Supporting Information

Enantioselective Vinylogous Mannich Reaction of Acyclic Vinylketene Silyl Acetals with Ketimines Using Chiral Bis(imidazoline)-Cu(II) Catalysts

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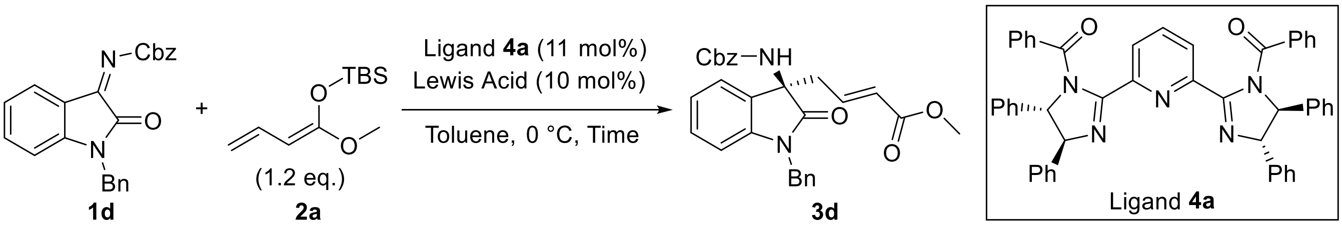
CONTENTS:

Experimental Section

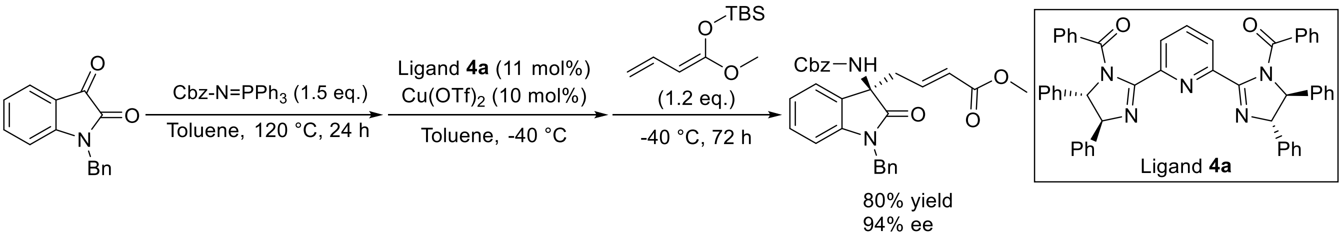
General method: All reactions were performed in oven-dried glassware under a positive pressure of argon. Solvents were transferred via syringe and were introduced into the reaction vessels through a rubber septum. All reactions were monitored by thin-layer chromatography (TLC) carried out on 0.25 mm Merck silica-gel (60-F254). The TLC plates were visualized with UV light and 7% phosphomolybdic acid or *p*-anisaldehyde in ethanol/heat. Column chromatography was carried out on a column packed with silica-gel 60N spherical neutral size 63-210 µm. The ^{1}H NMR (300 MHz) and ^{19}F NMR (282 MHz) spectra for solution in $CDCl_3$, CD_3OD or CD_3CN were recorded on Varian Mercury 300, or ^{1}H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectrum for solution in $CDCl_3$ or CD_3OD were recorded on Bruker Avance 500. Chemical shifts (δ) are expressed in ppm downfield from internal TMS. HPLC analyses were performed on a JASCO LC-2000plus using 4.6 x 250 mm of CHIRALPAK® IA, IA-3, IB-3, IB N-3, IC-3, and IF-3 column. ESI Mass spectra were recorded on a Waters SYNAPT G2 HDMS. Optical rotations were measured on a JASCO P-2200. Infrared spectra were recorded on a JASCO FT/IR-4600 spectrometer with ZnSe ATR unit. The bis(imidazoline) was synthesized by published procedures.[1)] Vinylketene silyl acetals were synthesized by published procedures.[2)]

Optimization of Lewis Acid



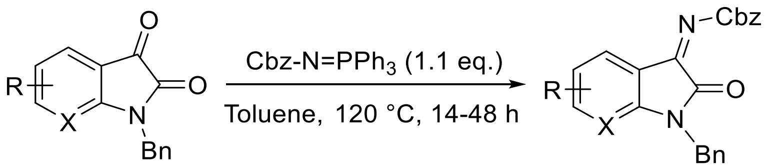
Entry	Lewis Acid	Time (h)	Yield (%)	Ee (%)[a]
1	$Cu(OTf)_2$	24	93	93(*R*)
2	$Cu(NTf_2)_2$	25	82	47(*R*)
3	CuOTf・1/2toluene	25	98	89(*R*)
4	CuI	90	84	0
5	$Zn(OTf)_2$	24	99	28(*S*)
6	$In(OTf)_3$	72	17	1(*R*)

One-pot procedure for vinylogous Mannich reaction of *N*-benzyl isatin



General procedure for the synthesis of ketimines:

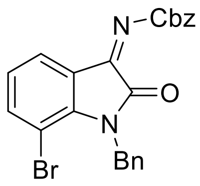
Ketimines **1a-f, h, j-l** are synthesized by previous reported method.[3)]



1g: X= CH, R= 7-Br 59% yield
1i: X= CH, R= 7-CF_3 66% yield
1n: X= CH, R= 5,7-CH_3 66% yield
1o : X= N, 16% yield

N-Benzyl isatin (3 mmol) and *N*-benzyloxycarbonylaminotriphenylphosphine (1.46 g, 3.3 mmol) was dissolved in toluene (3.0 mL) at room temperature, and the reaction mixture was refluxed for 14-48 h. Then the resulting mixture was cooling to room temperature, solvents were removed under reduced pressure. The crude residue was purified by flash silica gel chromatography (benzene : ethyl acetate = 99 : 1), and recrystallized from hexane and ethyl acetate or diethyl ether to afford ketimine **1**.

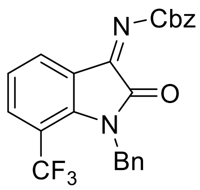
Benzyl 1-benzyl-7-bromo-2-oxoindolin-3-ylidenecarbamate (1g)



According to the general procedure, the reaction using *N*-benzyl 7-bromoisatin (948.5 mg, 3 mmol) and *N*-benzyloxycarbonylaminotriphenylphosphine (1.46 g, 3.3 mmol) gave **1g** as a red solid (790.0 mg, 59% yield).

m.p. 92.2-92.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.38 (s, 4H), 6.96 (s, 1H), 7.22-7.45 (m, 10H), 7.55 (d, *J* = 8.1 Hz, 1H), 7.66 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 44.7, 69.2, 103.7, 122.3, 123.9, 125.0, 126.5, 127.5, 128.6, 128.7, 128.7, 134.9, 136.0, 141.4, 144.6, 153.5, 158.0, 161.6; IR (ATR) 2948, 1730, 1685, 1610, 1345, 1209, 1185, 1124, 755, 722, 698 cm^{-1}; HRMS (ESI, positive) m/z for $C_{23}H_{17}BrN_2NaO_3$ [M+Na]$^+$: calcd. 471.0315, found 471.0321.

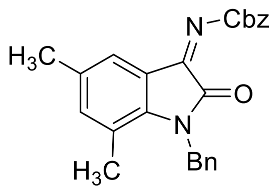
Benzyl 1-benzyl-7-trifluoromethyl-2-oxoindolin-3-ylidenecarbamate (1i)



According to the general procedure, the reaction using *N*-benzyl 7-trifluoromethylisatin (915.8 mg, 3 mmol) and *N*-benzyloxycarbonylaminotriphenylphosphine (1.46 g, 3.3 mmol) gave **1i** as a yellow solid (865.4 mg, 66% yield).

m.p. 105.0-105.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.18 (s, 2H), 5.37 (s, 2H), 7.12 (d, *J* = 7.8 Hz, 2H), 7.21-7.42 (m, 9H), 7.42 (d, *J* = 4.5 Hz, 1H), 7.76 (d, *J* = 8.1 Hz, 1H), 7.92 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 46.0-46.1 (m), 69.3, 114.4 (q, $J_{C\text{-}F}$ = 33.4 Hz), 119.3, 121.5, 121.7, 123.4, 123.7, 125.8, 127.4, 128.1, 128.6 (d, $J_{C\text{-}F}$ = 3.5 Hz), 128.8, 133.4-133.5 (m), 134.8, 134.9, 145.4 (d, $J_{C\text{-}F}$ = 2.0 Hz), 152.5, 158.3, 161.5; IR (ATR) 2951, 1730, 1685, 1610, 1345, 1209, 1185, 1124, 755, 722, 698 cm^{-1}; HRMS (ESI, positive) m/z for $C_{24}H_{17}F_3N_2NaO_3$ [M+Na]$^+$: calcd. 461.1083, found 461.1081.

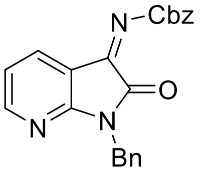
Benzyl 1-benzyl-5,7-dimethyl-2-oxoindolin-3-ylidenecarbamate (1n)



According to the general procedure, the reaction using *N*-benzyl 5,7-dimethylisatin (795.3 mg, 3 mmol) and *N*-benzyloxycarbonylamino triphenylphosphine (1.46 g, 3.3 mmol) gave **1n** as a red solid (787.2 mg, 66% yield).

m.p. 163.5-164.2 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.17 (s, 3H), 2.23 (s, 3H), 5.11 (s, 2H), 5.38 (s, 2H), 6.95 (s, 1H), 7.16 (d, *J* = 8.1 Hz, 2H), 7.23-7.46 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 18.3, 20.4, 45.2, 68.9, 119.9, 121.1, 123.2, 125.7, 127.5, 128.6, 128.7, 129.0, 133.5, 135.2, 136.3, 140.5, 143.2, 154.9, 158.6, 162.2; IR (ATR) 2966, 1727, 1714, 1682, 1601, 1347, 1208, 1158, 989, 728, 695 cm^{-1}; HRMS (ESI, positive) m/z for $C_{25}H_{22}N_2NaO_3$ [M+Na]$^+$: calcd. 421.1523, found 421.1526.

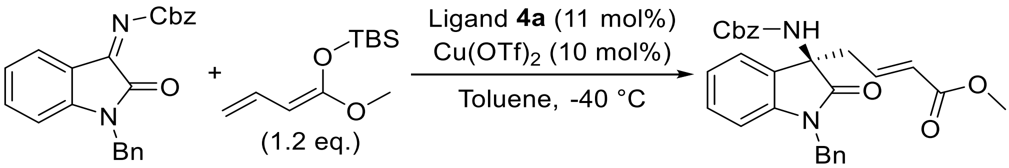
Benzyl 1-benzyl-2-oxo-1,2-dihydro-3H-pyrrolo[2,3-b]pyridin-3-ylidenecarbamate (1o)



According to the general procedure, the reaction using *N*-benzyl azaisatin (405.0 mg, 1.7 mmol) and *N*-benzyloxycarbonylaminotriphenylphosphine (782.9 mg, 1.9 mmol) gave **1o** as a yellow solid (102.5 mg, 16% yield).

m.p. 119.4-120.4 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 4.98 (s, 2H), 5.39 (s, 2H), 7.04 (s, 1H), 7.27-7.49 (m, 10H), 7.86 (s, 1H), 8.36 (d, *J* = 2.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 42.8, 69.2, 113.8, 119.4, 128.0, 128.6, 128.7, 128.7, 128.8, 132.1, 134.9, 135.4, 153.2, 153.6, 157.0, 160.5, 161.4; IR (ATR) 2933, 1720, 1682, 1592, 1444, 1220, 1170, 1095, 966, 753, 696 cm^{-1}; HRMS (ESI, positive) m/z for $C_{22}H_{17}N_3NaO_3$ $[M+Na]^+$: calcd. 394.1162, found 394.1161.

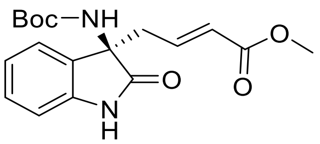
General procedure for the enantioselective vinylogous Mannich reaction of ketimines with acyclic vinylketene silyl acetals:



1d **2a** **3d**

A solution of **4a** (0.011 mmol, 11 mol%) and $Cu(OTf)_2$ (0.01 mmol, 10 mol%) in dry toluene (1.0 mL) was stirred at room temperature for 1 h. Ketimine **1d** (0.10 mmol) was added to the mixture and stirred at −40 °C. Vinylketene silyl acetal **2a** (0.12 mmol) was added. After completion of the reaction monitored by TLC, the reaction mixture was concentrated and purified by silica gel column chromatography (hexane/CH_2Cl_2/ethyl acetate = 4:1:1) to afford **3d**.

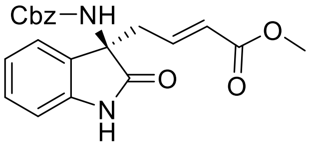
Methyl (*R*,*E*)-4-{3-[(*tert*-butoxycarbonyl)amino]-2-oxoindolin-3-yl}but-2-enoate (3a)



Reaction of ketimine **1a** (0.10 mmol) and vinylketene silyl acetal **2a** (0.12 mmol) using **4a** (0.01 mmol) and $Cu(OTf)_2$ (0.01 mmol) in toluene (1.00 mL) at 0 °C for 24 h gave (*R*)-**3a** (15.9 mg, 46% yield, 8% ee) as a white solid.

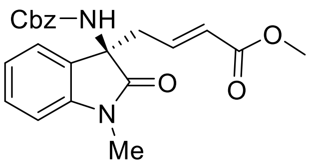
$[\alpha]_D^{25}$ −0.9 (c 0.28, $CHCl_3$); m.p. 181.2-182.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.28 (s, 9H), 2.63 (dd, *J* = 7.8, 13.8 Hz, 1H), 2.76 (dd, *J* = 7.8, 13.8 Hz, 1H), 3.73 (s, 3H), 5.27 (s, 1H), 5.94 (d, *J* = 15.6 Hz, 1H), 6.76-6.84 (m, 1H), 6.87 (d, *J* = 7.5 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 7.23-7.27 (m, 2H), 8.09 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.0, 39.9, 51.7, 61.2, 81.0, 110.4, 122.8, 123.2, 126.4, 129.1, 130.1, 139.8, 140.1, 153.9, 166.0, 178.1; IR (ATR) 3290, 2978, 1716, 1683, 1621, 1516, 1280, 1158, 1029, 966, 754 cm^{-1}; HRMS (ESI, positive) m/z for $C_{18}H_{22}N_2NaO_5$ $[M+Na]^+$: calcd. 369.1421, found 369.1414; HPLC (DAICEL CHIRALPAK IA-3®, hexane:*i*-PrOH = 80:20, 1.0 mL/min, 254 nm), tR = 9.6 min (major), 18.9 min (minor).

Methyl (*R*,*E*)-4-[3-(benzyloxycarbonyl)amino-2-oxoindolin-3-yl]but-2-enoate (3b)



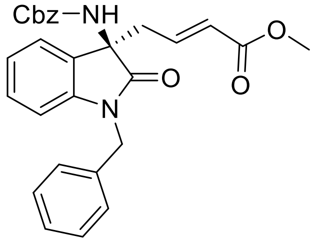
Reaction of ketimine **1b** (0.10 mmol) and vinylketene silyl acetal **2a** (0.12 mmol) using **4a** (0.01 mmol) and $Cu(OTf)_2$ (0.01 mmol) in toluene (1.0 mL) at 0 °C for 24 h gave (*R*)-**3b** (37.6mg, 99% yield, 66% ee) as a white solid. $[\alpha]_D{}^{25}$ −17.9 (c 0.36, $CHCl_3$); m.p. 123.6-124.4 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.62 (dd, *J* = 7.7, 13.8 Hz, 1H), 2.78 (dd, *J* = 7.7, 13.8 Hz, 1H), 3.69 (s, 3H), 4.97 (s, 2H), 5.86-5.94 (m, 2H), 6.76-6.84 (m, 2H), 7.05 (t, *J* = 7.5 Hz, 1H), 7.20-7.26 (m, 7H), 8.66 (br, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.6, 51.8, 61.4, 67.4, 110.7, 122.9, 123.4, 126.5, 128.1, 128.2, 128.5, 129.3, 135.6, 139.7, 140.4; 154.6, 166.0, 177.8; IR (ATR) 3285, 2950, 1716, 1618, 1509, 1470, 1203, 1038, 967, 739, 697 cm^{-1}; HRMS (ESI, positive) m/z for $C_{21}H_{20}N_2NaO_5$ $[M+Na]^+$: calcd. 403.1264, found 403.1266; HPLC (DAICEL CHIRALPAK IC-3®, hexane:*i*-PrOH = 80:20, 1.0 mL/min, 254 nm), tR = 23.7 min (minor), 32.6 min (major).

Methyl (*R*,*E*)-4-[3-(benzyloxycarbonyl)amino-1-methyl-2-oxoindolin-3-yl]but-2-enoate (3c)



Reaction of ketimine **1c** (0.10 mmol) and vinylketene silyl acetal **2a** (0.12 mmol) using **4a** (0.01 mmol) and $Cu(OTf)_2$ (0.01 mmol) in toluene (1.0 mL) at 0 °C for 24 h gave (*R*)-**3c** (35.1 mg, 89% yield, 85% ee) as a white solid. $[\alpha]_D{}^{25}$ −3.3 (c 0.32, $CHCl_3$); m.p. 103.2-104.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.63 (dd, *J* = 7.8, 14.0 Hz, 1H), 2.78 (dd, *J* = 7.8, 14.0 Hz, 1H), 3.18 (br, 3H), 3.71 (s, 3H), 4.93 (s, 2H), 5.44 (s, 1H), 5.91 (d, *J* = 15.6 Hz, 1H), 6.71-6.82 (m, 2H), 7.10 (t, *J* = 7.5 Hz, 1H), 7.29-7.36 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 26.5, 39.8, 51.7, 60.9, 67.4, 108.6, 123.0, 123.1, 126.5, 128.3, 128.3, 128.5, 129.0, 129.4, 135.5, 139.7, 143.2, 154.4, 165.9, 175.6; IR (ATR) 3311, 3033, 2951, 1704, 1613, 1470, 1252, 1028, 967, 752, 696 cm^{-1}; HRMS (ESI, positive) m/z for $C_{22}H_{22}N_2NaO_5$ $[M+Na]^+$: calcd. 417.1421, found 417.1419; HPLC (DAICEL CHIRALPAK IC-3®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 254 nm), tR = 29.5 min (minor), 52.2 min (major).

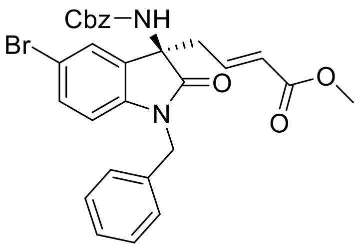
Methyl (*R*,*E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-2-oxoindolin-3-yl]but-2-enoate (3d)



Reaction of ketimine **1d** (0.10 mmol) and vinylketene silyl acetal **2a** (0.12 mmol) using **4a** (0.01 mmol) and $Cu(OTf)_2$ (0.01 mmol) in toluene (1.0 mL) at −40 °C for 72 h gave (*R*)-**3d** (47.1 mg, 99% yield, 97% ee) as a white solid. $[\alpha]_D{}^{25}$ −0.7 (c 1.38, $CHCl_3$); m.p. 47.0-48.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.70 (dd, *J* = 7.8, 13.5 Hz, 1H), 2.83 (dd, *J* = 7.8, 13.5 Hz, 1H), 3.68 (s, 3H), 4.97 (br, 4H), 5.72 (s, 1H), 5.91 (d, *J* = 15.6 Hz, 1H), 6.63-6.76 (m, 2H), 7.05 (t, *J* = 7.5 Hz, 1H), 7.16-

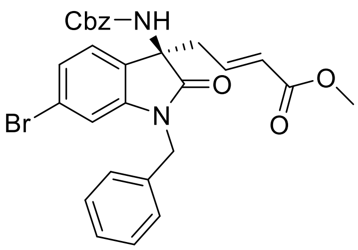
7.35 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.0, 44.1, 51.7, 61.0, 67.4, 109.7, 123.0, 123.1, 126.6, 127.1, 127.5, 128.3, 128.5, 128.8, 129.3, 135.4, 135.6, 139.5, 142.4, 154.3, 165.8, 175.7; IR (ATR) 3319, 3033, 2952, 1706, 1613, 1489, 1258, 1178, 1028, 750, 696 cm^{-1}; HRMS (ESI, positive) m/z for $C_{28}H_{26}N_2NaO_5$ $[M+Na]^+$: calcd. 493.1734, found 493.1748; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 254 nm), tR = 13.7 min (major), 33.1 min (minor).

Methyl (*R,E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-5-bromo-2-oxoindolin-3-yl]but-2-enoate (3e)



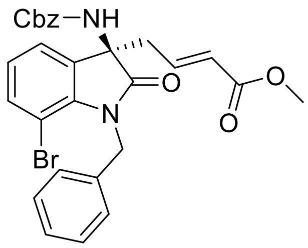
Reaction of ketimine **1e** (0.10 mmol) and vinylketene silyl acetal **2a** (0.12 mmol) using **4a** (0.01 mmol) and $Cu(OTf)_2$ (0.01 mmol) in toluene (1.0 mL) at −40 °C for 96 h gave (*R*)-**3e** (54.4 mg, 99% yield, 96% ee) as a white solid. $[\alpha]_D^{25}$ −6.2 (c 0.74, $CHCl_3$); m.p. 59.5-60.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 2.68-2.82 (m, 2H), 3.69 (s, 3H), 4.98 (br, 4H), 5.76 (s, 1H), 5.91 (d, *J* = 15.6 Hz, 1H), 6.51 (s, 1H), 6.59-6.69 (m, 1H), 7.23-7.40 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.8, 44.2, 51.7, 61.0, 67.5, 111.2, 115.8, 126.2, 126.9, 127.1, 127.7, 128.3, 128.4, 128.6, 128.9, 131.0, 132.2, 134.9, 135.4, 138.8, 141.5, 154.3, 165.7, 175.2; IR (ATR) 3318, 3032, 2950, 1709, 1608, 1483, 1257, 1176, 1041, 731, 696 cm^{-1}; HRMS (ESI, positive) m/z for $C_{28}H_{25}BrN_2NaO_5$ $[M+Na]^+$: calcd. 571.0839, found 571.0858; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 254 nm), tR = 11.4 min (major), 23.4 min (minor).

Methyl (*R,E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-6-bromo-2-oxoindolin-3-yl]but-2-enoate (3f)



Reaction of ketimine **1f** (0.10 mmol) and vinylketene silyl acetal **2a** (0.12 mmol) using **4a** (0.01 mmol) and $Cu(OTf)_2$ (0.01 mmol) in toluene (1.0 mL) at −40 °C for 96 h gave (*R*)-**3f** (54.3 mg, 99% yield, 98% ee) as a white solid. $[\alpha]_D^{25}$ −19.9 (c 0.53, $CHCl_3$); m.p. 58.2-59.0 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 2.67 (dd, *J* = 7.8, 14.0 Hz, 1H), 2.80 (dd, *J* = 7.8, 14.0 Hz, 1H), 3.70 (s, 3H), 4.97 (br, 4H), 5.74 (s, 1H), 5.91 (d, *J* = 15.6 Hz, 1H), 6.63-6.73 (m, 2H), 6.78 (s, 1H), 7.10-7.19 (m, 3H), 7.24-7.32 (m, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.7, 44.2, 51.7, 60.8, 67.5, 113.0, 112.9, 124.3, 125.9, 126.9, 127.1, 127.7, 127.9, 128.3, 128.4, 128.4, 128.5, 128.9, 134.9, 139.0, 143.7, 154.4, 165.7, 175.7; IR (ATR) 3237, 3032, 2951, 1710, 1605, 1486, 1254, 1177, 1028, 731, 696 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{28}H_{25}BrN_2NaO_5$ $[M+Na]^+$: calcd. 571.0839, found 571.0853; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 254 nm), tR = 12.8 min (major), 26.2 min (minor).

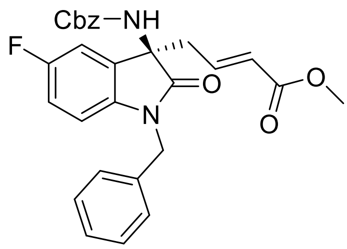
Methyl (*R,E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-7-bromo-2-oxoindolin-3-yl]but-2-enoate (3g)



Reaction of ketimine **1g** (0.10 mmol), and vinylketene silyl acetal **2a** (0.12 mmol) using **4a** (0.01 mmol) and $Cu(OTf)_2$ (0.01 mmol) in toluene (1.0 mL) at −40 °C for 72 h gave (*R*)-**3g** (54.4 mg, 99% yield, 97% ee) as a white solid.

$[\alpha]_D^{25}$ −3.2 (c 0.43, $CHCl_3$); m.p. 57.2-58.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.62-2.80 (m, 2H), 3.72 (s, 3H), 4.97 (s, 2H), 5.35 (s, 2H), 5.72 (s, 1H), 5.90 (d, *J* = 15.6 Hz, 1H), 6.67-6.77 (m, 1H), 6.94 (t, *J* = 7.8 Hz, 1H), 7.22-7.40 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.3, 44.9, 51.8, 60.4, 67.5, 102.9, 122.1, 124.2, 126.3, 126.9, 127.0, 128.3, 128.4, 128.5, 128.5, 128.6, 132.3, 135.3, 137.4, 138.9, 140.0, 154.3, 165.7, 176.6; IR (ATR) 3324, 3033, 2950, 1710, 1608, 1450, 1255, 1165, 1027, 732, 695 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{28}H_{25}BrN_2NaO_5$ $[M+Na]^+$: calcd. 571.0839, found 571.0843; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 254 nm), tR = 13.2 min (major), 35.2 min (minor).

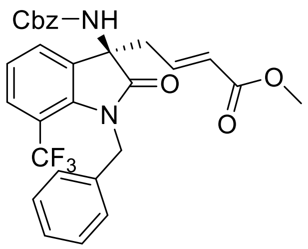
Methyl (*R,E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-5-fluoro-2-oxoindolin-3-yl]but-2-enoate (3h)



Reaction of ketimine **1h** (0.10 mmol) and vinylketene silyl acetal **2a** (0.12 mmol) using **4a** (0.01 mmol) and $Cu(OTf)_2$ (0.01 mmol) in toluene (1.0 mL) at −40 °C for 168 h gave (*R*)-**3h** (48.4 mg, 98% yield, 83% ee) as a white solid.

$[\alpha]_D^{25}$ −22.5 (c 0.54, $CHCl_3$); m.p. 47.2-47.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.68-2.86 (m, 2H), 3.70 (s, 3H), 4.99 (br, 4H), 5.67 (s, 1H), 5.92 (d, *J* = 15.6 Hz, 1H), 6.57 (s, 1H), 6.62-6.73 (m, 1H), 6.89 (t, *J* = 8.7 Hz, 1H), 7.06 (d, *J* = 7.8 Hz, 1H), 7.29-7.33 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.8, 44.3, 51.7, 61.3, 67.5, 110.4 (d, $J_{C\text{-}F}$ = 8.8 Hz), 111.3 (d, $J_{C\text{-}F}$ = 25.0 Hz), 115.6 (d, $J_{C\text{-}F}$ = 23.8 Hz), 126.8, 127.1, 127.7, 128.3, 128.4, 128.5, 128.9, 130.6, 135.1, 135.5, 138.3, 138.9, 154.4, 159.3 (d, $J_{C\text{-}F}$ = 239.8 Hz), 165.7, 175.5; ^{19}F NMR (282 MHz) δ −119.4; IR (ATR) 3316, 3033, 2952, 1707, 1619, 1491, 1237, 1173, 1028, 732, 696 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{28}H_{25}FN_2NaO_5$ $[M+Na]^+$: calcd. 511.1640, found 511.1636; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 254 nm), tR = 10.7 min (major), 21.8 min (minor).

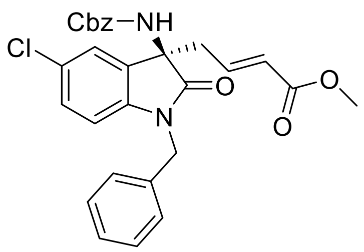
Methyl (*R,E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-7-trifluoromethyl-2-oxoindolin-3-yl]but-2-enoate (3i)



Reaction of ketimine **1i** (0.10 mmol) and vinylketene silyl acetal **2a** (0.12 mmol) using **4a** (0.01 mmol) and $Cu(OTf)_2$ (0.01 mmol) in toluene (1.0 mL) at −40 ºC for 168 h gave (*R*)-**3i** (53.4 mg, 99% yield, 97% ee) as a white solid.

$[\alpha]_D^{25}$ +41.4 (c 0.40, $CHCl_3$); m.p. 46.0-46.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.62-2.79 (m, 2H), 3.71 (s, 3H), 4.97 (s, 2H), 5.16 (s, 2H), 5.75 (s, 1H), 5.87 (d, *J* = 15.6 Hz, 1H), 6.66-6.77 (m, 1H), 7.17-7.30 (m, 11H), 7.47 (d, *J* = 7.5 Hz, 1H), 7.59 (d, *J* = 8.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.2, 46.3-46.4 (m), 51.8, 59.4, 67.6, 113.2 (q, $J_{C\text{-}F}$ = 33.3 Hz), 122.1, 122.5, 124.3, 125.8, 126.6, 126.8, 127.1, 127.4-127.5 (m), 128.3 (d, $J_{C\text{-}F}$ = 3.6 Hz), 128.4, 128.6, 132.1, 135.3, 136.2, 138.6, 140.7, 154.3, 165.6, 177.2; IR (ATR) 3325, 3034, 2953, 1715, 1597, 1453, 1258, 1120, 1028, 746, 695 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{29}H_{25}F_3N_2NaO_5$ $[M+Na]^+$: calcd. 561.1608, found 561.1615; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 254 nm), tR = 11.2 min (major), 27.5 min (minor).

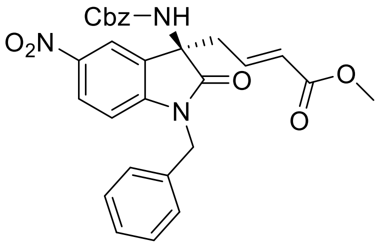
Methyl (*R,E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-5-chloro-2-oxoindolin-3-yl]but-2-enoate (3j)



Reaction of ketimine **1j** (0.10 mmol) and vinylketene silyl acetal **2a** (0.12 mmol) using **4a** (0.02 mmol) and $Cu(OTf)_2$ (0.02 mmol) in toluene (1.0 mL) at −40 ºC for 168 h gave (*R*)-**3j** (46.9 mg, 93% yield, 97% ee) as a white solid.

$[\alpha]_D^{25}$ −5.3 (c 1.56, $CHCl_3$); m.p. 61.2-62.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.68-2.83 (m, 2H), 3.70 (s, 3H), 4.98 (br, 4H), 5.67 (s, 1H), 5.92 (d, *J* = 15.6 Hz, 1H), 6.57-6.70 (m, 2H), 7.15 (dd, *J* = 2.1, 8.4 Hz, 2H), 7.26-7.32 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.8, 44.2, 51.7, 61.1, 67.5, 110.7, 123.5, 126.9, 127.1, 127.7, 128.3, 128.4, 128.5, 128.5, 128.9, 129.2, 130.7, 135.0, 135.4, 138.8, 141.0, 154.3, 165.7, 175.3; IR (ATR) 3310, 3033, 2951, 1715, 1611, 1487, 1257, 1176, 1042, 734, 696 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{28}H_{25}ClN_2NaO_5$ $[M+Na]^+$: calcd. 527.1344, found 527.1360; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 254 nm), tR = 23.4 min (major), 43.4 min (minor).

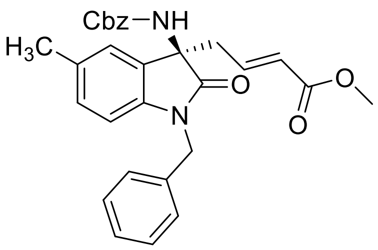
Methyl (*R,E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-5-nitro-2-oxoindolin-3-yl]but-2-enoate (3k)



Reaction of ketimine **1k** (0.10 mmol) and vinylketene silyl acetal **2a** (0.12 mmol) using **4a** (0.02 mmol) and $Cu(OTf)_2$ (0.02 mmol) in toluene (1.0 mL) at −40 °C for 192 h gave (*R*)-**3k** (33.6 mg, 65% yield, 79% ee) as a white solid.

$[\alpha]_D^{25}$ +8.0 (c 0.38, $CHCl_3$); m.p. 61.4-62.2 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 2.74-2.86 (m, 2H), 3.70 (s, 3H), 5.00 (br, 4H), 5.79 (s, 1H), 5.93 (d, *J* = 15.6 Hz, 1H), 6.58-6.72 (m, 2H), 7.26-7.34 (m, 10H), 8.14 (d, *J* = 10.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.5, 44.5, 51.8, 60.8, 67.7, 109.4, 118.7, 126.4, 127.1, 127.4, 128.0, 128.3, 128.4, 128.5, 128.6, 129.1, 130.0, 134.3, 135.2, 137.9, 143.6, 148.1, 154.3, 165.5, 176.0; IR (ATR) 3328, 3033, 2952, 1714, 1614, 1334, 1258, 1175, 1043, 732, 696 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{28}H_{25}N_3NaO_7$ $[M+Na]^+$: calcd. 538.1585, found 538.1578; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 254 nm), tR = 24.0 min (minor), 34.8 min (major).

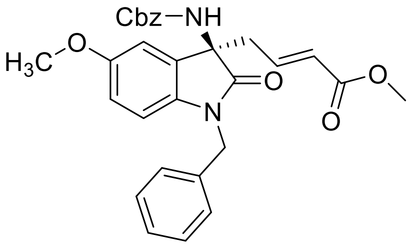
Methyl (*R,E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-5-methyl-2-oxoindolin-3-yl]but-2-enoate (3l)



Reaction of ketimine **1l** (0.10 mmol), and vinylketene silyl acetal **2a** (0.12 mmol) using **4a** (0.01 mmol) and $Cu(OTf)_2$ (0.01 mmol) in toluene (1.0 mL) at −40 °C for 168 h gave (*R*)-**3l** (48.0 mg, 99% yield, 92% ee) as a white solid.

$[\alpha]_D^{25}$ +25.7 (c 0.46, $CHCl_3$); m.p. 50.8-51.4 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 2.30 (s, 3H), 2.71 (dd, *J* = 7.8, 13.5 Hz, 1H), 2.82 (dd, *J* = 7.8, 13.5 Hz, 1H), 3.70 (s, 3H), 4.98 (br, 4H), 5.58 (s, 1H), 5.93 (d, *J* = 15.6 Hz, 1H), 6.54 (d, *J* = 8.1 Hz, 1H), 6.66-6.77 (m, 1H), 6.98 (d, *J* = 7.8 Hz, 1H), 7.11 (s, 1H), 6.96-7.29 (m, 10H); ^{13}C NMR (125 MHz, CD_3OD) δ 19.8, 39.2, 43.6, 50.7, 61.6, 66.4, 109.3, 122.9, 125.4, 127.0, 127.1, 127.6, 127.7, 128.1, 128.4, 129.1, 129.5, 132.8, 135.8, 136.4, 140.2, 140.3, 155.2, 166.1, 176.6; IR (ATR) 3322, 3032, 2950, 1705, 1604, 1496, 1235, 1179, 1044, 733, 696 cm^{-1}; HRMS (ESI, positive) m/z calcd for $C_{29}H_{28}N_2NaO_5$ $[M+Na]^+$: calcd. 507.1890, found 507.1894; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 254 nm), tR = 13.4 min (major), 33.7 min (minor).

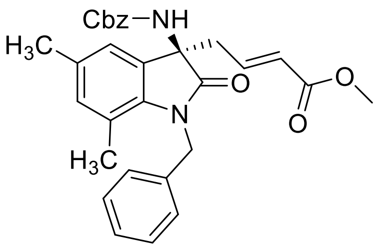
Methyl (*R*,*E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-5-methoxy-2-oxoindolin-3-yl]but-2-enoate (3m)



Reaction of **3m** (0.01 mmol), Cu(OTf)$_2$ (0.01 mmol), ketimine **1m** (0.10 mmol), and vinylketene silyl acetal **2a** (0.12 mmol) in toluene (1.0 mL) at −40 °C for 120 h gave (*R*)-**3m** (49.4 mg, 99% yield, 95% ee) as a white solid.

$[\alpha]_D^{25}$ −8.5 (c 0.43, CHCl$_3$); m.p. 49.4-50.2 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 2.72 (dd, *J* = 7.7, 13.5 Hz, 1H), 2.82 (dd, *J* = 7.7, 13.5 Hz, 1H), 3.68 (s, 3H), 3.74 (s, 3H), 4.95 (s, 2H), 4.98 (s, 2H), 5.67 (s, 1H), 5.91 (d, *J* = 15.7 Hz, 1H), 6.54 (d, *J* = 8.4 Hz, 1H), 6.64-6.74 (m, 2H), 6.92 (s, 1H), 7.23-7.34 (m, 10H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 40.0, 44.2, 51.7, 55.7, 61.4, 67.4, 110.2, 110.5, 113.5, 126.5, 127.1, 127.5, 128.3, 128.3, 128.5, 128.8, 130.2, 135.5, 135.6, 135.7, 139.5, 154.4, 156.1, 165.8, 175.4; IR (ATR) 3319, 3033, 2950, 1704, 1604, 1495, 1240, 1177, 1027, 733, 696 cm^{-1}; HRMS (ESI, positive) m/z calcd. for $C_{29}H_{28}N_2NaO_6$ [M+Na]$^+$: calc. 523.1840, found 523.1843; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 254 nm), tR = 18.9 min (major), 42.0 min (minor).

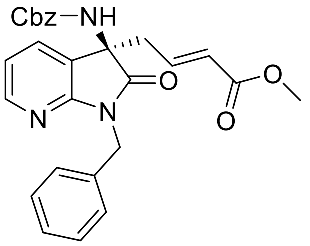
Methyl (*R*,*E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-5,7-dimethyl-2-oxoindolin-3-yl]but-2-enoate (3n)



Reaction of ketimine **1n** (0.10 mmol), and vinylketene silyl acetal **2a** (0.12 mmol) using **4a** (0.01 mmol) and Cu(OTf)$_2$ (0.01 mmol) in toluene (1.0 mL) at −40 °C for 144 h gave (*R*)-**3n** (49.3 mg, 99% yield, 93% ee) as a white solid.

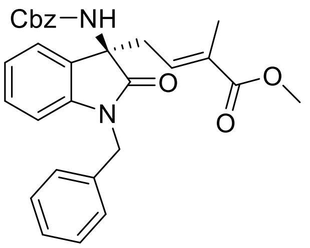
$[\alpha]_D^{25}$ +27.9 (c 0.43, CHCl$_3$); m.p. 58.0-59.0 °C; ^{1}H NMR (300 MHz, CDCl$_3$) δ 2.14 (s, 3H), 2.27 (s, 3H), 2.67-2.82 (m, 2H), 3.71 (s, 3H), 4.92-5.03 (m, 2H), 5.13 (s, 2H), 5.63 (s, 1H), 5.92 (d, *J* = 15.6 Hz, 1H), 6.70-6.78 (m, 2H), 6.97 (s, 1H), 7.21-7.31 (m, 10H); ^{13}C NMR (125 MHz, CDCl$_3$) δ 18.5, 20.8, 40.6 45.4, 51.7, 60.5, 67.3, 119.9, 121.6, 125.7, 126.4, 127.0, 128.2, 128.3, 128.5, 128.8, 129.8, 132.5, 133.9, 135.6, 137.6, 138.0, 139.9, 154.3, 165.9, 176.6; IR (ATR) 3314, 3032, 2951, 1704, 1604, 1482, 1250, 1174, 1026, 730, 696 cm^{-1}; HRMS (ESI, positive) m/z for $C_{30}H_{30}N_2NaO_5$ [M+Na]$^+$: calcd. 521.2047, found 521.2071; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 254 nm), tR = 13.8 min (major), 35.9 min (minor).

Methyl (*R,E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-3-yl]but-2-enoate (3o)



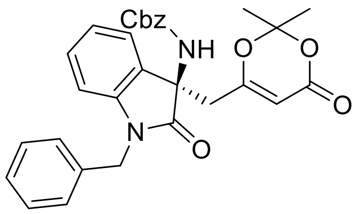
Reaction of ketimine **1o** (0.10 mmol), and vinylketene silyl acetal **2a** (0.12 mmol) using **4a** (0.011 mmol) and Cu(OTf)$_2$ (0.01 mmol) in toluene (1.0 mL) at −40 °C for 72 h gave (*R*)-**3o** (47.1 mg, 99% yield, 96% ee) as a white solid. $[\alpha]_D^{25}$ −14.2 (c 0.97, $CHCl_3$); m.p. 41.8-42.4 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 2.63 (dd, *J* = 7.8, 14.0 Hz, 1H), 2.82 (dd, *J* = 7.8, 14.0 Hz, 1H), 3.67 (s, 3H), 4.96 (br, 4H), 5.75 (s, 1H), 5.86 (d, *J* = 15.3 Hz, 1H) 6.61-6.72 (m, 1H), 6.95 (t, *J* = 6.3 Hz, 1H), 7.20-7.35 (m, 8H), 7.42 (d, *J* = 6.3 Hz, 2H), 7.54 (s, 1H), 8.21 (d, *J* = 5.4 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 39.2, 42.9, 51.7, 60.6, 67.4, 118.6, 123.4, 126.9, 127.4, 128.1, 128.1, 128.2, 128.3, 128.5, 131.1, 135.4, 136.3, 138.8, 148.2, 154.4, 156.0, 165.6, 175.4; IR (ATR) 3328, 3032, 2951, 1713, 1597, 1450, 1253, 1178, 1027, 738, 696 cm^{-1}; HRMS (ESI, positive) m/z for $C_{27}H_{25}N_3NaO_5$ $[M+Na]^+$: calcd. 494.1686, found 494.1688; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 254 nm), tR = 11.2 min (major), 28.6 min (minor).

Methyl (*R,E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-2-oxoindolin-3-yl]-2-methylbut-2-enoate (3p)



Reaction of ketimine **1d** (0.10 mmol) and vinylketene silyl acetal **2b** (0.30 mmol) using **4a** (0.011 mmol) and Cu(OTf)$_2$ (0.01 mmol) in toluene (1.0 mL) at 0 °C for 66 h gave (*R*)-**3p** (42.2 mg, 87% yield, 87% ee) as a white solid. $[\alpha]_D^{25}$ −8.1 (c 0.56, $CHCl_3$); m.p. 37.8-38.6 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 1.76 (s, 3H), 2.71-2.88 (m, 2H), 3.68 (s, 3H), 4.97 (br, 4H), 5.64 (s, 1H), 6.56-6.64 (m, 2H), 7.04 (t, *J* = 7.5 Hz, 1H), 7.16-7.30 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.8, 36.5, 44.1, 52.0, 61.1, 67.3, 109.6, 122.9, 123.0, 127.1, 127.5, 128.2, 128.4, 128.5, 128.7, 129.2, 132.2, 132.6, 135.5, 142.4, 154.4, 167.6, 176.0; IR (ATR) 3326, 3033, 2952, 1706, 1614, 1489, 1257, 1085, 1026, 735, 696 cm^{-1}; HRMS (ESI, positive) m/z for $C_{29}H_{28}N_2NaO_5$ $[M+Na]^+$: calcd. 507.1890, found 507.1894; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 254 nm), tR = 11.9 min (major), 27.8 min (minor).

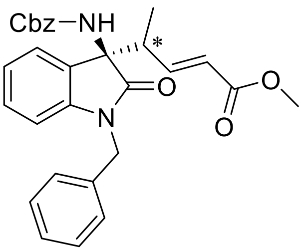
Benzyl (*R*)-[1-benzyl-3-(2,2-dimethyl-4-oxo-4H-1,3-dioxin-6-yl)methyl)-2-oxoindolin-3-yl]carbamate (3q)



Reaction of ketimine **1d** (0.10 mmol) and vinylketene silyl acetal **2c** (0.12 mmol) using **4a** (0.022 mmol) and $Cu(OTf)_2$ (0.02 mmol) in toluene (1.0 mL) at r.t. for 168 h gave (*R*)-**3q** (34.0 mg, 66% yield, 81% ee) as a white solid.

$[\alpha]_D^{25}$ −17.7 (c 0.52, $CHCl_3$); m.p. 53.2-53.8 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 1.32 (s, 3H), 1.49 (s, 3H), 2.86 (s, 2H), 4.87-5.05 (m, 4H), 5.17 (s, 1H), 5.86 (s, 1H), 6.71 (d, *J* = 8.1 Hz, 1H), 7.04 (t, *J* = 7.5 Hz, 1H), 7.18-7.36 (m, 12H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.6, 24.7, 40.3, 44.3, 60.6, 67.3, 97.1, 107.0, 109.6, 123.0, 124.2, 127.5, 127.8, 128.1, 128.3, 128.5, 128.9, 129.6, 135.2, 135.6, 142.6, 154.3, 160.1, 164.4, 174.9; IR (ATR) 3309, 3033, 2944, 1710, 1614, 1376, 1254, 1202, 1010, 750, 696 cm^{-1}; HRMS (ESI, positive) m/z for $C_{30}H_{28}N_2NaO_6$ $[M+Na]^+$: calcd. 535.1840, found 535.1851; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 254 nm), tR = 11.1 min (major), 27.1 min (minor).

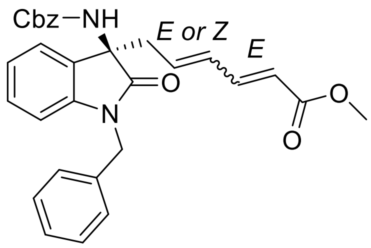
Methyl (*E*)-4-[(*R*)-1-benzyl-3-(benzyloxycarbonylamino)-2-oxoindolin-3-yl]-pent-2-enoate (3r)



Reaction of ketimine **1d** (0.10 mmol) and vinylketene silyl acetal **2d** (0.30 mmol) using **4a** (0.011 mmol) and $Cu(OTf)_2$ (0.01 mmol) in toluene (1.0 mL) at −40 °C for 96 h gave (*R*)-**3r** (48.5 mg, 99% yield, dr = 60:40; major: 93% ee, minor: 88% ee) as a white solid.

