Electronic Supplementary Material (ESI) for ChemComm.

Electronic Supplementary Information

Enantioselective dicarbofunctionalization of (*E*)-alkenyloxindoles with pyridinium salts by chiral Lewis acid/photo relay catalysis

Dong Zhang, Shunxi Dong, Qianwen He, Yao Luo, Yun Liu, Xiaohua Liu*, Xiaoming Feng*

Abstract: A highly efficient enantioselective dicarbofunctionalization reaction of (*E*)-alkenyloxindoles with pyridinium salts was realized. The process includes the chiral *N,N'*-dioxide-Sc(III) complex-catalyzed regio-, diastereo-, and enantioselective [3+2] cycloaddition reaction and the following photo-promoted aza-Norrish II type rearrangement. A series of 2-pyridyl substituted oxindole derivatives were obtained in good yields with moderate to good diastereo- and enantioselectivities.

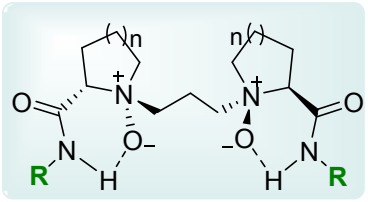
Table of Contents

(A) General information.

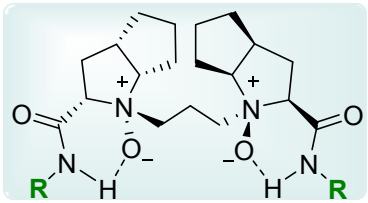
^{1}H NMR spectra were recorded on Bruker AMX-400 (400 MHz). Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard ($CDCl_3$, δ = 7.26). Spectra were reported as follows: chemical shift (δ ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, dt = doublet of triplets, td = triplet of doublets, ddd = doublet of doublet of doublets), coupling constants (Hz), integration and assignment. $^{13}C\{^{1}H\}$ NMR spectra were collected on Bruker AMX-400 (100 MHz) with complete proton decoupling. Chemical shifts were reported in ppm from the tetramethylsilane with the solvent resonance as internal standard ($CDCl_3$, δ = 77.0). $^{19}F\{^{1}H\}$ NMR spectra were collected on Bruker AMX-400 (376 MHz) with complete proton decoupling. HRMS was recorded on a commercial apparatus (ESI Source). Diastereomeric ratios (d.r.) were determined by ^{1}H NMR of the isolated products if not otherwise stated. Enantiomeric ratios (e.r.) were determined by HPLC analysis using the corresponding commercial chiralpak column as stated in the experimental procedures at 25 °C. Optical rotations were reported as follows: $[\alpha]^{T}_{D}$ (*c* g/100 mL, in solvent). IR spectra were recorded on BRUKER TENSOR II IR spectrophotometer. Fe(TPP)Cl [Iron(III) *meso*-tetraphenylporphine chloride, 95%, CAS: 16456-81-8] was purchased from Innochem. Unless otherwise noted, substituted pyridines obtained from commercial sources were used without further purification. Solvent were obtained from commercial suppliers and used without further purification except as indicated below: HCO_2Et and EtOAc were dried over anhydrous $CaCl_2$ and distilled under nitrogen just before use. A household 23 W LED lamp from Philips was used as the visible light source and a combination of 4×20 W blue LED lamps was used as the light source in the standard catalytic system. All catalytic reactions were weighed in glovebox.

(B) Typical procedure for chiral *N,N'*-dioxides preparation.

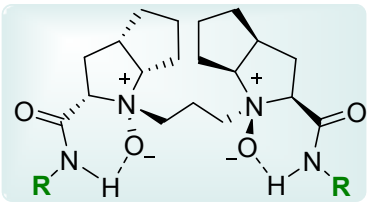
The *N,N'*-dioxide ligands were prepared by the similar procedure in the literatures.[1]



L_3-PrEt$_2$: **R** = 2,6-$Et_2C_6H_3$, n = 1
L_3-PrPr$_2$: **R** = 2,6-*i*$Pr_2C_6H_3$, n = 1
L_3-PiPr$_2$: **R** = 2,6-*i*$Pr_2C_6H_3$, n = 2
L_3-PiPr$_3$: **R** = 2,4,6-*i*$Pr_3C_6H_2$, n = 2



L_3-RaAd: **R** = 1-adamantyl
L_3-RaEt$_2$: **R** = 2,6-$Et_2C_6H_3$
L_3-RaPr$_2$: **R** = 2,6-*i*$Pr_2C_6H_3$
L_3-RaPr$_3$: **R** = 2,4,6-*i*$Pr_3C_6H_2$



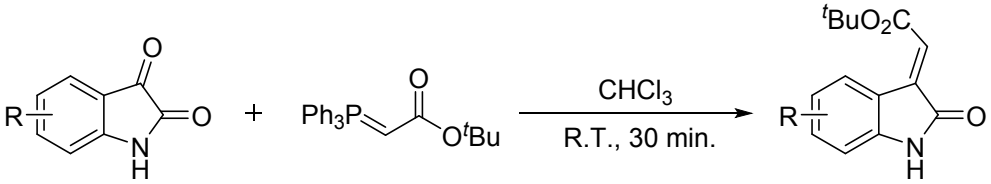
L_3-RaAd: **R** = 1-adamantyl
$[\alpha]^{19.1}_{D}$ = -30.5 (*c* 0.40, CH_2Cl_2)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.53 (s, 2H), 3.95 – 3.77 (m, 2H), 3.70 – 3.48 (m, 2H), 3.40 – 3.30 (m, 2H), 3.29 – 3.14 (m, 2H), 2.75 – 2.53 (m, 4H), 2.51 – 2.32 (m, 4H), 2.19 – 1.92 (m, 22H), 1.76 – 1.45 (m, 20H);

^{13}C NMR{1H} (100 MHz, Chloroform-*d*) δ 165.7, 83.4, 81.4, 77.2, 66.2, 51.4, 42.3, 41.7, 36.4, 34.6, 32.3, 29.4, 28.1, 26.5, 19.4.

(C) Typical procedure for substrates preparation.

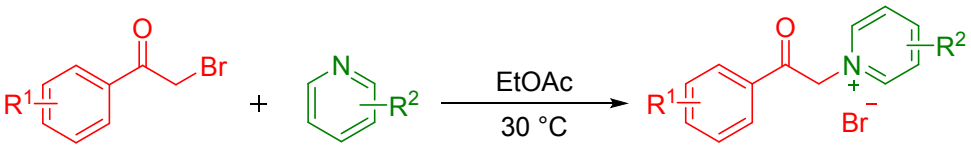
1. General procedure for the preparation of (*E*)-alkenyloxindoles **1a-1k**.[2]



1a-1k

Steps: Wittig reagent (2.0 mmol, 1.0 equiv) was added to a solution of the isatin (4.0 mmol, 2.0 equiv) in $CHCl_3$ (10.0 mL) in a 20 mL round bottom flask. The solution was stirred at room temperature for 30 minutes. Afterward, the crude mixture was subjected to column chromatography on silica gel (Eluent: petroleum ether/ethyl acetate 5:1 to 2:1) to afford the desired product **1a** in about 80% yield. Other (*E*)-alkenyloxindoles were prepared in a similar manner by using the above-mentioned method.

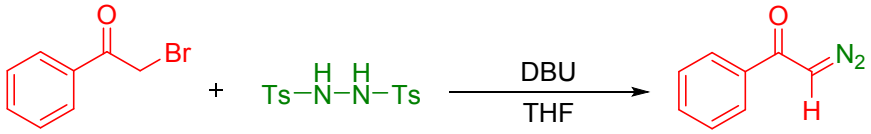
2. General procedure for the pyridinium salts preparation.[3]



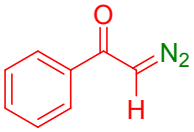
2a-2j

Steps: To a round-bottomed flask containing substituted 2-bromoacetophenone (6.0 mmol) and anhydrous ethyl acetate (10 mL) was added the corresponding substituted pyridine (5.0 mmol). The reaction solution was stirred at room temperature for 24 hours. Upon completion, the resulting precipitate was filtered off, the precipitate was washed with ethyl acetate three times (3×10 mL). The crude products were obtained in about 20-90% yields and the corresponding white solid was recrystallized by MeOH/EtOAc. Subsequently, the product was dried in vacuum for 2 hours.

3. General procedure for the α-diazoacetophenone preparation.[4]



Steps: α-Bromoacetophenone (1.99 g, 10.0 mmol) and *N,N'*-ditosylhydrazine (6.80 g, 20.0 mmol) were dissolved in THF (50 mL) and cooled to 0 °C. DBU (7.5 mL, 50.0 mmol) was added dropwise and the reaction was stirred at the same temperature for 10 minutes. Upon completion of the reaction (monitored by TLC), it was quenched by the addition of saturated $NaHCO_3$ solution, the solution was extracted with ethyl acetate three times (3×50 mL). The organic phase was washed with brine, dried over $MgSO_4$ and evaporated to give the crude α-diazoacetophenone. Finally, the crude mixture was purified by column chromatography using petroleum ether/ethyl acetate (10:1) to furnish α-diazoacetophenone in about 70% yield as a yellow solid.

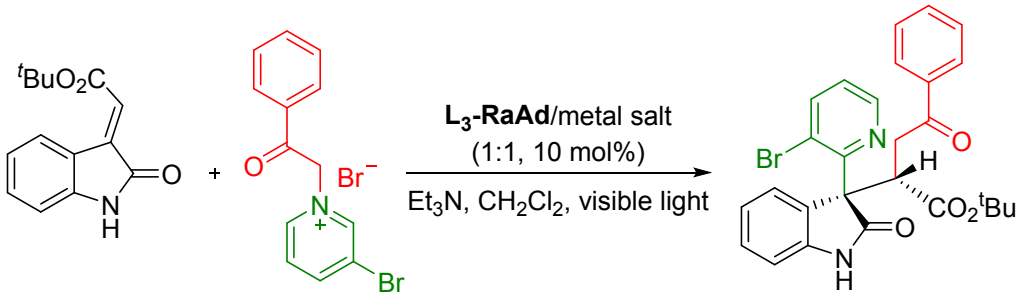


^{1}H NMR (400 MHz, Chloroform-d) δ 7.82 – 7.71 (m, 2H), 7.59 – 7.49 (m, 1H), 7.44 (dd, *J* = 8.4, 6.8 Hz, 2H), 5.92 (s, 1H);

^{13}C NMR{1H} (100 MHz, Chloroform-d) δ 186.34, 136.64, 132.72, 128.66, 126.69, 54.19.

(D) Optimization of the reaction conditions.

Table S1: Optimization of metal salts.

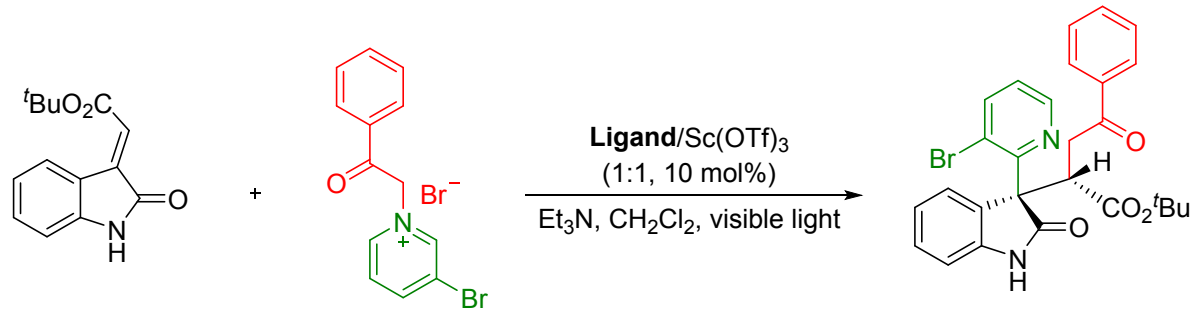


1a **2a** **4a**

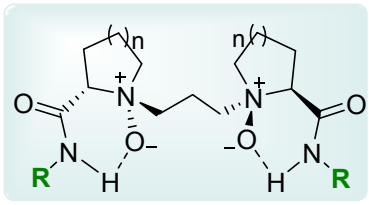
Entry[a]	Metal salt	Yield [%][b]	d.r.[c]	e.r.[c]
1	$Mg(OTf)_2$	28	>19:1	64:36
2	$Sc(OTf)_3$	34	>19:1	72:28
3	$Ni(OTf)_2$	26	>19:1	53:47
4	$Cu(OTf)_2$	21	>19:1	50:50
5	$Zn(OTf)_2$	35	>19:1	55:45
6	$Co(ClO_4)_2·6H_2O$	17	>19:1	55:45
7	$La(OTf)_3$	24	>19:1	55:45

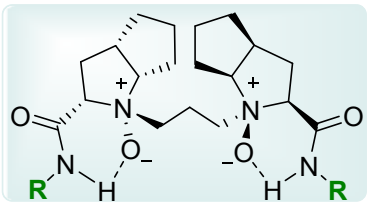
[a] Unless otherwise noted, the reactions were performed with (*E*)-alkenyloxindole **1a** (0.10 mmol), pyridinium salt **2a** (0.12 mmol), Et_3N (0.12 mmol), **L_3-RaAd**/metal salt (1:1, 10 mol%) in DCM (1.0 mL) under visible light (1×23 W LED) at room temperature for 24 h. OTf = trifluoromethanesulfonate. [b] Isolated yield. [c] Determined by HPLC analysis on a chiral stationary phase.

Table S2: Optimization of the chiral ligands.



1a **2a** **4a**





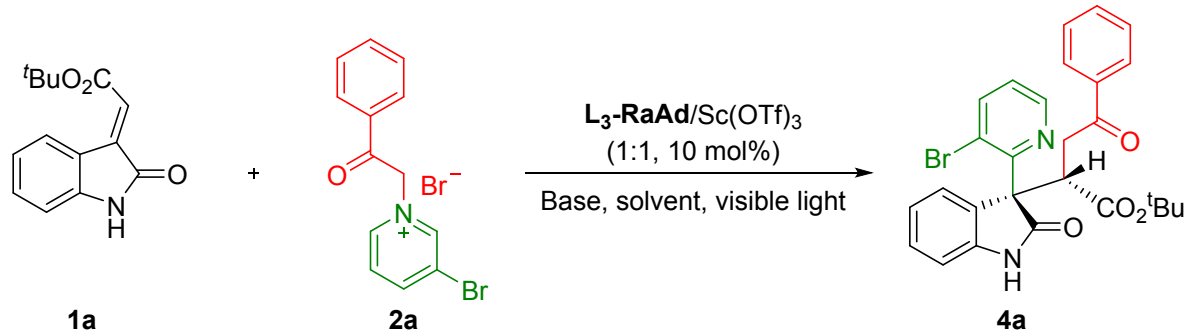
L_3-PrEt$_2$: **R** = 2,6-Et$_2$C$_6$H$_3$, n = 1
L_3-PrPr$_2$: **R** = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 1
L_3-PiPr$_2$: **R** = 2,6-*i*Pr$_2$C$_6$H$_3$, n = 2
L_3-PiPr$_3$: **R** = 2,4,6-*i*Pr$_3$C$_6$H$_2$, n = 2

L_3-RaAd: **R** = 1-adamantyl
L_3-RaEt$_2$: **R** = 2,6-Et$_2$C$_6$H$_3$
L_3-RaPr$_2$: **R** = 2,6-*i*Pr$_2$C$_6$H$_3$
L_3-RaPr$_3$: **R** = 2,4,6-*i*Pr$_3$C$_6$H$_2$

Entry[a]	Ligand	Yield [%][b]	d.r.[c]	e.r.[c]
1	**L_3-PrEt$_2$**	41	>19:1	52:48
2	**L_3-PrPr$_2$**	20	>19:1	61:39
3	**L_3-PiPr$_2$**	22	>19:1	51:49
4	**L_3-PiPr$_3$**	37	>19:1	56:44
5	**L_3-RaAd**	34	>19:1	72:28
6	**L_3-RaEt$_2$**	30	>19:1	58:42
7	**L_3-RaPr$_2$**	26	>19:1	66:34
8	**L_3-RaPr$_3$**	33	>19:1	56:44

[a] Unless otherwise noted, the reactions were performed with (*E*)-alkenyloxindole **1a** (0.10 mmol), pyridinium salt **2a** (0.12 mmol), Et_3N (0.12 mmol), **Ligand**/Sc(OTf)$_3$ (1:1, 10 mol%) in DCM (1.0 mL) under visible light (1×23 W LED) at room temperature (about 25 °C) for 24 h. [b] Isolated yield. [c] Determined by HPLC analysis on a chiral stationary phase.

Table S3: Optimization of solvents and bases.



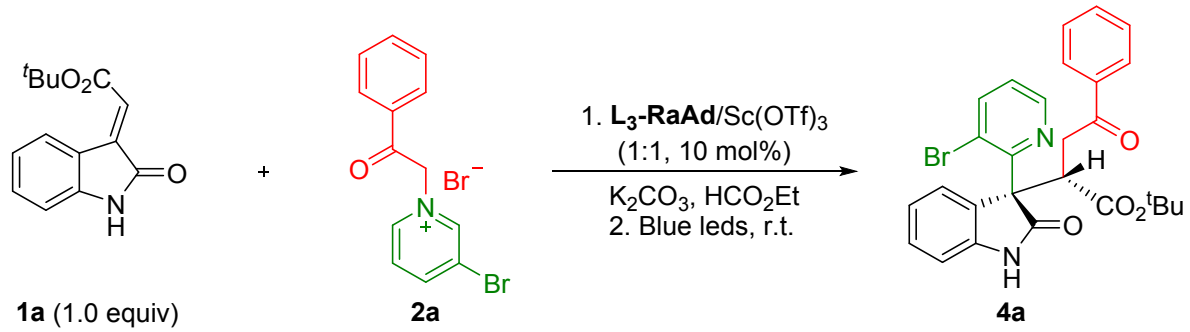
1a **2a** **4a**

Entry[a]	Base	Solvent	Yield [%][b]	d.r.[c]	e.r.[c]
1	Et_3N	EtOAc	44	>19:1	69:31
2	Et_3N	THF	32	>19:1	64:36
3	Et_3N	toluene	52	>19:1	66:34
4	Et_3N	HCO_2Et	52	>19:1	73:27
5	DBU	EtOAc	34	>19:1	53:47
6	DIPEA	EtOAc	35	>19:1	81:19
7	K_2CO_3	EtOAc	28	>19:1	87:13
8	DBACO	EtOAc	19	>19:1	87:13
9	TMEDA	EtOAc	38	>19:1	77:23
10	Na_2CO_3	EtOAc	30	>19:1	85:15
11	$KHCO_3$	EtOAc	44	>19:1	77:23

12	K_3PO_4	EtOAc	65	>19:1	67:33
13	K_2CO_3	MeOAc	31	>19:1	88:12
14	K_2CO_3	HCO_2Et	38	>19:1	91:9

[a] Unless otherwise noted, the reactions were performed with (*E*)-alkenyloxindole **1a** (0.10 mmol), pyridinium salt **2a** (0.12 mmol), base (0.12 mmol), **L_3-RaAd**/Sc(OTf)$_3$ (1:1, 10 mol%) in DCM (1.0 mL) under visible light (1×23 W LED) at room temperature (about 25 °C) for 24 h. [b] Isolated yield. [c] Determined by HPLC analysis on a chiral stationary phase.

Table S4: Optimization of the substrate ratio and temperature.



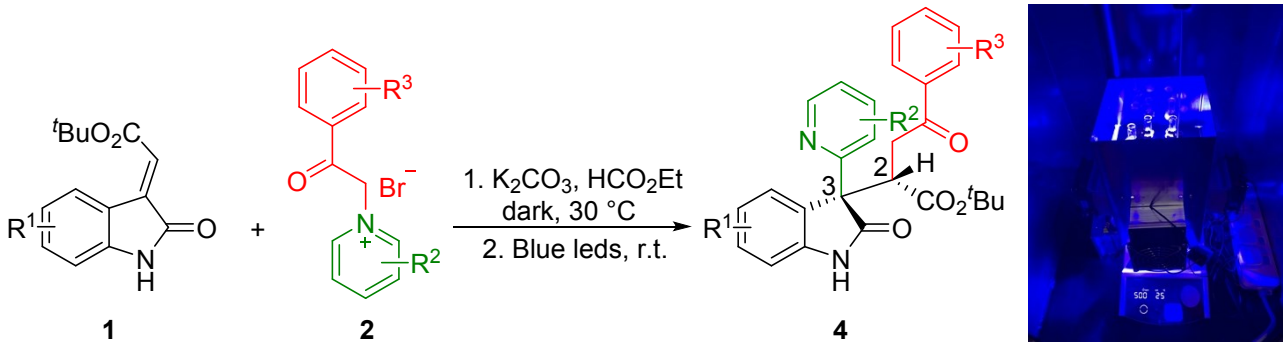
1a (1.0 equiv) **2a** **4a**

Entry[a]	**2a** (equiv)	K_2CO_3 (equiv)	T (°C)	Yield [%][b]	d.r.[c]	e.r.[c]
1	1.2	1.2	10	93	>19:1	92:8
2	1.2	1.2	0	96	>19:1	93:7
3	1.2	1.2	-10	92	>19:1	95:5
4	1.2	1.2	-20	95	>19:1	95:5
5	1.2	1.2	-30	90	>19:1	97:3
6	1.2	1.2	-40	93	>19:1	94:6
7	1.0	1.0	-30	93	>19:1	96:4
8	1.5	1.5	-30	94	>19:1	91:9
9	2.0	2.0	-30	92	>19:1	89:11

[a] Unless otherwise noted, the reactions were performed with (*E*)-alkenyloxindole **1a** (0.10 mmol), pyridinium salt **2a**, K_2CO_3, **L_3-RaAd**/Sc(OTf)$_3$ (1:1, 10 mol%) in HCO_2Et (1.0 mL) at indicated temperature for 24 h. Subsequently, the reaction mixture continues stirring at room temperature (ca. 30 °C) under blue LED lamps (4×20 W) for 10 h. [b] Isolated yield. [c] Determined by HPLC analysis on a chiral stationary phase.

(E) General procedure of the catalytic reactions.

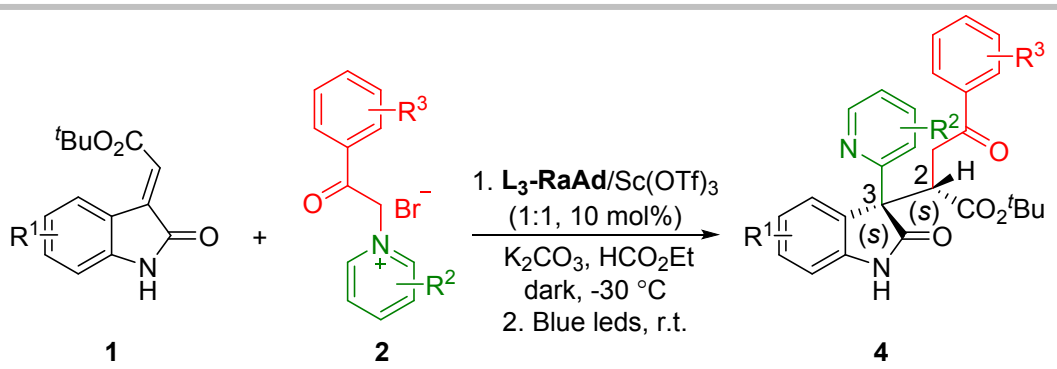
1. General procedure for the preparation of the racemic products.



1 **2** **4**

Steps: A dry reaction tube was charged with (*E*)-alkenyloxindole **1** (0.10 mmol), pyridinium salt **2** (0.20 mmol), K_2CO_3 (0.20 mmol) under N_2 atmosphere. Then, anhydrous HCO_2Et (1.0 mL) was added. The mixture was stirred at 30 °C for 12 h. Next, the reaction was stirred under blue LED lamps (4×20 W) at room temperature for 10 h. Finally, the crude mixture was subjected to column chromatography on silica gel (1/2, ethyl acetate/petroleum ether) to afford the desired racemic products.

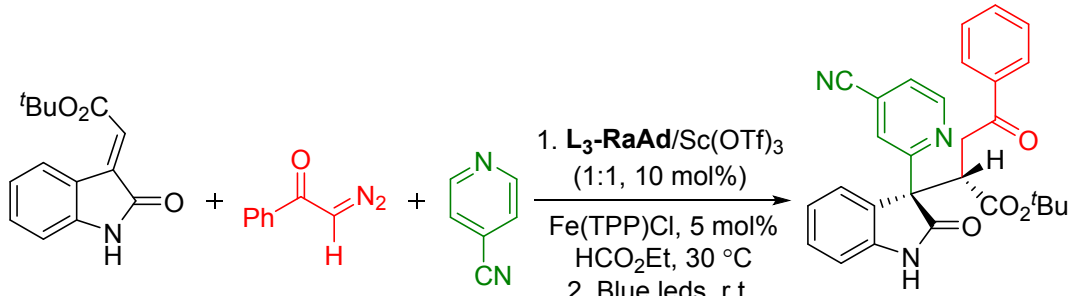
2. General procedure for the catalytic asymmetric synthesis of **4a-4t**.



1 **2** **4**

Steps: A dry reaction tube was charged with (*E*)-alkenyloxindole **1** (0.10 mmol), pyridinium salt **2** (0.10 mmol), K_2CO_3 (0.10 mmol), $Sc(OTf)_3$ (4.9 mg, 10 mol%) and the chiral ligand **L_3-RaAd** (6.5 mg, 10 mol%) under N_2 atmosphere. Then, HCO_2Et (1.0 mL) was added. The mixture was stirred at -30 °C for indicated hours. Next, the reaction was stirred under blue LED lamps (4×20 W) at room temperature for 10 h. Finally, the crude mixture was subjected to column chromatography on silica gel (1/2, ethyl acetate/petroleum ether) to afford the desired chiral products.

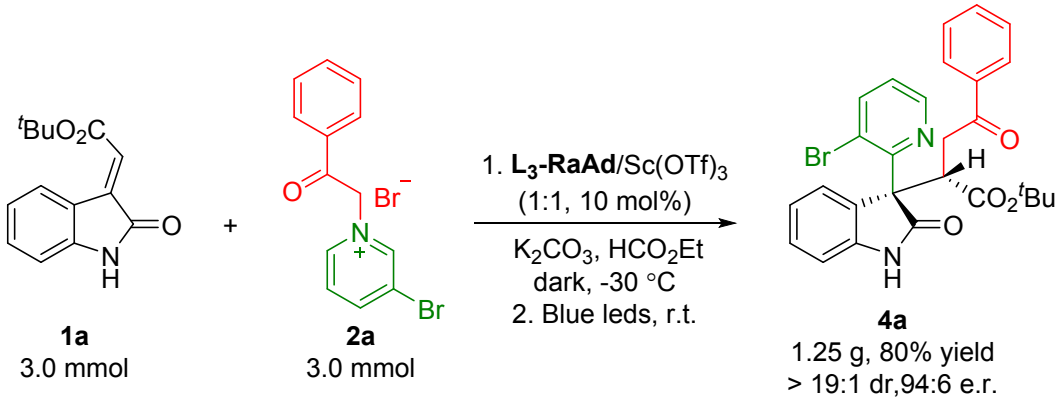
3. General procedure for the tandem reaction for the synthesis of **4n.**



1a

Steps: A dry reaction tube was charged with (*E*)-alkenyloxindole **1a** (24.5 mg, 0.10 mmol), Fe(TPP)Cl (3.5 mg, 5.0 mol%), $Sc(OTf)_3$ (4.9 mg, 10 mol%) and the chiral ligand **L_3-RaAd** (6.5 mg, 10 mol%) under N_2 atmosphere. Then, anhydrous HCO_2Et (1.0 mL) was added. The mixture was stirred at 30 °C for 0.5 h. Next, 4-cyanopyridine (31.3 mg, 0.30 mmol) and α-diazoacetophenone (22.1 mg, 0.15 mmol) were added successively. The mixture was stirred at 30 °C for 24 h and the reaction mixture was stirred under blue LED lamps (4×20 W) at room temperature for 10 h. Finally, the crude mixture was subjected to column chromatography on silica gel (1/1, ethyl acetate/petroleum ether) to afford the desired product **4n** in 43% yield, with > 19:1 dr and 82:18 e.r.

4. General procedure for the gram-scale reaction for the synthesis of **4a.**



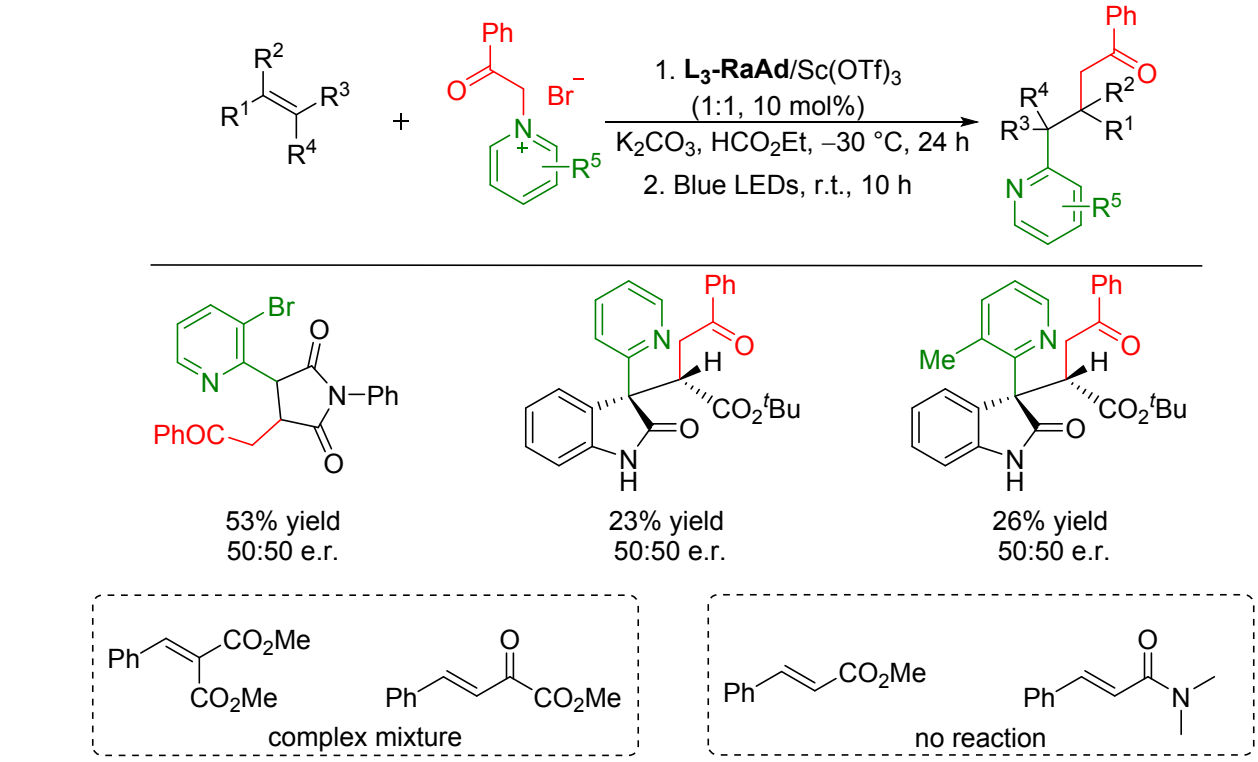
1a
3.0 mmol

2a
3.0 mmol

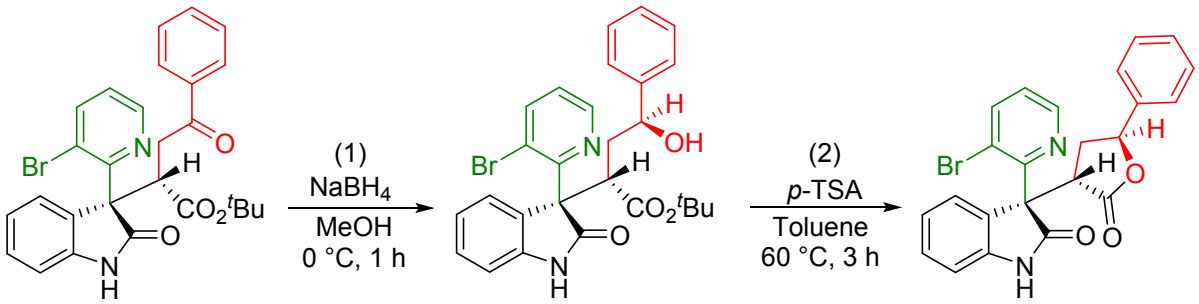
4a
1.25 g, 80% yield
> 19:1 dr,94:6 e.r.

Steps: A dry reaction tube was charged with (*E*)-alkenyloxindole **1a** (735.0 mg, 3.0 mmol), $Sc(OTf)_3$ (147 mg, 10 mol%) and the chiral ligand **L_3-RaAd** (195 mg, 10 mol%) under N_2 atmosphere. Then, anhydrous HCO_2Et (30.0 mL) was added. The mixture was stirred at 30 °C for 1.0 h. Next, pyridinium salt **2a** (1.074 g, 3.0 mmol) and K_2CO_3 (414.0 mg, 3.0 mmol) were added successively. The mixture was stirred at -30 °C for 60 h. Subsquently, the reaction was stirred under blue LED lamps (4×20 W) at room temperature for 10 h. After that, the solvent HCO_2Et was concentrated in vacuo, the crude mixture was subjected to column chromatography on silica gel (1/2, ethyl acetate/petroleum ether) to afford the desired chiral product **4a** (1.25 g, 80% yield, 94:6 e.r.).

(F) Unsuccessful substrates.



(G) Derivation of the product 4a.



(*S*, *S*)-**4a,** 99:1 e.r. (*S*, *S*, *S*)-**5a,** 97% yield, 91/9 dr 99:1 e.r. (*S*, *S*, *S*)-**6a,** 80% yield, 87/13 dr 99:1 e.r.

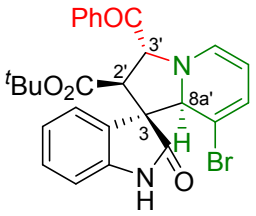
Procedure (1): To a solution of **4a** (0.05 mmol, 26.0 mg) in MeOH (1.0 mL) was added $NaBH_4$ (4.2 mg, 0.11 mmol) at 0 °C, the solution was stirred at 0 °C for 1.0 h. When the reaction completed, water (2.0 mL) was added. Then, the mixture was extract by EtOAc, and the aqueous layer was washed with EtOAc (3×2.0 mL). The combined organic phase was washed with brine (5.0 mL), and dried over anhydrous Na_2SO_4. After evaporation of the solvent, the residue was subjected to column chromatography on silica gel (1/1, ethyl acetate/petroleum ether). The product **5a** was obtained in 97% yield with 91:9 d.r. and 99:1 e.r.;

Procedure (2): To a solution of above mentioned product **5a** (0.05 mmol, 26.2 mg) in toluene (0.5 mL) was added *p*-TSA (*p*-toluenesulfonic acid) (17.2 mg, 0.10 mmol) at 30 °C, the solution was stirred at 60 °C for 3 h. When the reaction completed, the reaction mixture was directly purified by flash chromatography (1/2, ethyl acetate/petroleum ether) to afford the desired product **6a** in 80% yield with 87:13 d.r. and 99:1 e.r..

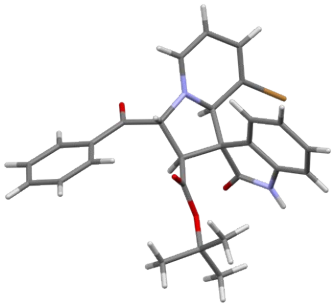
(H) X-ray diffraction analysis of the products.

