Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry

Supporting Information

A hypervalent iodine-mediated spirocyclization of 2-(4-hydroxybenzamido)acrylates – Unexpected formation of δ-spirolactones

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General Methods

^{1}H NMR spectra were recorded on an *Avance* 400 MHz instrument in deuterated chloroform ($CDCl_3$) , water (D_2O) or methanol (CD_3OD). Chemical shifts (δ) are given in parts per million (ppm). ^{1}H NMR spectra were referenced to the residual hydrogen signal in $CDCl_3$ at δ = 7.26 ppm, to the residual hydrogen signal in D_2O at δ = 4.79 ppm or to residual hydrogen singlet signal at δ = 4.84 ppm when measured in methanol-d^4. ^{13}C NMR spectra were recorded on 100 MHz and were fully decoupled by broad band decoupling. ^{13}C spectra were referenced to the $CDCl_3$ triplet signal at δ = 77.0 ppm or to septet signal at δ = 49.05 ppm in methanol-d^4. The following abbreviations were used to describe splitting patterns: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, sep = septet, m = multiplet. Coupling constants *J* are given in Hz. Mass spectra were recorded on a Finnigan MAT95 by using EI or FAB method. Thin layer chromatography was performed on fluorescence indicator marked precoated silca gel 60 plates (Macherey-Nagel, ALUGRAM Xtra SIL G/UV_{254}) and visualization was achieved by UV light (254 nm). Flash chromatography was performed on silica gel (0.040 – 0.063 mm). Unless otherwise stated all reactions were carried out under air. For air or moisture sensitive reactions standard Schlenk-techniques were applied under an argon atmosphere. Schlenk-glassware was heated in vacuo and flushed with argon several times before they were used. Reagents and solvents were added by syringe/septum techniques. IR spectra were recorded on JASCO FT/IR-4100. A selection of signals is given in reciprocal centimeters (cm^{-1}).

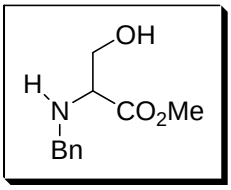
Solvents and reagents

Solvents for flash chromatography (hexane, ethyl acetate, dichloromethane) were distilled before use. Acetonitrile was dried over Al_2O_3 and stored over molecular sieve. Triethylamine was dried over calciumhydride and distilled before use. Unless stated, all other commercially available substances and reagents were used as received from their suppliers (Acros, Alfa Aesar, Sigma Aldrich) without further purification. 2-(4-Hydroxybenzamido)acrylates **3** were synthesized and purified as described. *O*-TMS protected 4-Hydroxybenzoyl chloride **1** and *N*-benzyl serine alkyl ester **2** were prepared from described procedures.[1],[2] The serine alkyl esters were also synthesized based on literature procedures.[3],[4],[5]

Synthesis of *N*-Benzyl serine alkyl ester 2a-2e

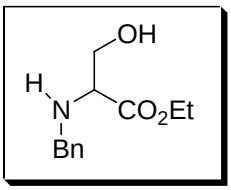
General preparation procedure according to literature:[2] To a solution of the corresponding serine alkyl ester (30 mmol, 1.00 equiv.), benzaldehyde (1.20 equiv.) and $MgSO_4$ (3.00 g) in dry DCM (50 mL) was added NEt_3 (1.20 equiv.) dropwise. The reaction mixture was stirred at room temperature for 24 hours, filtered and concentrated under reduced pressure. The residue was dissolved in MeOH (80 mL) and cooled to 0 °C before $NaBH_4$ (1.20 equiv.) was added portionwise. The resulting mixture was further stirred for 4 hours at room temperature and then quenched with water (35 mL) and EtOAc (35 mL). The aqueous layer was extracted with EtOAc (5 × 30 mL), and the combined organic layers were washed with brine (10 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was again dissolved in $CHCl_3$, filtered and concentrated under reduced pressure.

N-Benzyl serine methyl ester ***2a***: Yield: 82%, brown oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.28-



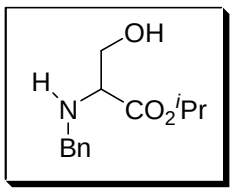
7.25 (m, 5H), 3.81 (d, 1H, $^2J_{HH}$ = 12.8 Hz), 3.70-3.60 (m, 1H), 3.67 (s, 3H), 3.64 (d, 1H, $^2J_{HH}$ = 12.8 Hz), 3.56-3.36 (m, 1H), 3.35-3.34 (m, 1H), 2.48 (bs, 2H). ^{13}C-NMR (100 MHz, $CDCl_3$) δ 173.4, 139.2, 128.5, 128.2, 127.3, 62.4, 61.8, 52.2, 52.0. MS (FAB) m/z = 210.3 $[M+H]^+$. IR ν_{max}/ cm^{-1} 1741, 1462, 1430, 1207, 1167, 1135, 1055, 1015, 744, 695. Compound is known to literature.[2]

