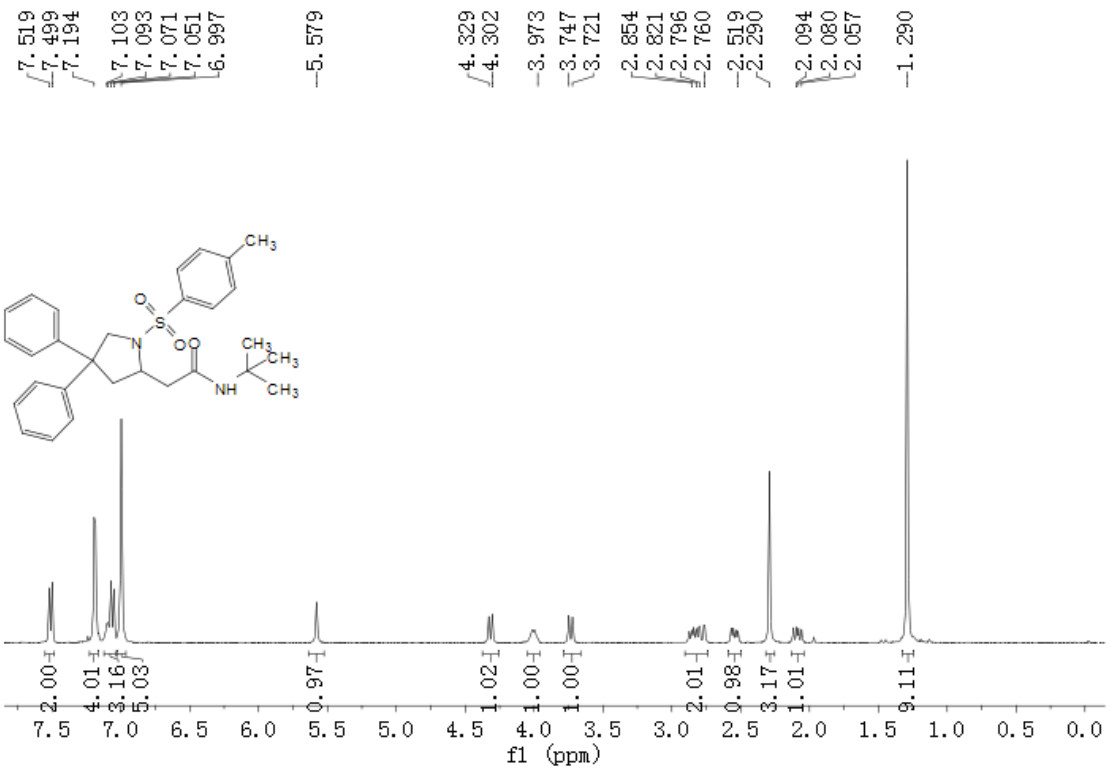


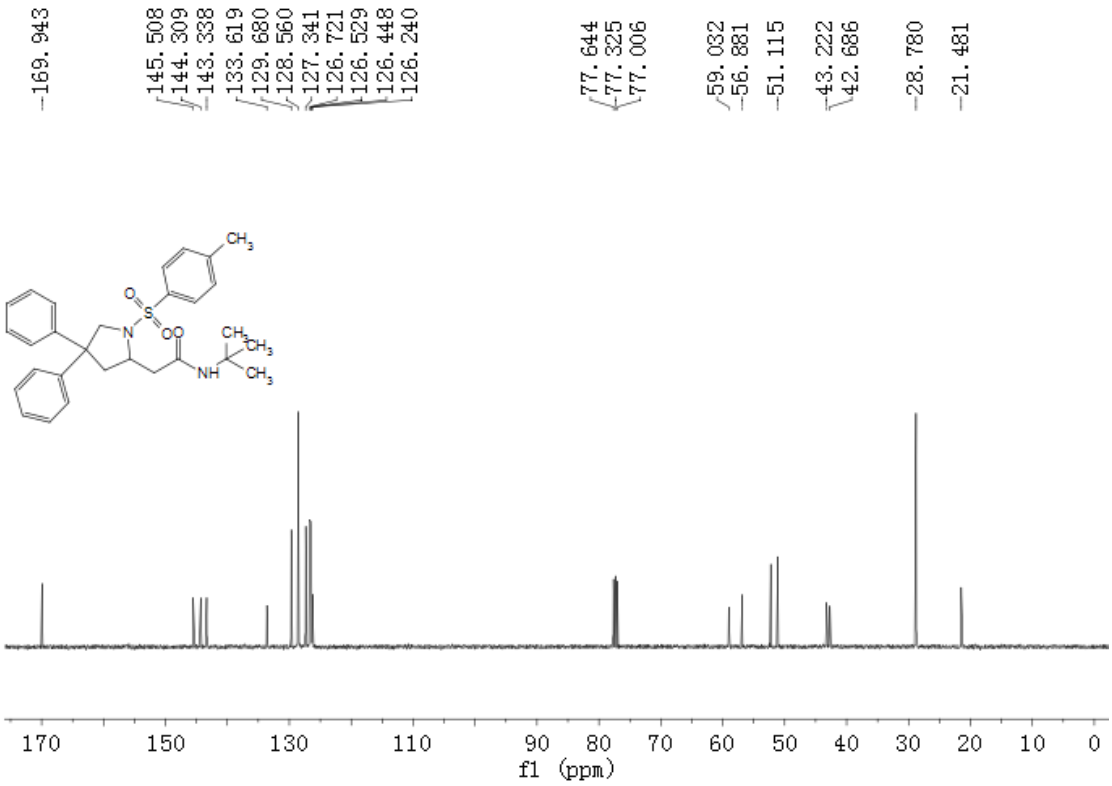
_N_-(_tert_-butyl)-2-(2-methyl-1-tosylindolin-2-yl)acetamide (3t)



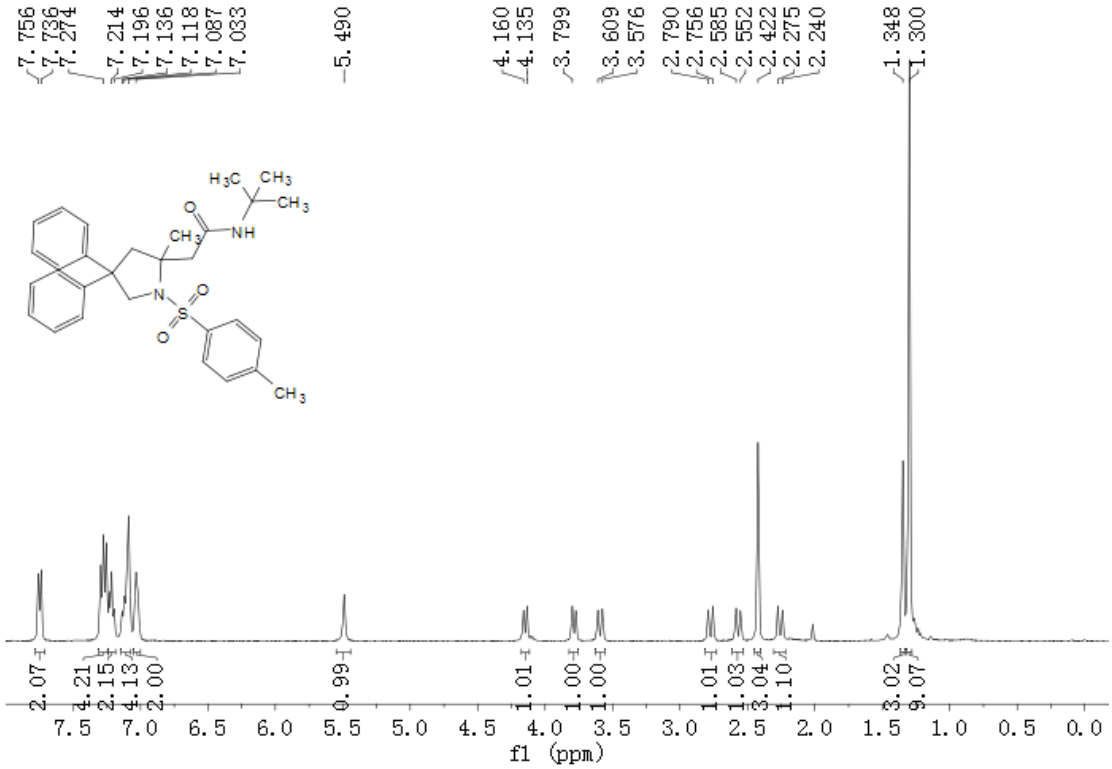


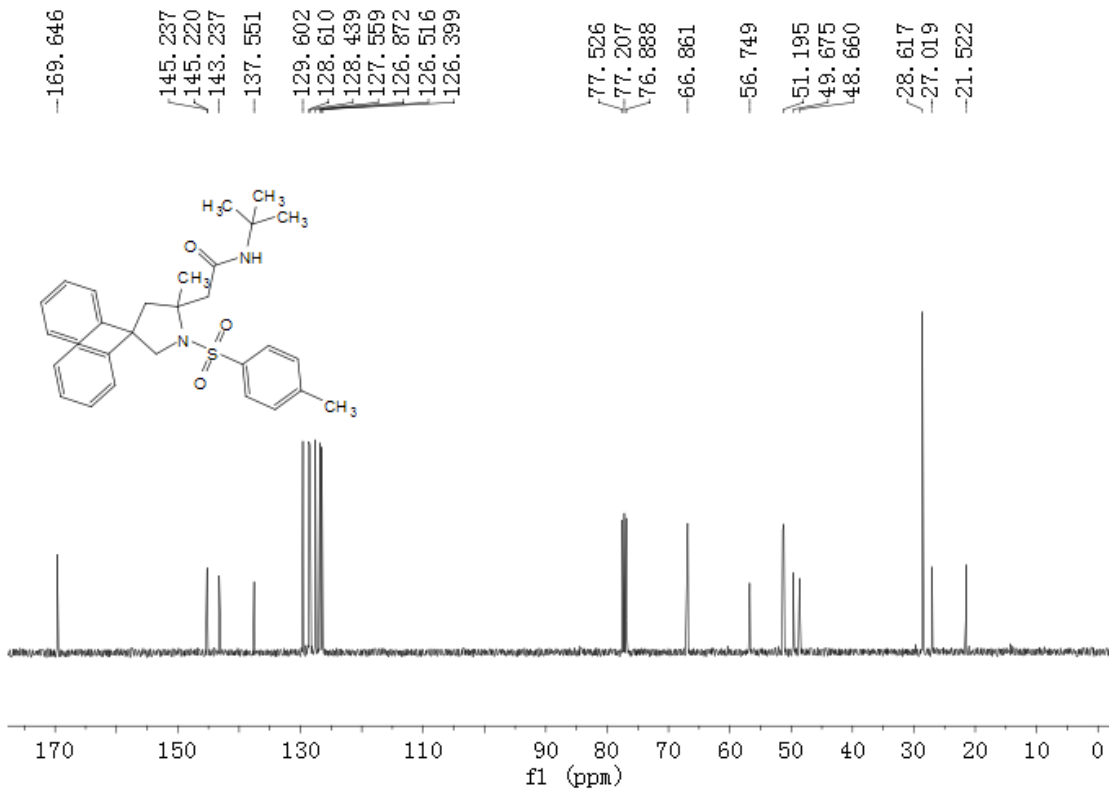
_N_-(tert-butyl)-2-(4,4-diphenyl-1-tosylpyrrolidin-2-yl)acetamide (3u)