$[\alpha]_D^{25}$ −15.5 (c 0.66, $CHCl_3$); m.p. 47.0-48.0 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 0.77 (d, *J* = 6.9 Hz, 3H, major), 1.00 (d, *J* = 6.9 Hz, 3H, minor), 2.87-3.02 (m, 2H) 3.71 (s, 3H, minor), 3.77 (s, 3H, major), 4.96 (br, 4H), 5.44 (s, 1H), 5.52 (s, 1H), 5.93 (d, *J* = 15.6 Hz, 1H, minor), 6.04 (d, *J* = 15.6 Hz, 1H, major), 6.64-6.72 (m, 2H), 6.87-6.99 (m, 2H), 7.03-7.08 (m, 2H), 7.18-7.34 (m, 11H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 13.6 (major), 14.1 (minor), 43.4 (major), 43.9 (minor), 44.2 (major), 44.4 (minor), 51.7 (minor), 51.9 (major), 63.7 (major), 63.8 (minor), 67.3 (minor), 67.4 (major), 109.4, 109.5, 122.9, 123.2, 123.9, 124.2, 124.6, 127.3, 127.4, 127.5, 127.6, 128.1, 128.3, 128.3, 128.4, 128.5, 128.5, 128.7 (minor), 128.8 (major), 129.3 (minor), 129.4 (major), 135.6, 143.3 (minor), 143.5 (major), 145.9 (minor), 145.9 (major), 154.1 (major), 154.4 (minor), 166.0, 175.3 (minor), 175.6 (major); IR (ATR) 3328, 3033, 2951, 1706, 1613, 1488, 1255, 1179, 1003, 729, 696 cm^{-1}; HRMS (ESI, positive) m/z for $C_{29}H_{28}N_2NaO_5$ $[M+Na]^+$: calcd. 507.1890, found 507.1910; HPLC (DAICEL CHIRALPAK IF-3®, hexane:*i*-PrOH = 80:20, 1.0 mL/min, 254 nm), major: tR = 21.3 min (major), 56.7 min (minor), minor: tR = 25.0 min (major), 46.5 min (minor).

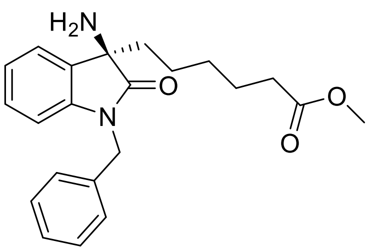
Methyl (2*E*)-6-[(*R*)-1-benzyl-3-(benzyloxycarbonylamino)-2-oxoindolin-3-yl]-hexa-2,4-dienoate methyl (3s)



Reaction of ketimine **1d** (0.10 mmol) and vinylketene silyl acetal **2e** (0.12 mmol) using **4a** (0.011 mmol) and $Cu(OTf)_2$ (0.01 mmol) in toluene (1.0 mL) at −40 °C for 168 h gave (*R*)-**3s** (40.3 mg, 81% yield, E/Z mixture, major:minor = 85:15) as a white solid. Ee was determined after transformation to **5**.

$[\alpha]_D^{25}$ −85.8 (c 0.27, $CHCl_3$); m.p. 52.4-53.2 °C; ^{1}H NMR (300 MHz, CD_3CN) δ 2.73 (dd, *J* = 7.5, 13.2 Hz, 1H, major), 2.82 (dd, *J* = 7.5, 13.2 Hz, 1H, major), 2.89-3.04 (m, 2H, minor) 3.70 (s, 3H, minor), 3.70 (s, 3H, major), 4.88-4.98 (m, 4H), 5.46 (dd, *J* = 8.7, 17.4 Hz, 1H, minor), 5.68-5.76 (m, 1H, major), 5.81 (d, *J* = 15.6 Hz, 1H, major), 5.89 (d, *J* = 15.6 Hz, 1H, minor), 6.11-6.24 (m, 1H), 6.63 (s, 1H), 6.72 (d, *J* = 7.8 Hz, 1H), 6.70-7.09 (m, 2H), 7.21-7.24 (t, *J* = 7.8 Hz, 1H), 7.30-7.46 (m, 10H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 35.9 (minor), 40.9 (major), 44.1, 51.6 (major), 51.7 (minor), 61.1 (minor), 61.4 (major), 67.3, 109.4 (minor), 109.6 (major), 121.4, 122.9 (major), 123.0 (minor), 123.2, 127.2 (major), 127.2 (minor), 127.3, 127.6, 128.2, 128.5, 128.7, 128.8, 129.1 (minor) 129.2 (major), 130.5, 131.2, 133.7 (major), 133.7 (minor), 135.5 (major), 135.6 (minor), 137.9, 142.4 (minor), 143.4, 154.4 (major), 154.4 (minor), 167.1 (minor), 167.2 (major), 175.8 (minor), 175.9 (major); IR (ATR) 3318, 3032, 2950, 1705, 1614, 1488, 1256, 1177, 1001, 732, 695 cm^{-1}; HRMS (ESI, positive) m/z for $C_{30}H_{28}N_2NaO_5$ $[M+Na]^+$: calcd. 519.1890, found 519.1887

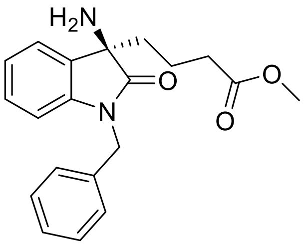
Methyl (*R*)-6-(3-amino-1-benzyl-2-oxoindolin-3-yl)hexanoate (5)



Pd/C (20 wt% on carbon, 8.1 mg) was added to a solution of **3s** (40.3 mg, 0.081 mmol) in methanol (0.8 mL). The reaction mixture was degassed in vacuo, placed under H_2 (balloon), stirred at r.t. for 3 h. The mixture was filtered and washed with methanol, then the solvent was removed under reduced pressure to give the crude product, which was purified by silica gel column chromatography (ethyl acetate) to afford **5** (27.8 mg, 94% yield, 89% ee) as a colorless oil.

$[\alpha]_D^{25}$ +23.0 (c 0.84, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.93-1.02 (m, 1H), 1.06-1.16 (m, 1H), 1.19-1.28 (m, 2H), 1.46-1.56 (m, 2H), 1.79 (s, 2H), 1.88 (t, *J* = 7.2 Hz, 2H), 2.20 (t, *J* = 7.5 Hz, 1H), 3.63 (s, 3H), 4.77 (d, *J* = 15.8 Hz, 1H), 5.01 (d, *J* = 15.8 Hz, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 7.20 (t, *J* = 7.8 Hz, 1H), 7.29-7.37 (m, 6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 23.4, 24.6, 33.8, 39.2, 43.8, 51.5, 61.1, 109.2, 122.9, 123.7, 127.4, 127.7, 128.8, 131.7, 135.9, 142.5, 174.1, 180.8; IR (ATR) 3361, 3032, 2935, 2858, 1710, 1613, 1466, 1348, 1172, 750, 697 cm^{-1}; HRMS (ESI, positive) m/z for $C_{22}H_{26}N_2NaO_3$ $[M+Na]^+$: calcd. 389.1836, found 389.1837; HPLC (for its *N*-*p*-methoxybenzenesulfonyl protected derivative, DAICEL CHIRALPAK IB N-3®, hexane:*i*-PrOH = 70:30, 1.0 mL/min, 254 nm), tR = 18.6 min (major), 35.4 min (minor).

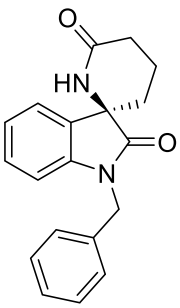
Methyl (*R*)-4-(3-amino-1-benzyl-2-oxoindolin-3-yl)butanoate (6)



Pd/C (20 wt% on carbon, 4.7 mg) was added to a solution of **3d** (23.5 mg, 0.05 mmol) in methanol (0.5 mL). The reaction mixture was degassed in vacuo, placed under H_2 (balloon), stirred at r.t. for 6 h. The mixture was filtered and washed with methanol, then the solvent was removed under reduced pressure to give the crude product, which was purified by silica gel column chromatography (ethyl acetate) to afford **6** (13.5 mg, 80% yield) as a colorless oil. Ee was determined after transformation to **6**.

$[\alpha]_D^{25}$ −3.3 (c 0.32, $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.34-1.52 (m, 2H), 1.73 (br, 2H), 1.84-1.97 (m, 2H), 2.18-2.27 (m, 2H), 3.62 (s, 3H), 4.81 (d, *J* = 15.6 Hz, 1H), 4.99 (d, *J* = 15.6 Hz, 1H), 6.74 (d, *J* = 7.8 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 7.20 (t, *J* = 7.8 Hz, 1H), 7.29-7.34 (m, 6H); ^{13}C NMR (125 MHz, CD_3OD) δ 19.1, 33.0, 38.0, 43.1, 50.5, 60.6, 109.3, 122.8, 123.2, 126.9, 127.0, 127.2, 128.3, 128.4, 128.6, 131.1, 135.8, 142.4, 173.5, 180.0; IR (ATR) 3031, 2950, 1709, 1612, 1466, 1348, 1254, 1173, 749, 697, 630 cm^{-1}; HRMS (ESI, positive) m/z for $C_{20}H_{22}N_2NaO_3$ $[M+Na]^+$: calcd. 361.1523, found 361.1516.

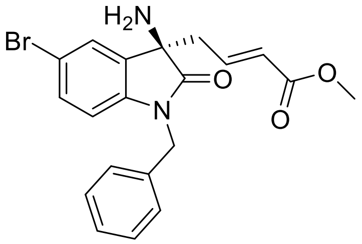
(*R*)-1-Benzylspiro[indoline-3,2'-piperidine]-2,6'-dione (7)



To a solution of **5** (13.5 mg, 0.04 mmol) in dry toluene (0.4 mL), trifluoroacetic acid (6.1 µL, 0.08 mmol) was added at r.t. under nitrogen atmosphere. The reaction mixture was heated at 90 ºC with oil bath for 6 h, and allowed to cool down to r.t., then quenched with sat. $NaHCO_3$, and aqueous layer was extracted with ethyl acetate. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to give the crude product, which was purified by silica gel column chromatography (ethyl acetate) to afford **7** (12.0 mg, 97% yield, 97% ee) as a white solid.

$[\alpha]_D^{25}$ +110.9 (c 0.25, $CHCl_3$); m.p. 170.4-171.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.90-2.12 (m, 3H), 2.47-2.69 (m, 3H), 4.79 (d, *J* = 15.6 Hz, 1H), 4.98 (d, *J* = 15.6 Hz, 1H), 5.76 (s, 1H), 6.75 (d, *J* = 7.8 Hz, 1H), 7.07 (t, *J* = 7.5 Hz, 1H), 7.21-7.36 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 16.4, 30.9, 32.6, 43.9, 61.6, 109.7, 123.3, 123.6, 127.3, 127.9, 128.9, 129.9, 130.5, 135.4, 141.6, 172.4, 176.6; IR (ATR) 3185, 3063, 2940, 1718, 1656, 1610, 1464, 1343, 1167, 758, 714 cm^{-1}; HRMS (ESI, positive) m/z for $C_{19}H_{18}N_2NaO_2$ $[M+Na]^+$: calcd. 329.1260, found 329.1264; HPLC (DAICEL CHIRALPAK IB-3®, hexane:*i*-PrOH = 80:20, 1.0 mL/min, 215 nm), tR = 17.0 min (major), 26.3 min (minor).

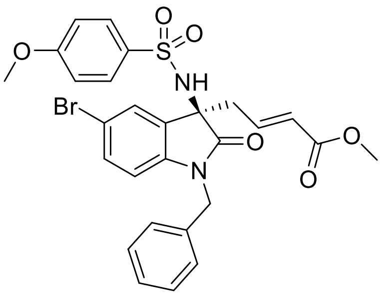
Methyl (*R,E*)-4-(3-amino-1-benzyl-5-bromo-2-oxoindolin-3-yl)but-2-enoate (8)



To a solution of **3e** (27.5 mg, 0.05 mmol) in dry dichloromethane (1.3 mL), anisole (81.7 µL, 0.75 mmol) at 0 °C, then trifluoromethanesulfonic acid (44.0 µL, 0.50 mmol) was added slowly. The reaction mixture was stirred for 4 h, then quenched with sat. $NaHCO_3$, and aqueous layer was extracted with dichloromethane. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to give the crude product, which was purified by silica gel column chromatography (hexane/CH_2Cl_2/ethyl acetate=2:1:1) to afford **8** (19.1 mg, 92% yield) as a colorless oil. Ee was determined after transformation to **9**.

$[\alpha]_D^{25}$ −43.8 (c 0.33, $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$) δ 1.79 (br, 2H), 2.67-2.82 (m, 2H), 3.69 (s, 3H), 4.67 (d, *J* = 15.8 Hz, 1H), 5.04 (d, *J* = 15.8 Hz, 1H), 5.87 (d, *J* = 15.6 Hz, 1H), 6.57 (d, *J* = 8.4 Hz, 1H), 6.61-6.71 (m, 1H), 7.21 (d, *J* = 7.8 Hz, 2H), 7.26-7.34 (m, 4H), 7.50 (d, *J* = 2.1 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 41.6, 43.9, 51.6, 60.7, 111.1, 115.9, 125.7, 127.1, 127.2, 127.8, 128.9, 132.3, 132.5, 134.9, 140.9, 141.2, 166.0, 179.0; IR (ATR) 3362, 3032, 2950, 1712, 1605, 1482, 1331, 1173, 809, 729, 697 cm^{-1}; HRMS (ESI, positive) m/z for $C_{20}H_{19}BrN_2NaO_3$ $[M+Na]^+$: calcd. 437.0471, found 437.0471.

Methyl (*R,E*)-4-[1-benzyl-5-bromo-3-(4-methoxybenzenesulfonamide)-2-oxoindolin-3-yl]but-2-enoate (9)

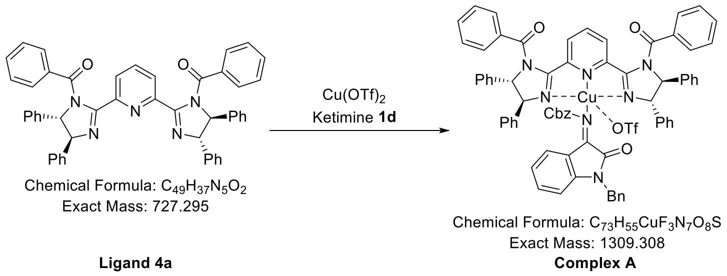


To a solution of **8** (27.5 mg, 8.7 µmol) in dry chloroform (44.0 µL), pyridine (1.05 µL, 13.0 µmol) at 0 °C, then 4-methoxybenzenesulfonyl Chloride (2.2 mg, 10.0 µmol) was added. The reaction mixture was warmed up to r.t. and stirred for 26 h, then quenched with H_2O, and aqueous layer was extracted with dichloromethane. The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure to give the crude product, which was purified by silica gel column chromatography (hexane/CH_2Cl_2/ethyl acetate=2:1:1) to afford **9** (5.1 mg, 99% yield, 95% ee) as a white solid. It was used X-ray crystal analysis to determine absolute stereochemistry.

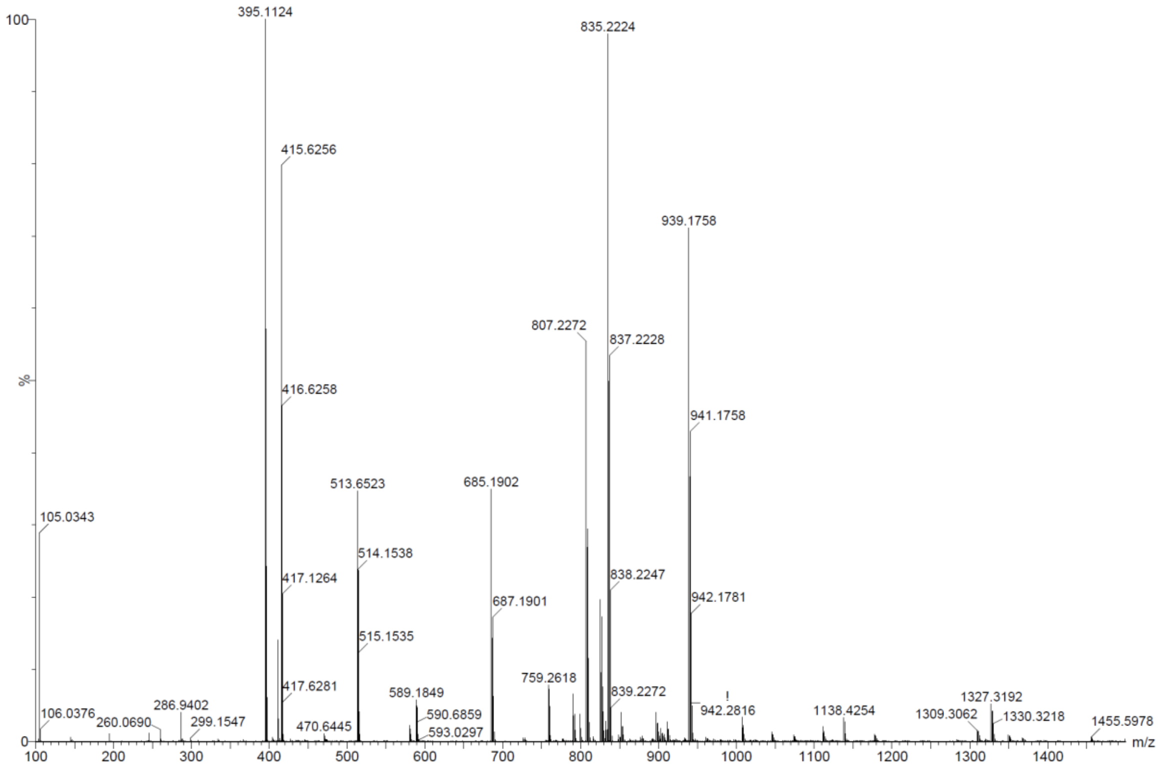
$[\alpha]_D^{25}$ −121.8 (c 0.12, $CHCl_3$); m.p. 177.0-178.0 °C; ^1H NMR (500 MHz, $CDCl_3$) δ 2.75-2.85 (m, 2H), 3.68 (s, 3H), 3.87 (s, 3H), 4.73 (d, *J* = 16.0 Hz, 1H), 5.02 (d, *J* = 16.0 Hz, 1H), 5.92 (d, *J* = 15.5 Hz, 1H), 6.05 (s, 1H), 6.44-6.49 (m, 1H), 6.51 (d, *J* = 8.5 Hz, 1H), 6.65 (d, *J* = 2.0 Hz, 1H), 6.79-6.82 (m, 2H), 7.23 (dd, *J* = 2.0, 8.5 Hz, 1H), 7.25-7.36 (m, 7H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 40.8, 44.6, 51.7, 55.6, 62.4, 111.3, 113.9, 115.3, 126.4, 127.1, 127.2, 127.8, 128.1, 128.9, 129.5, 132.0, 132.6, 134.8, 138.4, 142.1, 163.1, 165.7, 175.7; IR (ATR) 3230, 2948, 2841, 1717, 1596, 1330, 1260, 1151, 1091, 728, 697 cm^{-1}; HRMS (ESI, positive) m/z for $C_{27}H_{25}BrN_2NaO_6S$ $[M+Na]^+$: calcd. 607.0509, found 607.0507; HPLC

(DAICEL CHIRALPAK IA®, hexane:ethyl acetate = 70:30, 1.0 mL/min, 254 nm), tR = 23.4 min (major), 43.4 min (minor).

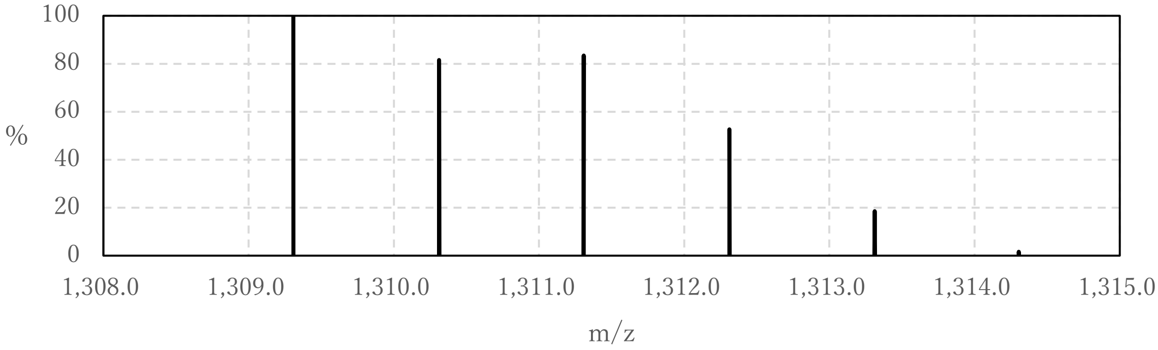
Figure S1. ESI-Mass spectroscopic analysis for complex between **4a** and $Cu(OTf)_2$ with ketimine **1d**



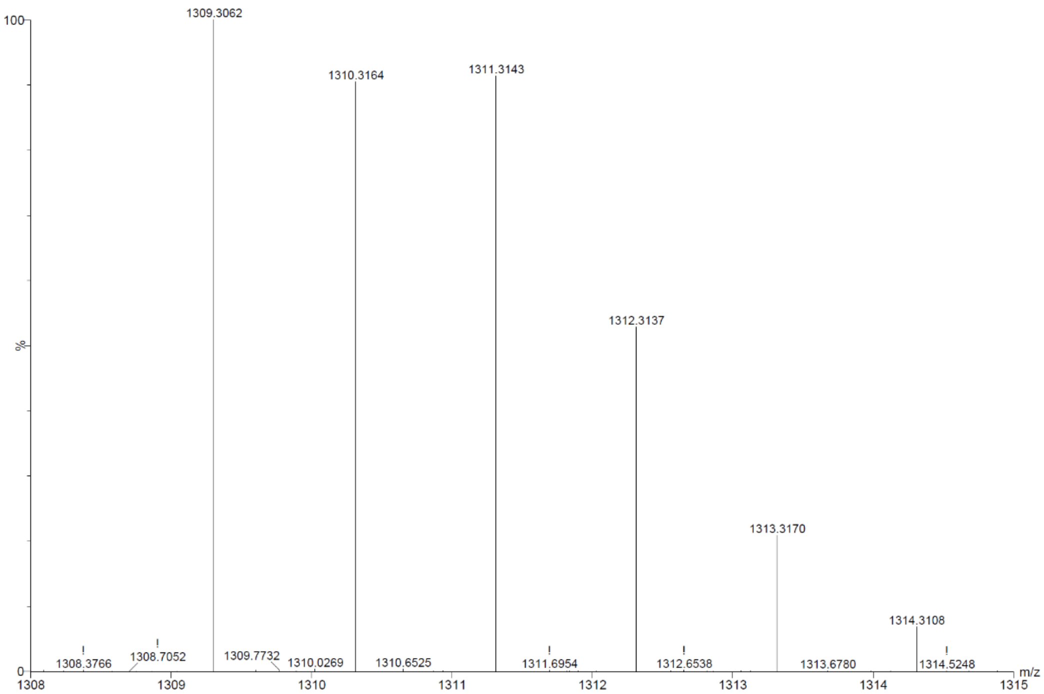
(a) The ESI-Mass spectrum of ligand **4a**, ketimine **1d** and $Cu(OTf)_2$.



(b) Theoretical peaks about Complex **A**



(c) Major peaks about Complex **A**



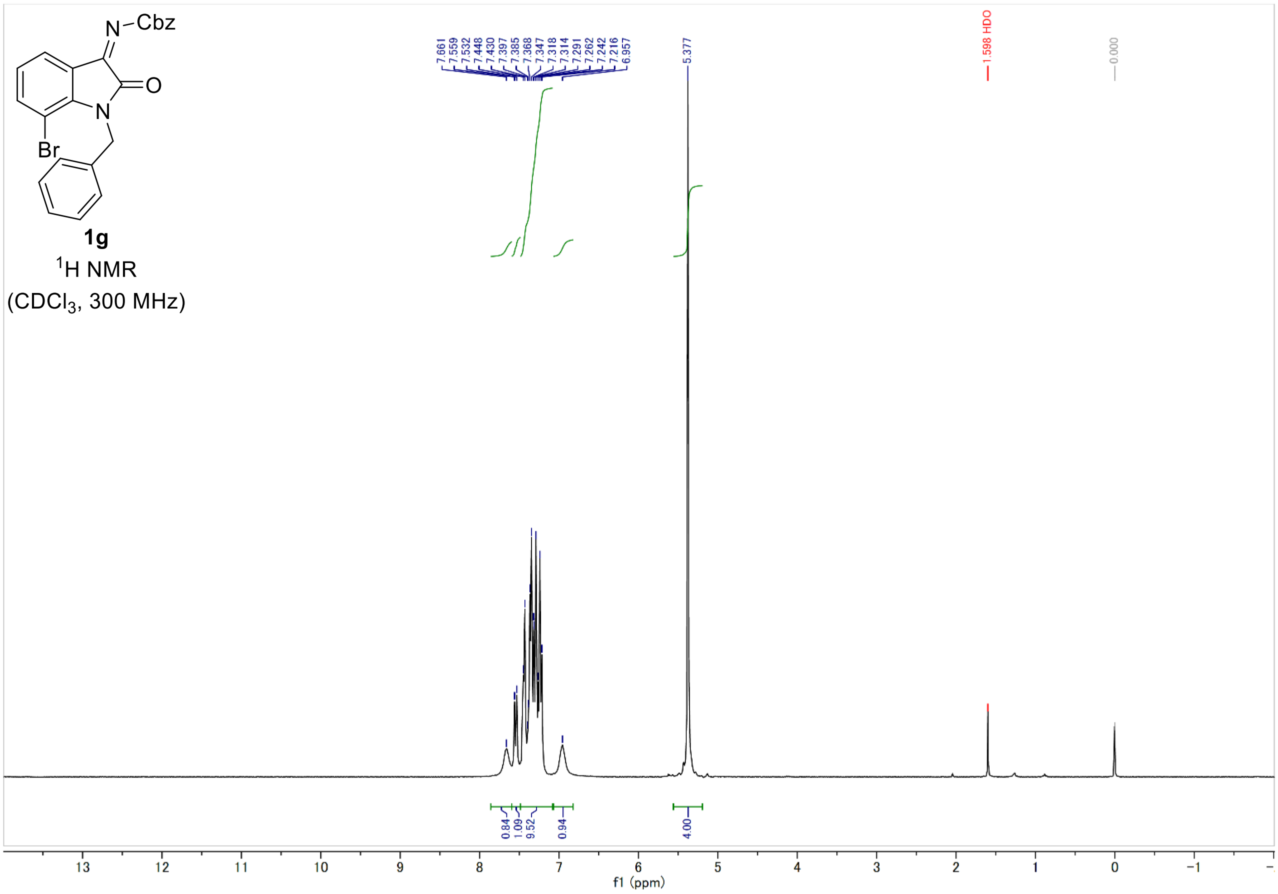
References

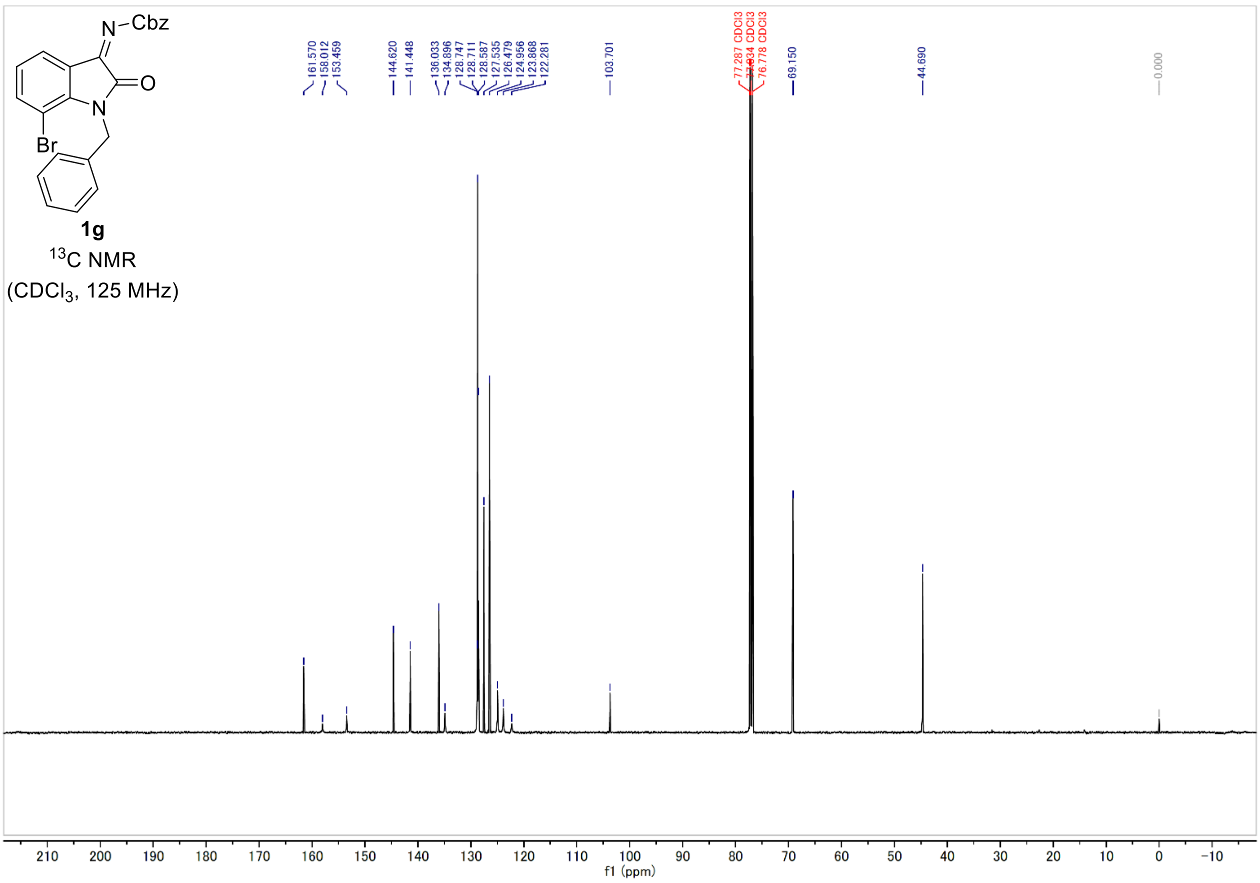
1) (a) Anilkumar, G.; Bhor, S.; Tse, M. K.; Kkawonn, M.; Bitterlich, B.; Beller, M. *Tetrahedron Asymmetry,* **2005**, *16*, 3536. (b) Nakamura, S.; Ohara, M.; Nakamura, Y.; Shibata, N.; Toru, T. *Chem. Eur. J.* **2010**, *16*, 2360.

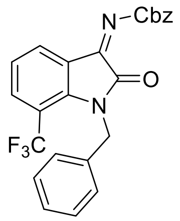
2) Ratjen, L.; Garcia-Garcia, P.; Lay, F.; Beck, M. E.; List, B. *Angew. Chem. Int. Ed.* **2011**, *50*, 754.

3) Yan, W.; Wang, D.; Feng, J.; Li, P.; Zhao, D.; Wang, R. *Org. Lett.* **2012**, *14*, 2512.

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



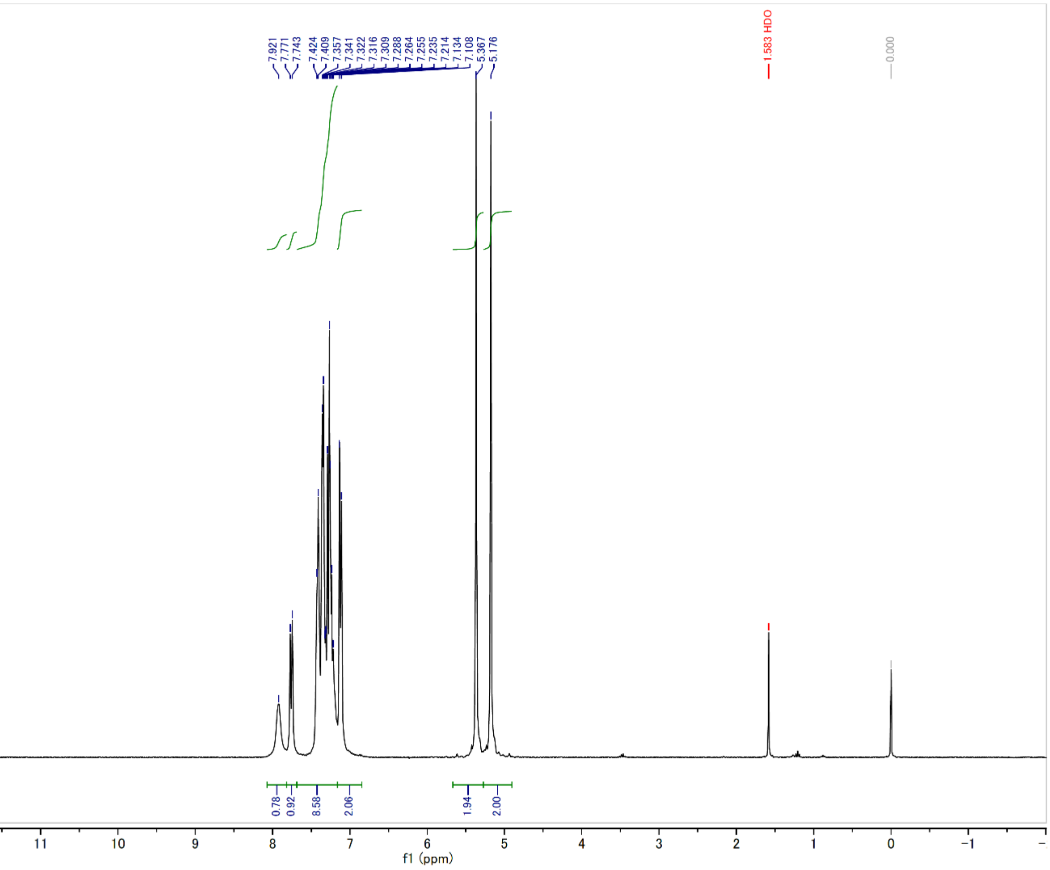


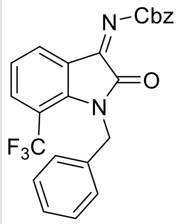


1i

^{1}H NMR

($CDCl_3$, 300 MHz)

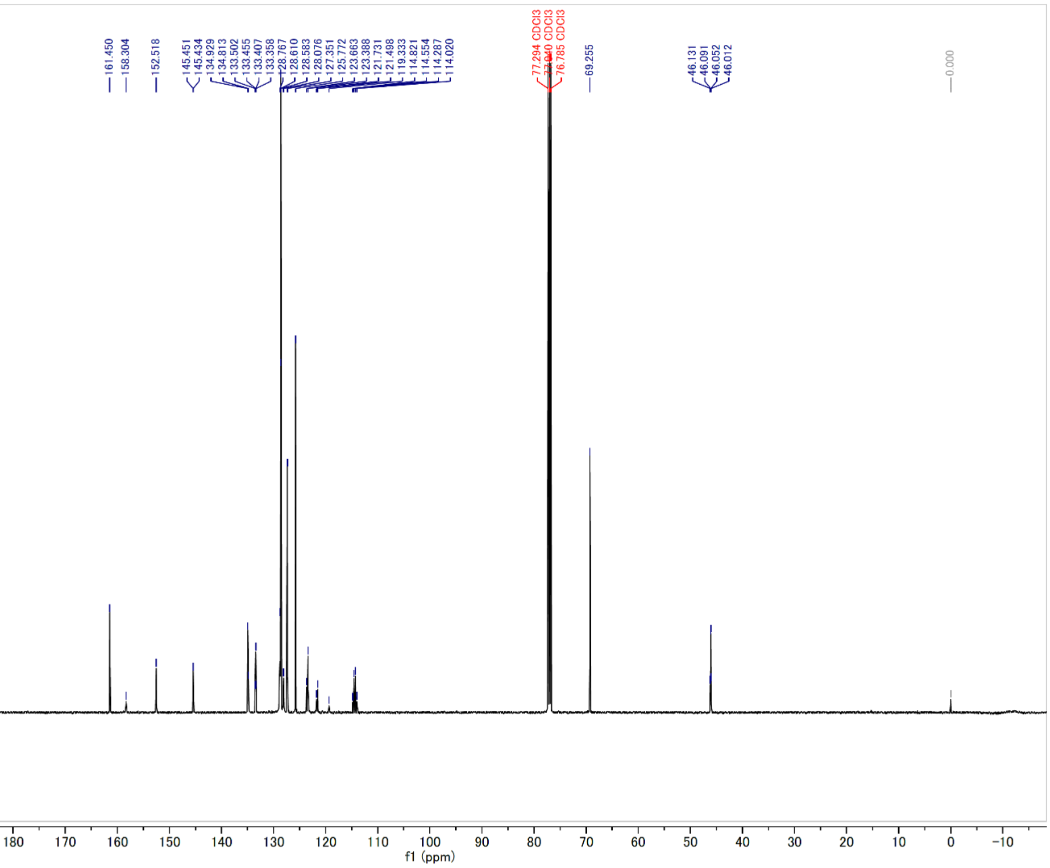


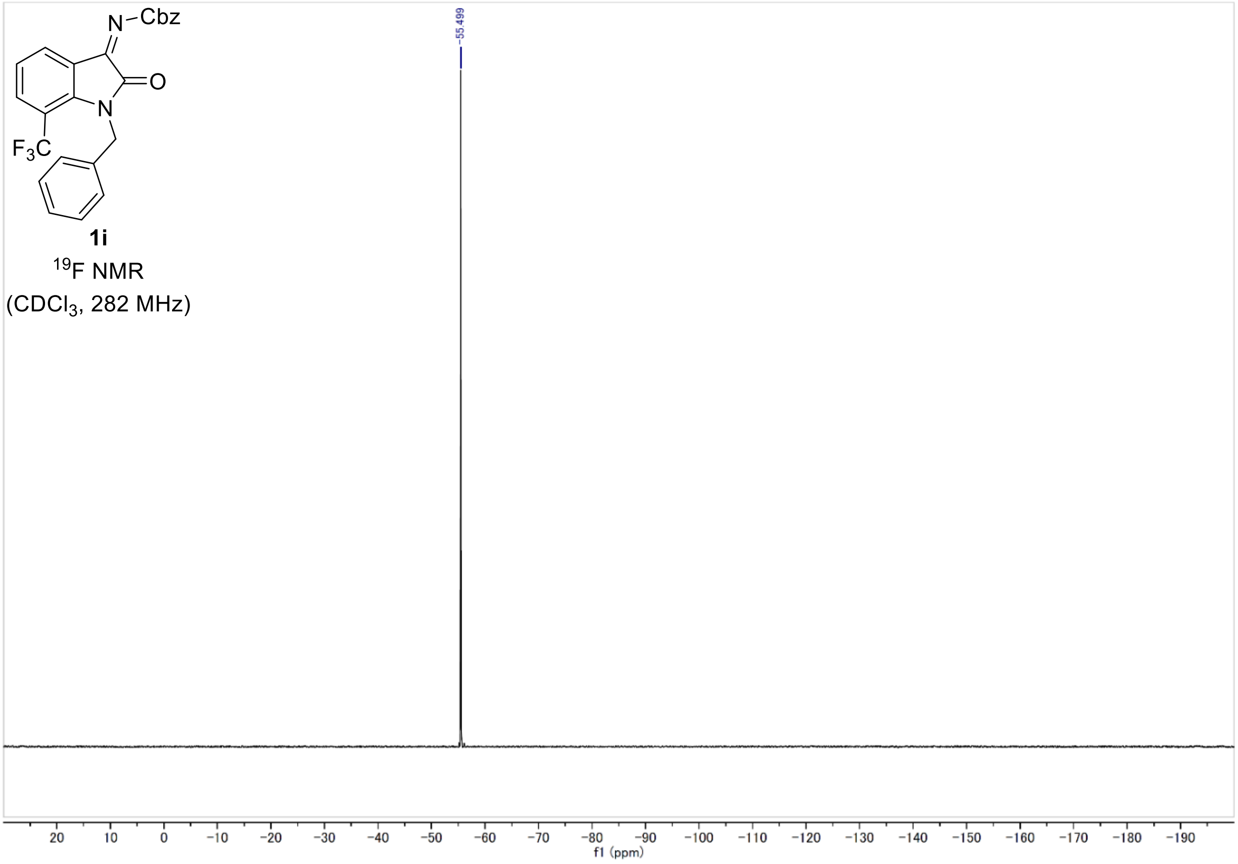


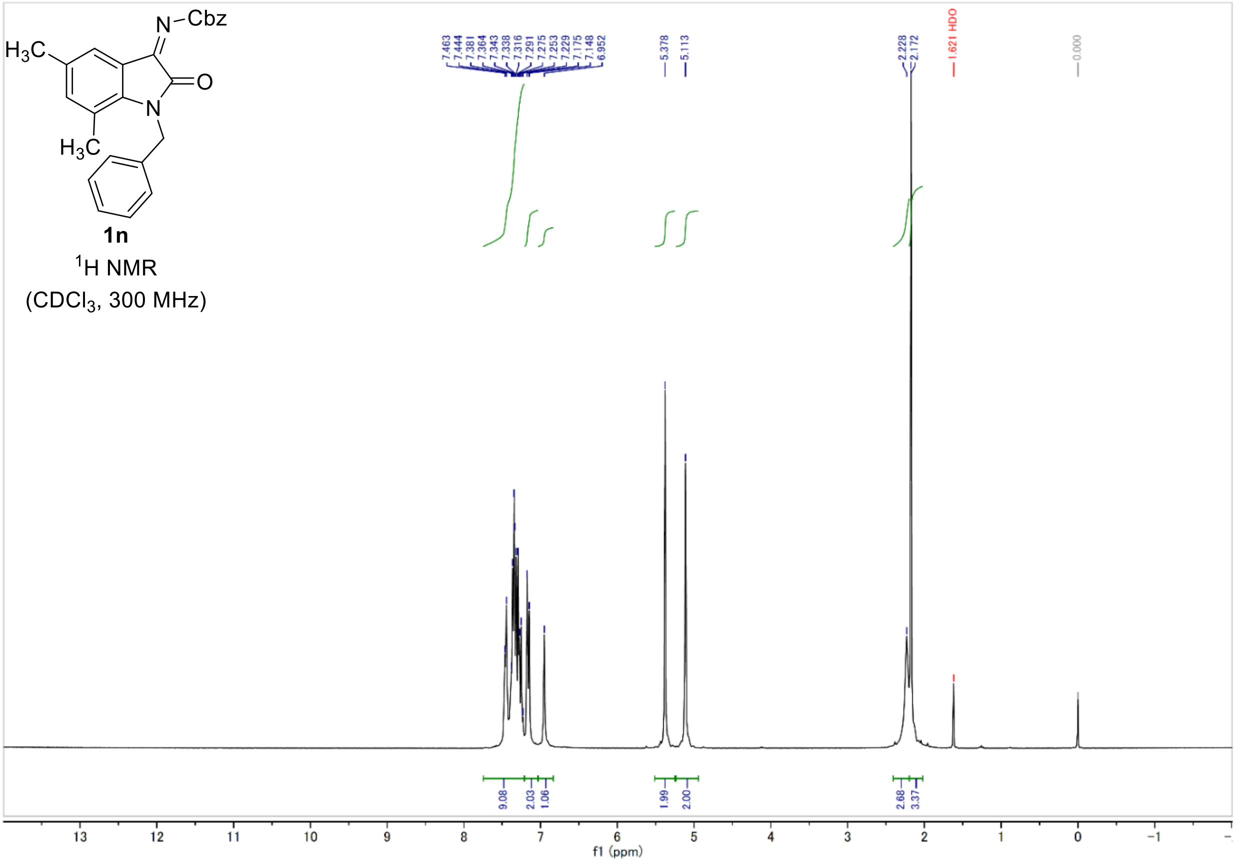
1i

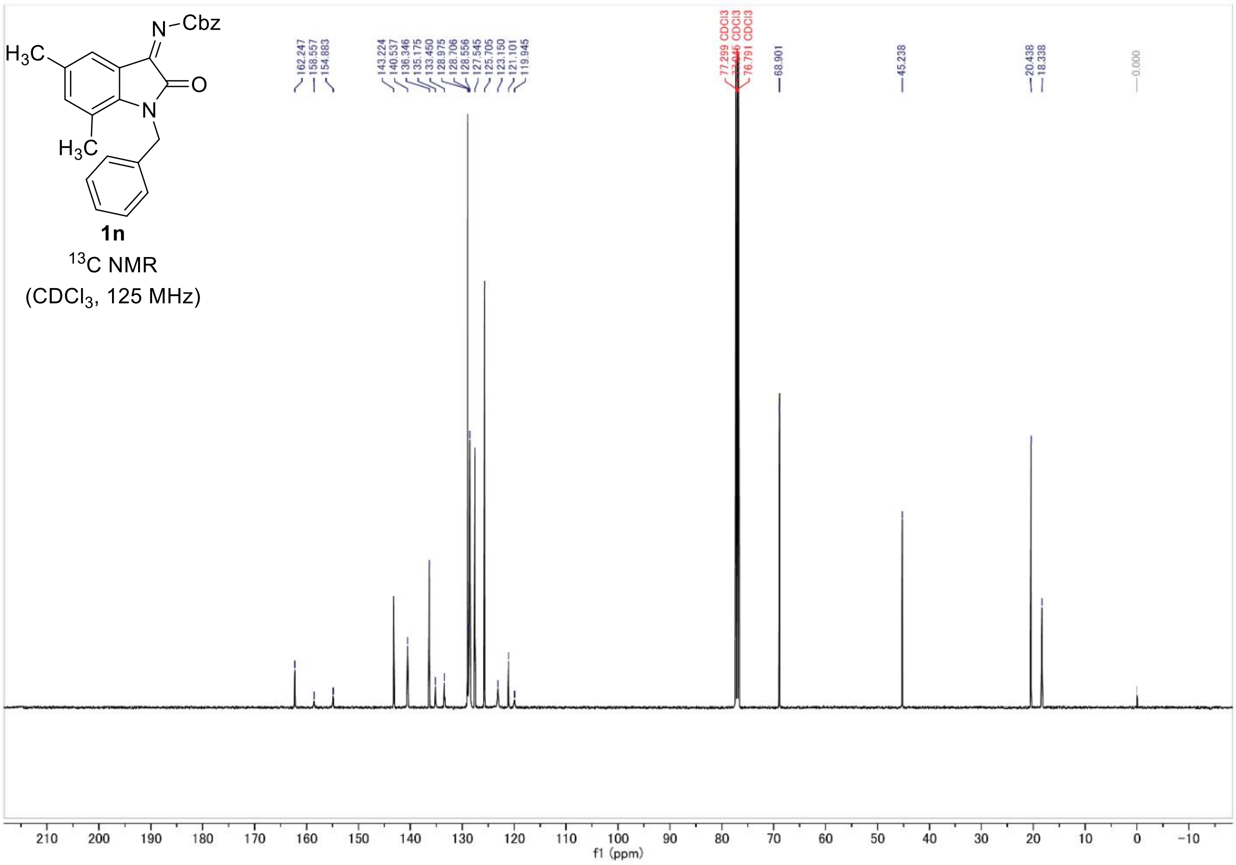
^{13}C NMR

($CDCl_3$, 125 MHz)




