

Annulation of Enaminones with Quinonediimides/ Quinoneimides for Selective Synthesis of Indoles and 2- Aminobenzofurans

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Table S1 Optimization on the synthesis of benzofuan

entry	catalyst	solvent	<i>t</i> (°C)	time (h)	yield (%) ^b
1	-	1,4-dioxane	50	8	0
2	Cu(OTf) ₂	1,4-dioxane	50	8	17
3	TFA	1,4-dioxane	50	8	0
4	Fe(OTf) ₃	1,4-dioxane	50	8	34
5	Fe(OTf) ₃	CH ₃ CN	50	8	39
6	Fe(OTf) ₃	DMF	50	8	34
7	Fe(OTf) ₃	DMSO	50	8	37
8	Fe(OTf) ₃	CH ₃ CN	30	8	43
9	Fe(OTf) ₃	CH ₃ CN	25	8	46
10	Fe(OTf) ₃	CH ₃ CN	0	8	51
11	Fe(OTf) ₃	CH ₃ CN	0	5	54
12	Fe(OTf) ₃	CH ₃ CN	0	3	57
13 ^c	Fe(OTf) ₃	CH ₃ CN	0	3	61
14 ^{c,d}	Fe(OTf) ₃	CH ₃ CN	0	3	73

^aGeneral conditions: **1a** (0.2 mmol), **4** (0.24 mmol), catalyst (0.04 mmol, 20 mol %), solvent (2 mL), stirred in a sealed tube for 8 h. ^bYield of isolated product. ^cWith 0.3 mmol of **4**. ^dCatalyst (0.05 mmol, 25 mol %)

General experimental information

All experiments were carried out under air atmosphere. All enaminones¹ **1** and quinonediimides/quinoneimides² **2** and **4** were synthesized following literature processes. Other chemicals and solvents used in the experiments were obtained from commercial sources and used directly without further treatment. The ¹H and ¹³C NMR spectra were recorded in 400 MHz apparatus and the frequencies for ¹H NMR and ¹³C NMR test are 400 MHz and 100 MHz, respectively. The chemical shifts were reported in ppm with TMS as internal standard. Melting points were tested in X-4A instrument without correcting temperature. The HRMS were obtained under ESI model in a mass spectrometer with TOF analyzer.

General procedure for the synthesis of 3

In a 10 mL sealed tube were added enaminone **1** (0.2 mmol, 1 equiv), quinonediimide **2** (0.24 mmol, 1.2 equiv), Zn(OTf)₂ (0.04 mmol, 20 mol %) and 1,4-dioxane (2 mL, 0.1 M). After sealing the tube with Teflon cap, the mixture was stirred at 50 °C with oil bath heating for 24 h. After being cooled down to room temperature, the mixture was transferred into the round bottom flask, and solvent was removed at reduced pressure. The residue obtained therein was subjected to flash silica gel column chromatography to provide pure products with the elution of mixed petroleum ether and ethyl acetate.

Procedure for the 1 mmol scale reaction for the synthesis of 3a

The In a 50 mL sealed tube were added enaminone **1** (1.0 mmol, 1 equiv), quinonediimide **2** (1.2mmol, 1.2 equiv), Zn(OTf)₂ (0.2 mmol, 20 mol %) and 1,4-dioxane (10 mL, 0.1 M). After sealing the tube with Teflon cap, the mixture was stirred at 50 °C with oil bath heating for 24 h. After being cooled down to room temperature, the mixture was transferred into a round bottom flask, and solvent was removed at reduced pressure. The residue obtained therein was subjected to flash silica gel column chromatography to provide pure product 3a (424 mg, 78% yield) with the elution of mixed petroleum ether and ethyl acetate (v/v = 2:1).

General procedure for the synthesis of 5

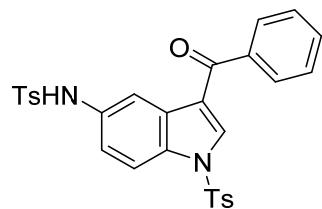
In a 10 mL sealed tube were added enaminone **1** (0.2 mmol, 1 equiv), quinoneimide **4** (0.3 mmol, 1.5 equiv), Fe(OTf)₃ (0.05 mmol, 25 mol %) and CH₃CN (2 mL, 0.1 M). After sealing the tube with Teflon cap, the mixture was stirred at 0 °C with ice bath for 3 h. Then the mixture was transferred into the round bottom flask, and solvent was removed at reduced pressure. The residue obtained therein was subjected to flash silica gel column chromatography to provide pure products with the elution of mixed petroleum ether and ethyl acetate.

Procedure for the 1 mmol scale reaction for the synthesis of 5a

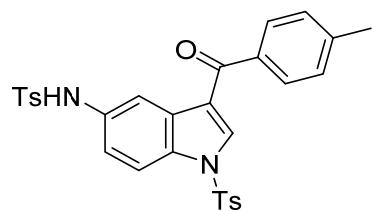
The In a 50 mL sealed tube were added enaminone **1** (1.0 mmol, 1 equiv), quinoneimide

4 (1.5 mmol, 1.5 equiv), Fe(OTf)₃ (0.25 mmol, 25 mol %) and CH₃CN (10 mL, 0.1 M). After sealing the tube with Teflon cap, the mixture was stirred at 0 °C with ice bath for 3 h. Then the mixture was transferred into a round bottom flask, and solvent was removed at reduced pressure. The residue obtained therein was subjected to flash silica gel column chromatography to provide pure product **3a** (295 mg, 68% yield) with the elution of mixed petroleum ether and ethyl acetate (v/v = 3:1).

Characterization data

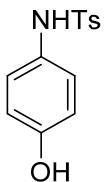


N-(3-Benzoyl-1-tosyl-1H-indol-5-yl)-4-methylbenzenesulfonamide (3a). Eluent: V_{PE}/V_{EA} = 2:1; white solid (92.5 mg, 85% yield); mp 105-106 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.98 (s, 1H), 7.90 (d, *J* = 2.3 Hz, 1H), 7.86 (d, *J* = 9.0 Hz, 1H), 7.81 (d, *J* = 6.9 Hz, 2H), 7.76 (d, *J* = 8.0 Hz, 2H), 7.61 (d, *J* = 8.2 Hz, 3H), 7.52 (s, 2H), 7.39 (s, 1H), 7.27 (s, 2H), 7.19 (s, 1H), 7.13 (d, *J* = 8.0 Hz, 2H), 2.36 (s, 3H), 2.31 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 190.8, 146.2, 143.8, 138.9, 136.2, 134.5, 134.3, 134.2, 132.5, 132.5, 130.3, 129.7, 129.6, 129.1, 129.0, 128.7, 127.3, 127.2, 126.5, 120.6, 120.0, 115.5, 113.9, 21.6, 21.5; HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₂₉H₂₄N₂O₅S₂ 545.1199; Found 545.1197.

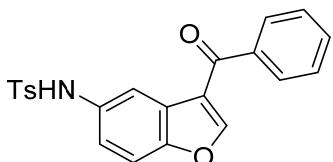


4-Methyl-N-(3-(4-methylbenzoyl)-1-tosyl-1H-indol-5-yl)benzenesulfonamide (3b). Eluent: V_{PE}/V_{EA} = 2:1; white solid (100.4 mg, 90% yield); mp 175-176 °C; ¹H NMR (400 MHz, CDCl₃) δ 7.98 (s, 1H), 7.93 (d, *J* = 2.2 Hz, 1H), 7.85 (d, *J* = 9.0 Hz, 1H), 7.75 (d, *J* = 8.0 Hz, 4H), 7.56 (d, *J* = 7.9 Hz, 3H), 7.41 (dd, *J* = 9.0, 2.2 Hz, 1H), 7.31 (d, *J* = 7.9 Hz, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.05 (d, *J* = 8.0 Hz, 2H), 2.44 (s, 3H), 2.33

Eluent: V_{PE}/V_{EA}=6:1; yellow liquid (27.79 mg, 21% yield); ¹H NMR (400 MHz, CDCl₃) δ 7.54 (d, *J* = 8.0 Hz, 2H), 7.42 (d, *J* = 7.7 Hz, 4H), 7.31 (t, *J* = 7.5 Hz, 4H), 7.24 (d, *J* = 4.9 Hz, 2H), 7.16 (d, *J* = 8.0 Hz, 2H), 6.95 (s, 1H), 6.75 (s, 1H), 6.72 (s, 1H), 6.53 (s, 1H), 3.83 (s, 2H), 2.36 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 157.3, 145.0, 143.6, 129.5, 129.1, 128.3, 127.5, 127.5, 127.4, 125.9, 124.7, 121.7, 109.6, 93.2, 44.1, 21.5.



N-(4-Hydroxyphenyl)-4-methylbenzenesulfonamide (7).⁴ Eluent: V_{PE}/V_{EA}=5:1; white solid (15.87 mg, 30 % yield); mp 151-152°C; ¹H NMR (400 MHz, DMSO-*d*₆) δ 9.67 (s, 1H), 9.31 (s, 1H), 7.55 (d, *J* = 7.9 Hz, 2H), 7.30 (d, *J* = 7.9 Hz, 2H), 6.85 (d, *J* = 8.3 Hz, 2H), 6.61 (d, *J* = 8.3 Hz, 2H), 2.32 (s, 3H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 155.2, 143.3, 137.2, 129.9, 129.1, 127.2, 124.4, 116.0, 21.4.

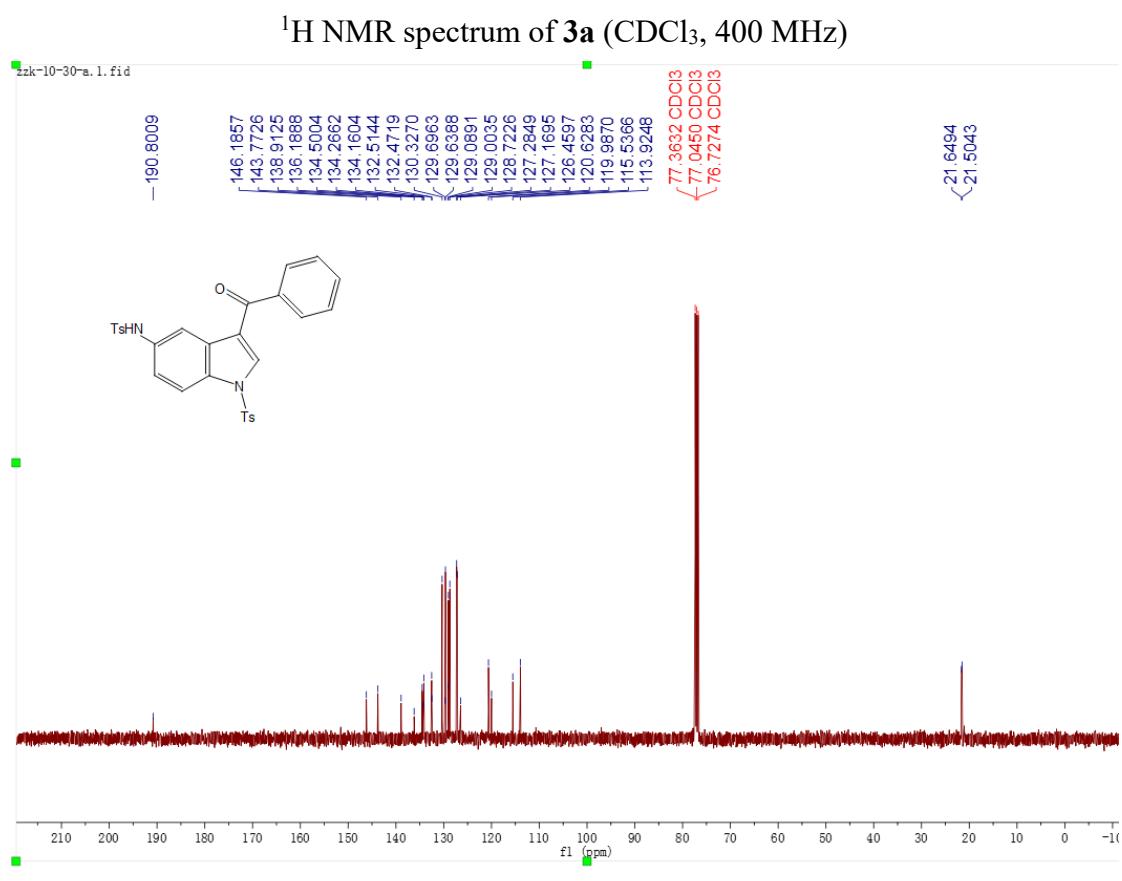
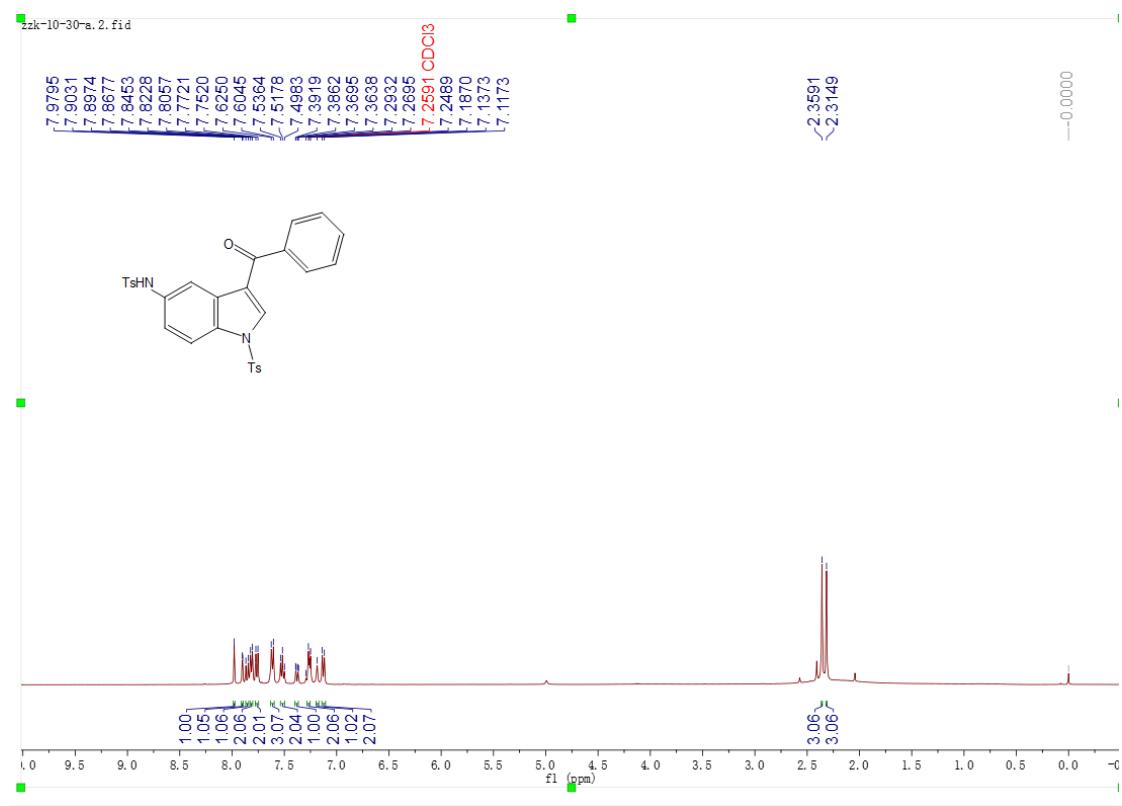


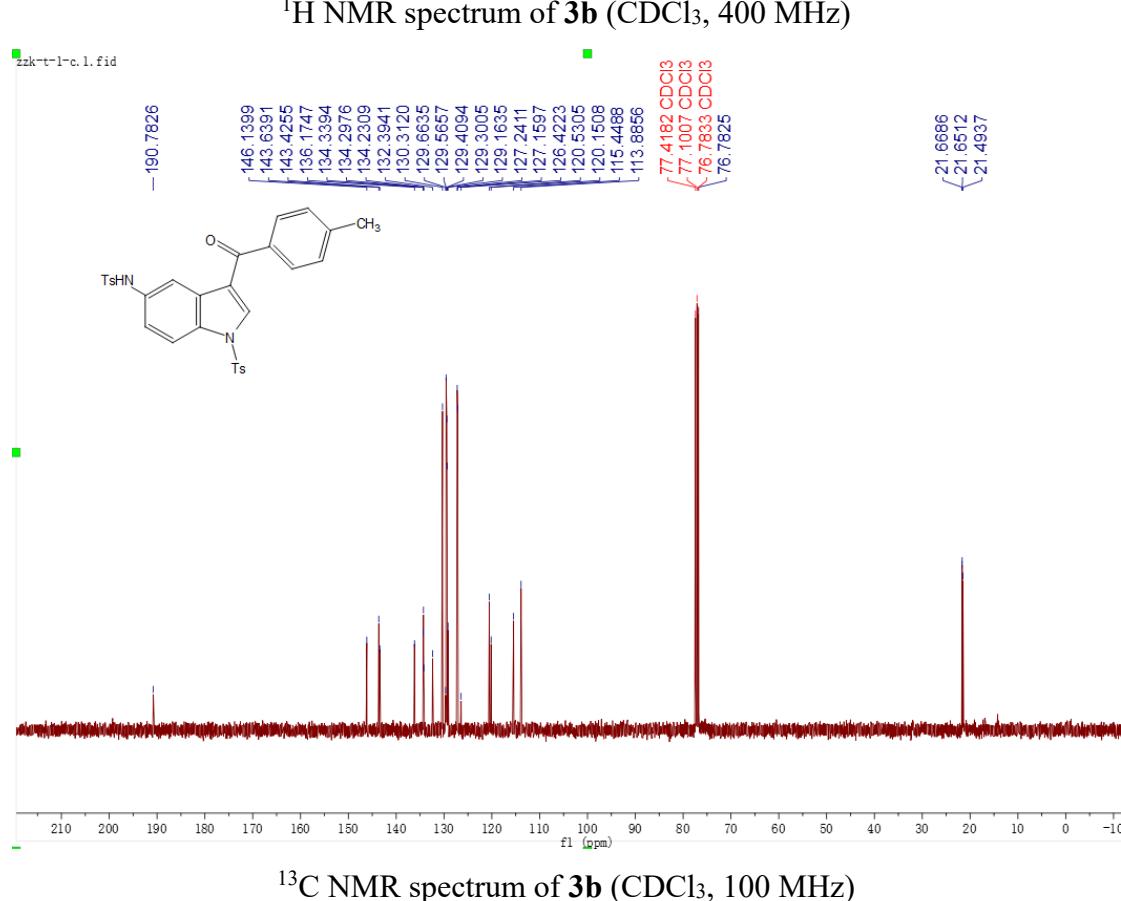
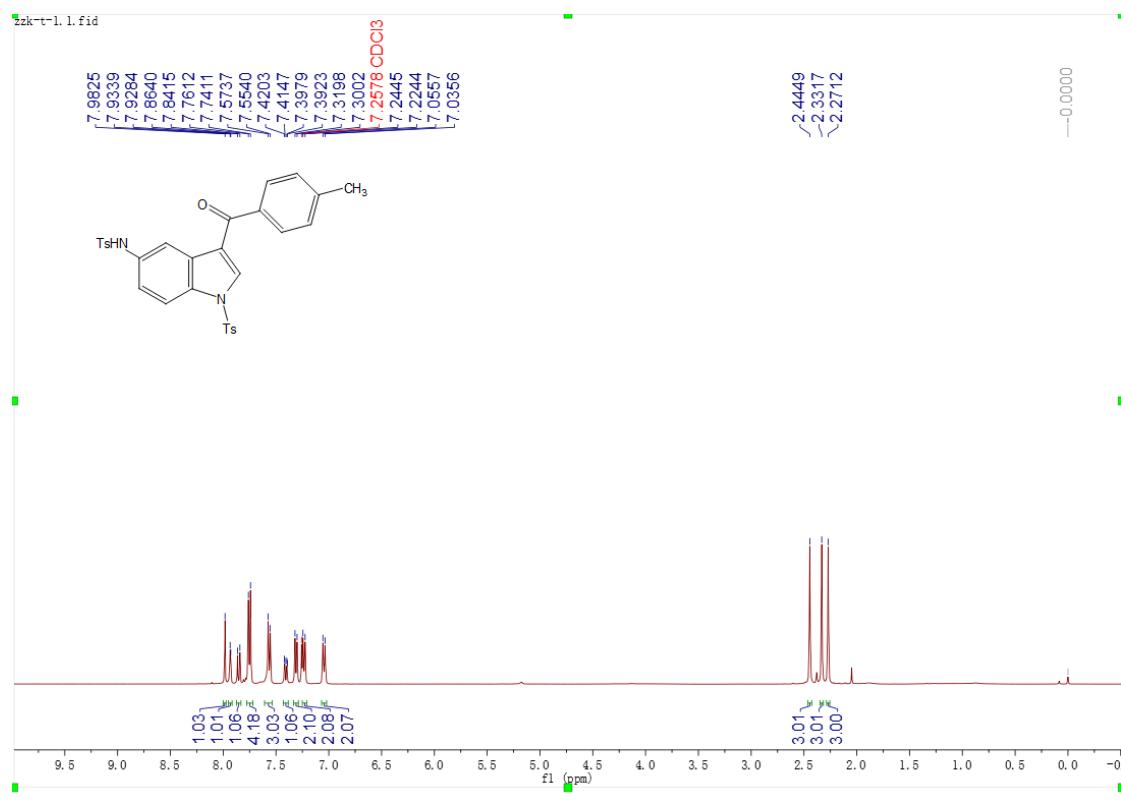
N-(3-Benzoylbenzofuran-5-yl)-4-methylbenzenesulfonamide (8). Eluent: V_{PE}/V_{EA}=4:1; white solid (41.45 mg, 53% yield); mp 190-191°C; ¹H NMR (400 MHz, CDCl₃) δ 8.05 (s, 1H), 7.90 – 7.83 (m, 3H), 7.61 (dd, *J* = 23.7, 9.7 Hz, 4H), 7.51 (d, *J* = 7.9 Hz, 2H), 7.43 (s, 1H), 7.40 (d, *J* = 2.2 Hz, 1H), 7.14 (d, *J* = 8.1 Hz, 2H), 2.31 (s, 3H); ¹³C NMR (100 MHz, CDCl₃) δ 190.3, 153.3, 143.7, 138.9, 136.1, 133.8, 132.7, 129.6, 128.9, 128.7, 127.3, 125.8, 121.2, 121.1, 116.3, 112.1, 21.5. HRMS (ESI-TOF) m/z: [M + H]⁺ Calcd for C₂₂H₁₈NO₄S 392.0951; Found 392.0951.