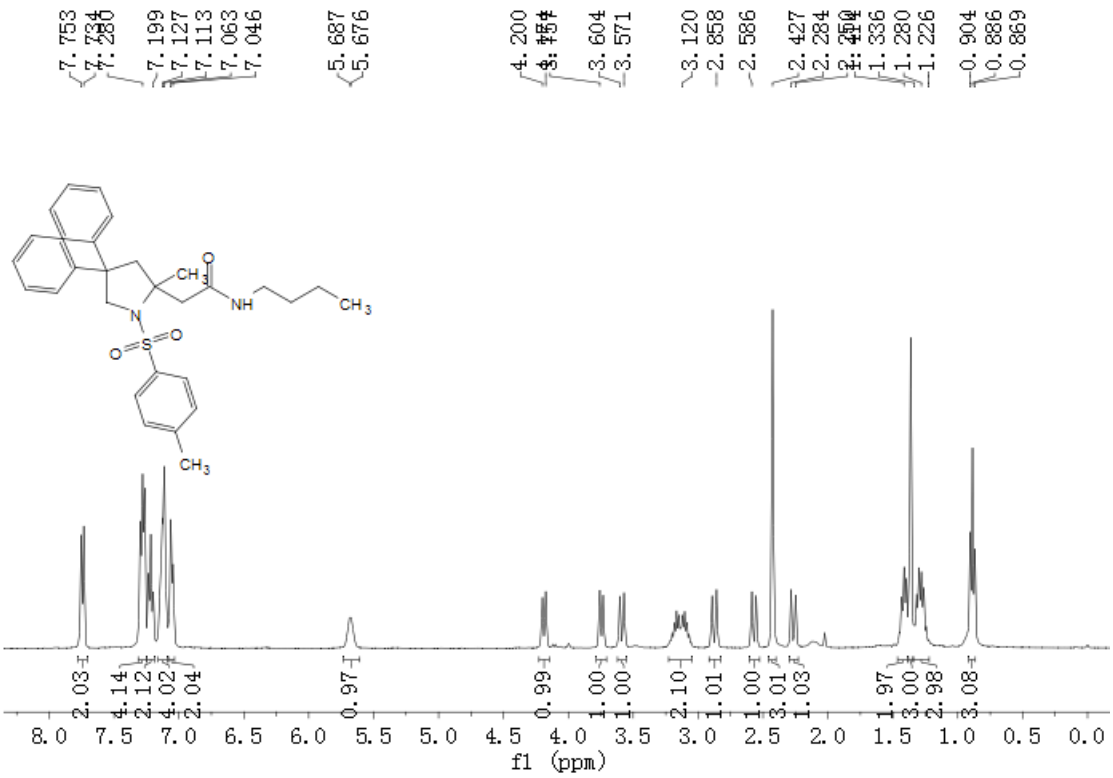


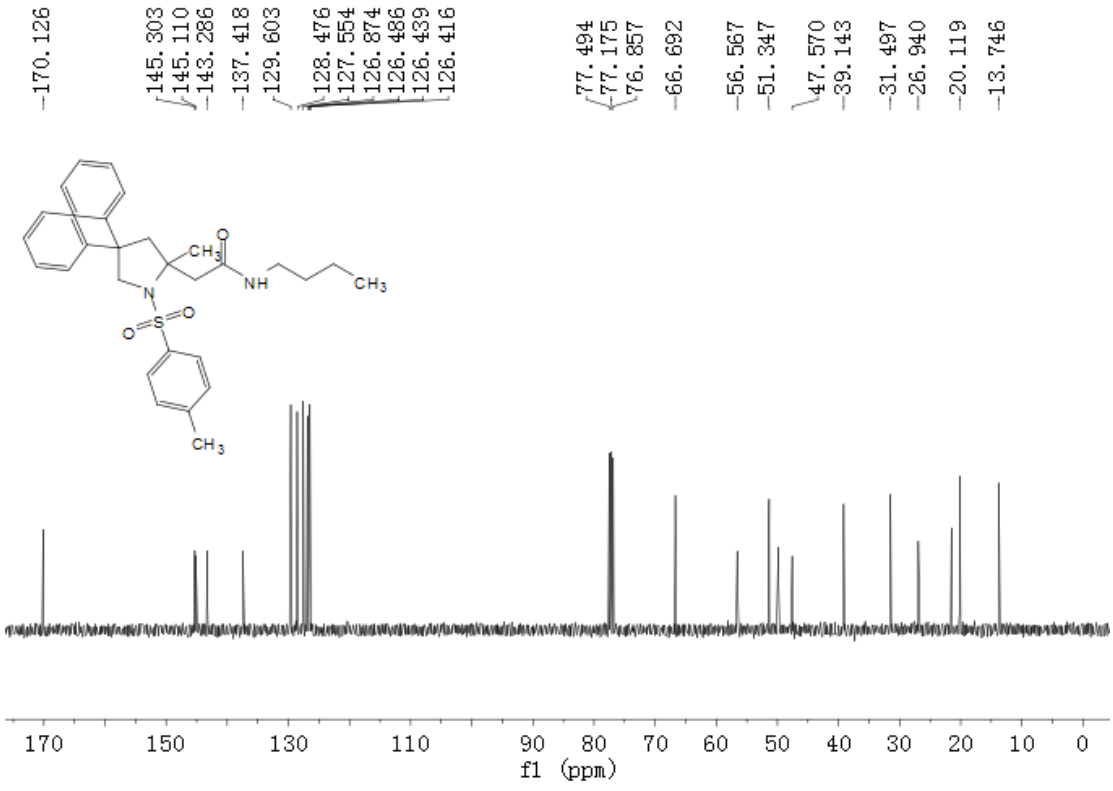
***N*-(*tert*-butyl)-2-(2-methyl-4,4-diphenyl-1-tosylpyrrolidin-2-yl)acetamide (3v)**



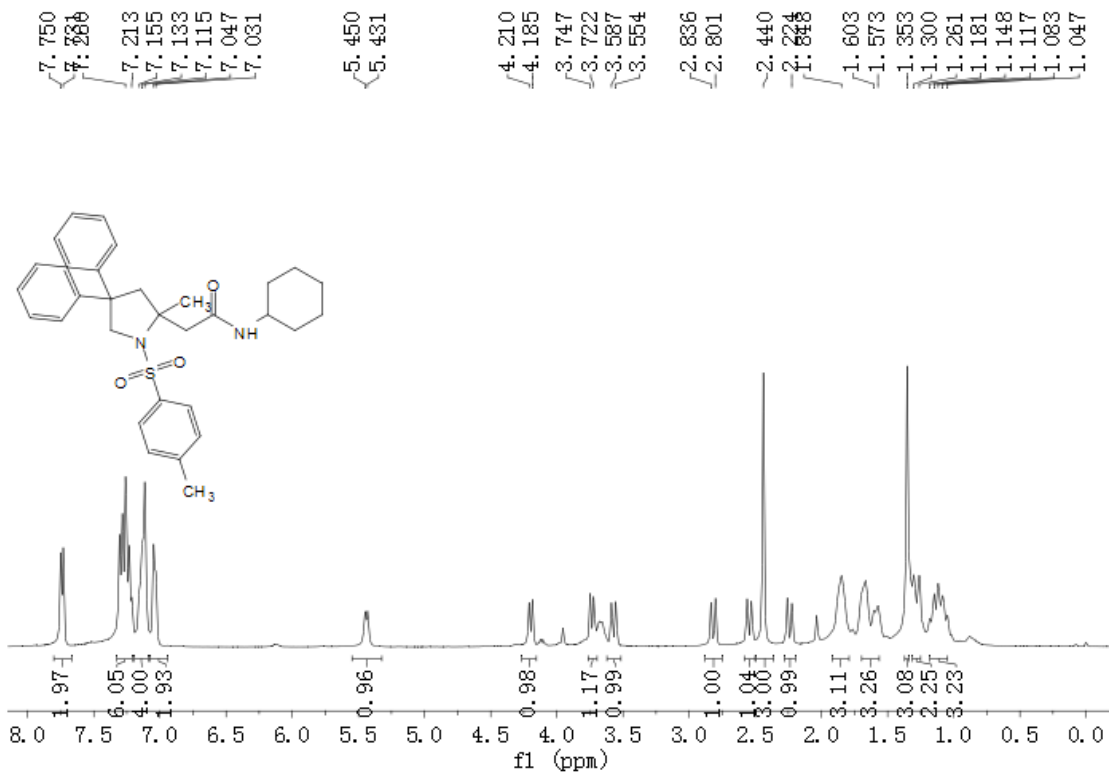


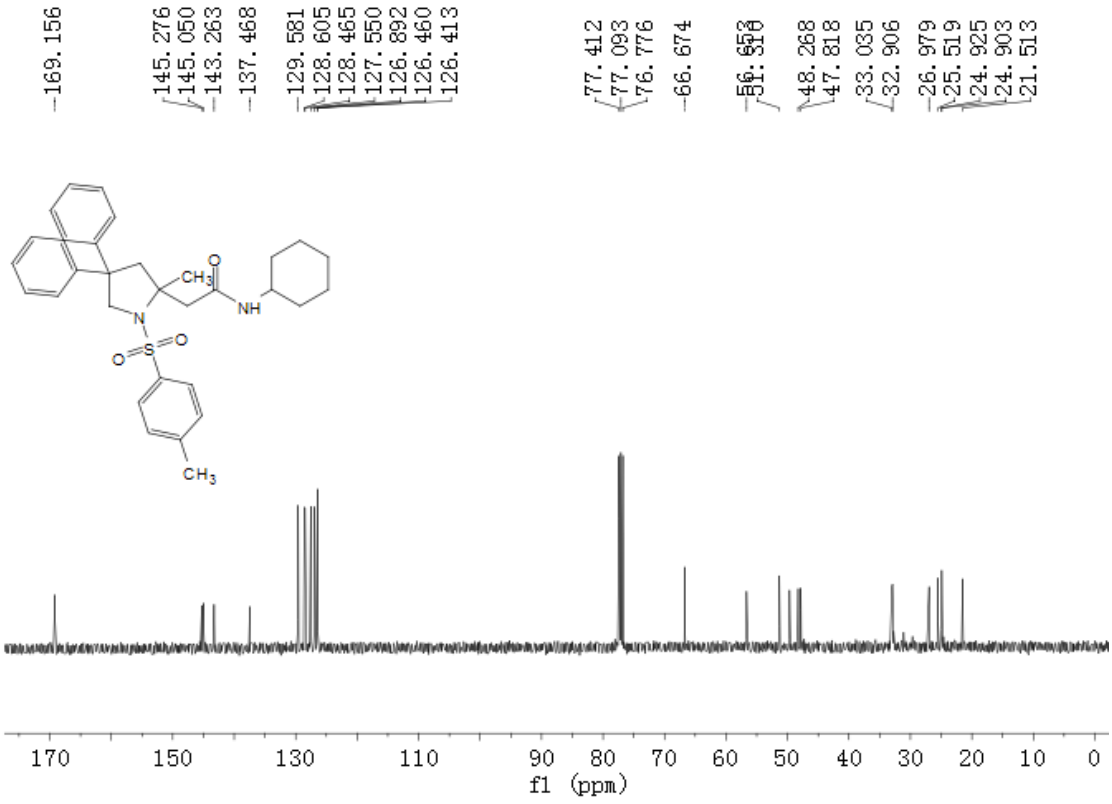
_N_-butyl-2-(2-methyl-4,4-diphenyl-1-tosylpyrrolidin-2-yl)acetamide (3w)



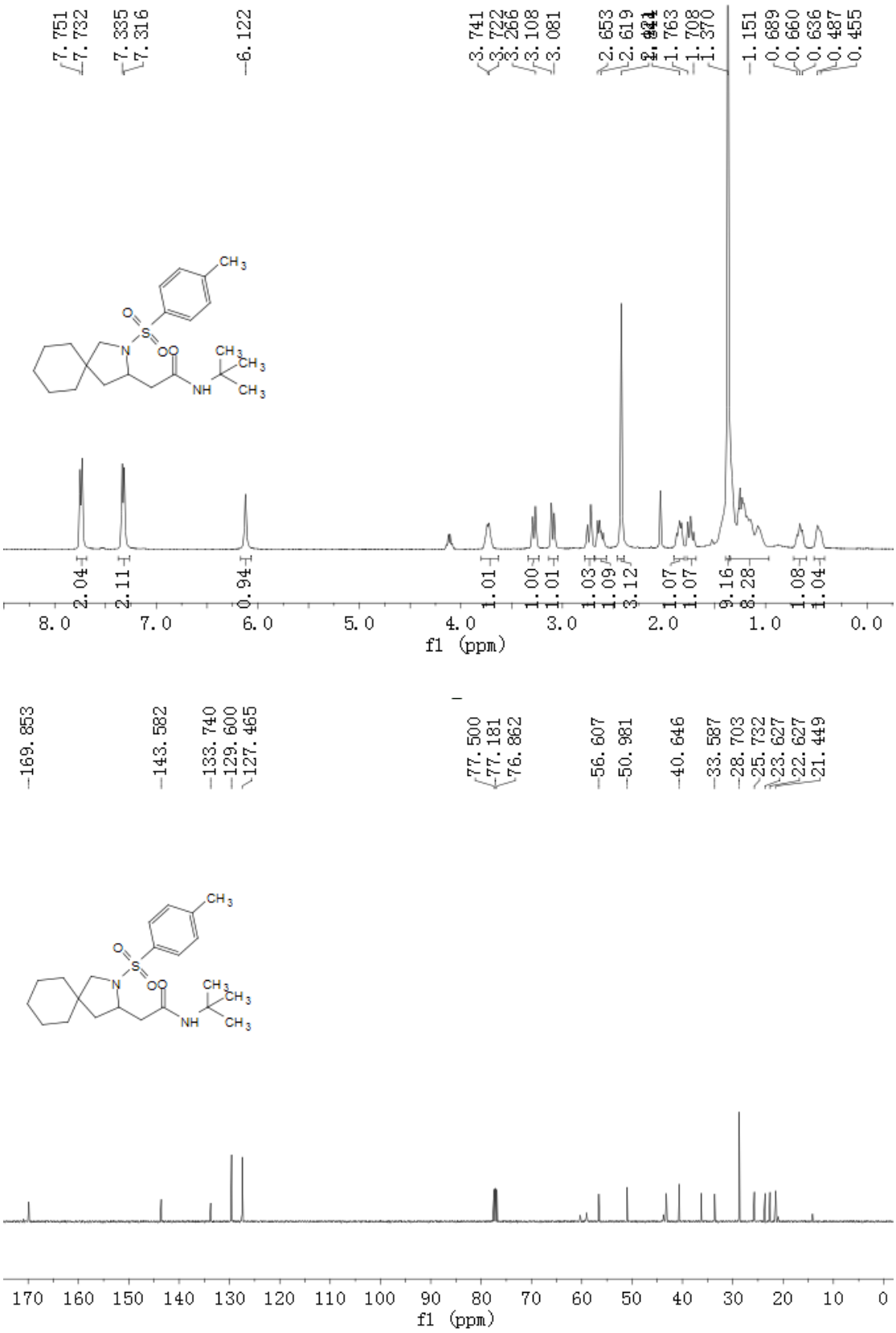


_N_-cyclohexyl-2-(2-methyl-4,4-diphenyl-1-tosylpyrrolidin-2-yl)acetamide (3x)