N-Benzyl serine ethyl ester ***2b***: Yield: 67%, brown oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.27-



7.16 (m, 5H), 4.12 (q, 2H, $^3J_{HH}$ = 7.1 Hz), 3.81 (d, 1H, $^2J_{HH}$ = 12.9 Hz), 3.71-3.67 (m, 1H), 3.68 (d, 1H, $^2J_{HH}$ = 12.9 Hz), 3.55-3.50 (m, 1H), 3.34-3.31 (m, 1H), 2.63 (bs, 2H), 1.21 (t, 3H, $^3J_{HH}$ = 7.1 Hz). ^{13}C{^{1}H}-NMR (100 MHz, $CDCl_3$) δ 172.8, 139.1, 128.5, 128.3, 127.3, 62.3, 61.8, 61.3, 52.0, 14.2. MS (FAB) m/z = 224.2 $[M+H]^+$. IR ν_{max}/cm^{-1} 1709, 1230, 1207, 1127, 1055, 1023, 855, 752, 695, 600. Compound is known to literature.[6]

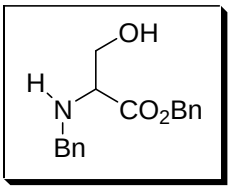
N-Benzyl serine isopropyl ester ***2c***: Yield: 77%, yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ



7.34-7.27 (m, 5H), 5.07 (sep, 1H, $^3J_{HH}$ = 6.3 Hz), 3.89 (d, 1H, $^2J_{HH}$ = 12.9 Hz), 3.79-3.73 (m, 1H), 3.74 (d, 1H, $^2J_{HH}$ = 12.9 Hz), 3.61-3.56 (m, 1H), 3.40-3.38 (m, 1H), 2.50 (bs, 2H), 1.27 (d, 3H, $^3J_{HH}$ = 6.1 Hz), 1.25 (d, 3H,

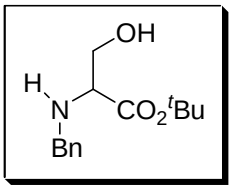
$^{3}J_{HH}$ = 6.2 Hz). $^{13}C\{^{1}H\}$-NMR (100 MHz, $CDCl_3$) δ 172.3, 139.2, 128.5, 128.3, 127.4, 68.9, 62.4, 61.9, 52.1, 21.9, 21.8. MS (FAB) m/z = 238.3 $[M+H]^+$. IR ν_{max}/cm^{-1} 1709, 1454, 1374, 1254, 1207, 1151, 1143, 1047, 735, 680. HRMS (ESI) m/z calculated to $C_{13}H_{19}NO_3$ $[M+H]^+$: 238.143770, found: 238.143697.

N-Benzyl serine benzyl ester ***2d***: Yield: 90%, brown oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.30-



7.18 (m, 10H), 5.14 (s, 2H), 3.80 (d, 1H, $^{2}J_{HH}$ = 12.9 Hz), 3.75-3.71 (m, 1H), 3.66 (d, 1H, $^{2}J_{HH}$ = 12.9 Hz), 3.60-3.56 (m, 1H), 3.42-3.39 (m, 1H), 2.63 (bs, 2H). $^{13}C\{^{1}H\}$-NMR (100 MHz, $CDCl_3$) δ 172.7, 139.0, 135.4, 128.6, 128.5, 128.4, 128.2, 128.1, 127.4, 67.0, 62.4, 61.8, 52.0. MS (FAB) m/z = 286.3 $[M+H]^+$. IR ν_{max}/cm^{-1} 3026, 1717, 1510, 1454, 1167, 1127, 1023, 727, 695, 568. HRMS (ESI) m/z calculated to $C_{17}H_{19}NO_3$ $[M+H]^+$: 286.143770, found: 286.143771. Compound is known to literature.[7]

N-Benzyl serine tert-butyl ester ***2e***: Yield: 66%, yellow oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ

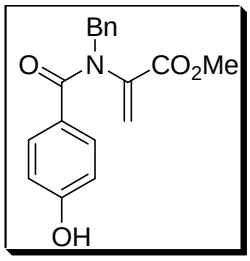


7.30-7.20 (m, 5H), 3.80 (d, 1H, $^{2}J_{HH}$ = 12.8 Hz), 3.70-3.66 (m, 1H), 3.65 (d, 1H, $^{2}J_{HH}$ = 12.8 Hz), 3.51-3.47 (m, 1H), 3.26-3.24 (m, 1H), 2.52 (bs, 2H), 1.41 (s, 9H). $^{13}C\{^{1}H\}$-NMR (100 MHz, $CDCl_3$) δ 172.1, 128.5, 128.4, 128.2, 126.9, 81.9, 65.2, 62.5, 52.1, 28.1. IR ν_{max}/cm^{-1} 1725, 1663, 1503, 1452, 1359, 1230, 1147, 1018, 740, 689. HRMS (ESI) m/z calculated to $C_{14}H_{21}NO_3$ $[M+H]^+$: 252.159420, found: 252.159292. Compound is known to literature.[8]

Synthesis of 2-(4-hydroxybenzamido)acrylates 3a-3e

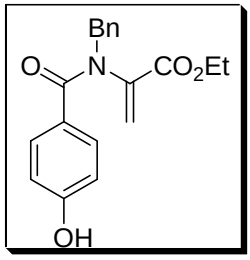
General preparation procedure:[9] In a vial, the *N*-Benzyl serine alkyl ester **2** (1.40 mmol, 1.0 equiv.) was dissolved in dry toluene (9 mL), followed by simultaneous addition of NEt_3 (440 µL, 3.10 mmol, 2.2 equiv.) and *p*-OTMS-benzoylchloride **1** (981 mg, 4.25 mmol 3.0 equiv.) at 0 °C. The resulting homogenous mixture was stirred at room temperature for 17 hours and extracted with 1M $KHSO_4$ solution (2 × 4 mL). The aqueous layer was extracted with EtOAc (3 × 4 mL), and combined organic layers were washed with brine (4 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was dissolved in dry DCM (9 mL) and cooled to 0 °C before DBU (470 µL, 3.10 mmol, 2.2 equiv.) was added dropwise. The mixture was stirred at 0 °C for 5 hours, and washed with 1M $KHSO_4$ solution (2 × 4 mL). The aqueous layer was extracted with DCM (4 × 4 mL), and the combined organic layers were washed with brine (4 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The products were obtained after flash chromatography using DCM and MeOH.

N-Benzyl-2-(4-hydroxybenzamido)methylacrylate ***3a***: Yield: 55%, white solid. ^{1}H-NMR



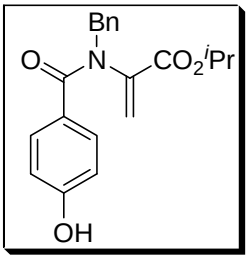
(400 MHz, $CDCl_3$) δ 7.28-7.17 (m, 7H), 6.59-6.57 (m, 2H), 5.88 (s, 1H), 5.22 (s, 1H), 4.85 (s, 2H), 3.50 (s, 3H). ^{13}C{1H}-NMR (100 MHz, $CDCl_3$) δ 172.0, 164.5, 158.9, 140.4, 136.7, 130.1, 128.5, 128.3, 128.1, 127.5, 126.3, 115.2, 52.7, 52.5. MS (FAB) m/z = 312.3 $[M+H]^+$. IR ν_{max}/cm^{-1} 1735, 1601, 1580, 1266, 1194, 1152, 848, 761, 725, 648. HRMS (ESI) m/z calculated to $C_{18}H_{17}NO_4$ $[M+Na]^+$: 334.104979, found: 334.104783.

N-Benzyl-2-(4-hydroxybenzamido)ethylacrylate ***3b***: Yield: 54%, white solid. ^{1}H-NMR



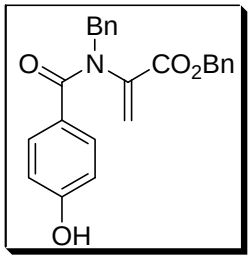
(400 MHz, $CDCl_3$) δ 7.44-7.42 (m, 2H), 7.34-7.28 (m, 5H), 6.70-6.68 (m, 2H), 5.96 (s, 1H), 5.30 (s, 1H), 4.94 (s, 2H), 4.00 (q, 2H, $^3J_{HH}$ = 7.0 Hz), 1.13 (t, 3H, $^3J_{HH}$ = 7.1 Hz). ^{13}C{1H}-NMR (100 MHz, $CDCl_3$) δ 171.6, 164.0, 158.6, 140.9, 136.9, 130.3, 128.5, 128.4, 128.3, 127.5, 126.9, 115.1, 61.8, 52.8, 13.9. MS (FAB) m/z = 326.4 $[M+H]^+$. IR ν_{max}/cm^{-1} 1717, 1589, 1446, 1366, 1342, 1254, 1158, 839, 744, 704. HRMS (ESI) m/z calculated to $C_{19}H_{19}NO_4$ $[M+Na]^+$: 348.120629, found: 348.120610.

