Supporting Information

An Atmosphere and Light Tuned Highly Diastereoselective Synthesis of Cyclobuta/penta[*b*]indoles from Aniline-tethered Alkylidenecyclopropanes with Alkynes

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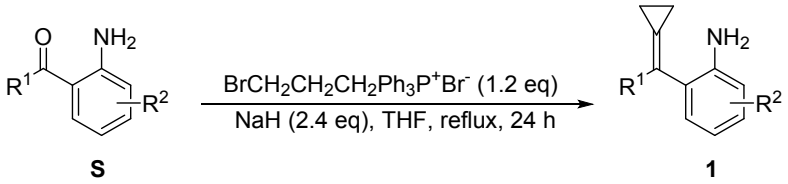
1. General Remarks.

Melting point (MP) was obtained with a Yanagimoto micro melting point apparatus and is uncorrected. Optical rotations were determined in a solution of CH_2Cl_2 at 20 ^oC by using a Perkin-Elmer-241 MC polarimeter; $[\alpha]_D$-values are given in units of 10^{-1} deg cm^2 g^{-1}. Infrared spectra were measured on a spectrometer. ^1H NMR spectra were recorded on a Agilent DD2 400-MR spectrometer for solution in $CDCl_3$ with tetramethylsilane (TMS) as internal standard; *J*-values are in Hz. ^{13}C NMR spectra were recorded at 100 MHz. ^{19}F NMR spectra were recorded at 376 MHz. Data for ^1H, ^{13}C, ^{19}F NMR were recorded as follows: chemical shift (δ, ppm), multiplicity (s = singlet, d = doublet, t = triplet, m = multiplet, q = quartet, br = broad). Mass spectra were recorded with a HP-5989 instrument and HRMS was measured by a Finnigan MA+ mass spectrometer. Organic solvents used were dried by standard methods when necessary. Commercially available reagents were used without further purification. All reactions were monitored by TLC with Huanghai GF_{254} silica gel coated plates. Flash column chromatography was carried out using 300-400 mesh silica gel at increased pressure. All reactions were performed under argon using standard Schlenk techniques.

Compounds **1**[1], [2] and **2A***[3] were prepared according to the previous literatures.

2. General procedure for synthesis of MCPs 1



S **1**

Under argon atmosphere, a solution of 3-bromopropyltriphenylphosphonium bromide (5.5 g, 12 mmol) and NaH (576 mg, 24 mmol) in THF (10 mL) was stirred at 70 ^{o}C for 12 h. Afterwards compound **S** (10 mmol) in THF (5 mL) was added and the reaction solution was stirred at 70 ^{o}C for another 12 h. Then the solvent was removed under reduced pressure and the residue was purified by a silica gel flash chromatography (eluent: petroleum ether/ethyl acetate = 50/1) to afford the product **1** in moderate yield.

3. General procedure for the argon controlled synthesis of cyclobuta[*b*]indoles 3 from aniline-tethered alkylidenecyclopropanes 1 with alkynes 2

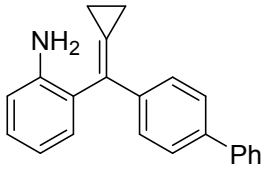
To a flame dried Schlenk tube was added aniline-tethered alkylidenecycopropanes **1** (0.2 mmol), alkynes (0.4 mmol) and DMSO (2.0 mL) under Argon. Then, the resulting solution was degassed, set under argon and stirred at 80 ^{o}C for 2 h. After cooling down to room temperature and the mixture was diluted with water (15 mL) followed by extraction with ethyl acetate (15 mL x 3). The combined organic collection was washed with brine (30 mL), and then dried over $NaSO_4$. The solvent was removed under reduced pressure and the residue was purified by a flash column chromatography on silica gel (PE/EA: 20:1 ~ 15/1) to give the desired products **3**.

4. General procedure for the oxygen controlled synthesis of cyclopenta[*b*]indoles 4 from aniline-tethered alkylidenecyclopropanes 1 with alkynes 2

To a flame dried Schlenk tube was added aniline-tethered alkylidenecycopropanes **1** (0.2 mmol), alkynes (0.4 mmol). Then, the tube was evacuated and backfilled with O_2 for 3 times, and

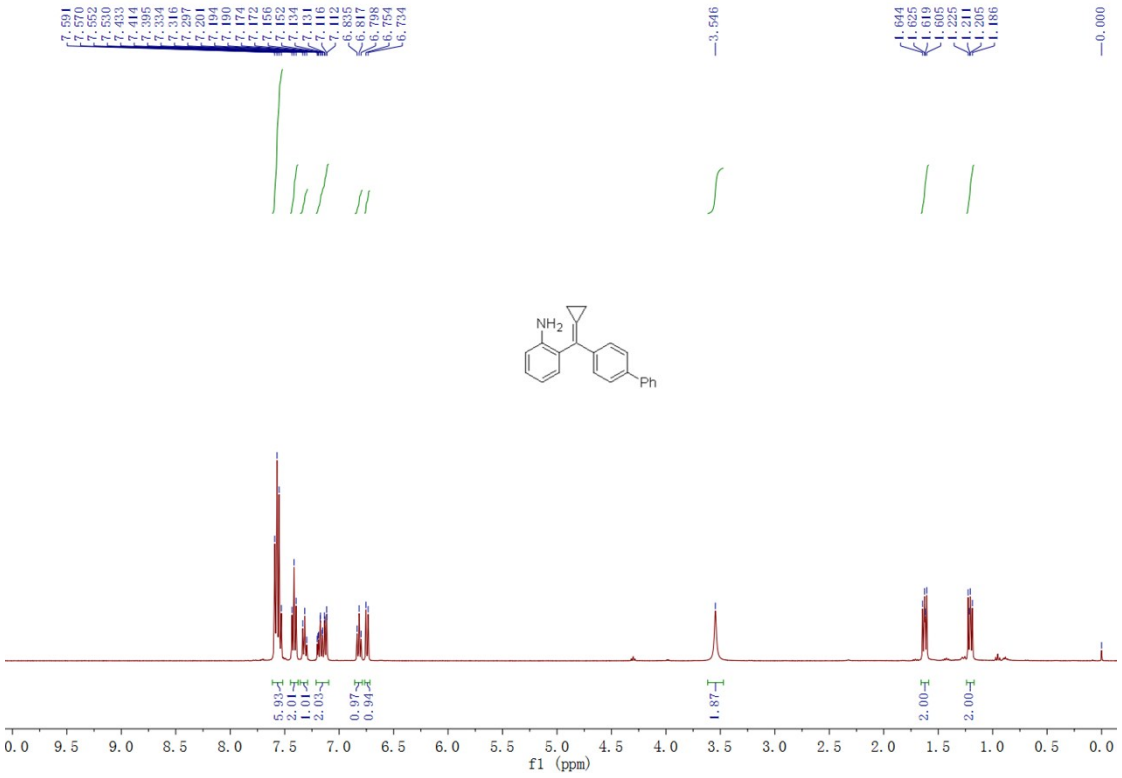
inserted an O_2 balloon. The solvent DMSO (2.0 mL) was added under O_2. Next, the resulting solution was allowed to stir at 80 ^oC for 12 h. After cooling down to room temperature and the mixture was diluted with water (15 mL) followed by extraction with ethyl acetate (15 mL x 3). The combined organic collection was washed with brine (30 mL), and then dried over $NaSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography on silica gel (PE/EA: 15:1 ~ 10/1) to give the desired products **4**.

5. Characterization and spectra charts for 1.



2-([1,1'-biphenyl]-4-yl(cyclopropylidene)methyl)aniline 1i

5.0 mmol scale, a light yellow solid, 55% yield (819.5 mg). M.p.: 125-128 ^oC. ^1H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.18-1.23 (m, 2H), 1.60-1.65 (m, 2H), 3.55 (s, 2H), 6.74 (d, *J* = 8.0 Hz, 1H), 6.82 (t, *J* = 7.6 Hz, 1H), 7.11-7.21 (m, 2H), 7.32 (t, *J* = 7.6 Hz, 1H), 7.41 (t, *J* = 7.6 Hz, 2H), 7.53-7.60 (m, 6H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 1.7, 5.5, 115.5, 118.3, 125.9, 126.4, 126.6, 126.9, 127.0, 127.1, 127.2, 128.3, 128.7, 130.8, 138.1, 139.7, 140.7, 144.2. IR (neat) ν 3480, 3382, 3081, 3059, 3026, 2967, 2923, 2859, 1732, 1607, 1484, 1444, 1304, 1266, 1178, 1158, 1008, 902, 839, 768, 741, 699 cm^{-1}. HRMS (ESI) Calcd. for $C_{22}H_{20}N^{+1}(M+H)^+$ requires: 298.1590, found: 298.1591.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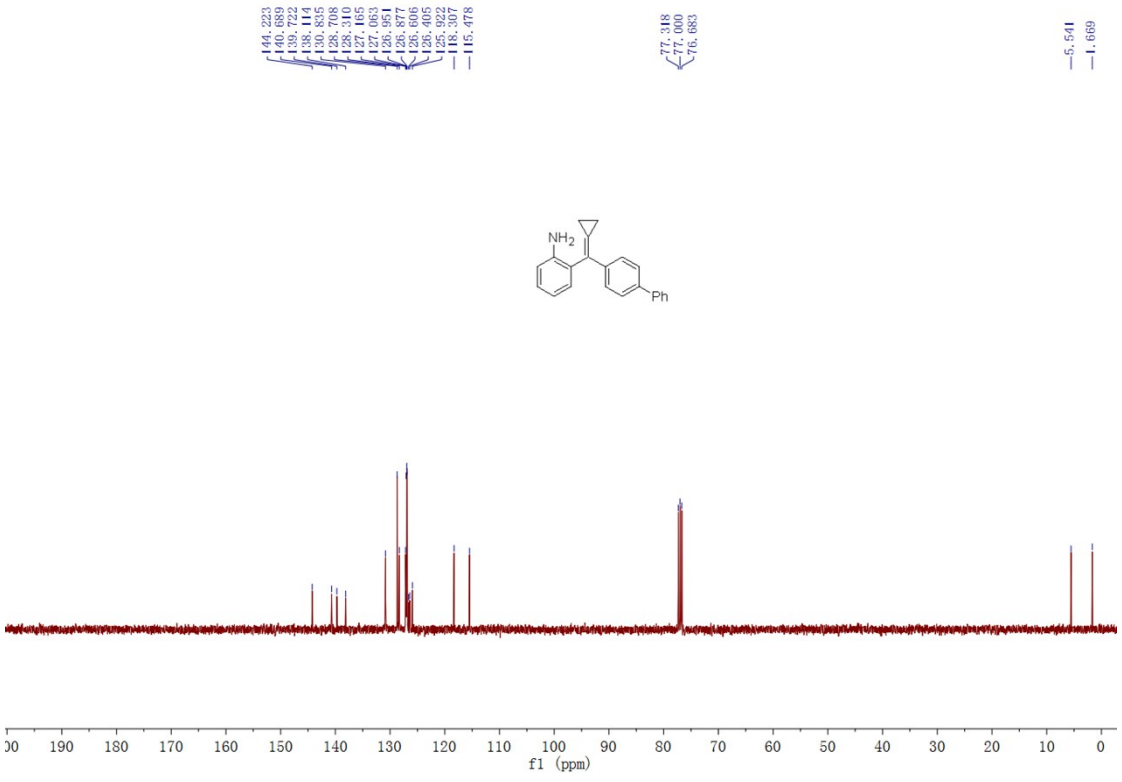
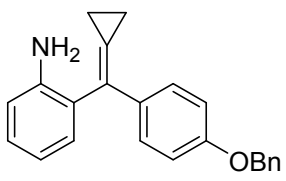
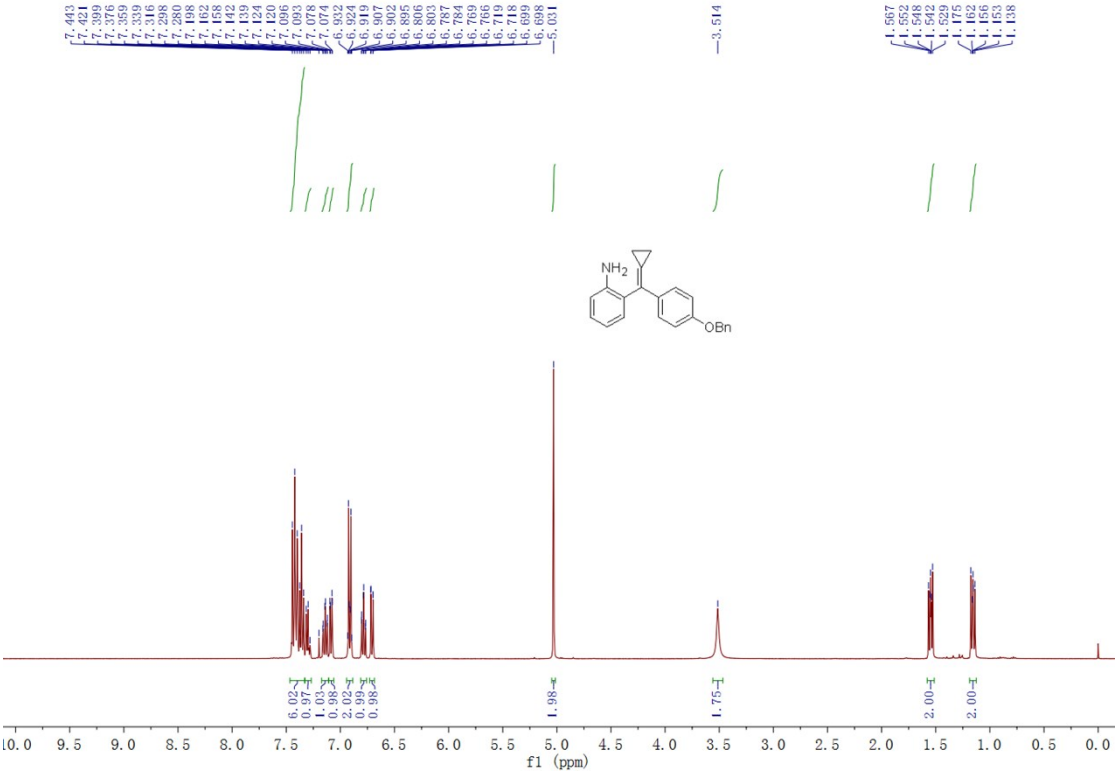
7.570
7.552
7.530
7.433
7.414
7.395
7.334
7.316
7.297
7.201
7.194
7.190
7.174
7.172
7.156
7.152
7.134
7.131
7.116
7.112
6.835
6.817
6.798
6.754
6.734
3.546
1.644
1.625
1.619
1.605
1.225
1.211
1.205
1.186
0.000
NH2
Ph
5.93
2.01
1.01
2.03
0.97
0.94
1.87
2.00
2.00
f1 (ppm)

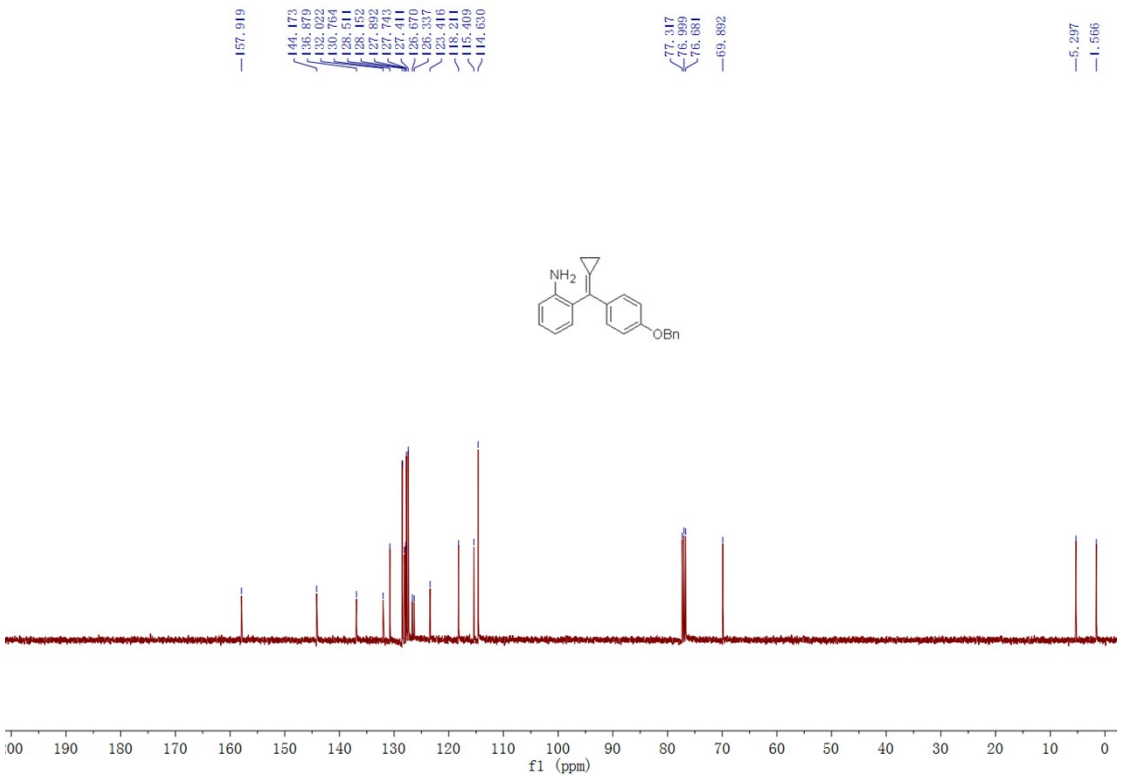

144.223
140.689
139.722
138.114
130.835
128.708
128.310
127.165
127.063
126.951
126.877
126.606
126.405
125.922
118.307
115.478
77.318
77.000
76.683
5.541
1.669
NH2
Ph
f1 (ppm)

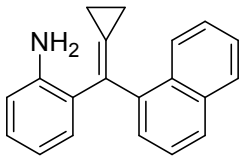

NH2
OBn

2-((4-(benzyloxy)phenyl)(cyclopropylidene)methyl)aniline 1j

5.0 mmol scale, a brown solid, 53% yield (866.6 mg). M.p.: 77-79 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.13-1.18 (m, 2H), 1.52-1.57 (m, 2H), 3.51 (s, 2H), 5.03 (s, 2H), 6.71 (dd, *J* = 0.4 Hz, 8.0 Hz, 1H), 6.79 (dt, *J* = 1.2 Hz, 7.2 Hz, 1H), 6.89-7.00 (m, 2H), 7.09 (dd, *J* = 1.2 Hz, 7.2 Hz, 1H), 7.12-7.17 (m, 1H), 7.28-7.32 (m, 1H), 7.33-7.45 (m, 6H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 1.6, 5.3, 69.9, 114.6, 115.4, 118.2, 123.4, 126.3, 126.7, 127.4, 127.7, 127.9, 128.2, 128.5, 130.8, 132.0, 136.9, 144.2, 157.9. IR (neat) ν 3470, 3377, 3092, 3067, 3045, 2974, 2956, 2923, 2870, 1614, 1506, 1490, 1452, 1386, 1246, 1171, 1025, 905, 829, 735, 693 cm^{-1}. HRMS (ESI) Calcd. for $C_{23}H_{22}N^{+1}(M+H)^+$ requires: 328.1696, found: 328.1697.

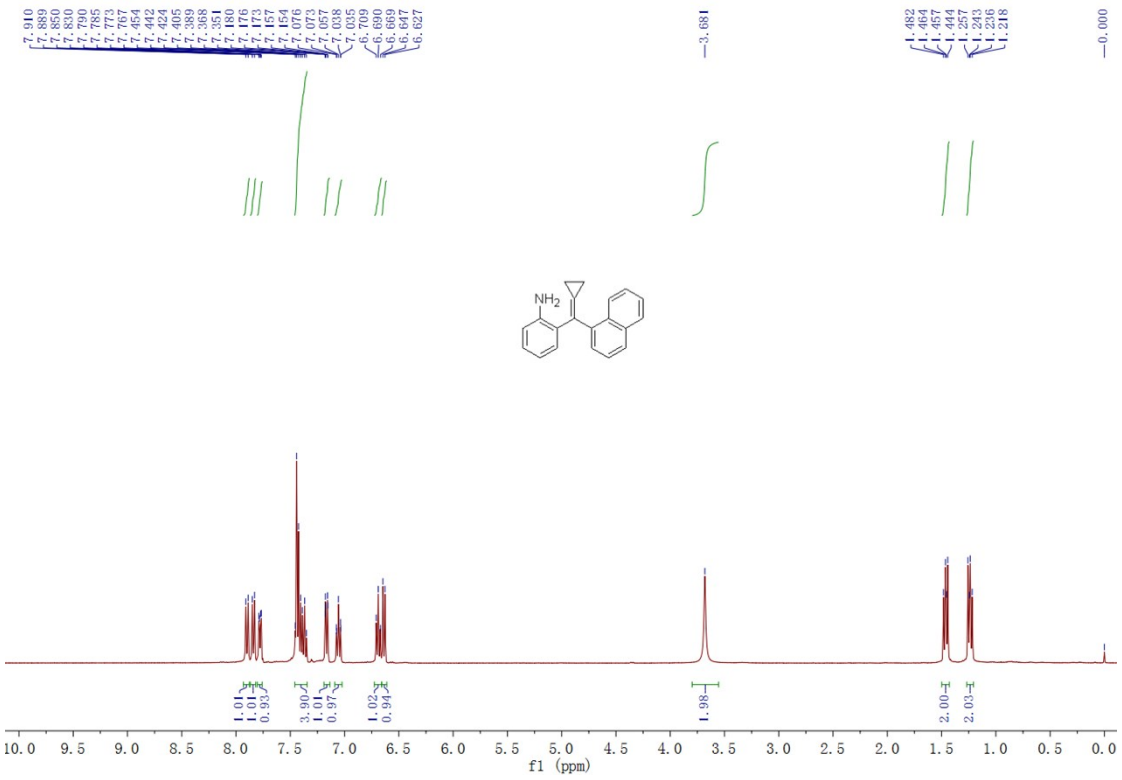


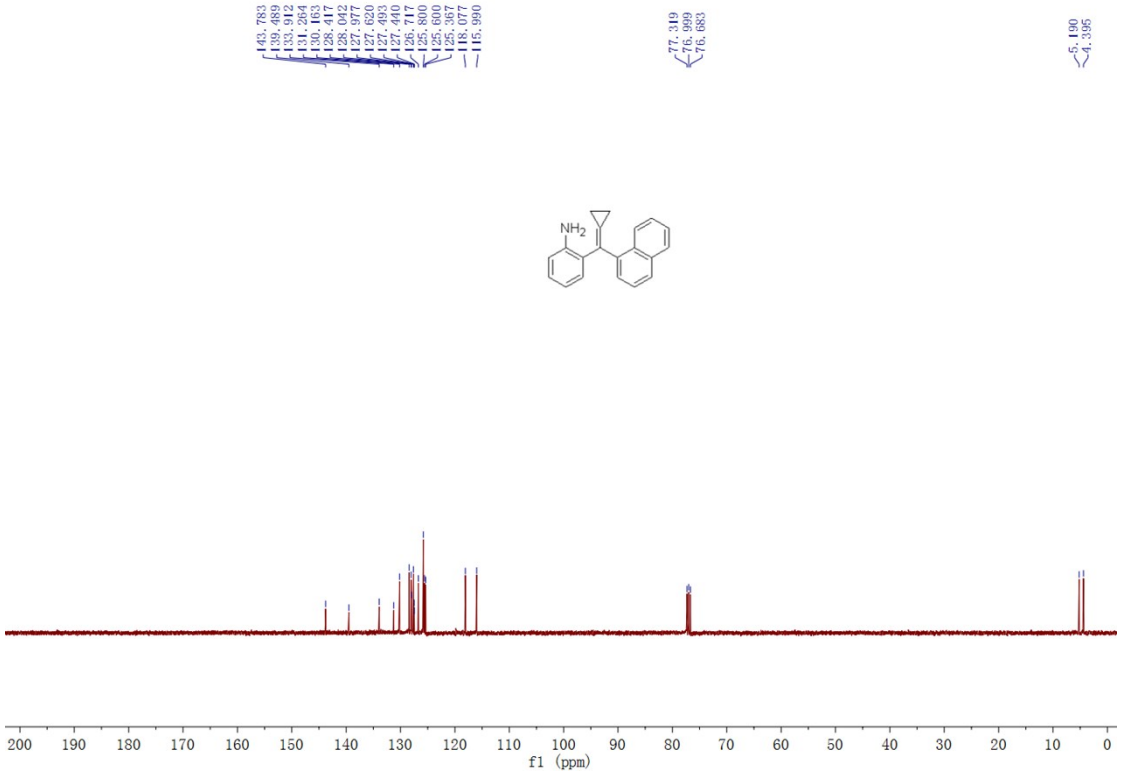


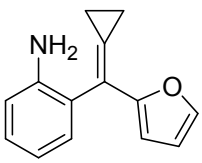


2-(cyclopropylidene(naphthalen-1-yl)methyl)aniline 1l

5.0 mmol scale, a light yellow solid, 50% yield (677.5 mg). M.p.: 88-90 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.21-1.26 (m, 2H), 1.44-1.49 (m, 2H), 3.68 (s, 2H), 6.64 (d, *J* = 8.0 Hz, 1H), 6.66-6.71 (m, 1H), 7.03-7.08 (m, 1H), 7.15-7.18 (m, 1H), 7.35-7.46 (m, 4H), 7.76-7.79 (m, 1H), 7.84 (d, *J* = 8.0 Hz, 1H), 7.90 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 4.4, 5.2, 116.0, 118.1, 125.4, 125.6, 125.8, 126.7, 127.4, 127.5, 127.6, 127.98, 128.04, 128.4, 130.2, 131.3, 133.9, 139.5, 143.8. IR (neat) ν 3465, 3376, 3057, 2971, 2928, 2859, 1612, 1573, 1489, 1451, 1392, 1336, 1302, 1256, 1156, 1142, 1105, 1069, 1046, 1020, 1001, 939, 902, 870, 852, 801, 776, 756, 745, 675 cm^{-1}. HRMS (ESI) Calcd. for $C_{20}H_{18}N^{+1}(M+H)^{+}$ requires: 272.1434, found: 272.1434.

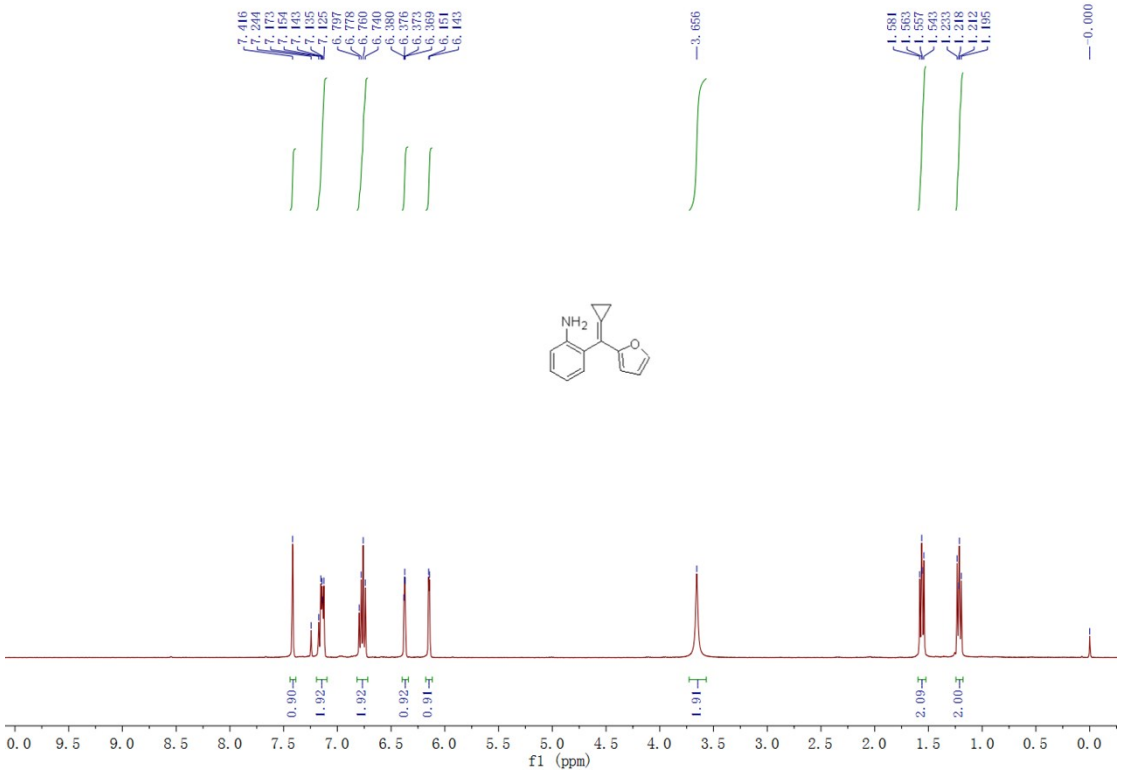


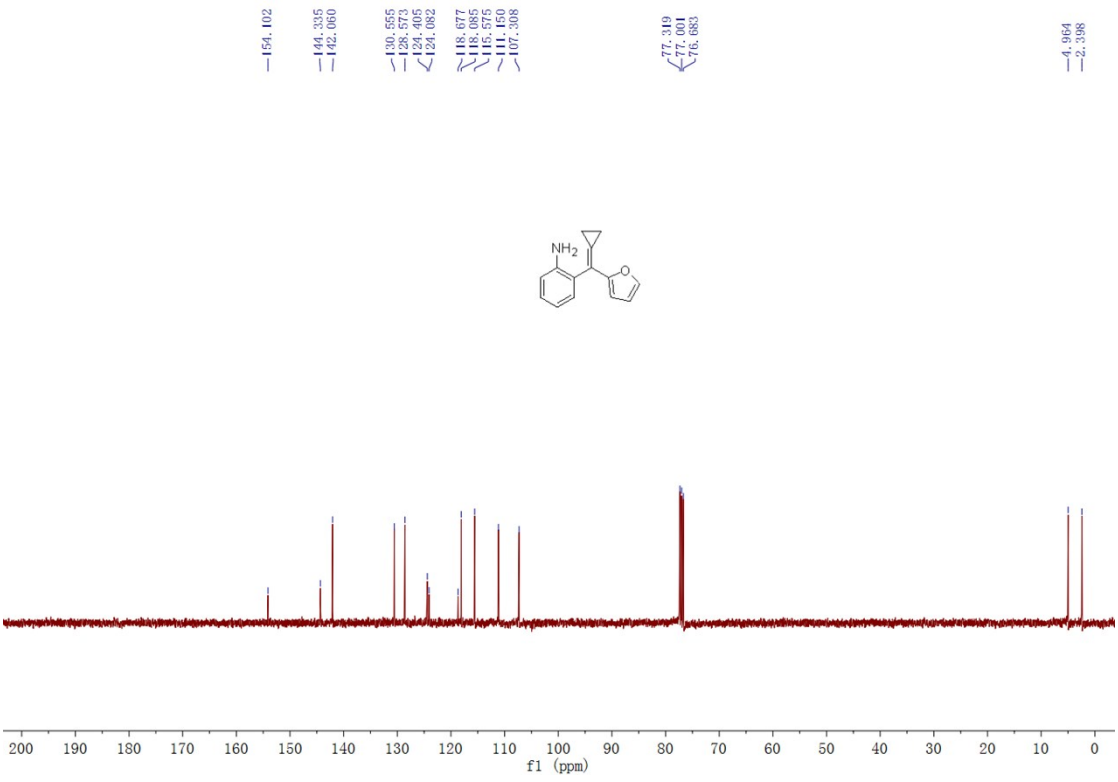


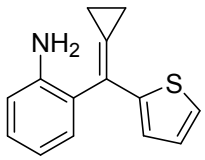


2-(cyclopropylidene(furan-2-yl)methyl)aniline 1m

5.0 mmol scale, a brown liquid, 53% yield (559.1 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.19-1.24 (m, 2H), 1.54-1.59 (m, 2H), 3.66 (s, 2H), 6.14 (d, *J* = 3.2 Hz, 1H), 6.36-6.38 (m, 1H), 6.74-6.80 (m, 2H), 7.12-7.18 (m, 2H), 7.42 (s, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 2.4, 5.0, 107.3, 111.2, 115.6, 118.1, 118.7, 124.1, 124.4, 128.6, 130.6, 142.1, 144.3, 154.1. IR (neat) ν 3467, 3378, 3111, 3050, 3024, 3972, 2920, 1671, 1612, 1492, 1452, 1300, 1255, 1208, 1151, 1007, 939, 886, 873, 808, 735, 692 cm^{-1}. HRMS (ESI) Calcd. for $C_{14}H_{14}NO^{+1}(M+H)^{+}$ requires: 212.1070, found: 212.1070.

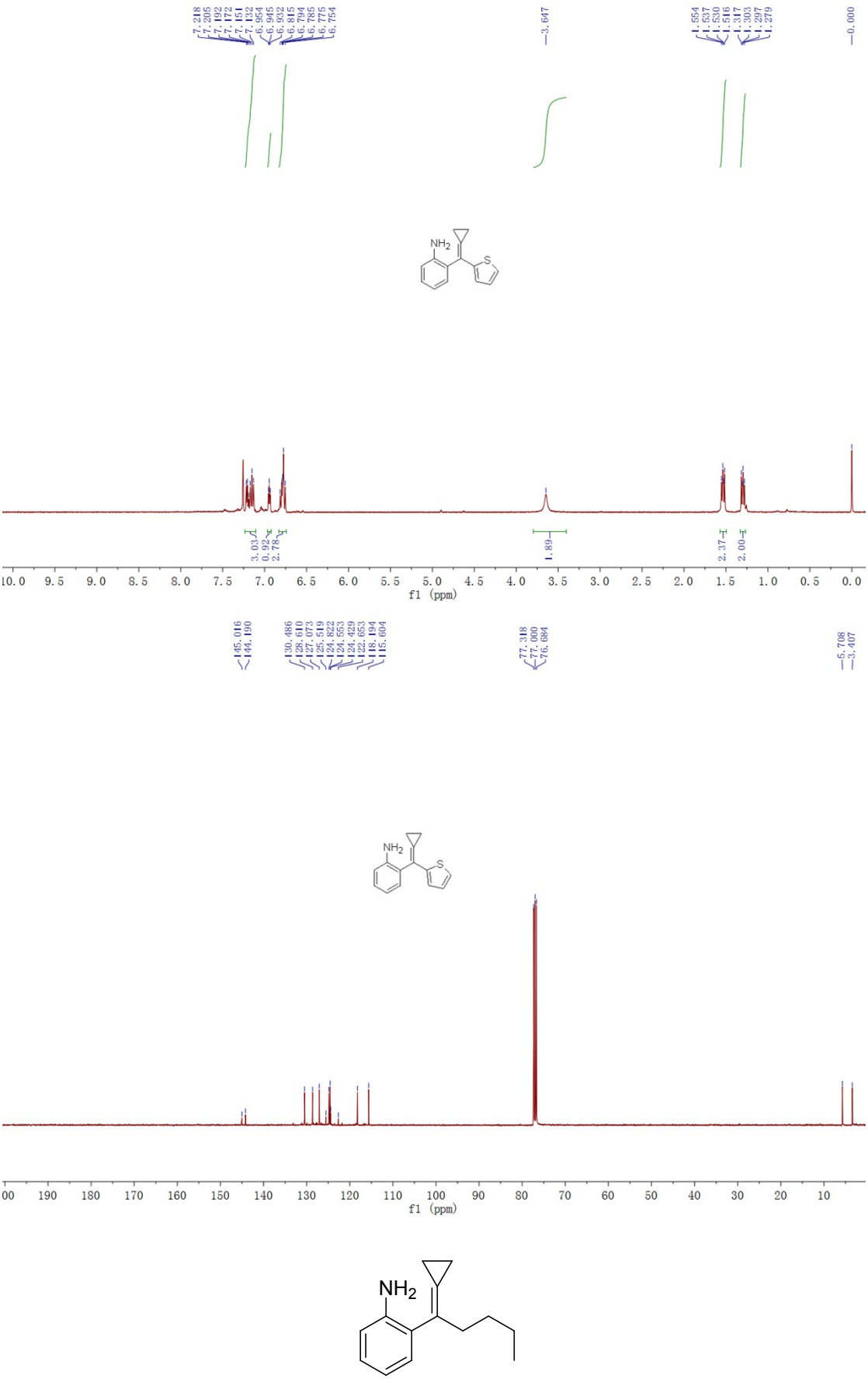






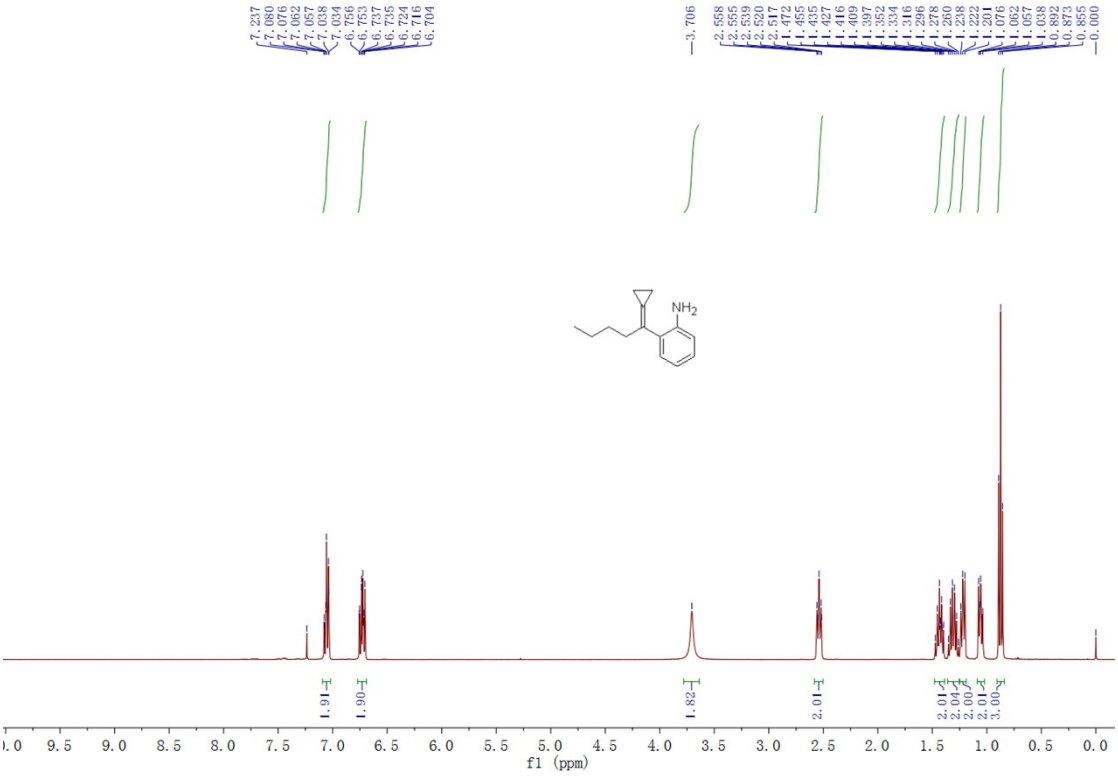
2-(cyclopropylidene(thiophen-2-yl)methyl)aniline 1n

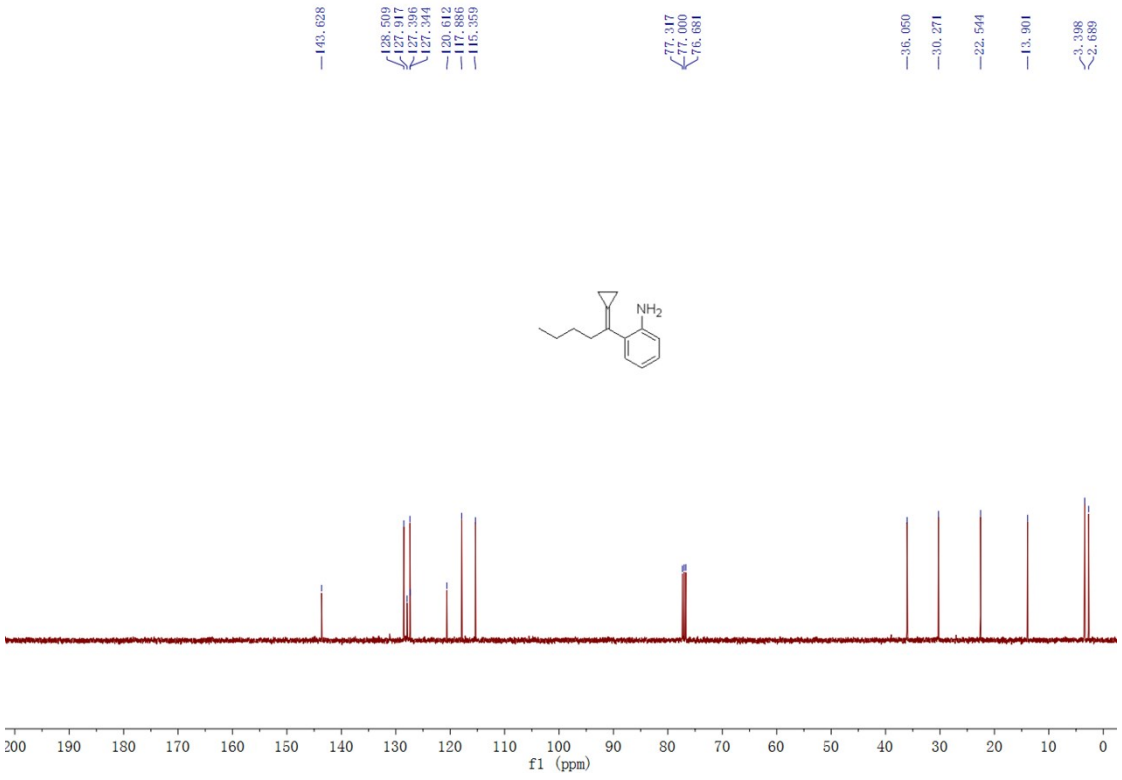
5.0 mmol scale, a brown solid, 45% yield (510.7 mg). M.p.: 48-50 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.27-1.32 (m, 2H), 1.51-1.56 (m, 2H), 3.65 (s, 2H), 6.75-6.82 (m, 3H), 6.93-6.96 (m, 1H), 7.13-7.22 (m, 3H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 3.4, 5.7, 115.6, 118.2, 122.7, 124.4, 124.6, 124.8, 125.5, 127.0, 128.6, 130.5, 144.2, 145.0. IR (neat) ν 3404, 3279, 3182, 3103, 3072, 3025, 2971, 2914, 2848, 1611, 1577, 1489, 1452, 1418, 1296, 1248, 1233, 1155, 1144, 1045, 1027, 1010, 878, 848, 836, 804, 753, 704, 691 cm^{-1}. HRMS (ESI) Calcd. for $C_{14}H_{14}NS^{+1}(M+H)^{+}$ requires: 228.0841, found: 228.0840.

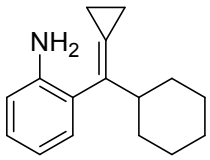


2-(1-cyclopropylidenepentyl)aniline 1p

5.0 mmol scale, a faint yellow liquid, 51% yield (512.6 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.87 (t, *J* = 7.2 Hz, 3H), 1.03-1.08 (m, 2H), 1.20-1.24 (m, 2H), 1.27-1.35 (m, 2H), 1.39-1.48 (m, 2H), 2.51-2.56 (m, 2H), 3.71 (s, 2H), 6.70-6.76 (m, 2H), 7.03-7.08 (m, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 2.7, 3.4, 13.9, 22.5, 30.3, 36.1, 115.4, 117.9, 120.6, 127.3, 127.4, 127.9, 128.5, 143.6. IR (neat) ν 3471, 3374, 3047, 3020, 2955, 2929, 2873, 2856, 1609, 1492, 1451, 1376, 1296, 1254, 1156, 1104, 1065, 999, 960, 931, 845, 744 cm^{-1}. HRMS (ESI) Calcd. for $C_{14}H_{20}N^{+1}(M+H)^{+}$ requires: 202.1590, found: 202.1589.

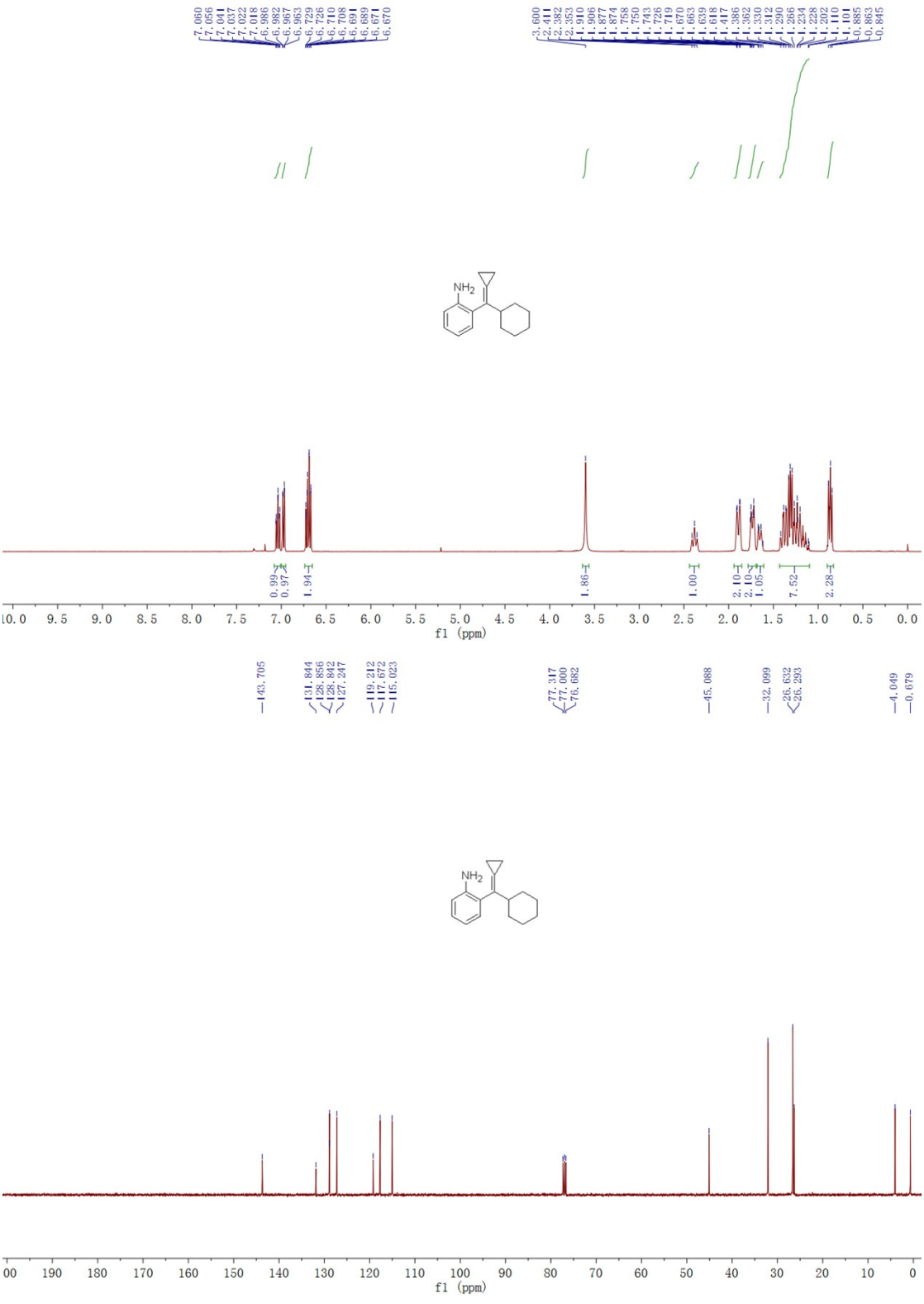




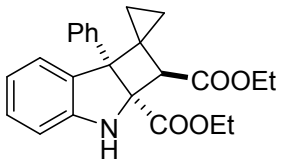


2-(cyclohexyl(cyclopropylidene)methyl)aniline 1q

5.0 mmol scale, a light yellow solid, 47% yield (533.5 mg). M.p.: 39-44 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.84-0.89 (m, 2H), 1.10-1.42 (m, 7H), 1.61-1.67 (m, 1H), 1.71-1.76 (m, 2H), 1.87-1.91 (m, 2H), 2.35-2.42 (m, 1H), 3.60 (s, 2H), 6.67-6.73 (m, 2H), 6.97 (dd, J = 1.6 Hz, 7.6 Hz, 1H), 7.01-7.06 (m, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 0.7, 4.0, 26.3, 26.6, 32.1, 45.1, 115.0, 117.7, 119.2, 127.2, 128.8, 128.9, 131.8, 143.7. IR (neat) ν 3405, 3308, 3200, 3075, 3053, 3036, 2973, 2922, 2848, 1611, 1574, 1489, 1449, 1413, 1316, 1290, 1264, 1246, 1155, 1142, 1063, 1049, 1040, 1011, 955, 937, 889, 859, 840, 807, 746 cm^{-1}. HRMS (ESI) Calcd. for $C_{16}H_{22}N^{+1}(M+H)^{+}$ requires: 228.1747, found: 228.1747.

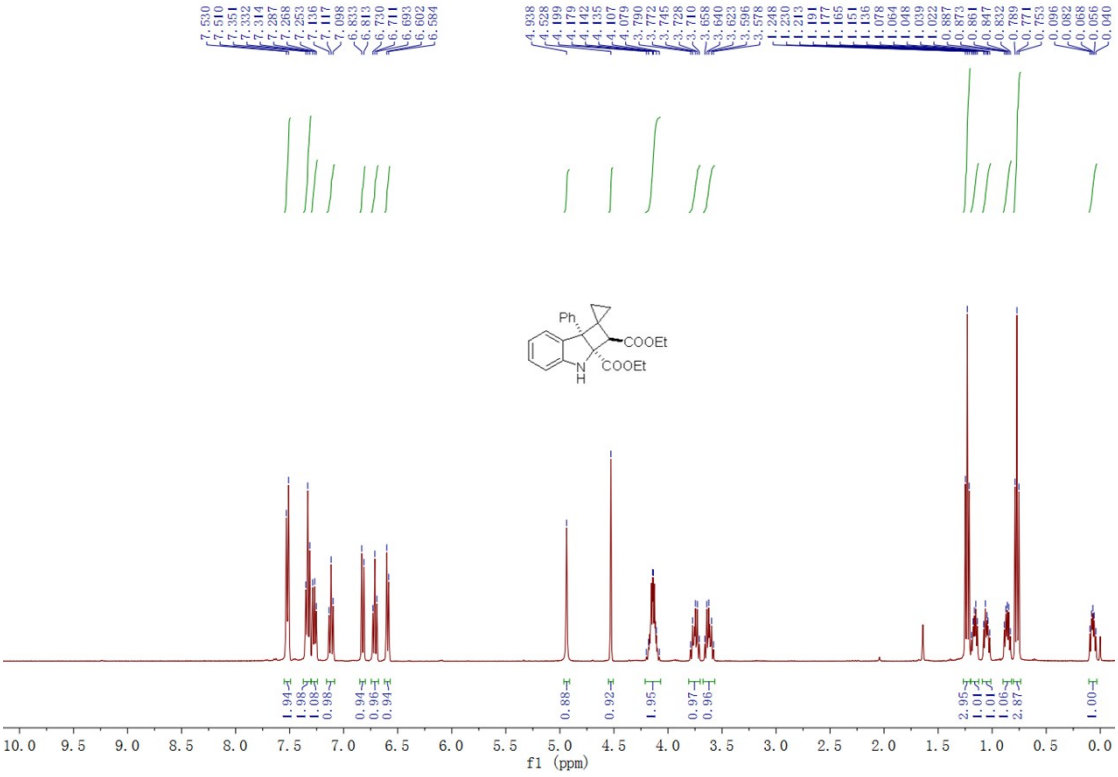


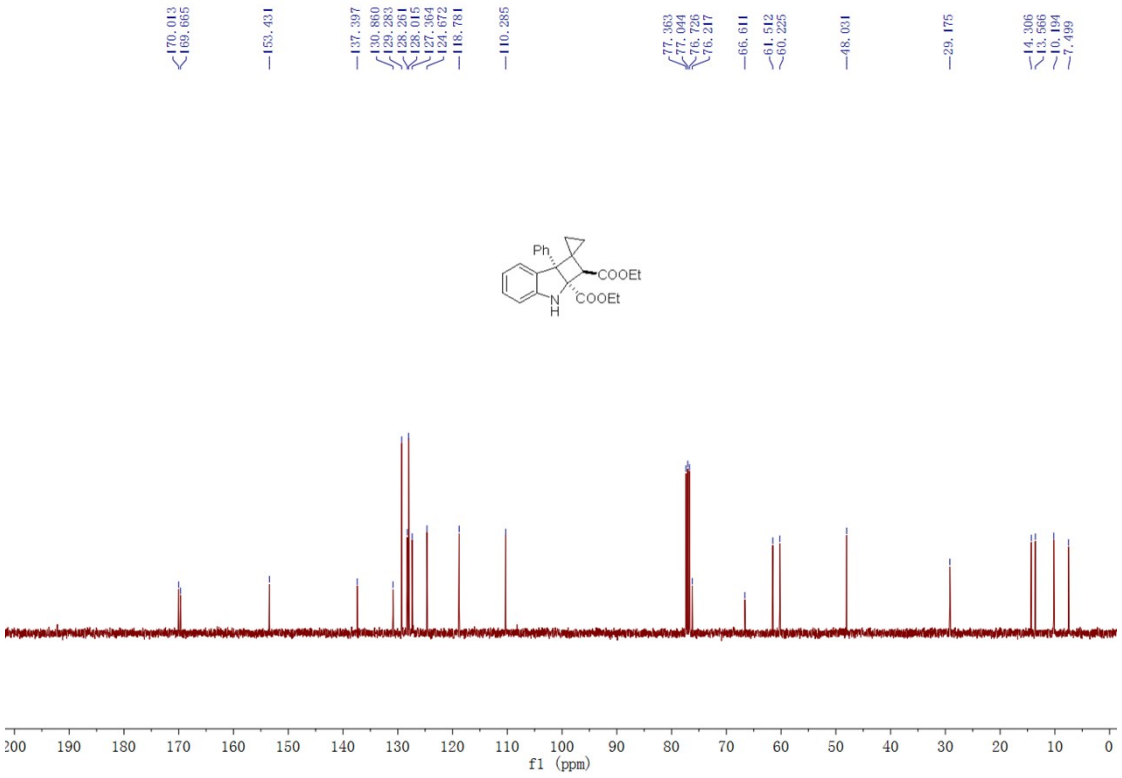
6. Characterization and spectra charts for 3.

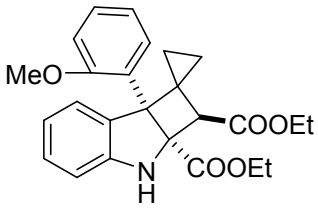


Diethyl-7*b*-phenyl-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3a

0.3 mmol scale, a light yellow solid, 83% yield (97.4 mg). M.p.: 100-101 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.04-0.10 (m, 1H), 0.77 (t, *J* = 7.2 Hz, 3H), 0.83-0.89 (m, 1H), 1.02-1.08 (m, 1H), 1.13-1.20 (m, 1H), 1.23 (t, *J* = 7.2 Hz, 3H), 3.57-3.66 (m, 1H), 3.71-3.79 (m, 1H), 4.07-4.20 (m, 2H), 4.53 (s, 1H), 4.94 (s, 1H), 6.59 (d, *J* = 7.2 Hz, 1H), 6.71 (dd, *J* = 7.2 Hz, 7.2 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 7.12 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 7.25-7.29 (m, 1H), 7.33 (dd, *J* = 7.6 Hz, 7.6 Hz, 2H), 7.52 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.5, 10.2, 13.6, 14.3, 29.2, 48.0, 60.2, 61.5, 66.6, 76.2, 110.3, 118.8, 124.7, 127.4, 128.0, 128.3, 129.3, 130.9, 137.4, 153.4, 169.7, 170.0. IR (neat) ν 3378, 2982, 2936, 2870, 2903, 0839, 1719, 1603, 1479, 1464, 1443, 1391, 1368, 1248, 1204, 1150, 1095, 1066, 1037, 942, 856, 820, 746, 718, 700, 675 cm^{-1}. HRMS (ESI) Calcd. for $C_{24}H_{26}NO_4^{+1}$(M+H)$^+$ requires: 392.1856, found: 392.1855.