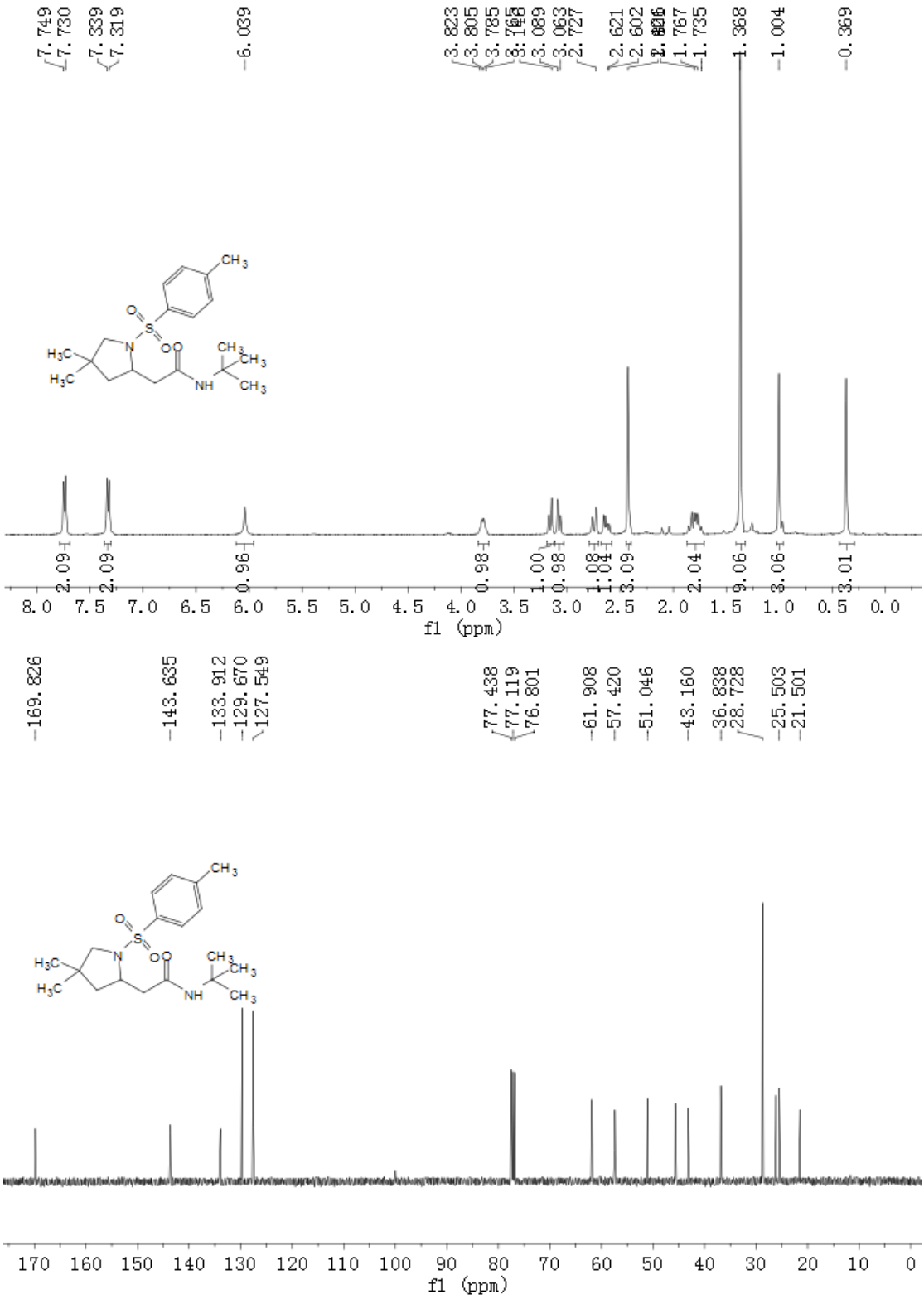




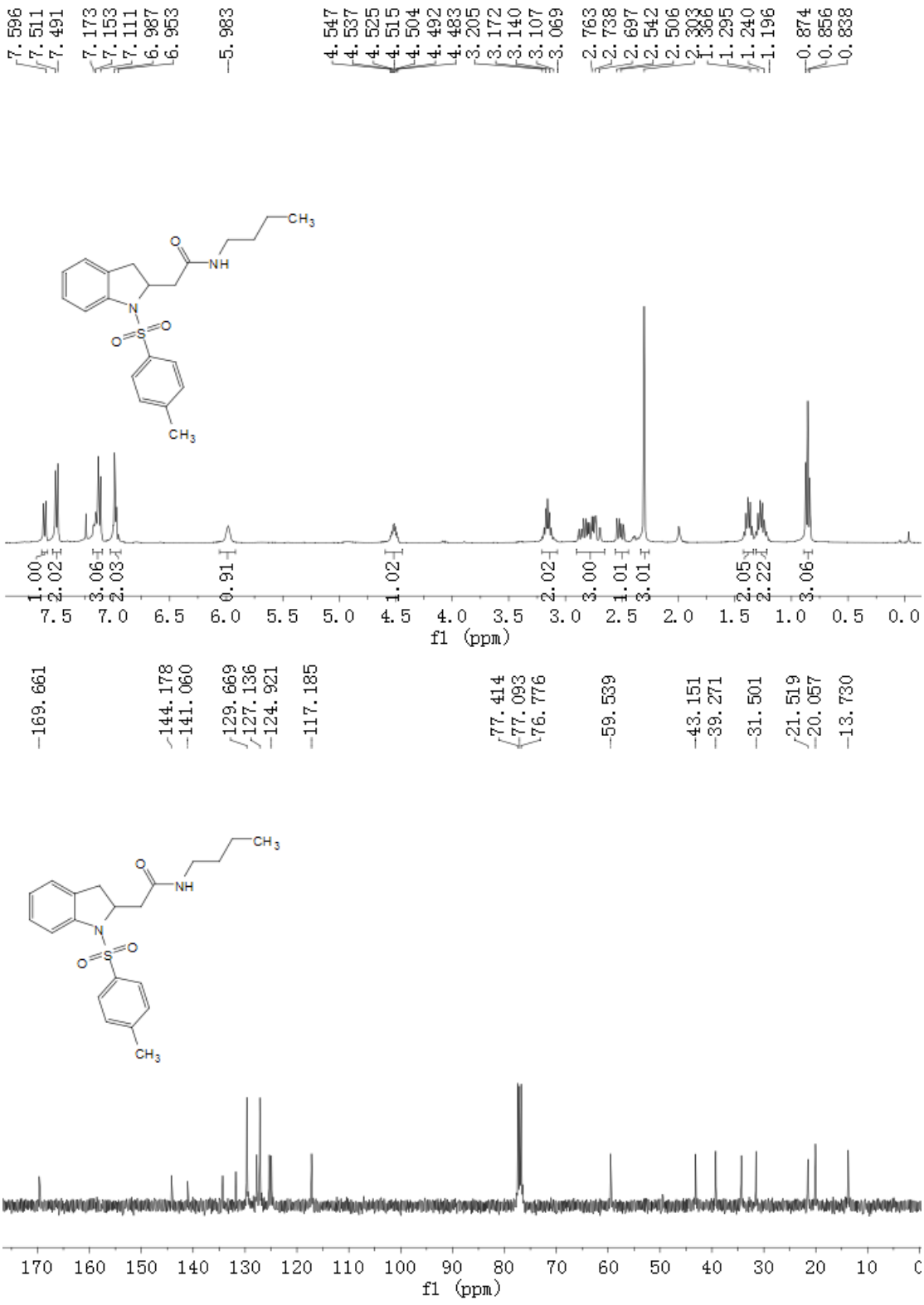
***N*-(*tert*-butyl)-2-(2-tosyl-2-azaspiro[4.5]decan-3-yl)acetamide (3y)**



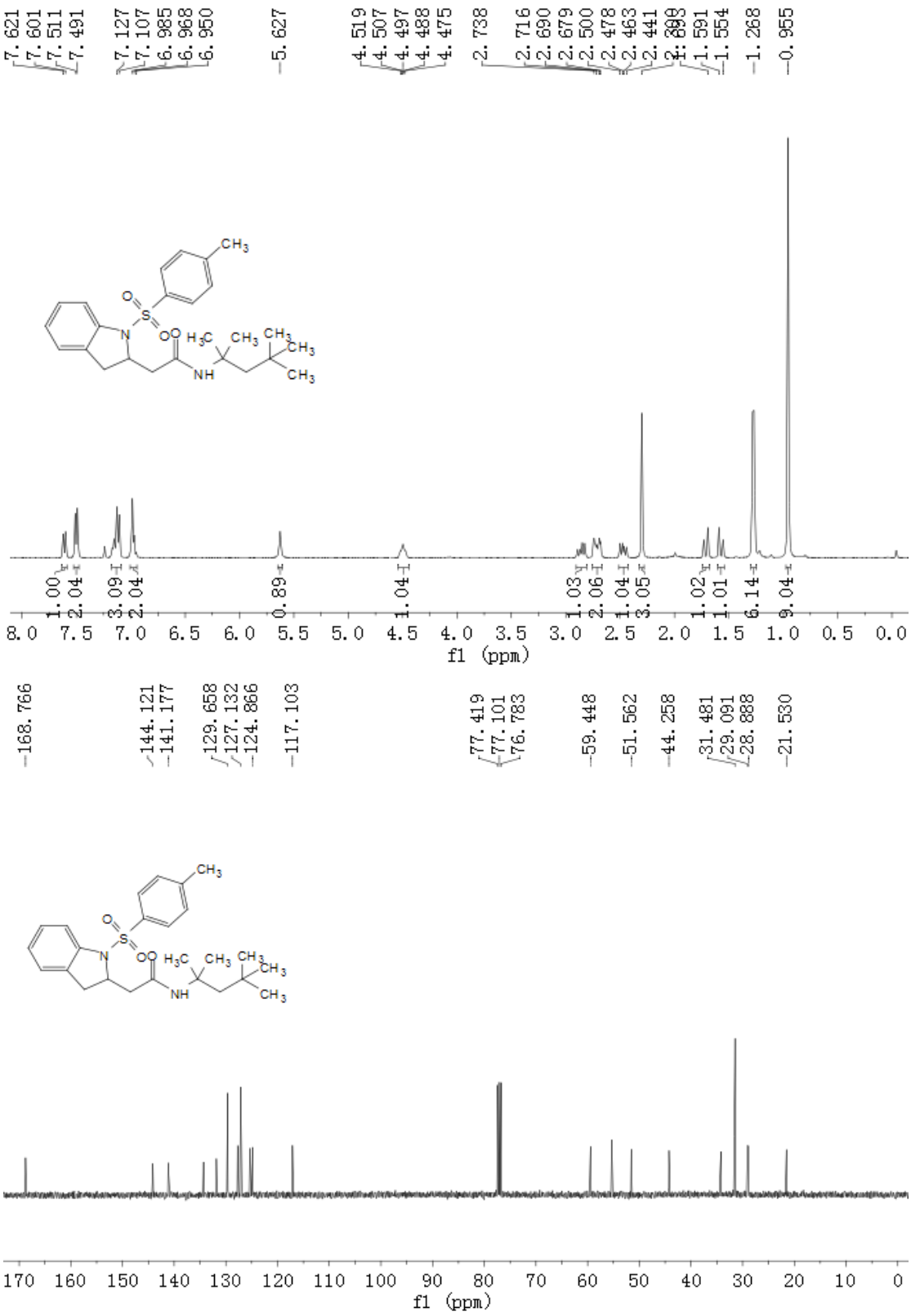
N-(tert-butyl)-2-(4,4-dimethyl-1-tosylpyrrolidin-2-yl)acetamide (3z)



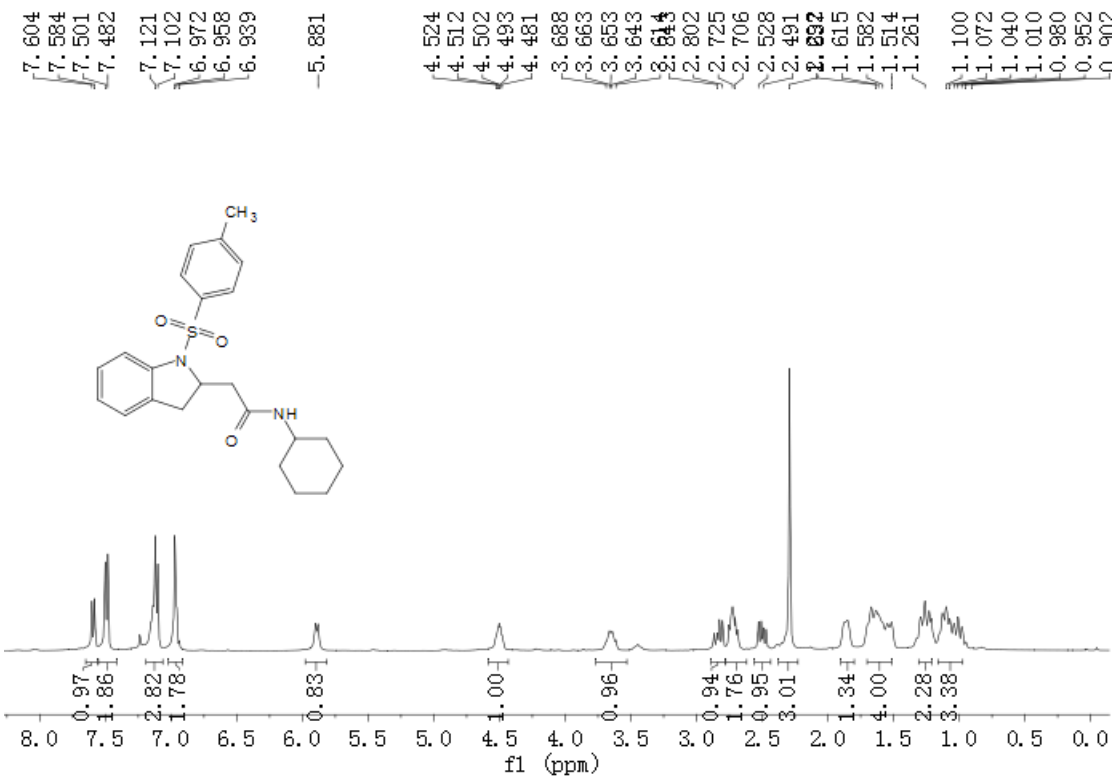
***N*-butyl-2-(1-tosylindolin-2-yl)acetamide (3za)**