N-Benzyl-2-(4-hydroxybenzamido)isopropylacrylate ***3c***: Yield: 63%, white solid. ^{1}H-NMR



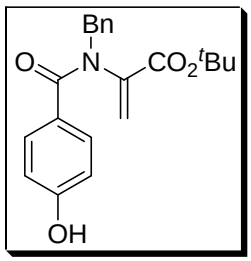
(400 MHz, $CDCl_3$) δ 7.44-7.42 (m, 2H), 7.34-7.28 (m, 5H), 6.72-6.70 (m, 2H), 5.96 (s, 1H), 5.31 (s, 1H), 4.94 (s, 2H), 4.84 (sep, 1H, $^{3}J_{HH}$ = 6.2 Hz), 1.09 (d, 6H, $^{3}J_{HH}$ = 6.2 Hz). ^{13}C{1H}-NMR (100 MHz, $CDCl_3$) δ 171.3, 163.1, 158.6, 140.8, 136.5, 130.1, 128.2, 128.0, 127.1, 126.2, 115.2, 114.8, 69.4, 52.7, 21.1. MS (FAB) m/z = 340.2 $[M+H]^+$. IR ν_{max}/cm^{-1} 1606, 1382, 1350, 1289, 1207, 1167, 799, 735, 695, 608. HRMS (ESI) m/z calculated to $C_{20}H_{21}NO_4$ $[M+Na]^+$: 362.136279, found: 362.136299.

N-Benzyl-2-(4-hydroxybenzamido)benzylacrylate ***3d***: Yield: 31%, white solid. ^{1}H-NMR



(400 MHz, $CDCl_3$) δ 7.37-7.19 (m, 12H), 6.66-6.64 (m, 2H), 6.00 (s, 1H), 5.32 (s, 1H), 5.00 (s, 2H), 4.94 (s, 2H). ^{13}C{1H}-NMR (100 MHz, $CDCl_3$) δ 164.2, 163.2, 161.2, 152.4, 136.0, 134.5, 132.2, 129.1, 128.3, 128.2, 128.0, 127.9, 127.4, 121.4, 120.3, 115.3, 67.6, 67.3. MS (FAB) m/z = 388.4 $[M+H]^+$. IR ν_{max}/cm^{-1} 1725, 1606, 1574, 1374, 1262, 1190, 848, 759, 695, 600. HRMS (ESI) m/z calculated to $C_{24}H_{21}NO_4$ $[M+Na]^+$: 410.136279, found: 410.136040.

N-Benzyl-2-(4-hydroxybenzamido)tert-butylacrylate ***3e***: Yield: 20%, white solid. ^{1}H-NMR

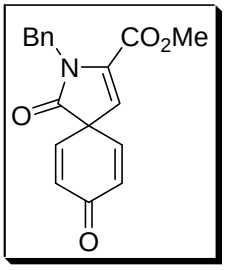


(400 MHz, $CDCl_3$) δ 7.42-7.40 (m, 2H), 7.34-7.23 (m, 5H), 6.68-6.65 (m, 2H), 5.96 (s, 1H), 5.35 (s, 1H), 4.92 (s, 2H), 1.19 (s, 9H). ^{13}C{1H}-NMR (100 MHz, $CDCl_3$) δ 162.8, 158.7, 142.1, 136.9, 132.3, 130.5, 128.4, 128.3, 127.4, 120.9, 115.3, 115.0, 82.4, 53.3, 27.4. IR ν_{max}/cm^{-1} 2364, 2338, 1745, 1606, 1565, 1282, 1235, 1142, 843, 719. HRMS (ESI) m/z calculated to $C_{21}H_{23}NO_4$ $[M+Na]^+$: 376.151929, found: 376.151978.

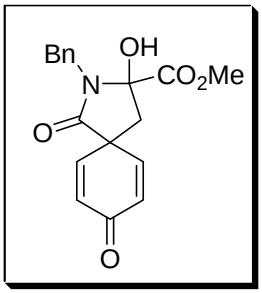
Spirocyclization of 2-(4-hydroxybenzamido)acrylates 3 to spirolactam 4

General preparation procedure: To a stirred solution of 2-(4-hydroxybenzamido)acrylate **3** (0.10 mmol, 1.0 equiv.) in 2 mL EtCN containing MS 3 Å at 90 °C was added PIFA (0.12 mmol, 1.2 equiv.) portionwise. After stirring at 90 °C for 10 minutes, the solvent was removed under reduced pressure and the crude product was purified by flash chromatography using DCM and MeOH.