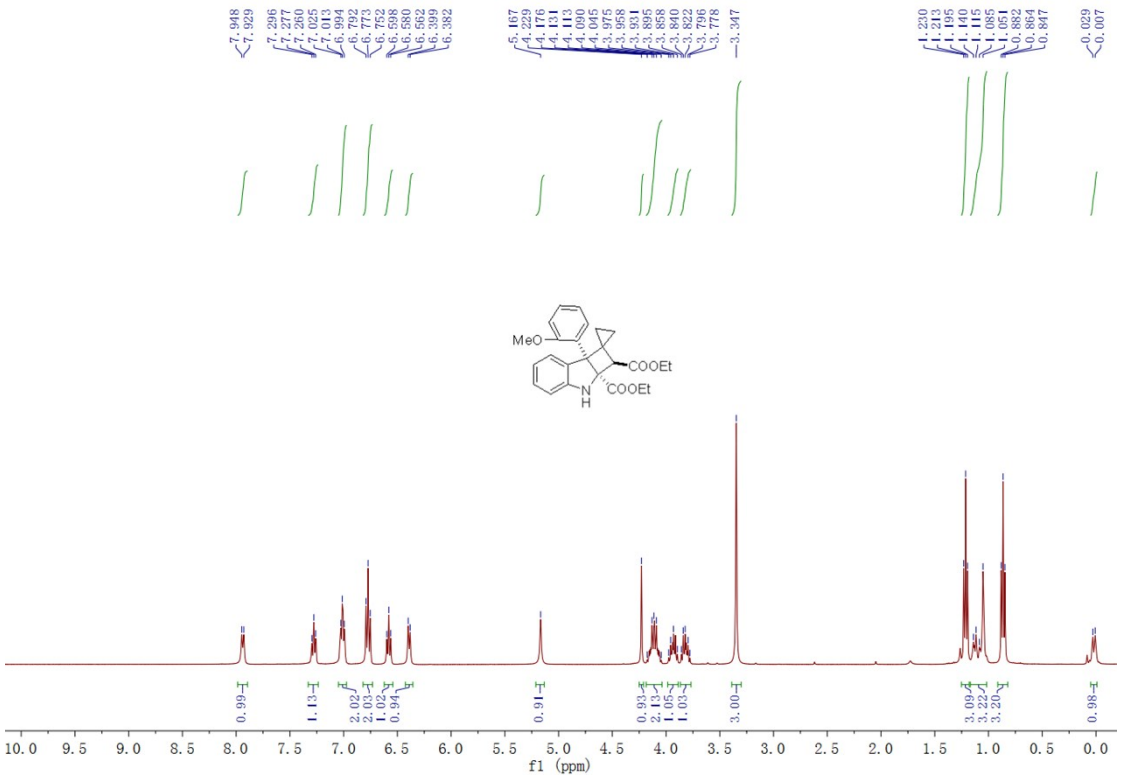






diethyl-7*b*-(2-methoxyphenyl)-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3b

0.3 mmol scale, a white solid, 88% yield (111.1 mg). M.p.: 90-92 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.01-0.03 (m, 1H), 0.86 (t, *J* = 7.2 Hz, 3H), 1.05-1.14 (m, 3H), 1.21 (t, *J* = 7.2 Hz, 3H), 3.35 (s, 3H), 3.77-3.86 (m, 1H), 3.89-3.98 (m, 1H), 4.04-4.18 (m, 2H), 4.23 (s, 1H), 5.17 (s, 1H), 6.39 (d, *J* = 7.2 Hz, 1H), 6.58 (dd, *J* = 7.2 Hz, 7.2 Hz, 1H), 6.77 (dd, *J* = 8.0 Hz, 8.0 Hz, 2H), 6.99-7.03 (m, 2H), 7.28 (dd, *J* = 7.2 Hz, 7.2 Hz, 1H), 7.94 (d, *J* = 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 5.9, 9.7, 13.5, 14.2, 28.7, 50.5, 54.4, 60.0, 61.0, 63.8, 75.1, 109.8, 110.6, 118.2, 119.9, 122.0, 126.8, 126.9, 128.3, 128.5, 133.7, 151.8, 158.2, 170.0, 170.4. IR (neat) ν 3392, 3084, 3050, 3028, 2984, 2934, 2903, 2834, 1727, 1712, 1605, 1482, 1463, 1371, 1274, 1232, 1188, 1162, 1122, 1066, 1054, 1027, 1002, 894, 783, 752, 742, 718 cm^{-1}. HRMS (ESI) Calcd. for $C_{25}H_{28}NO_5^{+1}$(M+H)$^+$ requires: 422.1962, found: 422.1961.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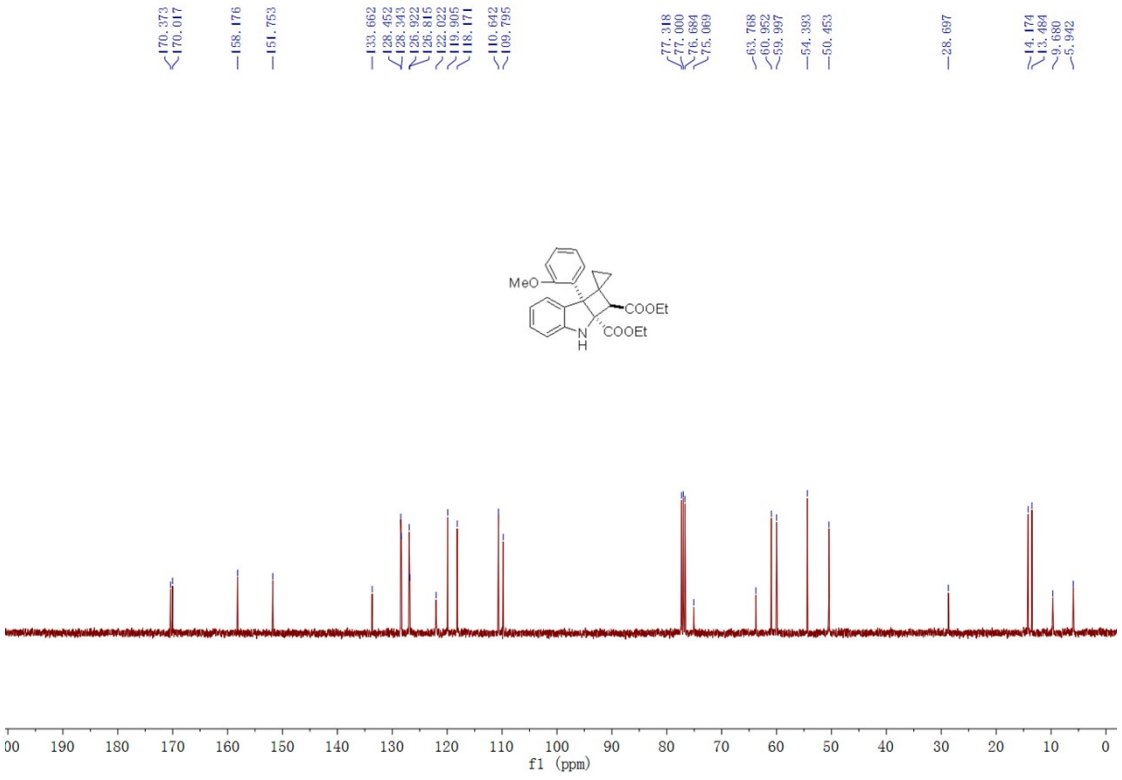
7.929
7.296
7.277
7.260
7.025
7.011
6.994
6.792
6.773
6.752
6.598
6.580
6.562
6.399
6.382
5.167
4.229
4.176
4.131
4.113
4.090
4.045
3.975
3.958
3.911
3.895
3.858
3.840
3.822
3.796
3.778
3.347
1.230
1.213
1.195
1.140
1.115
1.085
1.051
0.882
0.864
0.847
0.029
0.007
MeO
COOEt
COOEt
N
H
0.99
1.13
2.02
2.03
1.02
0.94
0.91
0.93
2.13
1.05
1.03
3.00
3.09
3.22
3.20
0.98
f1 (ppm)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170.017
158.176
151.753
133.662
128.452
128.343
126.922
126.815
122.022
119.905
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110.642
109.795
77.318
77.000
76.684
75.069
63.768
60.952
59.997
54.393
50.453
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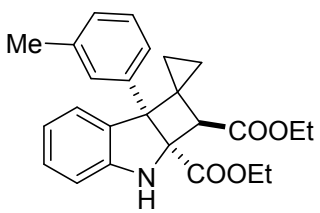
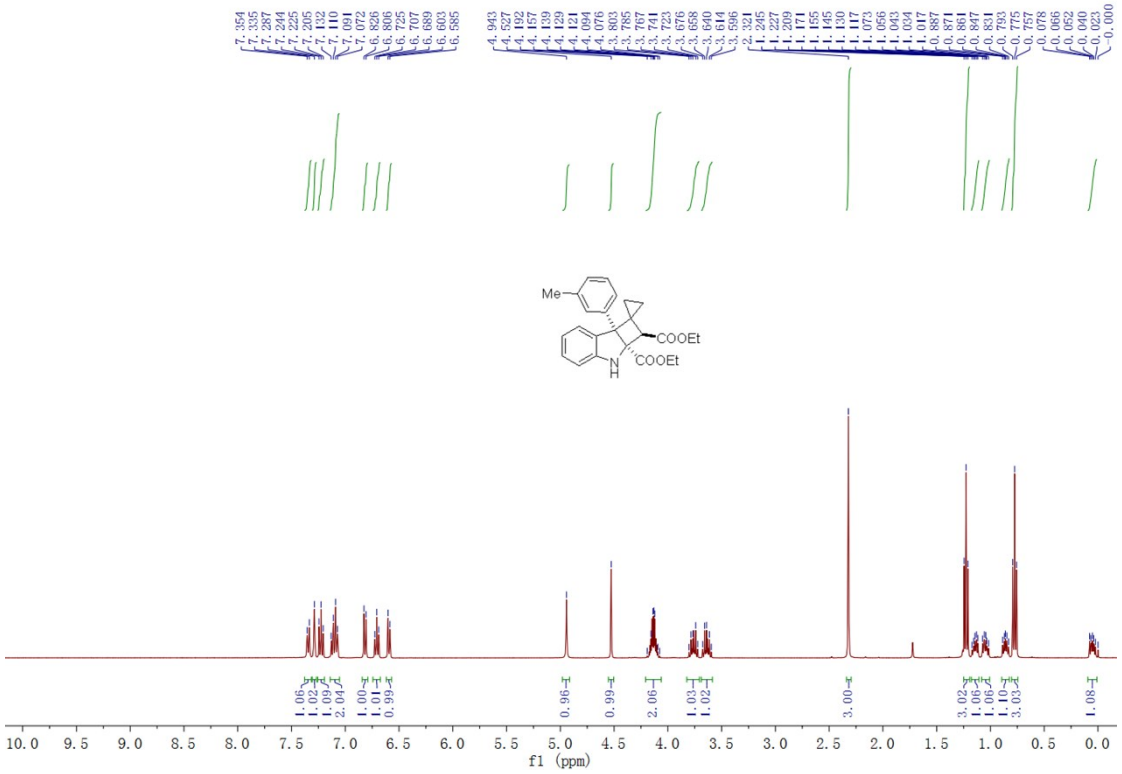
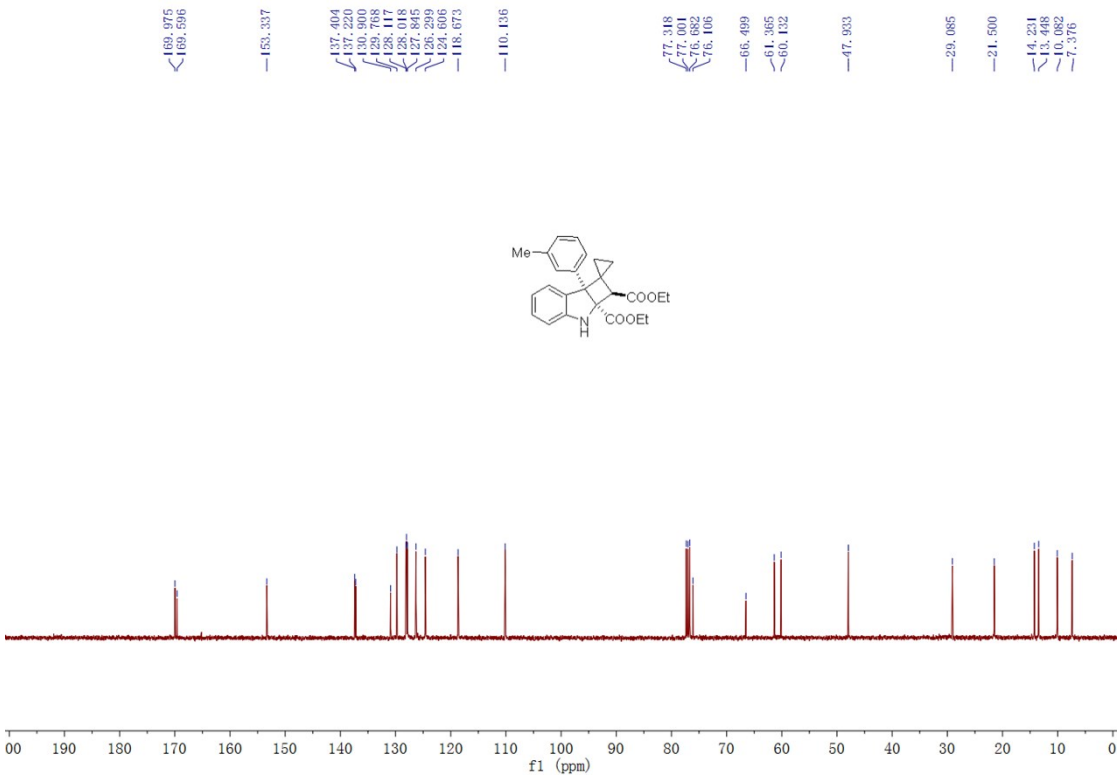
14.174
13.464
9.680
5.942
MeO
COOEt
COOEt
N
H
f1 (ppm)

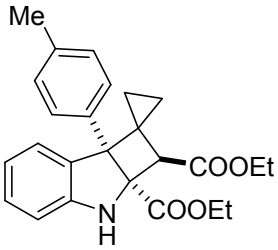

Me
COOEt
COOEt
N
H

diethyl-7*b*-(*m*-tolyl)-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3c

0.3 mmol scale, a faint yellow liquid, 84% yield (101.8 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.02-0.08 (m, 1H), 0.78 (t, *J* = 7.2 Hz, 3H), 0.83-0.89 (m, 1H), 1.01-1.08 (m, 1H), 1.11-1.18 (m, 1H), 1.23 (t, *J* = 7.2 Hz, 3H), 3.32 (s, 3H), 3.59-3.68 (m, 1H), 3.72-3.81 (m, 1H), 4.07-4.20 (m, 2H), 4.53 (s, 1H), 4.94 (s, 1H), 6.59 (d, *J* = 7.2 Hz, 1H), 6.71 (dd, *J* = 7.2 Hz, 7.2 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 7.07-7.14 (m, 2H), 7.23 (dd, *J* = 8.0 Hz, 8.0 Hz, 1H), 7.29 (s, 1H), 7.34 (d, *J* = 8.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.4, 10.1, 13.4, 14.2, 21.5, 29.1, 47.9, 60.1, 61.4, 66.5, 76.1, 110.1, 118.7, 124.6, 126.3, 127.8, 128.0, 128.1, 129.8, 130.9, 137.2, 137.4, 153.3, 169.6, 170.0. IR (neat) ν 3369, 3053, 2981, 2934, 2900, 2853, 1720, 1605, 1483, 1465, 1369, 1321, 1276, 1255, 1208, 1184, 1095, 1066, 1042, 1025, 941, 912, 865, 799, 779, 742, 722, 700 cm^{-1}. HRMS (ESI) Calcd. for $C_{25}H_{28}NO_4^{+1}$(M+H)$^+$ requires: 406.2013, found: 406.2012.



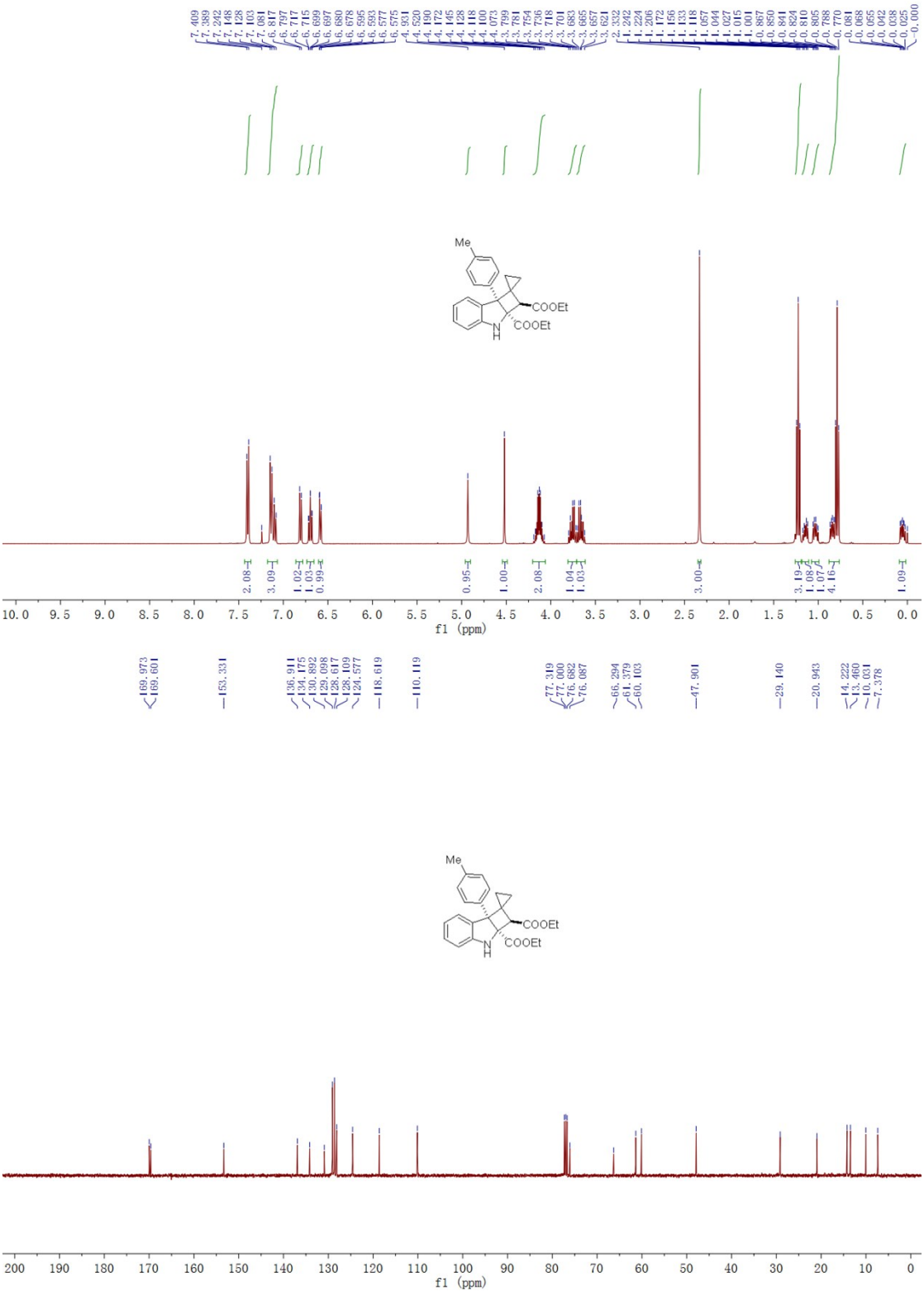


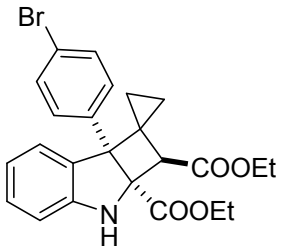


diethyl-7*b*-(*p*-tolyl)-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3d

0.3 mmol scale, a faint yellow solid, 91% yield (111.0 mg). M.p.: 102-105 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.02-0.09 (m, 1H), 0.79 (t, *J* = 7.2 Hz, 3H), 0.81-0.87 (m, 1H), 1.00-1.06 (m, 1H), 1.11-1.18 (m, 1H), 1.22 (t, *J* = 7.2 Hz, 3H), 2.33 (s, 3H), 3.62-3.71 (m, 1H), 3.72-3.80 (m, 1H), 4.07-4.19 (m, 2H), 4.52 (s, 1H), 4.93 (s, 1H), 6.59 (dd, *J* = 0.8 Hz, 7.2 Hz, 1H), 6.67-6.72 (m, 1H), 6.81 (d, *J* = 8.0 Hz, 1H), 7.08-7.15 (m, 3H), 7.40 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.4, 10.0, 13.5, 14.2, 20.9, 29.1, 47.9, 60.1, 61.4, 66.3, 76.1, 110.1, 118.6, 124.6, 128.1, 128.6, 129.1, 130.9, 134.2, 136.9, 153.3, 169.6, 170.0. IR (neat) ν 3379, 3089, 3053, 3025, 2986, 2970, 2924, 2875, 2850, 1731, 1719, 1608, 1514, 1485, 1470, 1371, 1345, 1317, 1274, 1259, 1233, 1215, 1185, 1151, 1113, 1063, 1039, 1024, 967, 934, 900, 867, 854, 814, 792, 746, 724, 710

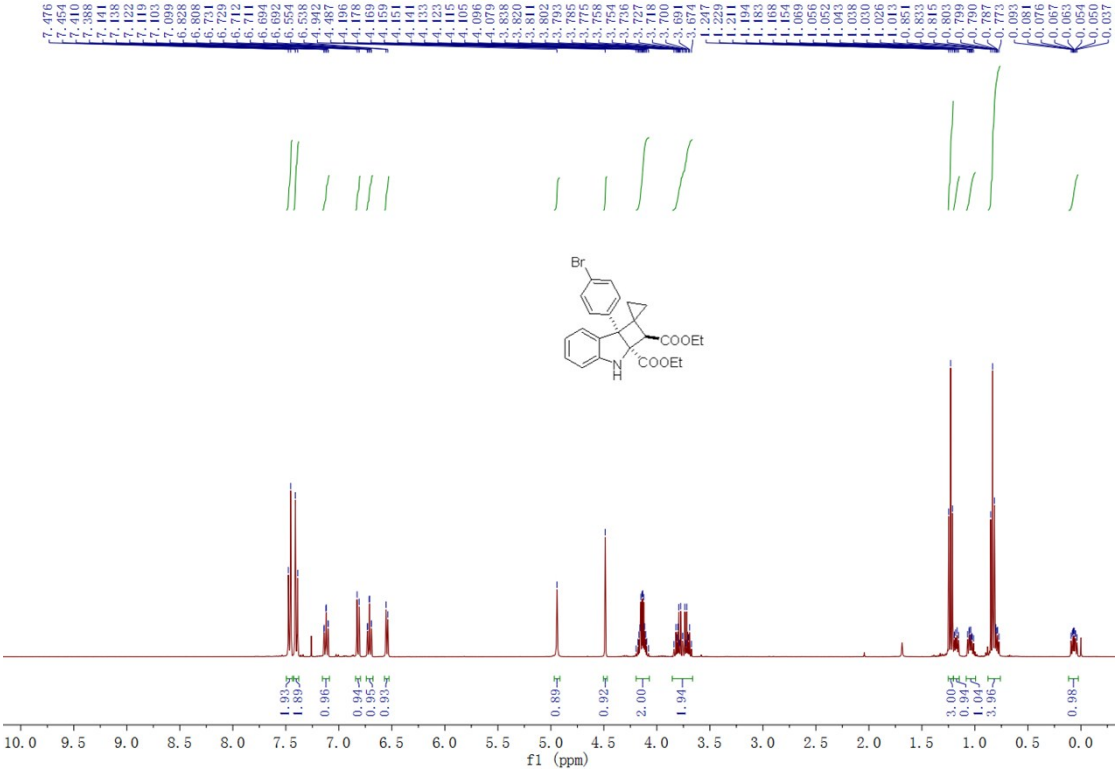
cm^{-1}. HRMS (ESI) Calcd. for $C_{25}H_{28}NO_4^{+1}(M+H)^+$ requires: 406.2013, found: 406.2014.

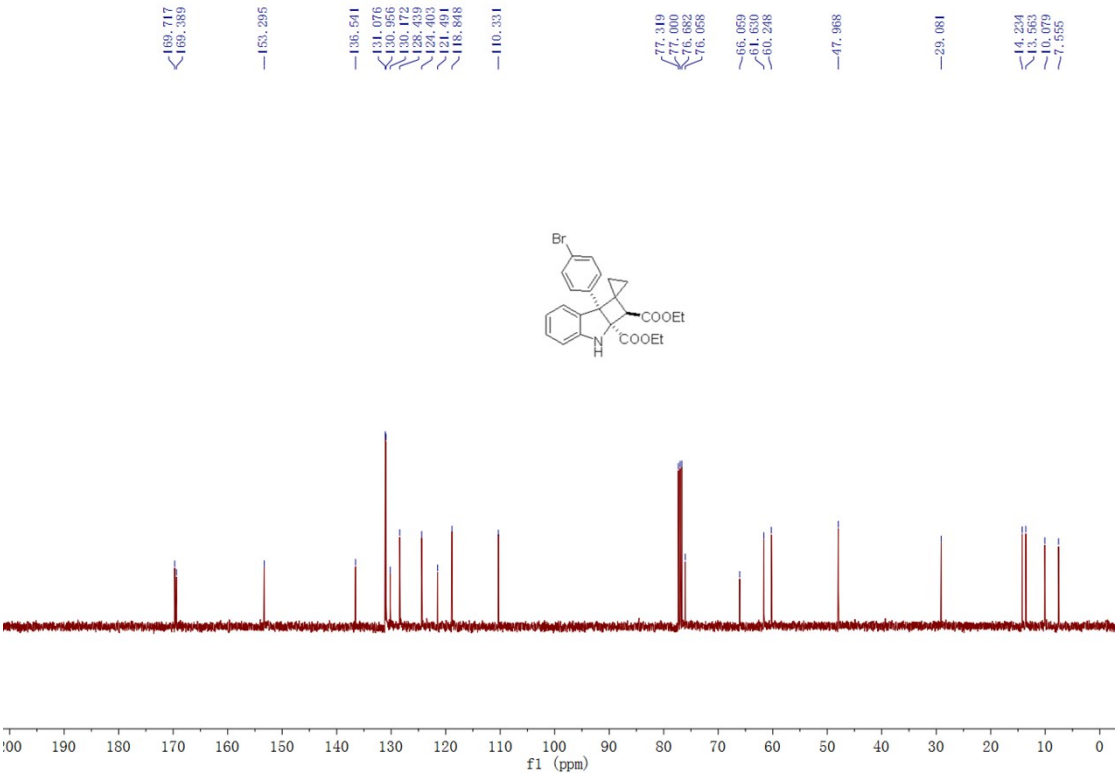


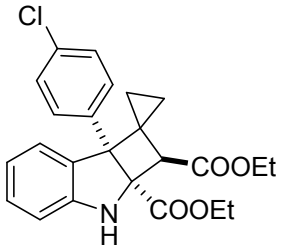


diethyl-7*b*-(4-bromophenyl)-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3e

0.3 mmol scale, a white solid, 84% yield (118.2 mg). M.p.: 109-111 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.05-0.10 (m, 1H), 0.77-0.86 (m, 4H), 1.01-1.07 (m, 1H), 1.15-1.20 (m, 1H), 1.23 (t, *J* = 7.2 Hz, 3H), 3.67-3.75 (m, 1H), 3.76-3.84 (m, 1H), 4.07-4.20 (m, 2H), 4.49 (s, 1H), 4.94 (s, 1H), 6.55 (d, *J* = 6.8 Hz, 1H), 6.69-6.74 (m, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 7.10-7.15 (m, 1H), 7.40 (d, *J* = 8.8 Hz, 2H), 7.47 (d, *J* = 8.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.6, 10.1, 13.6, 14.2, 29.1, 48.0, 60.2, 61.6, 66.1, 76.1, 110.3, 118.8, 121.5, 124.4, 128.4, 130.2, 131.0, 131.1, 136.5, 153.3, 169.4, 169.7. IR (neat) ν 3377, 3084, 30583, 2986, 2925, 2900, 2870, 1719, 1707, 1604, 1485, 1464, 1394, 1367, 1344, 1317, 1287, 1275, 1259, 1219, 1186, 1152, 1095, 1072, 1035, 1006, 966, 936, 898, 871, 819, 788, 744, 729, 710 cm^{-1}. HRMS (ESI) Calcd. for $C_{24}H_{25}NO_4Br^{+1}(M+H)^+$ requires: 470.0961, found: 470.0959.

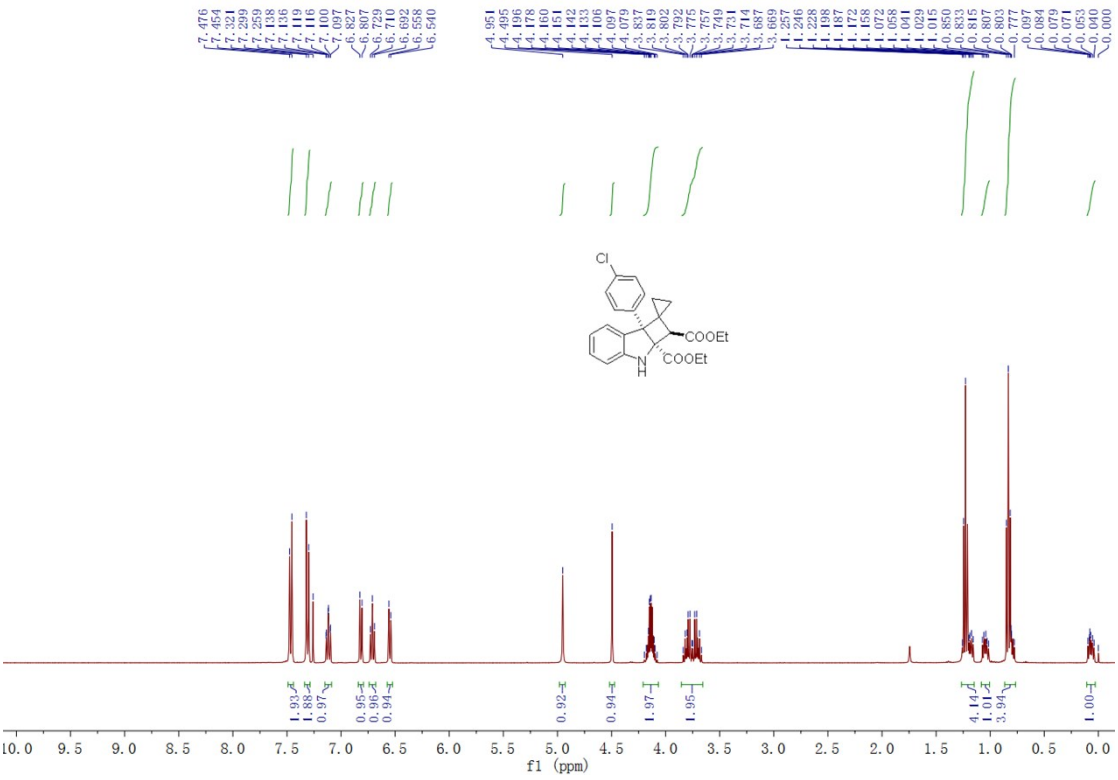


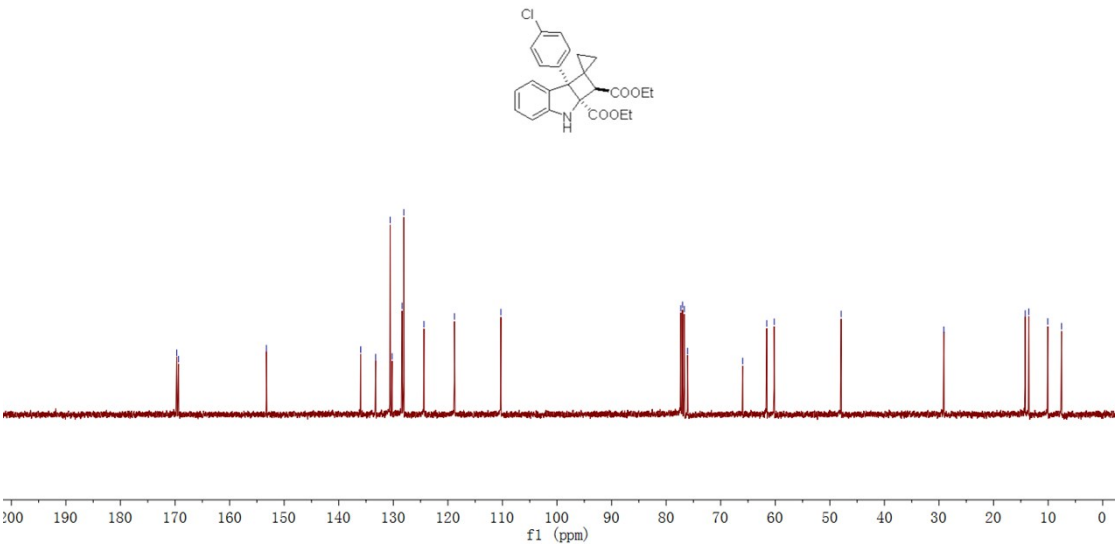


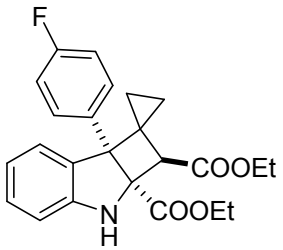


diethyl-7*b*-(4-chlorophenyl)-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3f

0.3 mmol scale, a white solid, 94% yield (119.6 mg). M.p.: 110-112 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.04-0.10 (m, 1H), 0.77-0.85 (m, 4H), 1.01-1.07 (m, 1H), 1.15-1.26 (m, 4H), 3.66-3.75 (m, 1H), 3.75-3.84 (m, 1H), 4.07-4.20 (m, 2H), 4.50 (s, 1H), 4.95 (s, 1H), 6.55 (d, J = 7.2 Hz, 1H), 6.71 (dd, J = 7.2 Hz, 7.2 Hz, 1H), 6.82 (d, J = 8.0 Hz, 1H), 7.09-7.14 (m, 1H), 7.31 (d, J = 8.8 Hz, 2H), 7.46 (d, J = 8.8 Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.5, 10.1, 13.5, 14.2, 29.1, 47.9, 60.2, 61.6, 66.0, 76.1, 110.3, 118.8, 124.4, 128.1, 128.4, 130.2, 130.6, 133.2, 136.0, 153.3, 169.4, 169.7. IR (neat) ν 3381, 3092, 3072, 3056, 3034, 2978, 2920, 2848, 1735, 1719, 1701, 1602, 1481, 1461, 1367, 1285, 1259, 1230, 1186, 1093, 1067, 1037, 1013, 840, 821, 743, 734 cm^{-1}. HRMS (ESI) Calcd. for $C_{24}H_{25}NO_4Cl^{+1}(M+H)^+$ requires: 426.1467, found: 426.1464.

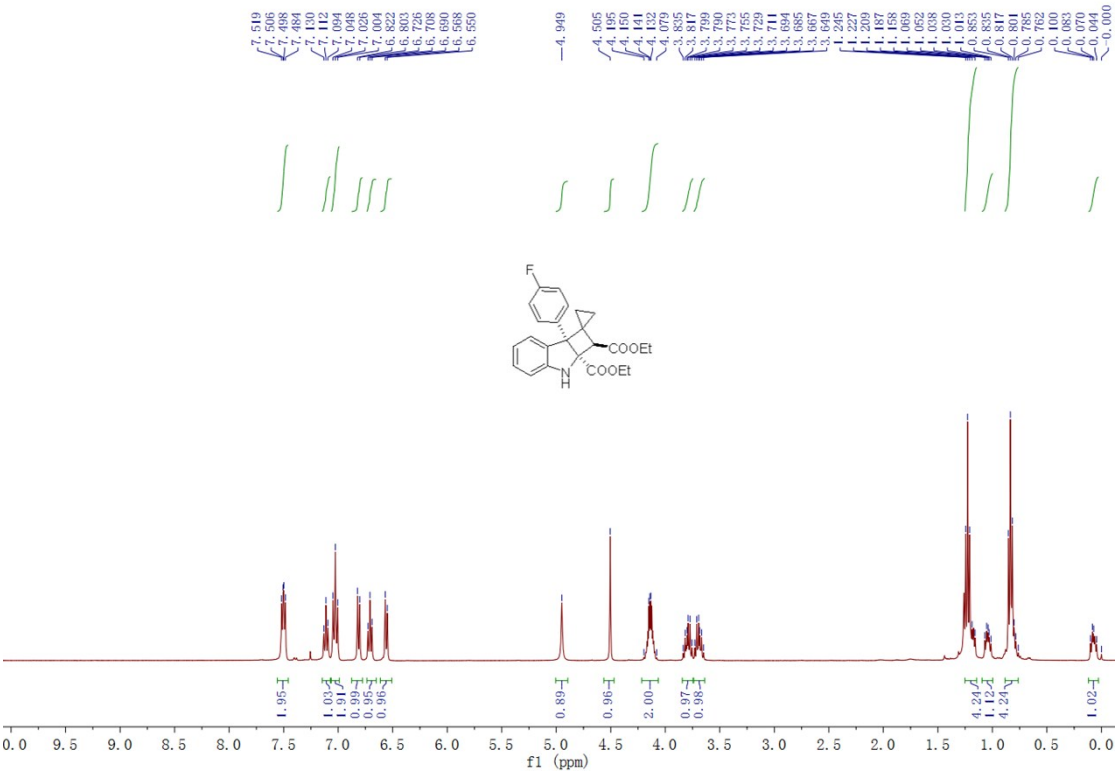

Cl
COOEt
COOEt
f1 (ppm)

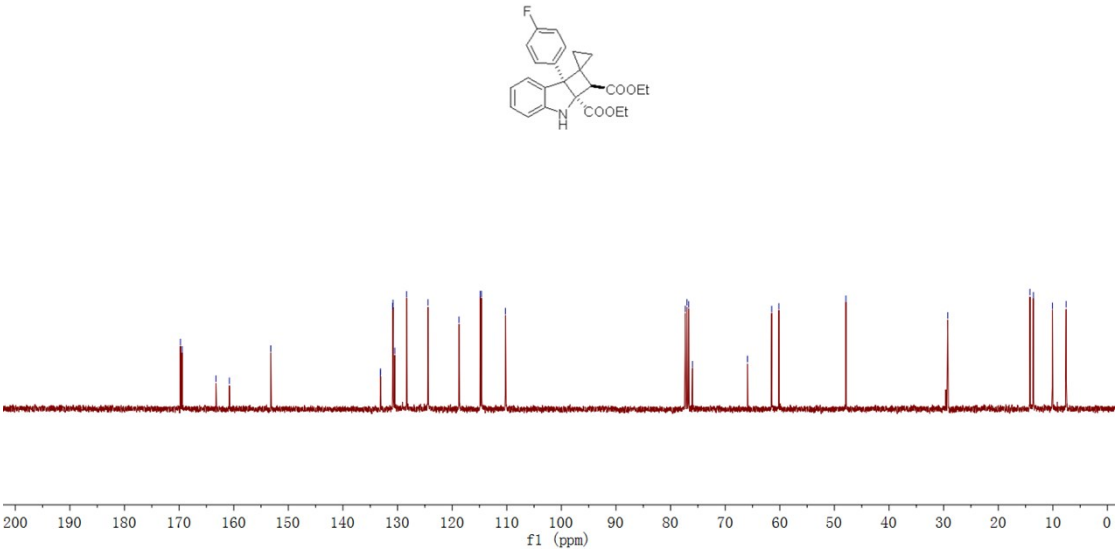

Cl
COOEt
COOEt
f1 (ppm)

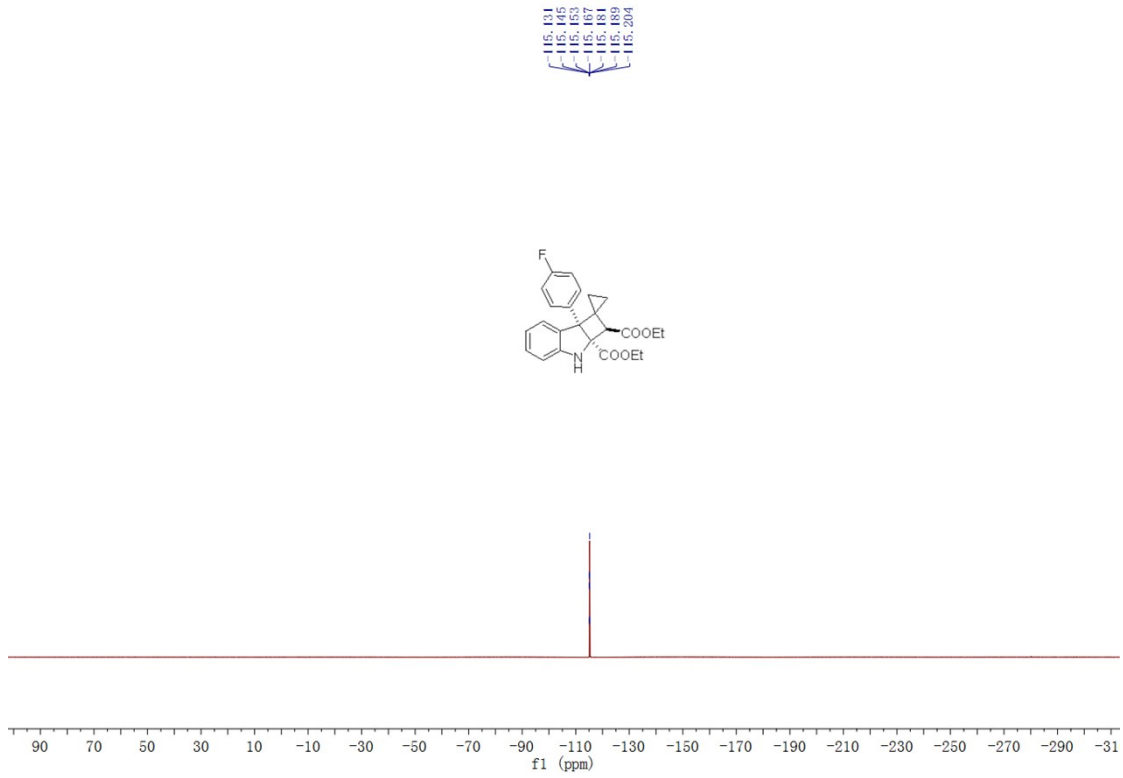


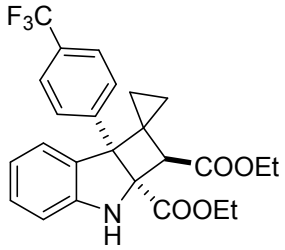
Diethyl-7*b*-(4-fluorophenyl)-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3g

0.3 mmol scale, a white solid, 89% yield (108.7 mg). M.p.: 117-120 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.04-0.10 (m, 1H), 0.76-0.86 (m, 4H), 1.01-1.07 (m, 1H), 1.15-1.25 (m, 4H), 3.64-3.73 (m, 1H), 3.75-3.84 (m, 1H), 4.07-4.20 (m, 2H), 4.51 (s, 1H), 4.95 (s, 1H), 6.56 (d, *J* = 7.2 Hz, 1H), 6.71 (dd, *J* = 7.2 Hz, 7.2 Hz, 1H), 6.82 (d, *J* = 7.2 Hz, 1H), 7.00-7.05 (m, 2H), 7.11 (d, *J* = 7.2 Hz, 1H), 7.48-7.52 (m, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.6, 10.1, 13.6, 14.2, 29.3, 47.9, 60.2, 61.5, 65.9, 76.0, 110.2, 114.8 (d, *J* = 20.0 Hz), 118.7, 124.4, 128.3, 130.5, 130.9 (d, *J* = 7.9 Hz), 133.1 (d, *J* = 3.2 Hz), 153.2, 162.0 (d, *J* = 245.3 Hz), 169.5, 169.8. ^{19}F NMR ($CDCl_3$, $CFCl_3$, 376 MHz) δ -115.20- -115.13 (m). IR (neat) ν 3391, 3081, 3050, 3031, 2989, 2956, 2925, 2848, 2831, 1711, 1603, 1509, 1481, 1462, 1371, 1289, 1276, 1228, 1188, 1163, 1067, 1054, 1038, 1027, 896, 839, 752, 741, 719 cm^{-1}. HRMS (ESI) Calcd. for $C_{24}H_{25}NO_4F^{+1}(M+H)^+$ requires: 410.1762, found: 410.1759.


F
COOEt
COOEt
H
f1 (ppm)


F
COOEt
COOEt
H
f1 (ppm)

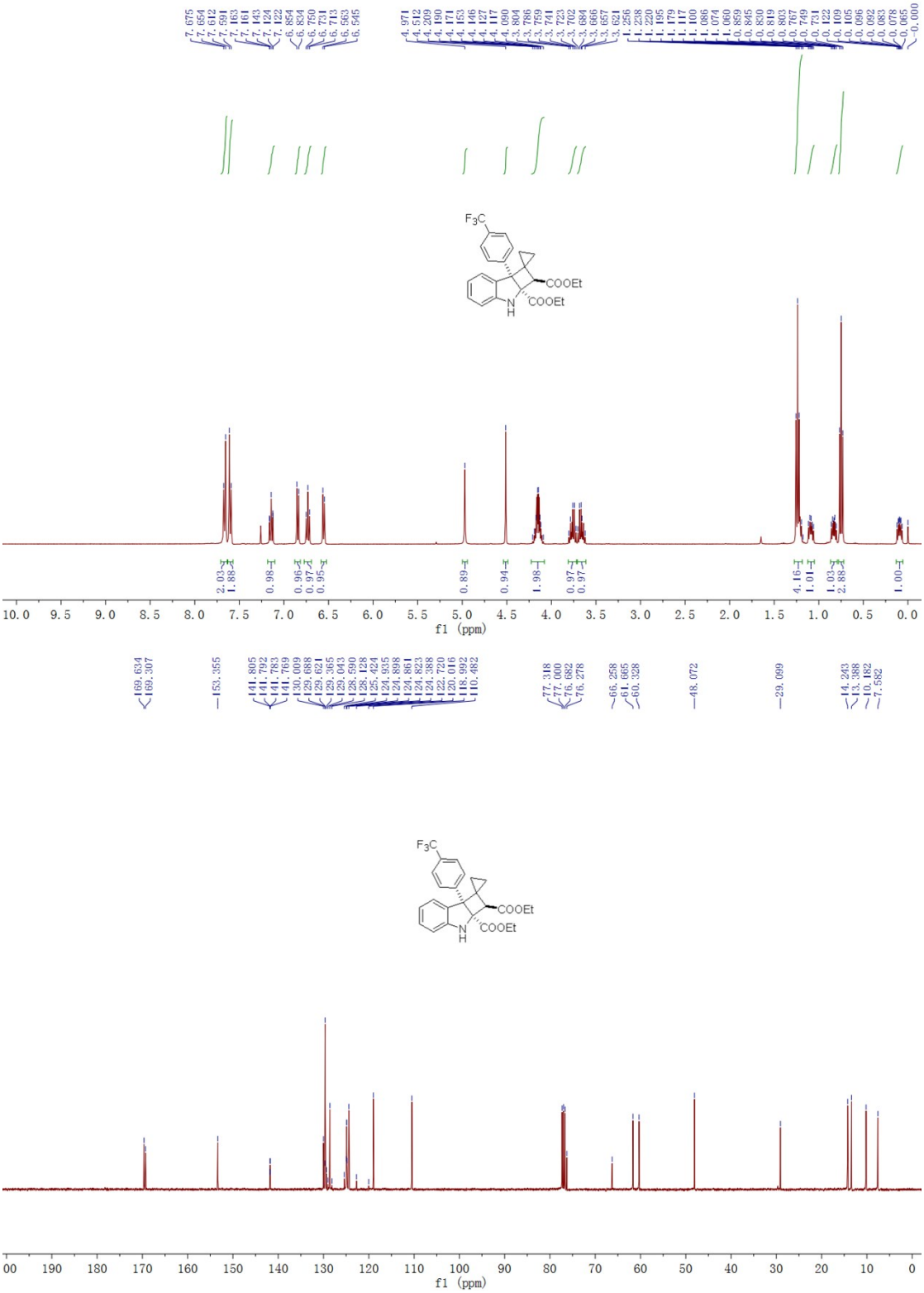


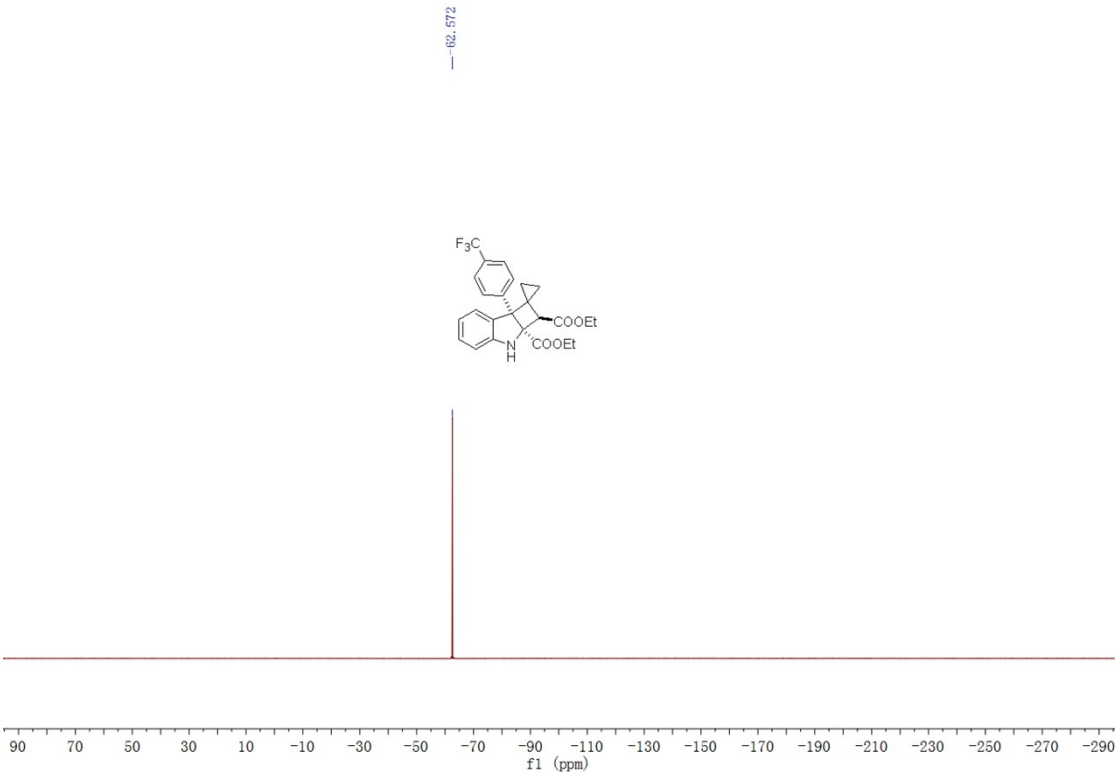


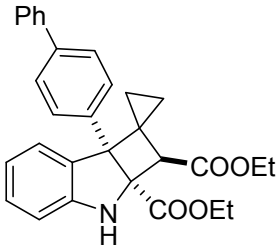
diethyl-7*b*-(4-(trifluoromethyl)phenyl)-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3h

0.3 mmol scale, a faint yellow solid, 87% yield (119.7 mg). M.p.: 77-80 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.06-0.12 (m, 1H), 0.75 (t, *J* = 7.2 Hz, 3H), 0.80-0.86 (m, 1H), 1.06-1.12 (m, 4H), 1.17-1.26 (m, 4H), 3.62-3.70 (m, 1H), 3.72-3.80 (m, 1H), 4.09-4.21 (m, 2H), 4.51 (s, 1H), 4.97 (s, 1H), 6.55 (d, *J* = 7.2 Hz, 1H), 6.73 (dd, *J* = 7.2 Hz, 7.2 Hz, 1H), 6.84 (d, *J* = 7.2 Hz, 1H), 7.12-7.17 (m, 1H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.66 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.6, 10.2, 13.4, 14.2, 29.1, 48.1, 60.3, 61.7, 66.3, 76.3, 110.5, 119.0, 124.1 (q, *J* = 270.4 Hz), 124.4, 124.9 (q, *J* = 3.8 Hz), 128.6, 129.5 (q, *J* = 32.2 Hz), 129.7, 130.0, 141.8 (q, *J* = 1.4 Hz), 153.4, 169.3, 169.6. ^{19}F NMR ($CDCl_3$, $CFCl_3$, 376 MHz) δ -62.6. IR (neat) ν 3397, 3047, 2989, 2961, 2942, 2900, 1734, 1724, 1713, 1618, 1606, 1482, 1466, 1407, 1324, 1276, 1262, 1166, 1115,

1068, 1055, 1035, 1016, 882, 832, 740, 715 cm^{-1}. HRMS (ESI) Calcd. for $C_{25}H_{25}NO_4F_3^{+1}(M+H)^+$ requires: 460.1730, found: 460.1728.



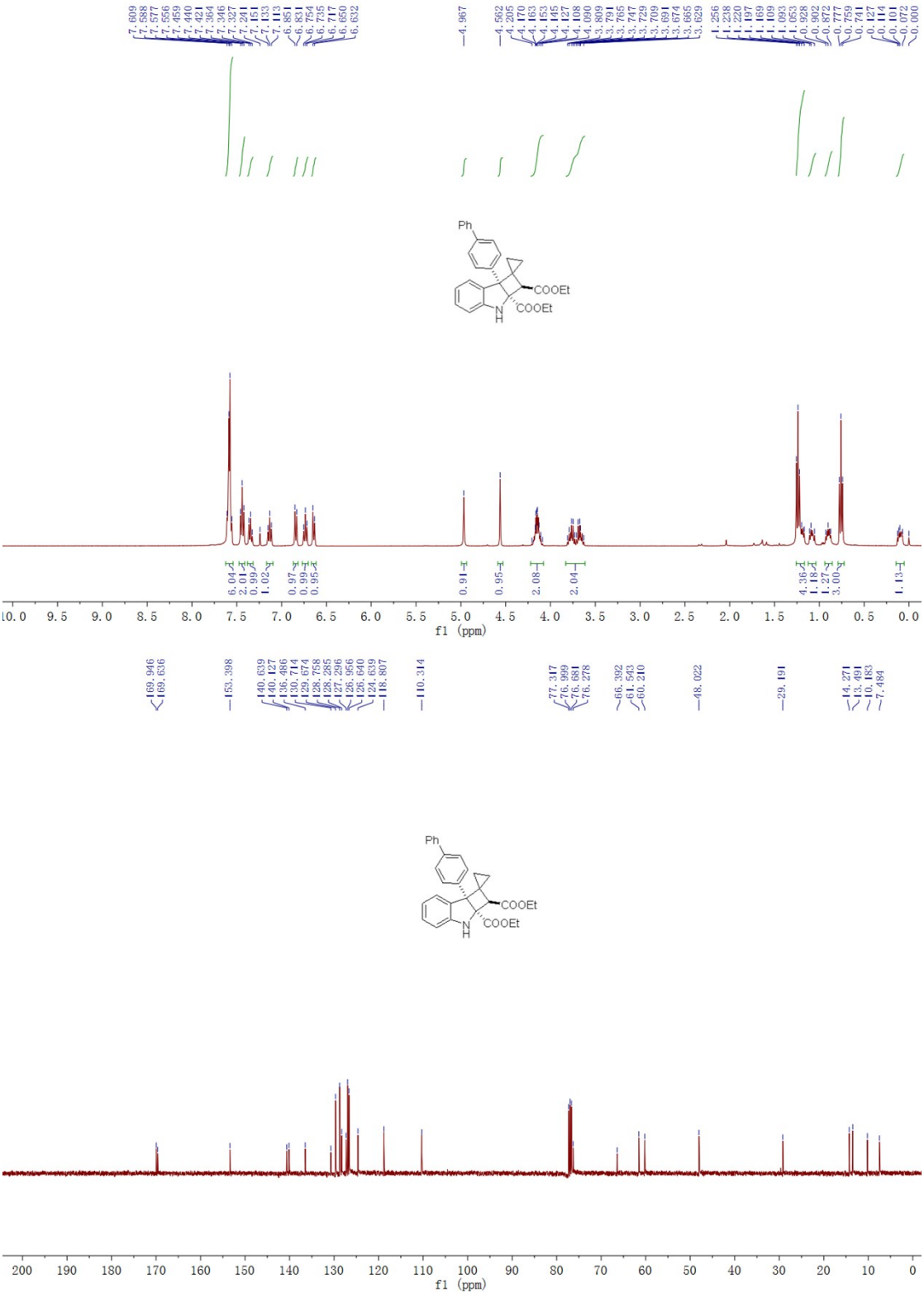


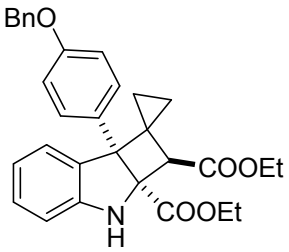


diethyl-7*b*-([1,1'-biphenyl]-4-yl)-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3i

0.3 mmol scale, a faint yellow solid, 74% yield (103.7 mg). M.p.: 40-42 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.07-0.13 (m, 1H), 0.76 (t, *J* = 7.2 Hz, 3H), 0.87-0.93 (m, 1H), 1.05-1.11 (m, 1H), 1.16-1.26 (m, 4H), 3.62-3.71 (m, 1H), 3.72-3.81 (m, 1H), 4.09-4.21 (m, 2H), 4.56 (s, 1H), 4.97 (s, 1H), 6.64 (d, *J* = 7.2 Hz, 1H), 6.74 (dd, *J* = 7.2 Hz, 7.2 Hz, 1H), 6.84 (d, *J* = 8.0 Hz, 1H), 7.13 (dd, *J* = 8.0 Hz, 8.0 Hz, 1H), 7.32-7.37 (m, 1H), 7.42-7.46 (m, 2H), 7.55-7.61 (m, 6H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.5, 10.2, 13.5, 14.3, 29.2, 48.0, 60.2, 61.5, 66.4, 76.3, 110.3, 118.8, 124.6, 126.6, 127.0, 127.3, 128.3, 128.8, 129.7, 130.7, 136.5, 140.1, 140.6, 153.4, 169.6, 169.9. IR (neat) ν 3379, 3056, 3028, 2980, 2956, 2926, 2870, 2853, 1723, 1604, 1485, 1465, 1391, 1369, 1322, 1280, 1258, 1186, 1095, 1066, 1037, 1025, 1007, 936, 899, 857, 830, 744, 697, 658

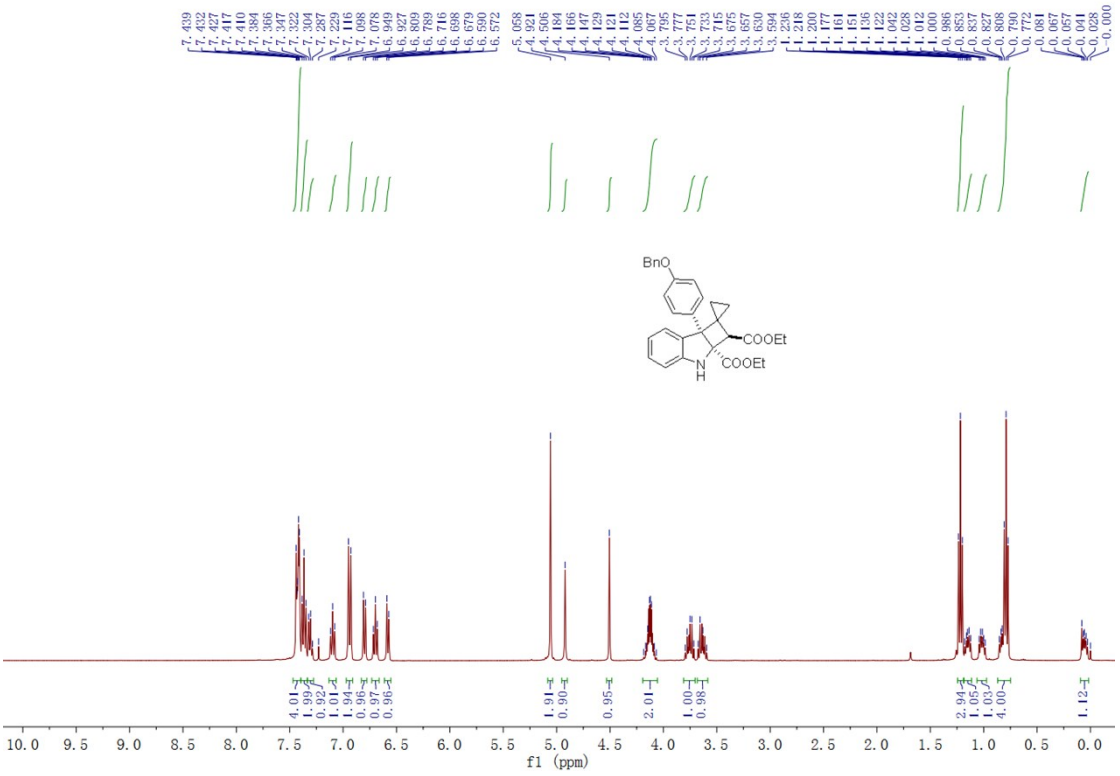
cm^{-1}. HRMS (ESI) Calcd. for $C_{30}H_{30}NO_4^{+1}(M+H)^+$ requires: 468.2169, found: 468.2167.