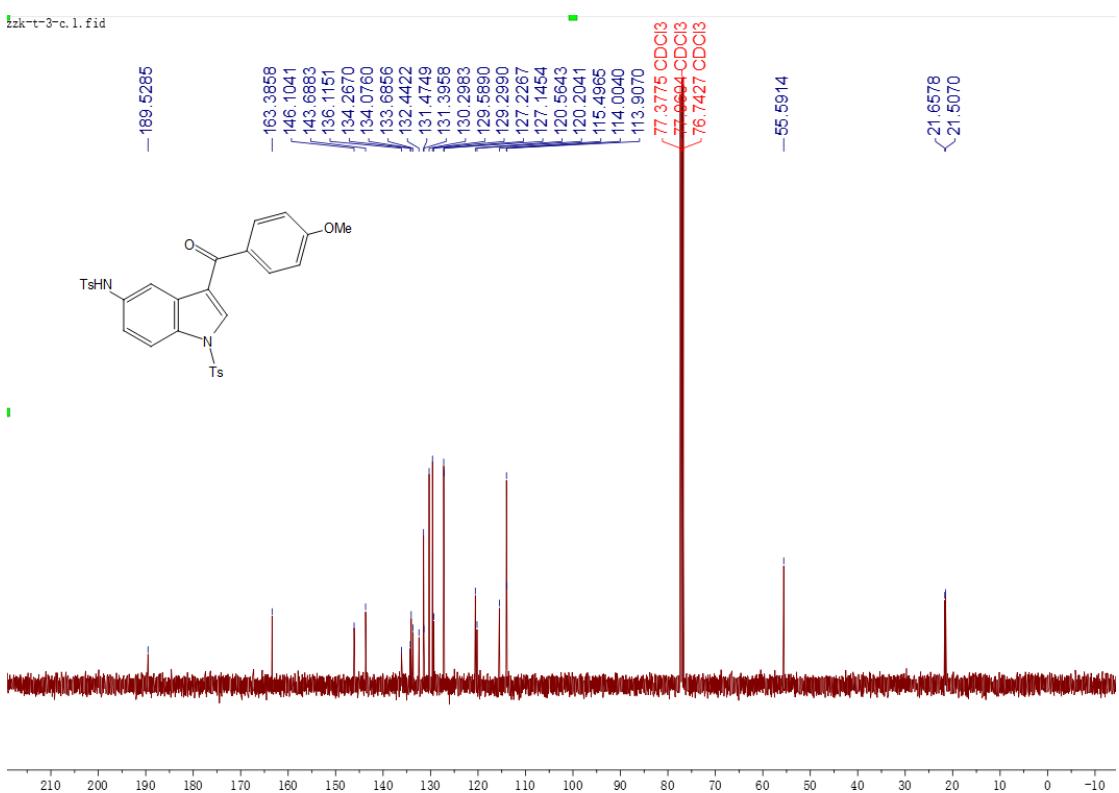
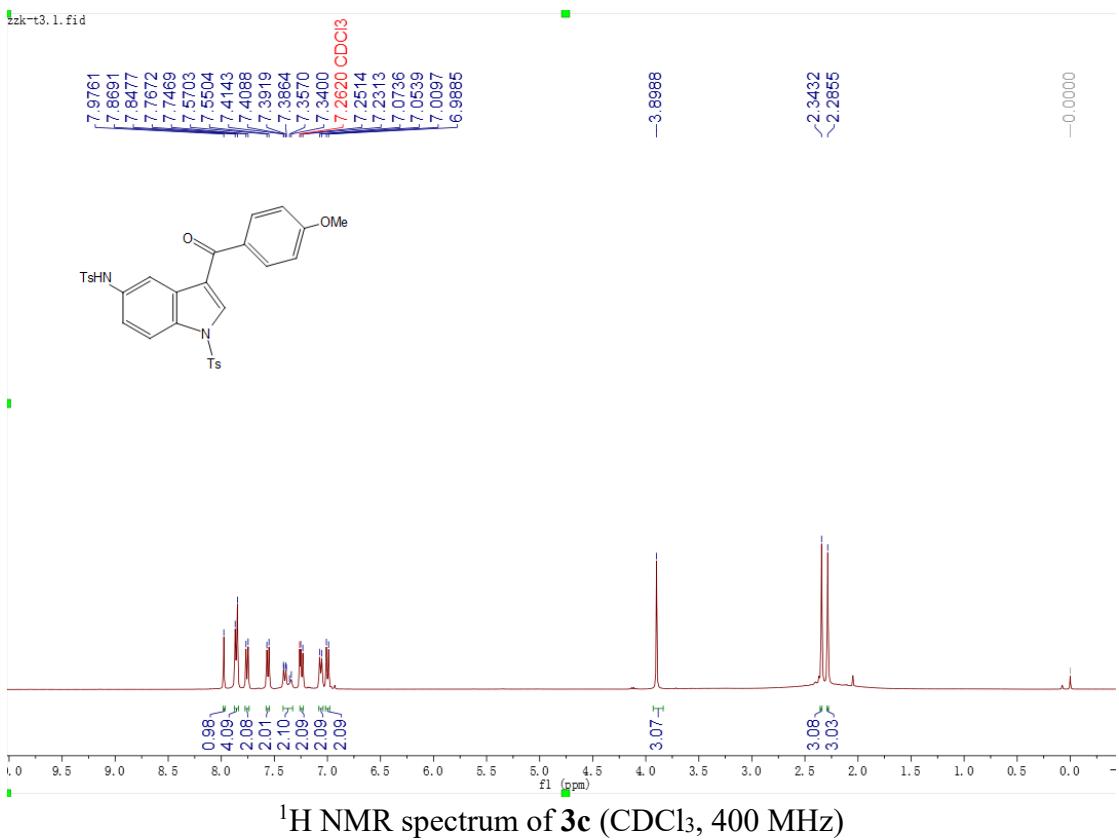
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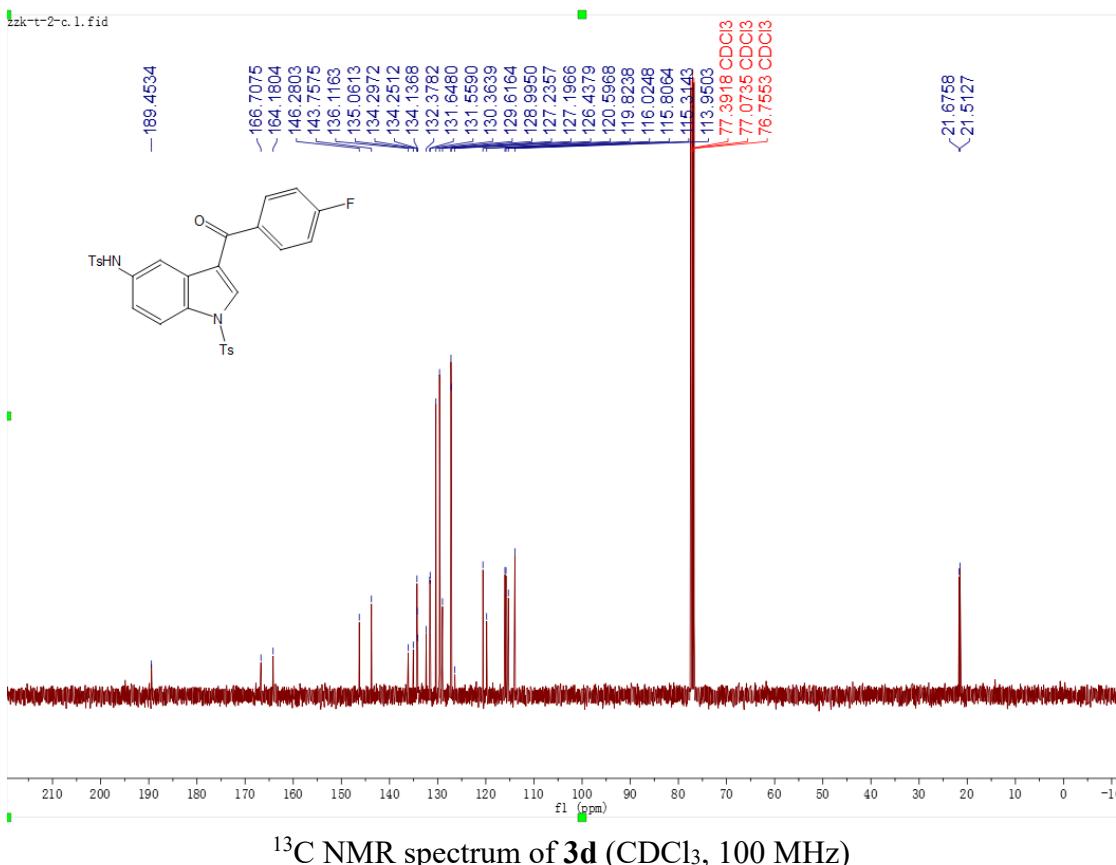
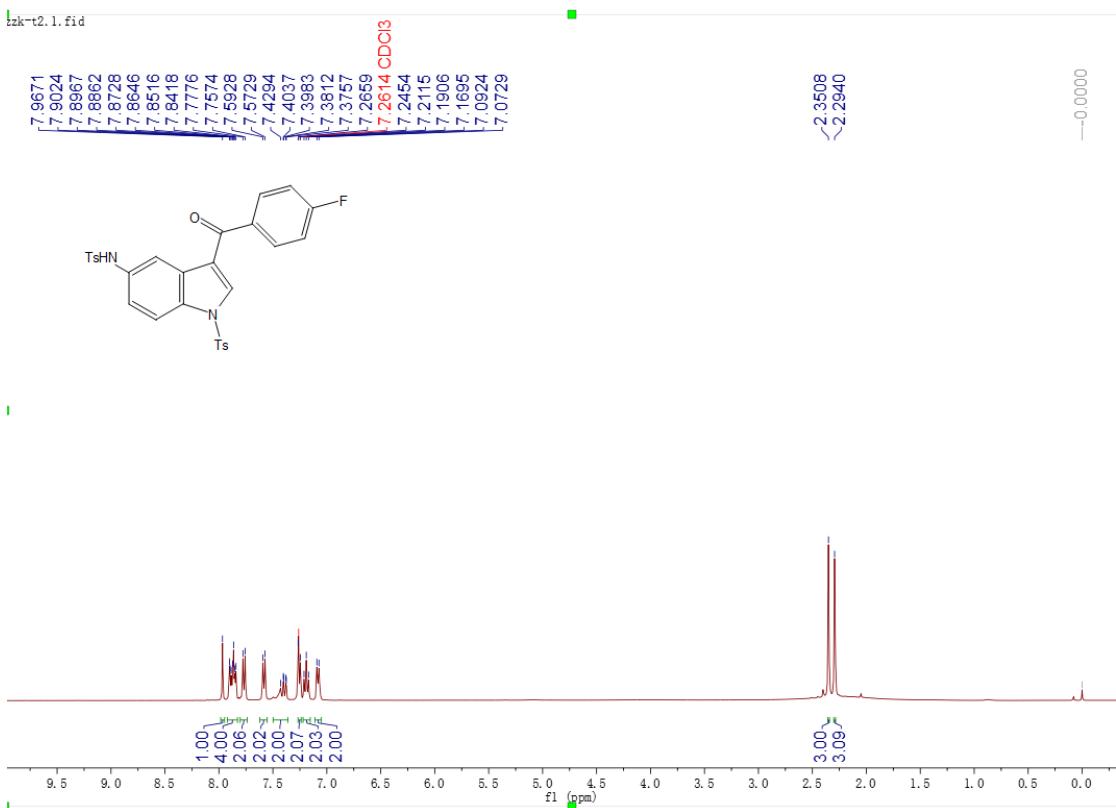
1. (a) Guo, H.; Tian, L.; Liu, Y.; Wan, J.-P., DMSO as a C1 Source for [2 + 2 + 1] Pyrazole Ring Construction via Metal-Free Annulation with Enaminones and Hydrazines. *Org. Lett.* **2022**, *24*, 228-233; (b) Ying, J.; Liu, T.; Liu, Y.; Wan, J.-P., Base-Promoted Annulative Difluoromethylenation of Enaminones with BrCF₂CO₂Et toward 2,2-Difluorinated 2,3-Dihydrofurans. *Org. Lett.* **2022**, *24*, 2404-2408.
2. (a) Liao, L.; Shu, C.; Zhang, M.; Liao, Y.; Hu, X.; Zhang, Y.; Wu, Z.; Yuan, W.; Zhang, X., Highly Enantioselective [3+2] Coupling of Indoles with Quinone Monoimines Promoted by a Chiral Phosphoric Acid. *Angew. Chem. Int. Ed.* **2014**, *53*, 10471-10475; (b) Ma, W.-Y.; Gelis, C.; Bouchet, D.; Retailleau, P.; Moreau, X.; Neuville, L.; Masson, G., Chiral Phosphoric Acid-Catalyzed Enantioselective Construction of 2,3-Disubstituted Indolines. *Org. Lett.* **2021**, *23*, 442-448.
3. Fan, R.; Li, W.; Ye, Y.; Wang, L. One-Pot Oxidative Heteroannulations of *N*-Sulfonylanilines with Styrenes for the Construction of 5-Aminocoumaran Derivatives. *Adv. Synth. Catal.* **2008**, *350*, 1531-1536.
4. Deng, X.; Mani, N. S. A facile, environmentaly benign sulfonamide synthesis in water. *Green Chem.* **2006**, *8*, 835-838.

The ^1H and ^{13}C NMR spectra



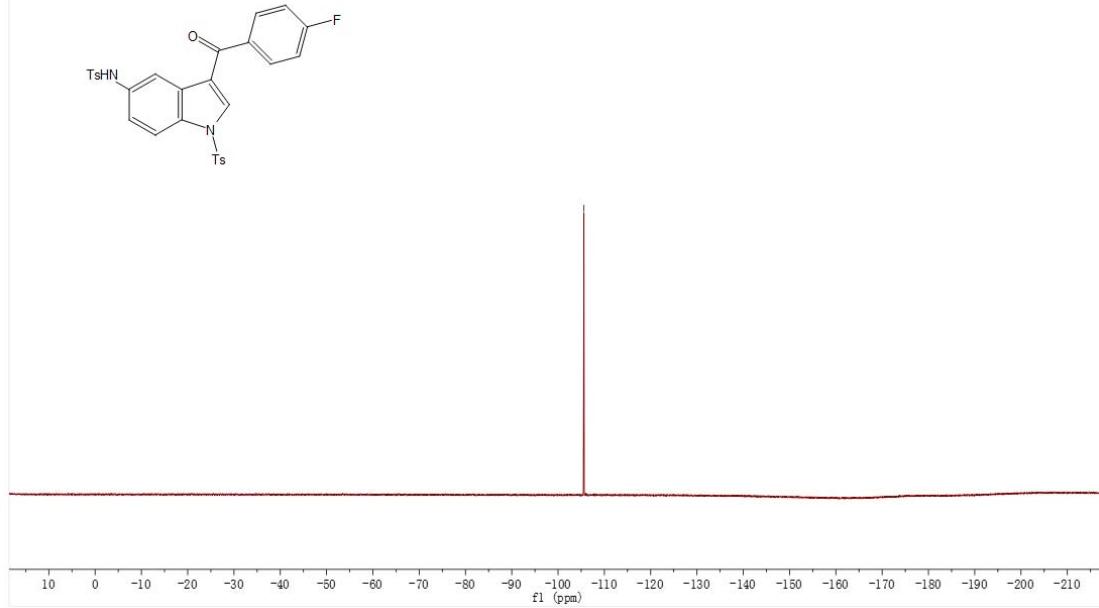






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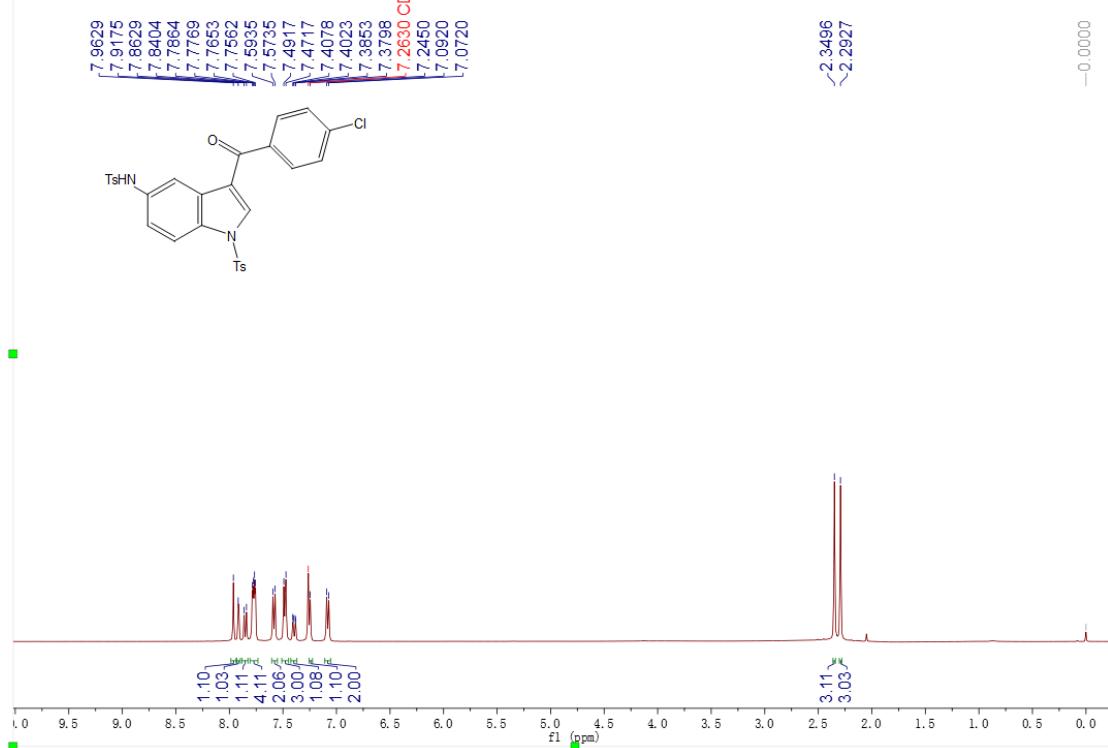
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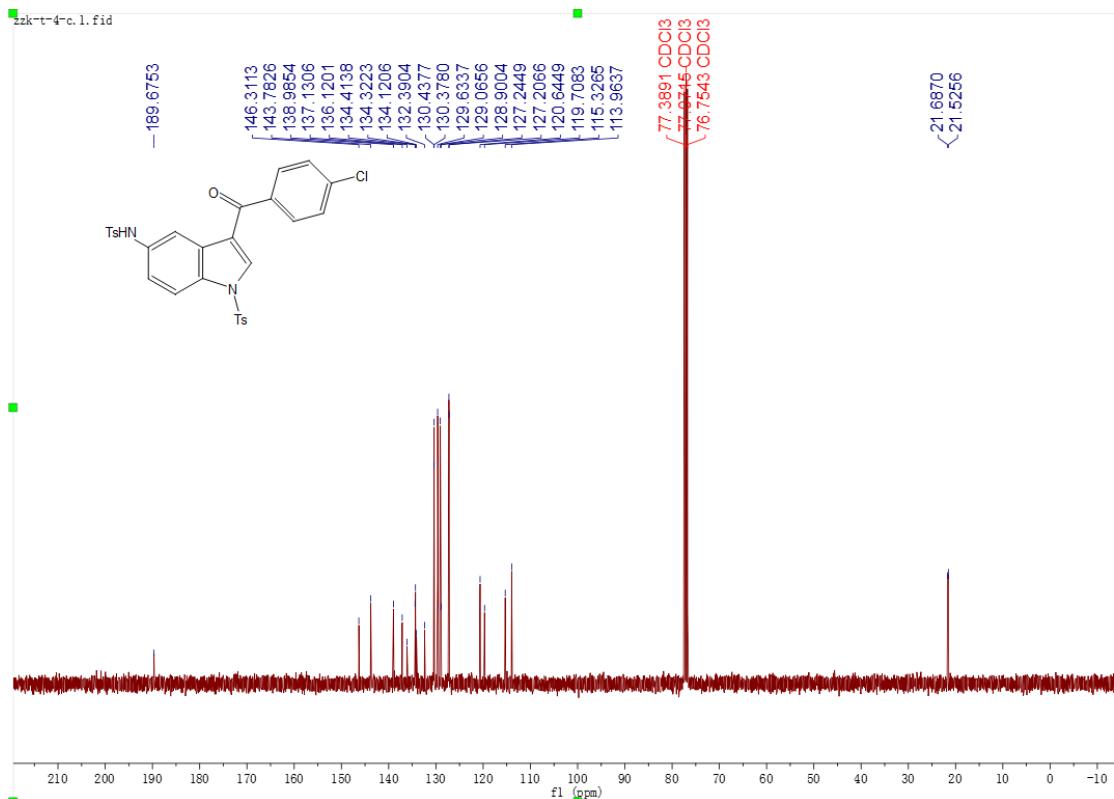
¹⁹F NMR spectrum of **3d** (CDCl_3 , 376 MHz)

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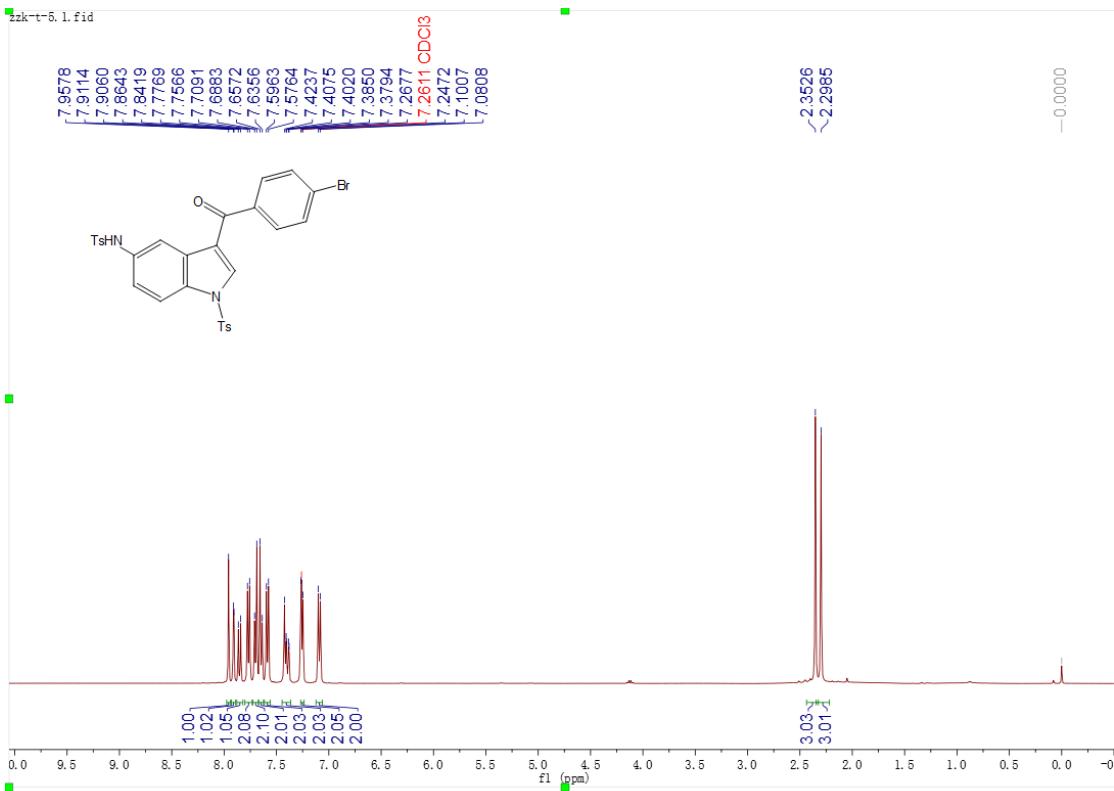
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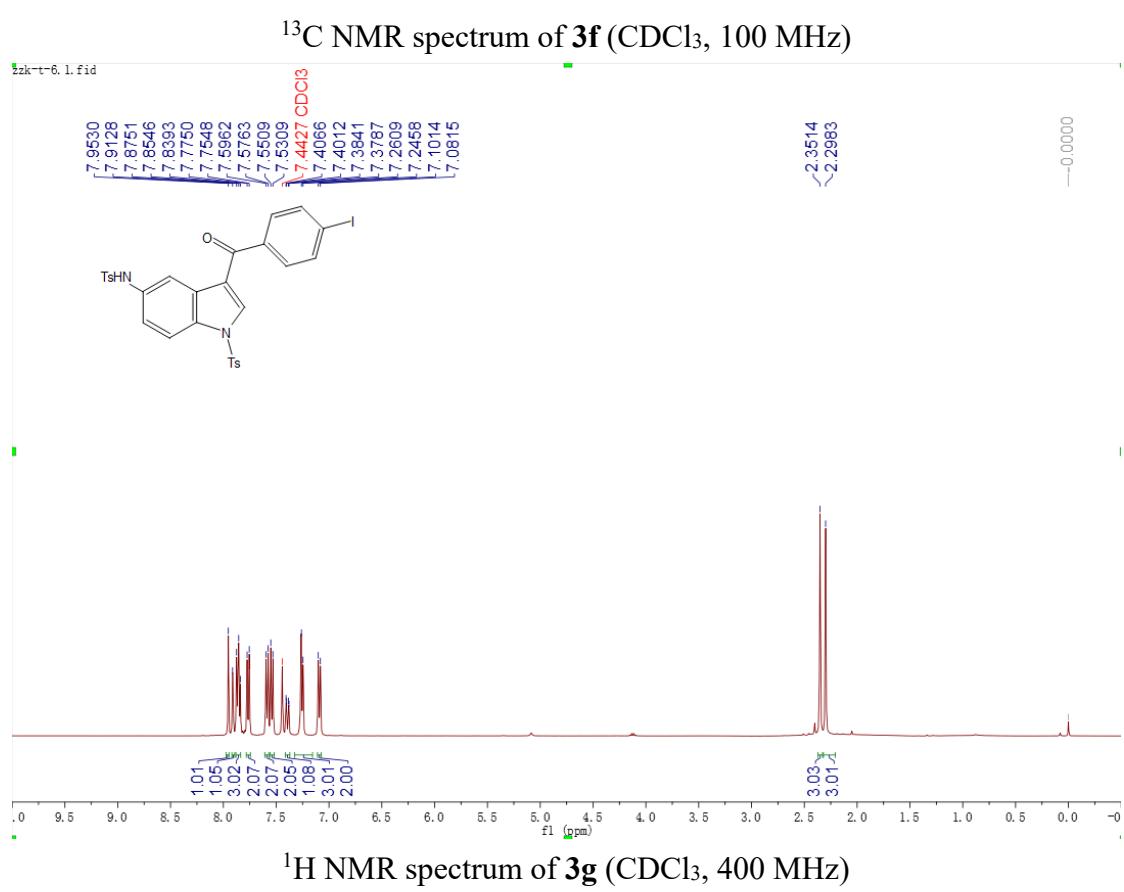
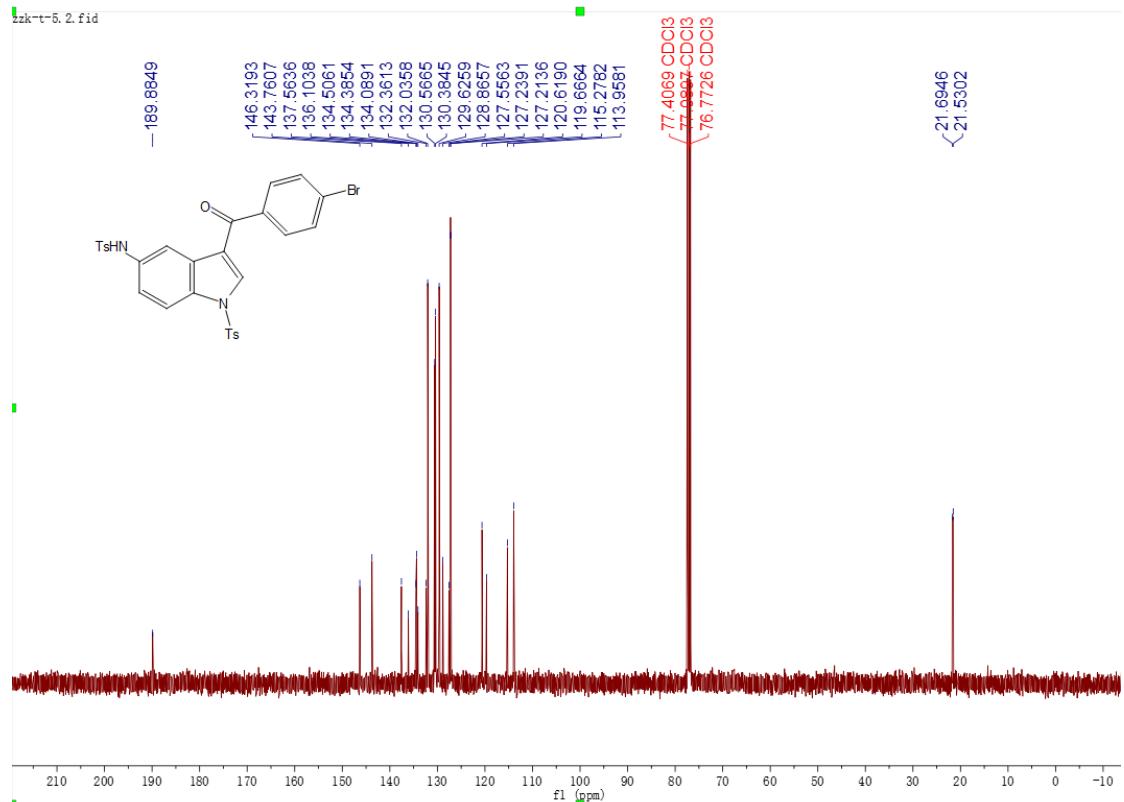
¹H NMR spectrum of **3e** (CDCl_3 , 400 MHz)

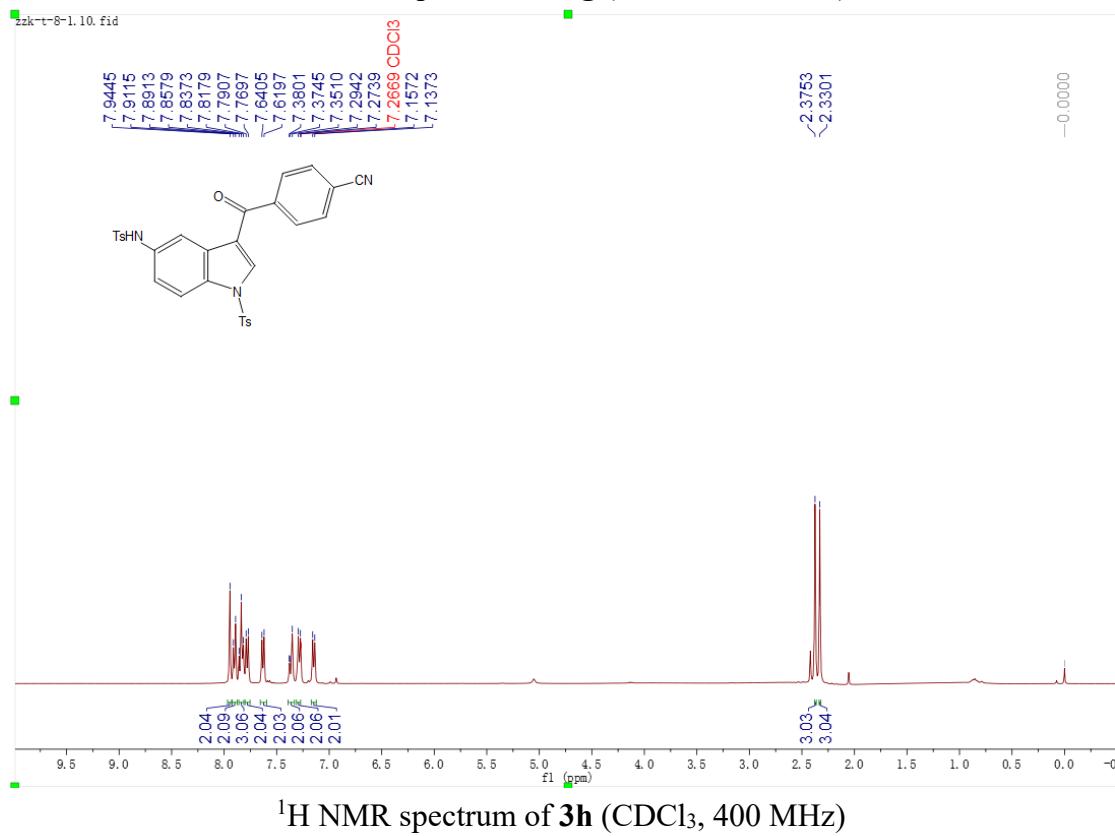
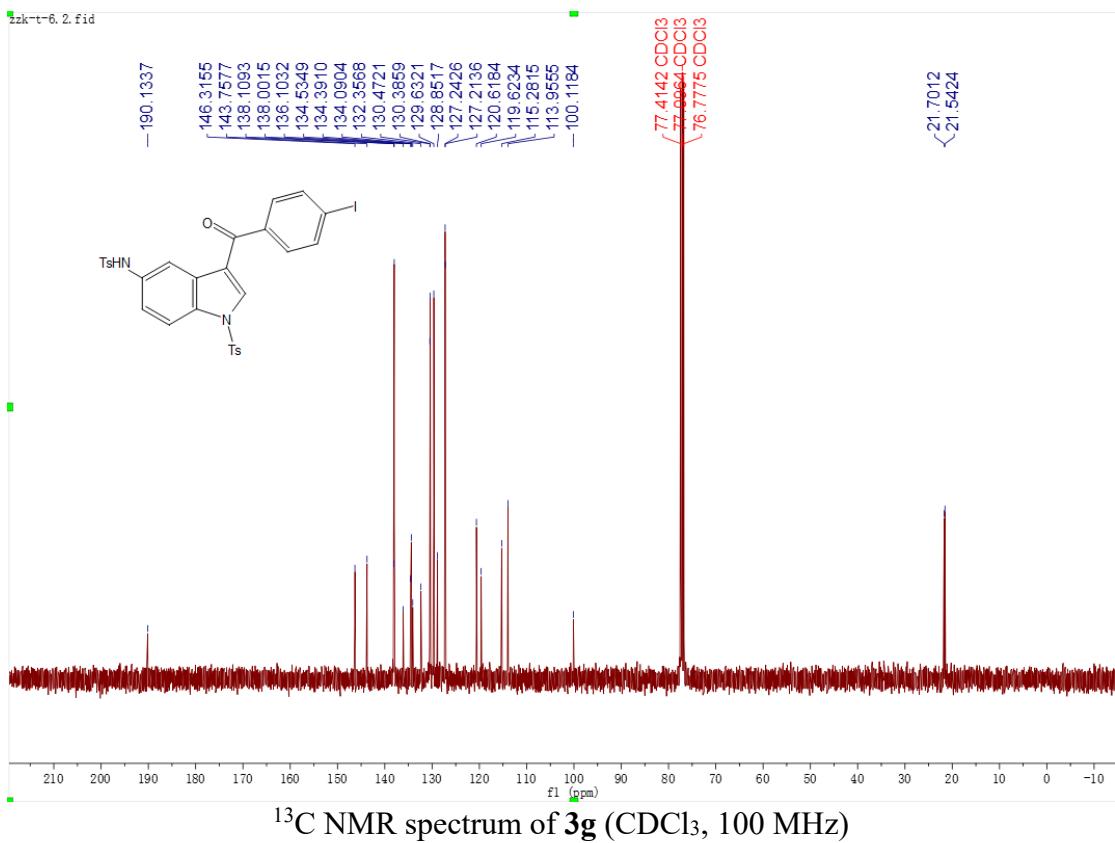