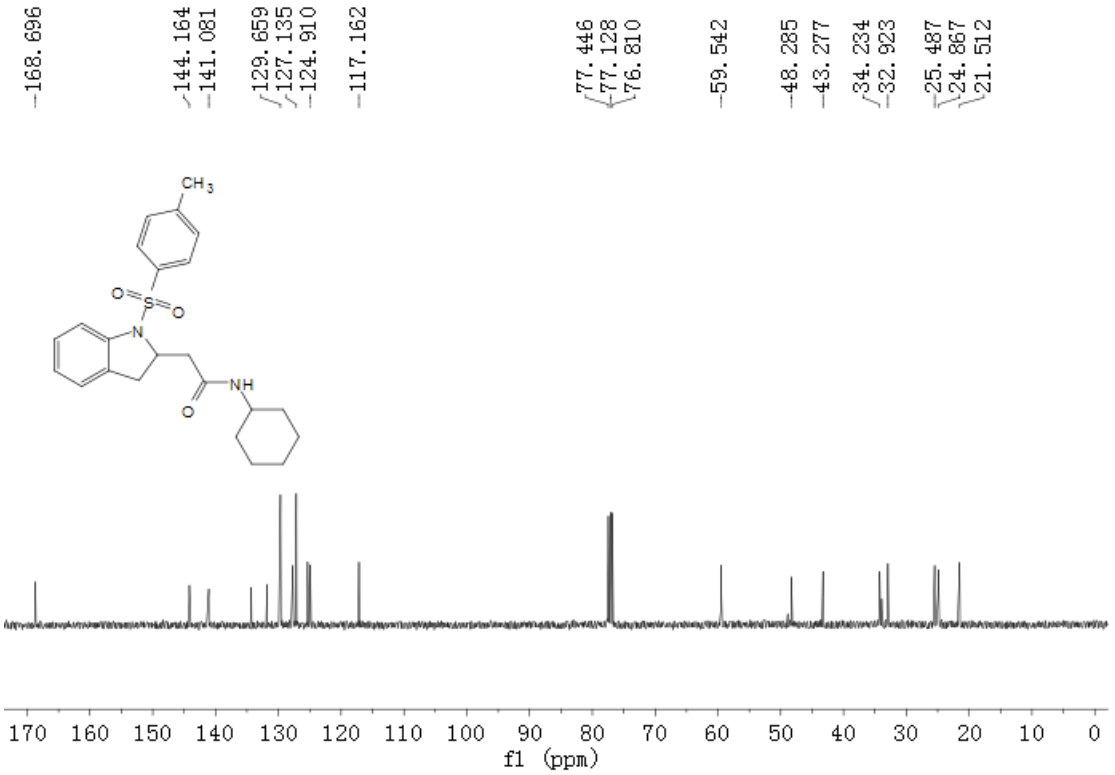


2-(1-tosylindolin-2-yl)-*N*-(2,4,4-trimethylpentan-2-yl)acetamide (3zb)

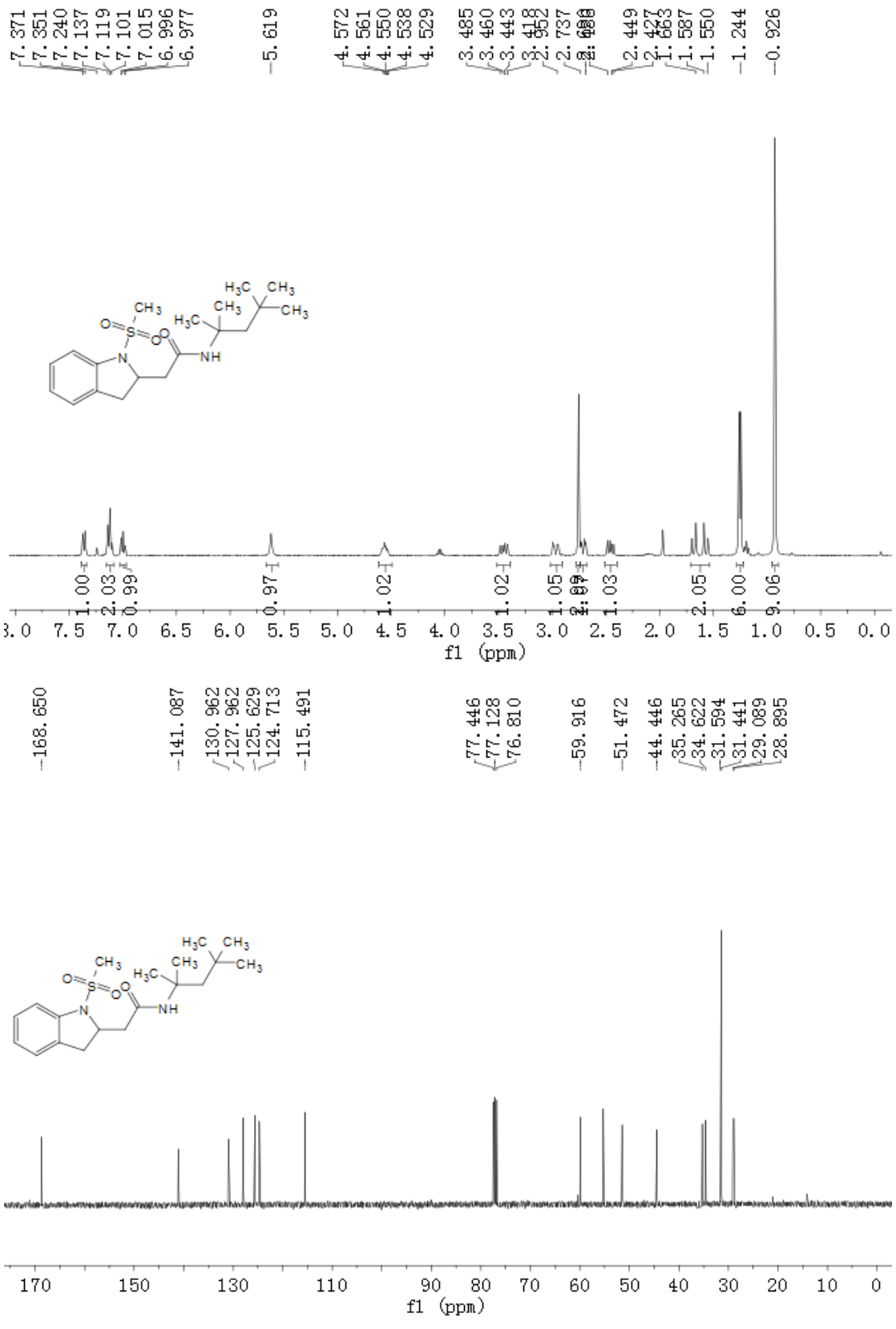


***N*-cyclohexyl-2-(1-tosylindolin-2-yl)acetamide (3zc)**

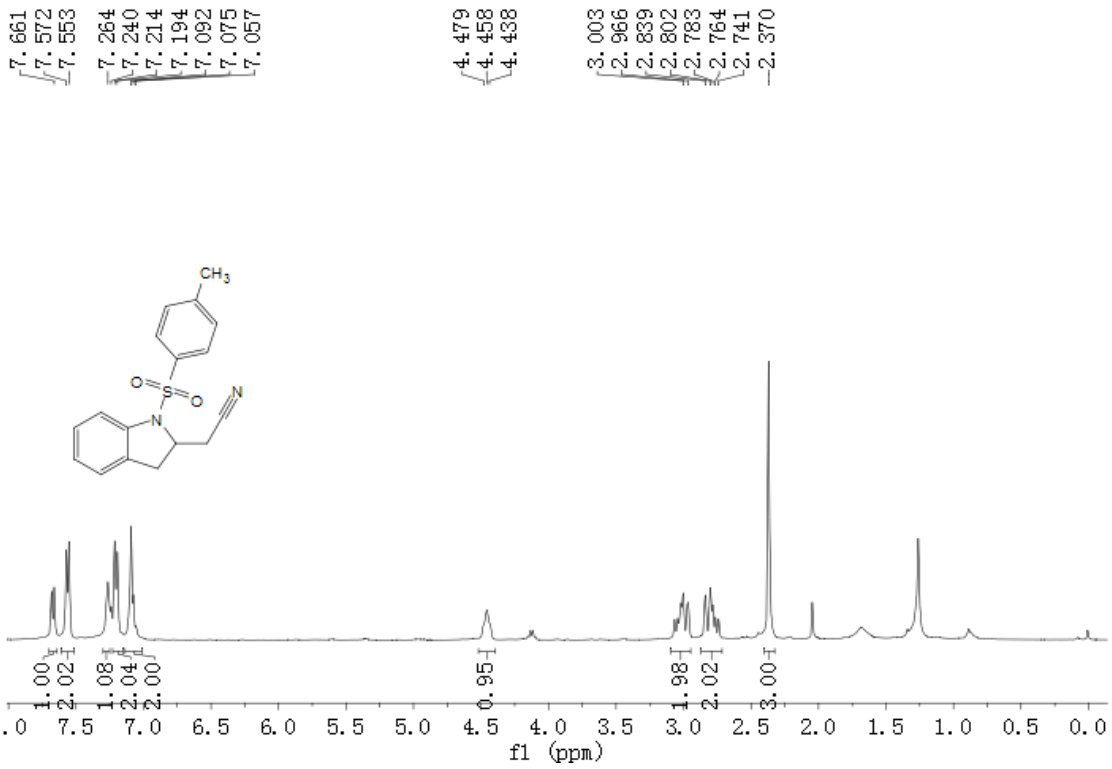


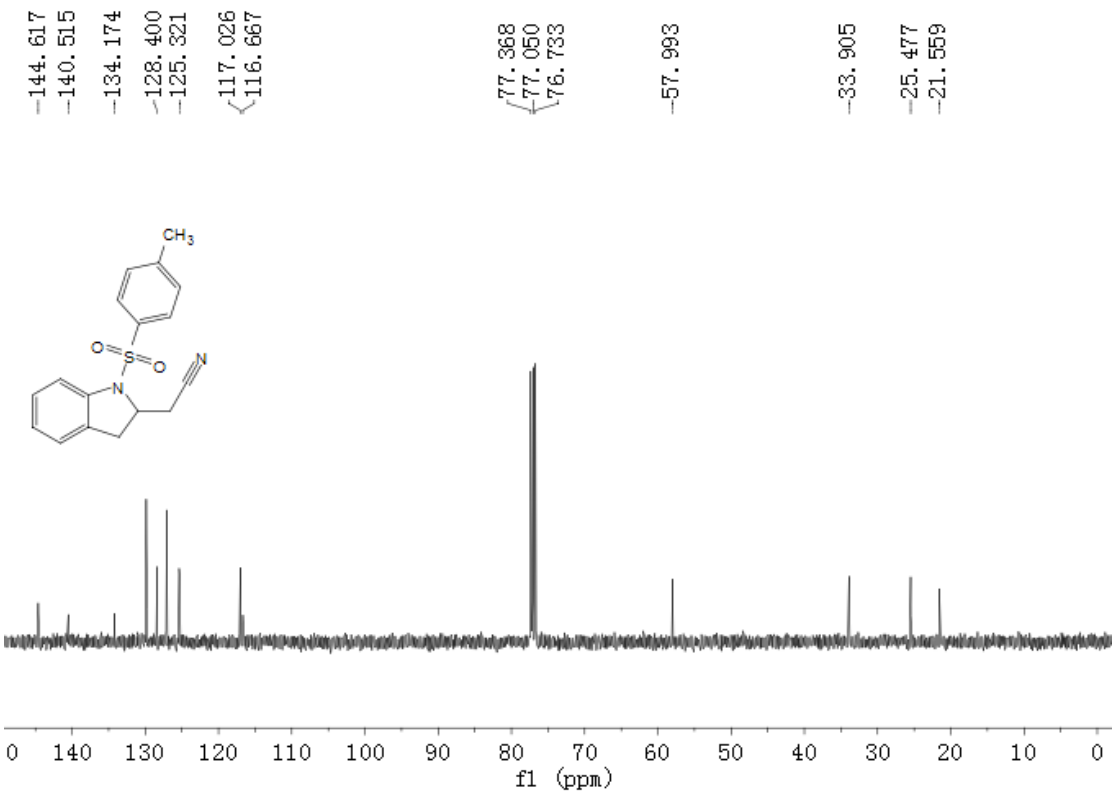


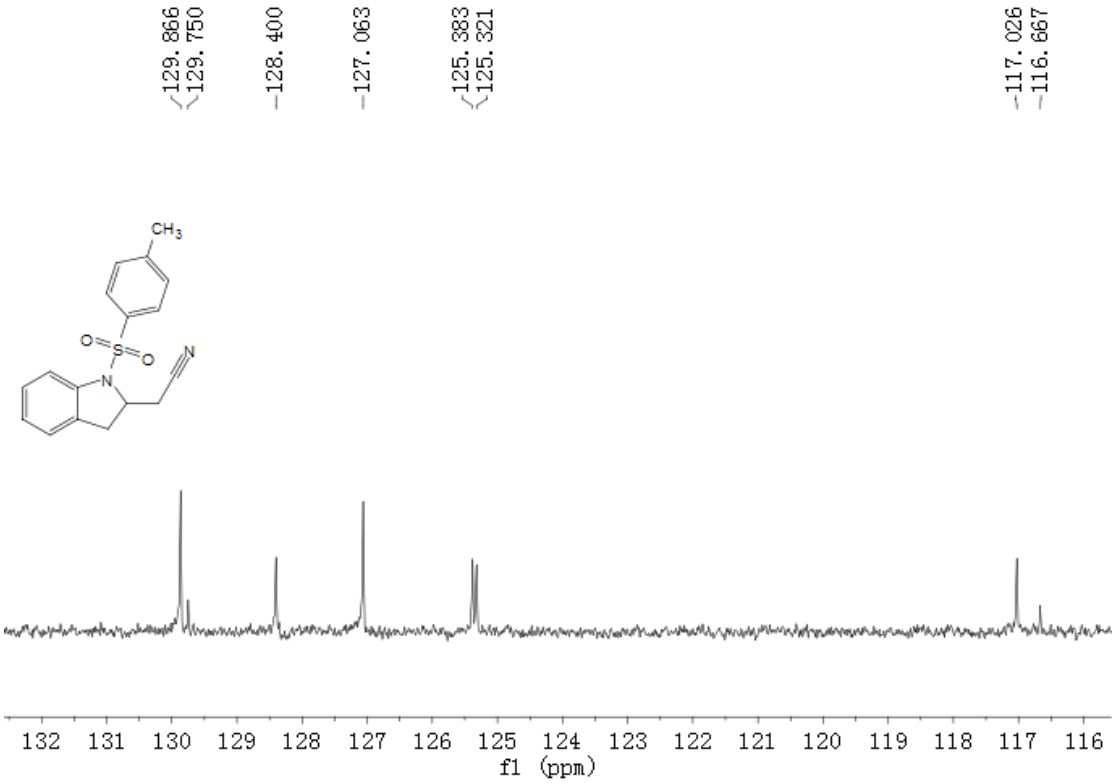
2-(1-(methylsulfonyl)indolin-2-yl)-*N*-(2,4,4-trimethylpentan-2-yl)acetamide (3zd)