(a) Tetrahydroindolizine 3a

The structure of tetrahydroindolizine intermediate **3a** was determined by X-ray chromatography analysis (thermal ellipsoids are shown with a 50% probability level). Single crystal of **3a** [$C_{27}H_{25}BrN_2O_4$] was obtained by slow evaporation in hexane/ethyl acetate at -20 °C. CCDC 2009353 contains the supplementary crystallographic data which can be obtained free of charge from The Cambrige Crystallographic Data Centere via www.ccdc.cam.ac.uk/data_request/cif.



Tetrahydroindolizine **3a**



rel-(2'*R*, 3*S*, 3'*R*, 8a'*R*)-**3a**
CCDC: 2009353

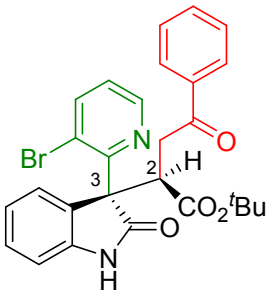
Crystallographic Data for $C_{27}H_{25}BrN_2O_4$

Formula	$C_{27}H_{25}BrN_2O_4$
Formula mass (amu)	520.39
Space group	P 21/c
a (Å)	13.2371 (4)
b (Å)	16.5924 (5)
c (Å)	11.5023 (3)
α (deg)	90
β (deg)	106.316 (1)
γ (deg)	90
V (Å^3)	2424.57 (12)
Z	4
λ (Å)	1.54178
T (K)	170 K
ρ_{calcd} (g cm^{-3})	1.428
μ (mm^{-1})	2.608
Transmission factors	0.738,0.889
$2\theta_{max}$ (deg)	72.401
No. of unique data, including $F_o^2 < 0$	4773
No. of unique data, with $F_o^2 > 2\sigma(F_o^2)$	4508
No. of variables	314
$R(F)$ for $F_o^2 > 2\sigma(F_o^2)$ [a]	0.0417
$R_w(F_o^2)$ [b]	0.1031
Goodness of fit	1.063

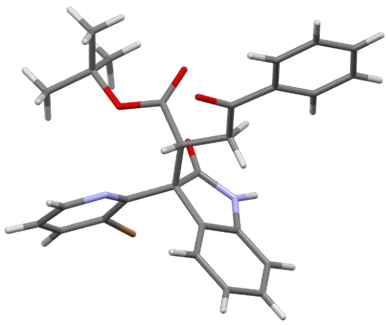
[a] $R(F) = \sum||F_o| - |F_c|| / \sum|F_o|$.
[b] $R_w(F_o^2) = [\sum[w(F_o^2 - F_c^2)^2] / \sum wF_o^4]^{1/2}$; $w^{-1} = [\sigma^2(F_o^2) + (Ap)^2 + Bp]$, where $p = [\max(F_o^2,0) + 2F_c^2] / 3$.

(b) Racemic 4a

The structure of the prodcut **4a** was determined by X-ray chromatography analysis (thermal ellipsoids are shown with a 50% probability level). Single crystal of **4a** [$C_{27}H_{25}BrN_2O_4$] was obtained by slow evaporation in hexane/DCM at 30 °C. CCDC 1992675 contains the supplementary crystallographic data which can be obtained free of charge from The Cambrige Crystallographic Data Centere via www.ccdc.cam.ac.uk/data_request/cif.



4a



rel-(2*R*, 3*R*)-**4a**
CCDC: 1992675

Crystallographic Data for $C_{27}H_{25}BrN_2O_4$

Formula	$C_{27}H_{25}BrN_2O_4$
Formula mass (amu)	520.39
Space group	P 21/n

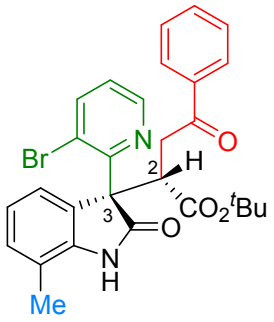
a (Å)	9.4091 (4)
b (Å)	11.5174 (4)
c (Å)	22.8668 (9)
α (deg)	90
β (deg)	91.996 (1)
γ (deg)	90
V (Å^3)	2476.53 (17)
Z	4
λ (Å)	0.71073
T (K)	169 K
ρ_{calcd} (g cm^{-3})	1.396
μ (mm^{-1})	1.695
Transmission factors	0.901,1.000
$2\theta_{max}$ (deg)	26.412
No. of unique data, including $F_o^2 < 0$	5071
No. of unique data, with $F_o^2 > 2\sigma(F_o^2)$	4302
No. of variables	310
$R(F)$ for $F_o^2 > 2\sigma(F_o^2)$ [a]	0.0331
$R_w(F_o^2)$ [b]	0.0916
Goodness of fit	1.086

[a] $R(F) = \sum||F_o| - |F_c|| / \sum|F_o|$.

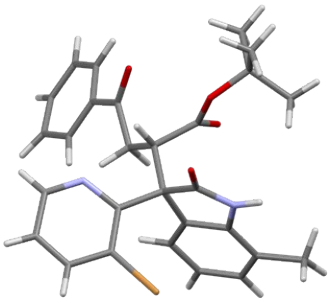
[b] $R_w(F_o^2) = [\sum[w(F_o^2 - F_c^2)^2] / \sum wF_o^4]^{1/2}$; $w^{-1} = [\sigma^2(F_o^2) + (Ap)^2 + Bp]$, where $p = [\max(F_o^2,0) + 2F_c^2] / 3$.

(c) Racemic 4e

The structure of the prodcut **4e** was determined by X-ray chromatography analysis (thermal ellipsoids are shown with a 50% probability level). Single crystal of **4e** [$C_{28}H_{27}BrN_2O_4$] was obtained by slow evaporation in hexane/DCM at 30 °C. CCDC 1984207 contains the supplementary crystallographic data which can be obtained free of charge from The Cambrige Crystallographic Data Centere via www.ccdc.cam.ac.uk/data_request/cif.



4e



rel-(2*S*, 3*S*)-**4e**
CCDC: 1984207

Crystallographic Data for $C_{28}H_{27}BrN_2O_4$

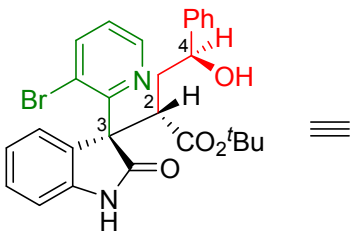
Formula	$C_{28}H_{27}BrN_2O_4$
Formula mass (amu)	535.42
Space group	P 21/c
a (Å)	10.9570 (13)
b (Å)	22.742 (2)
c (Å)	11.1670 (11)
α (deg)	90
β (deg)	110.062 (4)
γ (deg)	90
V (Å^3)	2613.7 (5)
Z	4
λ (Å)	0.71073
T (K)	170 K
ρ_{calcd} (g cm^{-3})	1.361
μ (mm^{-1})	1.608
Transmission factors	0.599, 0.746
$2\theta_{max}$ (deg)	28.412
No. of unique data, including $F_o^2 < 0$	6514
No. of unique data, with $F_o^2 > 2\sigma(F_o^2)$	3349

No. of variables	324
$R(F)$ for $F_o^2 > 2\sigma(F_o^2)$ [a]	0.0585
$R_w(F_o^2)$ [b]	0.1423
Goodness of fit	1.015

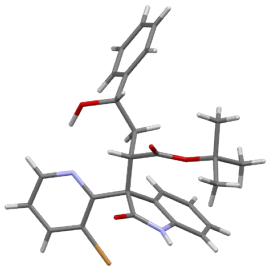
[a] $R(F) = \sum||F_o| - |F_c|| / \sum|F_o|$.
[b] $R_w(F_o^2) = [\sum[w(F_o^2 - F_c^2)^2] / \sum wF_o^4]^{1/2}$; $w^{-1} = [\sigma^2(F_o^2) + (Ap)^2 + Bp]$, where $p = [\max(F_o^2,0) + 2F_c^2] / 3$.

(d) Racemic 5a

The structure of the prodcut **5a** was determined by X-ray chromatography analysis (thermal ellipsoids are shown with a 50% probability level). Single crystal of **5a** [$C_{28}H_{27}BrN_2O_4$] was obtained by slow evaporation in hexane/ethyl acetate at 30 °C. CCDC 2010306 contains the supplementary crystallographic data which can be obtained free of charge from The Cambrige Crystallographic Data Centere via www.ccdc.cam.ac.uk/data_request/cif.



5a



rel-(2*S*, 3*S*, 4*S*)-**5a**
CCDC: 2010306

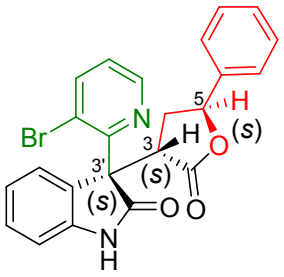
Crystallographic Data for $C_{28}H_{27}BrN_2O_4$

Formula	$C_{28}H_{27}BrN_2O_4$
Formula mass (amu)	523.41
Space group	C 2/c
a (Å)	21.8518 (7)
b (Å)	10.5122 (3)
c (Å)	22.7425 (8)
α (deg)	90
β (deg)	108.208 (2)
γ (deg)	90
V (Å^3)	4962.6 (3)
Z	8
λ (Å)	0.71073
T (K)	170 K
ρ_{calcd} (g cm^{-3})	1.401
μ (mm^{-1})	1.692
Transmission factors	0.701,0.905
$2\theta_{max}$ (deg)	27.546
No. of unique data, including $F_o^2 < 0$	5714
No. of unique data, with $F_o^2 > 2\sigma(F_o^2)$	4274
No. of variables	360
$R(F)$ for $F_o^2 > 2\sigma(F_o^2)$ [a]	0.0466
$R_w(F_o^2)$ [b]	0.1061
Goodness of fit	1.133

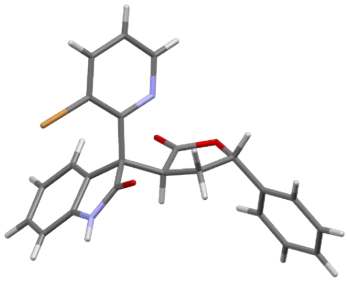
[a] $R(F) = \sum||F_o| - |F_c|| / \sum|F_o|$.
[b] $R_w(F_o^2) = [\sum[w(F_o^2 - F_c^2)^2] / \sum wF_o^4]^{1/2}$; $w^{-1} = [\sigma^2(F_o^2) + (Ap)^2 + Bp]$, where $p = [\max(F_o^2,0) + 2F_c^2] / 3$.

(e) Enantiomerically enriched **6a**

The absolute configuration of the product **6a** was determined to be (3*S*, 5*S*, 3'*S*) by X-ray chromatography analysis (thermal ellipsoids are shown with a 50% probability level). Single crystal of **6a** [$C_{23}H_{17}BrN_2O_3$] was obtained by slow evaporation in hexane/DCM at 30 °C. CCDC 1921882 contains the supplementary crystallographic data which can be obtained free of charge from The Cambrige Crystallographic Data Centere via www.ccdc.cam.ac.uk/data_request/cif.



6a



(3*S*,3'*S*,5*S*)-**6a**
CCDC: 1921882

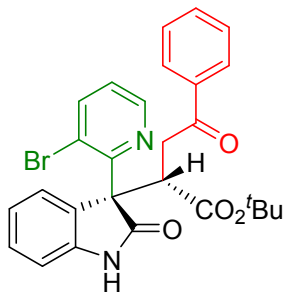
Crystallographic Data for $C_{23}H_{17}BrN_2O_3$.

Formula	$C_{23}H_{17}BrN_2O_3$
Formula mass (amu)	449.29
Space group	P 21 21 21
a (Å)	7.7448 (13)
b (Å)	15.656 (3)
c (Å)	18.122 (4)
α (deg)	90
β (deg)	90
γ (deg)	90
V (Å^3)	2197.4 (7)
Z	4
λ (Å)	0.71073
T (K)	235 K
ρ_{calcd} (g cm^{-3})	1.358
μ (mm^{-1})	1.895
Transmission factors	0.582, 0.746
$2\theta_{max}$ (deg)	28.456
No. of unique data, including $F_o^2 < 0$	5508
No. of unique data, with $F_o^2 > 2\sigma(F_o^2)$	3763
No. of variables	262
$R(F)$ for $F_o^2 > 2\sigma(F_o^2)$ [a]	0.0465
$R_w(F_o^2)$ [b]	0.1792
Goodness of fit	0.738

[a] $R(F) = \sum||F_o| - |F_c|| / \sum|F_o|$.

[b] $R_w(F_o^2) = [\sum[w(F_o^2 - F_c^2)^2] / \sum wF_o^4]^{1/2}$; $w^{-1} = [\sigma^2(F_o^2) + (Ap)^2 + Bp]$, where $p = [\max(F_o^2,0) + 2F_c^2] / 3$.

(I) Spectral characterization data for the products.



4a

***Tert*-Butyl (*S*)-2-[(*S*)-3-(3-bromopyridin-2-yl)-2-oxoindolin-3-yl]-4-oxo-4-phenylbutanoate**

0.1 mmol (**1a**) scale reaction:

Results: yellow solid, M.p. 84-87 °C, 93% yield, >19:1 d.r., 96:4 e.r.; $[\alpha]^{20}_{D}$ = 27.2 (*c* 0.26, CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 12.15 min, $t_{R(minor)}$ = 10.11 min);

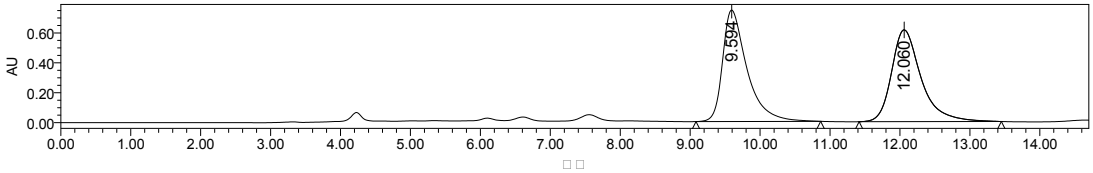
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.06 (s, 1H), 8.55 –8.53 (m, 1H), 7.90 – 7.88 (m, 2H), 7.81 – 7.78 (m, 1H), 7.53 – 7.49 (m, 1H), 7.42 – 7.38 (m, 2H), 7.24 – 7.20 (m, 2H), 7.10 – 7.07 (m, 1H), 7.00 – 6.96 (m, 1H), 6.89 – 6.87 (m, 1H), 4.90 (d, *J* = 9.6 Hz, 1H), 3.63 (dd, *J* = 17.2, 10.0 Hz, 1H), 3.21 (d, *J* = 17.6 Hz, 1H), 1.25 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 198.2, 170.4, 154.9, 146.5, 142.4, 137.0, 132.8, 129.91, 129.0, 128.4, 128.0, 125.2, 123.5, 122.2, 120.7, 110.1, 80.8, 62.0, 46.5, 37.2, 27.6, 14.2;

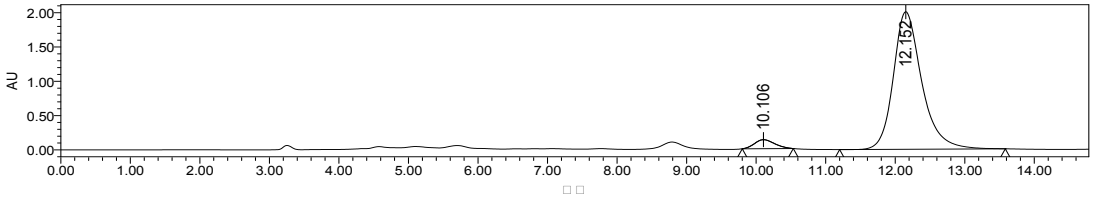
ESI-HRMS calcd for $[C_{27}H_{25}{}^{79}BrN_2O_4+Na^+]$: 543.0889, found 543.0882;

ESI-HRMS calcd for $[C_{27}H_{25}{}^{81}BrN_2O_5+Na^+]$: 545.0869, found 545.0863;

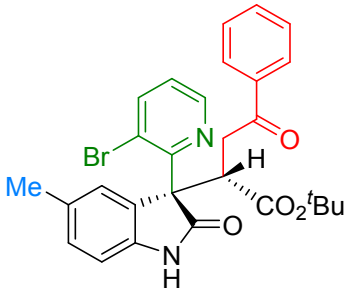
IR (neat): $\tilde{\nu}$ (cm-1) 2976, 1716, 1683, 1471, 1330, 1150, 1011, 751, 731, 689, 603.



	Retention Time	Area	% Area
1	9.594	18025647	50.02
2	12.060	18007893	49.98



	Retention Time	Area	% Area
1	10.106	2640920	4.44
2	12.152	56856730	95.56



4b

***Tert*-Butyl (*S*)-2-[(*S*)-3-(3-bromopyridin-2-yl)-5-methyl-2-oxoindolin-3-yl]-4-oxo-4-phenylbutanoate**

0.1 mmol (**1b**) scale reaction:

Results: yellow solid, M.p. 95-98 °C, 83% yield, >19:1 d.r., 95:5 e.r.; $[\alpha]^{20}_{D}$ = 5.20 (*c* 0.58, CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 10.65 min, $t_{R(minor)}$ = 8.92 min);

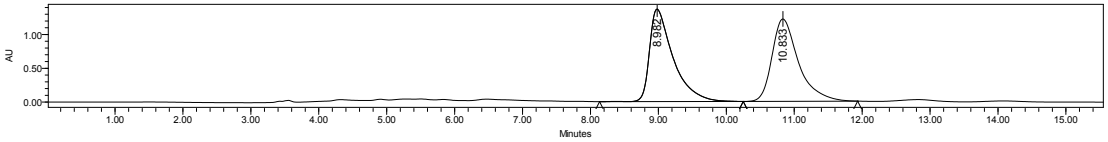
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.48 (s, 1H), 8.55 – 8.54 (m, 1H), 7.89 – 7.87 (m, 2H), 7.80 –7.78 (m, 1H), 7.52 – 7.48 (m, 1H), 7.40 – 7.36 (m, 2H), 7.09 – 7.06 (m, 1H), 7.02 – 6.98 (m, 2H), 6.77 – 6.75 (m, 1H), 4.96 (d, *J* = 9.6 Hz, 1H), 3.60 (dd, *J* = 16.8, 10.0 Hz, 1H), 3.23 – 2.94 (m, 1H), 2.24 (s, 3H), 1.26 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 198.4, 178.0, 170.5, 146.5, 142.4, 139.6, 137.0, 132.8, 131.8, 130.0, 129.4, 128.4, 128.1, 125.9, 123.4, 120.6, 109.8, 80.7, 62.1, 46.6, 37.0, 27.7, 21.3;

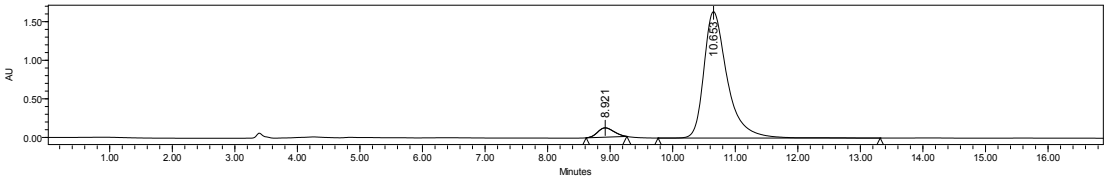
ESI-HRMS calcd for [$C_{28}H_{27}{}^{79}BrN_2O_4$+H$^+$]: 535.1227, found 535.1224;

ESI-HRMS calcd for [$C_{28}H_{27}{}^{81}BrN_2O_4$+H$^+$]: 537.1207, found 537.1208;

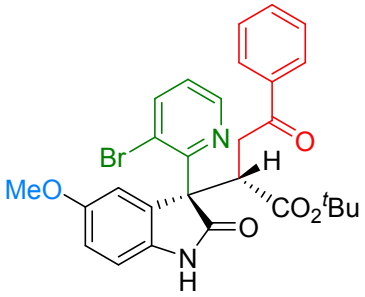
IR (neat): $\tilde{\nu}$ (cm-1) 2976, 2359, 1730, 1683, 1622, 1489, 1231, 1003, 809, 753, 687, 592.



	Retention Time	Area	% Area
1	8.982	32851475	49.90
2	10.833	32983542	50.10



	Retention Time	Area	% Area
1	8.921	2186717	4.90
2	10.653	42434875	95.10



4c

***Tert*-Butyl (*S*)-2-[(*S*)-3-(3-bromopyridin-2-yl)-5-methoxy-2-oxoindolin-3-yl]-4-oxo-4-phenylbutanoate**

0.1 mmol (**1c**) scale reaction:

Results: yellow solid, M.p. 74-77 °C, 86% yield, >19:1 d.r., 95:5 e.r.; $[\alpha]^{20}_{D}$ = 9.8 (*c* 0.37, CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 12.26 min, $t_{R(minor)}$ = 10.42 min);

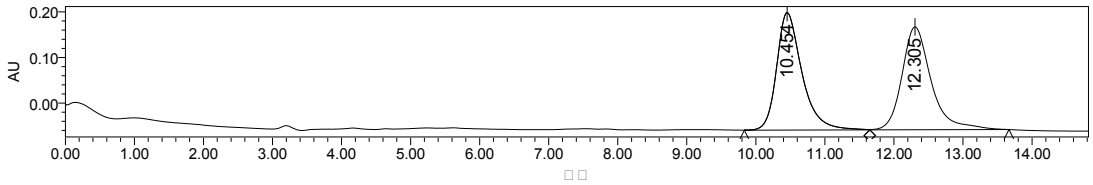
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.44 (s, 1H), 8.53 – 8.54 (m, 1H), 7.89 – 7.87 (m, 2H), 7.79 –7.77 (m, 1H), 7.54 – 7.47 (m, 1H), 7.40 – 7.39 (m, 2H), 7.10 –7.07 (m, 1H), 6.85 (s, 1H), 6.80 –6.71 (m, 2H), 4.95 (d, *J* = 10.0 Hz, 1H), 3.71 (d, *J* = 1.6 Hz, 3H), 3.62 (ddd, *J* = 17.2, 10.0, 1.6 Hz, 1H), 3.11 (d, *J* = 17.2 Hz, 1H), 1.26 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 198.25, 177.78, 170.41, 155.56, 146.52, 142.40, 137.01, 135.61, 132.81, 131.25, 128.41, 128.09, 123.53, 120.69, 113.31, 112.66, 110.37, 80.78, 62.46, 55.74, 46.5, 36.99, 27.65;

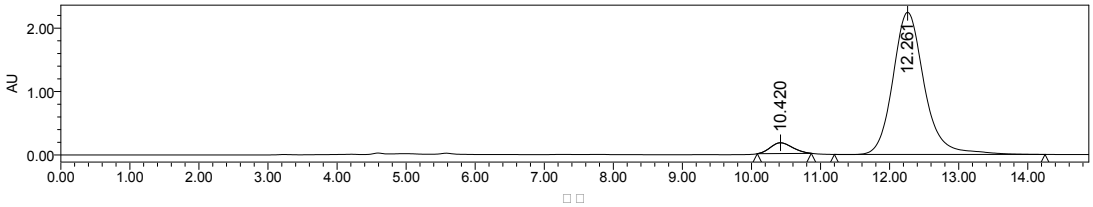
ESI-HRMS calcd for [$C_{28}H_{27}{}^{79}BrN_2O_5$+H$^+$]: 551.1176, found 551.1179;

ESI-HRMS calcd for [$C_{28}H_{27}{}^{81}BrN_2O_5$+H$^+$]: 553.1156, found 553.1162;

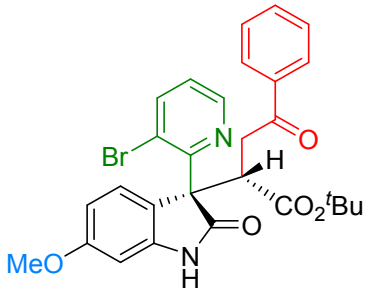
IR (neat): $\tilde{\nu}$ (cm-1) 2916, 2359, 1715, 1683, 1487, 1393, 1202, 1149, 1032, 730, 688, 618.



	Retention Time	Area	% Area
1	10.454	6554719	49.73
2	12.305	6624803	50.27



	Retention Time	Area	% Area
1	10.420	3755608	5.04
2	12.261	70720032	94.96



4d

***Tert*-Butyl (*S*)-2-[(*S*)-3-(3-bromopyridin-2-yl)-6-methoxy-2-oxoindolin-3-yl]-4-oxo-4-phenylbutanoate**

0.1 mmol (**1d**) scale reaction:

Results: yellow solid, M.p. 209-211 ºC, 83% yield, >19:1 d.r., 96:4 e.r.; $[\alpha]^{20}_{D}$ = 10.7 (*c* 0.36, CH_2Cl_2); HPLC (Daicel chiralcel ID, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 14.66 min, $t_{R(minor)}$ = 12.03 min);

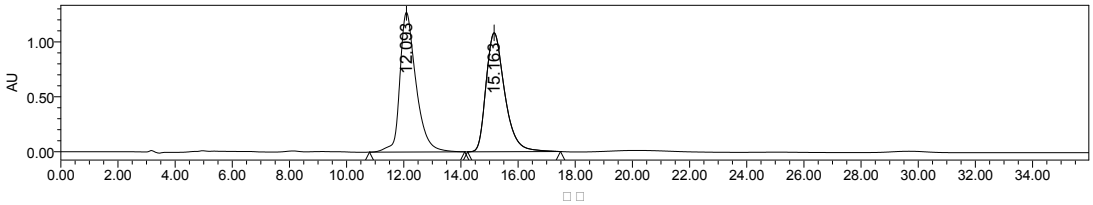
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.27 (s, 1H), 8.53 – 8.52 (m, 1H), 7.90 – 7.88 (m, 2H), 7.80 –7.78 (m, 1H), 7.53 – 7.48 (m, 1H), 7.42 – 7.38 (m, 2H), 7.13 – 7.05 (m, 2H), 6.50 – 6.46 (m, 2H), 4.91 (d, *J* = 9.6 Hz, 1H), 3.74 (s, 3H), 3.62 (dd, *J* = 17.2, 9.6 Hz, 1H), 3.18 (d, *J* = 17.2 Hz, 1H), 1.26 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-d) δ 198.3, 178.4, 170.6, 160.6, 155.3, 146.5, 143.3, 142.4, 137.1, 132.8, 128.4, 128.1, 126.1, 123.4, 121.9, 120.6, 107.2, 97.1, 80.8, 61.7, 55.4, 46.6, 37.2, 27.7;

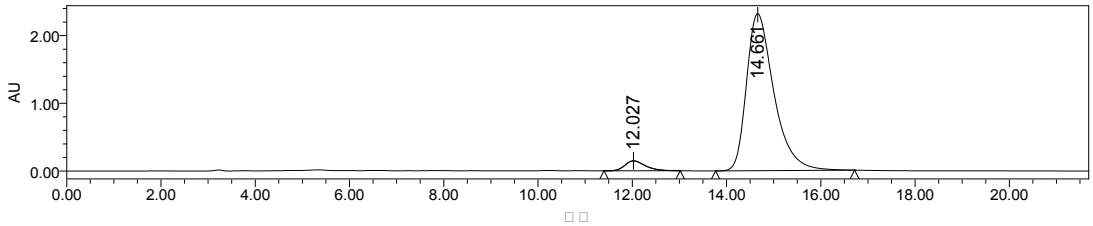
ESI-HRMS calcd for [$C_{28}H_{27}{}^{79}BrN_2O_5$+H$^+$]: 551.1176, found 551.1166;

ESI-HRMS calcd for [$C_{28}H_{27}{}^{81}BrN_2O_5$+H$^+$]: 553.1155, found 553.1145;

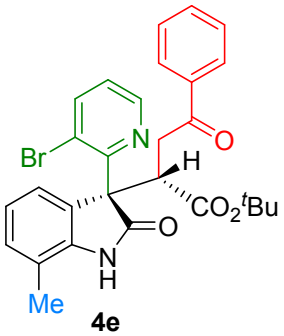
IR (neat): $\tilde{\nu}$ (cm-1) 2964, 2359, 1707, 1668, 1626, 1463, 1273, 1157, 1007, 794, 689, 542.



	Retention Time	Area	% Area
1	12.093	49808474	50.48
2	15.163	48869237	49.52



	Retention Time	Area	% Area
1	12.027	4159760	4.24
2	14.661	94053052	95.76



4e

***Tert*-Butyl (*S*)-2-[(*S*)-3-(3-bromopyridin-2-yl)-7-methyl-2-oxoindolin-3-yl]-4-oxo-4-phenylbutanoate**

0.1 mmol (**1e**) scale reaction:

Results: yellow solid, M.p. 218-223 °C, 91% yield, >19:1 d.r., 96:4 e.r.; $[\alpha]^{20}_{D}$ = 23.2 (*c* 1.09, CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 10.13 min, $t_{R(minor)}$ = 8.91 min);

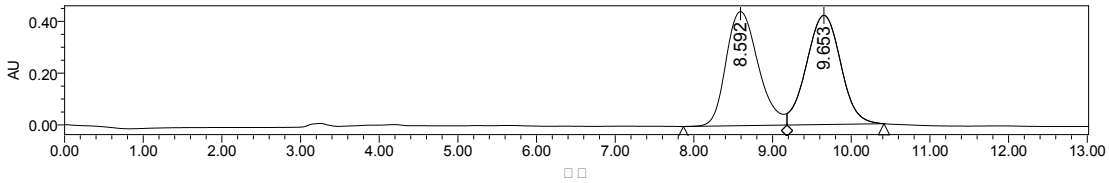
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.78 (s, 1H), 8.51 –8.50 (m, 1H), 7.88 – 7.86 (m, 2H), 7.80 – 7.78 (m, 1H), 7.51 – 7.47 (m, 1H), 7.39 – 7.35 (m, 2H), 7.12 – 7.00 (m, 3H), 6.91 – 6.87 (m, 1H), 5.01 (d, *J* = 9.6 Hz, 1H), 3.63 (dd, *J* = 17.2, 10.0 Hz, 1H), 3.06 (d, *J* = 17.2 Hz, 1H), 2.23 (s, 3H), 1.22 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 198.3, 178.4, 170.3, 146.5, 142.3, 140.8, 137.0, 132.7, 130.3, 129.6, 128.3, 128.0, 123.4, 122.5, 122.3, 120.5, 119.5, 80.7, 62.6, 37.0, 27.6, 16.7;

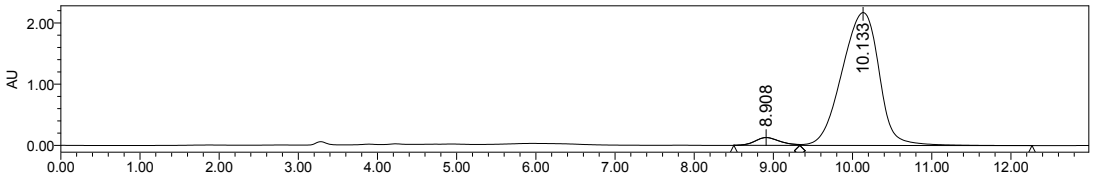
ESI-HRMS calcd for [$C_{28}H_{27}{}^{79}BrN_2O_4$+Na$^+$]: 557.1046, found 557.1042;

ESI-HRMS calcd for [$C_{28}H_{27}{}^{81}BrN_2O_4$+Na$^+$]: 559.1026 found 559.1020;

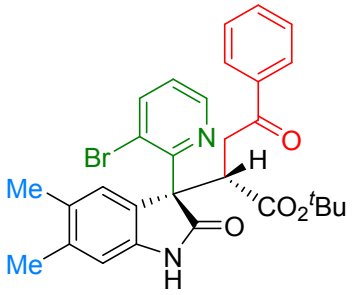
IR (neat): $\tilde{\nu}$ (cm-1) 2976, 2925, 2360, 1702, 1682, 1365, 956, 848, 759, 732, 696, 560.



	Retention Time	Area	% Area
1	8.592	12528926	49.62
2	9.653	12721158	50.38



	Retention Time	Area	% Area
1	8.908	2776832	3.78
2	10.133	70669878	96.22



4f

***Tert*-Butyl (*S*)-2-[(*S*)-3-(3-bromopyridin-2-yl)-5,6-dimethyl-2-oxoindolin-3-yl]-4-oxo-4-phenylbutanoate**

0.1 mmol (**1f**) scale reaction:

Results: yellow solid, M.p. 111-113 °C, 98% yield, >19:1 d.r., 97:3 e.r.; $[\alpha]^{25}_{D}$ = 23.78 (*c* 0.72, CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 12.11 min, $t_{R(minor)}$ = 9.91 min);

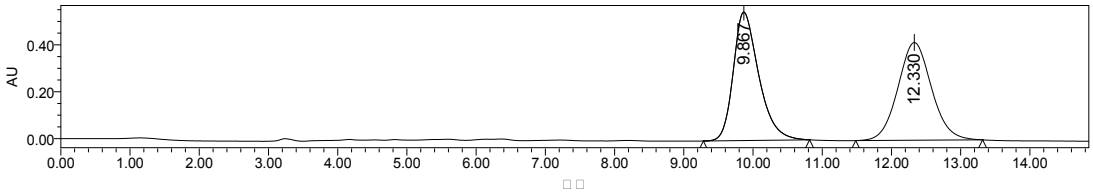
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.47 (s, 1H), 8.54 – 8.43 (m, 1H), 7.88 – 7.86 (m, 2H), 7.80 – 7.77 (m, 1H), 7.51 – 7.47 (m, 1H), 7.40 – 7.36 (m, 2H), 7.07 – 7.04 (m, 1H), 6.96 (s, 1H), 6.67 (s, 1H), 4.98 (d, *J* = 7.6 Hz, 1H), 3.59 (dd, *J* = 16.8, 10.0 Hz, 1H), 3.16 – 2.94 (m, 1H), 2.15 (s, 3H), 2.13 (s, 3H), 1.26 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 198.4, 178.1, 170.6, 155.5, 146.4, 142.3, 139.9, 137.4, 137.0, 132.7, 130.2, 128.3, 128.0, 127.2, 126.2, 123.2, 120.5, 111.4, 80.6, 62.1, 36.8, 27.6, 20.1, 19.6;

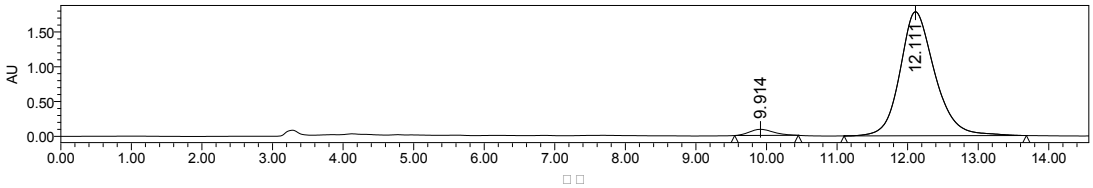
ESI-HRMS calcd for $[C_{29}H_{29}{}^{78.9183}BrN_2O_4+H^+]$: 549.1384, found 549.1378;

ESI-HRMS calcd for $[C_{29}H_{29}{}^{80.9163}BrN_2O_4+H^+]$: 551.1363, found 551.1357;

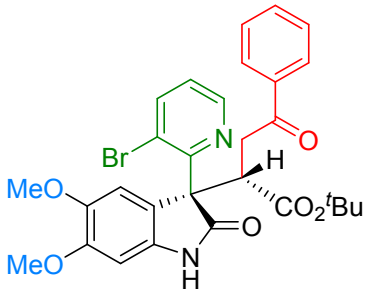
IR (neat): $\tilde{\nu}$ (cm-1) 2975, 1714, 1629, 1366, 1151, 1002, 848, 730, 689, 644, 628.