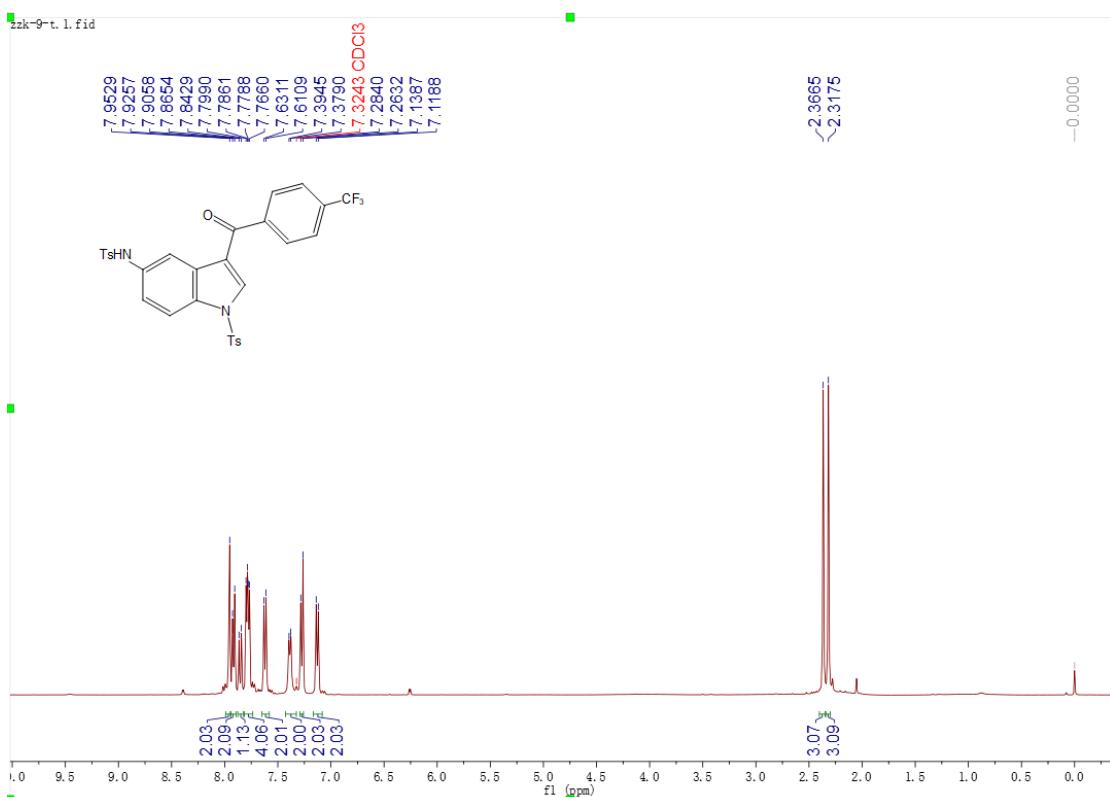
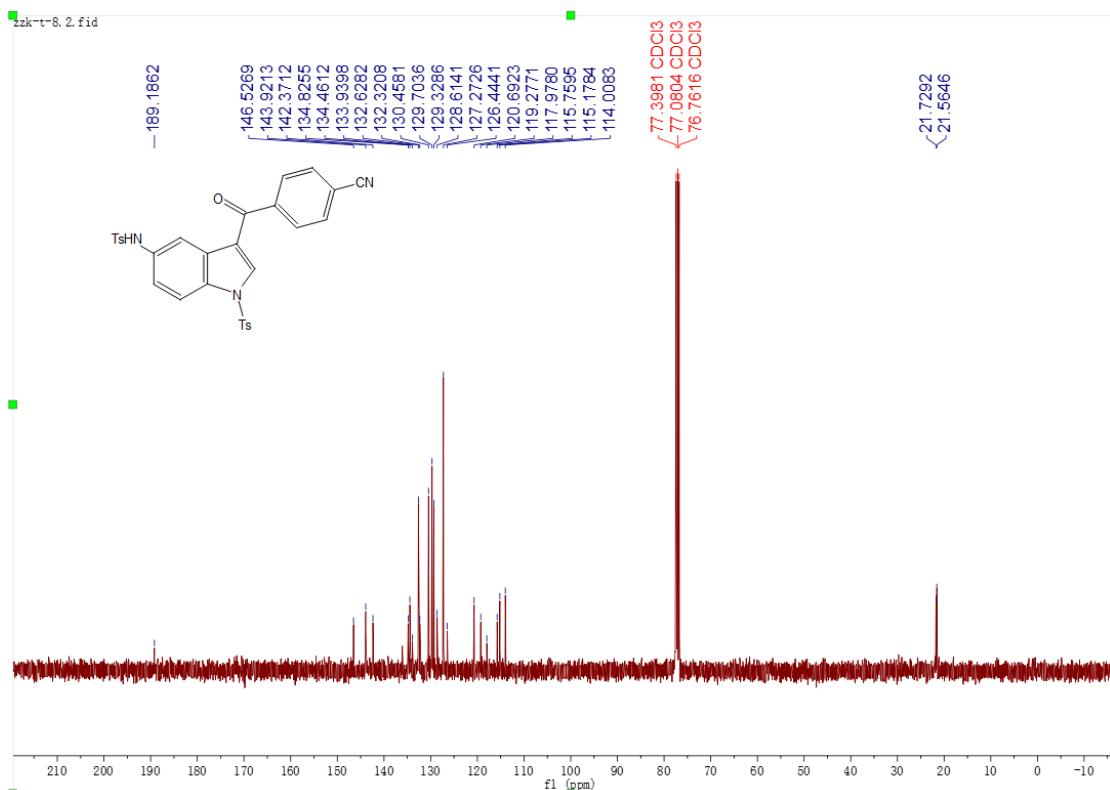
¹³C NMR spectrum of **3e** (CDCl_3 , 100 MHz)

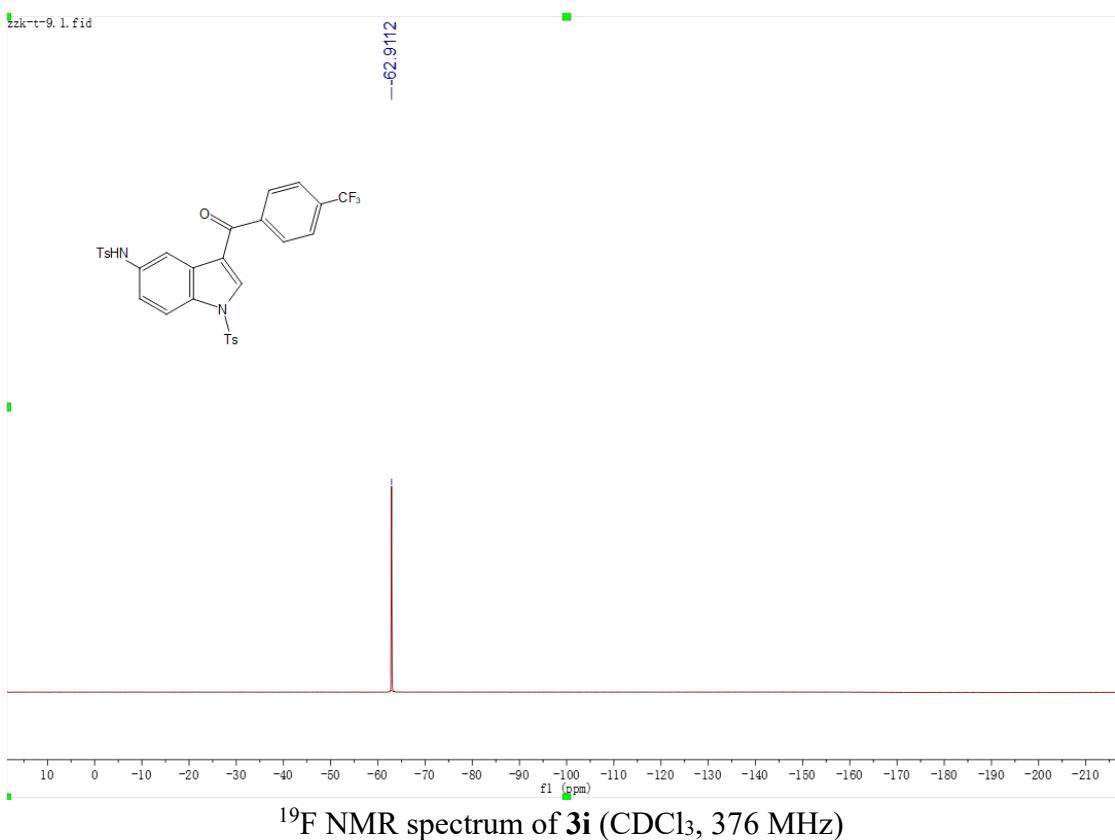
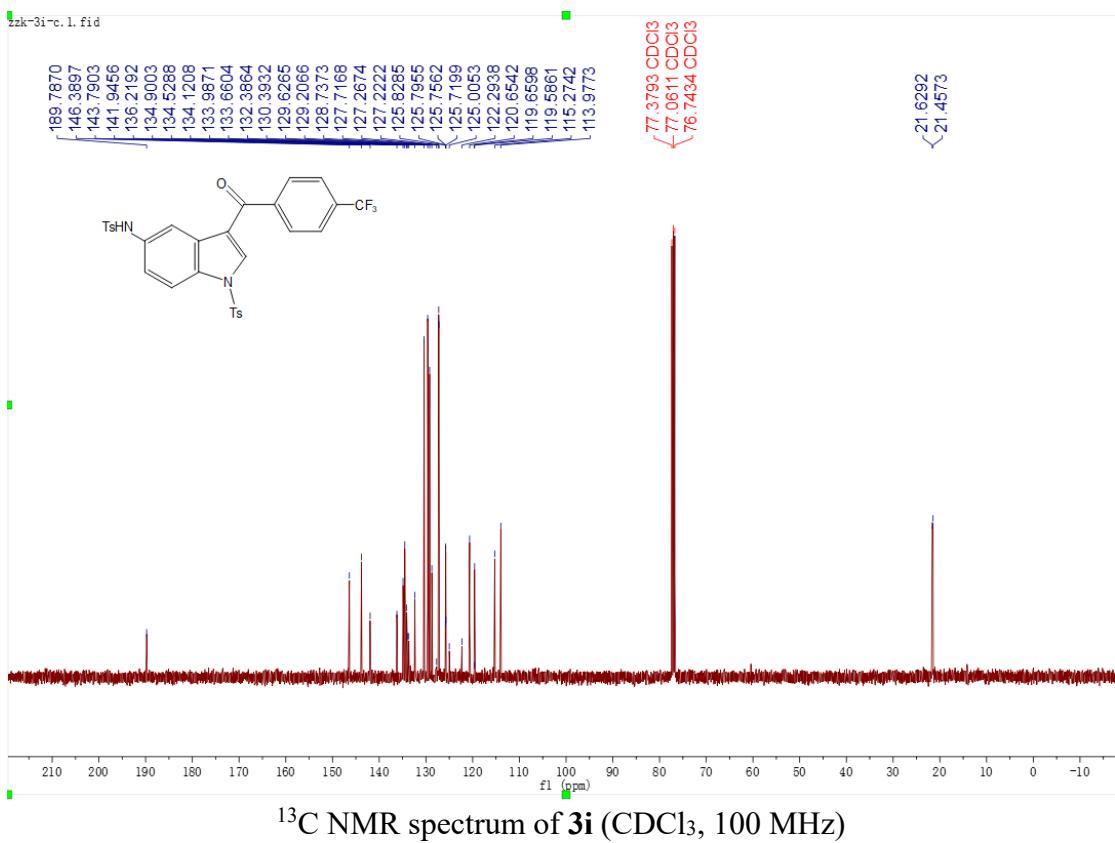


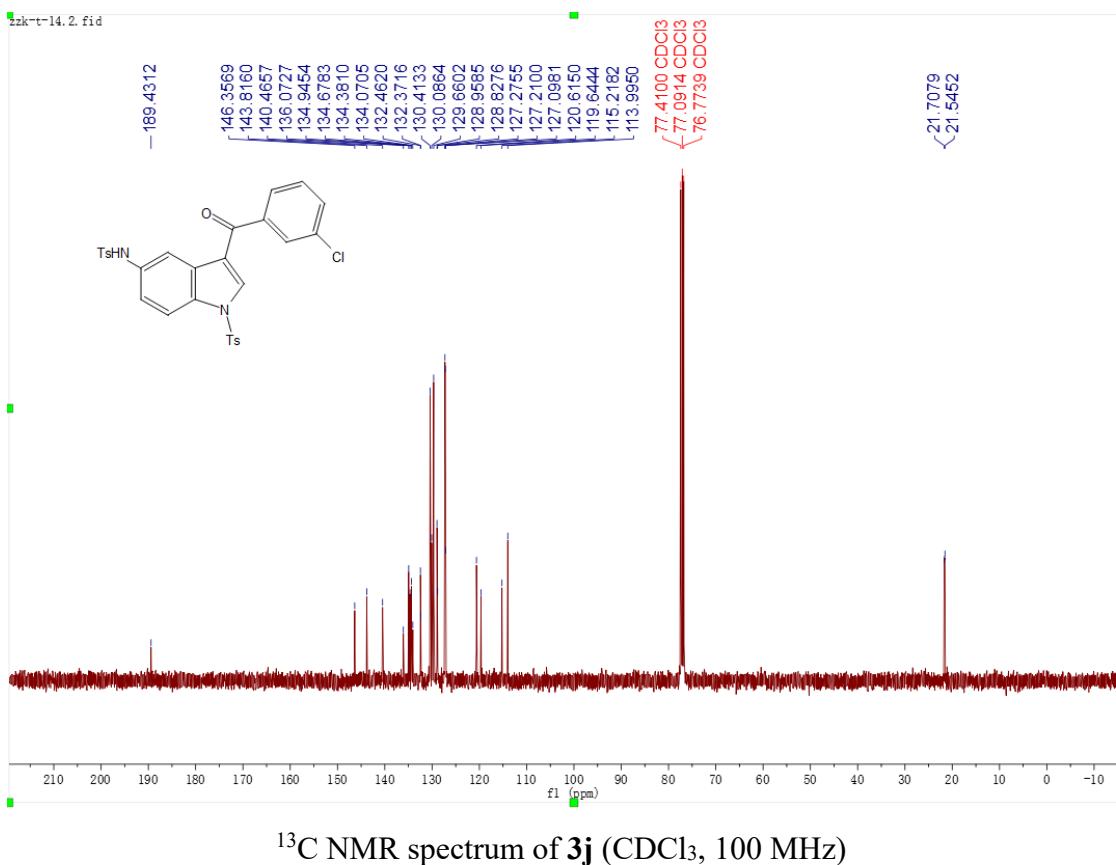
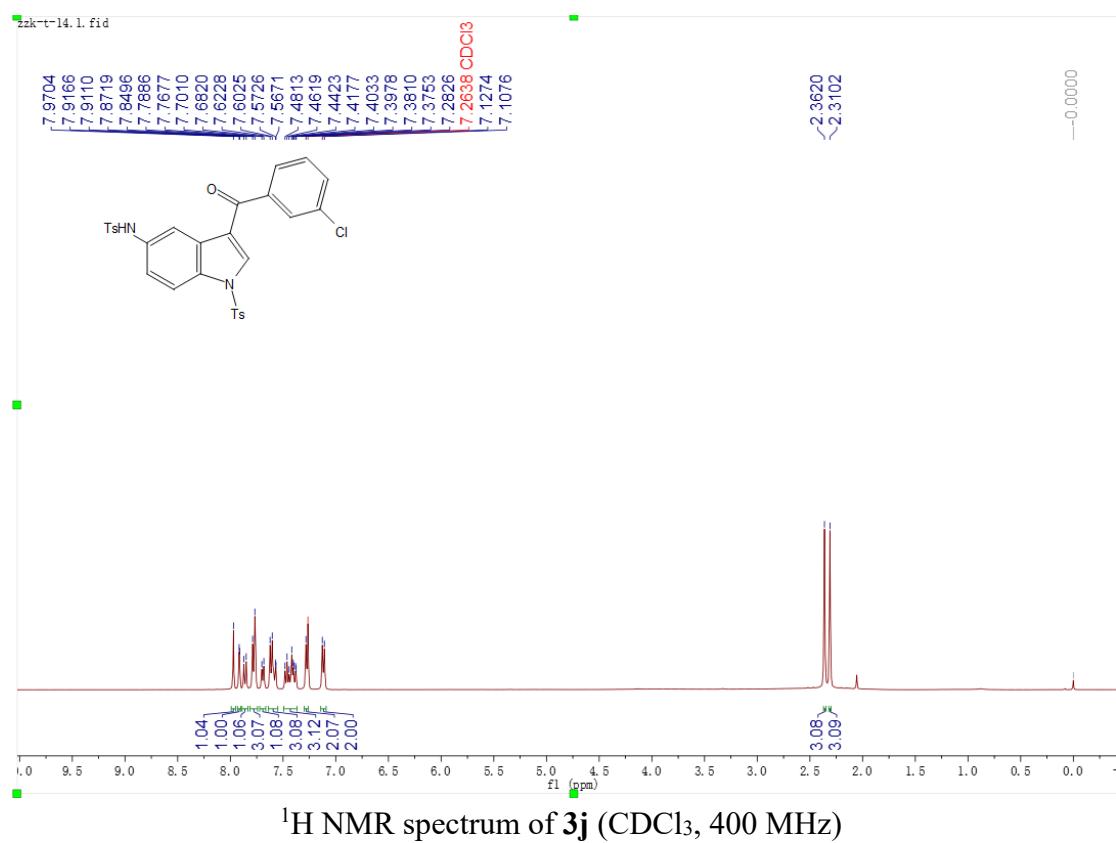
¹H NMR spectrum of **3f** (CDCl_3 , 400 MHz)

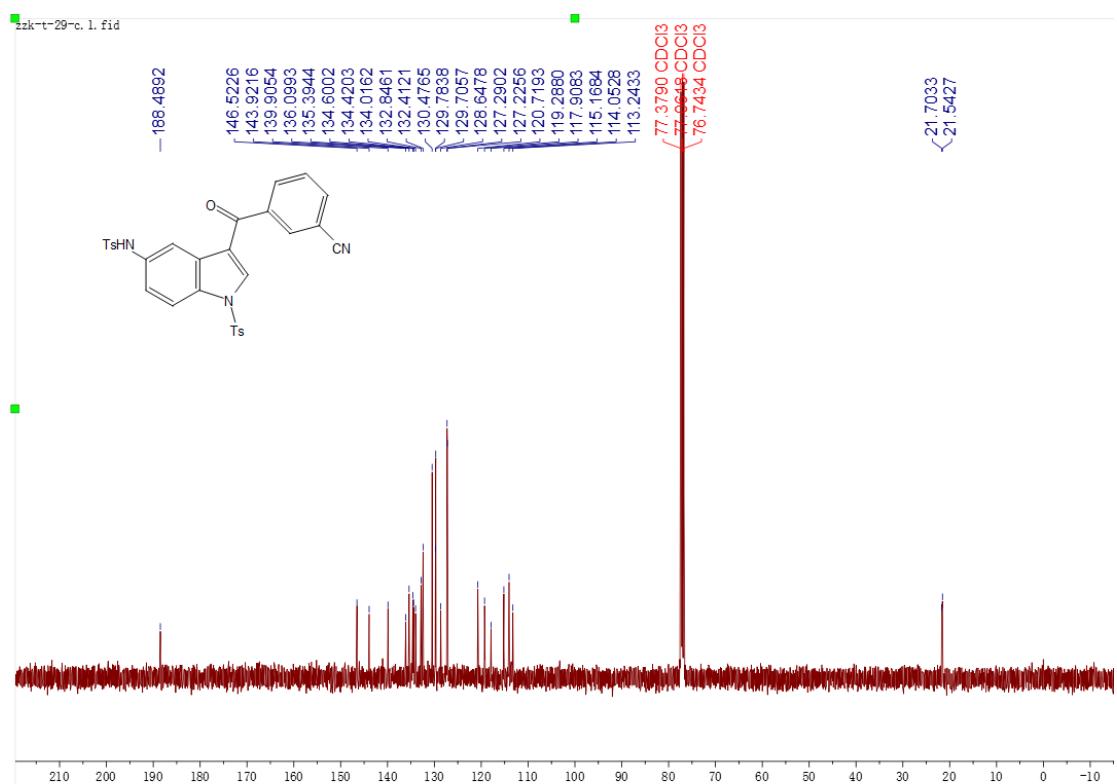
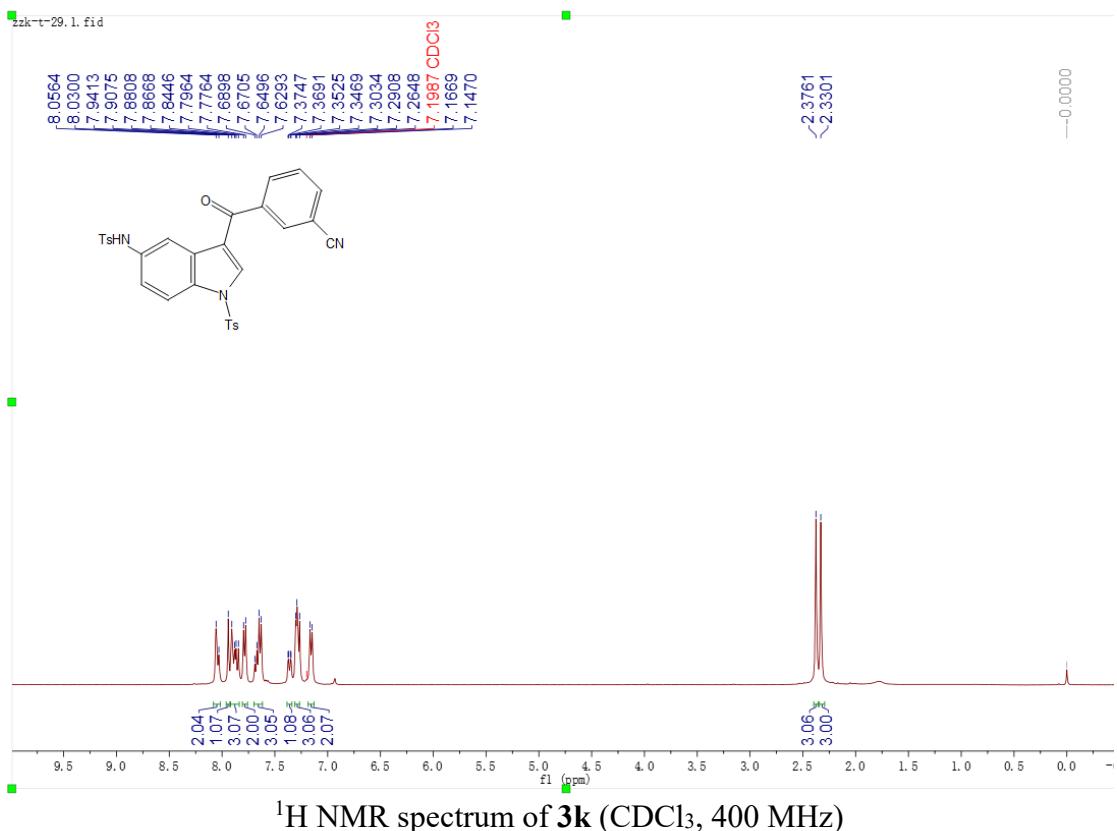