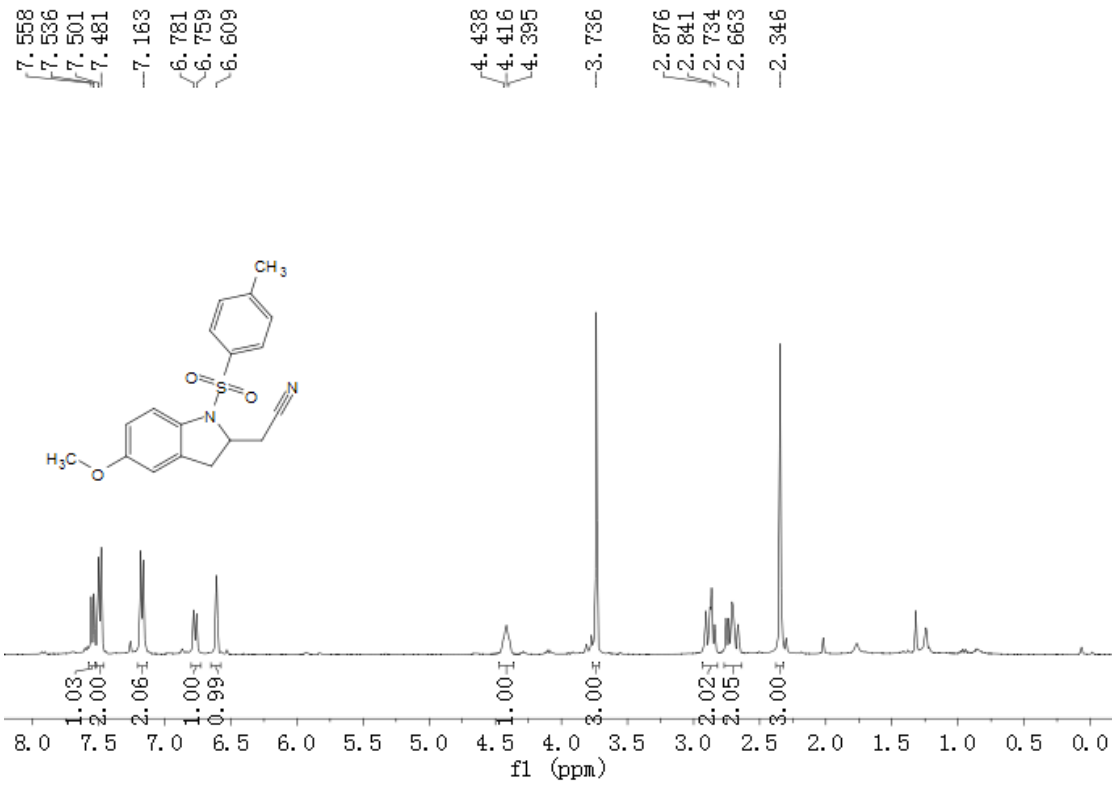
2-(1-tosylindolin-2-yl)acetonitrile (4a)

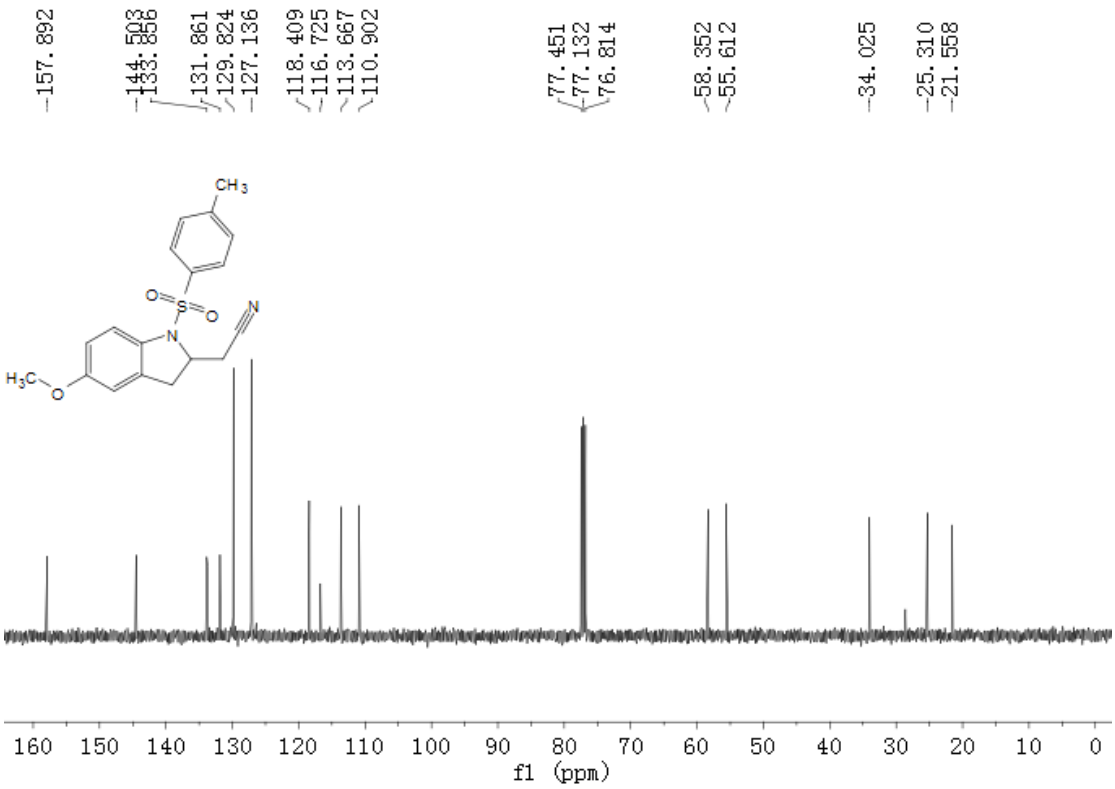

7.661
7.572
7.553
7.264
7.240
7.214
7.194
7.092
7.075
7.057
4.479
4.458
4.438
3.003
2.966
2.839
2.802
2.783
2.764
2.741
2.370
CH3
O
S
O
N
N
1.00
2.02
1.08
2.04
2.00
0.95
1.98
2.02
3.00
f1 (ppm)

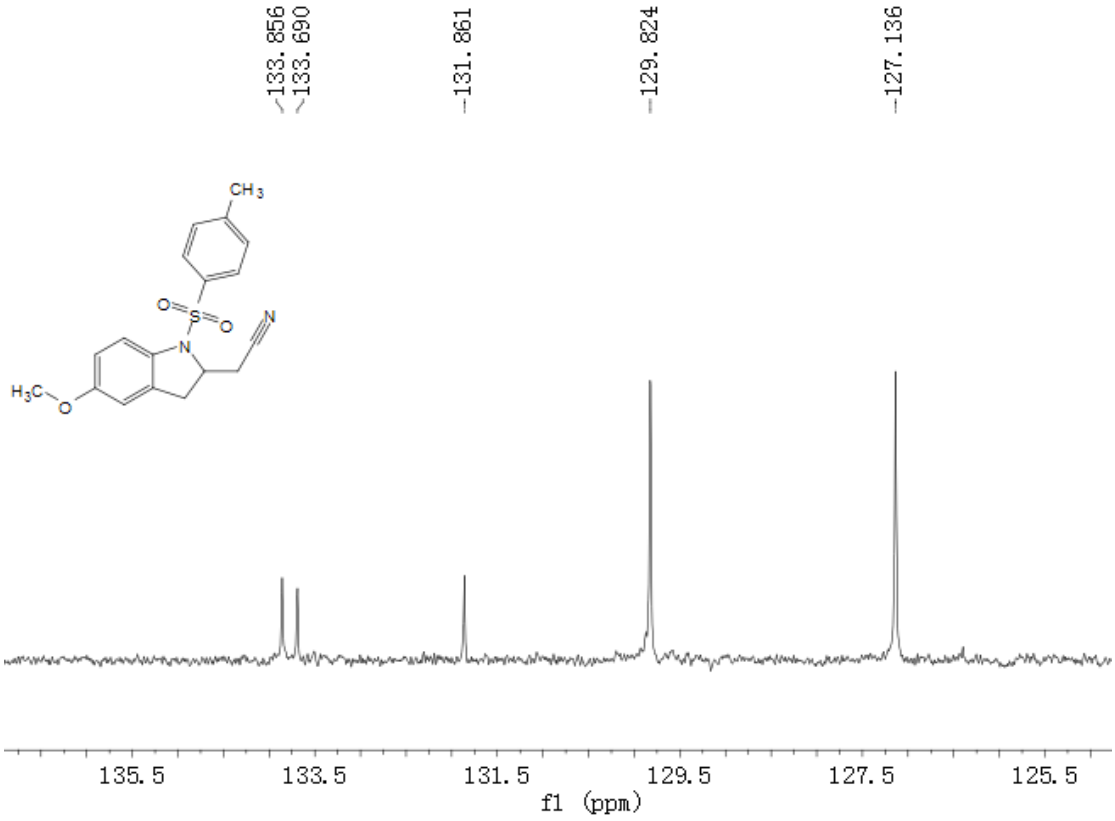

144.617
140.515
134.174
128.400
125.321
117.026
116.667
77.368
77.050
76.733
57.993
33.905
25.477
21.559
CH3
O
S
O
N
N
f1 (ppm)



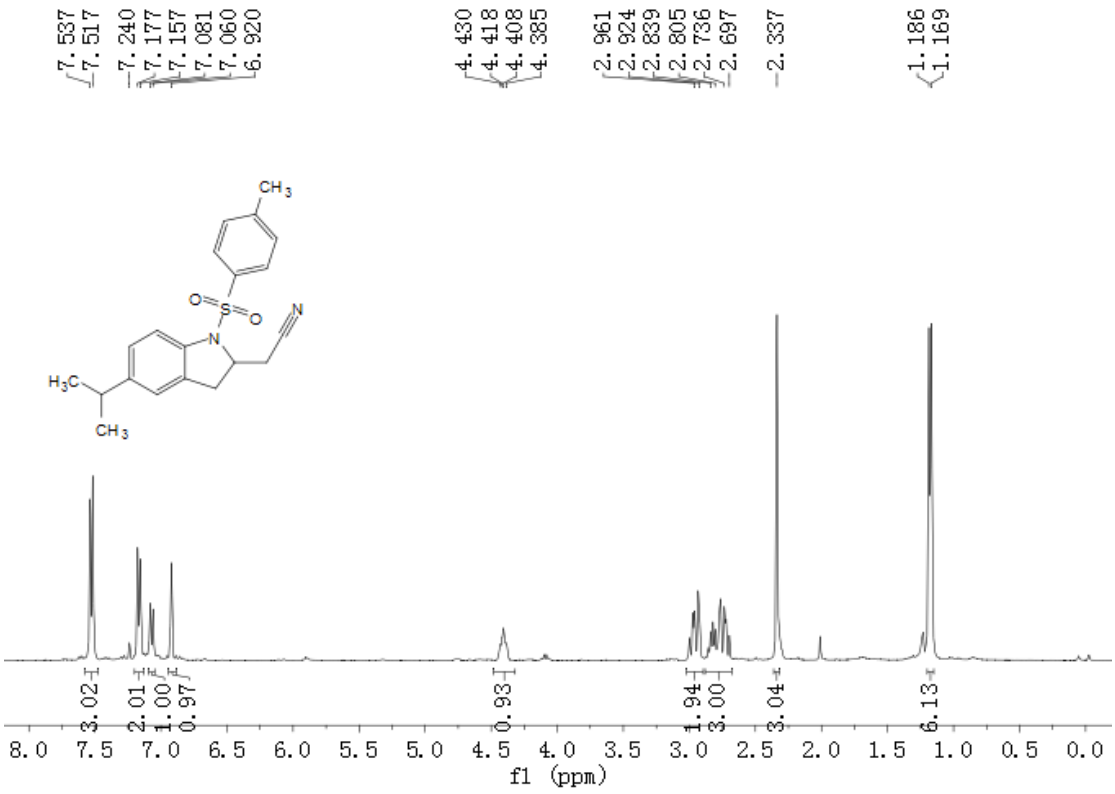
2-(5-methoxy-1-tosylindolin-2-yl)acetonitrile (4b)