	Retention Time	Area	% Area
1	9.867	13984699	49.86
2	12.330	14065853	50.14



	Retention Time	Area	% Area
1	9.914	2078667	3.30
2	12.111	60952782	96.70



4g

***Tert*-Butyl (*S*)-2-[(*S*)-3-(3-bromopyridin-2-yl)-5,6-dimethoxy-2-oxoindolin-3-yl]-4-oxo-4-phenylbutanoate**

0.1 mmol (**1g**) scale reaction:

Results: yellow solid, M.p. 84-87 °C, 97% yield, >19:1 d.r., 97:3 e.r.; $[\alpha]^{25}_{D}$ = 12.2 (*c* 1.03, CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 11.74 min, $t_{R(minor)}$ = 10.50 min);

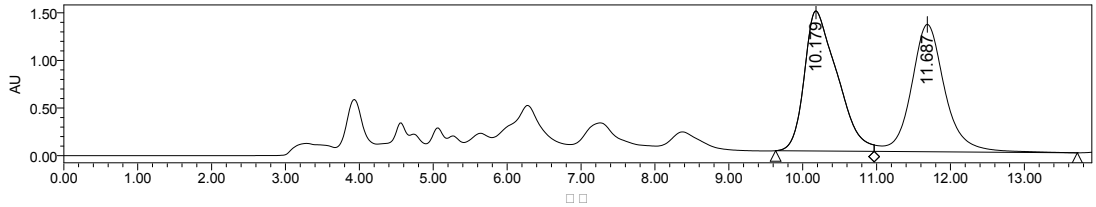
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.96 (s, 1H), 8.55 – 8.54 (m, 1H), 7.86 – 7.80 (m, 3H), 7.52 – 7.48 (m, 1H), 7.40 – 7.36 (m, 2H), 7.10 – 7.07 (m, 1H), 6.83 (s, 1H), 6.52 (s, 1H), 5.01 (d, *J* = 4.8 Hz, 1H), 3.77 (s, 3H), 3.76 (s, 3H), 3.60 (dd, *J* = 16.8, 9.2 Hz, 1H), 3.03 (d, *J* = 16.8 Hz, 1H), 1.26 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 198.2, 178.8, 170.6, 155.5, 150.1, 146.5, 144.9, 142.4, 136.9, 136.0, 132.8, 128.4, 128.0, 123.4, 120.4, 110.0, 95.7, 80.7, 62.6, 56.8, 56.8, 56.1, 56.1, 36.7, 27.7;

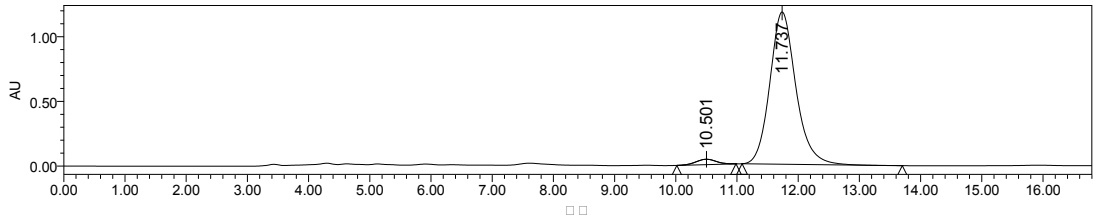
ESI-HRMS calcd for [$C_{29}H_{29}{}^{79}BrN_2O_6$+Na$^+$]: 603.1101, found 603.1101;

ESI-HRMS calcd for [$C_{29}H_{29}{}^{81}BrN_2O_6$+Na$^+$]: 605.1080, found 605.1074;

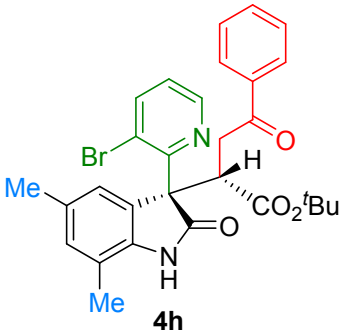
IR (neat): $\tilde{\nu}$ (cm-1) 2975, 2360, 1716, 1683, 1623, 1499, 1327, 1191, 1150, 1003, 845, 688, 575.



	Retention Time	Area	% Area
1	10.179	45318530	51.73
2	11.687	42293636	48.27



	Retention Time	Area	% Area
1	10.501	949228	2.66
2	11.737	34758796	97.34



4h

***Tert*-Butyl (*S*)-2-[(*S*)-3-(3-bromopyridin-2-yl)-5,7-dimethyl-2-oxoindolin-3-yl]-4-oxo-4-phenylbutanoate**

0.1 mmol (**1h**) scale reaction:

Results: yellow solid, M.p. 194-197 °C, 96% yield, >19:1 d.r., 97:3 e.r.; $[\alpha]^{20}_{D}$ = 15.1 (*c* 4.64, CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 30.20 min, $t_{R(minor)}$ = 25.91 min);

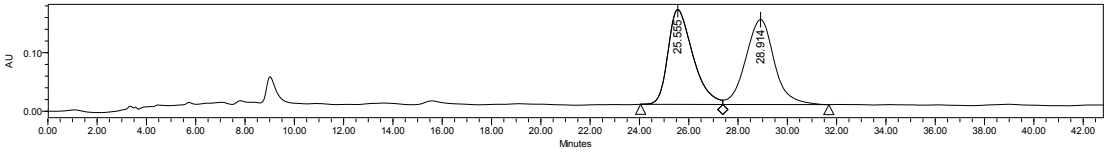
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.68 (s, 1H), 8.53 – 8.52 (m, 1H), 7.89 – 7.87 (m, 2H), 7.79 – 7.76 (m, 1H), 7.52 – 7.48 (m, 1H), 7.41 – 7.37 (m, 2H), 7.07 – 7.04 (m, 1H), 6.89 – 6.80 (m, 2H), 5.05 (d, *J* = 9.6 Hz, 1H), 3.64 – 3.57 (m, 1H), 2.97 (d, *J* = 17.2 Hz, 1H), 2.21 (s, 3H), 2.19 (s, 3H), 1.23 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 198.5, 178.4, 170.5, 146.5, 142.2, 138.2, 137.1, 132.8, 131.8, 130.9, 129.6, 128.3, 128.1, 123.3, 123.1, 120.4, 119.1, 80.6, 36.7, 29.7, 27.6, 21.2, 16.6;

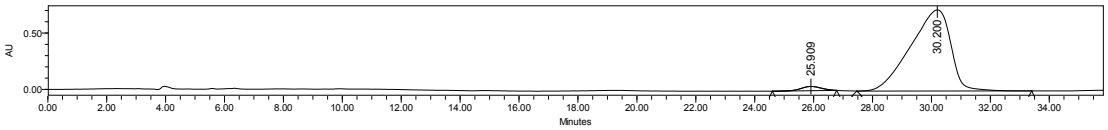
ESI-HRMS calcd for [$C_{29}H_{29}{}^{79}BrN_2O_4$+H$^+$]: 549.1384, found 549.1383;

ESI-HRMS calcd for [$C_{29}H_{29}{}^{81}BrN_2O_4$+H$^+$]: 551.1363, found 551.1360;

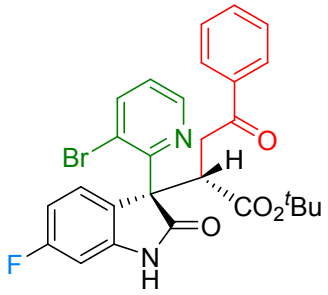
IR (neat): $\tilde{\nu}$ (cm-1) 2917, 2359, 1735, 1698, 1686, 1475, 1337, 1225, 1152, 1013, 846, 750, 685, 576.



	Retention Time	Area	% Area
1	25.555	11352976	49.32
2	28.914	11667932	50.68



	Retention Time	Area	% Area
1	25.909	1813775	2.58
2	30.200	68485912	97.42



4i

***Tert*-Butyl (*S*)-2-[(*S*)-3-(3-bromopyridin-2-yl)-6-fluoro-2-oxoindolin-3-yl]-4-oxo-4-phenylbutanoate**

0.1 mmol (**1i**) scale reaction:

Results: yellow solid, M.p. 87-90 °C, 90% yield, >19:1 d.r., 92:8 e.r.; $[\alpha]^{20}_{D}$ = 20.7 (*c* 1.34, CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 13.22 min, $t_{R(minor)}$ = 11.34 min);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.30 (s, 1H), 8.54 – 8.53 (m, 1H), 7.92 – 7.89 (m, 2H), 7.81 – 7.79 (m, 1H), 7.54 – 7.51 (m, 1H), 7.43 – 7.40 (m, 2H), 7.21 – 7.17 (m, 1H), 7.12 – 7.09 (m, 1H), 6.69 –6.60 (m, 2H), 4.90 – 4.71 (m, 1H), 3.73 – 3.57 (m, 1H), 3.30 (d, *J* = 17.2 Hz, 1H), 1.26 (s, 9H);

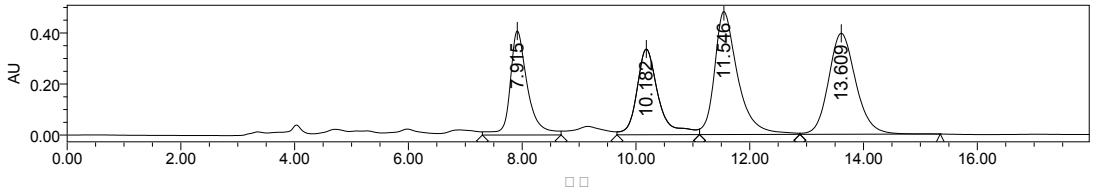
^{13}C NMR{^{1}H} (100 MHz, Chloroform-d) δ 198.1, 178.0, 170.4, 164.5, 162.0, 154.5, 146.5, 143.6 (*J* = 12.0 Hz), 142.5, 136.9, 132.9, 128.4, 128.0, 126.7, 125.5, 123.8, 120.8, 108.8 (*J* = 22.4 Hz), 98.9 (*J* = 27.3 Hz), 81.0, 61.5, 46.5, 37.3, 29.7, 27.6;

^{19}F NMR (376 MHz, Chloroform-*d*) δ -110.88;

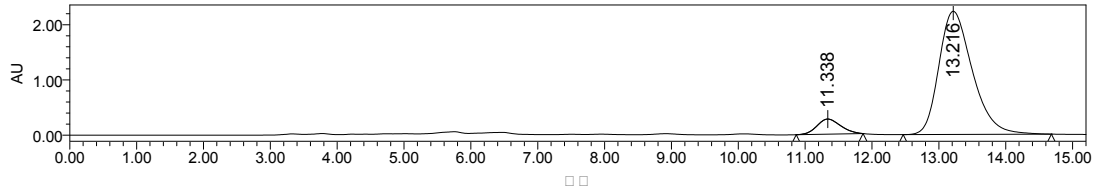
ESI-HRMS calcd for [$C_{27}H_{24}{}^{79}BrFN_2O_4$+Na$^+$]: 561.0796, found 561.0791;

ESI-HRMS calcd for [$C_{27}H_{24}{}^{81}BrFN_2O_4$+Na$^+$]: 563.0775, found 563.0765;

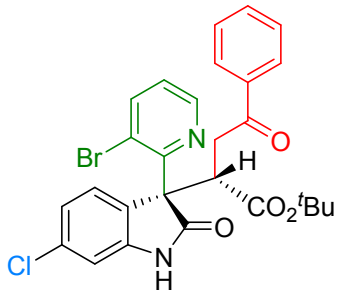
IR (neat): $\tilde{\nu}$ (cm-1) 2976, 2360,1716, 1683, 1624, 1498, 1141, 1098, 967, 843, 793, 689, 617.



	Retention Time	Area	% Area
1	7.915	8620366	19.57
2	10.182	8757070	19.88
3	11.546	13612266	30.90
4	13.609	13058823	29.65



	Retention Time	Area	% Area
1	11.338	6741844	7.99
2	13.216	77639945	92.01



4j

***Tert*-Butyl (*S*)-2-[(*S*)-3-(3-bromopyridin-2-yl)-6-chloro-2-oxoindolin-3-yl]-4-oxo-4-phenylbutanoate**

0.1 mmol (**1j**) scale reaction:

Results: yellow solid, M.p. 195-198 °C, 88% yield, >19:1 d.r., 91:9 e.r.; $[\alpha]^{20}_{D}$ = 11.3 (*c* 3.18, CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 13.43 min, $t_{R(minor)}$ = 11.39 min);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.52 (s, 1H), 8.54 – 8.53 (m, 1H), 7.92 – 7.86 (m, 2H), 7.79 – 7.81(m, 1H), 7.54 – 7.50 (m, 1H), 7.43 – 7.39 (m, 2H), 7.18 – 7.16 (m, 1H), 7.13 – 7.09 (m, 1H), 6.96 – 6.94 (m, 1H), 6.87 – 6.86 (m, 1H), 4.80 (s, 1H), 3.65 (ddd, *J* = 17.2, 9.2, 3.6 Hz, 1H), 3.30 (d, *J* = 17.2 Hz, 1H), 1.27 (s, 9 H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-d) δ 198.1, 178.0, 170.4, 146.6, 143.3, 142.5, 136.9, 134.7, 133.0, 128.5, 128.1, 126.5, 123.9, 122.3, 120.8, 110.8, 81.1, 61.8, 46.5, 37.4, 27.7;

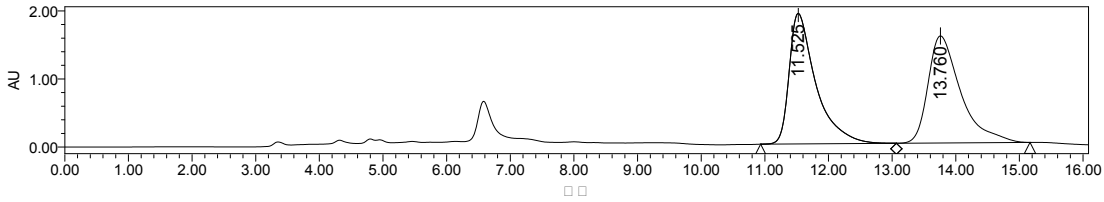
ESI-HRMS calcd for [$C_{27}H_{24}{}^{79}Br^{35}ClN_2O_4$+H$^+$]: 555.0681, found 555.0684;

ESI-HRMS calcd for [$C_{27}H_{24}{}^{79}Br^{37}ClN_2O_4$+H$^+$]: 556.0714, found 556.0716;

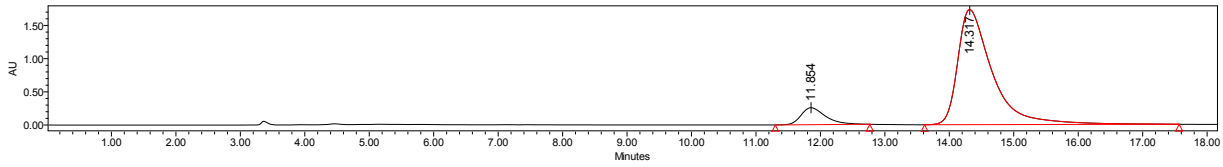
ESI-HRMS calcd for [$C_{27}H_{24}{}^{81}Br^{35}ClN_2O_4$+H$^+$]: 557.0660, found 557.0662;

ESI-HRMS calcd for [$C_{27}H_{24}{}^{81}Br^{37}ClN_2O_4$+H$^+$]: 558.0694, found 558.0692;

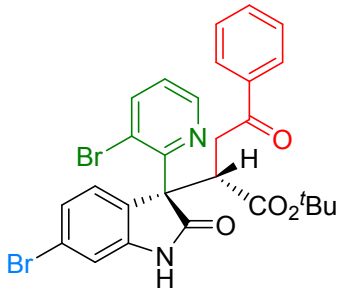
IR (neat): $\tilde{\nu}$ (cm-1) 2924, 2358, 1711, 1682, 1448, 1139, 1070, 1011, 916, 843, 802, 737, 689, 620, 531.



	Retention Time	Area	% Area
1	11.525	55765855	49.88
2	13.760	56031609	50.12



	Retention Time	Area	% Area
1	11.854	6755370	9.48
2	14.317	64520930	90.52



4k

***Tert*-Butyl (*S*)-2-[(*S*)-6-bromo-3-(3-bromopyridin-2-yl)-2-oxoindolin-3-yl]-4-oxo-4-phenylbutanoate**

0.1 mmol (**1k**) scale reaction:

Results: yellow solid, M.p. 192-195 °C, 80% yield, >19:1 d.r., 88:12 e.r.; $[\alpha]^{20}_{D}$ = 4.90 (*c* 1.94, CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 13.42 min, $t_{R(minor)}$ = 11.59 min);

^{1}H NMR (400 MHz, DMSO-d_6) δ 11.05 – 10.97 (m, 1H), 8.62 – 8.61(m, 1H), 8.07 – 8.02 (m, 3H), 7.70 – 7.66 (m, 1H), 7.57 – 7.53 (m, 2H), 7.38 – 7.34 (m, 2H), 7.27 – 7.26 (m, 1H), 7.20 – 7.16 (m, 1H), 4.46 – 4.33 (m, 1H), 3.75 –3.68 (m, 1H), 3.37 – 3.53 (m, 1H), 1.20 (s, 9H);

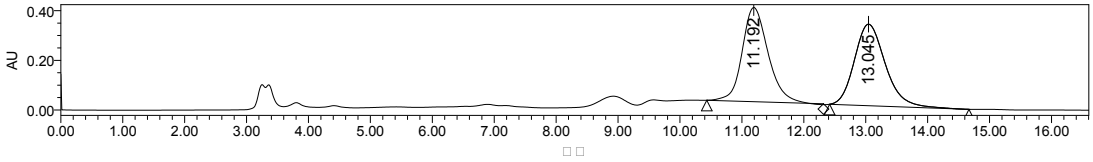
^{13}C NMR{^{1}H} (100 MHz, DMSO-d_6) δ 198.2, 175.6, 175.3, 169.8, 153.3, 146.9, 145.6, 142.9, 136.2, 133.3, 128.8, 128.7, 128.5, 127.9 127.7, 127.2, 124.6, 123.7, 121.5, 120.7, 112.2, 79.9, 79.6, 60.6, 59.4, 46.1, 27.1;

ESI-HRMS calcd for [$C_{27}H_{24}{}^{79}Br_2N_2O_4$+H$^+$]: 599.0176, found 599.0176;

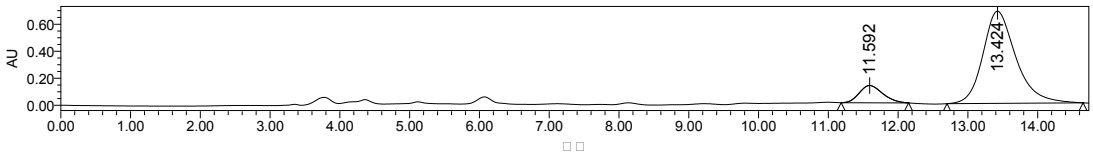
ESI-HRMS calcd for [$C_{27}H_{24}{}^{79}Br^{81}BrN_2O_4$+H$^+$]: 601.0155, found 601.0155;

ESI-HRMS calcd for [$C_{27}H_{24}{}^{81}Br_2N_2O_4$+H$^+$]: 603.0135, found 601.0137;

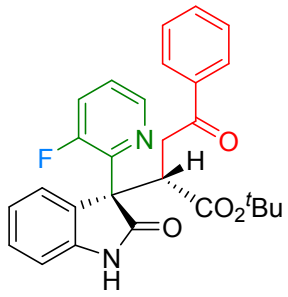
IR (neat): $\tilde{\nu}$ (cm-1) 2975, 2360, 1714, 1682, 1614, 1214, 1146, 1012, 908, 841, 804, 768, 688, 597.



	Retention Time	Area	% Area
1	11.192	11078756	49.28
2	13.045	11403612	50.72



	Retention Time	Area	% Area
1	11.592	2979186	12.00
2	13.424	21839762	88.00



4l

***Tert*-Butyl (*S*)-2-[(*S*)-3-(3-fluoropyridin-2-yl)-2-oxoindolin-3-yl]-4-oxo-4-phenylbutanoate**

0.1 mmol (**1a**) scale reaction:

Results: yellow solid, M.p. 238-241 °C, 86% yield, >19:1 d.r., 89:11 e.r.; $[\alpha]^{20}_{D}$ = 23.0 (*c* 0.52, CH_2Cl_2); HPLC (Daicel chiralcel IC, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 30.35 min, $t_{R(minor)}$ = 25.81 min);

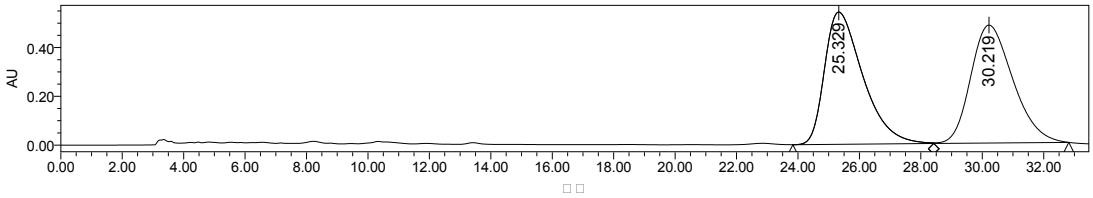
^{1}H NMR (400 MHz, Chloroform-d) δ 9.10 – 8.97 (m, 1H), 8.36 – 8.32 (m, 1H), 7.87 – 7.84 (m, 2H), 7.50 – 7.45 (m, 1H), 7.39 – 7.32 (m, 4H), 7.23 – 7.13 (m, 2H), 6.97 – 6.89 (m, 2H), 4.95 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.76 – 3.67 (m, 1H), 2.62 (dd, *J* = 17.2, 2.8 Hz, 1H), 1.16 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-d) δ 198.0, 177.2, 170.0, 156.6, 144.2 (*J* = 5.0 Hz), 141.2, 136.9, 132.9, 130.4, 129.0, 128.4, 128.4, 128.1, 124.7 (*J* = 4.1 Hz), 123.9, 123.7, 122.8, 110.2, 81.0, 77.2, 59.6, 59.6, 36.1, 27.6;

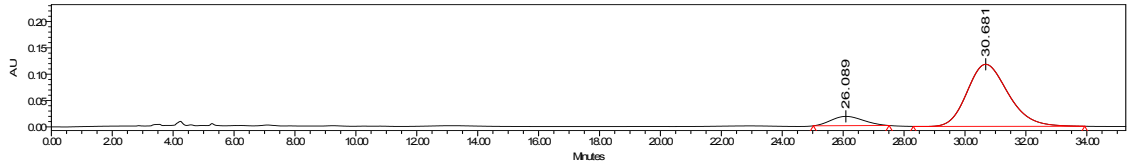
^{19}F NMR (376 MHz, Chloroform-*d*) δ -118.15;

ESI-HRMS calcd for [$C_{27}H_{25}FN_2O_4$+Na$^+$]: 483.1691, found 483.1690;

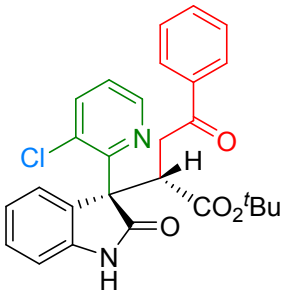
IR (neat): $\tilde{\nu}$ (cm-1) 2977, 2359, 1736, 1681, 1456, 1152, 1007, 842, 758, 675, 611.



	Retention Time	Area	% Area
1	25.329	46943280	50.45
2	30.219	46101315	49.55



	Retention Time	Area	% Area
1	26.089	1291595	10.49
2	30.681	11020638	89.51



4m

***Tert*-Butyl (*S*)-2-[(*S*)-3-(3-chloropyridin-2-yl)-2-oxoindolin-3-yl]-4-oxo-4-phenylbutanoate**

0.1 mmol (**1a**) scale reaction:

Results: yellow solid, M.p. 78-81 ºC, 94% yield, >19:1 d.r., 91:9 e.r.; $[\alpha]^{20}_{D}$ = 12.16 (*c* 1.16, CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 11.65 min, $t_{R(minor)}$ = 8.41 min);

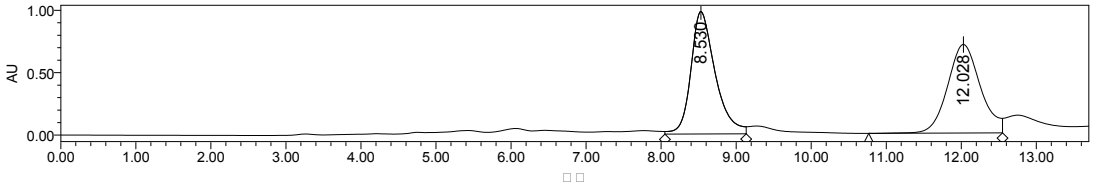
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.15 (s, 1H), 8.50 – 8.49 (m, 1H), 7.90 – 7.88 (m, 2H), 7.60 – 7.58 (m, 1H), 7.52 – 7.48 (m, 1H), 7.41 – 7.37 (m, 2H), 7.24 – 7.15 (m, 3H), 6.98 – 6.94 (m, 1H), 6.89 – 6.87 (m, 1H), 4.96 (dd, *J* = 10.4, 2.8 Hz, 1H), 3.63 (dd, *J* = 17.2, 10.0 Hz, 1H), 3.14 – 3.10 (m, 1H), 1.24 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 198.2, 177.7, 170.3, 154.3, 146.1, 141.8, 138.7, 137.0, 132.8, 131.2, 129.9, 129.0, 128.4, 128.0, 125.1, 123.3, 122.3, 110.0, 80.8, 61.1, 46.0, 37.0, 27.6;

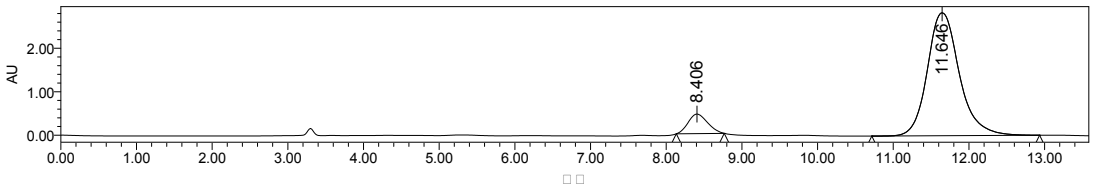
ESI-HRMS calcd for $[C_{27}H_{25}{}^{35}ClN_2O_4+H^+]$: 477.1576, found 477.1566;

ESI-HRMS calcd for $[C_{27}H_{25}{}^{37}ClN_2O_4+H^+]$: 479.1546, found 479.1538;

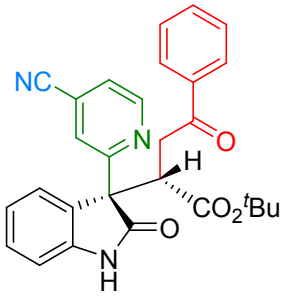
IR (neat): $\tilde{\nu}$ (cm-1) 2976, 2360, 1716, 1683, 1616, 1471, 1330, 1150, 845, 751, 688, 644, 604.



	Retention Time	Area	% Area
1	8.530	22106359	50.69
2	12.028	21503529	49.31



	Retention Time	Area	% Area
1	8.406	8004112	8.80
2	11.646	82949024	91.20



4n

***Tert*-Butyl (*S*)-2-[(*S*)-3-(4-cyanopyridin-2-yl)-2-oxoindolin-3-yl]-4-oxo-4-phenylbutanoate**

0.1 mmol (**1a**) scale reaction:

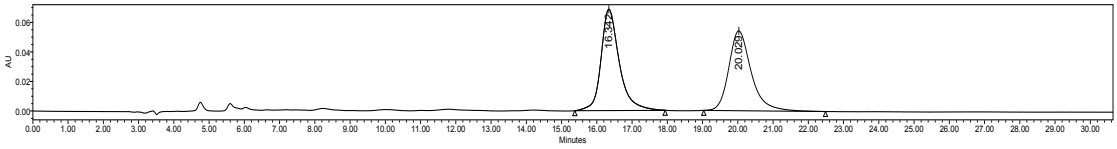
Results: yellow solid, M.p. 155-158 °C, 83% yield, 90:10 d.r., 93:7 e.r.; $[\alpha]^{20}_{D}$ = 74.3 (*c* 1.43, CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 80/20, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 17.73 min, $t_{R(minor)}$ = 22.42 min);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.26 – 9.07 (m, 1H), 8.87 – 8.83 (m, 1H), 7.93 – 7.85 (m, 2H), 7.64 – 7.50 (m, 2H), 7.53 – 7.50 (m, 1H), 7.42 – 7.38 (m, 3H), 7.29 – 7.23 (m, 1H), 7.10 – 7.07 (m, 1H), 7.00 – 6.95 (m, 1H), 4.75 (dt, *J* = 10.4, 3.2 Hz, 1H), 3.75 (dd, *J* = 17.2, 10.4 Hz, 1H), 2.52 (ddd, *J* = 17.2, 9.2, 3.2 Hz, 1H), 1.14 (s, 9H);

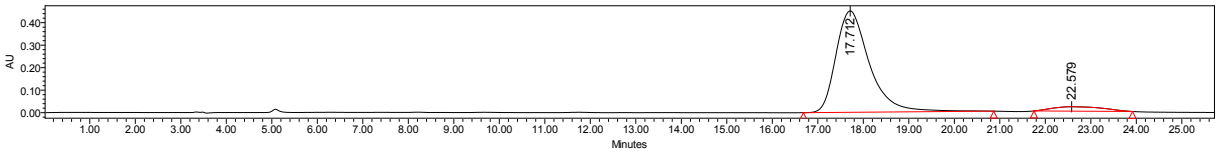
^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 197.5, 177.1, 169.6, 161.2, 159.4, 150.5, 141.0, 136.7, 133.1, 129.4, 129.0, 128.5, 128.1, 128.0, 126.4, 123.7, 123.5, 123.1, 121.0, 116.4, 110.4, 81.5, 60.2, 47.8, 35.8, 27.5, 14.2;

ESI-HRMS calcd for [$C_{28}H_{25}N_3O_4$+Na$^+$]: 490.1737, found 490.1735;

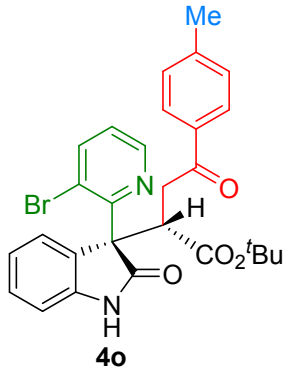
IR (neat): $\tilde{\nu}$ (cm-1) 2976, 2360, 1716, 1697, 1472, 1151, 839, 749, 687, 617, 546.



	Retention Time	Area	% Area
1	16.342	2464279	50.84
2	20.029	2382616	49.16



	Retention Time	Area	% Area
1	17.734	24359730	92.98
2	22.417	1839891	7.02



4o

***Tert*-Butyl (*S*)-2-[(*S*)-3-(3-bromopyridin-2-yl)-2-oxoindolin-3-yl]-4-oxo-4-(*p*-tolyl)butanoate**

0.1 mmol (**1a**) scale reaction:

Results: yellow solid, M.p. 202-205 °C, 92% yield, >19:1 d.r., 92:8 e.r.; $[\alpha]^{20}_{D}$ = 21.4 (*c* 2.1 CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 80/20, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 22.41 min, $t_{R(minor)}$ = 15.73 min);

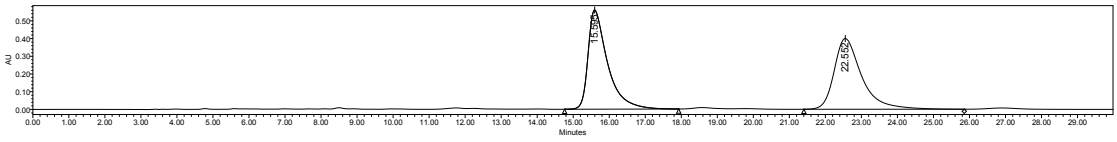
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.41 (s, 1H), 8.53 – 8.47 (m, 1H), 7.89 –7.77 (m, 3H), 7.23 – 7.18 (m, 4H), 7.10 – 7.06 (m, 1H), 6.99 – 6.95 (m, 1H), 6.91 – 6.89 (m, 1H), 4.88 (d, *J* = 9.6 Hz, 1H), 3.63 – 3.56 (m, 1H), 3.21 (d, *J* = 17.2 Hz, 1H), 2.37 (s, 3H), 1.24 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 197.9, 177.9, 170.5, 146.5, 143.5, 142.4, 142.3, 134.6, 130.0, 129.1, 129.0, 128.4, 128.2, 125.3, 123.6, 122.3, 120.8, 110.2, 80.8, 62.1, 46.56, 37.2, 27.6, 21.6;

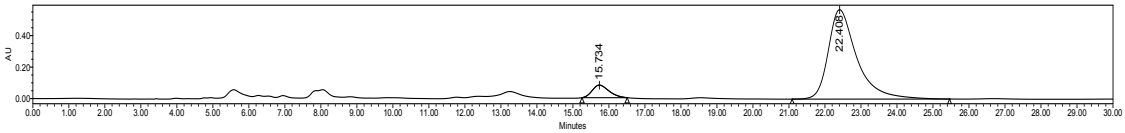
ESI-HRMS calcd for [$C_{28}H_{27}{}^{79}BrN_2O_4$+H$^+$]: 535.1227, found 535.1227;

ESI-HRMS calcd for [$C_{28}H_{27}{}^{81}BrN_2O_5$+H$^+$]: 537.1206, found 537.1207;

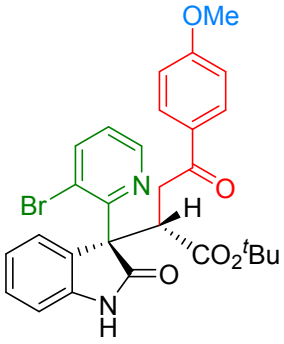
IR (neat): $\tilde{\nu}$ (cm-1) 2972, 2355, 1728, 1701, 1682, 1156, 1007, 812, 672, 604, 548.



	Retention Time	Area	% Area
1	15.595	21056499	49.82
2	22.552	21211551	50.18



	Retention Time	Area	% Area
1	15.734	2573957	7.60
2	22.408	31312742	92.40



4p

***Tert*-Butyl (*S*)-2-[(*S*)-3-(3-bromopyridin-2-yl)-2-oxoindolin-3-yl]-4-(4-methoxyphenyl)-4-oxobutanoate**

0.1 mmol (**1a**) scale reaction:

Results: yellow solid, M.p. 80-85 ºC, 75% yield, >19:1 d.r., 91:9 e.r.; $[\alpha]^{20}_{D}$ = 18.4 (*c* 0.36, CH_2Cl_2); HPLC (Daicel chiralcel IA2, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 23.93 min, $t_{R(minor)}$ = 13.81 min);

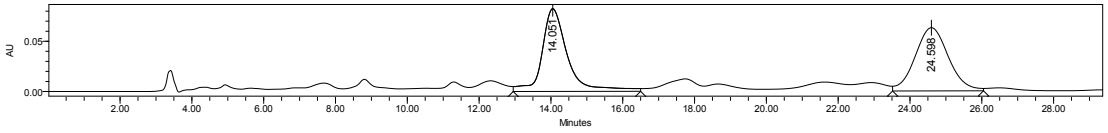
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.08 (s, 1H), 8.54 – 8.53 (m, 1H), 7.89 – 7.80 (m, 2H), 7.79 – 7.80 (m, 1H), 7.24 – 7.20 (m, 2H), 7.10 – 7.07 (m, 1H), 6.99 – 6.95 (m, 1H), 6.89 – 6.84 (m, 3H), 4.90 (d, *J* = 9.6 Hz, 1H), 3.84 (s, 3H), 3.64 – 3.51 (m, 1H), 3.15 (d, *J* = 16.8 Hz, 1H), 1.23 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 196.7, 177.6, 170.5, 163.2, 146.5, 142.4, 142.1, 130.3, 130.1, 130.0, 129.0, 125.3, 123.5, 122.2, 120.8, 113.5, 110.0, 80.7, 62.1, 55.4, 36.8, 27.6;

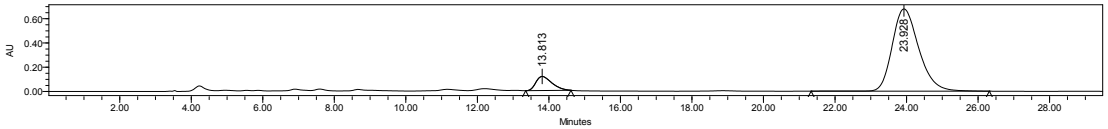
ESI-HRMS calcd for [$C_{28}H_{27}{}^{79}BrN_2O_5$+H$^+$]: 551.1176, found 551.1172;

ESI-HRMS calcd for [$C_{28}H_{27}{}^{81}BrN_2O_5$+H$^+$]: 553.1156, found 553.1154;

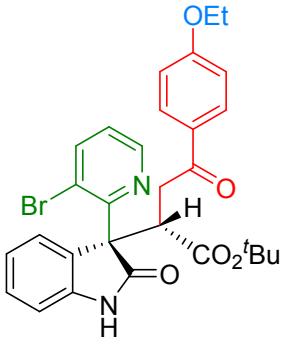
IR (neat): $\tilde{\nu}$ (cm-1) 2976, 2360, 1716, 1598, 1471, 1253, 1150, 1015, 957, 832, 751, 677, 603, 562.