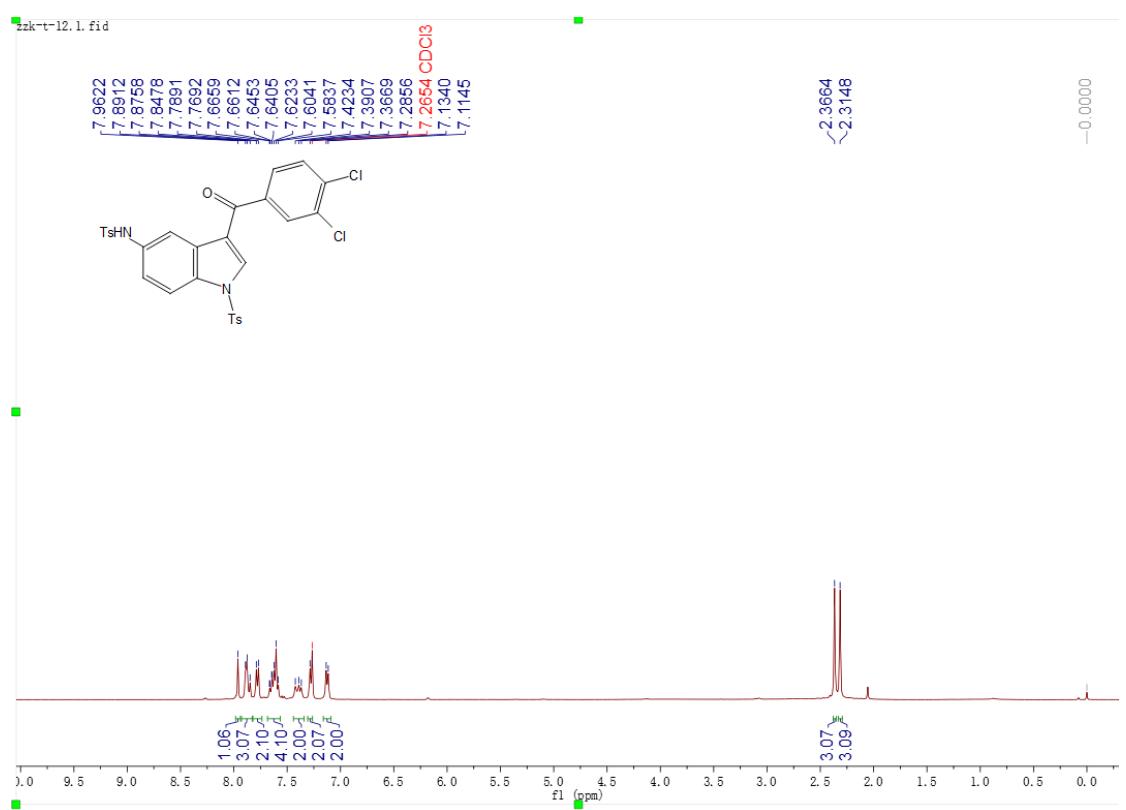




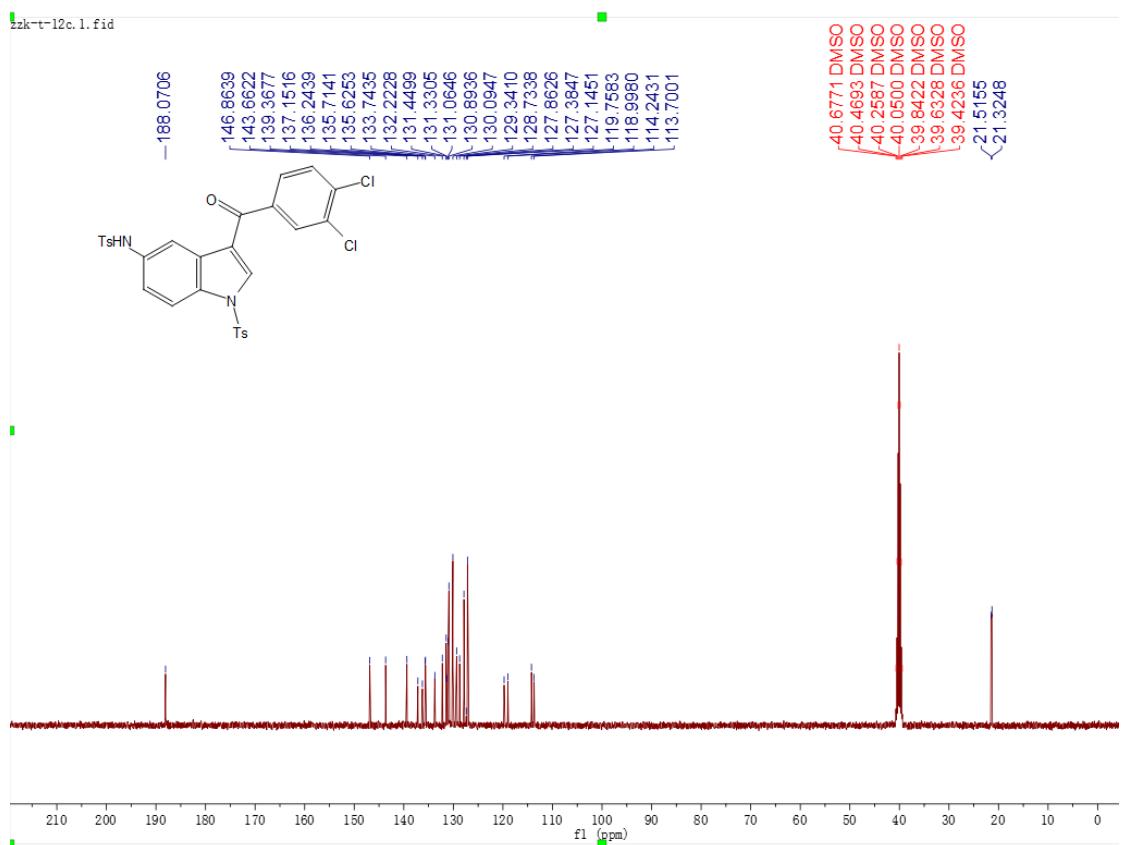






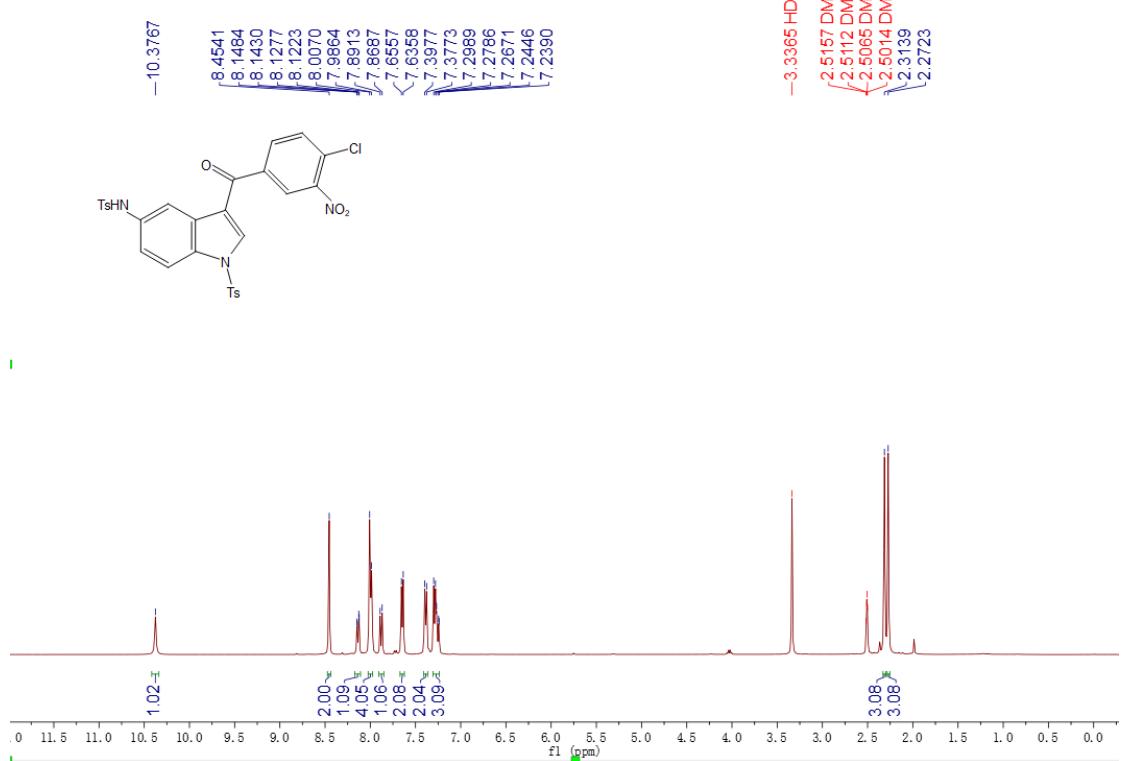


¹H NMR spectrum of **3I** (CDCl₃, 400 MHz)

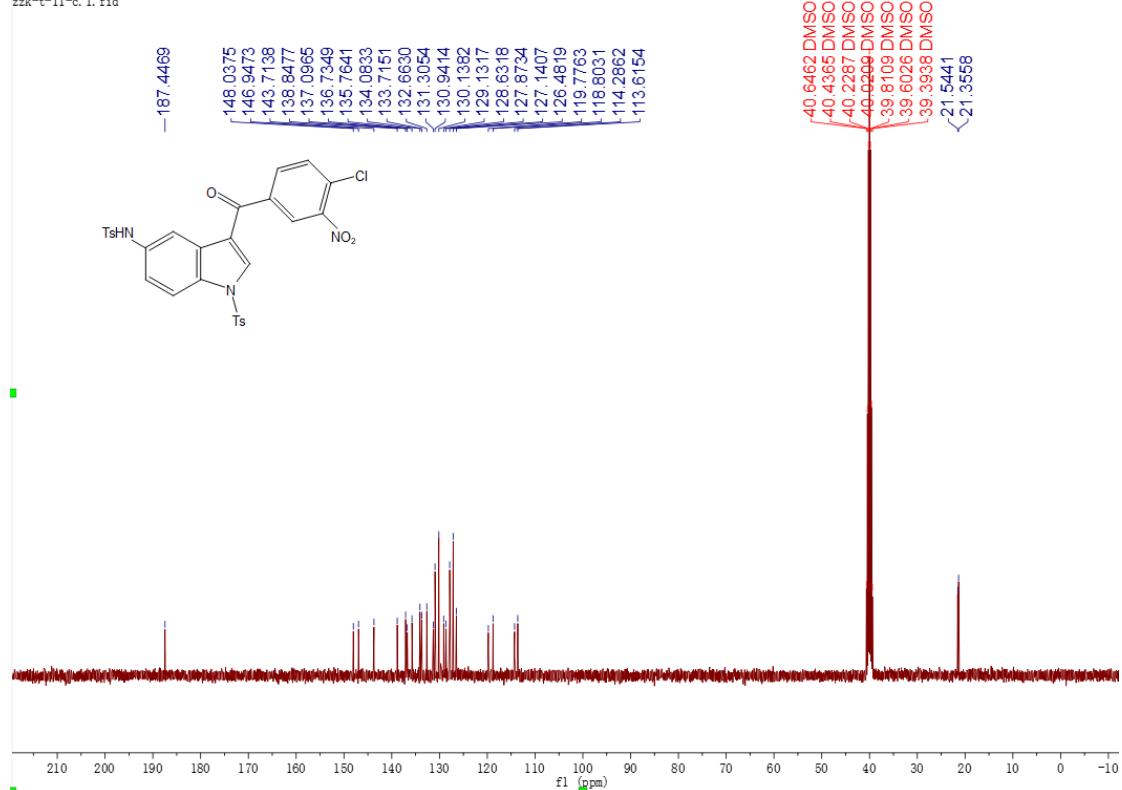


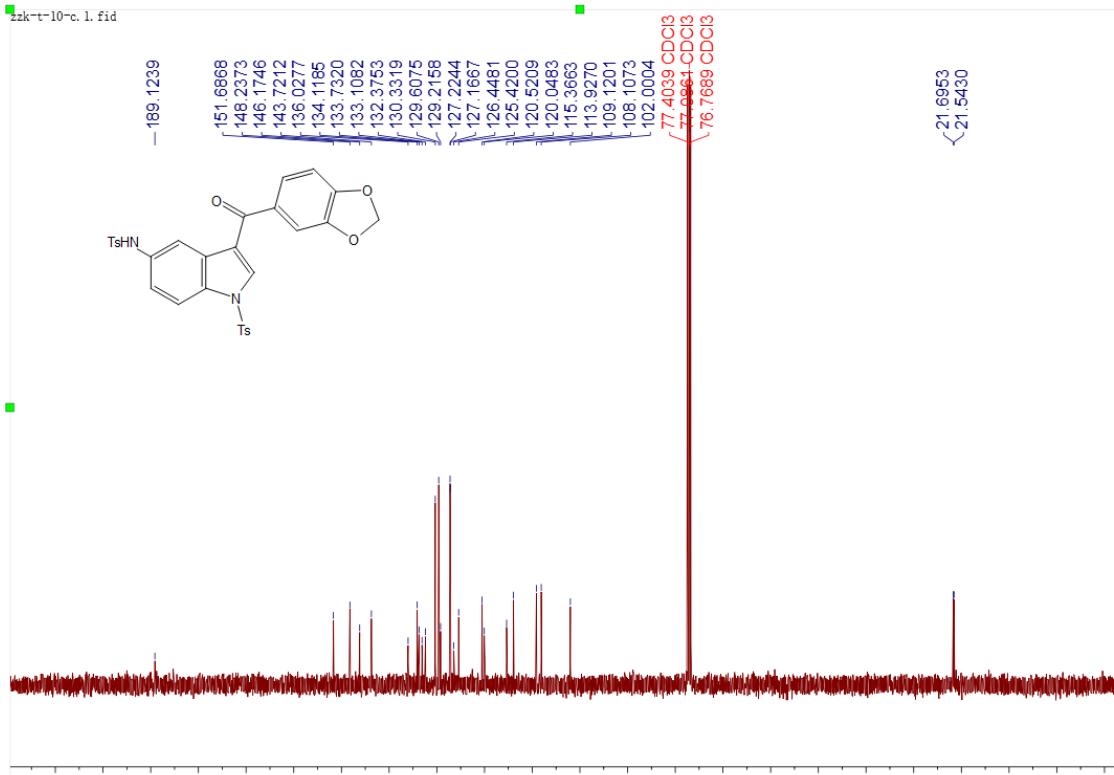
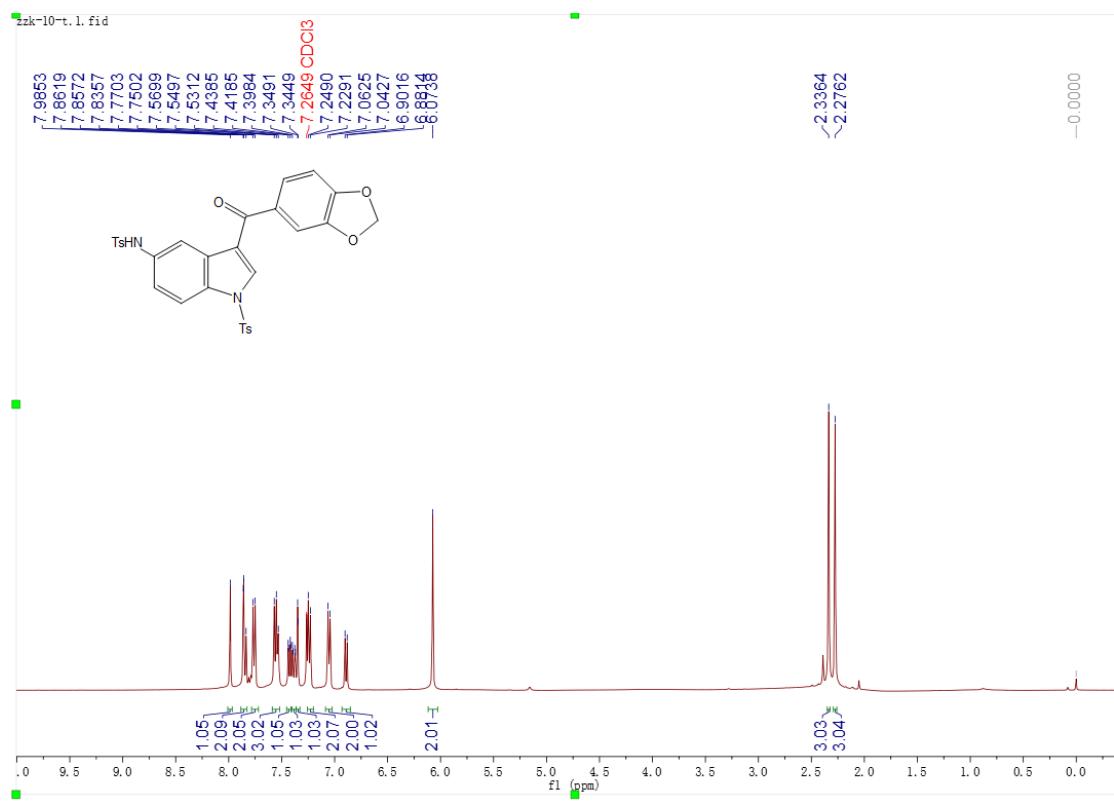
¹³C NMR spectrum of **3I** (DMSO-*d*₆, 100 MHz)

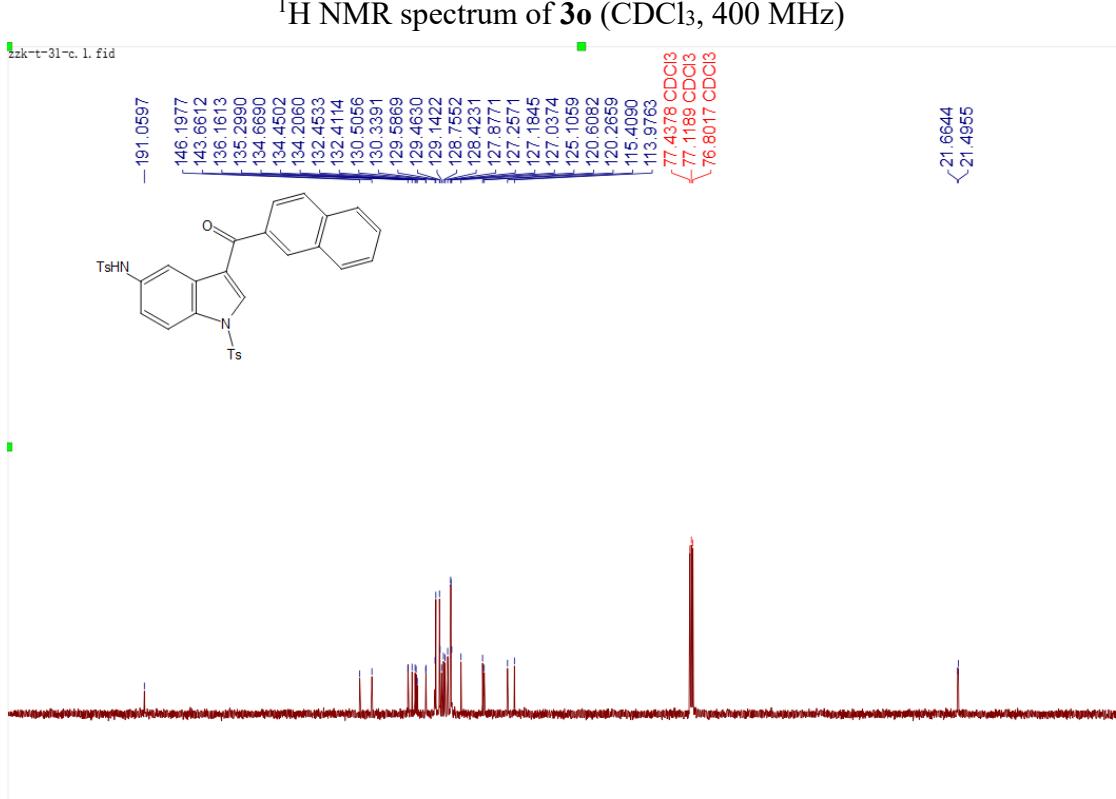
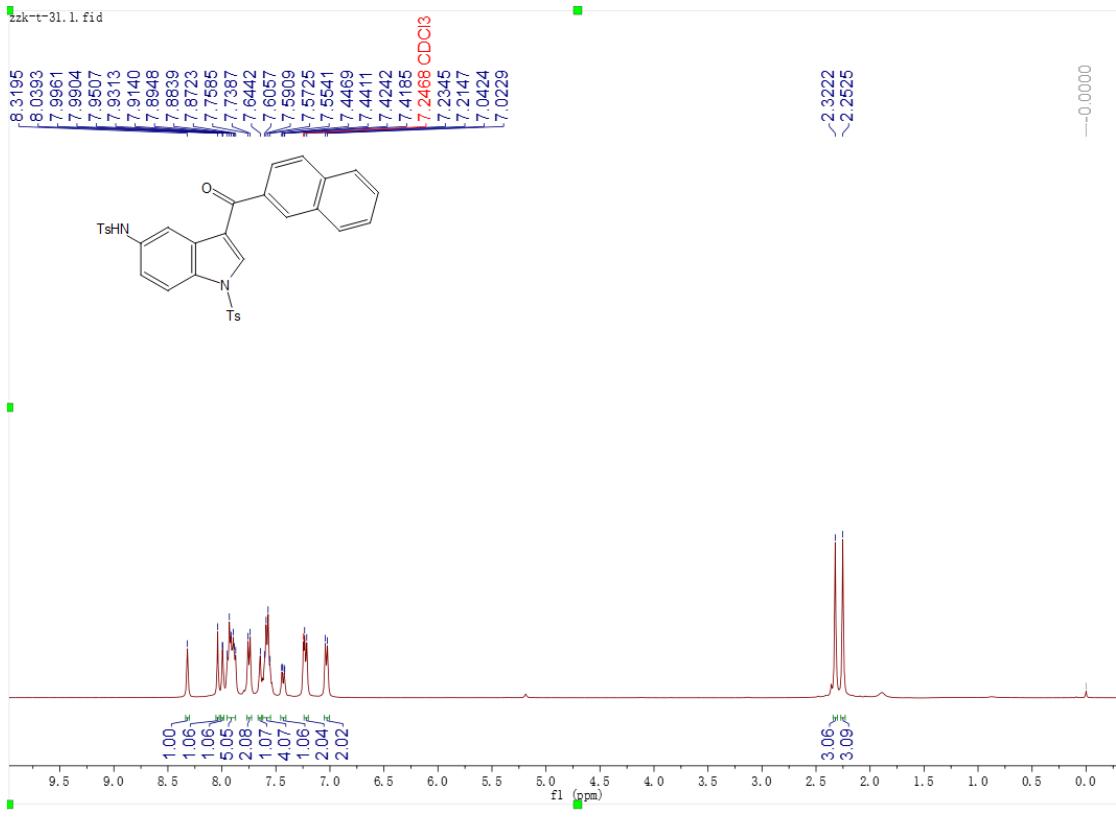
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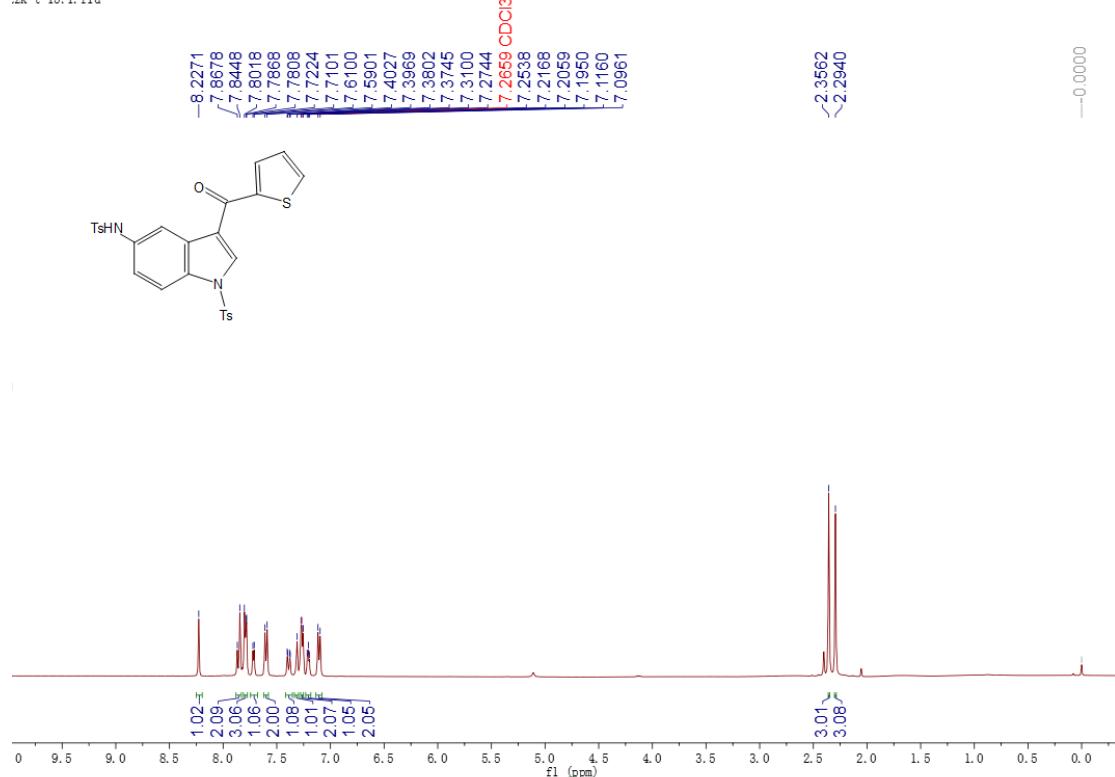
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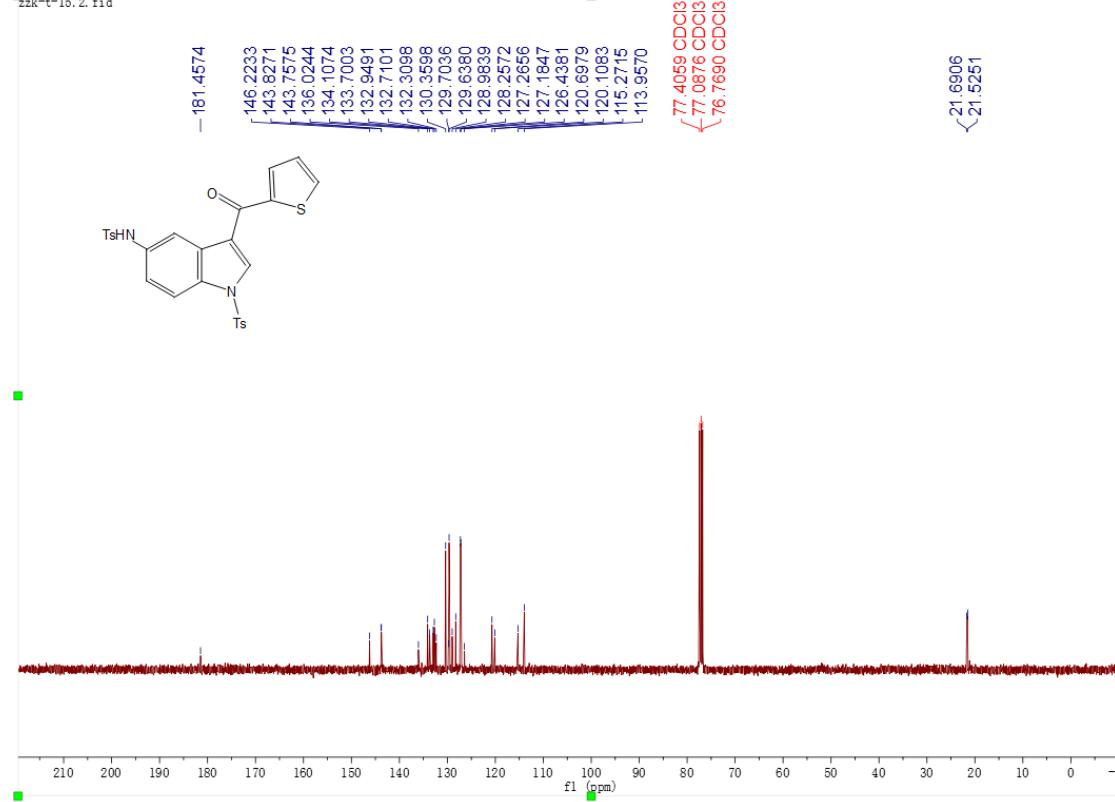