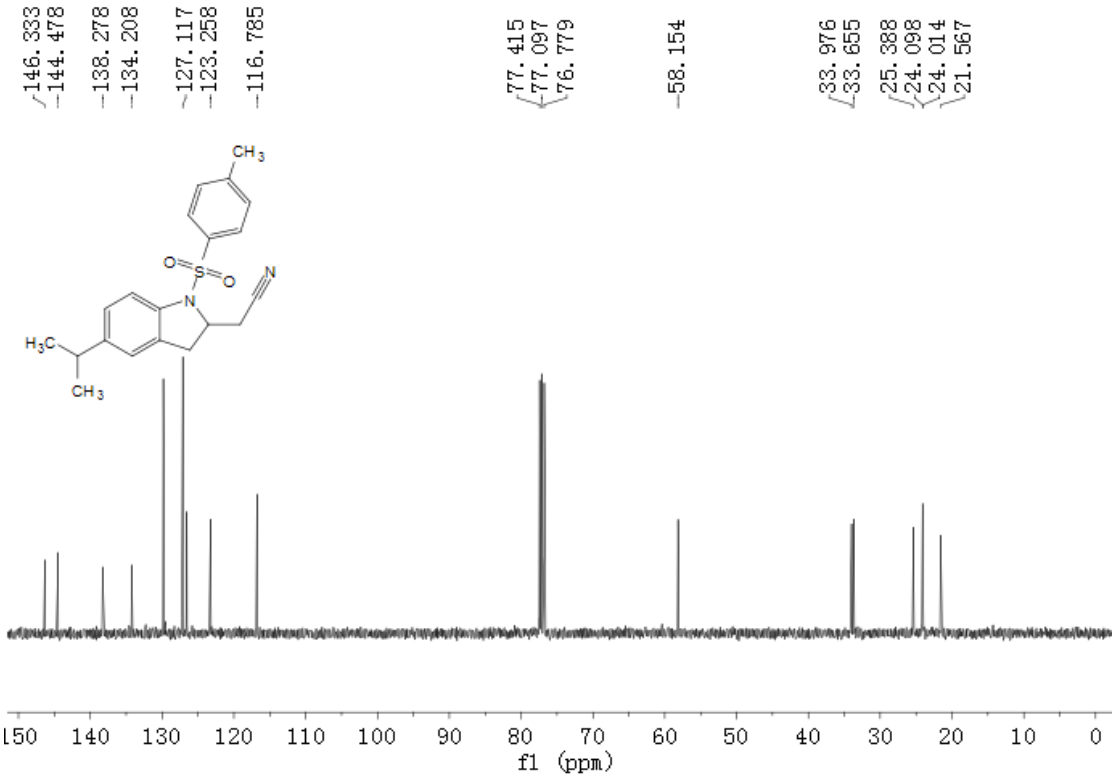




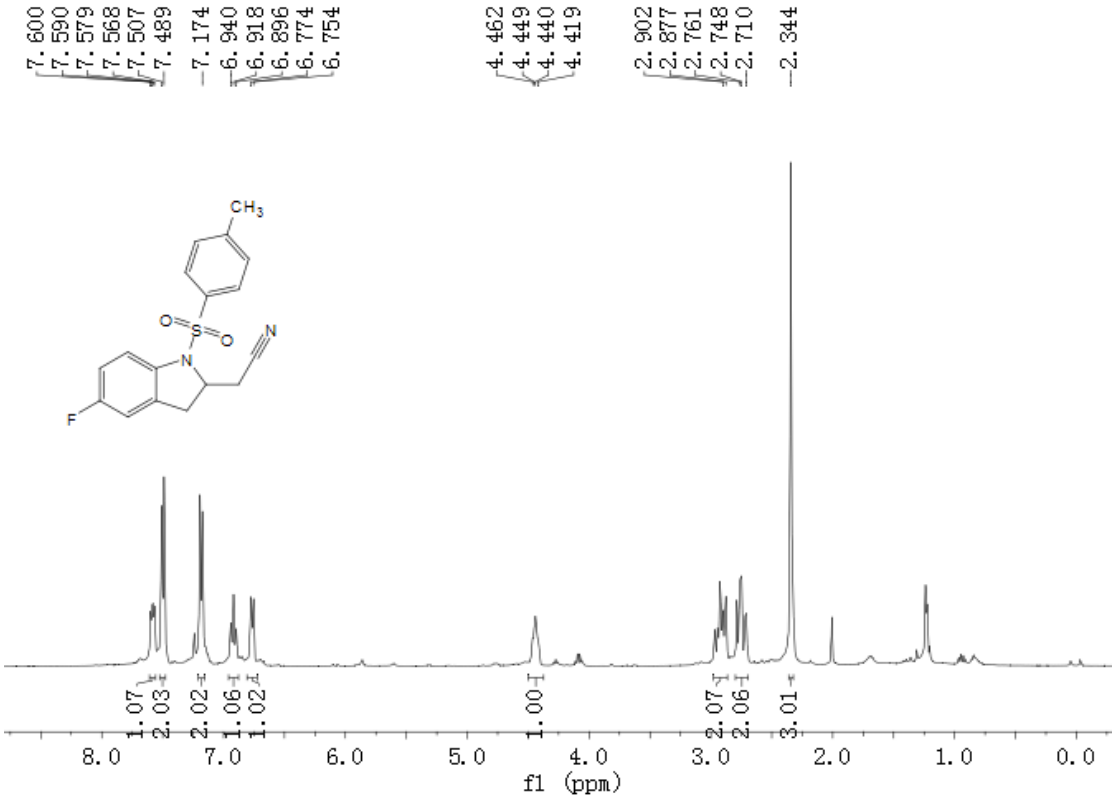


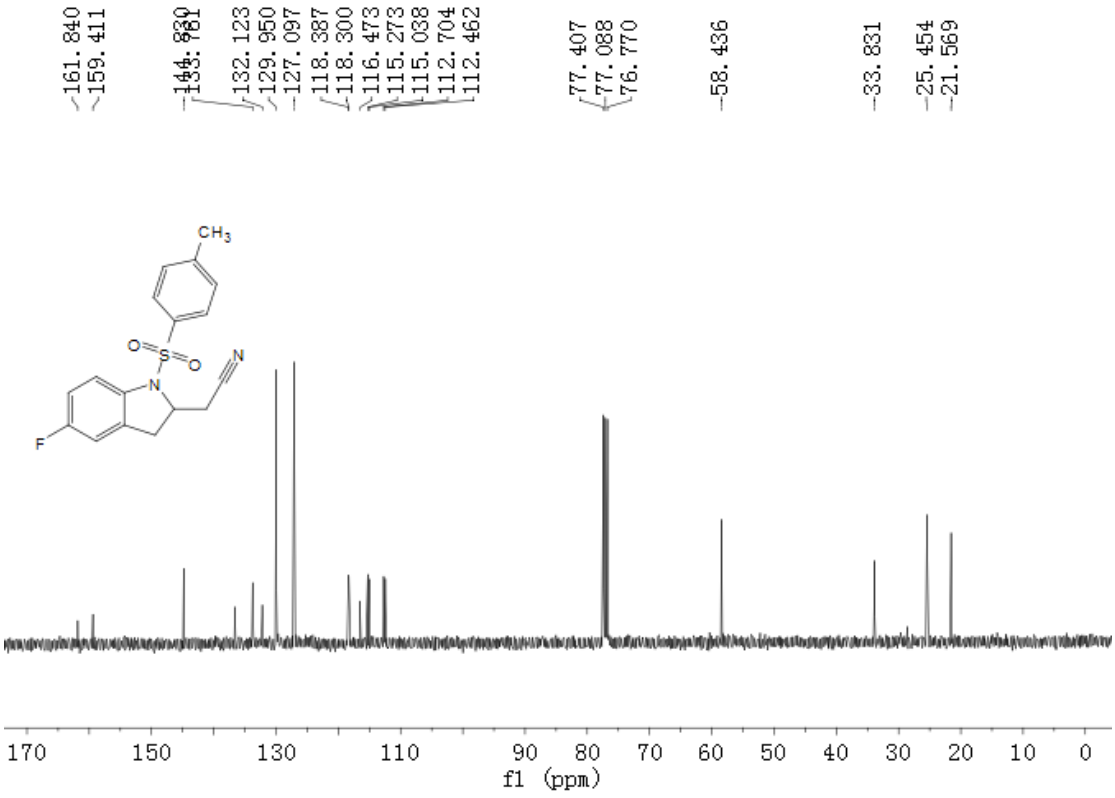
2-(5-isopropyl-1-tosylindolin-2-yl)acetonitrile (4c)



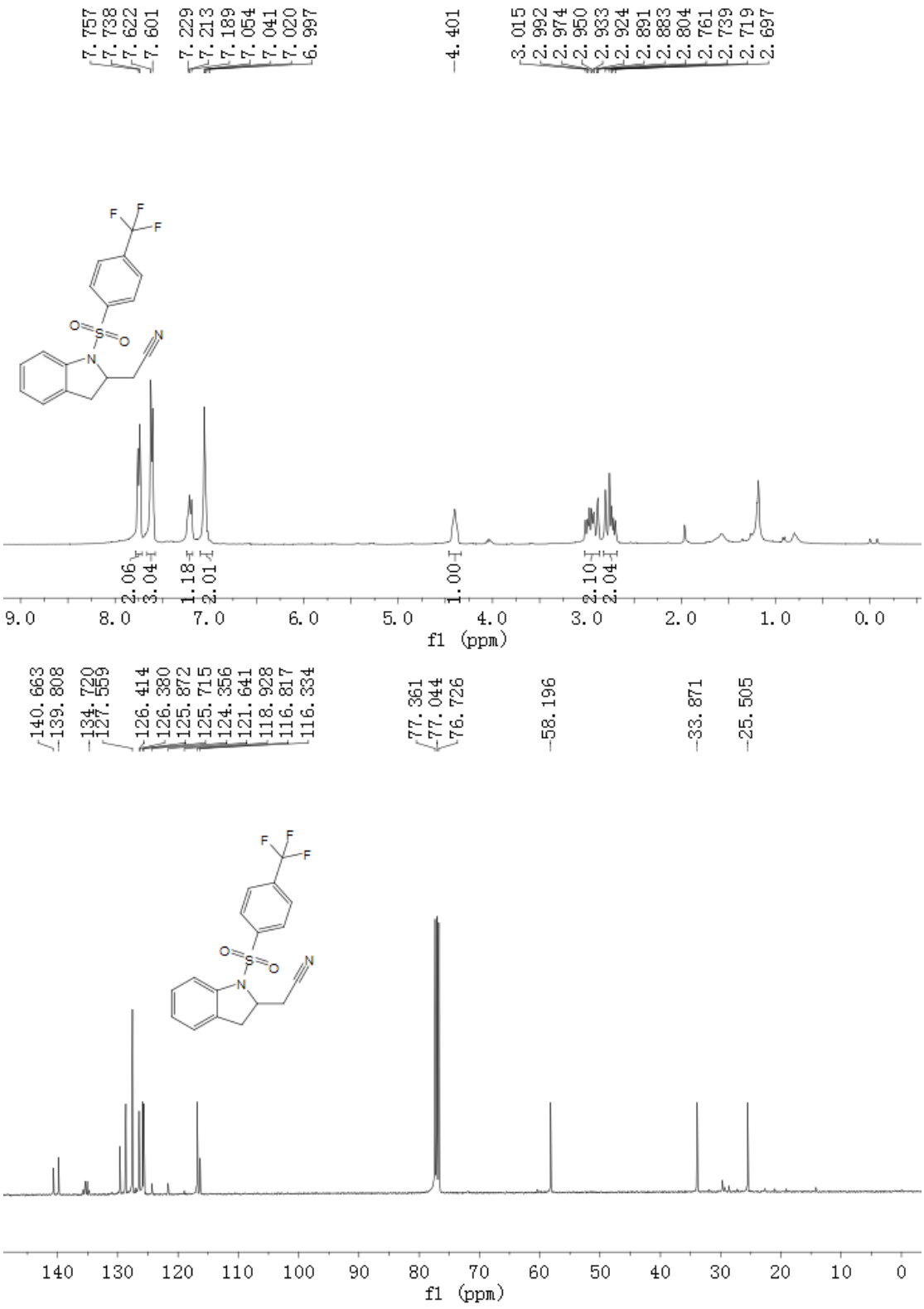


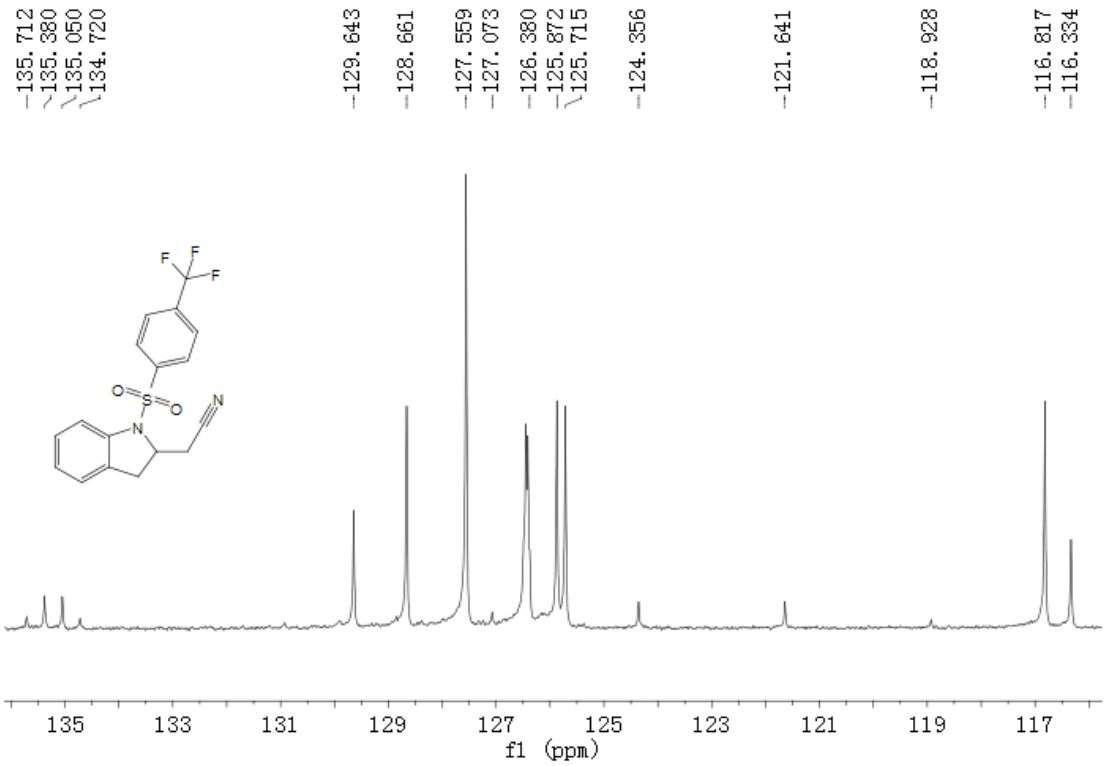
2-(5-fluoro-1-tosylindolin-2-yl)acetonitrile (4d)