	Retention Time	Area	% Area
1	14.051	4047765	49.88
2	24.598	4067049	50.12



	Retention Time	Area	% Area
1	13.813	3629331	9.39
2	23.928	35026690	90.61



4q

***Tert*-Butyl (*S*)-2-[(*S*)-3-(3-bromopyridin-2-yl)-2-oxoindolin-3-yl]-4-(4-ethoxyphenyl)-4-oxobutanoate**

0.1 mmol (**1a**) scale reaction:

Results: yellow solid, M.p. 87-92 °C, 71% yield, >19:1 d.r., 91:9 e.r.; $[\alpha]^{20}_{D}$ = 14.9 (*c* 1.88, CH_2Cl_2); HPLC (Daicel chiralcel IE, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 30.28 min, $t_{R(minor)}$ = 13.08 min);

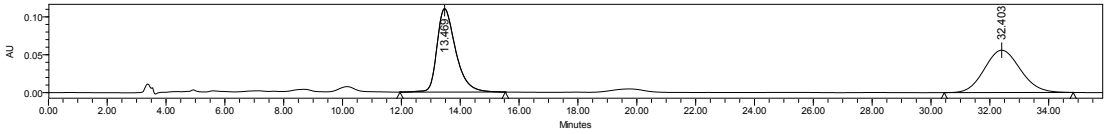
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.04 (s, 1H), 8.53 – 8.53 (m, 1H), 7.88 – 7.78 (m, 3H), 7.24 – 7.20 (m, 2H), 7.10 – 7.06 (m, 1H), 6.99 – 6.95 (m, 1H), 6.90 – 6.85 (m, 3H), 4.89 (d, *J* = 9.6 Hz, 1H), 4.06 (q, *J* = 7.2 Hz, 2H), 3.60 – 3.53 (m, 1H), 3.15 (d, *J* = 16.8 Hz, 1H), 1.42 (t, *J* = 7.2 Hz, 3H), 1.23 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-d) δ 196.7, 177.6, 170.5, 162.7, 146.5, 142.4, 142.1, 130.3, 130.0, 129.9, 125.3, 123.6, 122.3, 120.8, 114.0, 110.0, 80.7, 63.7, 62.1, 36.8, 27.6, 14.7;

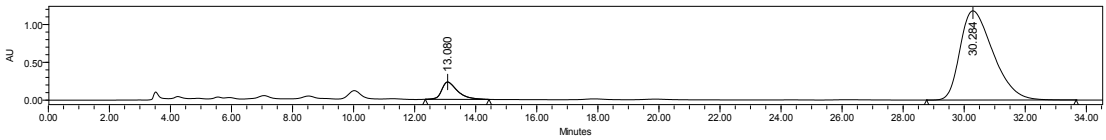
ESI-HRMS calcd for [$C_{29}H_{29}{}^{79}BrN_2O_5$+H$^+$]: 565.1333, found 565.1335;

ESI-HRMS calcd for [$C_{29}H_{29}{}^{81}BrN_2O_5$+H$^+$]: 567.1312, found 567.1317.

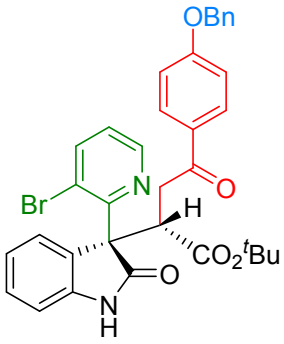
IR (neat): $\tilde{\nu}$ (cm-1) 2928, 2360, 1716, 1598, 1472, 1242, 1150, 1040, 751, 729, 637.



	Retention Time	Area	% Area
1	13.469	4839134	50.50
2	32.403	4742989	49.50



	Retention Time	Area	% Area
1	13.080	8714450	8.97
2	30.284	88399932	91.03



4r

***Tert*-Butyl (*S*)-4-(4-(benzyloxy)phenyl)-2-[(*S*)-3-(3-bromopyridin-2-yl)-2-oxoindolin-3-yl]-4-oxobutanoate**

0.1 mmol (**1a**) scale reaction:

Results: yellow solid, M.p. 85-88 ºC, 81% yield, 10:1 d.r., 92:8 e.r.; $[\alpha]^{20}_{D}$ = 21.3 (*c* 2.1 CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 46.77 min, $t_{R(minor)}$ = 19.21 min);

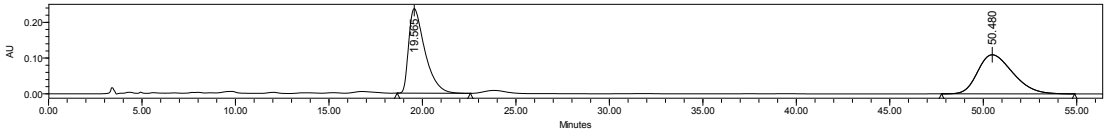
^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.04 (s, 1H), 8.53 – 8.52 (m, 1H), 7.88 – 7.80 (m, 1H), 7.80 – 7.77 (m, 1H), 7.42 – 7.33(m, 6H), 7.23 – 7.19 (m, 2H), 7.09 – 7.06 (m, 1H), 6.98 – 6.93 (m, 3H), 6.89 – 6.87 (m, 1H), 5.10 (s, 2H), 4.89 (d, *J* = 9.6 Hz, 1H), 3.60 – 3.53 (m, 1H), 3.15 (d, *J* = 16.8 Hz, 1H), 1.23 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 196.7, 177.6, 170.5, 162.4, 146.5, 142.4, 142.1, 136.2, 130.3, 130.3, 130.0, 129.0 128.6, 128.2, 127.4, 125.3, 123.5, 122.3, 120.8, 114.4, 110.0, 80.7, 70.0, 62.0, 46.5, 36.9, 27.6;

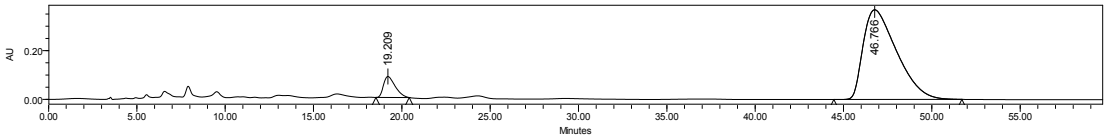
ESI-HRMS calcd for [$C_{34}H_{31}{}^{79}BrN_2O_5$+H$^+$]: 627.1489, found 627.1488;

ESI-HRMS calcd for [$C_{34}H_{31}{}^{81}BrN_2O_3$+H$^+$]: 629.1469, found 629.1459;

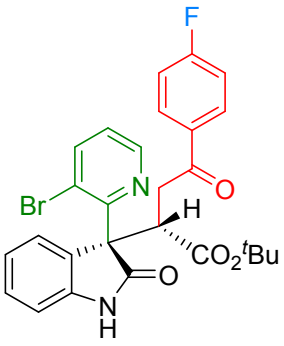
IR (neat): $\tilde{\nu}$ (cm-1) 2976, 2360, 1716, 1597, 1471, 1336, 1224, 1150, 731, 696, 604.



	Retention Time	Area	% Area
1	19.565	14242740	50.01
2	50.480	14237319	49.99



	Retention Time	Area	% Area
1	19.209	3957414	7.56
2	46.766	48391598	92.44



4s

***Tert*-butyl (*S*)-2-[(*S*)-3-(3-bromopyridin-2-yl)-2-oxoindolin-3-yl]-4-(4-fluorophenyl)-4-oxobutanoate**

0.1 mmol (**1a**) scale reaction:

Results: yellow solid, M.p. 93-97 °C, 73% yield, 10:1 d.r., 90:10 e.r.; $[\alpha]^{20}_{D}$ = 19.9 (*c* 1.36, CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 80/20, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 34.13 min, $t_{R(minor)}$ = 16.04 min);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.25 (s, 1H), 8.55 – 8.53 (m, 1H), 7.95 – 7.90 (m, 2H), 7.82 –7.79 (m, 1H), 7.20 – 7.12 (m, 2H), 7.11 – 7.02 (m, 3H), 7.00 – 6.96 (m, 1H), 6.90 – 6.88 (m, 1H), 4.89 (d, *J* = 9.6 Hz, 1H), 3.60 (dd, *J* = 17.2, 9.6 Hz, 1H), 3.18 (d, *J* = 17.2 Hz, 1H), 1.24 (s, 9H);

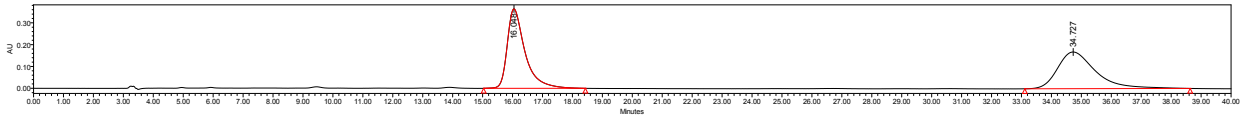
^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 196.7, 177.8, 170.4, 166.9, 164.3, 146.5, 142.5, 142.1, 133.4, 130.7 (*J* = 9.1 Hz), 130.7, 129.9, 129.1, 125.4, 123.6, 122.4, 120.8, 115.6 (*J* = 21.5 Hz), 115.4, 110.2, 81.0, 77.2, 62.0, 46.6, 37.1, 27.6;

^{19}F NMR (376 MHz, Chloroform-*d*) δ -105.77;

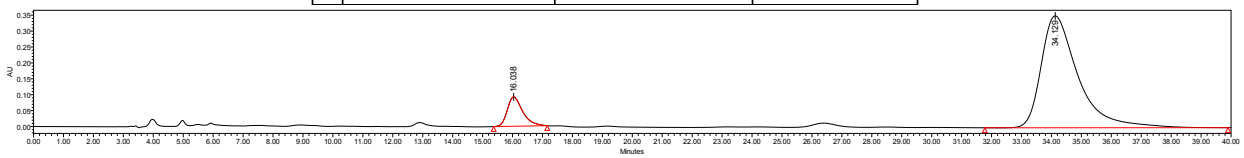
ESI-HRMS calcd for [$C_{27}H_{24}{}^{79}BrFN_2O_4$+H$^+$]: 539.0976, found 539.0977;

ESI-HRMS calcd for [$C_{27}H_{24}{}^{81}BrFN_2O_4$+H$^+$]: 541.0956, found 541.0958;

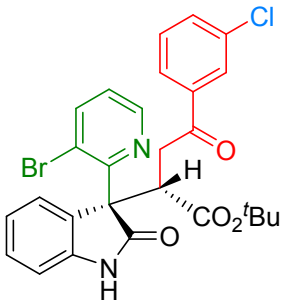
IR (neat): $\tilde{\nu}$ (cm-1) 2975, 2360, 1730, 1685, 1597, 1225, 1154, 1005, 834, 752, 671, 604, 547.



	Retention Time	Area	% Area
1	16.048	14965778	50.24
2	34.727	14823423	49.76



	Retention Time	Area	% Area
1	16.038	3293661	9.85
2	34.129	30146559	90.15



4t

***Tert*-Butyl (*S*)-2-[(*S*)-3-(3-bromopyridin-2-yl)-2-oxoindolin-3-yl]-4-(3-chlorophenyl)-4-oxobutanoate**

0.1 mmol (**1a**) scale reaction:

Results: yellow solid, M.p. 85-87 °C, 84% yield, >19:1 d.r., 91:9 e.r.; $[\alpha]^{20}_{D}$ = 25.0 (*c* 0.26, CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 13.80 min, $t_{R(minor)}$ = 9.96 min);

^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.02 (s, 1H), 8.56 – 8.55 (m, 1H), 7.89 – 7.88 (m, 1H), 7.80 – 7.76 (m, 2H), 7.50 – 7.47 (m, 1H), 7.37 – 7.33 (m, 1H), 7.24 – 7.24 (m, 2H), 7.12 – 7.09 (m, 1H), 7.01 – 6.97 (m, 1H), 6.91 – 6.89 (m, 1H), 4.83 (d, *J* = 10.0 Hz, 1H), 3.61 – 3.54 (m, 1H), 3.28 (t, *J* = 16.8 Hz, 1H), 1.25 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 197.1, 177.5, 170.3, 146.5, 142.5, 142.1, 138.6, 134.7, 132.8, 129.8, 129.1, 128.2, 126.2, 125.4, 123.7, 122.4, 120.9, 110.1, 81.1, 61.9, 37.6, 27.6;

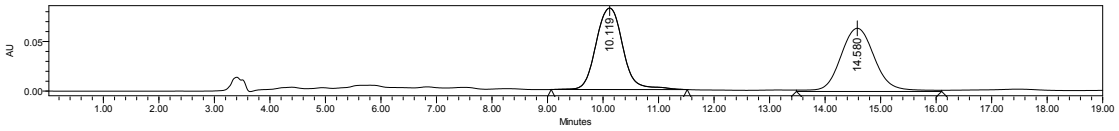
ESI-HRMS calcd for $[C_{27}H_{24}{}^{79}Br^{35}ClN_2O_4+H^+]$: 555.0681, found 555.0677;

ESI-HRMS calcd for $[C_{27}H_{24}{}^{79}Br^{37}ClN_2O_4+H^+]$: 556.0714, found 556.0702;

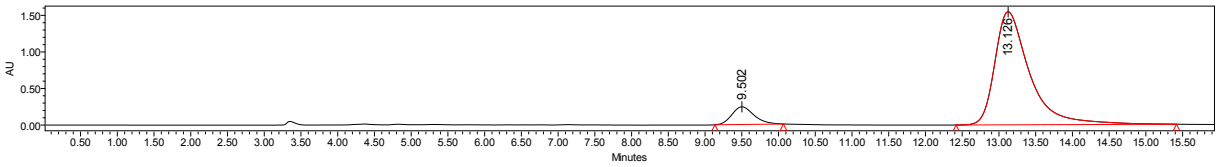
ESI-HRMS calcd for $[C_{27}H_{24}{}^{81}Br^{35}ClN_2O_4+H^+]$: 557.0660, found 557.0658;

ESI-HRMS calcd for $[C_{27}H_{24}{}^{81}Br^{37}ClN_2O_4+H^+]$: 558.0694, found 558.0685;

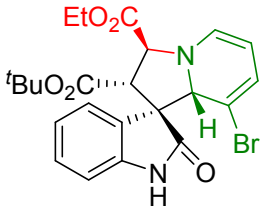
IR (neat): $\tilde{\nu}$ (cm-1) 2977, 2359, 1715, 1617, 1471, 1150, 1016, 792, 751, 678, 603.



	Retention Time	Area	% Area
1	10.119	2750553	50.08
2	14.580	2741232	49.92

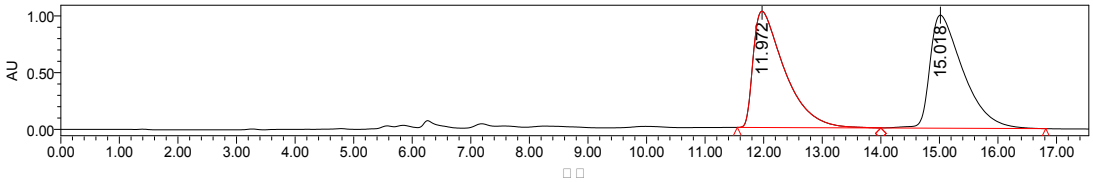


	Retention Time	Area	% Area
1	9.502	5062844	9.05
2	13.126	50896246	90.95

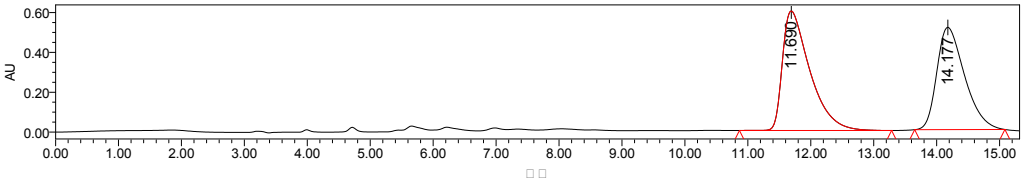


3u

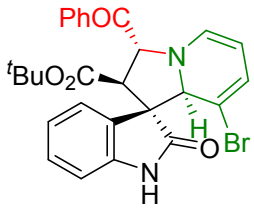
2'-(*Tert*-Butyl) 3'-ethyl (2'*S*, 3*R*, 3'*S*, 8a'*S*)-8'-bromo-2-oxo-2',3'-dihydro-8a'*H*-spiro[indoline-3,1'-indolizine]-2',3'-dicarboxylate
0.1 mmol (**1a**) scale reaction:
Results: yellow solid, M.p. 114-117 °C, 91% yield, >19:1 d.r., 54:46 e.r.; HPLC (Daicel chiralcel ID, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, t_R(major) = 11.69 min, t_R(minor) = 14.18 min);
^{1}H NMR (400 MHz, Chloroform-d) δ 9.00 (s, 1H), 7.32 – 7.26 (m, 2H), 7.02 – 6.96 (m, 2H), 6.31 (d, *J* = 7.2 Hz, 1H), 6.02 (dt, *J* = 6.4, 1.2 Hz, 1H), 5.36 (d, *J* = 1.2 Hz, 1H), 4.83 (d, *J* = 7.2 Hz, 1H), 4.51 (t, *J* = 6.8 Hz, 1H), 4.29 (q, *J* = 7.2 Hz, 2H), 3.79 (d, *J* = 7.6 Hz, 1H), 1.33 (t, *J* = 7.2 Hz, 3H), 1.01 (s, 9H);
^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 177.5, 170.9, 167.2, 142.4, 133.2, 129.2, 128.1, 126.7, 124.6, 122.3, 109.9, 108.1, 94.1, 82.5, 72.9, 64.8, 63.8, 62.1, 52.7, 27.4, 27.2, 14.2;
ESI-HRMS calcd for [$C_{23}H_{25}{}^{79}BrN_2O_5$+Na$^+$]: 511.0839, found 511.0846;
ESI-HRMS calcd for [$C_{23}H_{25}{}^{81}BrN_2O_5$+Na$^+$]: 513.0819, found 513.0825.



	Retention Time	Area	% Area
1	11.972	38312310	49.42
2	15.018	39211078	50.58



	Retention Time	Area	% Area
1	11.690	18128545	53.55
2	14.177	15727557	46.45



3a

***Tert*-Butyl (2'*R*,3*S*,3'*R*,8a'*R*)-3'-benzoyl-8'-bromo-2-oxo-2',3'-dihydro-8a'H-spiro[indoline-3,1'-indolizine]-2'-carboxylate**

0.1 mmol (**1a**) scale reaction:

yellow solid, M.p. 95-98 °C, 96% yield, >19:1 d.r., 95:5 e.r.; HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 11.42 min, $t_{R(minor)}$ = 28.92 min);

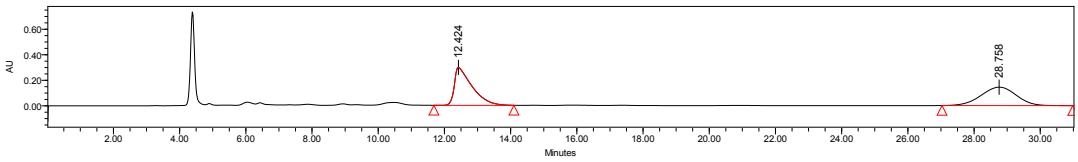
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.66 (s, 1H), 8.07 – 8.01 (m, 2H), 7.64 – 7.57 (m, 1H), 7.52 – 7.45 (m, 2H), 7.42 (d, *J* = 7.6 Hz, 1H), 7.28 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.04 – 6.98 (m, 1H), 6.96 – 6.91 (m, 1H), 6.24 (d, *J* = 7.2 Hz, 1H), 6.04 (dt, *J* = 6.4, 1.2 Hz, 1H), 5.74 (dd, *J* = 6.0, 0.8 Hz, 1H), 5.37 (d, *J* = 1.2 Hz, 1H), 4.50 (td, *J* = 6.8, 6.4, 0.8 Hz, 1H), 3.66 (dd, *J* = 6.0, 0.8 Hz, 1H), 0.95 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 196.3, 177.5, 167.9, 142.4, 135.0, 133.8, 132.9, 132.2, 129.1, 128.9, 128.9, 128.2, 127.2, 125.1, 122.2, 109.7, 107.8, 93.9, 82.6, 73.5, 66.6, 64.4, 53.3, 28.1, 27.1;

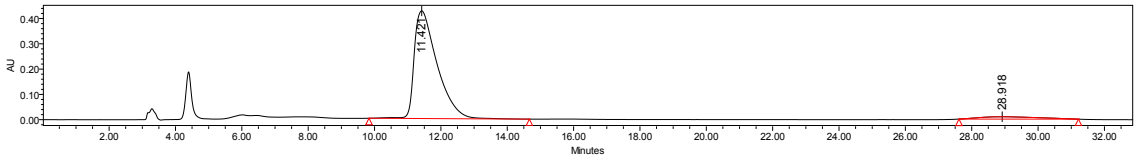
ESI-HRMS calcd for [$C_{27}H_{25}{}^{79}BrN_2O_4$+Na$^+$]: 543.0889, found 543.0893;

ESI-HRMS calcd for [$C_{27}H_{25}{}^{81}BrN_2O_5$+Na$^+$]: 545.0869, found 545.0872;

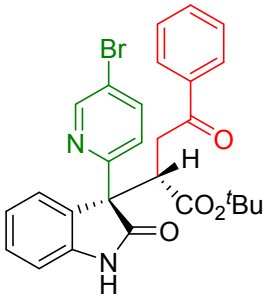
IR (neat): $\tilde{\nu}$ (cm-1) 2360, 1732, 1707, 1441, 1218, 1149, 843, 695, 680.



	Retention Time	Area	% Area
1	12.424	10942592	50.64
2	28.758	10667202	49.36



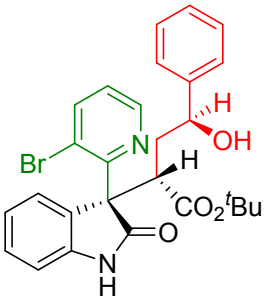
	Retention Time	Area	% Area
1	11.421	20396048	94.55
2	28.918	1176209	5.45



4a'

***Tert*-Butyl (2'*R*,3*S*,3'*R*,8a'*R*)-3'-benzoyl-8'-bromo-2-oxo-2',3'-dihydro-8a'H-spiro[indoline-3,1'-indolizine]-2'-carboxylate**

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.96 (s, 1H), 8.48 (dd, *J* = 4.4, 1.6 Hz, 1H), 7.98 (dt, *J* = 7.2, 1.6 Hz, 2H), 7.80 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.53 – 7.48 (m, 1H), 7.40 (dd, *J* = 7.2, 1.6 Hz, 2H), 7.26 – 7.19 (m, 1H), 7.08 (dd, *J* = 8.0, 4.4 Hz, 1H), 7.02 – 6.96 (m, 2H), 6.91 (d, *J* = 7.6 Hz, 1H), 4.75 (dd, *J* = 10.8, 2.4 Hz, 1H), 3.89 (dd, *J* = 18.0, 10.8 Hz, 1H), 3.58 (dd, *J* = 18.0, 2.8 Hz, 1H), 1.08 (s, 9H);
^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 199.0, 177.3, 171.9, 154.3, 146.6, 142.6, 142.0, 136.9, 132.8, 129.7, 128.9, 128.4, 128.3, 128.2, 128.1, 125.4, 123.9, 122.3, 121.7, 109.9, 80.4, 60.2, 48.1, 37.5, 27.3;
ESI-HRMS calcd for [$C_{27}H_{25}{}^{79}BrN_2O_4$+$H^+$]: 521.1070, found 521.1077;
ESI-HRMS calcd for [$C_{27}H_{25}{}^{81}BrN_2O_5$+$H^+$]: 523.1050, found 523.1059;
IR (neat): $\tilde{\nu}$ (cm-1) 2974, 1708, 1617, 1471, 1332, 1148, 829, 731, 689, 601.



5a

***Tert*-Butyl (2*S*,4*S*)-2-[(*S*)-3-(3-bromopyridin-2-yl)-2-oxoindolin-3-yl]-4-hydroxy-4-phenylbutanoate**

0.05 mmol (**4a**) scale reaction:

Results: white solid, M.p. 97-100 °C, 92% yield, 91:9 d.r., 99:1 e.r.; $[\alpha]^{19.8}_{D}$ = 40.0 (*c* 0.25, CH_2Cl_2); HPLC (Daicel chiralcel IA, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 26.55 min, $t_{R(minor)}$ = 10.24 min);

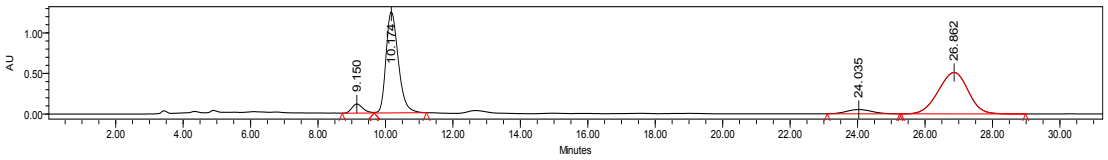
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.93 (s, 1H), 8.67–8.65 (m, 1H), 7.85 – 7.82 (m, 1H), 7.31 – 7.27 (m, 4H), 7.25 – 7.18 (m, 3H), 6.96 – 6.85 (m, 3H), 4.83 – 4.73 (m, 2H), 4.37 – 4.34 (m, 1H), 2.32 – 2.26 (m, 1H), 2.13 – 2.05 (m, 1H), 1.34 (s, 9H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 176.8, 171.2, 154.5, 146.4, 144.9, 143.3, 142.8, 129.1, 129.0, 128.3, 127.1, 125.5, 124.7, 124.2, 122.4, 121.9, 109.9, 81.4, 72.6, 61.5, 48.3, 39.6, 27.8;

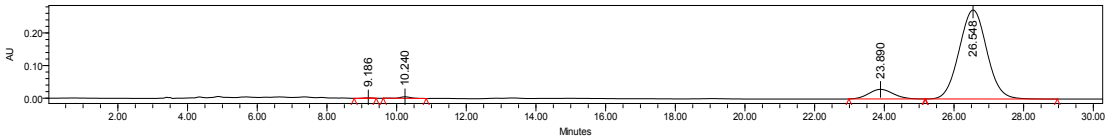
ESI-HRMS calcd for [$C_{27}H_{27}{}^{79}BrN_2O_4$+Na$^+$]: 545.1046, found 545.1039;

ESI-HRMS calcd for [$C_{27}H_{27}{}^{81}BrN_2O_4$+Na$^+$]: 547.1026, found 547.1024;

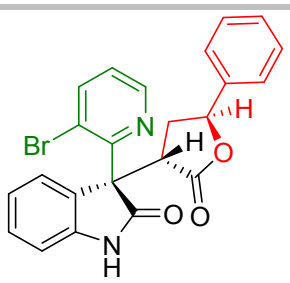
IR (neat): $\tilde{\nu}$ (cm-1) 2975, 2359, 1716, 1617, 1471, 1322 1148, 1023, 749, 699, 604.



	Retention Time	Area	% Area
1	9.150	2577271	3.78
2	10.174	31472682	46.13
3	24.035	2765762	4.05
4	26.862	31410685	46.04



	Retention Time	Area	% Area
1	9.186	18574	0.11
2	10.240	104199	0.63
3	23.890	1440670	8.67
4	26.548	15052579	90.59



6a

(*S*)-3-(3-bromopyridin-2-yl)-3-((3*S*,5*S*)-2-oxo-5-phenyltetrahydrofuran-3-yl)indolin-2-one

0.05 mmol (**5a**) scale reaction:

Results: white solid, M.p. 115-120 °C, 80% yield, 87:13 d.r., 99:1 e.r.; $[\alpha]^{20}_{D}$ = 2.75 (*c* 1.42, CH_2Cl_2); HPLC (Daicel chiralcel ID, *n*-hexane/*i*-PrOH 70/30, 1.0 mL/min, λ = 254 nm, $t_{R(major)}$ = 26.07 min, $t_{R(minor)}$ = 31.38 min);

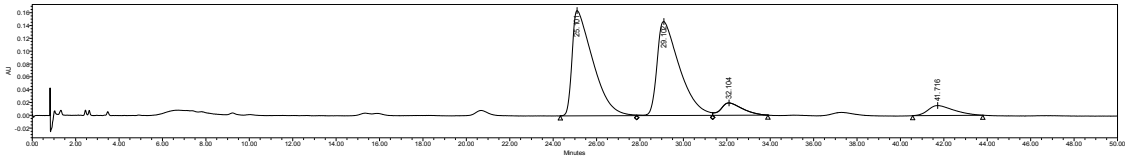
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.62 – 8.61(m, 1H), 8.38 (s, 1H), 7.84 – 7.82 (m, 1H), 7.55 – 7.50 (m, 1H), 7.36 – 7.32 (m, 2H), 7.29 – 7.24 (m, 4H), 7.19 – 7.17 (m, 1H), 7.04 – 7.00 (m, 1H), 6.90 – 6.88 (m, 1H), 5.72 (s, 1H), 5.39 – 5.33 (m, 1H), 3.38 (s, 1H), 2.36 (d, *J* = 14.4 Hz, 1H);

^{13}C NMR{^{1}H} (100 MHz, Chloroform-*d*) δ 177.6, 153.2, 146.2, 142.4, 129.1, 128.7, 128.5, 127.9, 125.0, 124.3, 122.5, 121.8, 109.7, 78.1, 60.7, 33.4;

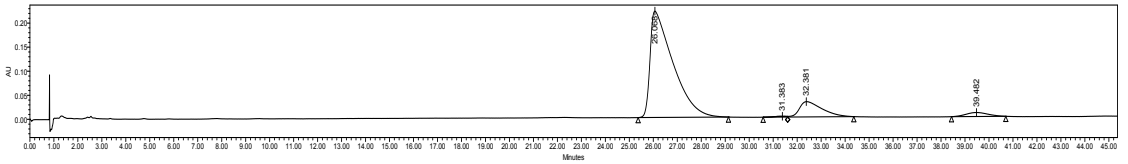
ESI-HRMS calcd for [$C_{23}H_{17}{}^{79}BrN_2O_3$+Na$^+$]: 471.0315, found 471.0317;

ESI-HRMS calcd for [$C_{23}H_{17}{}^{81}BrN_2O_3$+Na$^+$]: 473.0294, found 473.0296;

IR (neat): $\tilde{\nu}$ (cm-1) 2361, 1719, 1616, 1483, 1170, 978, 755, 727, 704, 601.