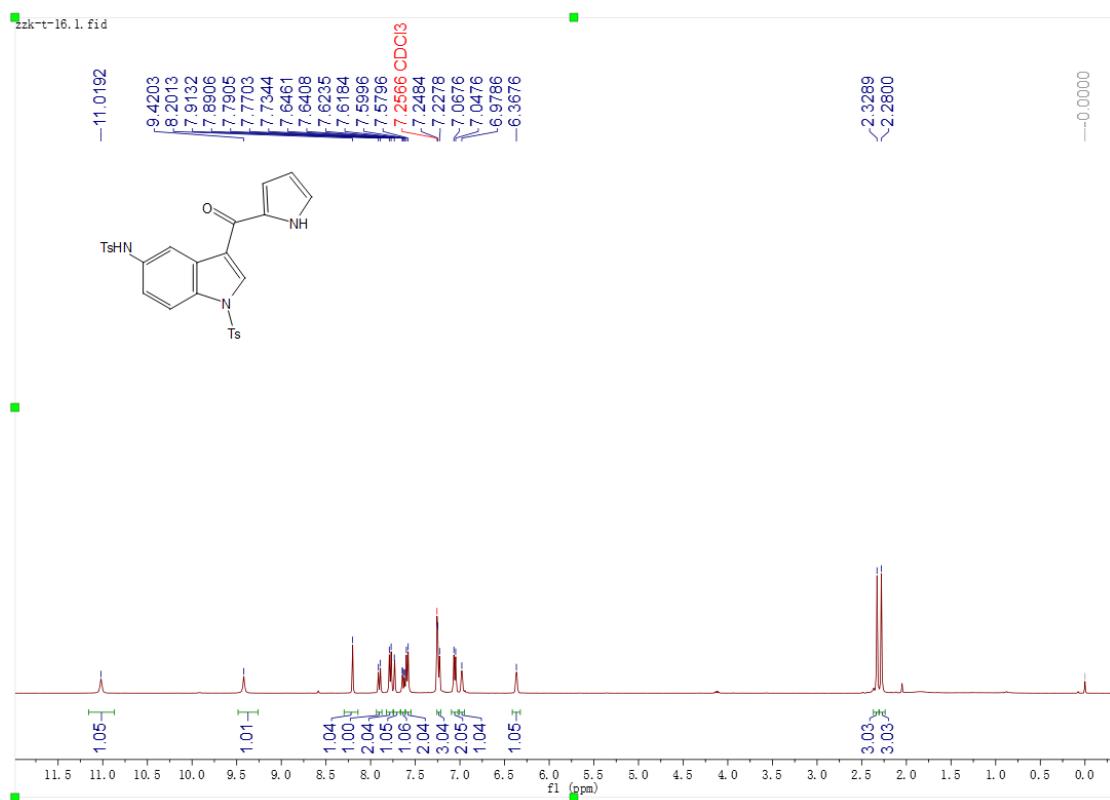


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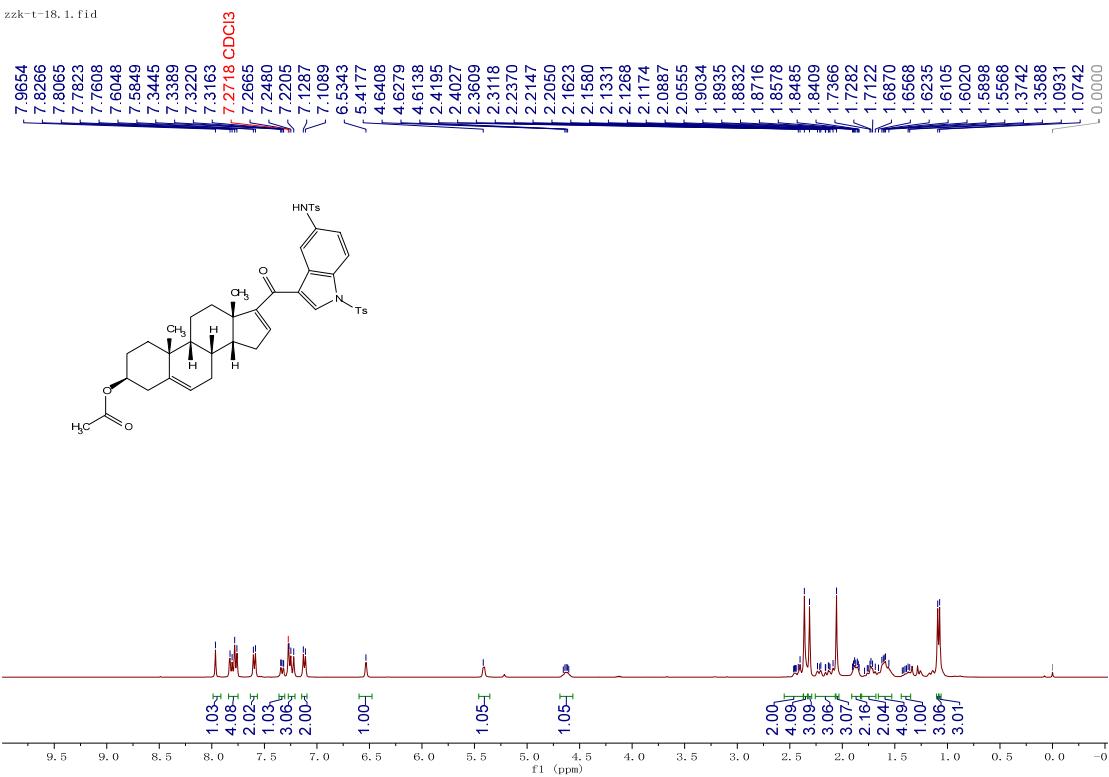


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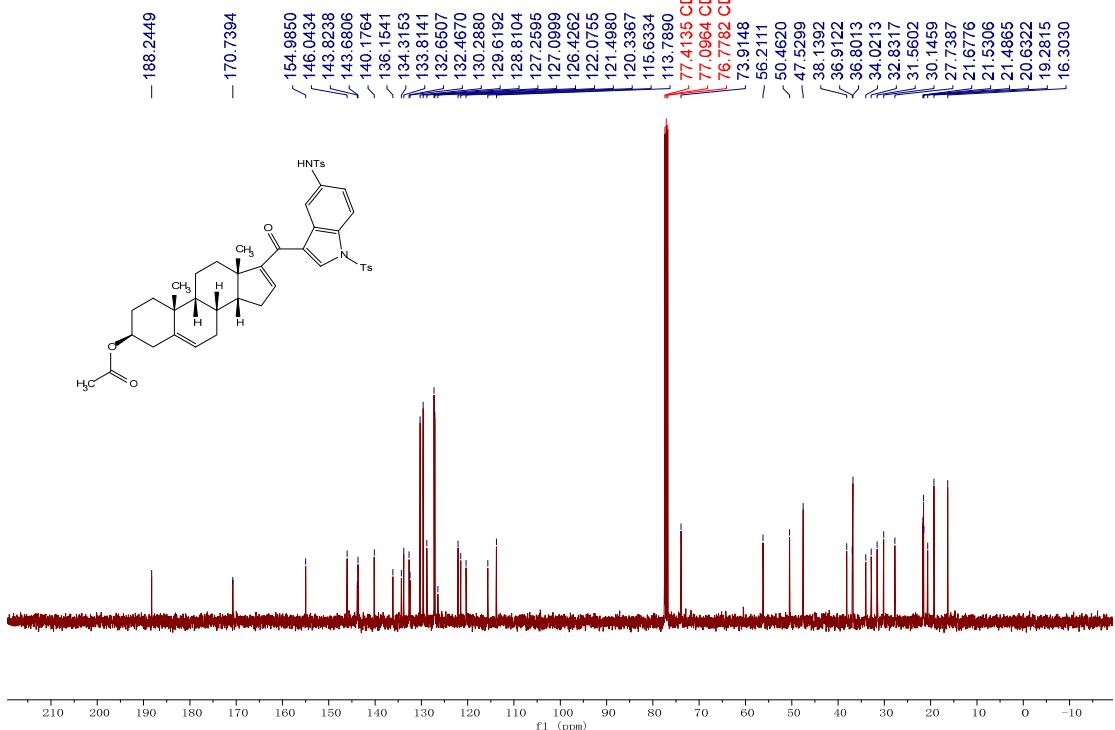


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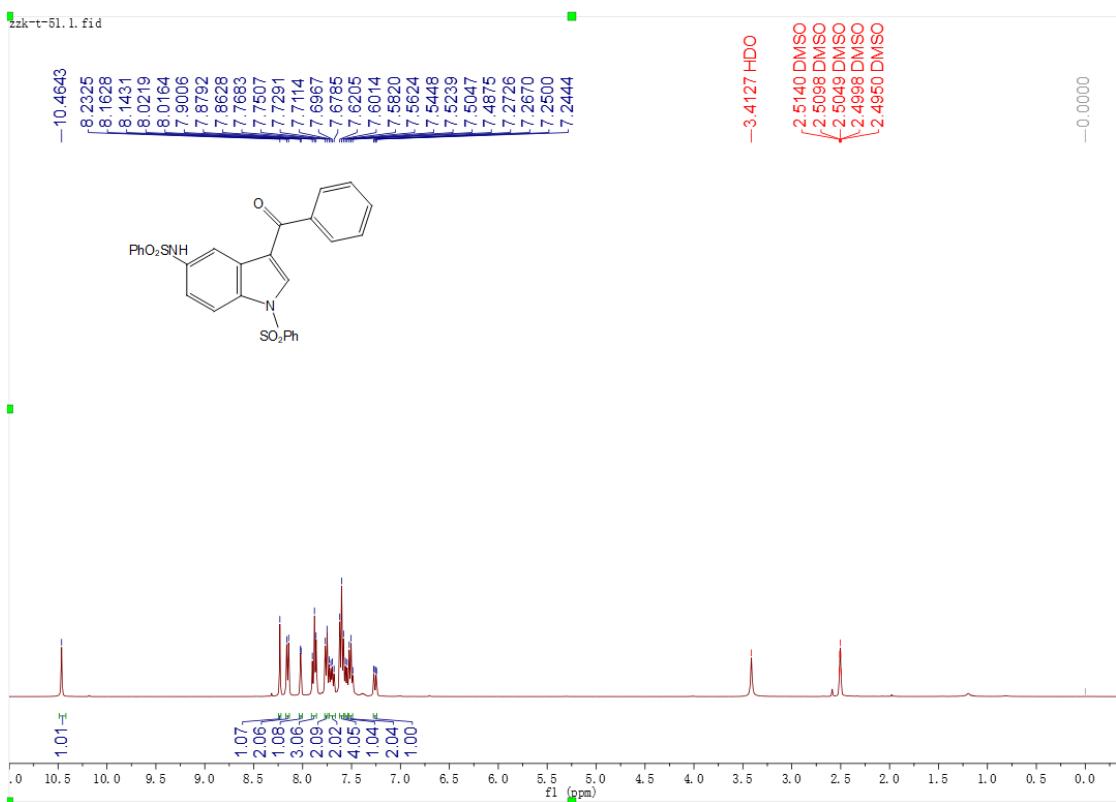


^1H NMR spectrum of **3r** (CDCl_3 , 400 MHz)

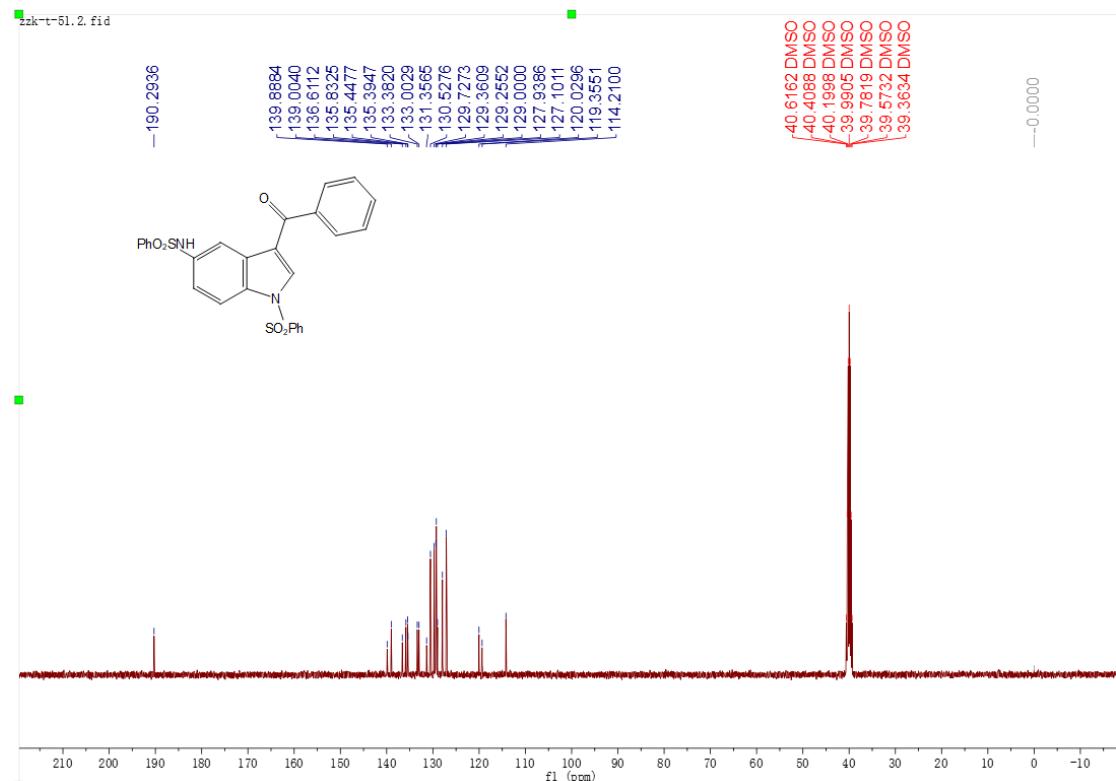
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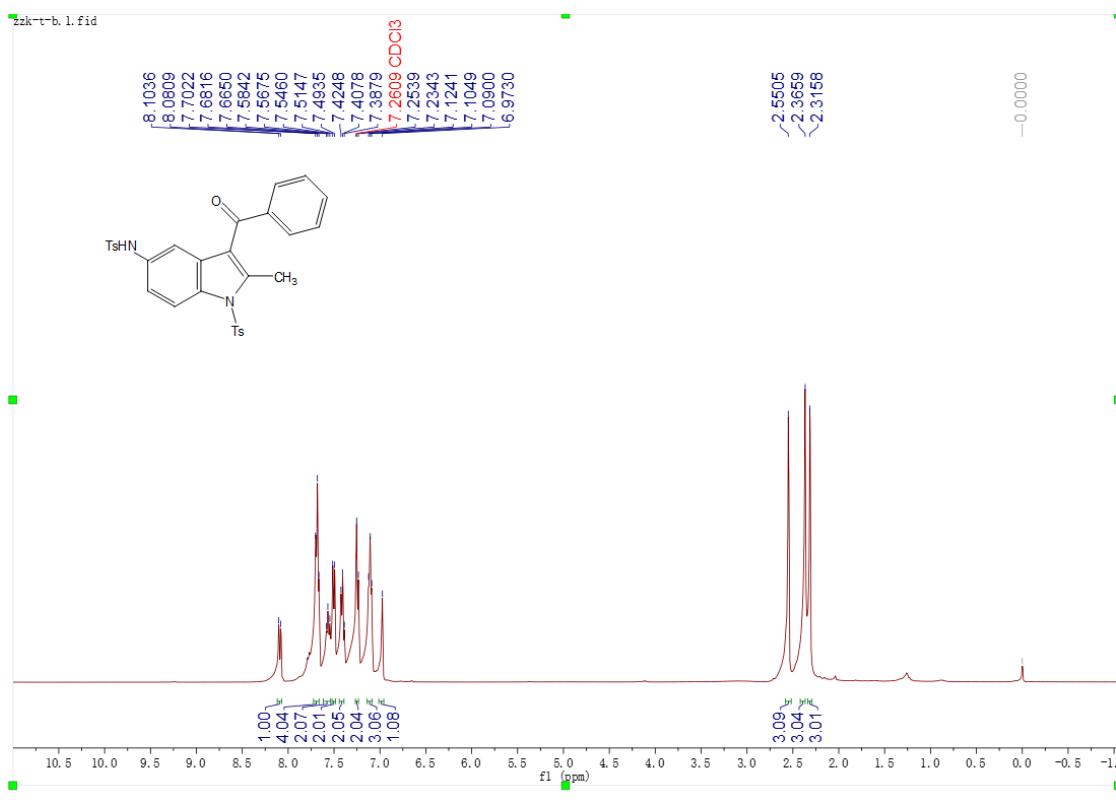
^{13}C NMR spectrum of **3r** (CDCl_3 , 100 MHz)



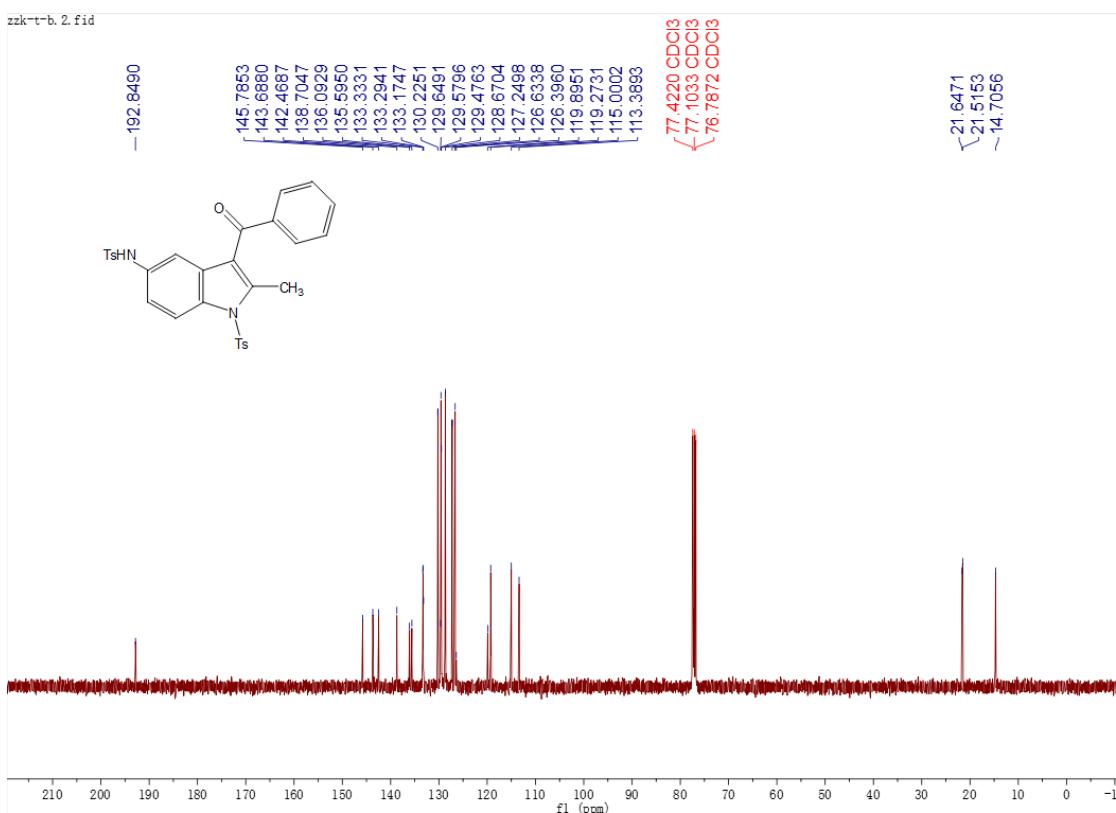
¹H NMR spectrum of **3s** (DMSO-*d*₆, 400 MHz)



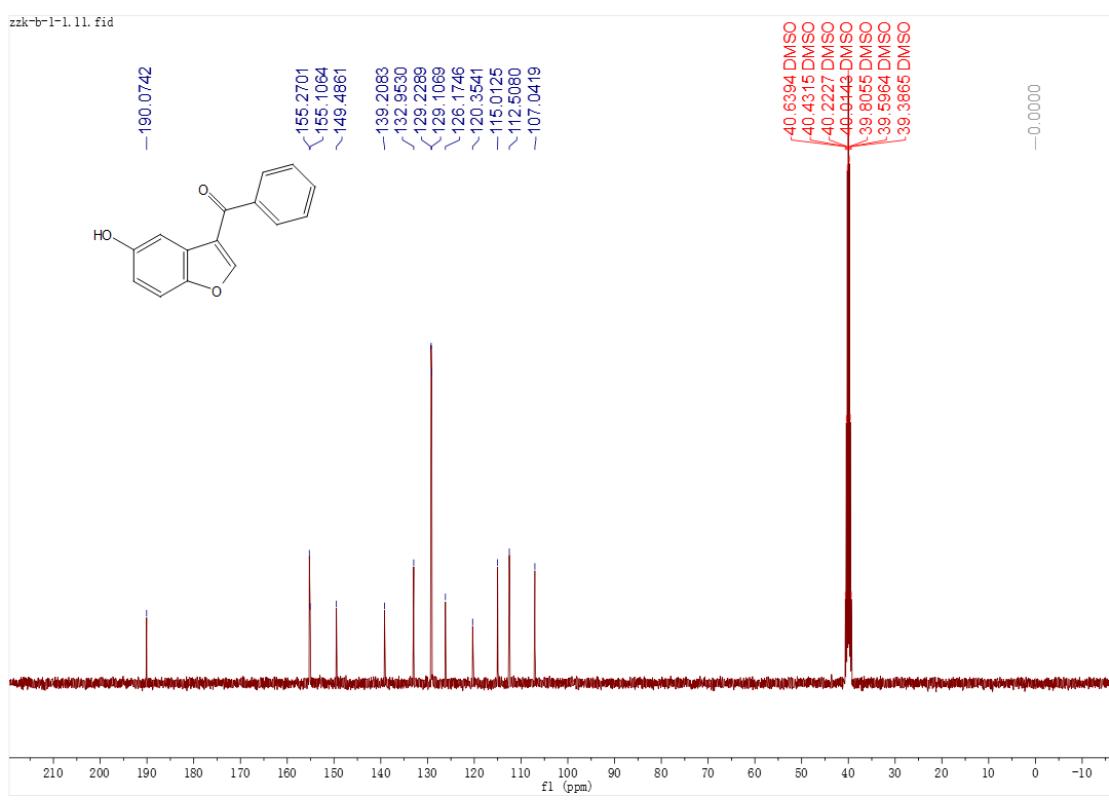
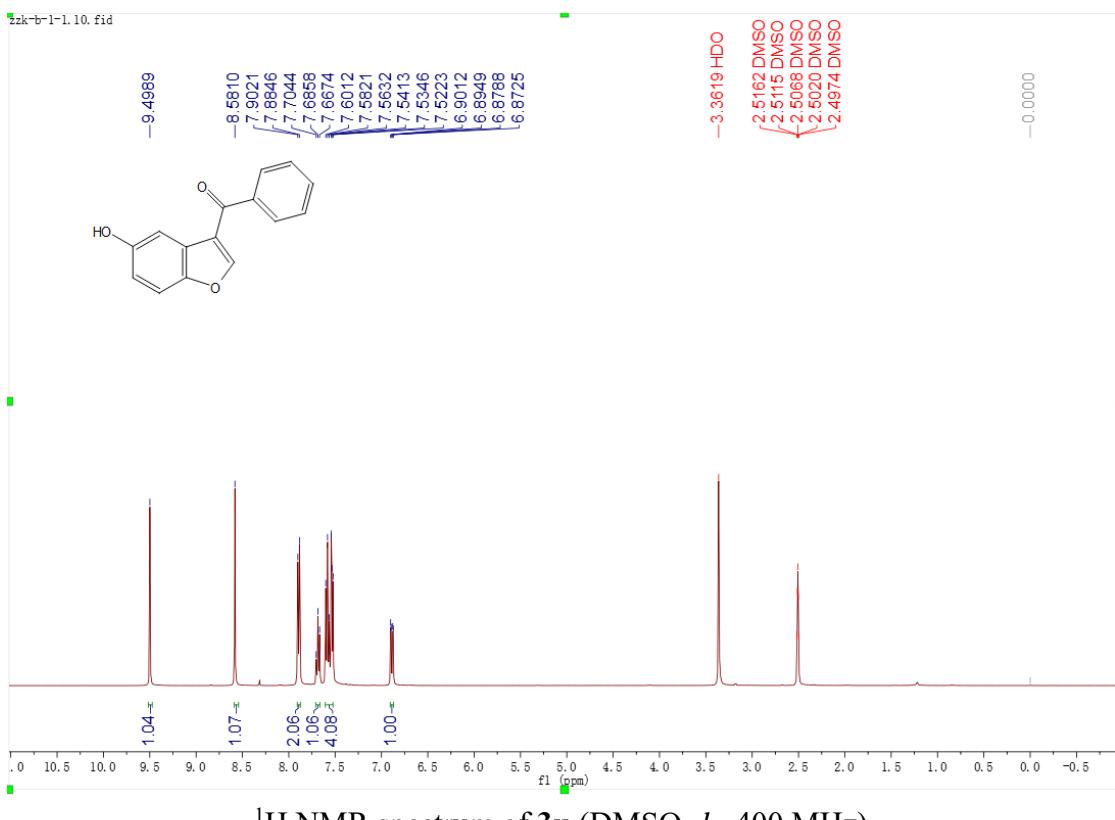
¹³C NMR spectrum of **3s** (DMSO-*d*₆, 100 MHz)

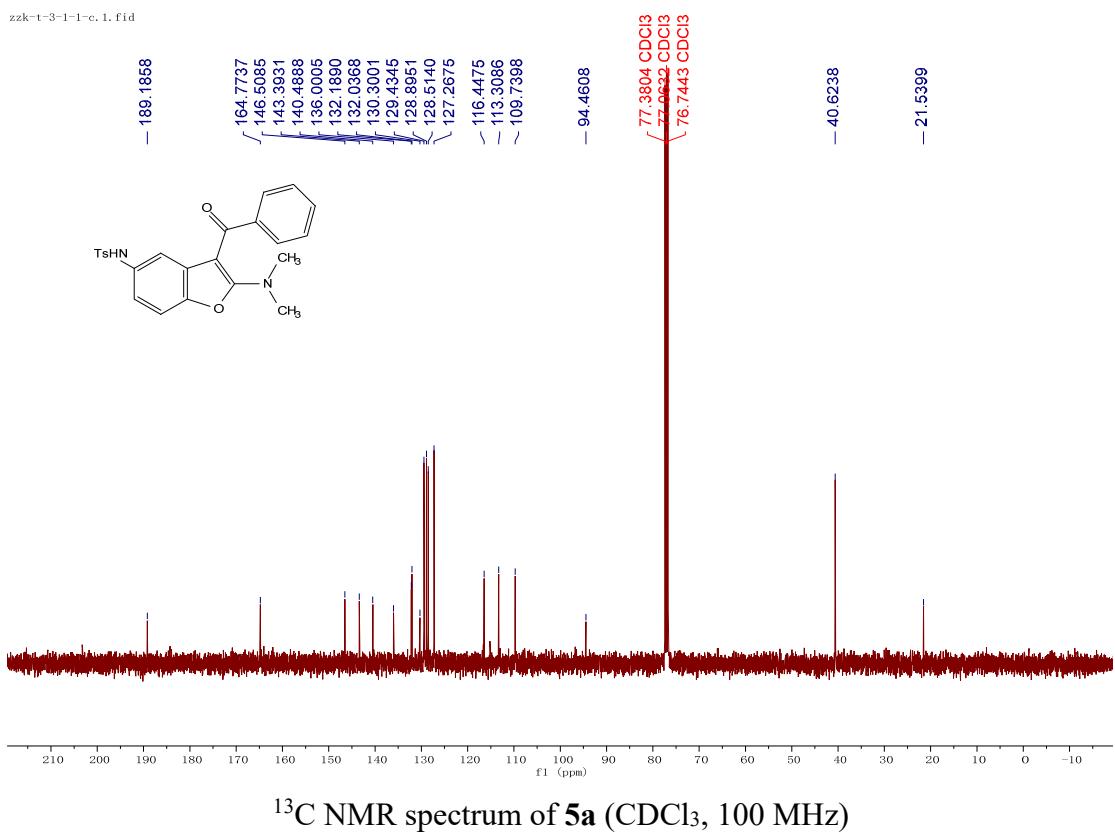
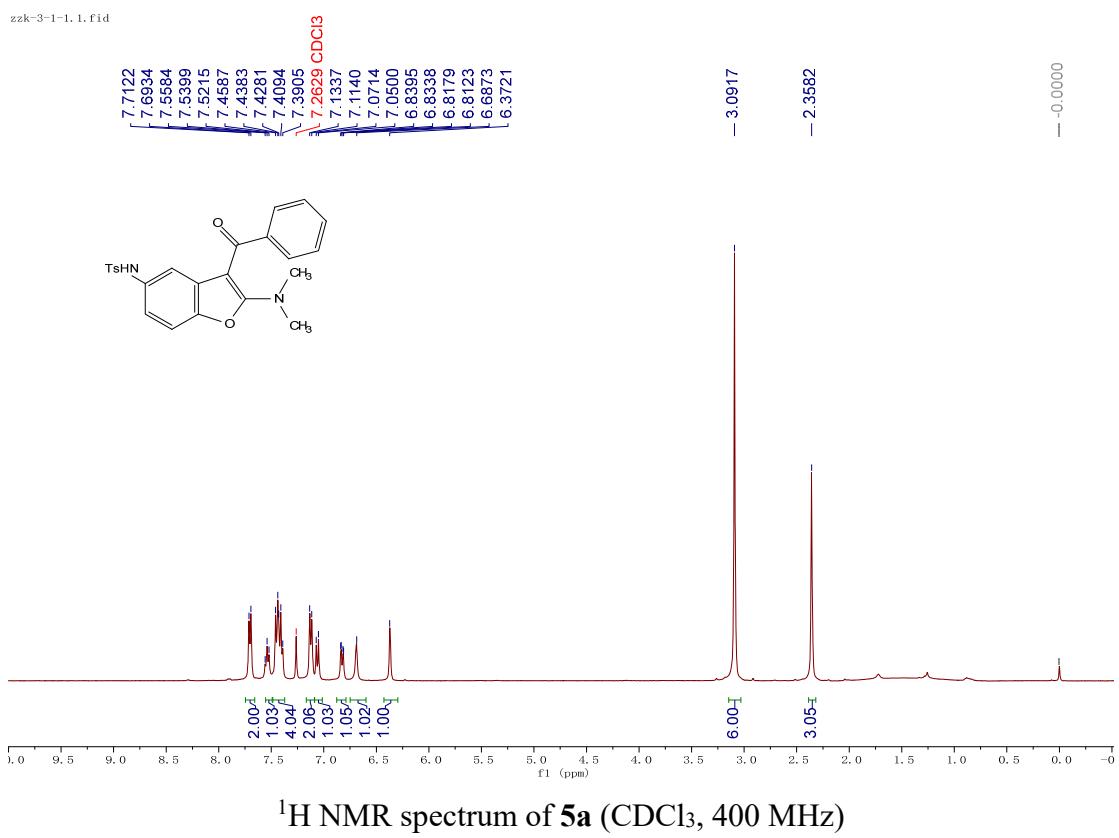