N–Cbz
O
N
F3C
1i
19F NMR
(CDCl3, 282 MHz)
-55.499
20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190
f1 (ppm)


N–Cbz
H3C
O
N
H3C
1n
1H NMR
(CDCl3, 300 MHz)
f1 (ppm)


N–Cbz
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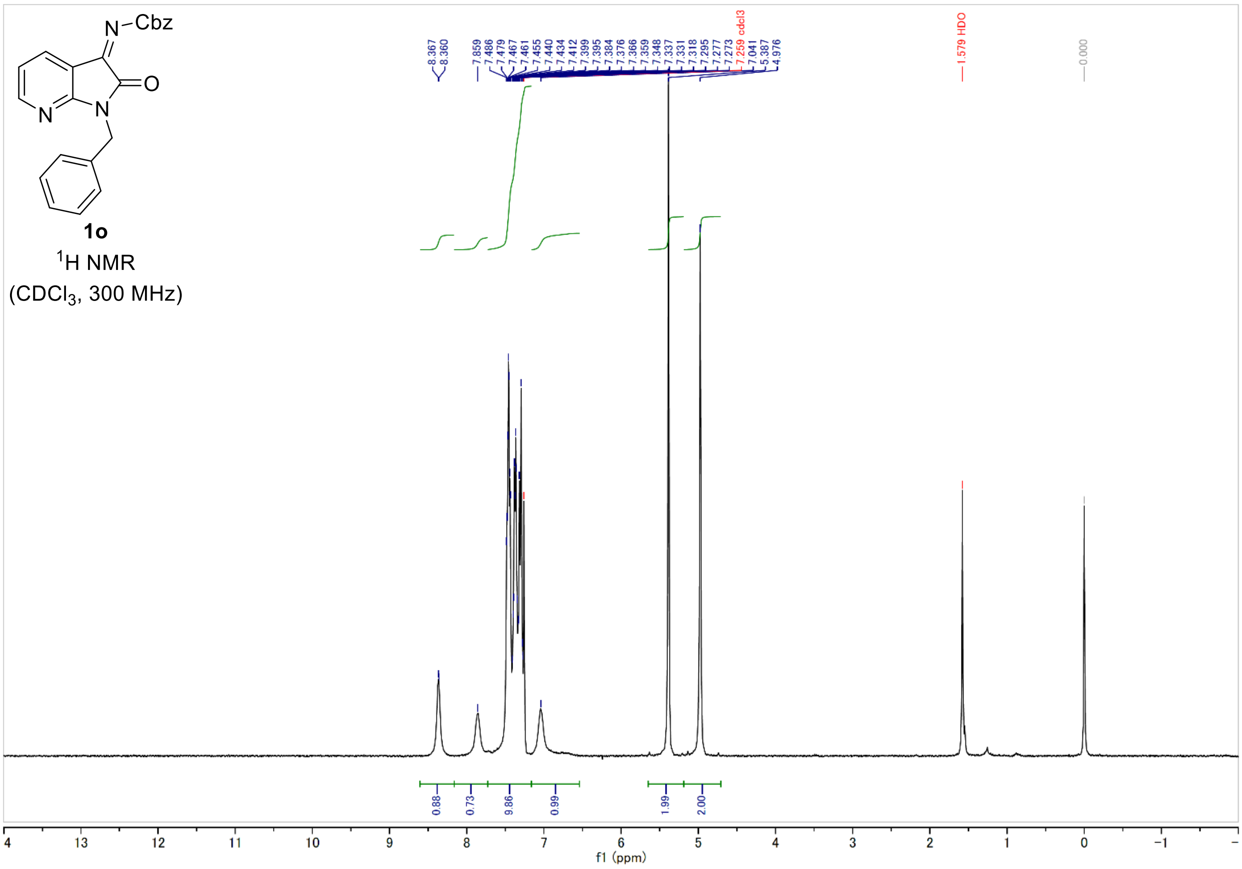
O
N
H3C
1n
13C NMR
(CDCl3, 125 MHz)
f1 (ppm)


N-Cbz
O
N
N
1o
1H NMR
(CDCl3, 300 MHz)
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1.579 HDO
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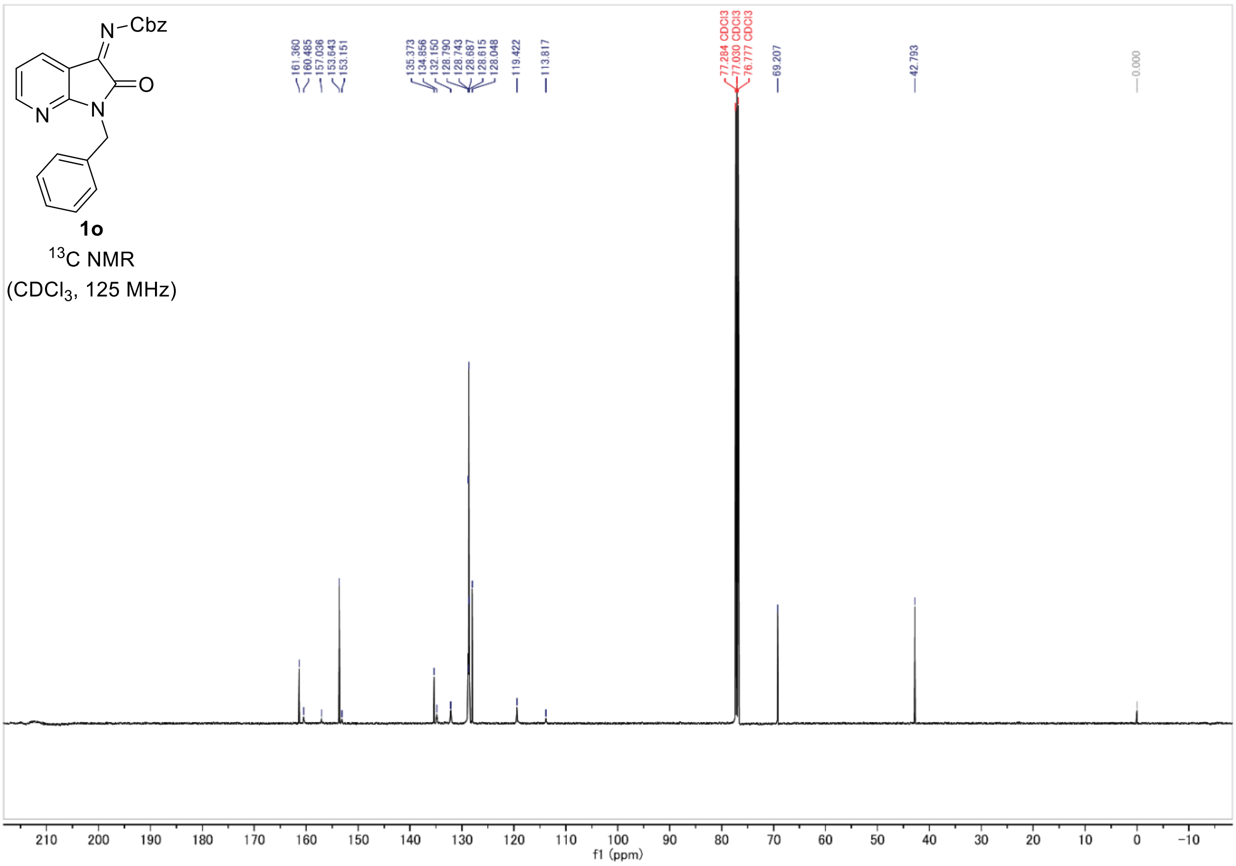
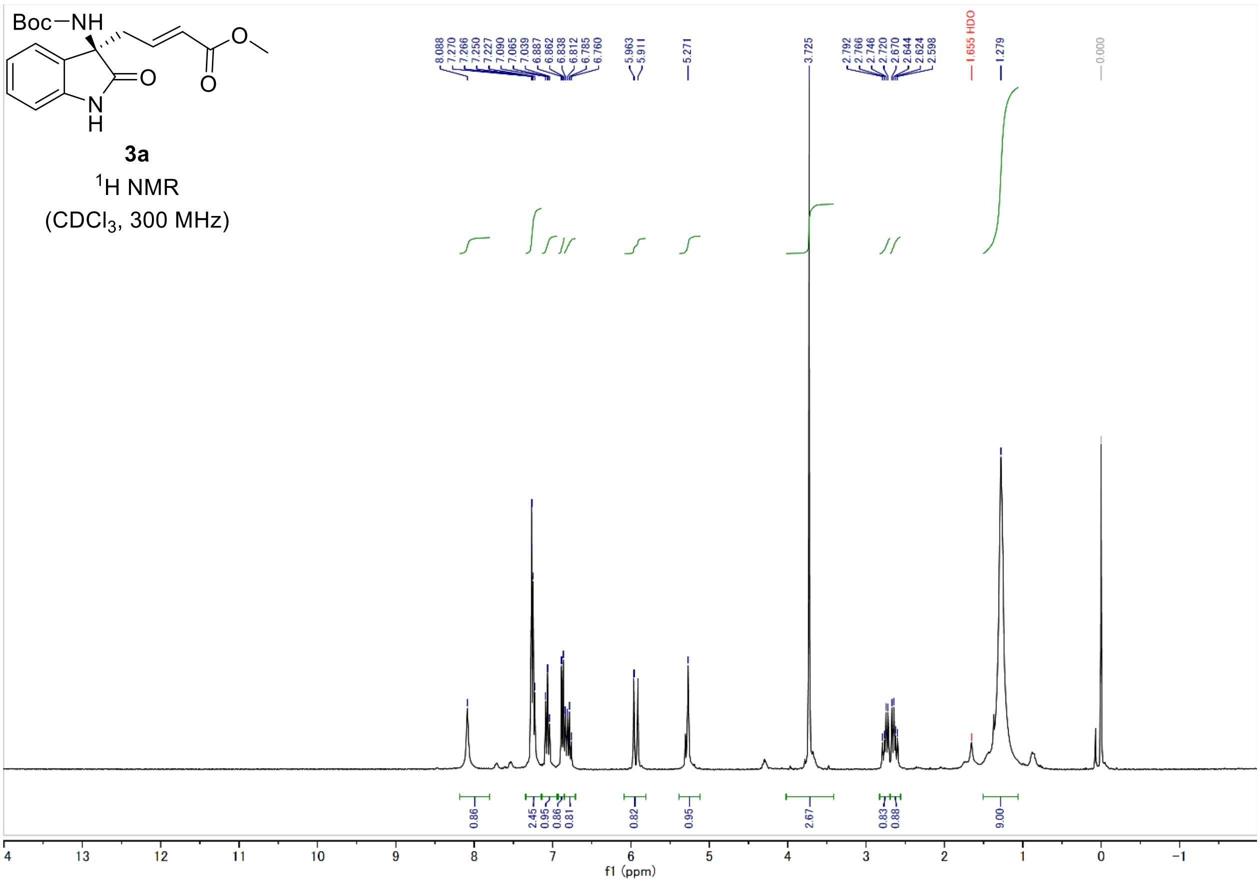
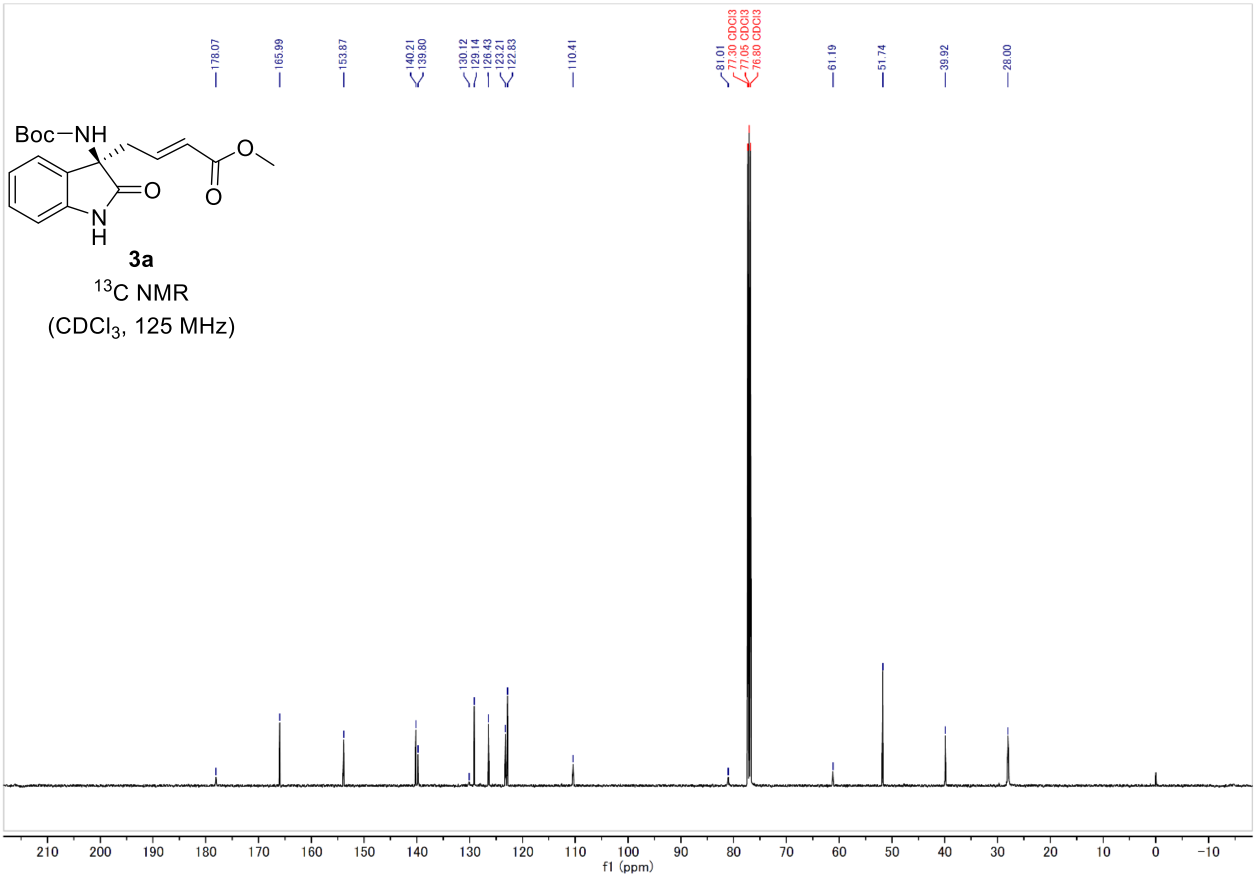
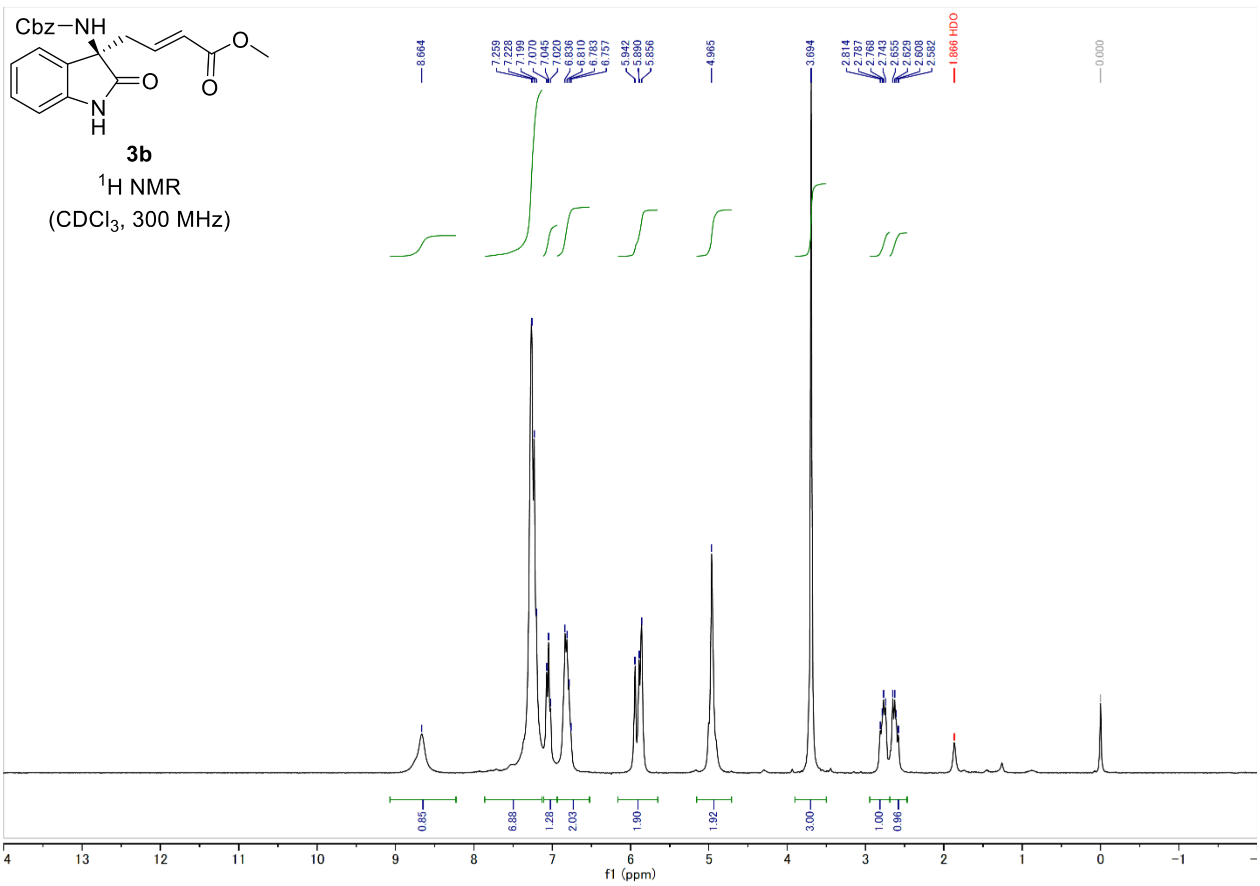
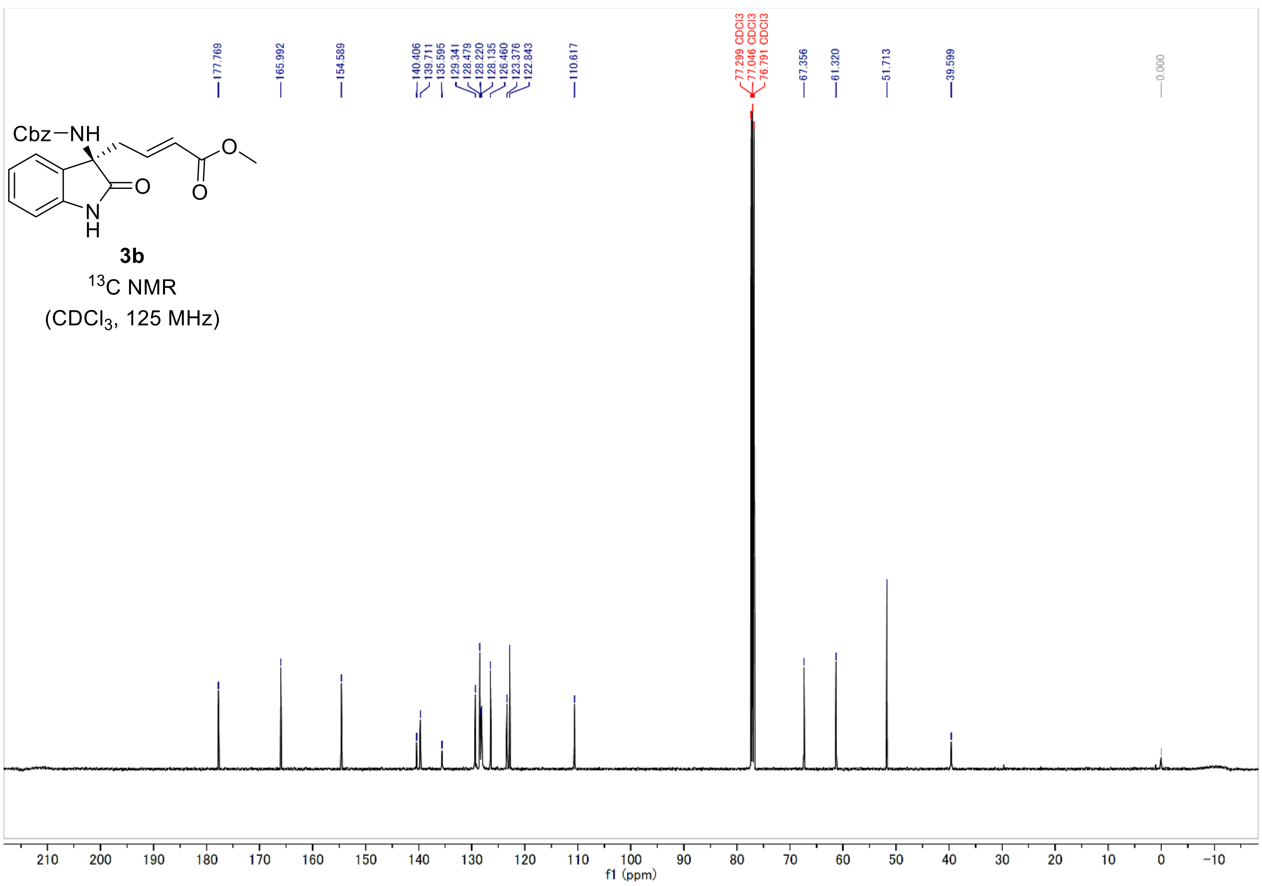
0.88
0.73
9.86
0.99
1.99
2.00
f1 (ppm)

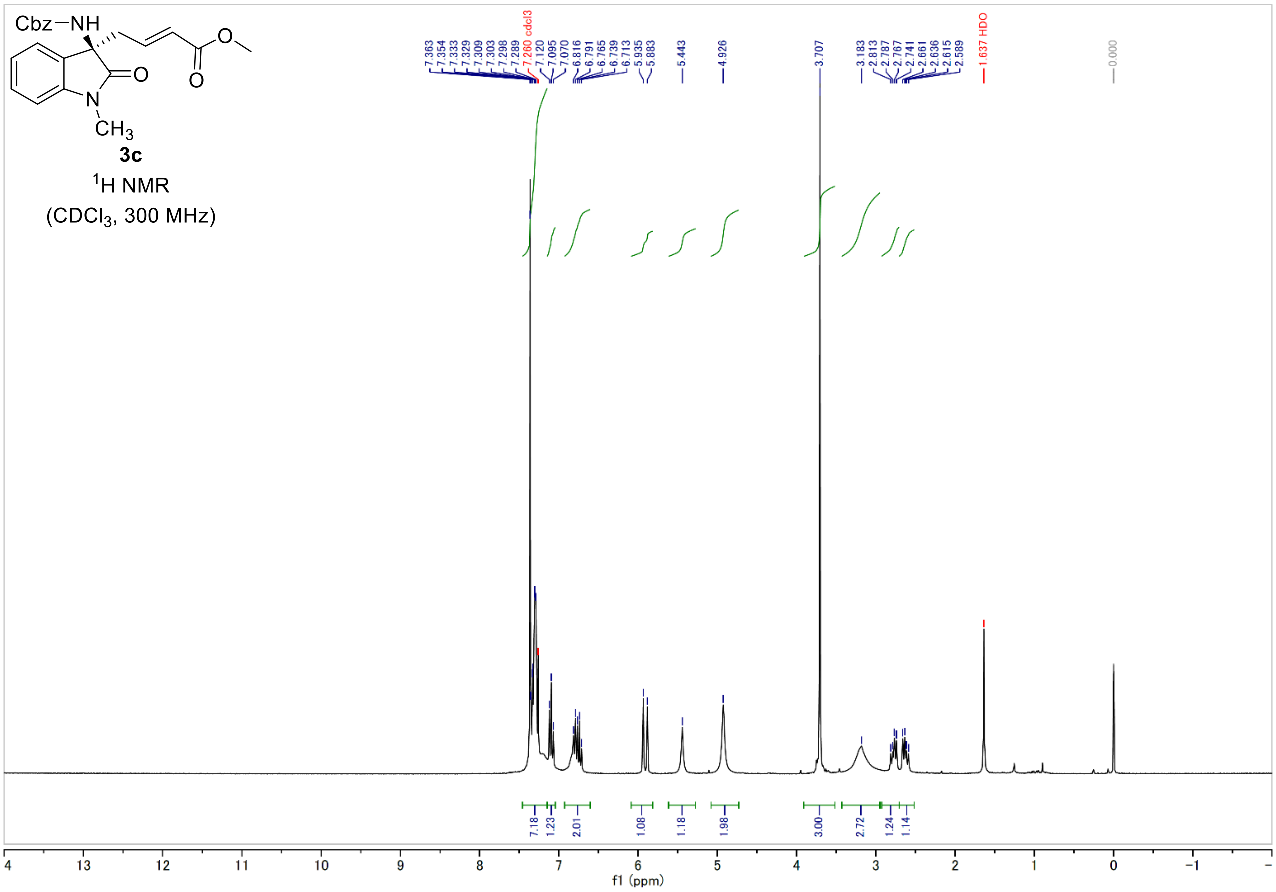

N-Cbz
O
N
N
1o
13C NMR
(CDCl3, 125 MHz)
161.360
160.485
157.036
153.643
153.151
135.373
134.856
132.150
128.790
128.743
128.687
128.615
128.048
119.422
113.817
77.284 CDCl3
77.030 CDCl3
76.777 CDCl3
69.207
42.793
0.000
f1 (ppm)

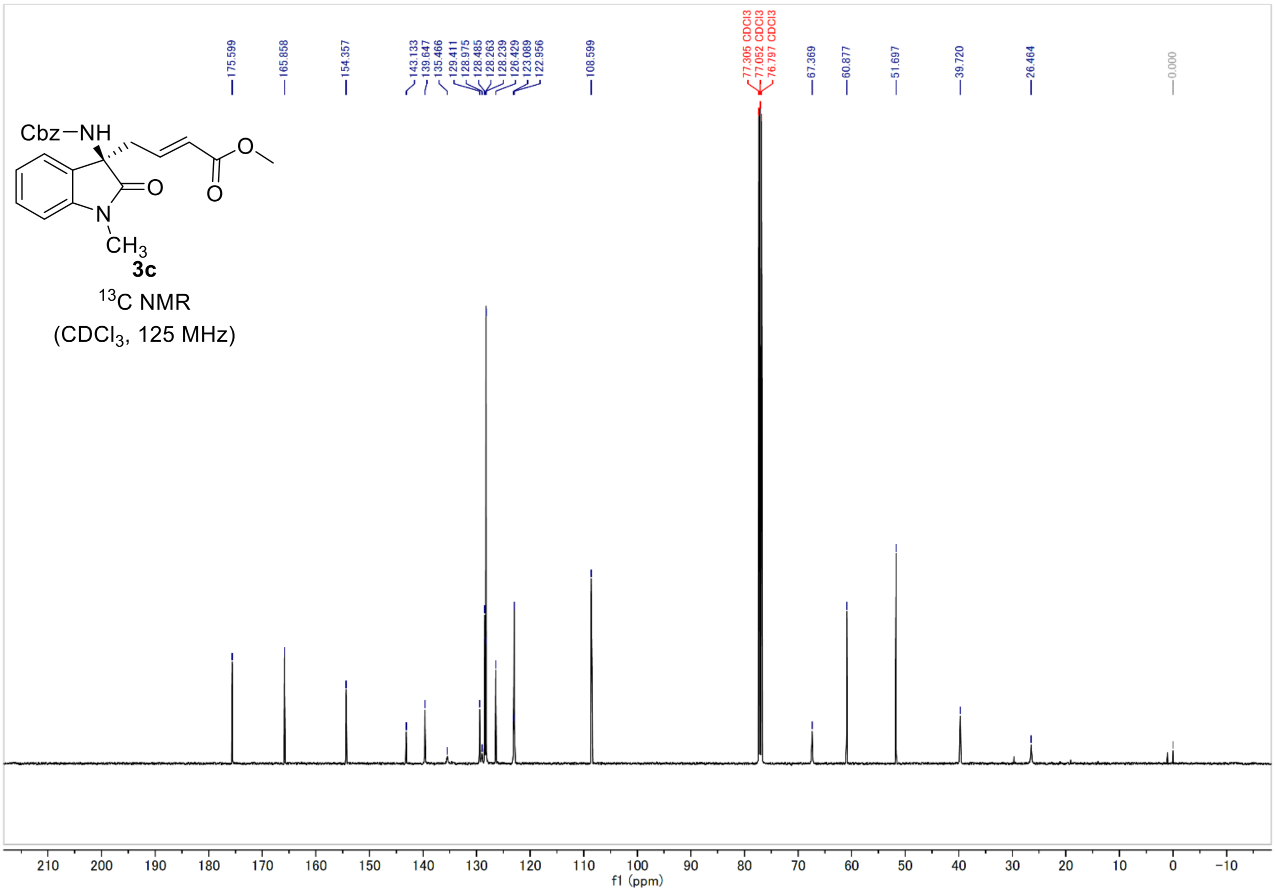

Boc−NH
O
O
N
H
O
3a
^{1}H NMR
($CDCl_3$, 300 MHz)
8.088 7.270 7.266 7.250 7.227 7.090 7.065 7.039 6.887 6.862 6.838 6.812 6.785 6.760
5.963 5.911
5.271
3.725
2.792 2.766 2.746 2.720 2.670 2.644 2.624 2.598
1.655 HDO
1.279
0.000
0.86 2.45 0.95 0.86 0.81 0.82 0.95 2.67 0.83 0.88 9.00
f1 (ppm)

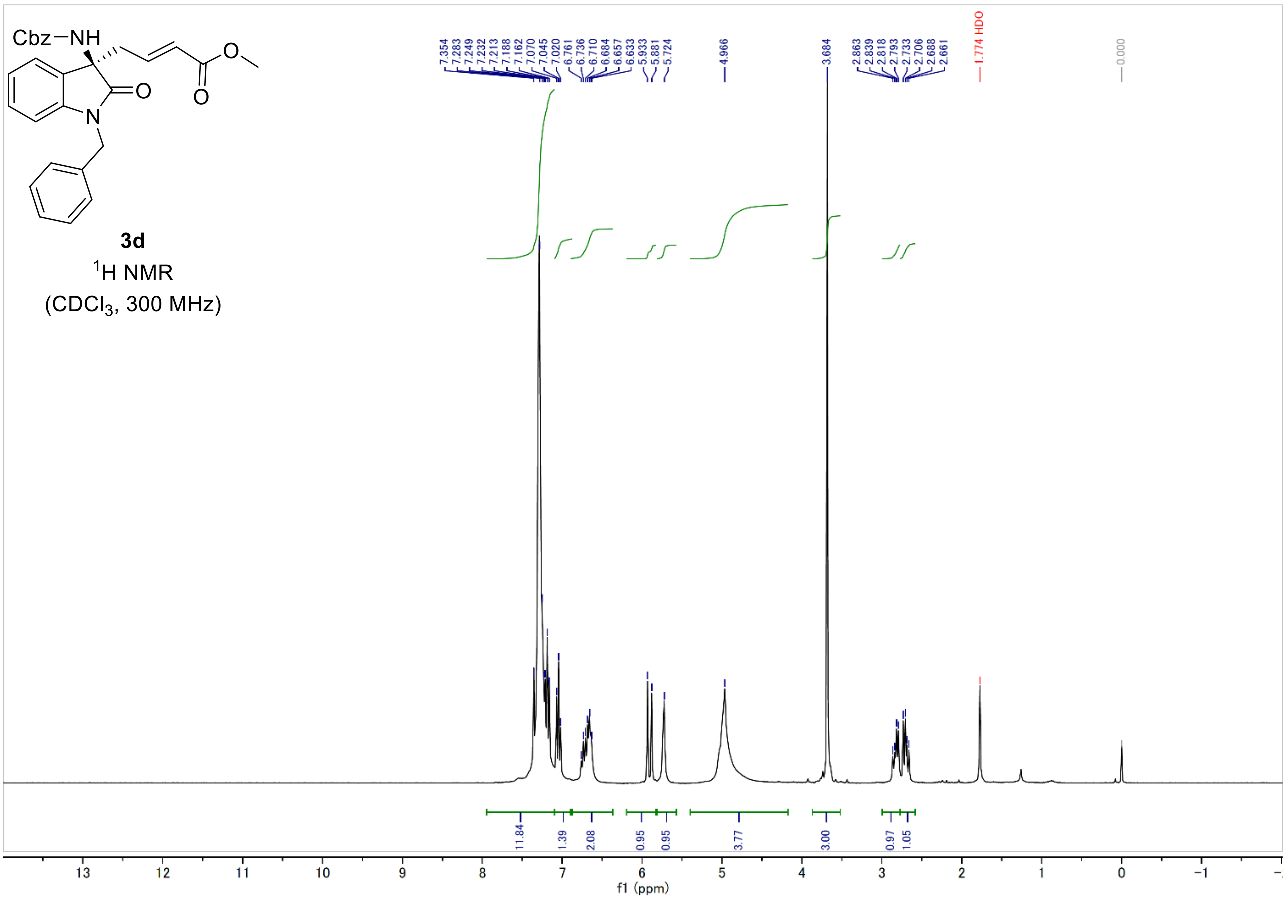

178.07
165.99
153.87
140.21 139.80
130.12 129.14 126.43 123.21 122.83
110.41
81.01 77.30 CDCl3 77.05 CDCl3 76.80 CDCl3
61.19
51.74
39.92
28.00
Boc−NH
O
O
N
H
O
3a
^{13}C NMR
($CDCl_3$, 125 MHz)
f1 (ppm)

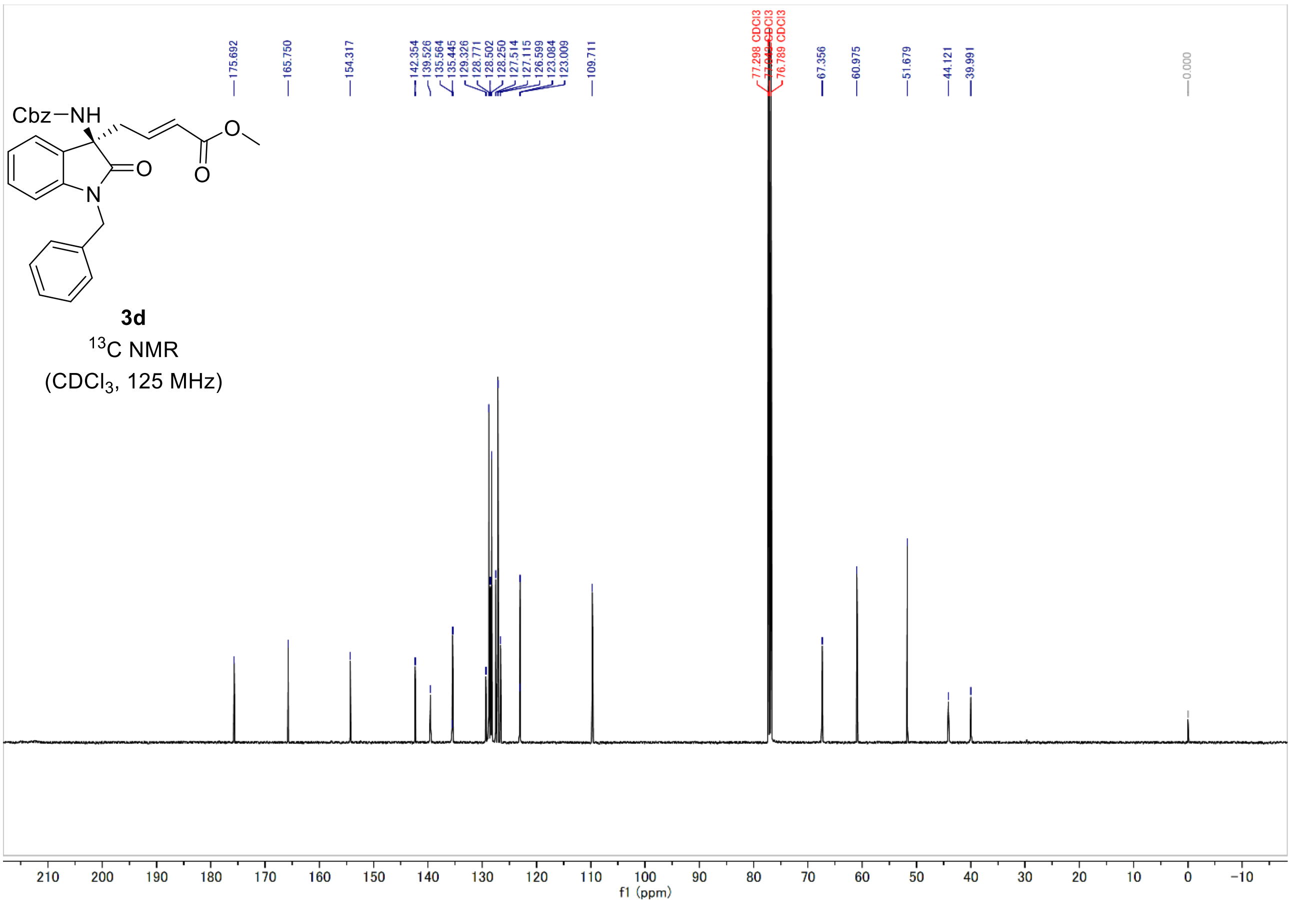

Cbz—NH
O
O
O
N
H
3b
1H NMR
(CDCl3, 300 MHz)
f1 (ppm)

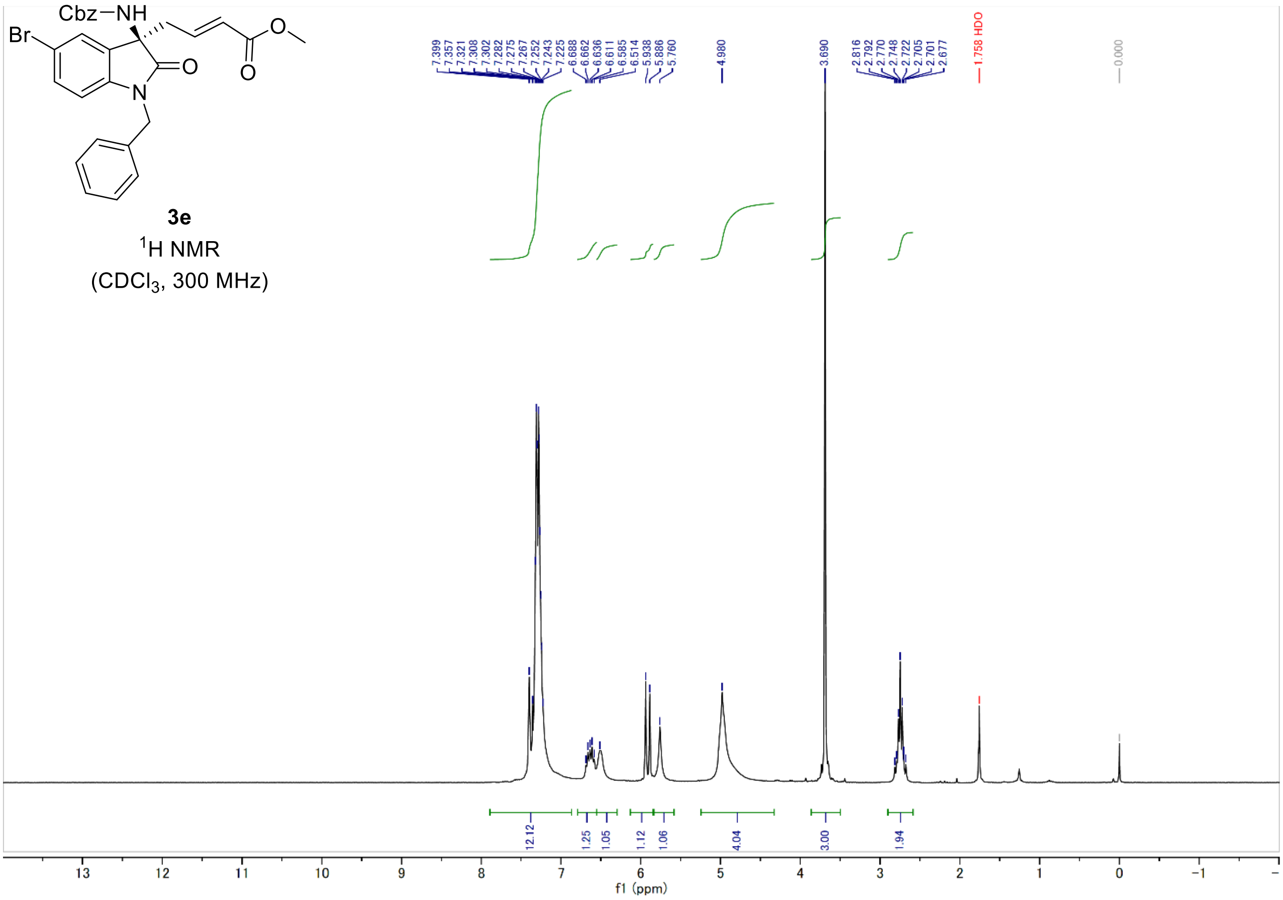

Cbz—NH
O
O
O
N
H
3b
13C NMR
(CDCl3, 125 MHz)
f1 (ppm)

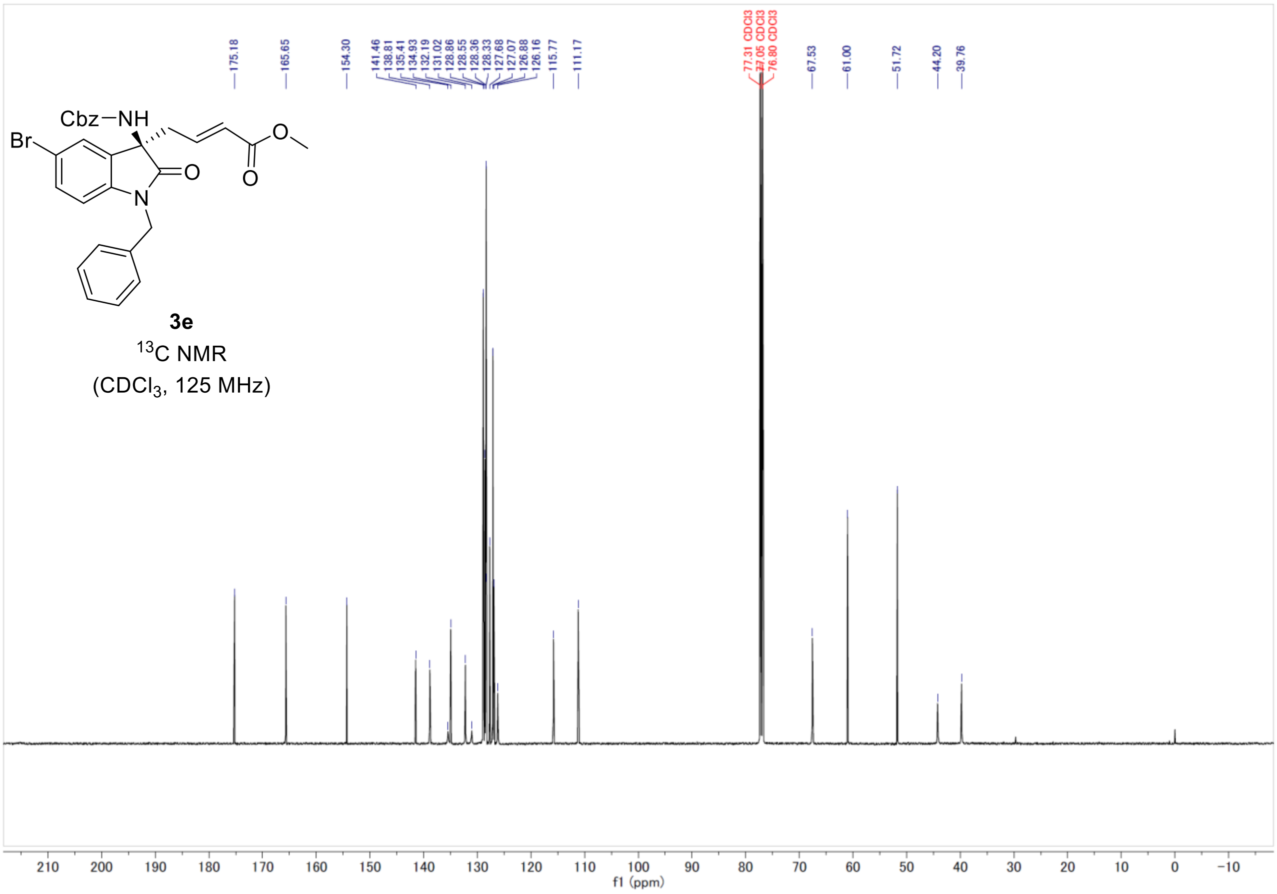

Cbz−NH
O
O
N
CH3
3c
1H NMR
(CDCl3, 300 MHz)
f1 (ppm)