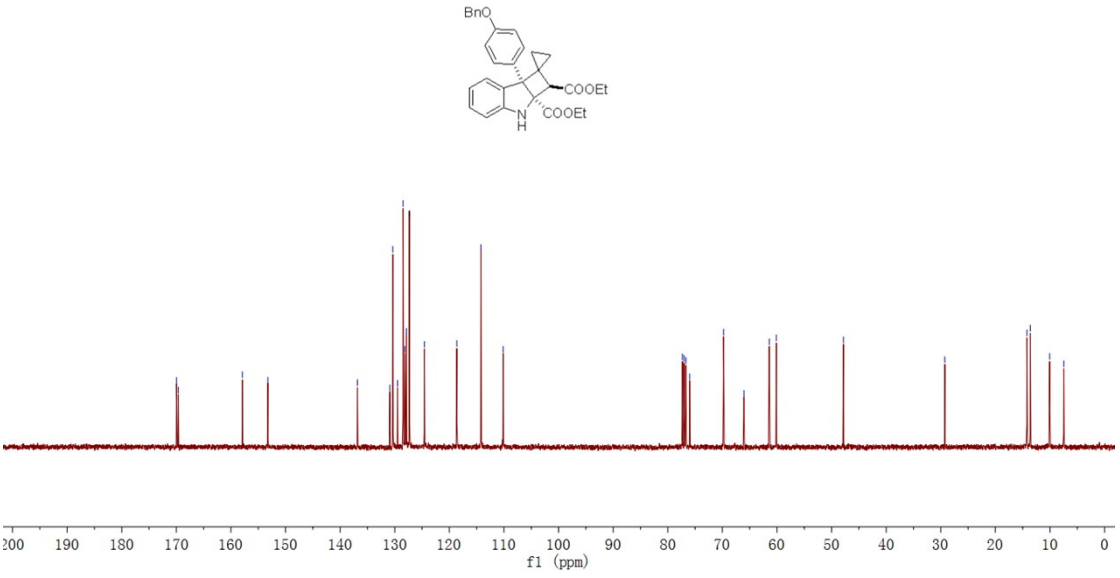


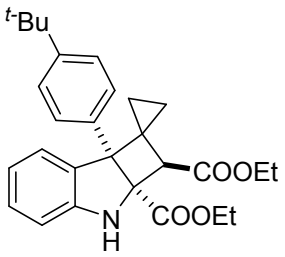


diethyl-7*b*-(4-(benzyloxy)phenyl)-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3j

0.3 mmol scale, a faint yellow solid, 88% yield (131.2 mg). M.p.: 99-101 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.02-0.09 (m, 1H), 0.77-0.85 (m, 4H), 0.98-1.05 (m, 1H), 1.12-1.17 (m, 1H), 1.22 (t, *J* = 7.2 Hz, 3H), 3.59-3.68 (m, 1H), 3.72-3.80 (m, 1H), 4.07-4.19 (m, 2H), 4.51 (s, 1H), 4.92 (s, 1H), 5.06 (s, 2H), 6.58 (d, *J* = 7.2 Hz, 1H), 6.70 (dd, *J* = 7.2 Hz, 7.2 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.94 (d, *J* = 8.8 Hz, 2H), 7.10 (dd, *J* = 8.0 Hz, 8.0 Hz, 1H), 7.28-7.33 (m, 1H), 7.34-7.38 (m, 2H), 7.41-7.44 (m, 4H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.5, 10.1, 13.6, 14.2, 29.3, 47.8, 60.1, 61.4, 66.1, 69.8, 76.0, 110.1, 114.2, 118.6, 124.6, 127.3, 127.9, 128.1, 128.5, 129.5, 130.4, 130.9, 136.8, 153.2, 157.9, 169.6, 170.0. IR (neat) ν 3378, 3064, 3042, 3028, 2989, 2942, 2903, 2870, 1721, 1710, 1600, 1509, 1483, 1461, 1365, 1292, 1254, 1219, 1186, 1157, 1076, 1039, 1010, 871, 839, 804, 788, 755, 741, 703 cm^{-1}. HRMS (ESI) Calcd. for $C_{31}H_{32}NO_5^{+1}(M+H)^+$ requires: 498.2275, found: 498.2277.

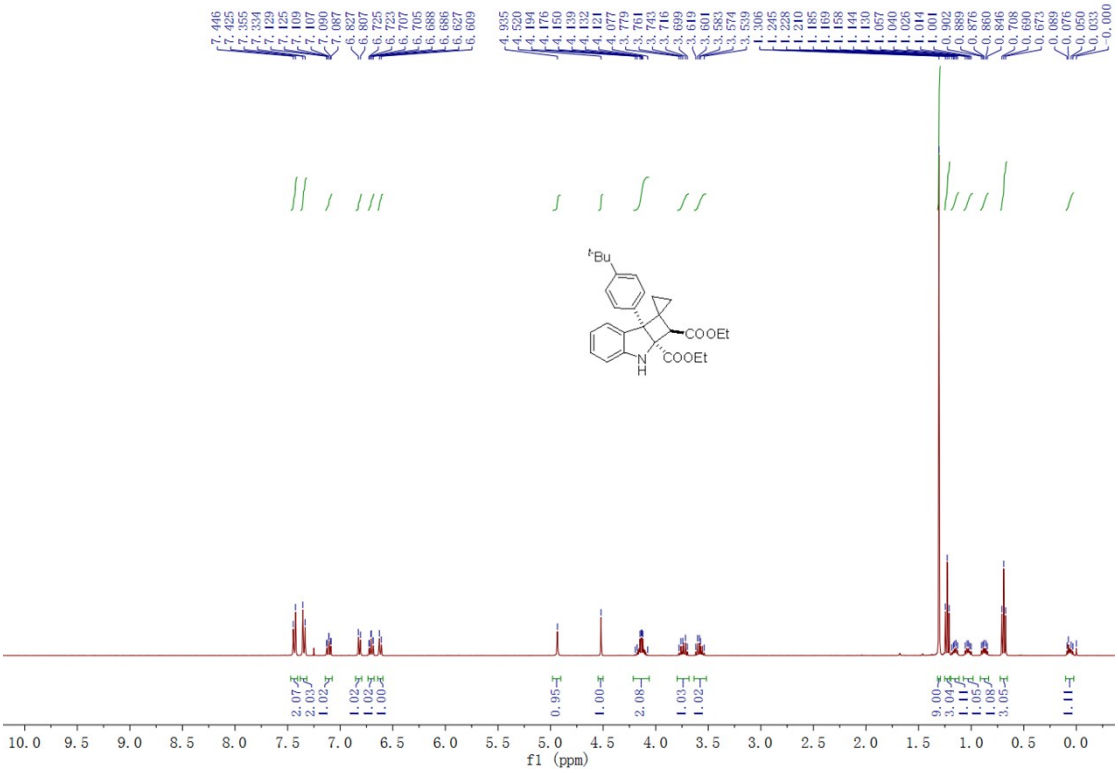

BnO
COOEt
COOEt
N
H
f1 (ppm)

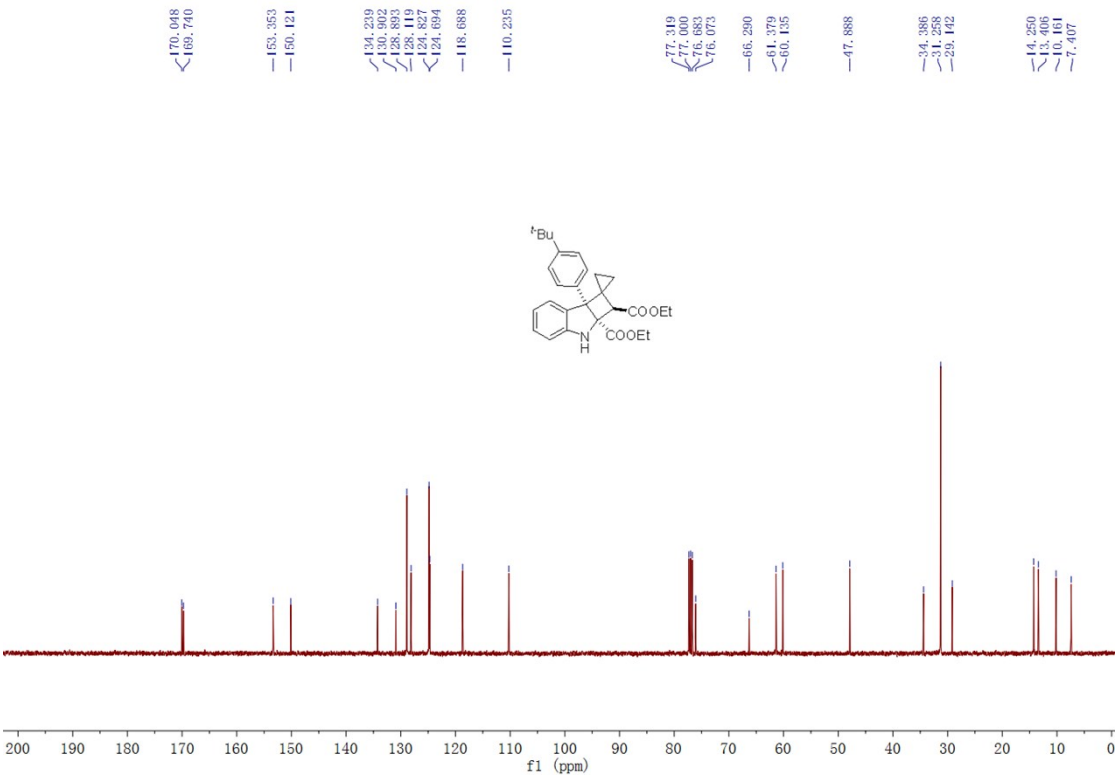

BnO
COOEt
COOEt
N
H
f1 (ppm)

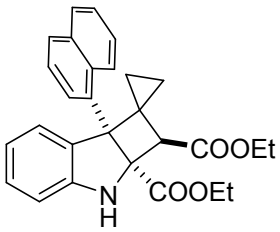


diethyl-7*b*-(4-(tert-butyl)phenyl)-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3k

0.3 mmol scale, a white solid, 91% yield (122.4 mg). M.p.: 44-46 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.03-0.09 (m, 1H), 0.69 (t, *J* = 7.2 Hz, 3H), 0.84-0.91 (m, 1H), 1.00-1.06 (m, 1H), 1.13-1.19 (m, 1H), 1.23 (t, *J* = 7.2 Hz, 3H), 1.31 (s, 9H), 3.53-3.62 (m, 1H), 3.69-3.78 (m, 1H), 4.07-4.20 (m, 2H), 4.52 (s, 1H), 4.94 (s, 1H), 6.61 (d, *J* = 7.2 Hz, 1H), 6.68-6.73 (m, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 7.08-7.13 (m, 1H), 7.34 (d, *J* = 8.4 Hz, 2H), 7.44 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.4, 10.2, 13.4, 14.3, 29.1, 31.3, 34.4, 47.9, 60.1, 61.3, 66.3, 76.1, 110.2, 118.7, 124.7, 124.8, 128.1, 128.9, 130.9, 134.2, 150.1, 153.4, 169.7, 170.0. IR (neat) ν 3381, 3086, 3050, 3028, 2961, 2931, 2903, 2867, 1722, 1606, 1509, 1484, 1464, 1390, 1367, 1255, 1212, 1184, 1066, 1038, 1018, 935, 869, 826, 742, 702 cm^{-1}. HRMS (ESI) Calcd. for $C_{28}H_{34}NO_4^{+1}$(M+H)$^+$ requires: 448.2482, found: 448.2484.



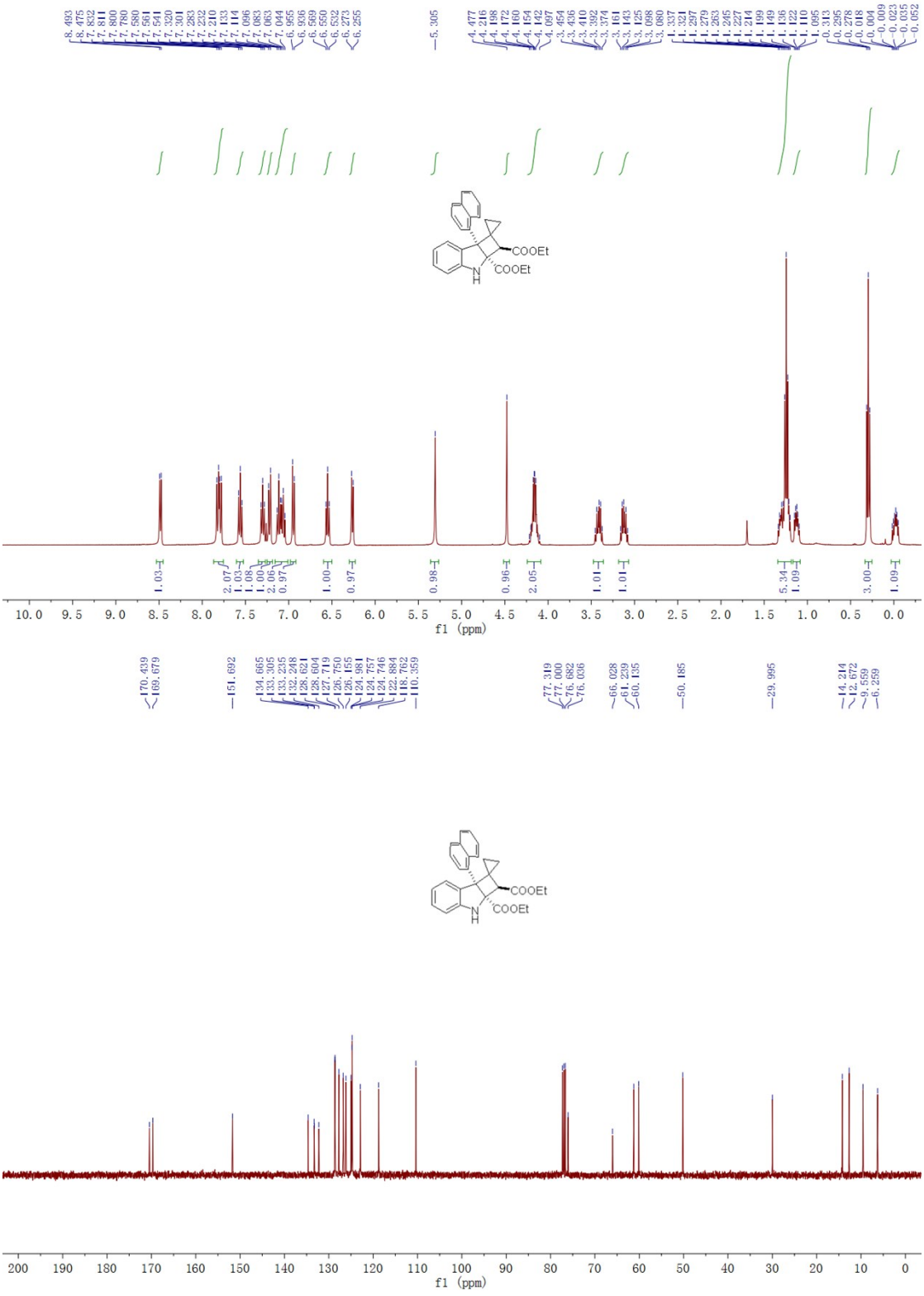


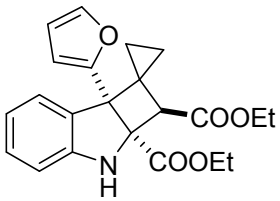


diethyl-7*b*-(naphthalen-1-yl)-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3l

0.3 mmol scale, a white solid, 82% yield (108.7 mg). M.p.: 135-136 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ -0.05-0.02 (m, 1H), 0.30 (t, *J* = 7.2 Hz, 3H), 1.09-1.15 (m, 1H), 1.19-1.34 (m, 5H), 3.08-3.17 (m, 1H), 3.37-3.46 (m, 1H), 4.09-4.22 (m, 2H), 4.45 (s, 1H), 5.31 (s, 1H), 6.26 (d, *J* = 7.2 Hz, 1H), 6.55 (dd, *J* = 7.2 Hz, 7.2 Hz, 1H), 6.95 (d, *J* = 7.2 Hz, 1H), 7.04-7.14 (m, 2H), 7.22 (d, *J* = 8.0 Hz, 1H), 7.30 (dd, *J* = 8.0 Hz, 8.0 Hz, 1H), 7.56 (dd, *J* = 8.0 Hz, 8.0 Hz, 1H), 7.78-7.84 (m, 2H), 8.48 (d, *J* = 7.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 6.3, 9.6, 12.7, 14.2, 30.0, 50.2, 60.1, 61.2, 66.0, 76.0, 110.4, 118.8, 122.9, 124.75, 124.76, 125.0, 126.2, 126.8, 127.7, 128.60, 128.62, 132.2, 133.2, 133.3, 134.7, 151.7, 169.7, 170.4. IR (neat) ν 3376, 3084, 3050, 2981, 2959, 2939, 2925, 2900, 2867, 1741, 1710, 1603, 1483, 1469, 1390, 1369, 1286, 1257, 1202, 1186, 1150, 1058, 1035, 871, 857, 799, 780, 769, 759, 732, 717 cm^{-1}. HRMS (ESI) Calcd. for

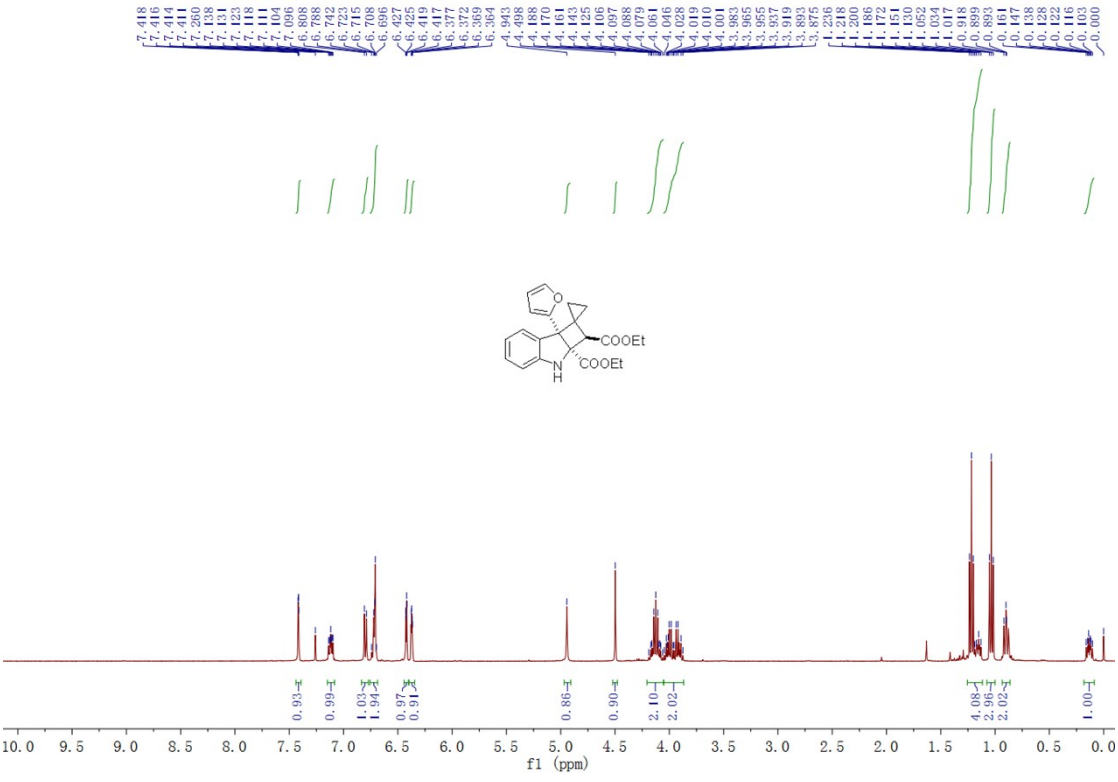
$C_{28}H_{28}NO_4^{+1}(M+H)^+$ requires: 442.2013, found: 442.2010.

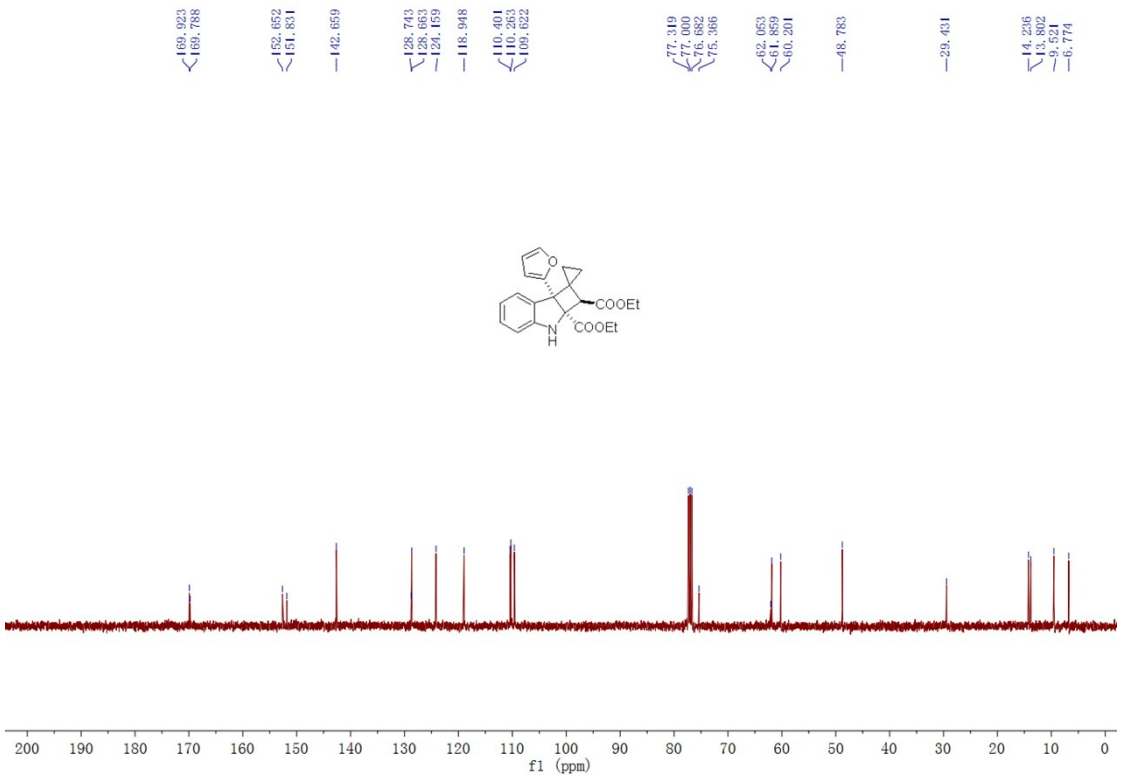


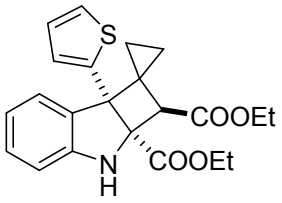


diethyl-7*b*-(furan-2-yl)-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3m

0.3 mmol scale, a yellow solid, 50% yield (57.2 mg). M.p.: 89-90 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.10-0.17 (m, 1H), 0.89-0.92 (m, 2H), 1.03 (t, *J* = 7.2 Hz, 3H), 1.13-1.19 (m, 1H), 1.22 (t, *J* = 7.2 Hz, 3H), 3.87-3.96 (m, 1H), 3.97-4.05 (m, 1H), 4.06-4.19 (m, 2H), 4.50 (s, 1H), 4.94 (s, 1H), 6.37 (dd, *J* = 2.0 Hz, 3.2 Hz, 1H), 6.42 (dd, *J* = 0.8 Hz, 3.2 Hz, 1H), 6.69-6.75 (m, 2H), 6.80 (d, *J* = 8.0 Hz, 1H), 7.09-7.14 (m, 1H), 7.42 (dd, *J* = 0.8 Hz, 2.0 Hz, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 6.8, 9.5, 13.8, 14.2, 29.4, 48.8, 60.2, 61.9, 62.1, 75.4, 109.6, 110.3, 110.4, 118.9, 124.2, 128.66, 128.74, 142.7, 151.8, 152.7, 169.8, 169.9. IR (neat) ν 3411, 3367, 3339, 3056, 3975, 2956, 2934, 2900, 2867, 1712, 1651, 1604, 1482, 1467, 1447, 1369, 1324, 1286, 1254, 1216, 1178, 1095, 1066, 1036, 1014, 974, 860, 821, 750, 741, 720 cm^{-1}. HRMS (ESI) Calcd. for $C_{22}H_{24}NO_5^{+1}$(M+H)$^+$ requires: 382.1649, found: 382.1648.

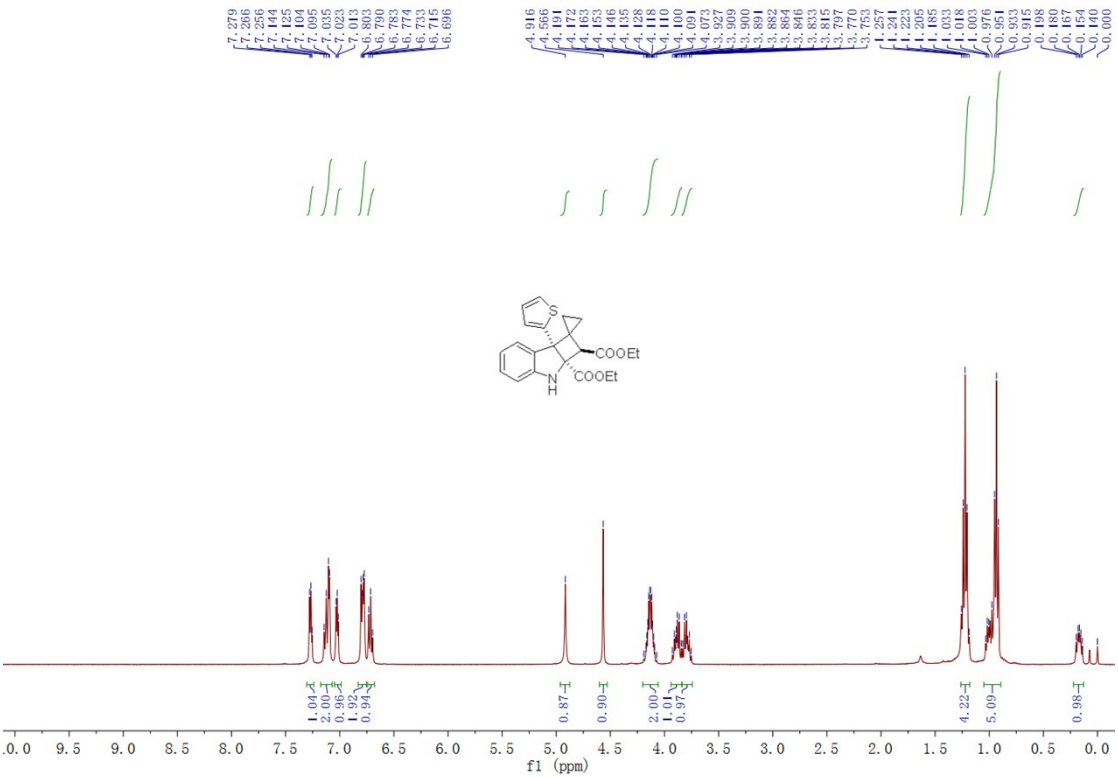


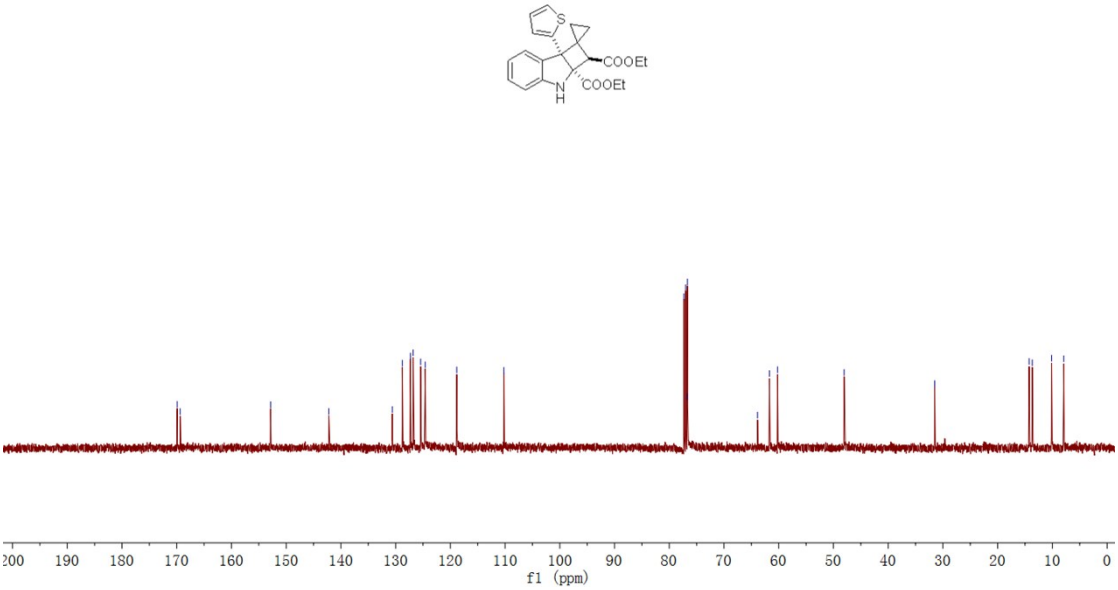


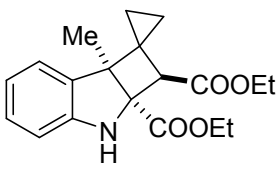


diethyl-7*b*-(thiophen-2-yl)-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3n

0.3 mmol scale, a yellow solid, 73% yield (86.9 mg). M.p.: 91-93 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.14-0.20 (m, 1H), 0.92-1.04 (m, 5H), 1.18-1.26 (m, 4H), 3.75-3.84 (m, 1H), 3.86-3.93 (m, 1H), 4.07-4.20 (m, 2H), 4.57 (s, 1H), 4.92 (s, 1H), 6.72 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 6.77-6.81 (m, 2H), 7.01-7.04 (m, 1H), 7.09-7.15 (m, 2H), 7.27 (d, *J* = 4.2 Hz, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.9, 10.1, 13.7, 14.2, 31.5, 48.0, 60.2, 61.7, 63.9, 76.7, 110.2, 118.8, 124.6, 125.4, 126.8, 127.3, 128.8, 130.6, 142.2, 152.8, 169.4, 169.9. IR (neat) ν 3385, 3064, 2986, 2974, 2924, 2873, 2850, 1719, 1608, 1484, 1471, 1417, 1370, 1347, 1317, 1280, 1257, 1236, 1210, 1190, 1149, 1114, 1081, 1065, 1051, 1035, 1022, 936, 865, 824, 797, 747, 716, 699 cm^{-1}. HRMS (ESI) Calcd. for $C_{22}H_{24}NO_4S^{+1}(M+H)^+$ requires: 398.1421, found: 398.1418.



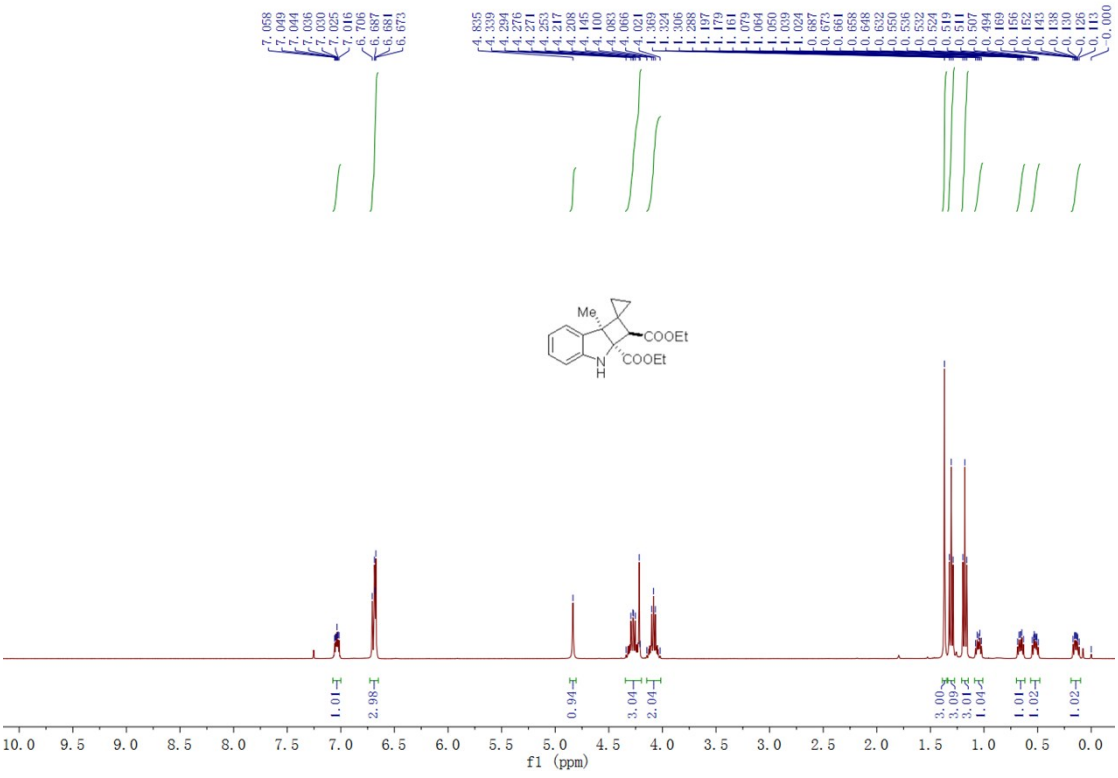


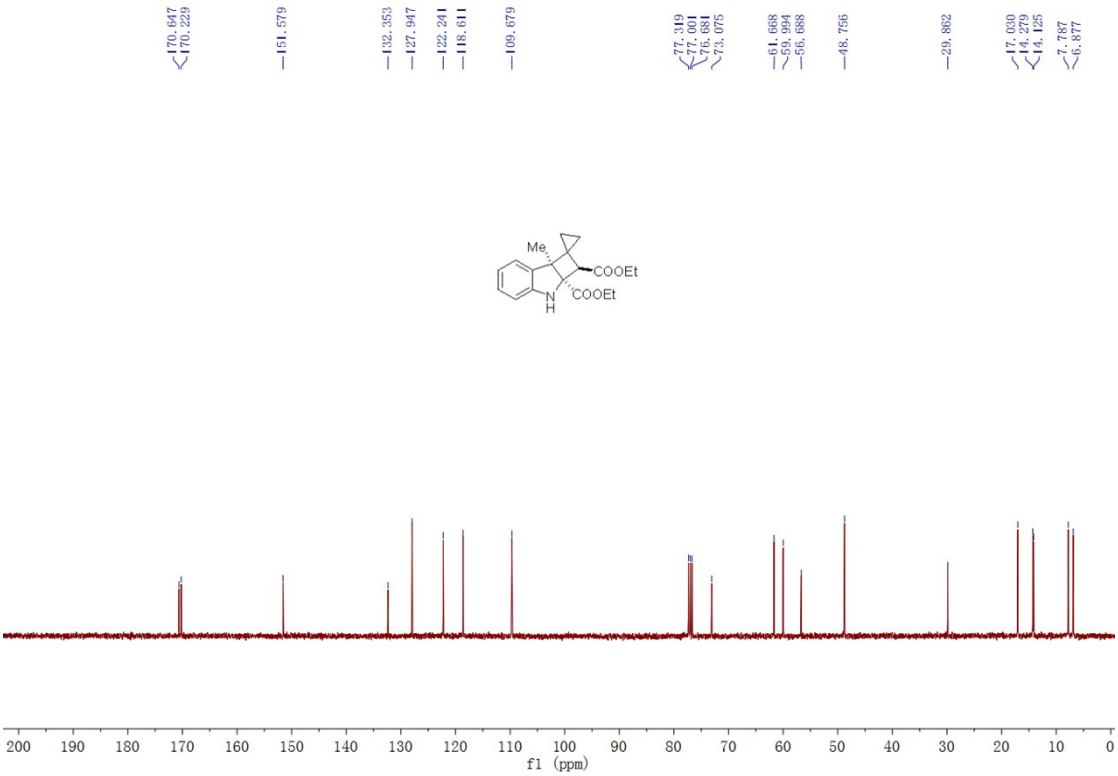


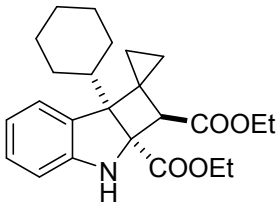
diethyl-7*b*-methyl-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-

dicarboxylate 3o

0.3 mmol scale, a yellow oil, 81% yield (79.9 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.11-0.17 (m, 1H), 0.49-0.55 (m, 1H), 0.63-0.69 (m, 1H), 1.02-1.08 (m, 1H), 1.18 (t, *J* = 7.2 Hz, 3H), 1.31 (t, *J* = 7.2 Hz, 3H), 1.37 (s, 3H), 4.02-4.15 (m, 2H), 4.20-4.34 (m, 3H), 4.84 (s, 1H), 6.67-6.71 (m, 3H), 7.01-7.06 (m, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 6.9, 7.8, 14.1, 14.3, 17.0, 29.9, 48.8, 56.7, 60.0, 61.7, 73.1, 109.7, 118.6, 122.2, 127.9, 132.4, 151.6, 170.2, 170.6. IR (neat) ν 3399, 2979, 2956, 2945, 2925, 2900, 2867, 1721, 1607, 1484, 1468, 1449, 1370, 1320, 1287, 1258, 1239, 1185, 1158, 1130, 1096, 1074, 1036, 1016, 865, 819, 750, 702, 685 cm^{-1}. HRMS (ESI) Calcd. for $C_{19}H_{24}NO_4^{+1}$(M+H)$^+$ requires: 330.1700, found: 330.1701.

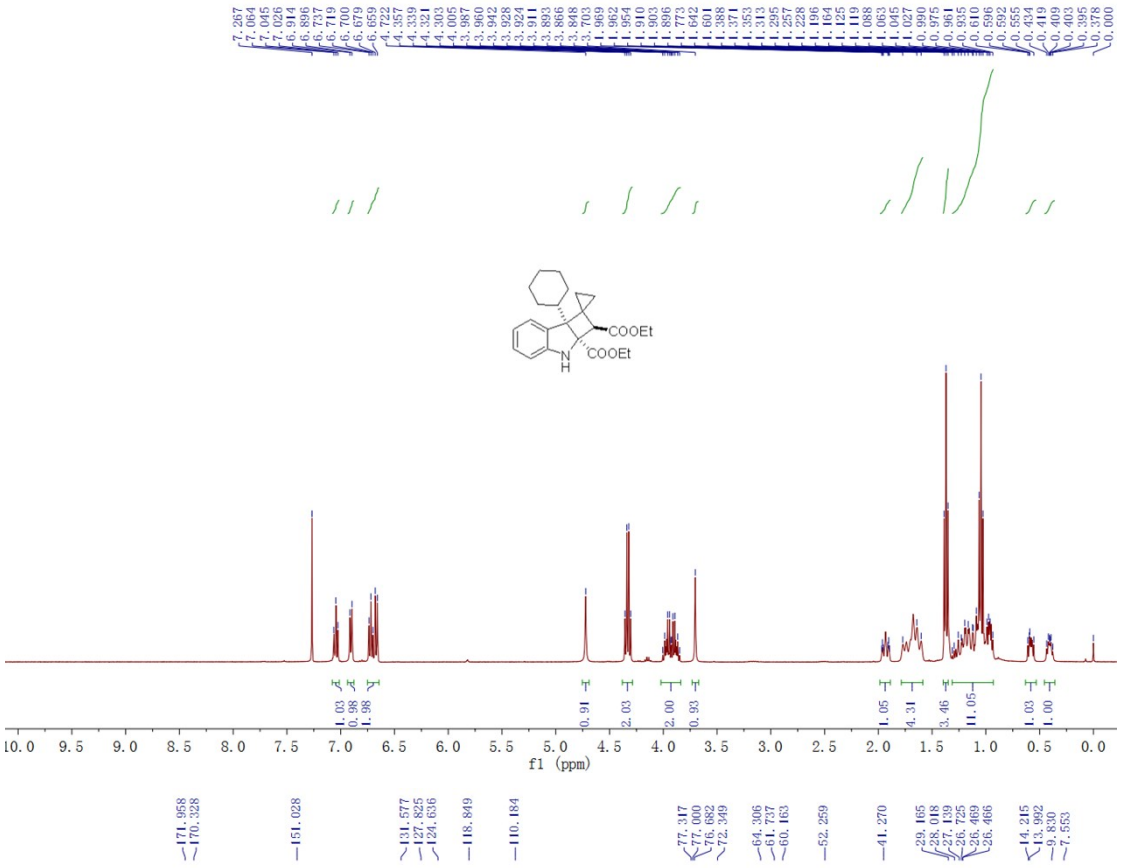


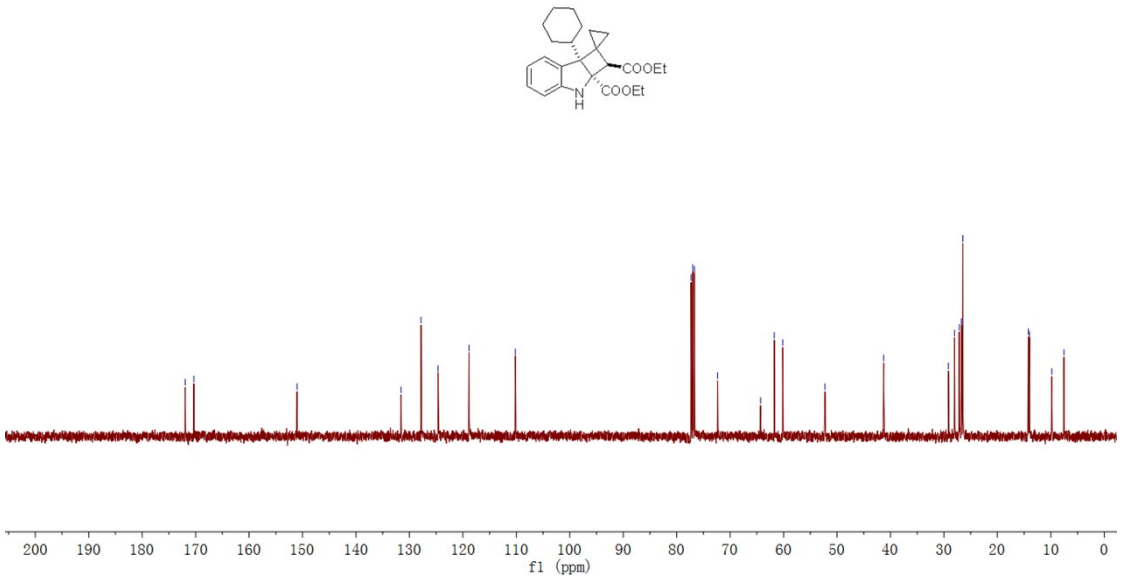


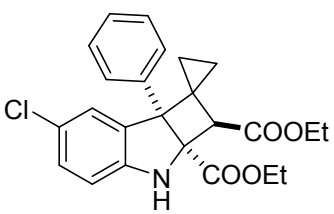


diethyl-7*b*-cyclohexyl-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3q

0.3 mmol scale, a white oil, 99% yield (117.3 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.37-0.44 (m, 1H), 0.55-0.61 (m, 1H), 0.93-1.32 (m, 11H), 1.37 (t, *J* = 7.2 Hz, 3H), 1.60-1.77 (m, 4H), 1.89-1.97 (m, 1H), 3.70 (s, 1H), 3.84-4.01 (m, 2H), 4.33 (q, *J* = 7.2 Hz, 2H), 4.72 (s, 1H), 6.67 (d, *J* = 7.6 Hz, 1H), 6.72 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 6.91 (d, *J* = 7.6 Hz, 1H), 7.05 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.6, 9.8, 14.0, 14.2, 26.466, 26.469, 26.7, 27.1, 28.0, 29.2, 41.3, 52.3, 60.2, 61.7, 64.3, 72.3, 110.2, 118.8, 124.6, 127.8, 131.6, 151.0, 170.3, 172.0. IR (neat) ν 3373, 3084, 3053, 2979, 2930, 2851, 1720, 1643, 1605, 1483, 1465, 1390, 1368, 1346, 1324, 1250, 1184, 1153, 1095, 1065, 1036, 912, 860, 738 cm^{-1}. HRMS (ESI) Calcd. for $C_{24}H_{32}NO_4^{+1}(M+H)^+$ requires: 398.2326, found: 398.2327.

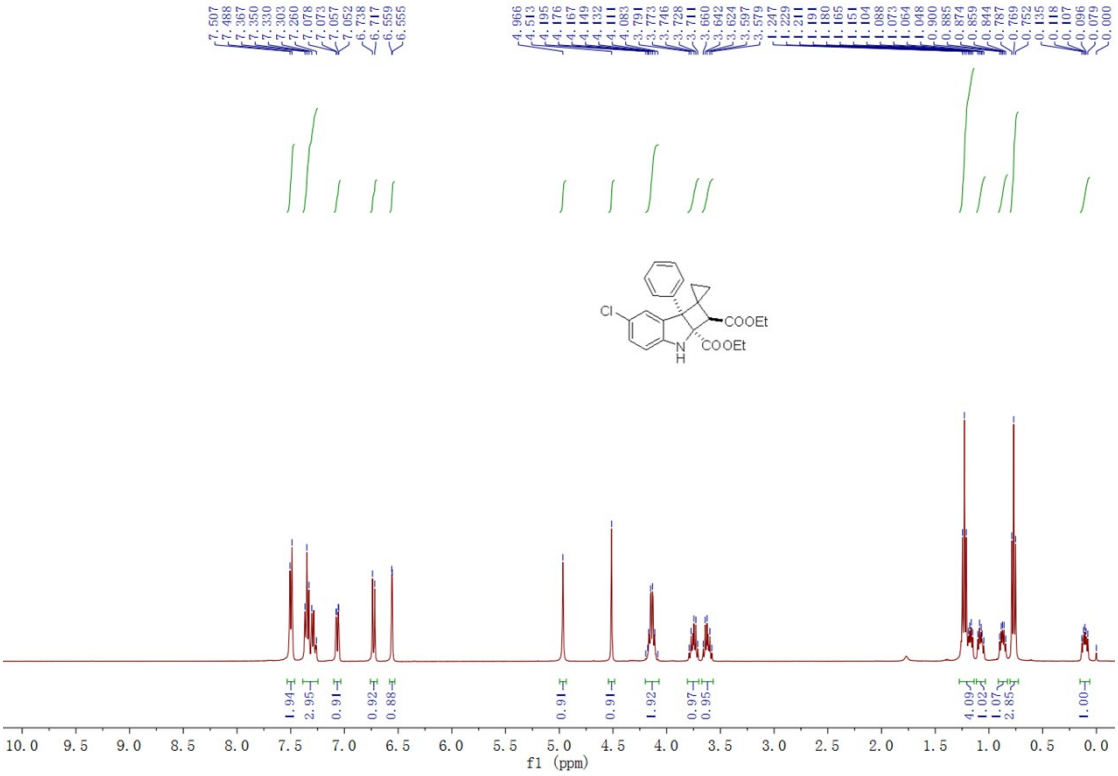

COOEt
COOEt
f1 (ppm)

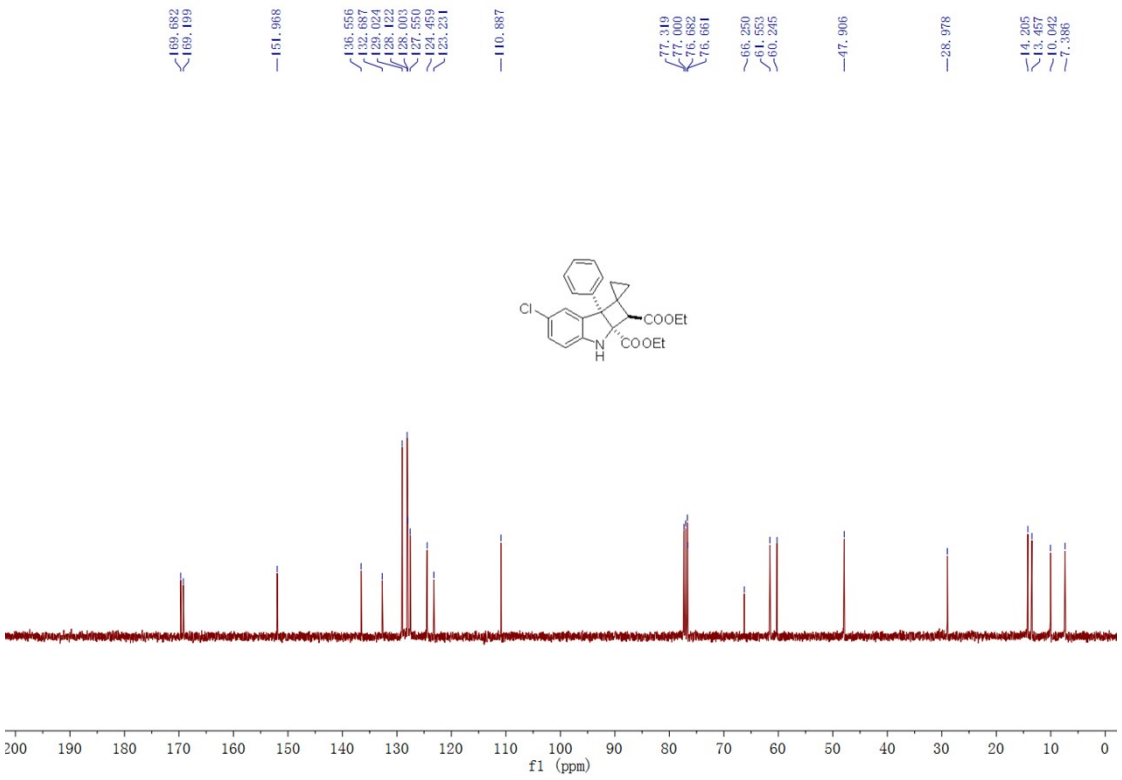

COOEt
COOEt
f1 (ppm)

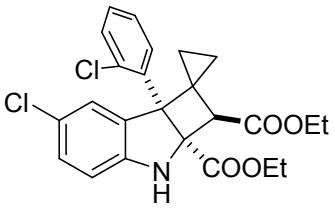

Cl
COOEt
COOEt
N
H

diethyl-6-chloro-7b-phenyl-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3r

0.3 mmol scale, a white solid, 86% yield (109.7 mg). M.p.: 146-147 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.07-0.14 (m, 1H), 0.77 (t, *J* = 7.2 Hz, 3H), 0.84-0.90 (m, 1H), 1.04-1.11 (m, 1H), 1.15-1.25 (m, 4H), 3.57-3.66 (m, 1H), 3.71-3.80 (m, 1H), 4.08-4.20 (m, 2H), 4.51 (s, 1H), 4.97 (s, 1H), 6.56 (d, *J* = 1.6 Hz, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 7.07 (dd, *J* = 1.6 Hz, 8.4 Hz, 1H), 7.26-7.37 (m, 3H), 7.50 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.4, 10.0, 13.5, 14.2, 29.0, 47.9, 60.2, 61.6, 66.3, 76.7, 110.9, 123.2, 124.5, 127.6, 128.0, 128.1, 129.0, 132.7, 136.6, 152.0, 169.2, 169.7. IR (neat) ν 3384, 3339, 3059, 3034, 2986, 2956, 2928, 2900, 2867, 1737, 1715, 1654, 1603, 1475, 1446, 1370, 1265, 1216, 1196, 1175, 1116, 1067, 1039, 944, 865, 823, 809, 747, 713, 697, 659 cm^{-1}. HRMS (ESI) Calcd. for $C_{24}H_{25}NO_4Cl^{+1}(M+H)^+$ requires: 426.1467, found: 426.1463.

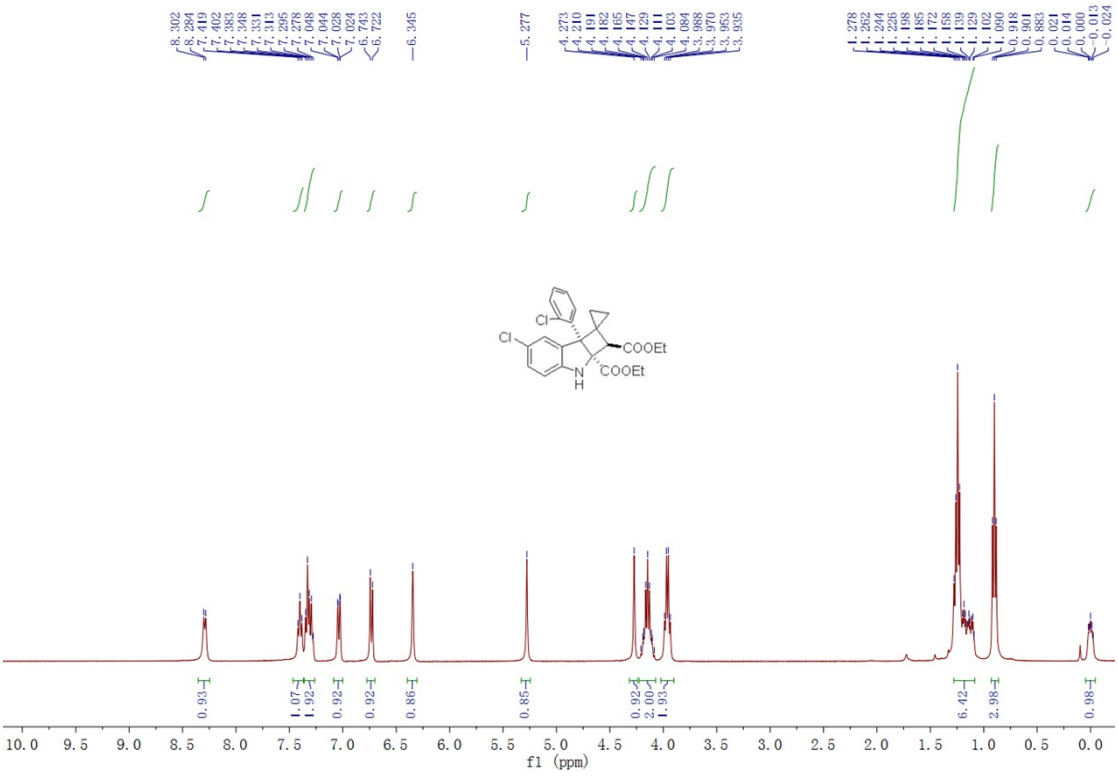


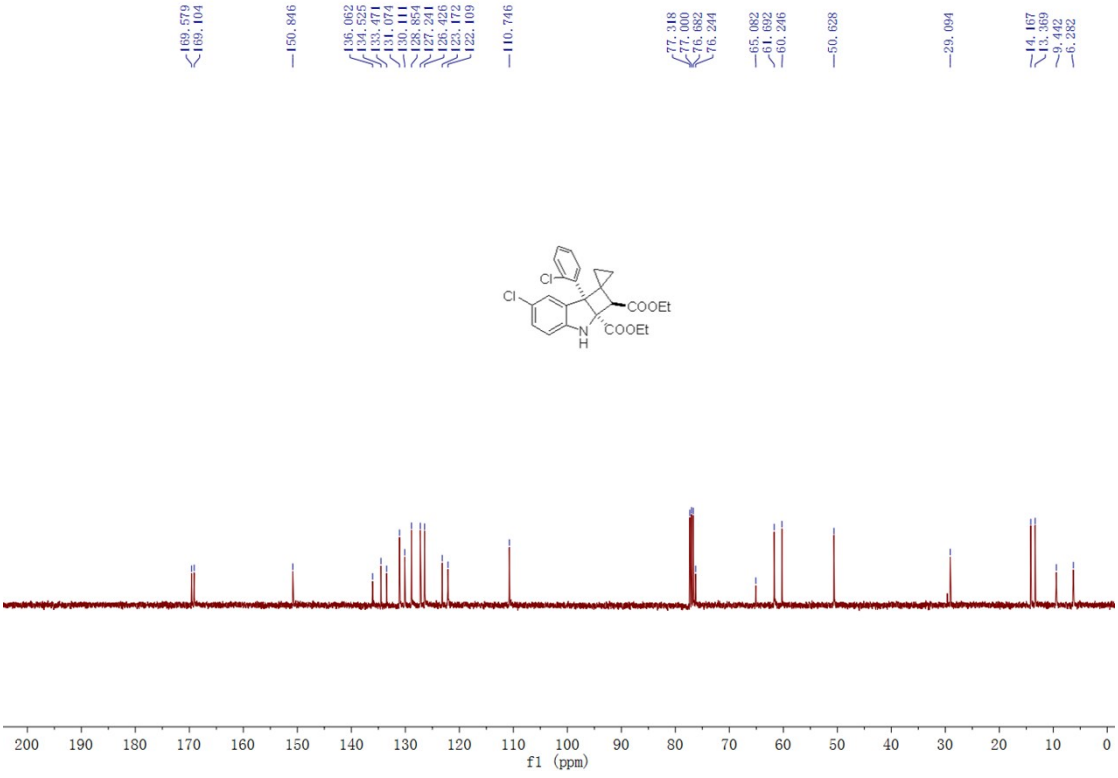


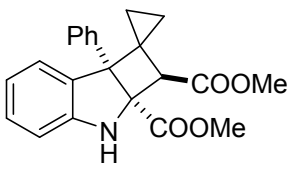


diethyl-6-chloro-7*b*-(2-chlorophenyl)-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3s

0.3 mmol scale, a white solid, 79% yield (108.8 mg). M.p.: 147-149 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ -0.02-0.03 (m, 1H), 0.90 (t, *J* = 7.2 Hz, 3H), 1.09-1.28 (m, 6H), 3.96 (q, *J* = 7.2 Hz, 2H), 4.08-4.21 (m, 2H), 4.27 (s, 1H), 5.23 (s, 1H), 6.35 (s, 1H), 6.73 (d, *J* = 8.4 Hz, 1H), 7.07 (dd, *J* = 1.6 Hz, 8.4 Hz, 1H), 7.27-7.35 (m, 2H), 7.40 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 8.29 (d, *J* = 7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 6.3, 9.4, 13.4, 14.2, 29.1, 50.6, 60.2, 61.7, 65.1, 76.2, 110.7, 122.1, 123.2, 126.4, 127.2, 128.9, 130.1, 131.1, 133.5, 134.5, 136.1, 150.8, 169.1, 169.6. IR (neat) ν 3378, 3342, 3059, 2978, 2959, 2931, 2903, 2867, 1731, 1699, 1652, 1603, 1475, 1446, 1369, 1255, 1234, 1208, 1175, 1096, 1066, 1039, 862, 822, 809, 799, 751, 740, 713 cm^{-1}. HRMS (ESI) Calcd. for $C_{24}H_{24}NO_4Cl_2^{+1}(M+H)^+$ requires: 460.1077, found: 460.1072.



