Supplementary Information

2-Indolymethanols as 4-Atom-Synthons in oxa-Michael Reaction Cascade: Access to Tetracyclic Indoles

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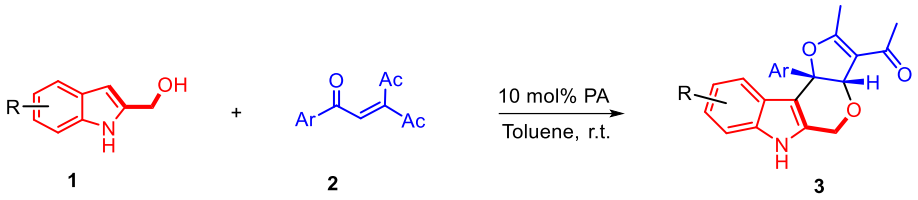
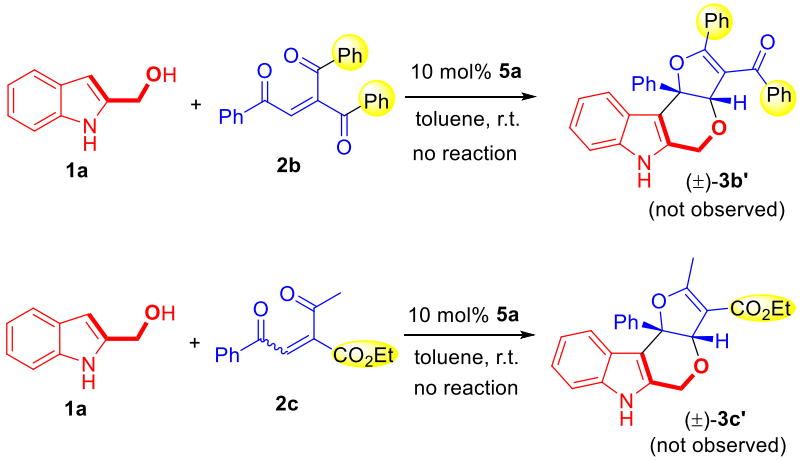
1. General Methods

Unless otherwise specified, all reactions were conducted under an inert atmosphere and anhydrous conditions. All chemicals which are commercially available were employed without further purification. Thin‐layer chromatography (TLC) was performed on silica gel plates (60F‐254) using UV‐light (254 nm). Flash chromatography was conducted on silica gel (200–300 mesh). ^{1}H and ^{13}C NMR spectra were recorded at ambient temperature in d_6-DMSO and $CDCl_3$ on a 400 MHz NMR spectrometer. Chemical shifts were reported in parts per million (ppm). The data are reported as follows: for ^{1}H NMR, chemical shift in ppm from tetramethylsilane with the solvent as internal standard ($CDCl_3$ δ 7.26 ppm; d_6-DMSO δ 2.50 ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet or overlap of non-equivalent resonances), integration; for ^{13}C NMR, chemical shift in ppm from tetramethylsilane with the solvent as internal indicator ($CDCl_3$ δ 77.1 ppm; d_6-DMSO δ 2.50 ppm), multiplicity with respect to protons. All high-resolution mass spectra were obtained on a Q-TOF Micro LC/MS System ESI spectrometer to be given in m/z. trione alkenes **2** were synthesized according to modified literature-reported procedures;[1] 2-Indolymethanols **1** were either employed directly from commercial sources or prepared according to the literature.[2]

2. General Procedures for the oxa-Michael Reaction Cascade



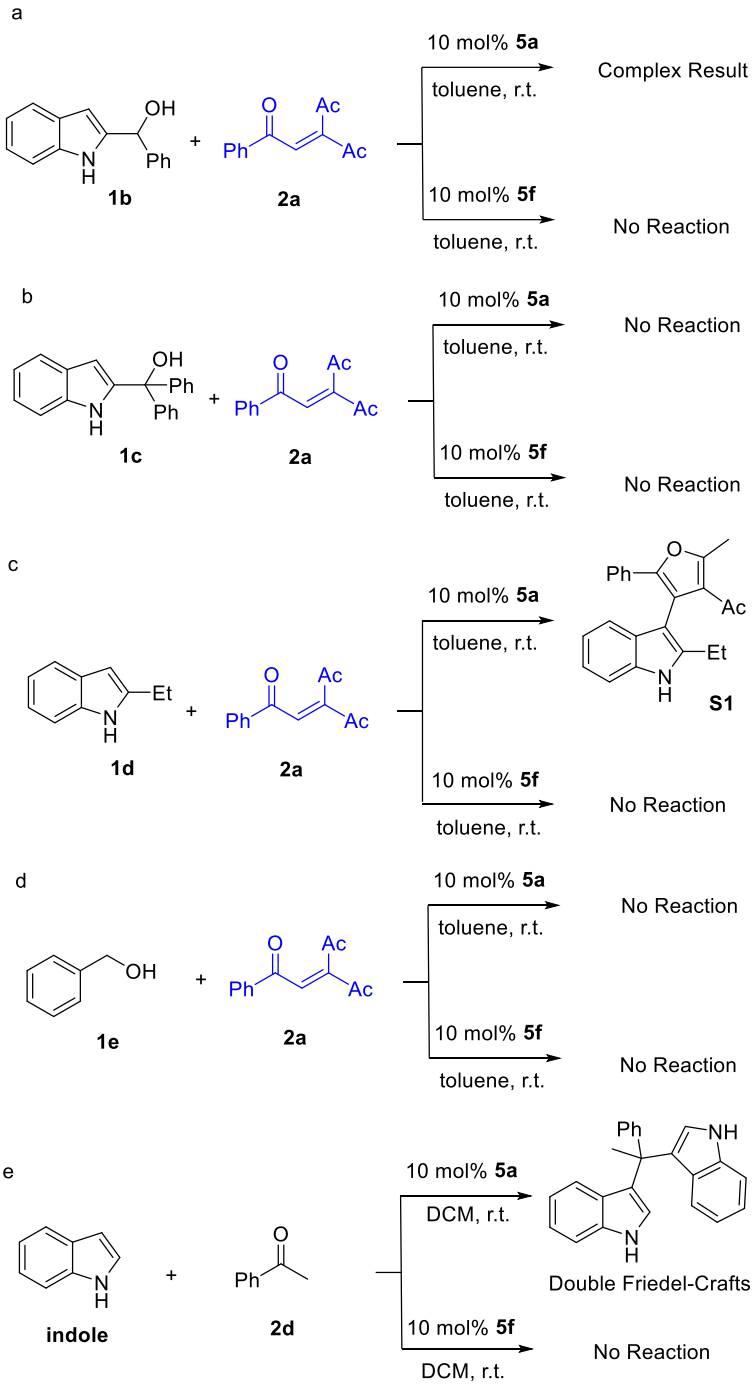
2-Indolymethanol **1** (0.12mmol) and 3-acetyl-1-phenylpent-2-ene-1,4-dione **2** (0.1mmol) (ratio of 1:2 = 1:1.2) was dissolved in toluene and PA (10mol%) was added. The reaction mixture was stirred for 0.5h at room temperature. The solvents were removed in vacuo and the crude product was separated by flash column chromatography on silica gel (petroleum ether/ethyl acetate 4:1–2:1).



To further examine the tolerance of trione alkene, Bz-substituted **2b** and **2c** were employed under standard conditions. However, both of them were ineffective to this reaction, which indicated that whether increasing or decreasing the activity of olefins was unfavourable.

Mechanism studies:

Firstly, 2-indolymehtanols **1b** &**1c** and 2-ethyl indole **1d** were utilized to examine the importance of the O3' nucleophilicity (Scheme S1 a-c). Under standard conditions, secondary 2-indolymethanol led to a complex result, due to the decomposition of substrate. Tertiary 2-indolymethanol gave the result with no reaction. When 2-ethyl indole was employed, strong acid catalyst **5a** afforded the 3,3'-indolylfuran **S2**. These results indicated that the formation of tetracyclic indole **3a** was initiated by the oxa-Michael addition reaction.



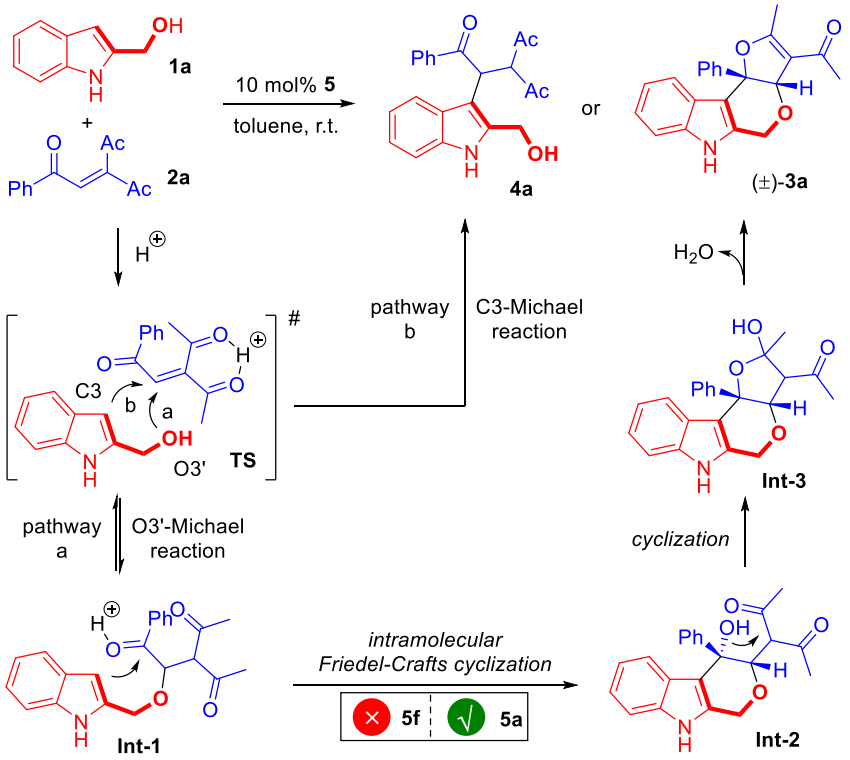
Scheme S1. Control experiments.

Weak acid **5f** failed to catalyze the C-Michael addition reaction in the cases of secondary 2-indolymethanol and tertiary 2-indolymethanol (Scheme S1 a-b), demonstrating the steric effect had some influence. Moreover, the C-Michael addition reaction between 2-ethyl indole and trione alkene was also failed under the catalysis of **5f** (Scheme S1 c). Maybe the OH group of indolylmethanol **1a** severed as a

directing group to activate the substrate via hydrogen-bonding interaction with weak acid **5f** catalyst.

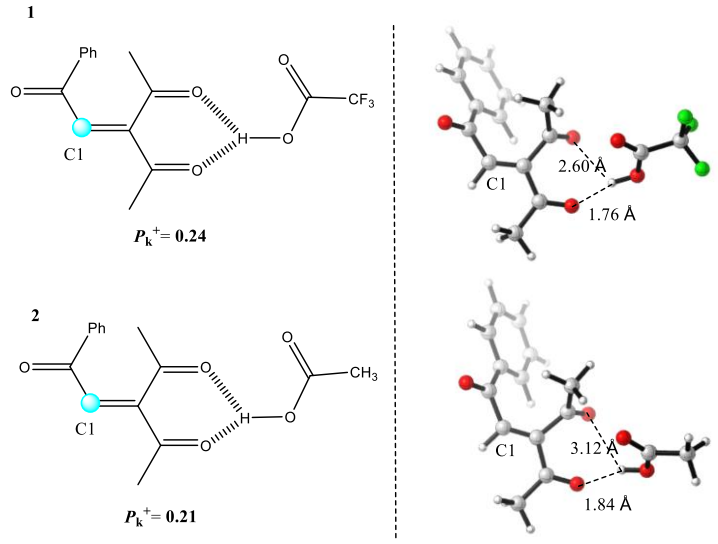
Then, benzyl alcohol **1e** was employed to examine the oxa-Michael process. As shown in Scheme S1 d, in the presence of strong acid **5a** or weak acid **5f**, starting materials were recovered after a standard reaction time, implying that the oxa-Michael addition process could be reversible.

In addition, the feasibility of Friedel-Crafts reaction between indole and acetophenone **2d** was investigated (Scheme S1 e). Notably, under the catalysis of strong acid **5a**, the double Friedel-Crafts reaction occurred smoothly (known reaction).[3] However, weak acid **5f** failed to catalyze this Friedel-Crafts reaction. So, the regioselectivity of the projected reaction stems from the intramolecular Friedel-Crafts reaction. The intramolecular Friedel-Crafts cyclization (**Int-1** to **Int 2**) can only be catalyzed by a strong acid such as **5a**. When it comes to weak acid **5f**, **Int-1** would go through a retro-oxa-Michael addition reaction, and then result in the observed C-Michael selectivity.



Scheme S2. Proposed reaction pathway.

Computational calculation



Scheme S3. The electrophilicity study of trione alkene **2a**.

The local electrophilicity (P_k^+) Parr[4] function analysis has been employed to calculate the electrophilicity of the C1 electrophilicity of **2a**. Parr function analysis is based on the calculation of Mulliken atomic spin density (ASD) of the free radical anion corresponding to the study molecule. The calculation results show that the P_k^+ (0.24) of C1 (blue highlight) of molecule 1 is higher than that of C1 (blue highlight) of molecule 2. So, in the presence of strong acid catalyst, trione alkene **2a** has a stronger electrophilicity, which also contributes to the oxa-Michael process (Fig. S1).

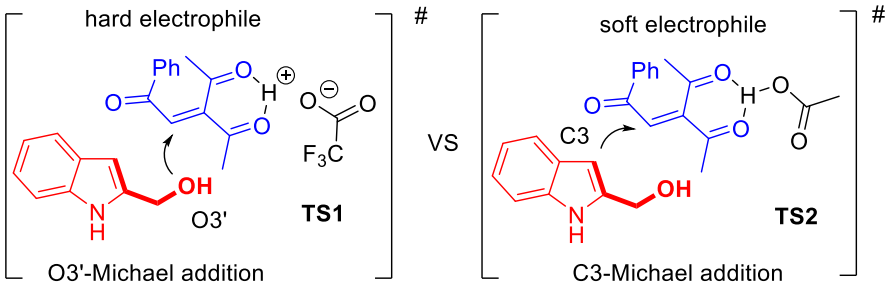
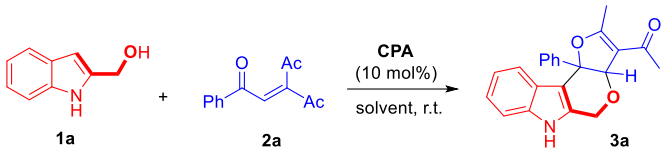
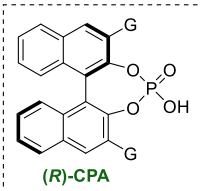


Figure S1. O3'-Michael addition vs C3-Michael addition.

Table S1. Preliminary investigations of catalytic asymmetric version.





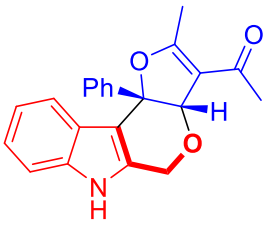
CPA1, G = 9-anthracenyl
CPA2, G = 2,4,6-(i-Pr)$_3$C$_6$H$_2$
CPA3, G = 3,5-(CH$_3$)$_2$C$_6$H$_3$
CPA4, G = SiPh$_3$
CPA5, G = 3,5-(CF$_3$)$_2$C$_6$H$_3$
CPA6, G = 1-naphthyl
CPA7, G = 2-naphthyl

Entry	Cat.	solvent	yield (%)[b]	*ee* (%)[c]
1	**CPA1**	toluene	78	12
2	**CPA2**	toluene	<5	-
3	**CPA3**	toluene	58	8
4	**CPA4**	toluene	<5	-
5	**CPA5**	toluene	45	0
6	**CPA6**	toluene	80	14
7	**CPA7**	toluene	88	22
8	**CPA7**	THF	<5	-
9	**CPA7**	EtOAc	86	10
10	**CPA7**	CH_2Cl_2	85	15

[a]Unless indicated otherwise, the reaction was carried out at 0.1 mmol scale and catalyzed by 1 mol% of **CPA** in a solvent (1 mL) at rt for 0.5 h, and the molar ratio of **1a**:**2a** was 1:1.2, the d.r. of **3a** was > 20:1. [b]Isolated yield. [c]The *ee* value was determined by HPLC. EA = ethyl acetate.

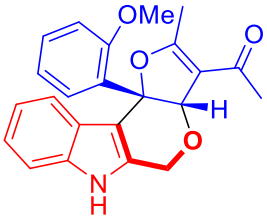
3. Characterization of Tetracyclic Indoles

2-Methyl-10c-phenyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3a:**



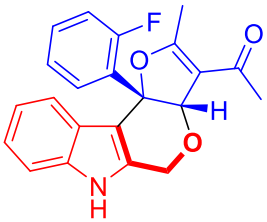
A colorless solid; 33.1 mg; isolated yield=96%; m.p. 117.6-118.6℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28 (s, 1H), 7.37 – 7.21 (m, 6H), 7.14 – 7.11 (m, 1H), 7.07 – 7.05 (m, 1H), 6.98 – 6.91 (m, 1H), 5.05 (s, 1H), 4.97 – 4.89 (m, 2H), 2.50 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 195.3, 173.9, 141.5, 135.9, 135.2, 128.5, 127.7, 125.4, 125.3, 122.5, 120.6, 119.5, 112.0, 111.2, 107.7, 87.3, 87.0, 60.3, 29.0, 15.6; HRMS (ESI) m/z calcd for $C_{22}H_{20}NO_3$ $[M + H]^+$ = 346.1438, found = 346.1430.

10c-(2-methoxyphenyl)-2-methyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3b:**



A colorless oil; 36.8 mg; isolated yield=98%;^{1}H NMR (400 MHz, $CDCl_3$) δ 8.39 (s, 1H), 7.83 – 7.56 (m, 1H), 7.33 – 7.18 (m, 2H), 7.13 (d, *J* = 7.9 Hz, 1H), 7.05 – 7.02 (m, 2H), 6.93 – 6.89 (m, 1H), 6.74 (d, *J* = 8.1 Hz, 1H), 5.36 (s, 1H), 4.81 (d, *J* = 1.7 Hz, 2H), 3.38 (s, 3H), 2.45 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 173.1, 156.6, 135.6, 135.4, 129.4, 128.9, 125.9, 125.5, 121.8, 120.7, 120.1, 119.0, 114.2, 112.6, 111.2, 106.5, 86.1, 82.8, 60.7, 55.5, 29.1, 15.7; HRMS (ESI) m/z calcd for $C_{24}H_{24}NO_5$ $[M + H]^+$ = 376.1543, found = 376.1544.

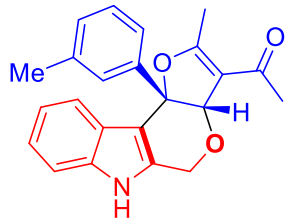
10c-(2-fluorophenyl)-2-methyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3c:**



A colorless oil; 32.7 mg; isolated yield=86%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (s, 1H), 7.71 – 7.67 (m, 1H), 7.31 – 7.17 (m, 3H), 7.15 – 7.03 (m, 2H), 7.00 – 6.82 (m,

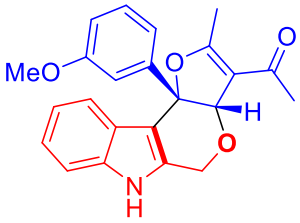
2H), 5.25 (d, *J* = 2.8 Hz, 1H), 5.05 – 4.76 (m, 2H), 2.47 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.4, 173.2, 159. 8 (d, *J* = 246 Hz), 137.3, 135.8, 135.1, 129.9(d, *J* = 9 Hz), 128.5 (d, *J* = 9 Hz), 128.3, 126.6, 126.6, 125.3, 124.1 (d, *J* = 3 Hz), 122.2, 121.8, 120.4, 118.8, 116.7 (d, *J* = 22 Hz), 113.6, 113.2, 111.3, 110.8, 105.9, 84.7, 84.6, 83.9, 83.9, 60.7, 29.1, 15.5; HRMS (ESI) m/z calcd for $C_{22}H_{19}FNO_3$ $[M + H]^+$ = 364.1343, found = 364.1344.

2-methyl-10c-(m-tolyl)-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3d:**



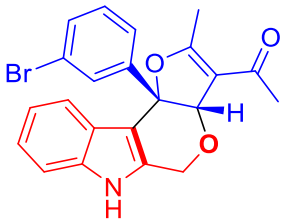
A colorless solid; 35.6 mg; isolated yield=94%; m.p. 117.6-118.6℃; ^{1}H NMR (400 MHz, DMSO) δ 11.32 (s, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.22 – 7.18 (m, 1H), 7.15 – 6.97 (m, 4H), 6.91 (d, *J* = 7.7 Hz, 1H), 6.83 (d, *J* = 7.4 Hz, 1H), 5.07 – 5.03 (m, 2H), 4.90 (d, *J* = 14.8 Hz, 1H), 2.43 (s, 3H), 2.25 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 194.6, 173.1, 142.5, 137.9, 136.8, 136.2, 128.6, 126.3, 125.4, 122.9, 121.7, 119.8, 118.9, 112.7, 112.1, 111.5, 106.5, 87.6, 86.1, 79.7, 60.6, 29.3, 21.6, 15.4; HRMS (ESI) m/z calcd for $C_{23}H_{21}NNaO_3$ $[M + Na]^+$ = 382.1414, found = 382.1416; IR: 3386, 2919, 1665, 1579, 1233, 755, 635.

10c-(3-methoxyphenyl)-2-methyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3e:**



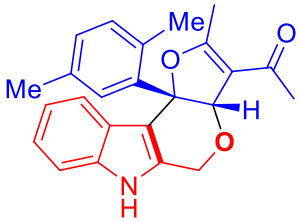
A colorless solid; 33.2 mg; isolated yield=84%; m.p. 202.2-203.0℃; ^{1}H NMR (400 MHz, DMSO) δ 11.40 (s, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.26 – 7.22 (m, 1H), 7.03 (s, 1H), 6.93 (d, *J* = 7.8 Hz, 1H), 6.90 – 6.75 (m, 4H), 5.08 – 5.04 (m, 2H), 4.89 (d, *J* = 14.8 Hz, 1H), 3.69 (s, 3H), 2.42 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 194.6, 173.0, 159.5, 144.2, 136.9, 136.2, 129.9, 125.4, 121.7, 119.8, 118.8, 118.2, 112.9, 112.4, 112.3, 112.1, 106.2, 87.5, 85.9, 60.6, 55.4, 29.3, 15.4; HRMS (ESI) m/z calcd for $C_{23}H_{21}NNaO_4$ $[M + Na]^+$ = 398.1363, found = 398.1362; IR: 3284, 2925, 1651, 1574, 1236, 741, 701.

10c-(3-bromophenyl)-2-methyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3f:**



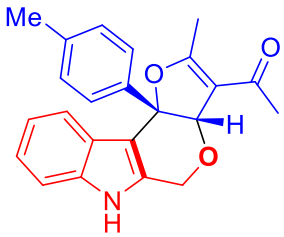
A colorless solid; 41.6 mg; isolated yield=98%; m.p. 214.4-215.6℃; ^{1}H NMR (400 MHz, DMSO) δ 11.39 (s, 1H), 7.51 – 7.44 (m, 1H), 7.43 – 7.34 (m, 3H), 7.32 – 7.28 (m, 1H), 7.06 – 7.02 (m, 1H), 6.86 (d, *J* = 6.4 Hz, 2H), 5.12 – 5.08 (m, 2H), 4.89 (d, *J* = 14.8 Hz, 1H), 2.43 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (10o MHz, DMSO) δ 194.6, 172.8, 145.2, 137.2, 136.2, 131.0, 128.6, 125.2, 125.1, 122.2, 121.9, 120.0, 118.5, 112.7, 112.2, 105.7, 87.0, 85.7, 60.6, 29.3, 15.3; HRMS (ESI) m/z calcd for $C_{22}H_{18}BrNNaO_3$ $[M + Na]^+$ = 446.0362, found = 446.0362; IR: 3310, 2933, 1663, 1576, 1230, 800, 750.

1-(10c-(2,5-dimethylphenyl)-2-methyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3g:**



A colorless solid; 26.1 mg; isolated yield=80%; m.p. 212.9-213.8℃; ^{1}H NMR (400 MHz, DMSO) δ 11.22 (s, 1H), 7.33 (d, *J* = 7.9 Hz, 1H), 7.19 (d, *J* = 1.9 Hz, 1H), 7.01 – 6.97 (m, 2H), 6.87 – 6.78 (m, 3H), 5.23 (s, 1H), 4.93 – 4.73 (m, 2H), 3.75 (s, 3H), 3.32 (s, 3H), 2.40 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 194.5, 172.1, 153.6, 150.8, 136.8, 135.8, 131.0, 125.6, 121.3, 119.6, 118.5, 115.1, 114.3, 113.3, 112.3, 111.9, 105.1, 85.9, 82.4, 60.8, 56.7, 55.8, 29.3, 15.3; HRMS (ESI) m/z calcd for $C_{24}H_{24}NO_3$ $[M + H]^+$ = 374.1751, found = 374.1759; IR: 3259, 2920, 1661, 1580, 1239, 760, 685.