7.600
7.590
7.579
7.568
7.507
7.489
7.174
6.940
6.918
6.896
6.774
6.754
4.462
4.449
4.440
4.419
2.902
2.877
2.761
2.748
2.710
2.344
CH3
O
S
O
N
N
F
1.07
2.03
2.02
1.06
1.02
1.00
2.07
2.06
3.01
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
f1 (ppm)

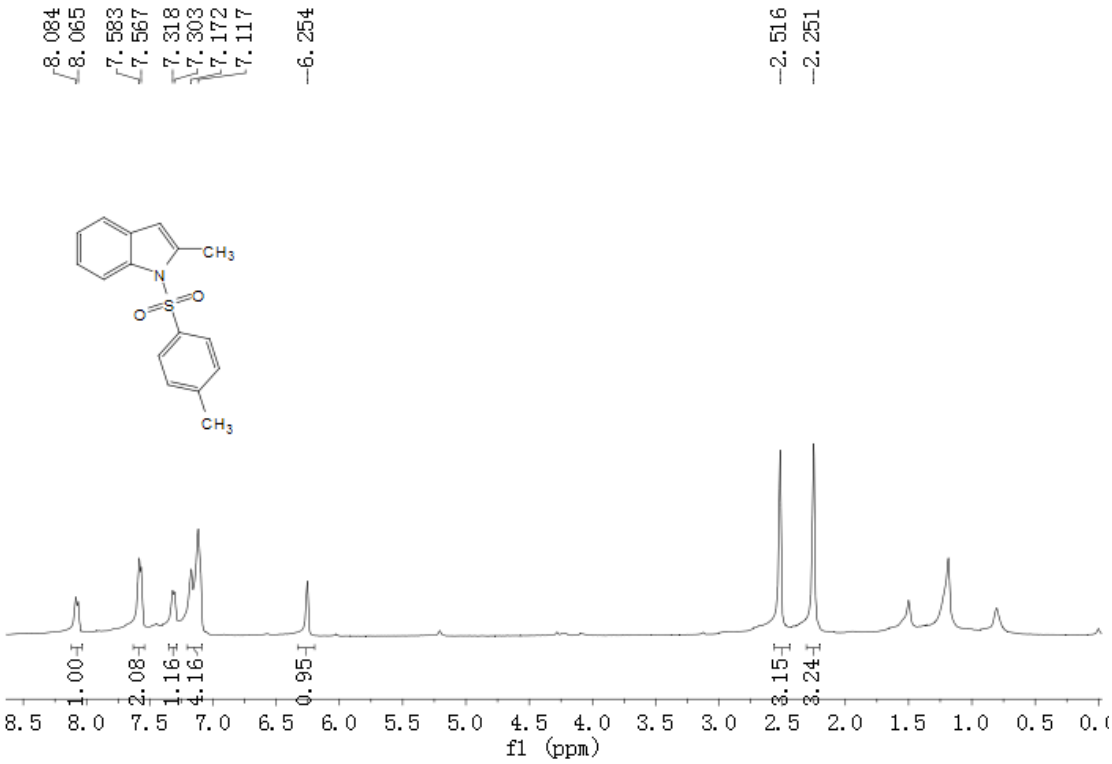

161.840
159.411
132.123
129.950
127.097
118.387
118.300
116.473
115.273
115.038
112.704
112.462
77.407
77.088
76.770
58.436
33.831
25.454
21.569
CH3
O
S
O
N
N
F
170
150
130
110
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

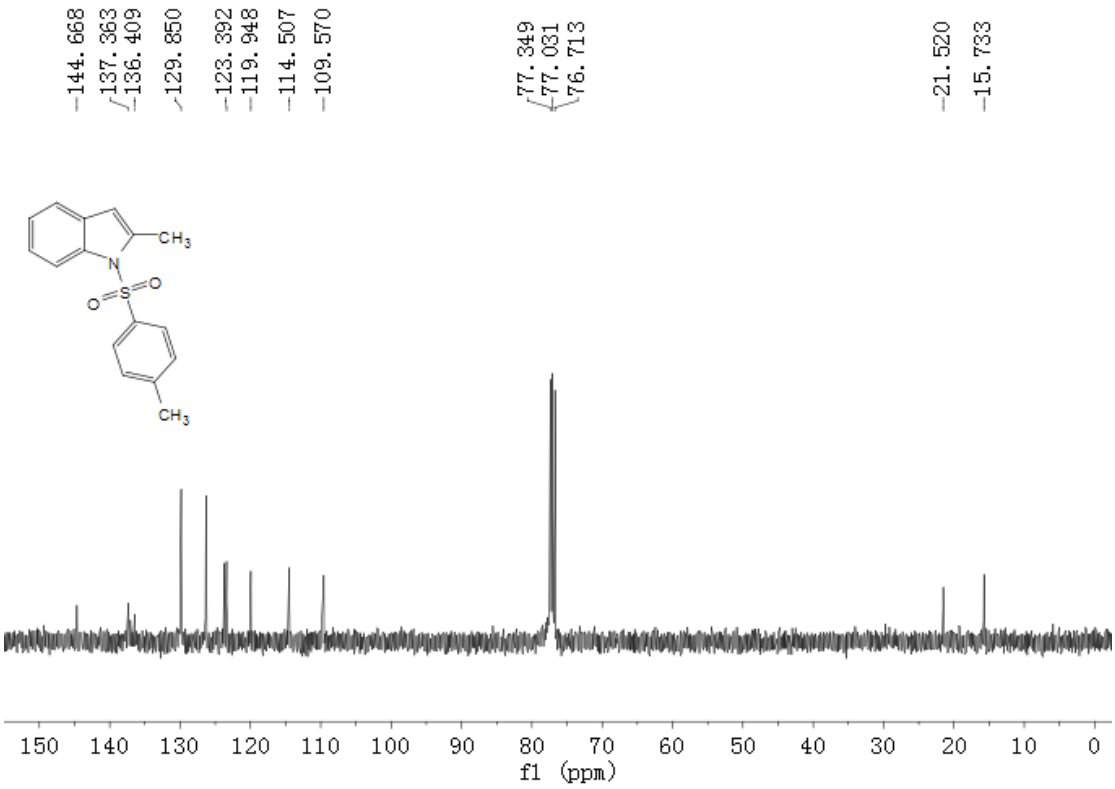
2-(1-((4-(trifluoromethyl)phenyl)sulfonyl)indolin-2-yl)acetonitrile (4e)



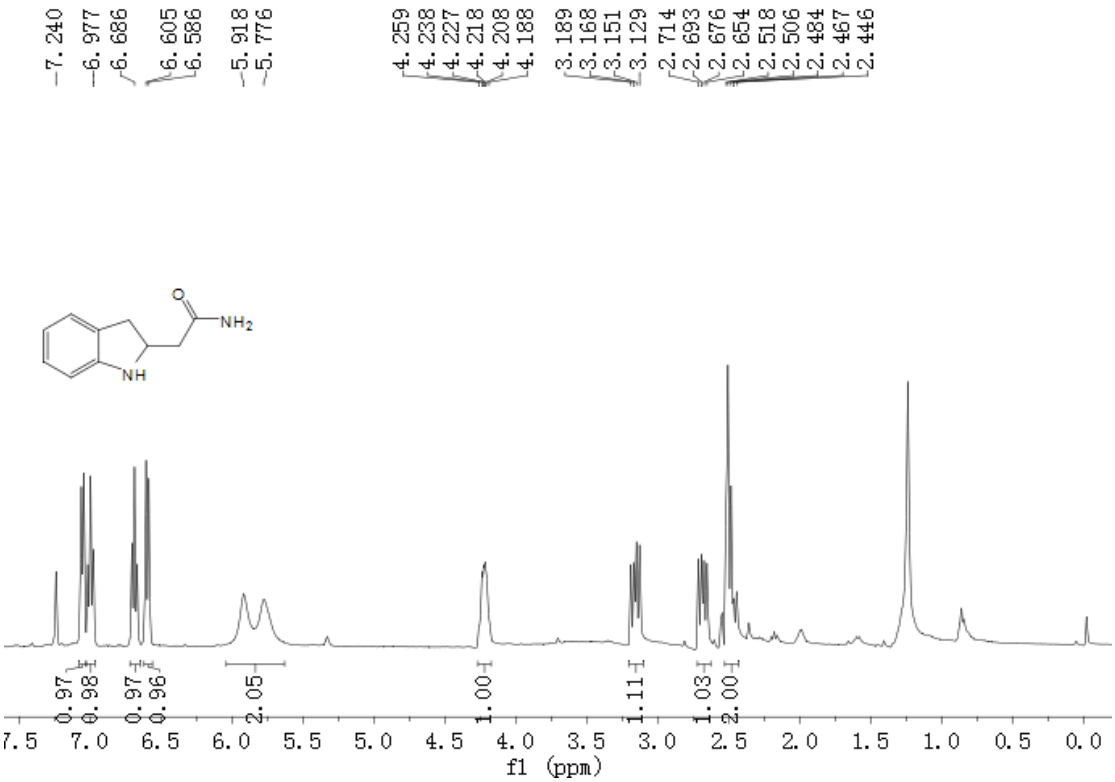


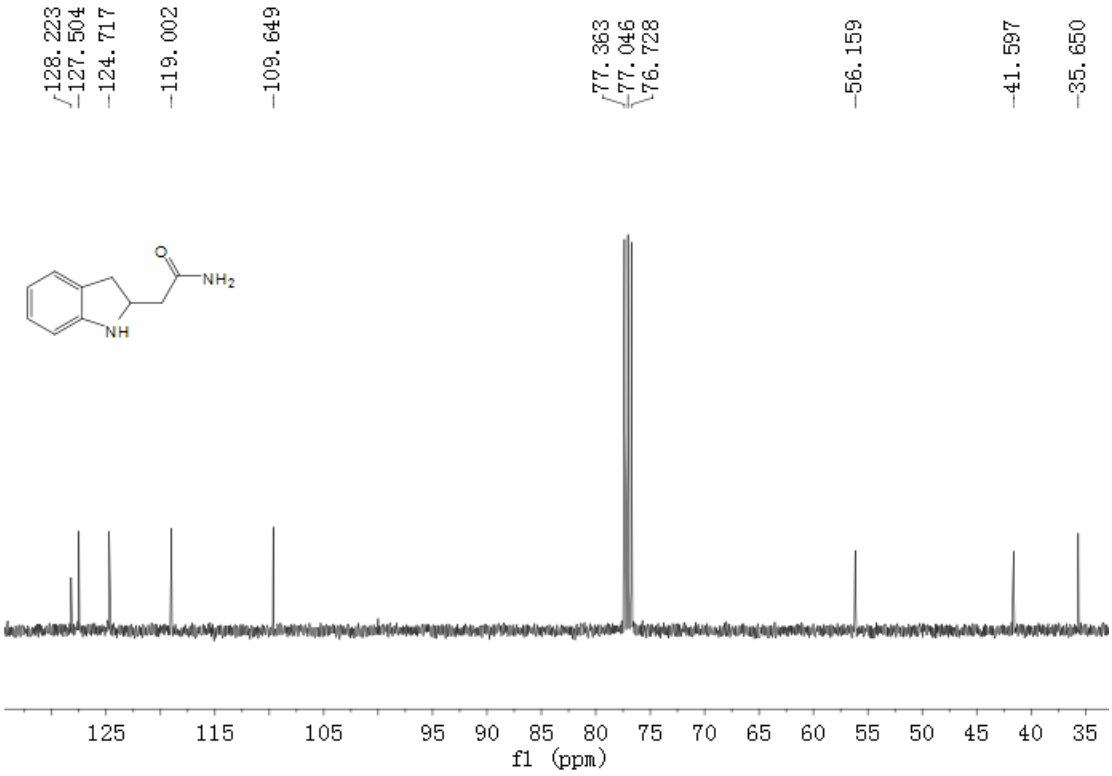
2-methyl-1-tosyl-1H-indole (5)