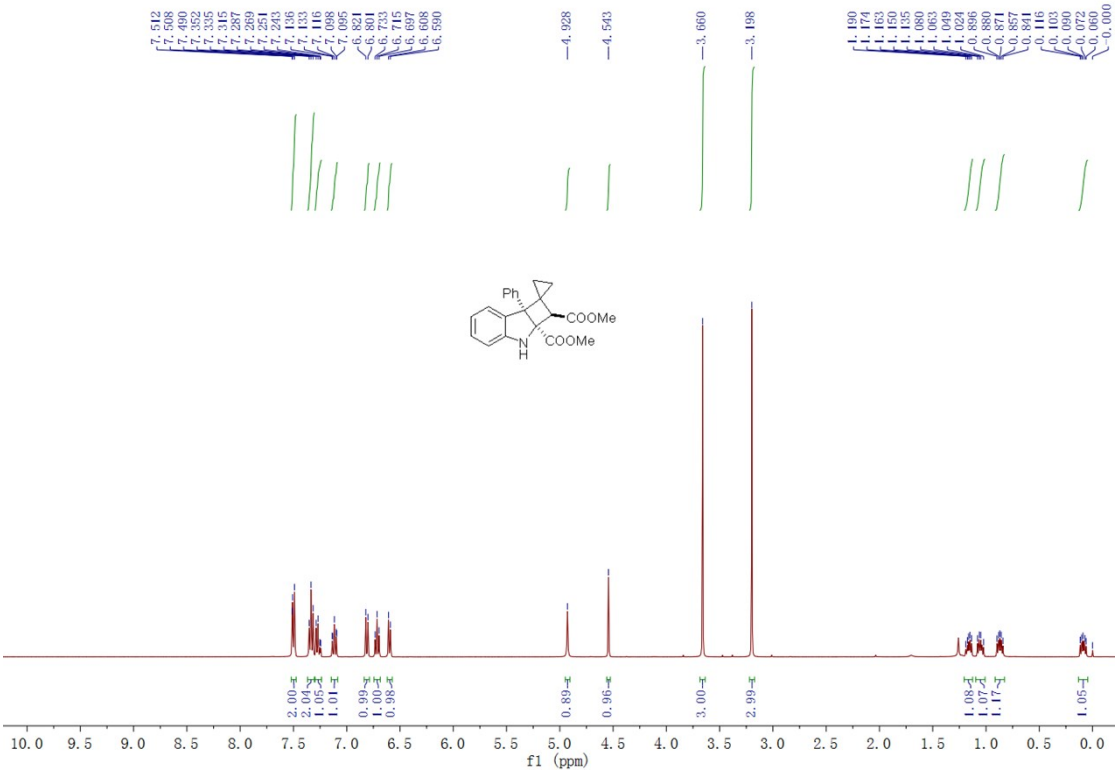


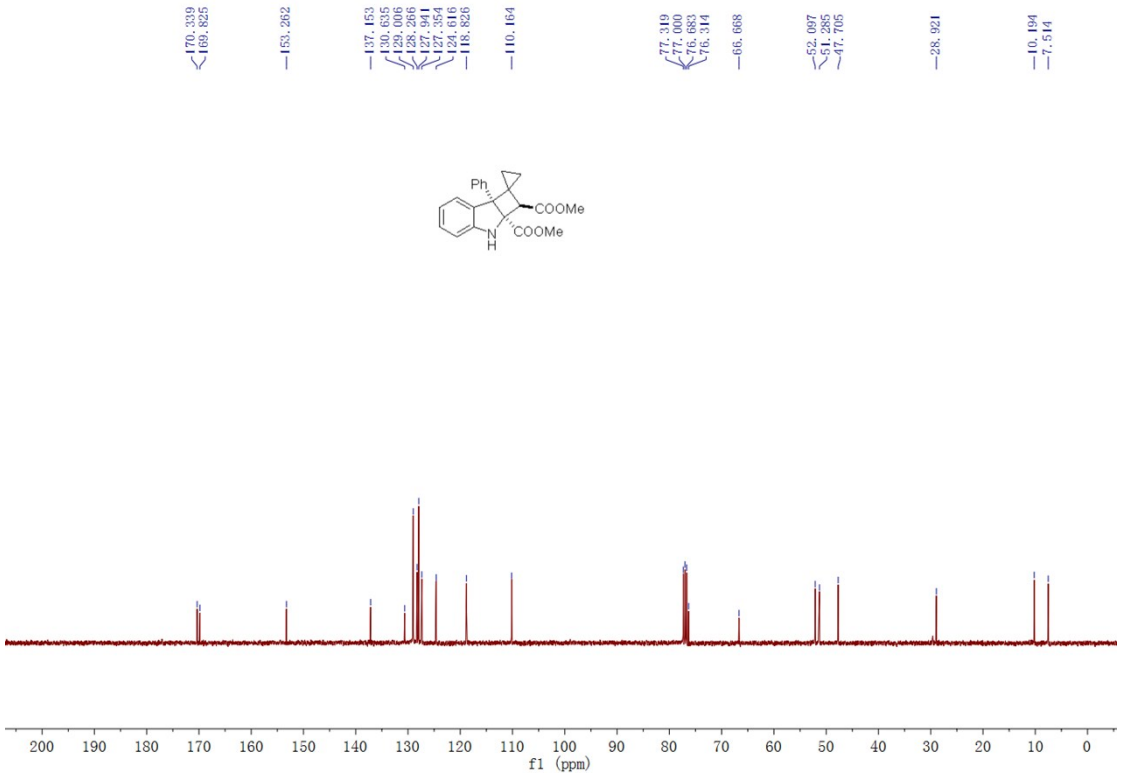


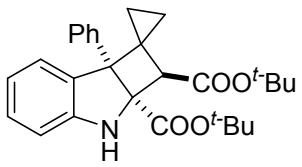
dimethyl-7*b*-phenyl-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-

dicarboxylate 3t

0.3 mmol scale, a white solid, 93% yield (101.7 mg). M.p.: 115-116 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.06-0.12 (m, 1H), 0.84-0.90 (m, 1H), 1.02-1.08 (m, 1H), 1.13-1.19 (m, 1H), 3.20 (s, 3H), 3.66 (s, 3H), 4.54 (s, 1H), 4.93 (s, 1H), 6.60 (d, J = 7.2 Hz, 1H), 6.72 (dd, J = 7.2 Hz, 7.2 Hz, 1H), 6.81 (d, J = 8.0 Hz, 1H), 7.01-7.14 (m, 1H), 7.24-7.29 (m, 1H), 7.31-7.36 (m, 2H), 7.49-7.52 (m, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.5, 10.2, 28.9, 47.7, 51.3, 52.1, 66.7, 76.3, 110.2, 118.8, 124.6, 127.4, 127.9, 128.3, 129.0, 130.6, 137.2, 153.3, 169.8, 170.3. IR (neat) ν 3375, 3358, 3081, 3056, 3034, 2989, 2953, 2920, 2842, 1737, 1716, 1605, 1485, 1469, 1435, 1357, 1318, 1285, 1263, 1197, 1185,1158, 1063, 1040, 1021, 963, 871, 812, 750, 738, 717, 701 cm^{-1}. HRMS (ESI) Calcd. for $C_{22}H_{22}NO_4^{+1}$(M+H)$^+$ requires: 364.1543, found: 364.1541.

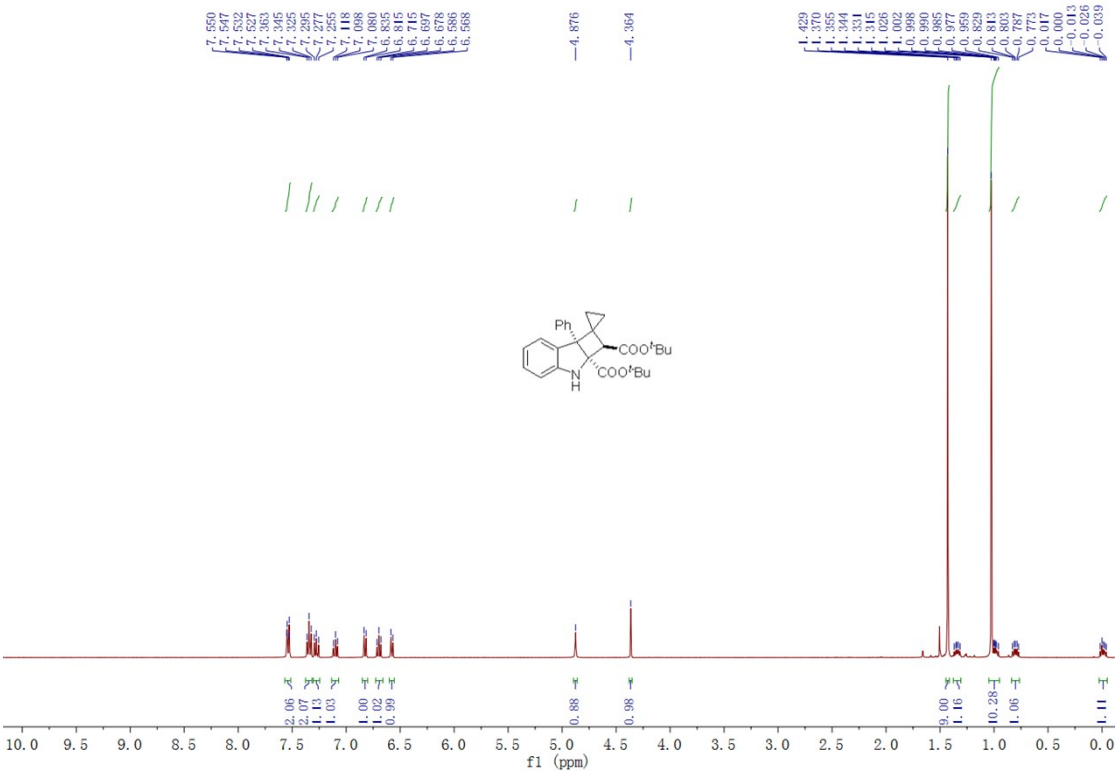


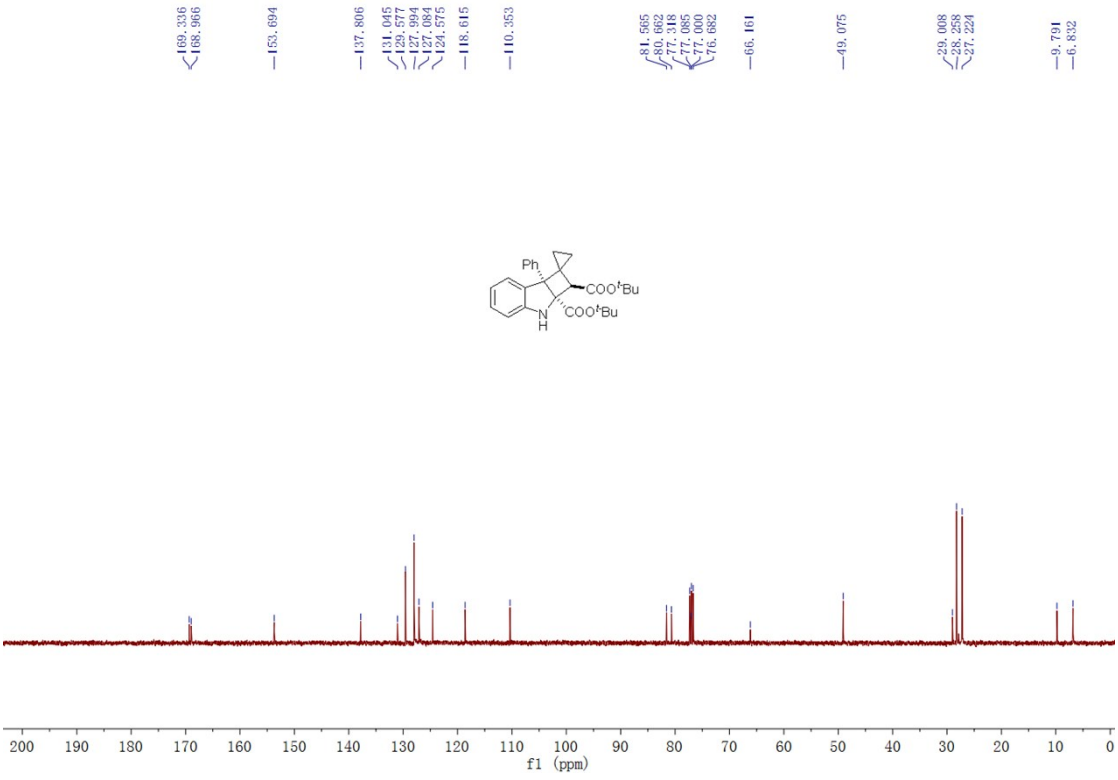


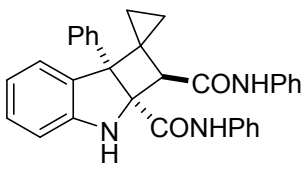


di-tert-butyl-7*b*-phenyl-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3u

0.3 mmol scale, a white solid, 64% yield (85.9 mg). M.p.: 150-153 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ -0.04-0.02 (m, 1H), 0.77-0.83 (m, 1H), 0.95-1.01 (m, 1H), 1.03 (s, 9H), 1.31-1.37 (m, 1H), 1.43 (s, 9H), 4.36 (s, 1H), 4.88 (s, 1H), 6.58 (d, J = 8.0 Hz, 1H), 6.70 (dd, J = 7.6 Hz, 7.6 Hz, 1H), 6.83 (d, J = 8.0 Hz, 1H), 7.08-7.12 (m, 1H), 7.25-7.30 (m, 1H), 7.32-7.37 (m, 2H), 7.52-7.55 (m, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 6.8, 9.8, 27.2, 28.3, 29.0, 49.1, 66.2, 77.1, 80.7, 81.6, 110.4, 118.6, 124.6, 127.1, 128.0, 129.6, 131.0, 137.8, 153.7, 169.0, 169.3. IR (neat) ν 3368, 3084, 3053, 3003, 2979, 2932, 2914, 2900, 2873, 1729, 1605, 1483, 1465, 1392, 1367, 1323, 1284, 1260, 1216, 1202, 1157, 1096, 1070, 1027, 969, 947, 845, 813, 744, 710 cm^{-1}. HRMS (ESI) Calcd. for $C_{28}H_{34}NO_4^{+1}(M+H)^+$ requires: 448.2482, found: 448.2479.



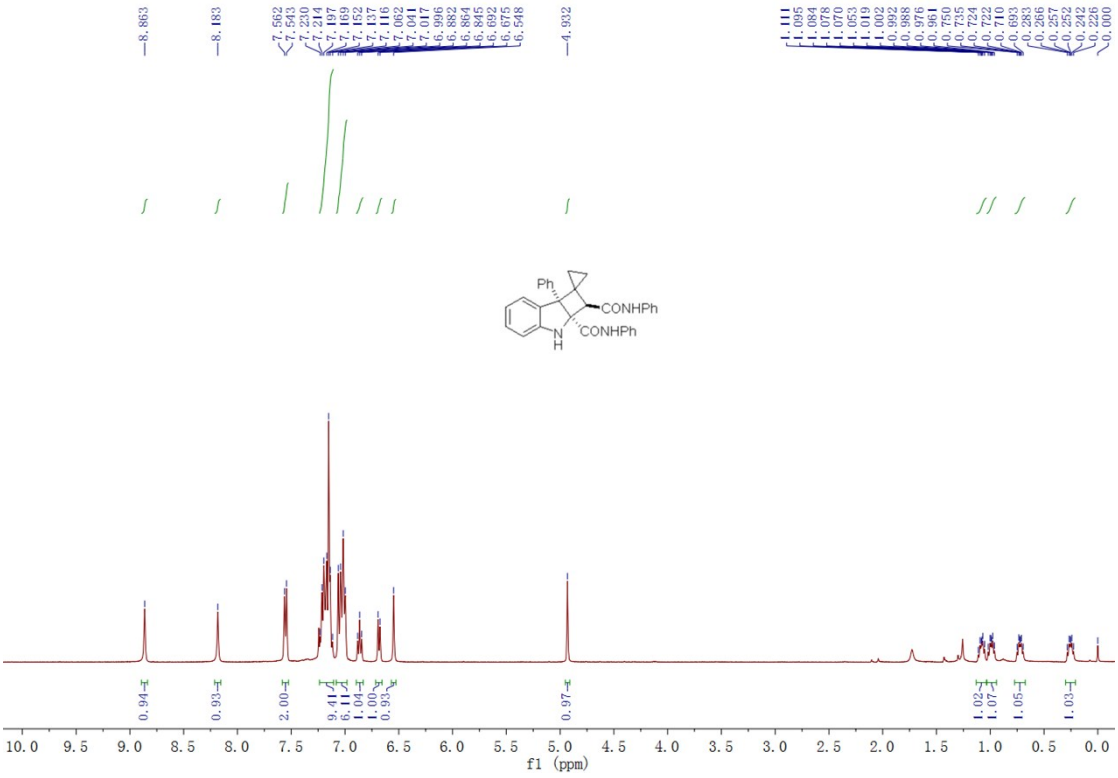


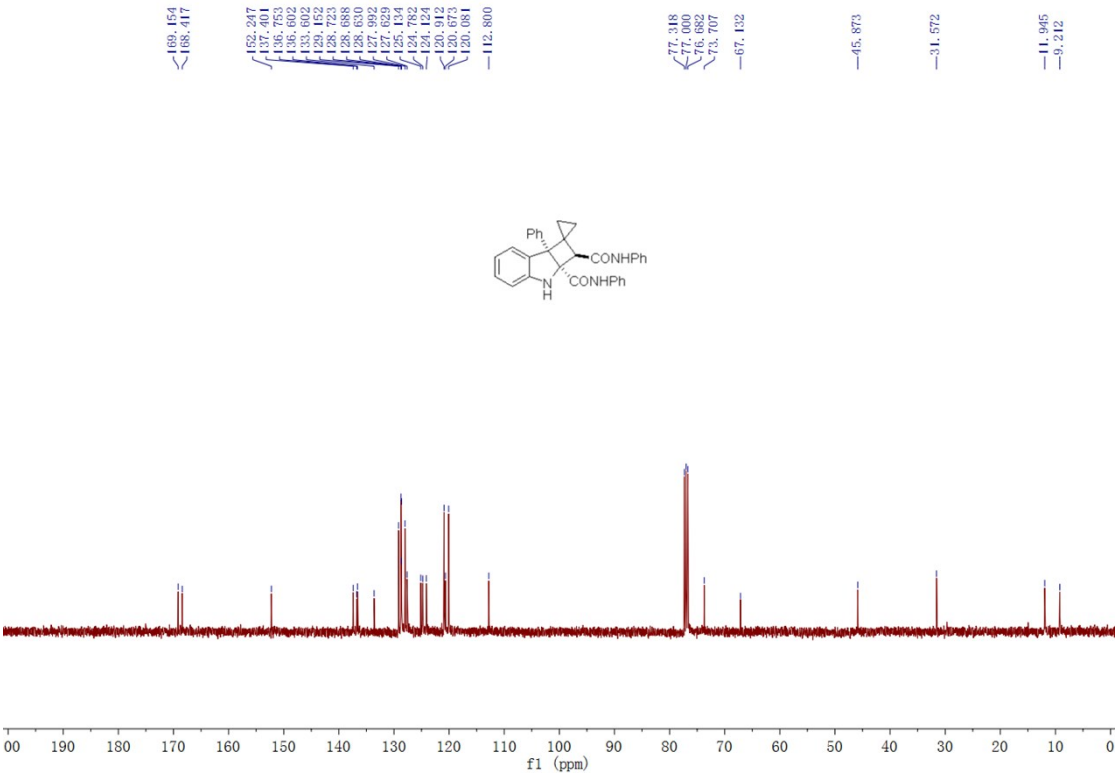


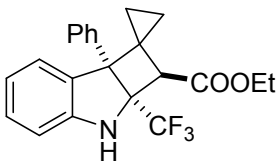
N^2,N^{2a},7*b*-triphenyl-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-

dicarboxamide 3v

0.3 mmol scale, a white solid, 35% yield (50.9 mg). M.p.: 209-212 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.22-0.29 (m, 1H), 0.69-0.75 (m, 1H), 0.96-1.02 (m, 1H), 1.05-1.12 (m, 1H), 4.93 (s, 1H), 6.56 (s, 1H), 6.68 (d, *J* = 6.8 Hz, 1H), 6.86 (dd, *J* = 7.2 Hz, 7.2 Hz, 1H), 6.99-7.07 (m, 6H), 7.11-7.23 (m, 9H), 7.55 (d, *J* = 7.6 Hz, 2H), 8.18 (s, 1H), 8.86 (s, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 9.2, 11.9, 31.6, 45.9, 67.1, 73.7, 112.8, 120.1, 120.7, 120.9, 124.1, 124.8, 125.1, 127.6, 128.0, 128.6, 128.69, 128.72, 129.2, 133.6, 136.6, 136.8, 137.4, 152.2, 168.4, 169.2. IR (neat) ν 3307, 3258, 3197, 3142, 3060, 3022, 2998, 2956, 2923, 2859, 1655, 1599, 1544, 1525, 1498, 1483, 1466, 1442, 1374, 1309, 1261, 1186, 1152, 1103, 1080, 1018, 976, 963, 918, 898, 878, 832, 799, 749, 690 cm^{-1}. HRMS (ESI) Calcd. for $C_{32}H_{28}N_3O_2^{+1}$(M+H)$^{+}$ requires: 486.2176, found: 486.2174.

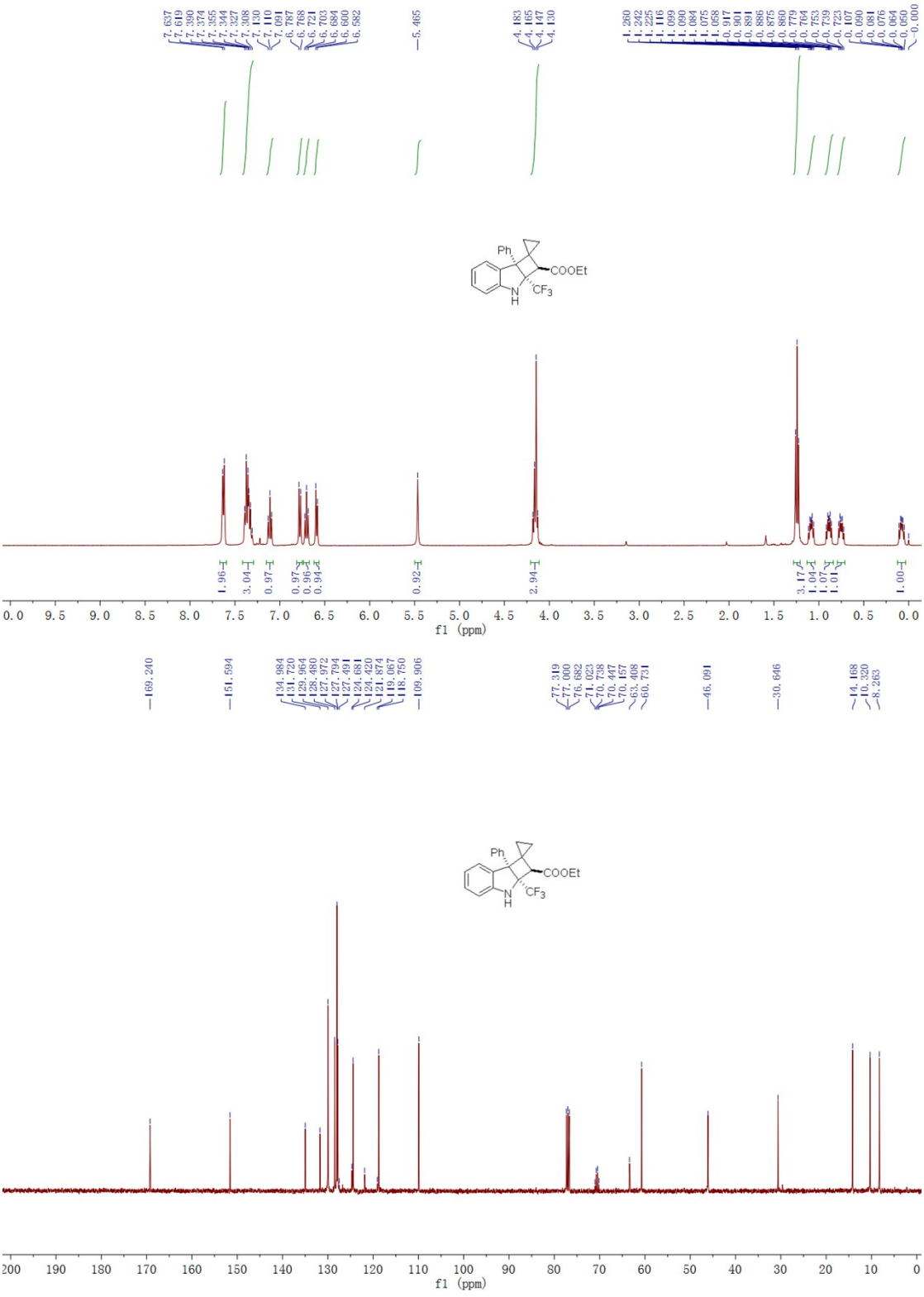






ethyl-7*b*-phenyl-2*a*-(trifluoromethyl)-2,2*a*,3,7*b*-tetrahydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2-carboxylate 3y

0.3 mmol scale, a white solid, 93% yield (108.0 mg). M.p.: 120-123 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.05-0.11 (m, 1H), 0.72-0.78 (m, 1H), 0.86-0.92 (m, 1H), 1.05-1.12 (m, 1H), 1.24 (t, *J* = 7.2 Hz, 3H), 4.15 (s, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 5.47 (s, 1H), 6.59 (d, *J* = 7.2 Hz, 1H), 6.70 (dd, *J* = 7.2 Hz, 7.2 Hz, 1H), 6.78 (d, *J* = 7.6 Hz, 1H), 7.11 (d, *J* = 7.6 Hz, 1H), 7.30-7.39 (m, 3H), 7.63 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 8.3, 10.3, 14.2, 30.6, 46.1, 60.7, 63.4, 70.6 (q, *J* = 29.0 Hz), 109.9, 118.8, 123.3 (q, *J* = 280.7 Hz), 124.4, 127.8, 128.0, 128.5, 130.0, 131.7, 135.0, 151.6, 169.2. ^{19}F NMR ($CDCl_3$, $CFCl_3$, 376 MHz) δ -76.5. IR (neat) ν 3402, 3328, 3089, 3059, 3034, 2998, 2976, 2934, 2920, 2853, 1719, 1610, 1497, 1484, 1466, 1449, 1390, 1374, 1328, 1301, 1267, 1206, 1178, 1143, 1093, 1038, 1023, 960, 949, 934, 921, 896, 860, 818, 795, 759, 743, 716, 702, 661 cm^{-1}. HRMS (ESI) Calcd. for $C_{22}H_{21}NO_2F_3^{+1}(M+H)^+$ requires: 388.1519, found: 388.1516.


7.637
7.619
7.390
7.374
7.355
7.344
7.327
7.308
7.110
7.091
6.787
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6.703
6.684
6.600
6.582
5.465
4.183
4.165
4.147
4.130
1.260
1.242
1.225
1.116
1.099
1.090
1.084
1.075
1.058
0.917
0.901
0.891
0.886
0.875
0.860
0.779
0.764
0.753
0.739
0.723
0.107
0.090
0.084
0.075
0.064
0.050
0.000
Ph
COOEt
N
H
CF3
1.96
3.04
0.97
0.97
0.96
0.94
0.92
2.94
3.17
1.04
1.07
1.01
1.00
f1 (ppm)
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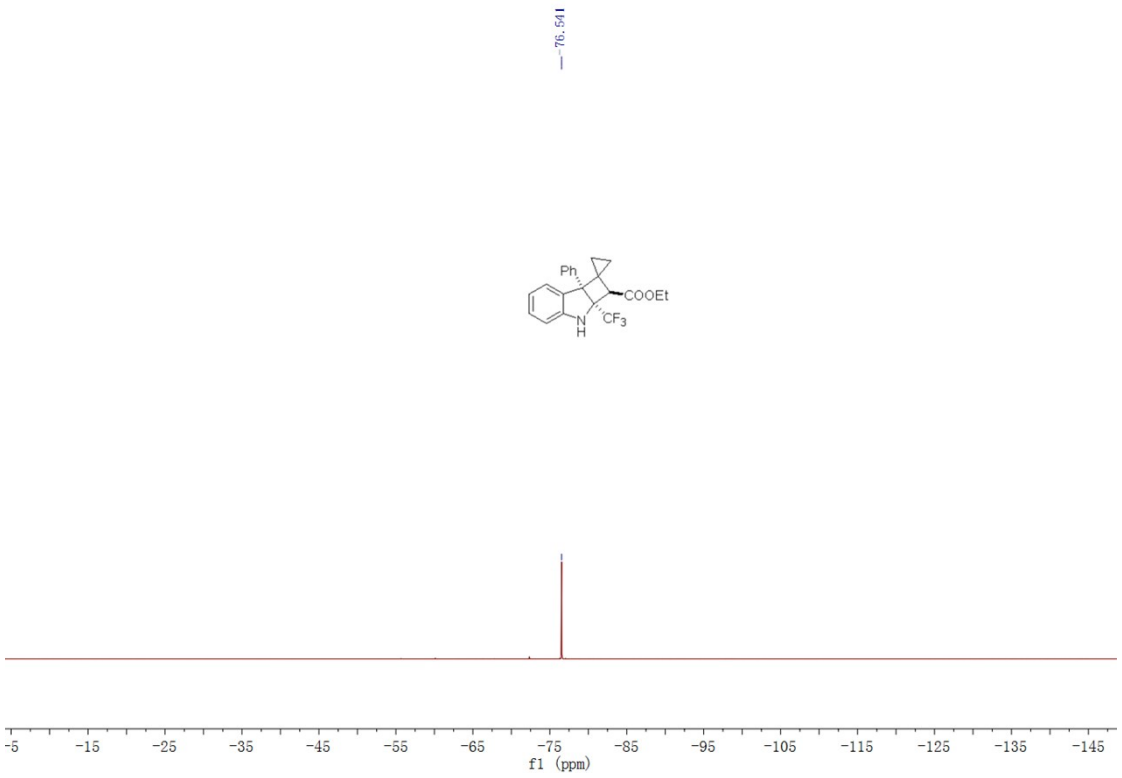
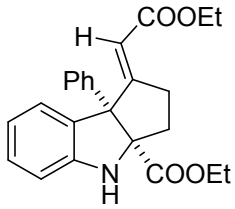
Ph
COOEt
N
H
CF3
f1 (ppm)



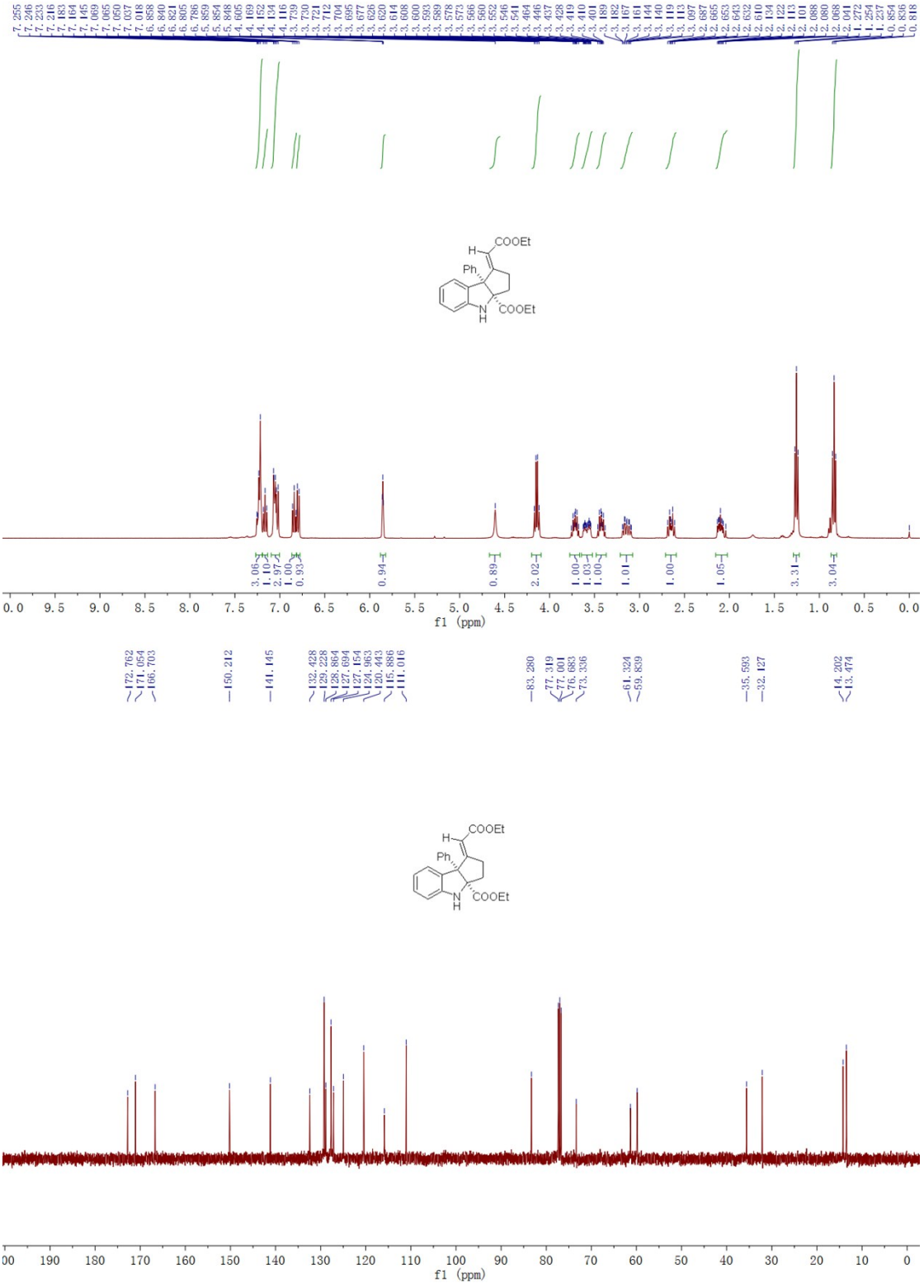
7. Characterization and spectra charts for 4.

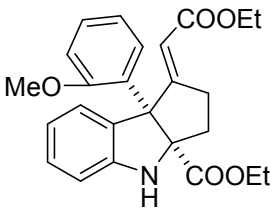


ethyl-(*E*)-1-(2-ethoxy-2-oxoethylidene)-8*b*-phenyl-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3a(1*H*)-carboxylate 4a

0.3 mmol scale, a light yellow gem, 75% yield (87.9 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.84 (t, *J* = 7.2 Hz, 3H), 1.25 (t, *J* = 7.2 Hz, 3H), 2.04-2.14 (m, 1H), 2.61-2.69 (m, 1H), 3.09-3.19 (m, 1H), 3.38-3.46 (m, 1H), 3.54-3.63 (m, 1H), 3.67-3.76 (m, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 4.61 (s, 1H), 5.85 (t, *J* = 2.4 Hz, 1H), 6.80 (d, *J* = 7.6 Hz, 1H), 6.84 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 7.01-7.07 (m, 3H), 7.16 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 7.21-7.26 (m, 3H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.4, 14.2, 32.1, 35.6, 59.8, 61.3, 73.3, 83.3, 111.0, 115.9, 120.4, 125.0, 127.2, 127.7, 128.9, 129.2, 132.4, 141.1, 150.2, 166.7, 171.1, 172.8. IR (neat) ν 3362, 3086, 3053, 2978, 2955, 2928, 2900, 2870, 2850, 1709, 1647, 1603, 1483, 1466, 1446, 1391, 1368, 1346, 1255, 1231, 1205, 1163, 1097, 1069, 1037, 931, 862, 795, 747, 699 cm^{-1}. HRMS (ESI) Calcd. for

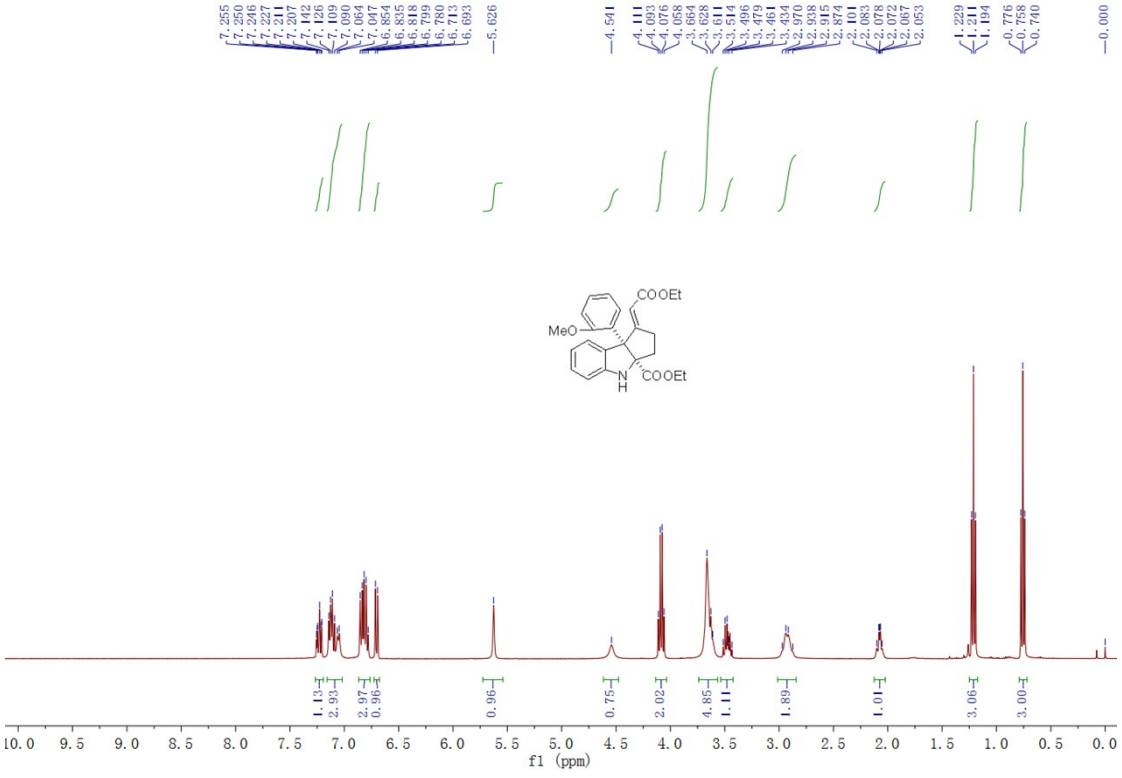
$C_{24}H_{26}NO_4^{+1}(M+H)^+$ requires: 392.1856, found: 392.1856.

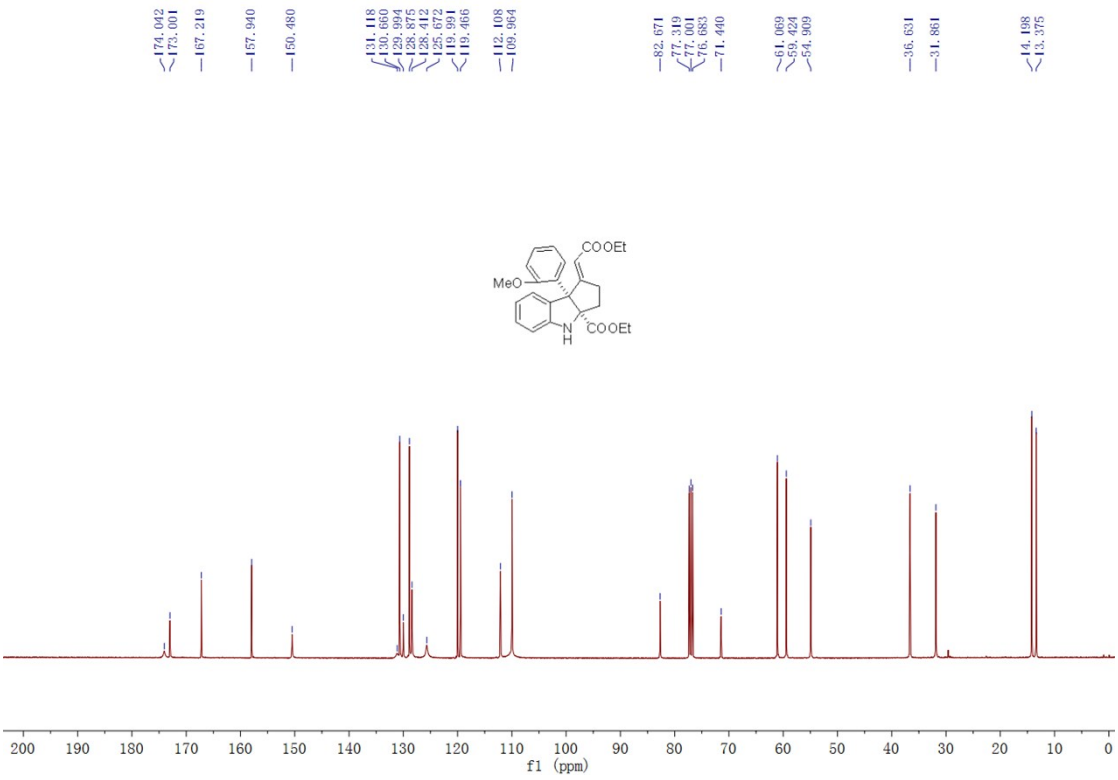


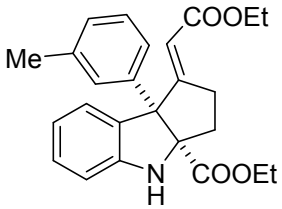


ethyl-(*E*)-1-(2-ethoxy-2-oxoethylidene)-8*b*-(2-methoxyphenyl)-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4b

0.3 mmol scale, a white solid, 90% yield (113.7 mg). M.p.: 50-52 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.76 (t, *J* = 7.2 Hz, 3H), 1.21 (t, *J* = 7.2 Hz, 3H), 2.05-2.11 (m, 1H), 2.87-2.97 (m, 2H), 3.43-3.52 (m, 1H), 3.61-3.67 (m, 5H), 4.08 (q, *J* = 7.2 Hz, 2H), 4.54 (s, 1H), 5.63 (s, 1H), 6.70 (d, *J* = 8.0 Hz, 1H), 6.78-6.86 (m, 3H), 7.04-7.15 (m, 3H), 7.20-7.26 (m, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.4, 14.2, 31.9, 36.6, 54.9, 59.4, 61.1, 71.4, 82.7, 110.0, 112.1, 119.5, 120.0, 125.7, 128.4, 128.9, 130.0, 130.7, 131.1, 150.5, 157.9, 167.2, 173.0, 174.0. IR (neat) ν 3365, 3053, 2979, 2936, 2898, 2873, 2834, 1706, 1646, 1599, 1486, 1466, 1390, 1368, 1346, 1282, 1248, 1227, 1203, 1161, 1115, 1069, 1023, 930, 898, 857, 791, 748 cm^{-1}. HRMS (ESI) Calcd. for $C_{25}H_{28}NO_5^{+1}(M+H)^+$ requires: 422.1962, found: 422.1960.

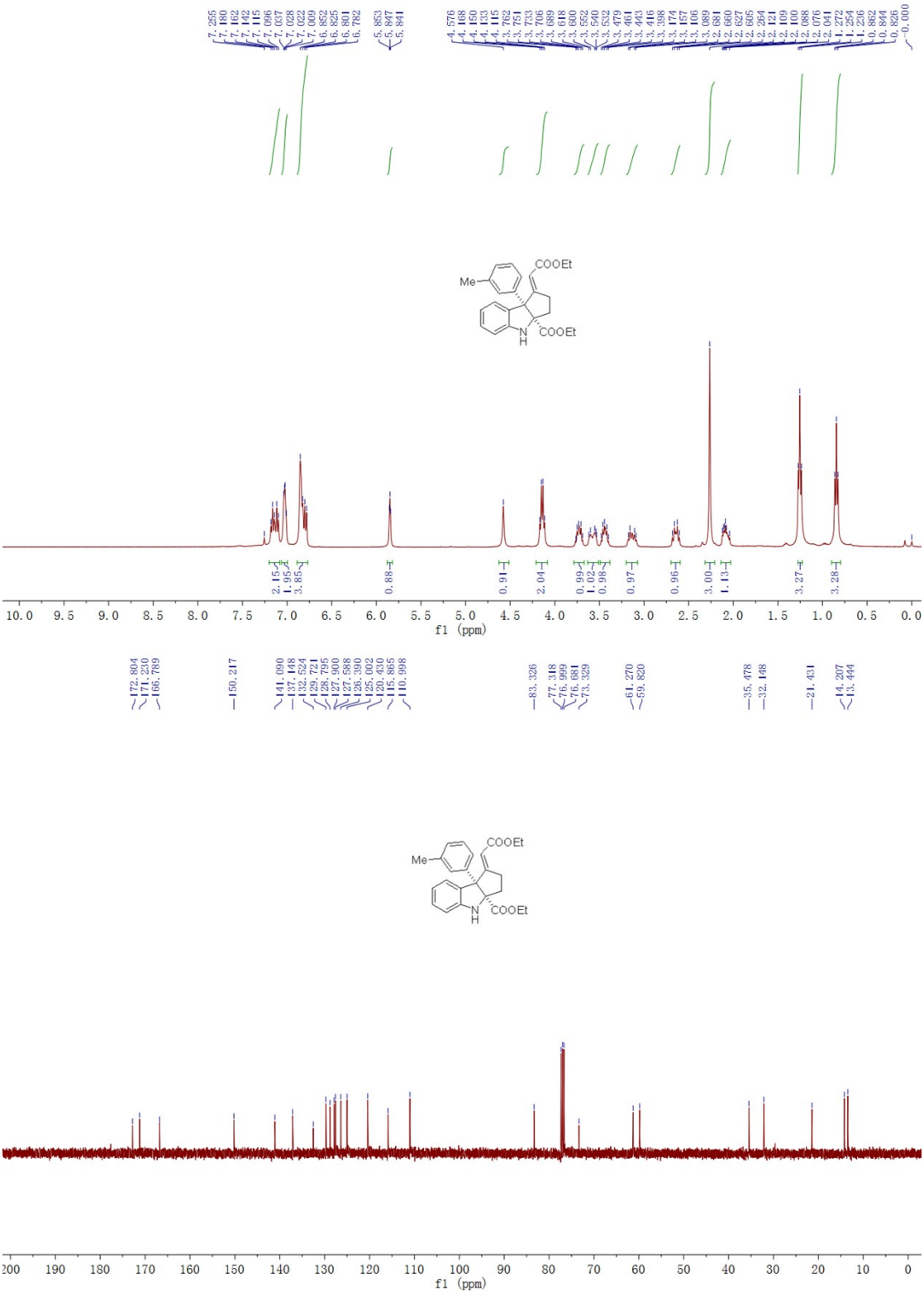






ethyl-(*E*)-1-(2-ethoxy-2-oxoethylidene)-8*b*-(*m*-tolyl)-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4c

0.3 mmol scale, a faint yellow oil, 66% yield (79.6 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.84 (t, *J* = 7.2 Hz, 3H), 1.25 (t, *J* = 7.2 Hz, 3H), 2.04-2.12 (m, 1H), 2.26 (s, 3H), 2.60-2.69 (m, 1H), 3.08-3.17 (m, 1H), 3.39-3.48 (m, 1H), 3.53-3.62 (m, 1H), 3.68-3.77 (m, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 4.58 (s, 1H), 5.85 (t, *J* = 2.4 Hz, 1H), 6.78-6.86 (m, 4H), 7.00-7.04 (m, 2H), 7.09-7.18 (m, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.4, 14.2, 21.4, 32.1, 35.5, 59.8, 61.3, 73.3, 83.3, 111.0, 115.9, 120.4, 125.0, 126.4, 127.6, 127.9, 128.8, 129.7, 132.5, 137.1, 141.1, 150.2, 166.8, 171.2, 172.8. IR (neat) ν 3359, 3053, 3036, 2978, 2928, 2898, 2870, 1709, 1647, 1603, 1484, 1466, 1391, 1368, 1345, 1259, 1210, 1188, 1158, 1115, 1095, 1069, 1039, 991, 864, 780, 722, 701 cm^{-1}. HRMS (ESI) Calcd. for $C_{25}H_{28}NO_4^{+1}(M+H)^+$ requires: 406.2013, found: 406.2015.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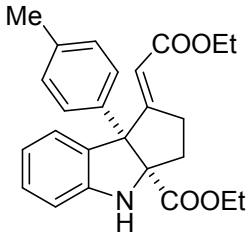
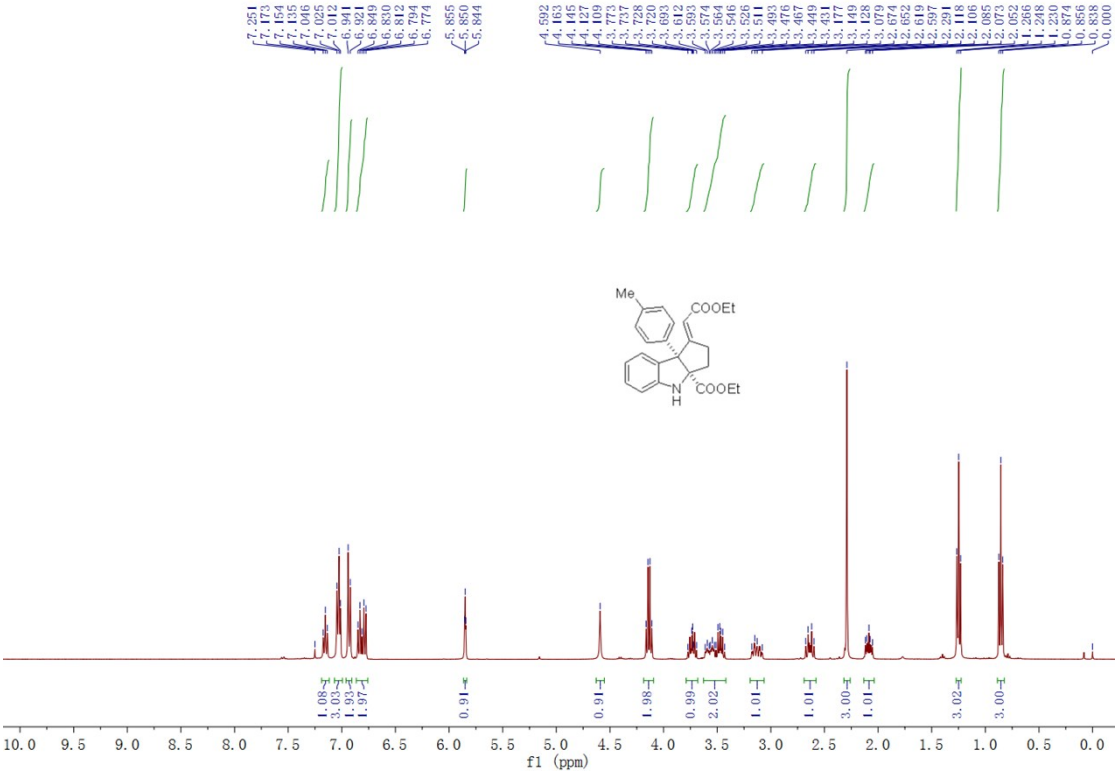
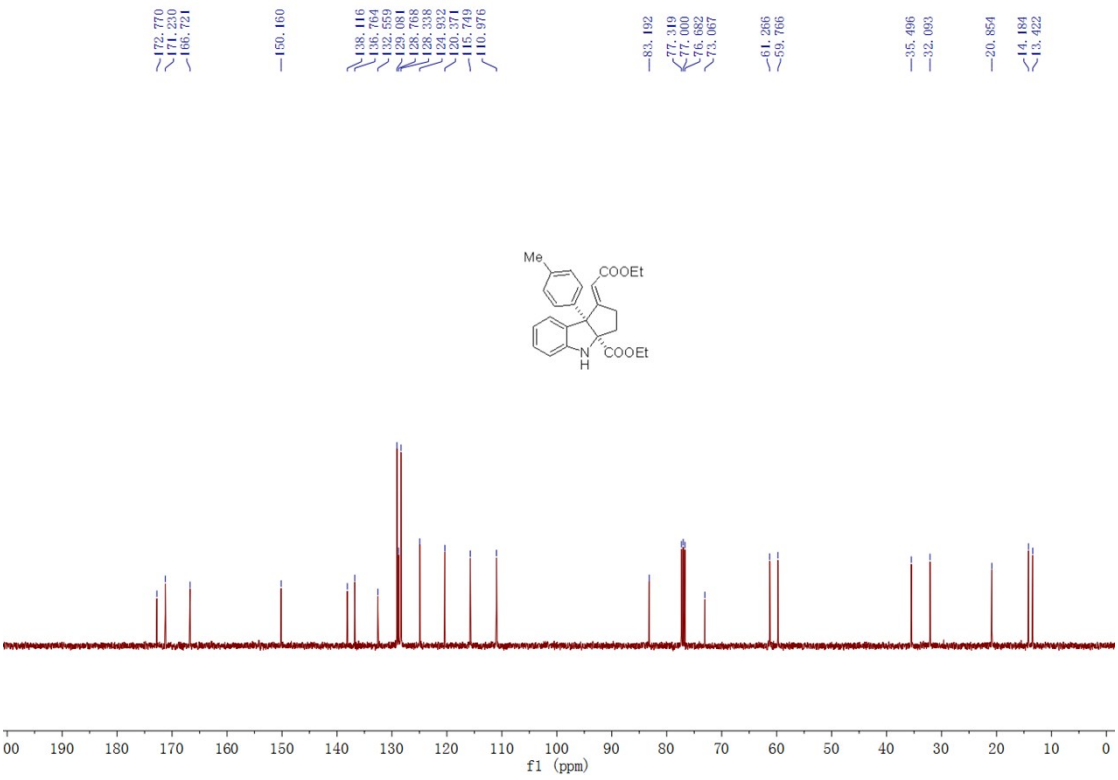
7.180
7.162
7.142
7.115
7.096
7.037
7.028
7.022
7.009
6.852
6.825
6.801
6.782
5.853
5.847
5.841
4.576
4.168
4.150
4.133
4.115
3.762
3.751
3.733
3.706
3.689
3.618
3.600
3.552
3.540
3.532
3.479
3.461
3.443
3.416
3.398
3.174
3.157
3.106
3.089
2.681
2.660
2.627
2.605
2.264
2.121
2.109
2.100
2.088
2.076
2.041
1.272
1.254
1.236
0.862
0.844
0.826
0.000
COOEt
Me
COOEt
N
H
2.15
1.95
3.85
0.88
0.91
2.04
0.99
1.02
0.98
0.97
0.96
3.00
1.13
3.27
3.28
f1 (ppm)
172.804
171.230
166.789
150.217
141.090
137.148
132.524
129.721
128.795
127.900
127.588
126.390
125.002
120.430
115.865
110.998
83.326
77.318
76.999
76.681
73.329
61.270
59.820
35.478
32.148
21.431
14.207
13.444
COOEt
Me
COOEt
N
H
f1 (ppm)

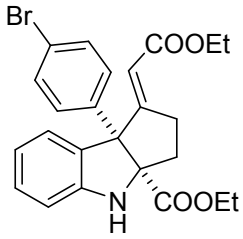


ethyl-(*E*)-1-(2-ethoxy-2-oxoethylidene)-8*b*-(*p*-tolyl)-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4d

0.3 mmol scale, a faint yellow solid, 70% yield (85.3 mg). M.p.: 131-134 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.86 (t, *J* = 7.2 Hz, 3H), 1.25 (t, *J* = 7.2 Hz, 3H), 2.05-2.12 (m, 1H), 2.29 (s, 3H), 2.59-2.68 (m, 1H), 3.07-3.17 (m, 1H), 3.43-3.52 (m, 1H), 3.53-3.62 (m, 1H), 3.69-3.78 (m, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 4.59 (s, 1H), 5.85 (t, *J* = 2.4 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.83 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 6.93 (d, *J* = 8.0 Hz, 2H), 7.01-7.18 (m, 3H), 7.15 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.4, 14.2, 20.9, 32.1, 35.5, 59.8, 61.3, 73.1, 83.2, 111.0, 115.7, 120.4, 124.9, 128.3, 128.8, 129.1, 132.6, 136.8, 138.1, 150.2, 166.7, 171.2, 172.8. IR (neat) ν 3378, 3321, 3053, 3025, 2953, 2939, 2923, 2900, 2867, 1722, 1698, 1648, 1603, 1484, 1470, 1370, 1346, 1285, 1274, 1258, 1236, 1217, 1185, 1165, 1150, 1113, 1070, 1041, 1022, 1011, 861, 811, 792, 757, 745, 740, 723, 666, 655 cm^{-1}. HRMS (ESI) Calcd. for $C_{25}H_{28}NO_4^{+1}$(M+H)$^+$ requires: 406.2013, found: 406.2014.