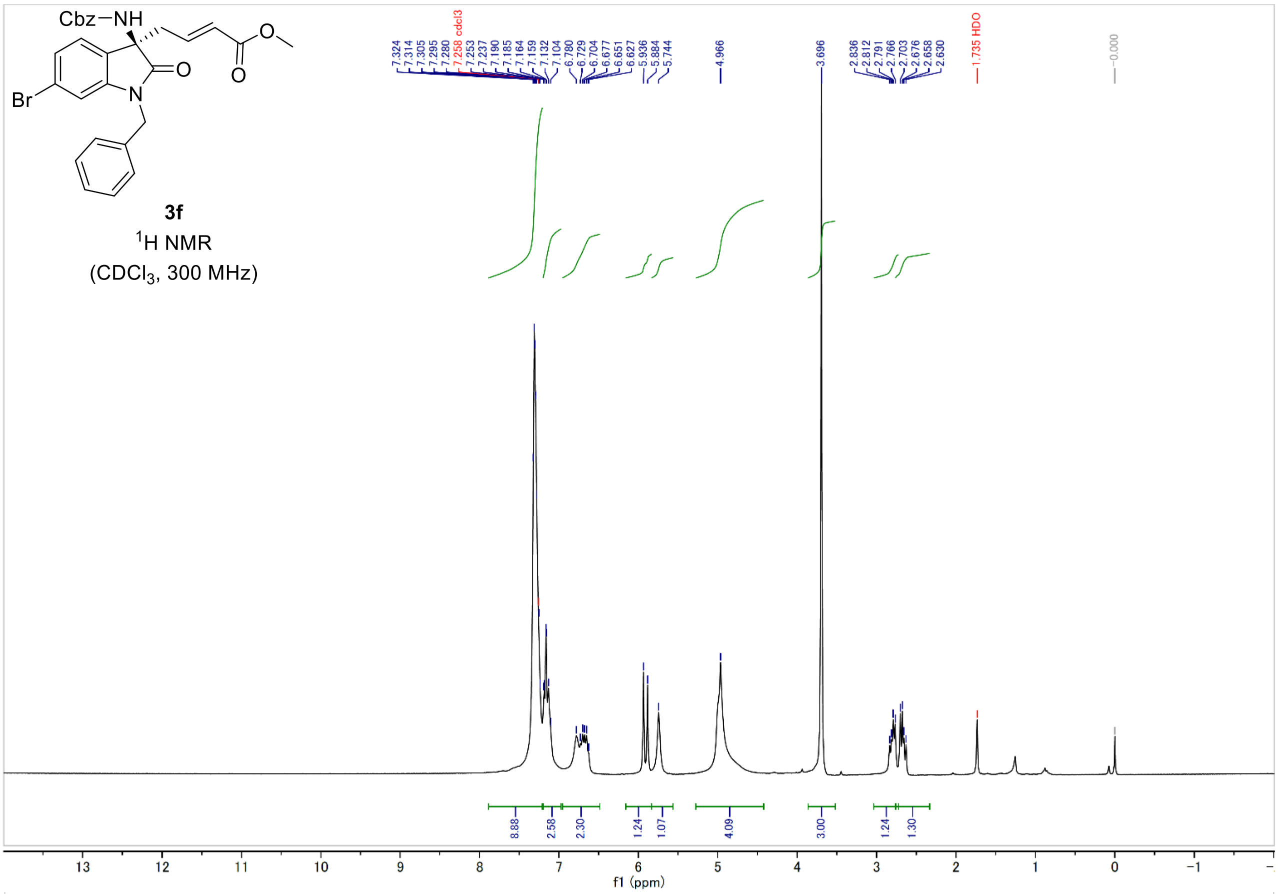

Cbz−NH
O
O
N
CH3
3c
13C NMR
(CDCl3, 125 MHz)
f1 (ppm)

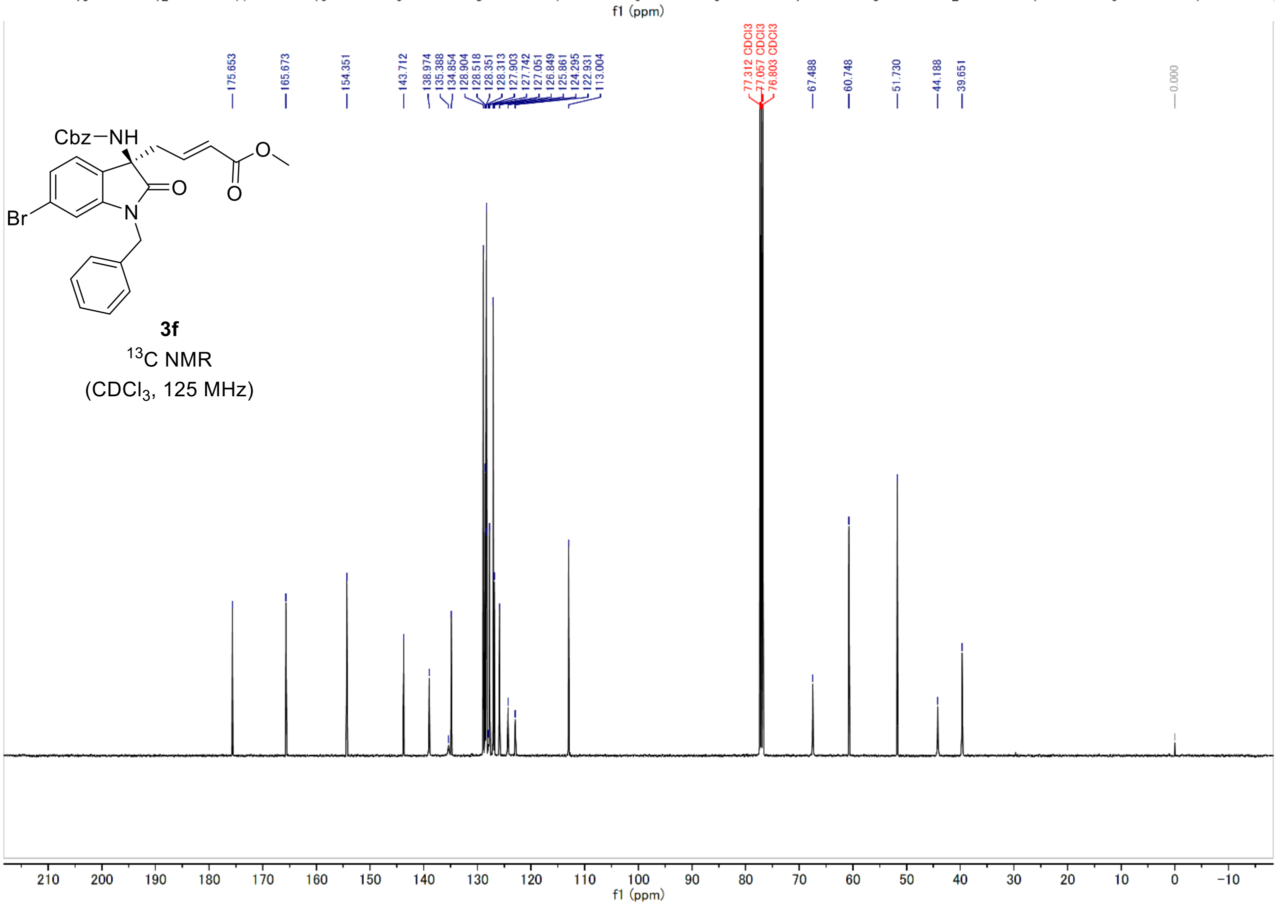

Cbz−NH
O
O
O
N
3d
1H NMR
(CDCl3, 300 MHz)
7.354
7.283
7.249
7.232
7.213
7.188
7.162
7.070
7.045
7.020
6.761
6.736
6.710
6.684
6.657
6.633
5.933
5.881
5.724
4.966
3.684
2.863
2.839
2.818
2.793
2.733
2.706
2.688
2.661
1.774 HDO
0.000
11.84
1.39
2.08
0.95
0.95
3.77
3.00
0.97
1.05
f1 (ppm)

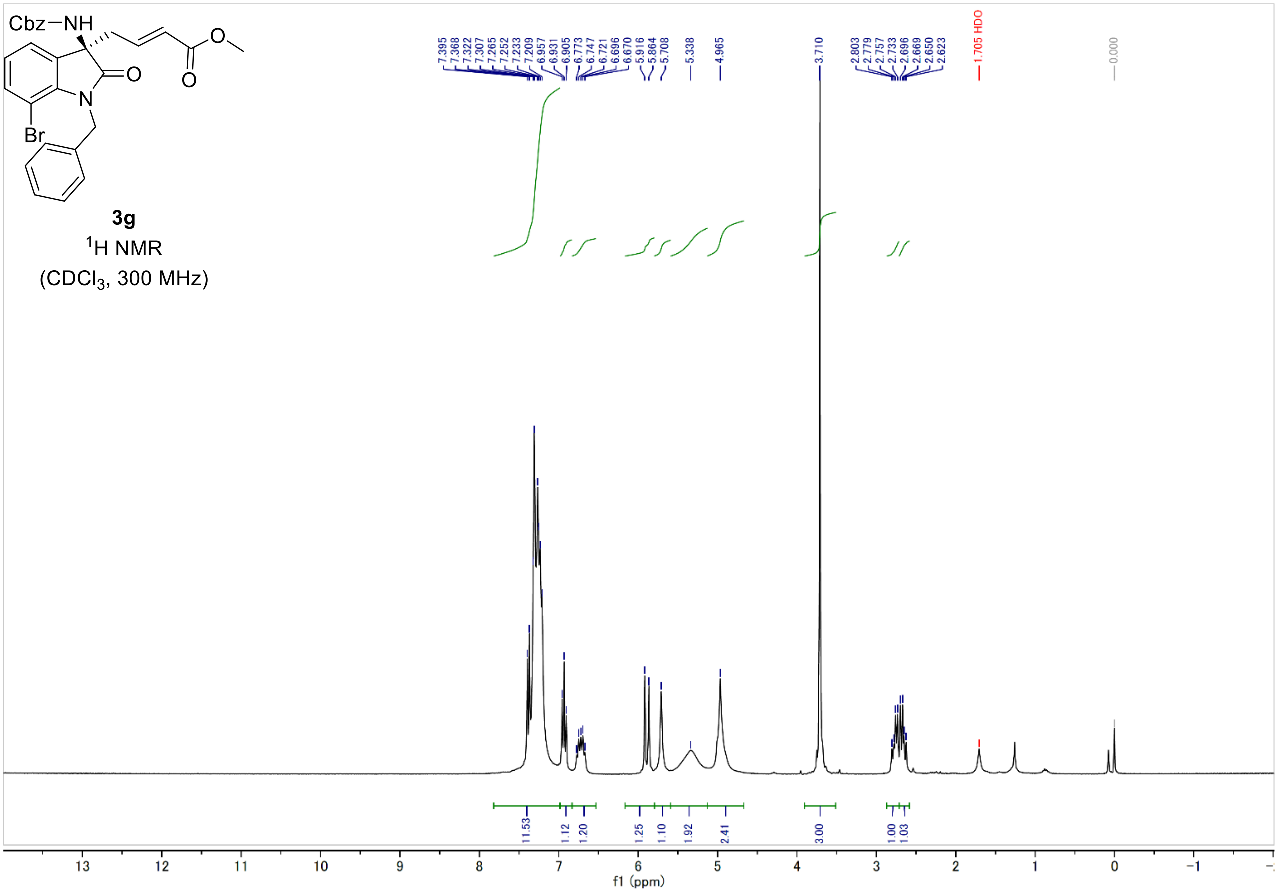

Cbz−NH
O
O
O
N
3d
13C NMR
(CDCl3, 125 MHz)
175.692
165.750
154.317
142.254
139.526
135.564
135.445
129.326
128.771
128.502
128.250
127.514
127.115
126.599
123.084
123.009
109.711
77.298 CDCl3
76.789 CDCl3
67.356
60.975
51.679
44.121
39.991
0.000
f1 (ppm)

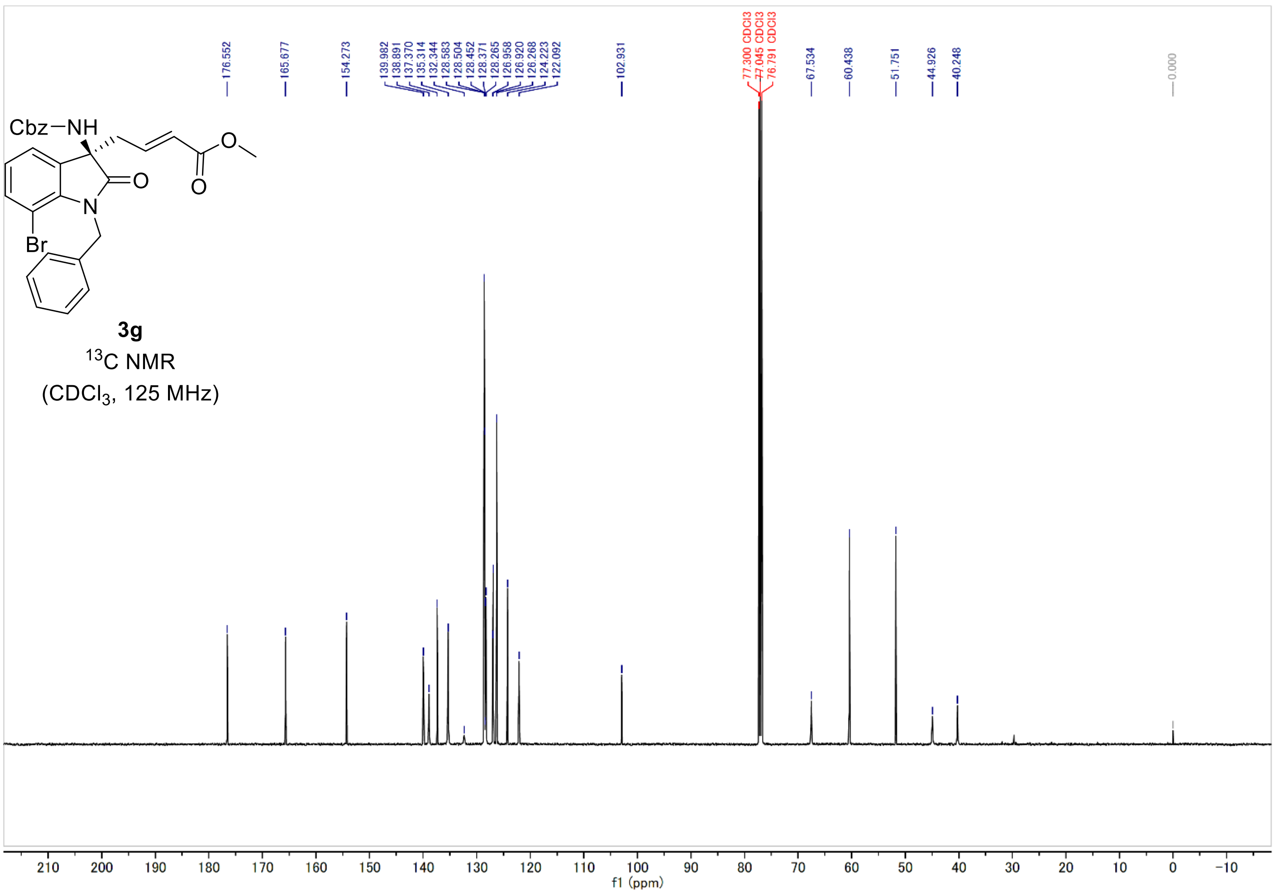

Cbz−NH
Br
O
O
O
N
3e
1H NMR
(CDCl3, 300 MHz)
7.399 7.357 7.321 7.308 7.302 7.282 7.275 7.267 7.252 7.243 7.225 6.688 6.662 6.636 6.611 6.585 6.514 5.938 5.886 5.760
4.980
3.690
2.816 2.792 2.770 2.748 2.722 2.705 2.701 2.677
1.758 HDO
0.000
12.12 1.25 1.05 1.12 1.06 4.04 3.00 1.94
f1 (ppm)

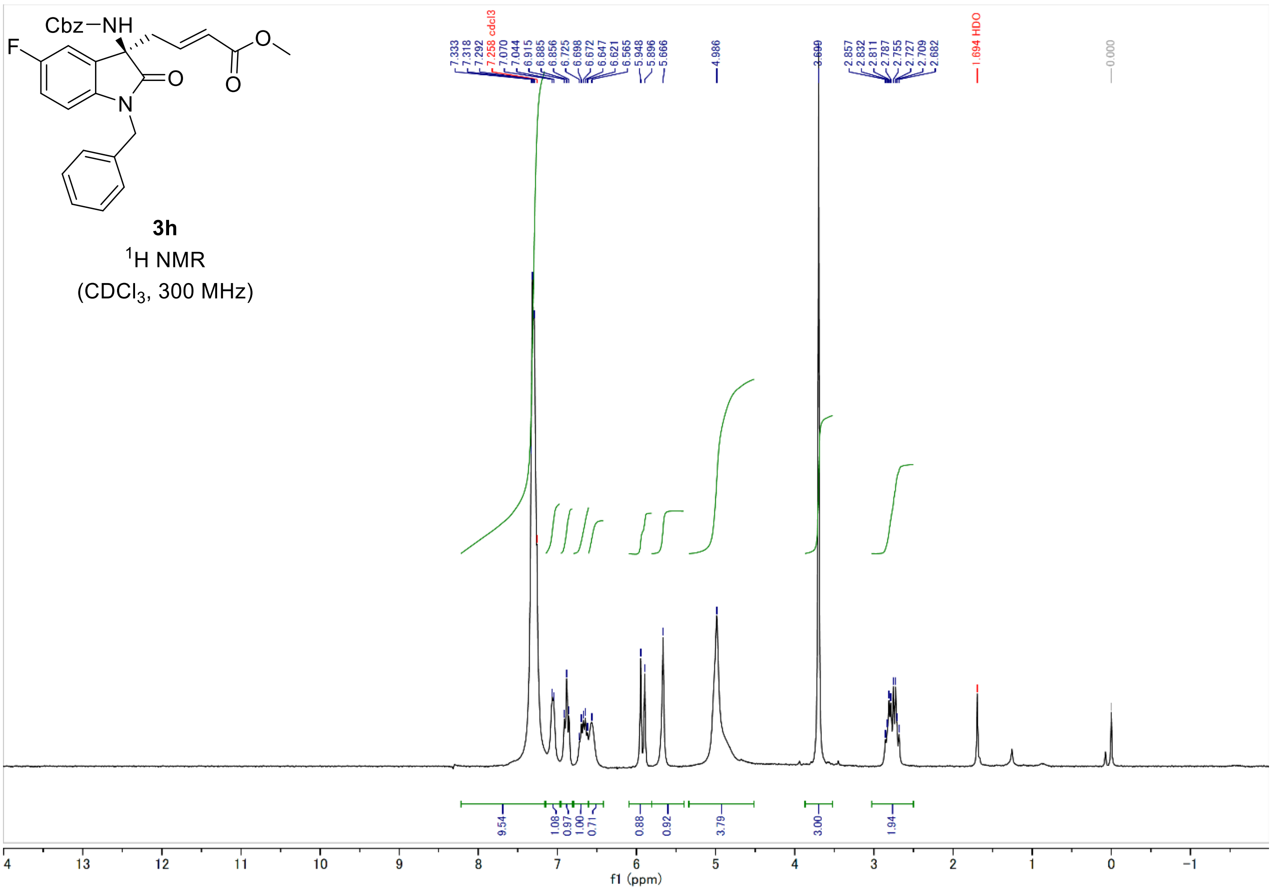

175.18
165.65
154.30
141.46 138.81 135.41 134.93 132.19 131.02 128.86 128.55 128.36 128.33 127.68 127.07 126.88 126.16
115.77
111.17
77.31 CDCl3 77.05 CDCl3 76.80 CDCl3
67.53
61.00
51.72
44.20
39.76
Cbz−NH
Br
O
O
O
N
3e
13C NMR
(CDCl3, 125 MHz)
f1 (ppm)

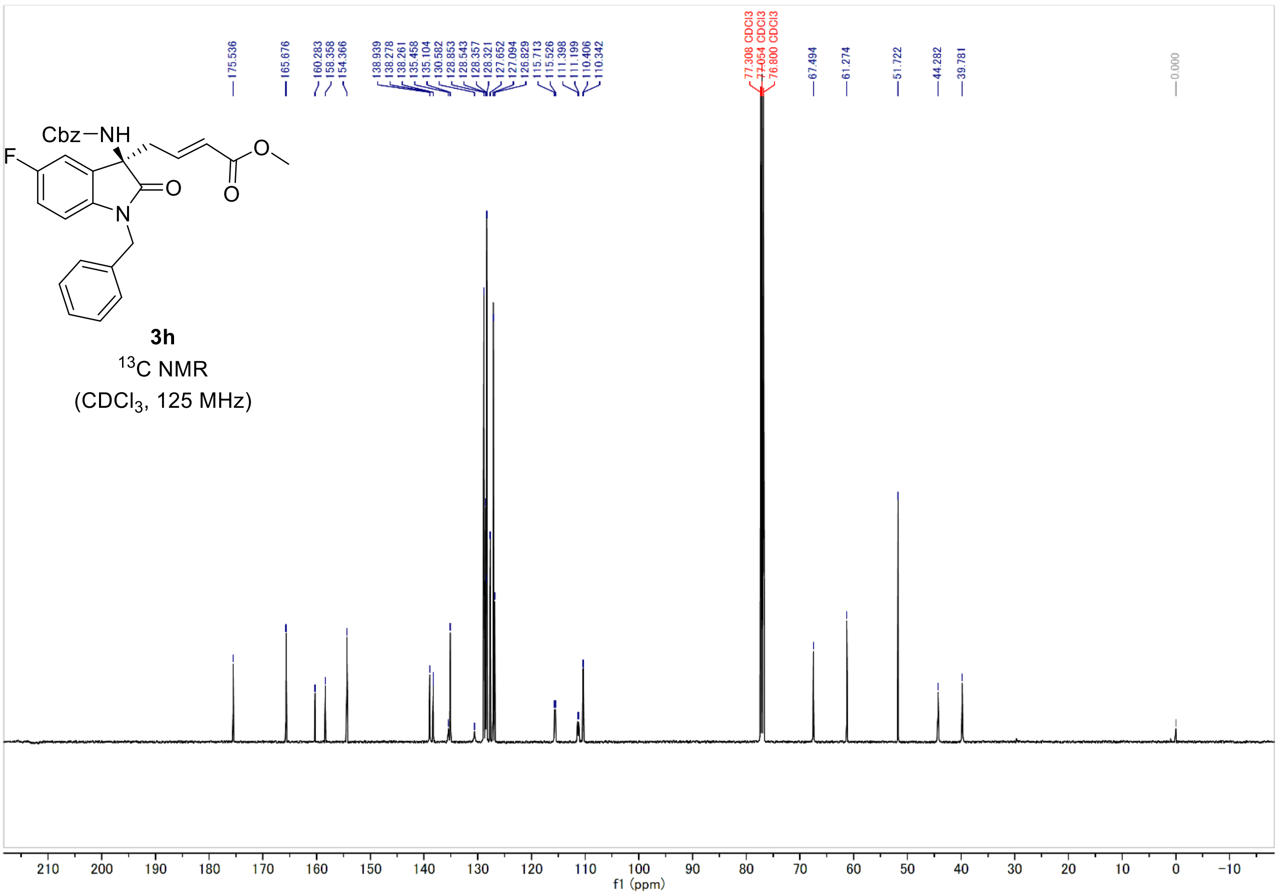

Cbz–NH
Br
N
O
3f
1H NMR
(CDCl3, 300 MHz)
f1 (ppm)

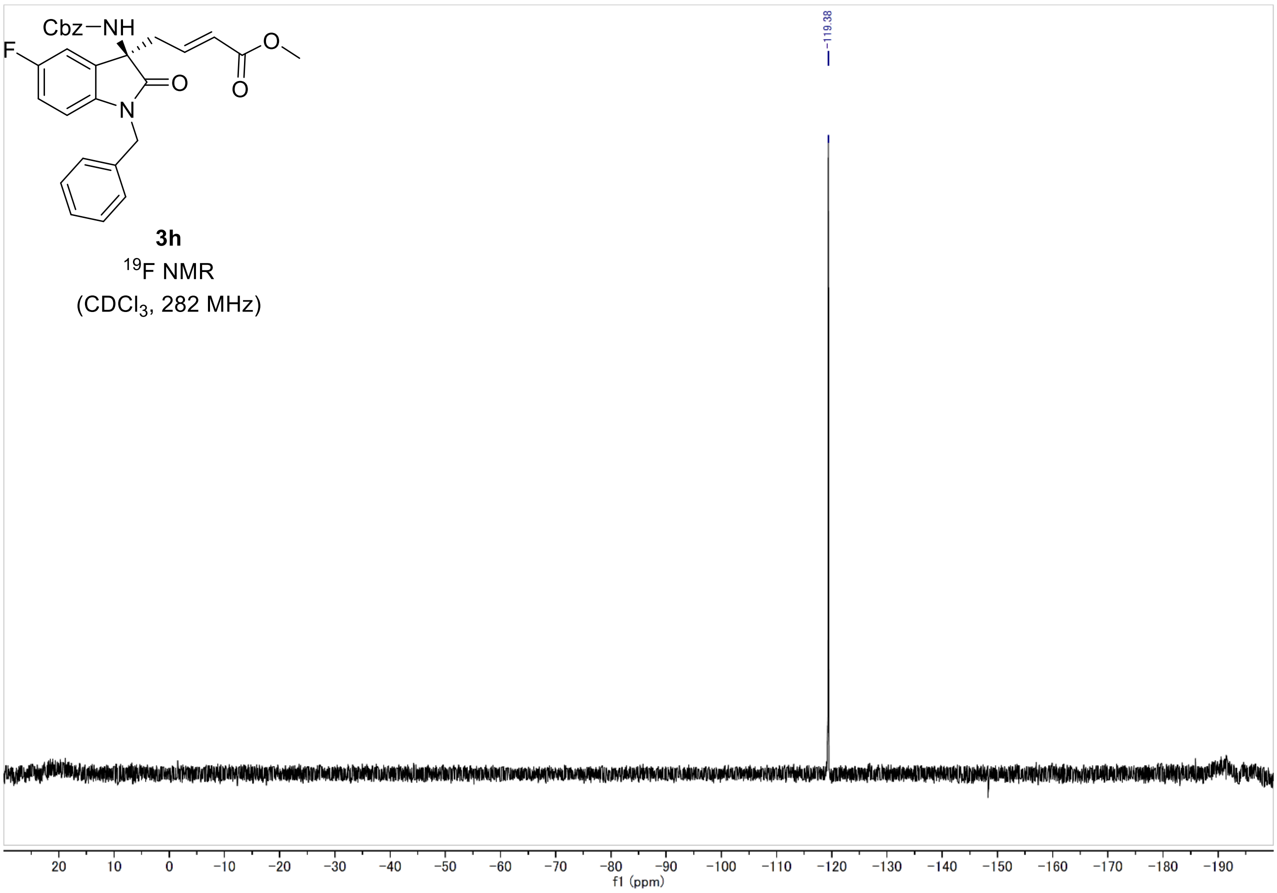

Cbz–NH
Br
N
O
3f
13C NMR
(CDCl3, 125 MHz)
f1 (ppm)


Cbz−NH
O
O
N
O
Br
3g
^{1}H NMR
($CDCl_3$, 300 MHz)
1.705 HDO
f1 (ppm)

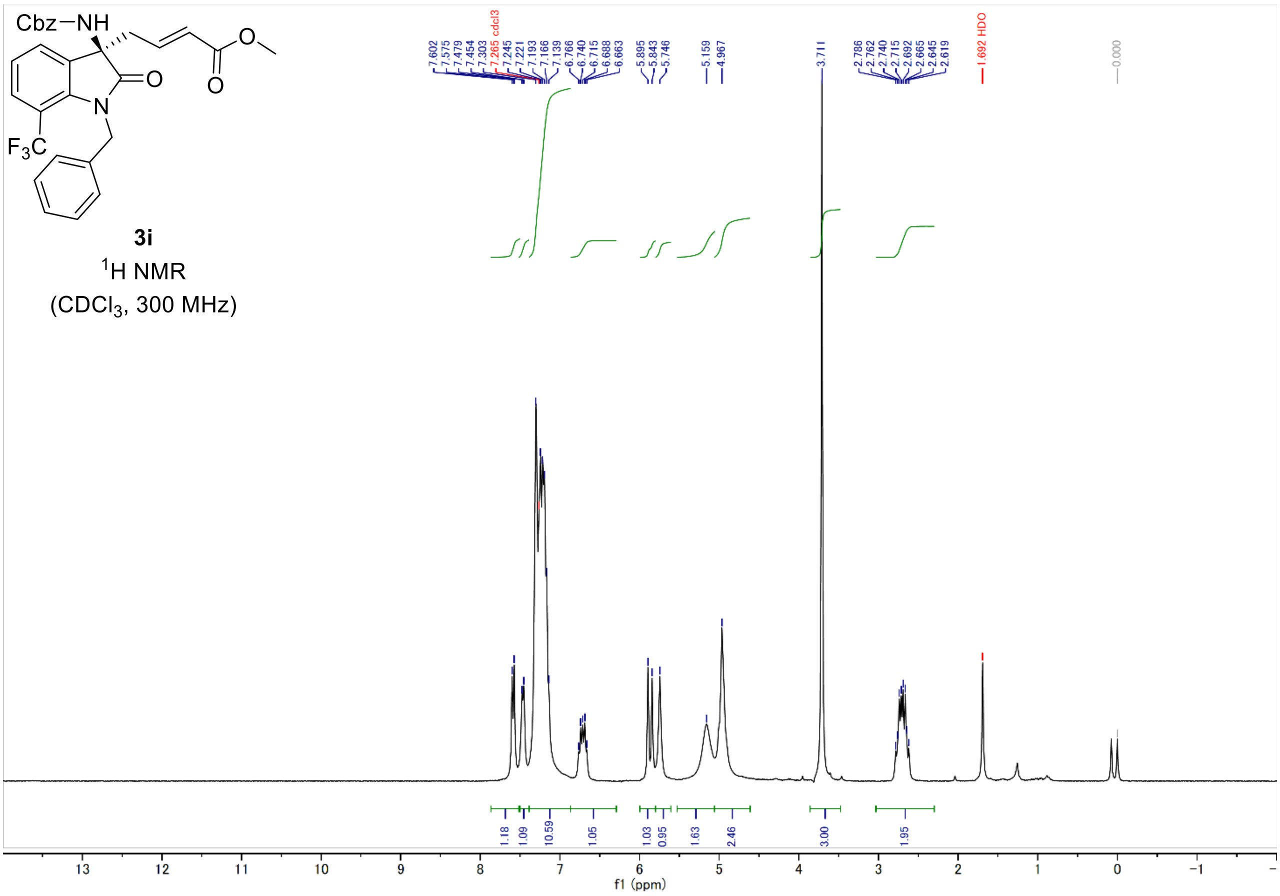

Cbz−NH
O
O
N
O
Br
3g
^{13}C NMR
($CDCl_3$, 125 MHz)
f1 (ppm)

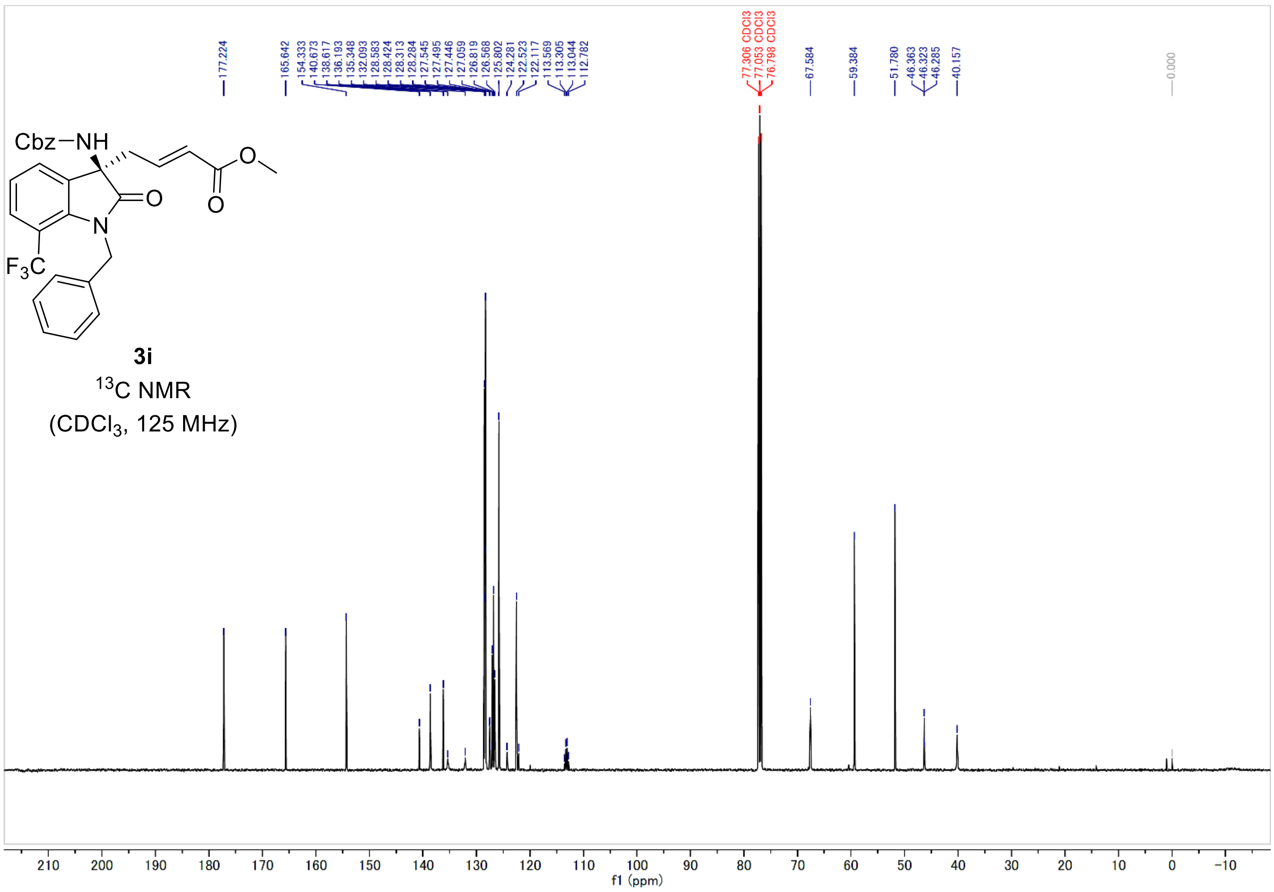

Cbz−NH
F
O
N
O
O
3h
¹H NMR
(CDCl₃, 300 MHz)
7.333
7.318
7.292
7.258 cdcl3
7.070
7.044
6.915
6.885
6.856
6.725
6.698
6.672
6.647
6.621
6.565
5.948
5.896
5.666
4.986
3.690
2.857
2.832
2.811
2.787
2.755
2.727
2.709
2.682
1.694 HDO
0.000
9.54
1.08
0.97
1.00
0.71
0.88
0.92
3.79
3.00
1.94
f1 (ppm)

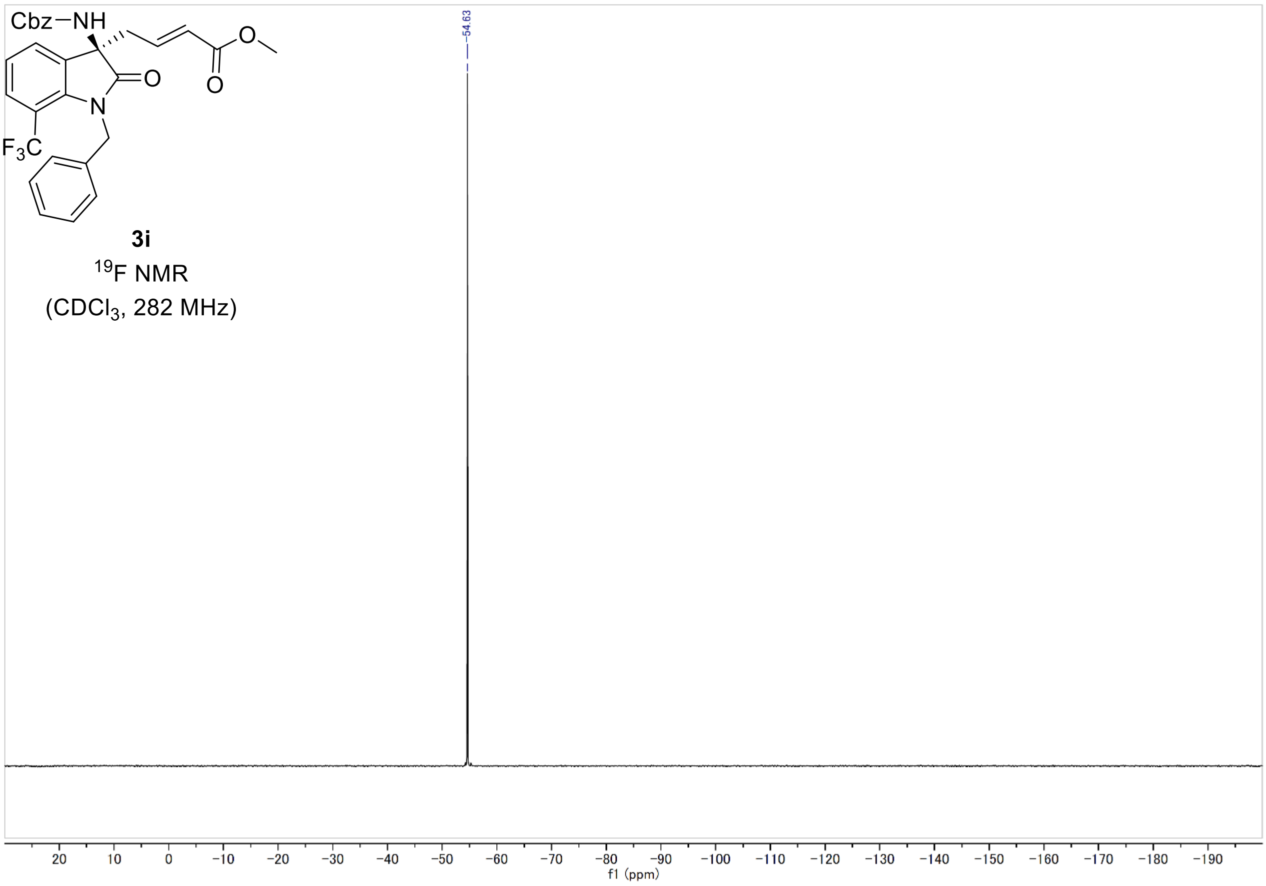

175.536
165.676
160.283
158.358
154.366
138.939
138.278
138.261
135.458
135.104
130.582
128.853
128.543
128.357
128.321
127.652
127.094
126.829
115.713
115.526
111.398
111.199
110.406
110.342
77.308 CDCl3
77.054 CDCl3
76.800 CDCl3
67.494
61.274
51.722
44.282
39.781
0.000
Cbz−NH
F
O
N
O
O
3h
¹³C NMR
(CDCl₃, 125 MHz)
f1 (ppm)



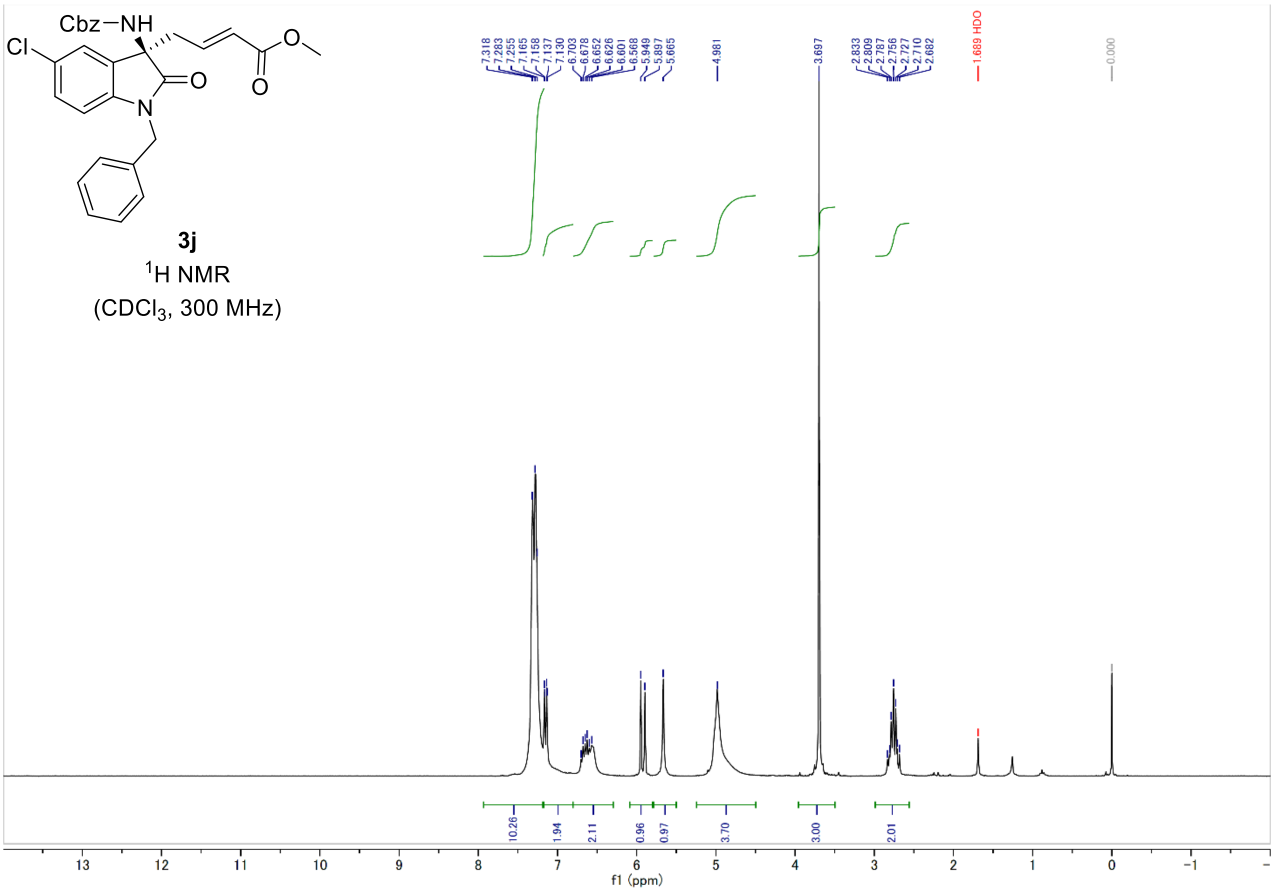
Cbz—NH
F
O
N
O
O
3h
^{19}F NMR
(CDCl$_3$, 282 MHz)
−119.38
20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190
f1 (ppm)

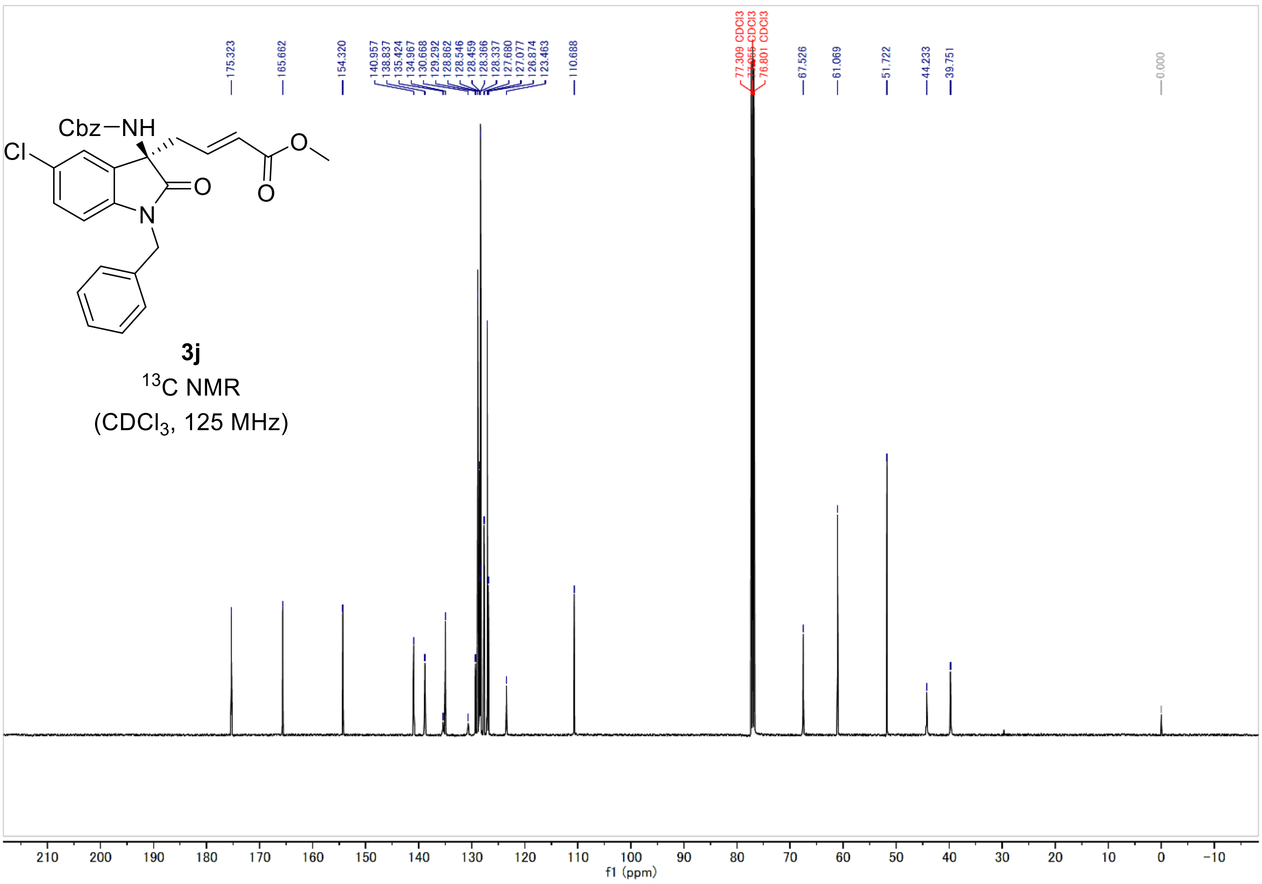

Cbz−NH
O
O
O
N
F3C
3i
1H NMR
(CDCl3, 300 MHz)
f1 (ppm)