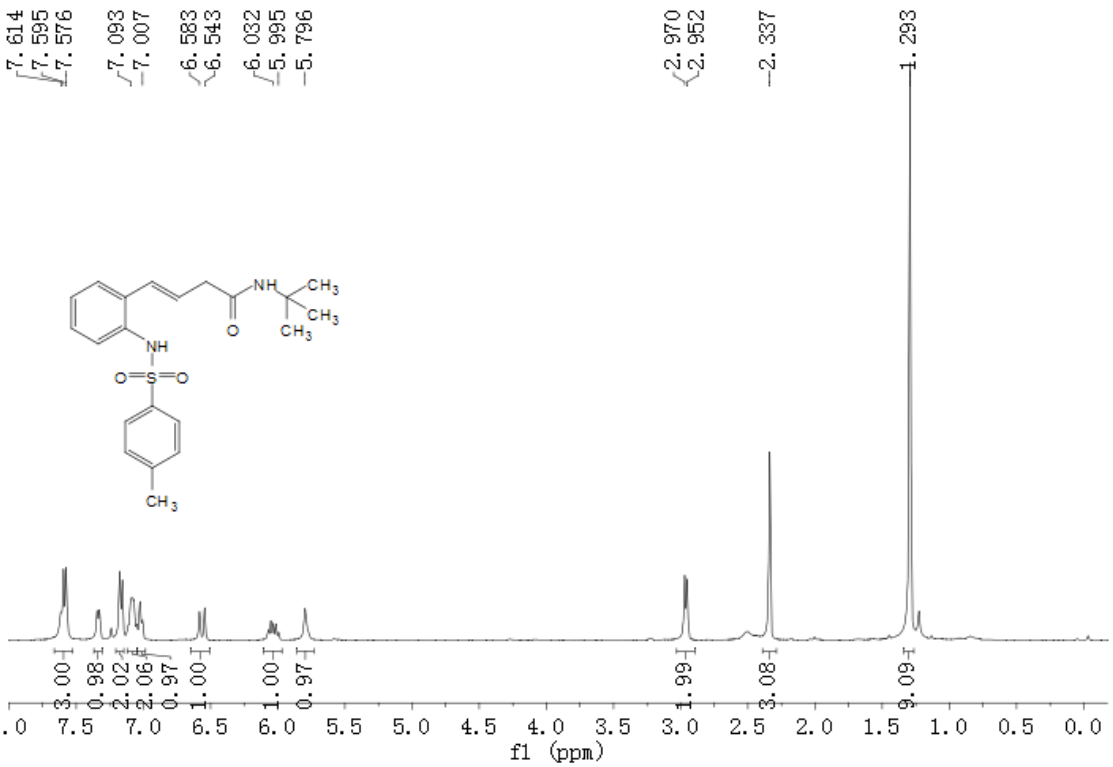


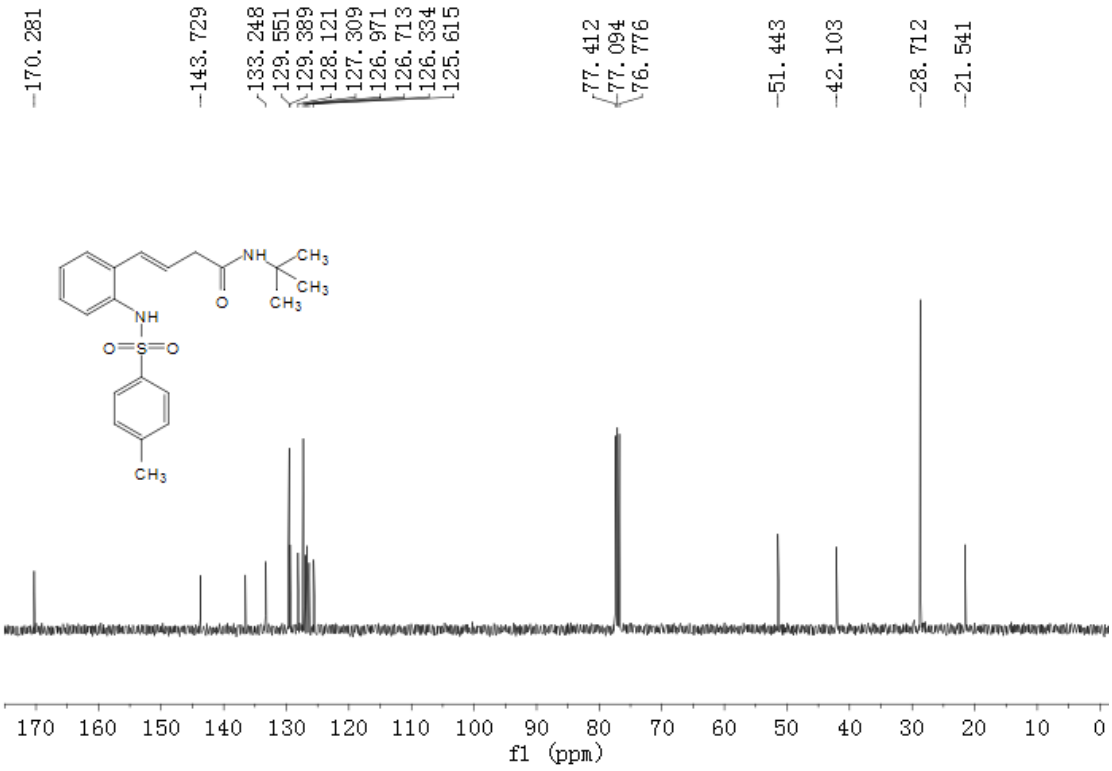
2-(indolin-2-yl)acetamide (6)



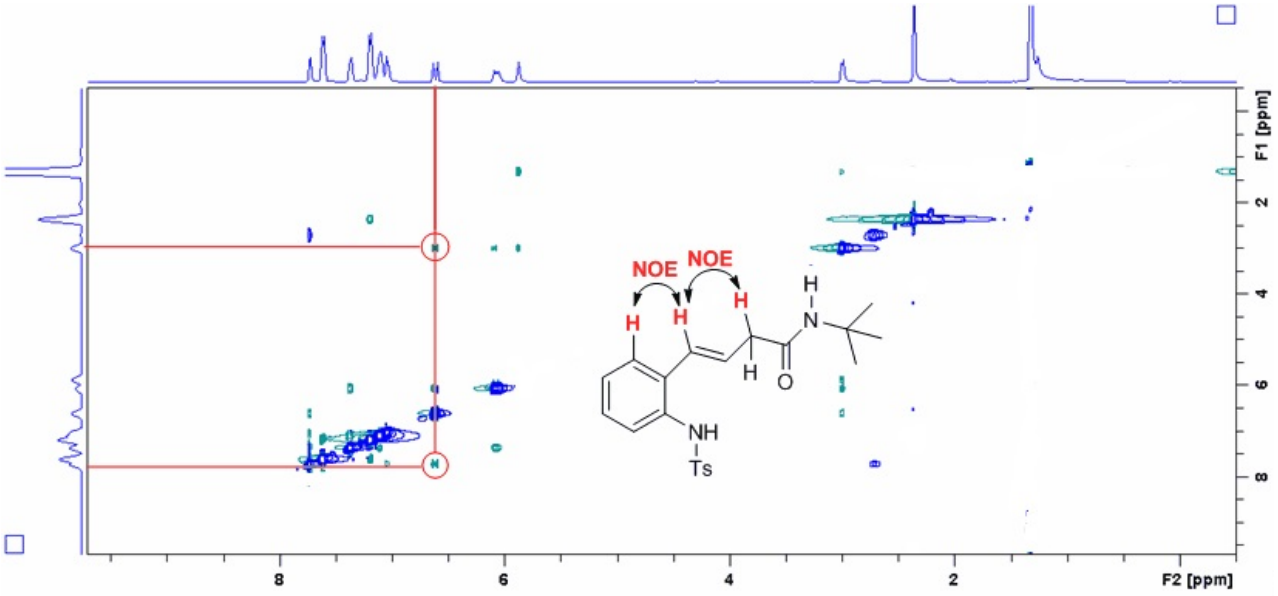


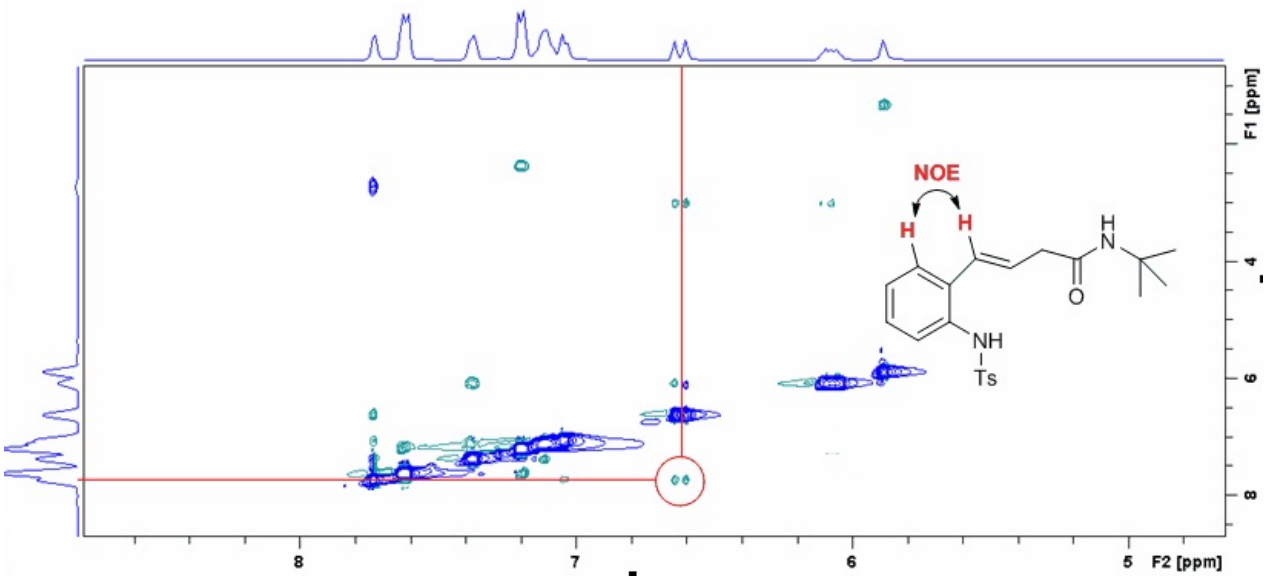
(E)-*N*-(tert-butyl)-4-(2-(4-methylphenylsulfonamido)phenyl)but-3-enamide (7)





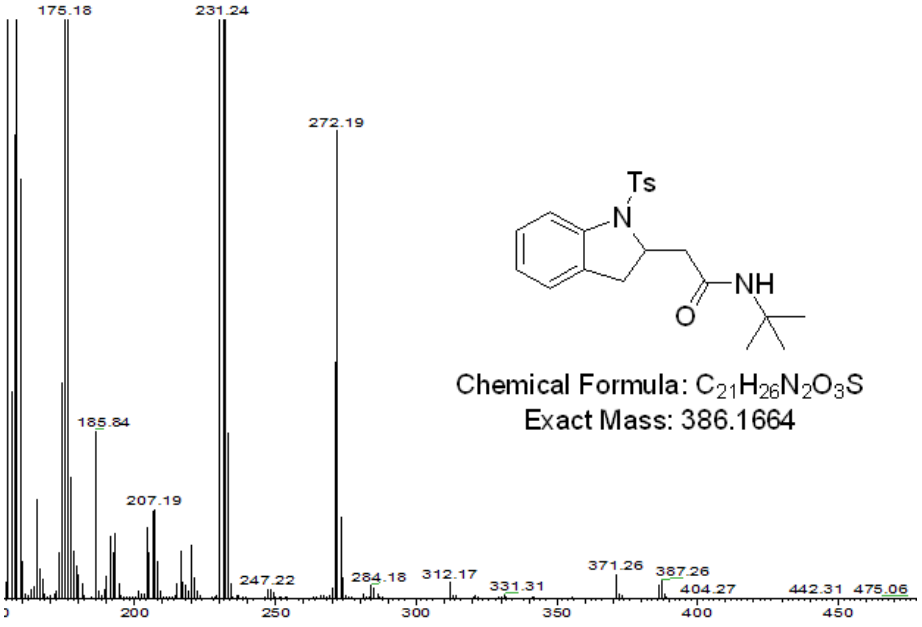
NOE Spectra for Compound (E)-*N*-(tert-butyl)-4-(2-(4-methylphenylsulfonamido)phenyl)but-3-enamide (7)





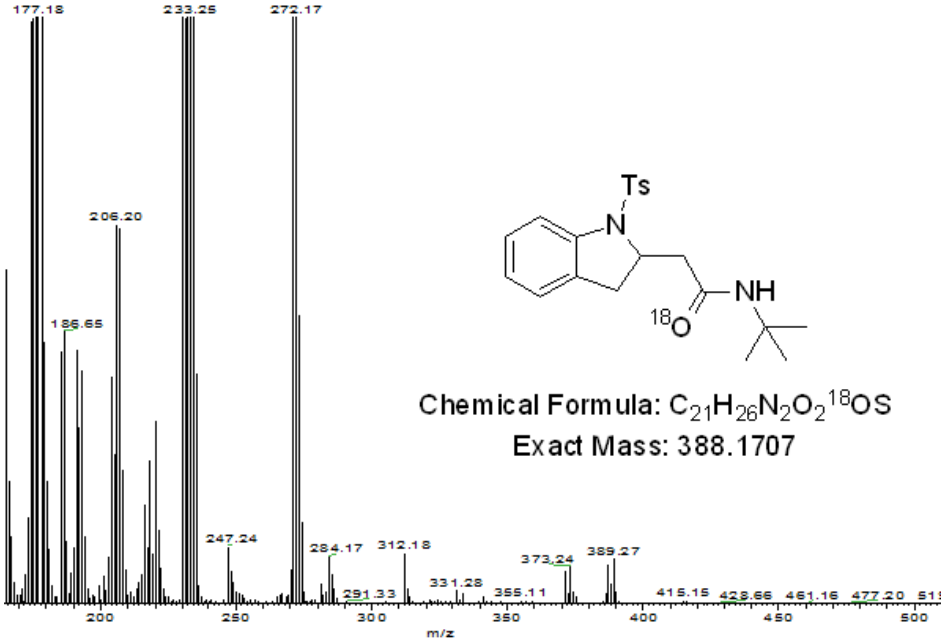
MS Spectra for Compounds 3a and 3a-^{18}O

MS Spectra for Compounds 3a:



Chemical Formula: $C_{21}H_{26}N_2O_3S$
Exact Mass: 386.1664

MS Spectra for Compounds 3a-^{18}O:


177.18
233.25
272.17
206.20
186.65
247.24
284.17
312.18
373.24
389.27
331.28
291.33
355.11
415.15
428.66
461.16
477.20
200
250
300
350
400
450
500
m/z
Ts
N
NH
18O
Chemical Formula: C21H26N2O218OS
Exact Mass: 388.1707