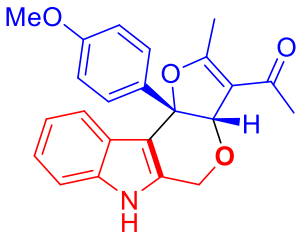
1-((3aS,10cS)-2-methyl-10c-(p-tolyl)-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3h:**



A colorless solid; 36.0 mg; isolated yield=99%; m.p. 175.7-176.5℃; ^{1}H NMR (400 MHz, DMSO) δ 11.31 (s, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.18 –7.10 (m, 4H), 7.05 – 6.98 (m, 1H), 6.89 (d, *J* = 7.7 Hz, 1H), 6.84 – 6.80 (m, 1H), 5.10 – 4.96 (m, 2H), 4.89 (d, *J* = 14.8 Hz, 1H), 2.42 (s, 3H), 2.24 (s, 3H), 2.17 (s, 3H); ^{13}C NMR (100 MHz,

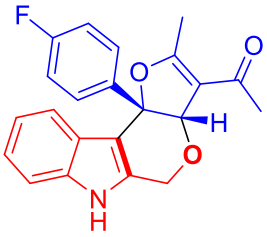
DMSO) δ 194.5, 173.1, 139.4, 137.1, 136.9, 136.3, 129.3, 125.8, 125.4, 121.7, 119.7, 118.9, 112.7, 112.1, 106.4, 87.6, 86.1, 60.7, 29.2, 21.02, 15.4; HRMS (ESI) m/z calcd for $C_{23}H_{21}NNaO_3$ $[M + Na]^+$ = 382.1414, found = 382.1414; IR: 3320, 2925, 1666, 1586, 1235, 755, 710.

10c-(4-methoxyphenyl)-2-methyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3i:**



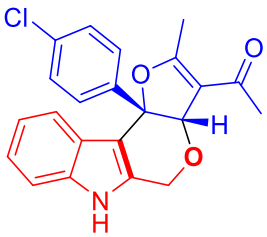
A colorless solid; 32.6 mg; isolated yield=83%; m.p. 206.9-207.5℃; ^{1}H NMR (400 MHz, DMSO) δ 11.38 (s, 1H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.18 (d, *J* = 8.8 Hz, 1H), 7.04 – 7.00 (m, 1H), 6.90 – 6.81 (m, 1H), 5.09 – 4.95 (m, 1H), 4.89 (d, *J* = 14.8 Hz, 1H), 3.70 (s, 1H), 2.42 (s, 1H), 2.18 (s, 1H); ^{13}C NMR (100 MHz, DMSO) δ 194.6, 173.1, 158.9, 136.9, 136.3, 134.0, 127.1, 125.5, 121.7, 119.8, 118.9, 114.1, 112.7, 112.1, 106.4, 87.5, 86.1, 60.6, 55.5, 29.2, 15.4; HRMS (ESI) m/z calcd for $C_{23}H_{22}NO_4$ $[M + H]^+$ = 376.1543, found = 376.1546; IR: 3402, 2912, 1662, 1565, 1239, 742, 630.

10c-(4-fluorophenyl)-2-methyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3j:**



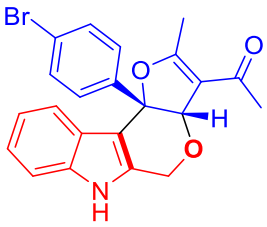
A colorless solid; 36.7 mg; isolated yield=96%; m.p. 217.7-219.3℃; ^{1}H NMR (400 MHz, DMSO) δ 11.47 (s, 1H), 7.38 (d, *J* = 8.1 Hz, 1H), 7.34 – 7.31 (m, 2H), 7.16 – 7.11 (m, 2H), 7.07 – 7.01 (m, 1H), 6.86 – 6.83 (m, 2H), 5.05 (d, *J* = 17.1 Hz, 2H), 4.91 (d, *J* = 14.8 Hz, 1H), 2.43 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 194.6, 172.9, 161.8 (d, *J* = 242 Hz), 138.4 (d, *J* = 3 Hz), 137.0, 136.3, 128.1 (d, *J* = 8 Hz), 125.3, 121.8, 119.9, 118.7, 115.5 (d, *J* = 22 Hz), 112.6, 112.2, 106.1, 87.3, 85.9, 60.7, 29.3, 15.3; HRMS (ESI) m/z calcd for $C_{22}H_{18}FNNaO_3$ $[M + Na]^+$ = 386.1163, found = 386.1163; IR: 3397, 2924, 1666, 1578, 1231, 751, 709.

10c-(4-chlorophenyl)-2-methyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3k:**



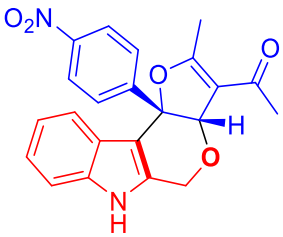
A colorless solid; 37.1 mg; isolated yield=98%; m.p. 221.3-222.7℃; ^{1}H NMR (400 MHz, DMSO) δ 11.52 (s, 1H), 7.41 – 7.34 (m, 3H), 7.34 – 7.27 (m, 2H), 7.06 – 7.00 (m, 1H), 6.91 – 6.80 (m, 2H), 5.03 (d, *J* = 4.5 Hz, 2H), 4.91 (d, *J* = 14.8 Hz, 1H), 2.43 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 194.6, 172.9, 141.4, 137.1, 136.3, 132.5, 128.7, 127.9, 125.2, 121.8, 119.9, 118.6, 112.6, 112.2, 105.8, 87.2, 85.8, 60.7, 29.3, 15.3; HRMS (ESI) m/z calcd for $C_{22}H_{18}ClNNaO_3$ $[M + Na]^+$ = 402.0867, found = 402.0867; IR: 3397, 2931, 1669, 1581, 1231, 751, 671.

10c-(4-bromophenyl)-2-methyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3l:**



A colorless solid; 39.0 mg; isolated yield=92%; m.p. 230.6-232.0℃; ^{1}H NMR (400 MHz, DMSO) δ 11.37 (s, 1H), 7.50 (d, *J* = 8.6 Hz, 2H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.25 (d, *J* = 8.6 Hz, 2H), 7.06 – 7.02 (m, 1H), 6.88 – 6.83 (m, 2H), 5.11 – 4.99 (m, 2H), 4.90 (d, *J* = 14.8 Hz, 1H), 2.43 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 194.5, 172.9, 141.9, 137.1, 136.3, 131.7, 128.3, 125.2, 121.9, 121.1, 119.9, 118.7, 112.6, 112.2, 105.8, 87.2, 85.8, 29.3, 15.3; HRMS (ESI) m/z calcd for $C_{22}H_{18}BrNNaO_3$ $[M + Na]^+$ = 446.0362, found = 446.0362; IR: 3303, 2927, 1666, 1581, 1236, 756, 637.

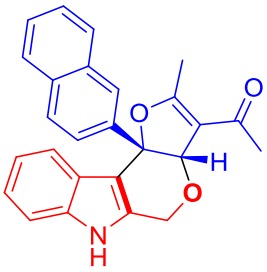
2-methyl-10c-(4-nitrophenyl)-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3m:**



A colorless oil; 34.3 mg; isolated yield=88%; ^{1}H NMR (400 MHz, DMSO) δ 11.52 (s, 1H), 8.17 (d, *J* = 8.2 Hz, 2H), 7.61 (d, *J* = 8.1 Hz, 2H), 7.39 (d, *J* = 8.1 Hz, 1H), 7.10 – 6.99 (m, 1H), 6.91 – 6.75 (m, 2H), 5.13 – 5.09 (m, 2H), 4.95 (d, *J* = 14.9 Hz, 1H), 2.46 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 194.5, 172.9, 150.0, 147.4, 137.2, 136.3, 127.6, 125.0, 123.9, 121.9, 120.1, 118.4, 112.7, 112.3, 105.3, 87.3, 85.5,

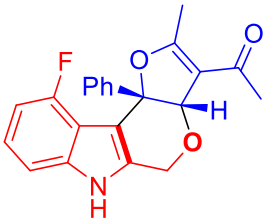
60.8, 29.3, 15.3; HRMS (ESI) m/z calcd for $C_{22}H_{18}N_2NaO_5$ $[M + Na]^+$ = 413.1108, found = 413.1108.

2-methyl-10c-(naphthalen-2-yl)-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3n:**



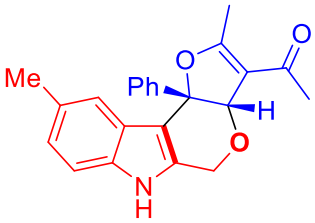
A colorless solid; 38.7 mg; isolated yield=98%; m.p. 237.8-238.6℃; ^{1}H NMR (400 MHz, DMSO) δ 11.39 (s, 1H), 7.97 (s, 2H), 7.89 – 7.76 (m, 2H), 7.59 – 7.44 (m, 2H), 7.37 (d, *J* = 8.1 Hz, 1H), 7.32 – 7.29 (m, 1H), 7.02 – 6.98 (m, 1H), 6.87 (d, *J* = 7.8 Hz, 1H), 6.77 – 6.73 (t, 1H), 5.26 – 5.07 (m, 2H), 4.96 (d, *J* = 14.8 Hz, 1H), 2.53 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (101 MHz, DMSO) δ 194.6, 173.2, 139.7, 137.1, 136.3, 132.9, 132.7, 128.6, 128.5, 127.9, 126.8, 126.7, 125.4, 124.6, 123.9, 121.8, 119.8, 118.7, 112.7, 112.1, 106.2, 87.7, 85.7, 60.7, 29.3, 15.4; HRMS (ESI) m/z calcd for $C_{26}H_{21}NNaO_3$ $[M + Na]^+$ = 418.1414, found = 418.1416; IR: 3401, 2925, 1664, 1584, 1237, 810, 744.

10-fluoro-2-methyl-10c-phenyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3o:**



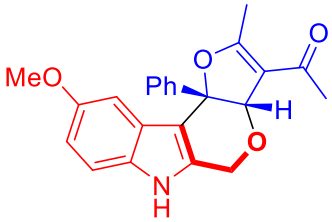
A solid; 30.9 mg; isolated yield=85%; m.p. 226.7-227.5℃; ^{1}H NMR (400 MHz, DMSO) δ 11.65 (s, 1H), 7.29 – 7.16 (m, 6H), 7.03 – 6.98 (m, 1H), 6.60 – 6.56 (m, 1H), 5.04 (d, *J* = 14.8 Hz, 1H), 4.98 – 4.85 (m, 2H), 2.45 (s, 3H), 2.16 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 194.5, 173.2, 156.4, 154.0, 142.9, 139.2, 139.1, 137.5, 128.4, 127.7, 125.9, 122.6, 122.6, 114.1, 113.9, 112.6, 108.4, 108.4, 105.2, 105.0, 104.9, 104.9, 87.2, 86.7, 60.6, 29.2, 15.3; HRMS (ESI) m/z calcd for $C_{22}H_{19}FNO_3$ $[M + H]^+$ = 364.1343, found = 346.1338; IR: 3327, 2889, 1659, 1571, 1233, 754, 698.

2,9-dimethyl-10c-phenyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3p:**



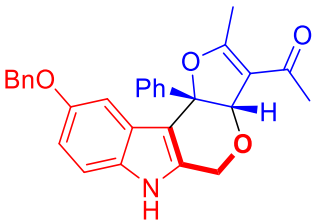
A colorless oil; 32.4 mg; isolated yield=81%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (s, 1H), 7.44 – 7.12 (m, 6H), 6.95 (d, *J* = 8.3 Hz, 1H), 6.84 (s, 1H), 5.03 (s, 1H), 4.99 – 4.82 (m, 2H), 2.51 (s, 3H), 2.27 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.2, 173.9, 141.5, 135.2, 134.2, 129.9, 128.5, 127.7, 125.6, 125.5, 124.1, 119.2, 111.9, 110.8, 107.2, 87.5, 87.1, 60.4, 29.0, 21.4, 15.6; HRMS (ESI) m/z calcd for $C_{23}H_{21}NNaO_3$ $[M + Na]^+$ = 382.1414, found = 382.1412.

9-methoxy-2-methyl-10c-phenyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3q**



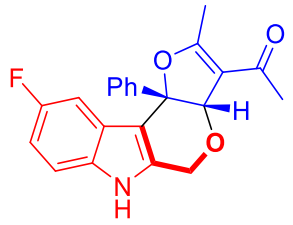
A colorless oil; 37.8 mg; isolated yield=97%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.47 (s, 1H), 7.36 – 7.20 (m, 5H), 7.17 (d, *J* = 8.8 Hz, 1H), 6.76 – 6.73 (m, 1H), 6.48 (d, *J* = 1.9 Hz, 1H), 5.03 (s, 1H), 4.90 – 4.81 (m, 2H), 3.61 (s, 3H), 2.50 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.4, 174.1, 154.4, 141.3, 136.0, 130.9, 128.5, 127.8, 125.9, 125.5, 112.2, 112.0, 111.9, 107.3, 101.8, 87.6, 86.9, 60.4, 55.7, 29.1, 15.7; HRMS (ESI) m/z calcd for $C_{23}H_{21}NNaO_4$ $[M + Na]^+$ = 398.1363, found = 398.1360.

9-(benzyloxy)-2-methyl-10c-phenyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3r:**



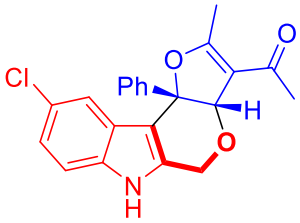
A colorless oil; 44.6 mg; isolated yield=98%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 7.34 – 7.21 (m, 10H), 7.17 (d, *J* = 8.8 Hz, 1H), 6.84 – 6.81 (m, 1H), 6.59 (d, *J* = 2.3 Hz, 1H), 5.03 (s, 1H), 4.93 – 4.75 (m, 4H), 2.50 (s, 3H), 2.26 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.3, 173.9, 153.6, 141.3, 137.3, 136.0, 131.1, 128.5, 128.5, 127.8, 127.7, 125.9, 125.4, 112.8, 112.1, 111.9, 107.4, 103.3, 87.4, 86.9, 70.6, 60.4, 29.0, 15.7; HRMS (ESI) m/z calcd for $C_{29}H_{25}NNaO_4$ $[M + Na]^+$ = 474.1676, found = 474.1672; IR: 3313, 2921, 1664, 1584, 1233, 740, 695.

9-fluoro-2-methyl-10c-phenyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3s:**



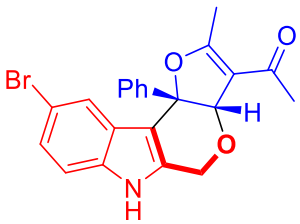
A colorless oil; 36.1 mg; isolated yield=99%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (s, 1H), 7.37 – 7.11 (m, 6H), 6.86 – 6.81 (m, 1H), 6.71 – 6.68 (m, 1H), 5.05 (s, 1H), 4.93 – 4.76 (m, 2H), 2.49 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.6, 174.2, 158.0 (d, *J* = 235 Hz), 140.9, 137.1, 132.4, 128.6, 127.9, 125.8 (d, *J* = 10 Hz), 125.3, 112.3, 112.0 (d, *J* = 10 Hz), 110.7 (d, *J* = 26 Hz), 107.7 (d, *J* = 4 Hz), 104.6 (d, *J* = 24 Hz), 87.3, 86.9, 60.3, 29.1, 15.7; HRMS (ESI) m/z calcd for $C_{22}H_{89}FNNaO_3$ $[M + Na]^+$ = 386.1163, found = 386.1160; IR: 3300, 2926, 1663, 1583, 1236, 736, 698.

9-chloro-2-methyl-10c-phenyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3t:**



A colorless oil; 37.2 mg; isolated yield=98%; ^{1}H NMR (400 MHz, DMSO) δ 11.58 (s, 1H), 7.41 (d, *J* = 8.6 Hz, 1H), 7.37 – 7.24 (m, 5H), 7.06 – 7.03 (m, 1H), 6.80 (d, *J* = 1.8 Hz, 1H), 5.09 – 5.05 (m, 2H), 4.92 (d, *J* = 15.0 Hz, 1H), 2.44 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 194.5, 173.1, 141.9, 138.9, 134.8, 128.9, 128.1, 126.5, 125.8, 124.3, 121.7, 117.7, 113.8, 112.7, 106.4, 87.1, 86.0, 60.6, 29.3, 15.3; HRMS (ESI) m/z calcd for $C_{22}H_{18}ClNNaO_3$ $[M + Na]^+$ = 402.0867, found = 402.0864.

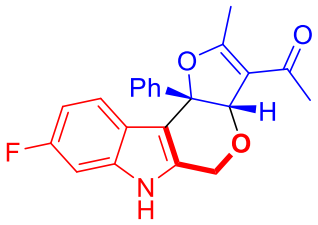
9-bromo-2-methyl-10c-phenyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3u:**



A colorless oil; 37.9 mg; isolated yield=89%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 7.37 – 7.09 (m, 8H), 5.03 (s, 1H), 4.93 – 4.79 (m, 2H), 2.49 (s, 3H), 2.27 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 174.1, 140.9, 136.6, 134.7, 128.7, 128.1, 127.0,

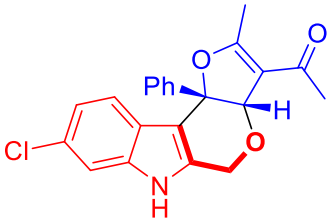
125.4, 125.3, 121.9, 113.8, 112.8, 112.2, 107.3, 87.1, 87.0, 60.3, 29.1, 15.7; HRMS (ESI) m/z calcd for $C_{22}H_{18}BrNNaO_3$ $[M + Na]^+$ = 446.0362, found = 446.0352.

8-fluoro-2-methyl-10c-phenyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3v:**



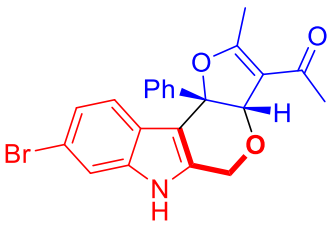
A colorless solid; 35.9 mg; isolated yield=98%; m.p. 81.6-82.2℃; ^{1}H NMR (400 MHz, DMSO) δ 11.45 (s, 1H), 7.36 – 7.23 (m, 5H), 7.20 – 7.17 (m, 1H), 6.86 – 6.79 (m, 1H), 6.73 – 6.68 (m, 1H), 5.04 (t, *J* = 7.4 Hz, 2H), 4.90 (d, *J* = 14.9 Hz, 1H), 2.44 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 194.6, 173.1, 159.2 (d, *J* = 233 Hz), 142.1, 137.7 (d, *J* = 3 Hz), 136.2 (d, *J* = 13 Hz), 128.8, 127.9, 125.8, 122.1, 119.5 (d, *J* = 11 Hz), 112.7, 108.2 (d, *J* = 25 Hz), 106.5, 98.5 (d, *J* = 24 Hz), 87.3, 86.0, 60.6, 29.3, 15.3; HRMS (ESI) m/z calcd for $C_{22}H_{18}FNNaO_3$ $[M + Na]^+$ = 386.1163, found = 386.1153; IR: 3358, 2924, 1673, 1588, 1227, 765, 698.

8-chloro-2-methyl-10c-phenyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3w:**



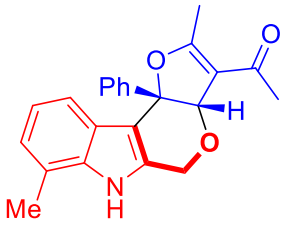
A colorless solid; 32.5 mg; isolated yield=82%; m.p. 232.2-233.2℃; ^{1}H NMR (400 MHz, DMSO) δ 11.56 (s, 1H), 7.44 (d, *J* = 1.4 Hz, 1H), 7.37 – 7.21 (m, 5H), 6.88 – 6.81 (m, 2H), 5.07 – 5.03 (m, 2H), 4.91 (d, *J* = 15.0 Hz, 1H), 2.44 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 190.5, 169.1, 136.4, 131.2, 129.9, 123.8, 123.2, 121.8, 120.6, 120.1, 117.1, 114.0, 107.3, 104.3, 99.9, 82.3, 82.2, 24.3, 10.9; HRMS (ESI) m/z calcd for $C_{22}H_{18}ClNNaO_3$ $[M + Na]^+$ = 402.0867, found = 402.0860; IR: 3190, 2924, 1660, 1581, 1238, 751, 702.

8-bromo-2-methyl-10c-phenyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3x:**



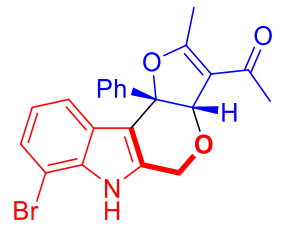
A colorless solid; 42.9 mg; isolated yield=98%; m.p. 96.2-96.8℃; ^{1}H NMR (400 MHz, DMSO) δ 11.52 (s, 1H), 7.59 (d, *J* = 1.6 Hz, 1H), 7.37 – 7.20 (m, 5H), 7.00 – 6.97 (m, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 5.07 – 5.03 (m, 2H), 4.92 (d, *J* = 15.0 Hz, 1H), 2.44 (s, 3H), 2.18 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 194.5, 173.1, 142.0, 138.1, 137.2, 128.8, 128.0, 125.8, 124.5, 122.8, 120.3, 114.8, 114.4, 112.7, 106.7, 87.2, 86.0, 60.5, 29.3, 15.3; HRMS (ESI) m/z calcd for $C_{22}H_{18}BrNNaO_3$ $[M + Na]^+$ = 446.0362, found = 446.0355; IR: 3393, 2920, 1662, 1581, 1220, 751, 698.

2,7-dimethyl-10c-phenyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl) ethan-1-one **3y:**



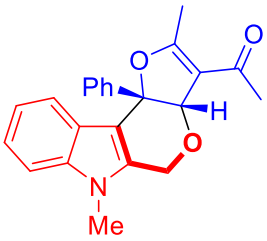
A colorless solid; 32.5 mg; isolated yield=86%; m.p. 200.3-201.3℃; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (s, 1H), 7.39 – 7.18 (m, 5H), 6.93 – 6.84 (m, *J* = 14.4, 7.4 Hz, 3H), 5.05 (s, 1H), 4.98 – 4.87 (m, 2H), 2.49 (s, 3H), 2.45 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 195.5, 174.2, 141.5, 135.5, 135.0, 128.5, 127.7, 125.5, 124.9, 123.1, 120.7, 120.4, 117.2, 112.1, 107.9, 87.5, 86.9, 60.4, 29.1, 16.7, 15.7; HRMS (ESI) m/z calcd for $C_{23}H_{21}NNaO_3$ $[M + Na]^+$ = 382.1414, found = 382.1409; IR: 3206, 2922, 1651, 1568, 1241, 758, 697.

7-bromo-2-methyl-10c-phenyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl)ethan-1-one **3z:**



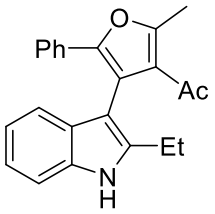
A colorless oil; 29.8 mg; isolated yield=68%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.58 (s, 1H), 7.35 – 7.19 (m, 6H), 7.00 (d, *J* = 7.9 Hz, 1H), 6.85 – 6.81 (m, 1H), 5.06 (s, 1H), 5.04 – 4.91 (m, 2H), 2.51 (s, 3H), 2.28 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 195.7, 174.3, 141.6, 136.4, 135.1, 129.0, 128.4, 127.0, 125.8, 125.3, 122.3, 119.2, 112.5, 109.5, 105.2, 87.5, 87.4, 60.7, 29.5, 16.1; HRMS (ESI) m/z calcd for $C_{22}H_{18}BrNNaO_3$ $[M + H]^+$ = 446.0362, found = 446.0353.

2,6-dimethyl-10c-phenyl-3a,5,6,10c-tetrahydrofuro[2',3':5,6]pyrano[3,4-*b*]indol-3-yl) ethan-1-one **3a':**



A colorless solid; 26.4 mg; isolated yield=74%; m.p. 224.6-225.2℃; ^{1}H NMR (400 MHz, DMSO) δ 7.45 (d, *J* = 8.3 Hz, 1H), 7.37 – 7.21 (m, 5H), 7.13 – 7.03 (m, 1H), 6.86 (d, *J* = 6.4 Hz, 2H), 5.15 – 4.97 (m, 3H), 3.72 (s, 3H), 2.43 (s, 3H), 2.19 (s, 3H); ^{13}C NMR (100 MHz, DMSO) δ 194.5, 173.1, 142.3, 138.2, 137.3, 133.6, 129.0, 128.7, 127.9, 125.9, 125.1, 121.7, 120.0, 118.9, 112.7, 110.3, 106.0, 87.5, 86.1, 59.7, 30.1, 29.3, 15.3; HRMS (ESI) m/z calcd for $C_{23}H_{21}NNaO_3$ $[M + H]^+$ = 382.1414, found = 382.1409.