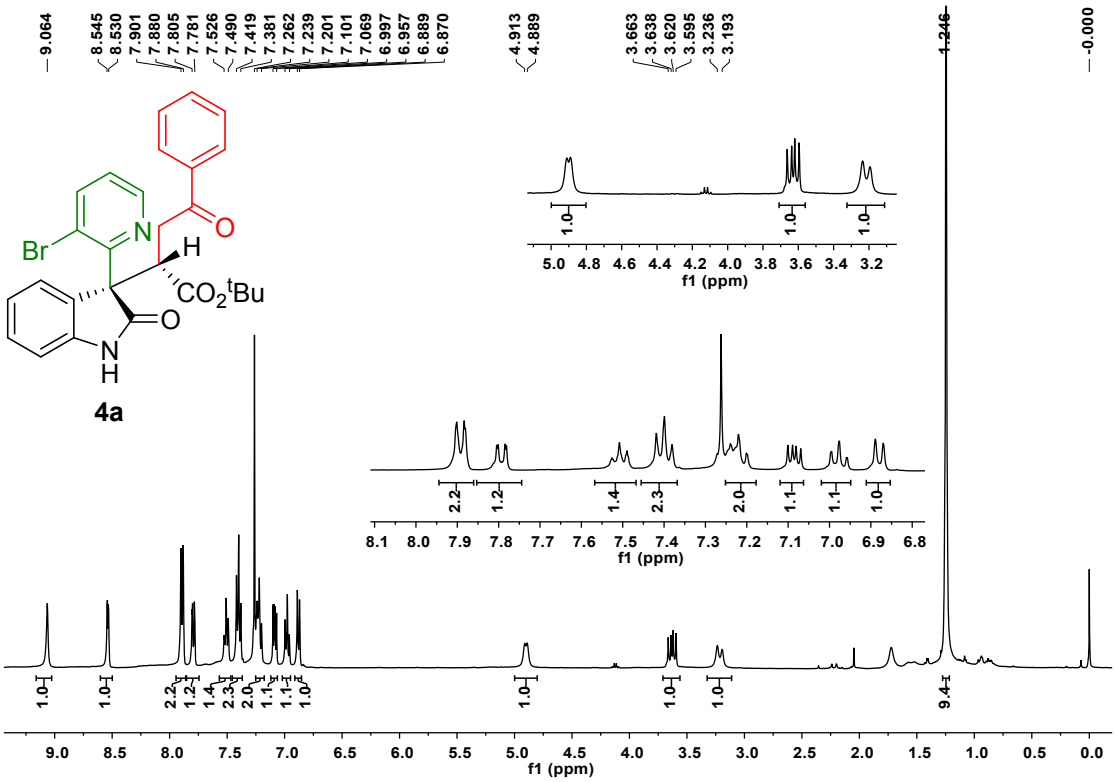


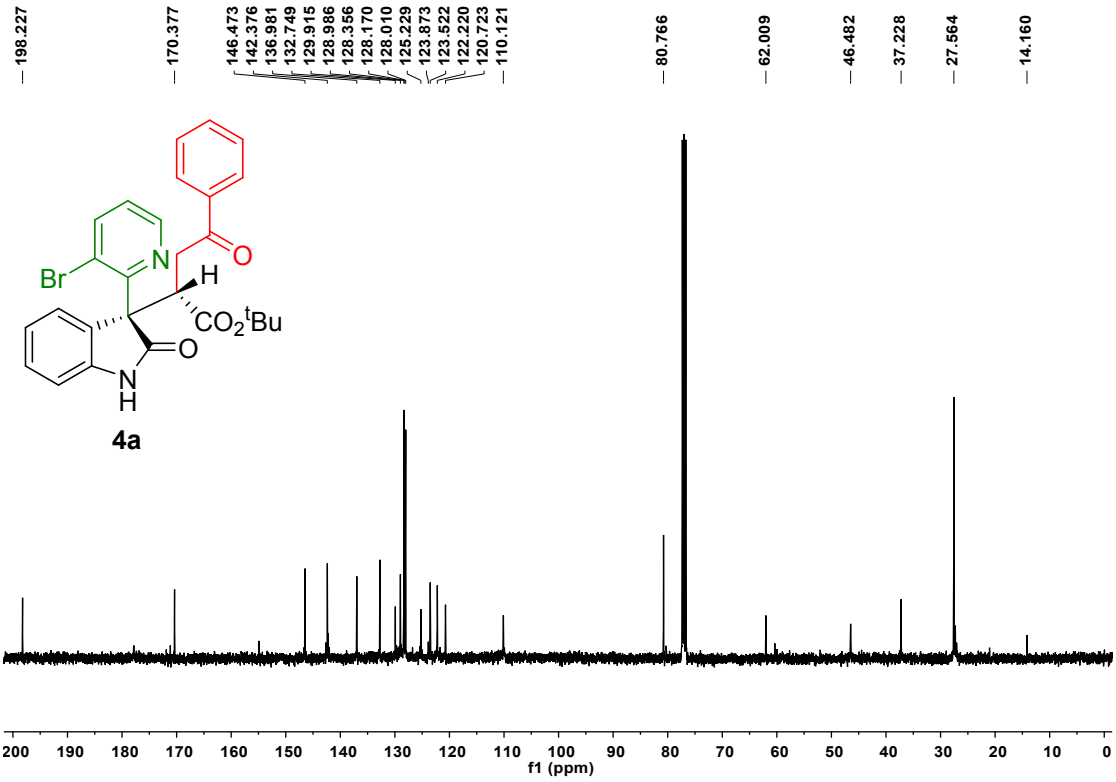
	Retention Time	Area	% Area
1	25.101	10902415	45.42
2	29.102	10504366	43.76
3	32.104	1314010	5.47
4	41.716	1285255	5.35

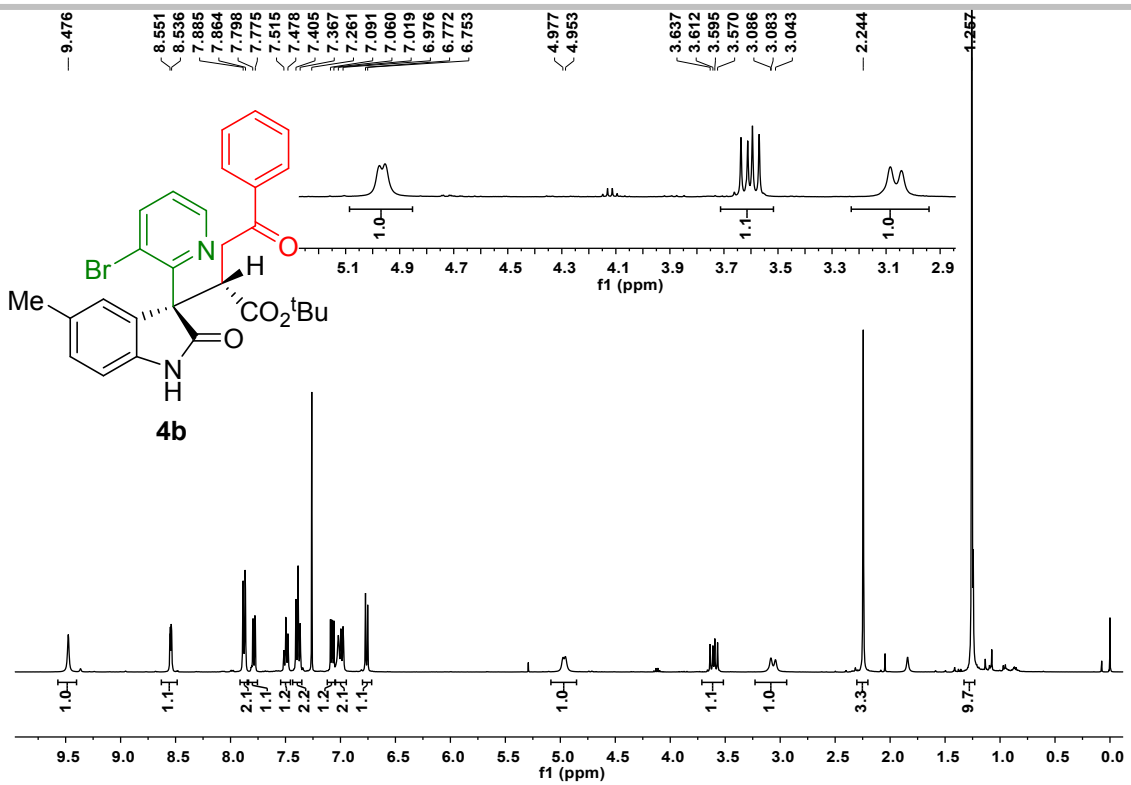


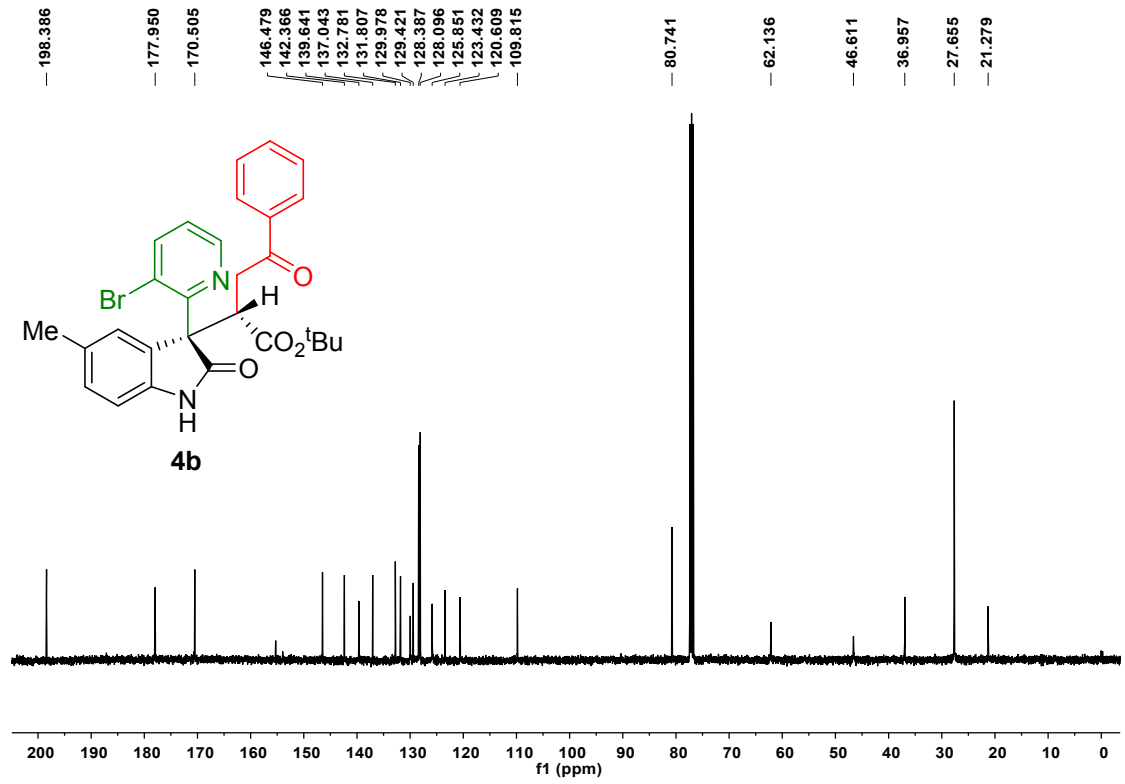
	Retention Time	Area	% Area
1	26.068	14613516	84.60
2	31.383	56267	0.33
3	32.381	2071556	11.99
4	39.482	533257	3.09

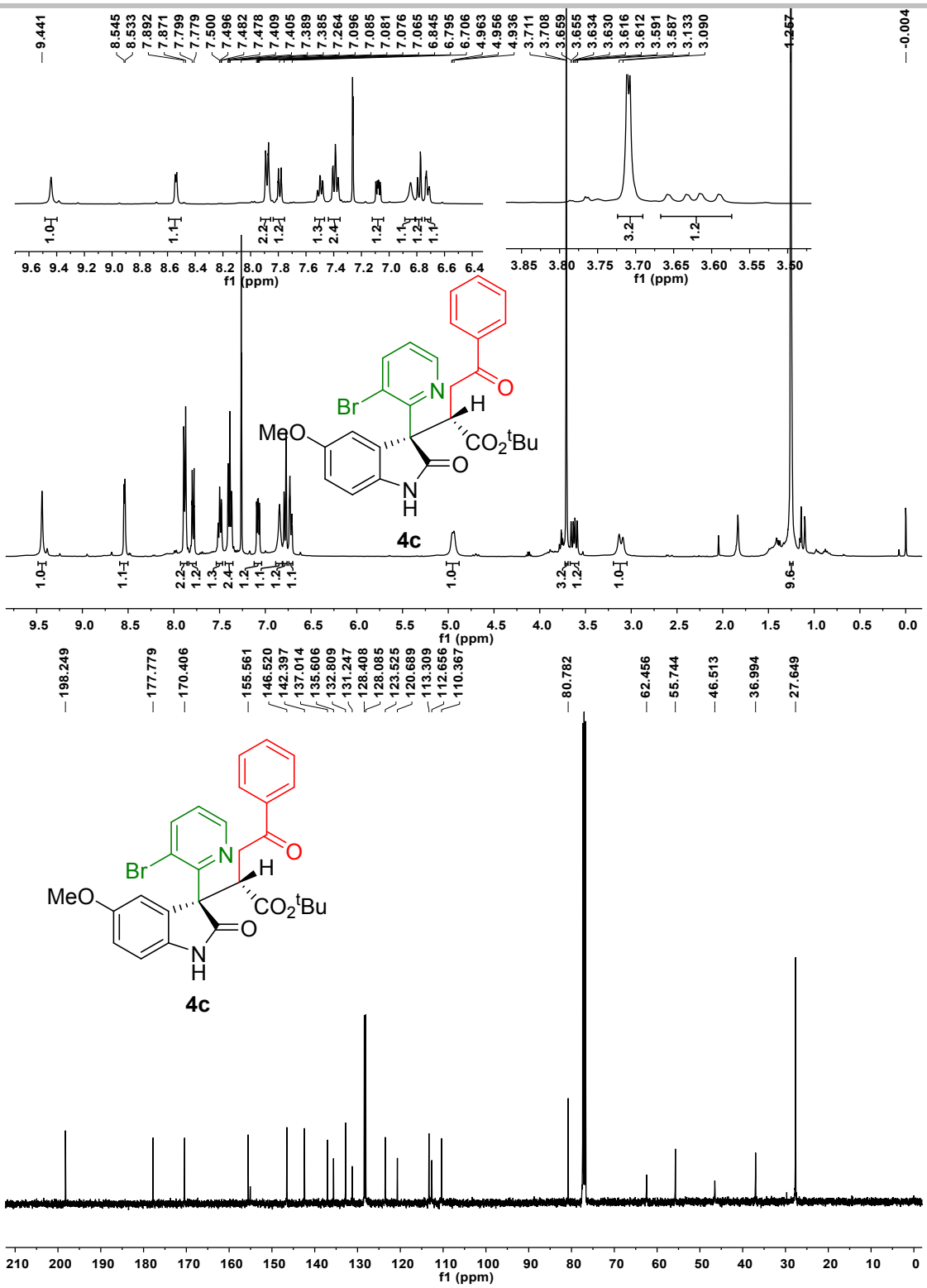
(J) Copies of NMR spectra for the reaction products.

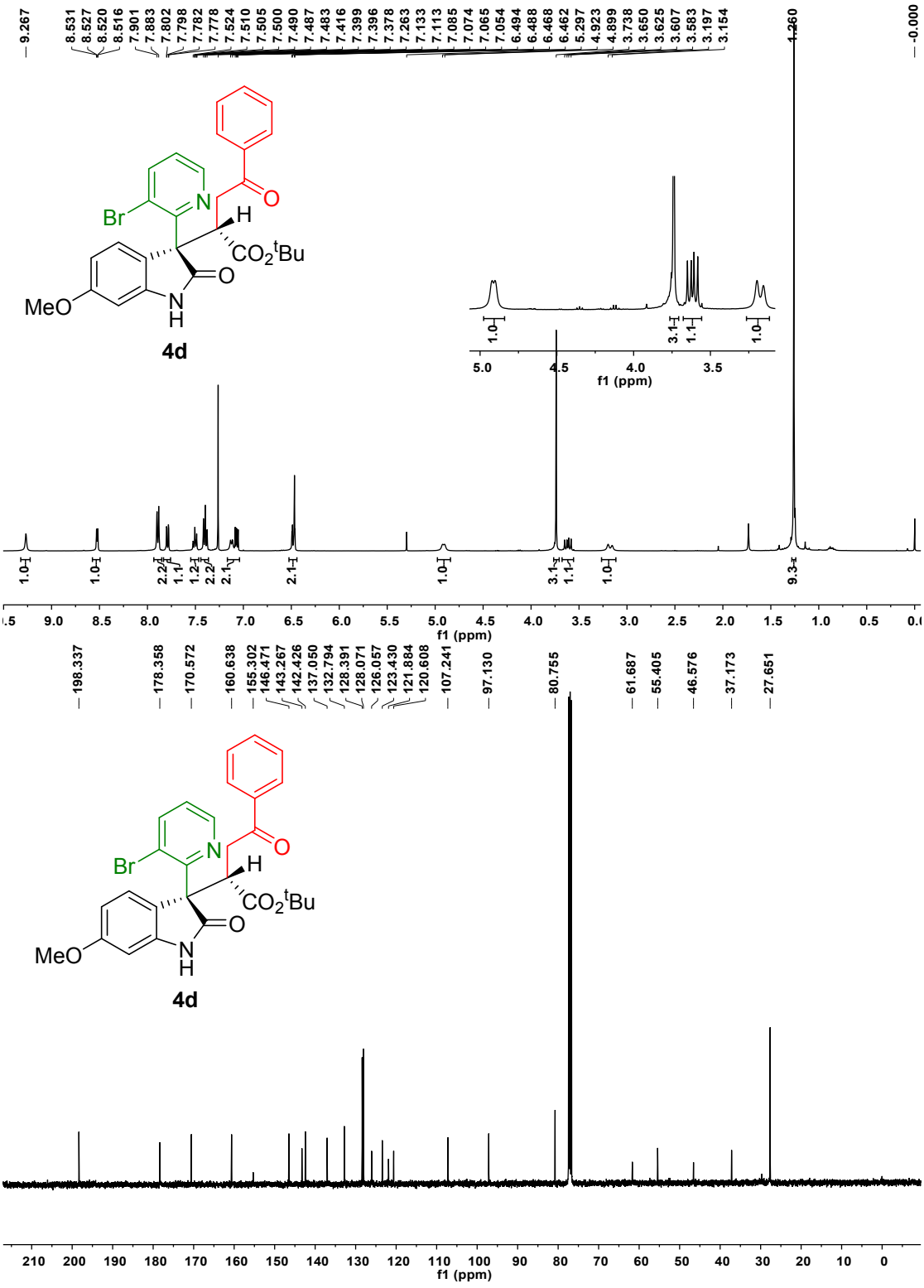


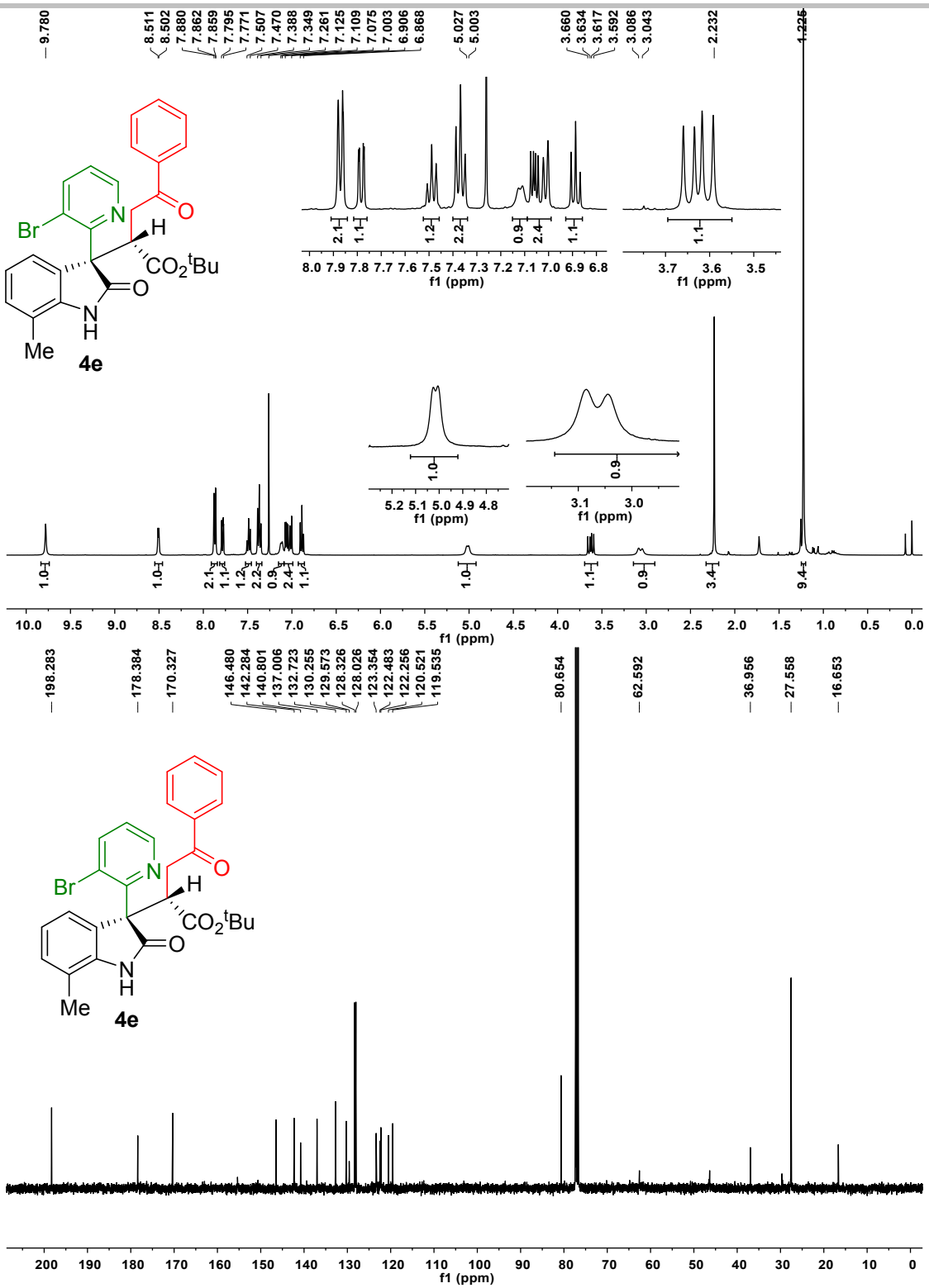


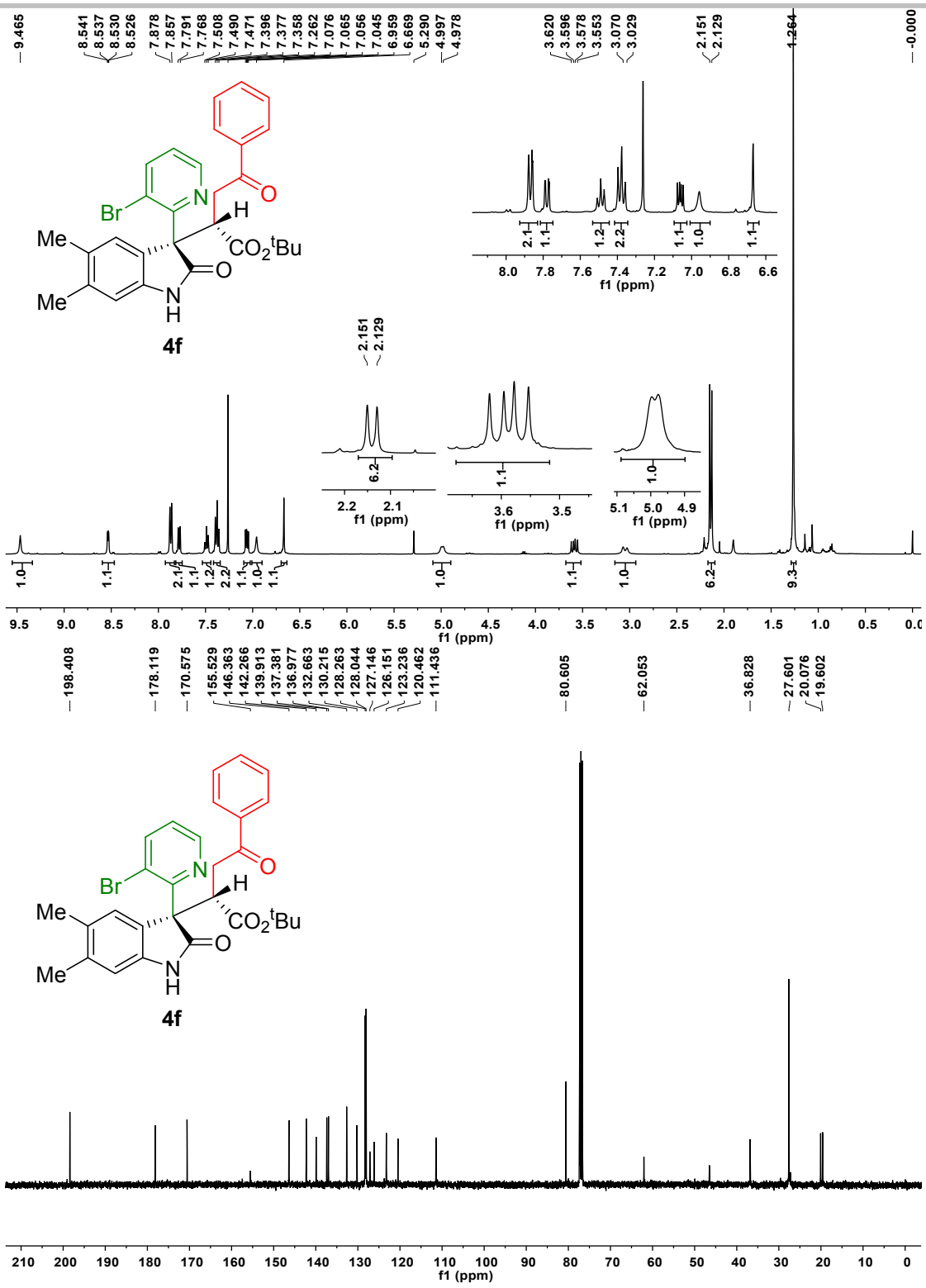

9.476
8.551
8.536
7.885
7.864
7.798
7.775
7.515
7.478
7.405
7.367
7.261
7.091
7.060
7.019
6.976
6.772
6.753
4.977
4.953
3.637
3.612
3.595
3.570
3.086
3.083
3.043
2.244
1.267
Br
N
H
O
Me
CO2tBu
O
N
H
4b
f1 (ppm)
f1 (ppm)

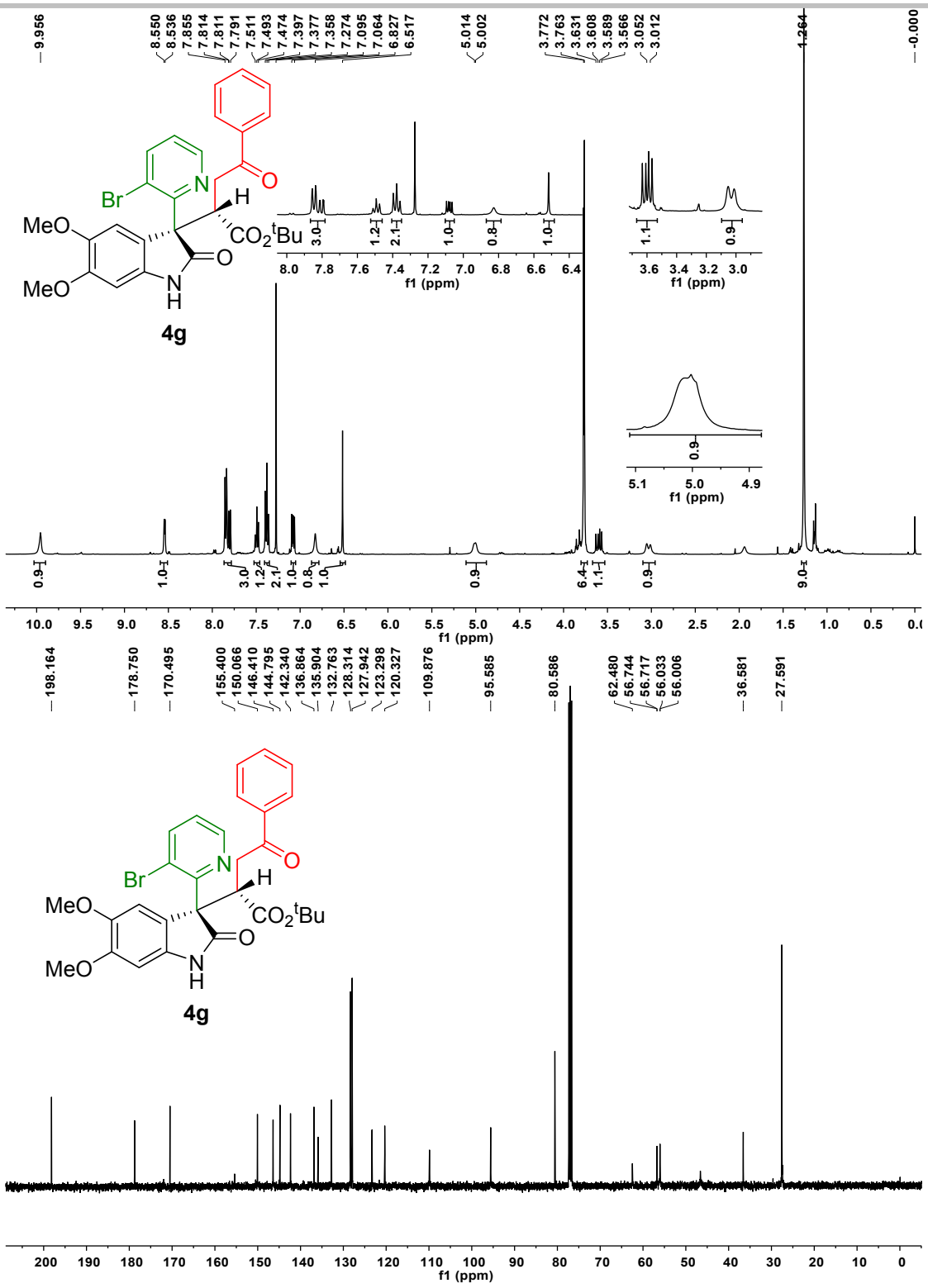

198.386
177.950
170.505
146.479
142.366
139.641
137.043
132.781
131.807
129.978
129.421
128.387
128.096
125.851
123.432
120.609
109.815
80.741
62.136
46.611
36.957
27.655
21.279
Br
N
H
O
Me
CO2tBu
O
N
H
4b
f1 (ppm)

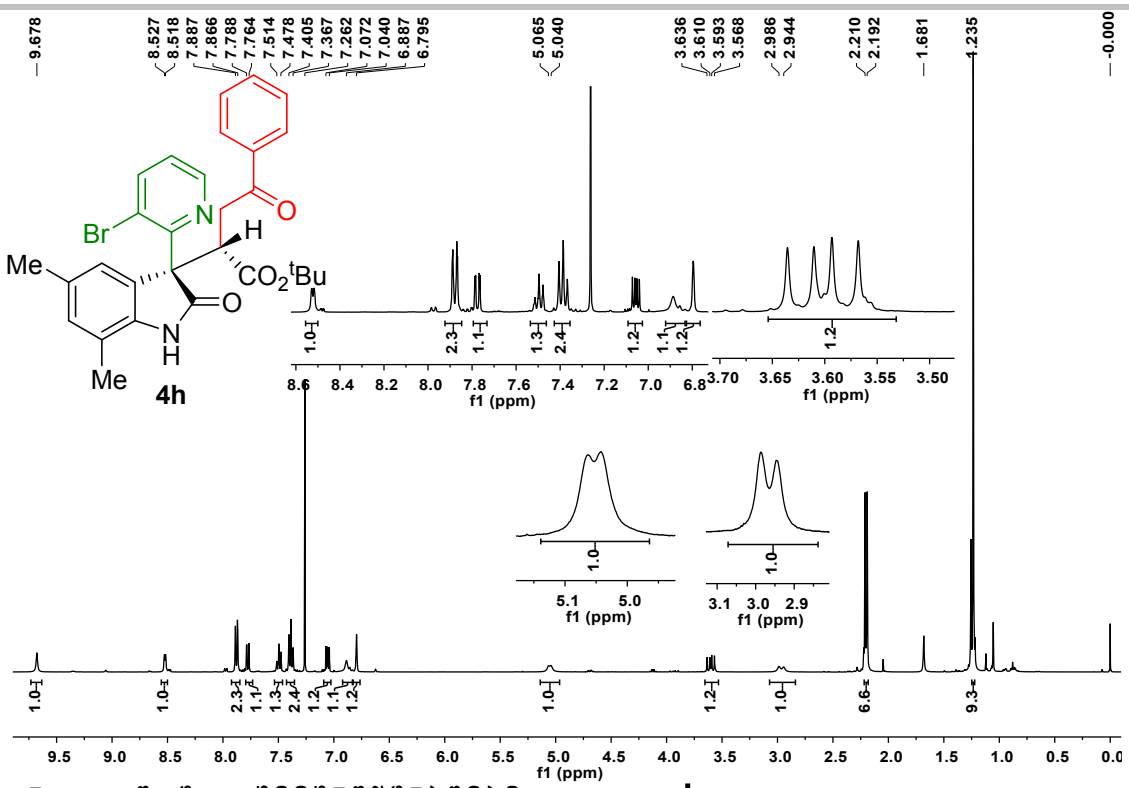

9.441
8.545
8.533
7.892
7.871
7.799
7.779
7.500
7.496
7.482
7.478
7.409
7.405
7.389
7.385
7.264
7.096
7.085
7.081
7.076
7.065
6.845
6.795
6.706
4.963
4.956
4.936
3.711
3.708
3.659
3.655
3.634
3.630
3.616
3.612
3.591
3.587
3.133
3.090
1.257
-0.004
f1 (ppm)
Br
N
O
H
MeO
CO2tBu
O
N
H
4c
198.249
177.779
170.406
155.561
146.520
142.397
137.014
135.606
132.809
131.247
128.408
128.085
123.525
120.689
113.309
112.656
110.367
80.782
62.456
55.744
46.513
36.994
27.649
f1 (ppm)

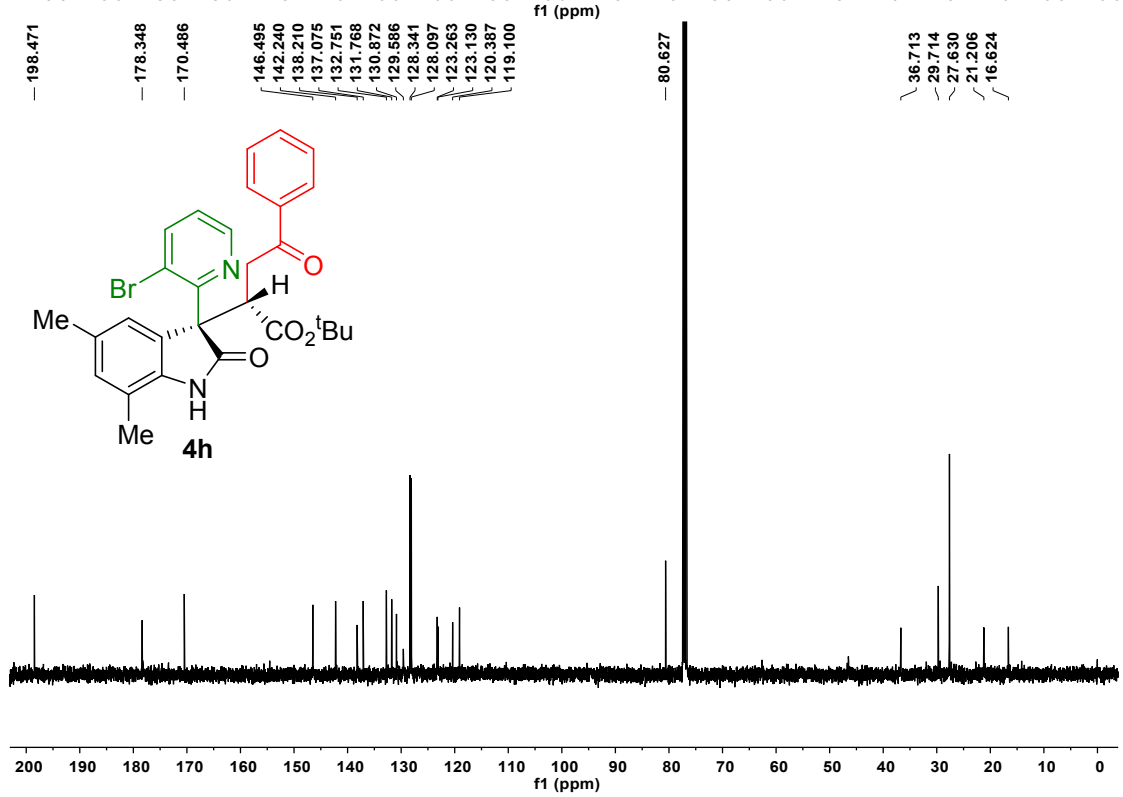

9.267
8.531
8.527
8.520
8.516
7.901
7.883
7.802
7.798
7.782
7.778
7.524
7.510
7.505
7.500
7.490
7.487
7.483
7.416
7.399
7.396
7.378
7.263
7.133
7.113
7.085
7.074
7.065
7.054
6.494
6.488
6.468
6.462
5.297
4.923
4.899
3.738
3.650
3.625
3.607
3.583
3.197
3.154
1.260
-0.000
Br
N
O
H
CO2tBu
O
MeO
N
H
4d
1.0
3.1
1.1
1.0
5.0
4.5
4.0
3.5
f1 (ppm)
1.0
1.0
2.2
1.1
1.2
2.2
2.1
2.1
1.0
3.1
1.1
1.0
9.3
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
f1 (ppm)
198.337
178.358
170.572
160.638
155.302
146.471
143.267
142.426
137.050
132.794
128.391
128.071
126.057
123.430
121.884
120.608
107.241
97.130
80.755
61.687
55.405
46.576
37.173
27.651
Br
N
O
H
CO2tBu
O
MeO
N
H
4d
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