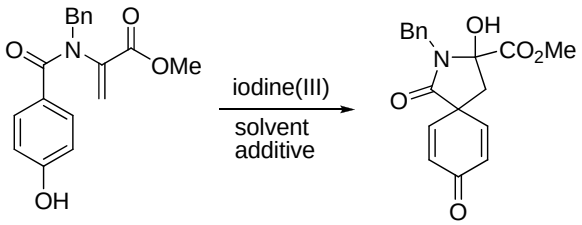
N-Benzyl-3-(methoxycarbonyl)-2-azaspiro[4.5]dec-3,6,9-trien-1,8-dione ***4a:*** Yield: 52%, brown solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.31-7.25 (m, 5H), 6.56-6.47 (m, 4H), 5.97 (s, 1H), 5.10 (s, 2H), 3.81 (s, 3H). ^{13}C{1H}-NMR (100 MHz, $CDCl_3$) δ 184.7, 172.8, 159.5, 140.9, 137.5, 137.0, 132.5, 128.7, 127.8, 127.7, 117.3, 56.7, 52.6, 45.5. MS (FAB) m/z = 310.2 $[M+H]^+$. IR ν_{max}/cm^{-1} 1720, 1647, 1436, 1328, 1266, 1194, 1147, 1049, 859, 704. HRMS (ESI) m/z calculated to $C_{18}H_{15}NO_4$ $[M+Na]^+$: 332.089329, found: 332.089236.



N-Benzyl-3-(hydroxy)-3-(methoxycarbonyl)-2-azaspiro[4.5]dec-6,9-dien-1,8-dione **5**: pale yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.33-7.24 (m, 5H), 7.00-6.88 (m, 2H), 6.50-6.43 (m, 2H), 4.83 (d, 1H, $^{2}J_{HH}$ = 15.1 Hz), 4.13 (d, 1H, $^{2}J_{HH}$ = 15.1 Hz), 3.29 (s, 3H), 2.81 (d, 1H, $^{2}J_{HH}$ = 14.2 Hz), 2.41 (d, 1H, $^{2}J_{HH}$ = 14.2 Hz). ^{13}C{1H}-NMR (100 MHz, $CDCl_3$) δ 184.6, 171.3, 170.1, 146.7, 146.4, 134.0, 131.2, 130.3, 128.6, 128.2, 127.7, 86.0, 53.5, 50.3, 43.7, 41.8. MS (FAB) m/z = 328.2 $[M+H]^+$. HRMS (ESI) m/z calculated to $C_{18}H_{17}NO_5$ $[M+Na]^+$: 350.099894, found: 350.099844.



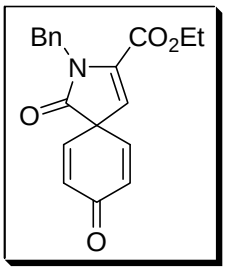
Optimization studies towards the formation of **5**



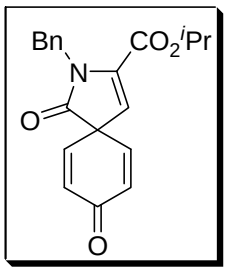
20 **21**

entry	iodine(III)	equiv.	solvent	Additive (equiv.)	T [°C]	T [min]	Yield [%]
1	PIFA	1.2	MeCN	-	0	90	30
2	PIFA	1.2	MeCN	TFA (1.2)	0	120	44
3	**PIFA**	**1.2**	**MeCN**	**TFA (1.2) H_2O (1.1)**	**0**	**100**	**56**
4	PIFA	1.2	MeCN	-	RT	15	33
5	PIFA	1.2	MeCN	H_2O (1.1)	RT	15	40
6	PIFA	1.2	MeCN	H_2O (2.1)	RT	20	35
7	PIFA	2	MeCN	H_2O (1.1)	RT	20	18
8	PIFA	2	MeCN	H_2O (2.1)	RT	20	44
9	PIFA	1.2	MeCN	TFA (1.2) H_2O (1.1)	RT	20	51
10	PIFA	1.2	MeCN	-	60	15	11
11	PIFA	1.2	MeCN	TFA (1.2)	60	10	15