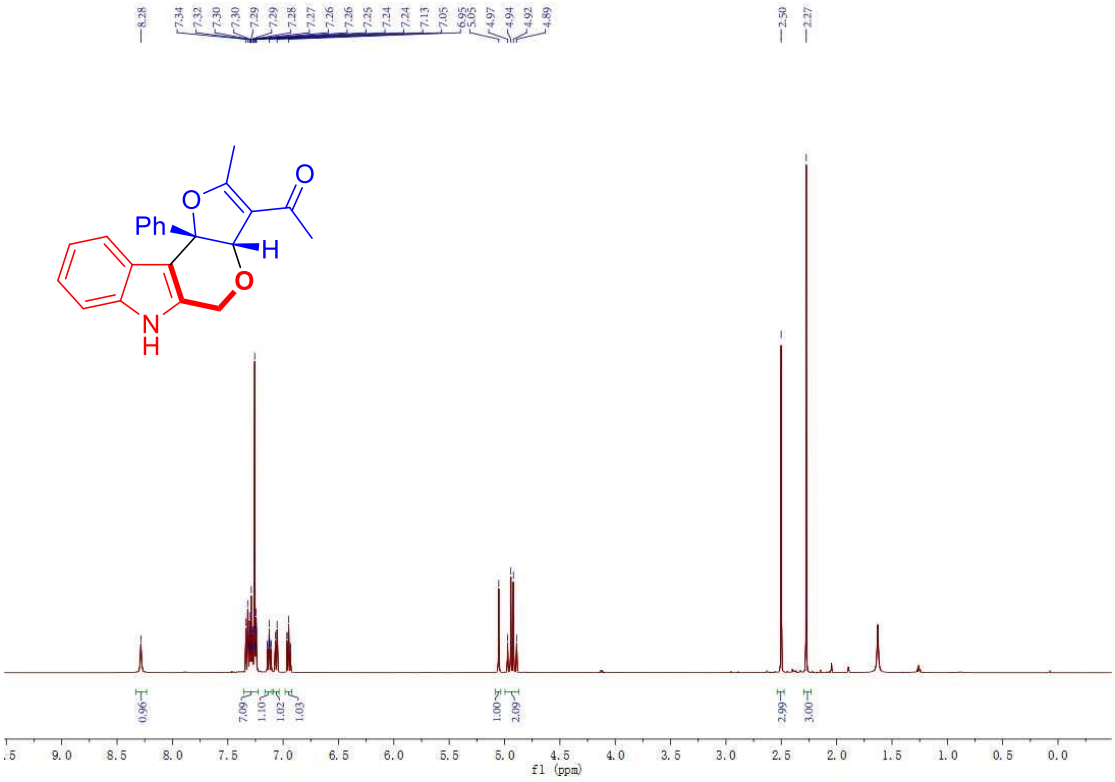
1-(4-(2-ethyl-1H-indol-3-yl)-2-methyl-5-phenylfuran-3-yl)ethan-1-one **S1:**

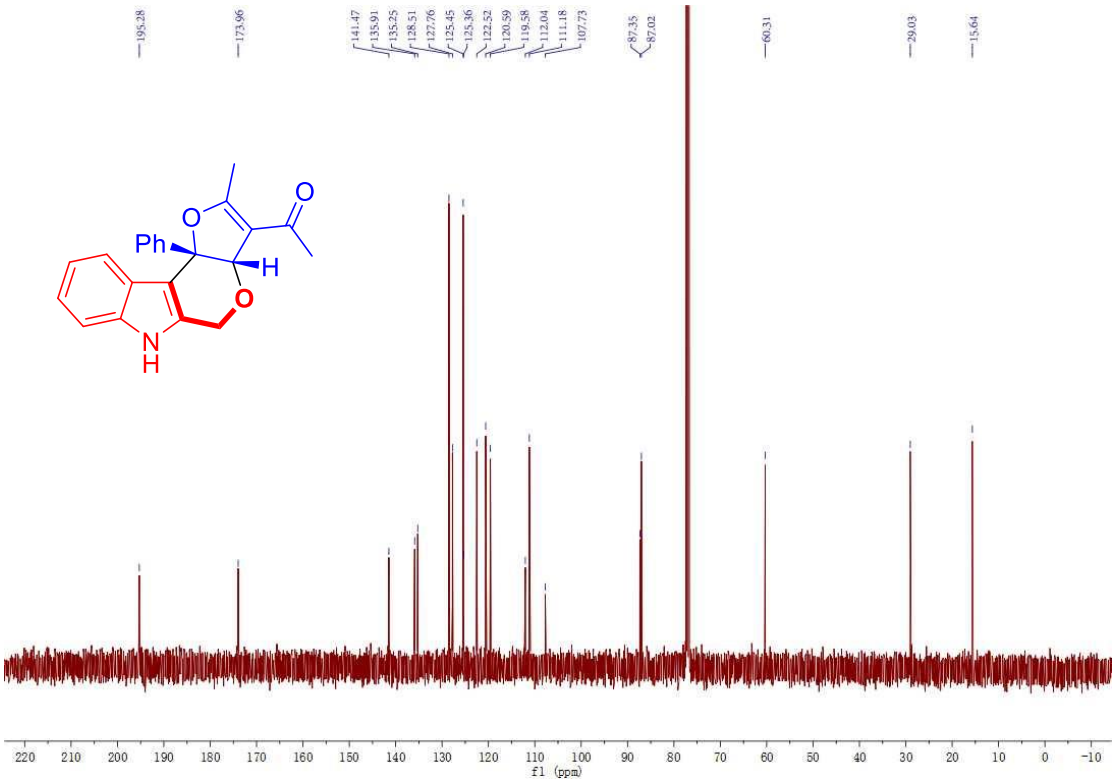


A yellowish oil; isolated yield=90%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.19 (s, 1H), 7.43 – 7.29 (m, 4H), 7.22 – 7.01 (m, 5H), 2.71 (s, 3H), 2.66 – 2.49 (m, 2H), 1.82 (s, 3H), 1.10 (t, *J* = 7.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.7, 158.0, 148.5, 138.2, 135.6, 130.7, 128.9, 128.3, 127.1, 125.1, 124.8, 121.8, 120.3, 119.1, 113.0, 110.5, 104.6, 29.6, 19.8, 14.8, 13.2; HRMS (ESI) m/z calcd for $C_{23}H_{22}NO_2$ $[M + H]^+$ = 344.1645, found = 344.1640.

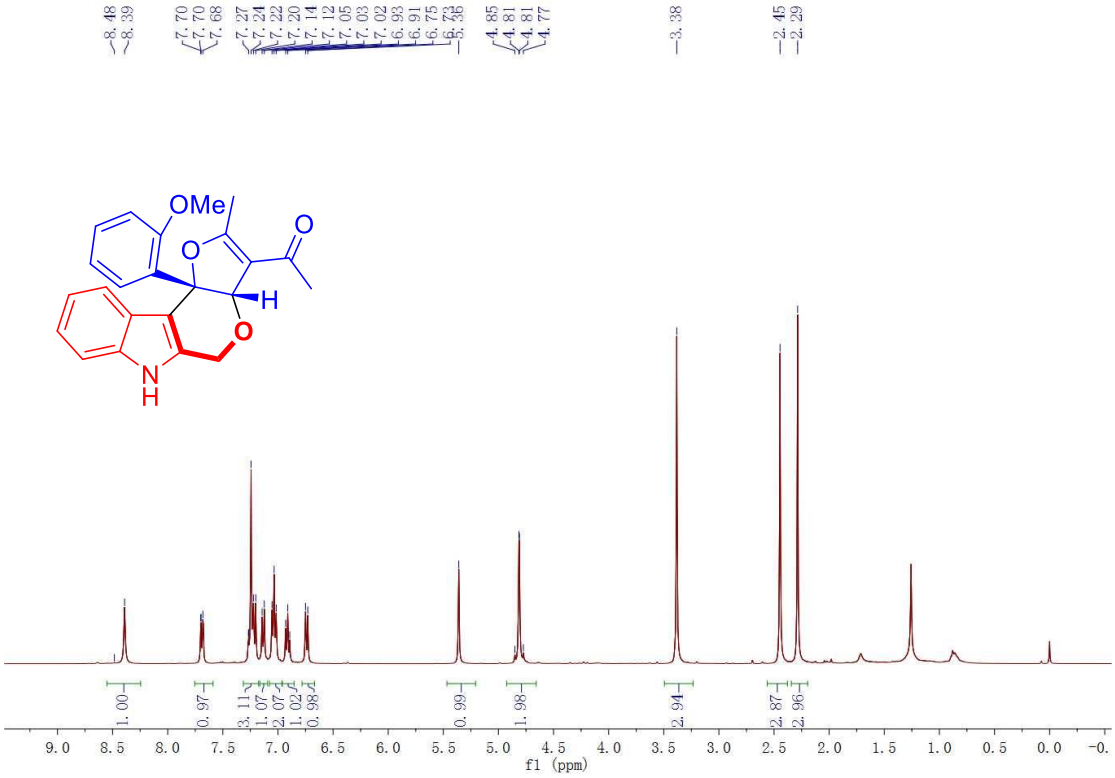
4. NMR Spectra of Compounds

3a





3b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7.03
7.02
6.93
6.91
6.75
6.73
6.58
4.85
4.81
4.81
4.77
3.38
2.45
2.29
OMe
O
O
H
O
N
H
1.00
0.97
3.11
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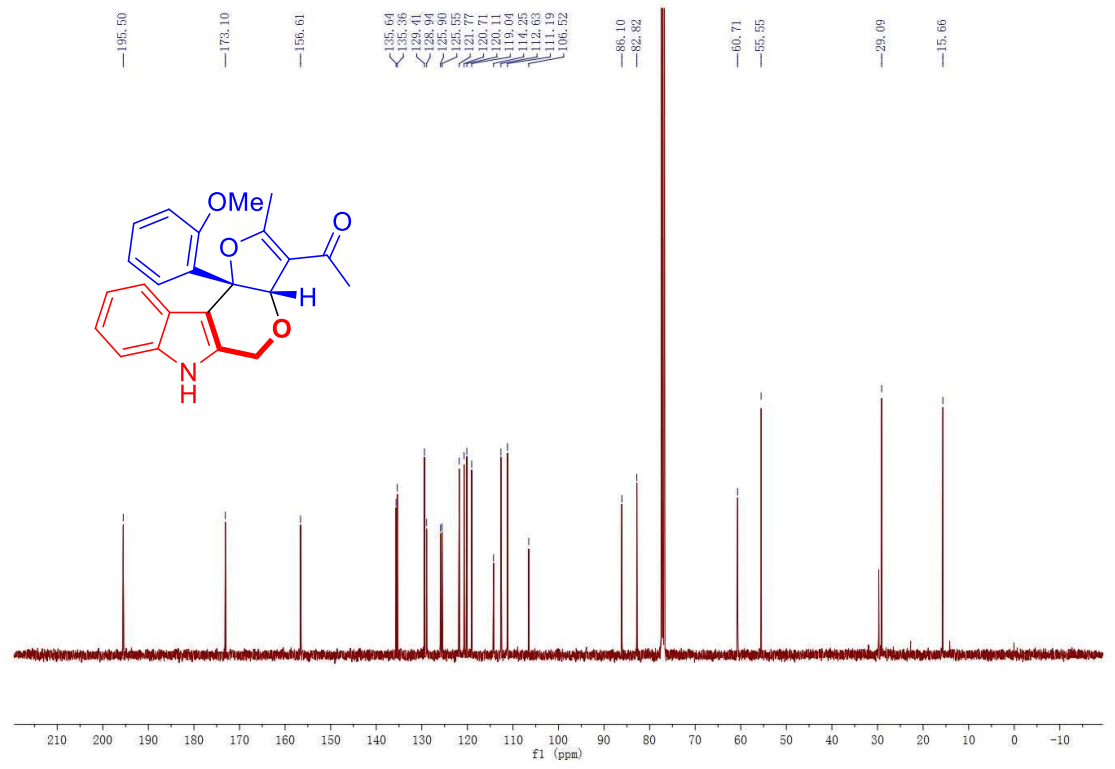
2.07
1.02
0.98
0.99
1.98
2.94
2.87
2.96
f1 (ppm)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125.90
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120.71
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119.04
114.25
112.63
111.19
106.52
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55.55
29.09
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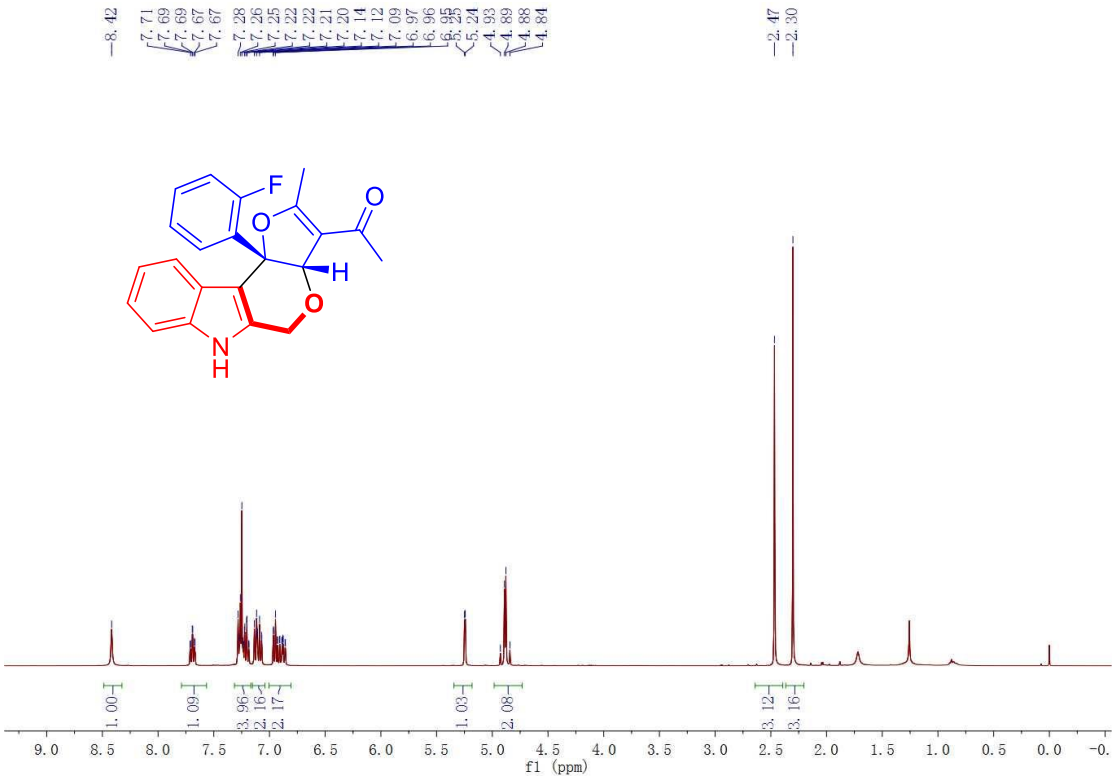
H
O
N
H
f1 (ppm)

3c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7.22
7.21
7.20
7.14
7.12
7.09
6.97
6.96
6.95
6.25
5.24
4.93
4.89
4.88
4.84
2.47
2.30
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O
O
H
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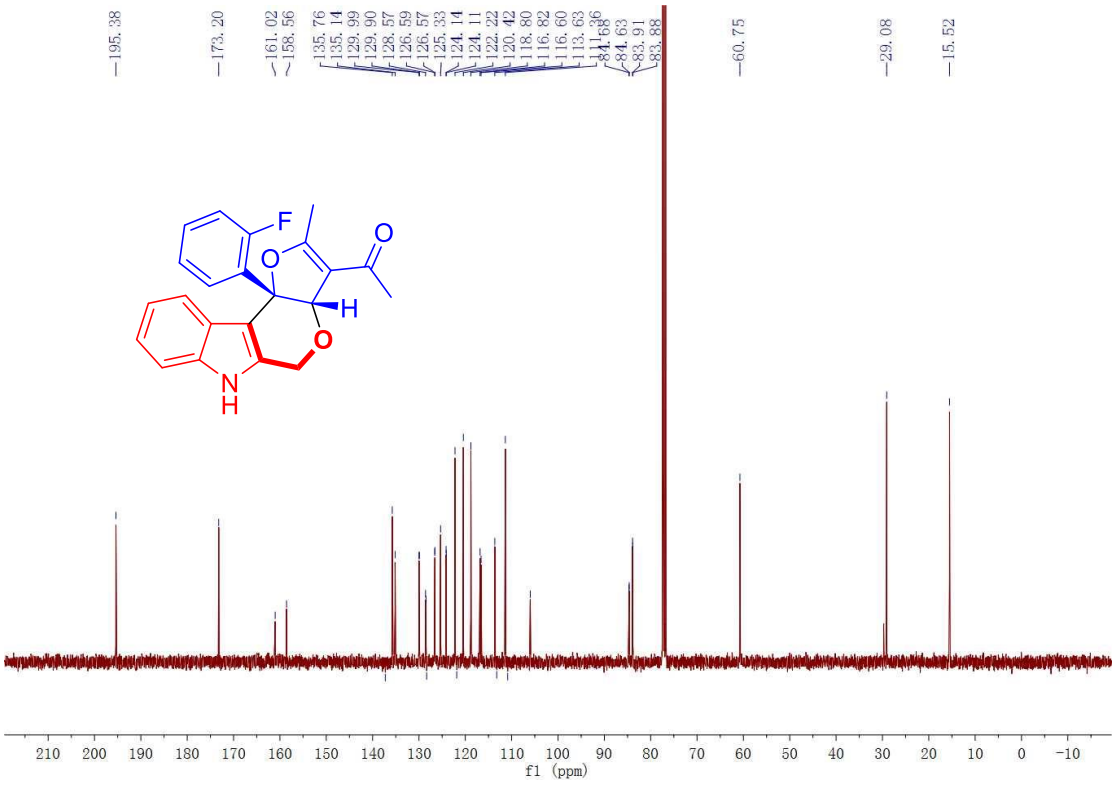
2.08
3.12
3.16
f1 (ppm)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126.57
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124.14
124.11
122.22
120.42
118.80
116.82
116.60
113.63
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60.75
29.08
15.52
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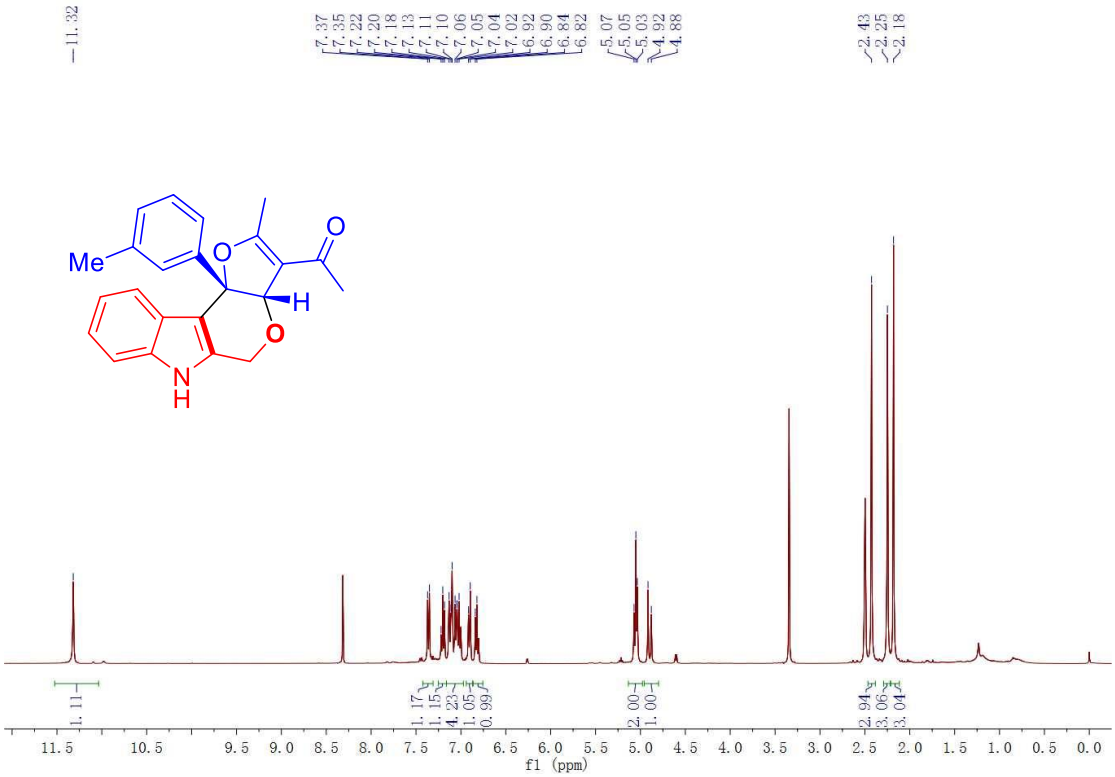
O
H
O
N
H
f1 (ppm)

3d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7.11
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7.05
7.04
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2.43
2.25
2.18
Me
O
O
H
O
N
H
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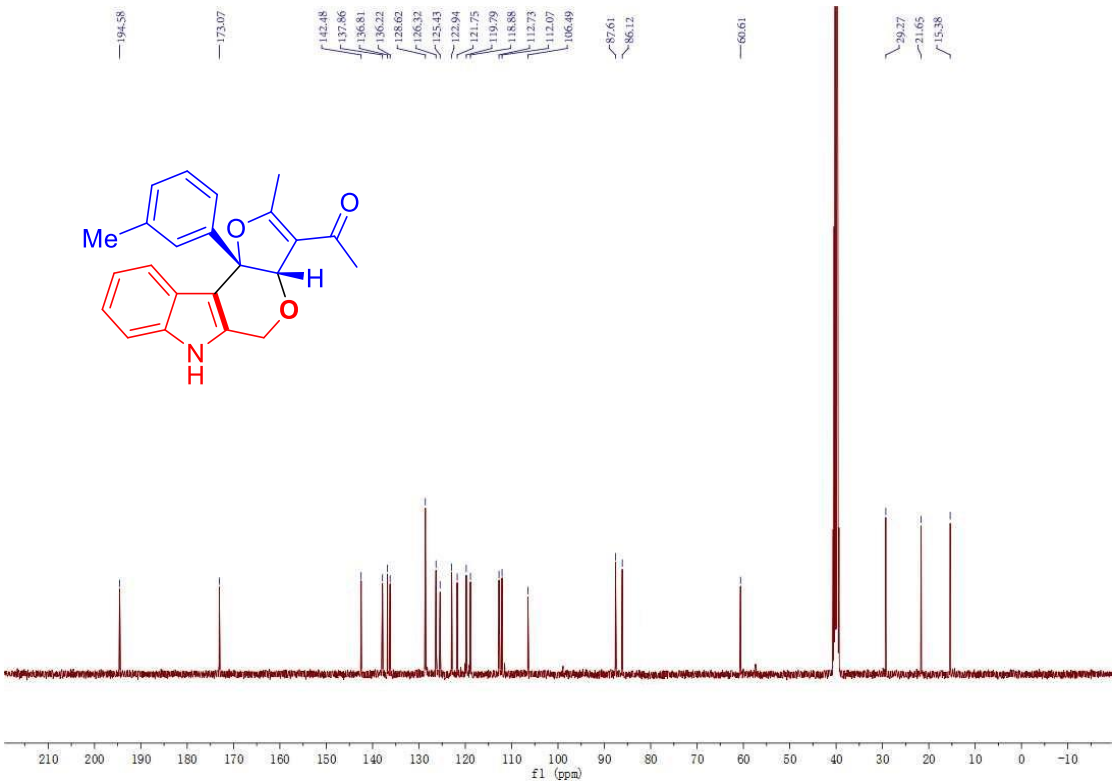
3.04
f1 (ppm)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112.07
106.49
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29.27
21.65
15.38
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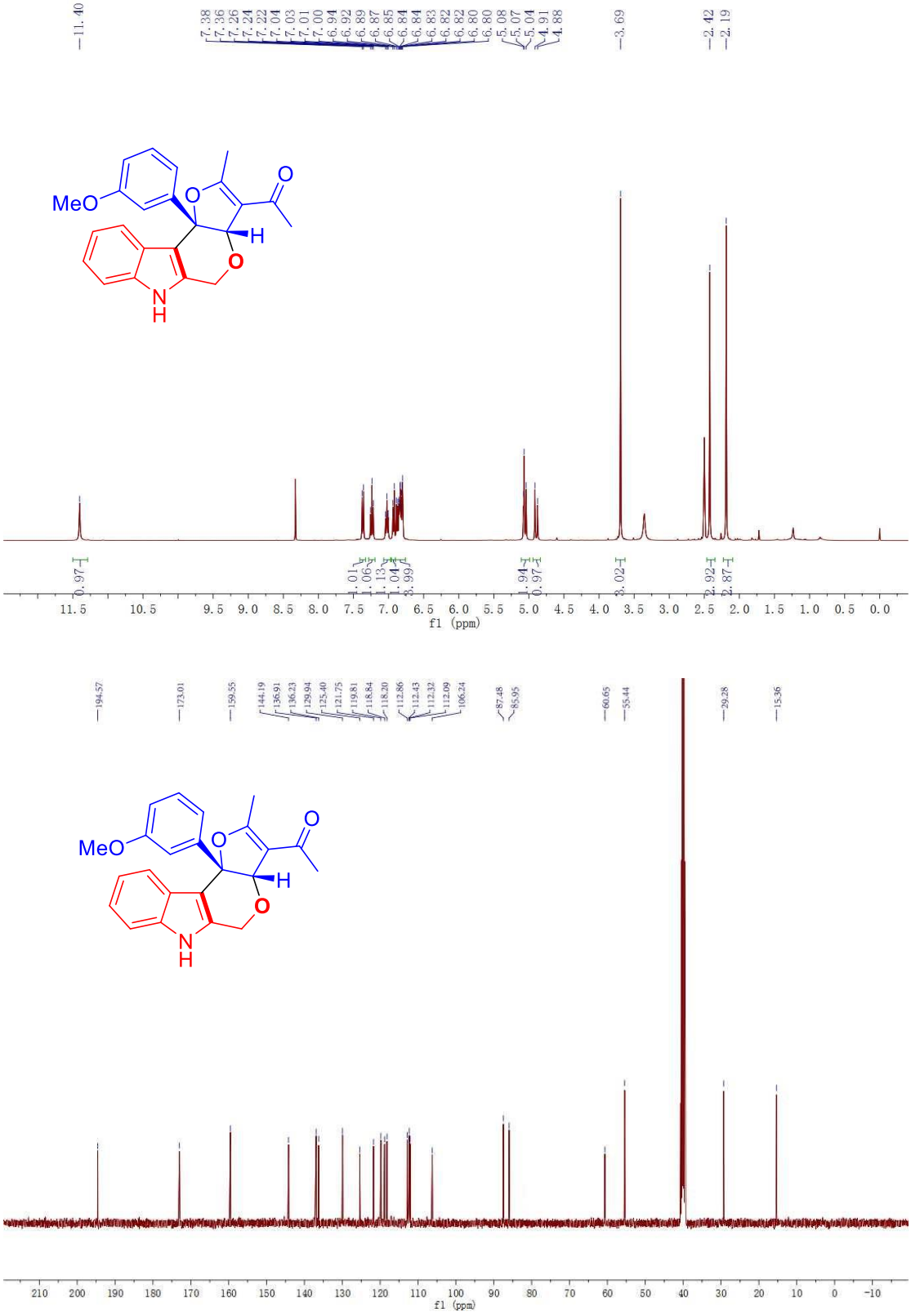
H
O
N
H
f1 (ppm)