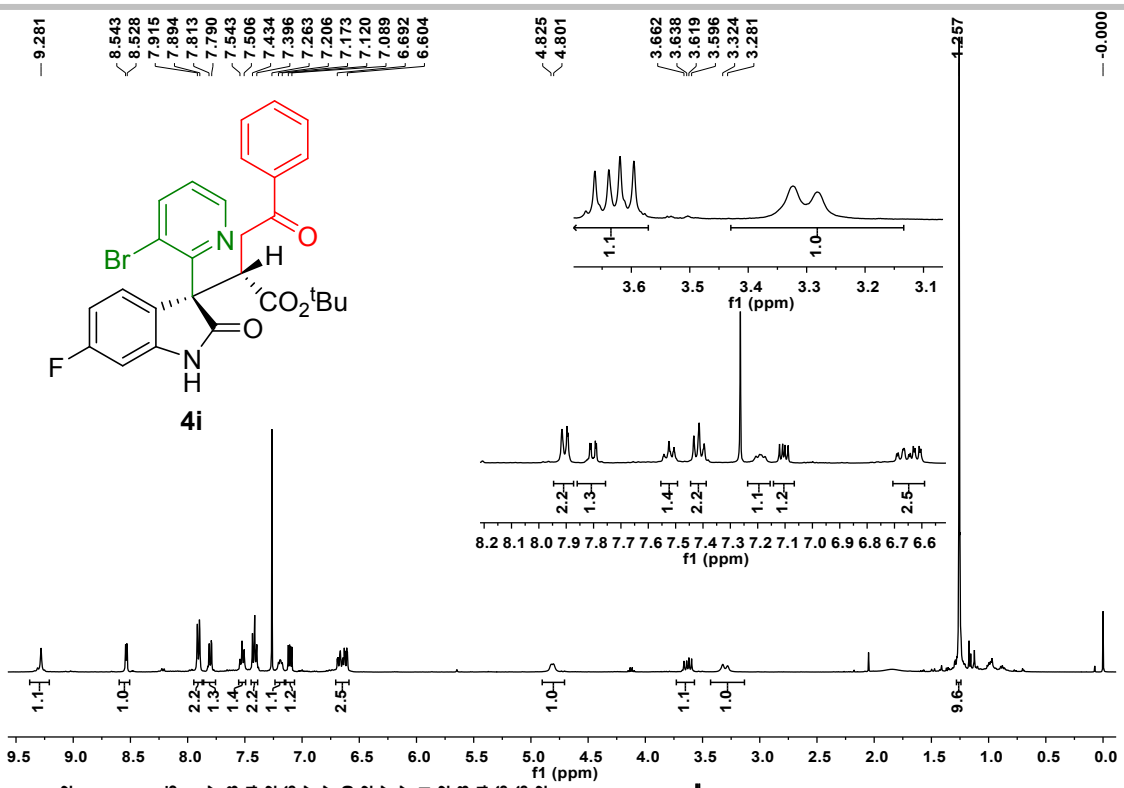

9.780
8.511
8.502
7.880
7.862
7.859
7.795
7.771
7.507
7.470
7.388
7.349
7.261
7.125
7.109
7.075
7.003
6.906
6.868
5.027
5.003
3.660
3.634
3.617
3.592
3.086
3.043
2.232
1.235
Br
N
O
H
CO2tBu
O
N
H
Me
4e
f1 (ppm)
198.283
178.384
170.327
146.480
142.284
140.801
137.006
132.723
130.255
129.573
128.326
128.026
123.354
122.483
122.256
120.521
119.535
80.654
62.592
36.956
27.558
16.653

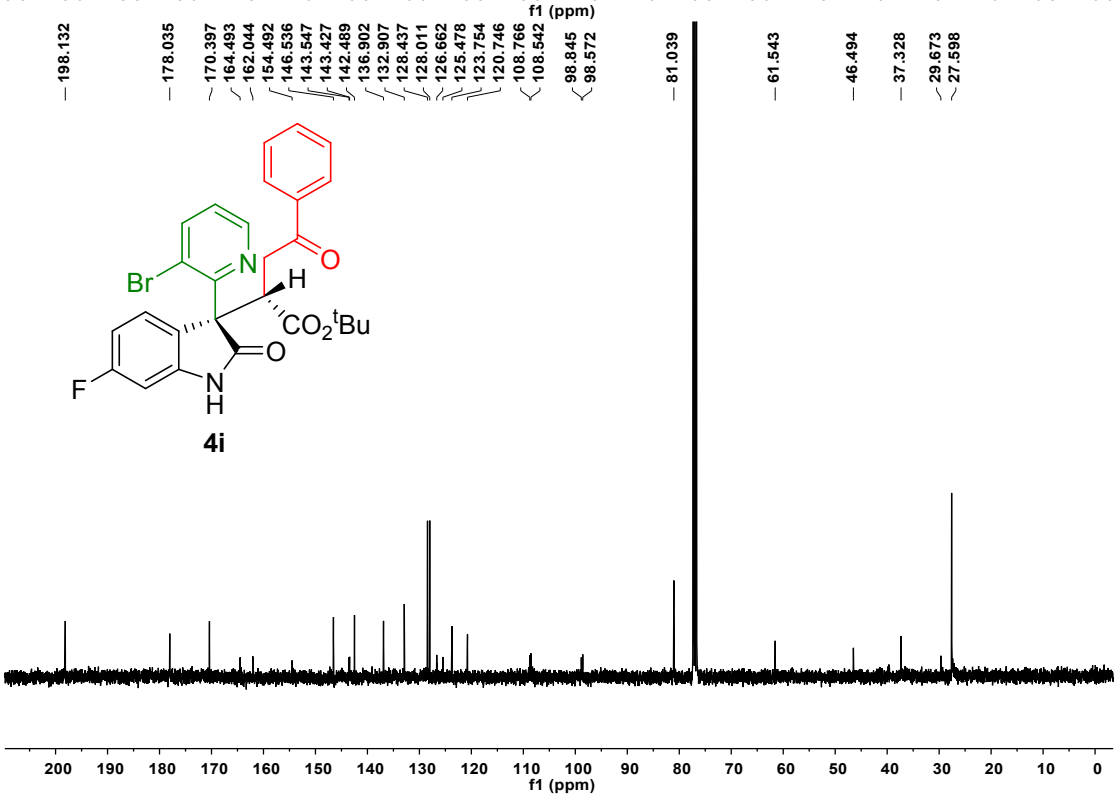

9.465
8.541
8.537
8.530
8.526
7.878
7.857
7.791
7.768
7.508
7.490
7.471
7.396
7.377
7.358
7.262
7.076
7.065
7.056
7.045
6.959
6.669
5.290
4.997
4.978
3.620
3.596
3.578
3.553
3.070
3.029
2.151
2.129
1.264
-0.000
Br
N
O
H
Me
Me
CO2tBu
O
N
H
4f
f1 (ppm)
198.408
178.119
170.575
155.529
146.363
142.266
139.913
137.381
136.977
132.663
130.215
128.263
128.044
127.146
126.151
123.236
120.462
111.436
80.605
62.053
36.828
27.601
20.076
19.602

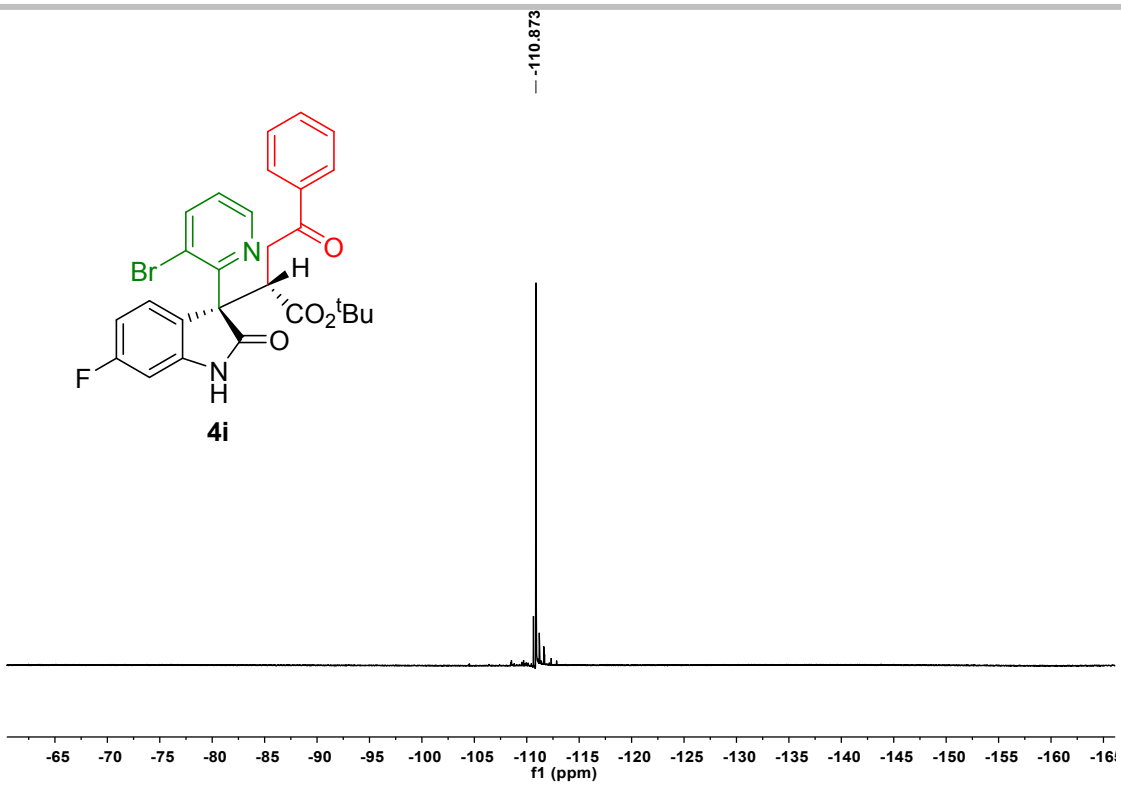

9.956
8.550
8.536
7.855
7.814
7.811
7.791
7.511
7.493
7.474
7.397
7.377
7.358
7.274
7.095
7.064
6.827
6.517
5.014
5.002
3.772
3.763
3.631
3.608
3.589
3.566
3.052
3.012
1.264
-0.000
Br
N
O
H
MeO
MeO
CO2tBu
O
N
H
4g
f1 (ppm)
198.164
178.750
170.495
155.400
150.066
146.410
144.795
142.340
136.864
135.904
132.763
128.314
127.942
123.298
120.327
109.876
95.585
80.586
62.480
56.744
56.717
56.033
56.006
36.581
27.591


9.678
8.527
8.518
7.887
7.866
7.788
7.764
7.514
7.478
7.405
7.367
7.262
7.072
7.040
6.887
6.795
5.065
5.040
3.636
3.610
3.593
3.568
2.986
2.944
2.210
2.192
1.681
1.235
-0.000
Br
N
O
H
Me
CO2tBu
O
N
H
Me
4h
f1 (ppm)

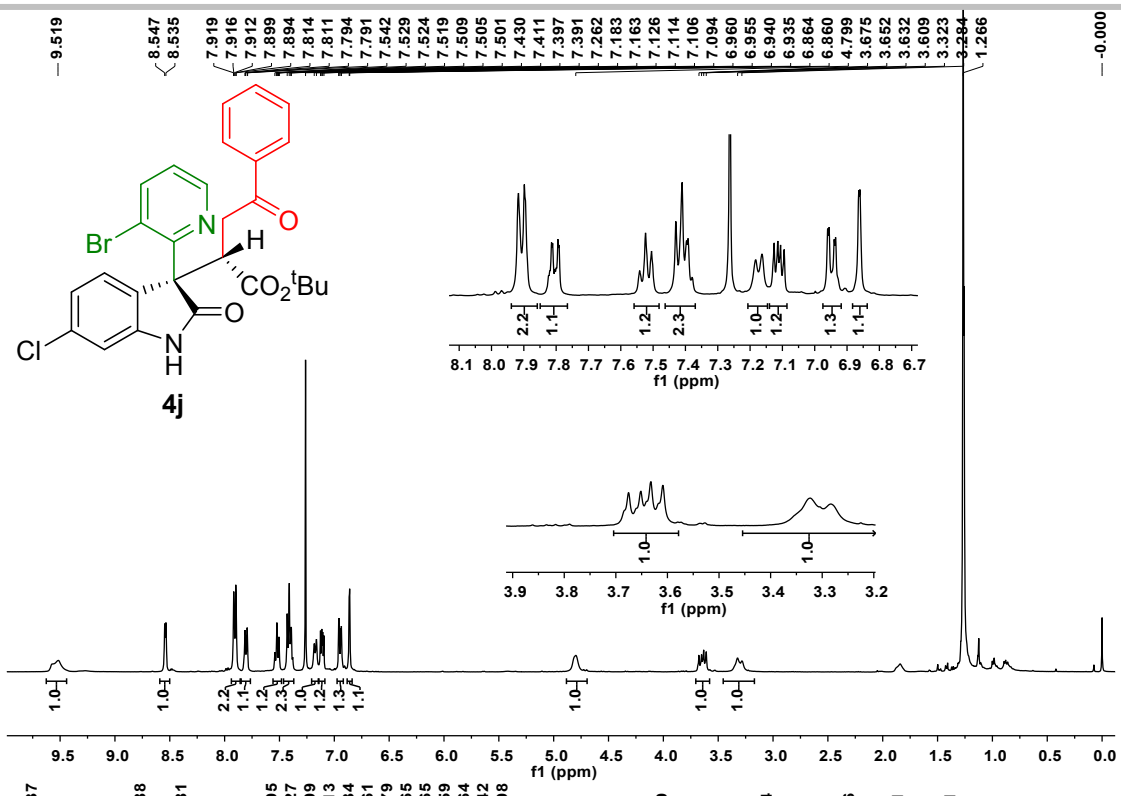

198.471
178.348
170.486
146.495
142.240
138.210
137.075
132.751
131.768
130.872
129.586
128.341
128.097
123.263
123.130
120.387
119.100
80.627
36.713
29.714
27.630
21.206
16.624
Br
N
O
H
Me
CO2tBu
O
N
H
Me
4h
f1 (ppm)

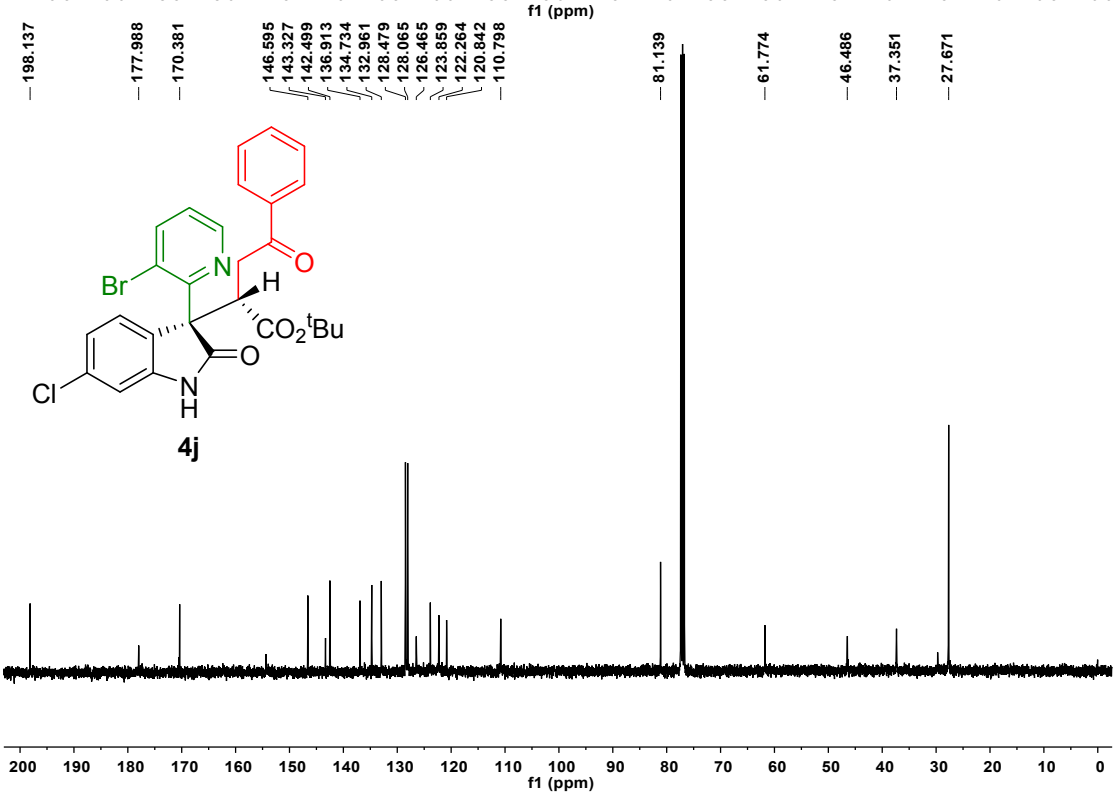

9.281
8.543
8.528
7.915
7.894
7.813
7.790
7.543
7.506
7.434
7.396
7.263
7.206
7.173
7.120
7.089
6.692
6.604
4.825
4.801
3.662
3.638
3.619
3.596
3.324
3.281
1.257
0.000
Br
N
O
H
CO2tBu
O
N
H
F
4i
f1 (ppm)

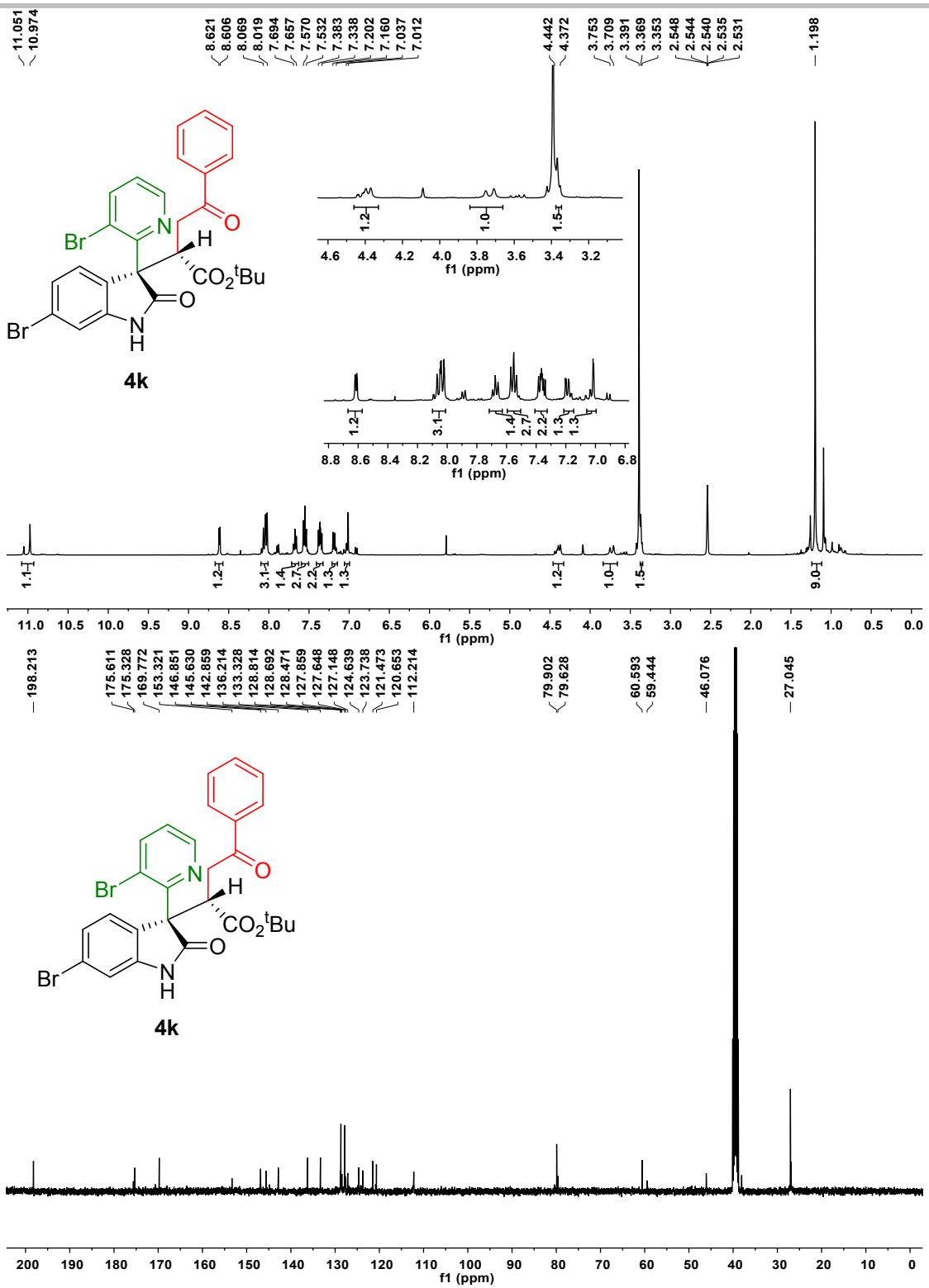

198.132
178.035
170.397
164.493
162.044
154.492
146.536
143.547
143.427
142.489
136.902
132.907
128.437
128.011
126.662
125.478
123.754
120.746
108.766
108.542
98.845
98.572
81.039
61.543
46.494
37.328
29.673
27.598
Br
N
O
H
CO2tBu
O
N
H
F
4i
f1 (ppm)

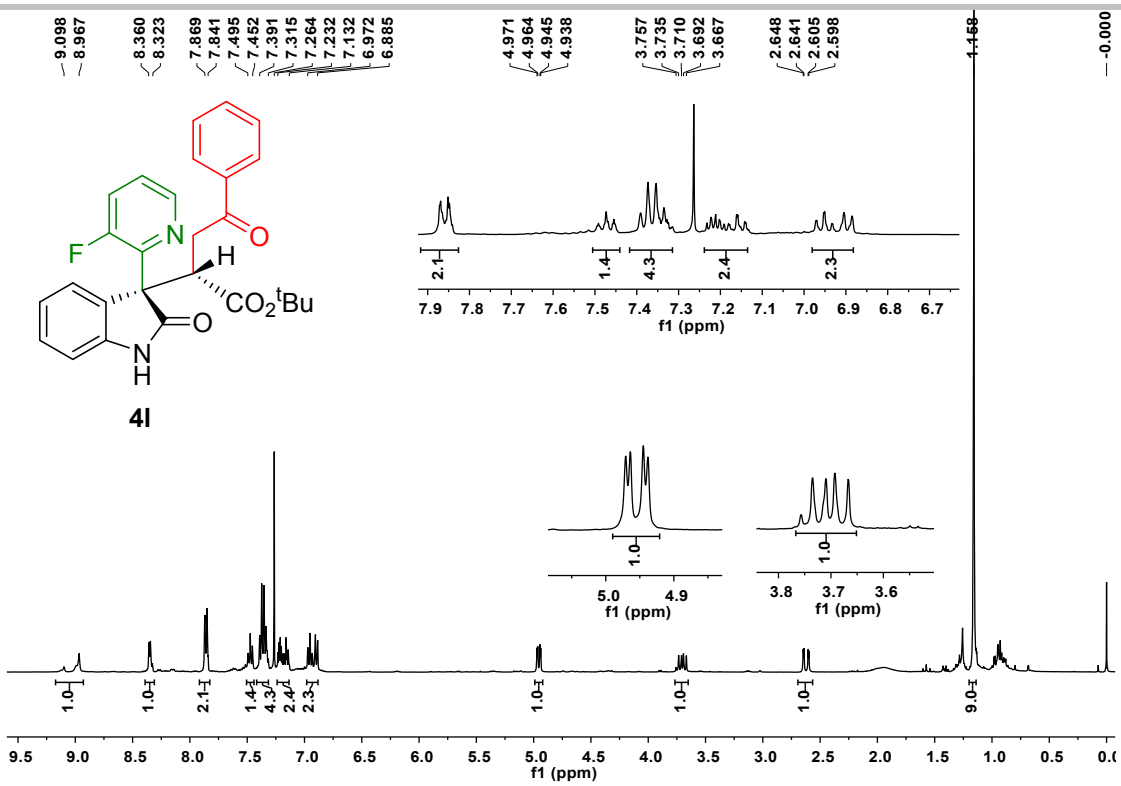

-110.873
Br
N
O
H
CO2tBu
O
F
N
H
-65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160
f1 (ppm)

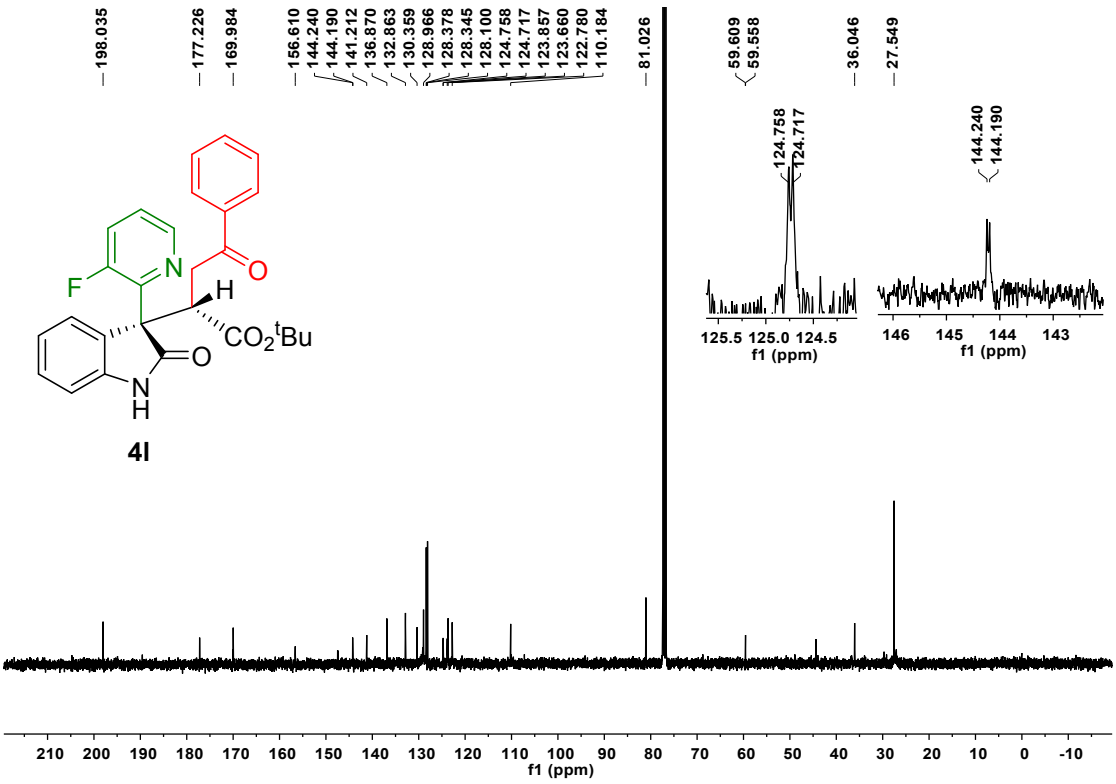
4i

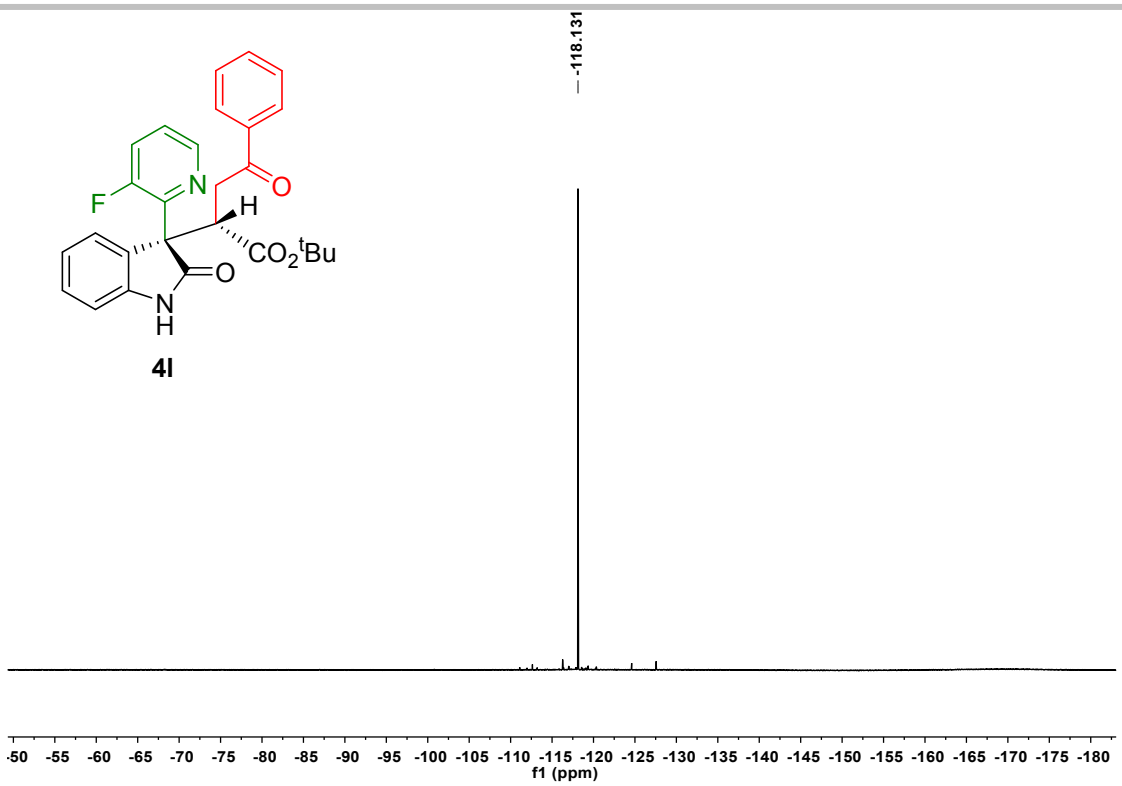

9.519
8.547
8.535
7.919
7.916
7.912
7.899
7.894
7.814
7.811
7.794
7.791
7.542
7.529
7.524
7.519
7.509
7.505
7.501
7.430
7.411
7.397
7.391
7.262
7.183
7.163
7.126
7.114
7.106
7.094
6.960
6.955
6.940
6.935
6.864
6.860
4.799
3.675
3.652
3.632
3.609
3.323
3.284
1.266
-0.000
Br
N
O
H
CO2tBu
O
N
H
Cl
4j
f1 (ppm)
f1 (ppm)
f1 (ppm)


198.137
177.988
170.381
146.595
143.327
142.499
136.913
134.734
132.961
128.479
128.065
126.465
123.859
122.264
120.842
110.798
81.139
61.774
46.486
37.351
27.671
Br
N
O
H
CO2tBu
O
N
H
Cl
4j
f1 (ppm)

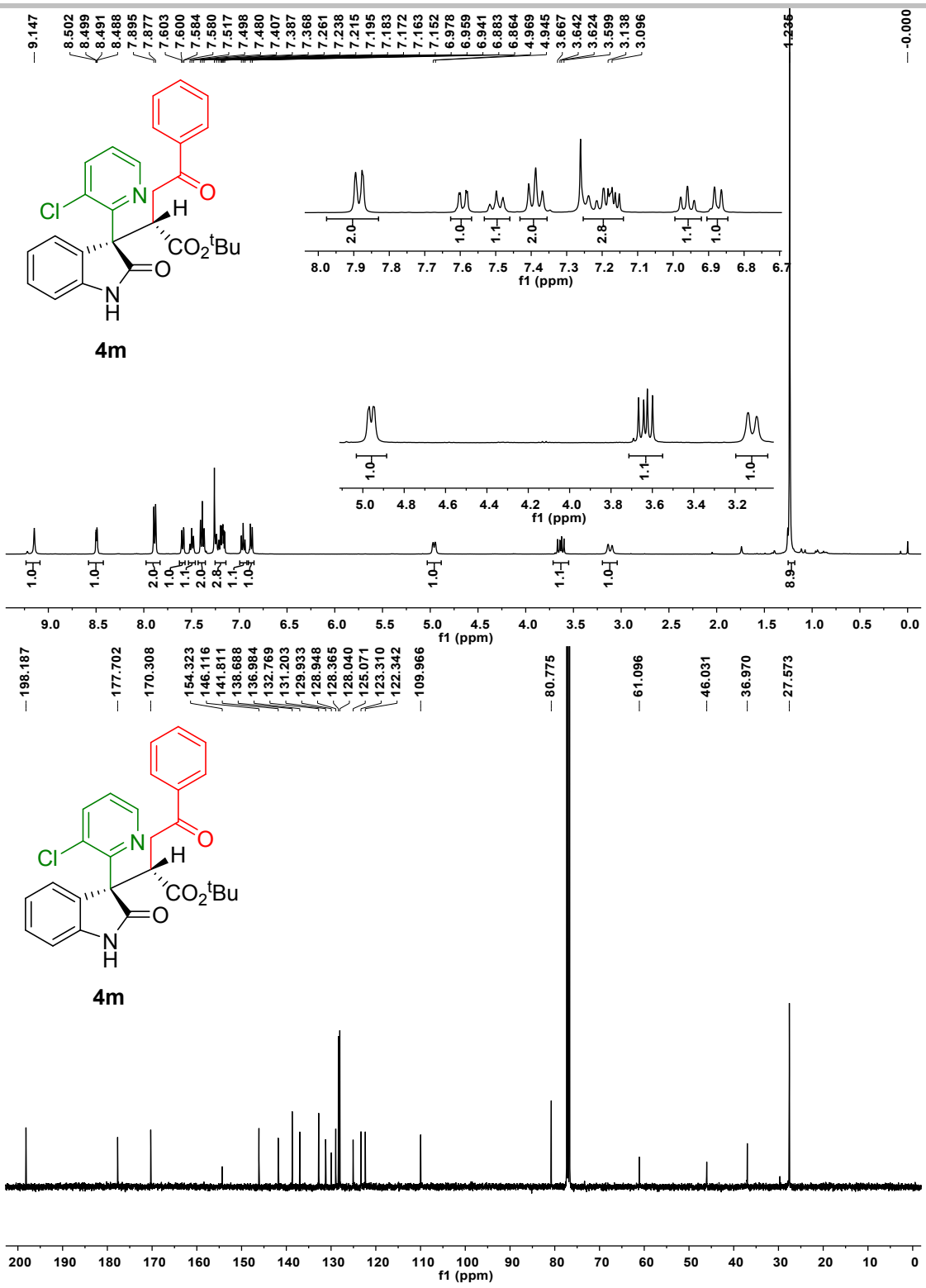

11.051
10.974
8.621
8.606
8.069
8.019
7.694
7.657
7.570
7.532
7.383
7.338
7.202
7.160
7.037
7.012
4.442
4.372
3.753
3.709
3.391
3.369
3.353
2.548
2.544
2.540
2.535
2.531
1.198
Br
N
H
O
CO2tBu
O
N
H
Br
4k
f1 (ppm)
198.213
175.611
175.328
169.772
153.321
146.851
145.630
142.859
136.214
133.328
128.814
128.692
128.471
127.859
127.648
127.148
124.639
123.738
121.473
120.653
112.214
79.902
79.628
60.593
59.444
46.076
27.045
4k
f1 (ppm)