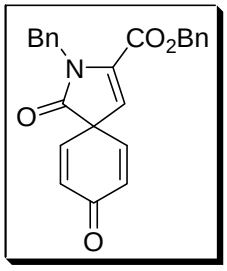
N-Benzyl-3-(ethoxycarbonyl)-2-azaspiro[4.5]dec-3,6,9-trien-1,8-dione ***4b:*** Yield: 35%, brown solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.30-7.24 (m, 5H), 6.55-6.47 (m, 4H), 5.96 (s, 1H), 5.10 (s, 2H), 4.26 (q, 2H, $^{3}J_{HH}$ = 7.1 Hz), 1.28 (t, 3H, $^{3}J_{HH}$ = 7.1 Hz). ^{13}C{1H}-NMR (100 MHz, $CDCl_3$) δ 184.6, 172.8, 159.1, 140.9, 137.9, 137.0, 132.5, 128.7, 127.7, 127.6, 116.9, 62.0, 56.6, 45.5, 13.9. MS (FAB) m/z = 324.2 $[M+H]^+$. IR ν_{max}/cm^{-1} 1720, 1653, 1328, 1261, 1189, 1137, 1054, 853, 740, 694. HRMS (ESI) m/z calculated to $C_{19}H_{17}NO_4$ $[M+Na]^+$: 346.104979, found: 346.105199.



N-Benzyl-3-(isopropoxycarbonyl)-2-azaspiro[4.5]dec-3,6,9-trien-1,8-dione ***4c:*** Yield: 38%, brown solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.32-7.23 (m, 5H), 6.55-6.48 (m, 4H), 5.92 (s, 1H), 5.10 (sep, 1H, $^{3}J_{HH}$ = 6.3 Hz), 5.09 (s, 2H), 1.23 (d, 6H, $^{3}J_{HH}$ = 6.3 Hz). ^{13}C{1H}-NMR (100 MHz, $CDCl_3$) δ 184.6, 172.8, 158.7, 141.1, 138.3, 137.0, 132.4, 128.7, 127.7, 127.6, 116.4, 70.1, 56.6, 45.4, 21.5. MS (FAB) m/z = 338.1 $[M+H]^+$. IR ν_{max}/cm^{-1} 1740, 1720, 1663, 1261, 1179, 1147, 1101, 1049, 859, 694. HRMS (ESI) m/z calculated to $C_{20}H_{19}NO_4$ $[M+Na]^+$: 360.120629, found: 360.120596.

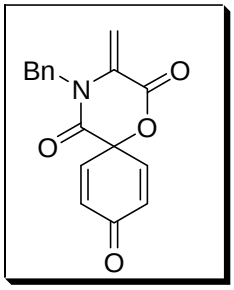


N-Benzyl-3-(benzyloxycarbonyl)-2-azaspiro[4.5]dec-3,6,9-trien-1,8-dione ***4d:*** Yield: 35%, brown solid. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.38-7.21 (m, 10H), 6.53-6.47 (m, 4H), 5.99 (s, 1H), 5.22 (s, 2H), 5.10 (s, 2H). ^{13}C{1H}-NMR (100 MHz, $CDCl_3$) δ 184.5, 172.7, 158.9, 140.8, 137.6, 136.9, 134.4, 132.4, 128.8, 128.7, 128.7, 128.5, 127.7, 127.7, 117.4, 67.5, 56.6, 45.4. MS (FAB) m/z = 386.1 $[M+H]^+$. IR ν_{max}/cm^{-1} 1720, 1653, 1405, 1338, 1266, 1179, 1147, 853, 730, 694. HRMS (ESI) m/z calculated to $C_{24}H_{19}NO_4$ $[M+Na]^+$: 408.120629, found: 408.120530.



Spirocyclization of 2-(4-hydroxybenzamido)acrylates 3 to δ-spirolactone 6

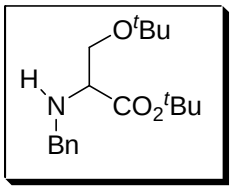
To a stirred solution of 2-(4-hydroxybenzamido)acrylate **3** (0.10 mmol, 1.0 equiv.) in 2 mL TFE containing MS 3 Å at 0 °C was added TFA (0.20 mmol, 2.0 equiv.) and then PIFA (0.20 mmol, 2.0 equiv.). After stirring at 0 °C for 1 hour, the solvent was removed under reduced pressure and the crude product was purified by flash chromatography

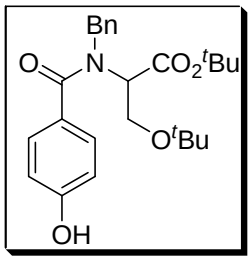


(Hex : EE 5:1 → 3:1) to give the title compound as a pale yellow solid (up to 70%).^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.37-7.15 (m, 5H), 6.89-6.86 (m, 2H), 6.49-6.46 (m, 2H), 6.00 (d, 1H, $^{2}J_{HH}$ = 2.1 Hz), 5.30 (d, 1H, $^{2}J_{HH}$ = 2.1 Hz), 4.99 (s, 2H). ^{13}C{1H}-NMR (100 MHz, $CDCl_3$) δ 183.0, 160.7, 157.6, 139.3, 134.0, 132.0, 131.6, 128.9, 127.9, 126.4, 110.3, 76.9, 47.9. MS (FAB) m/z = 296.2 $[M+H]^+$. IR ν_{max}/cm^{-1} 1741, 1677, 1613, 1342, 1262, 1138, 1055, 911, 839, 688. HRMS (ESI) m/z calculated to $C_{17}H_{13}NO_4$ $[M+Na]^+$: 318.073679, found: 318.073889.