¹H NMR spectrum of 3t (CDCl₃, 400 MHz)

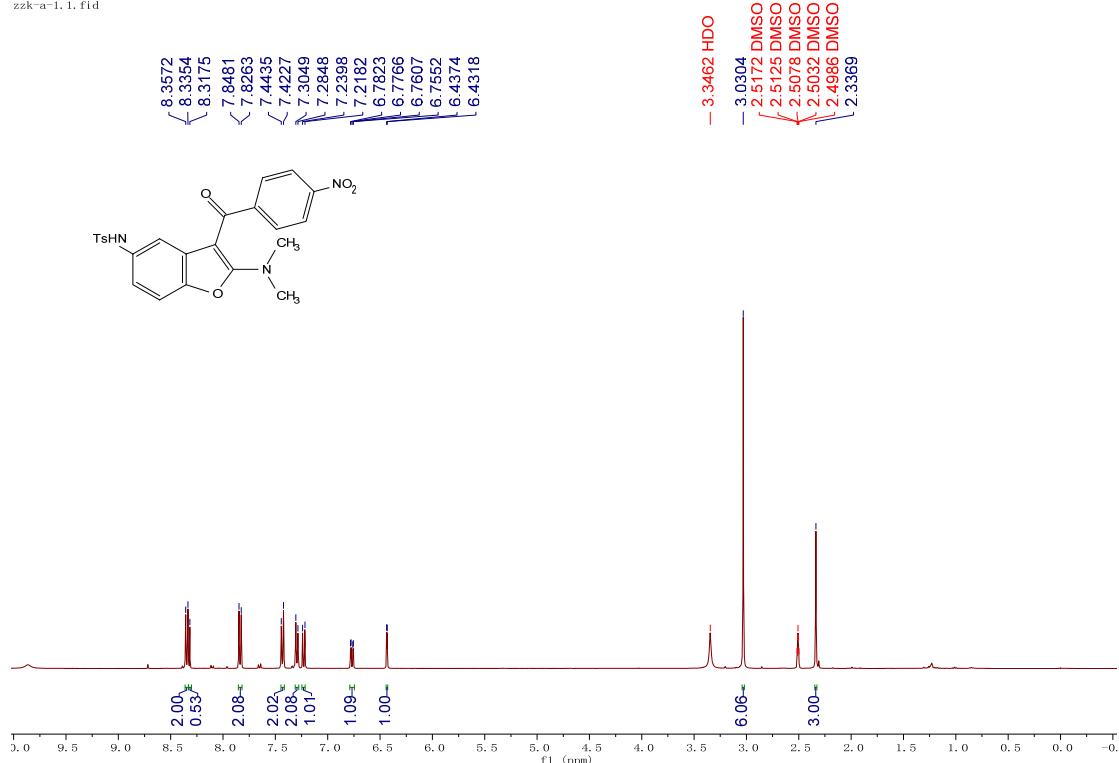


¹³C NMR spectrum of 3t (CDCl₃, 100 MHz)



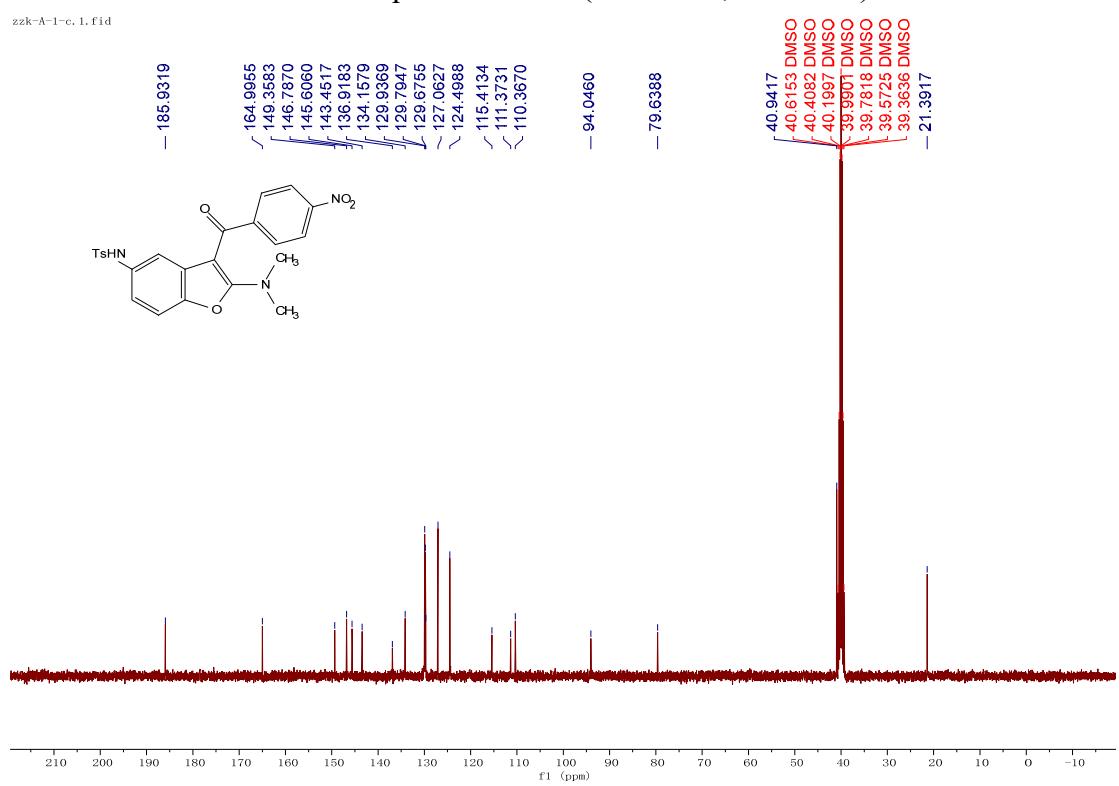


zzk-a-1, 1, fid



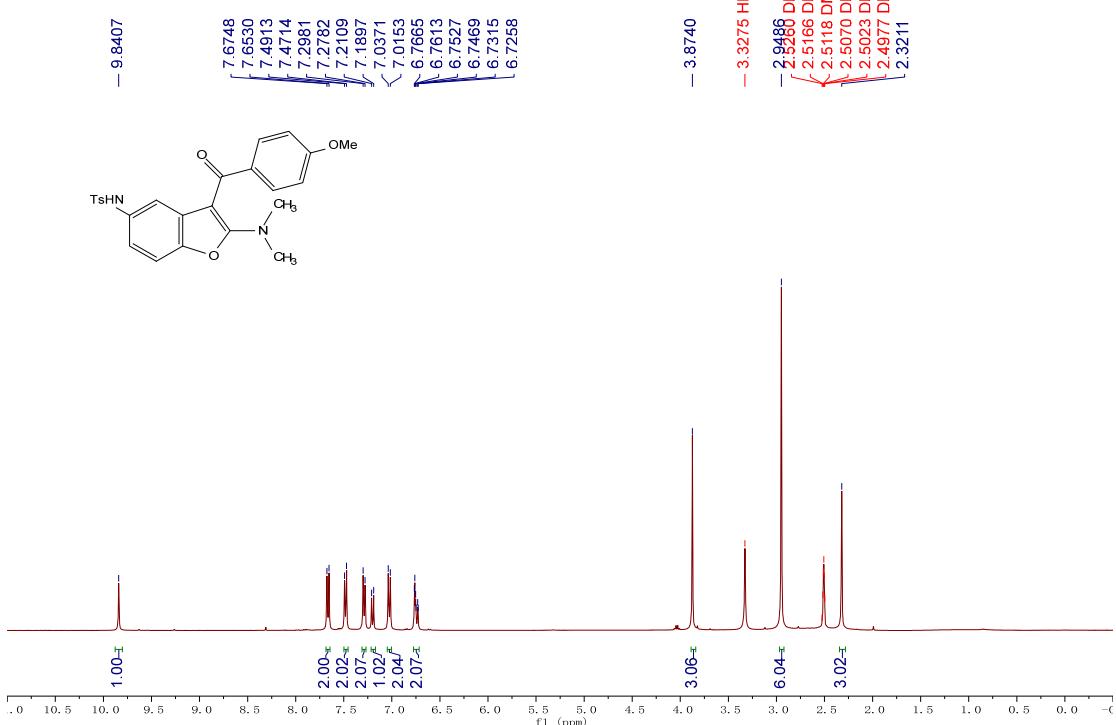
¹H NMR spectrum of **5b** (DMSO-*d*₆, 400 MHz)

zzk-A-1-c, 1, fid



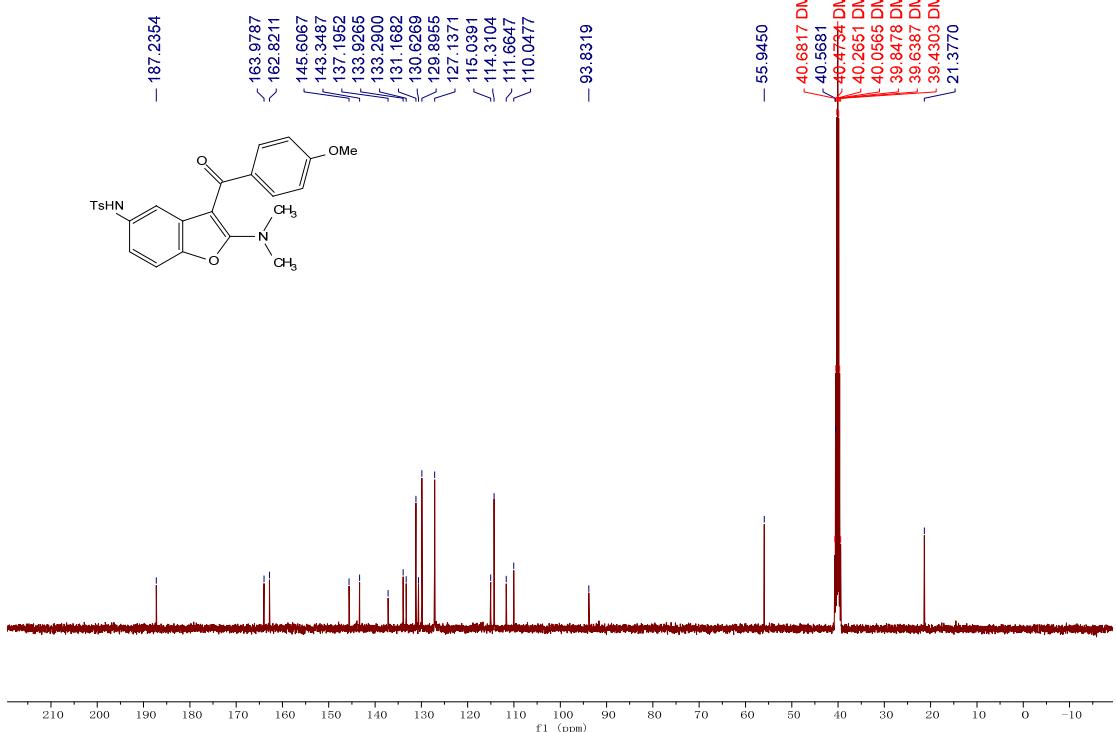
¹³C NMR spectrum of **5b** (DMSO-*d*₆, 100 MHz)

zzk-a-50.1.fid



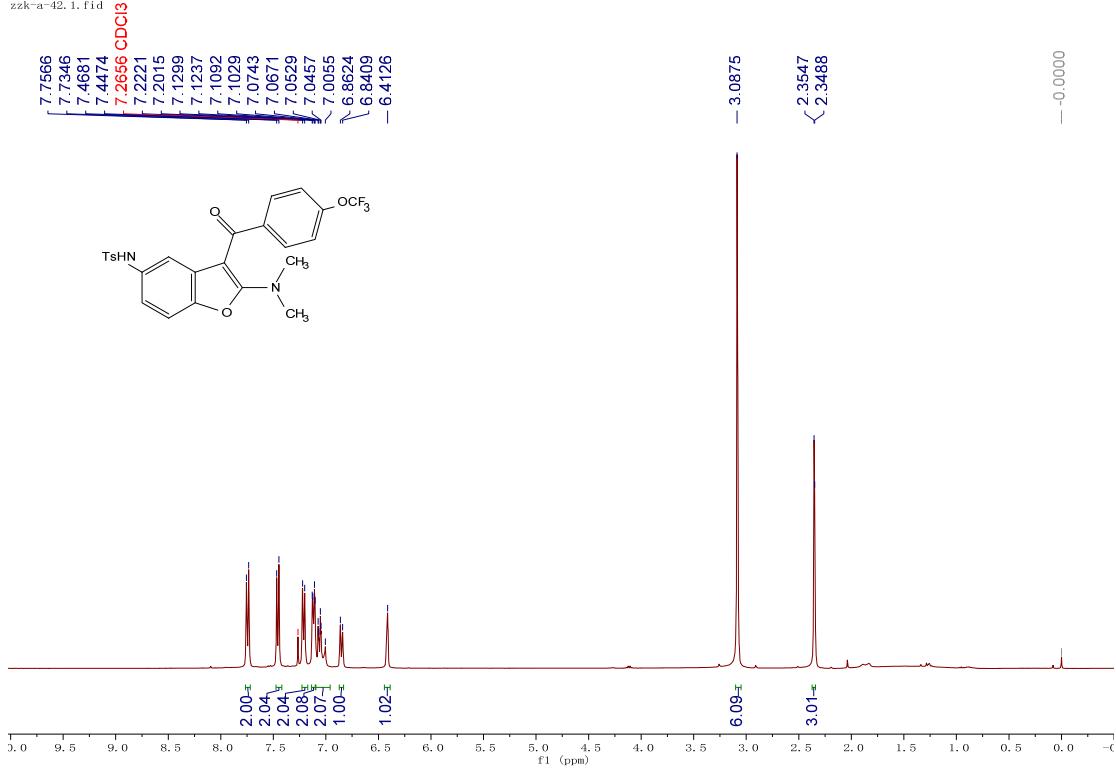
^1H NMR spectrum of **5c** (DMSO- d_6 , 400 MHz)

zzk-a-50.2.fid



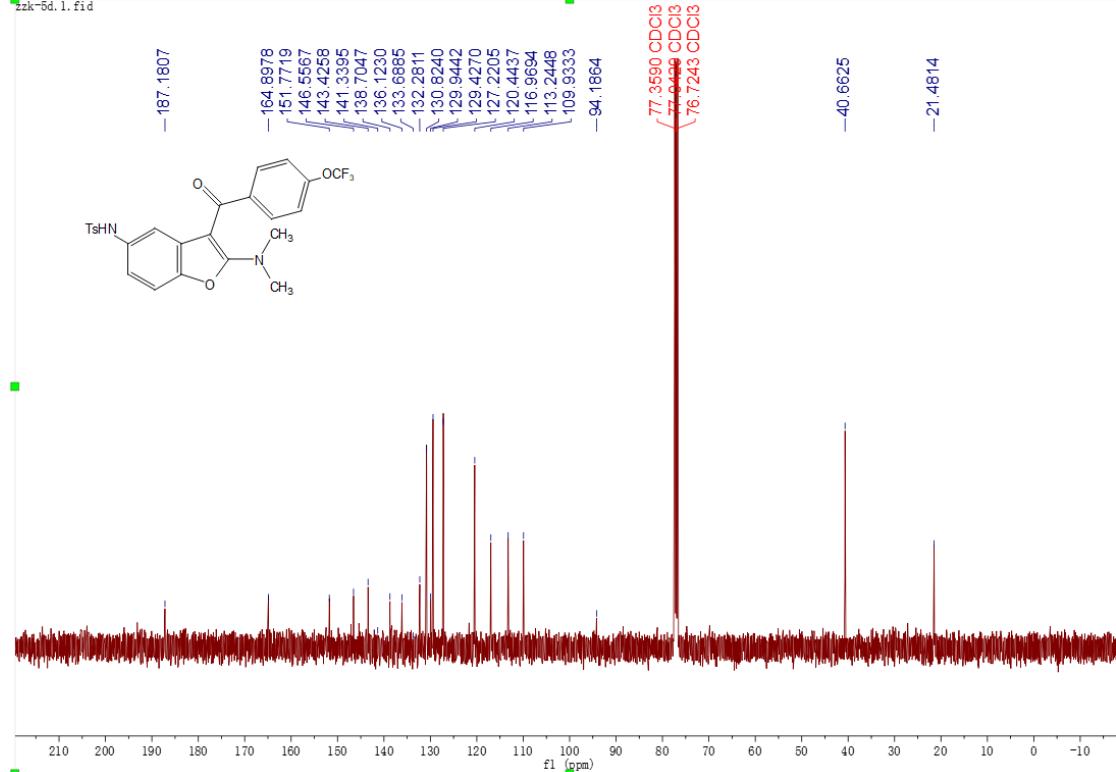
^{13}C NMR spectrum of **5c** (DMSO- d_6 , 100 MHz)

zzk-a-42.1.fid

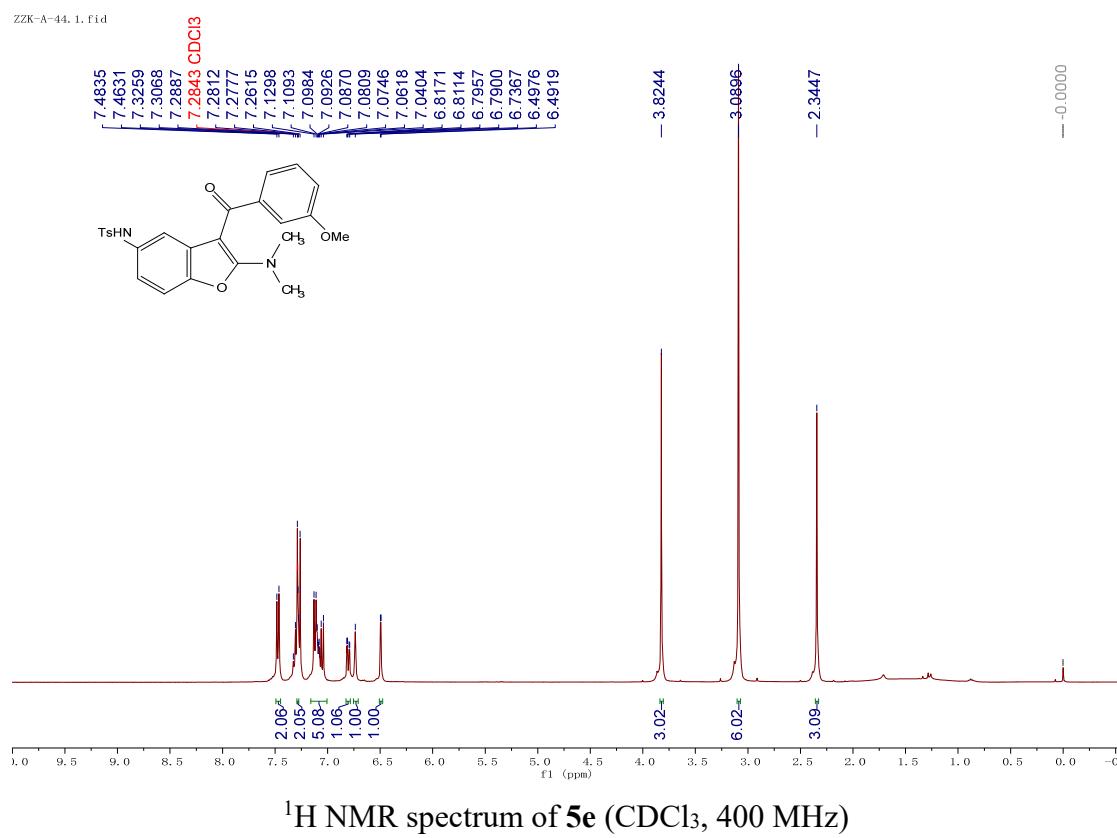
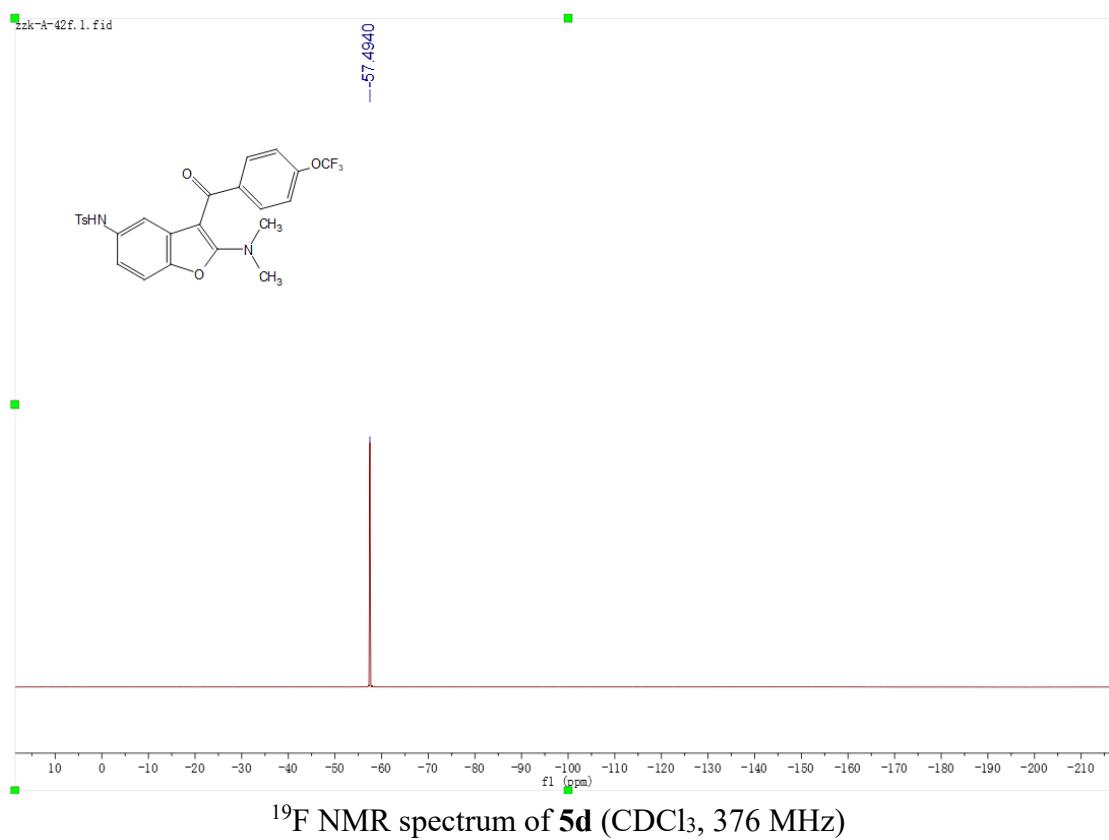


^1H NMR spectrum of **5d** (CDCl_3 , 400 MHz)

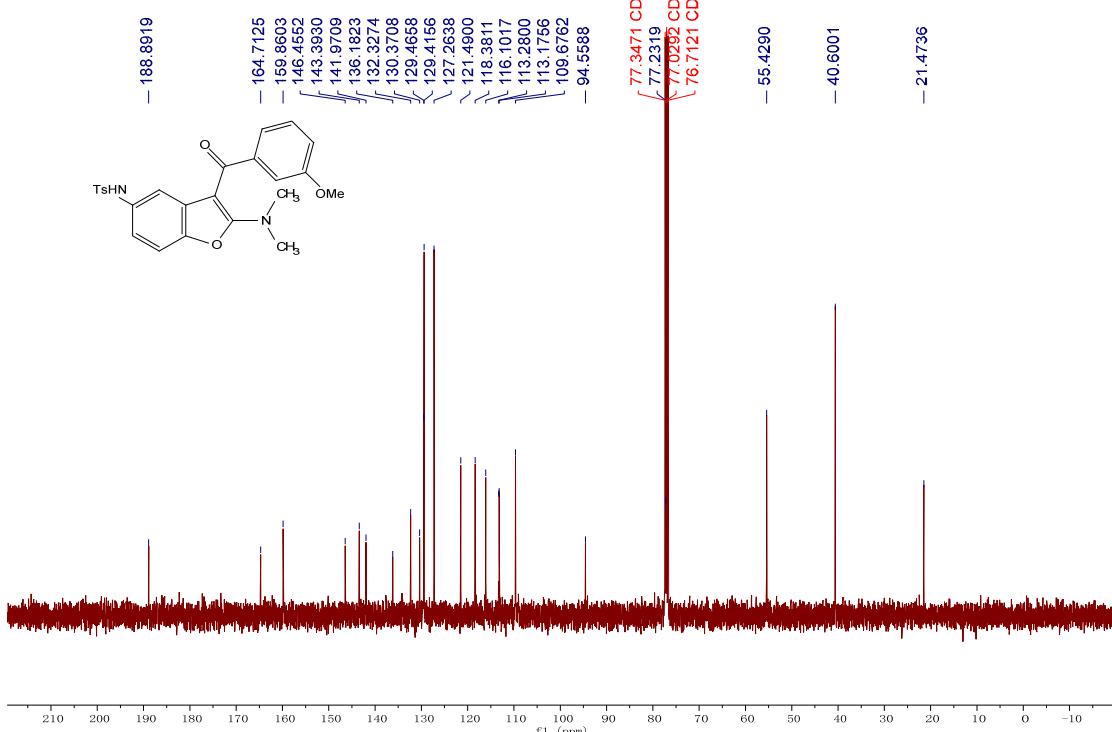
zzk-5d.1.fid



^{13}C NMR spectrum of **5d** (CDCl_3 , 100 MHz)