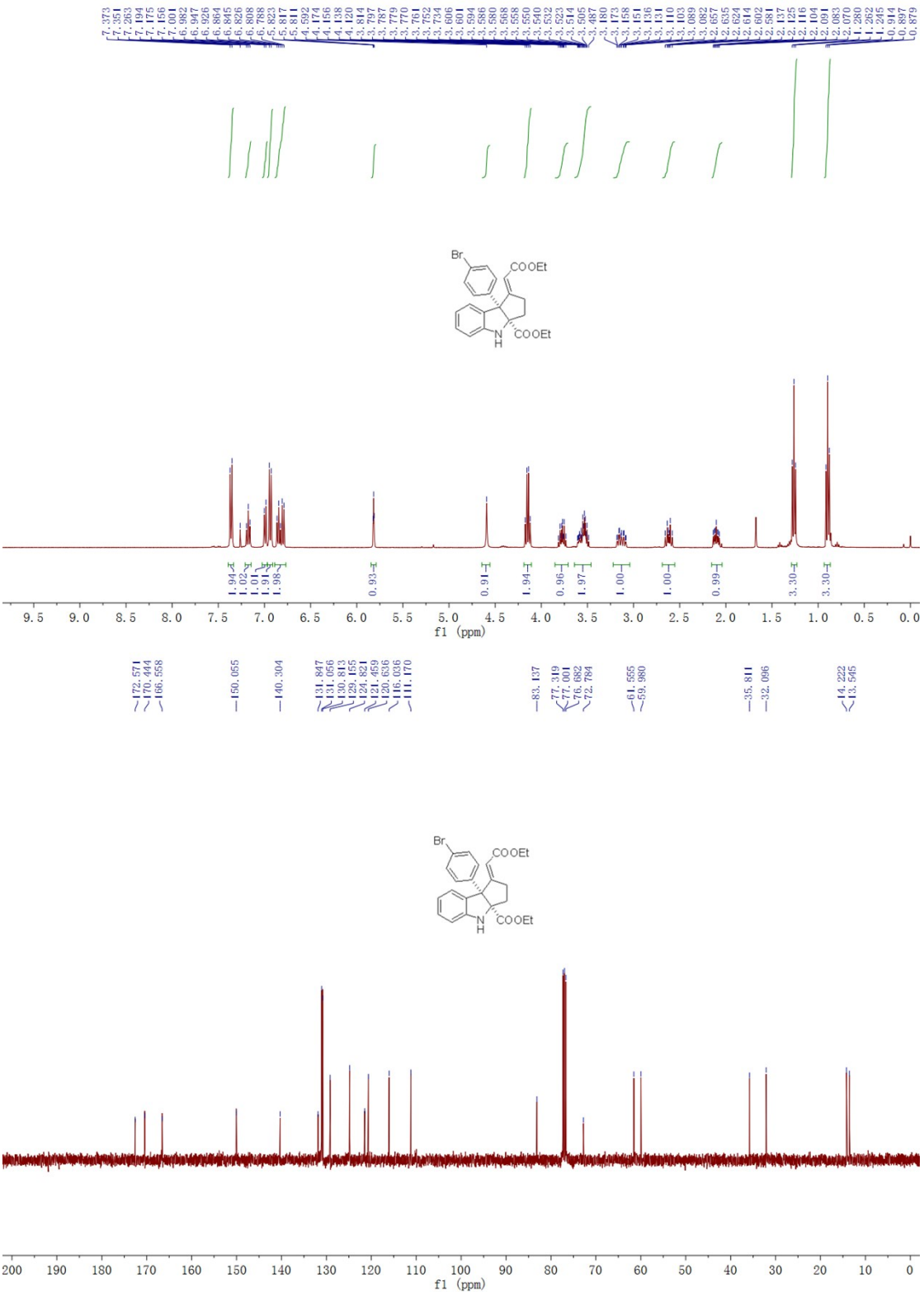


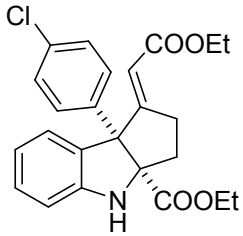




ethyl-(*E*)-8*b*-(4-bromophenyl)-1-(2-ethoxy-2-oxoethylidene)-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4e

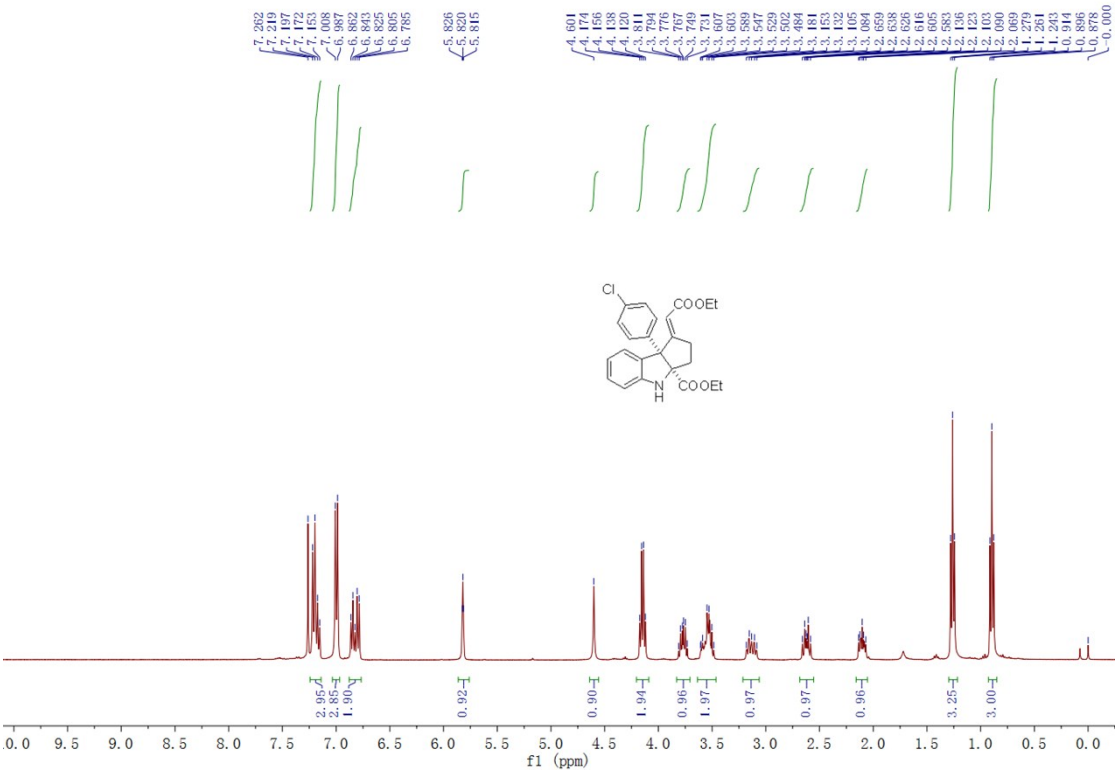
0.3 mmol scale, a yellow solid, 66% yield (92.9 mg). M.p.: 106-108 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.90 (t, *J* = 7.2 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 2.07-2.14 (m, 1H), 2.58-2.66 (m, 1H), 3.08-3.18 (m, 1H), 3.48-3.61 (m, 2H), 3.73-3.82 (m, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 4.59 (s, 1H), 5.82 (t, *J* = 2.4 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.85 (dd, *J* = 8.0 Hz, 8.0 Hz, 1H), 6.93 (d, *J* = 8.0 Hz, 2H), 6.99 (d, *J* = 8.0 Hz, 1H), 7.18 (dd, *J* = 8.0 Hz, 8.0 Hz, 1H), 7.36 (d, *J* = 8.0 Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.5, 14.2, 32.1, 35.8, 60.0, 61.6, 72.8, 83.1, 111.2, 116.0, 120.6, 121.5, 124.8, 129.2, 130.8, 131.1, 131.8, 140.3, 150.1, 166.6, 170.4, 172.6. IR (neat) ν 3320, 2978, 2960, 2922, 2870, 2850, 1723, 1698, 1650, 1601, 1483, 1468, 1392, 1369, 1344, 1312, 1285, 1257, 1165, 1095, 1070, 1037, 1011, 859, 815, 739, 721, 712, 702, 662 cm^{-1}. HRMS (ESI) Calcd. for $C_{24}H_{25}NO_4Br^{+1}$(M+H)$^+$ requires: 470.0961, found: 470.0954.

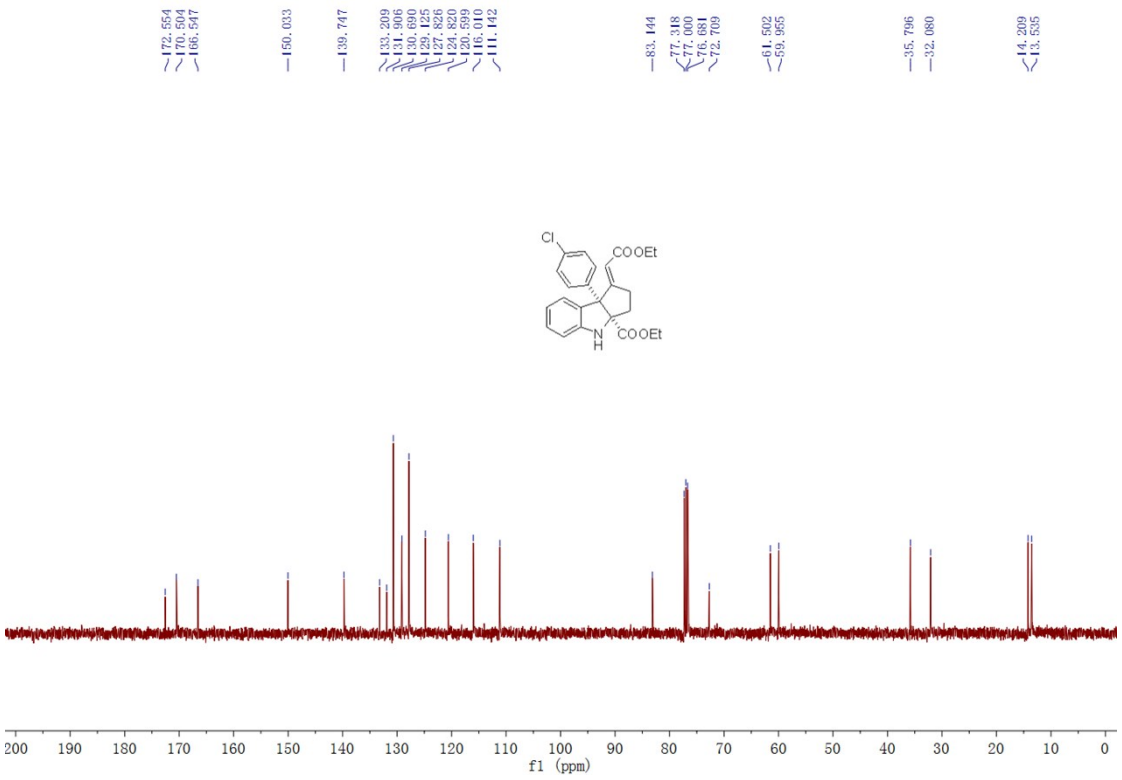

Br
COOEt
N
H
COOEt
f1 (ppm)
f1 (ppm)

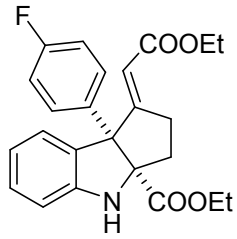


ethyl-(*E*)-8*b*-(4-chlorophenyl)-1-(2-ethoxy-2-oxoethylidene)-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4f

0.3 mmol scale, a yellow solid, 70% yield (89.8 mg). M.p.: 104-106 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.90 (t, *J* = 7.2 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 2.06-2.14 (m, 1H), 2.58-2.66 (m, 1H), 3.08-3.18 (m, 1H), 3.48-3.61 (m, 2H), 3.73-3.81 (m, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 4.60 (s, 1H), 5.82 (t, *J* = 2.4 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.84 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 6.98-7.01 (m, 3H), 7.15-7.22 (m, 3H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.5, 14.2, 32.1, 35.8, 60.0, 61.5, 72.7, 83.1, 111.1, 116.0, 120.6, 124.8, 127.8, 129.1, 130.7, 131.9, 133.2, 139.7, 150.0, 166.5, 170.5, 172.6. IR (neat) ν 3364, 3050, 2975, 2950, 2931, 2895, 2853, 1721, 1701, 1651, 1603, 1482, 1468, 1367, 1286, 1257, 1232, 1209, 1184, 1162, 1092, 1072, 1037, 1014, 858, 822, 740 cm^{-1}. HRMS (ESI) Calcd. for $C_{24}H_{25}NO_4Cl^{+1}(M+H)^+$ requires: 426.1467, found: 426.1463.



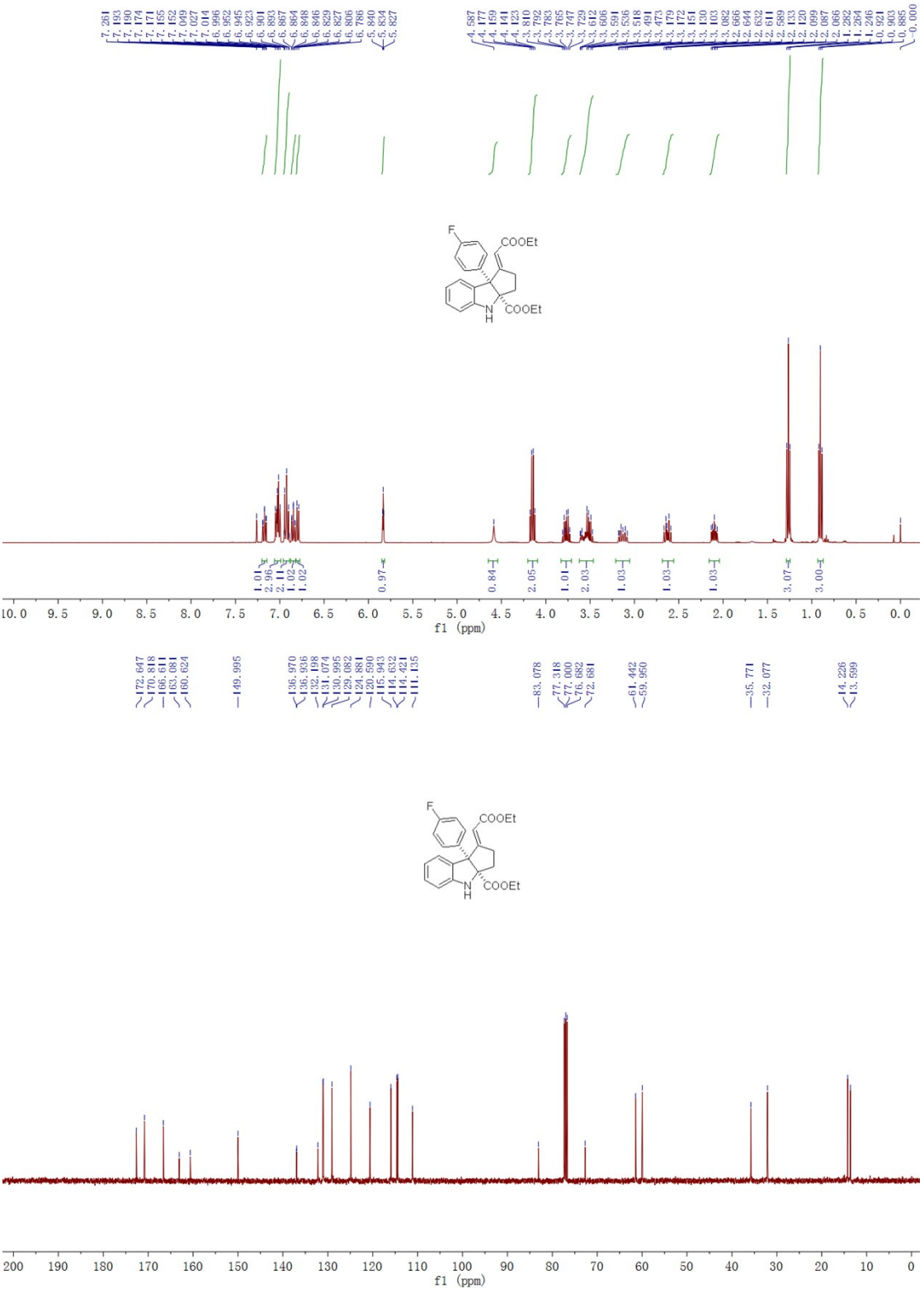


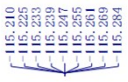


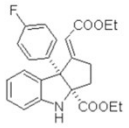
ethyl-(*E*)-1-(2-ethoxy-2-oxoethylidene)-8*b*-(4-fluorophenyl)-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4g

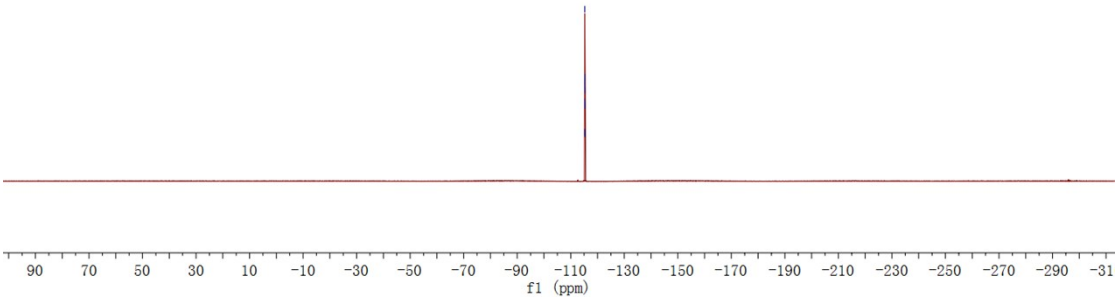
0.3 mmol scale, a yellow solid, 77% yield (94.8 mg). M.p.: 49-52 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.90 (t, *J* = 7.2 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 2.06-2.14 (m, 1H), 2.58-2.67 (m, 1H), 3.08-3.18 (m, 1H), 3.47-3.62 (m, 2H), 3.72-3.81 (m, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 4.59 (s, 1H), 5.83 (t, *J* = 2.4 Hz, 1H), 6.80 (d, *J* = 8.0 Hz, 1H), 6.82-6.87 (m, 1H), 6.89-6.95 (m, 2H), 6.99-7.05 (m, 3H), 7.15-7.20 (m, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.6, 14.2, 32.1, 35.8, 60.0, 61.4, 72.7, 83.1, 111.1, 114.5 (d, *J* = 21.1 Hz), 115.9, 120.6, 124.9, 129.1, 131.0 (d, *J* = 7.9 Hz), 132.2, 137.0 (d, *J* = 3.4 Hz), 150.0, 161.9 (d, *J* = 245.7 Hz), 166.6, 170.8, 172.6. ^{19}F NMR ($CDCl_3$, $CFCl_3$, 376 MHz) δ -115.28- -115.21 (m). IR (neat) ν 3394, 3361, 3050, 2981, 2936, 2903, 2873, 1711, 1650, 1603, 1506, 1482, 1465, 1369, 1256, 1227, 1161, 1116, 1096, 1068, 1039, 1028, 862, 827, 813, 751, 742 cm^{-1}. HRMS (ESI) Calcd. for $C_{24}H_{25}NO_4F^{+1}(M+H)^+$ requires: 410.1762, found:

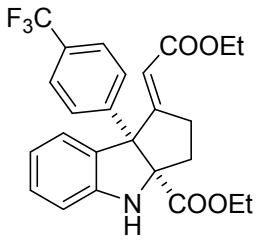
410.1761.







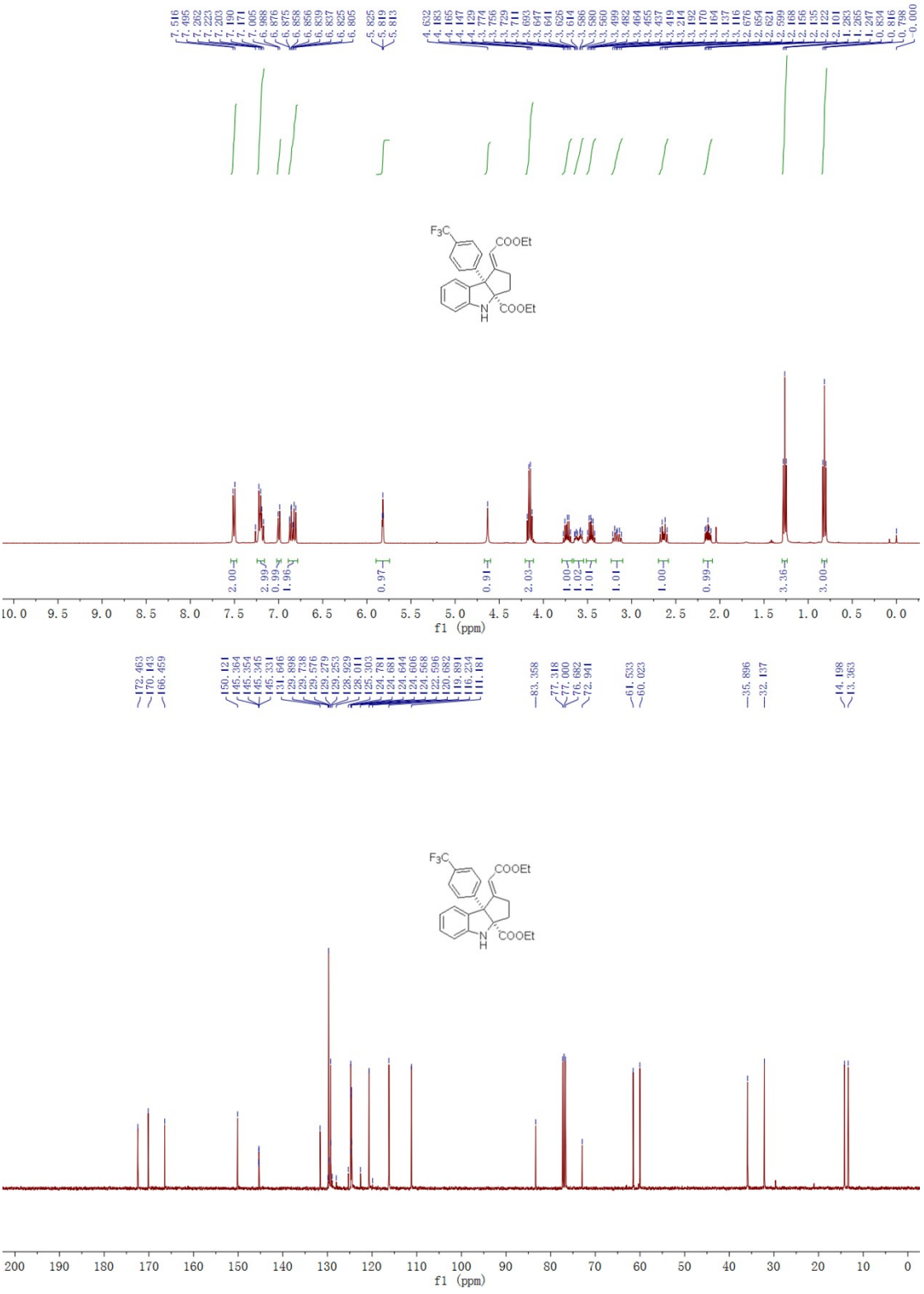


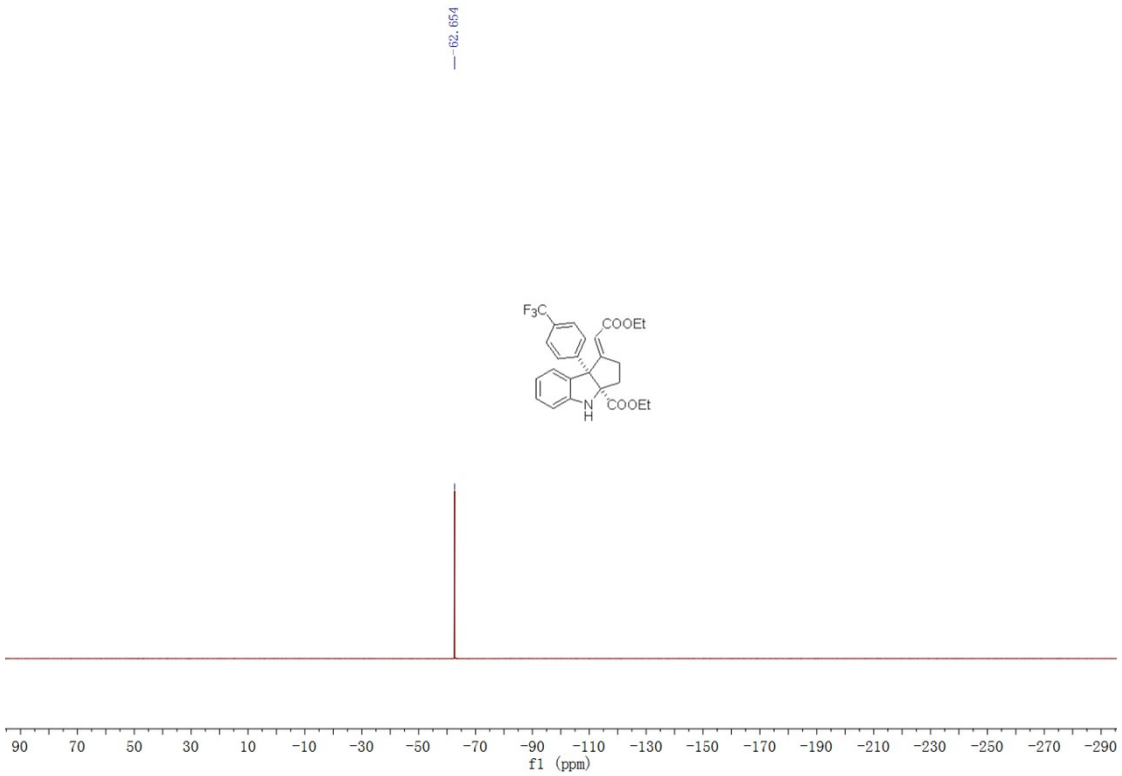


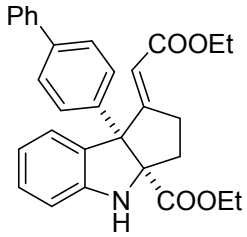
ethyl-(*E*)-1-(2-ethoxy-2-oxoethylidene)-8*b*-(4-(trifluoromethyl)phenyl)-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4h

0.3 mmol scale, a faint yellow solid, 85% yield (117.0 mg). M.p.: 42-45 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.82 (t, *J* = 7.2 Hz, 3H), 1.27 (t, *J* = 7.2 Hz, 3H), 2.10-2.17 (m, 1H), 2.59-2.68 (m, 1H), 3.11-3.22 (m, 1H), 3.41-3.50 (m, 1H), 3.56-3.65 (m, 1H), 3.69-3.78 (m, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 4.63 (s, 1H), 5.82 (t, *J* = 2.4 Hz, 1H), 6.82 (d, *J* = 8.0 Hz, 1H), 6.83-6.88 (m, 1H), 7.00 (d, *J* = 6.8 Hz, 1H), 7.17-7.23 (m, 3H), 7.51 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.4, 14.2, 32.1, 35.9, 60.0, 61.5, 72.9, 83.4, 111.2, 116.2, 120.7, 123.9 (q, *J* = 270.8 Hz), 124.6 (q, *J* = 3.8 Hz), 124.8, 129.3, 129.4 (q, *J* = 32.2 Hz), 129.7, 131.6, 145.3 (q, *J* = 1.4 Hz), 150.1, 166.5, 170.1, 172.5. ^{19}F NMR ($CDCl_3$, $CFCl_3$, 376 MHz) δ -62.6. IR (neat) ν 3397, 3053, 2992, 2956, 2920, 2900, 2853, 1712, 1651, 1607, 1482, 1468, 1407, 1368, 1323, 1257, 1209, 1162, 1116, 1068, 1036, 1016, 862, 829, 741, 688 cm^{-1}. HRMS (ESI) Calcd. for $C_{25}H_{25}NO_4F_3^{+1}(M+H)^+$

requires: 460.1730, found: 460.1729.



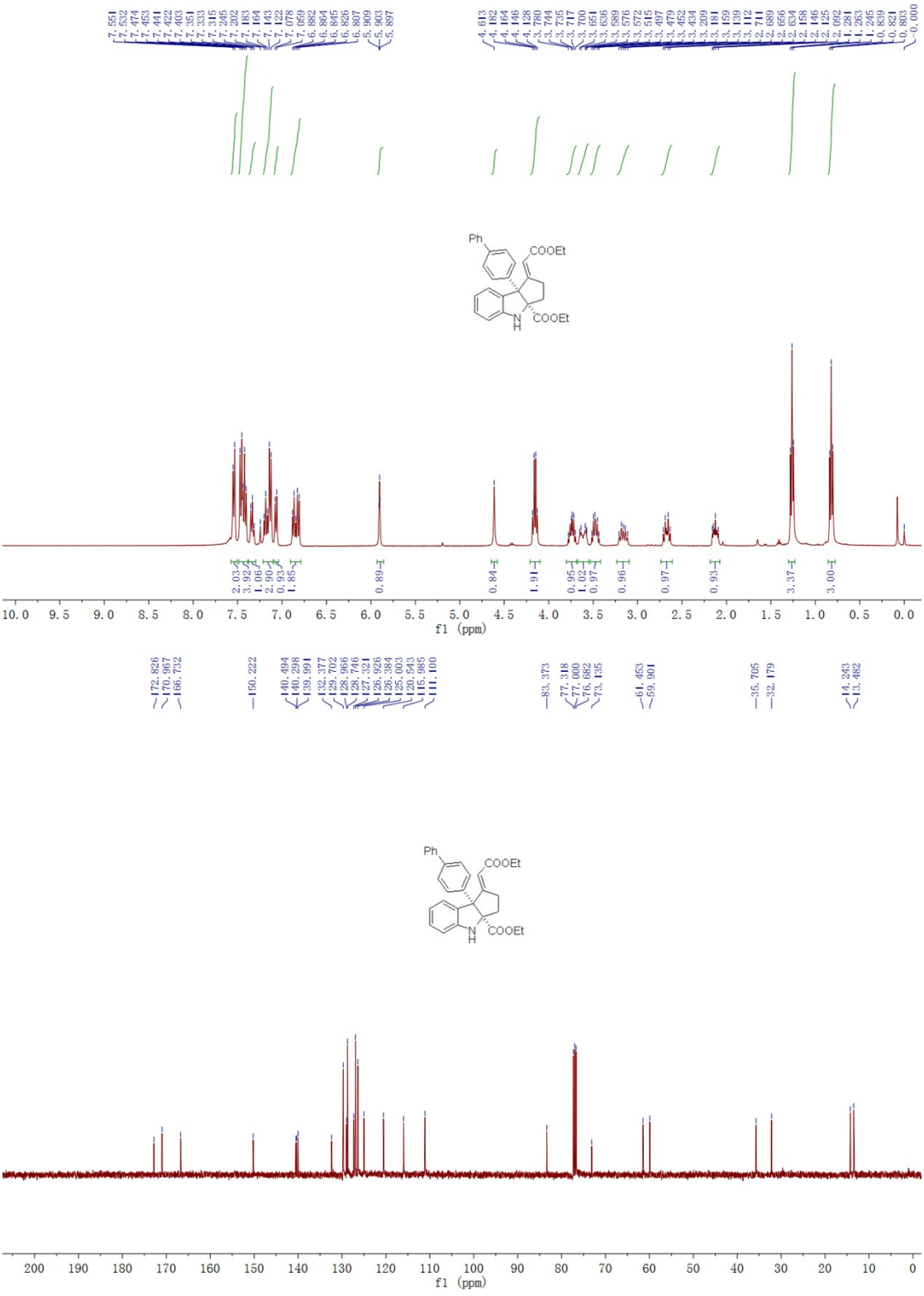


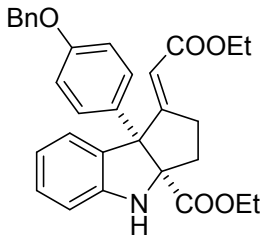


ethyl-(*E*)-8*b*-([1,1'-biphenyl]-4-yl)-1-(2-ethoxy-2-oxoethylidene)-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4i

0.3 mmol scale, a yellow solid, 83% yield (116.3 mg). M.p.: 165-168 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.82 (t, *J* = 7.2 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 2.09-2.16 (m, 1H), 2.63-2.72 (m, 1H), 3.11-3.21 (m, 1H), 3.43-3.52 (m, 1H), 3.57-3.66 (m, 1H), 3.70-3.78 (m, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 4.61 (s, 1H), 5.90 (t, *J* = 2.4 Hz, 1H), 6.82 (d, *J* = 7.6 Hz, 1H), 6.86 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 7.07 (d, *J* = 7.6 Hz, 1H), 7.12-7.21 (m, 3H), 7.31-7.36 (m, 1H), 7.40-7.48 (m, 4H), 7.54 (d, *J* = 7.6 Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.5, 14.2, 32.2, 35.7, 59.9, 61.5, 73.1, 83.4, 111.1, 116.0, 120.5, 125.0, 126.4, 126.9, 127.3, 128.7, 129.0, 129.7, 132.4, 140.0, 140.3, 140.5, 150.2, 166.7, 171.0, 172.8. IR (neat) ν 3383, 3053, 3031, 2981, 2961, 2936, 2923, 2898, 2870, 2848, 1721, 1706, 1648, 1599, 1485, 1468, 1367, 1256, 1214, 1201, 1176, 1166, 1135, 1112, 1068, 1036, 1008, 871, 830, 768, 756, 728, 701, 659 cm^{-1}. HRMS (ESI) Calcd. for

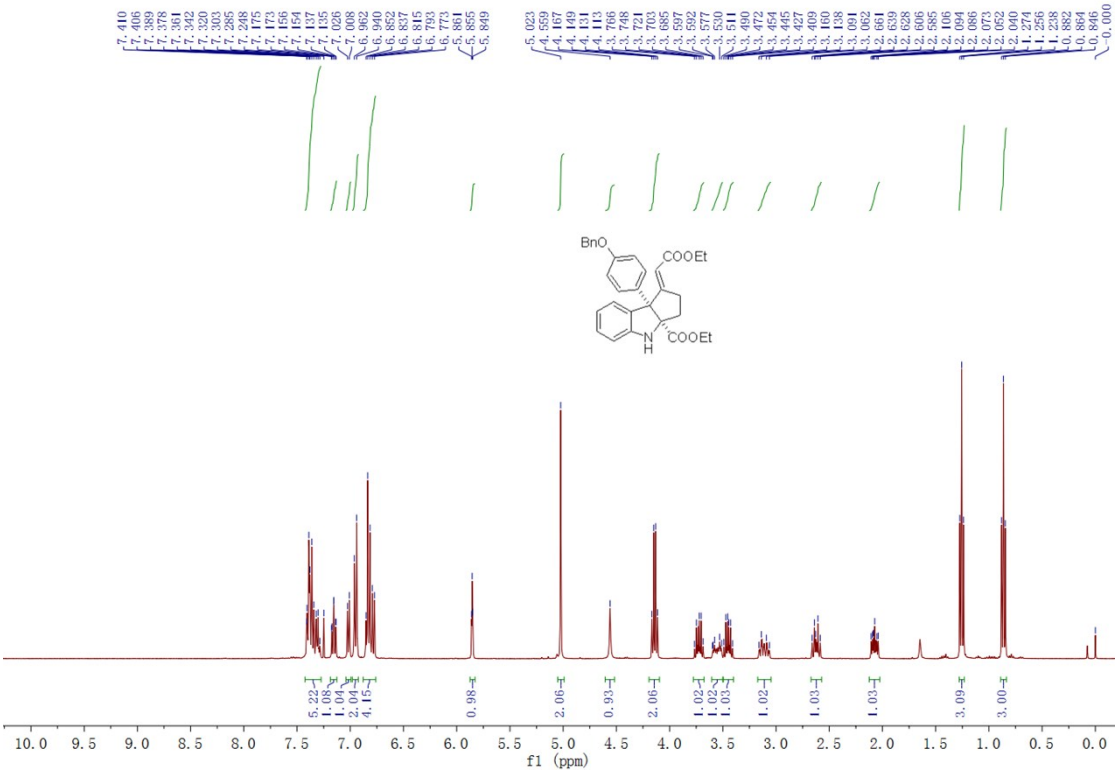
$C_{24}H_{25}NO_4Cl^{+1}(M+H)^+$ requires: 468.2169, found: 468.2167.

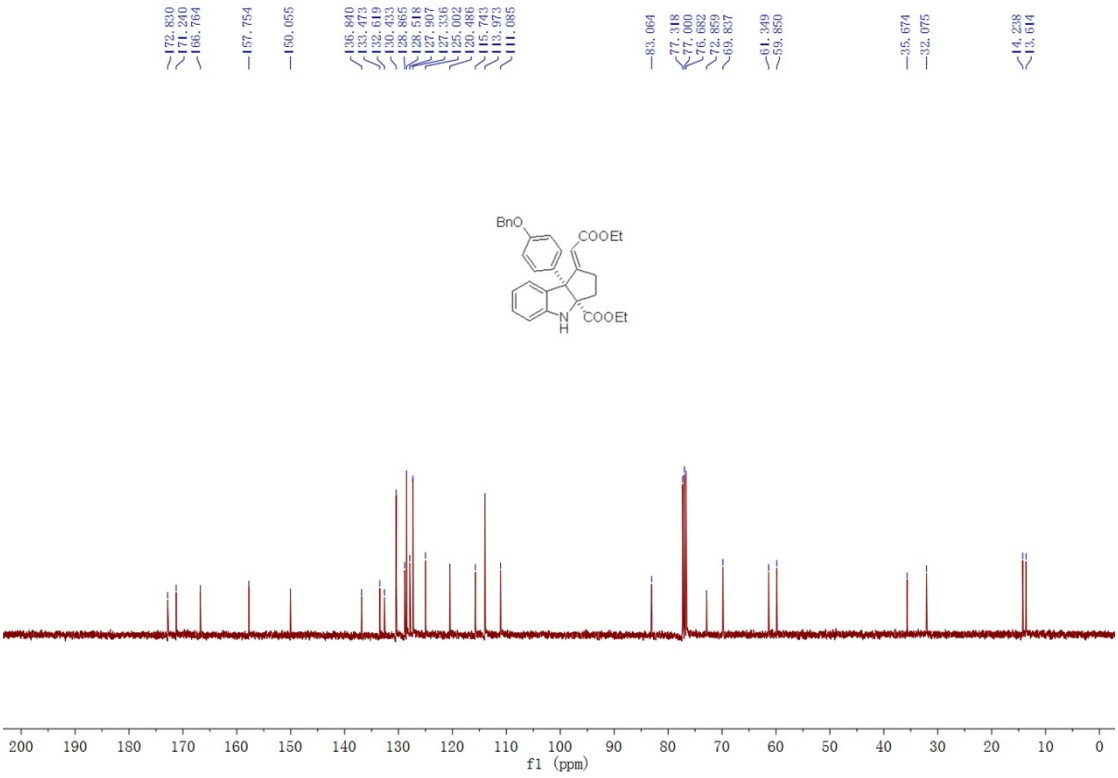


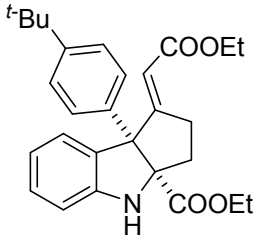


ethyl-(*E*)-8*b*-(4-(benzyloxy)phenyl)-1-(2-ethoxy-2-oxoethylidene)-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4j

0.3 mmol scale, a yellow solid, 68% yield (101.4 mg). M.p.: 49-52 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.86 (t, *J* = 7.2 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 2.04-2.11 (m, 1H), 2.58-2.67 (m, 1H), 3.01-3.16 (m, 1H), 3.40-3.49 (m, 1H), 3.51-3.60 (m, 1H), 3.68-3.77 (m, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 4.56 (s, 1H), 5.02 (s, 2H), 5.86 (t, *J* = 2.4 Hz, 1H), 6.77-6.86 (m, 4H), 6.95 (d, *J* = 8.8 Hz, 2H), 7.02 (d, *J* = 7.2 Hz, 1H), 7.13-7.18 (m, 1H), 7.28-7.41 (m, 5H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.6, 14.2, 32.1, 35.7, 59.9, 61.3, 69.8, 72.9, 83.1, 111.1, 114.0, 115.7, 120.5, 125.0, 127.3, 127.9, 128.5, 128.9, 130.4, 132.6, 133.5, 136.8, 150.1, 157.8, 166.8, 171.2, 172.8. IR (neat) ν 3383, 3028, 2980, 2936, 2901, 1722, 1706, 1649, 1600, 1485, 1468, 1449, 1392, 1368, 1346, 1256, 1219, 1201, 1176, 1165, 1135, 1112, 1067, 1037, 1009, 871, 829, 793, 768, 756, 728, 701, 659 cm^{-1}. HRMS (ESI) Calcd. for $C_{31}H_{32}NO_5^{+1}$(M+H)$^+$ requires: 498.2275, found: 498.2275.

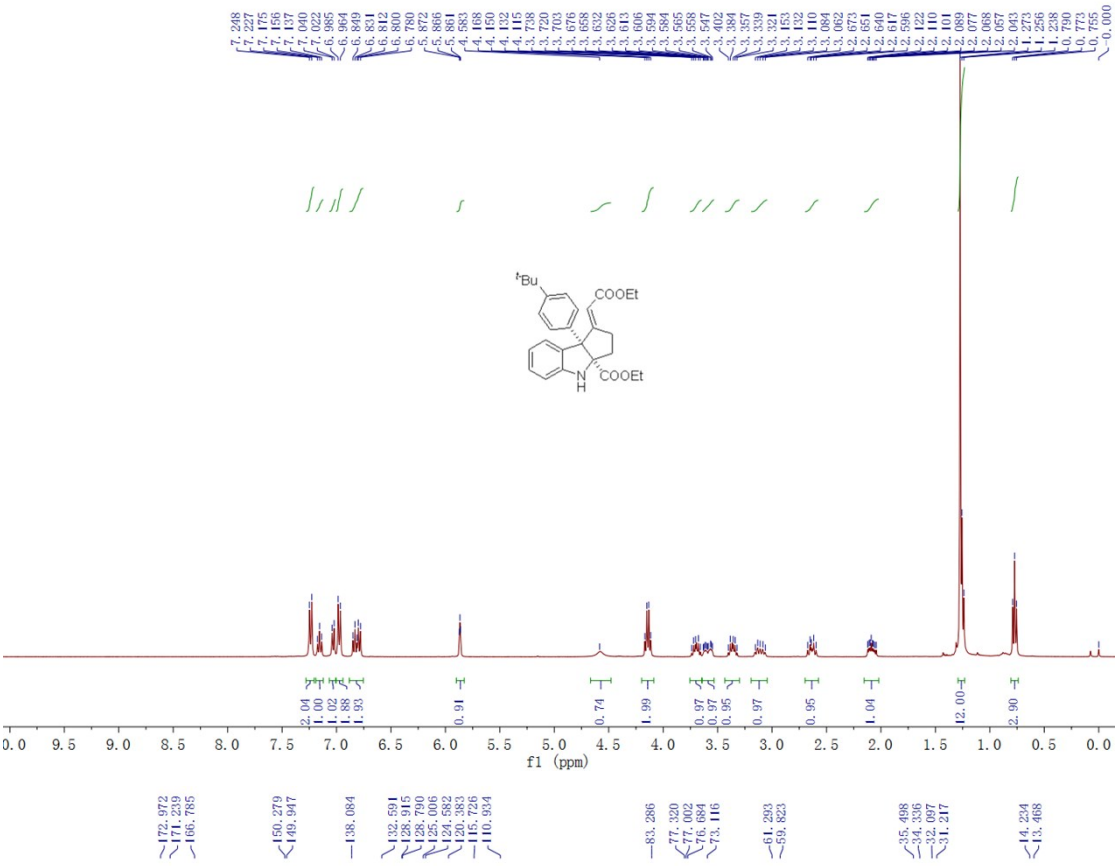


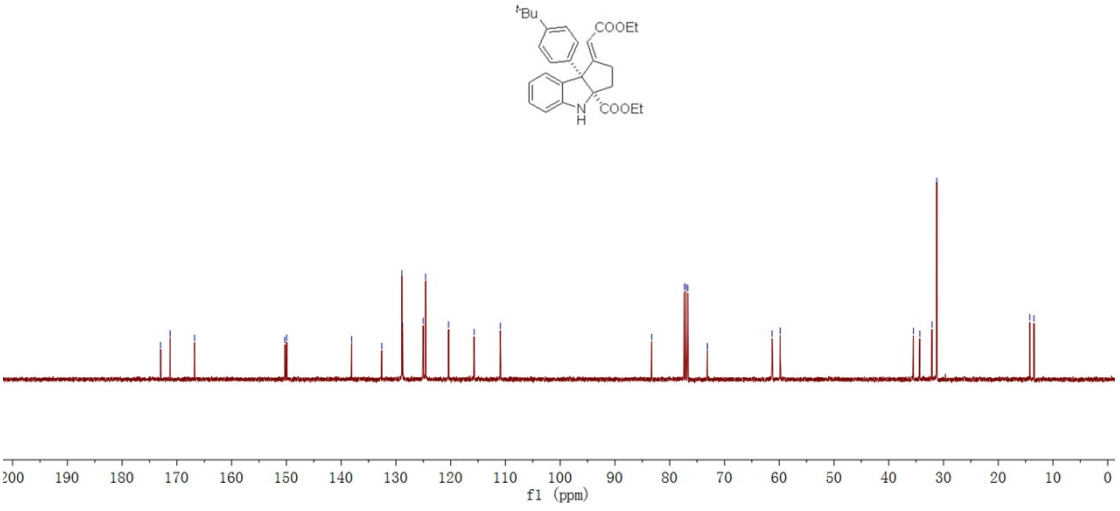


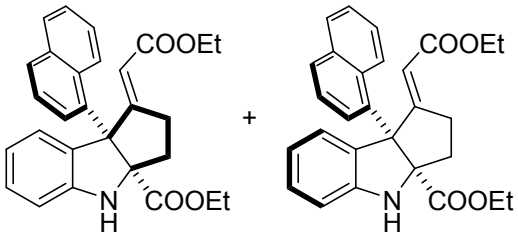


ethyl-(*E*)-8*b*-(4-(tert-butyl)phenyl)-1-(2-ethoxy-2-oxoethylidene)-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4k

0.3 mmol scale, an orange solid, 75% yield (100.1 mg). M.p.: 143-145 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.77 (t, *J* = 7.2 Hz, 3H), 1.23-1.28 (m, 12H), 2.04-2.12 (m, 1H), 2.59-2.68 (m, 1H), 3.06-3.16 (m, 1H), 3.32-3.41 (m, 1H), 3.54-3.64 (m, 1H), 3.65-3.74 (m, 1H), 4.14 (q, *J* = 7.2 Hz, 2H), 4.58 (s, 1H), 5.87 (t, *J* = 2.4 Hz, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 6.83 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 6.97 (d, *J* = 8.4 Hz, 2H), 7.03 (d, *J* = 7.6 Hz, 1H), 7,16 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 7.24 (d, *J* = 8.4 Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.5, 14.2, 31.2, 32.1, 34.3, 35.5, 59.8, 61.3, 73.1, 83.3, 110.9, 115.7, 120.4, 124.6, 125.0, 128.8, 128.9, 132.6, 138.1, 149.9, 150.3, 166.8, 171.2, 173.0. IR (neat) ν 3336, 3081, 3050, 3034, 2956, 2931, 2898, 2864, 1731, 1700, 1654, 1602, 1485, 1471, 1369, 1255, 1218, 1175, 1112, 1096, 1066, 1038, 862, 822, 739 cm^{-1}. HRMS (ESI) Calcd. for $C_{28}H_{34}NO_4^{+1}$(M+H)$^+$ requires: 448.2482, found: 448.2484.

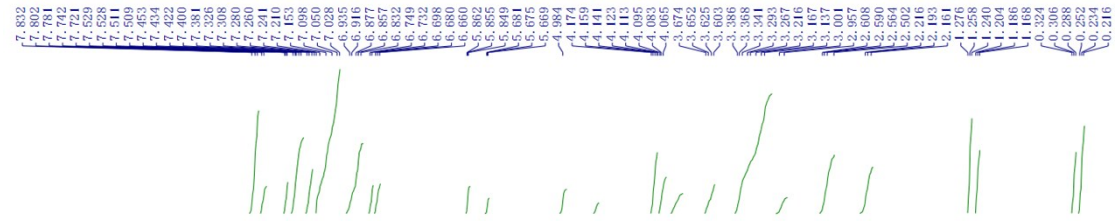

tBu
COOEt
N
H
COOEt
f1 (ppm)

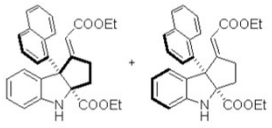

tBu
COOEt
N
H
COOEt
f1 (ppm)

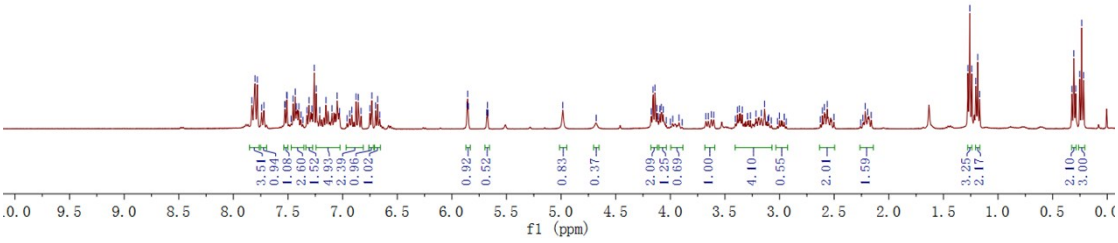


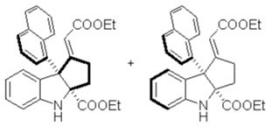
compounds 4l and 4l′

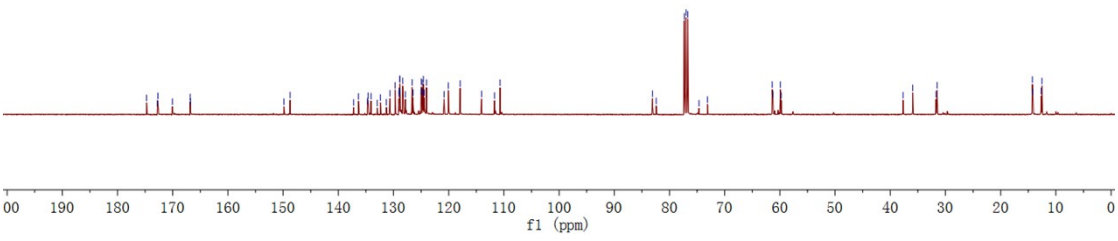
0.3 mmol scale, a brown solid, 51% yield (67.5 mg), dr = 3:2, inseparable (atropisomers). M.p.: 47-68 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.23 (t, *J* = 7.2 Hz, 3H), 0.31 (t, *J* = 7.2 Hz, 2H), 1.19 (t, *J* = 7.2 Hz, 2H), 1.26 (t, *J* = 7.2 Hz, 3H), 2.16-2.26 (m, 1.59H), 2.50-2.63 (m, 2H), 2.93-3.02 (m, 0.55H), 3.07-3.41 (m, 4.10H), 3.60-3.68 (m, 1H), 4.68 (s, 0.37H), 4.98 (s, 1H), 5.68 (t, *J* = 2.4 Hz, 0.52H), 5.86 (t, *J* = 2.4 Hz, 1H), 6.80 (dd, *J* = 7.2 Hz, 7.2 Hz, 1H), 6.74 (t, *J* = 7.2 Hz, 1H), 6.83-6.96 (m, 2.39H), 7.02-7.21 (m, 4.93H), 7.28-7.33 (m, 1.52H), 7.36-7.48 (m, 2.60H), 7.50-7.53 (m, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 12.5, 12.7, 14.2, 14.3, 31.5, 31.7, 35.9, 37.7, 59.8, 59.9, 61.2, 61.4, 73.1, 74.7, 82.4, 83.1, 110.7, 111.7, 114.0, 117.9, 120.1, 120.8, 124.0, 124.4, 124.60, 124.68, 124.74, 124.96, 125.02, 126.5, 126.6, 127.9, 128.3, 128.84, 128.87, 128.90, 128.99, 129.02, 129.7, 130.6, 131.3, 132.4, 133.0, 134.1, 134.6, 134.7, 136.3, 137.2, 148.7, 149.9, 166.78, 166.84, 170.1, 172.7, 172.8, 174.7. IR (neat) ν 3363, 3049, 2980, 2953, 2935, 2902, 2866, 1707, 1645, 1599, 1509, 1483, 1466, 1394, 1368, 1344, 1255, 1201, 1160, 1136, 1107, 1069, 1038, 863, 799, 775, 733, 702, 662 cm^{-1}. HRMS (ESI) Calcd. for $C_{28}H_{28}NO_4^{+1}(M+H)^+$ requires: 442.2013, found: 442.2008.

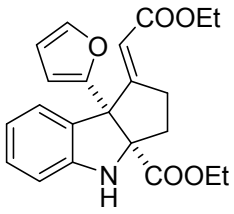



COOEt
COOEt
N
H
COOEt
+
COOEt
COOEt
N
H


f1 (ppm)

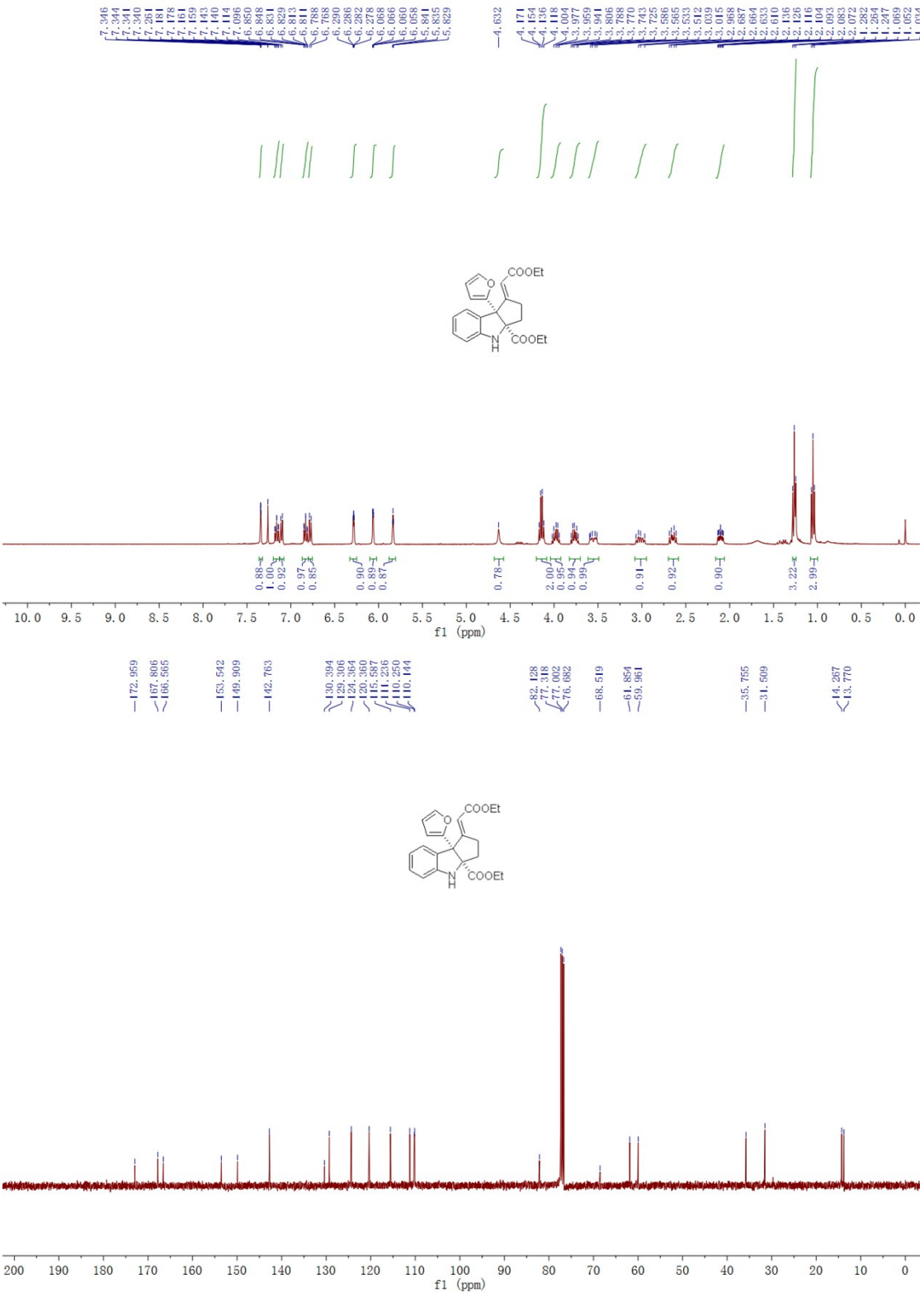

COOEt
COOEt
N
H
COOEt
+
COOEt
COOEt
N
H

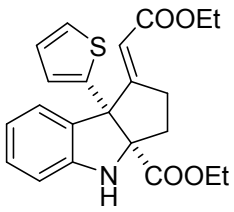

f1 (ppm)



ethyl-(*E*)-1-(2-ethoxy-2-oxoethylidene)-8*b*-(furan-2-yl)-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4m

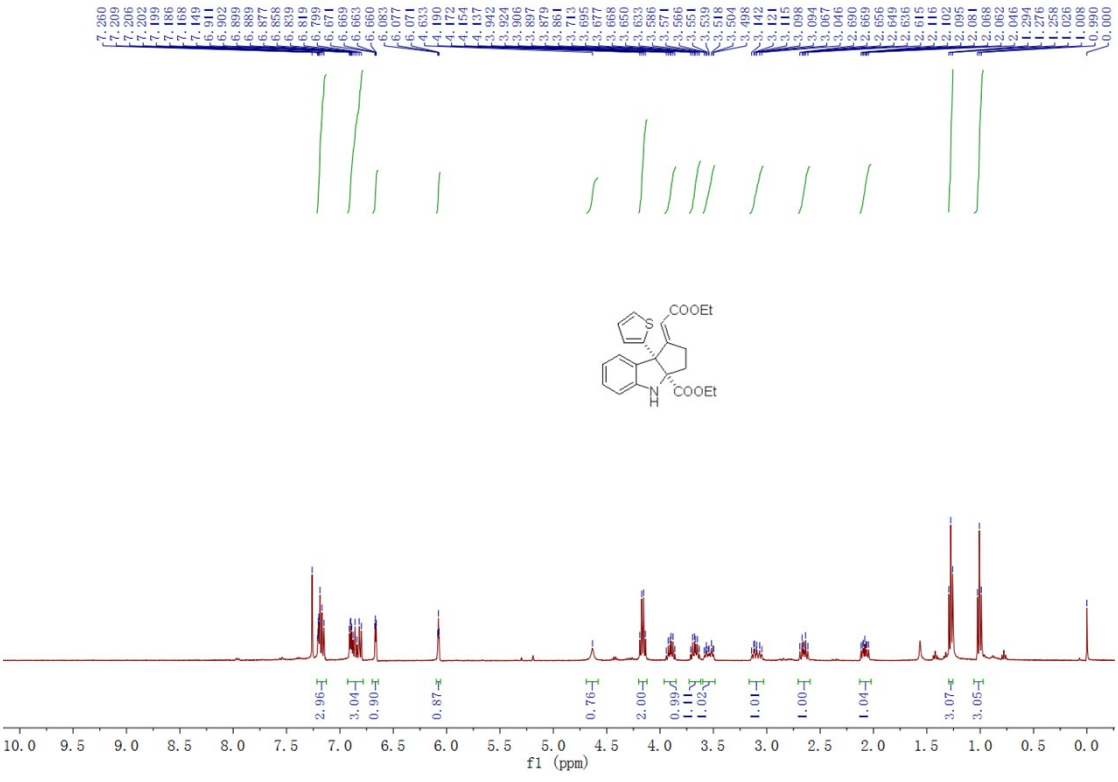
0.3 mmol scale, a white solid, 40% yield (45.7 mg). M.p.: 83-85 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.05 (t, *J* = 7.2 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 2.07-2.14 (m, 1H), 2.61-2.69 (m, 1H), 2.96-3.07 (m, 1H), 3.51-3.60 (m, 1H), 3.72-3.81 (m, 1H), 3.94-4.03 (m, 1H), 4.15 (q, *J* = 7.2 Hz, 2H), 4.63 (s, 1H), 5.84 (t, *J* = 2.4 Hz, 1H), 6.06 (dd, *J* = 0.8 Hz, 3.2 Hz, 1H), 6.28 (dd, *J* = 1.6 Hz, 3.2 Hz, 1H), 6.78 (d, *J* = 8.0 Hz, 1H), 6.81-6.85 (m, 1H), 7.11 (d, *J* = 7.2 Hz, 1H), 7.15-7.19 (m, 1H), 7.34 (dd, *J* = 0.8 Hz, 1.6 Hz, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.8, 14.3., 31.5, 35.8, 60.0, 61.9, 68.5, 82.1, 110.1, 110.3, 111.2, 115.6, 120.4, 124.4, 129.3, 130.4, 142.8, 149.9, 153.5, 166.6, 167.8, 173.0. IR (neat) ν 3362, 3136, 3117, 3050, 2979, 2925, 2903, 2870, 2850, 1707, 1651, 1605, 1483, 1467, 1391, 1369, 1346, 1243, 1220, 1206, 1171, 1154, 1114, 1099, 1071, 1040, 1015, 954, 858, 811, 746 cm^{-1}. HRMS (ESI) Calcd. for $C_{22}H_{24}NO_5^{+1}$(M+H)$^{+}$ requires: 382.1649, found: 382.1649.