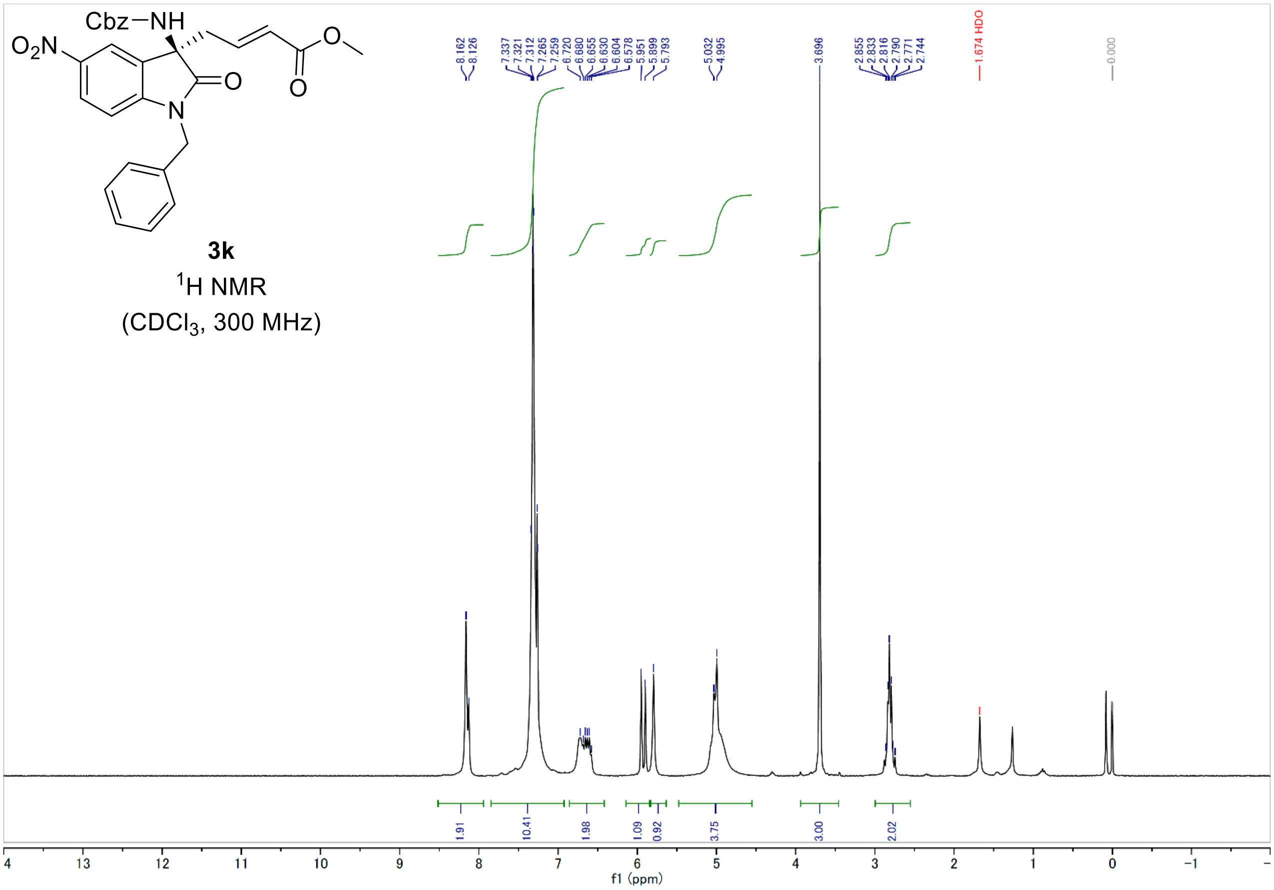

Cbz−NH
O
O
O
N
F3C
3i
13C NMR
(CDCl3, 125 MHz)
f1 (ppm)



Cbz−NH
O
O
O
N
F3C
3i
19F NMR
(CDCl3, 282 MHz)
−54.63
20 10 0 −10 −20 −30 −40 −50 −60 −70 −80 −90 −100 −110 −120 −130 −140 −150 −160 −170 −180 −190
f1 (ppm)


Cbz−NH
Cl
O
O
O
N
3j
1H NMR
(CDCl3, 300 MHz)
1.689 HDO
f1 (ppm)

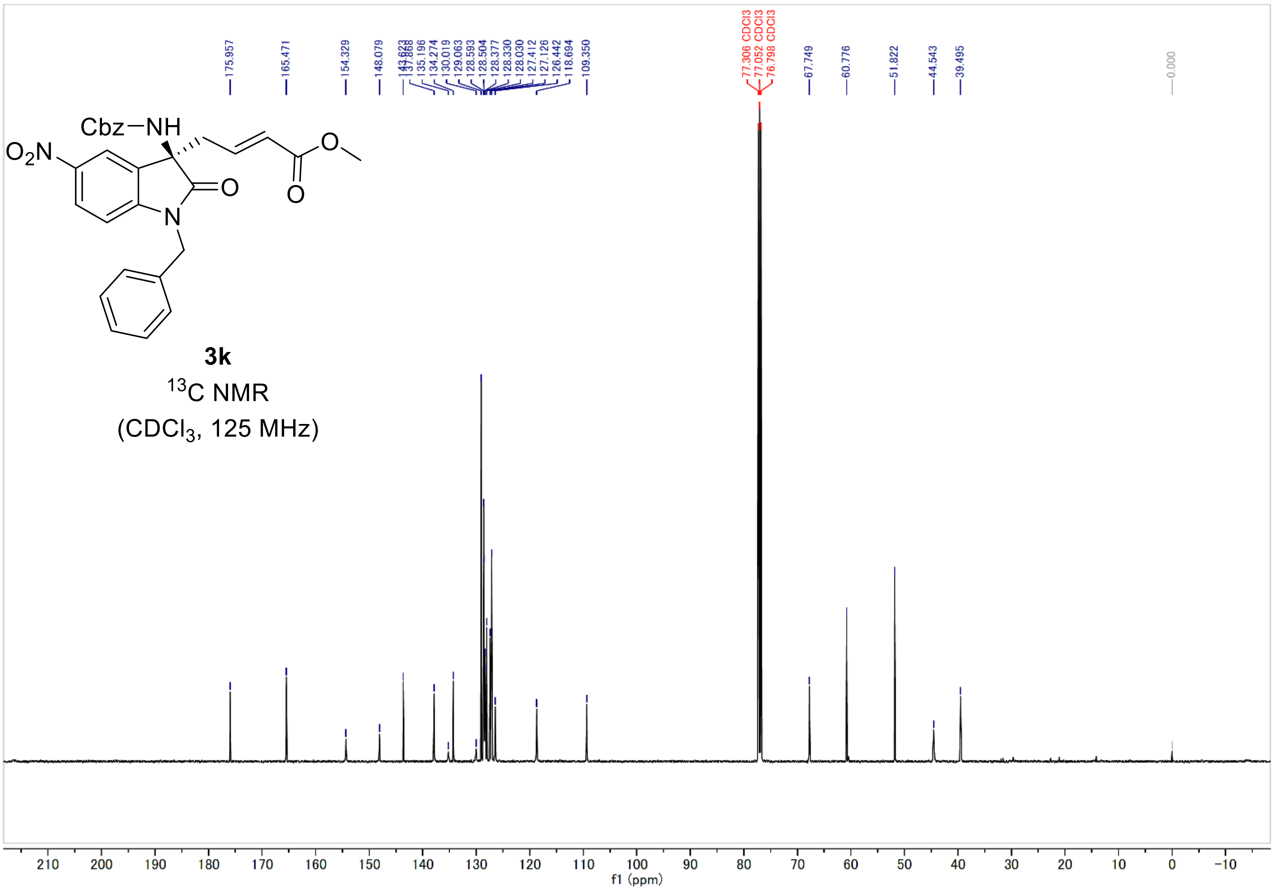

Cbz−NH
Cl
O
O
O
N
3j
13C NMR
(CDCl3, 125 MHz)
f1 (ppm)



3k

^{1}H NMR

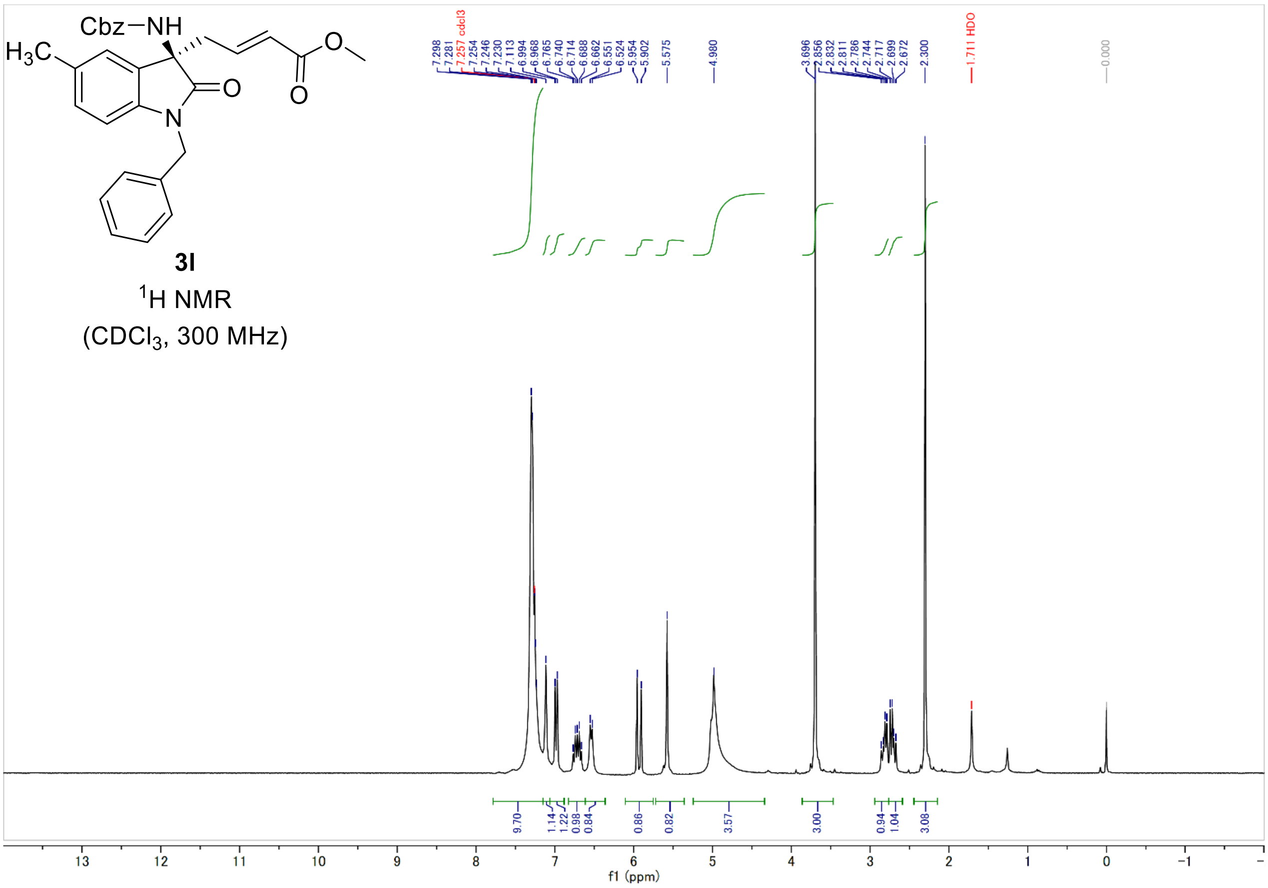
($CDCl_3$, 300 MHz)

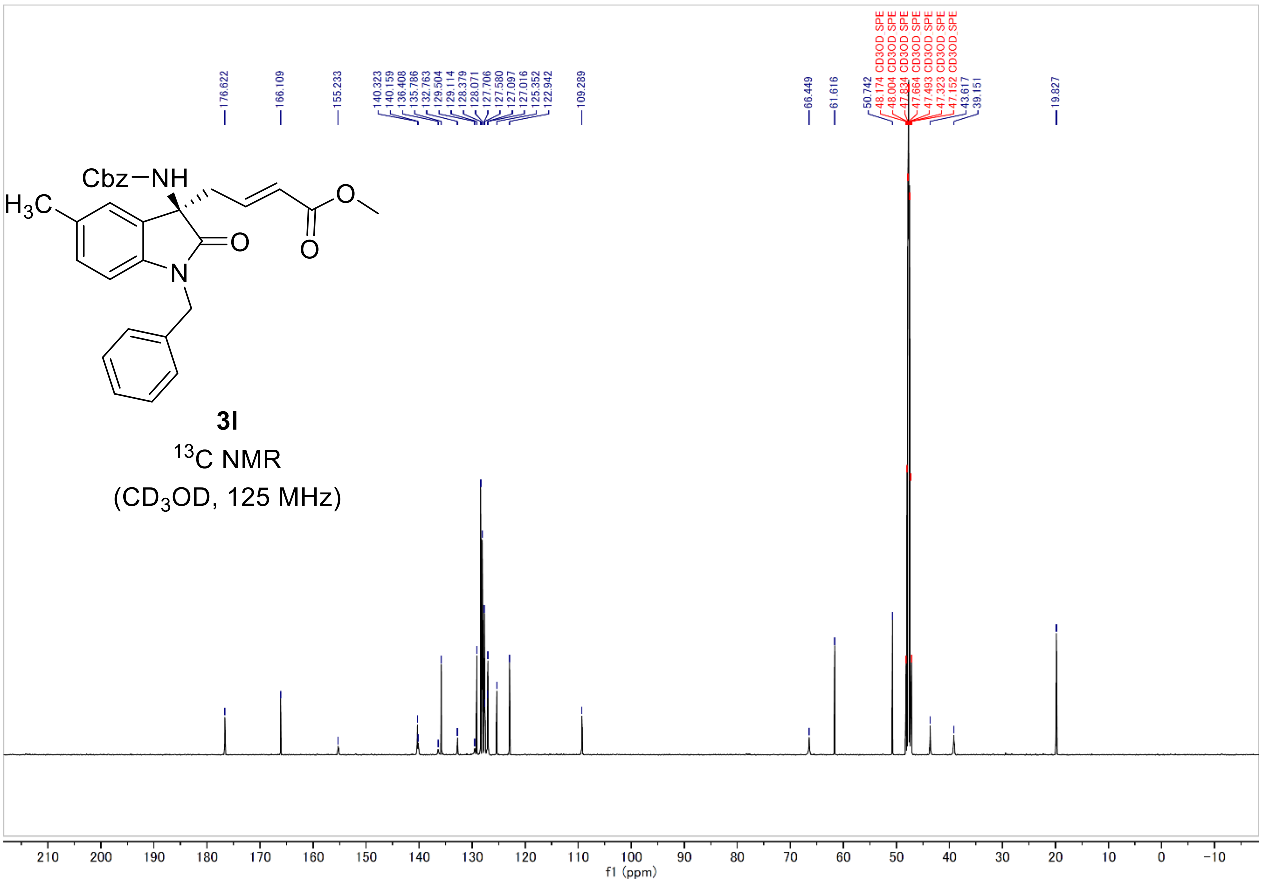


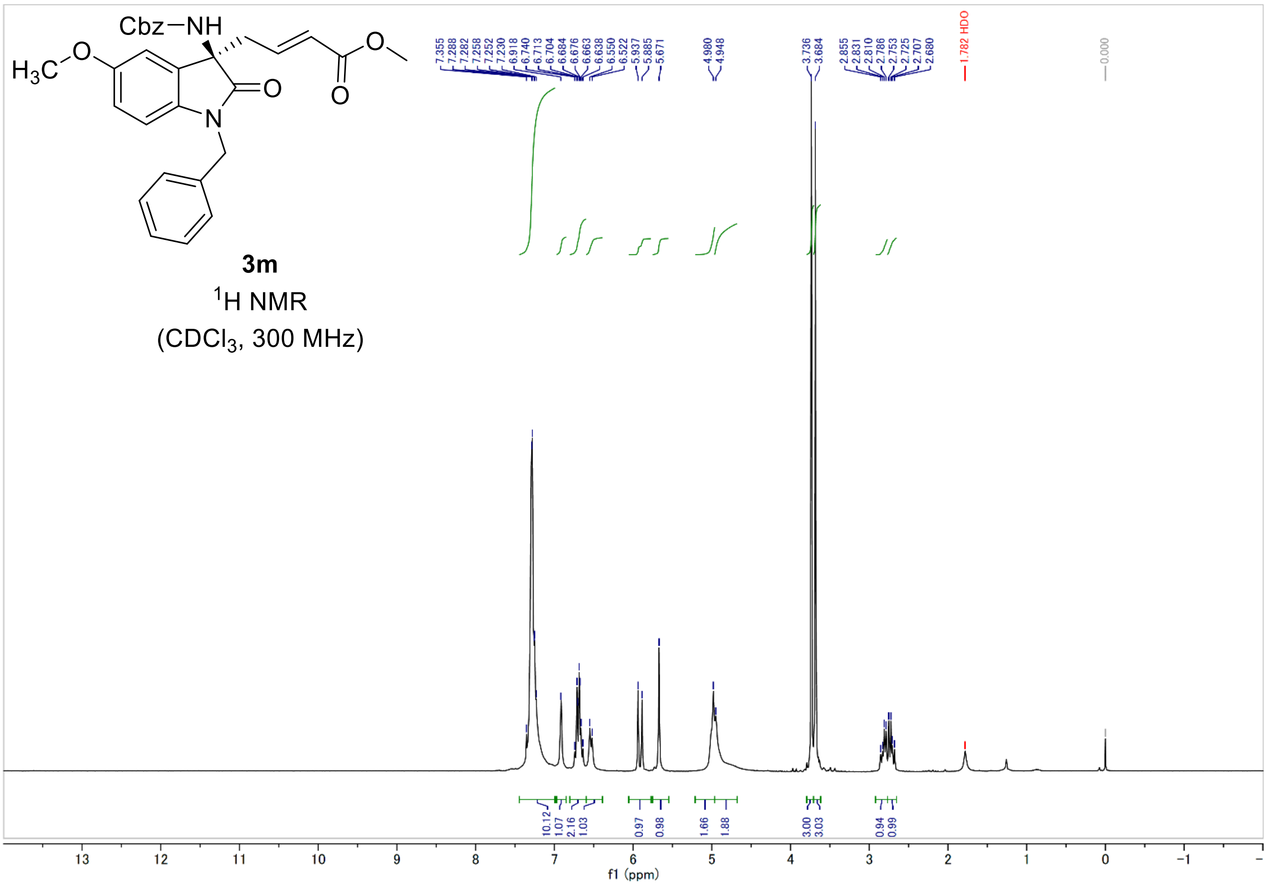
3k

^{13}C NMR

($CDCl_3$, 125 MHz)


Cbz—NH
H3C
3l
1H NMR
(CDCl3, 300 MHz)
f1 (ppm)

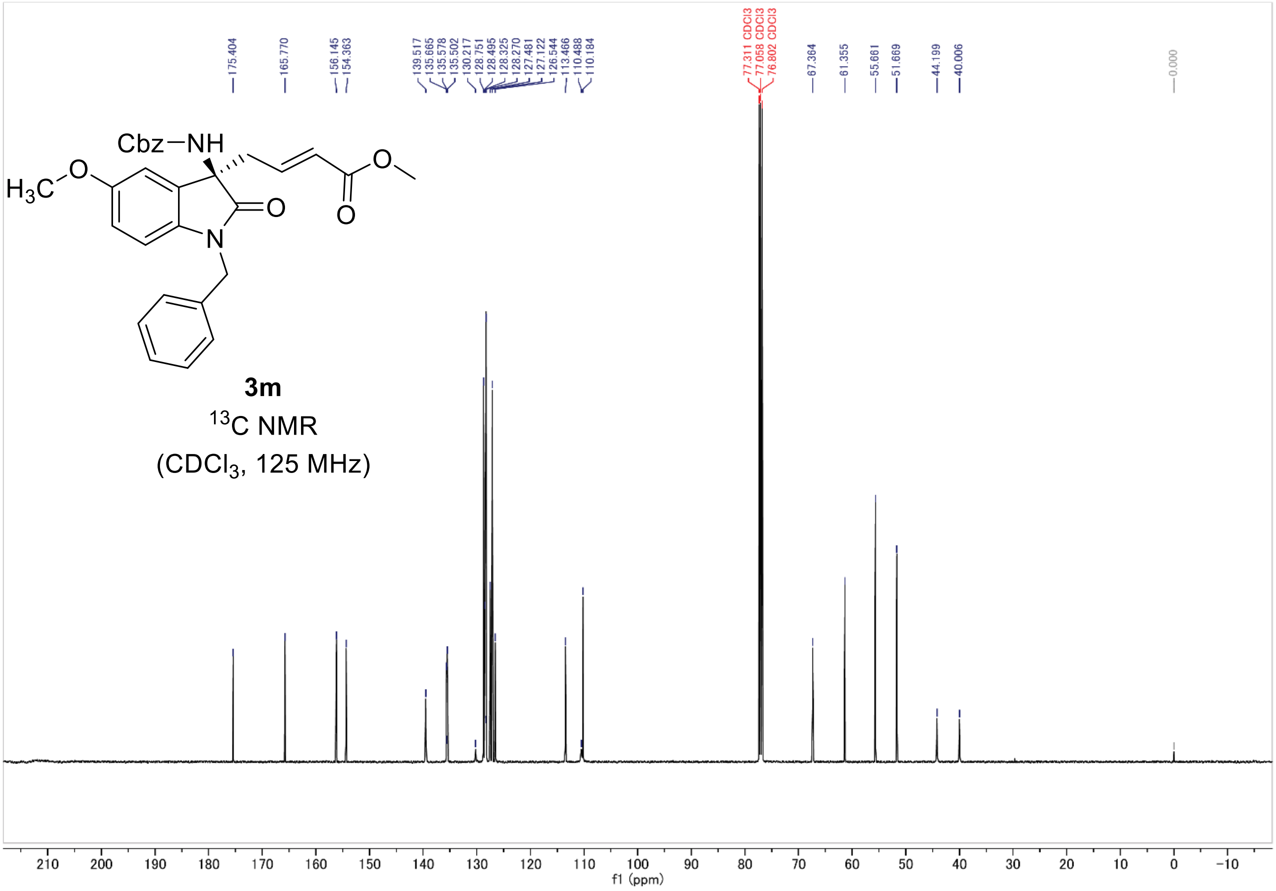

Cbz—NH
H3C
3l
13C NMR
(CD3OD, 125 MHz)
f1 (ppm)



3m

^{1}H NMR

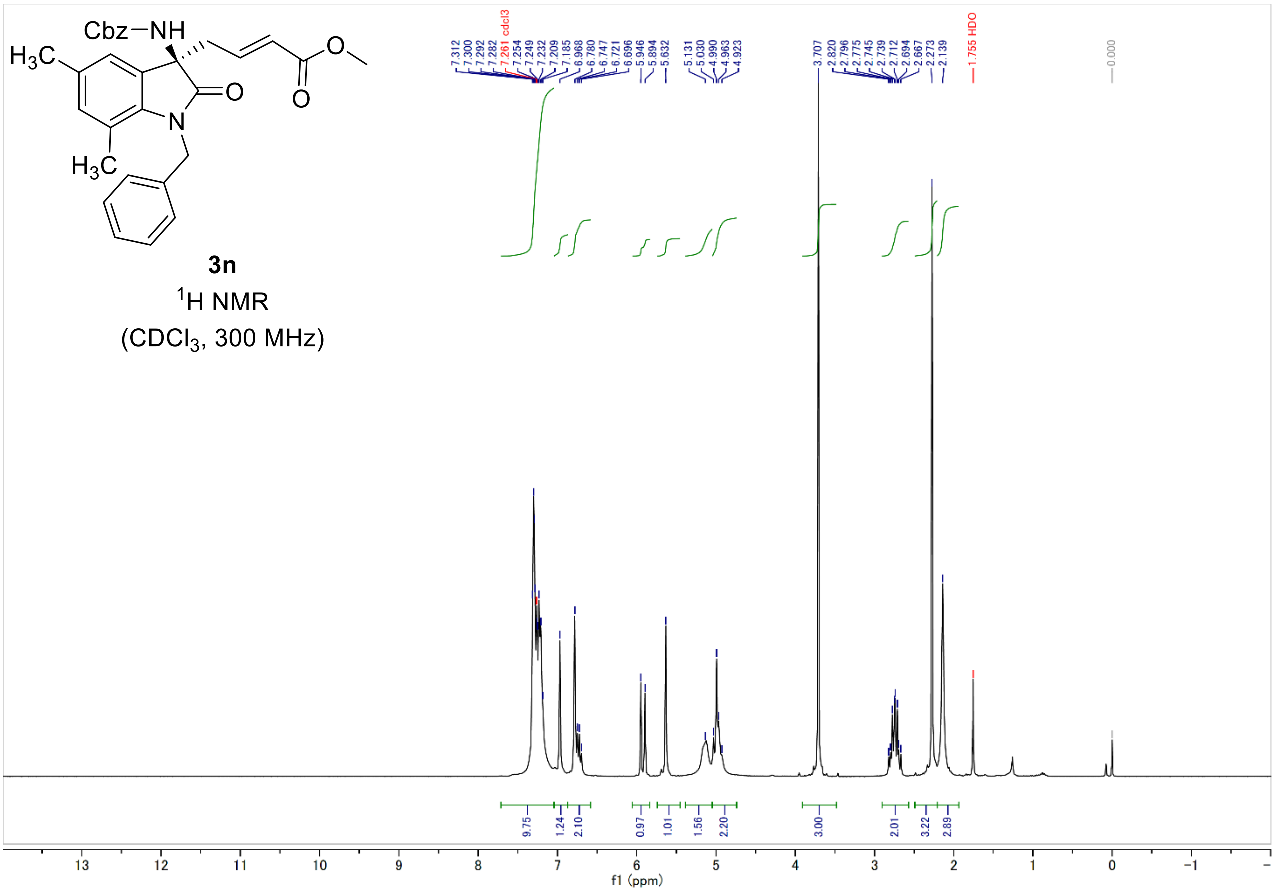
($CDCl_3$, 300 MHz)

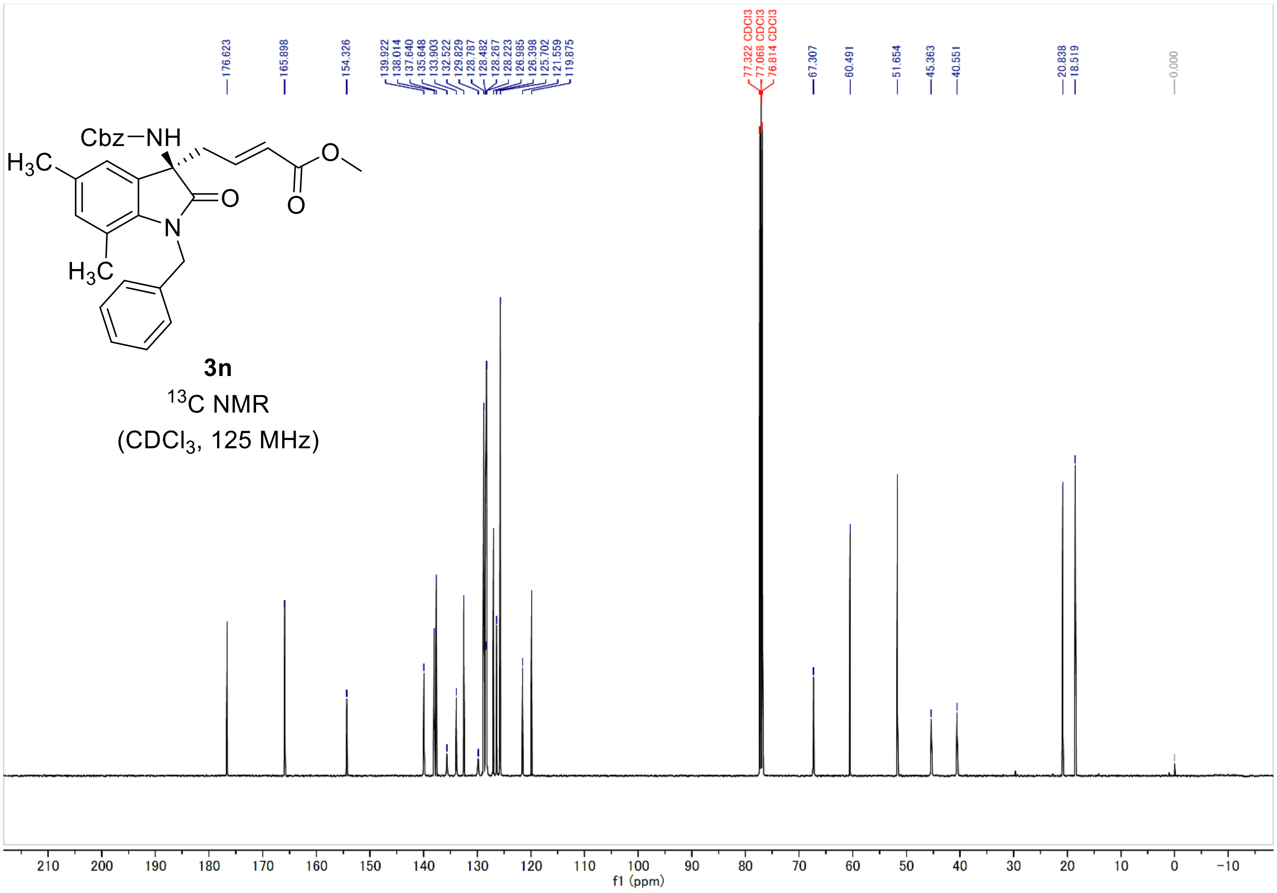


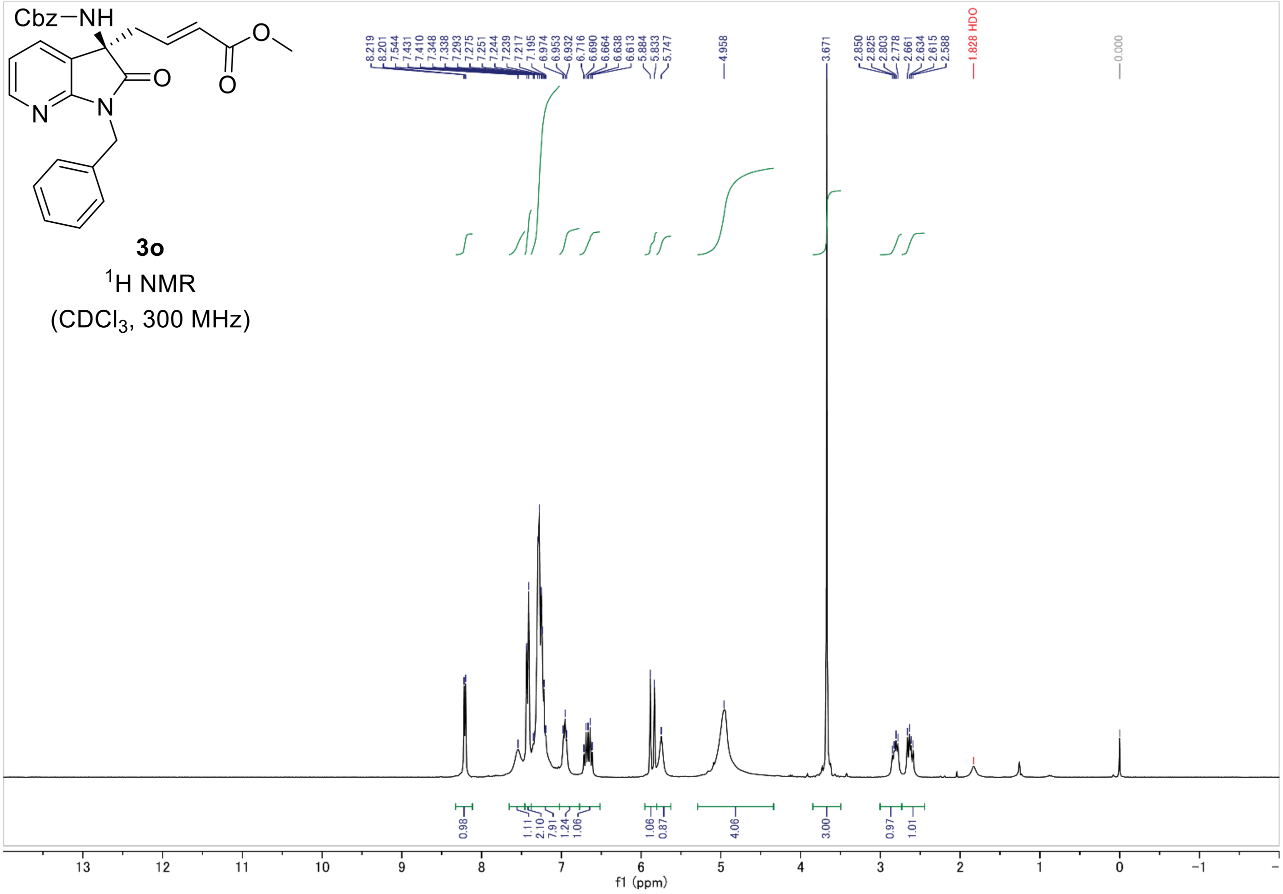
3m

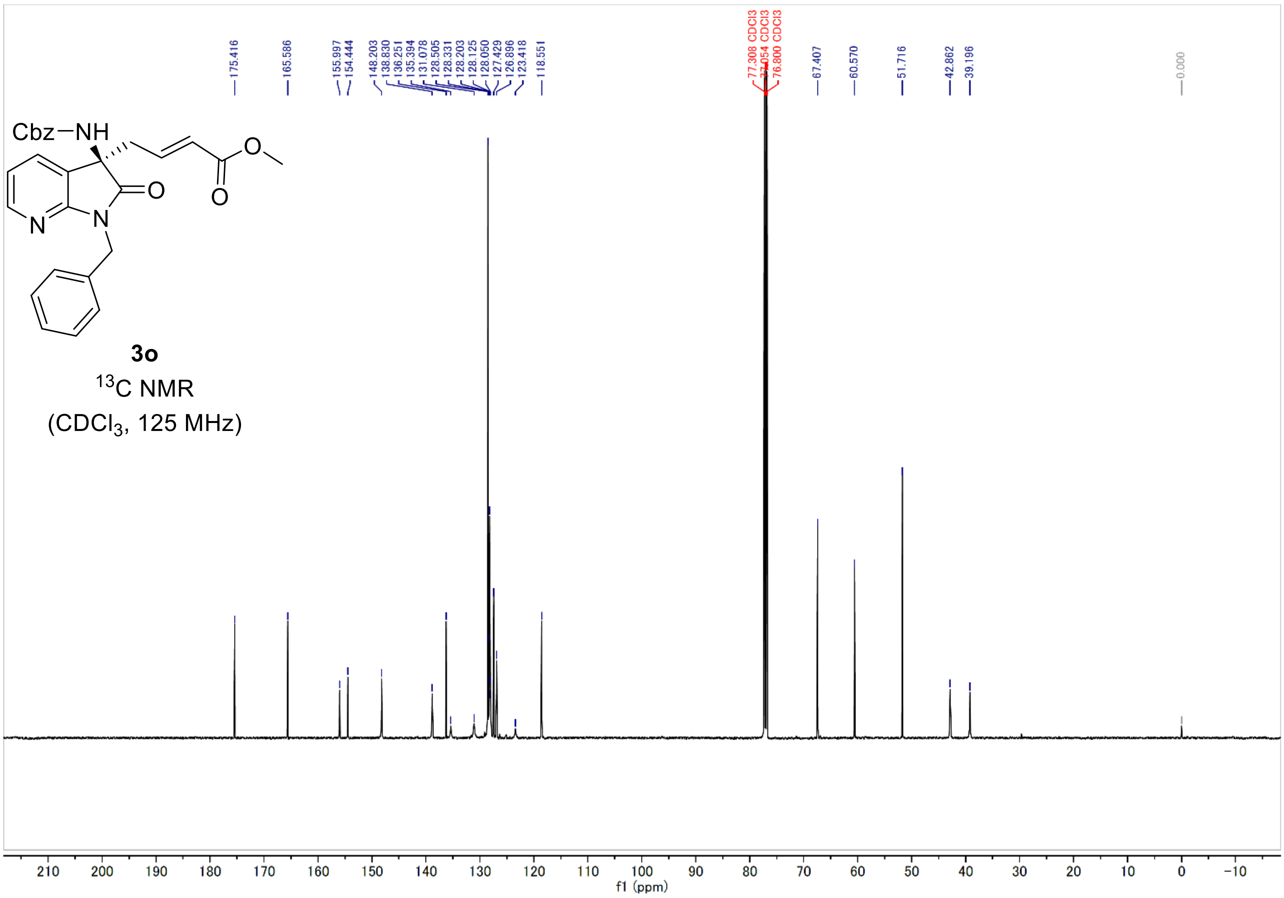
^{13}C NMR

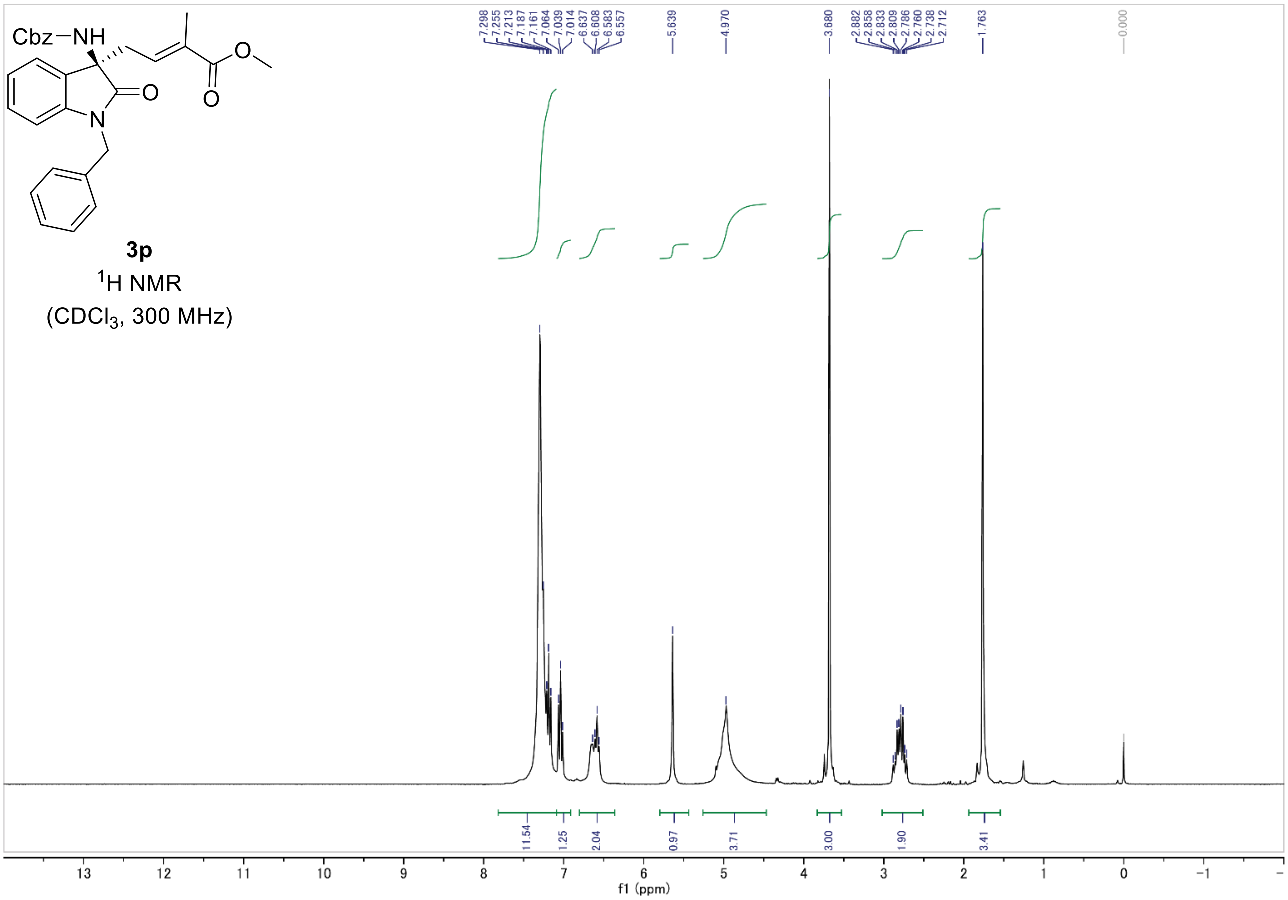
($CDCl_3$, 125 MHz)


Cbz—NH
H3C
H3C
O
N
3n
1H NMR
(CDCl3, 300 MHz)
f1 (ppm)

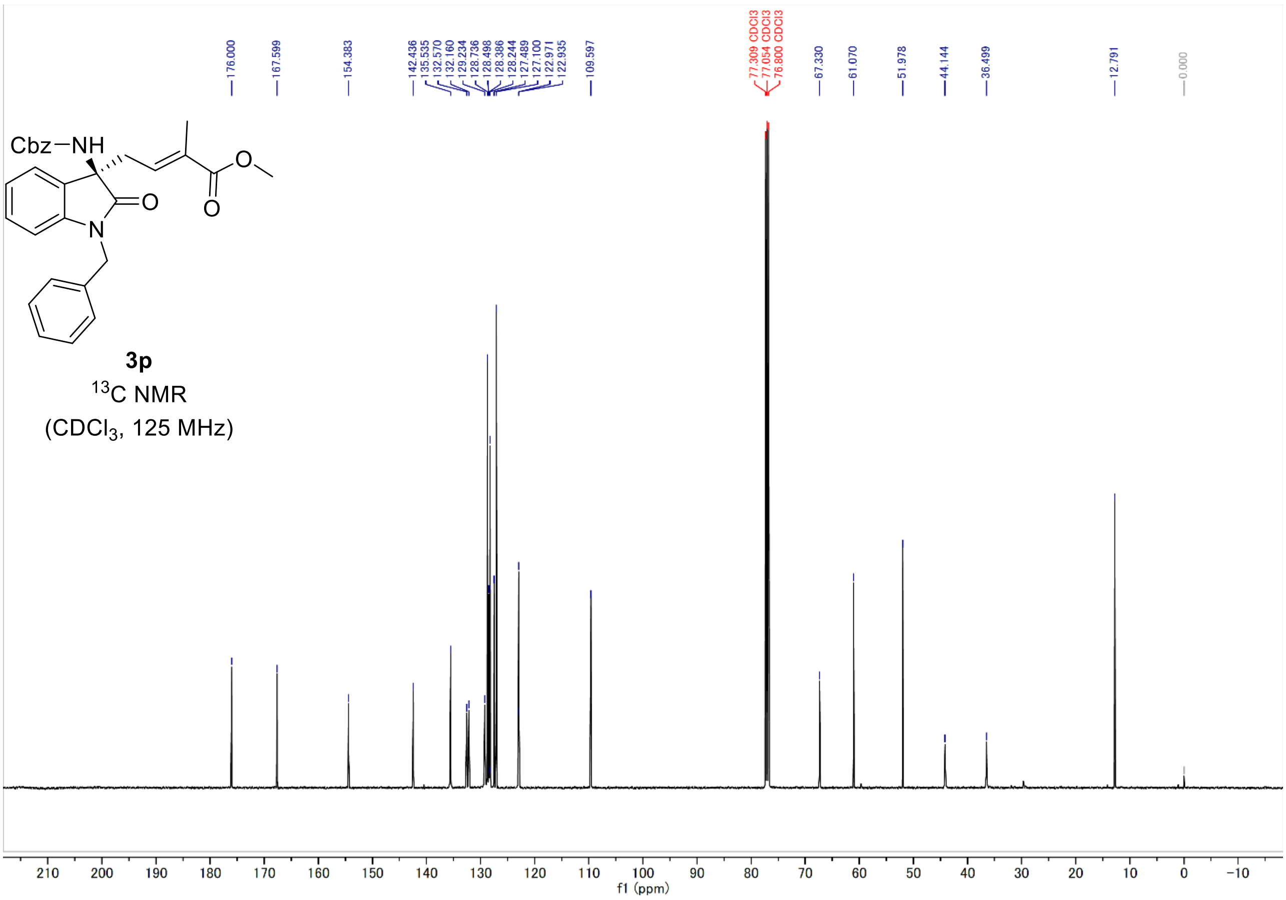

Cbz—NH
H3C
H3C
O
N
3n
13C NMR
(CDCl3, 125 MHz)
f1 (ppm)


Cbz−NH
N
O
O
O
N
3o
¹H NMR
(CDCl3, 300 MHz)
8.219
8.201
7.544
7.431
7.410
7.348
7.338
7.293
7.275
7.251
7.244
7.239
7.217
7.195
6.974
6.953
6.932
6.716
6.690
6.664
6.638
6.613
5.884
5.833
5.747
4.958
3.671
2.850
2.825
2.803
2.778
2.661
2.634
2.615
2.588
1.828 HDO
0.000
0.98
1.11
2.10
7.91
1.24
1.06
1.06
0.87
4.06
3.00
0.97
1.01
f1 (ppm)

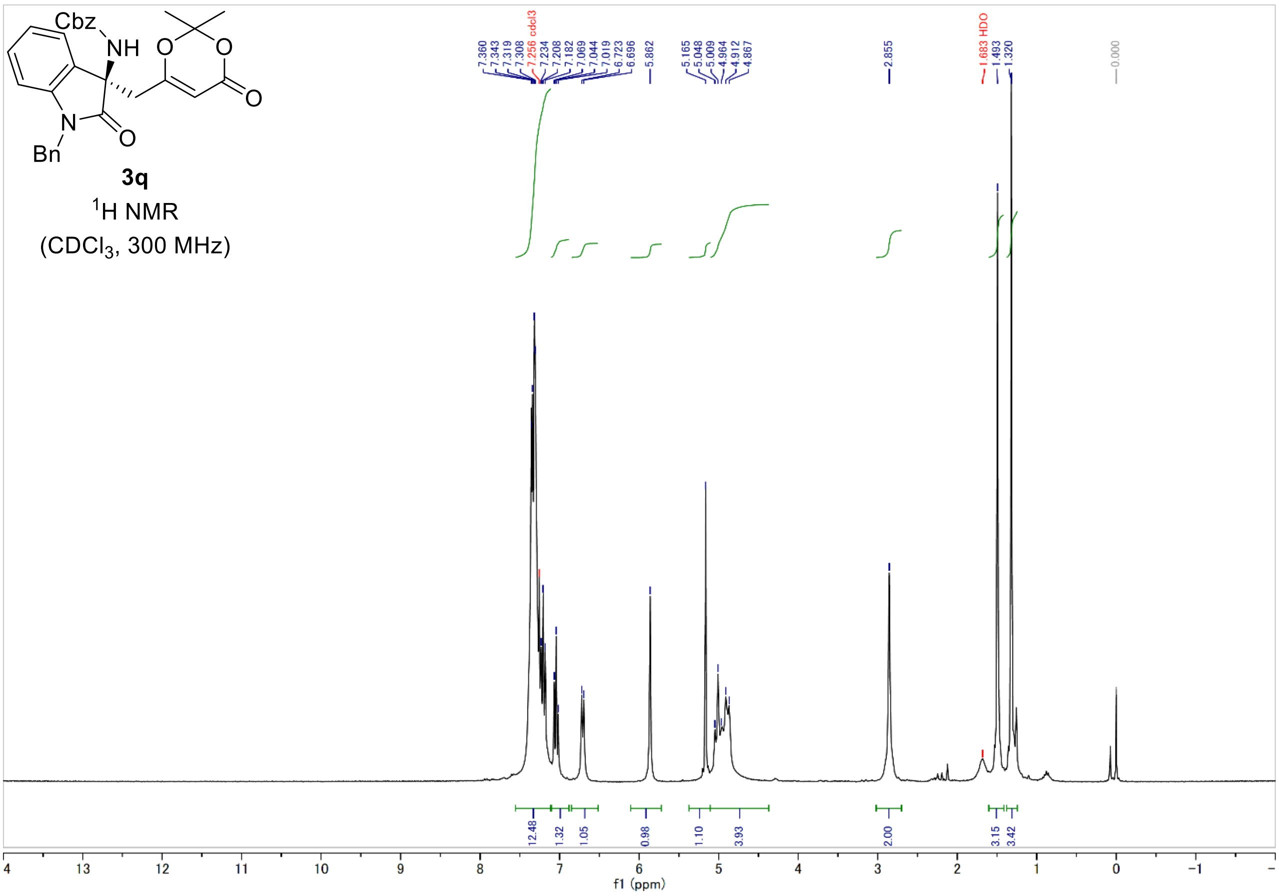

175.416
165.586
155.997
154.444
148.203
138.830
136.251
135.394
131.078
128.505
128.331
128.203
128.125
128.050
127.429
126.896
123.418
118.551
77.308 CDCl3
77.054 CDCl3
76.800 CDCl3
67.407
60.570
51.716
42.862
39.196
0.000
Cbz−NH
N
O
O
O
N
3o
¹³C NMR
(CDCl3, 125 MHz)
f1 (ppm)