3e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6.89
6.87
6.85
6.84
6.84
6.83
6.82
6.82
6.80
6.80
5.08
5.07
5.04
4.91
4.88
3.69
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H
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1.06
1.13
1.04
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0.97
3.02
2.92
2.87
f1 (ppm)
194.57
173.01
159.55
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136.91
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129.94
125.40
121.75
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118.84
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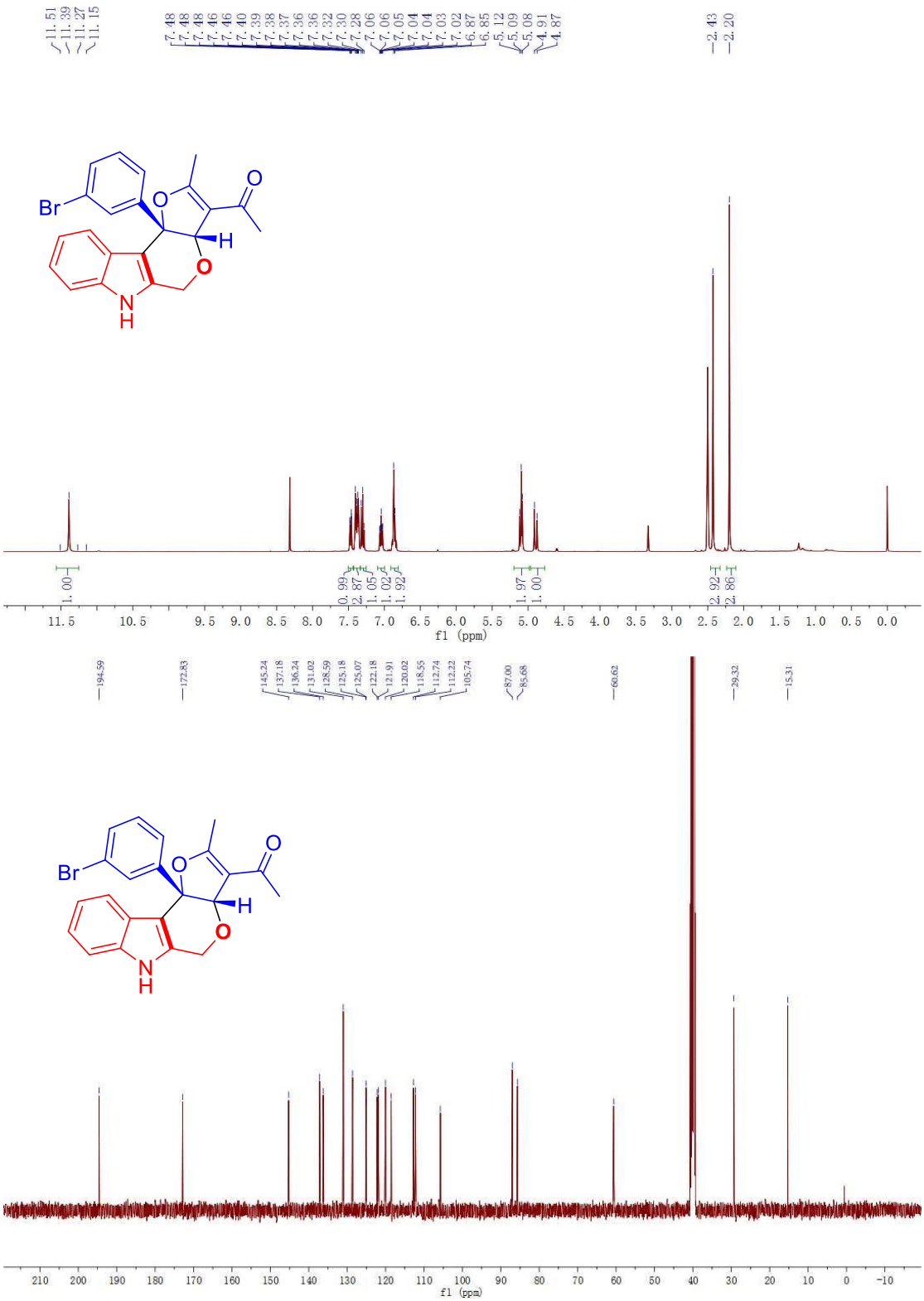
H
f1 (ppm)

3f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7.28
7.06
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7.04
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7.03
7.02
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4.87
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6.0
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5.0
4.5
4.0
3.5
3.0
2.5
2.0
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0.0
f1 (ppm)
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172.83
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120.02
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15.31
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H
O
N
H
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180
170
160
150
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80
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60
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20
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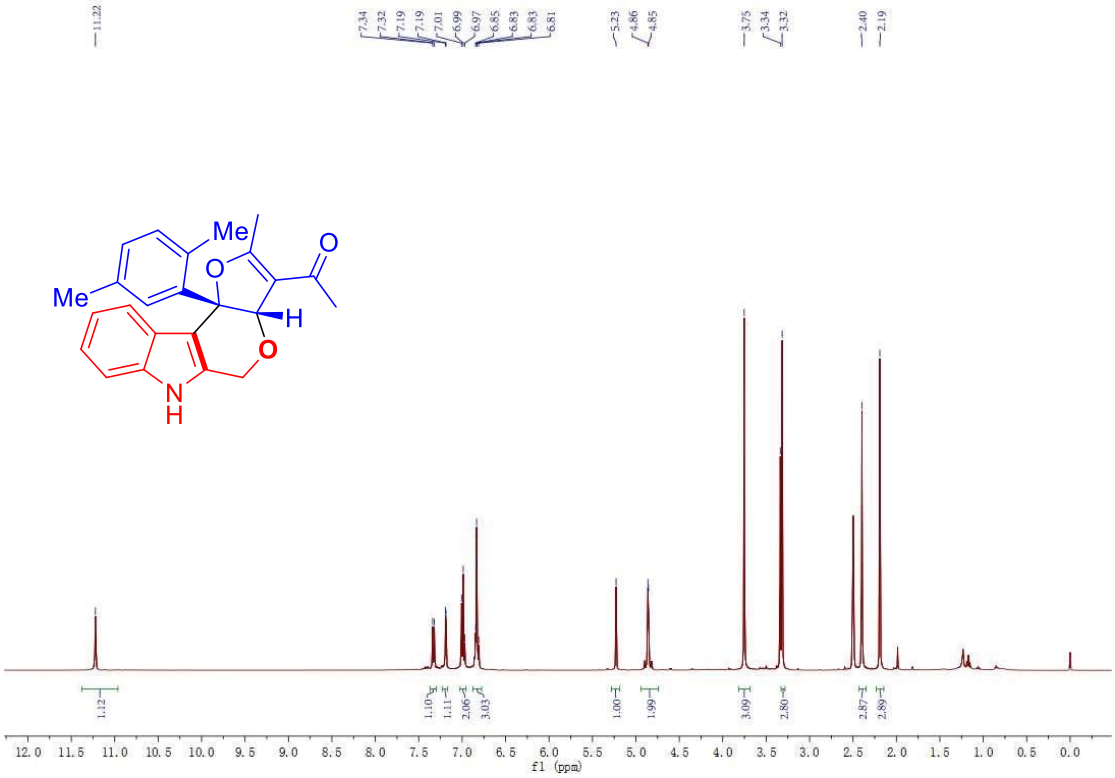
f1 (ppm)

3g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4.85
3.75
3.34
3.32
2.40
2.19
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H
O
N
H
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1.10
1.11
2.06
3.03
1.00
1.99
3.09
2.80
2.87
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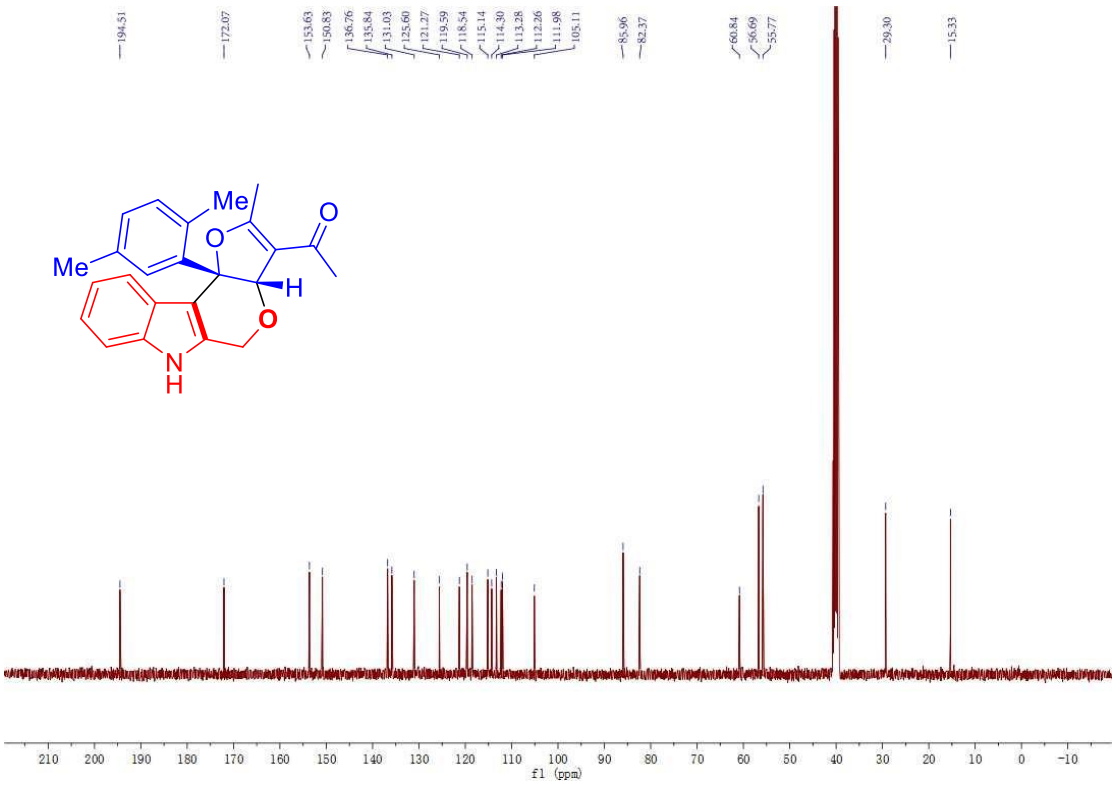
f1 (ppm)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56.69
55.77
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15.33
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H
O
N
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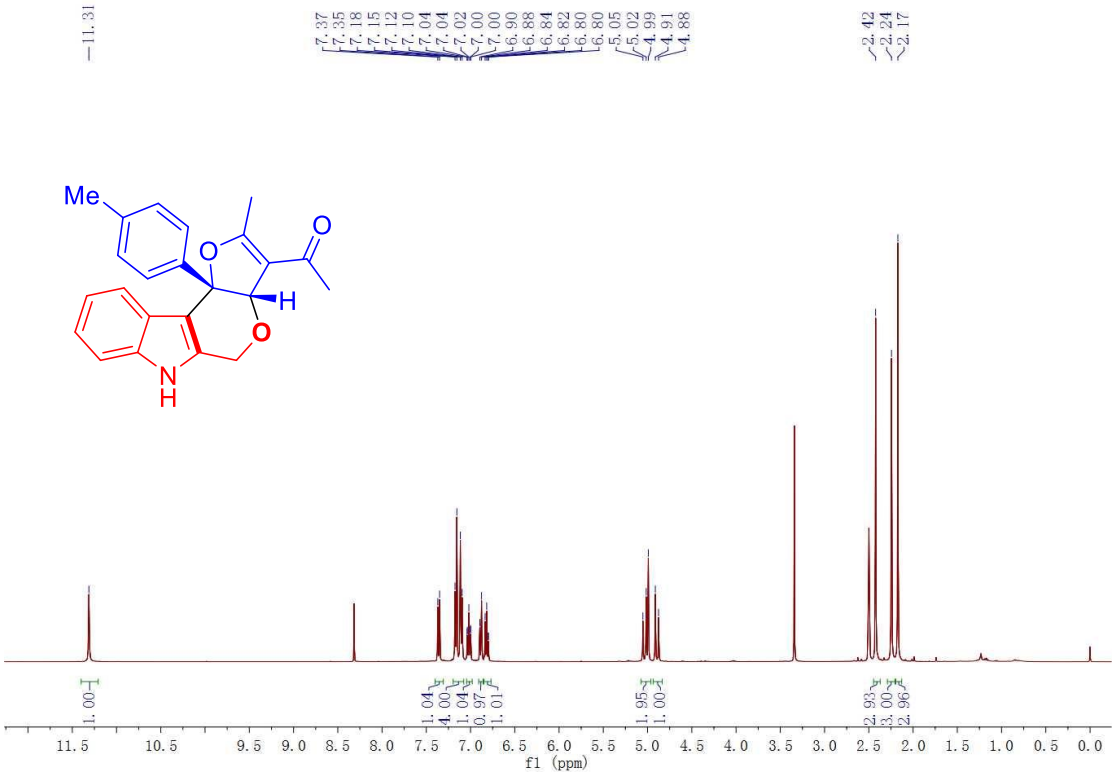
f1 (ppm)

3h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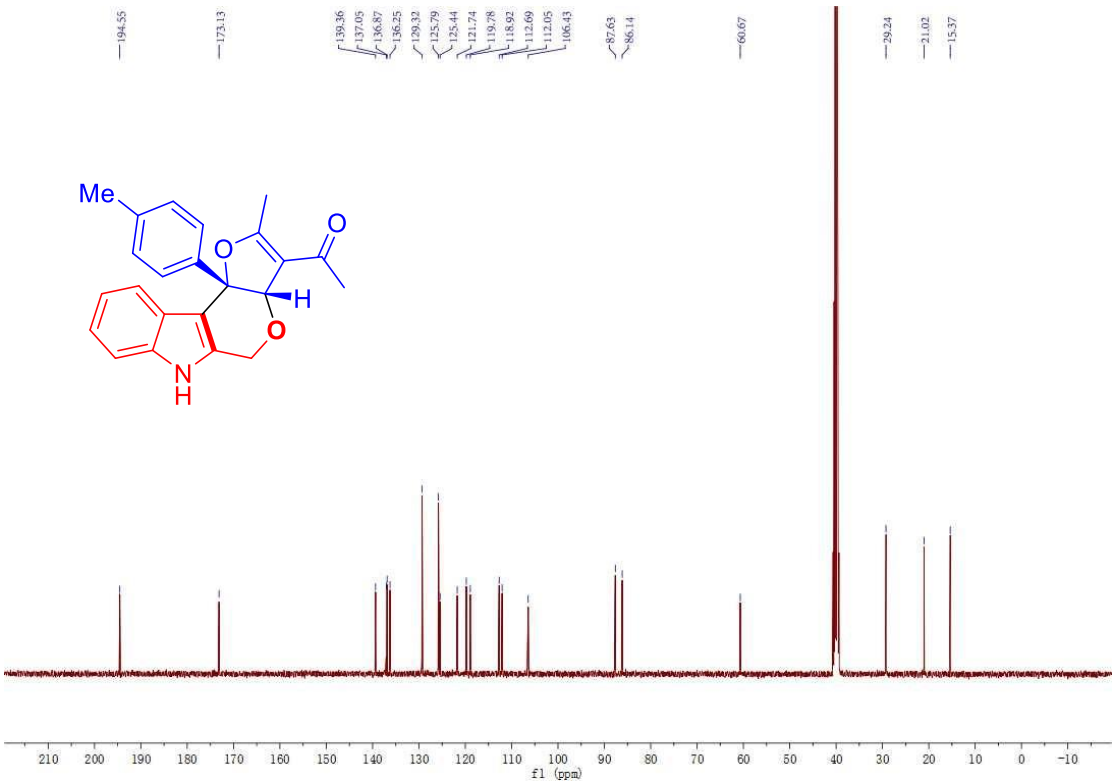
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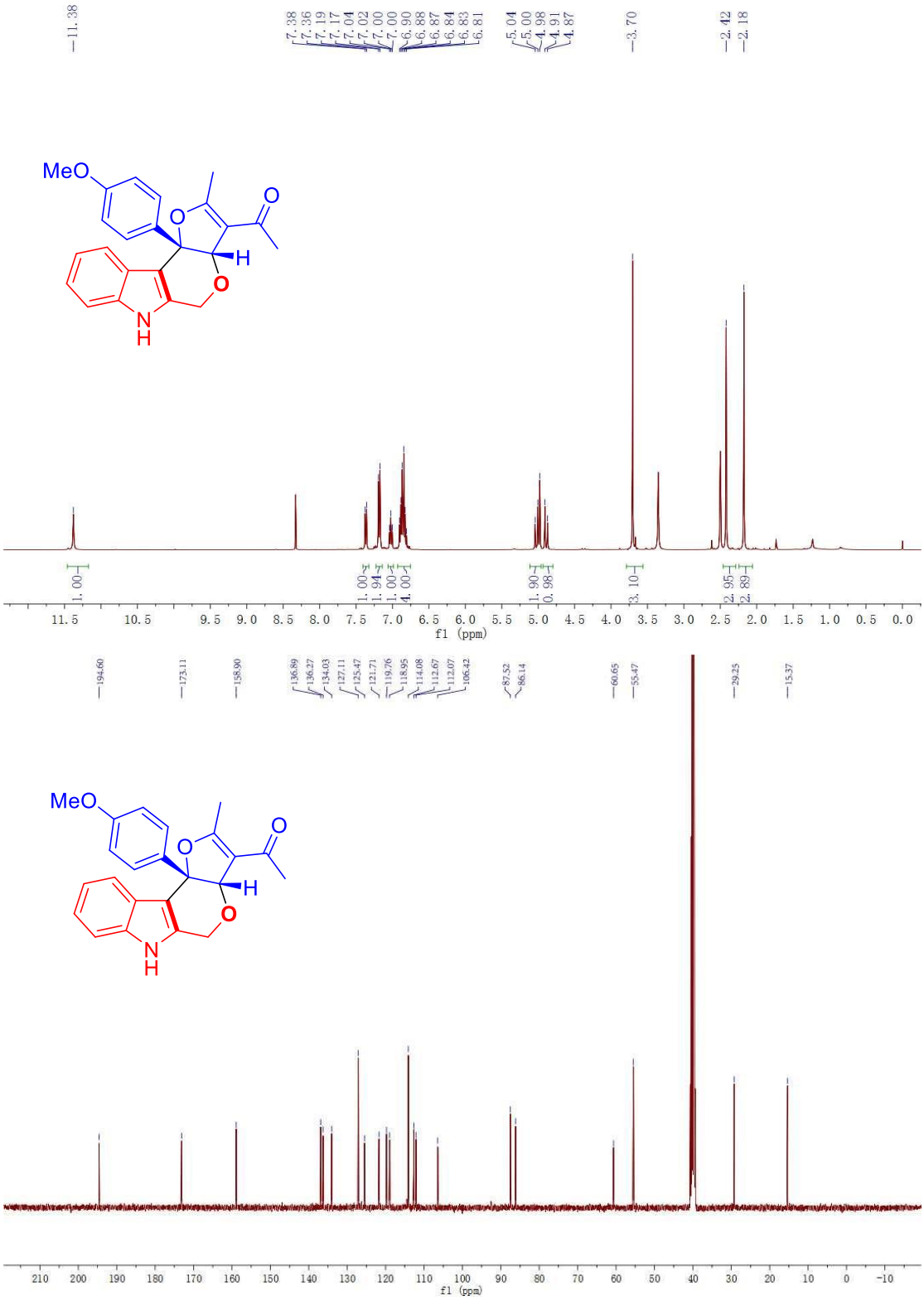
f1 (ppm)

3i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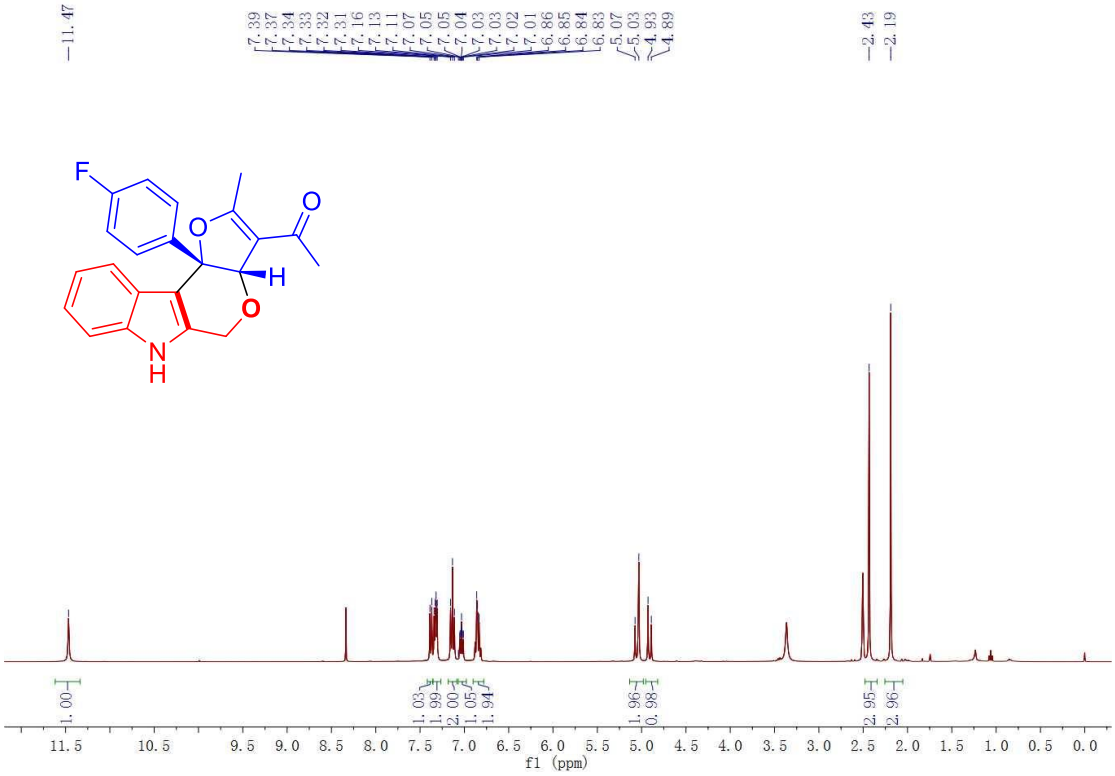
f1 (ppm)