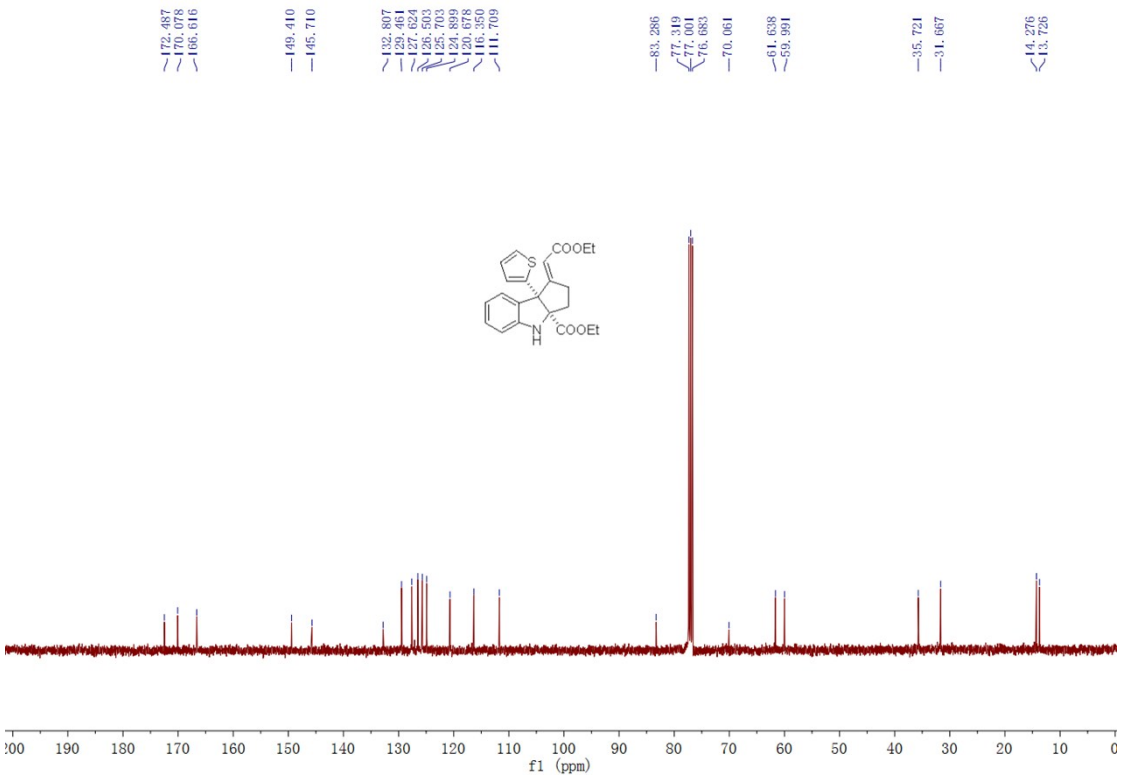

COOEt
COOEt
f1 (ppm)
f1 (ppm)

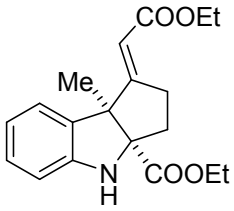


ethyl-(*E*)-1-(2-ethoxy-2-oxoethylidene)-8*b*-(thiophen-2-yl)-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4n

0.3 mmol scale, a yellow solid, 40% yield (63.5 mg). M.p.: 134-137 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.01 (t, *J* = 7.2 Hz, 3H), 1.28 (t, *J* = 7.2 Hz, 3H), 2.04-2.14 (m, 1H), 2.62-2.69 (m, 1H), 3.04-3.15 (m, 1H), 3.49-3.59 (m, 1H), 3.63-3.72 (m, 1H), 3.86-3.94 (m, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 4.63 (s, 1H), 6.08 (t, *J* = 2.4 Hz, 1H), 6.67 (dd, *J* = 1.2 Hz, 3.6 Hz, 1H), 6.79-6.92 (m, 3H), 7.14-7.21 (m, 3H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.7, 14.3, 31.7, 35.7, 60.0, 61.6, 70.1, 83.3, 111.7, 116.4, 120.7, 124.9, 125.7, 126.5, 127.6, 129.5, 132.8, 145.7, 149.4, 166.6, 170.1, 172.5. IR (neat) ν 3388, 3064, 2975, 2942, 2875, 1714, 1652, 1608, 1485, 1471, 1417, 1369, 1346, 1274, 1252, 1238, 1210, 1191, 1176, 1114, 1066, 1036, 1021, 936, 865, 824, 747, 699 cm^{-1}. HRMS (ESI) Calcd. for $C_{22}H_{24}NO_4S^{+1}$(M+H)$^{+}$ requires: 398.1421, found: 398.1418.

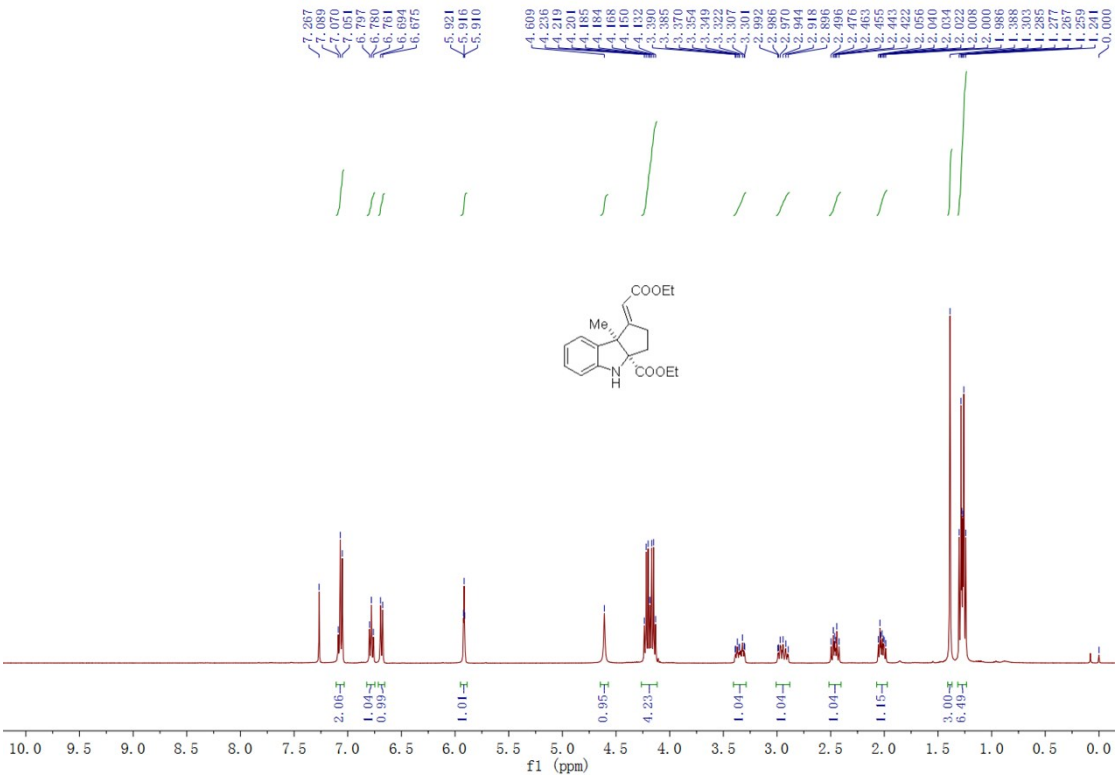






ethyl-(*E*)-1-(2-ethoxy-2-oxoethylidene)-8*b*-methyl-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4o

0.3 mmol scale, a yellow oil, 81% yield (80.3 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.26 (t, *J* = 7.2 Hz, 3H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.39 (s, 3H), 1.98-2.06 (m, 1H), 2.42-2.50 (m, 1H), 2.89-3.00 (m, 1H), 3.30-3.39 (m, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 4.21 (q, *J* = 7.2 Hz, 2H), 4.61 (s, 1H), 5.92 (t, *J* = 2.4 Hz, 1H), 6.68 (d, *J* = 7.6 Hz, 1H), 6.78 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 7.05-7.09 (m, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 14.1, 14.2, 22.4, 31.4, 35.8, 59.7, 61.4, 62.6, 80.2, 110.6, 112.4, 119.9, 122.6, 128.5, 133.2, 148.2, 166.6, 171.4, 173.3. IR (neat) ν 3367, 3053, 2977, 2934, 2903, 2870, 1709, 1650, 1603, 1482, 1466, 1368, 1347, 1253, 1235, 1185, 1158, 1116, 1096, 1066, 1030, 957, 862, 744 cm^{-1}. HRMS (ESI) Calcd. for $C_{19}H_{24}NO_4^{+1}(M+H)^+$ requires: 330.1700, found: 330.1702.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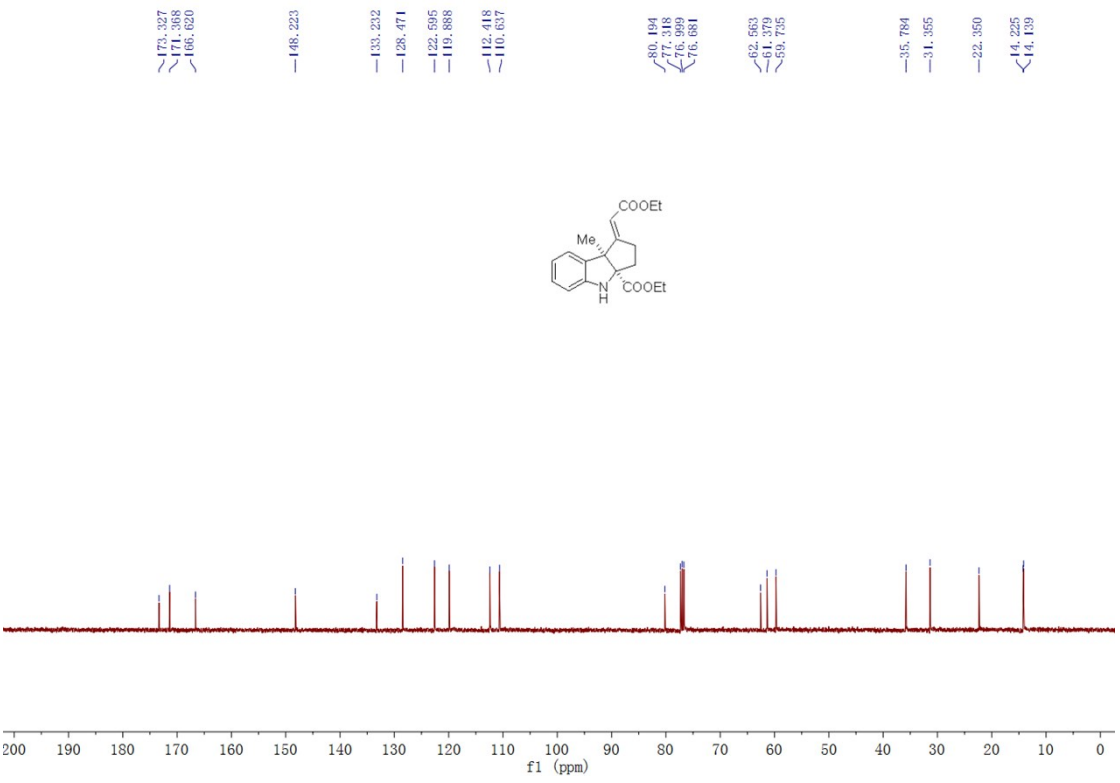
1.285
1.277
1.257
1.259
1.241
0.000
COOEt
Me
N
H
COOEt
2.06
1.04
0.99
1.01
0.95
4.23
1.04
1.04
1.04
1.15
3.00
6.49
f1 (ppm)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76.681
62.563
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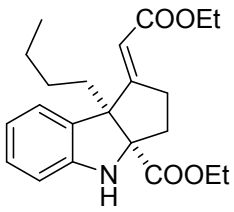
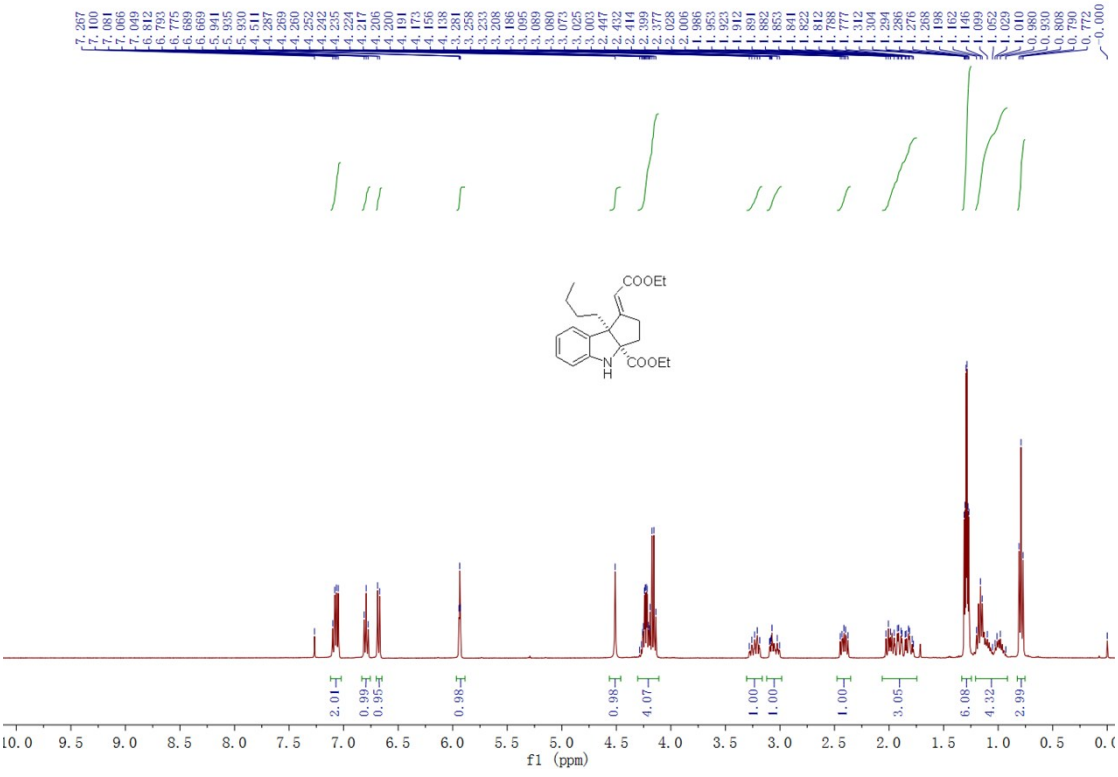
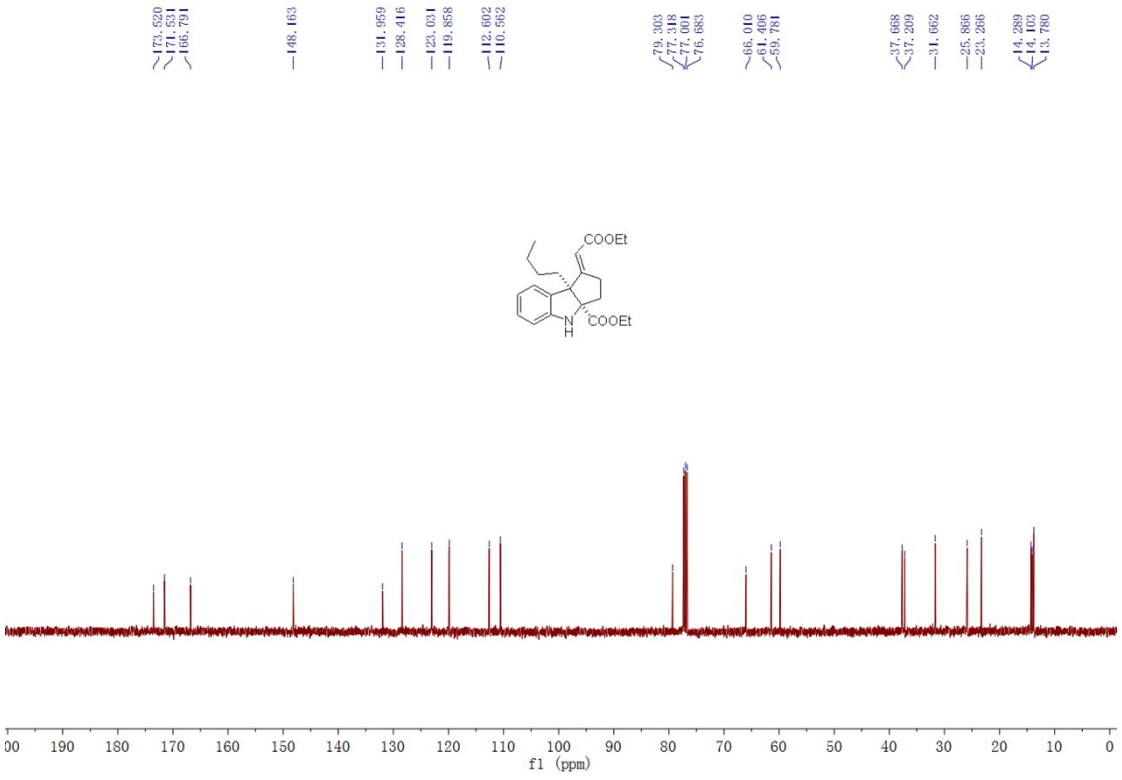
14.225
14.139
COOEt
Me
N
H
COOEt
f1 (ppm)

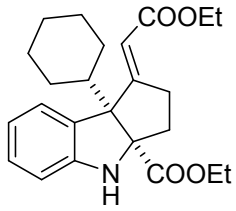


ethyl-(E)-8*b*-butyl-1-(2-ethoxy-2-oxoethylidene)-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3a(1*H*)-carboxylate 4p

0.3 mmol scale, a yellow oil, 98% yield (109.1 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.79 (t, *J* = 7.2 Hz, 3H), 0.93-1.20 (m, 4H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.77-2.03 (m, 3H), 2.37-2.45 (m, 1H), 3.00-3.10 (m, 1H), 3.18-3.29 (m, 1H), 4.13-4.29 (m, 4H), 4.51 (s, 1H), 5.94 (t, *J* = 2.4 Hz, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 6.79 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 7.04-7.10 (m, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.8, 14.1, 14.3, 23.3, 25.9, 31.7, 37.2, 37.7, 59.8, 61.4, 66.0, 79.3, 110.6, 112.6, 119.9, 123.0, 128.4, 132.0, 148.2, 166.8, 171.5, 173.5. IR (neat) ν 3367, 3047, 2953, 2934, 2906, 2867, 1709, 1647, 1604, 1482, 1466, 1368, 1251, 1220, 1206, 1153, 1096, 1066, 1038, 910, 859, 741 cm^{-1}. HRMS (ESI) Calcd. for $C_{22}H_{30}NO_4^{+1}(M+H)^+$ requires: 372.2169, found: 372.2168.

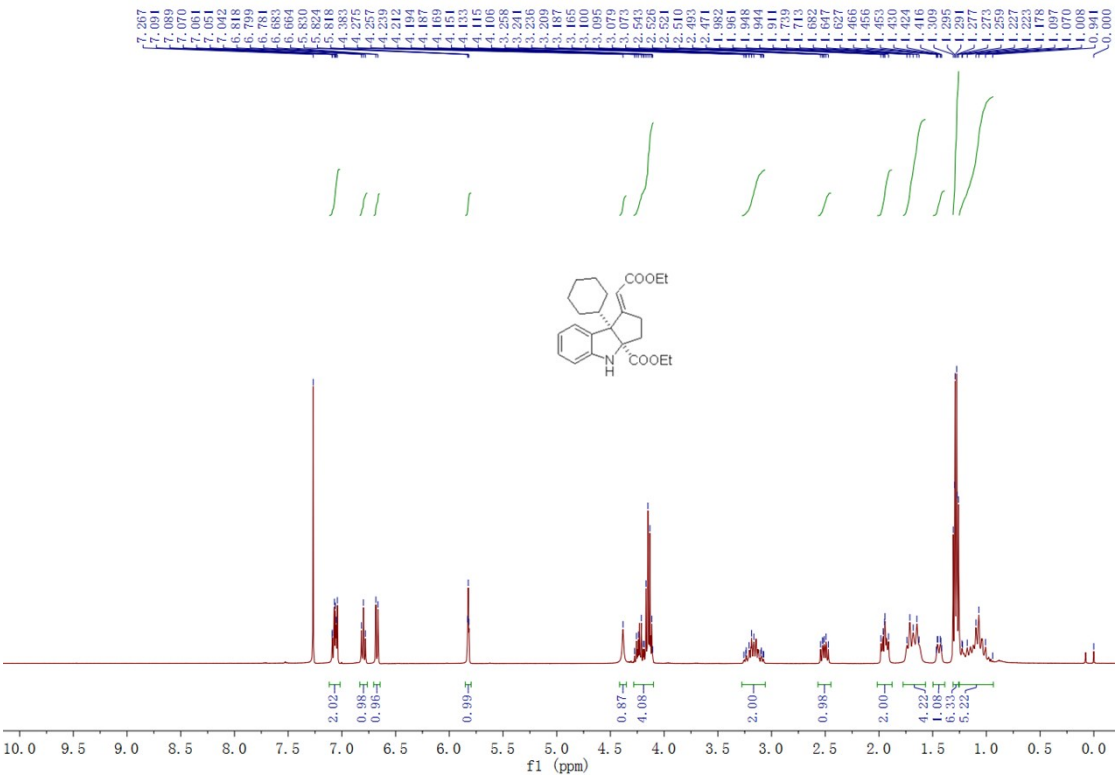


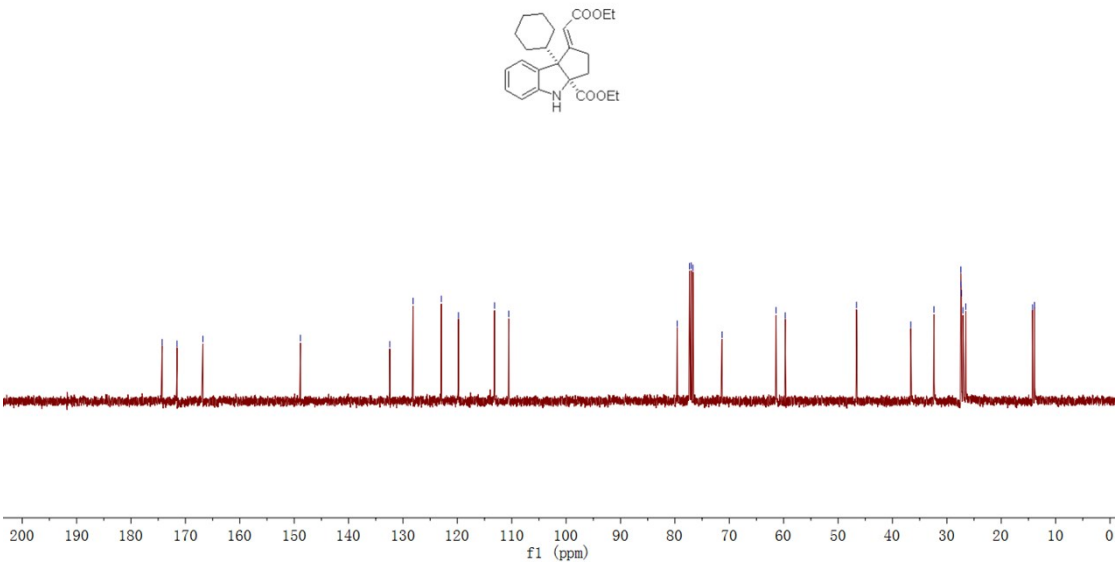


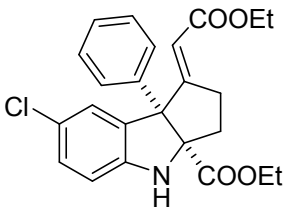


ethyl-(*E*)-8*b*-cyclohexyl-1-(2-ethoxy-2-oxoethylidene)-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4q

0.3 mmol scale, a yellow oil, 89% yield (106.2 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.94-1.23 (m, 5H), 1.28 (t, *J* = 7.2 Hz, 3H), 1.29 (t, *J* = 7.2 Hz, 3H), 1.41-1.47 (m, 1H), 1.62-1.74 (m, 4H), 1.91-1.99 (m, 2H), 2.47-2.55 (m, 1H), 3.07-3.26 (m, 2H), 4.10-4.28 (m, 4H), 4.38 (s, 1H), 5.82 (t, *J* = 2.4 Hz, 1H), 6.67 (d, *J* = 7.6 Hz, 1H), 6.80 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 7.04-7.10 (m, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.9, 14.2, 26.5, 27.0, 27.3, 27.42, 27.43, 32.4, 36.6, 46.6, 59.7, 61.4, 71.3, 79.6, 110.5, 113.2, 119.8, 122.9, 128.1, 132.4, 148.8, 166.8, 171.5, 174.3. IR (neat) ν 3363, 3053, 2979, 2933, 2851, 1712, 1642, 1603, 1482, 1466, 1448, 1390, 1368, 1345, 1274, 1249, 1226, 1213, 1184, 1153, 1107, 1067, 1039, 912, 859, 734 cm^{-1}. HRMS (ESI) Calcd. for $C_{24}H_{32}NO_4^{+1}(M+H)^+$ requires: 398.2326, found: 398.2329.

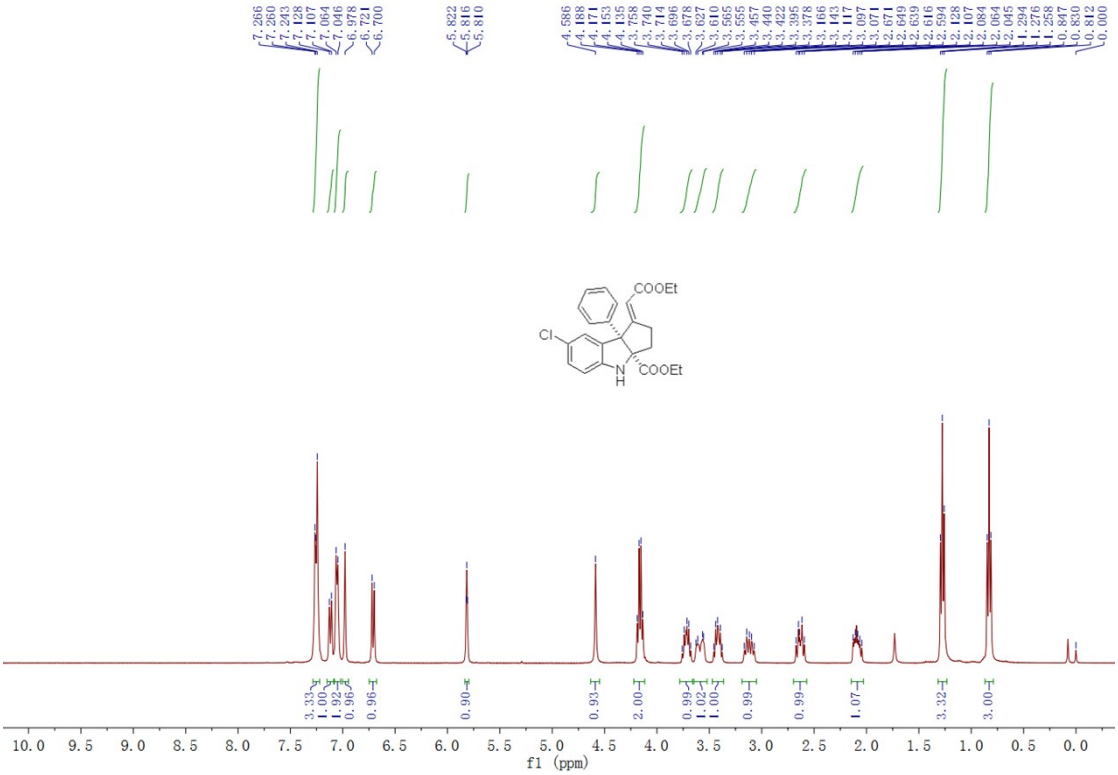

COOEt
COOEt
N
H
f1 (ppm)

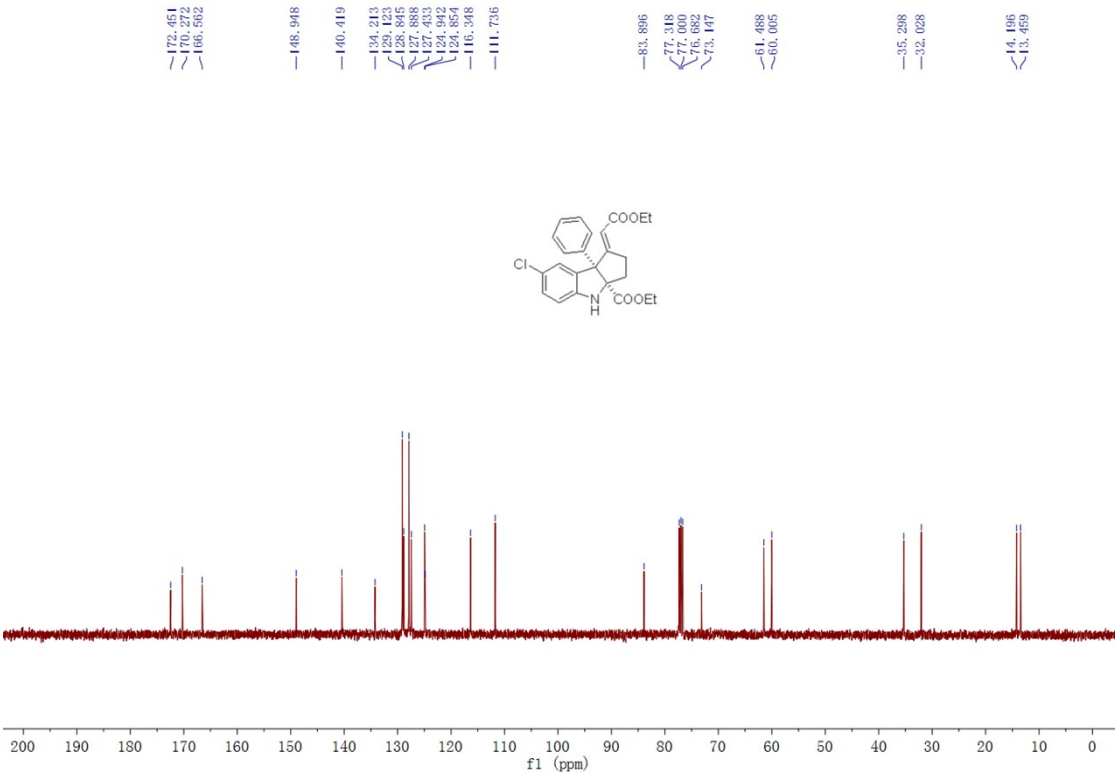

COOEt
COOEt
N
H
f1 (ppm)

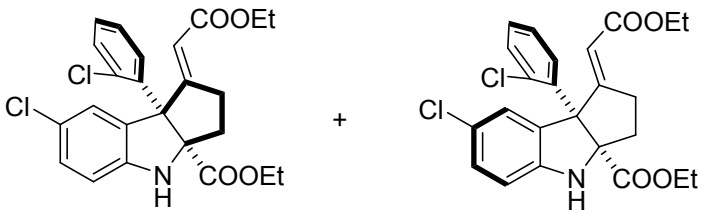


ethyl-(*E*)-7-chloro-1-(2-ethoxy-2-oxoethylidene)-8*b*-phenyl-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4r

0.3 mmol scale, a faint yellow solid, 86% yield (110.1 mg). M.p.: 130-132 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.83 (t, *J* = 7.2 Hz, 3H), 1.28 (t, *J* = 7.2 Hz, 3H), 2.04-2.13 (m, 1H), 2.59-2.68 (m, 1H), 3.07-3.17 (m, 1H), 3.37-3.46 (m, 1H), 3.55-3.63 (m, 1H), 3.67-3.76 (m, 1H), 4.16 (q, *J* = 7.2 Hz, 2H), 4.59 (s, 1H), 5.82 (t, *J* = 2.4 Hz, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.98 (s, 1H), 7.04-7.07 (m, 2H), 7.12 (d, *J* = 8.4 Hz, 1H), 7.24-7.27 (m, 3H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.5, 14.2, 32.0, 35.3, 60.0, 61.5, 73.1, 83.9, 111.7, 116.3, 124.85, 124.94, 127.4, 127.9, 128.8, 129.1, 134.2, 140.4, 148.9, 166.6, 170.3, 172.5. IR (neat) ν 3364, 3342, 3056, 3036, 2978, 2953, 2931, 2895, 2859, 1729, 1699, 1650, 1603, 1477, 1447, 1368, 1344, 1252, 1233, 1207, 1174, 1163, 1095, 1068, 1039, 877, 858, 799, 752, 738, 713, 703, 659 cm^{-1}. HRMS (ESI) Calcd. for $C_{24}H_{25}NO_4Cl^{+1}(M+H)^+$ requires: 426.1467, found: 426.1462.



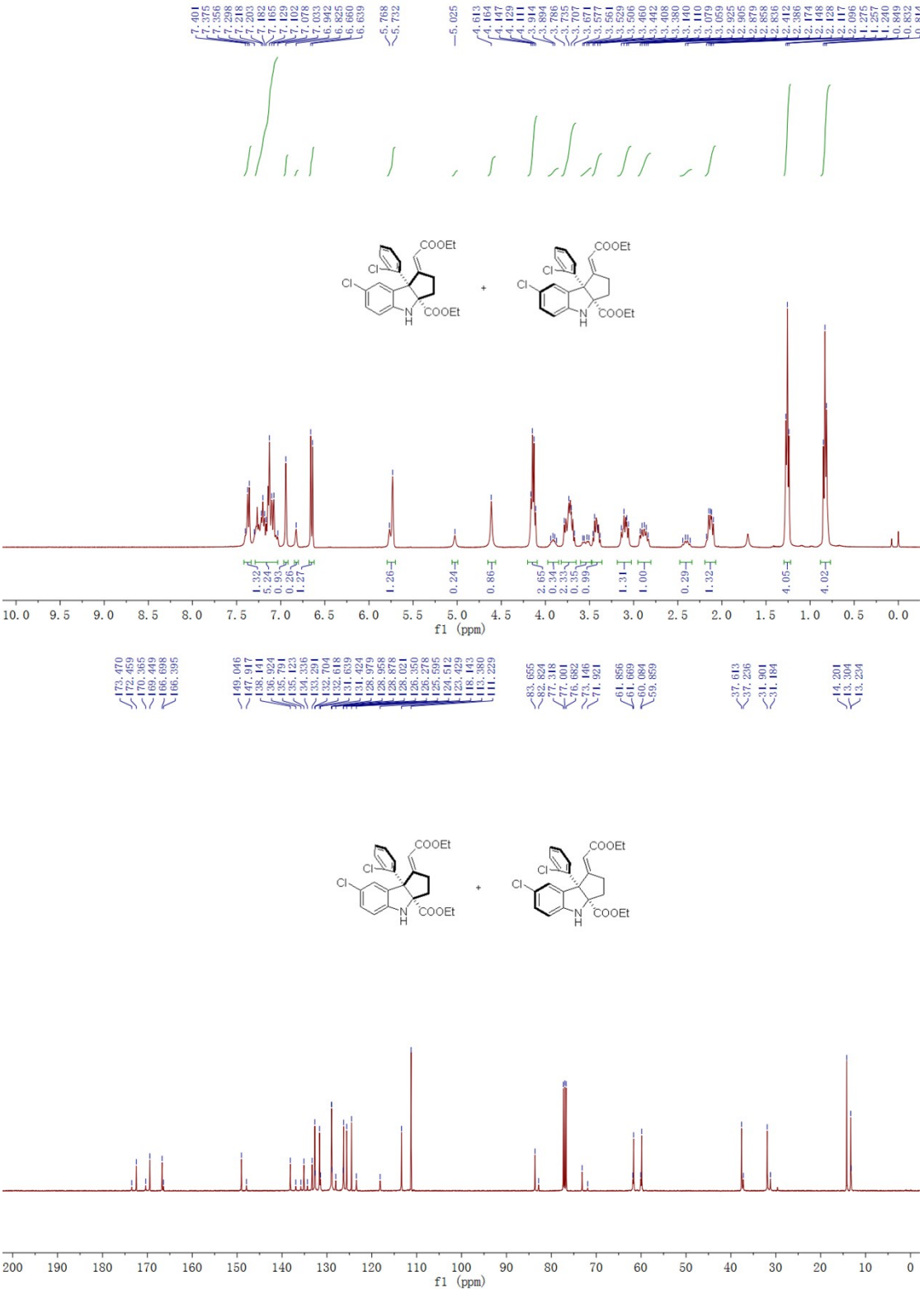


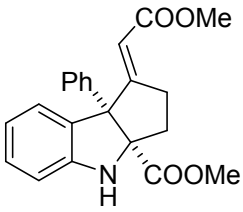


compounds 4s and 4s′

0.3 mmol scale, a faint yellow solid, 88% yield (121.2 mg), dr = 3:1, inseparable atropisomers. M.p.: 66-68 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.83 (t, *J* = 7.2 Hz, 4H), 1.26 (t, *J* = 7.2 Hz, 4H), 2.09-2.18 (m, 1.32H), 2.36-2.45 (m, 0.29H), 2.83-2.93 (m, 1H), 3.05-3.14 (m, 1.31H), 3.38-3.46 (m, 1H), 3.50-3.58 (m, 0.35H), 3.67-3.79 (m, 2.33H), 3.87-3.94 (m, 0.34H), 4.14 (q, *J* = 7.2 Hz, 2.65H), 4.61 (s, 1H), 5.03 (s, 0.24H), 5.73 (s, 1H), 5.77 (s, 0.26H), 6.65 (d, *J* = 8.4 Hz, 1.27H), 6.83 (s, 0.26H), 6.94 (s, 1H), 7.07-7.30 (m, 5.24H), 7.35-7.41 (m, 1.32H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.2, 13.3, 14.2, 31.2, 31.9, 37.2, 37.6, 59.9, 60.1, 61.7, 61.9, 71.9, 73.1, 82.8, 83.7, 111.2, 113.4, 118.1, 123.4, 124.5, 125.6, 126.3, 126.4, 128.0, 128.88, 128.96, 128.98, 131.4, 131.6, 132.6, 132.7, 133.3, 134.3, 135.1, 135.8, 136.9, 138.1, 147.9, 149.0, 166.4, 166.7, 169.4, 170.4, 172.5, 173.5. IR (neat) ν 3365, 3059, 2981, 2953, 2935, 2902, 2868, 1705, 1648, 1600, 1480, 1432, 1391, 1368, 1346, 1291, 1255, 1205, 1166, 1119, 1071, 1042, 943, 919, 861, 808, 755, 734, 696

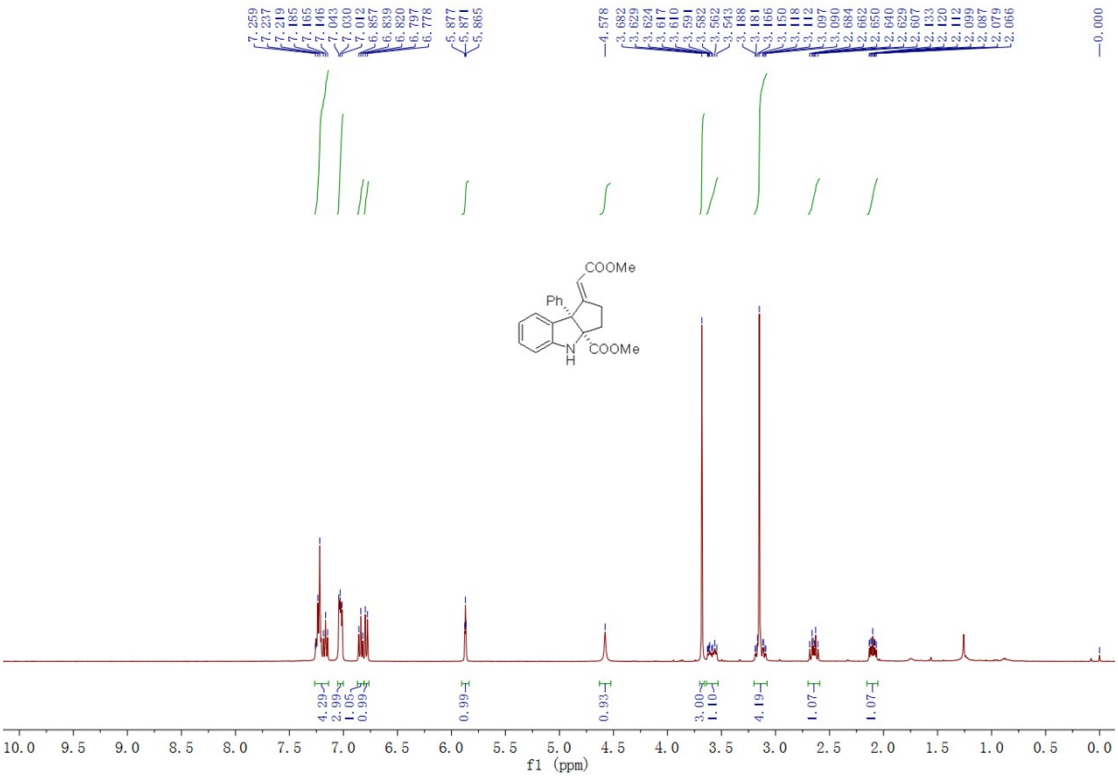
cm^{-1}. HRMS (ESI) Calcd. for $C_{24}H_{24}NO_4Cl_2^{+1}(M+H)^+$ requires: 460.1077, found: 460.1077.

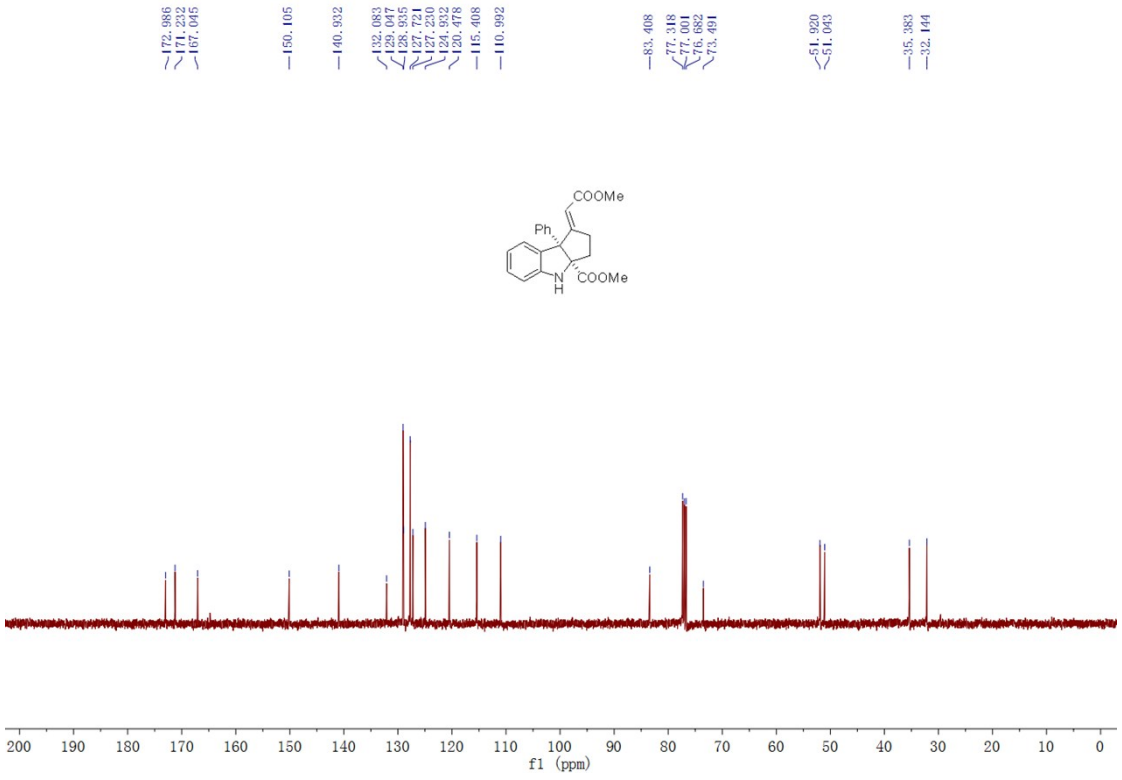


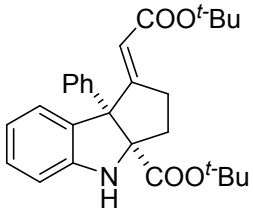


methyl-(*E*)-1-(2-methoxy-2-oxoethylidene)-8*b*-phenyl-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4t

0.3 mmol scale, a light yellow solid, 71% yield (77.2 mg). M.p.: 51-53 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 2.06-2.14 (m, 1H), 2.60-2.69 (m, 1H), 3.09-3.19 (m, 1H), 3.15 (s, 3H), 3.54-3.63 (m, 1H), 3.68 (s, 3H), 4.58 (s, 1H), 5.87 (t, *J* = 2.4 Hz, 1H), 6.79 (d, *J* = 7.6 Hz, 1H), 6.84 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 7.01-7.05 (m, 3H), 7.14-7.26 (m, 4H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 32.1, 35.4, 51.0, 51.9, 73.5, 83.4, 111.0, 115.4, 120.5, 124.9, 127.2, 127.7, 128.9, 129.0, 132.1, 140.9, 150.1, 167.0, 171.2, 173.0. IR (neat) ν 3383, 3358, 3084, 3053, 3031, 2984, 2948, 2920, 2845, 1736, 1717, 1646, 1604, 1484, 1468, 1435, 1357, 1284, 1261, 1207, 1186, 1164, 1066, 1039, 1021, 966, 863, 813, 750, 737, 717, 700 cm^{-1}. HRMS (ESI) Calcd. for $C_{22}H_{22}NO_4^{+1}$(M+H)$^+$ requires: 364.1543, found: 364.1541.

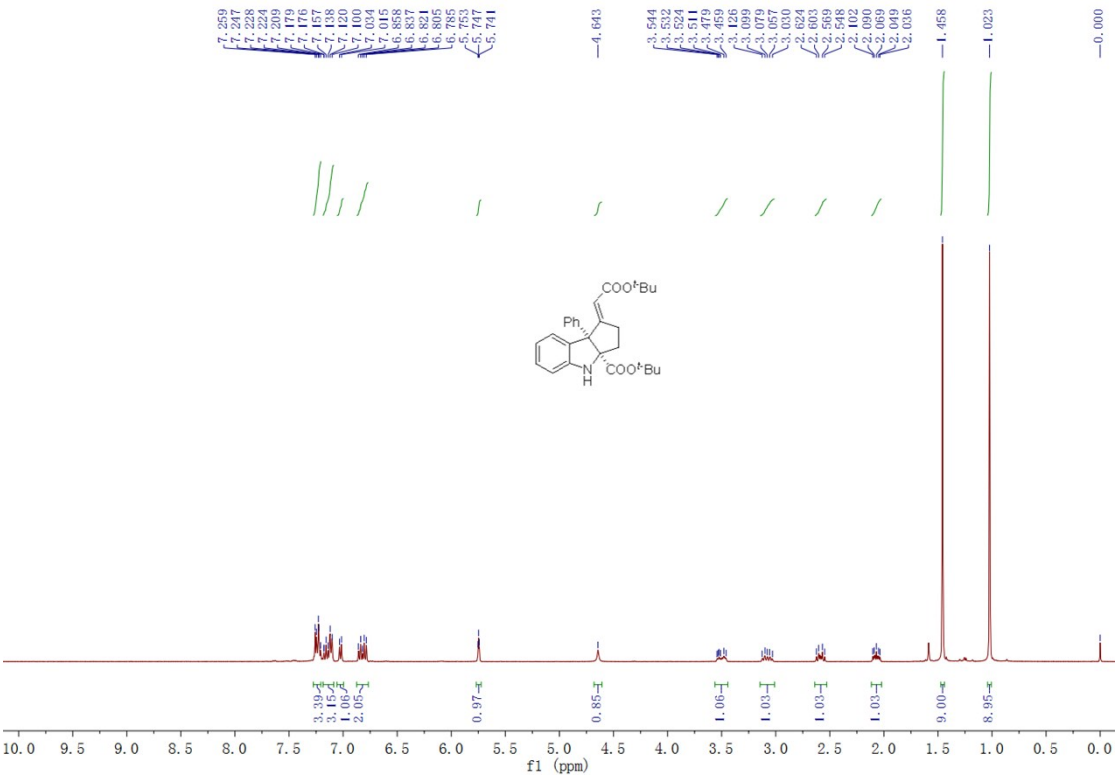






tert-butyl-(*E*)-1-(2-(tert-butoxy)-2-oxoethylidene)-8*b*-phenyl-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4u

0.3 mmol scale, a light yellow solid, 47% yield (63.2 mg). M.p.: 177-179 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.02 (s, 9H), 1.46 (s, 9H), 2.03-2.11 (m, 1H), 2.54-2.63 (m, 1H), 3.03-3.13 (m, 1H), 3.45-3.55 (m, 1H), 4.64 (s, 1H), 5.75(t, *J* = 2.4 Hz, 1H), 6.78-6.86 (m, 2H), 7.02 (d, *J* = 7.6 Hz, 1H), 7.10-7.18 (m, 3H), 7.20-7.26 (m, 3H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 27.3, 28.3, 31.8, 36.8, 72.7, 79.9, 81.9, 83.1, 111.1, 117.7, 120.4, 125.2, 127.0, 127.8, 128.7, 129.8, 133.3, 141.7, 150.2, 166.3, 169.8, 171.9. IR (neat) ν 3336, 3086, 3059, 3003, 2979, 2953, 2931, 1716, 1691, 1654, 1605, 1488, 1473, 1453, 1391, 1364, 1303, 1284, 1266, 1254, 1229, 1151, 1116, 1101, 1068, 1038, 1002, 857, 847, 826, 763, 747, 733, 700, 659 cm^{-1}. HRMS (ESI) Calcd. for $C_{28}H_{34}NO_4^{+1}(M+H)^+$ requires: 448.2482, found: 448.2480.


7.259
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7.176
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7.120
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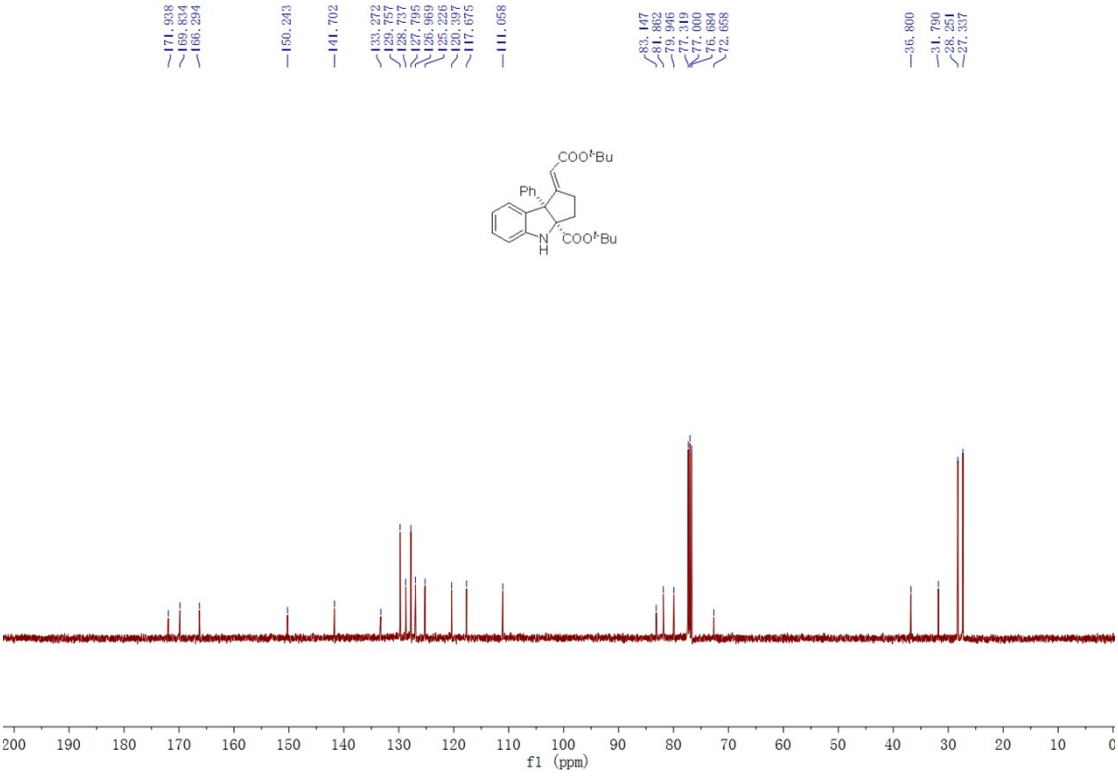
3.030
2.624
2.603
2.569
2.548
2.102
2.090
2.069
2.049
2.036
1.458
1.023
0.000
COO^{t}Bu
Ph
N
H
COO^{t}Bu
3.39
3.15
1.06
2.05
0.97
0.85
1.06
1.03
1.03
1.03
9.00
8.95
f1 (ppm)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126.969
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111.058
83.147
81.862
79.946
77.319
77.000
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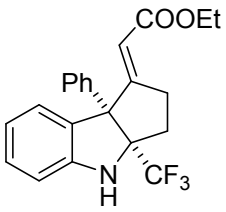
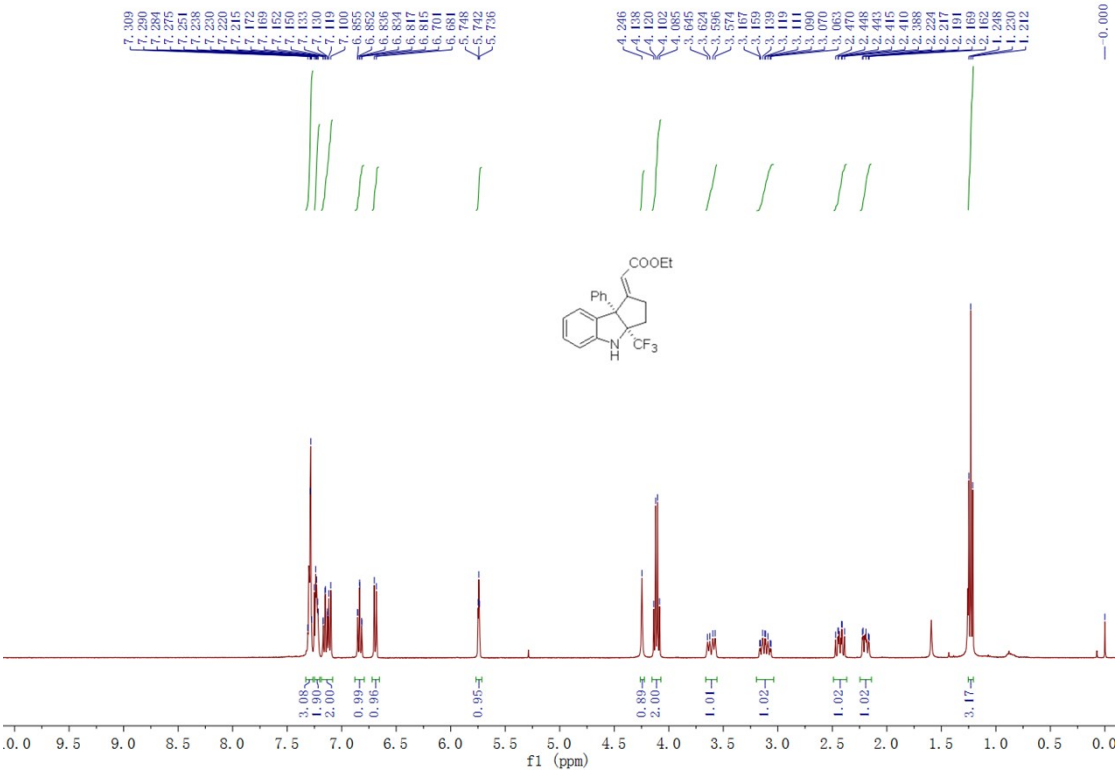
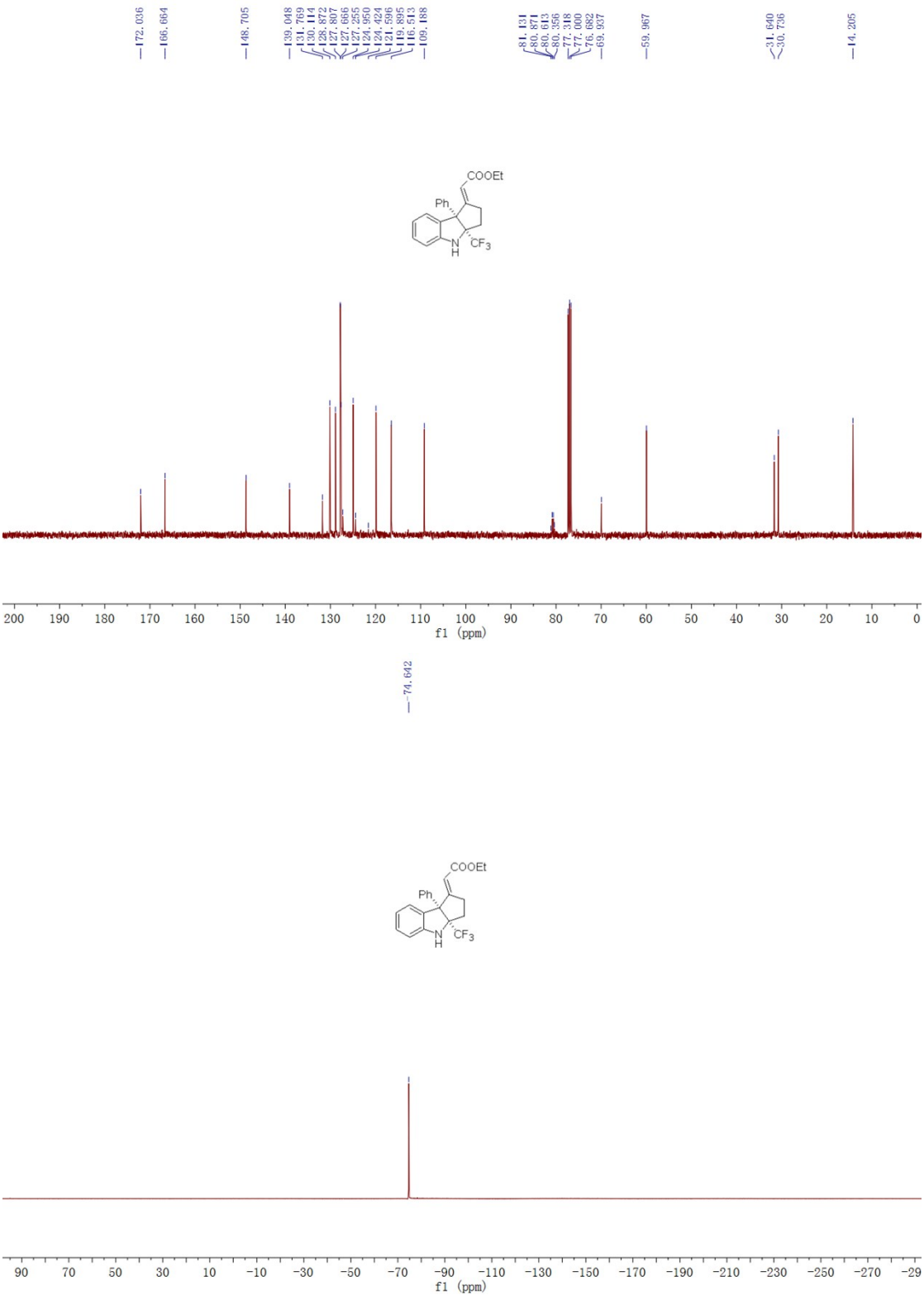
COO^{t}Bu
Ph
N
H
COO^{t}Bu
f1 (ppm)



ethyl-(*E*)-2-(8*b*-phenyl-3*a*-(trifluoromethyl)-3,3*a*,4,8*b*-tetrahydrocyclopenta[*b*]indol-1(2*H*)-ylidene)acetate 4y

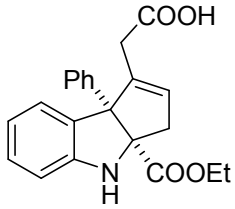
0.3 mmol scale, a white solid, 67% yield (77.8 mg). M.p.: 54-57 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.23 (t, *J* = 7.2 Hz, 3H), 2.16-2.23 (m, 1H), 2.38-2.47 (m, 1H), 3.06-3.17 (m, 1H), 3.57-3.65 (m, 1H), 4.11 (q, *J* = 7.2 Hz, 2H), 4.25 (s, 1H), 5.74 (t, *J* = 2.4 Hz, 1H), 6.69 (d, *J* = 8.0 Hz, 1H), 6.81-6.86 (m, 1H), 7.11 (d, *J* = 7.6 Hz, 1H), 7.13-7.18 (m, 1H), 7.21-7.24 (m, 2H), 7.27-7.31 (m, 3H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 14.2, 30.7, 31.6, 60.0, 69.9, 80.7 (q, *J* = 25.7 Hz), 109.2, 116.5, 119.9, 125.0, 125.8 (q, *J* = 282.8 Hz), 127.3, 127.7, 127.8, 128.9, 130.1, 131.8, 139.0, 148.7, 166.7, 172.0. ^{19}F NMR ($CDCl_3$, $CFCl_3$, 376 MHz) δ -74.6. IR (neat) ν 3347, 3056, 3025, 2972, 2936, 2895, 1698, 1648, 1606, 1481, 1454, 1418, 1371, 1347, 1291, 1270, 1222, 1189, 1163, 1150, 1122, 1110, 1072, 1041, 990, 927, 878, 804, 750, 723, 700 cm^{-1}. HRMS (ESI) Calcd. for $C_{22}H_{21}NO_2F_3^{+1}(M+H)^+$ requires: 388.1519, found: 388.1517.