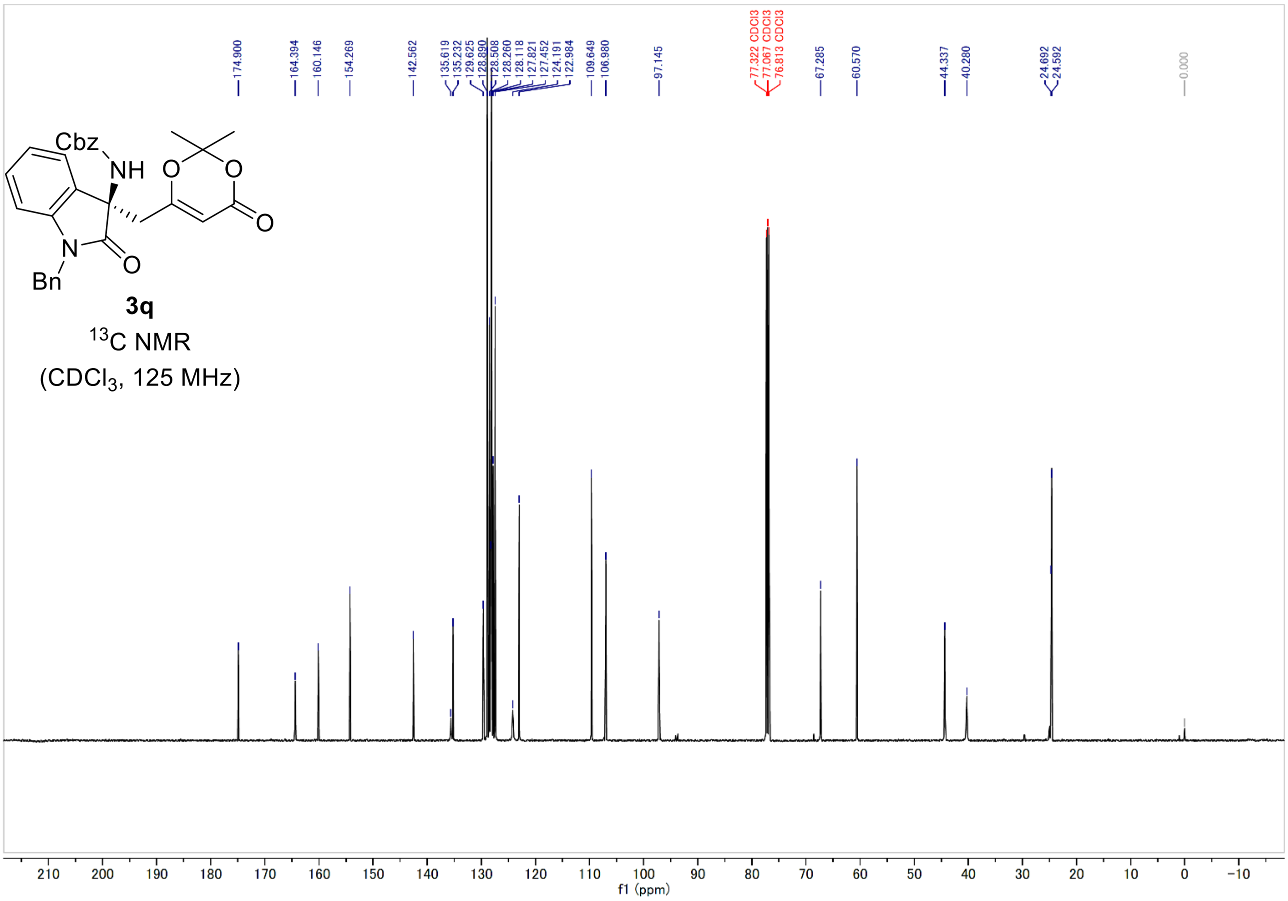


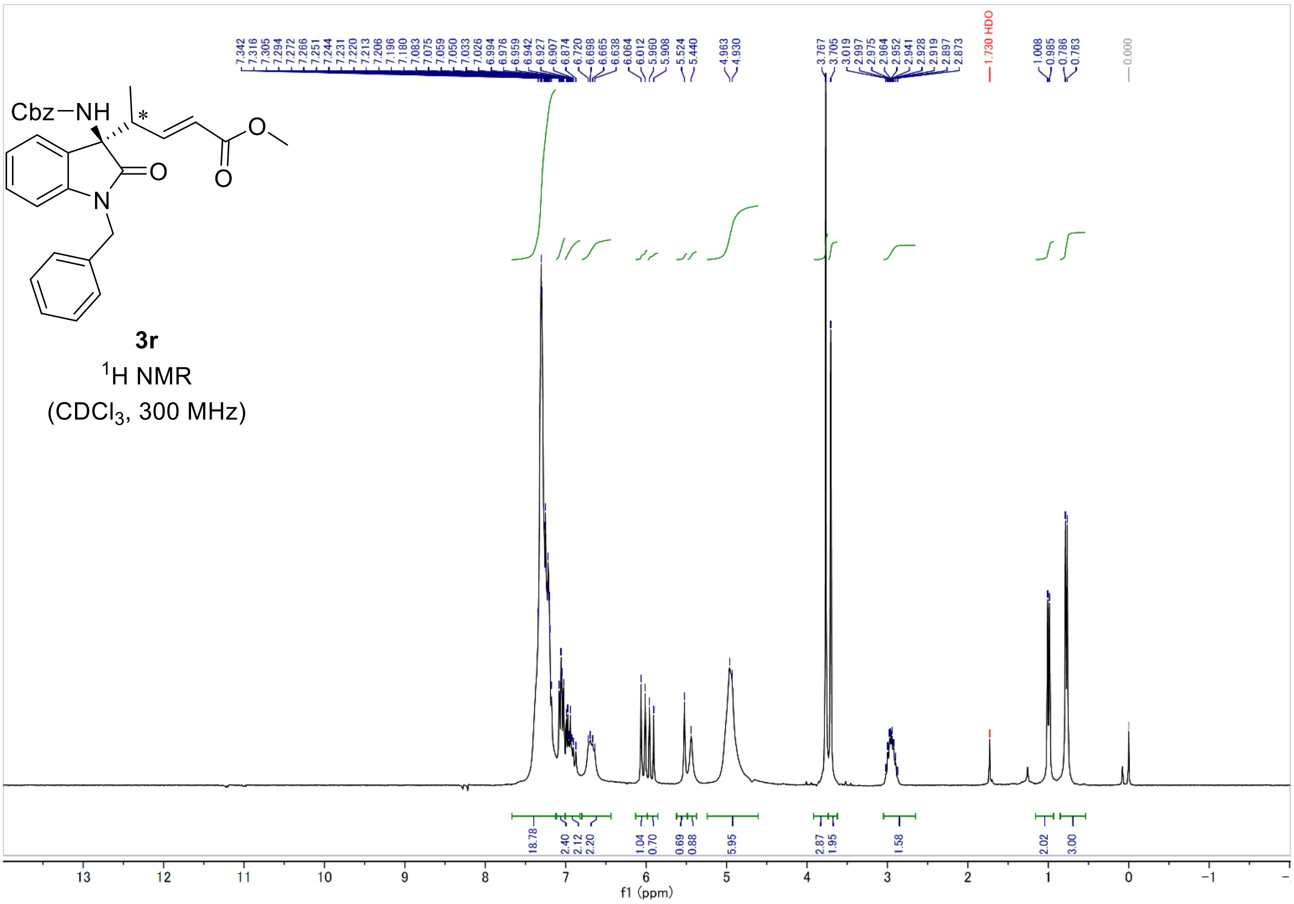
3p
^{1}H NMR
($CDCl_3$, 300 MHz)

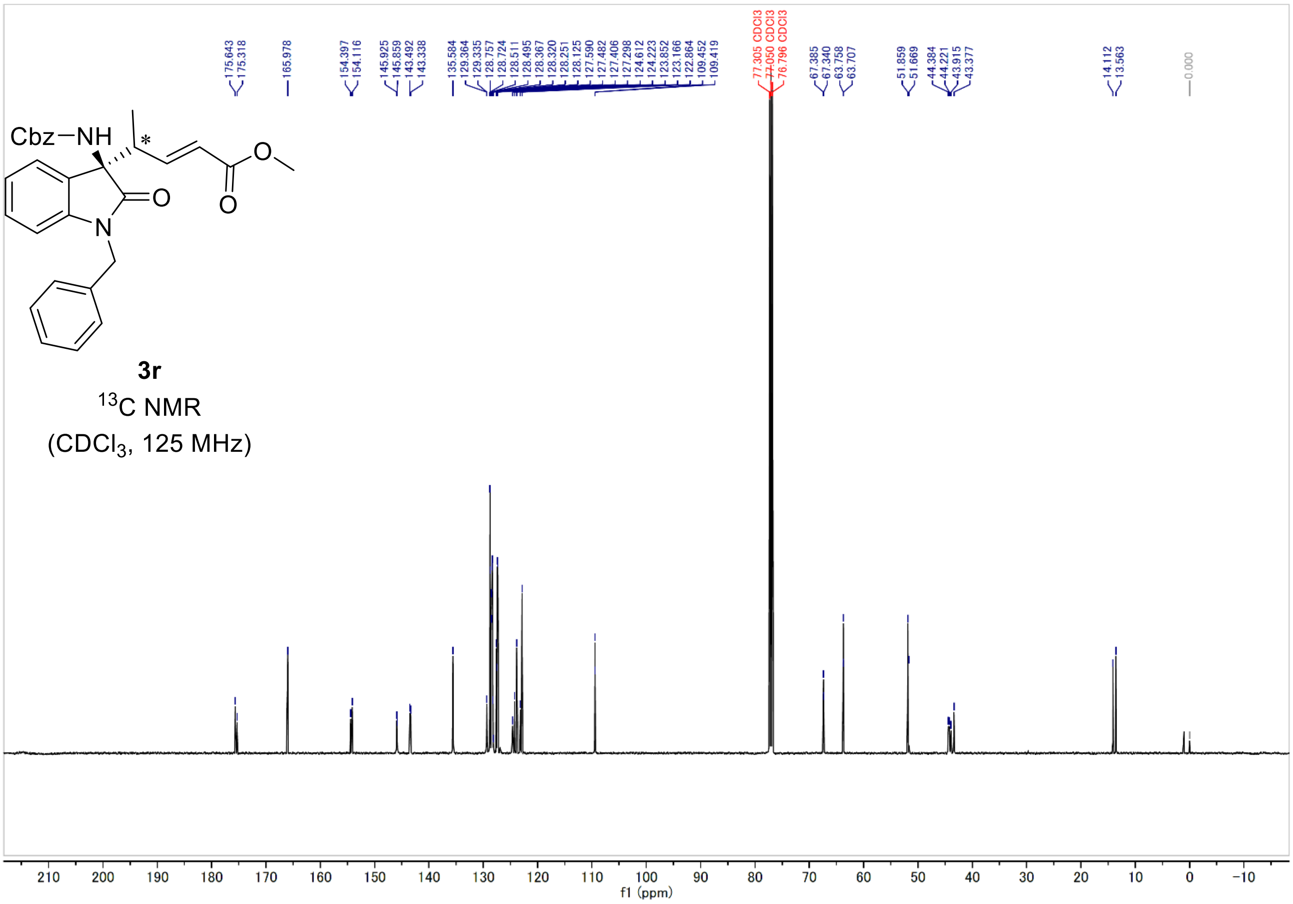


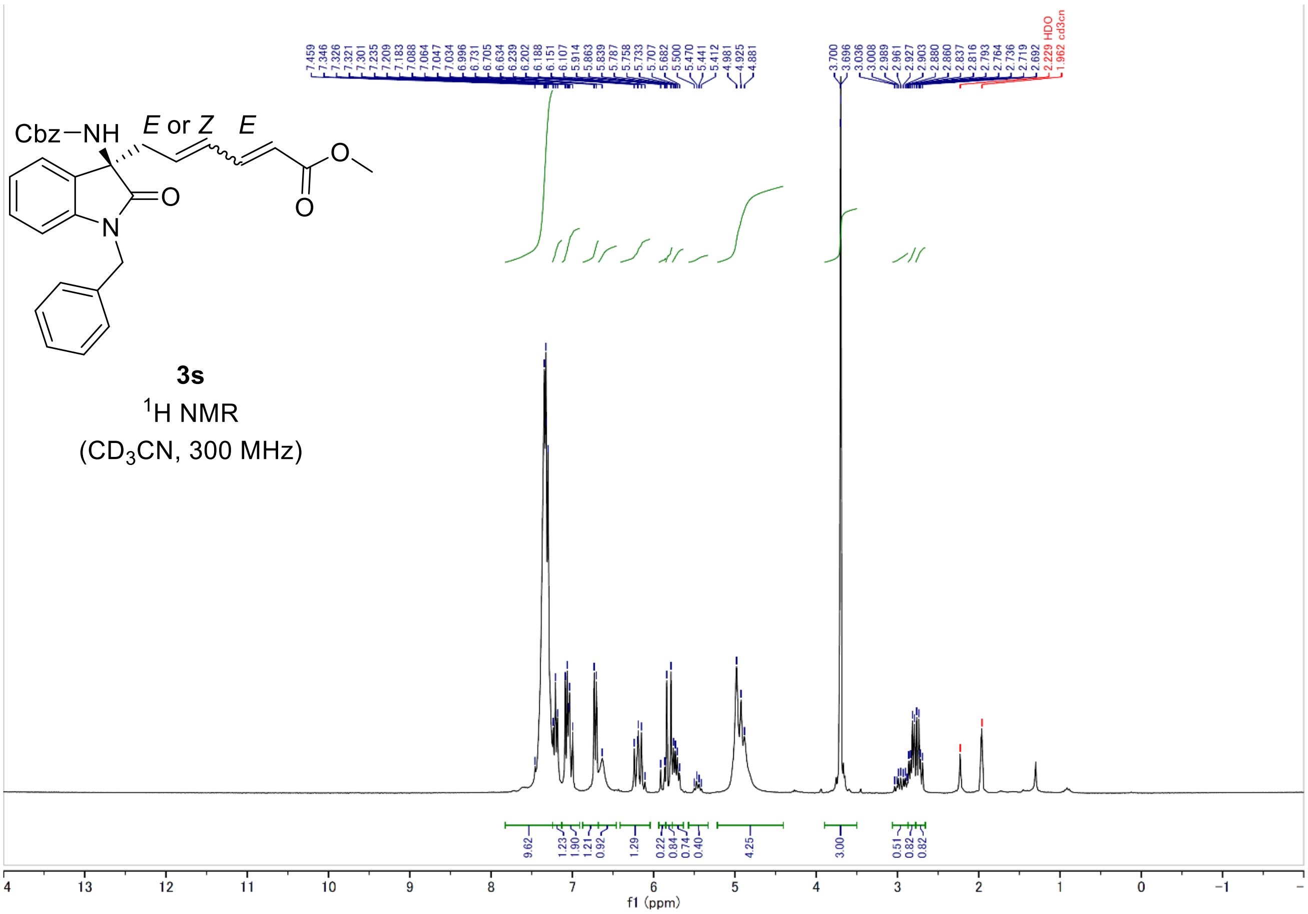
3p
^{13}C NMR
($CDCl_3$, 125 MHz)


Cbz
NH
O
O
O
N
O
Bn
3q
^{1}H NMR
($CDCl_3$, 300 MHz)
f1 (ppm)

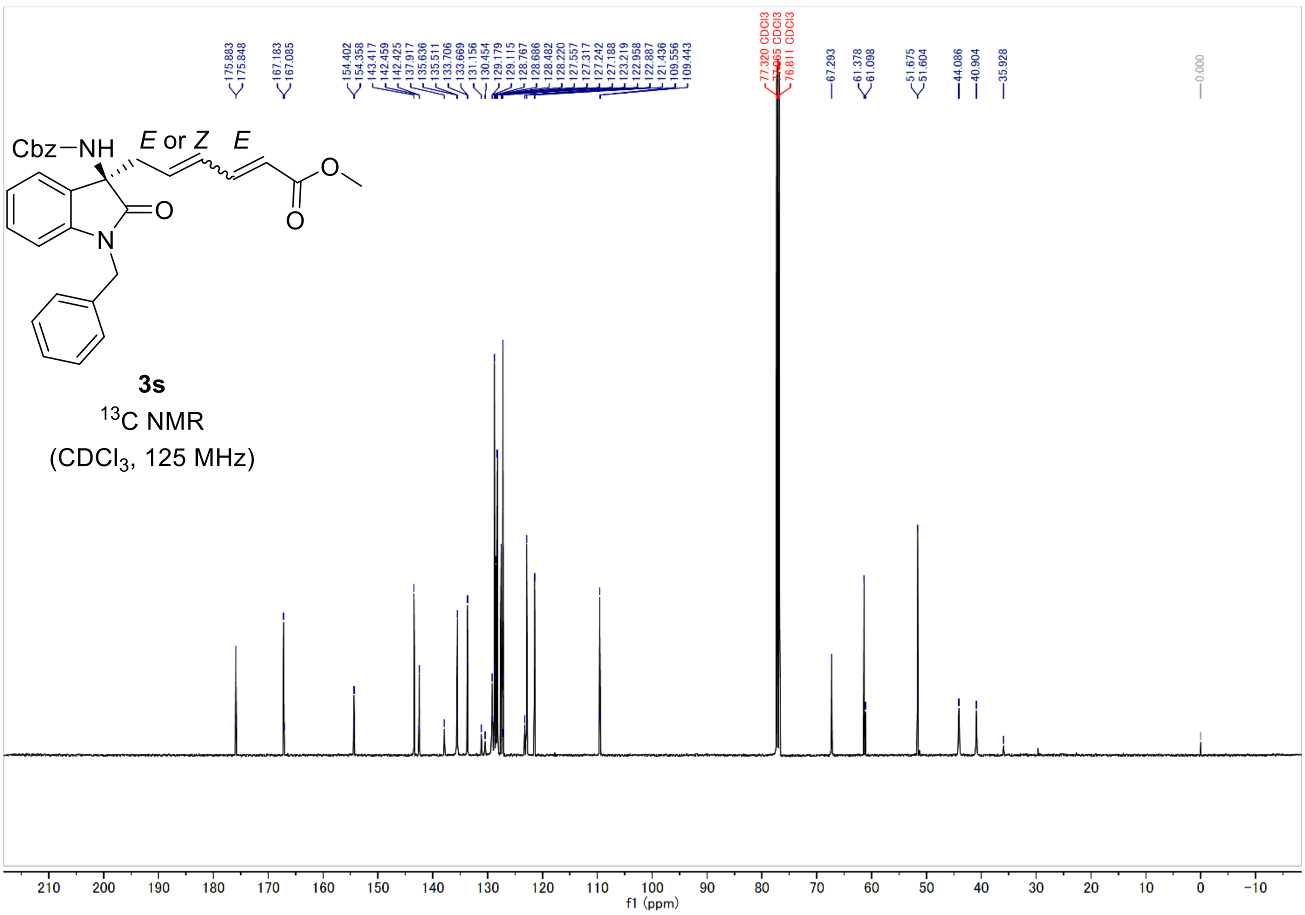

Cbz
NH
O
O
O
N
O
Bn
3q
^{13}C NMR
($CDCl_3$, 125 MHz)
f1 (ppm)


Cbz−NH
*
O
O
N
O
3r
¹H NMR
(CDCl3, 300 MHz)
f1 (ppm)

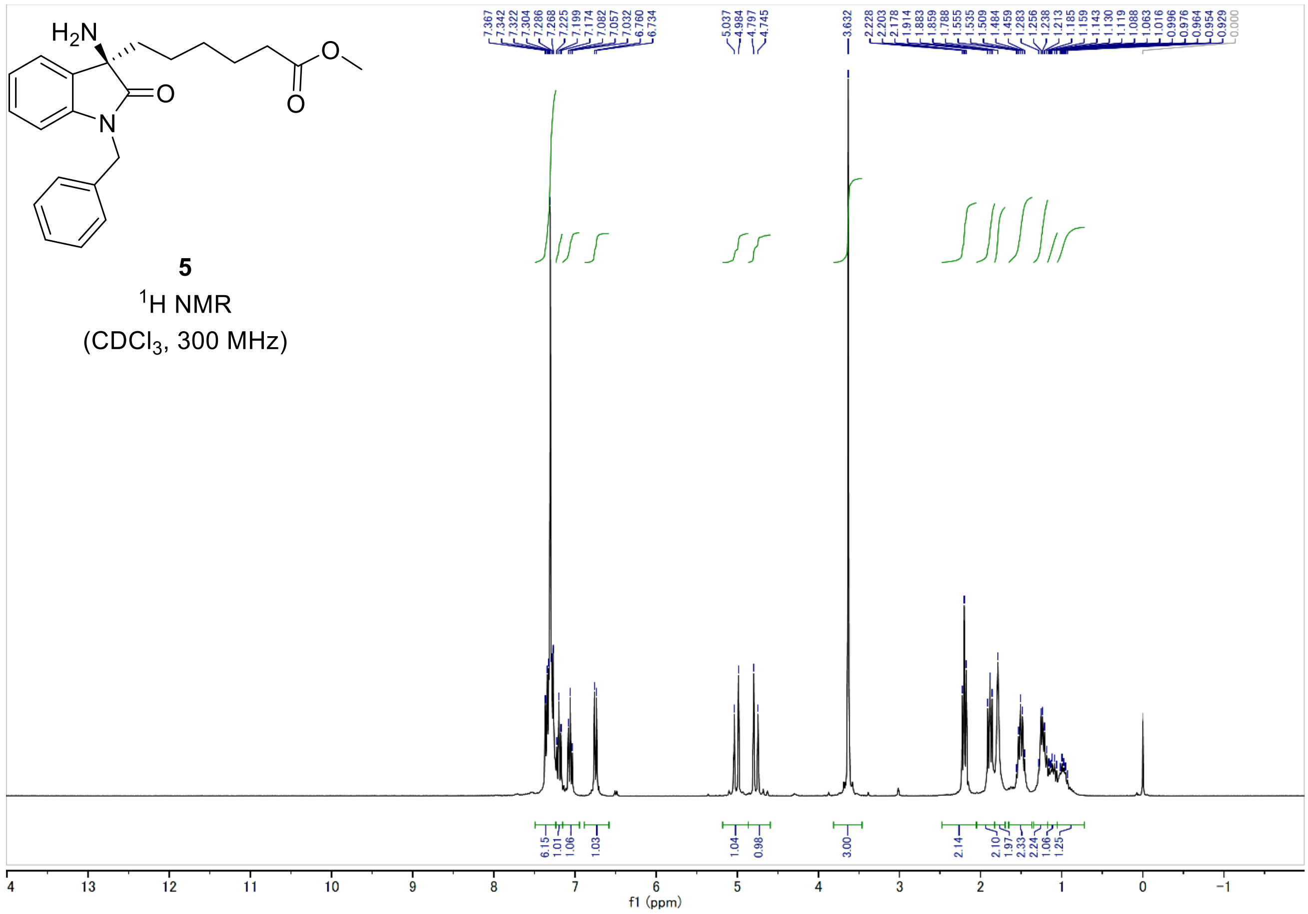

Cbz−NH
*
O
O
N
O
3r
¹³C NMR
(CDCl3, 125 MHz)
f1 (ppm)

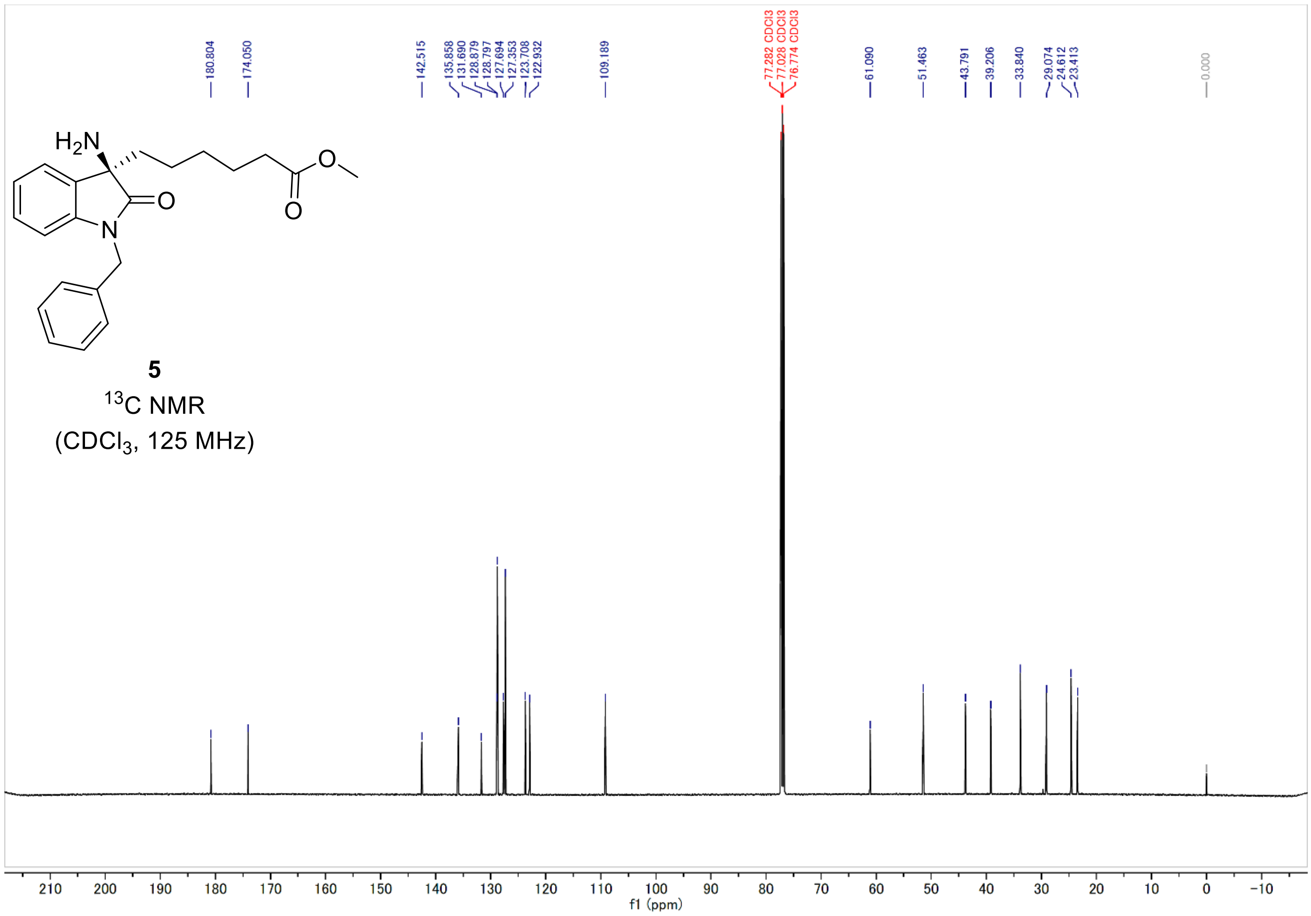


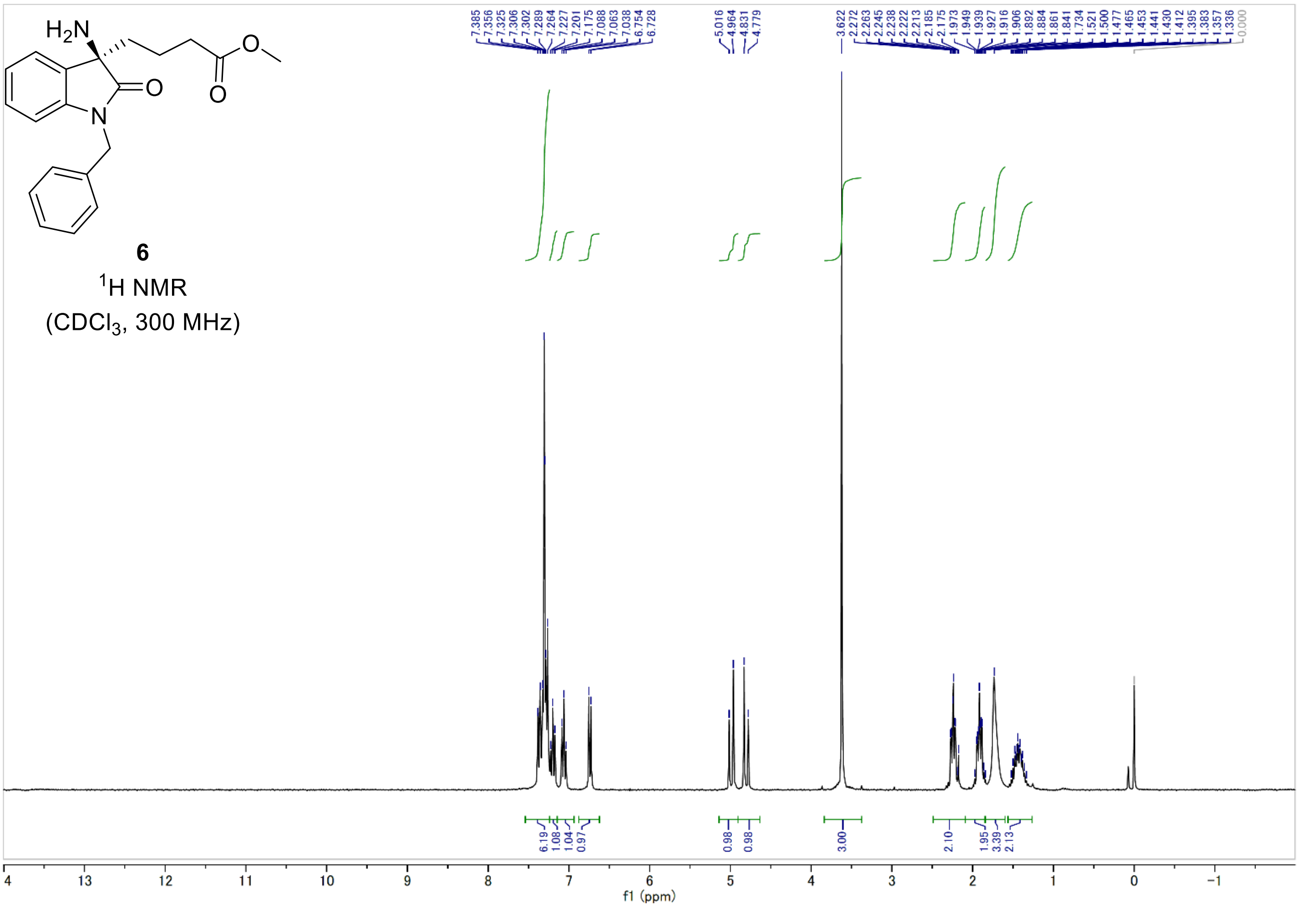
3s
^{1}H NMR
(CD_3CN, 300 MHz)



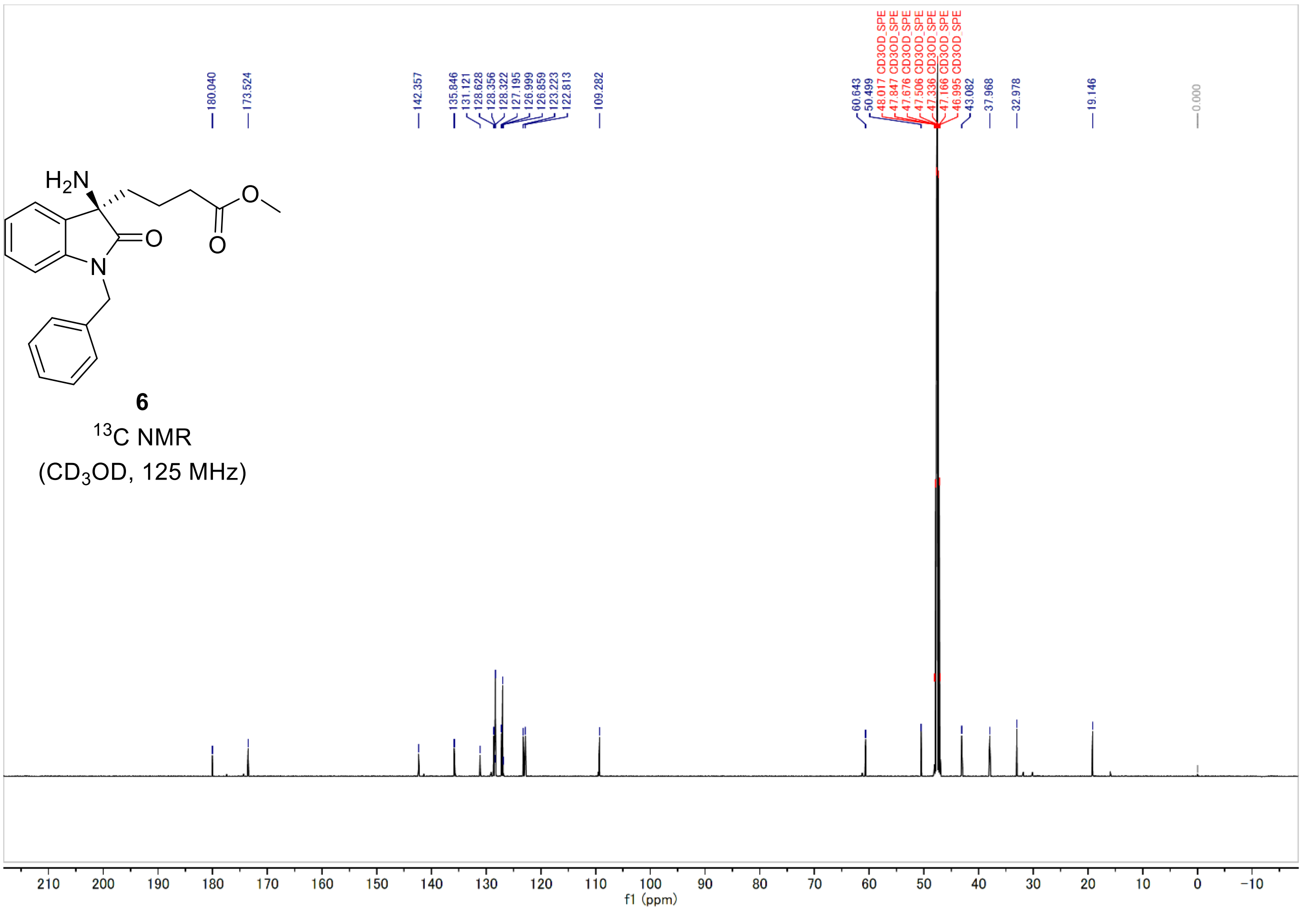
3s
^{13}C NMR
($CDCl_3$, 125 MHz)


5
^{1}H NMR
($CDCl_3$, 300 MHz)
f1 (ppm)

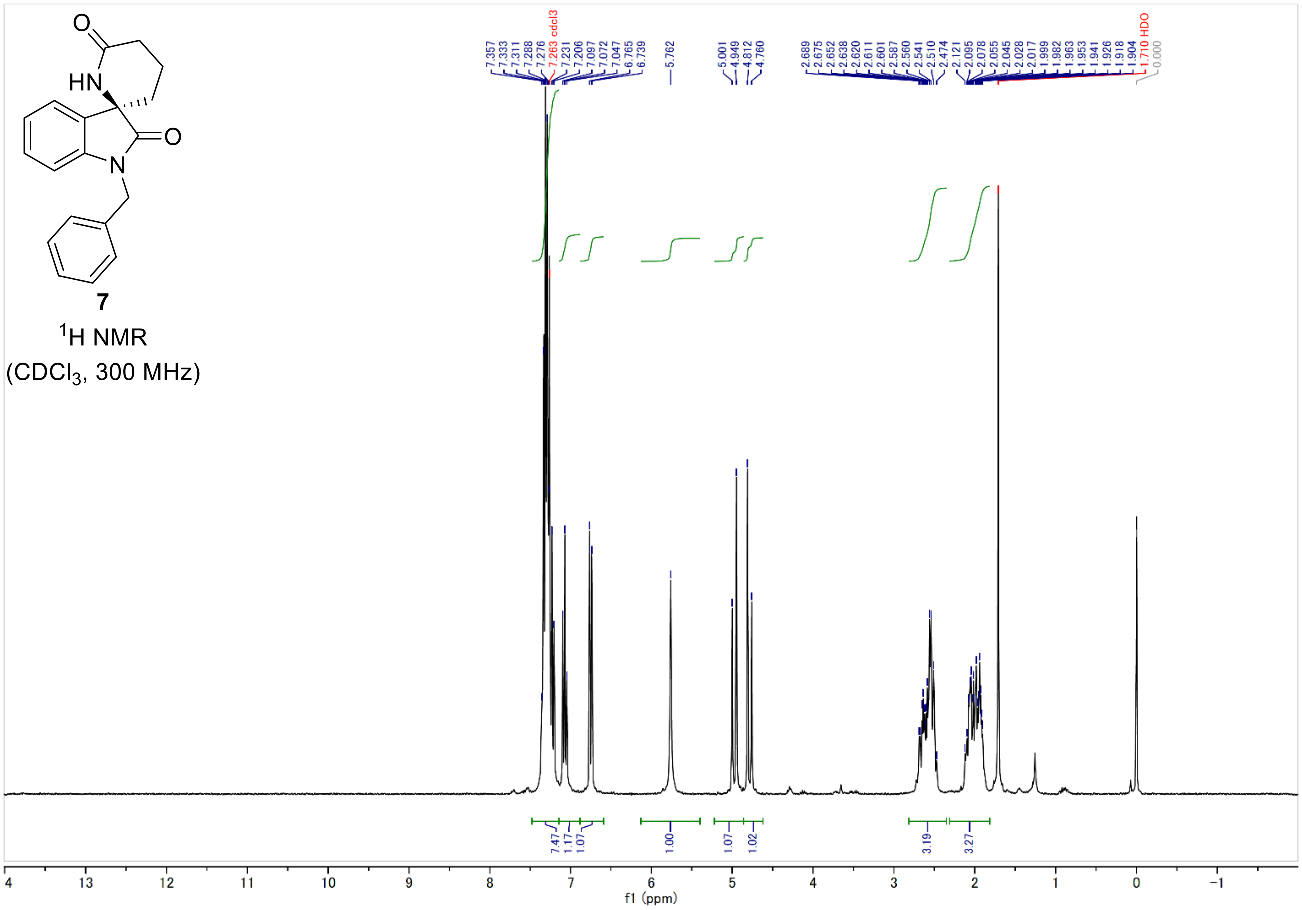

5
^{13}C NMR
($CDCl_3$, 125 MHz)
f1 (ppm)

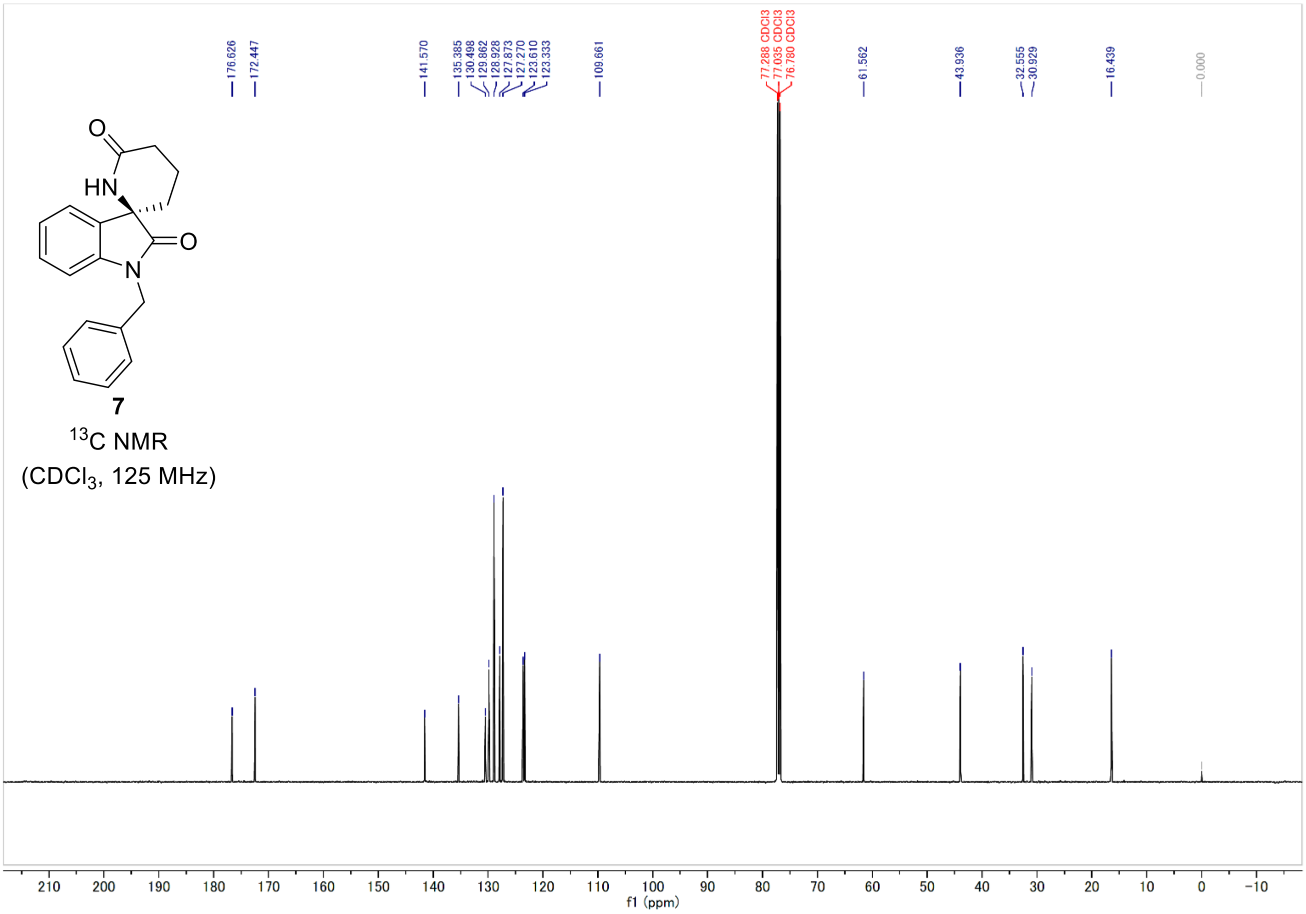


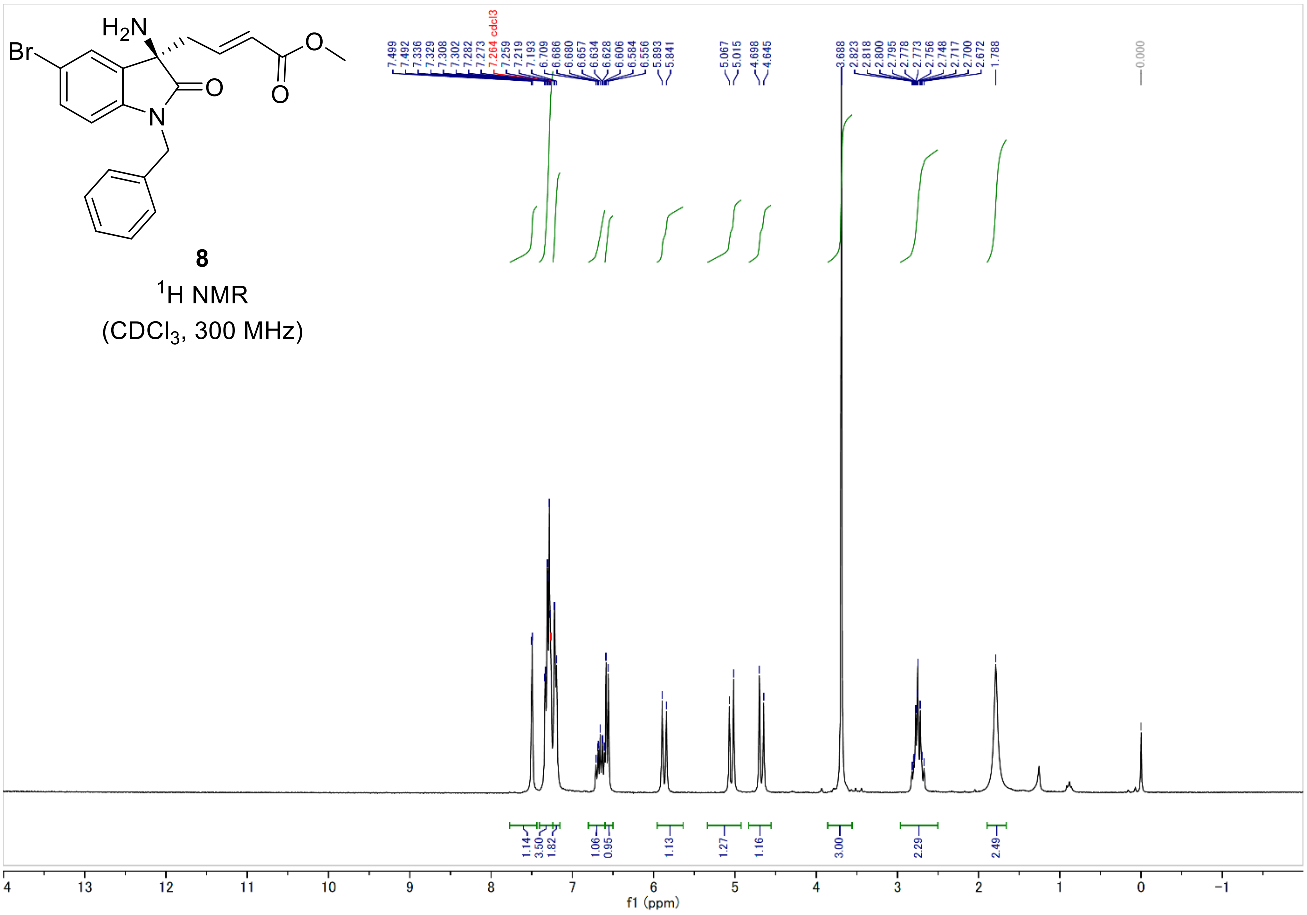
6
^{1}H NMR
($CDCl_3$, 300 MHz)