3j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H
O
N
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2.00
1.05
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2.95
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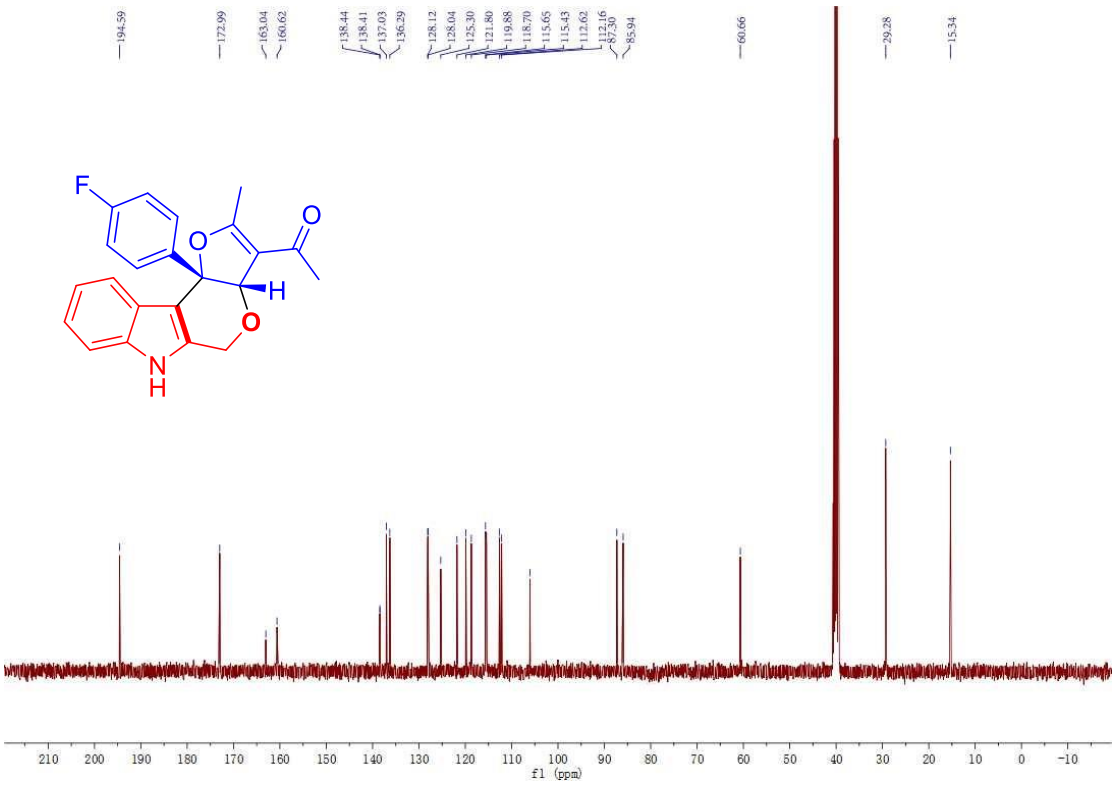
0.0
f1 (ppm)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118.70
115.65
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112.62
112.16
87.30
85.94
60.66
29.28
15.34
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O
O
H
O
N
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200
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180
170
160
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20
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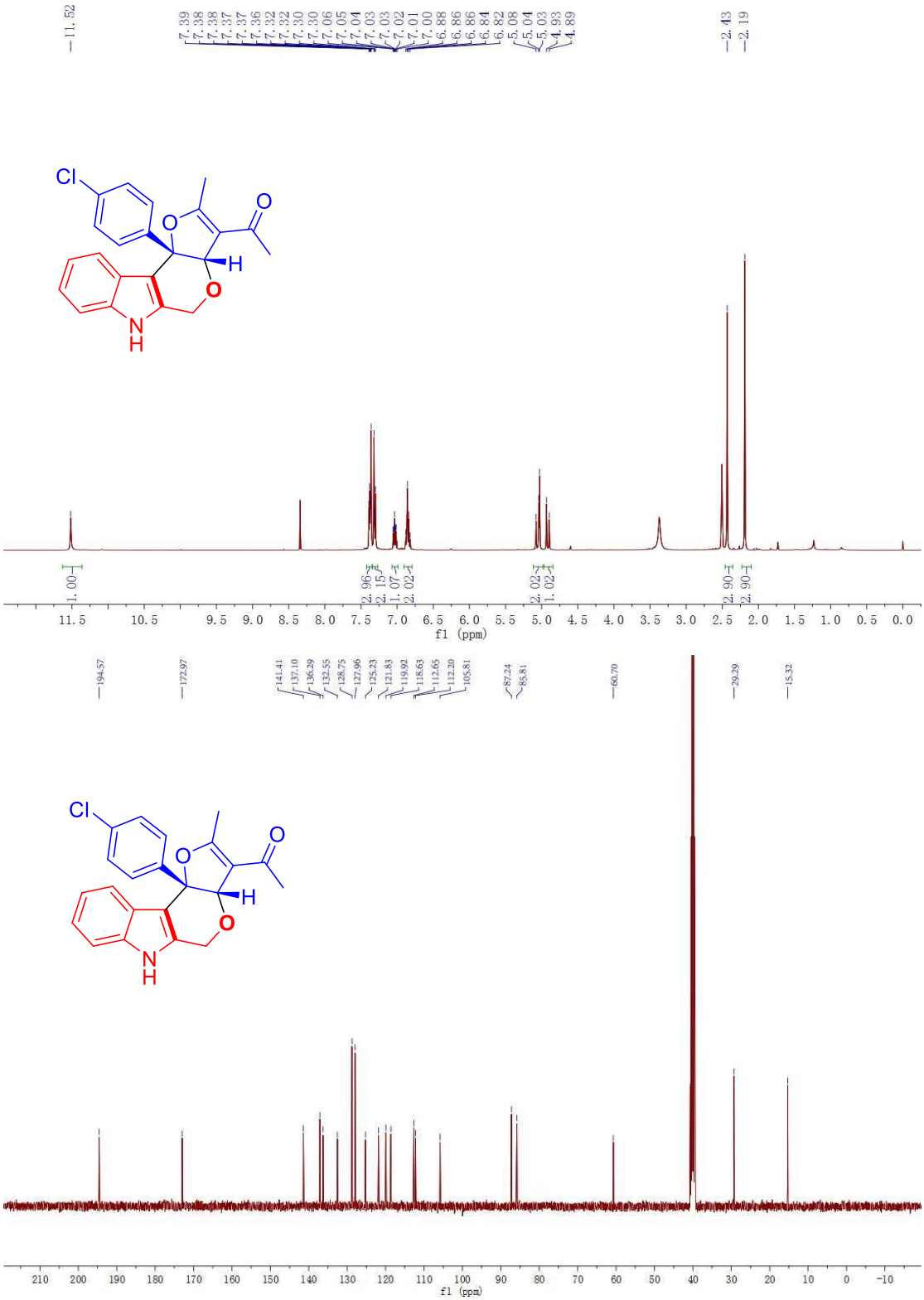
f1 (ppm)

3k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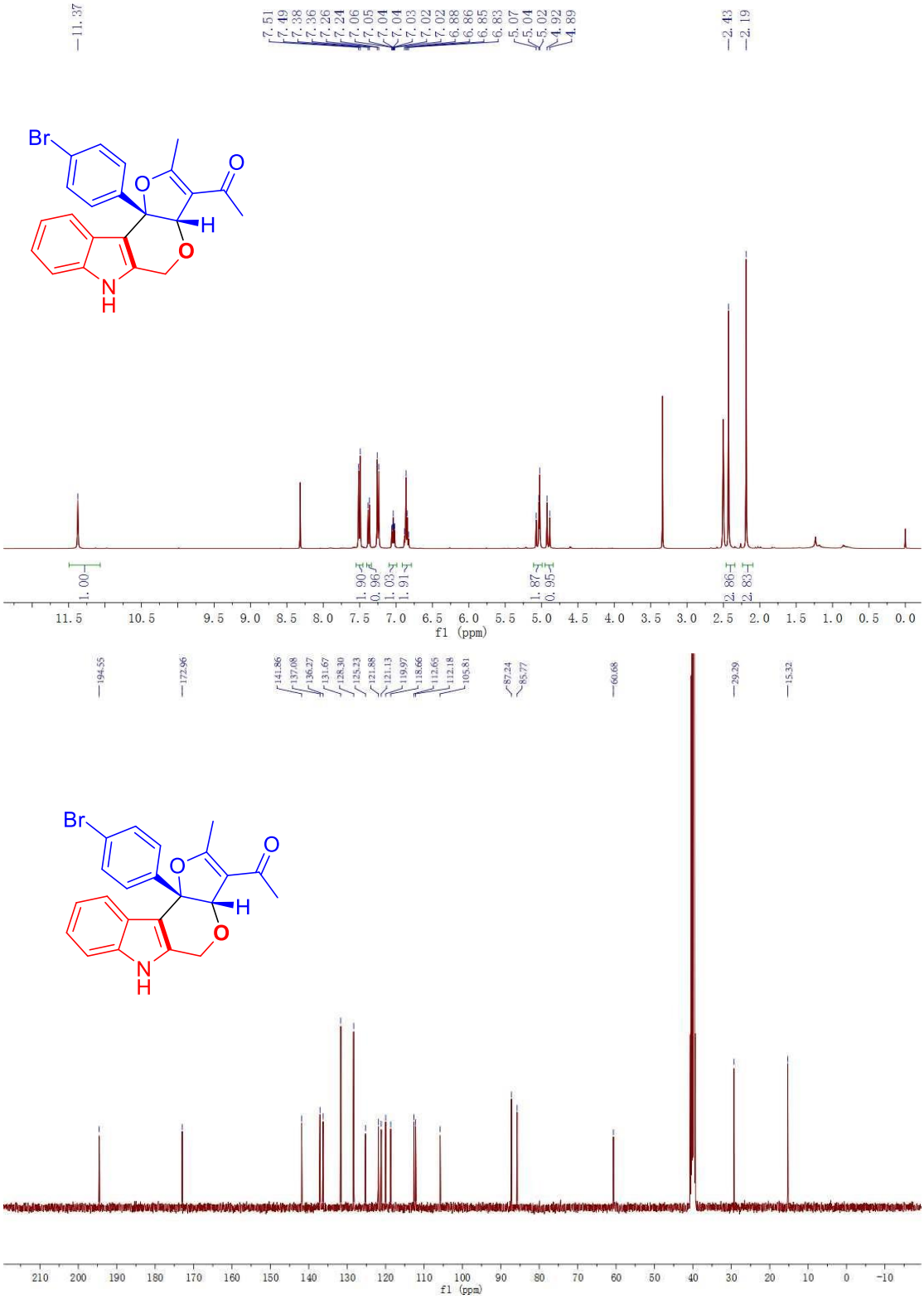
7.37
7.36
7.32
7.32
7.30
7.30
7.06
7.05
7.04
7.03
7.03
7.02
7.01
7.00
6.88
6.86
6.86
6.84
6.82
5.08
5.04
5.03
4.93
4.89
2.43
2.19
Cl
O
O
H
O
N
H
1.00
2.96
2.15
1.07
2.02
2.02
1.02
2.90
2.90
f1 (ppm)
194.57
172.97
141.41
137.10
136.29
132.55
128.75
127.96
125.23
121.83
119.92
118.63
112.65
112.20
105.81
87.24
85.81
60.70
29.29
15.32
Cl
O
O
H
O
N
H
f1 (ppm)

3l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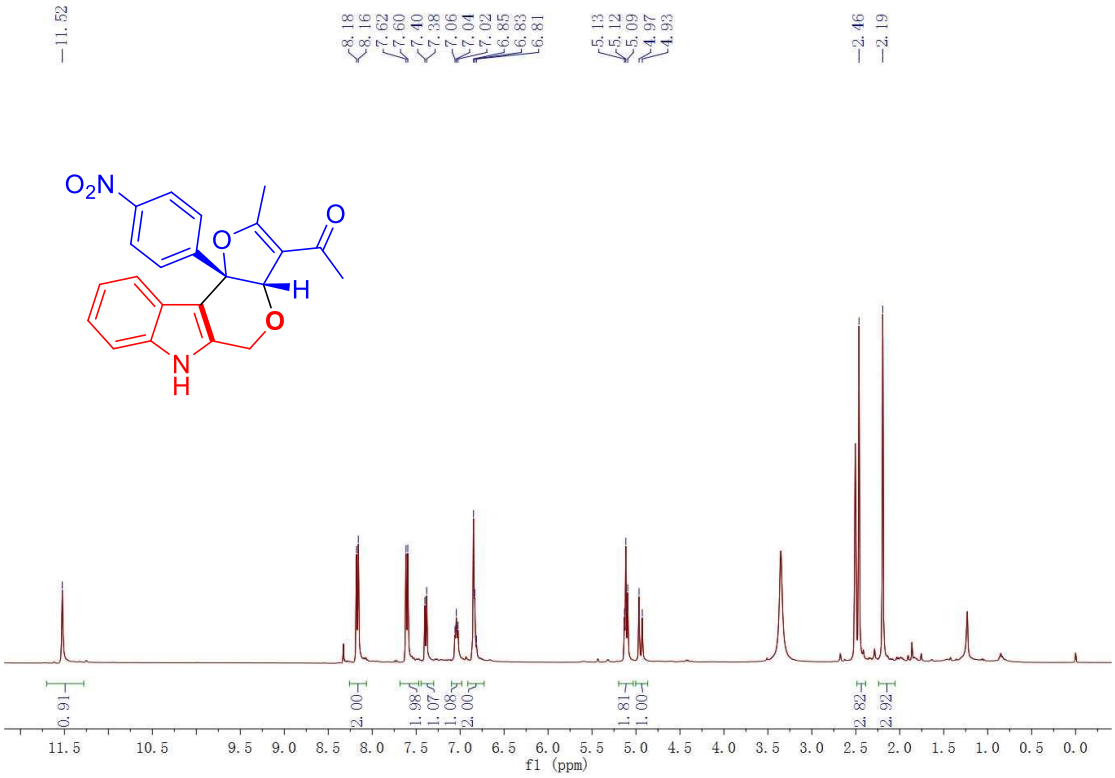
7.51
7.49
7.38
7.36
7.26
7.24
7.06
7.05
7.04
7.04
7.03
7.02
7.02
6.88
6.86
6.85
6.83
5.07
5.04
5.02
4.92
4.89
2.43
2.19
Br
O
O
H
O
N
H
1.00
1.90
0.96
1.03
1.91
1.87
0.95
2.86
2.83
f1 (ppm)
194.55
172.96
141.86
137.08
136.27
131.67
128.30
125.23
121.88
121.13
119.97
118.66
112.65
112.18
105.81
87.24
85.77
60.68
29.29
15.32
f1 (ppm)

3m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8.18
8.16
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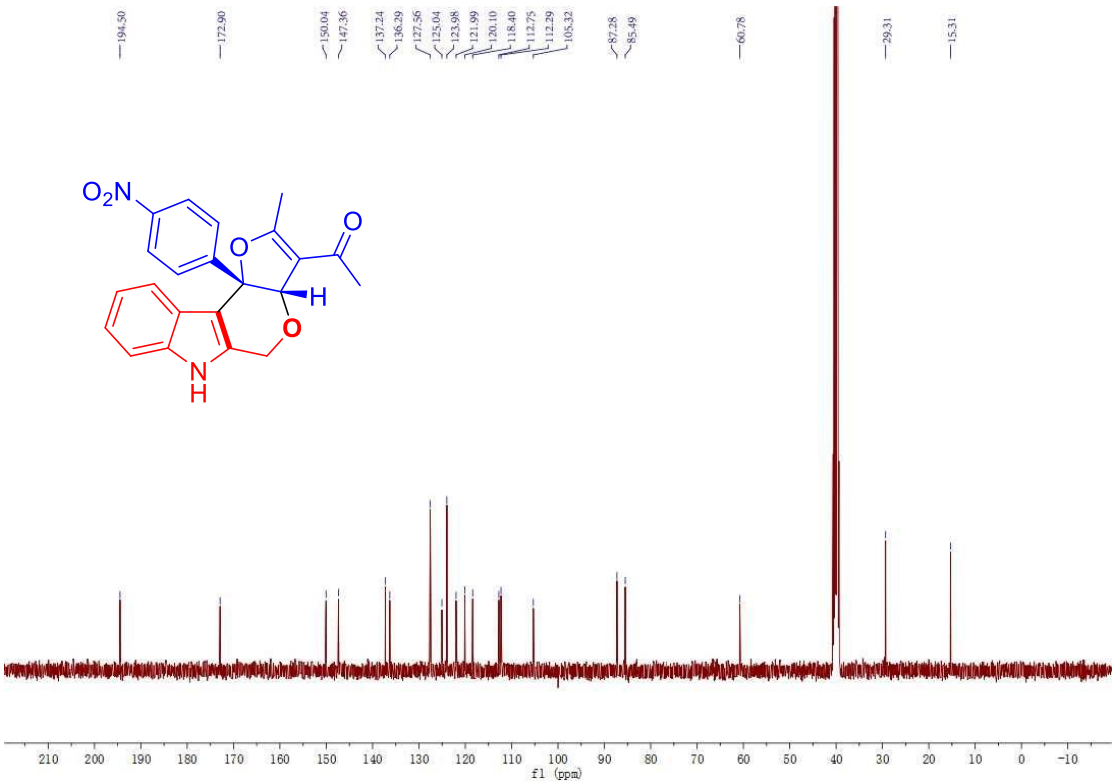
7.60
7.40
7.38
7.06
7.04
7.02
6.85
6.83
6.81
5.13
5.12
5.09
4.97
4.93
2.46
2.19
O2N
O
O
H
O
N
H
0.91
2.00
1.98
1.07
1.08
2.00
1.81
1.00
2.82
2.92
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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136.29
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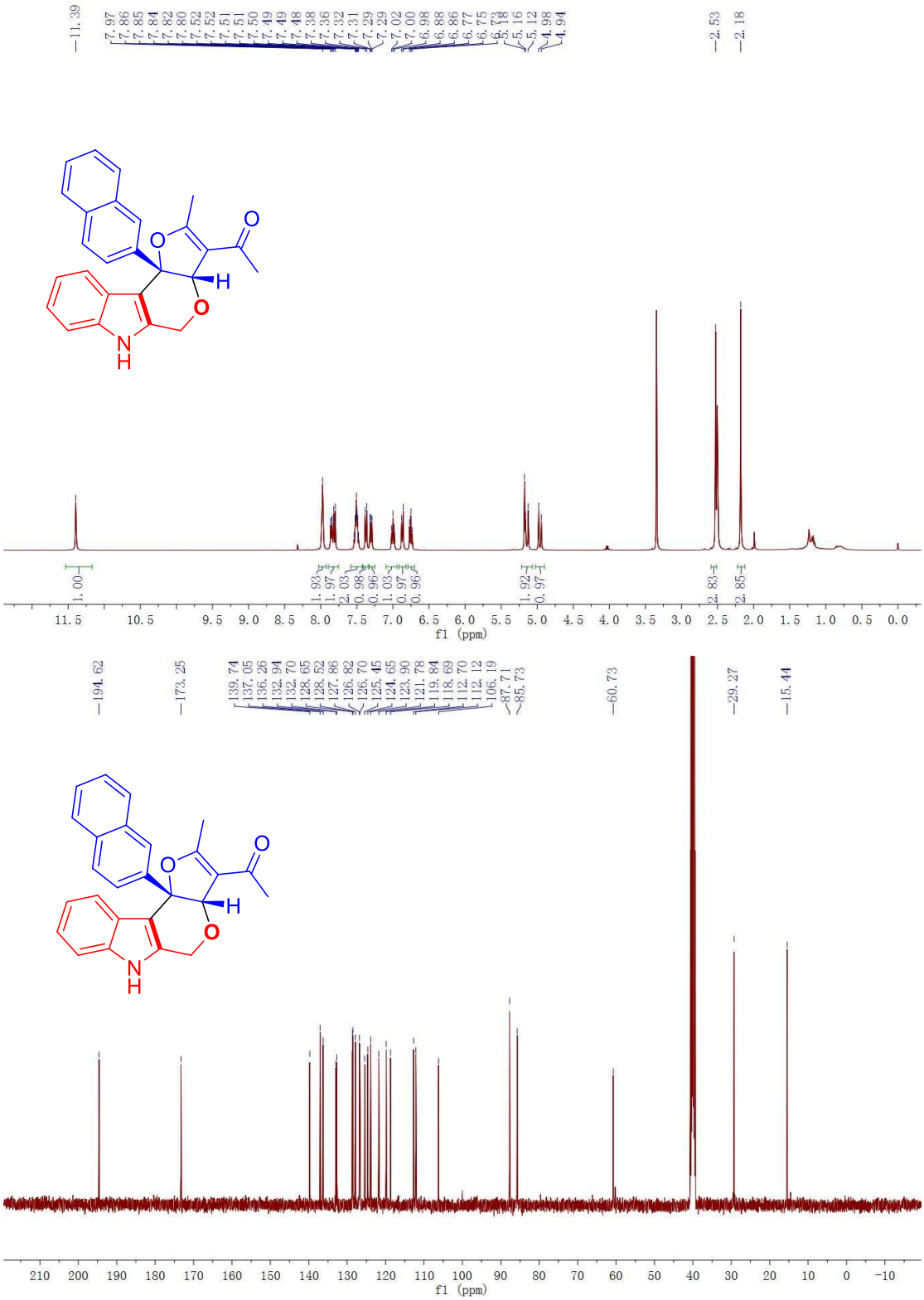
125.04
123.98
121.99
120.10
118.40
112.75
112.29
105.32
87.28
85.49
60.78
29.31
15.31
O2N
O
O
H
O
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

3n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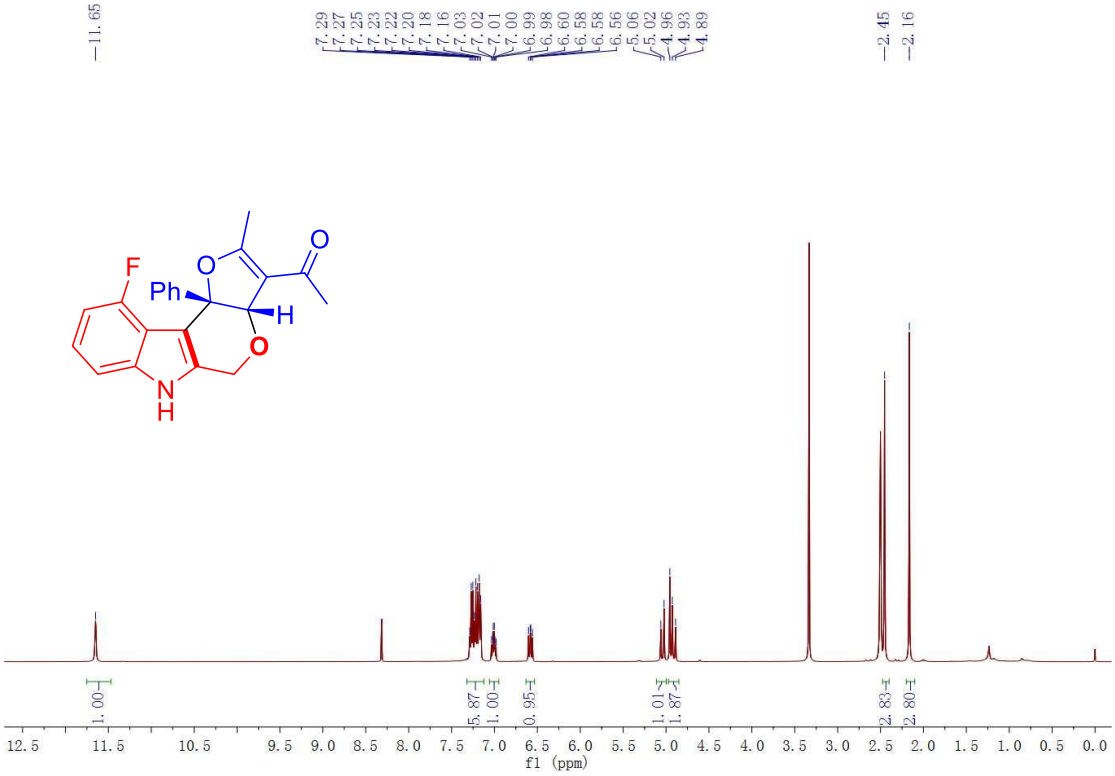
7.84
7.82
7.80
7.52
7.52
7.51
7.51
7.50
7.49
7.49
7.48
7.38
7.36
7.32
7.31
7.29
7.29
7.02
7.00
6.98
6.88
6.86
6.77
6.75
6.73
5.18
5.16
5.12
4.98
4.94
2.53
2.18
O
O
H
O
N
H
1.00
1.93
1.97
2.03
0.98
0.96
1.03
0.97
0.96
1.92
0.97
2.83
2.85
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
194.62
173.25
139.74
137.05
136.26
132.94
132.70
128.65
128.52
127.86
126.82
126.70
125.45
124.65
123.90
121.78
119.84
118.69
112.70
112.12
106.19
87.71
85.73
60.73
29.27
15.44
O
O
H
O
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