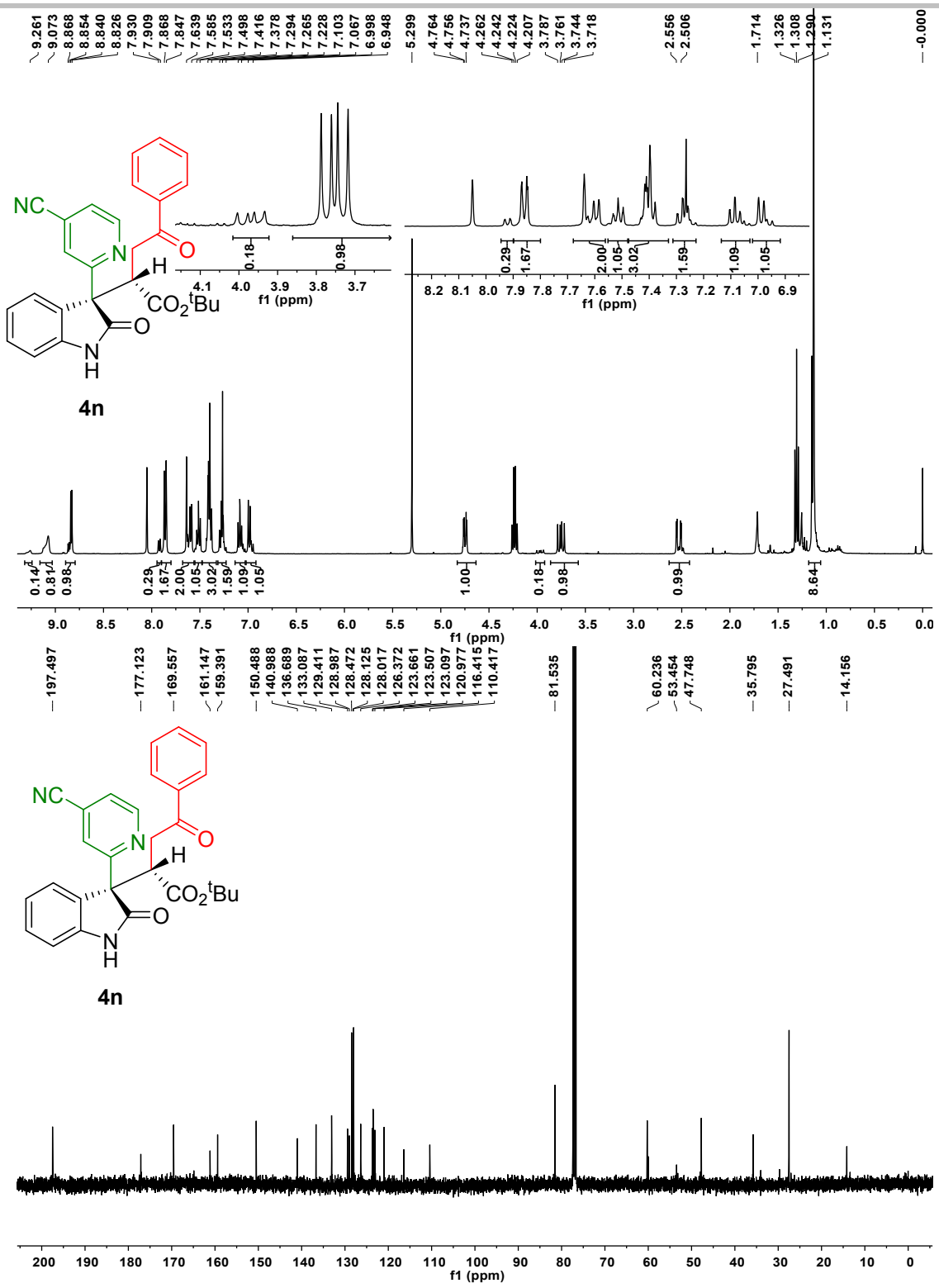

9.098
8.967
8.360
8.323
7.869
7.841
7.495
7.452
7.391
7.315
7.264
7.232
7.132
6.972
6.885
4.971
4.964
4.945
4.938
3.757
3.735
3.710
3.692
3.667
2.648
2.641
2.605
2.598
1.158
-0.000
F
N
O
H
CO2tBu
O
N
H
4l
f1 (ppm)

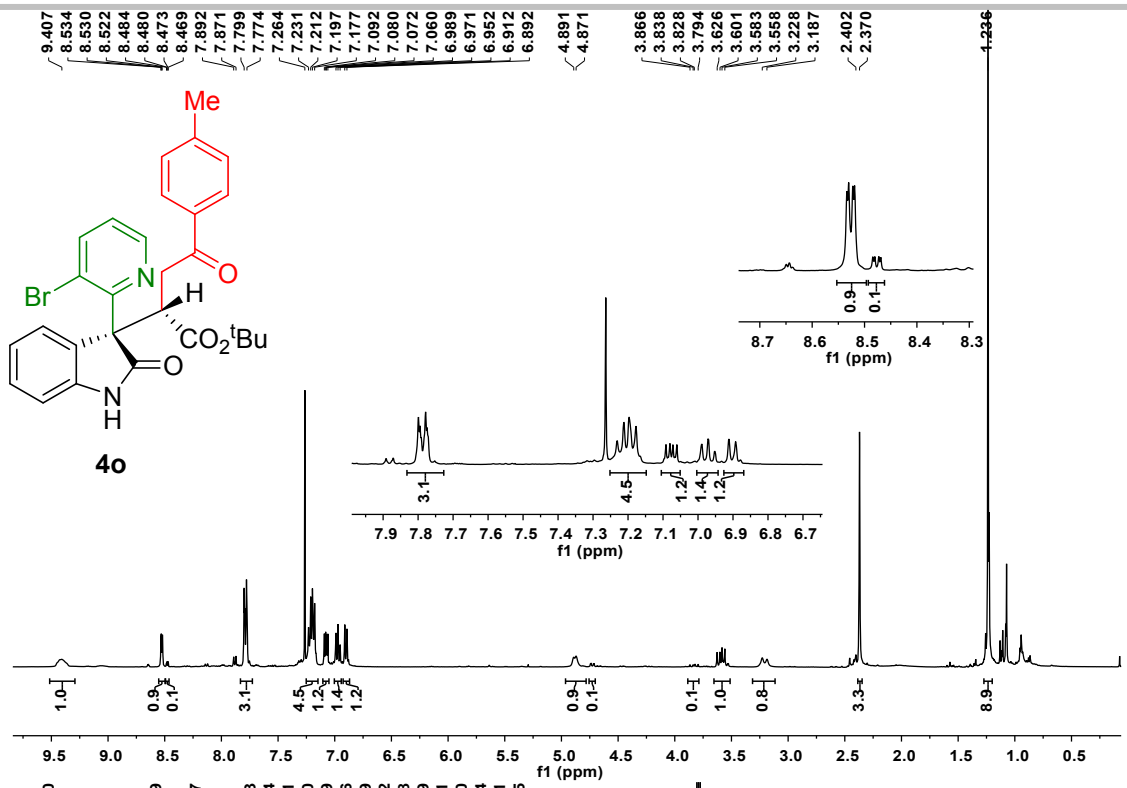

198.035
177.226
169.984
156.610
144.240
144.190
141.212
136.870
132.863
130.359
128.966
128.378
128.345
128.100
124.758
124.717
123.857
123.660
122.780
110.184
81.026
59.609
59.558
36.046
27.549
F
N
O
H
CO2tBu
O
N
H
4l
f1 (ppm)


-118.131
F
N
O
H
CO2tBu
O
N
H
-50 -55 -60 -65 -70 -75 -80 -85 -90 -95 -100 -105 -110 -115 -120 -125 -130 -135 -140 -145 -150 -155 -160 -165 -170 -175 -180
f1 (ppm)

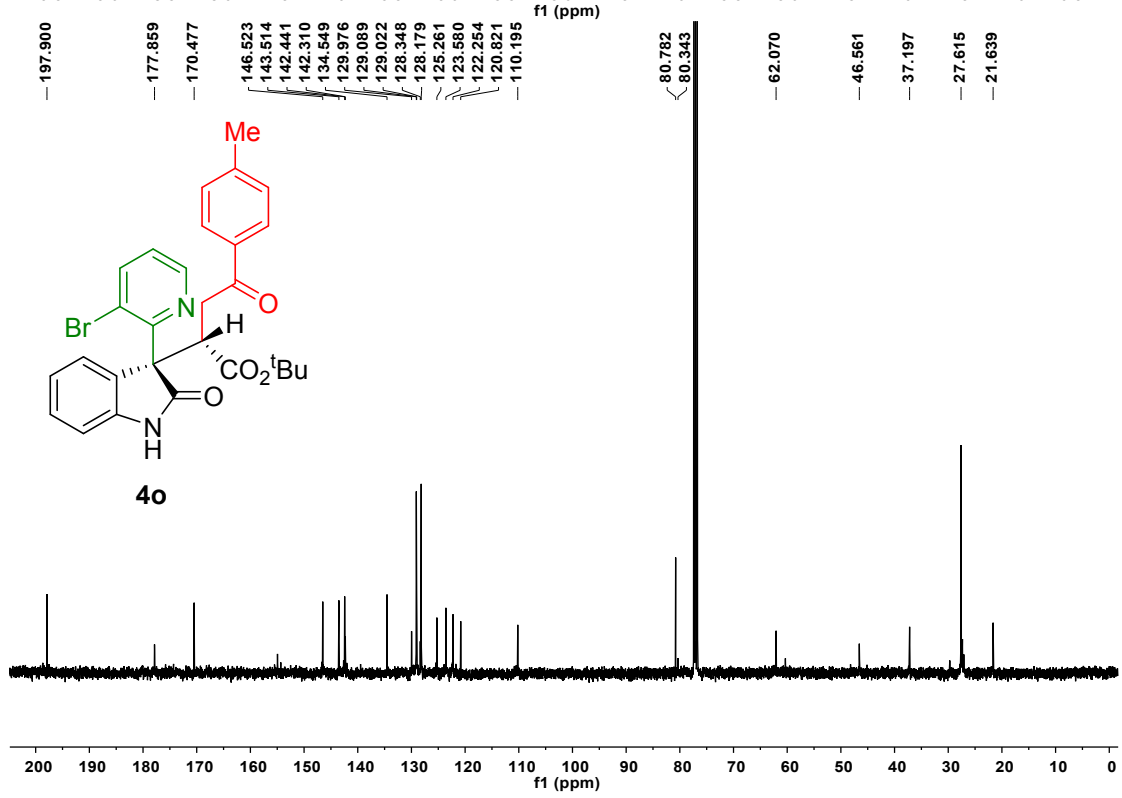
4l

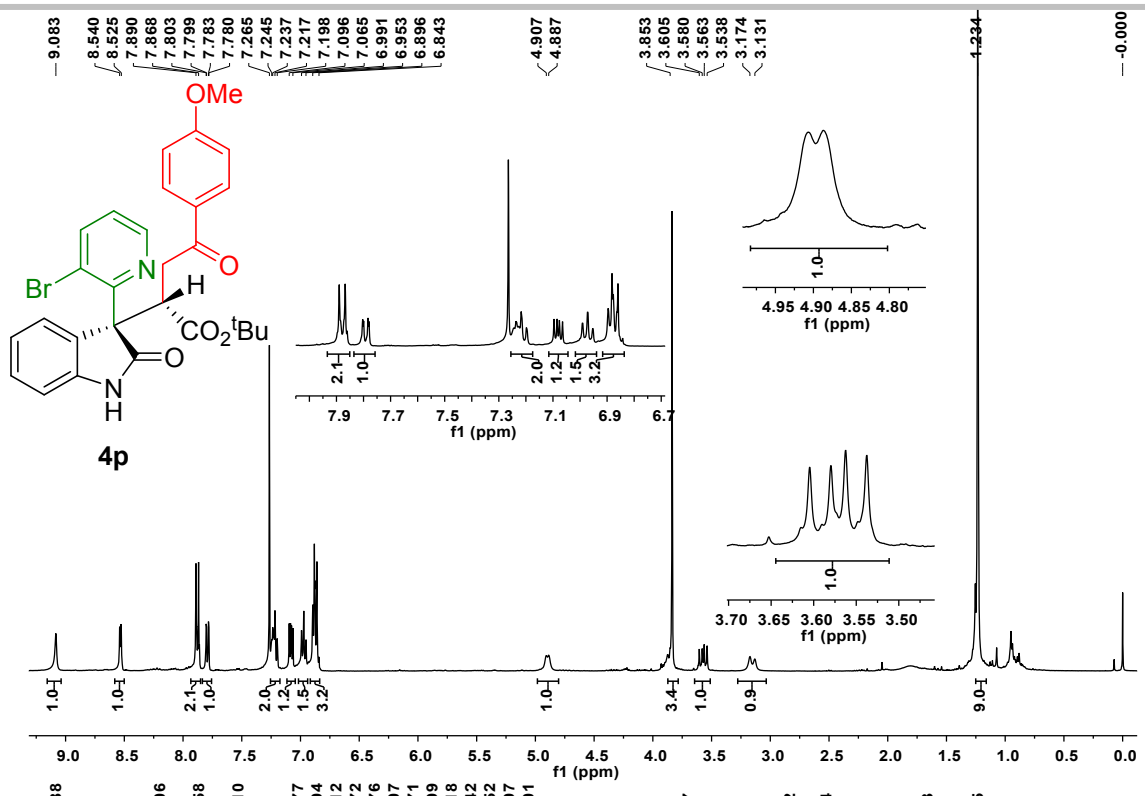

9.147
8.502
8.499
8.491
8.488
7.895
7.877
7.603
7.600
7.584
7.580
7.517
7.498
7.480
7.407
7.387
7.368
7.261
7.238
7.215
7.195
7.183
7.172
7.163
7.152
6.978
6.959
6.941
6.883
6.864
4.969
4.945
3.667
3.642
3.624
3.599
3.138
3.096
1.235
-0.000
Cl
N
O
H
CO2tBu
O
N
H
4m
f1 (ppm)
198.187
177.702
170.308
154.323
146.116
141.811
138.688
136.984
132.769
131.203
129.933
128.948
128.365
128.040
125.071
123.310
122.342
109.966
80.775
61.096
46.031
36.970
27.573
4m
f1 (ppm)

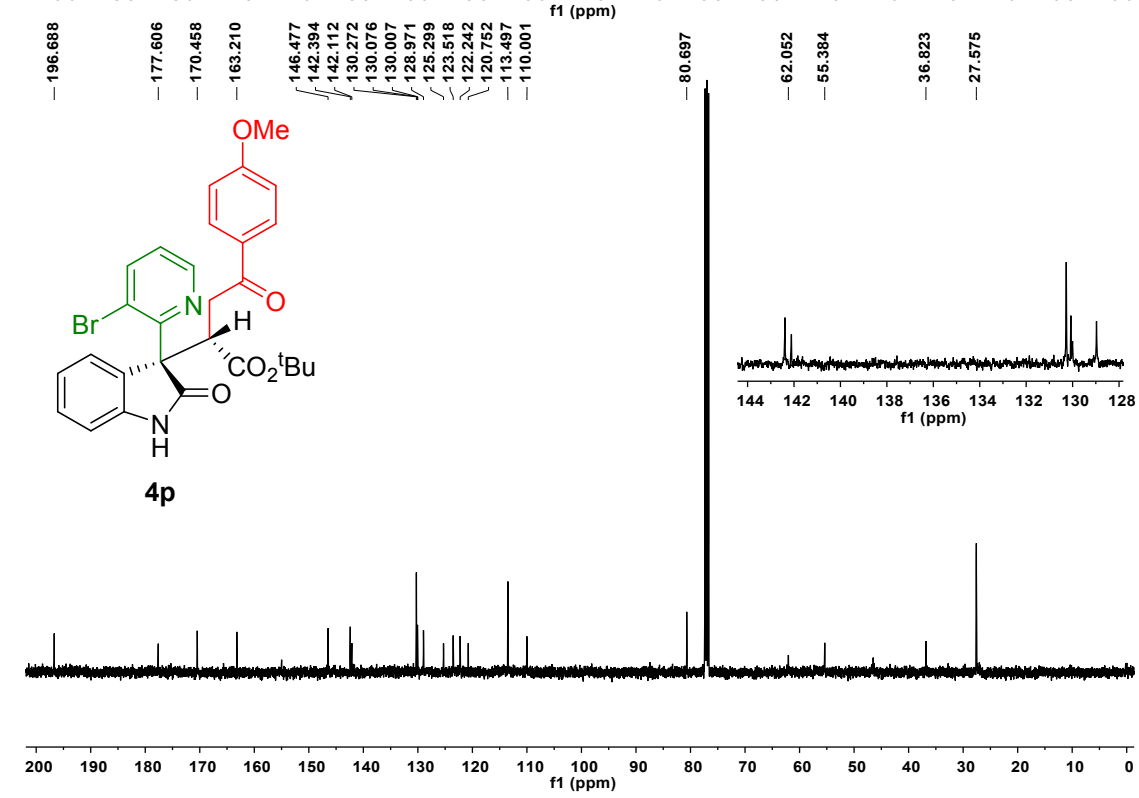

NC
N
O
H
CO2tBu
O
N
H
4n
f1 (ppm)
NC
N
O
H
CO2tBu
O
N
H
4n
f1 (ppm)

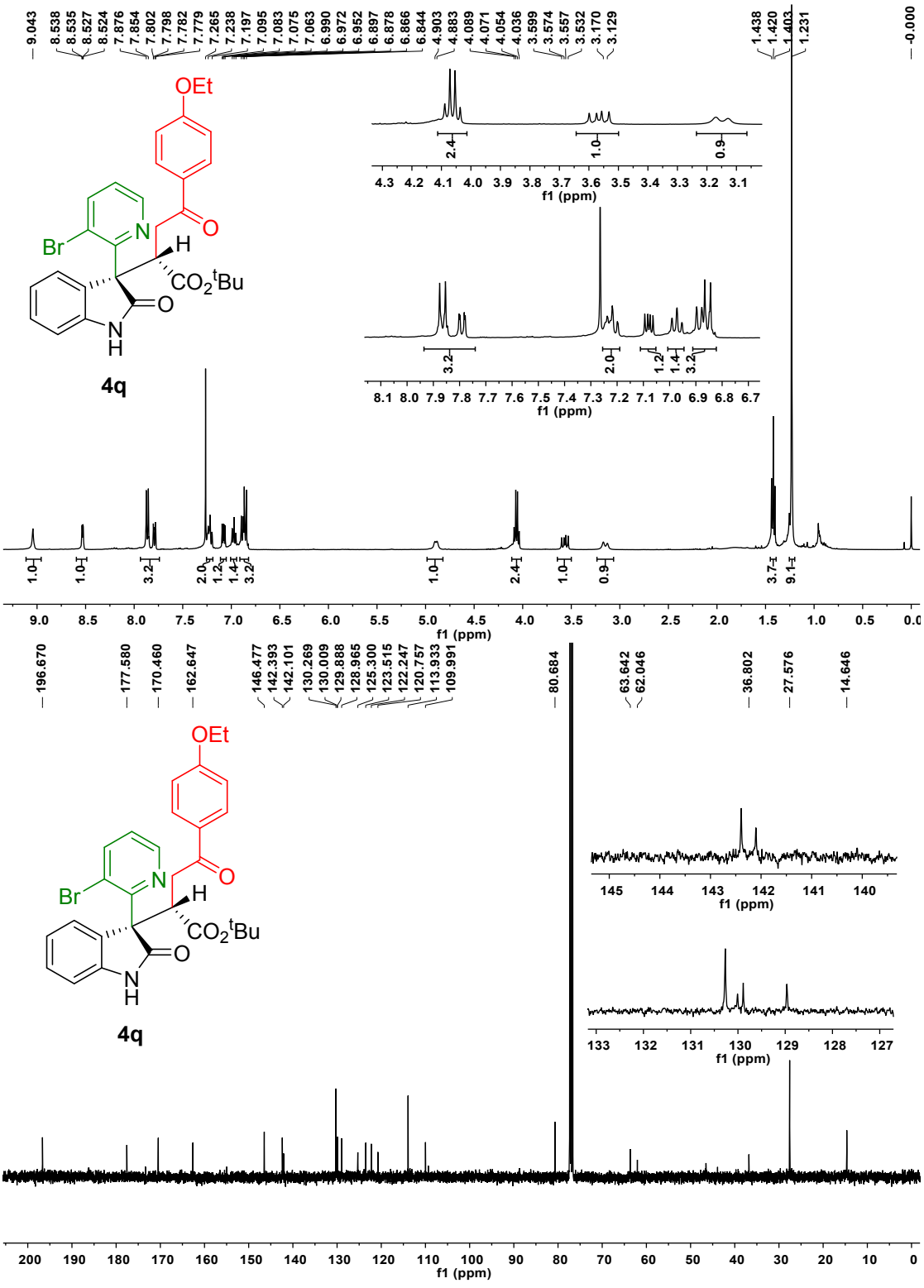

Me
Br
N
H
O
CO2tBu
O
N
H
4o

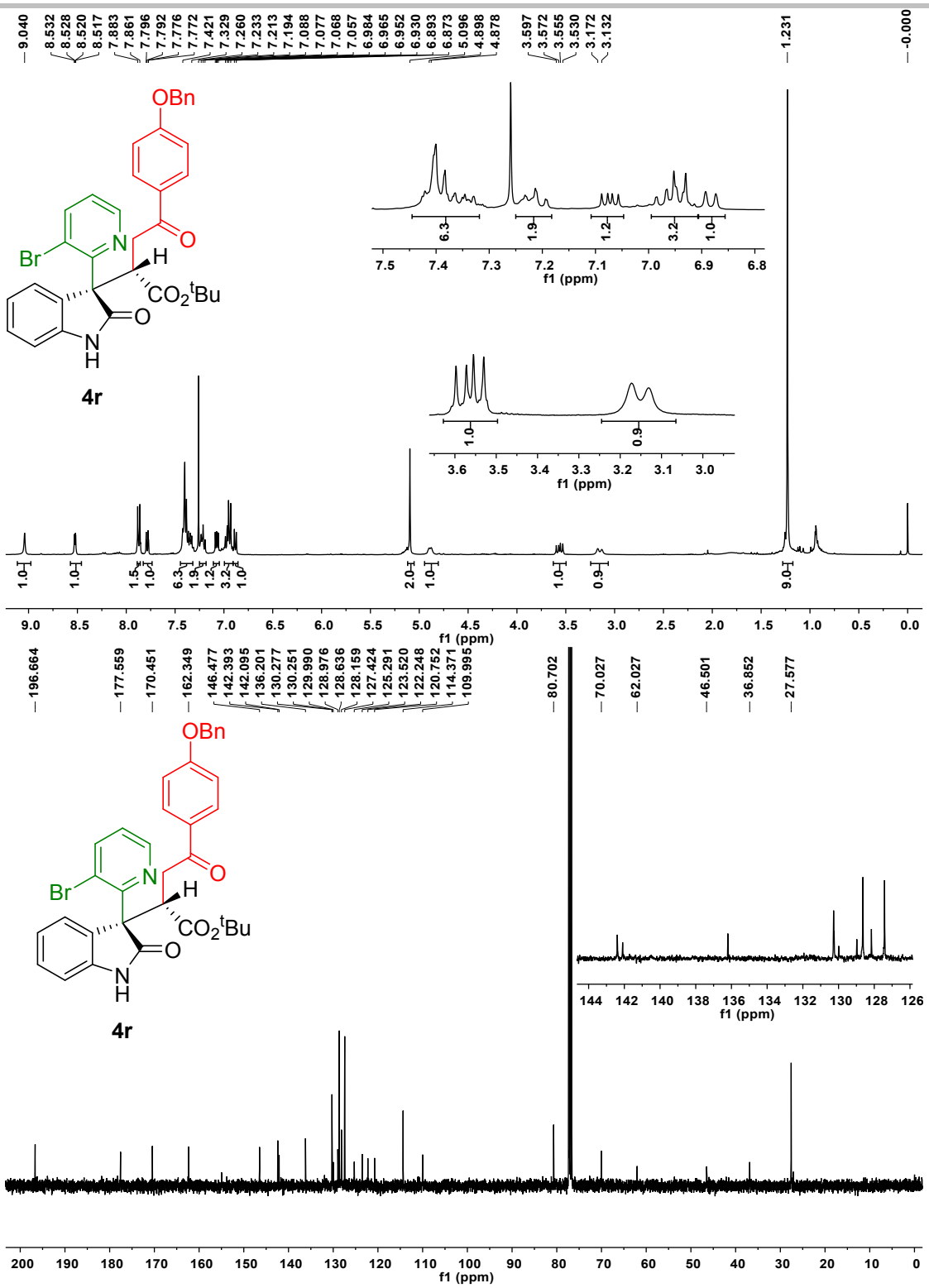
9.407
8.534
8.530
8.522
8.484
8.480
8.473
8.469
7.892
7.871
7.799
7.774
7.264
7.231
7.212
7.197
7.177
7.092
7.080
7.072
7.060
6.989
6.971
6.952
6.912
6.892
4.891
4.871
3.866
3.838
3.828
3.794
3.626
3.601
3.583
3.558
3.228
3.187
2.402
2.370
1.236
f1 (ppm)

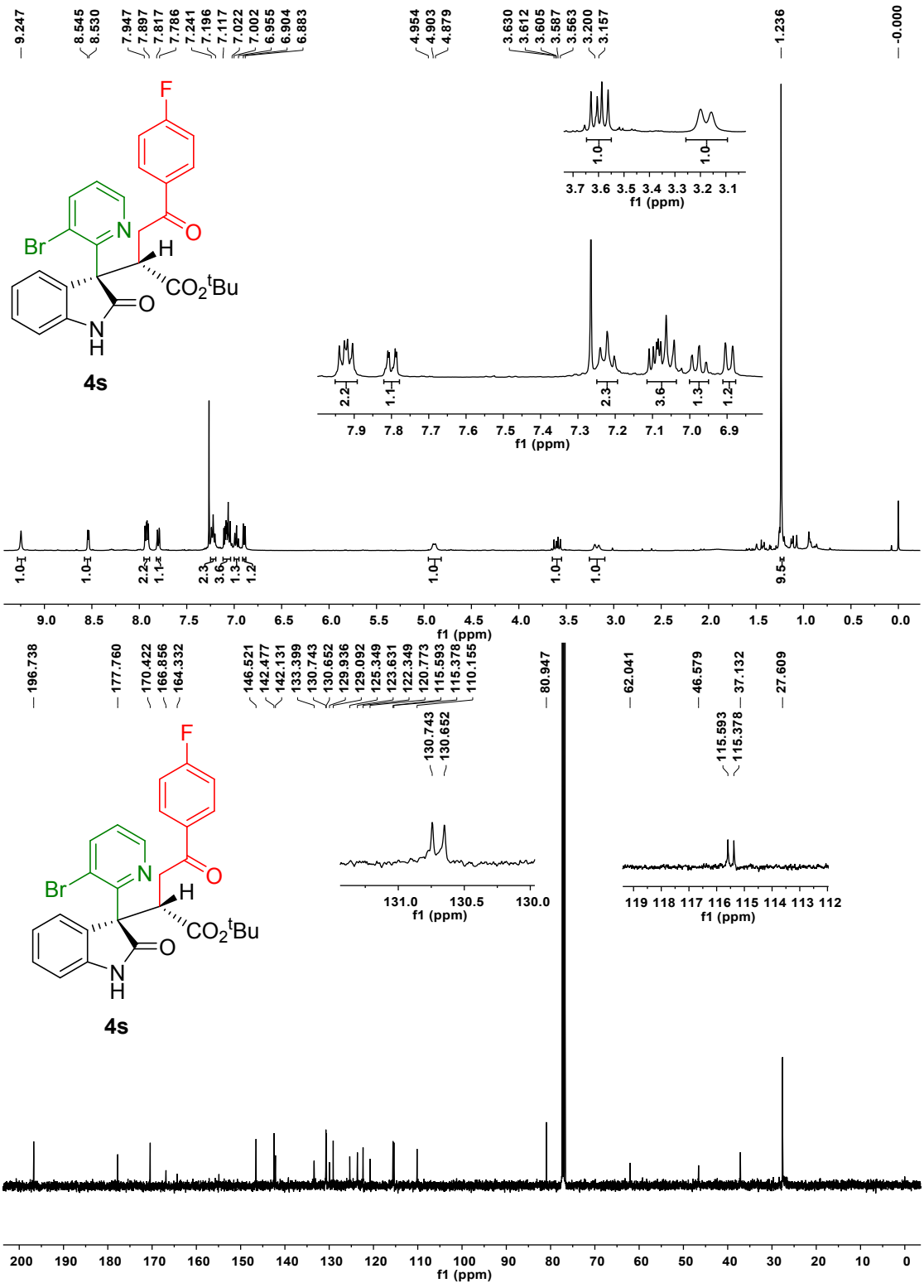

197.900
177.859
170.477
146.523
143.514
142.441
142.310
134.549
129.976
129.089
129.022
128.348
128.179
125.261
123.580
122.254
120.821
110.195
80.782
80.343
62.070
46.561
37.197
27.615
21.639
f1 (ppm)

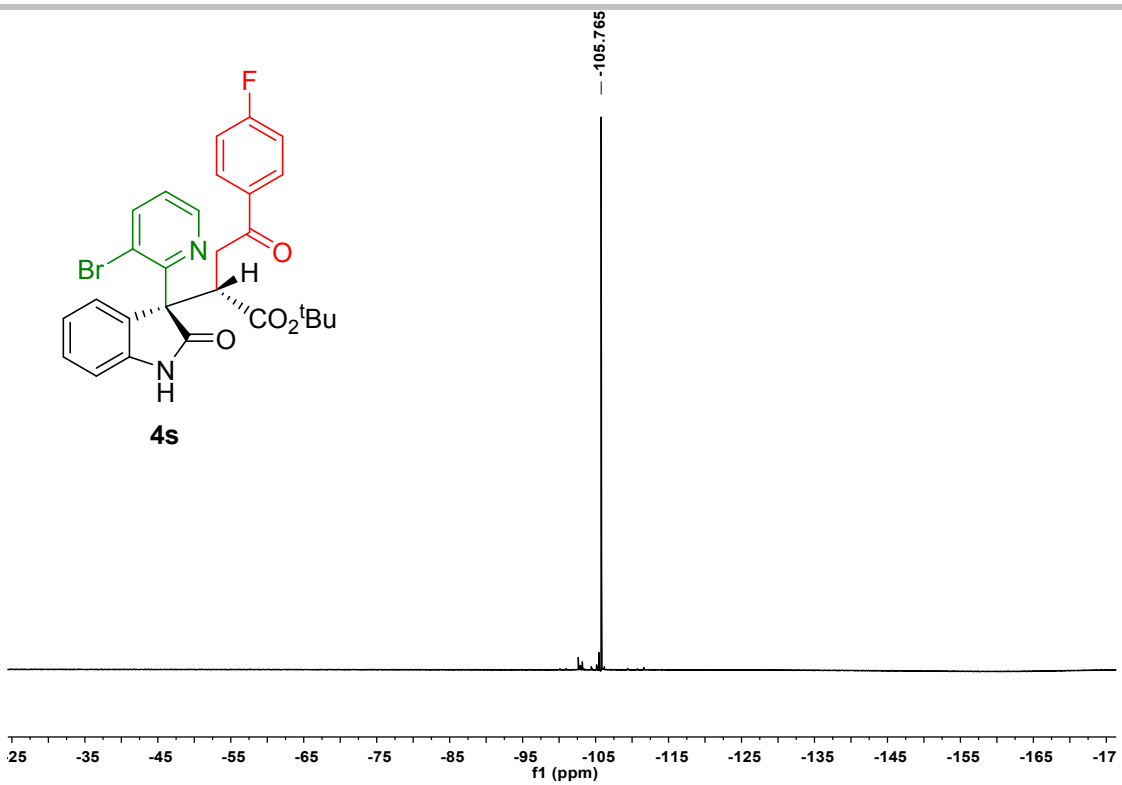

9.083
8.540
8.525
7.890
7.868
7.803
7.799
7.783
7.780
7.265
7.245
7.237
7.217
7.198
7.096
7.065
6.991
6.953
6.896
6.843
4.907
4.887
3.853
3.605
3.580
3.563
3.538
3.174
3.131
1.234
-0.000
OMe
Br
N
H
O
CO2tBu
O
N
H
4p
f1 (ppm)

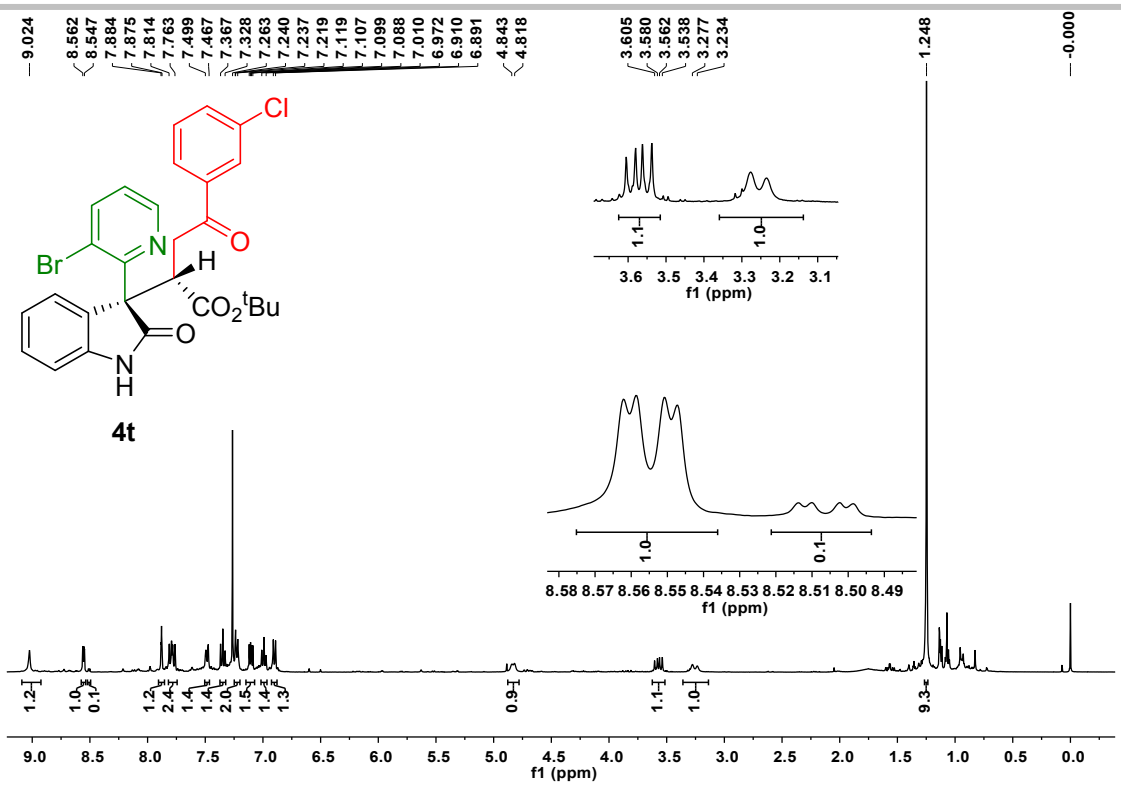

196.688
177.606
170.458
163.210
146.477
142.394
142.112
130.272
130.076
130.007
128.971
125.299
123.518
122.242
120.752
113.497
110.001
80.697
62.052
55.384
36.823
27.575
OMe
Br
N
H
O
CO2tBu
O
N
H
4p
f1 (ppm)