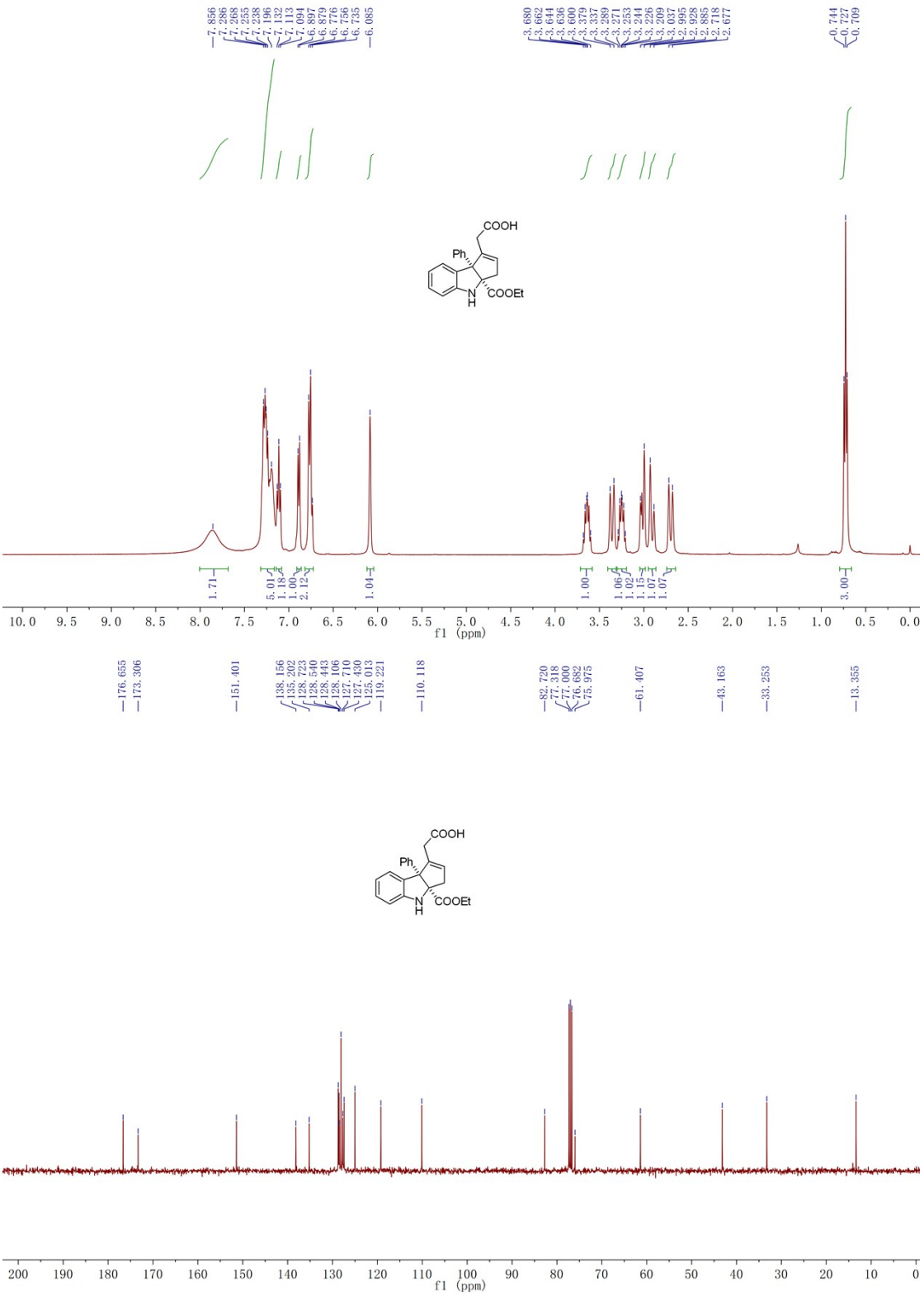
8. General procedure for the synthesis of 5-10, 3A1*, 3A2*, 11*, 4A1*, 4A2*, and 8* and their characterization and spectra charts

To a solution of **4a** (1.2 mmol, 1.0 equiv.) and LiOH (6.0 mmol, 5.0 equiv.) in MeOH (30 mL) was refluxed for 5 hours at 80 °C under argon. The solvent was removed under vacuum and the residue was purified by a silica gel column chromatography (PE/EA = 8/1) to give the desired product **5** as a brown solid.



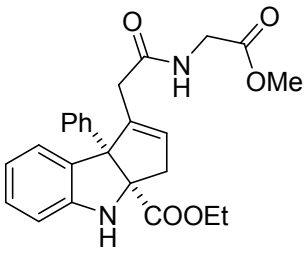
2-(-3*a*-(ethoxycarbonyl)-8*b*-phenyl-3,3*a*,4,8*b*-tetrahydrocyclopenta[*b*]indol-1-yl)acetic acid 5

1.2 mmol scale, a brown solid, 87% yield (380.0 mg). M.p.: 157-159 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.73 (t, *J* = 6.8 Hz, 3H), 2.70 (d, *J* = 16.4 Hz, 1H), 2.91 (d, *J* = 17.2 Hz, 1H), 3.02 (d, *J* = 17.2 Hz, 1H), 3.21-3.29 (m, 1H), 3.36 (d, *J* = 16.4 Hz, 1H), 3.60-3.68 (m, 1H), 6.09 (s, 1H), 6.73-6.78 (m, 2H), 6.89 (d, *J* = 7.6 Hz, 1H), 7.11 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 7.19-7.29 (m, 5H), 7.86 (br, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.4, 33.3, 43.2, 61.4, 76.0, 82.7, 110.1, 119.2, 125.0, 127.4, 127.7, 128.1, 128.4, 128.5, 128.7, 135.2, 138.2, 151.4, 173.3, 176.7. IR (neat) ν 3376, 3081, 3053, 3028, 2982, 2925, 2898, 1709, 1604, 1484, 1466, 1446, 1400, 1366, 1261, 1227, 1197, 1065, 1034, 934, 859, 809, 749, 735, 701 cm^{-1}. HRMS (ESI) Calcd. for $C_{22}H_{22}NO_4^{+1}(M+H)^+$ requires: 364.1543, found: 364.1537.



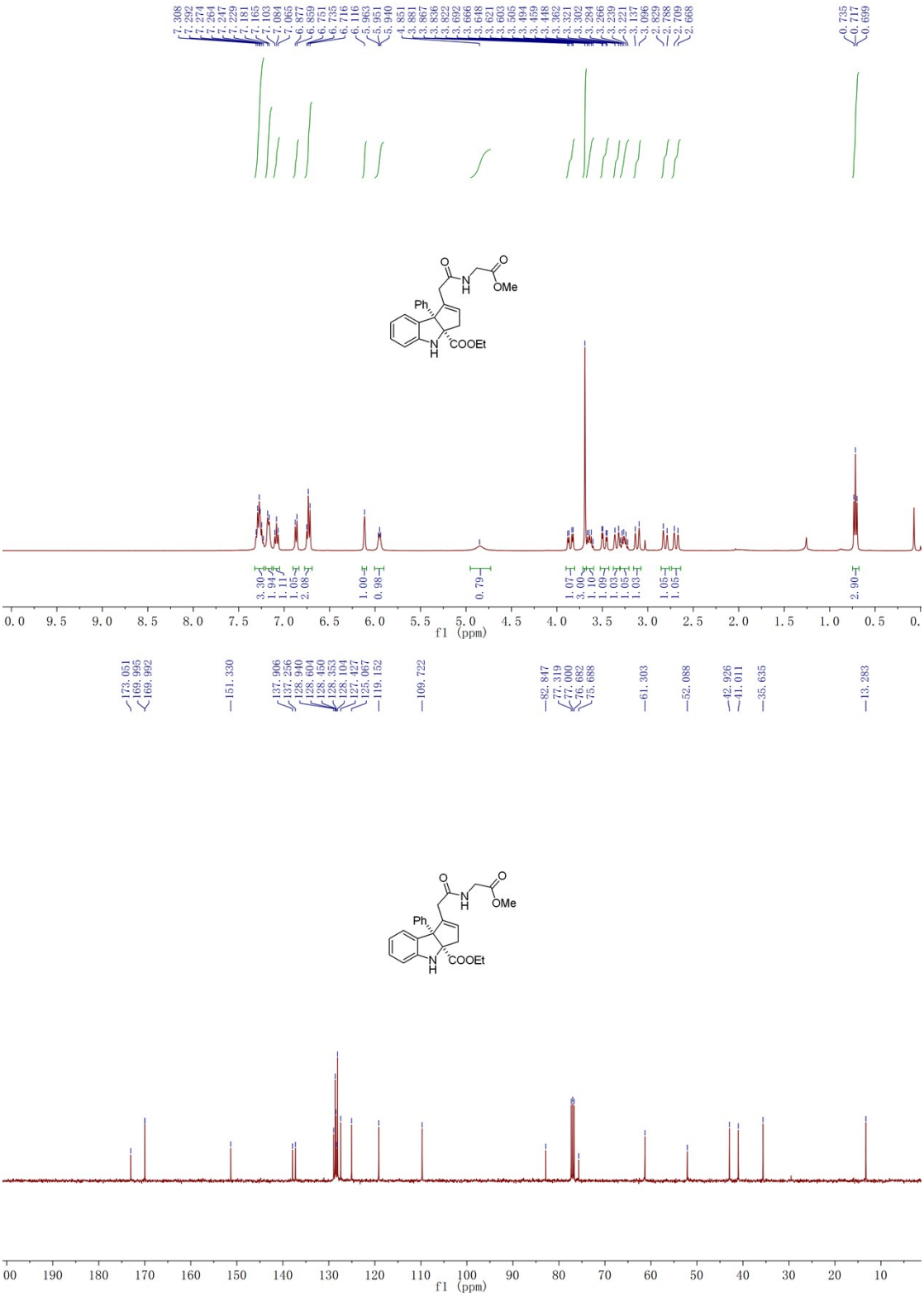
To a reaction tube was added **5** (0.2 mmol, 1.0 equiv.), EDCI (0.4 mmol, 2.0 equiv.), HOBt (0.6 mmol, 3.0 equiv.), Et_3N (0.5 mmol, 2.5 equiv.) and DMF (3.0 mL) at 0 °C for 15 min. Then, the glucine methyl ester hydrochloride (0.3 mmol, 1.5 equiv.) in 2 mL DMF was added at 0 °C.

The resulting mixture was allowed to warm to room temperature and was stirred for 12 hours. Next, the reaction was quenched by water (10 mL) and extracted with ethyl acetate (15 mL x 3). The combined organic collection was washed with brine (30 mL), and then dried over $NaSO_4$. The solvent was removed under reduced pressure and the residue was purified by a flash column chromatography on silica gel (PE/EA: 2:1) to give the desired products **6** as a light red solid.



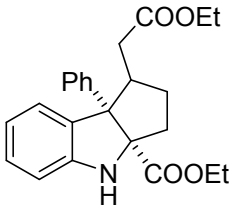
ethyl-1-(2-((2-methoxy-2-oxoethyl)amino)-2-oxoethyl)-8*b*-phenyl-4,8*b*-dihydrocyclopenta[*b*]indole-3*a*(3*H*)-carboxylate 6

0.2 mmol scale, a light red solid, 88% yield (76.4 mg). M.p.: 142-144 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.72 (t, *J* = 7.2 Hz, 3H), 2.69 (d, *J* = 16.4 Hz, 1H), 2.81 (d, *J* = 16.4 Hz, 1H), 3.12 (d, *J* = 16.4 Hz, 1H), 3.22-3.33 (m, 1H), 3.34 (d, *J* = 16.4 Hz, 1H), 3.48 (dd, *J* = 4.4 Hz, 18.4 Hz, 1H), 3.60-3.67 (m, 1H), 3.69 (s, 3H), 3.85 (dd, *J* = 5.6 Hz, 18.4 Hz, 1H), 4.85 (br, 1H), 5.95 (t, *J* = 4.4 Hz, 1H), 6.12 (s, 1H), 6.71-6.76 (m, 2H), 6.87 (d, *J* = 7.2 Hz, 1H), 7.08 (dd, *J* = 7.6 Hz, 7.6 Hz, 1H), 7.16-7.19 (m, 2H), 7.22-7.31 (m, 3H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.3, 35.6, 41.0, 42.9, 52.1, 61.3, 75.7, 82.8, 109.7, 119.2, 125.1, 127.4, 128.1, 128.4, 128.5, 128.6, 128.9, 137.3, 137.9, 151.3, 169.992, 169.995, 173.1. IR (neat) ν 3364, 3305, 3083, 3055, 3023, 2979, 2953, 2928, 2899, 2848, 1747, 1723, 1666, 1604, 1525, 1484, 1466, 1437, 1405, 1367, 1261, 1198, 1176, 1101, 1066, 1034, 1011, 936, 859, 802, 735, 701 cm^{-1}. HRMS (ESI) Calcd. for $C_{25}H_{27}N_2O_5^{+1}(M+H)^+$ requires: 435.1914, found: 435.1909.



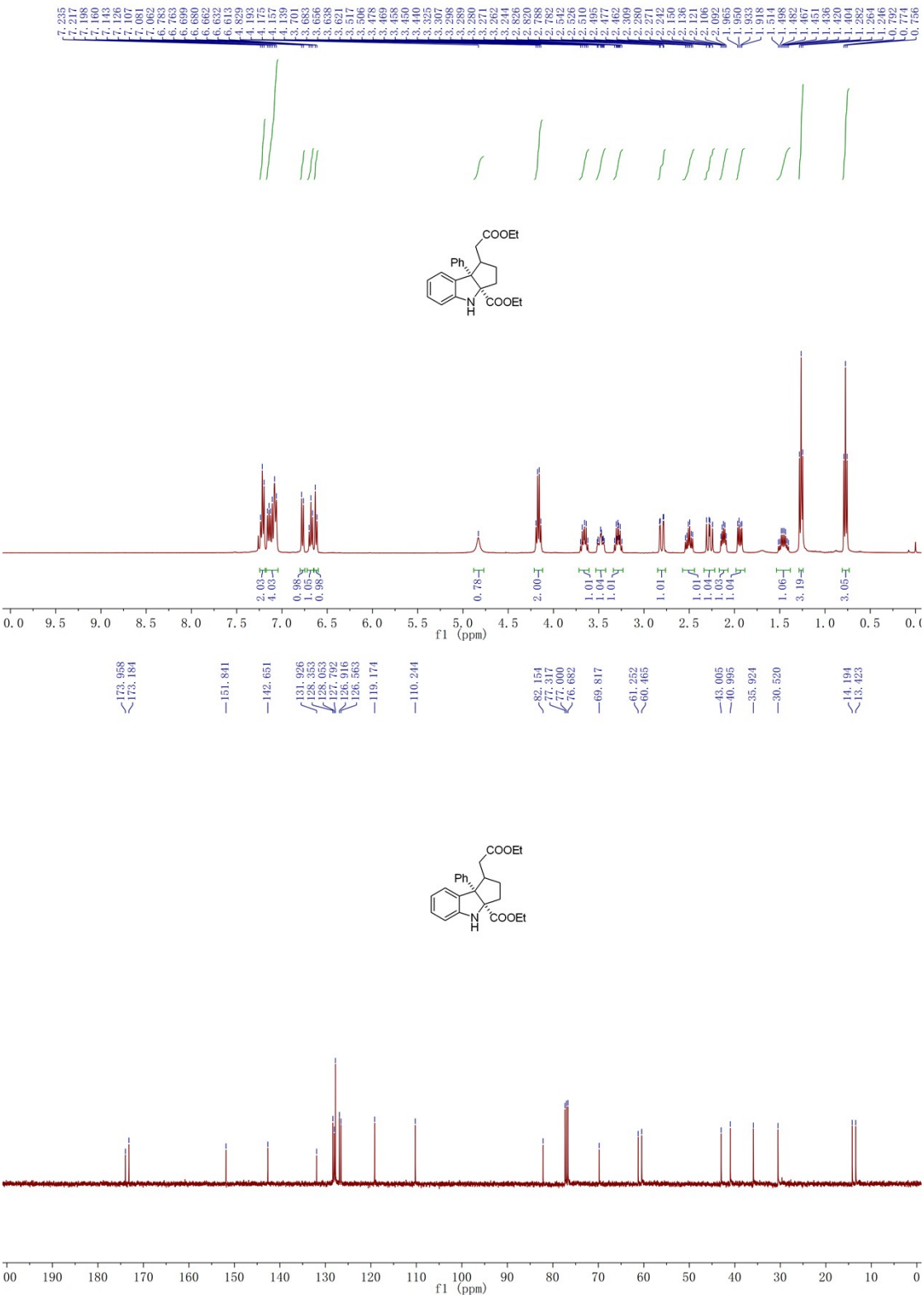
To a Schlenk tube was added **4a** (0.5 mmol) and Pd/C (0.05 mmol) and MeOH (1.0 mL). Then, the resulting solution was evacuated and backfilled with H_2 for 3 times and stirred at 25 ^oC for 48 h under H_2. The solvent was removed under vacuum and the residue was purified by a silica gel

column chromatography (PE/EA = 8/1) to give the desired product **7** as a yellow liquid.



ethyl-1-(2-ethoxy-2-oxoethyl)-8*b*-phenyl-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 7

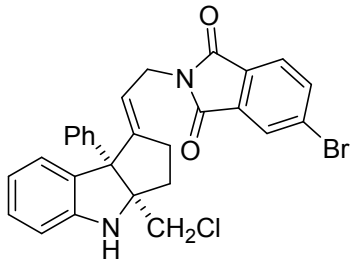
0.5 mmol scale, a yellow liquid, 60% yield (117.9 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.77 (t, *J* = 7.2 Hz, 3H), 1.26 (t, *J* = 7.2 Hz, 3H), 1.40-1.51 (m, 1H), 1.94 (dd, *J* = 6.0 Hz, 12.8 Hz, 1H), 2.09-2.15 (m, 1H), 2.28 (dd, *J* = 11.6 Hz, 15.2 Hz, 1H), 2.46-2.55 (m, 1H), 2.80 (dd, *J* = 2.4 Hz, 15.2 Hz, 1H), 3.24-3.33 (m, 1H), 3.44-3.52 (m, 1H), 3.62-3.70 (m, 1H), 4.17 (q, *J* = 7.2 Hz, 2H), 4.83 (br, 1H), 6.62 (d, *J* = 7.6 Hz, 1H), 6.68 (t, *J* = 7.6 Hz, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 7.06-7.16 (m, 4H), 6.19-7.24 (m, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 13.4, 14.2, 30.5, 35.9, 41.0, 43.0, 60.5, 61.3, 69.8, 82.2, 110.2, 119.2, 126.6, 126.9, 127.8, 128.1, 128.4, 131.9, 142.7, 151.8, 173.2, 174.0. IR (neat) ν 3364, 3089, 3053, 3034, 2977, 2956, 2939, 2900, 2869, 1724, 1603, 1486, 1465, 1444, 1367, 1300, 1280, 1255, 1211, 1157, 1092, 1058, 1029, 859, 740, 698 cm^{-1}. HRMS (ESI) Calcd. for $C_{24}H_{28}NO_4^{+1}$(M+H)$^+$ requires: 394.2013, found: 394.2007.



To a solution of **4a** (0.5 mmol, 1.0 eq) in dry THF was added dropwise into a solution of $LiAlH_4$ (3 mmol, 6.0 eq) in THF while the temperature was maintained at 0 °C. The resulting mixture was allowed to warm to room temperature and was stirred for 2 hours. Then the mixture

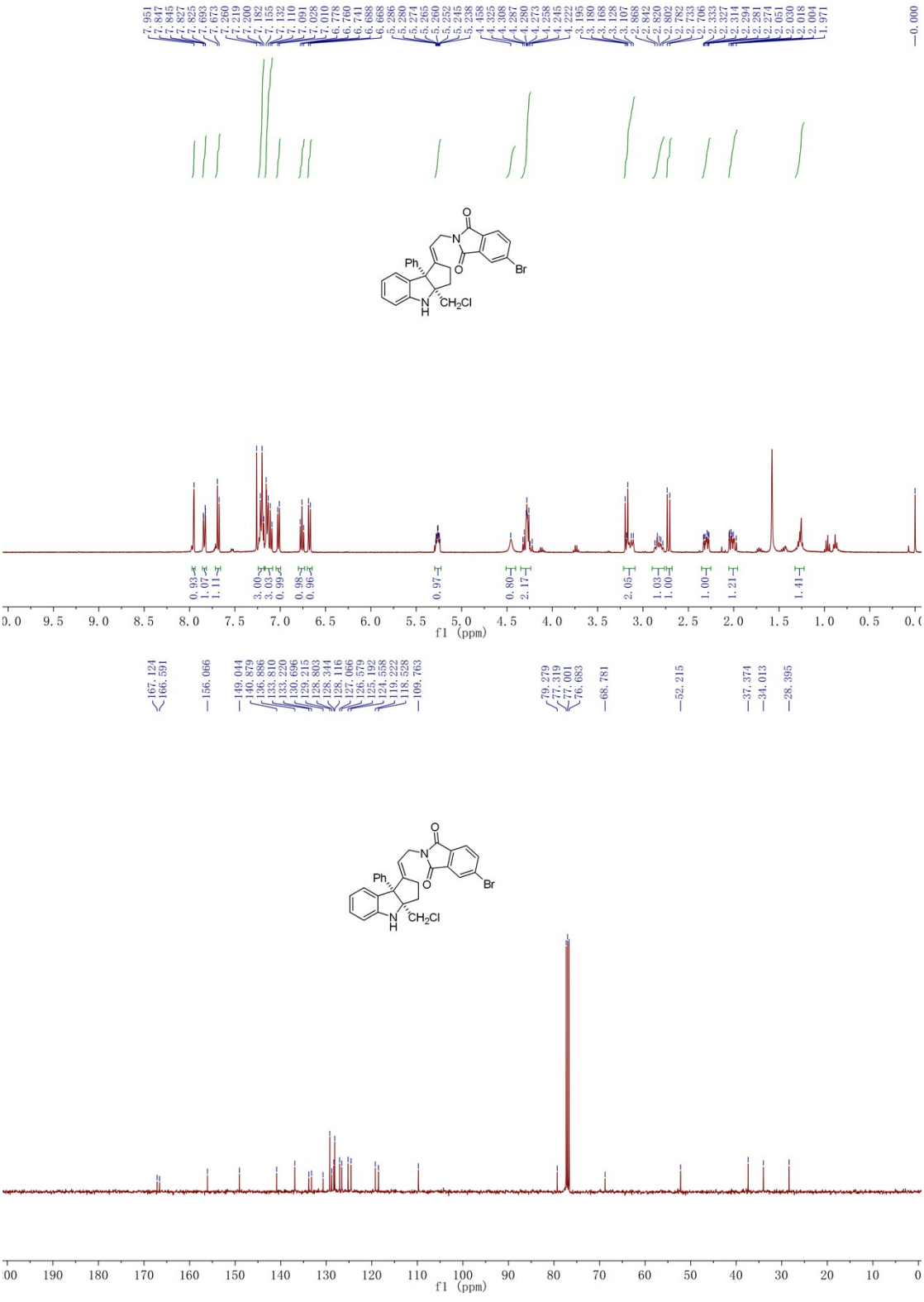
was hydrolyzed by addition of H_2O (0.5 mL) and 5% NaOH (0.5 mL). The resulting suspension was filtered, and the precipitate was washed with ethyl acetate. Next, the solvent was removed under vacuum and the residue was purified by a silica gel column chromatography (PE/EA = 8/1) to give the desired product **8** as a white solid in 89% yield.

To a solution of **8** (0.1 mmol, 1.0 equiv.), 5-bromoisoindoline-1,3-dione (0.11 mmol, 1.1 equiv.), LiCl (0.11 mmol, 1.1 equiv.), and triphenylphosphine (0.25 mmol, 2.5 equiv.) in THF (5 mL), (2.5 mmol, 1.2 equiv.) DEAD was added dropwise at 0 °C. The resulting mixture was allowed to warm to room temperature and was stirred for 12 hours. Then, the resulting solution was concentrated in vacuum and the residue was purified by a silica gel flash chromatography PE/EA = 8/1) to give product **9** as a white solid.



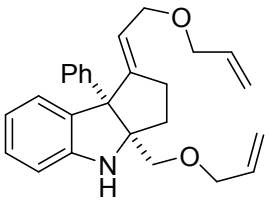
5-bromo-2-((*E*)-2-(-3*a*-(chloromethyl)-8*b*-phenyl-3,3*a*,4,8*b*-tetrahydrocyclopenta[*b*]indol-1(2*H*)-ylidene)ethyl)isoindoline-1,3-dione 9

0.1 mmol scale, a white solid, 32% yield (17.5 mg). M.p.: 181-183 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.97-2.05 (m, 1H), 2.27-2.33 (m, 1H), 2.72 (d, *J* = 10.8 Hz, 1H), 2.78-2.87 (m, 1H), 3.10-3.18 (m, 1H), 3.18 (d, *J* = 10.8 Hz, 1H), 4.22-4.33 (m, 2H), 4.46 (br, 1H), 5.23-5.29 (m, 1H), 6.68 (d, *J* = 8.0 Hz, 1H), 6.76 (t, *J* = 7.2 Hz, 1H), 7.02 (d, *J* = 7.2 Hz, 1H), 7.09-7.16 (m, 3H), 7.18-7.22 (m, 3H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.82-7.85 (m, 1H), 7.95 (s, 1H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 28.4, 34.0, 37.4, 52.2, 68.8, 79.3, 109.8, 118.5, 119.2, 124.6, 125.2, 126.6, 127.1, 128.1, 128.3, 128.8, 129.2, 130.7, 133.2, 133.8, 136.9, 140.9, 149.0, 156.1, 166.6, 167.1. IR (neat) ν 3367, 3093, 3052, 3026, 2959, 2922, 2851, 1772, 1713, 1604, 1482, 1464, 1431, 1417, 1387, 1355, 1326, 1262, 1229, 1186, 1168, 1101, 1079, 1048, 947, 894, 842, 795, 738, 703, 662 cm^{-1}. HRMS (ESI) Calcd. for $C_{28}H_{23}BrClN_2O_4^{+1}(M+H)^+$ requires: 533.0626, found: 533.0627.



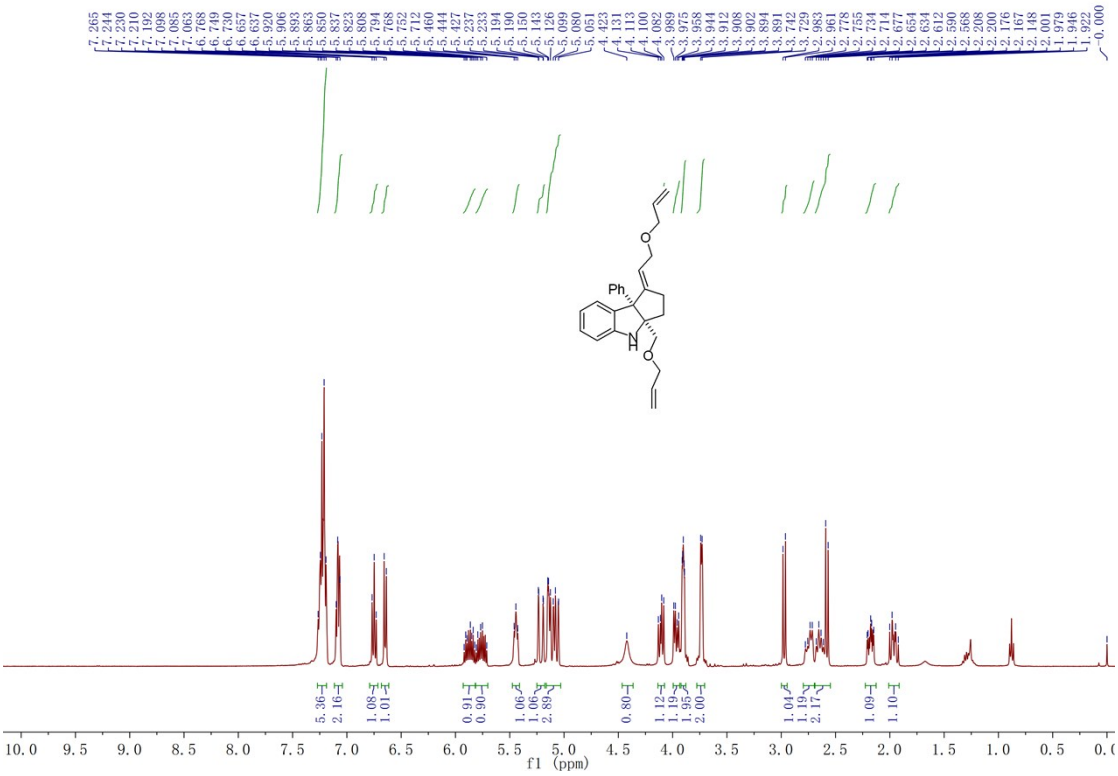
To a flame dried Schlenk tube was added **8** (1.0 mmol, 1.0 equiv.), NaH (2.3 mmol, 2.3 equiv.) and THF (30.0 mL) under Argon at 0 °C for 0.5 h. Then, the 3-bromoprop-1-ene (2.5 mmol, 2.5 equiv.) was added at 0 °C. The resulting mixture was allowed to warm to room temperature and

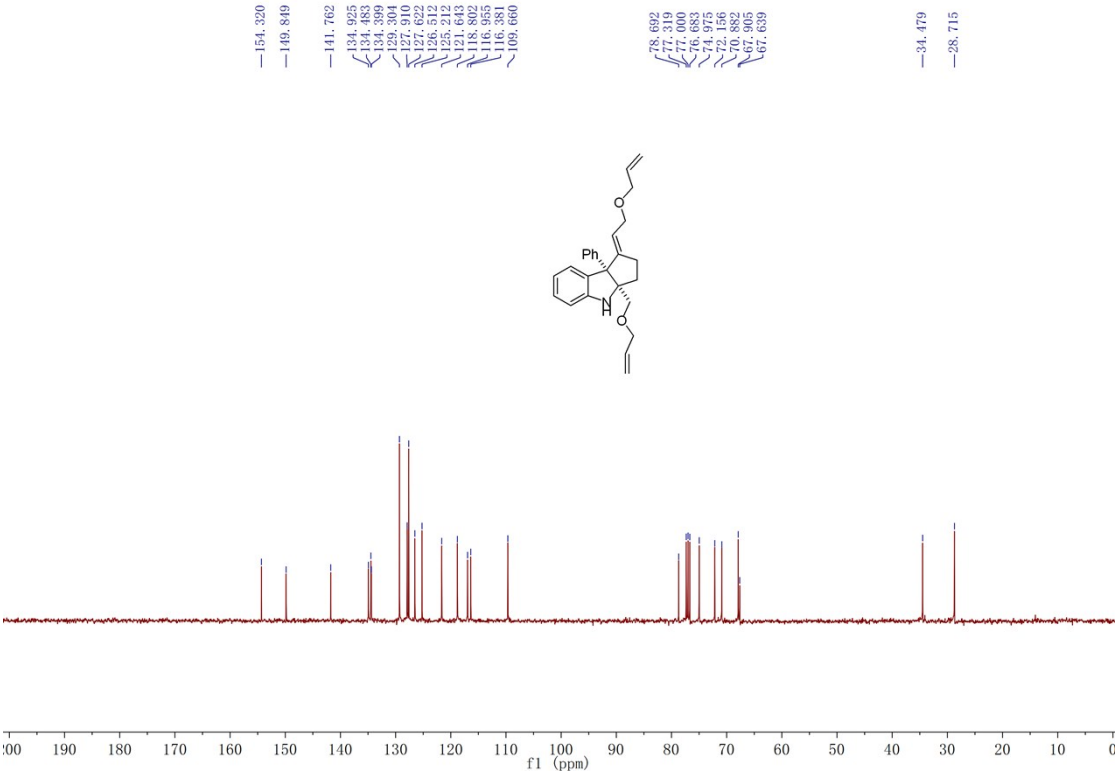
was stirred for 2 hours. Next, the reaction was quenched by water (10 mL) and extracted with ethyl acetate (15 mL x 3). The combined organic collection was washed with brine (30 mL), and then dried over $NaSO_4$. The solvent was removed under reduced pressure and the residue was purified by a flash column chromatography on silica gel (PE/EA: 40:1) to give the desired product **10** as a colorless oil.



(*E*)-1-(2-(allyloxy)ethylidene)-3*a*-((allyloxy)methyl)-8*b*-phenyl-1,2,3,3*a*,4,8*b*-hexahydrocyclopenta[*b*]indole 10

1.0 mmol scale, a colorless oil, 64% yield (247.1 mg). ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.92-2.01 (m, 1H), 2.14-2.21 (m, 1H), 2.58 (d, *J* = 8.8 Hz, 1H), 2.61-2.68 (m, 1H), 2.71-2.78 (m, 1H), 2.97 (d, *J* = 8.8 Hz, 1H), 3.72-3.75 (m, 2H), 3.89-3.92 (m, 2H), 3.97 (dd, *J* = 5.6 Hz, 12.4 Hz, 1H), 4.11 (dd, *J* = 7.2 Hz, 12.4 Hz, 1H), 4.42 (br, 1H), 5.05-5.15 (m, 3H), 5.19-5.24 (m, 1H), 5.42-5.46 (m, 1H), 5.71-5.81 (m, 1H), 5.82-5.92 (m, 1H), 6.65 (d, *J* = 8.0 Hz, 1H), 6.75 (t, *J* = 7.6 Hz, 1H), 7.06-7.10 (m, 2H), 7.19-7.27 (m, 5H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 28.7, 34.5, 67.6, 67.9, 70.9, 72.2, 75.0, 78.7, 109.7, 116.4, 117.0, 118.8, 121.6, 125.2, 126.5, 127.6, 127.9, 129.3, 134.4, 134.5, 134.9, 141.8, 149.8, 154.3. IR (neat) ν 3376, 3077, 3054, 3029, 2959, 2917, 2853, 1727, 1645, 1603, 1481, 1464, 1446, 1425, 1383, 1347, 1320, 1308, 1253, 1185, 1079, 1008, 990, 926, 792, 741, 702 cm^{-1}. HRMS (ESI) Calcd. for $C_{26}H_{30}NO_2^{+1}(M+H)^+$ requires: 388.2271, found: 388.2266.


7.265 7.244 7.230 7.210 7.192 7.098 7.085 7.063 6.768 6.749 6.730 6.657 6.637 6.920 5.906 5.893 5.863 5.850 5.837 5.823 5.808 5.794 5.768 5.752 5.712 5.460 5.444 5.427 5.237 5.233 5.194 5.190 5.150 5.143 5.126 5.089 5.051 4.423 4.131 4.113 4.100 4.082 3.989 3.975 3.958 3.944 3.912 3.908 3.902 3.894 3.891 3.742 3.729 2.983 2.961 2.778 2.755 2.734 2.714 2.677 2.654 2.634 2.612 2.590 2.568 2.208 2.200 2.176 2.167 2.148 2.001 1.979 1.946 1.922 0.000
Ph
N
O
5.36 2.16 1.08 1.01 0.91 0.90 1.06 1.06 2.89 0.80 1.12 1.19 1.95 2.00 1.04 1.19 2.17 1.09 1.10
f1 (ppm)


154.320 149.849 141.762 134.925 134.483 134.399 129.304 127.910 127.622 126.512 125.212 121.643 118.802 116.955 116.381 109.660
78.692 77.319 77.000 76.683 74.975 72.156 70.882 67.905 67.639
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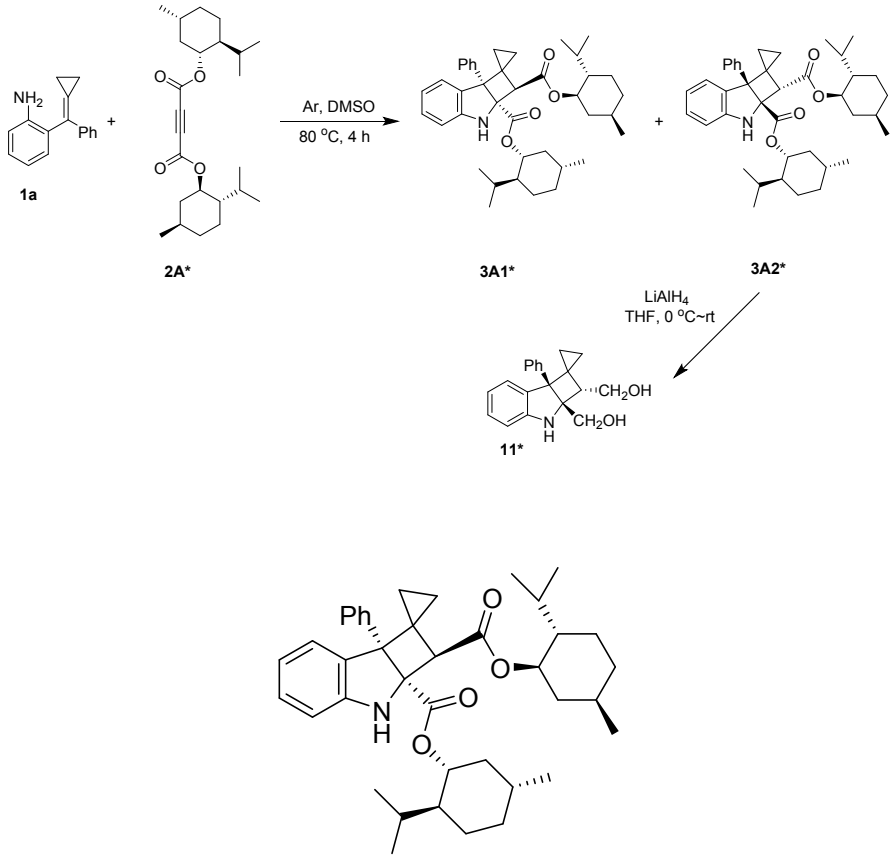
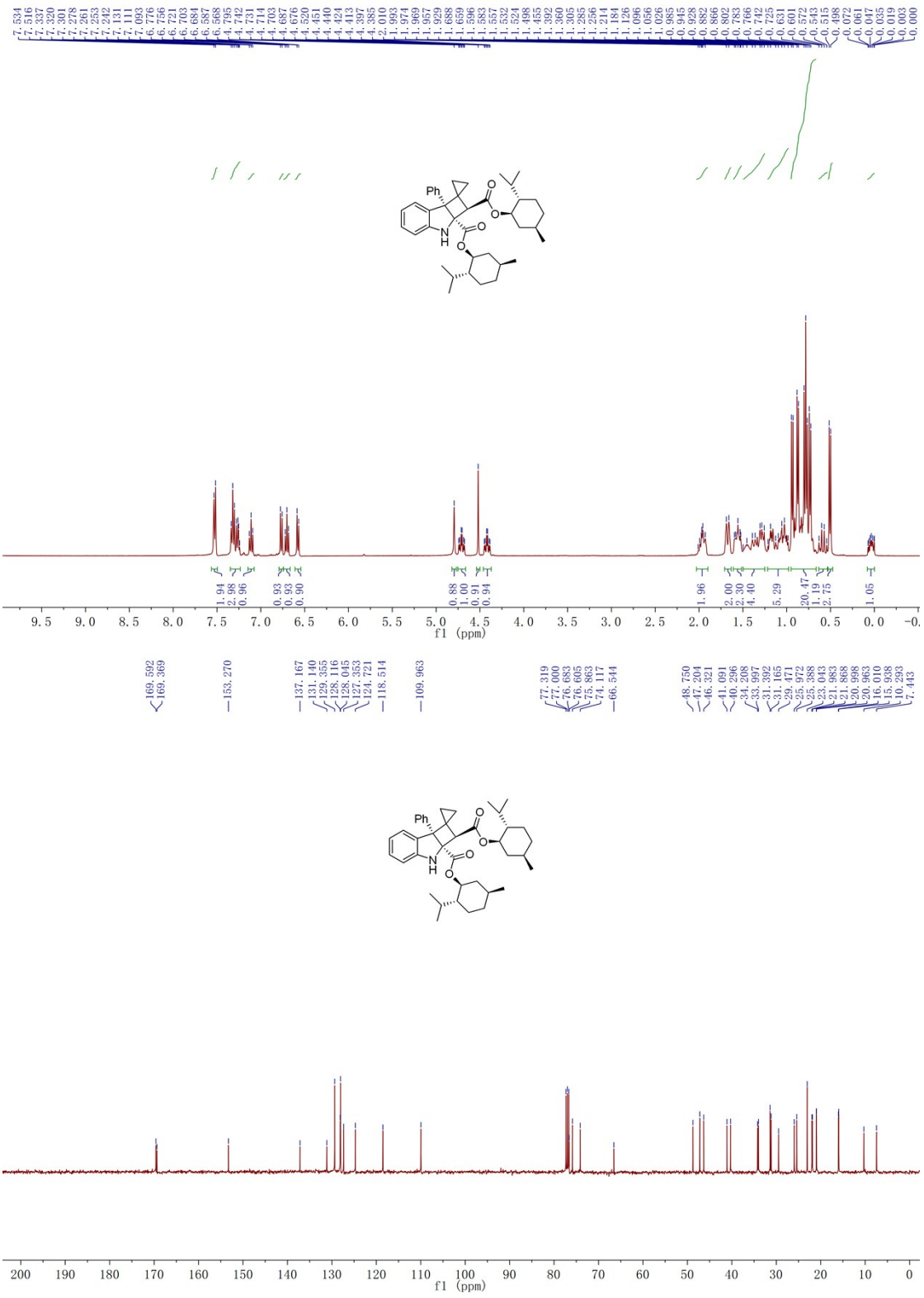
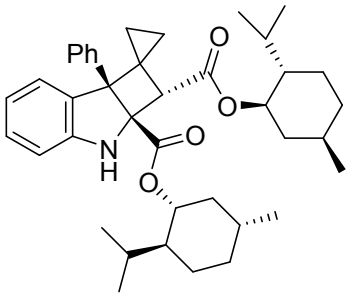
Ph
N
O
f1 (ppm)



bis((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl)(2*R*,2*aR*,7*bS*)-7*b*-phenyl-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3A1*

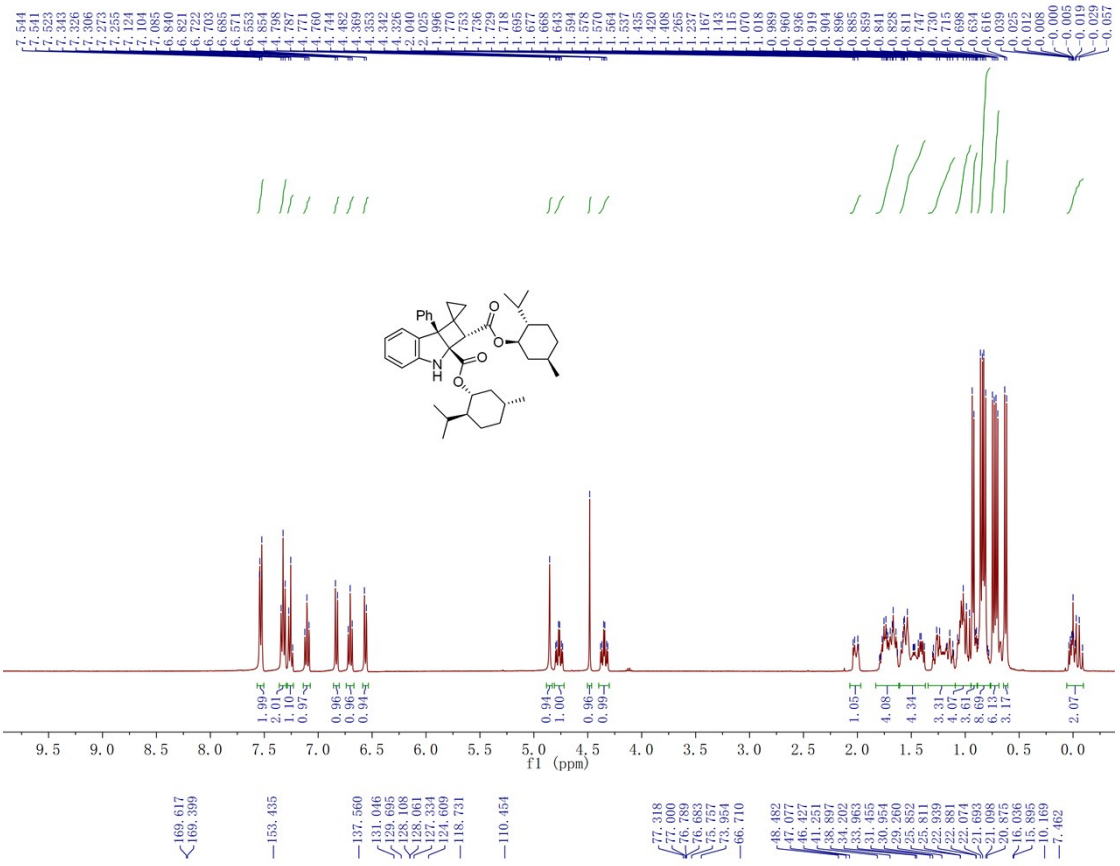
1.5 mmol scale, a white solid, 48% yield (439.9 mg). M.p.: 68-70 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.01-0.08 (m, 1H), 0.51 (d, *J* = 6.8 Hz, 3H), 0.54-0.64 (m, 1H), 0.72-0.95 (m, 20H), 0.98-1.22 (m, 5H), 1.25-1.50 (m, 4H), 1.52-1.60 (m, 2H), 1.65-1.69 (m, 2H), 1.92-2.01 (m, 2H), 4.42 (ddd, *J* = 4.8 Hz, 11.2 Hz, 15.6 Hz, 1H), 4.52 (s, 1H), 4.71 (ddd, *J* = 4.4 Hz, 10.8 Hz, 15.2 Hz, 1H), 4.80 (s, 1H), 6.58 (d, *J* = 7.6 Hz, 1H), 6.70 (t, *J* = 7.6 Hz, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 7.11 (t, *J* = 7.6 Hz, 1H), 7.24-7.34 (m, 3H), 7.53 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.4, 10.3, 15.9, 16.0, 20.96, 21.00, 21.9, 22.0, 23.0, 25.4, 26.0, 29.5, 31.2, 31.4, 34.0, 34.2, 40.3, 41.1, 46.3, 47.2, 48.8, 66.5, 74.1, 75.9, 76.6, 110.0, 118.5, 124.7, 127.4, 128.0, 128.1, 129.4, 131.1, 137.2, 153.3, 169.4, 169.6. IR (neat) ν 3375, 3089, 3056, 3031, 2952, 2925, 2867, 1718, 1606, 1495, 1484, 1465, 1386, 1369, 1320, 1278, 1253, 1179, 1151, 1080, 1065, 1037, 1026, 1003, 981, 954, 913, 844, 743, 716, 699 cm^{-1}. HRMS (ESI) Calcd. for $C_{40}H_{54}NO_4^{+1}$(M+H)$^+$ requires: 612.4047, found: 612.4041. $[\alpha]_D^{20}$ = -83.4 (c = 0.100, CH_2Cl_2).

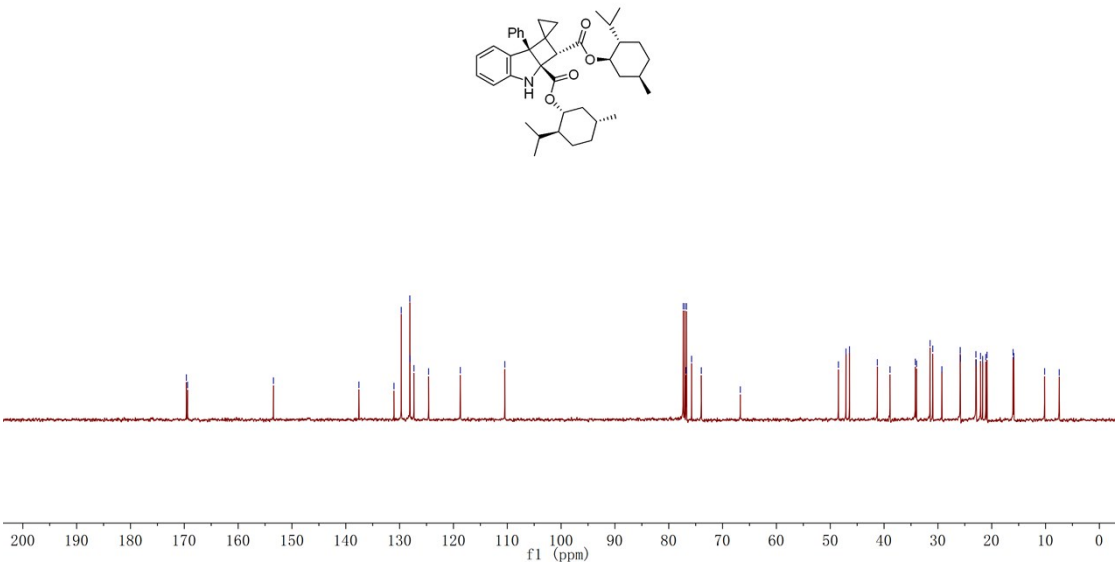


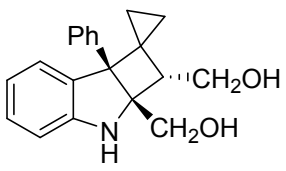


bis((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl)(2*S*,2*aS*,7*bR*)-7*b*-phenyl-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropane]-2,2*a*(2*H*)-dicarboxylate 3A2*

1.5 mmol scale, a white solid, 49% yield (449.1 mg). M.p.: 67-70 ^{o}C.^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ -0.09-0.04 (m, 2H), 0.63 (d, *J* = 7.2 Hz, 3H), 0.71 (d, *J* = 7.2 Hz, 3H), 0.74 (d, *J* = 7.2 Hz, 3H), 0.78-0.89 (m, 4H), 0.96-1.07 (m, 4H), 1.10-1.31 (m, 3H), 1.37-1.59 (m, 4H), 1.62-1.80 (m, 4H), 1.99-2.04 (m, 1H), 4.35 (ddd, *J* = 4.4 Hz, 10.8 Hz, 15.2 Hz, 1H), 4.48 (s, 1H), 4.77 (ddd, *J* = 4.4 Hz, 10.8 Hz, 15.2 Hz, 1H), 4.85 (s, 1H), 6.56 (d, *J* = 7.2 Hz, 1H), 6.70 (t, *J* = 7.6 Hz, 1H), 6.83 (d, *J* = 7.6 Hz, 1H), 7.08-7.13 (m, 1H), 7.23-7.28 (m, 1H), 7.30-7.35 (m, 2H), 7.52-7.55 (m, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.5, 10.2, 15.9, 16.0, 20.9, 21.1, 21.7, 22.1, 22.9, 23.0, 25.8, 25.9, 29.3, 31.0, 31.5, 34.0, 34.2, 38.9, 41.3, 46.4, 47.1, 48.5, 66.7, 74.0, 75.8, 76.8, 110.5, 118.7, 124.6, 127.3, 128.06, 128.11, 129.7, 131.0, 137.6, 153.4, 169.4, 169.6. IR (neat) ν 3372, 3089, 3059, 3031, 2954, 2927, 2868, 1716, 1606, 1484, 1465, 1386, 1369, 1279, 1259, 1191, 1151, 1065, 1037, 1026, 982, 955, 913, 841, 744, 717, 699 cm^{-1}. HRMS (ESI) Calcd. for $C_{40}H_{54}NO_4^{+1}$(M+H)$^{+}$ requires: 612.4047, found: 612.4040. $[\alpha]_D^{20}$ = -31.1 (c = 0.100, CH_2Cl_2).



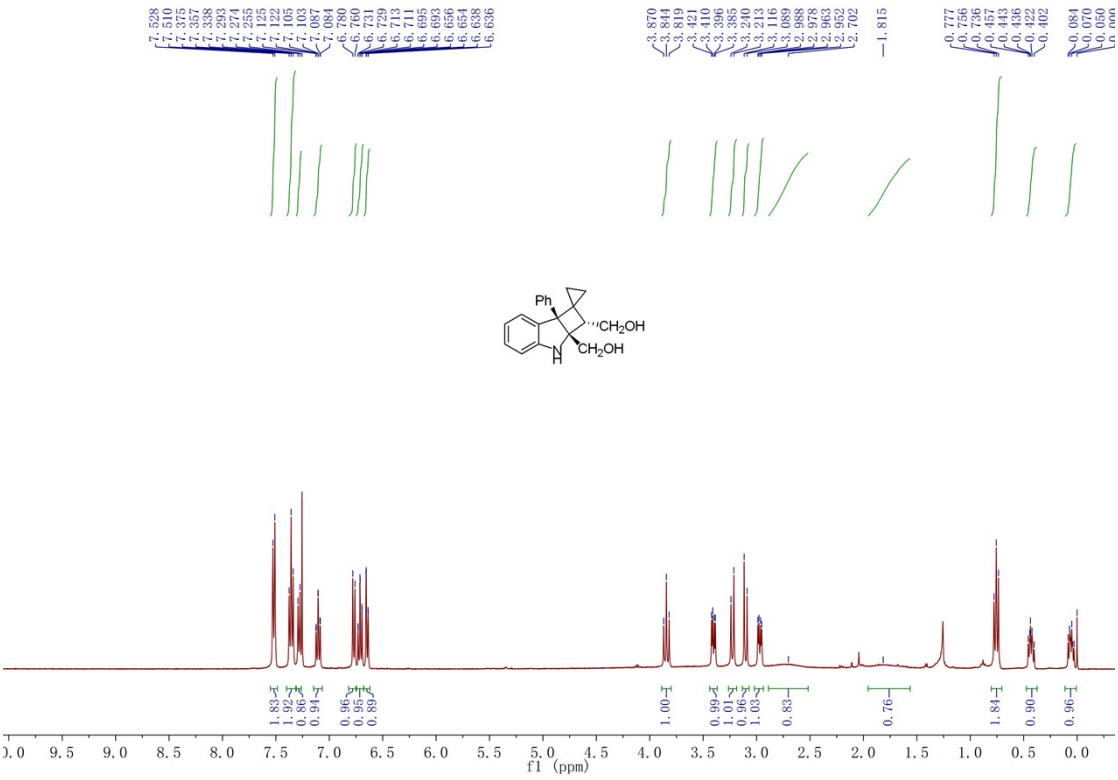


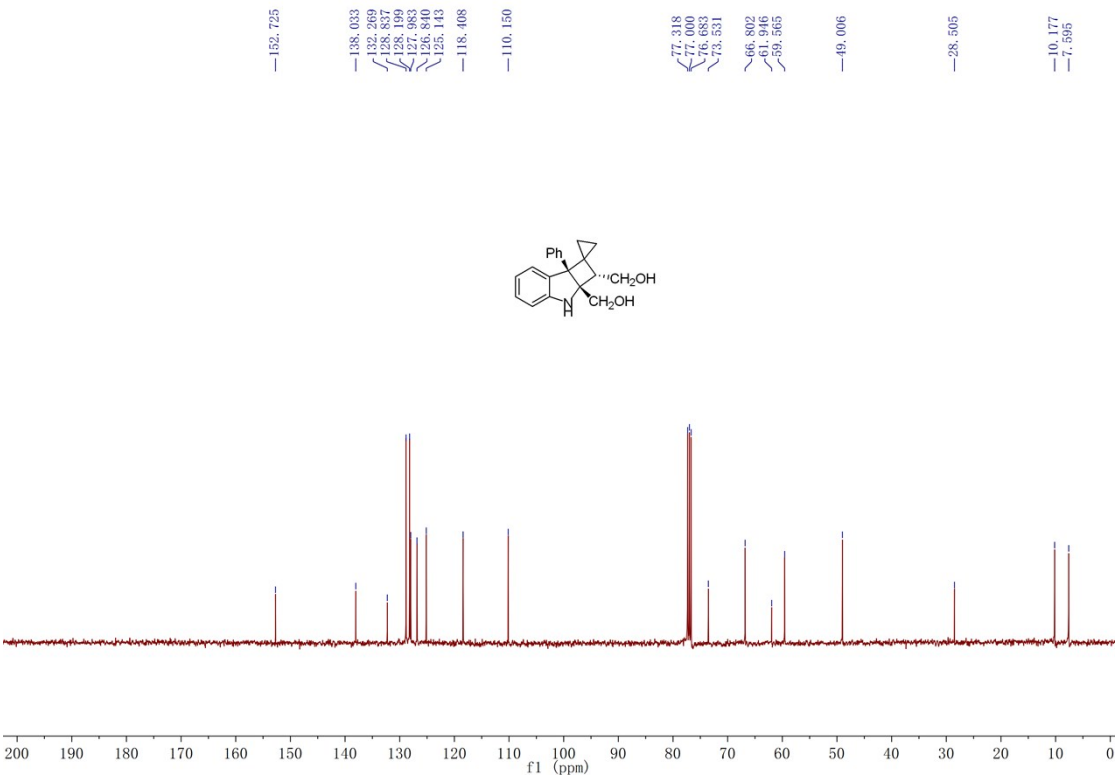


((2*S*,2*aS*,7*bR*)-7*b*-phenyl-3,7*b*-dihydrospiro[cyclobuta[*b*]indole-1,1'-cyclopropan]-2,2*a*(2*H*)-

diyl)dimethanol 11*

0.2 mmol scale, a brown solid, 48% yield (27.2 mg). M.p.: 147-149 °C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.02-0.09 (m, 1H), 0.40-0.46 (m, 1H), 0.76 (t, *J* = 8.0 Hz, 2H), 1.81 (br, 1H), 2.70 (br, 1H), 2.97 (dd, *J* = 8.0 Hz, 10.0 Hz, 1H), 3.10 (d, *J* = 10.8 Hz, 1H), 3.23 (d, *J* = 10.8 Hz, 1H), 3.40 (dd, *J* = 4.4 Hz, 10.0 Hz, 1H), 3.84 (t, *J* = 10.0 Hz, 1H), 6.65 (dd, *J* = 0.8 Hz, 7.2 Hz, 1H), 6.71 (dt, *J* = 0.8 Hz, 7.2 Hz, 1H), 6.77 (d, *J* = 8.0 Hz, 1H), 7.10 (dt, *J* = 1.2 Hz, 8.0 Hz, 1H), 7.25-7.30 (m, 1H), 7.33-7.38 (m, 2H), 7.52 (d, *J* = 7.2 Hz, 2H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 7.6, 10.2, 28.5, 49.0, 59.6, 61.9, 66.8, 73.5, 110.2, 118.4, 125.1, 126.8, 128.0, 128.2, 128.8, 132.3, 138.0, 152.7. IR (neat) ν 3358, 3067, 3023, 2995, 2926, 2878, 2853, 1644, 1604, 1481, 1463, 1445, 1414, 1393, 1322, 1261, 1244, 1150, 1091, 1019, 968, 944, 908, 884, 800, 736, 747, 705 cm^{-1}. HRMS (ESI) Calcd. for $C_{20}H_{22}NO_2^{+1}$(M+H)$^+$ requires: 308.1645, found: 308.1641. $[\alpha]_D^{20}$ = +73.2 (c = 0.100, CH_2Cl_2).