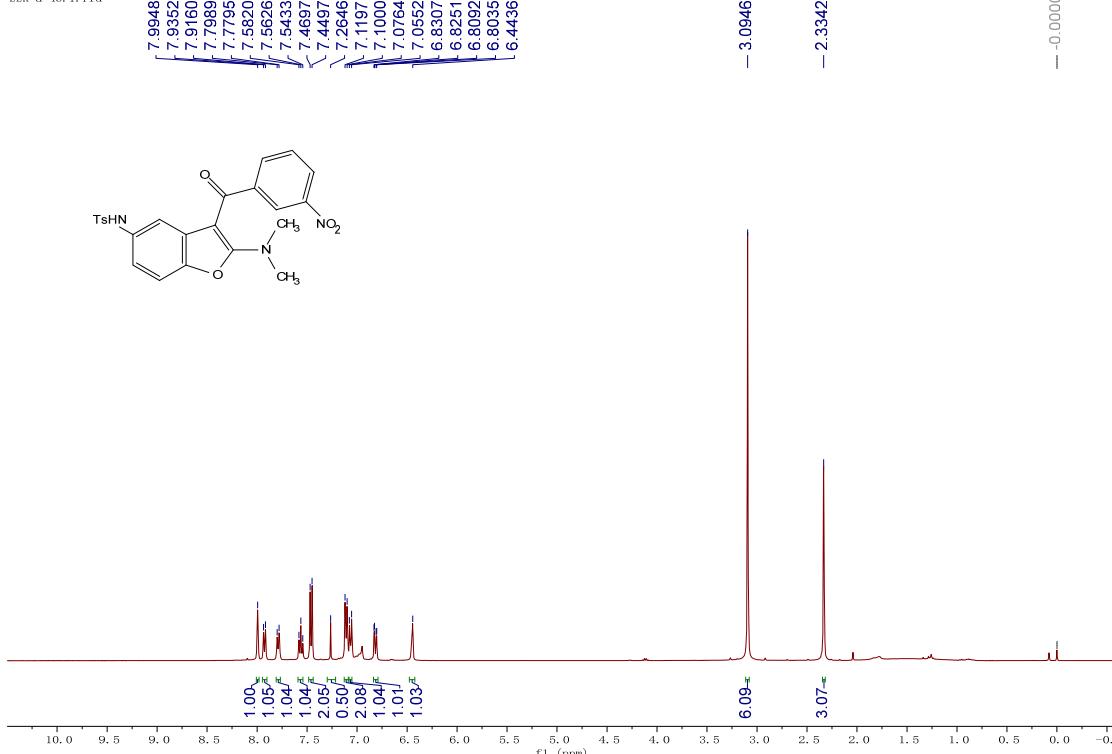


zzk-A-44.2. fid



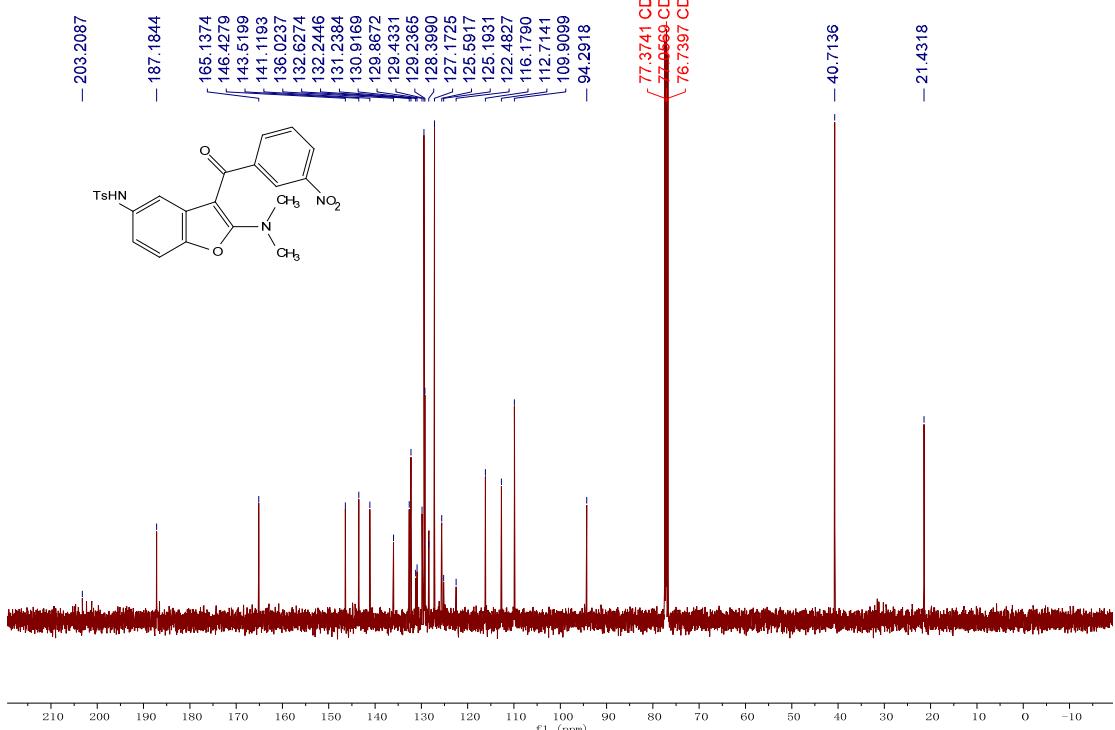
¹³C NMR spectrum of **5e** (CDCl₃, 100 MHz)

zzk-a-43.1. fid



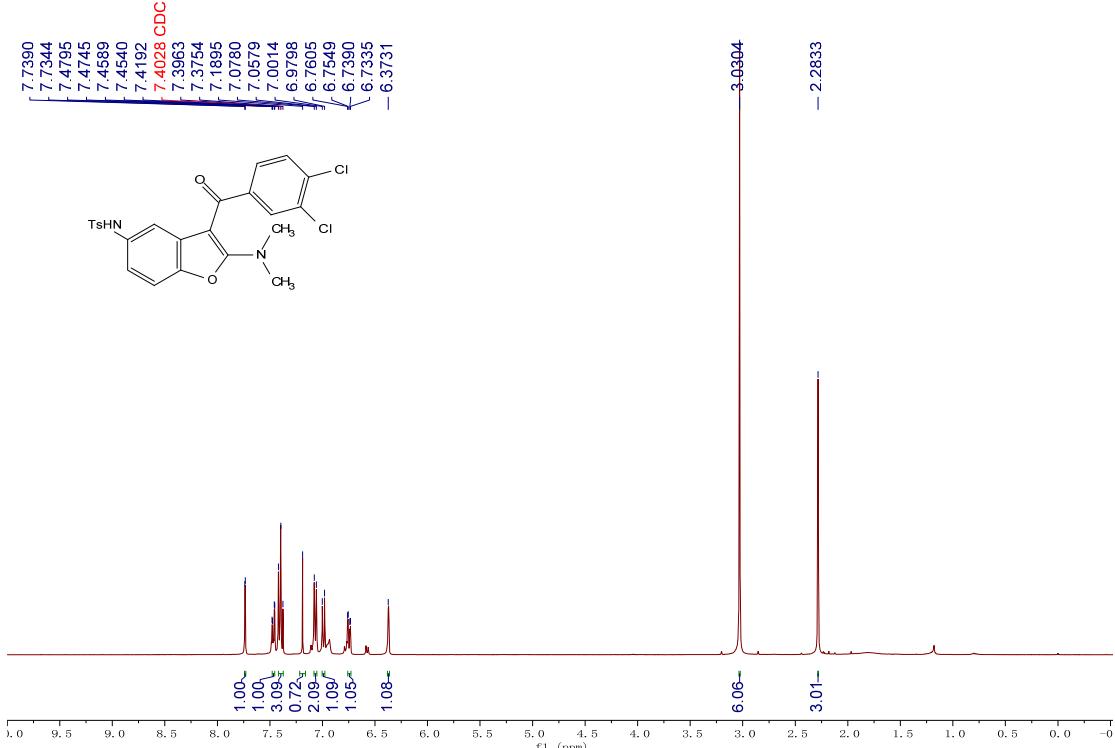
¹H NMR spectrum of **5f** (CDCl₃, 400 MHz)

zzk-a-43-e, 1, fid



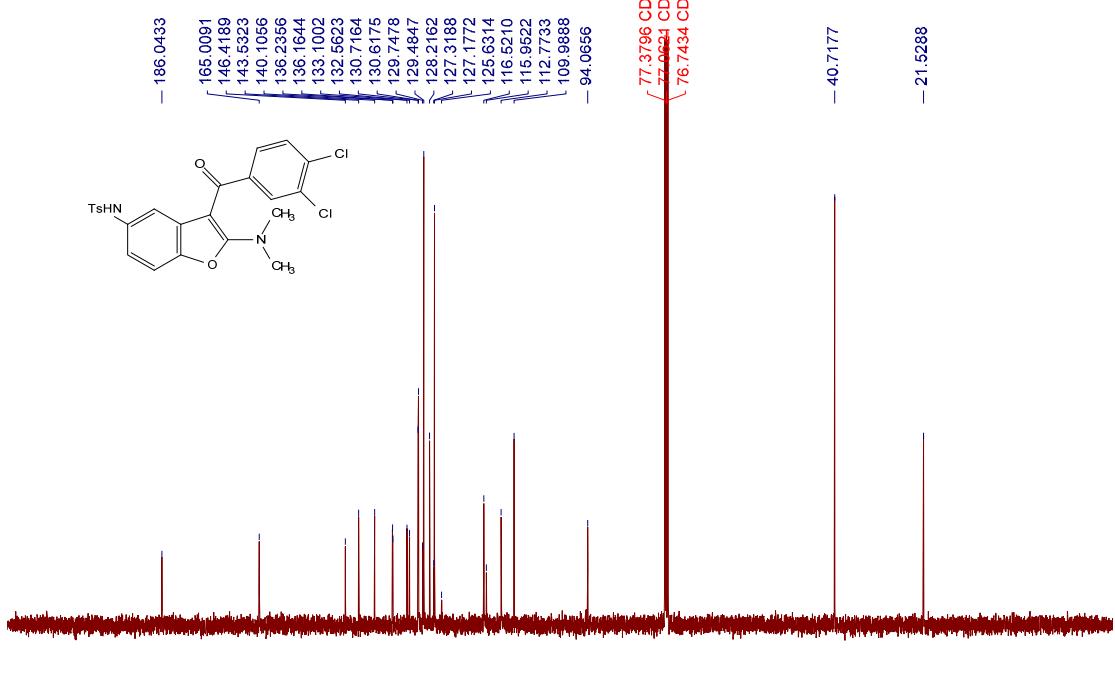
^{13}C NMR spectrum of **5f** (CDCl_3 , 100 MHz)

zzk-a-8, 1, fid



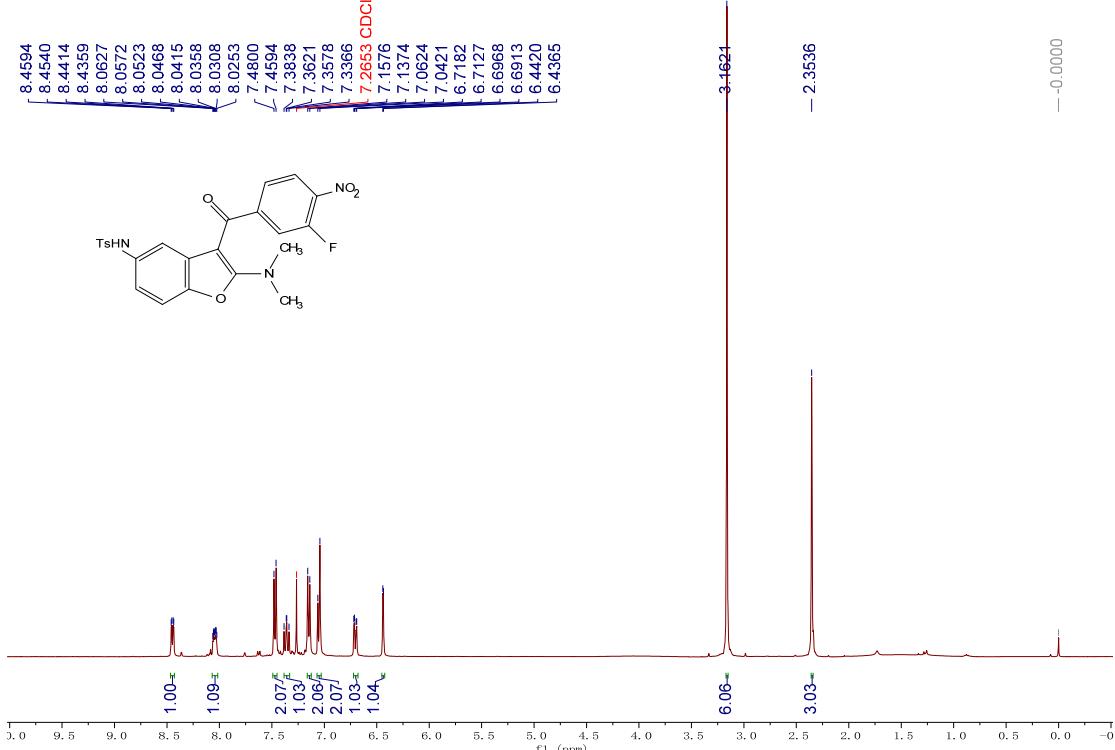
^1H NMR spectrum of **5g** (CDCl_3 , 400 MHz)

zzk-a-8c.1.fid



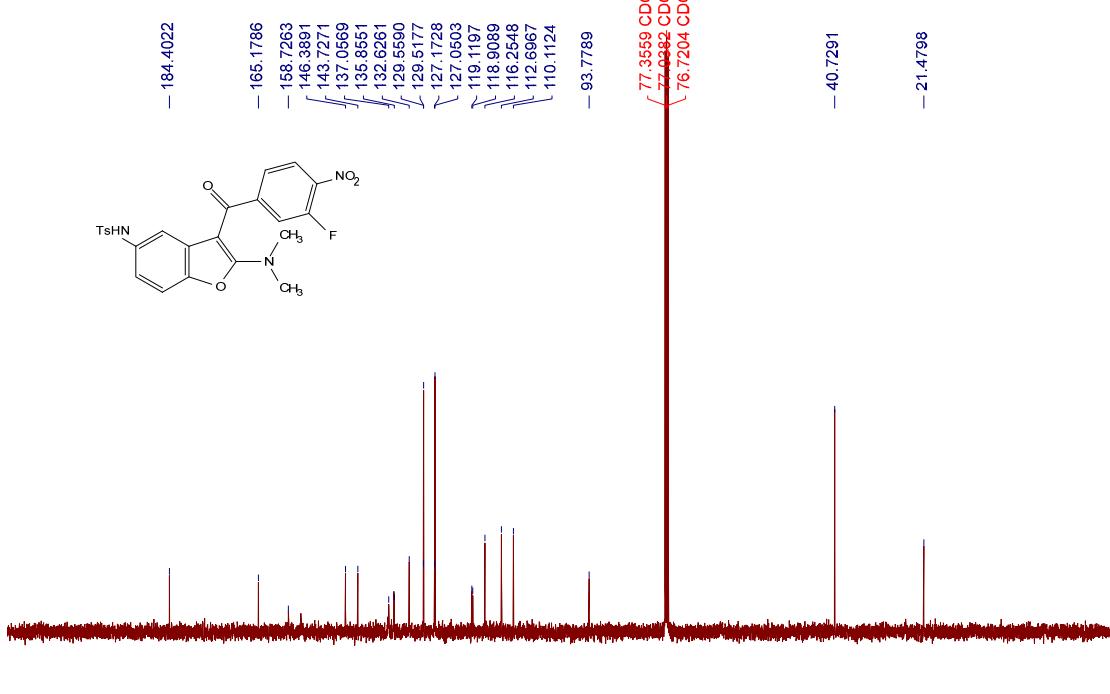
^{13}C NMR spectrum of **5g** (CDCl_3 , 100 MHz)

zzk-a-41.1.fid



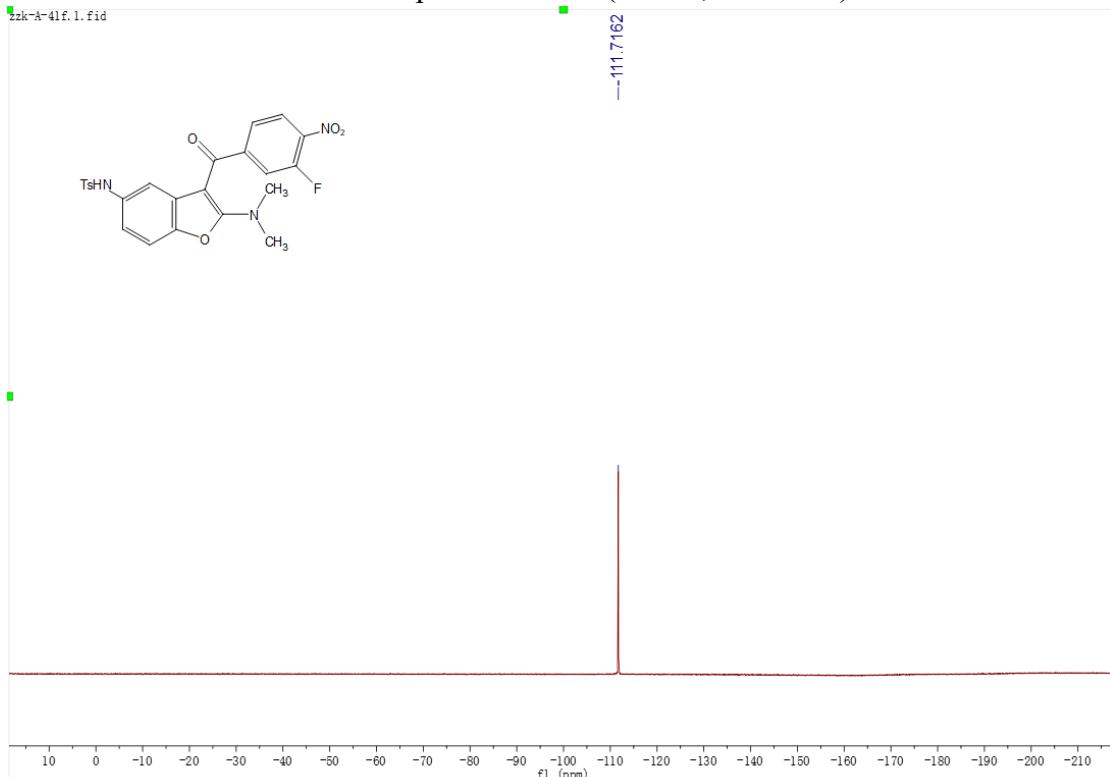
^1H NMR spectrum of **5h** (CDCl_3 , 400 MHz)

zzk-a-41-c, 1, fid



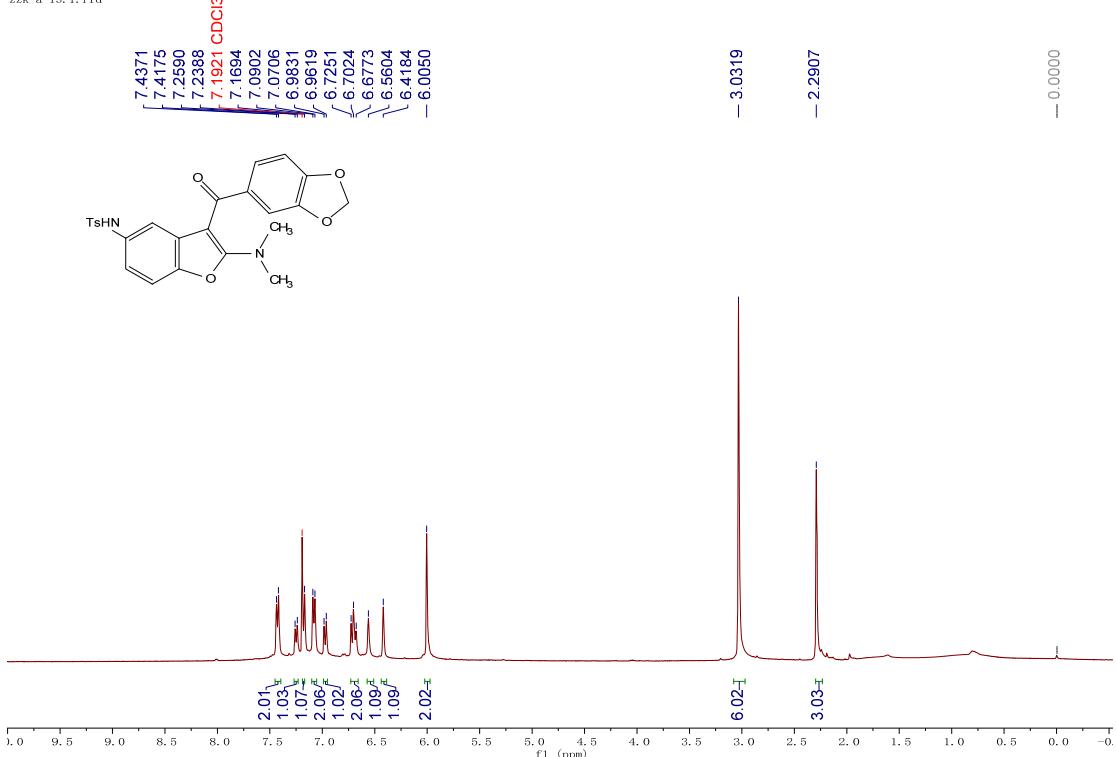
^{13}C NMR spectrum of **5h** (CDCl_3 , 100 MHz)

zzk-A-41f. 1, fid



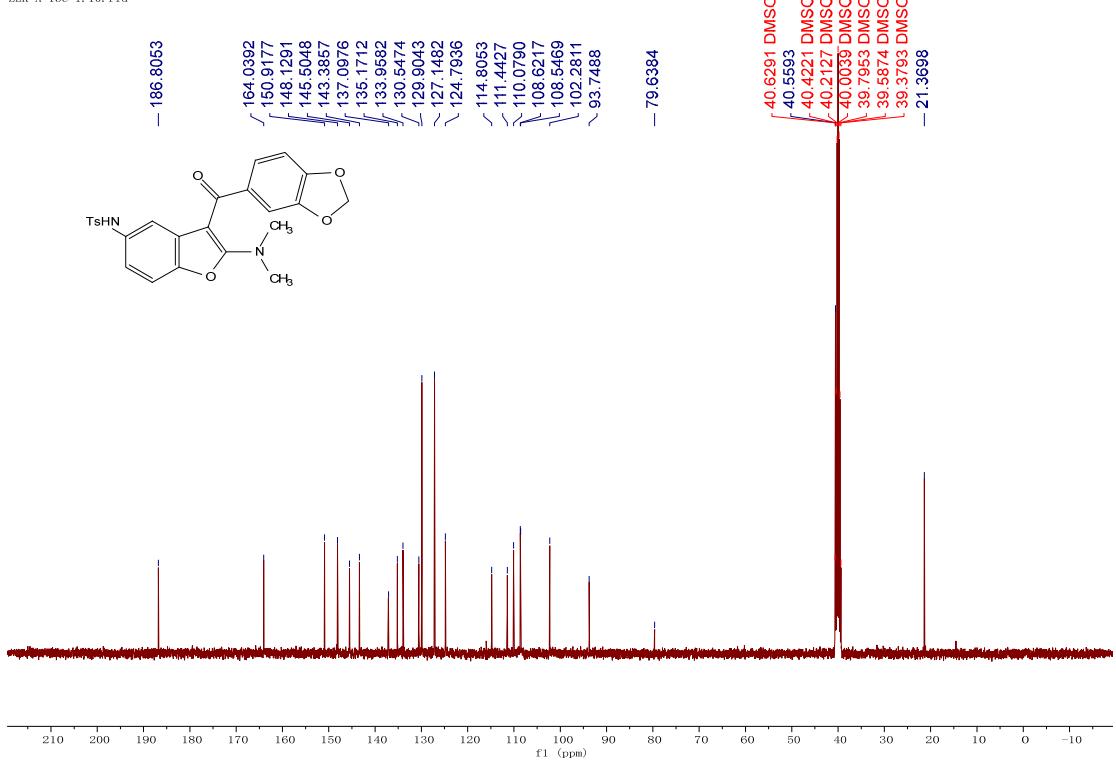
^{19}F NMR spectrum of **5h** (CDCl_3 , 376 MHz)

zzk-a-13. 1. fid



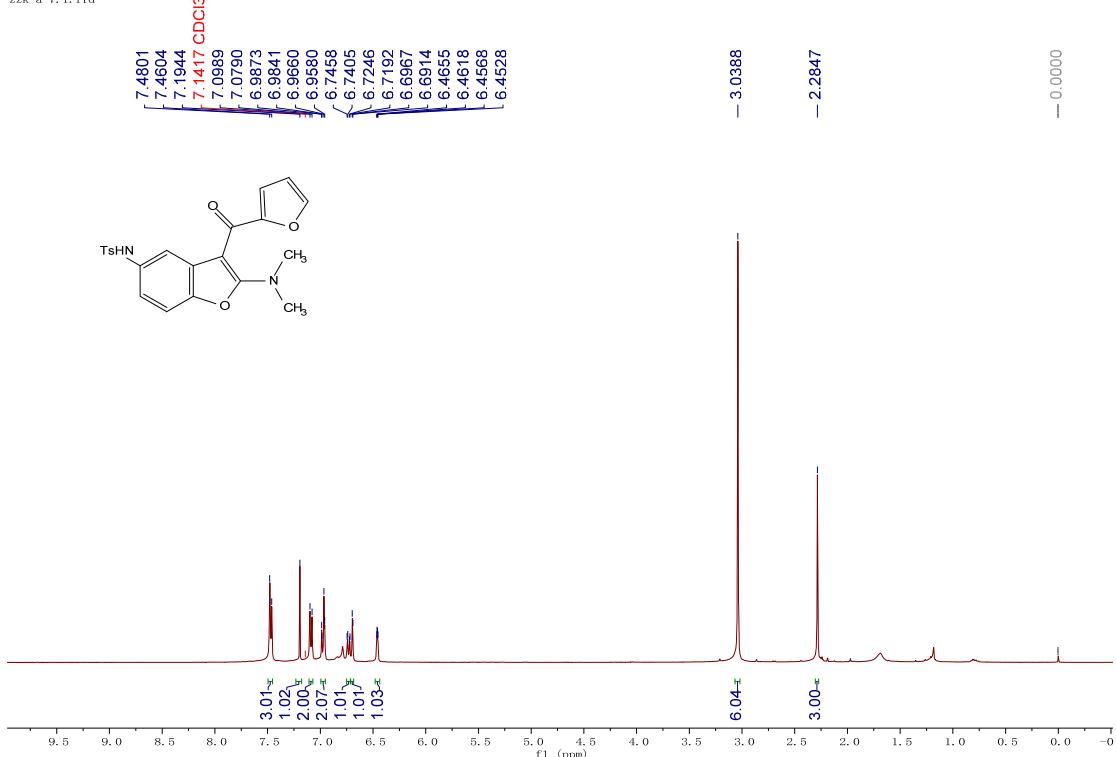
^1H NMR spectrum of **5i** (CDCl_3 , 400 MHz)

ZZK-A-13C-1. 10. fid

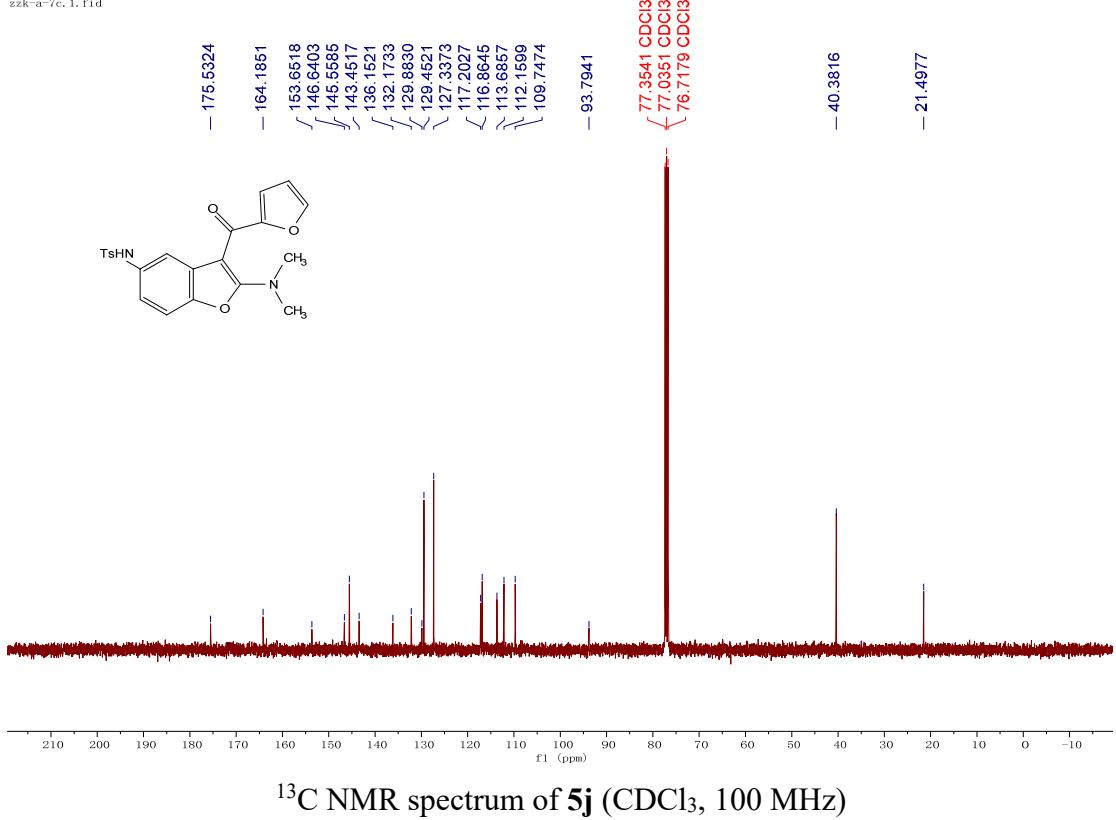


^{13}C NMR spectrum of **5i** (CDCl_3 , 100 MHz)