Synthesis of 7

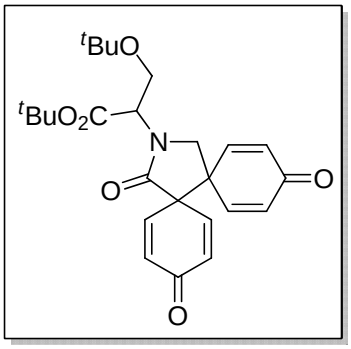
N-Benzyl O-tert-butyl serine tert-butyl ester was prepared according to the procedure described for compounds **2a-2e** starting from *O-tert*-butyl serin *tert*-butyl-ester:[4]: Yield: 71%, brown oil. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.28-7.13 (m, 5H), 3.83 (d, 1H, $^{2}J_{HH}$ = 12.9 Hz), 3.63 (d, 1H, $^{2}J_{HH}$ = 12.9 Hz), 3.53-3.41 (m, 2H), 3.23-3.21 (m, 1H), 2.16 (bs, 1H), 1.40 (s, 9H), 1.07 (s, 9H). ^{13}C{^{1}H}-NMR (100 MHz, $CDCl_3$) δ 172.6, 139.9, 128.4, 128.3, 126.8, 80.8, 72.8, 63.3, 61.4, 51.84, 28.1, 27.3. MS (FAB) m/z = 308.2 $[M+H]^+$. IR ν_{max}/cm^{-1} 2977, 1735, 1462, 1359, 1184, 1137, 1085, 1018, 740, 689. HRMS (ESI) m/z calculated to $C_{18}H_{29}NO_3$ $[M+H]^+$: 308.222020, found: 308.222230.





N-Benzyl *O-tert*-butyl serine *tert*-butyl ester (170 mg, 0.60 mmol, 1.0 equiv.) was dissolved in dry toluene (6 mL), followed by simultaneous addition of NEt_3 (183 µL, 1.32 mmol, 2.2 equiv.) and *p*-OTMS-benzoylchloride **1** (412 mg, 1.80 mmol, 3.0 equiv.) at 0 °C. The resulting homogenous mixture was stirred at room temperature for 17 hours and extracted with 1M $KHSO_4$ solution (2 × 4 mL). The aqueous layer was extracted with EtOAc (3 × 4 mL), and combined organic layers were washed with brine (4 mL), dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (DCM : MeOH 200:1 → 50:1) to give the title compound **7** as a white solid (164 mg, 0.40 mmol, 66%). ^{1}H-NMR (400 MHz, DMSO-d_6) δ 9.84 (s, 1H) 7.33-7.22 (m, 7H), 6.76 (m, 2H), 4.76-3.56 (m, 3H), 3.32 (s, 2H), 1.36 (s, 9H), 0.98 (s, 9H). ^{13}C{1H}-NMR (100 MHz, $CDCl_3$) δ 173.3, 168.1, 158.5, 137.1, 132.4, 128.9, 128.3, 127.3, 126.3, 115.5, 81.8, 73.8, 60.6, 55.2, 51.8, 27.9, 27.3. MS (FAB) m/z = 428.2 $[M+H]^+$. IR ν_{max}/cm^{-1} 1749, 1613, 1566, 1414, 1279, 1239, 1143, 1111, 848, 727. HRMS (ESI) m/z calculated to $C_{25}H_{33}NO_5$ $[M+Na]^+$: 450.225094, found: 450.224677.