3o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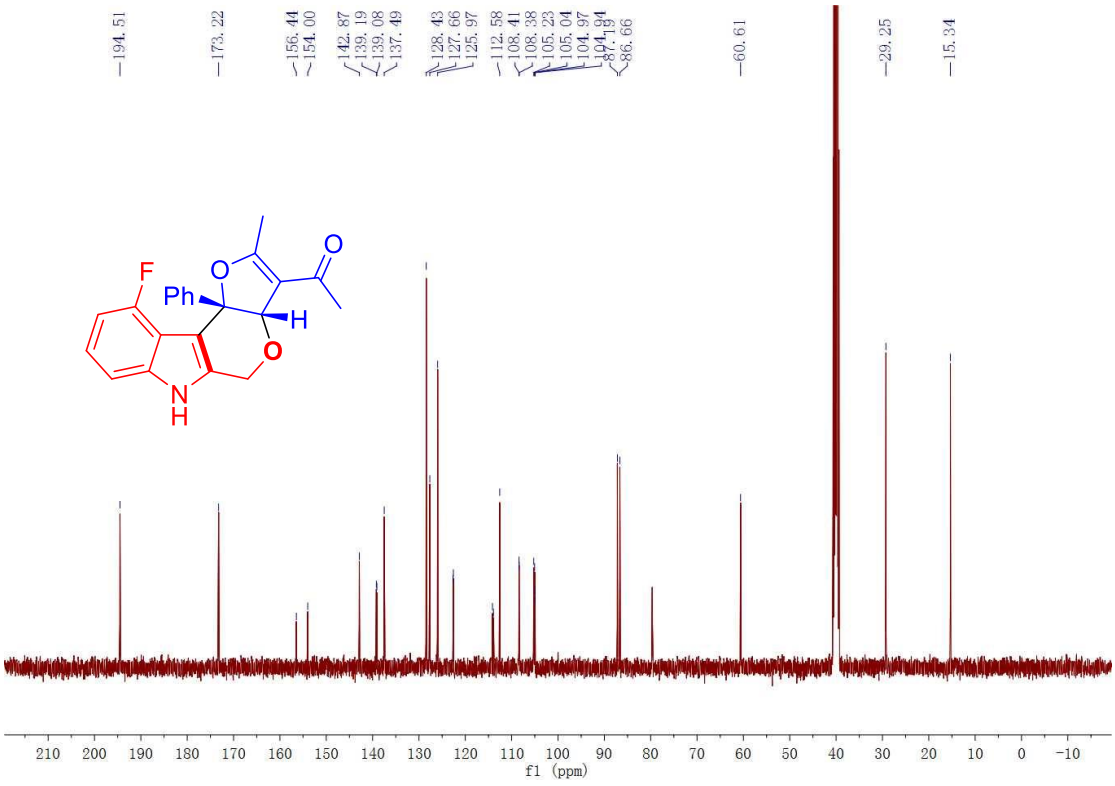
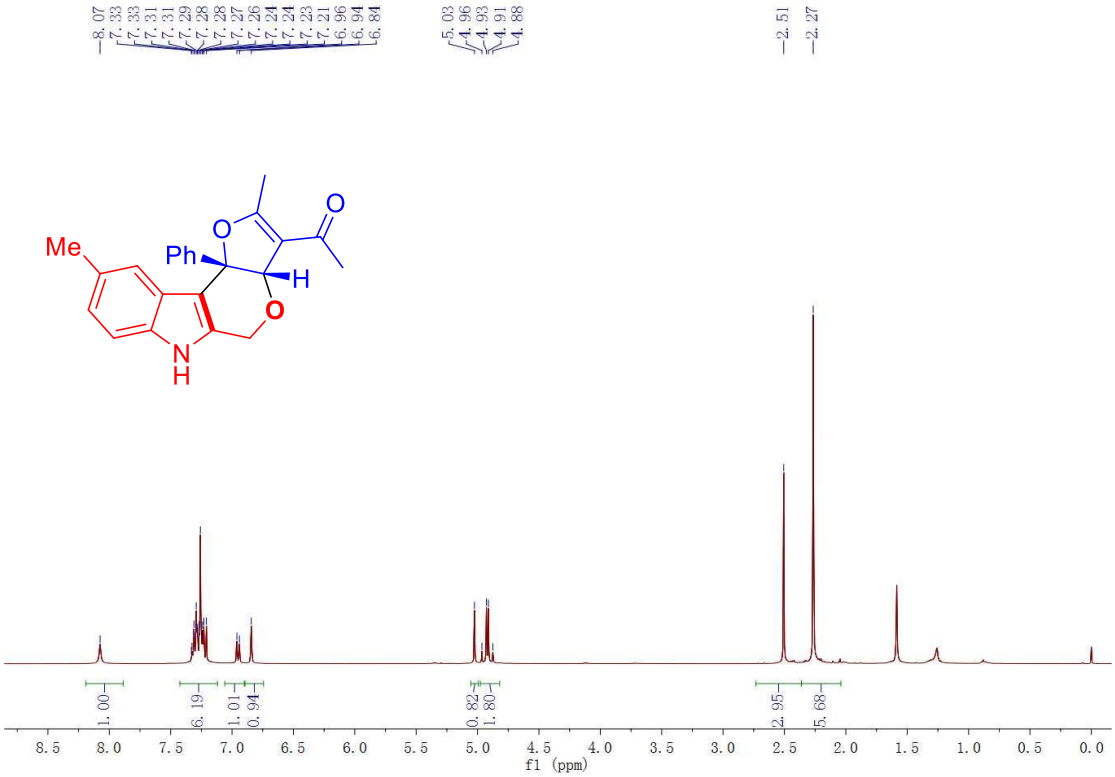
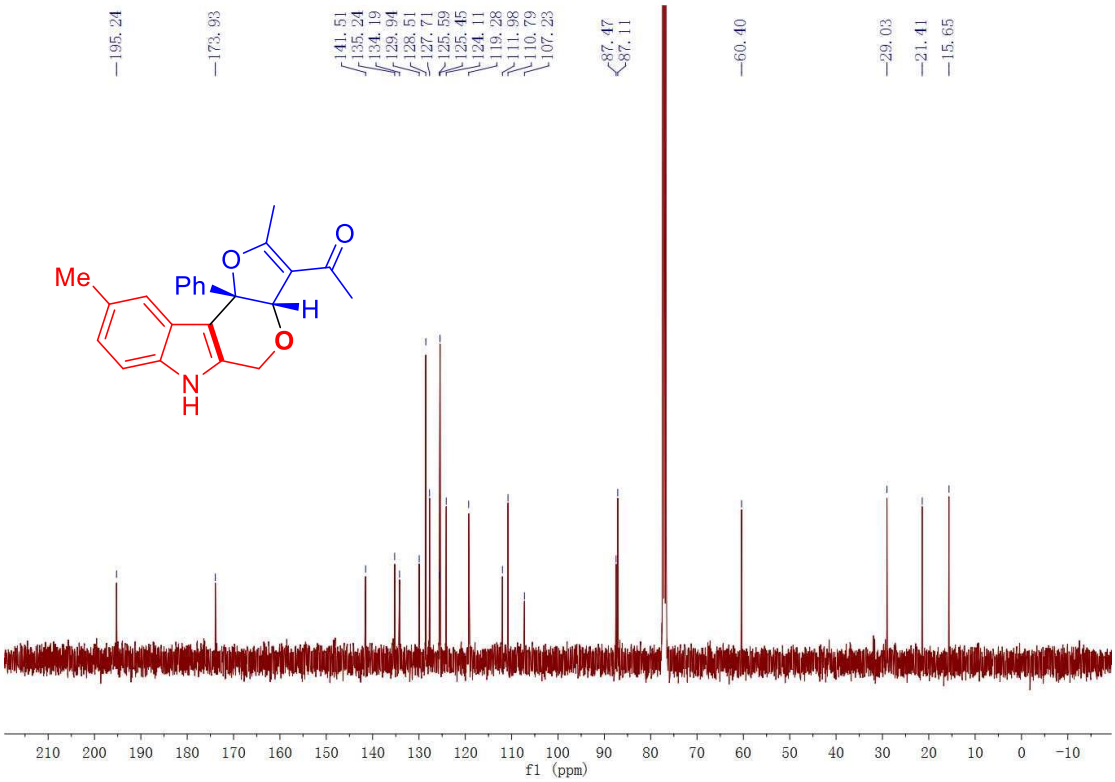
7.23
7.22
7.20
7.18
7.16
7.03
7.02
7.01
7.00
6.99
6.98
6.60
6.58
6.58
6.56
5.06
5.02
4.96
4.93
4.89
2.45
2.16
F
O
Ph
H
O
N
H
O
1.00
5.87
1.00
0.95
1.01
1.87
2.83
2.80
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

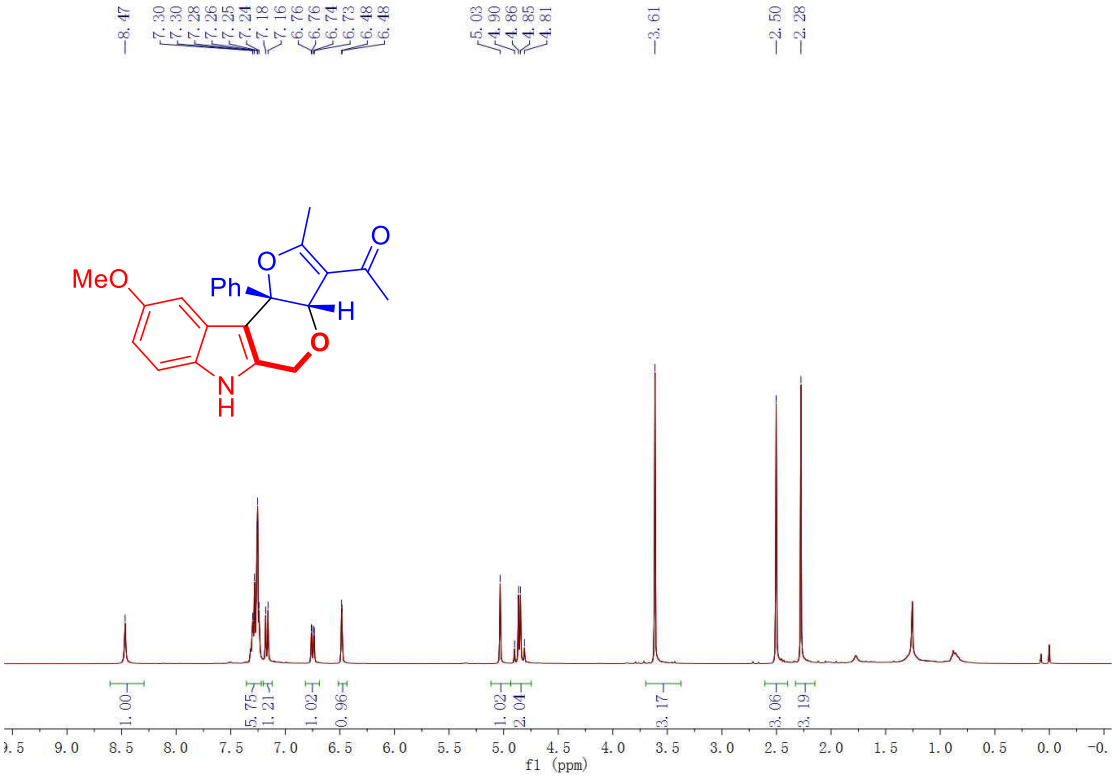

194.51
173.22
156.44
154.00
142.87
139.19
139.08
137.49
128.43
127.66
125.97
112.58
108.41
108.38
105.23
105.04
104.97
104.94
87.19
86.66
60.61
29.25
15.34
F
O
Ph
H
O
N
H
O
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

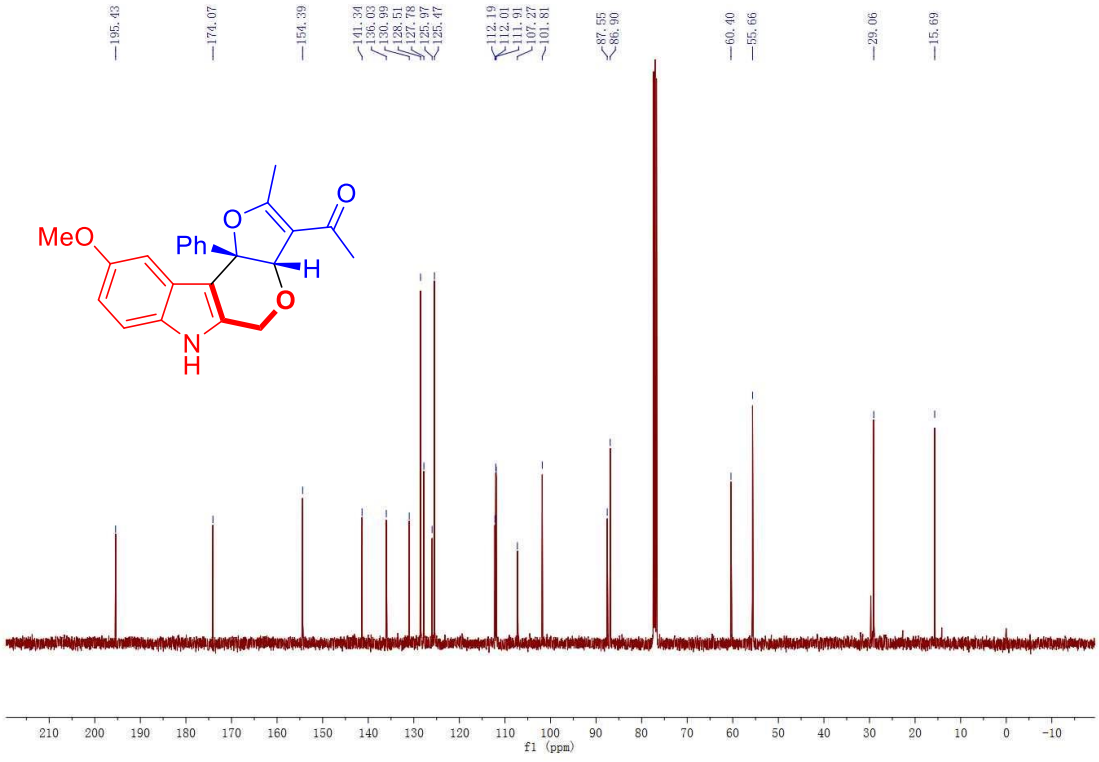
3p


8.07
7.33
7.33
7.31
7.31
7.29
7.28
7.28
7.27
7.26
7.24
7.24
7.23
7.21
6.96
6.94
6.84
5.03
4.96
4.93
4.91
4.88
2.51
2.27
Me
Ph
H
O
O
N
H
1.00
6.19
1.01
0.94
0.82
1.80
2.95
5.68
f1 (ppm)


195.24
173.93
141.51
135.24
134.19
129.94
128.51
127.71
125.59
125.45
124.11
119.28
111.98
110.79
107.23
87.47
87.11
60.40
29.03
21.41
15.65
Me
Ph
H
O
O
N
H
f1 (ppm)

3q


8.47
7.30
7.30
7.28
7.26
7.25
7.24
7.18
7.16
6.76
6.76
6.74
6.73
6.48
6.48
5.03
4.90
4.86
4.85
4.81
3.61
2.50
2.28
MeO
Ph
H
O
N
H
1.00
5.75
1.21
1.02
0.96
1.02
2.04
3.17
3.06
3.19
f1 (ppm)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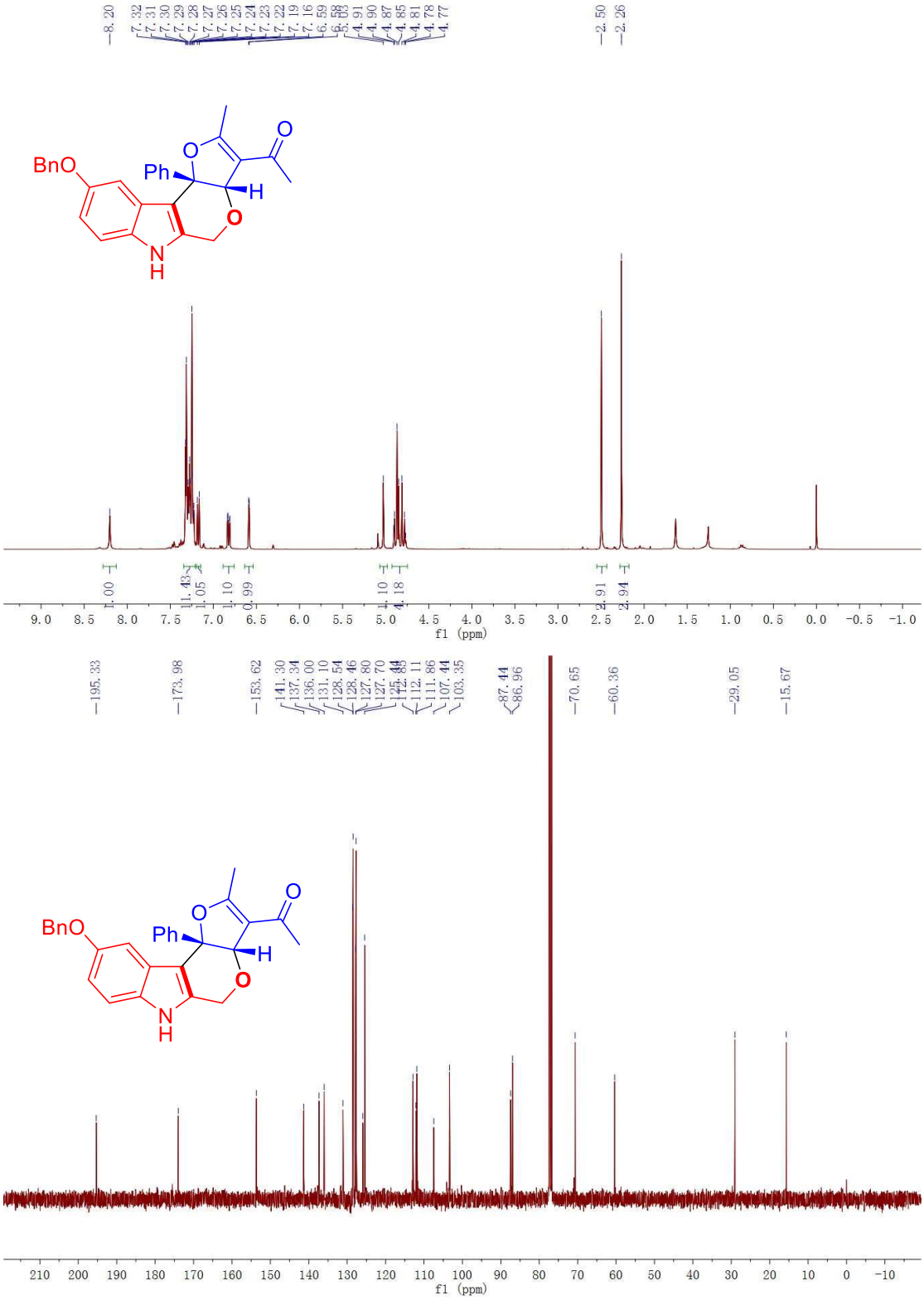
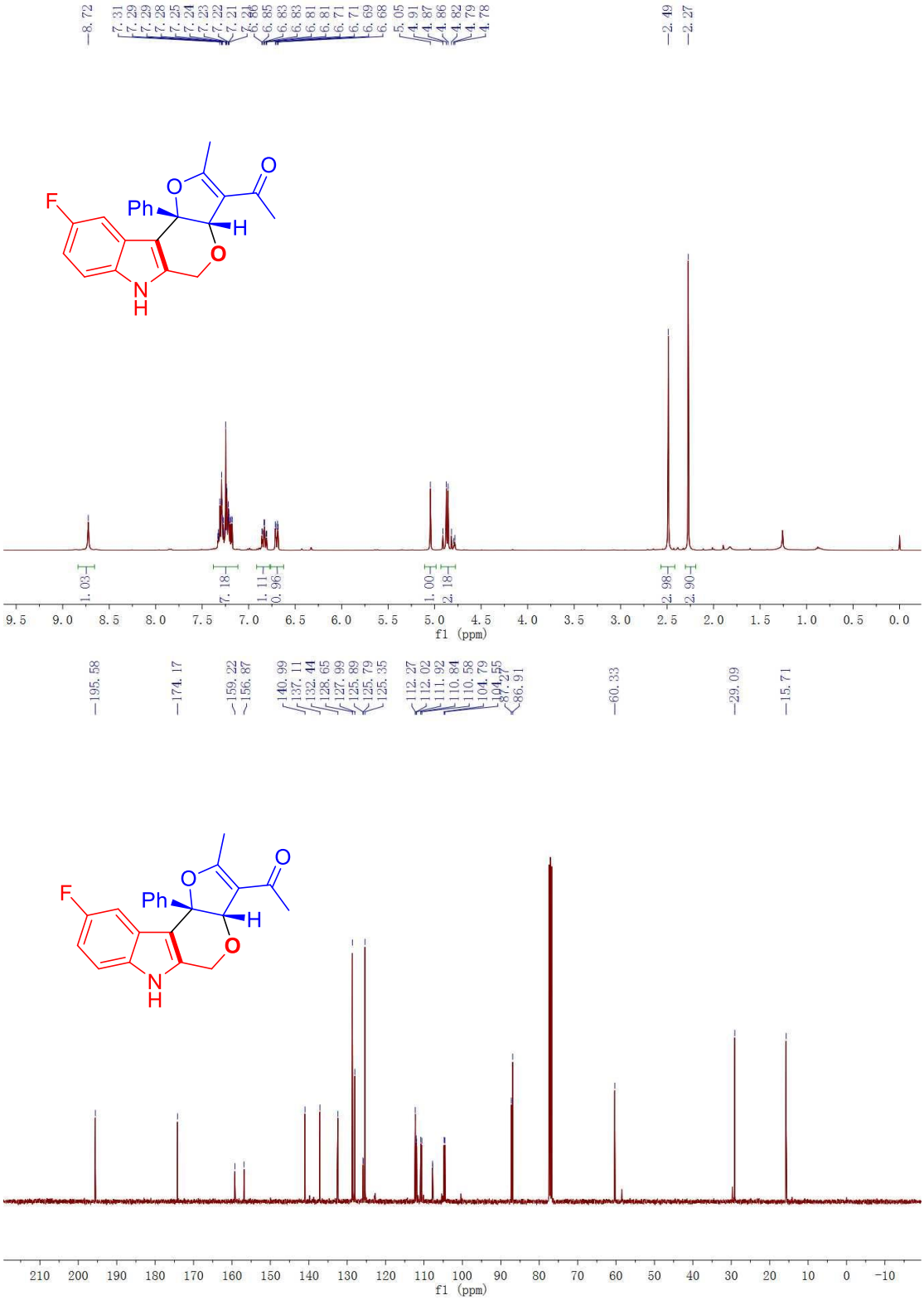
174.07
154.39
141.34
136.03
130.99
128.51
127.78
125.97
125.47
112.19
112.01
111.91
107.27
101.81
87.55
86.90
60.40
55.66
29.06
15.69
MeO
Ph
H
O
N
H
f1 (ppm)

3r



3s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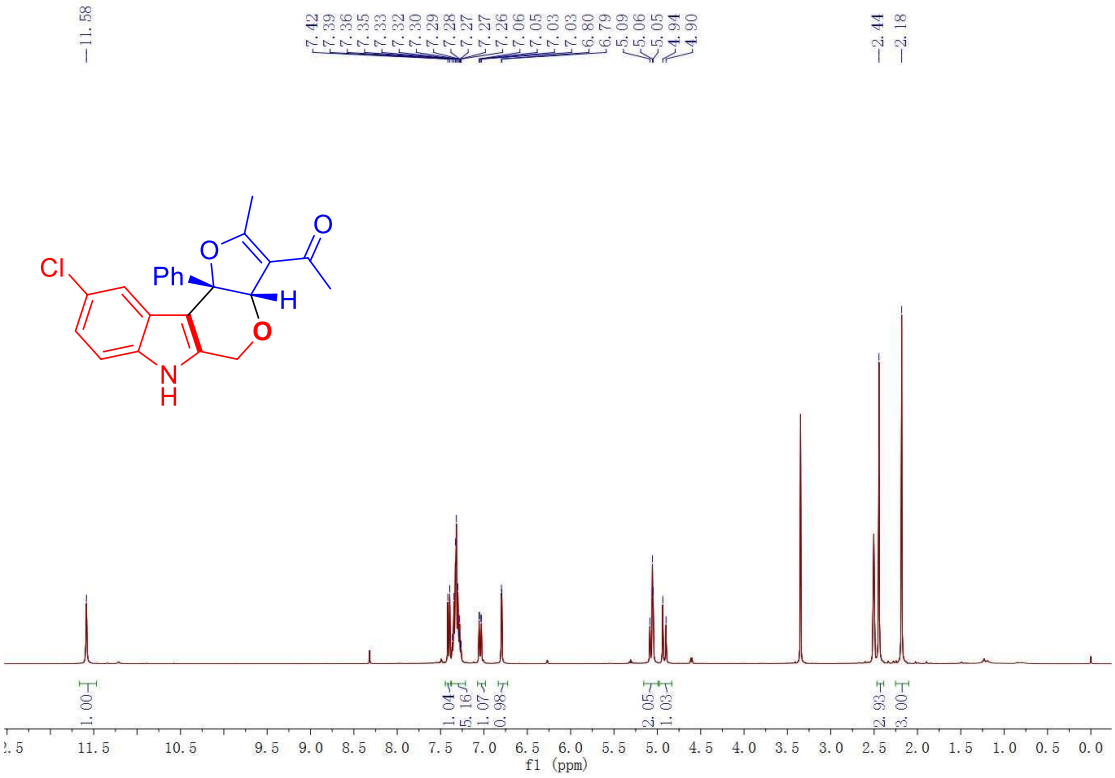
7.31
7.29
7.29
7.28
7.25
7.24
7.23
7.22
7.21
6.85
6.83
6.81
6.81
6.71
6.71
6.69
6.68
5.05
4.91
4.87
4.86
4.82
4.79
4.78
2.49
2.27
F
Ph
O
O
H
O
N
H
1.03
7.18
1.11
0.96
1.00
2.18
2.98
2.90
f1 (ppm)
195.58
174.17
159.22
156.87
140.99
137.11
132.44
128.65
127.99
125.89
125.79
125.35
112.27
112.02
111.92
110.84
110.58
104.79
104.55
87.27
86.91
60.33
29.09
15.71
f1 (ppm)