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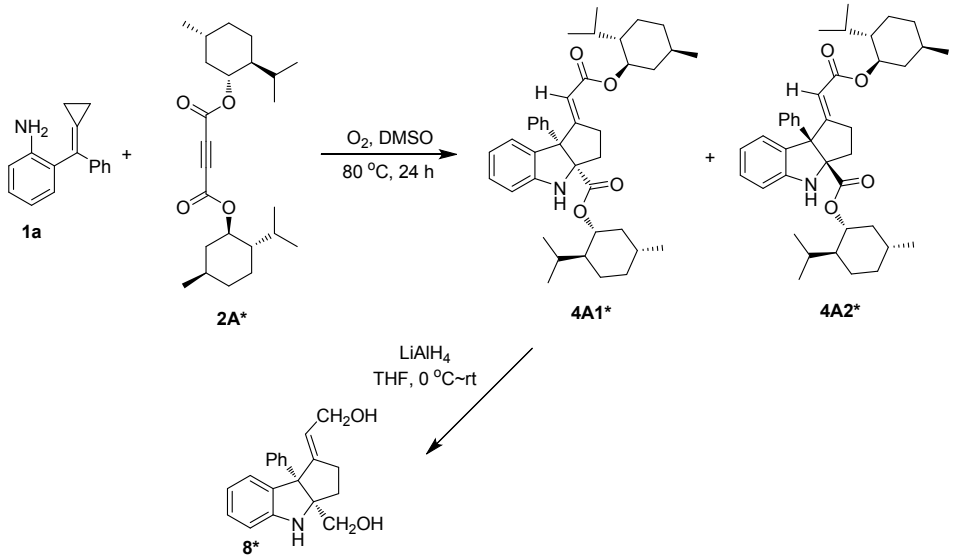
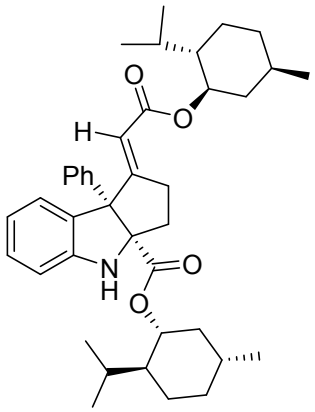
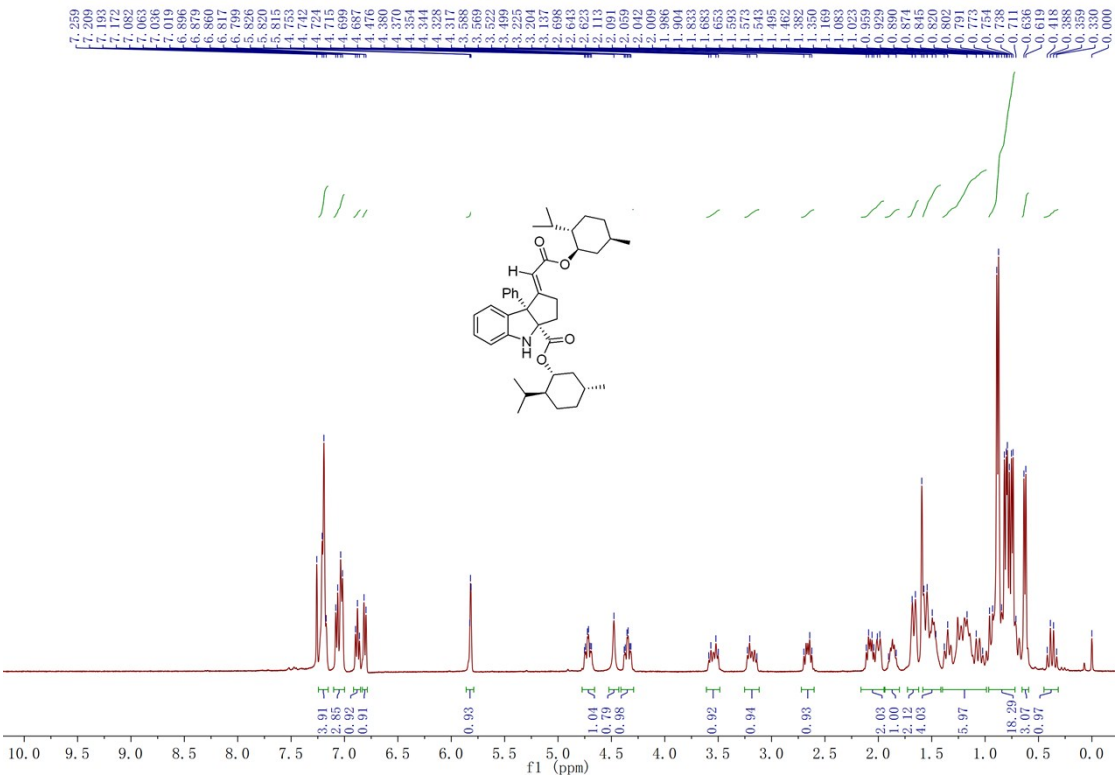
138.033
132.269
128.837
128.199
127.983
126.840
125.143
118.408
110.150
77.318
77.000
76.683
73.531
66.802
61.946
59.565
49.006
28.505
10.177
7.595
Ph
CH2OH
CH2OH
N
H
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

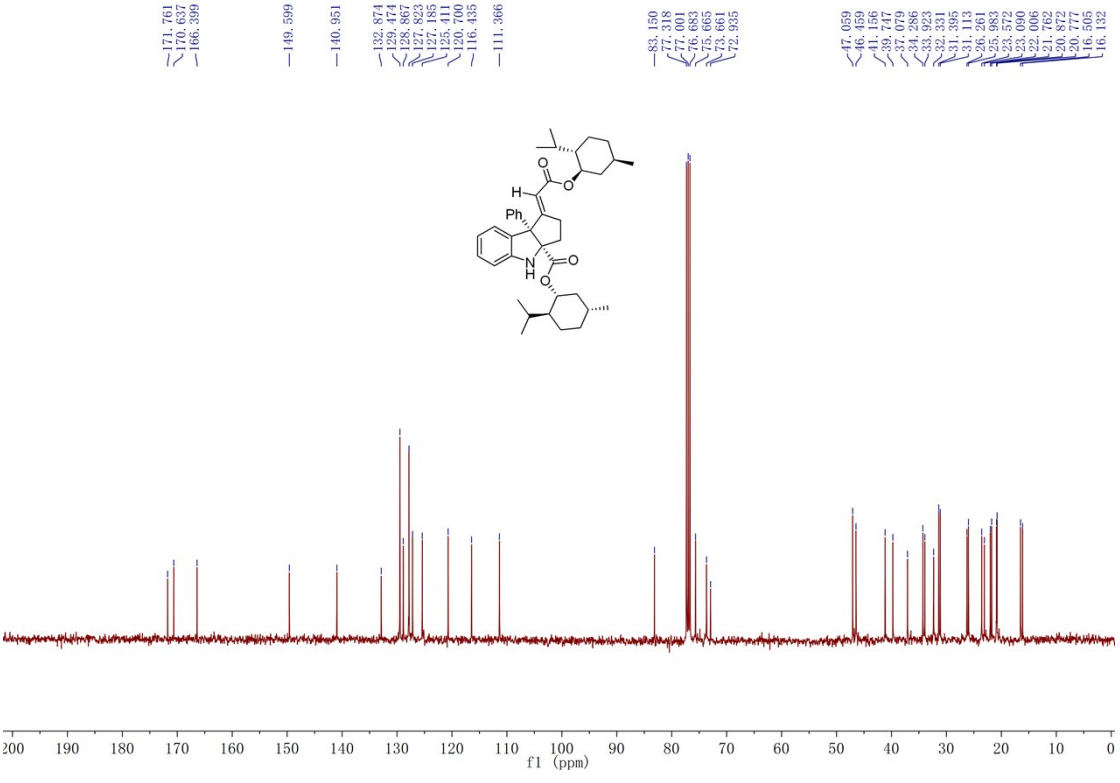

NH2
Ph
1a
+
O
O
O
O
2A*
O2, DMSO
80 °C, 24 h
H
Ph
N
H
O
O
O
4A1*
+
4A2*
LiAlH4
THF, 0 °C~rt
CH2OH
Ph
N
H
CH2OH
8*

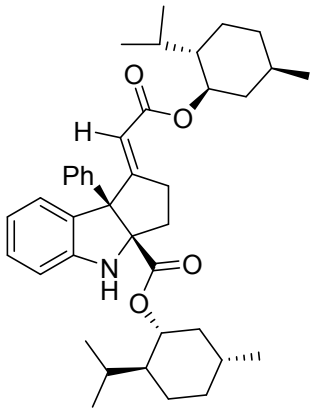


(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl(3*aR*,8*bS*,*E*)-1-(2-(((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl)oxy)-2-oxoethylidene)-8*b*-phenyl-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4A1*

1.5 mmol scale, a white solid, 38% yield (348.8 mg). M.p.: 76-78 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.37 (q, *J* = 12.0 Hz, 1H), 0.63 (d, *J* = 6.8 Hz, 3H), 0.71-0.96 (m, 18H), 1.02-1.39 (m, 6H), 1.35-1.60 (m, 4H), 1.67 (d, *J* = 12.0 Hz, 2H), 1.83-1.91 (m, 1H), 1.98-2.12 (m, 2H), 2.62-2.70 (m, 1H), 3.13-3.23 (m, 1H), 3.49-3.59 (m, 1H), 4.35 (ddd, *J* = 4.0 Hz, 10.8 Hz, 14.8 Hz, 1H), 4.48 (s, 1H), 4.72 (ddd, *J* = 4.4 Hz, 11.6 Hz, 15.2 Hz, 1H), 5.82 (t, *J* = 2.4 Hz, 1H), 6.61 (d, *J* = 7.2 Hz, 1H), 6.88 (t, *J* = 7.2 Hz, 1H), 7.01-7.09 (m, 3H), 7.17-7.21 (m, 4H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 16.1, 16.5, 20.8, 20.9, 21.8, 22.0, 23.1, 23.6, 26.0, 26.3, 31.1, 31.4, 32.3, 33.9, 34.3, 37.1, 39.7, 41.2, 46.5, 47.1, 72.9, 73.7, 75.7, 83.2, 111.4, 116.4, 120.7, 125.4, 127.2, 127.8, 128.9, 129.5, 132.9, 141.0, 149.6, 166.4, 170.6, 171.8. IR (neat) ν 3367, 3085, 3052, 3026, 2953, 2868, 1708, 1647, 1604, 1484, 1466, 1453, 1386, 1368, 1284, 1251, 1205, 1167, 1137, 1117, 1097, 1068, 1036, 1020, 981, 955, 913, 865, 847, 746, 698, 669 cm^{-1}. HRMS (ESI) Calcd. for $C_{40}H_{54}NO_4^{+1}$(M+H)$^+$ requires: 612.4047, found: 612.4042. $[\alpha]_D^{20}$ = -221.1 (c = 0.100, CH_2Cl_2).

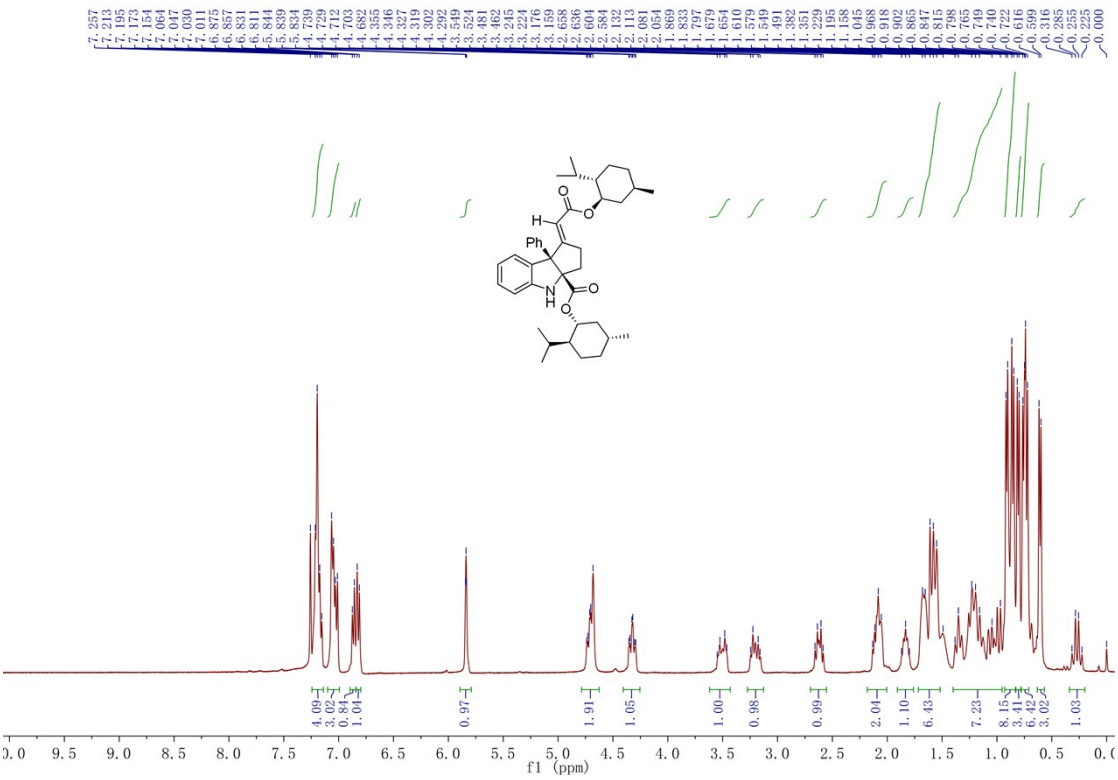

7.259
7.209
7.193
7.172
7.082
7.063
7.036
7.019
6.896
6.879
6.860
6.817
6.799
5.826
5.820
5.815
4.753
4.742
4.724
4.715
4.699
4.687
4.476
4.380
4.370
4.354
4.344
4.328
4.317
3.588
3.569
3.522
3.499
3.225
3.204
3.137
2.698
2.643
2.623
2.113
2.091
2.059
2.042
2.009
1.986
1.904
1.833
1.683
1.653
1.593
1.573
1.545
1.495
1.462
1.382
1.350
1.169
1.083
1.023
0.959
0.929
0.890
0.874
0.845
0.820
0.802
0.791
0.773
0.754
0.738
0.711
0.636
0.619
0.418
0.398
0.359
0.330
0.000
H
Ph
N
H
O
O
O
O
3.91
2.85
0.92
0.91
0.93
1.04
0.79
0.98
0.92
0.94
0.93
2.03
1.00
2.12
4.03
5.97
18.29
3.07
0.97
10.0
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)

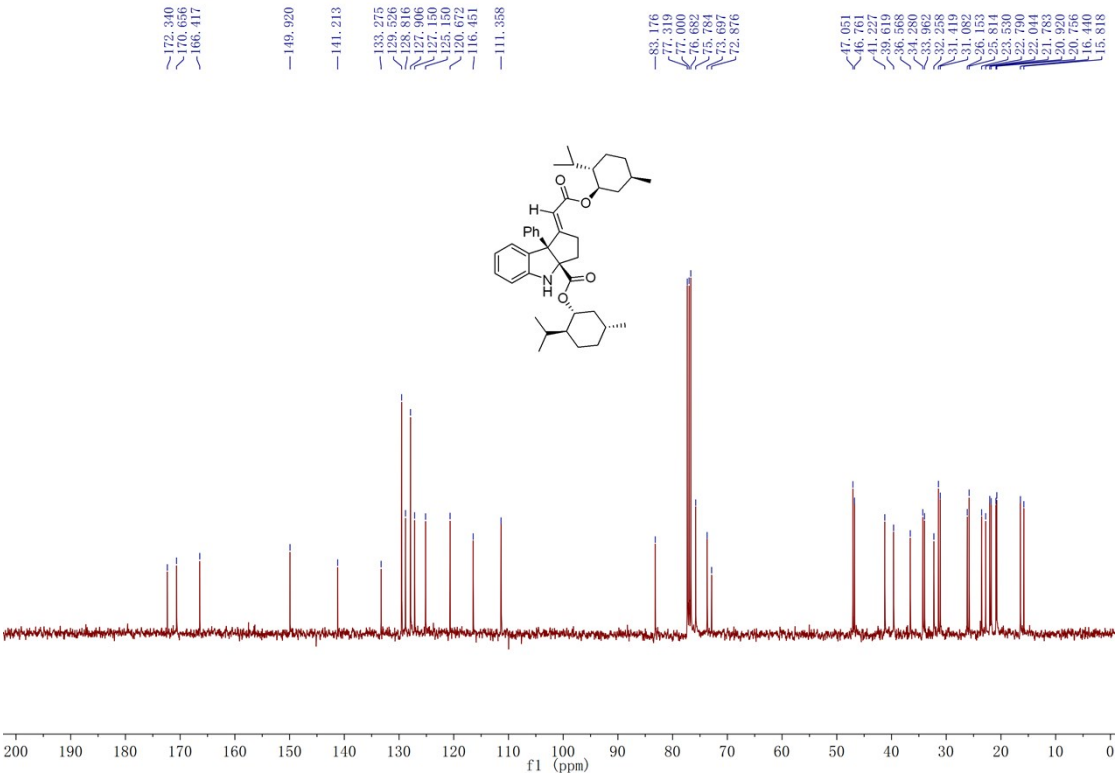

171.761
170.637
166.399
149.599
140.951
132.874
129.474
128.867
127.823
127.185
125.411
120.700
116.435
111.366
83.150
77.318
77.001
76.683
75.665
73.661
72.935
47.059
46.459
41.156
39.747
37.079
34.286
33.323
32.331
31.395
31.113
26.261
25.983
23.572
23.090
22.006
21.762
20.872
20.777
16.505
16.132
H
Ph
N
H
O
O
O
O
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

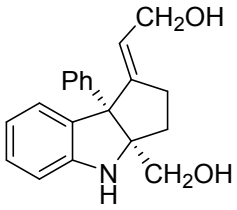


(1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl(3*aS*,8*bR*,*E*)-1-(2-(((1*R*,2*S*,5*R*)-2-isopropyl-5-methylcyclohexyl)oxy)-2-oxoethylidene)-8*b*-phenyl-2,3,4,8*b*-tetrahydrocyclopenta[*b*]indole-3*a*(1*H*)-carboxylate 4A2*

1.5 mmol scale, a white solid, 39% yield (358.0 mg). M.p.: 68-70 ^{o}C.^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 0.27 (q, *J* = 12.0 Hz, 1H), 0.61 (d, *J* = 6.8 Hz, 3H), 0.72-0.77 (m, 6H), 0.81 (d, *J* = 6.8 Hz, 3H), 0.84-0.92 (m, 8H), 0.96-1.39 (m, 7H), 1.49-1.68 (m, 6H), 1.79-1.87 (m, 1H), 2.05-2.14 (m, 2H), 2.58-2.66 (m, 1H), 3.15-3.25 (m, 1H), 3.46-3.55 (m, 1H), 4.32 (ddd, *J* = 4.0 Hz, 10.8 Hz, 14.0 Hz, 1H), 4.68 (s, 1H), 4.71 (ddd, *J* = 4.0 Hz, 10.8 Hz, 14.4 Hz, 1H), 5.84 (d, *J* = 2.0 Hz, 1H), 6.82 (t, *J* = 8.0 Hz, 1H), 6.87 (d, *J* = 7.2 Hz, 1H), 7.01-7.07 (m, 3H), 7.15-7.22 (m, 4H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 15.8, 16.4, 20.8, 20.9, 21.8, 22.0, 22.8, 23.5, 25.8, 26.2, 31.1, 31.4, 32.3, 34.0, 34.3, 36.6, 39.6, 41.2, 46.8, 47.1, 72.9, 73.7, 75.8, 83.2, 111.4, 116.5, 120.7, 125.2, 127.2, 127.9, 128.8, 129.5, 133.3, 141.2, 149.9, 166.4, 170.7, 172.3. IR (neat) ν 3367, 3090, 3052, 3031, 2953, 2924, 2867, 1707, 1647, 1603, 1484, 1465, 1455, 1386, 1368, 1285, 1275, 1254, 1232, 1205, 1165, 1115, 1097, 1068, 1036, 1017, 981, 955, 914, 864, 846, 743, 698, 669 cm^{-1}. HRMS (ESI) Calcd. for $C_{40}H_{54}NO_4^{+1}$(M+H)$^+$ requires: 612.4047, found: 612.4039. $[\alpha]_D^{20}$ = +106.8 (c = 0.100, CH_2Cl_2).

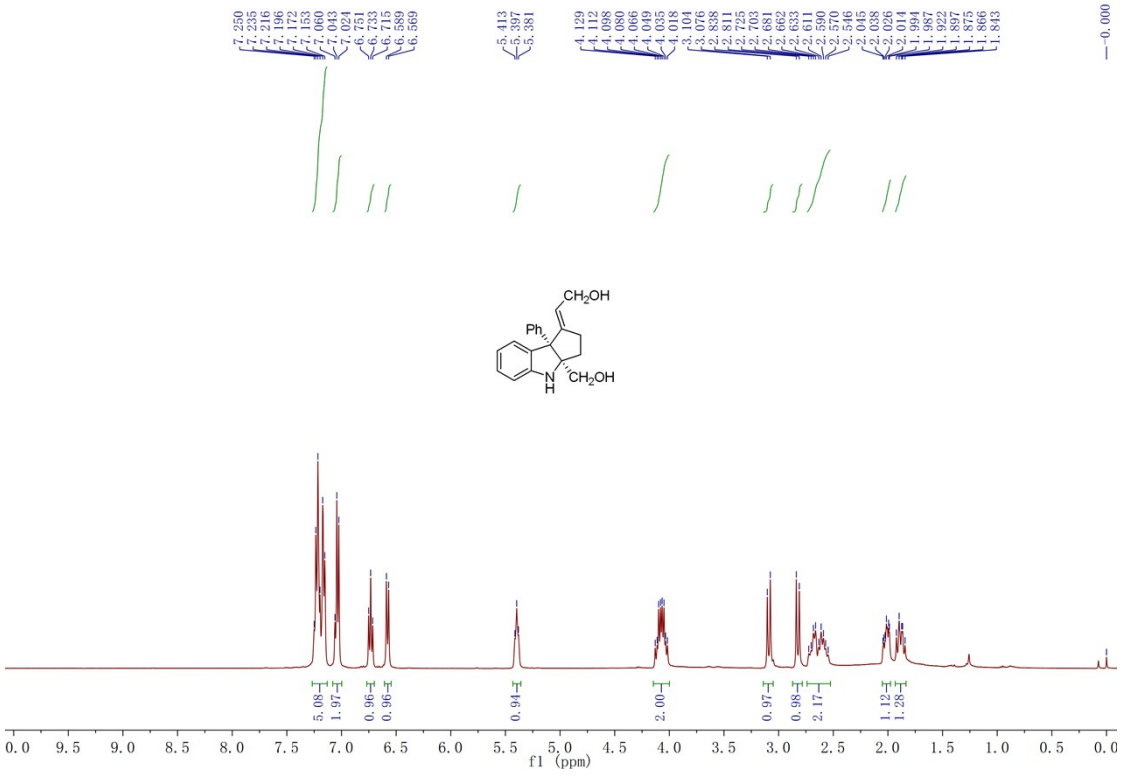

7.257
7.213
7.195
7.173
7.154
7.064
7.047
7.030
7.011
6.875
6.857
6.831
6.811
6.844
5.839
5.834
4.739
4.729
4.712
4.703
4.682
4.355
4.346
4.327
4.319
4.302
4.292
3.549
3.524
3.481
3.462
3.245
3.224
3.176
3.159
2.638
2.636
2.604
2.584
2.132
2.113
2.081
2.054
1.869
1.833
1.797
1.679
1.654
1.610
1.579
1.549
1.491
1.382
1.351
1.229
1.195
1.158
1.045
0.968
0.918
0.902
0.865
0.847
0.815
0.798
0.765
0.749
0.740
0.722
0.616
0.599
0.316
0.285
0.255
0.225
0.000
Ph
H
N
O
4.09
3.02
0.84
1.04
0.97
1.91
1.05
1.00
0.98
0.99
2.04
1.10
6.43
7.23
8.15
3.41
6.42
3.02
1.03
f1 (ppm)

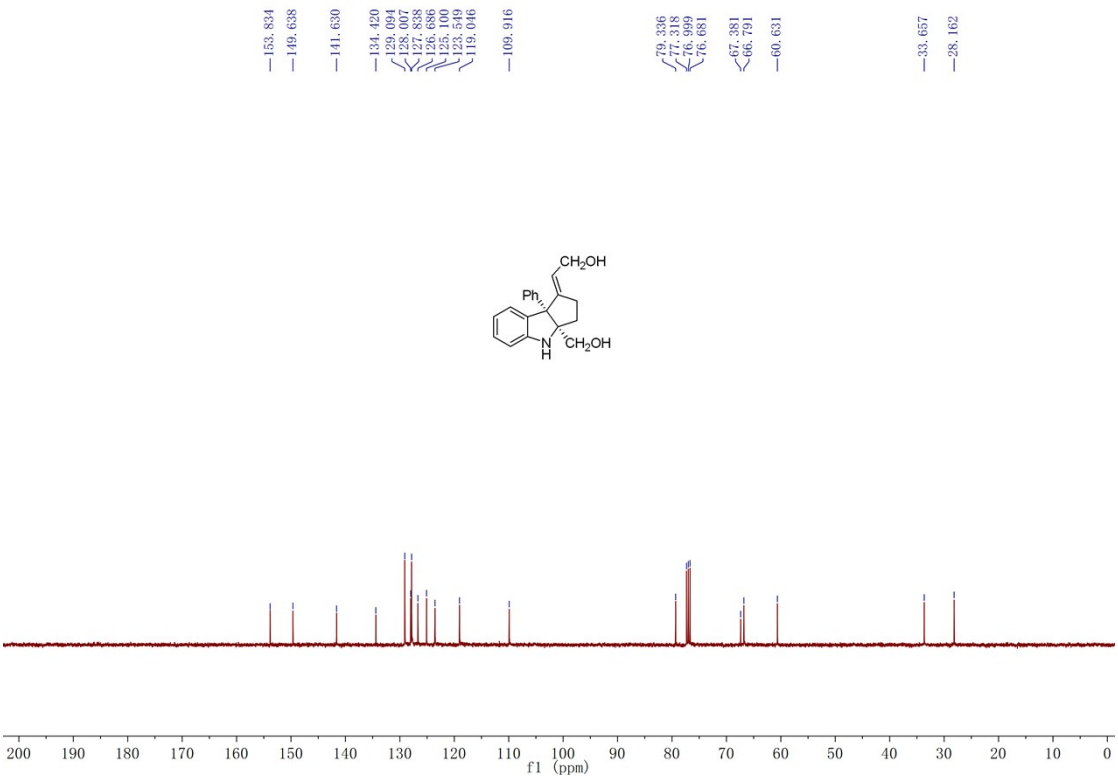

172.340
170.656
166.417
149.920
141.213
133.275
129.526
128.816
127.906
127.150
125.150
120.672
116.451
111.358
83.176
77.319
77.000
76.682
75.784
73.697
72.876
47.051
46.761
41.227
39.619
36.568
34.969
33.962
33.258
31.419
31.082
26.153
25.814
23.530
22.790
22.044
21.783
20.920
20.756
16.440
15.818
Ph
H
N
O
f1 (ppm)



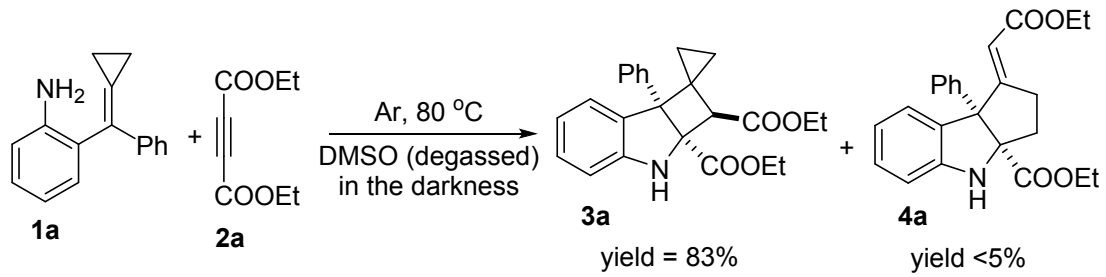
(*E*)-2-((3*aR*,8*bS*)-3*a*-(hydroxymethyl)-8*b*-phenyl-3,3*a*,4,8*b*-tetrahydrocyclopenta[*b*]indol-1(2*H*)-ylidene)ethan-1-ol 8*

0.1 mmol scale, a white solid, 62% yield (18.1 mg). M.p.: 65-68 ^{o}C. ^{1}H NMR ($CDCl_3$, TMS, 400 MHz) δ 1.84-1.92 (m, 1H), 1.98-2.05 (m, 1H), 2.54-2.73 (m, 2H), 2.82 (d, *J* = 10.8 Hz, 1H), 3.09 (d, *J* = 10.8 Hz, 1H), 4.01-4.13 (m, 2H), 5.38-5.42 (m, 1H), 6.58 (d, *J* = 8.0 Hz, 1H), 6.73 (t, *J* = 7.2 Hz, 1H), 7.02-7.06 (m, 2H), 7.15-7.25 (m, 5H). ^{13}C NMR ($CDCl_3$, TMS, 100 MHz) δ 28.2, 33.7, 60.6, 66.8, 67.4, 79.3, 109.9, 119.0, 123.5, 125.1, 126.7, 127.8, 128.0, 129.1, 134.4, 141.6, 149.6, 153.8. IR (neat) ν 3349, 3081, 3050, 3028, 2928, 2873, 1671, 1601, 1481, 1462, 1445, 1388, 1319, 1251, 1183, 1152, 1100, 1062, 1021, 982, 931, 842, 796, 740, 702, 667 cm^{-1}. HRMS (ESI) Calcd. for $C_{20}H_{22}NO_2^{+1}$(M+H)$^+$ requires: 308.1645, found: 308.1643. $[\alpha]_D^{20}$ = -120.0 (c = 0.100, CH_2Cl_2).

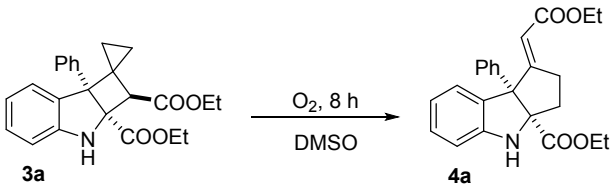



153.834
149.638
141.630
134.420
129.094
128.007
127.838
126.686
125.100
123.549
119.046
109.916
79.326
77.318
76.999
76.681
67.381
66.791
60.631
33.657
28.162
CH2OH
Ph
N
H
CH2OH
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

9. Control experiments



To gain some insights into the mechanism of the formation of **3a**, the control experiment was investigated. When **1a** and **2a** was used as the substrate in carefully degassed DMSO (firstly bubbled by Ar for 15 min, then degassed by an argon purging and freezing-degassing process three times) under Ar at 80 °C in the darkness for 8 hours, **3a** was cleanly obtained in 83% yield. The result indicated that the formation of **3a** is not promoted by light nor O_2



1) O_2, 80 °C, household light, **3a**: -, **4a**: 86%.
2) freezing-degassed Ar, 80 °C, household light, **3a**: 73%, **4a**: 14%.
3) O_2, 80 °C, in the dark, **3a**: 73%, **4a**: 7%.
4) O_2, 25 °C, blue LEDs, **3a**: <5%, **4a**: 77%
5) O_2, TEMPO (2.0 equiv.), 80 °C, household light, **3a**:95%, **4a**: trace.

To gain some insights into the mechanism, some control experiments were investigated (Scheme 6). When **3a** was used as the substrate in DMSO under O_2 at 80 °C in household light for 8 hours, **4a** was cleanly obtained in 86% yield. Moreover, when the solution of **3a** in DMSO was carefully degassed by an argon purging and freezing-degassing process three times, the reaction only produced **4a** in 14% yield for 8 hours. Then, **3a** was conducted in DMSO in the absolute darkness under O_2 at 80 °C for 8 hours, the transformation was also restrained. When **3a** was performed under blue LEDs at 25 °C for 12 hours, the reaction proceeded smoothly, affording **4a** in 77% yield. However, when 2.0 equivalents of TEMPO were added in the reaction, **3a** was restrained to be transformed into **4a**, which indicated a radical procedure. The experimental results suggested that the household light and oxygen promoted the formation of **4a** from **3a**.

10. Experimental results for electronic circular dichroism (ECD) of product 8*.

ECD experiment

ECD and UV spectra of **8***, at a concentration of 0.1 mg/mL in acetonitrile, were recorded in a 1.0 mm path length quartz cuvette, using a Chirascan circular dichroism spectrometer (Applied Photophycis Ltd., Leatherhead, UK). The experimental conditions were as follows: bandwidth, 1 nm; wavelength range, 185-400 nm; wavelength step size, 1 nm; time-per-point, 0.5 s; temperature, 25 ^{o}C. Acetonitrile was measured under the same conditions to obtain baseline.

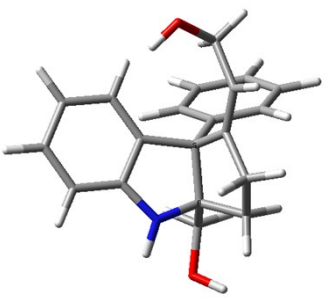
ECD computations

Molecular model of (*3R,*8*S*)-**8*** was built and subjected to a conformational analysis using the Monte Carlo protocol at the molecular mechanic force field MMFF94 level with Compute VOA (BioTools Inc., Jupiter, FL). Within a 10 kcal/mol window, 75 conformers were predicted. Geometry optimization of the conformers were then carried out in the framework of density functional theory (DFT) using the B3LYP hybrid density functional and 6-31G(d) basis set with Gaussian 09 (Gaussian Inc., Wallingford, CT). The polarizable continuum model (PCM) was adopted to consider solvent effects. Frequency calculations were also carried out to confirm the geometries obtained were true minima of the potential energy surface by exhibiting no imaginary frequencies. Structures and population percentages based on DFT//B3LYP/6-31G(d) relative energies of the 14 conformers in the initial 1.4 kcal/mol range, accounting for 96.6% of the total population, are shown in Figure SI-1.

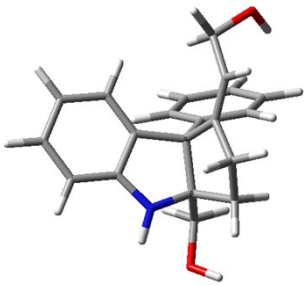
Rotatory strengths in velocity form (R_{vel}) and length form (R_{len}), oscillator strengths and excitation energies of the 50 lowest electronic transitions were calculated for each conformer employing time-dependent density functional theory (TDDFT) at B3LYP/6-31G(d). R_{vel}, oscillator strengths and ó = 0.25 eV (UV peak half-width at half height) were adopted to simulate ECD and UV curves with GaussView 5. Boltzmann-population-weighted composite ECD and UV spectra were then generated.

Figure SI-2 and Figure SI-3 show the observed and calculated ECD and UV spectra of **8*** over the range of 160-360 nm. The experimental ECD spectrum has negative Cotton effects at 308 nm, 248 nm and 197 nm, which can be assigned to the calculated bands of (*3R,*8*S*)-**8*** at 291 nm, 225

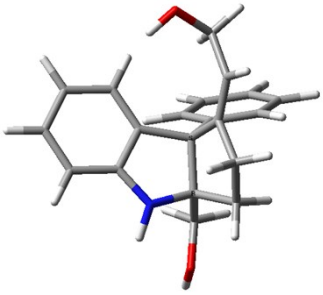
nm and 177 nm respectively. The observed positive Cotton effects at 206 nm and 187 nm can be assigned to the calculated bands of (*3R,*8*S*)-8* at 189 nm and 166 nm. The calculated bands are blue-shifted by 10-30 nm to the measured ones. According to the good agreement between the corresponding spectra, **8*** is assigned to have (*3R,*8*S*) configuration unambiguously.



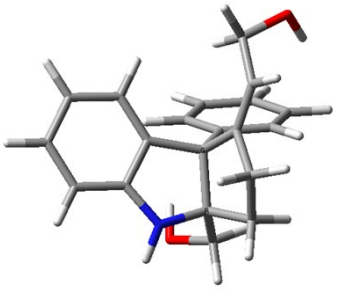
a (19.2%)



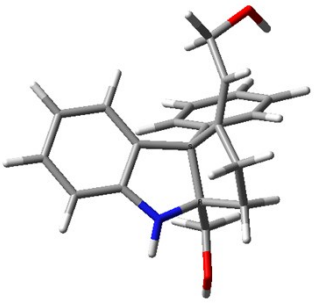
b (17.9%)



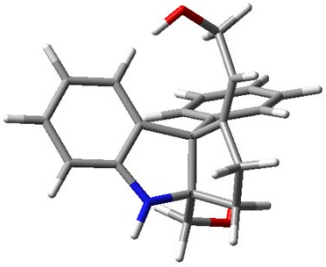
c (7.9%)



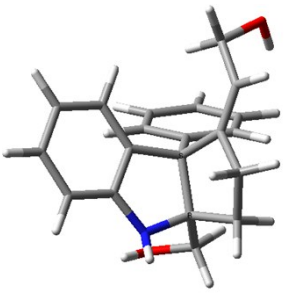
d (7.5%)



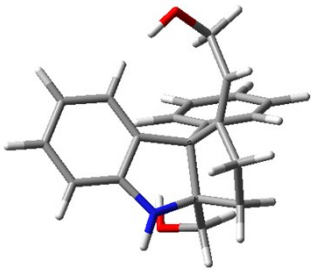
e (7.1%)



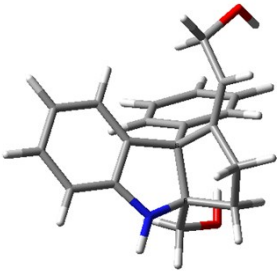
f (6.6%)



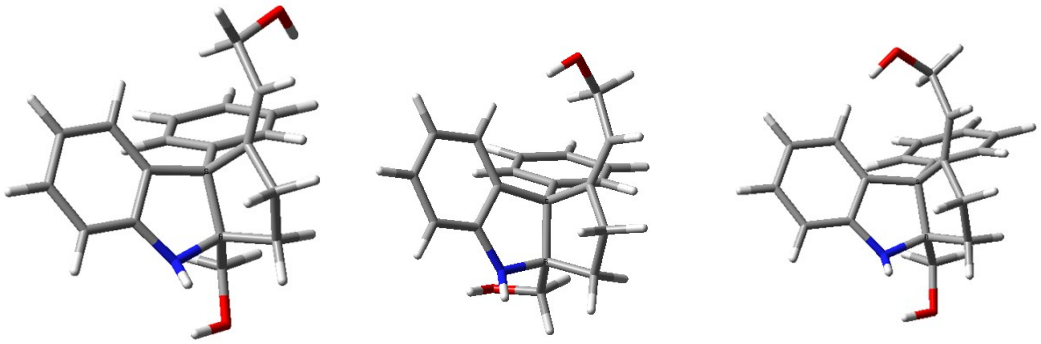
g (6.5%)



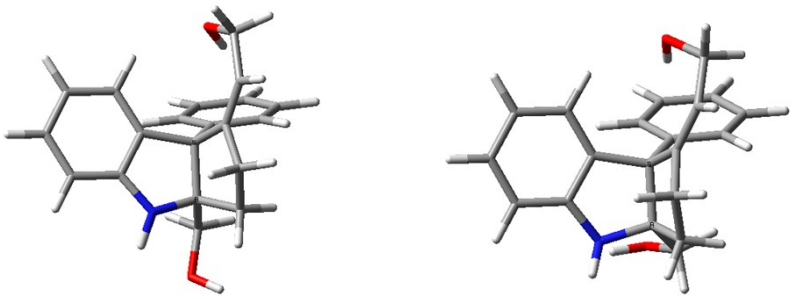
h (5.7%)



i (5.2%)



j (3.6%) k (2.9%) l (2.4%)



m (2.2%) n (1.9%)

Figure SI-1. TDDFT//B3LYP/6-31G(d) minimum energy structures of (*3R,*8*S*)-**8***

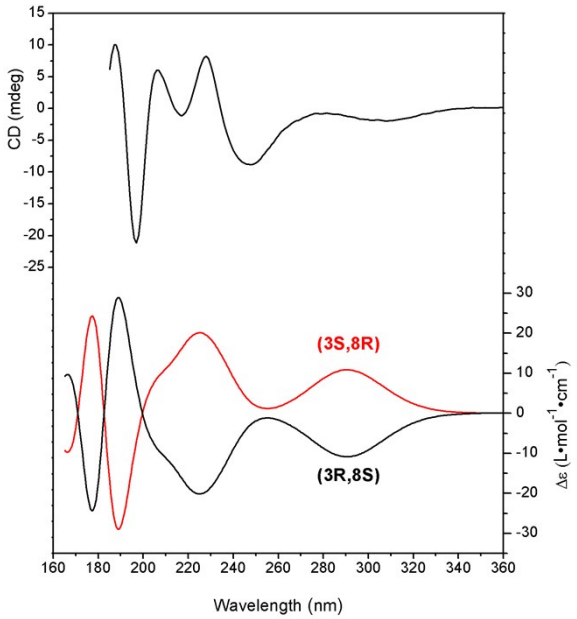


Figure SI-2. Comparison of the experimental (top) and calculated (bottom) ECD spectra of **8***

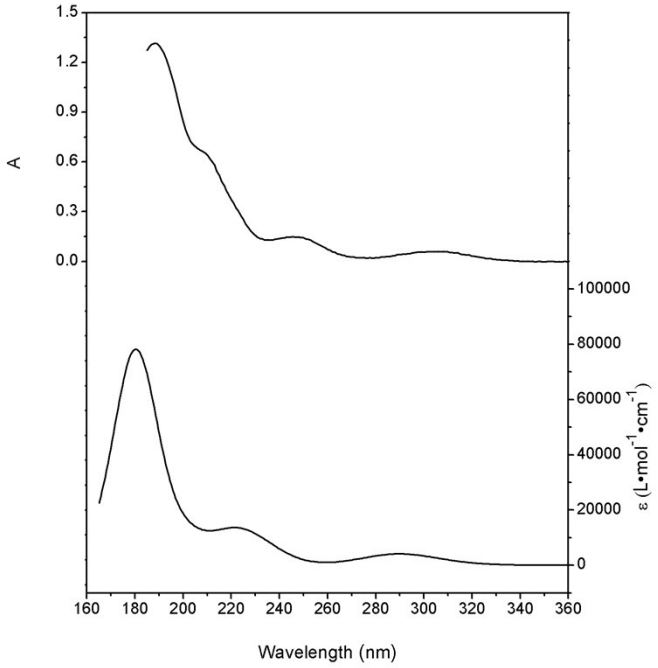


Figure SI-3. Comparison of the experimental (top) and calculated (bottom) UV spectra of **8***

11. **UV-vis absorption spectra of 1a, 2a, 3a and 4a**

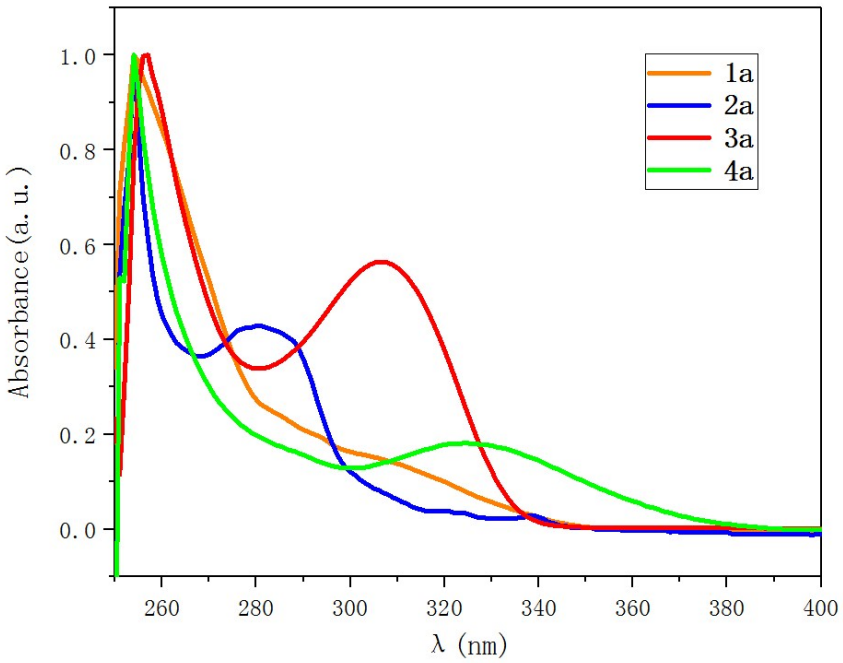
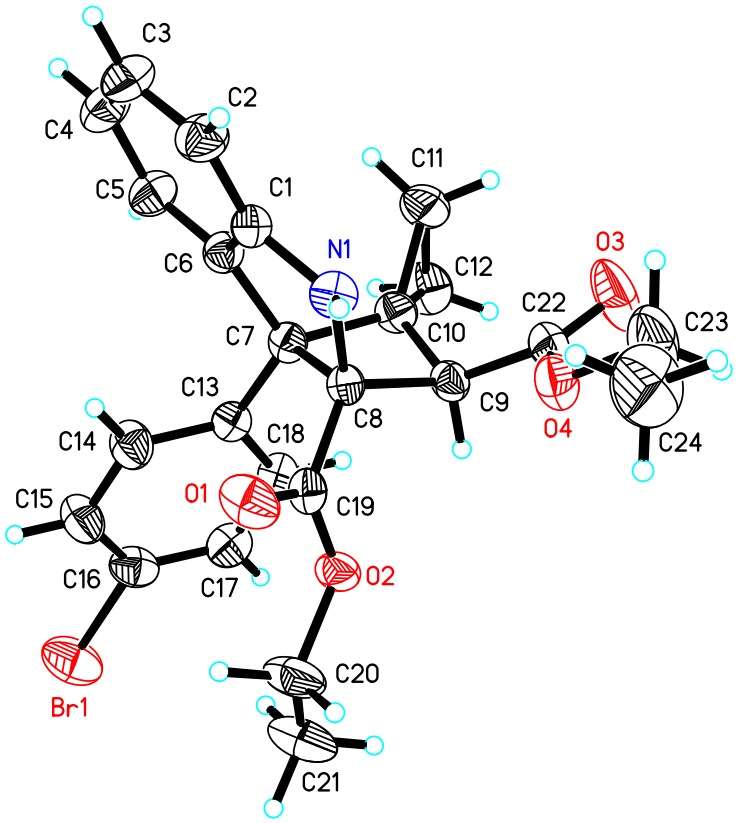
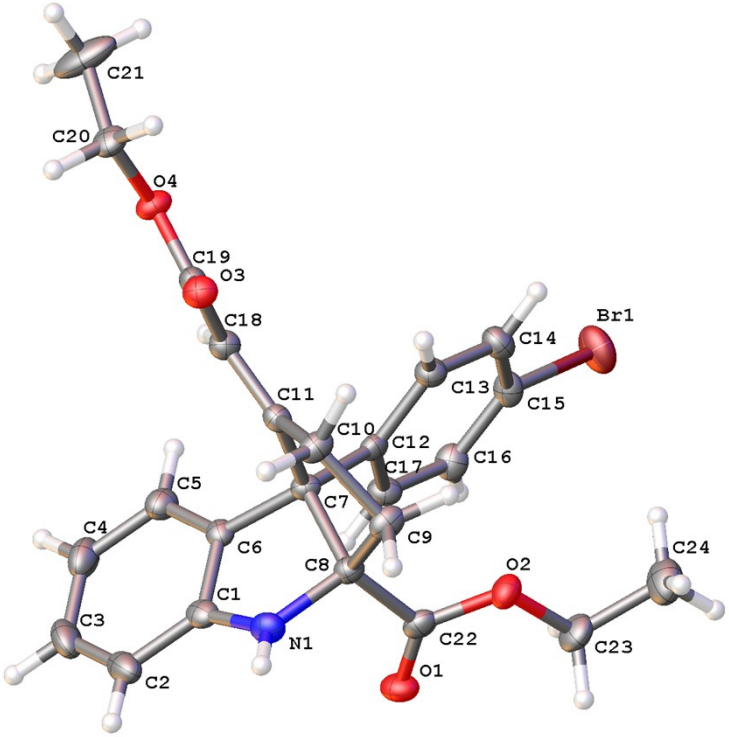


Figure SI-4. UV-Absorption Spectra of **1a, 2a, 3a and 4a** (5.0×10^{-5} M in all cases) in DMSO

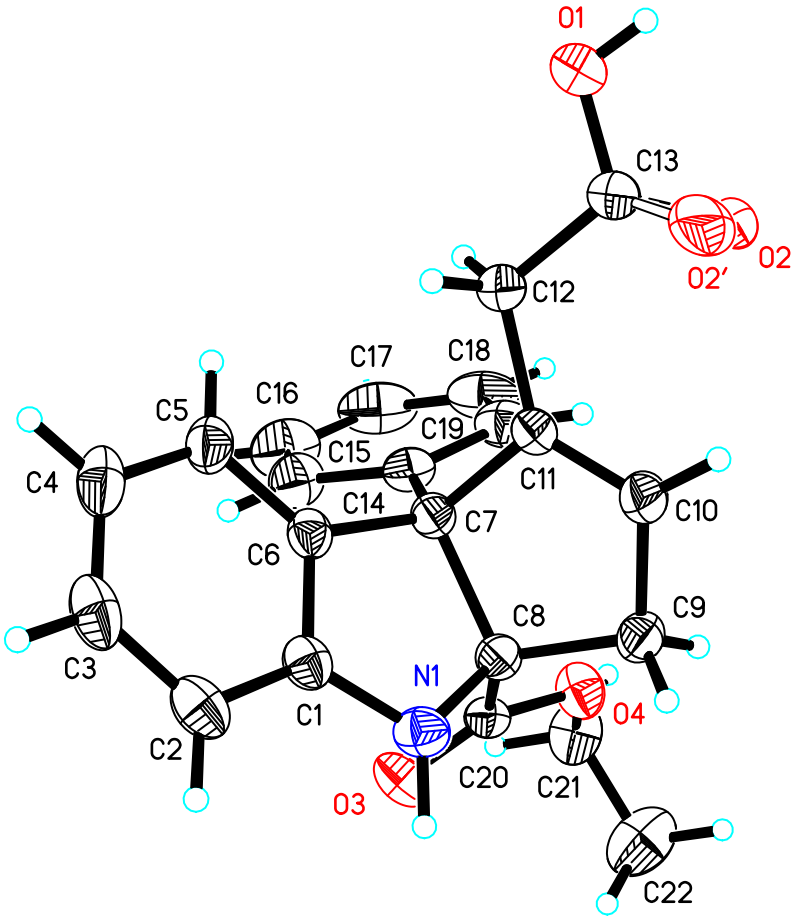
12. X-ray crystallographic information of products 3e, 4e, 5, 9 and 11*



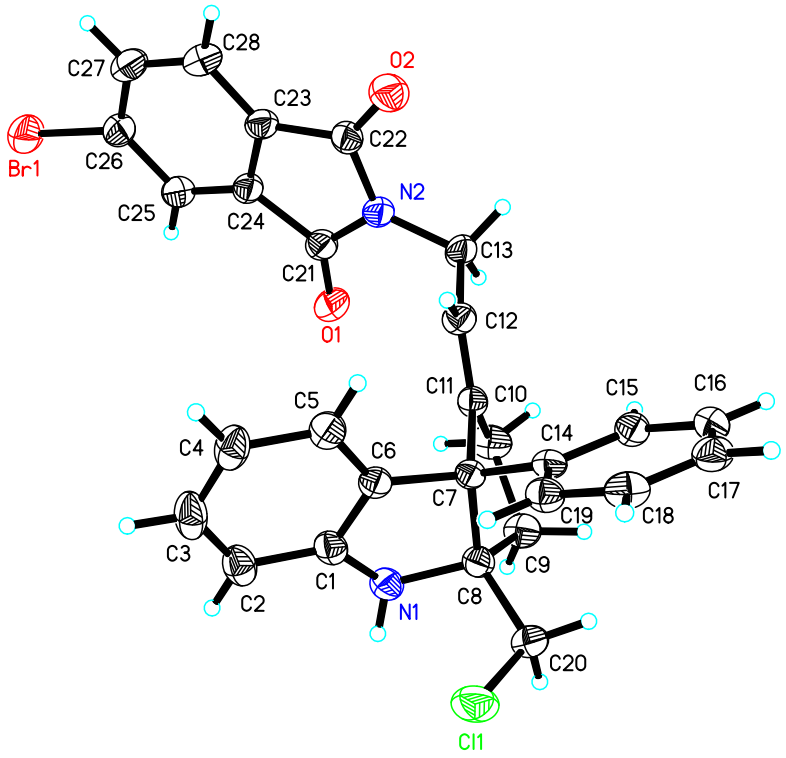
The crystal data of **3e** have been deposited in CCDC with number 1518992. Empirical Formula: $C_{24}H_{24}BrNO_4$; Formula Weight: 470.35; Crystal Color, Habit: colorless, Crystal Dimensions: 0.200 x 0.170 x 0.130 mm^3; Crystal System: Triclinic; Lattice Parameters: a = 9.1087(12)Å, b = 9.6236(13)Å, c = 13.9209(18)Å, α = 106.948(3)°, β = 95.031(3)°, γ = 99.718(3)°, V = 1138.3(3)$Å^3$; Space group: P -1; Z = 2; D_{calc}= 1.372 g/cm^3; F_{000} = 484; Final R indices [I>2sigma(I)] R1 = 0.0486, wR2 = 0.1117.



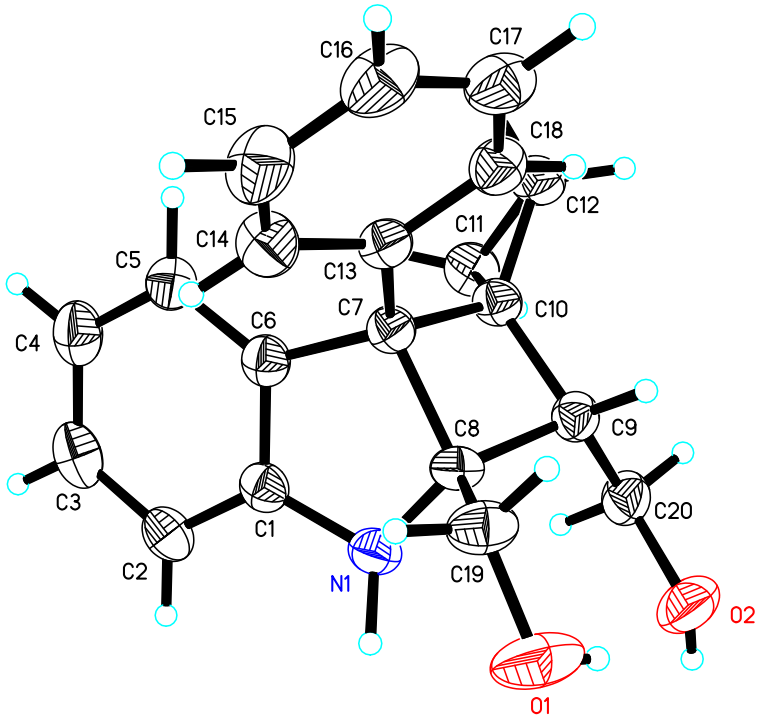
The crystal data of **4e** have been deposited in CCDC with number 1522872. Empirical Formula: $C_{24}H_{24}BrNO_4$; Formula Weight: 470.35; Crystal Color, Habit: colorless, Crystal Dimensions: 0.15 x 0.1 x 0.05 mm^3; Crystal System: Monoclinic; Lattice Parameters: a = 11.8749(12)Å, b = 13.1162(14)Å, c = 14.6639(16)Å, α = 90°, β = 106.809(2)°, γ = 90°, V = 2186.4(4)$Å^3$; Space group: P 1 21/c 1; Z = 4; D_{calc}= 1.429 g/cm^3; F_{000} = 968; Final R indices [I>2sigma(I)] R1 = 0.0461, wR2 = 0.0957.



The crystal data of **5** have been deposited in CCDC with number 1580815. Empirical Formula: $C_{22}H_{21}NO_4$; Formula Weight: 363.40; Crystal Color, Habit: colorless, Crystal Dimensions: 0.170 x 0.120 x 0.070 mm^3; Crystal System: Orthorhombic; Lattice Parameters: a = 17.5019(5)Å, b = 8.4032(3)Å, c = 12.4676(4)Å, α = 90°, β = 90°, γ = 90°, V = 1833.63(10)$Å^3$; Space group: P c a 21; Z = 4; D_{calc} = 1.316 g/cm^3; F_{000} = 768; Final R indices [I>2sigma(I)] R1 = 0.0439, wR2 = 0.1117.



The crystal data of **9** have been deposited in CCDC with number 1579530. Empirical Formula: $C_{28}H_{22}BrClN_2O_2$; Formula Weight: 533.83; Crystal Color, Habit: colorless, Crystal Dimensions: 0.170 x 0.150 x 0.120 mm^3; Crystal System: Monoclinic; Lattice Parameters: a = 32.328(10)Å, b = 10.078(3)Å, c = 15.161(4)Å, α = 90°, β = 109.440(8)°, γ = 90°, V = 4658(2)$Å^3$; Space group: C 2/c; Z = 8; D_{calc} = 1.523 g/cm^3; F_{000} = 2176; Final R indices [I>2sigma(I)] R1 = 0.0497, wR2 = 0.1140.



The crystal data of **11*** have been deposited in CCDC with number 1579529. Empirical Formula: $C_{20}H_{21}NO_2$; Formula Weight: 307.38; Crystal Color, Habit: colorless, Crystal Dimensions: 0.170 x 0.130 x 0.070 mm^3; Crystal System: Monoclinic; Lattice Parameters: a = 14.0718(2)Å, b = 7.93280(10)Å, c = 14.6162(2)Å, α = 90°, β = 92.8680(10)°, γ = 90°, V = 1629.55(4)$Å^3$; Space group: P 21; Z = 4; D_{calc} = 1.253 g/cm^3; F_{000} = 656; Final R indices [I>2sigma(I)] R1 = 0.0539, wR2 = 0.1152.

13. References

[1] S. V. Frye, M. C. Johnson, N. L. Valvano, *J. Org. Chem.* **1991**, *56*, 3750.

[2] (a) K. Chen, Z. Zhang, Y. Wei, M. Shi, *Chem. Commun.* **2012**, *48*, 7696. (b) Y.-C. Yuan, H.-B. Yang, X.-Y. Tang, Y. Wei, M. Shi, *Chem.-Eur. J.* **2016**, *22*, 5146. (c) B. Cao, M. Simaan, I. Marek, Y. Wei, M. Shi, *Chem. Commun.* **2017**, *53*, 216.

[3] W. P. Forrest, J. G. Weis, J. M. John, J. C. Axtell, J. H. Simpson, T. M. Swager, R. R. Schrock, *J. Am. Chem. Soc.* **2014**, *136*, 10910.