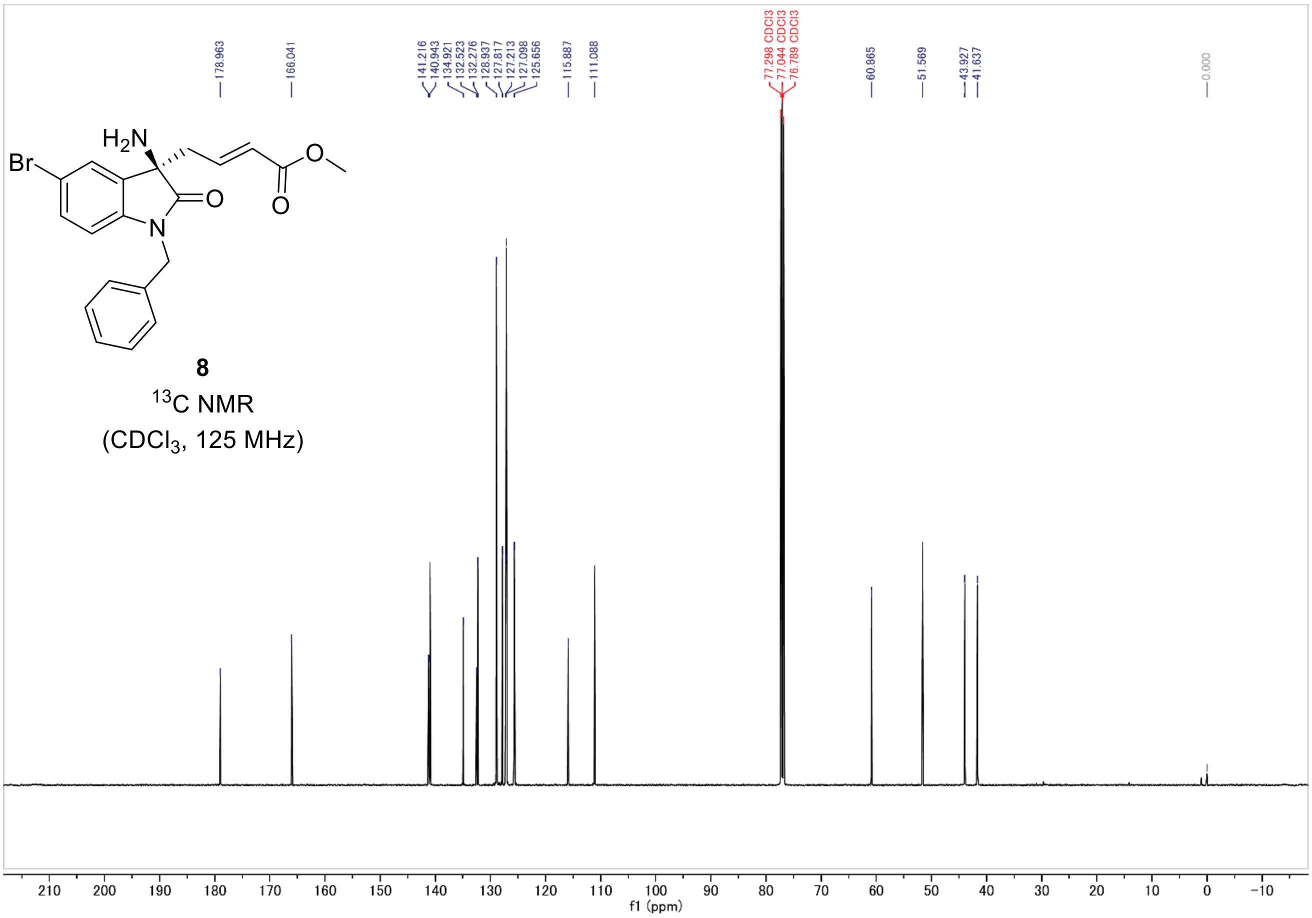


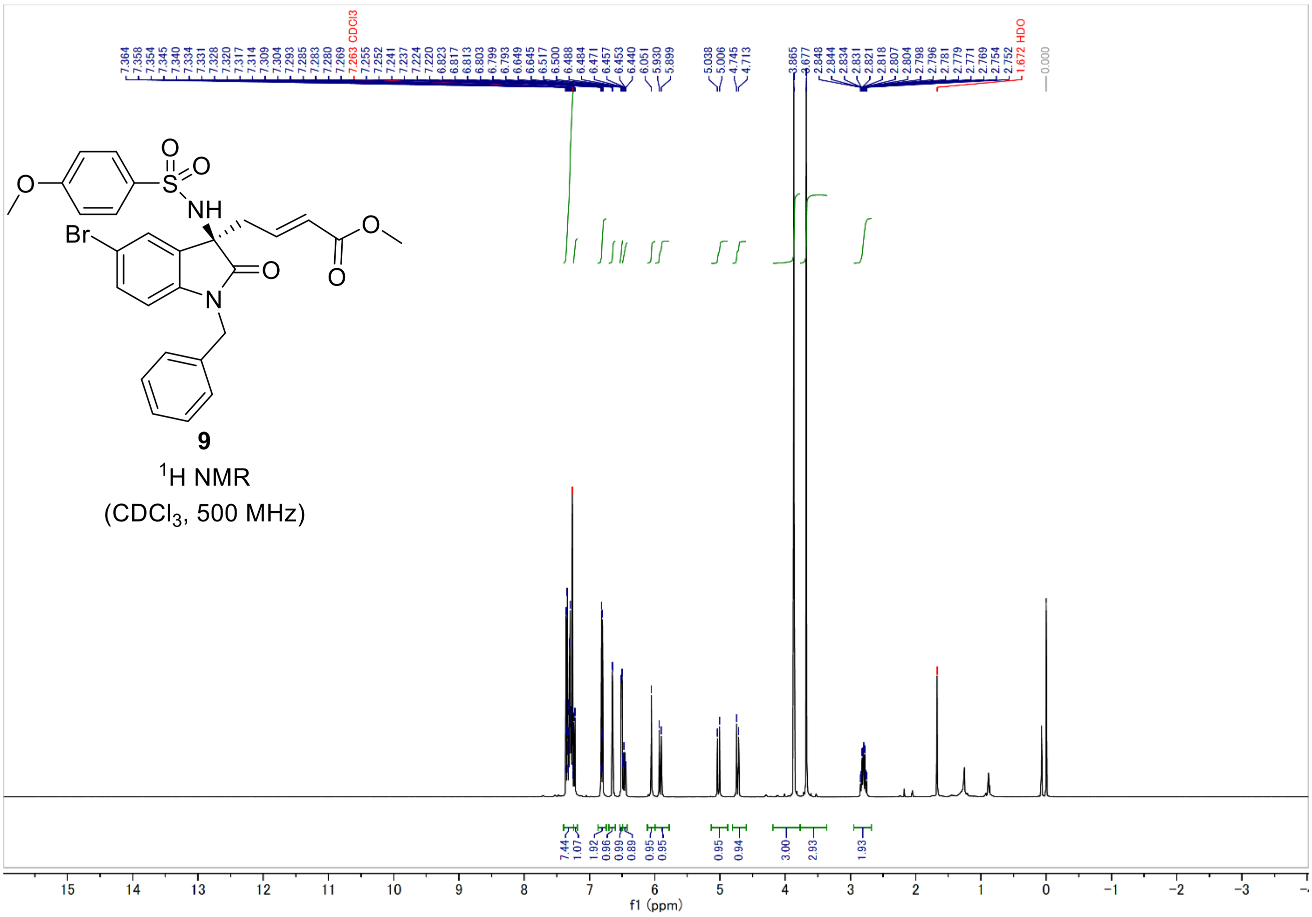
6
^{13}C NMR
(CD_3OD, 125 MHz)

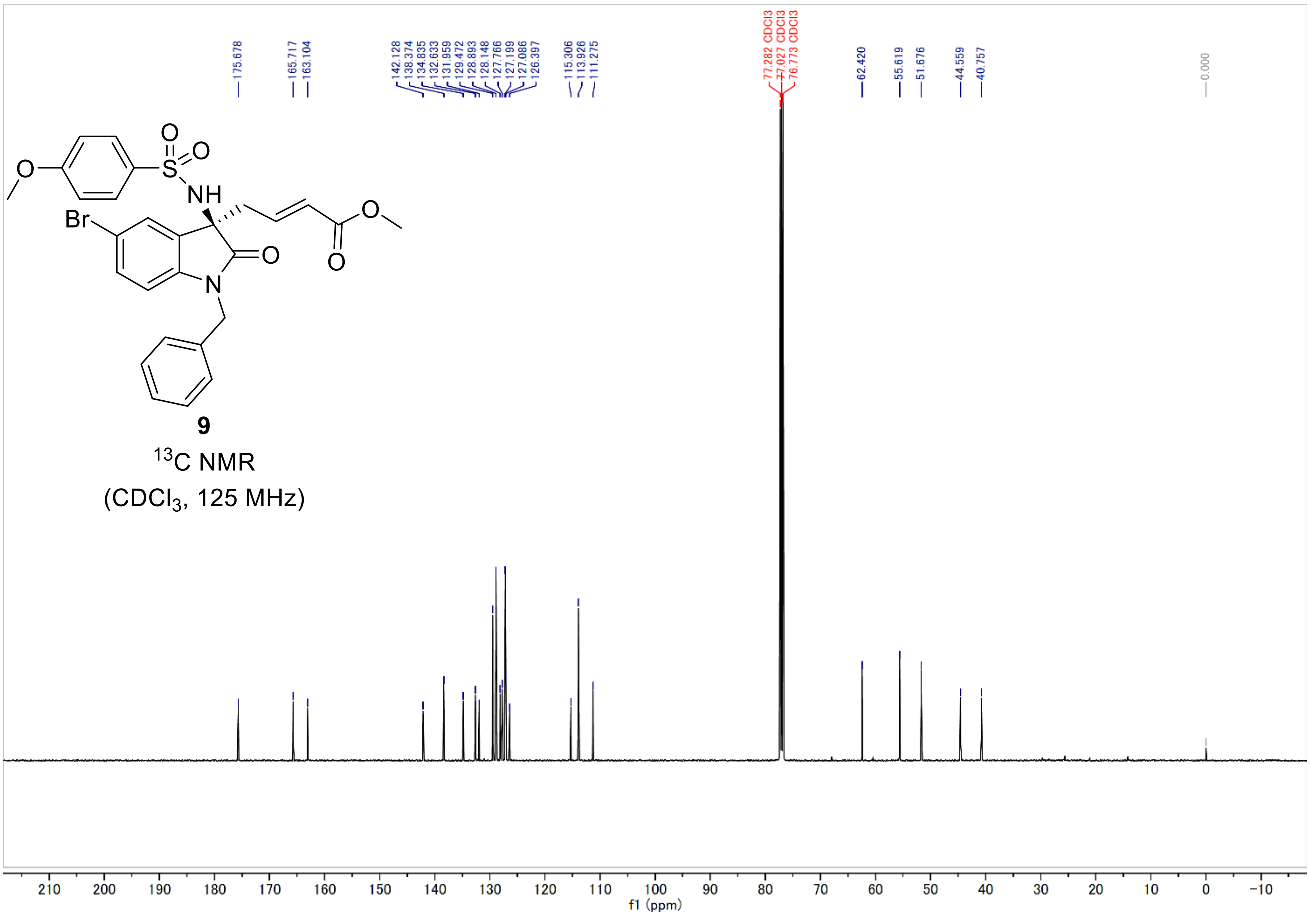

7
1H NMR
(CDCl3, 300 MHz)
7.357 7.333 7.311 7.288 7.276 7.263 cdcl3 7.231 7.206 7.097 7.072 7.047 6.765 6.739
5.762
5.001 4.949 4.812 4.760
2.689 2.675 2.652 2.638 2.620 2.611 2.601 2.587 2.560 2.541 2.510 2.474 2.121 2.095 2.078 2.055 2.045 2.028 2.017 1.999 1.982 1.963 1.953 1.941 1.926 1.918 1.904 1.710 HDO 0.000
7.47 1.17 1.07 1.00 1.07 1.02 3.19 3.27
f1 (ppm)


7
13C NMR
(CDCl3, 125 MHz)
176.626 172.447 141.570 135.385 130.498 129.862 128.928 127.873 127.270 123.610 123.333 109.661
77.288 CDCl3 77.035 CDCl3 76.780 CDCl3
61.562 43.936 32.555 30.929 16.439 0.000
f1 (ppm)



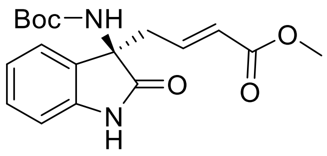



9
^{1}H NMR
(CDCl$_3$, 500 MHz)
f1 (ppm)

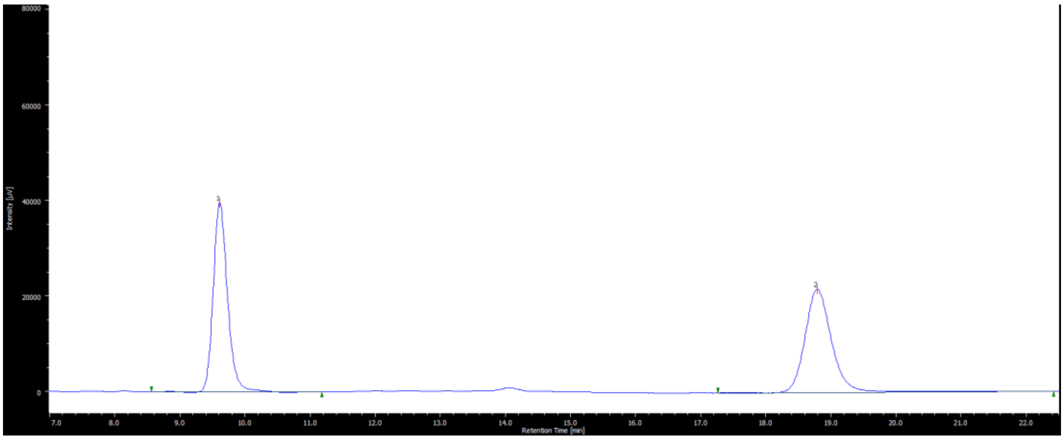

9
^{13}C NMR
(CDCl$_3$, 125 MHz)
f1 (ppm)

HPLC analysis

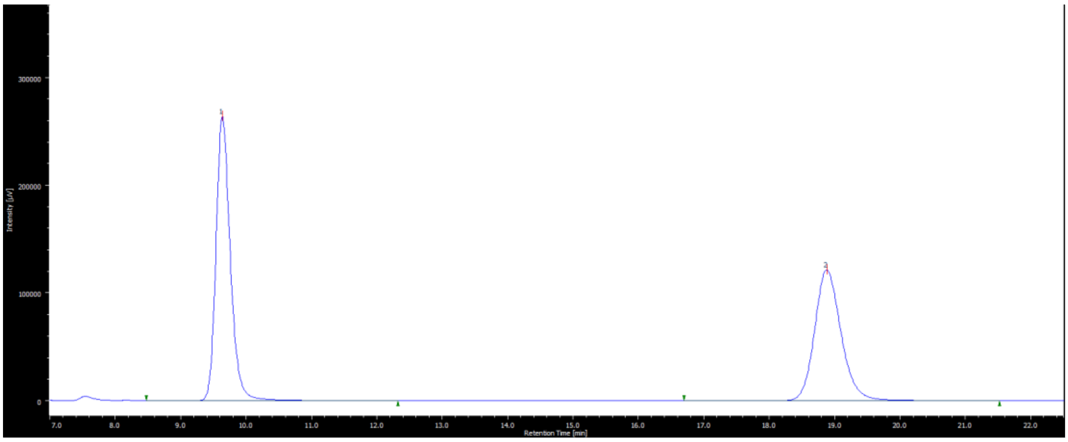
Methyl (*R*,*E*)-4-{3-[(*tert*-butoxycarbonyl)amino]-2-oxoindolin-3-yl}but-2-enoate (3a)



racemic-**3a**



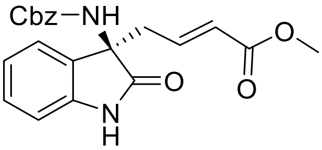
(*R*)-**3a**



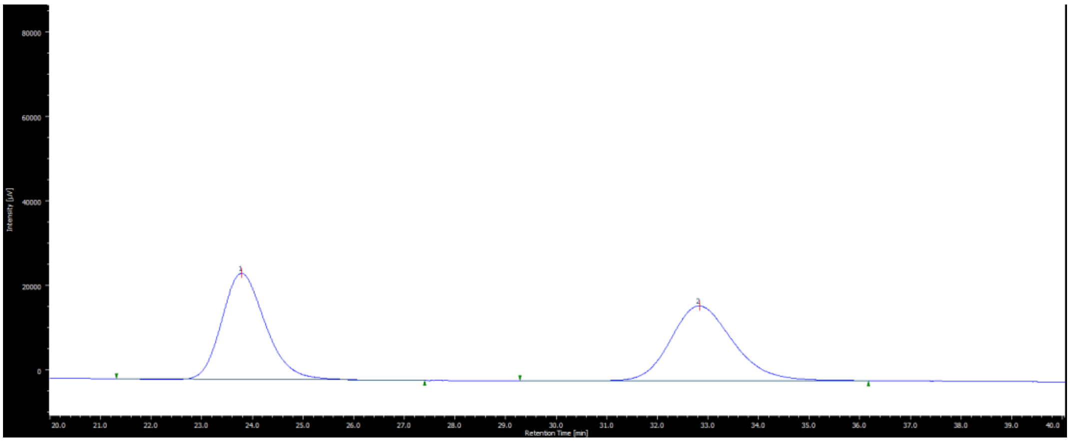
racemic-**3a**		
Peak	tR (min)	Area (%)
1	9.6	49.8
2	18.8	50.0

(*R*)-**3a**		
Peak	tR (min)	Area (%)
1	9.6	54.0
2	18.9	46.0

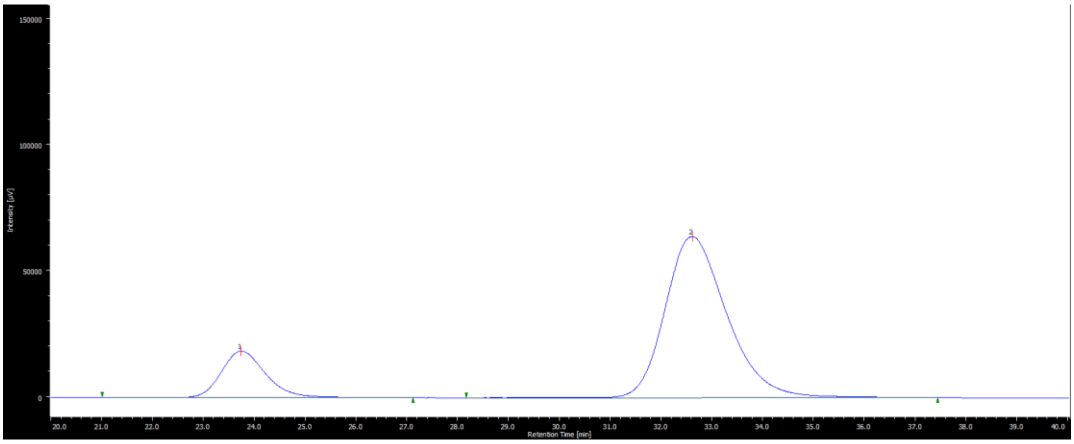
Methyl (*R*,*E*)-4-[3-(benzyloxycarbonyl)amino-2-oxoindolin-3-yl]but-2-enoate (3b)



racemic-**3b**



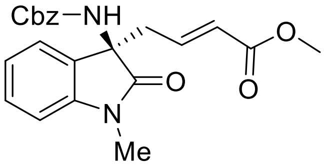
(*R*)-**3b**



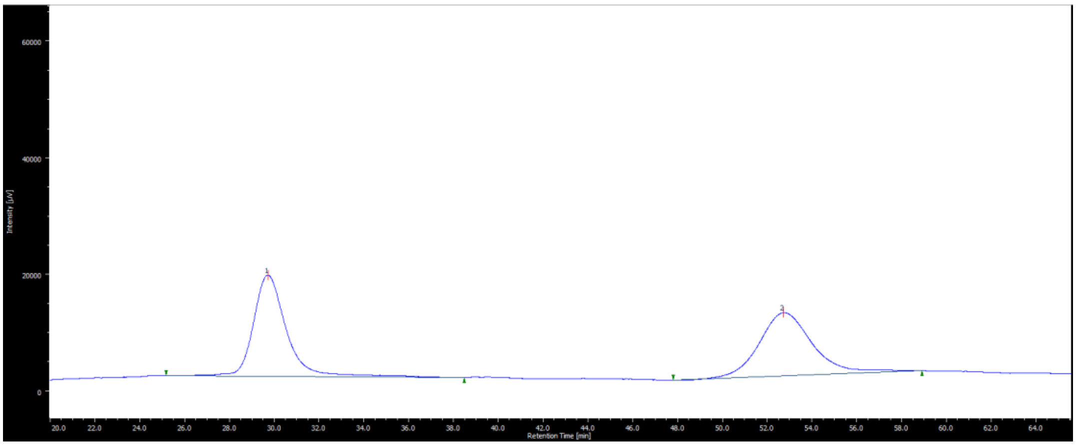
racemic-**3b**		
Peak	tR (min)	Area (%)
1	23.8	49.9
2	32.8	50.1

(*R*)-**3b**		
Peak	tR (min)	Area (%)
1	23.7	17.0
2	32.6	83.0

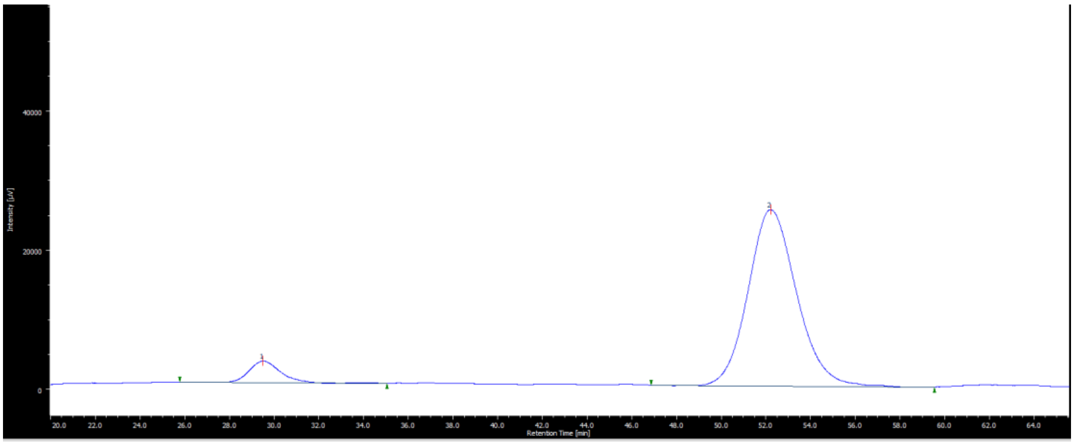
Methyl (*R*,*E*)-4-[1-methyl-3-(benzyloxycarbonylamino)-2-oxoindolin-3-yl]but-2-enoate (3c)



racemic-**3c**



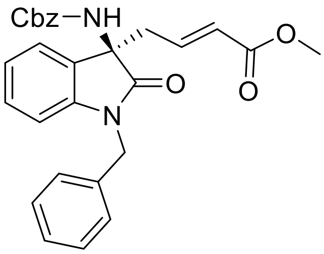
(*R*)-**3c**



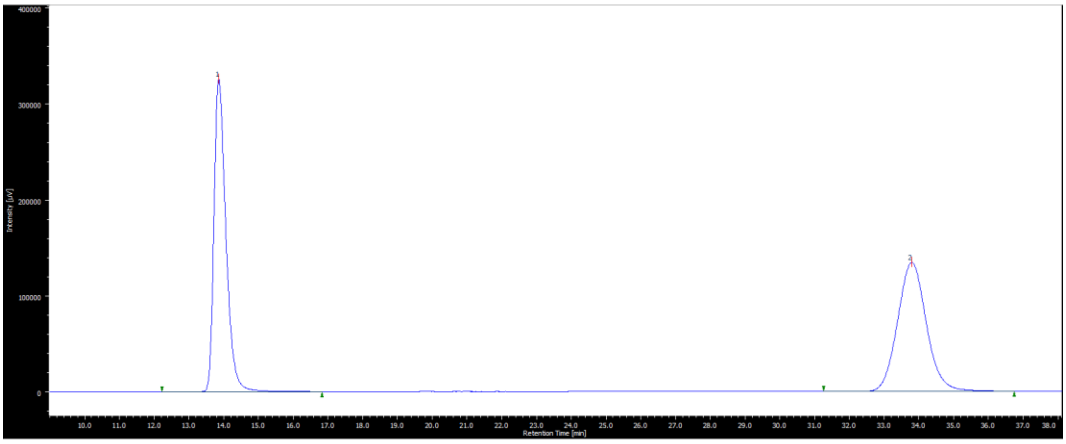
racemic-**3c**		
Peak	tR (min)	Area (%)
1	29.7	49.8
2	52.7	50.2

(*R*)-**3c**		
Peak	tR (min)	Area (%)
1	29.5	7.3
2	52.2	92.7

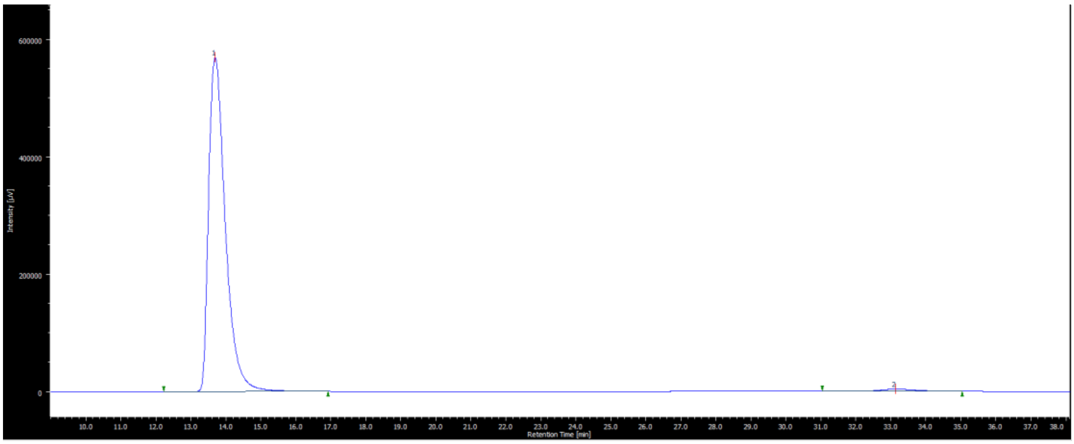
Methyl (*R*,*E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-2-oxoindolin-3-yl]but-2-enoate (3d)



racemic-**3d**



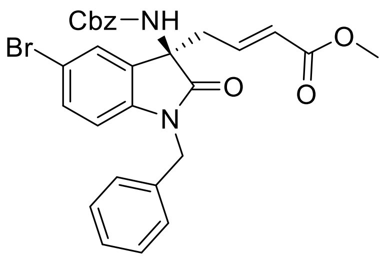
(*R*)-**3d**



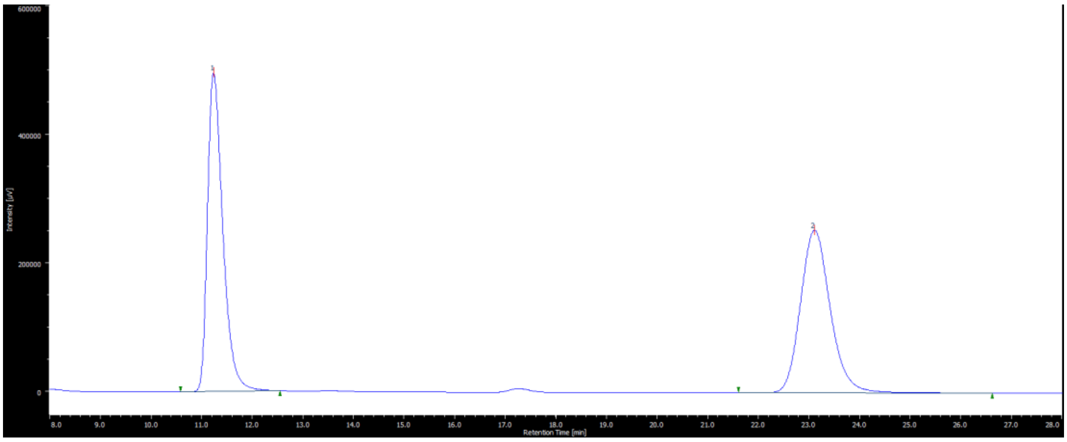
racemic-**3d**		
Peak	tR (min)	Area (%)
1	13.9	50.0
2	33.8	50.0

(*R*)-**3d**		
Peak	tR (min)	Area (%)
1	9.1	98.6
2	33.1	1.4

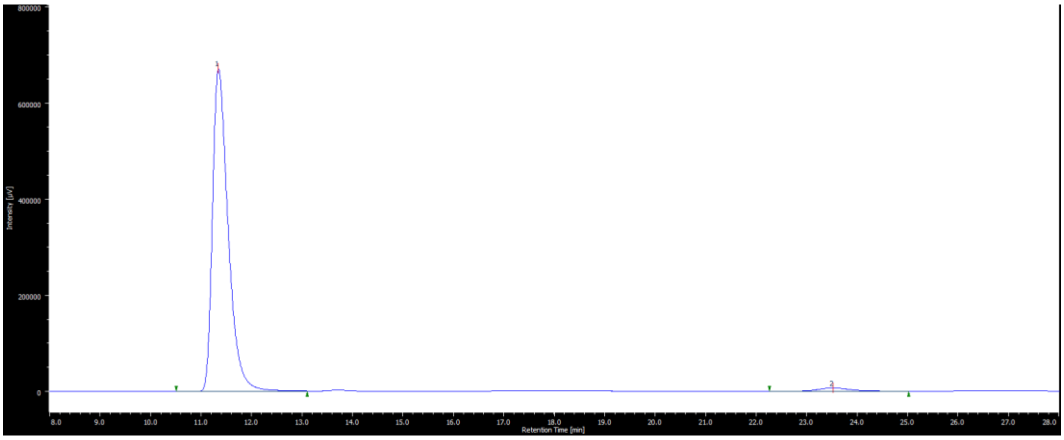
Methyl (*R*,*E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-5-bromo-2-oxoindolin-3-yl]but-2-enoate (3e)



racemic-**3e**

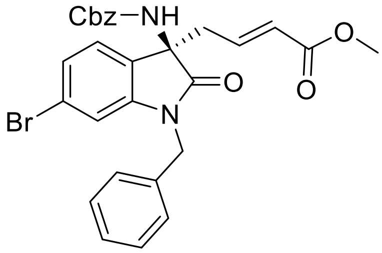


(*R*)-**3e**

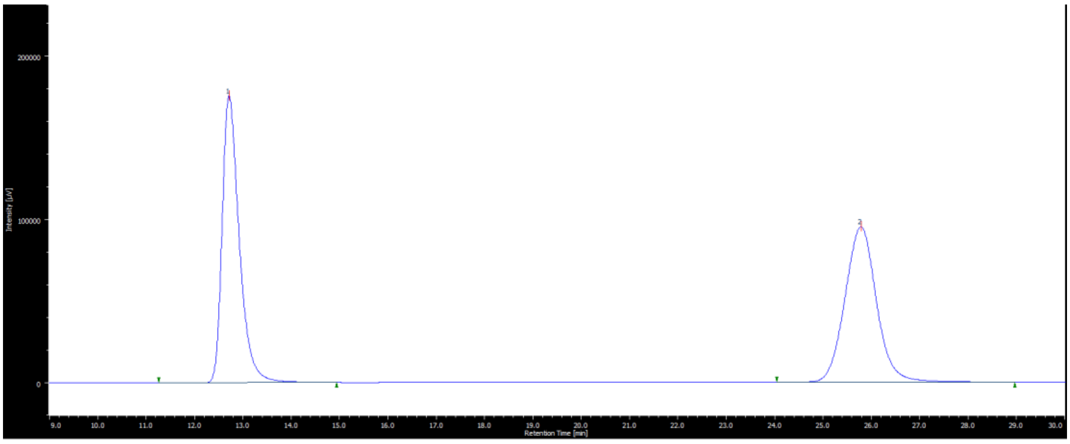


racemic-**3e**			(*R*)-**3e**		
Peak	tR (min)	Area (%)	Peak	tR (min)	Area (%)
1	11.2	50.1	1	11.3	98.0
2	23.1	49.9	2	23.5	2.0

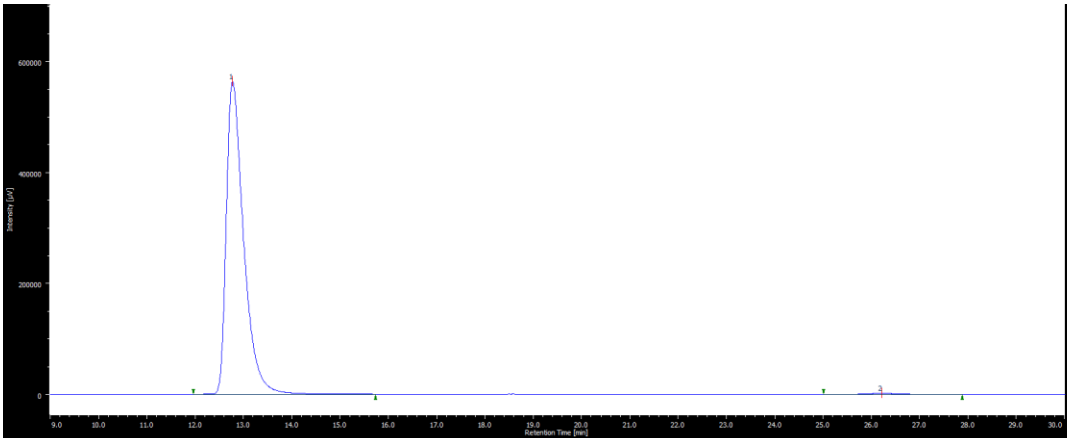
Methyl (*R*,*E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-6-bromo-2-oxoindolin-3-yl]but-2-enoate (3f)



racemic-**3f**

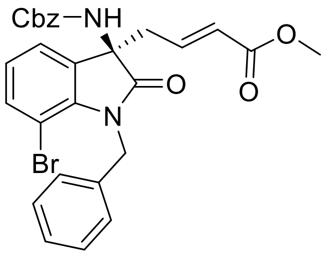


(*R*)-**3f**

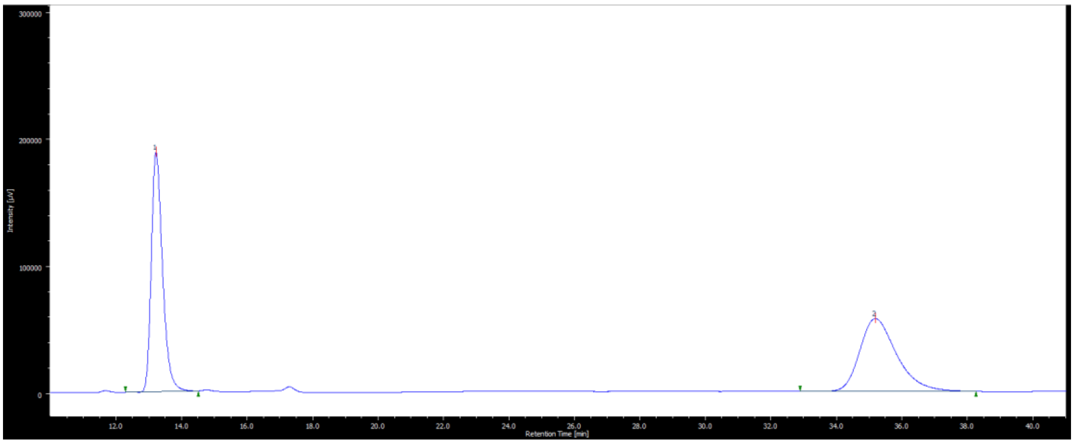


racemic-**3f**			(*R*)-**3f**		
Peak	tR (min)	Area (%)	Peak	tR (min)	Area (%)
1	12.7	50.1	1	12.8	99.3
2	25.8	49.9	2	26.2	0.7

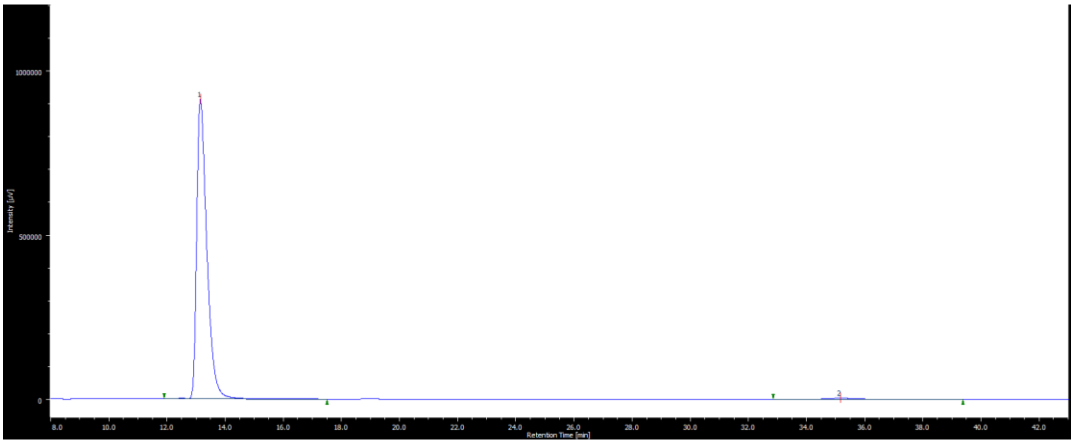
Methyl (*R*,*E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-7-bromo-2-oxoindolin-3-yl]but-2-enoate (3g)



racemic-**3g**



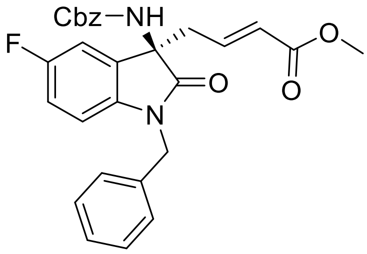
(*R*)-**3g**



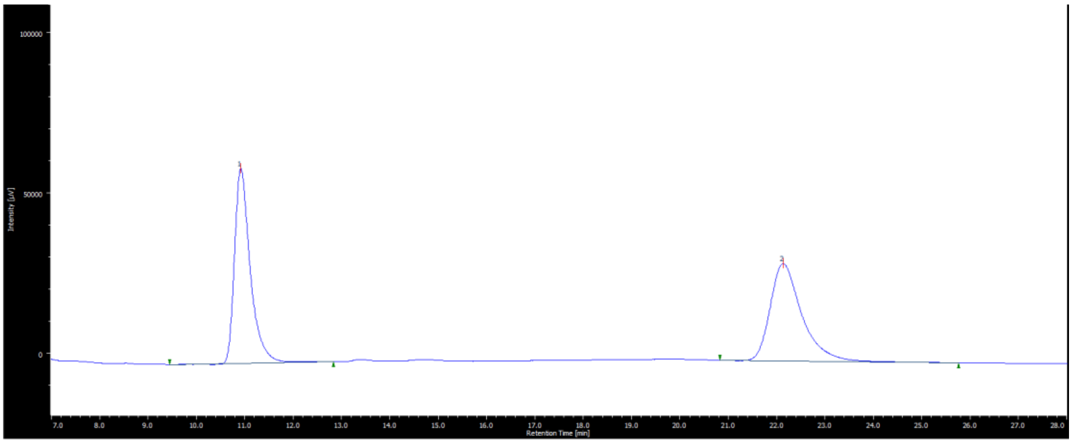
racemic-**3g**		
Peak	tR (min)	Area (%)
1	13.2	50.0
2	35.2	50.0

(*R*)-**3g**		
Peak	tR (min)	Area (%)
1	13.1	98.7
2	35.1	1.3

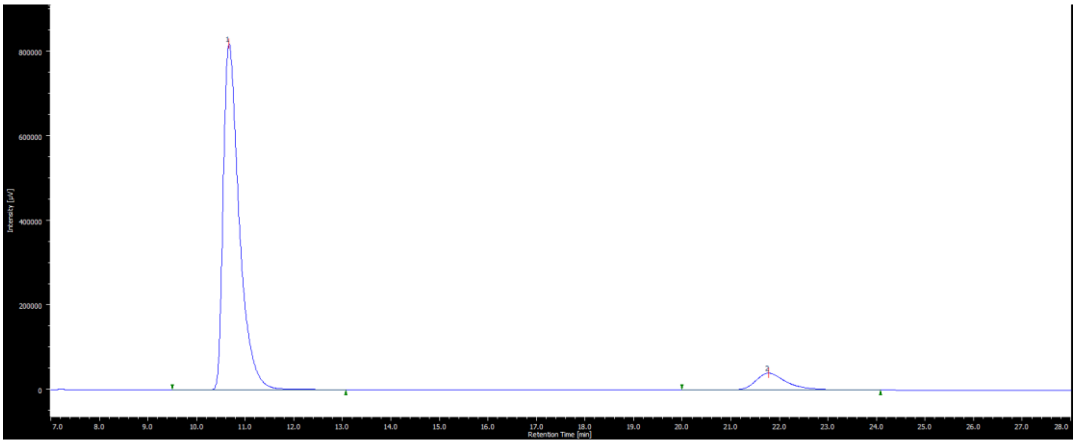
Methyl (*R*,*E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-5-fluoro-2-oxoindolin-3-yl]but-2-enoate (3h)



racemic-**3h**



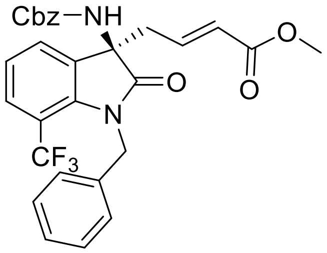
(*R*)-**3h**



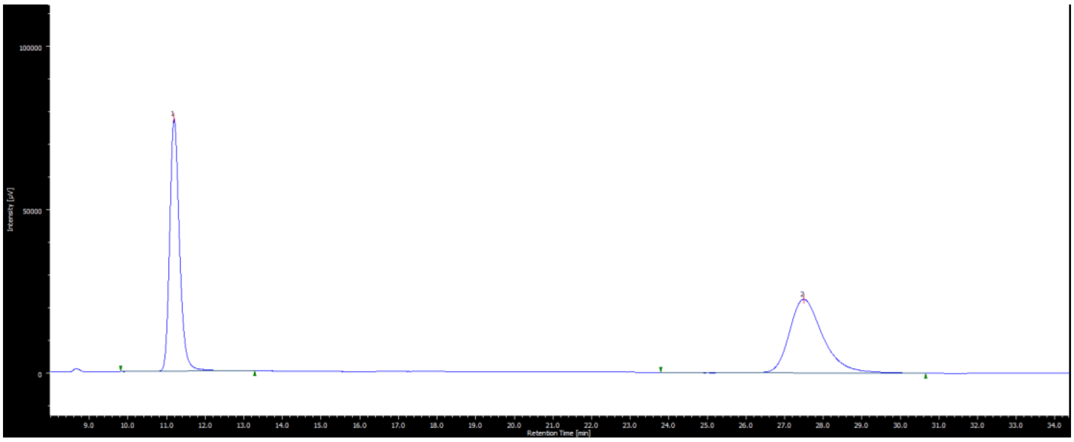
racemic-**3h**		
Peak	tR (min)	Area (%)
1	10.9	49.9
2	22.1	50.1