3t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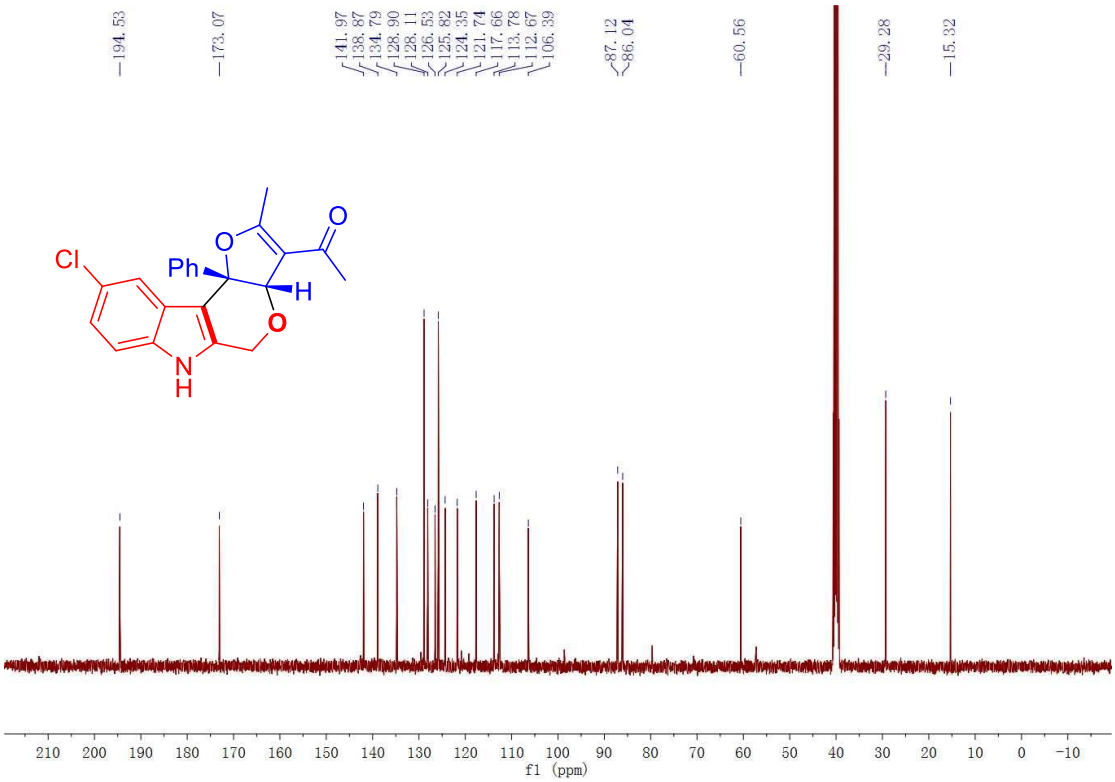
7.33
7.32
7.30
7.29
7.28
7.27
7.27
7.26
7.06
7.05
7.03
7.03
6.80
6.79
5.09
5.06
5.05
4.94
4.90
2.44
2.18
Cl
Ph
O
H
O
N
H
O
1.00
1.04
5.16
1.07
0.98
2.05
1.03
2.93
3.00
f1 (ppm)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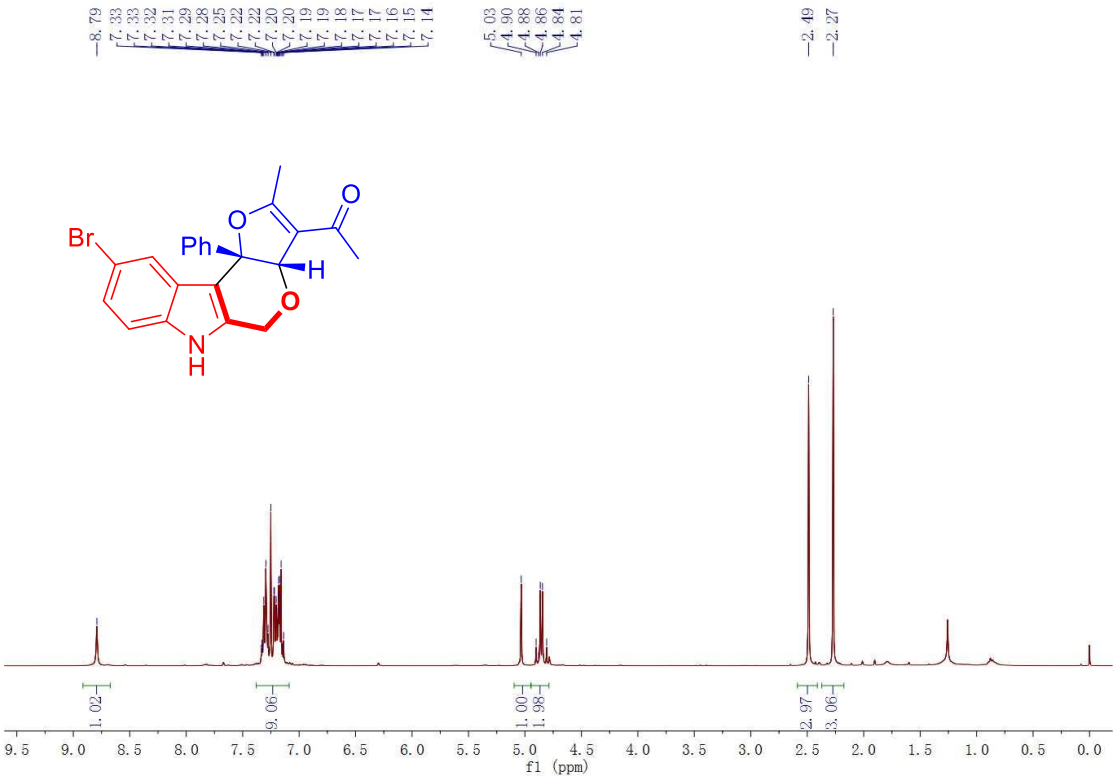
173.07
141.97
138.87
134.79
128.90
128.11
126.53
125.82
124.35
121.74
117.66
113.78
112.67
106.39
87.12
86.04
60.56
29.28
15.32
Cl
Ph
O
H
O
N
H
O
f1 (ppm)

3u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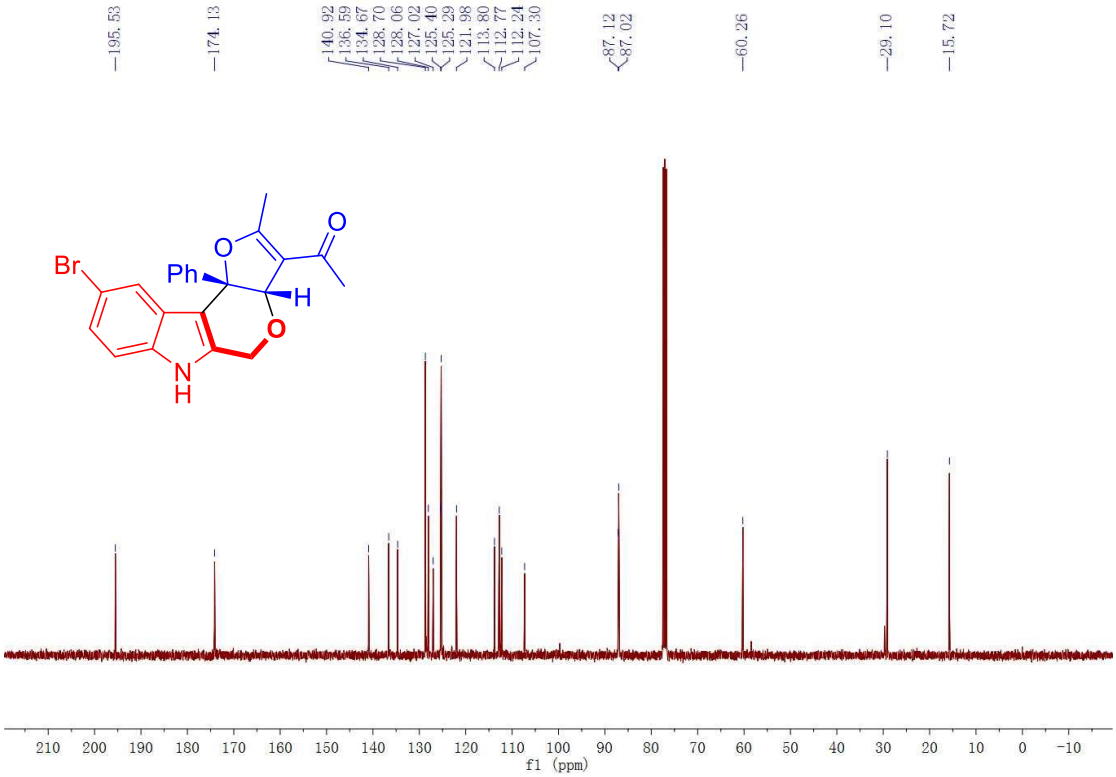
7.32
7.31
7.29
7.28
7.25
7.22
7.22
7.20
7.20
7.19
7.19
7.18
7.17
7.17
7.16
7.15
7.14
5.03
4.90
4.88
4.86
4.84
4.81
2.49
2.27
Br
Ph
O
H
N
H
1.02
9.06
1.00
1.98
2.97
3.06
f1 (ppm)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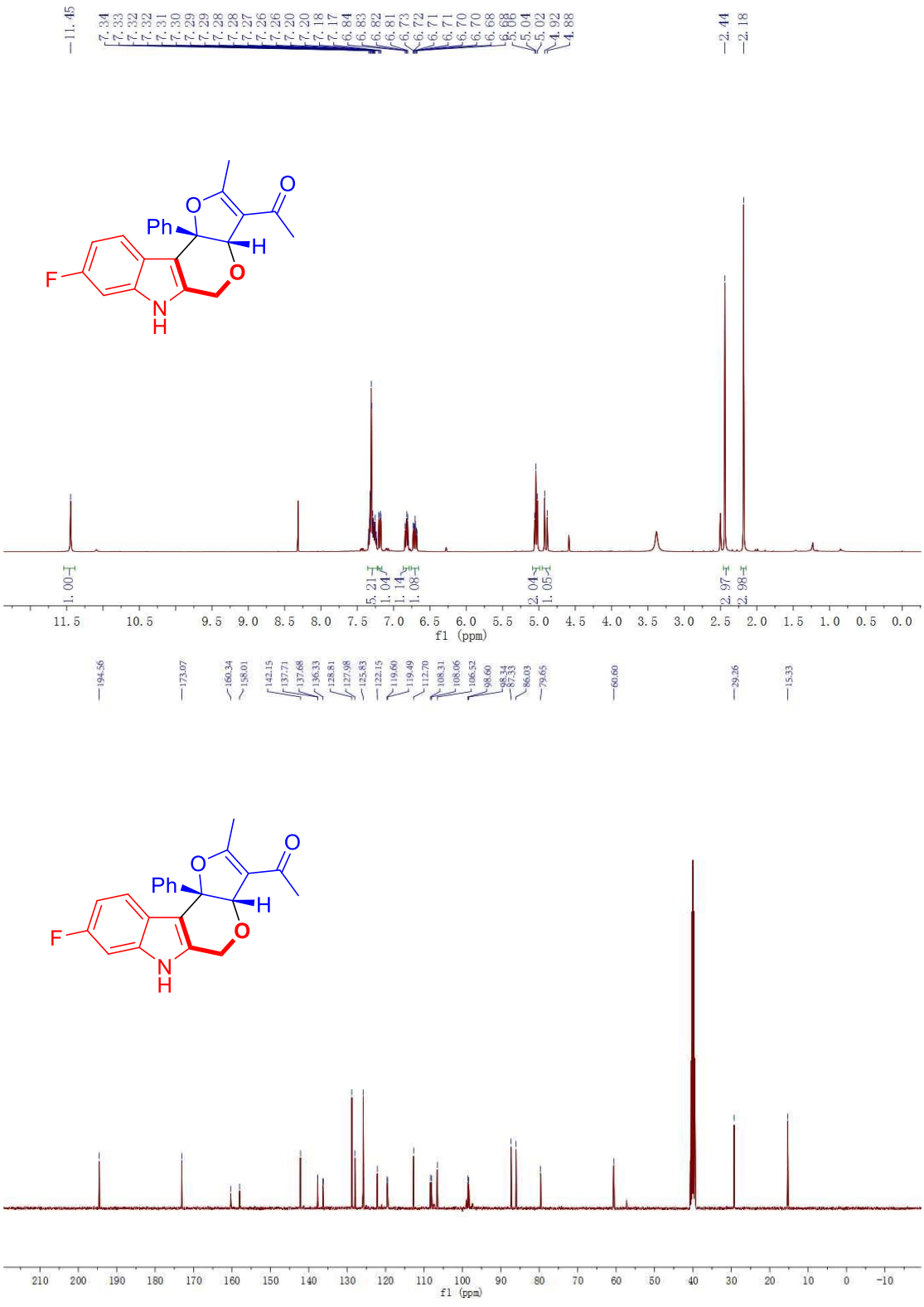
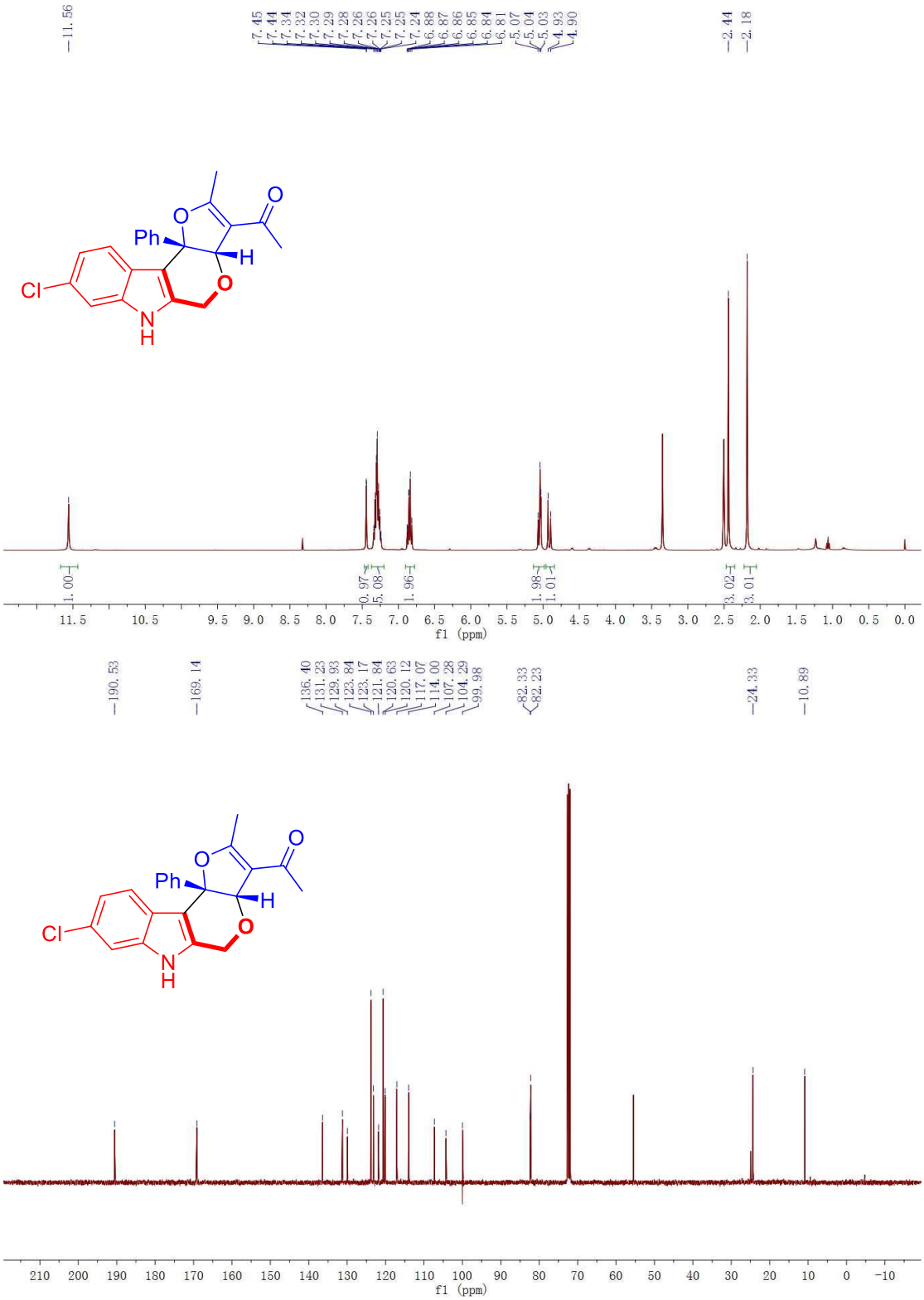
174.13
140.92
136.59
134.67
128.70
128.06
127.02
125.40
125.29
121.98
113.80
112.77
112.24
107.30
87.12
87.02
60.26
29.10
15.72
Br
Ph
O
H
N
H
f1 (ppm)

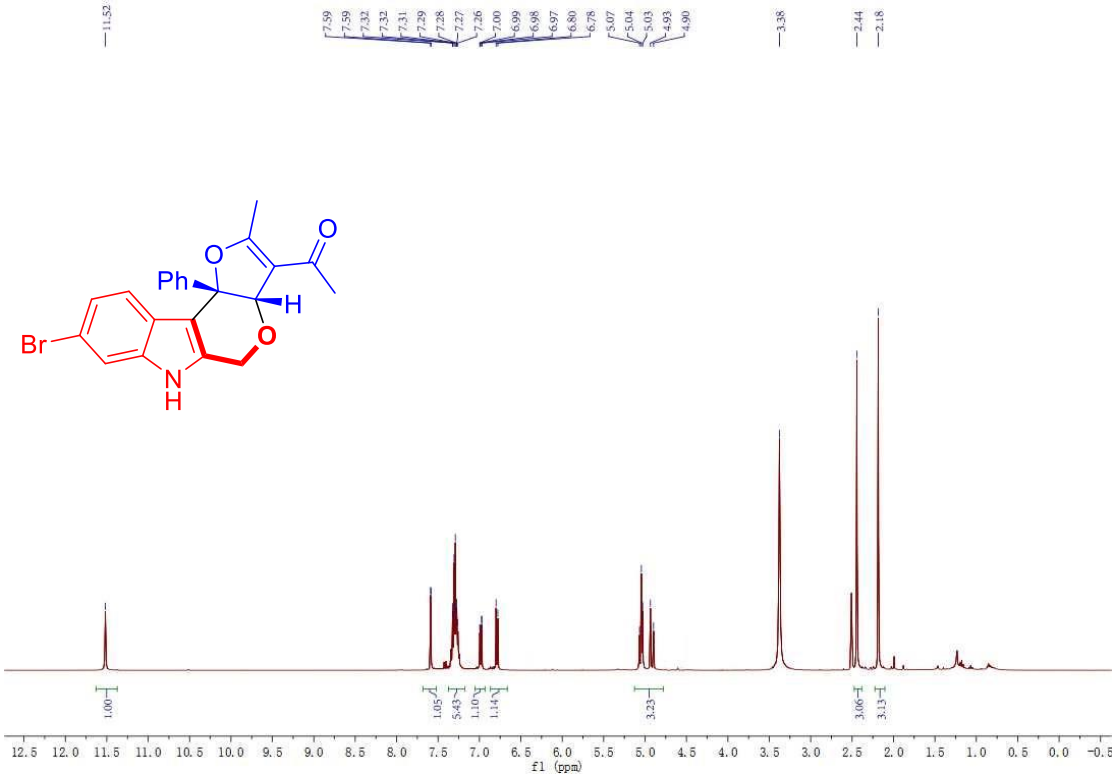
3v


11.45
7.34
7.33
7.32
7.32
7.31
7.30
7.29
7.29
7.28
7.28
7.27
7.26
7.26
7.20
7.20
7.18
7.17
6.84
6.83
6.82
6.81
6.73
6.72
6.71
6.71
6.70
6.70
6.68
6.68
5.06
5.04
5.02
4.92
4.88
2.44
2.18
O
O
Ph
H
F
O
N
H
1.00
5.21
1.04
1.14
1.08
2.04
1.05
2.97
2.98
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
194.56
173.07
160.34
158.01
142.15
137.71
137.68
136.33
128.81
127.98
125.83
122.15
119.60
119.49
112.70
108.31
108.06
106.52
98.60
88.34
87.33
86.03
79.65
60.60
29.26
15.33
O
O
Ph
H
F
O
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

3w


11.56
7.45
7.44
7.34
7.32
7.30
7.29
7.28
7.26
7.26
7.25
7.25
7.24
6.88
6.87
6.86
6.85
6.84
6.81
5.07
5.04
5.03
4.93
4.90
2.44
2.18
O
Ph
H
O
Cl
N
H
1.00
0.97
5.08
1.96
1.98
1.01
3.02
3.01
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
190.53
169.14
136.40
131.23
129.93
123.84
123.17
121.84
120.63
120.12
117.07
114.00
107.28
104.29
99.98
82.33
82.23
24.33
10.89
O
Ph
H
O
Cl
N
H
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

3x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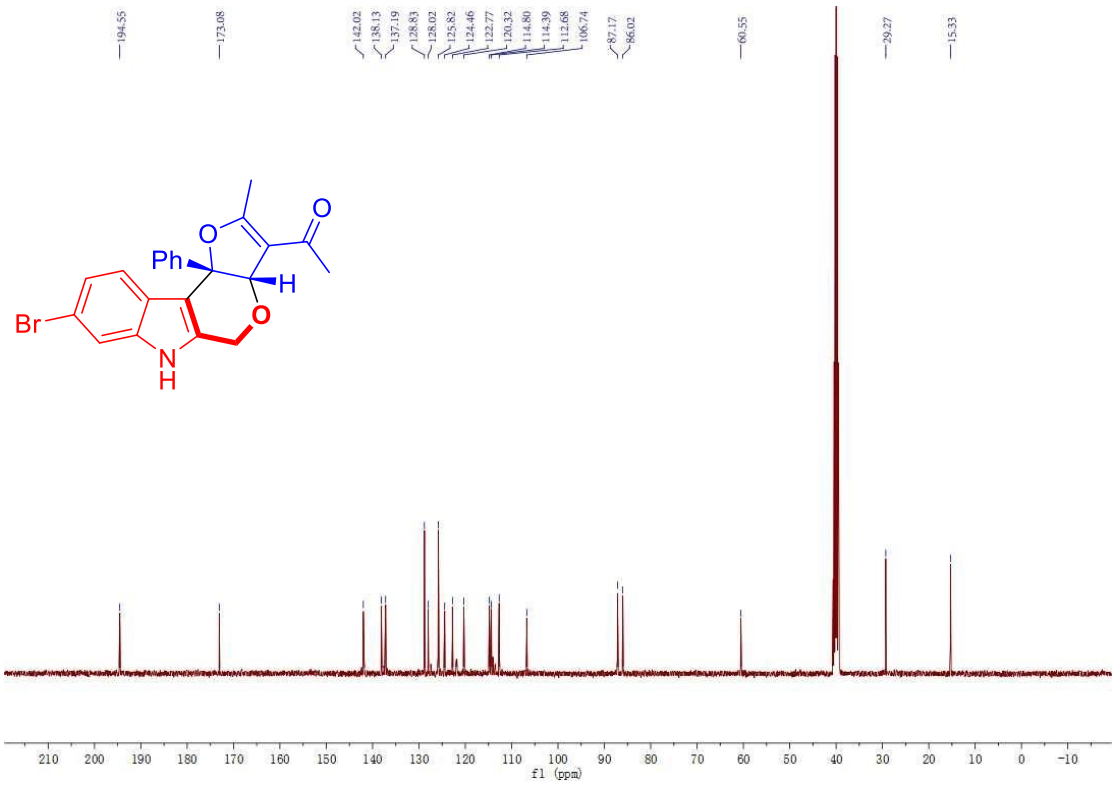
7.59
7.59
7.32
7.32
7.31
7.29
7.28
7.27
7.26
7.00
6.99
6.98
6.97
6.80
6.78
5.07
5.04
5.03
4.93
4.90
3.38
2.44
2.18
O
Ph
H
O
Br
N
H
1.00
1.05
5.43
1.10
1.14
3.23
3.06
3.13
f1 (ppm)