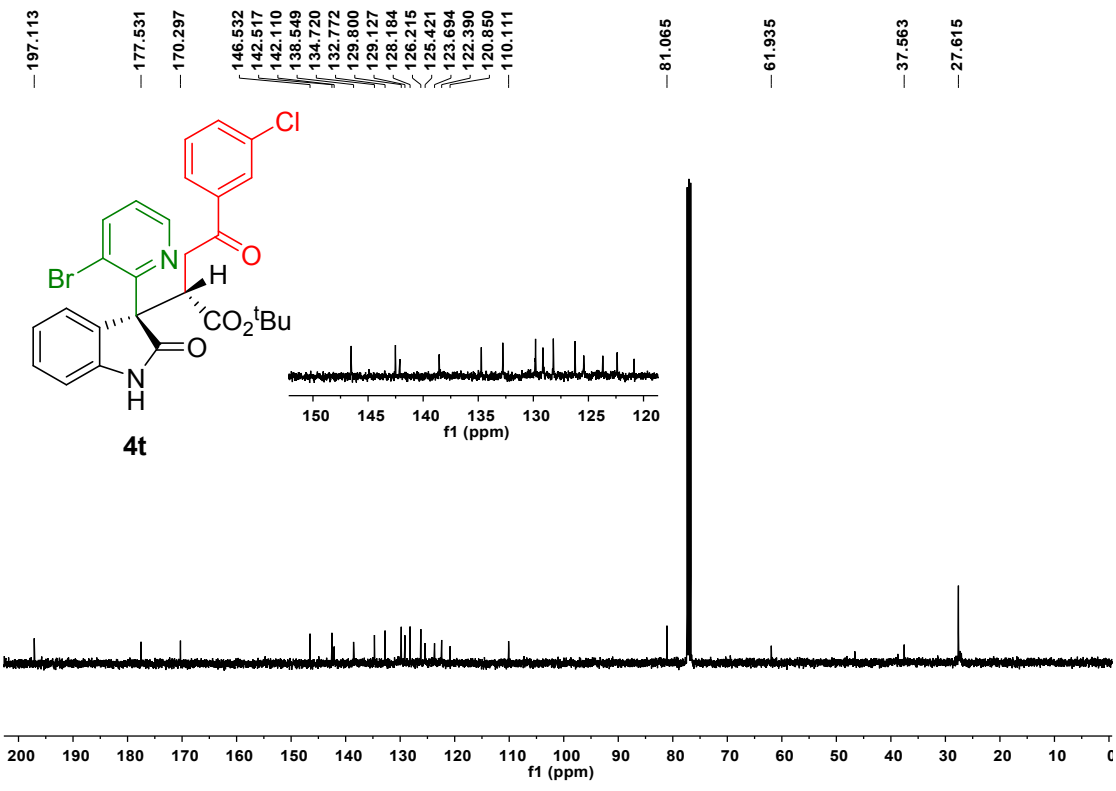

4q
4q

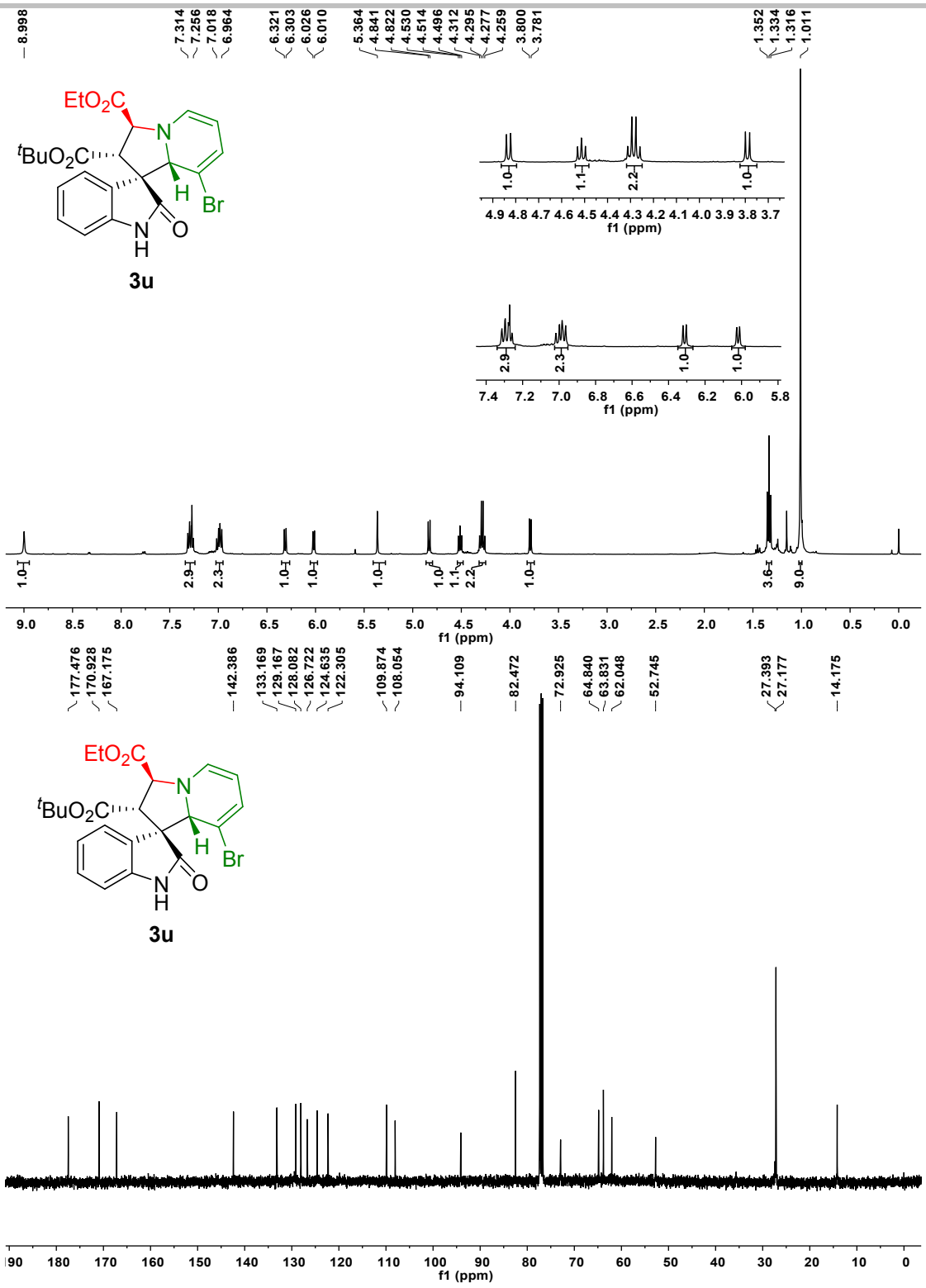

9.040
8.532
8.528
8.520
8.517
7.883
7.861
7.796
7.792
7.776
7.772
7.421
7.329
7.260
7.233
7.213
7.194
7.088
7.077
7.068
7.057
6.984
6.965
6.952
6.930
6.893
6.873
5.096
4.898
4.878
3.597
3.572
3.555
3.530
3.172
3.132
1.231
-0.000
OBn
Br
N
O
H
CO2tBu
O
N
H
4r
6.3
1.9
1.2
3.2
1.0
7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8
f1 (ppm)
1.0
0.9
3.6 3.5 3.4 3.3 3.2 3.1 3.0
f1 (ppm)
1.0 1.0 1.5 1.0 6.3 1.9 1.2 3.2 1.0 2.0 1.0 1.0 0.9 9.0
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)
196.664
177.559
170.451
162.349
146.477
142.393
142.095
136.201
130.277
130.251
129.990
128.976
128.636
128.159
127.424
125.291
123.520
122.248
120.752
114.371
109.995
80.702
70.027
62.027
46.501
36.852
27.577
OBn
Br
N
O
H
CO2tBu
O
N
H
4r
144 142 140 138 136 134 132 130 128 126
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)

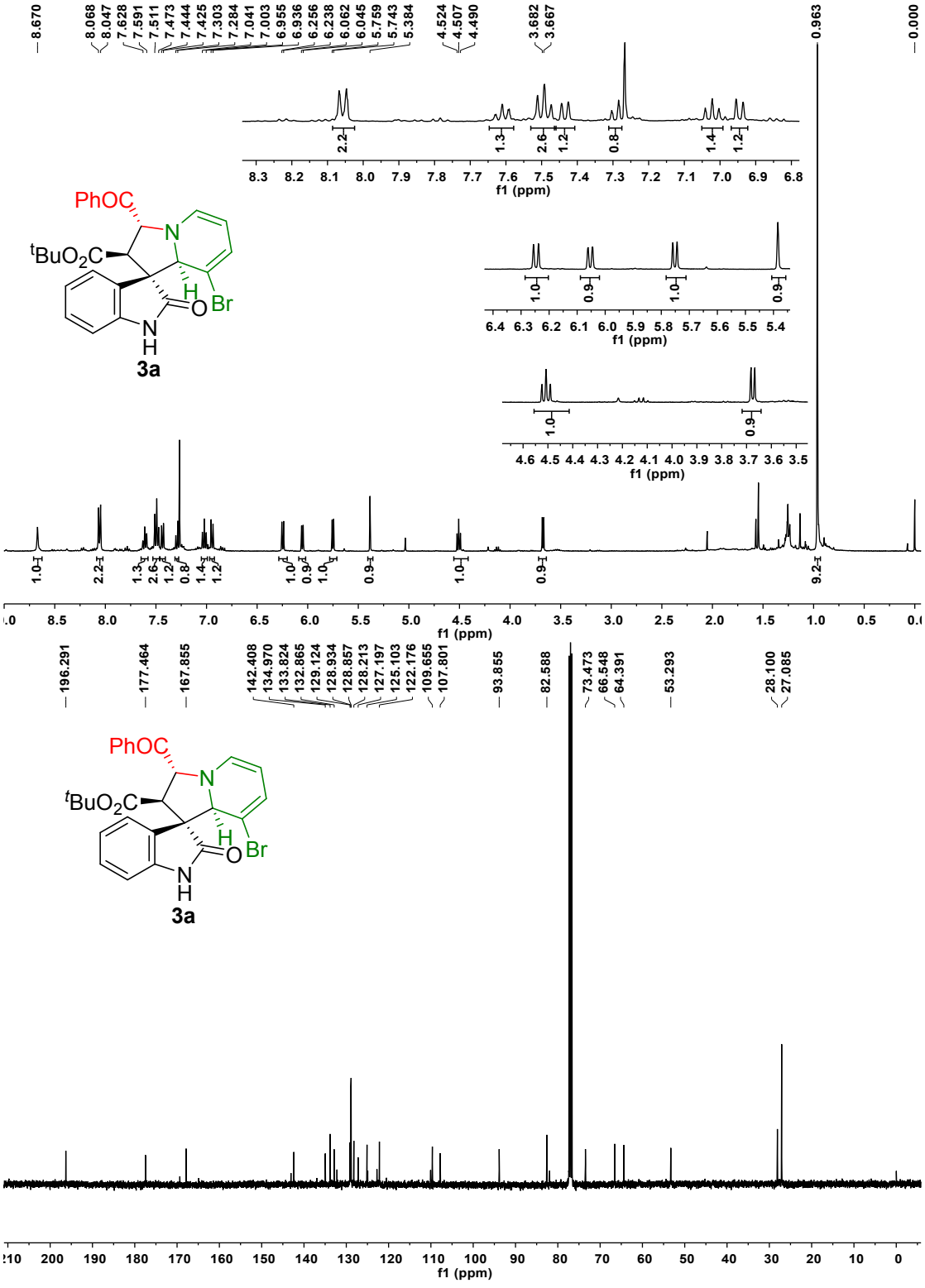

4s
4s

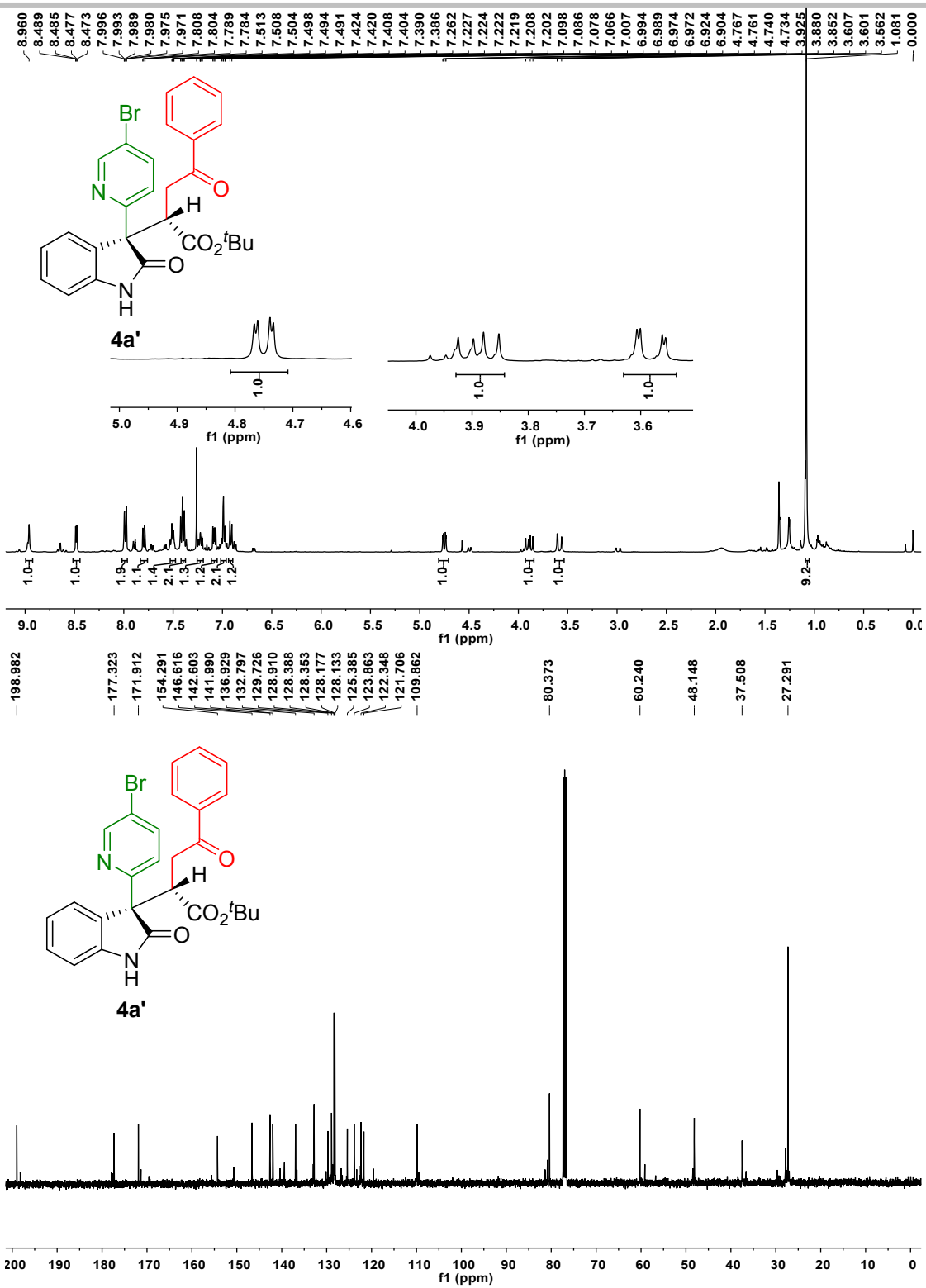

F
O
N
Br
H
CO2tBu
O
N
H
4s
-105.765
25
-35
-45
-55
-65
-75
-85
-95
-105
-115
-125
-135
-145
-155
-165
-17
f1 (ppm)

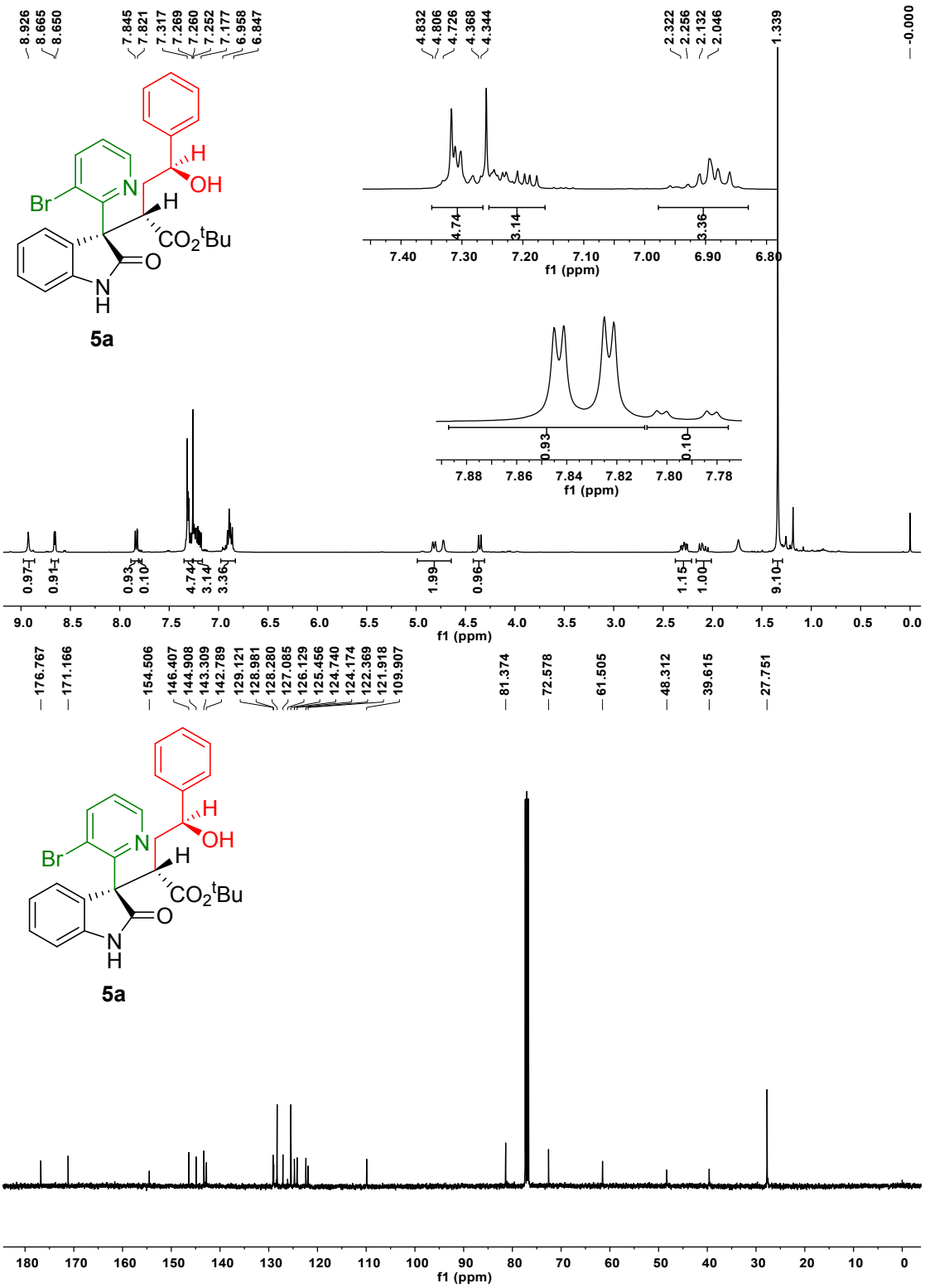

9.024
8.562
8.547
7.884
7.875
7.814
7.763
7.499
7.467
7.367
7.328
7.263
7.240
7.237
7.219
7.119
7.107
7.099
7.088
7.010
6.972
6.910
6.891
4.843
4.818
3.605
3.580
3.562
3.538
3.277
3.234
1.248
-0.000
Cl
O
N
H
Br
CO2tBu
O
N
H
4t
1.1
1.0
3.6 3.5 3.4 3.3 3.2 3.1
f1 (ppm)
1.0
0.1
8.58 8.57 8.56 8.55 8.54 8.53 8.52 8.51 8.50 8.49
f1 (ppm)
1.2
1.0
0.1
1.2
2.4
1.4
1.4
2.0
1.5
1.4
1.3
0.9
1.1
1.0
9.3
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)

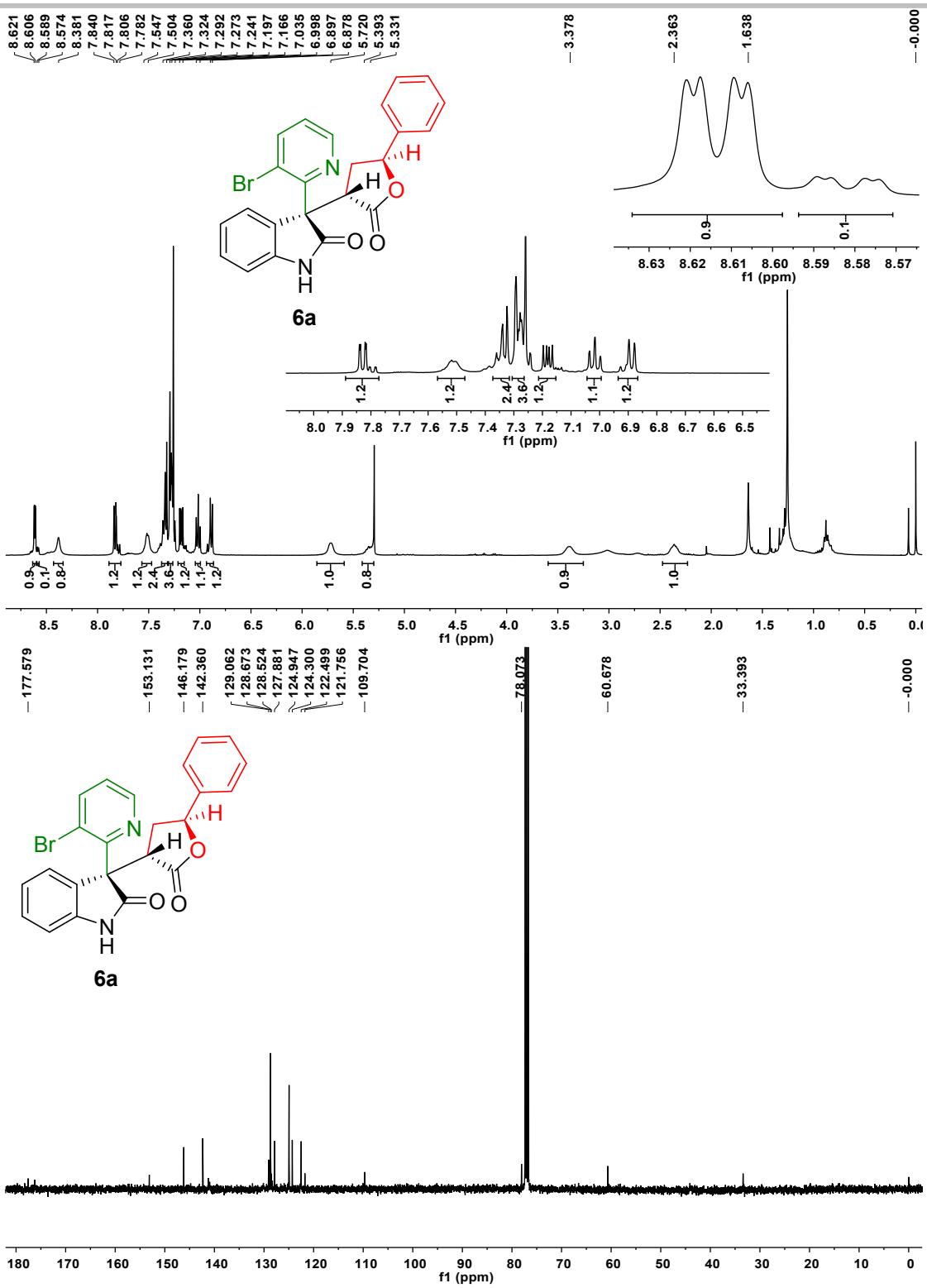

197.113
177.531
170.297
146.532
142.517
142.110
138.549
134.720
132.772
129.800
129.127
128.184
126.215
125.421
123.694
122.390
120.850
110.111
81.065
61.935
37.563
27.615
Cl
O
N
H
Br
CO2tBu
O
N
H
4t
150 145 140 135 130 125 120
f1 (ppm)
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

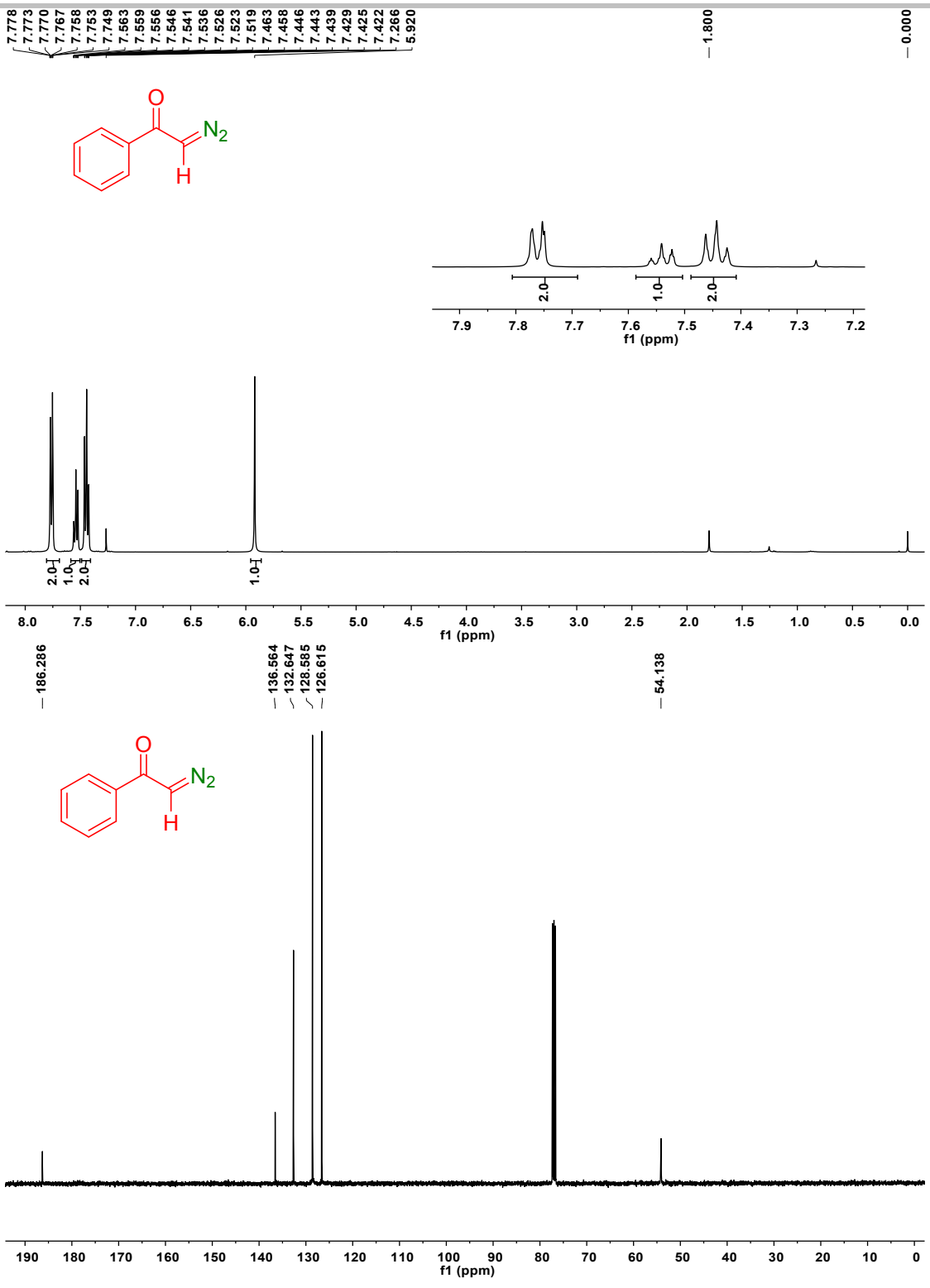

8.998
7.314
7.256
7.018
6.964
6.321
6.303
6.026
6.010
5.364
4.841
4.822
4.530
4.514
4.496
4.312
4.295
4.277
4.259
3.800
3.781
1.352
1.334
1.316
1.011
EtO2C
tBuO2C
N
H
Br
N
H
O
3u
f1 (ppm)
177.476
170.928
167.175
142.386
133.169
129.167
128.082
126.722
124.635
122.305
109.874
108.054
94.109
82.472
72.925
64.840
63.831
62.048
52.745
27.393
27.177
14.175
f1 (ppm)

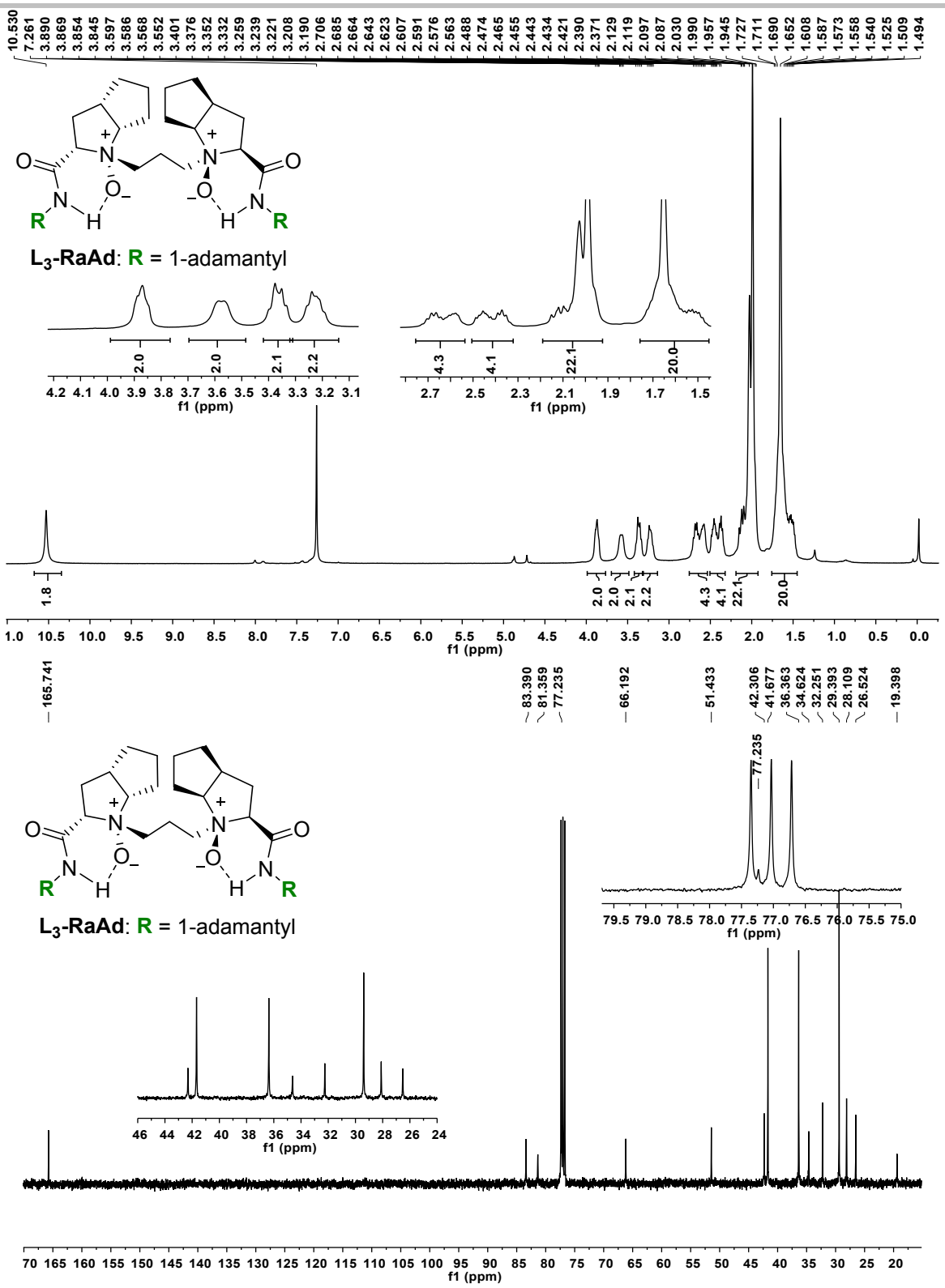

PhOC
tBuO2C
N
H
O
Br
N
H
3a
f1 (ppm)


8.960 8.489 8.485 8.477 8.473 7.996 7.993 7.989 7.980 7.975 7.971 7.808 7.804 7.789 7.784 7.513 7.508 7.504 7.498 7.494 7.491 7.424 7.420 7.408 7.404 7.390 7.386 7.262 7.227 7.224 7.222 7.219 7.208 7.202 7.098 7.086 7.078 7.066 7.007 6.994 6.989 6.974 6.972 6.924 6.904 4.767 4.761 4.740 4.734 3.925 3.880 3.852 3.607 3.601 3.562 1.081 0.000
Br
N
O
H
CO2tBu
O
N
H
4a'
1.0
5.0 4.9 4.8 4.7 4.6
f1 (ppm)
1.0 1.0
4.0 3.9 3.8 3.7 3.6
f1 (ppm)
1.0 1.0 1.9 1.1 1.4 2.1 1.3 1.2 2.1 1.2 1.0 1.0 1.0 9.2
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)
198.982 177.323 171.912 154.291 146.616 142.603 141.990 136.929 132.797 129.726 128.910 128.388 128.353 128.177 128.133 125.385 123.863 122.348 121.706 109.862 80.373 60.240 48.148 37.508 27.291
Br
N
O
H
CO2tBu
O
N
H
4a'
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


8.926
8.665
8.650
7.845
7.821
7.317
7.269
7.260
7.252
7.177
6.958
6.847
4.832
4.806
4.726
4.368
4.344
2.322
2.256
2.132
2.046
1.339
-0.000
Br
N
H
OH
H
CO2tBu
O
N
H
5a
4.74
3.14
3.36
7.40
7.30
7.20
7.10
7.00
6.90
6.80
f1 (ppm)
0.93
0.10
7.88
7.86
7.84
7.82
7.80
7.78
f1 (ppm)
0.97
0.91
0.93
0.10
4.74
3.14
3.36
1.99
0.96
1.15
1.00
9.10
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)
176.767
171.166
154.506
146.407
144.908
143.309
142.789
129.121
128.981
128.280
127.085
126.129
125.456
124.740
124.174
122.369
121.918
109.907
81.374
72.578
61.505
48.312
39.615
27.751
Br
N
H
OH
H
CO2tBu
O
N
H
5a
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


8.621
8.606
8.589
8.574
8.381
7.840
7.817
7.806
7.782
7.547
7.504
7.360
7.324
7.292
7.273
7.241
7.197
7.166
7.035
6.998
6.897
6.878
5.720
5.393
5.331
3.378
2.363
1.638
-0.000
Br
N
H
O
O
O
N
H
6a
f1 (ppm)
f1 (ppm)
f1 (ppm)
177.579
153.131
146.179
142.360
129.062
128.673
128.524
127.881
124.947
124.300
122.499
121.756
109.704
78.073
60.678
33.393
-0.000
6a
f1 (ppm)


7.778
7.773
7.770
7.767
7.758
7.753
7.749
7.563
7.559
7.556
7.546
7.541
7.536
7.526
7.523
7.519
7.463
7.458
7.446
7.443
7.439
7.429
7.425
7.422
7.266
5.920
1.800
0.000
O
N2
H
2.0
1.0
2.0
7.9
7.8
7.7
7.6
7.5
7.4
7.3
7.2
f1 (ppm)
2.0
1.0
2.0
1.0
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)
186.286
136.564
132.647
128.585
126.615
54.138
O
N2
H
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


10.530 7.261 3.890 3.869 3.854 3.845 3.597 3.586 3.568 3.552 3.401 3.376 3.352 3.332 3.259 3.239 3.221 3.208 3.190 2.706 2.685 2.664 2.643 2.623 2.607 2.591 2.576 2.563 2.488 2.474 2.465 2.455 2.443 2.434 2.421 2.390 2.371 2.129 2.119 2.097 2.087 2.030 1.990 1.957 1.945 1.727 1.711 1.690 1.652 1.608 1.587 1.573 1.558 1.540 1.525 1.509 1.494
L3-RaAd: R = 1-adamantyl
1.8 2.0 2.0 2.1 2.2 4.3 4.1 22.1 20.0
f1 (ppm)
165.741 83.390 81.359 77.235 66.192 51.433 42.306 41.677 36.363 34.624 32.251 29.393 28.109 26.524 19.398
L3-RaAd: R = 1-adamantyl
f1 (ppm)

(K) References.

[1] For the synthesis of chiral *N,N'*-dioxide Liagnds, see: (a) X. H. Liu, L. L. Lin, X. M. Feng, *Acc. Chem. Res.* 2011, **44**, 574; (b) X. H. Liu, L. L. Lin, X. M. Feng, *Org. Chem. Front.* 2011, **1**, 298.

[2] For the synthesis of (*E*)-alkenyloxindoles **1a-1k**, see: Y. M. Cao, X. X. Jiang, L. P. Liu, F. F. Shen, F. T. Zhang, R. Wang, *Angew. Chem. Int. Ed.* 2011, **50**, 9124.

[3] For the synthesis of pyridnium salts, see: Hu R. B.; Sun S.; Su Y. *Angew. Chem. Int. Ed.* 2017, **56**, 10877.

[4] For the synthesis of α-diazoacetophenone: T. B. Mete, D. Laha, R. G. Bhat, *ChemistrySelect.* 2018, **3**, 7656.

(L) Author contributions.

Dong Zhang: data curation (lead), formal analysis (lead), investigation (lead), writing of original draft (lead)

Shunxi Dong, Qianwen He, Yao Luo: data curation (supporting), formal analysis (supporting)

Yun Liu: repeating some experiments (supporting)

Xiaohua Liu*: project administration (equal)

Xiaoming Feng*: funding acquisition (equal), project administration (equal)