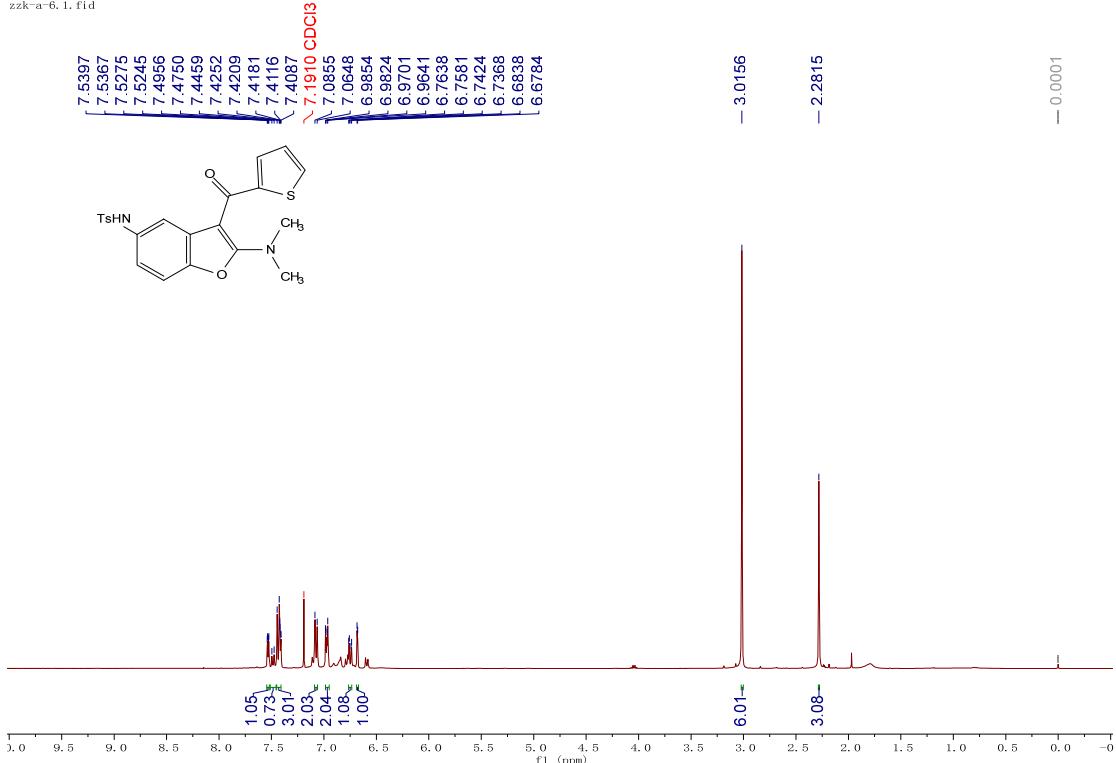
zzk-a-7.1.fid



zzk-a-7c.1.fid

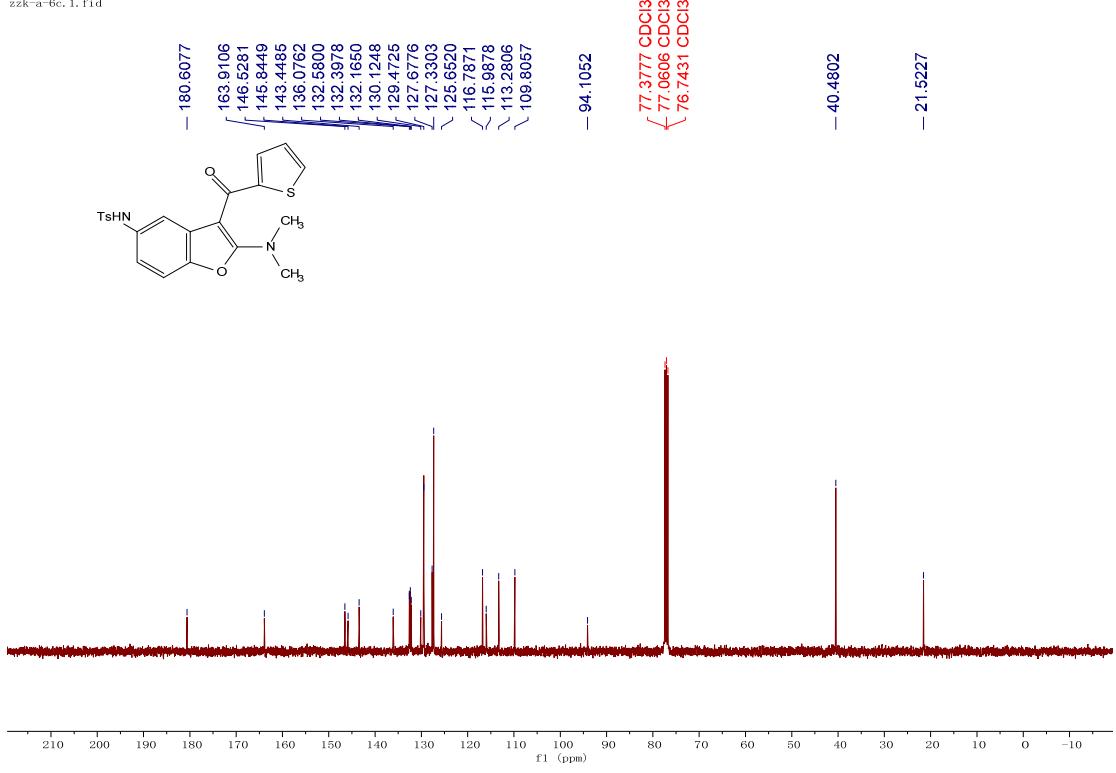


zzk-a-6.1.fid



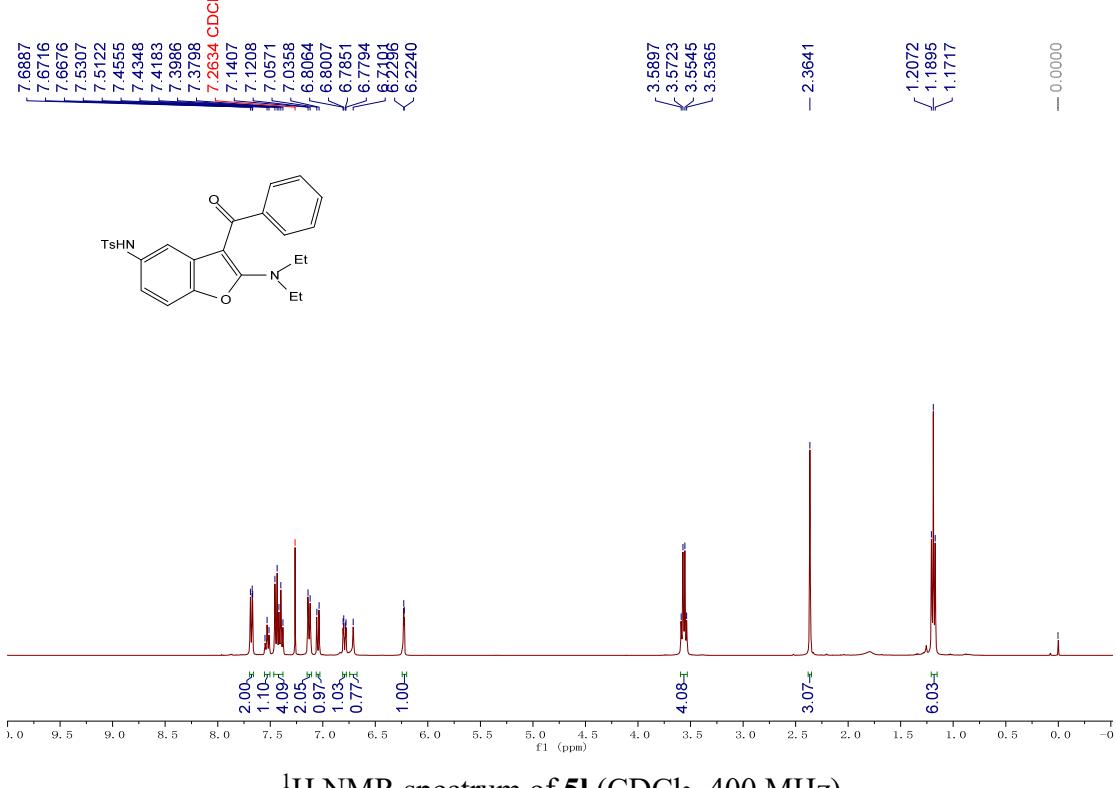
¹H NMR spectrum of **5k** (CDCl₃, 400 MHz)

zzk-a-6c.1.fid

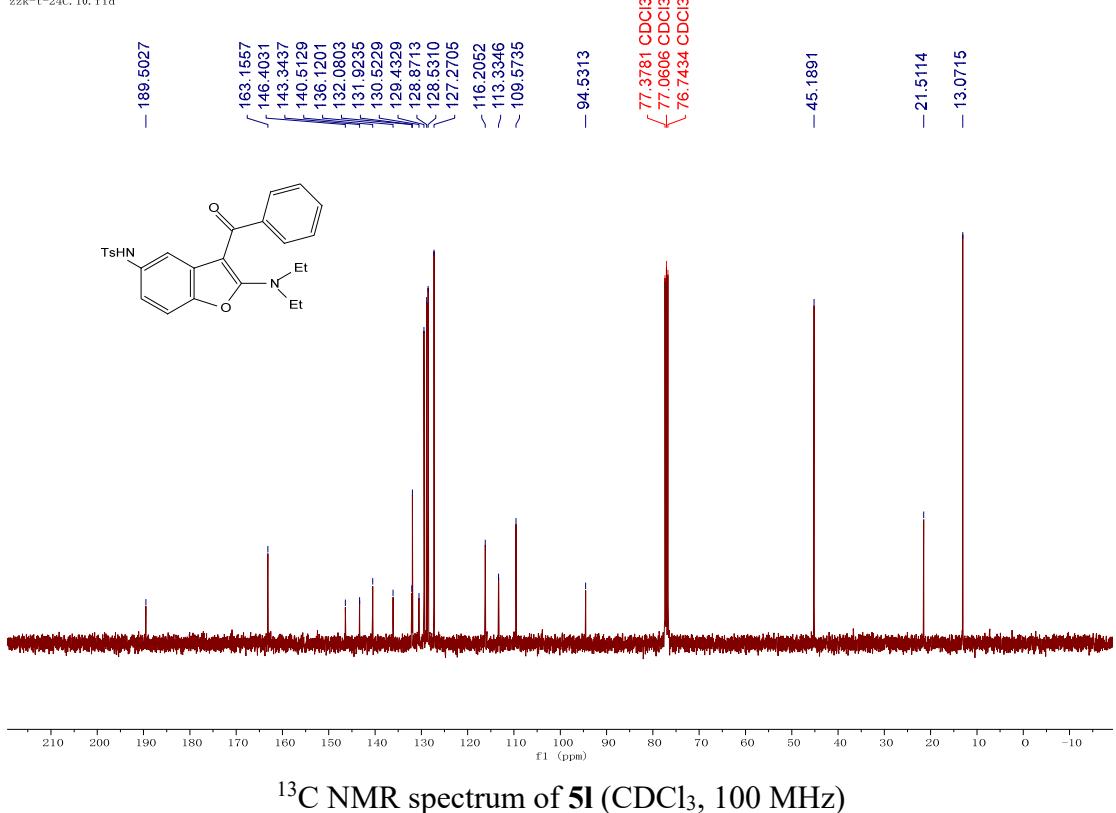


¹³C NMR spectrum of **3d** (CDCl₃, 100 MHz)

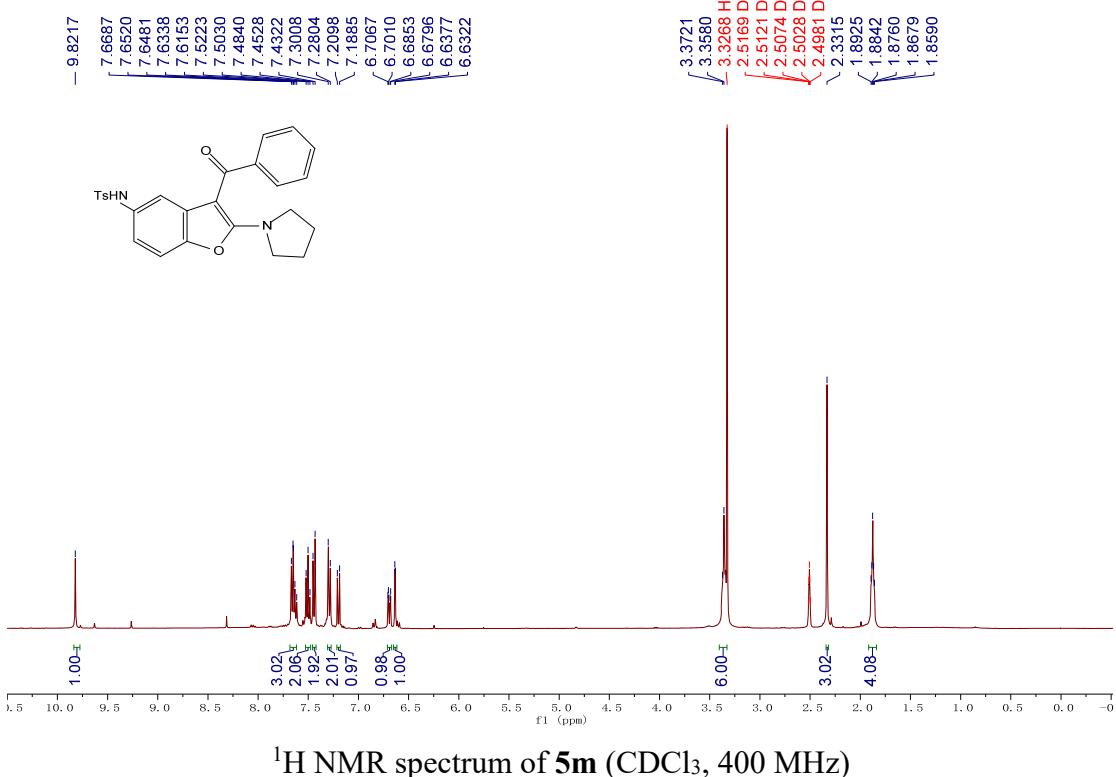
zzk-t-24.1.fid



zzk-t-24C.10.fid

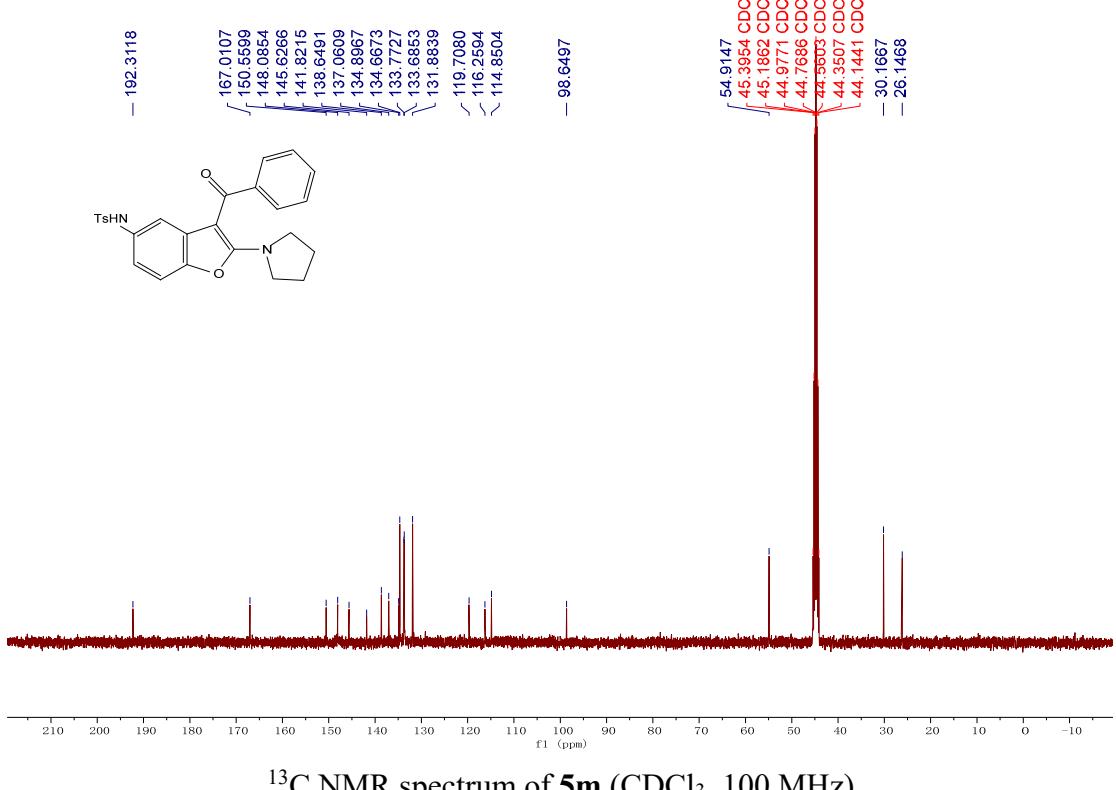


zzk-a-25-1, 10. fid



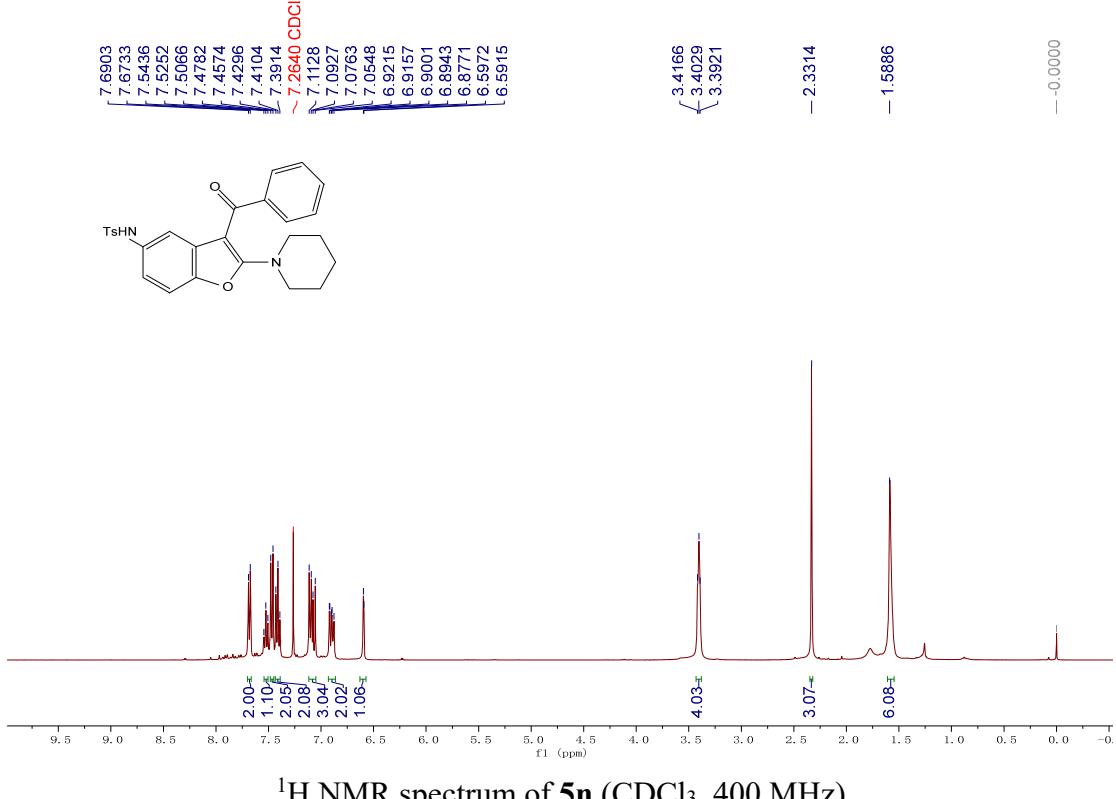
¹H NMR spectrum of **5m** (CDCl₃, 400 MHz)

ZZK-A-25. 1. fid

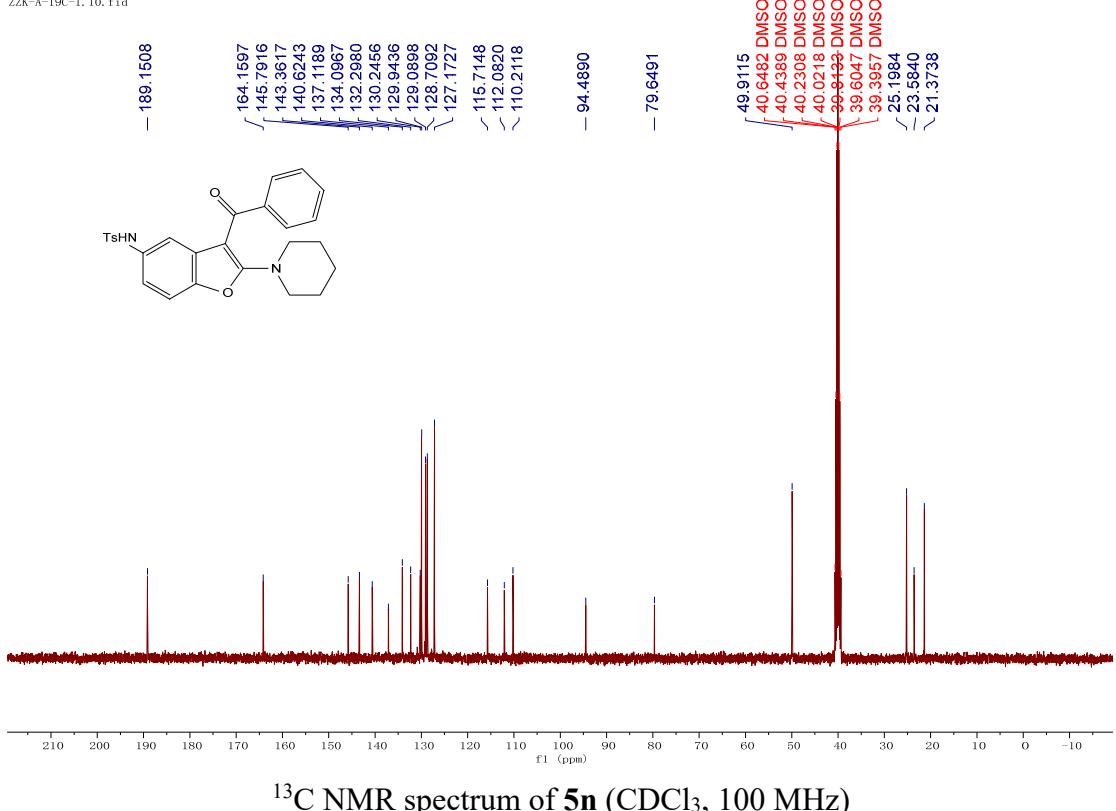


¹³C NMR spectrum of **5m** (CDCl₃, 100 MHz)

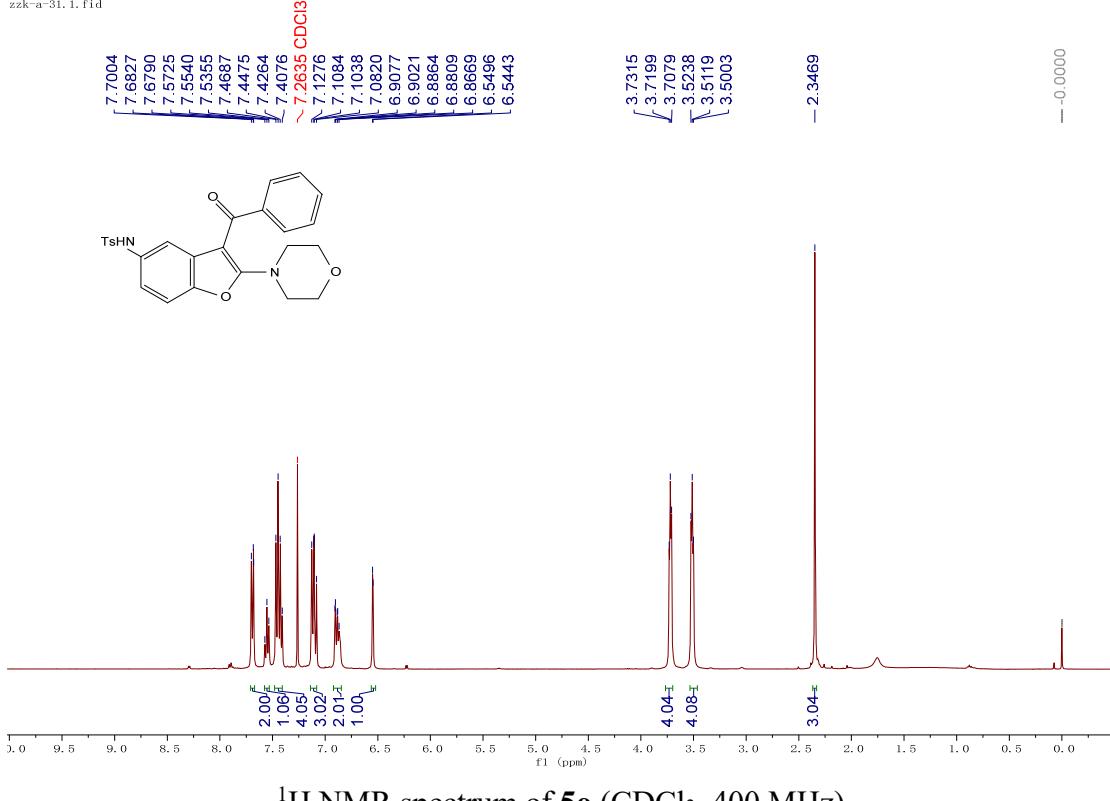
ZZK-A-19. 1. fid



ZZK-A-19C-1. 10. fid

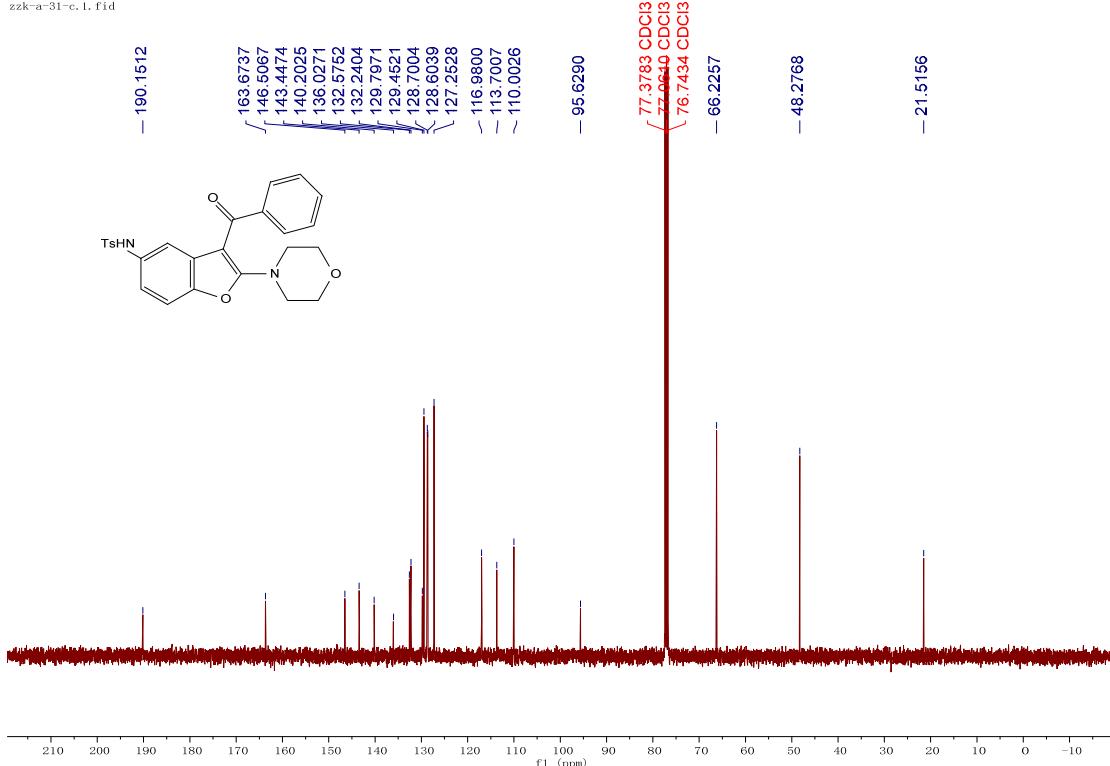


zzk-a-31.1.fid



^1H NMR spectrum of **5o** (CDCl_3 , 400 MHz)

zzk-a-31-c.1.fid



^{13}C NMR spectrum of **5o** (CDCl_3 , 100 MHz)