194.55
173.08
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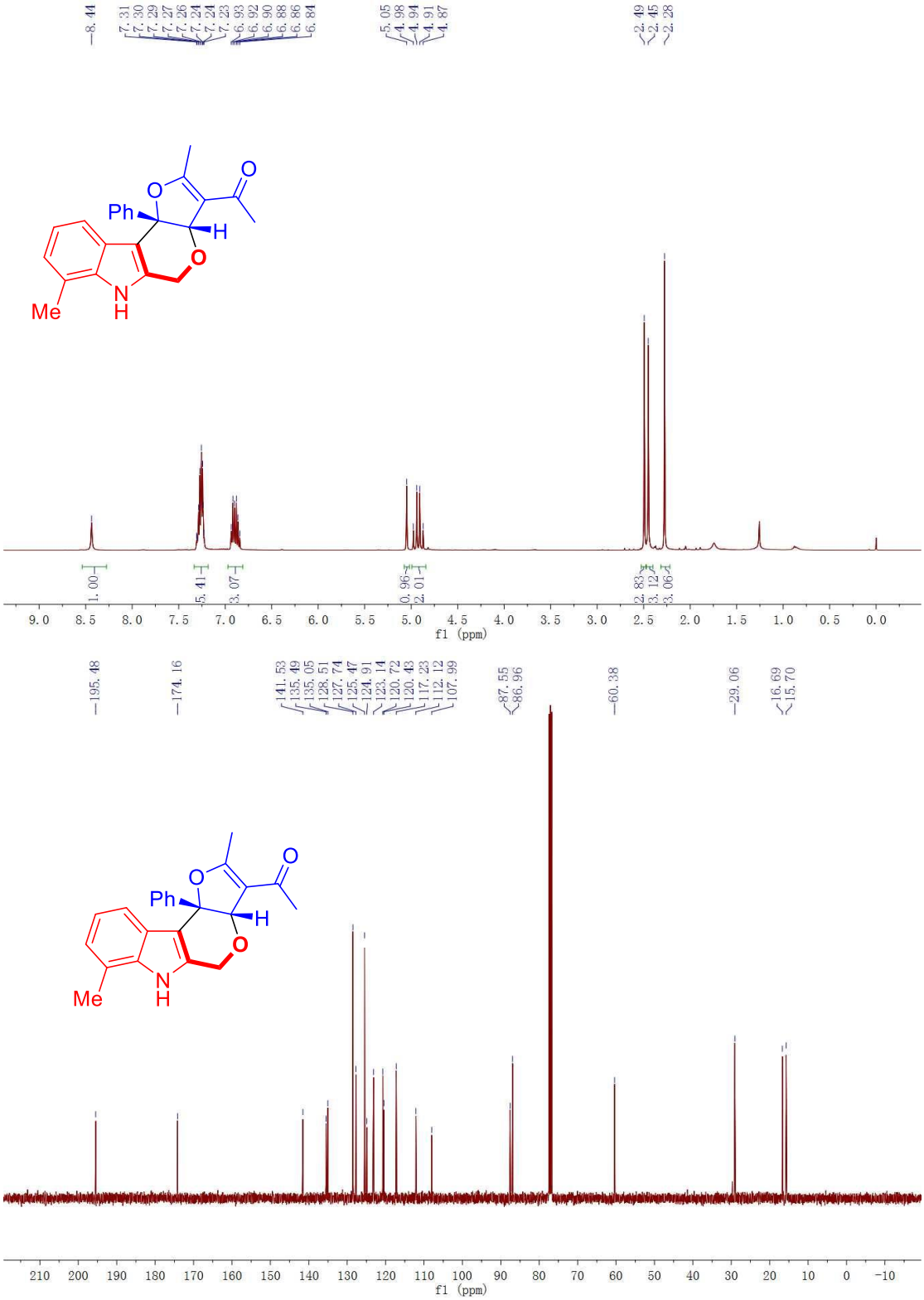
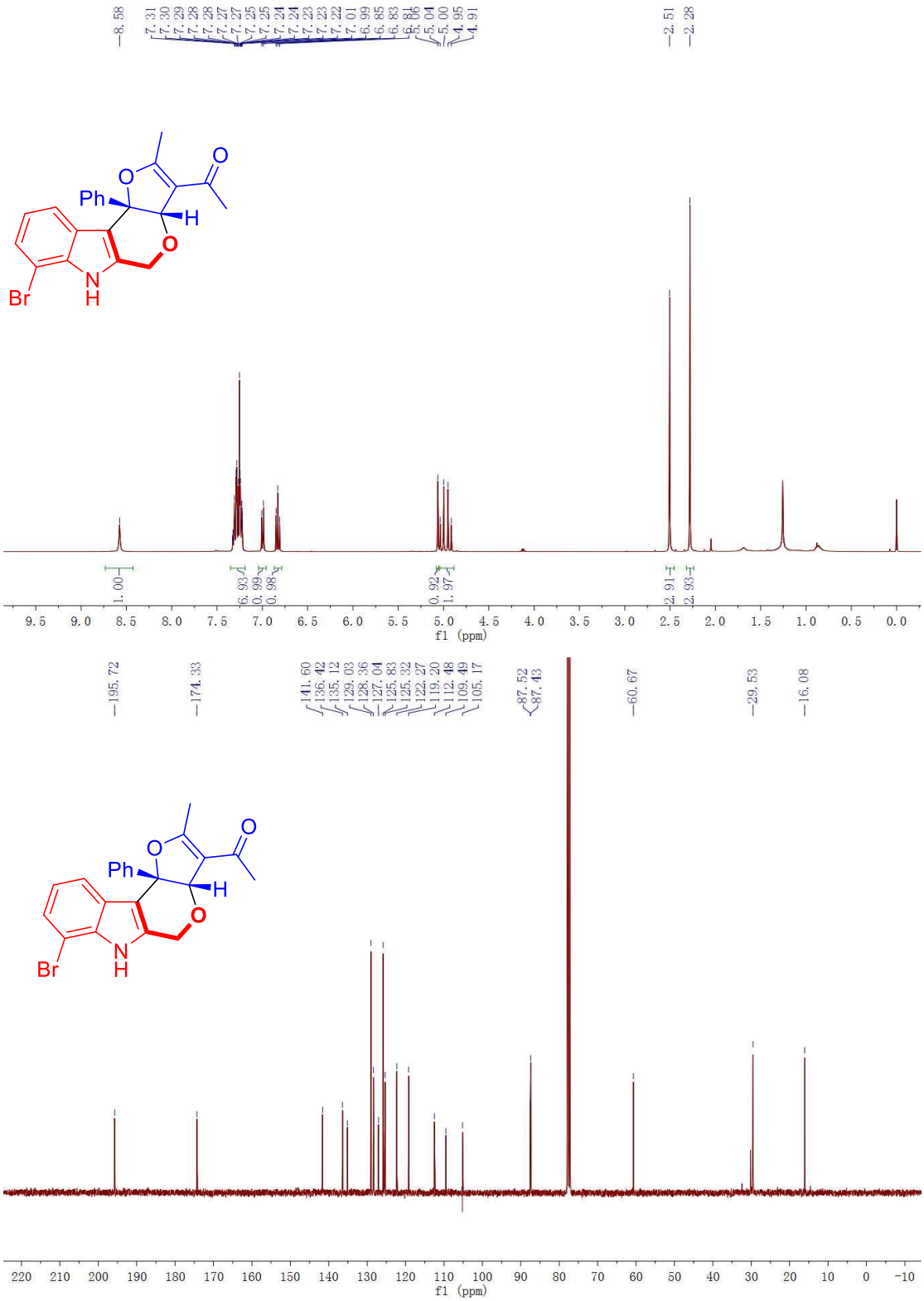
138.13
137.19
128.83
128.02
125.82
124.46
122.77
120.32
114.80
114.39
112.68
106.74
87.17
86.02
60.55
29.27
15.33
O
Ph
H
O
Br
N
H
f1 (ppm)

3y


8.44
7.31
7.30
7.29
7.27
7.26
7.24
7.24
7.23
6.93
6.92
6.90
6.88
6.86
6.84
5.05
4.98
4.94
4.91
4.87
2.49
2.45
2.28
O
Ph
H
O
N
H
Me
1.00
5.41
3.07
0.96
2.01
2.83
3.12
3.06
f1 (ppm)
195.48
174.16
141.53
135.49
135.05
128.51
127.74
125.47
124.91
123.14
120.72
120.43
117.23
112.12
107.99
87.55
86.96
60.38
29.06
16.69
15.70
f1 (ppm)

3z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7.30
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7.28
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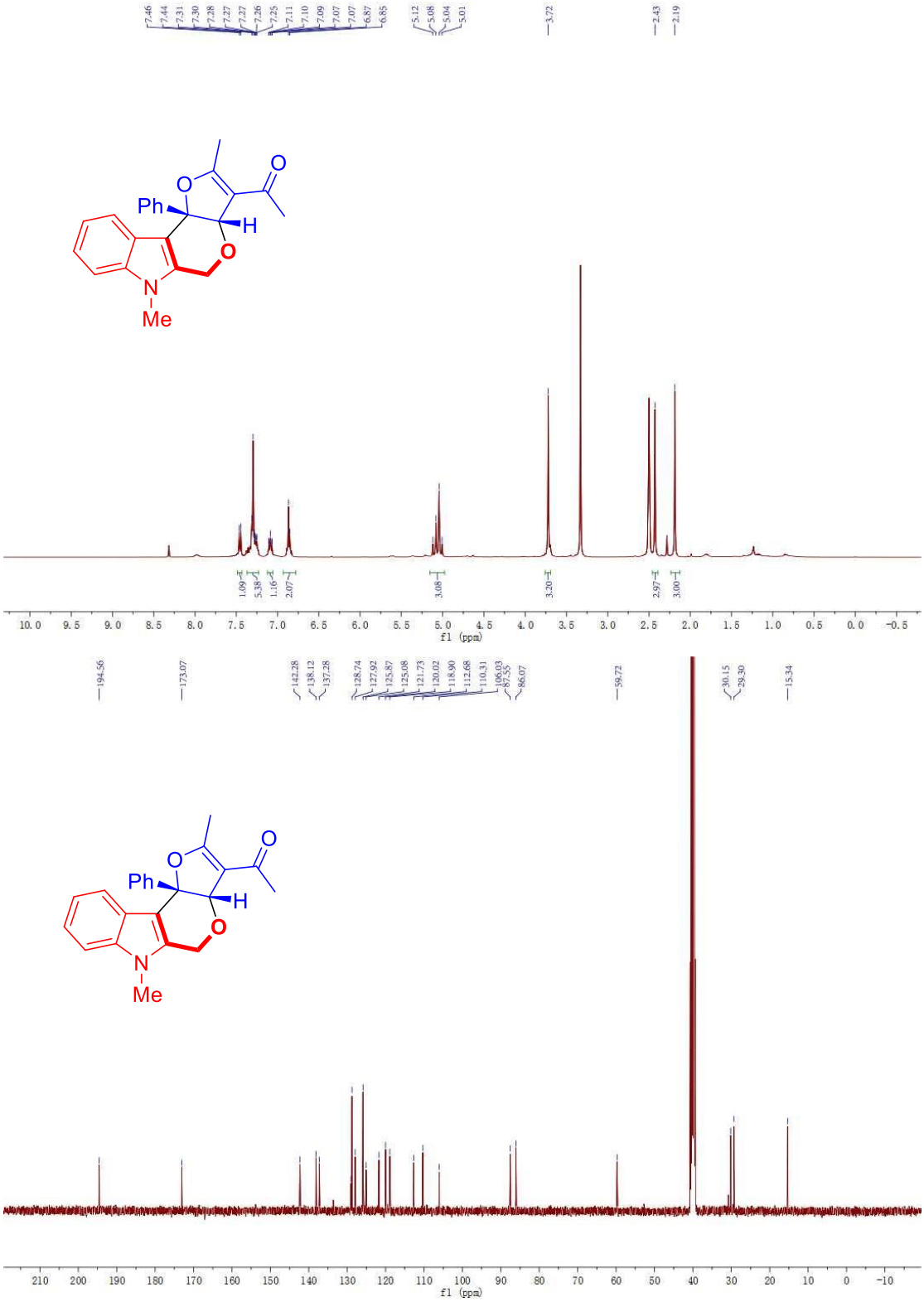
7.27
7.25
7.25
7.24
7.24
7.23
7.23
7.22
7.01
6.99
6.85
6.83
6.81
6.80
5.04
5.00
4.95
4.91
2.51
2.28
O
Ph
H
O
N
H
Br
1.00
6.93
0.99
0.98
0.92
1.97
2.91
2.93
f1 (ppm)
195.72
174.33
141.60
136.42
135.12
129.03
128.36
127.04
125.83
125.32
122.27
119.20
112.48
109.49
105.17
87.52
87.43
60.67
29.53
16.08
f1 (ppm)

3a'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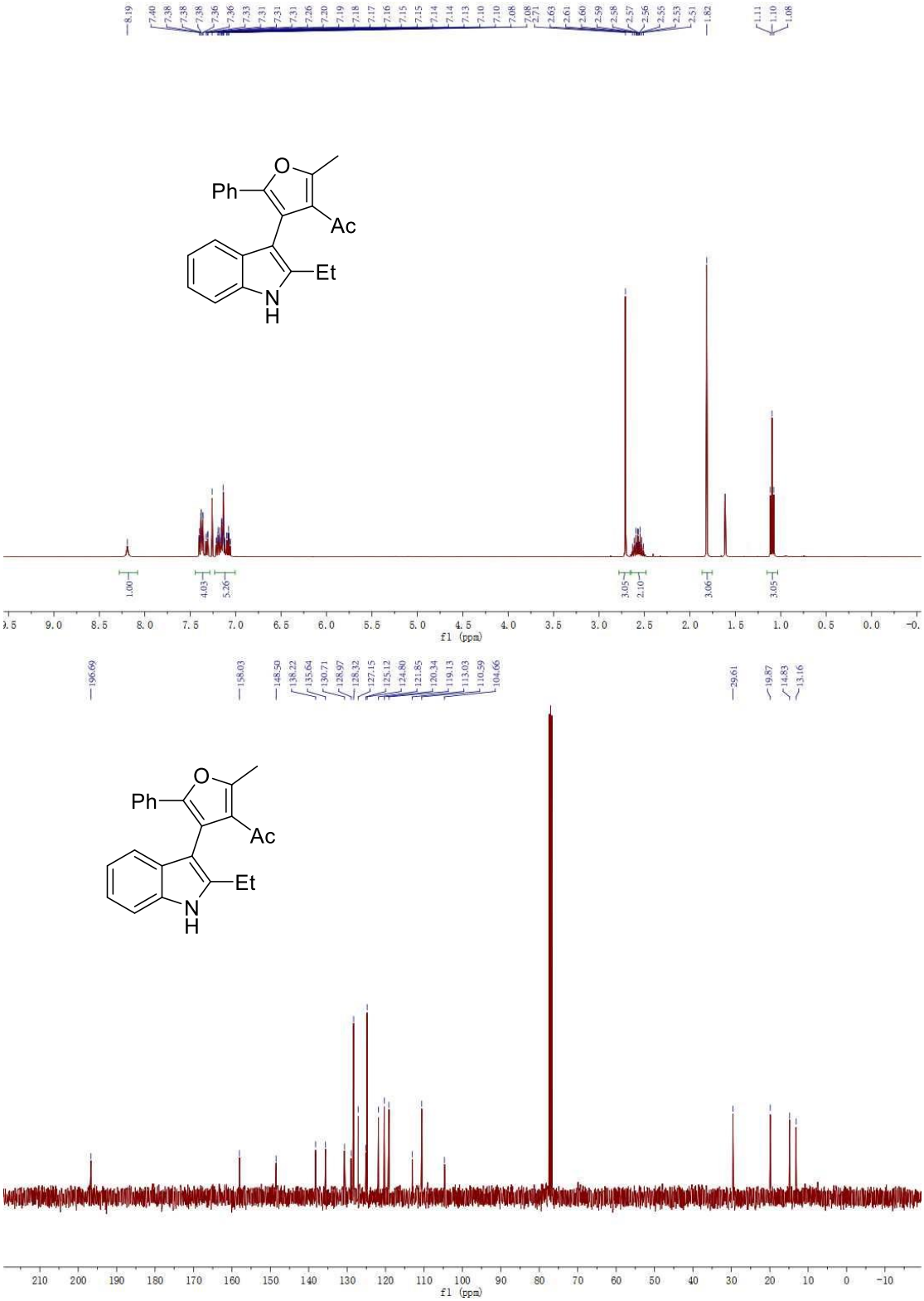
7.44
7.31
7.30
7.28
7.27
7.27
7.26
7.25
7.11
7.10
7.09
7.07
7.07
6.87
6.85
5.12
5.08
5.04
5.01
3.72
2.43
2.19
O
O
Ph
H
O
N
Me
1.09
5.38
1.16
2.07
3.08
3.20
2.97
3.00
f1 (ppm)
194.56
173.07
142.28
138.12
137.28
128.74
127.92
125.87
125.08
121.73
120.02
118.90
112.68
110.31
106.03
87.55
86.07
59.72
30.15
29.30
15.34
f1 (ppm)

S1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7.36
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7.33
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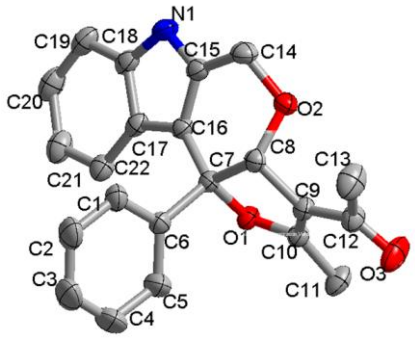
7.31
7.31
7.26
7.20
7.19
7.18
7.17
7.16
7.15
7.15
7.14
7.14
7.13
7.10
7.10
7.08
7.08
2.71
2.63
2.61
2.60
2.59
2.58
2.57
2.56
2.55
2.53
2.51
1.82
1.11
1.10
1.08
O
Ph
Ac
Et
N
H
1.00
4.03
5.26
3.05
2.10
3.06
3.05
f1 (ppm)
196.69
158.03
148.50
138.22
135.64
130.71
128.97
128.32
127.15
125.12
124.80
121.85
120.34
119.13
113.03
110.59
104.66
29.61
19.87
14.83
13.16
f1 (ppm)

5. X-ray crystal structure of 3a and 3l



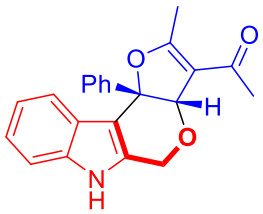
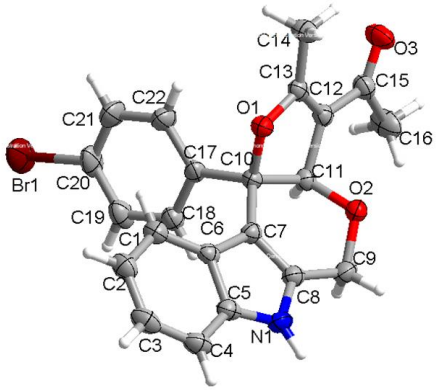


Table 1 Crystal data and structure refinement for 202104102.

Identification code	202104102
Empirical formula	$C_{22}H_{19}NO_3$
Formula weight	345.38
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	8.34646(16)
b/Å	28.3786(5)
c/Å	8.67019(14)
α/°	90
β/°	94.7923(18)
γ/°	90
Volume/Å^3	2046.45(6)

Z	4
$\rho_{calc}g/cm^3$	1.121
μ/mm^{-1}	0.601
F(000)	728.0
Crystal size/mm^3	0.16 × 0.08 × 0.06
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	10.636 to 134.048
Index ranges	-7 ≤ h ≤ 9, -33 ≤ k ≤ 33, -9 ≤ l ≤ 10
Reflections collected	14602
Independent reflections	3649 [R_{int} = 0.0328, R_{sigma} = 0.0272]
Data/restraints/parameters	3649/0/241
Goodness-of-fit on F^2	1.034
Final R indexes [I>=2σ (I)]	R_1 = 0.0493, wR_2 = 0.1455
Final R indexes [all data]	R_1 = 0.0625, wR_2 = 0.1591
Largest diff. peak/hole / e $Å^{-3}$	0.15/-0.17



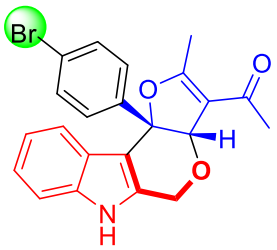


Table 1 Crystal data and structure refinement for 202104106.

Identification code	202104106
Empirical formula	$C_{22}H_{18}BrNO_3$
Formula weight	424.28
Temperature/K	293(2)
Crystal system	monoclinic
Space group	$P2_1/c$
a/Å	8.1529(6)
b/Å	30.7743(11)
c/Å	8.7822(4)
α/°	90
β/°	95.200(5)
γ/°	90
Volume/Å^3	2194.41(19)
Z	4
ρ_{calc}g/cm^3	1.284
μ/mm^{-1}	2.711
F(000)	864.0
Crystal size/mm^3	0.14 × 0.1 × 0.06
Radiation	CuKα (λ = 1.54184)
2Θ range for data collection/°	10.516 to 134.124

Index ranges	$-9 \leq h \leq 8, -36 \leq k \leq 36, -8 \leq l \leq 10$
Reflections collected	8408
Independent reflections	3918 [R_{int} = 0.0293, R_{sigma} = 0.0443]
Data/restraints/parameters	3918/0/250
Goodness-of-fit on F^2	1.038
Final R indexes [I>=2σ (I)]	R_1 = 0.0578, wR_2 = 0.1529
Final R indexes [all data]	R_1 = 0.0755, wR_2 = 0.1675
Largest diff. peak/hole / e $Å^{-3}$	0.21/-0.44

6. Computational Methods:

All the calculations were performed using the Gaussian 09 program[5]. The B3LYP[6-7] density functional was used to optimize the geometries of the molecules. The 6-31G(d, p) basis set was applied for the atoms.

Geometrical Coordinates of the Listed Complexes

1

1

Zero-point correction= 0.258528

Thermal correction to Energy= 0.281256

Thermal correction to Enthalpy= 0.282200

Thermal correction to Gibbs Free Energy= 0.201867

Sum of electronic and zero-point Energies= -1254.815741

Sum of electronic and thermal Energies= -1254.793013

Sum of electronic and thermal Enthalpies= -1254.792069

Sum of electronic and thermal Free Energies= -1254.872402

Cartesian coordinates

C	0.316535	0.089101	0.123255
C	0.304566	-0.500052	1.511427
H	1.183311	-0.224944	2.099186
H	-0.582716	-0.102095	2.018932
H	0.203345	-1.584610	1.447035
C	0.860718	1.498399	-0.052091
C	-0.101225	2.524619	-0.579202
C	0.340252	3.970199	-0.701460
H	1.167070	4.070717	-1.412182
H	-0.508048	4.554722	-1.056564
H	0.678917	4.364669	0.261507
C	2.146858	1.823706	0.182077
H	2.477808	2.847611	0.028067
C	3.221648	0.966590	0.801469
O	3.707090	1.389396	1.843812
C	3.684751	-0.288988	0.156346
C	4.621135	-1.075435	0.850999
C	3.254423	-0.688717	-1.119056
C	5.106054	-2.247607	0.285026
H	4.949237	-0.743159	1.830020
C	3.747219	-1.863781	-1.684495
H	2.536131	-0.090715	-1.668262
C	4.668641	-2.643356	-0.984202
H	5.824401	-2.855314	0.826623

H	3.409309	-2.170453	-2.669173
H	5.048082	-3.560009	-1.426079
O	-0.137199	-0.486260	-0.848299
O	-1.242485	2.220332	-0.903833
H	-2.361980	0.858868	-0.968530
C	-3.468099	-0.151053	0.195549
C	-4.729726	-1.042391	0.146302
O	-2.880518	0.073693	1.229360
O	-3.170796	0.289408	-1.013090
F	-5.055138	-1.461200	1.373531
F	-4.513671	-2.120719	-0.629536
F	-5.772980	-0.360885	-0.362423

Vibrational frequencies

-14.8013	11.5634	24.7906
28.1699	33.3970	44.5457
59.7401	74.9399	82.9602
93.7881	100.5658	106.2972
115.7411	151.2320	160.1901
178.5094	191.6117	197.7425
242.3955	249.2433	256.8840
263.2903	352.3583	385.6756
398.7635	415.3588	426.7944
429.7921	442.7815	500.3487
509.0193	526.5303	558.1054
588.9821	599.1237	629.3739
638.8775	668.3219	675.7188
689.8058	703.8120	740.0421
761.0852	771.8994	807.7419
809.2443	851.1648	867.5370
893.6616	908.4415	960.0771
991.2685	993.3885	1015.2621
1016.9340	1019.0460	1047.3290
1050.2751	1063.9951	1089.8892
1114.1175	1190.8429	1195.8696
1200.4305	1207.3225	1213.1821
1248.4381	1254.5887	1296.8923
1323.8143	1346.3763	1366.5842
1370.2178	1402.1365	1406.8108
1474.1168	1480.3174	1482.4515
1485.2992	1489.8693	1491.4023
1531.5987	1632.2976	1653.0406
1660.5614	1738.2202	1745.7956
1799.8362	1855.4817	3055.3266
3057.9690	3124.5688	3130.5617

3169.5053	3175.7507	3188.7470
3189.2833	3201.0717	3209.6115
3221.7691	3224.7119	3408.5538

2

Zero-point correction= 0.281498

Thermal correction to Energy= 0.303402

Thermal correction to Enthalpy= 0.304346

Thermal correction to Gibbs Free Energy= 0.225616

Sum of electronic and zero-point Energies= -957.092659

Sum of electronic and thermal Energies= -957.070756

Sum of electronic and thermal Enthalpies= -957.069812

Sum of electronic and thermal Free Energies= -957.148542

Cartesian coordinates

C	-0.363057	-0.338344	-0.171617
C	-0.500325	-1.080711	1.130392
H	0.196573	-0.717405	1.890766
H	-1.521370	-0.906663	1.498091
H	-0.365556	-2.150337	0.960251
C	-0.168759	1.171340	-0.112779
C	-1.330304	1.988113	-0.597140
C	-1.204120	3.496263	-0.688425
H	-0.370107	3.787493	-1.334548
H	-2.134803	3.891556	-1.094877
H	-1.028969	3.934589	0.299585
C	0.966892	1.759135	0.307967
H	1.035181	2.844124	0.319353
C	2.154964	1.105786	0.965881
O	2.435233	1.506788	2.089248
C	2.959091	0.066220	0.270484
C	3.967891	-0.582383	1.004875
C	2.778458	-0.248753	-1.085494
C	4.770502	-1.539083	0.396383
H	4.099058	-0.315383	2.047979
C	3.590592	-1.205035	-1.693348
H	2.004177	0.242020	-1.663749
C	4.582529	-1.851251	-0.954909
H	5.543885	-2.042578	0.968404
H	3.444960	-1.447143	-2.741265
H	5.210886	-2.598772	-1.430353
O	-0.449098	-0.867975	-1.263279
O	-2.384380	1.449681	-0.909377
H	-3.436854	-0.063760	-0.852120
C	-4.459597	-1.121573	0.353949

C	-5.678016	-2.013629	0.386447
O	-3.784809	-0.844019	1.329031
O	-4.209657	-0.669903	-0.881712
H	-6.555229	-1.457801	0.042258
H	-5.840894	-2.376881	1.400330
H	-5.539691	-2.856210	-0.297381

Vibrational frequencies

13.8640	24.3320	25.1306
35.2821	44.9056	48.6204
69.5985	78.2869	83.3071
96.3927	112.5336	121.6757
131.3332	161.3199	162.8944
180.1037	189.4370	211.1509
239.8586	253.0466	343.8917
392.5910	416.6681	434.2152
438.1442	447.7465	494.8250
518.9456	557.4652	584.5408
600.1758	603.9997	629.6178
637.4092	672.7600	676.1787
705.0508	738.9953	768.9965
807.5241	822.8745	868.9270
884.9867	892.9141	907.7083
961.4605	992.2334	993.5876
1014.4418	1016.9682	1018.9113
1020.4247	1048.8906	1050.2123
1068.3639	1069.7657	1091.1246
1114.3493	1190.2639	1202.4932
1208.7763	1247.6693	1270.2985
1298.2632	1347.2809	1366.1195
1370.1508	1383.0853	1402.8545
1410.1031	1442.1771	1477.6962
1483.3689	1485.2212	1489.8213
1490.1268	1491.2722	1491.4436
1532.0164	1632.8674	1653.7870
1665.4726	1737.7861	1752.6677
1799.6079	1822.8956	3032.0440
3057.1797	3066.4828	3114.1611
3123.5210	3132.2220	3162.7605
3173.8780	3181.9860	3185.3856
3187.1921	3199.7226	3208.9992
3221.3644	3227.0040	3553.0064

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