(*R*)-**3h**		
Peak	tR (min)	Area (%)
1	10.7	91.4
2	21.8	8.6

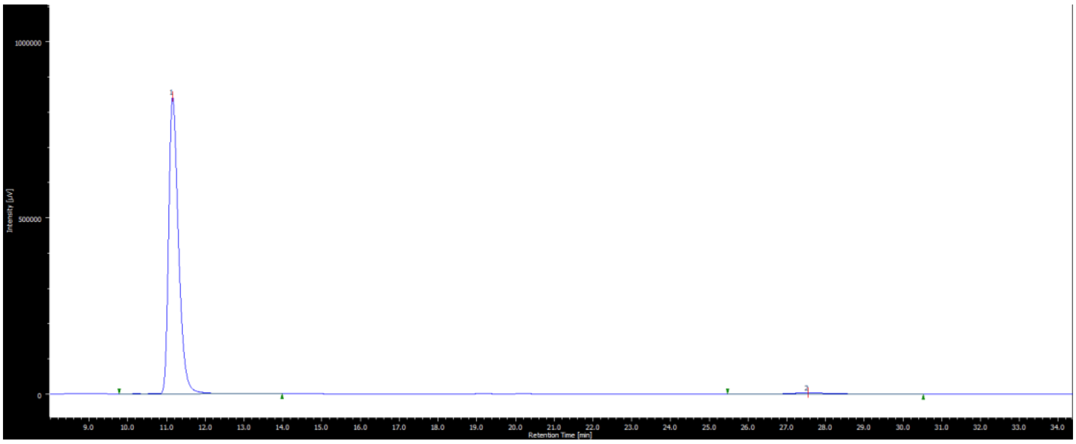
Methyl (*R*,*E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-7-trifluoromethyl-2-oxoindolin-3-yl]but-2-enoate (3i)



racemic-**3i**



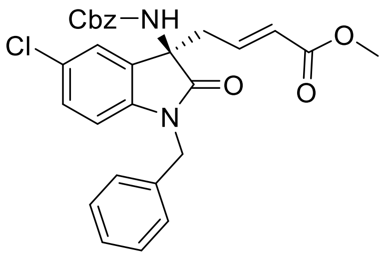
(*R*)-**3i**



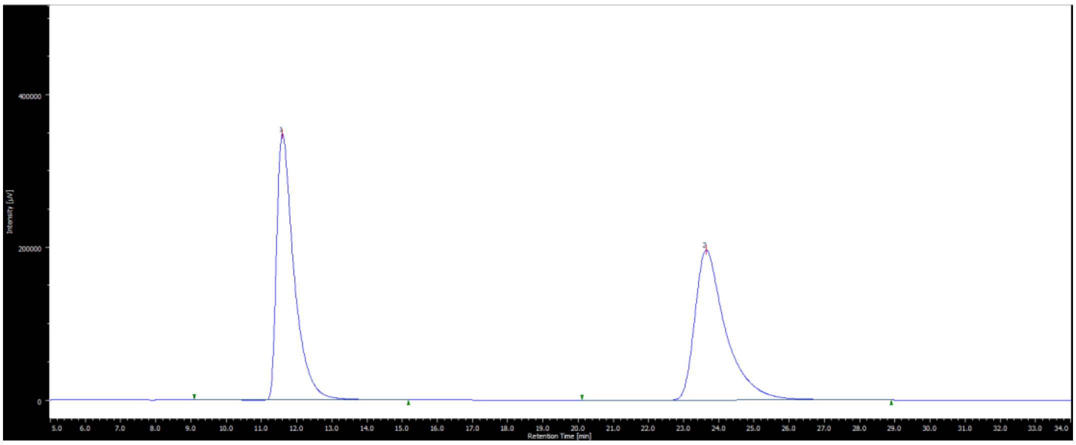
racemic-**3i**		
Peak	tR (min)	Area (%)
1	11.2	50.2
2	27.5	49.8

(*R*)-**3i**		
Peak	tR (min)	Area (%)
1	13.1	98.7
2	35.1	1.3

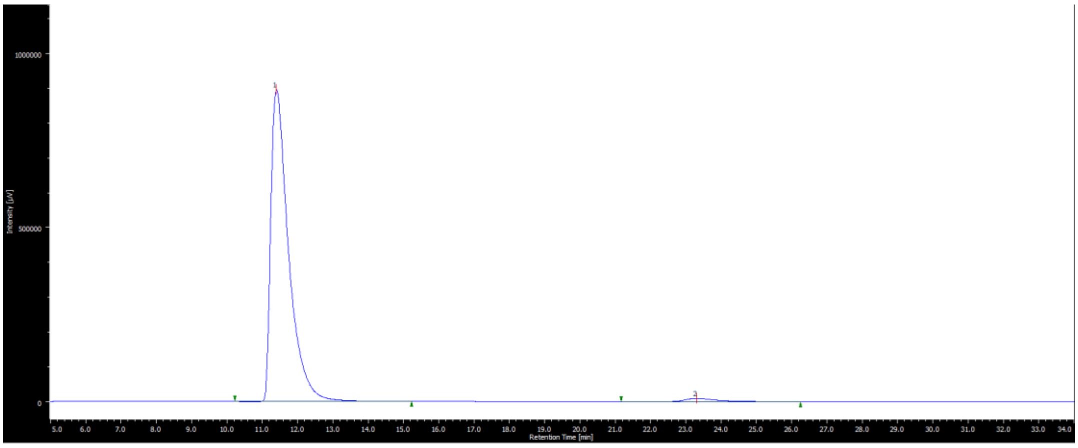
Methyl (*R*,*E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-5-chloro-2-oxoindolin-3-yl]but-2-enoate (3j)



racemic-**3j**



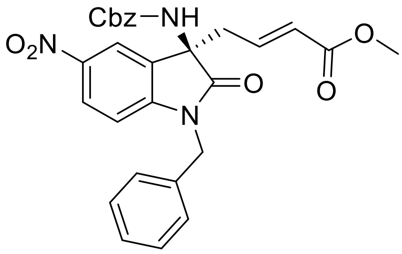
(*R*)-**3j**



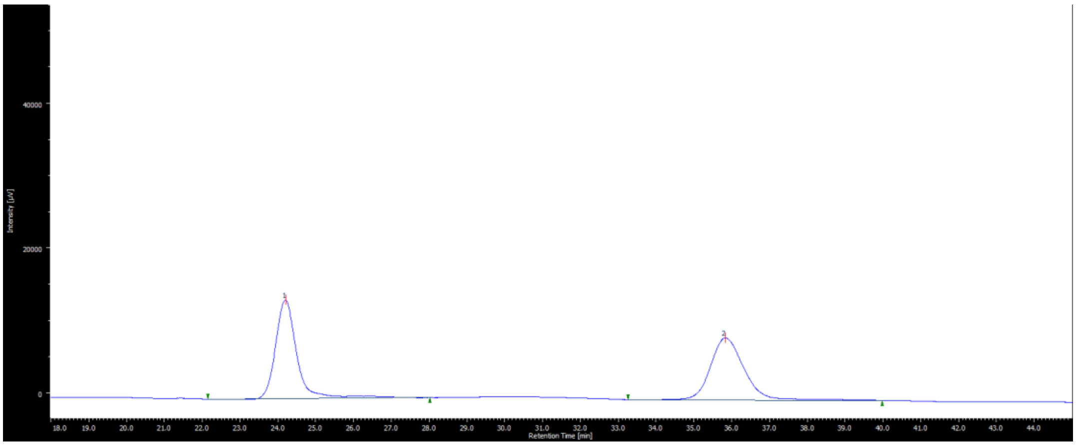
racemic-**3j**		
Peak	tR (min)	Area (%)
1	11.6	50.1
2	23.6	49.9

(*R*)-**3j**		
Peak	tR (min)	Area (%)
1	11.4	98.3
2	23.3	1.7

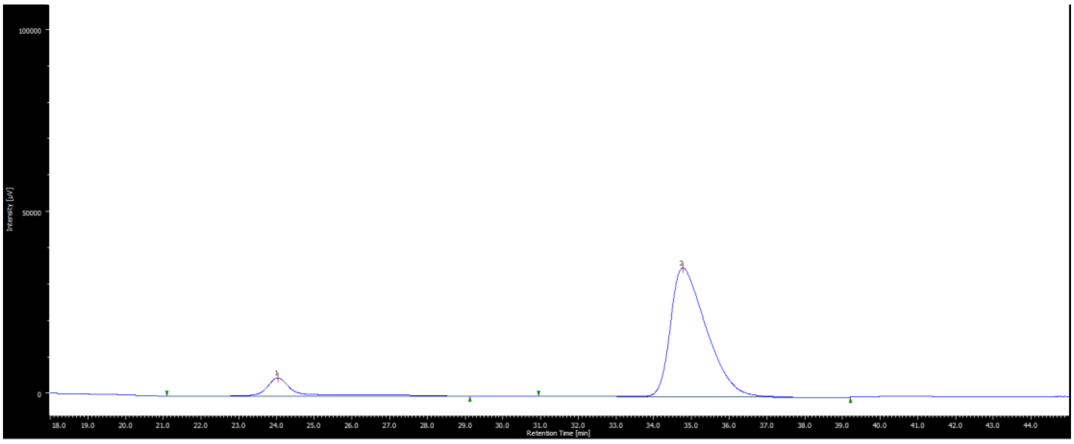
Methyl (*R*,*E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-5-nitro-2-oxoindolin-3-yl]but-2-enoate (3k)



racemic-**3k**

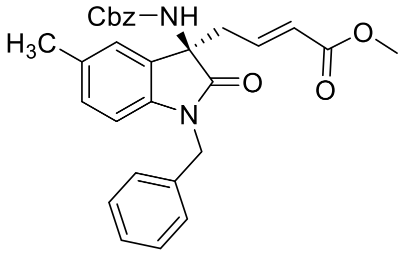


(*R*)-**3k**

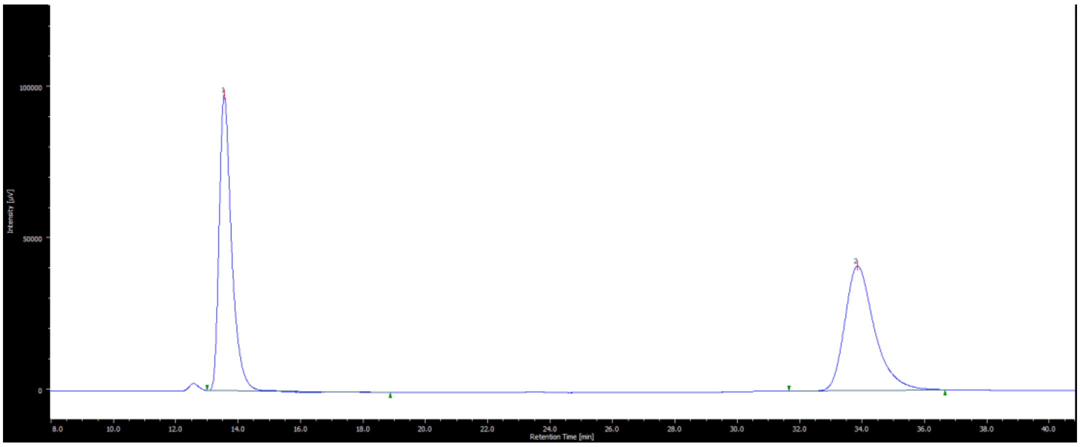


racemic-**3k**				(*R*)-**3k**		
Peak	tR (min)	Area (%)		Peak	tR (min)	Area (%)
1	24.2	50.1		1	24.0	10.4
2	35.8	49.9		2	34.8	89.6

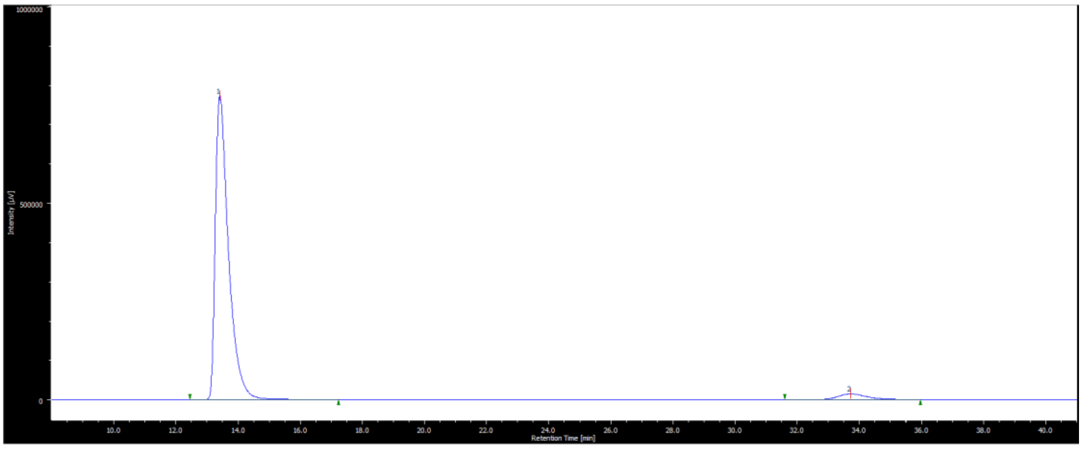
Methyl (*R*,*E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-5-methyl-2-oxoindolin-3-yl]but-2-enoate (3l)



racemic-**3l**



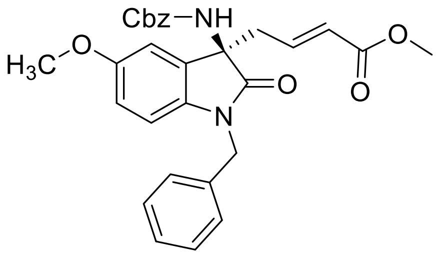
(*R*)-**3l**



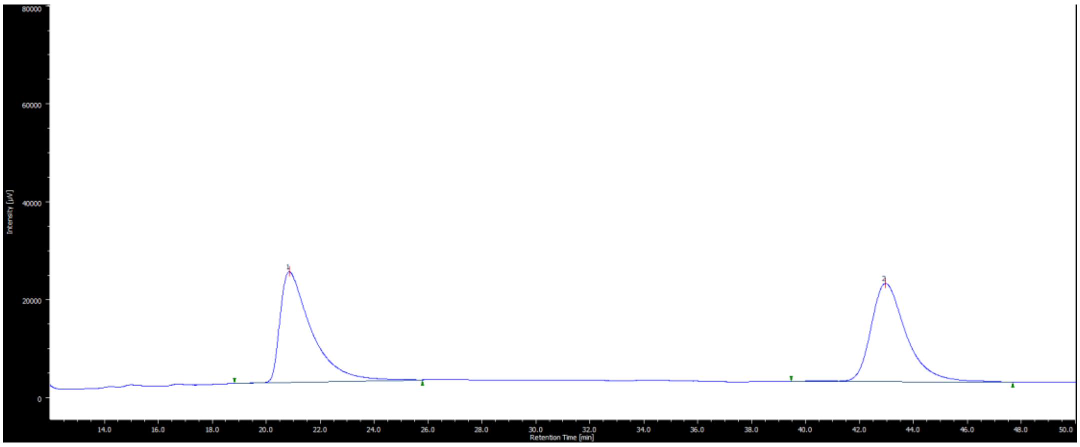
racemic-**3l**		
Peak	tR (min)	Area (%)
1	13.6	50.0
2	33.8	50.0

(*R*)-**3l**		
Peak	tR (min)	Area (%)
1	13.4	96.0
2	33.7	4.0

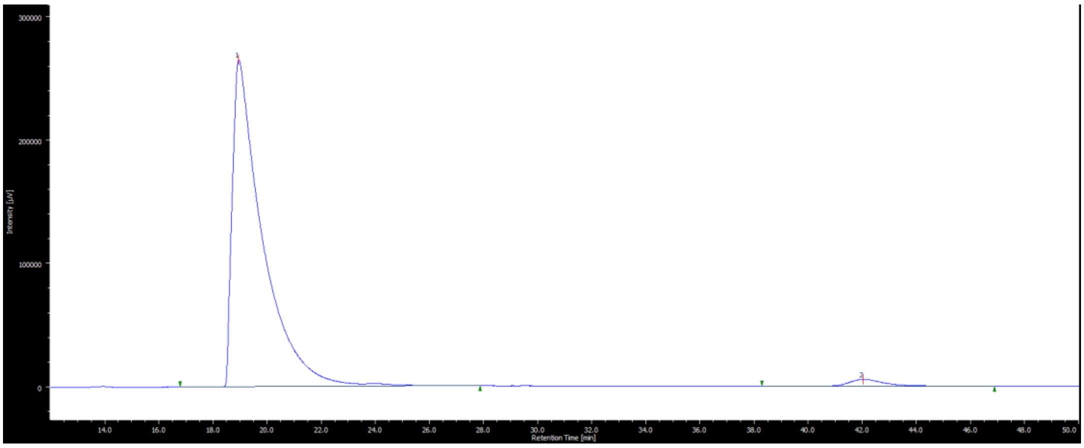
Methyl (*R,E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-5-methoxy-2-oxoindolin-3-yl]but-2-enoate (3m)



racemic-**3m**



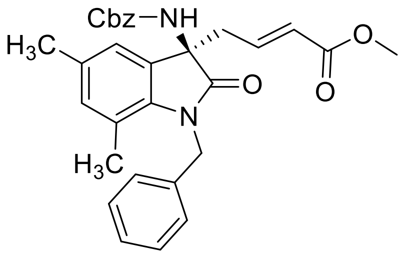
(*R*)-**3m**



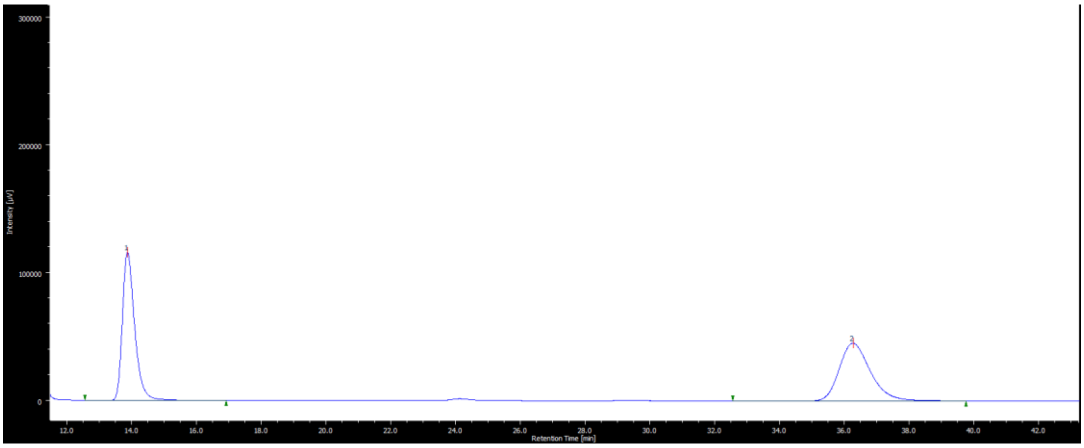
racemic-**3m**		
Peak	tR (min)	Area (%)
1	20.9	50.3
2	42.9	49.7

(*R*)-**3m**		
Peak	tR (min)	Area (%)
1	19.0	97.7
2	42.0	2.3

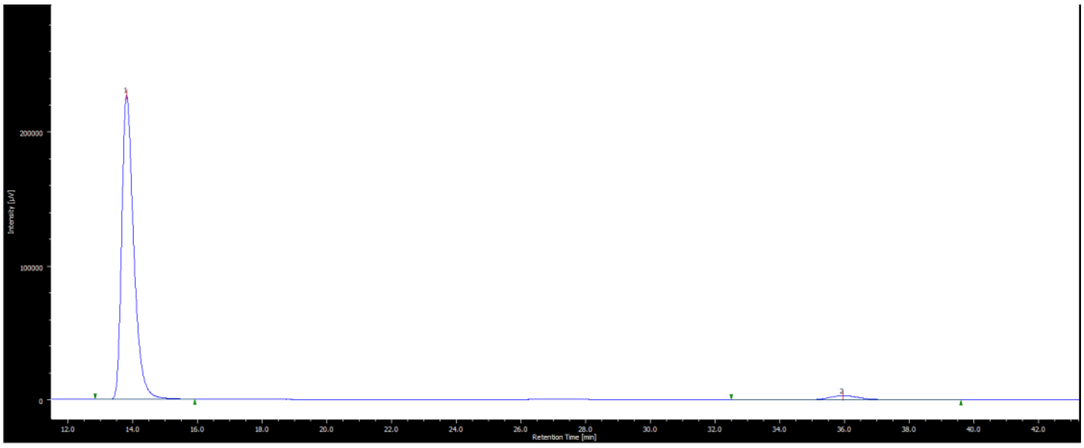
Methyl (*R*,*E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-5,7-dimethyl-2-oxoindolin-3-yl]but-2-enoate (3n)



racemic-**3n**



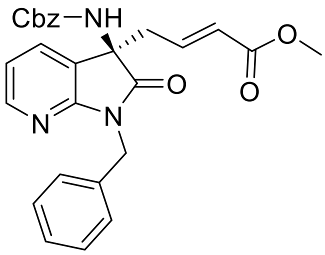
(*R*)-**3n**



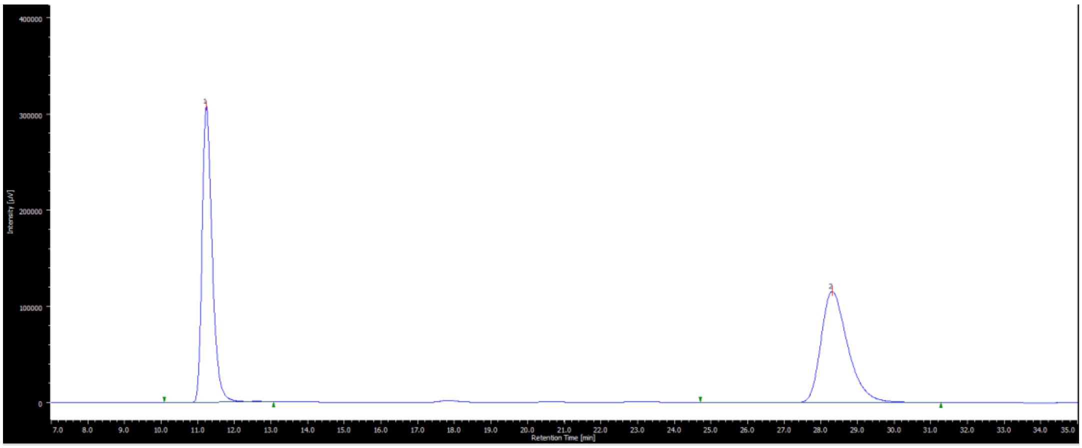
racemic-**3n**		
Peak	tR (min)	Area (%)
1	13.8	50.2
2	36.3	49.8

(*R*)-**3n**		
Peak	tR (min)	Area (%)
1	13.8	96.8
2	35.9	3.2

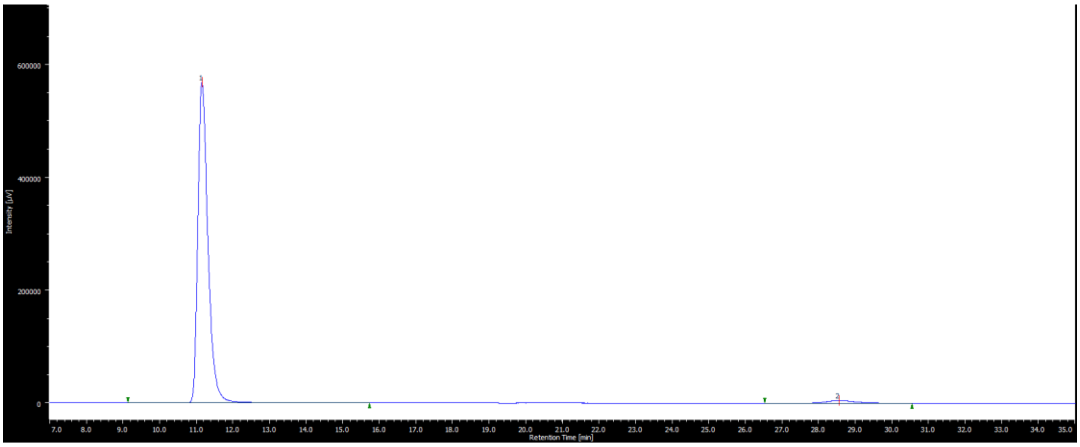
Methyl (*R,E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-2-oxo-2,3-dihydro-1H-pyrrolo[2,3-b]pyridin-3-yl]but-2-enoate (3o)



racemic-**3o**



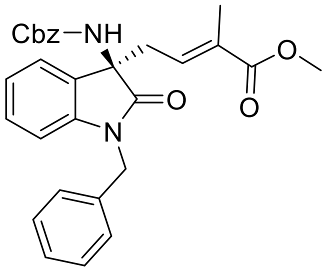
(*R*)-**3o**



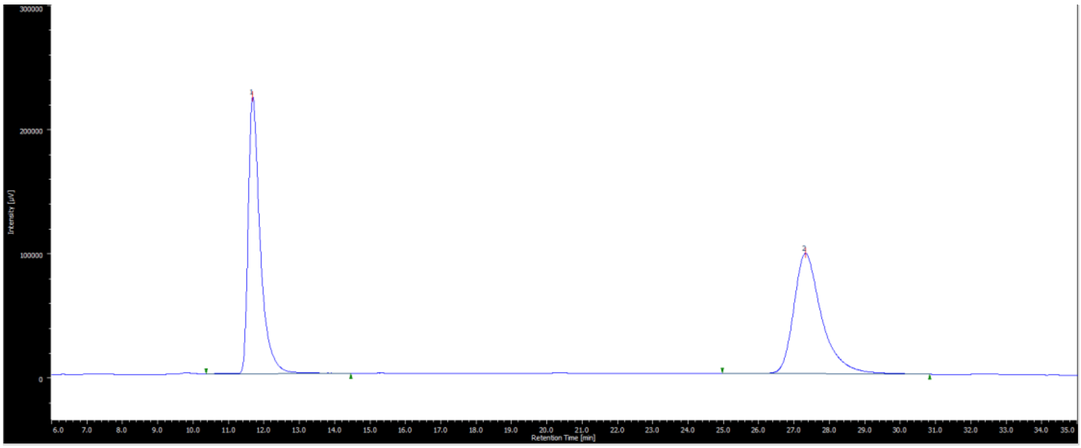
racemic-**3o**		
Peak	tR (min)	Area (%)
1	11.2	50.3
2	28.3	49.7

(*R*)-**3o**		
Peak	tR (min)	Area (%)
1	11.2	97.8
2	28.6	2.2

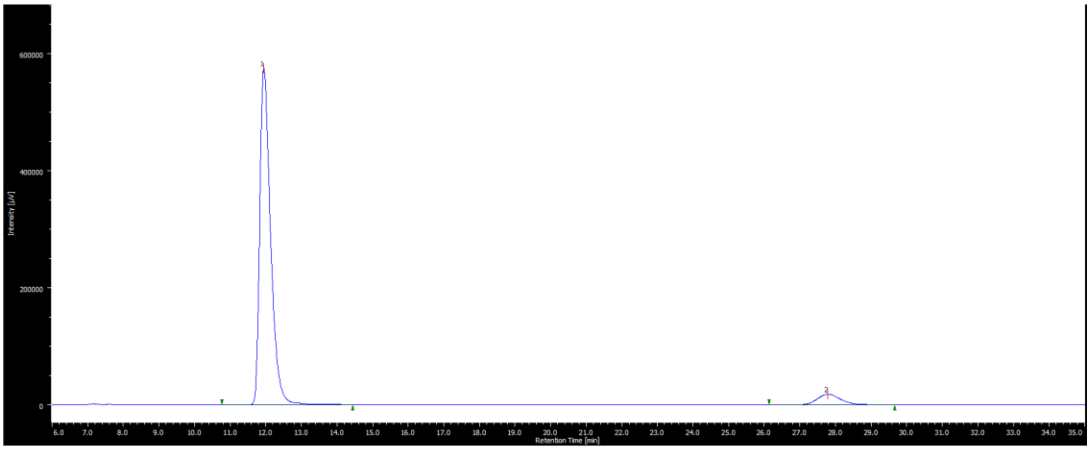
Methyl (*R,E*)-4-[1-benzyl-3-(benzyloxycarbonylamino)-2-oxoindolin-3-yl]-2-methylbut-2-enoate (3p)



racemic-**3p**

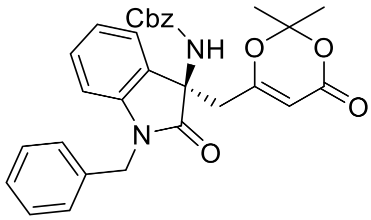


(*R*)-**3p**

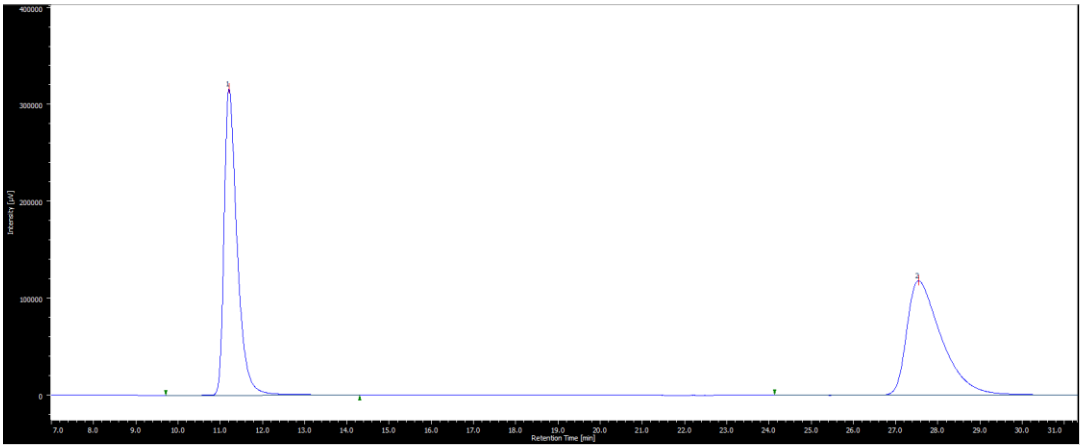


racemic-**3p**			(*R*)-**3p**		
Peak	tR (min)	Area (%)	Peak	tR (min)	Area (%)
1	11.7	49.6	1	11.9	93.6
2	27.3	50.4	2	27.8	6.4

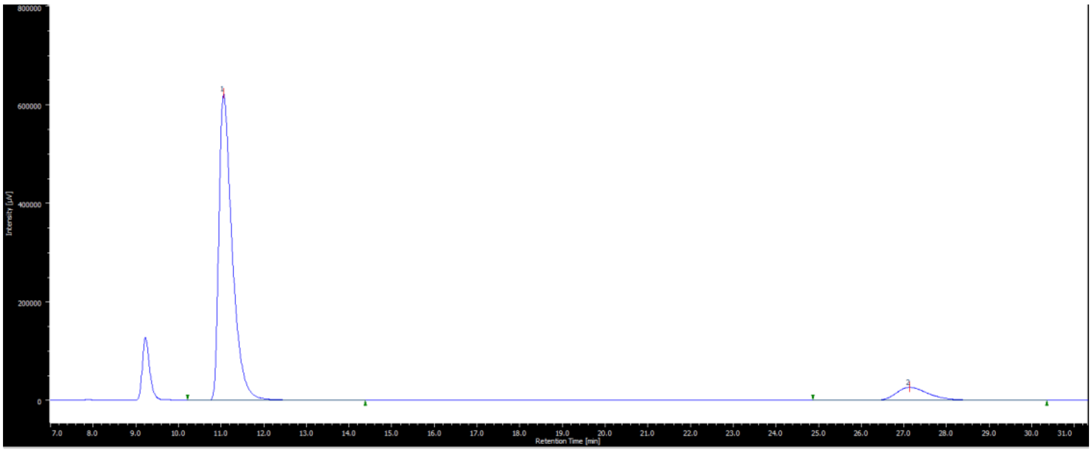
Benzyl (*R*)-[1-benzyl-3-(2,2-dimethyl-4-oxo-4H-1,3-dioxin-6-yl)methyl)-2-oxoindolin-3-yl]carbamate (3q)



racemic-**3q**



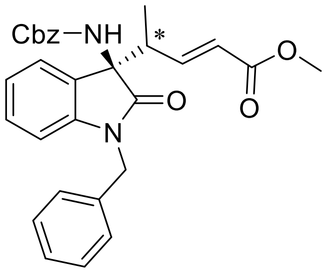
(*R*)-**3q**



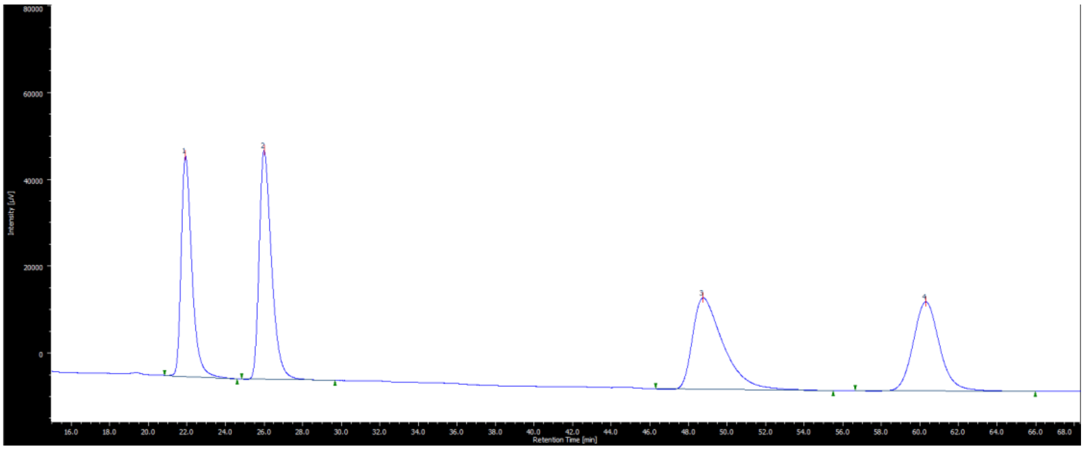
racemic-**3q**		
Peak	tR (min)	Area (%)
1	11.2	50.1
2	27.5	49.9

(*R*)-**3q**		
Peak	tR (min)	Area (%)
1	11.1	90.4
2	27.1	9.6

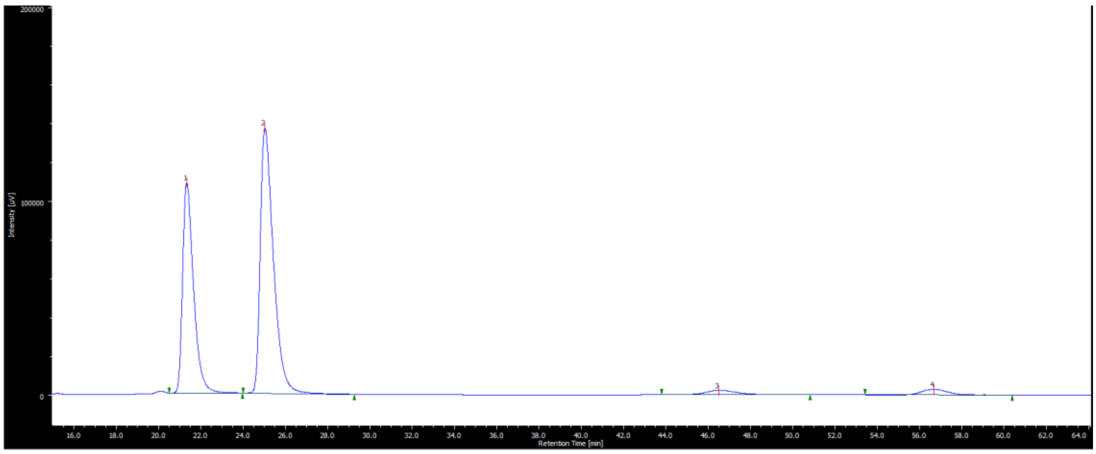
Methyl (*E*)-4-[(*R*)-1-benzyl-3-(benzyloxycarbonylamino)-2-oxoindolin-3-yl]-pent-2-enoate (3r)



racemic-**3r**



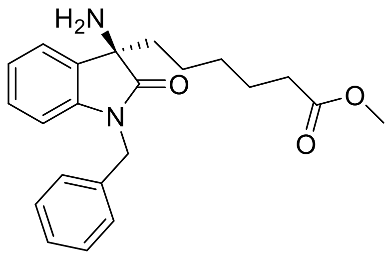
(*R*)-**3r**



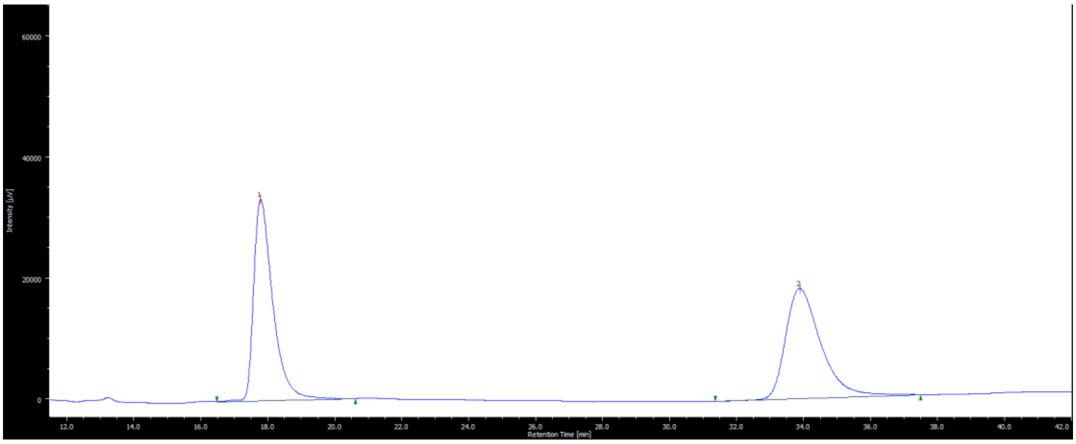
racemic-**3r**					
Peak	tR (min)	Area (%)	Peak	tR (min)	Area (%)
1	21.9	22.7	2	26.0	27.5
3	48.7	27.2	4	60.3	22.5

chiral-**3r**					
Peak	tR (min)	Area (%)	Peak	tR (min)	Area (%)
1	21.3	38.1	2	25.0	57.3
3	46.5	2.1	4	56.7	2.5

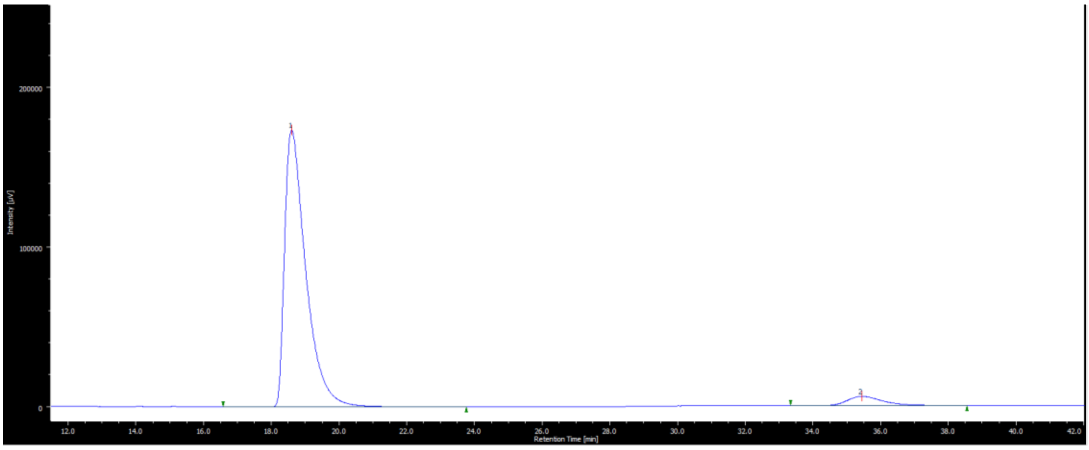
Methyl (*R*)-6-(3-amino-1-benzyl-2-oxoindolin-3-yl)hexanoate (5)



racemic-**5**

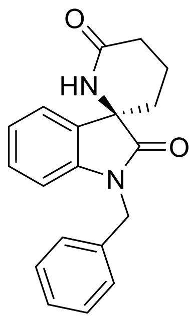


(*R*)-**5**

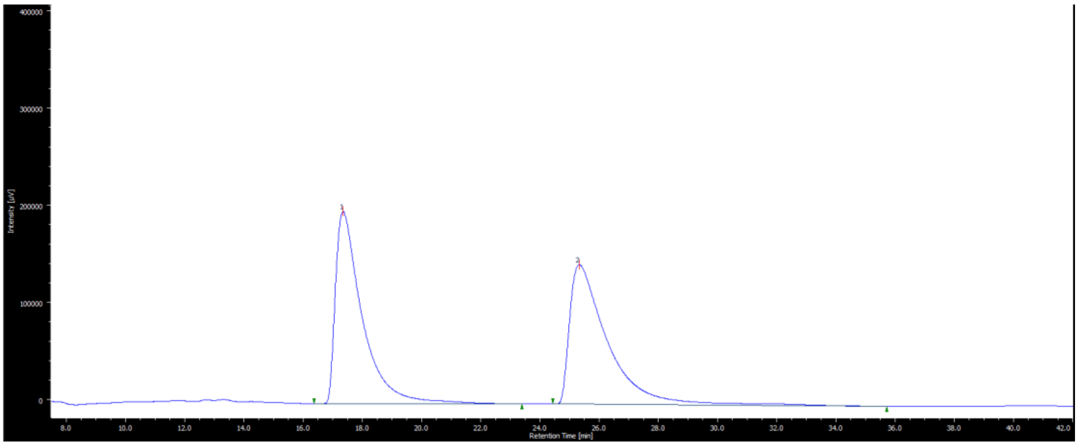


racemic-**5**			(*R*)-**5**		
Peak	tR (min)	Area (%)	Peak	tR (min)	Area (%)
1	17.8	49.8	1	18.6	94.5
2	33.9	50.2	2	35.4	5.5

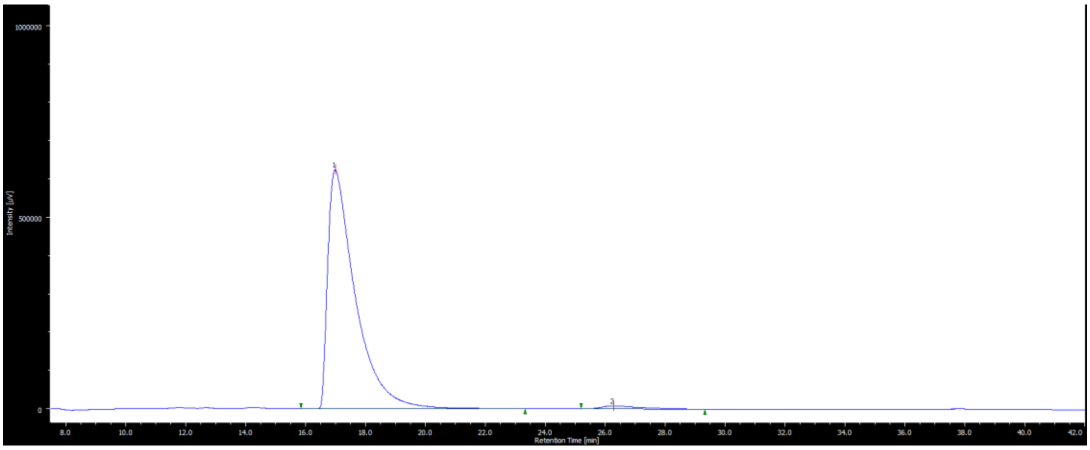
(*R*)-1-Benzylspiro[indoline-3,2'-piperidine]-2,6'-dione (7)



racemic-**7**



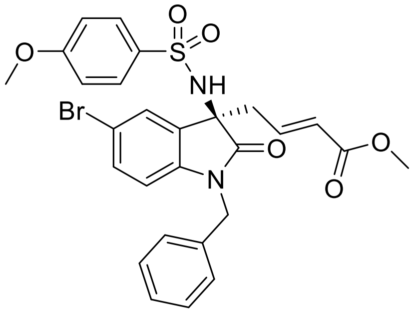
(*R*)-**7**



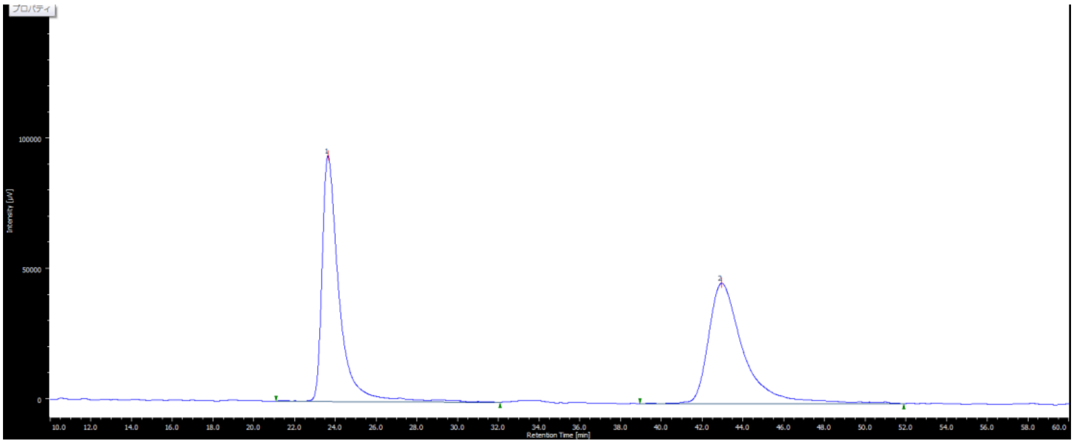
racemic-**7**		
Peak	tR (min)	Area (%)
1	17.3	49.2
2	25.3	50.8

(*R*)-**7**		
Peak	tR (min)	Area (%)
1	17.0	98.4
2	25.3	1.6

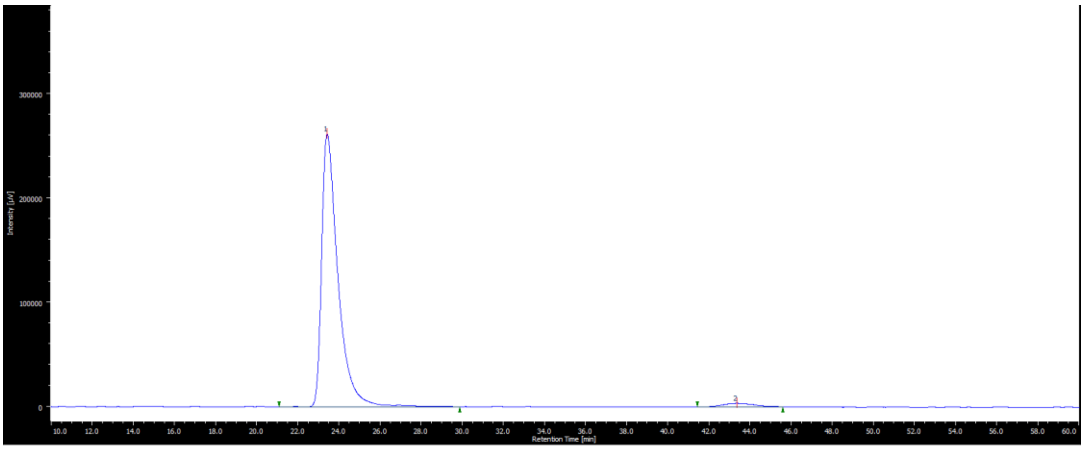
Methyl (*R,E*)-4-[1-benzyl-5-bromo-3-(4-methoxybenzenesulfonamide)-2-oxoindolin-3-yl]but-2-enoate (9)



racemic-**9**



(*R*)-**9**



racemic-**9**		
Peak	tR (min)	Area (%)
1	23.6	49.6
2	43.0	50.4

(*R*)-**9**		
Peak	tR (min)	Area (%)
1	23.4	97.5
2	43.4	2.5