Spirocyclization of 7 to bis(cyclohexa-2,5-dien-4-one) 9



To a stirred solution of **7** (41 mg, 0.10 mmol, 1.0 equiv.) in 2 mL TFE containing MS 3 Å at 0 °C was added TFA (14.3 µL; 0.20 mmol, 2.0 equiv.) and then PIFA (81.0 mg, 0.20 mmol, 2.0 equiv.). After stirring at 0 °C for 1 hour, the solvent was removed under reduced pressure and the crude product was purified by flash chromatography (Hex : EE 3:1 → 1:1) to give the title compound as a pale yellow solid (27.0 mg, 0.06 mmol, 61%).^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.21-6.84 (m, 4H), 6.49-6-37 (m, 4H), 4.92-4.90 (m, 1H), 4.02 (d, 1H, $^{2}J_{HH}$ = 10.9 Hz), 3.90-3.86 (m, 1H), 3.81 (d, 1H, $^{2}J_{HH}$ = 10.9 Hz), 3.71-3.68 (m, 1H), 1.49 (s, 9H), 1.20 (s, 9H). ^{13}C{1H}-NMR (100 MHz, $CDCl_3$) δ 184.2, 184.0, 169.3, 167.3, 146.4, 146.1, 141.9, 141.6, 133.2. 133.2, 131.5, 131.4, 83.1, 73.9, 60.5, 59.2, 55.9, 51.6, 50.7, 28.1, 27.4. MS (FAB) m/z = 442.1 $[M+H]^+$, 464.1 $[M+Na]^+$. IR ν_{max}/cm^{-1} 1741, 1702, 1663, 1620, 1366, 1230, 1190, 1158, 1087, 871. HRMS (ESI) m/z calculated to $C_{25}H_{31}NO_6$ $[M+Na]^+$: 464.204359, found: 464.204242.

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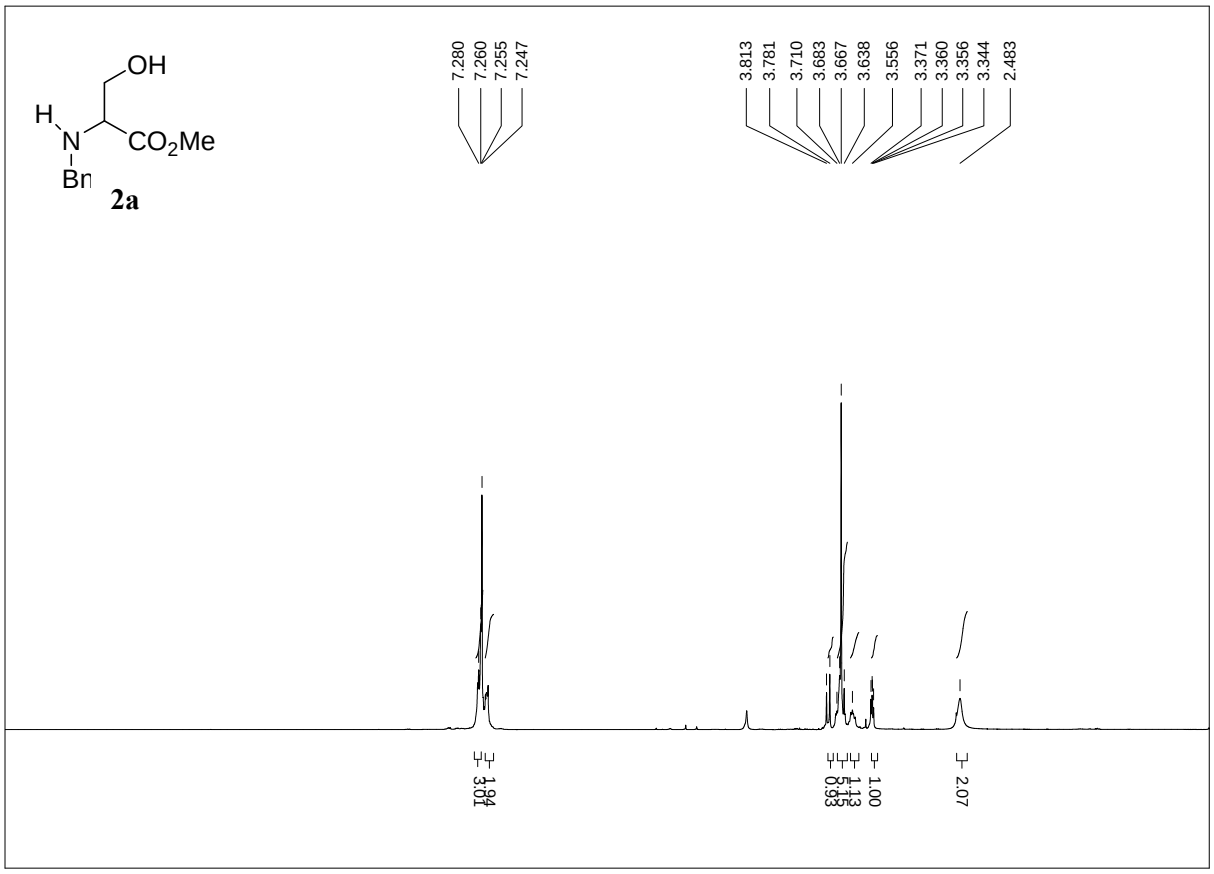

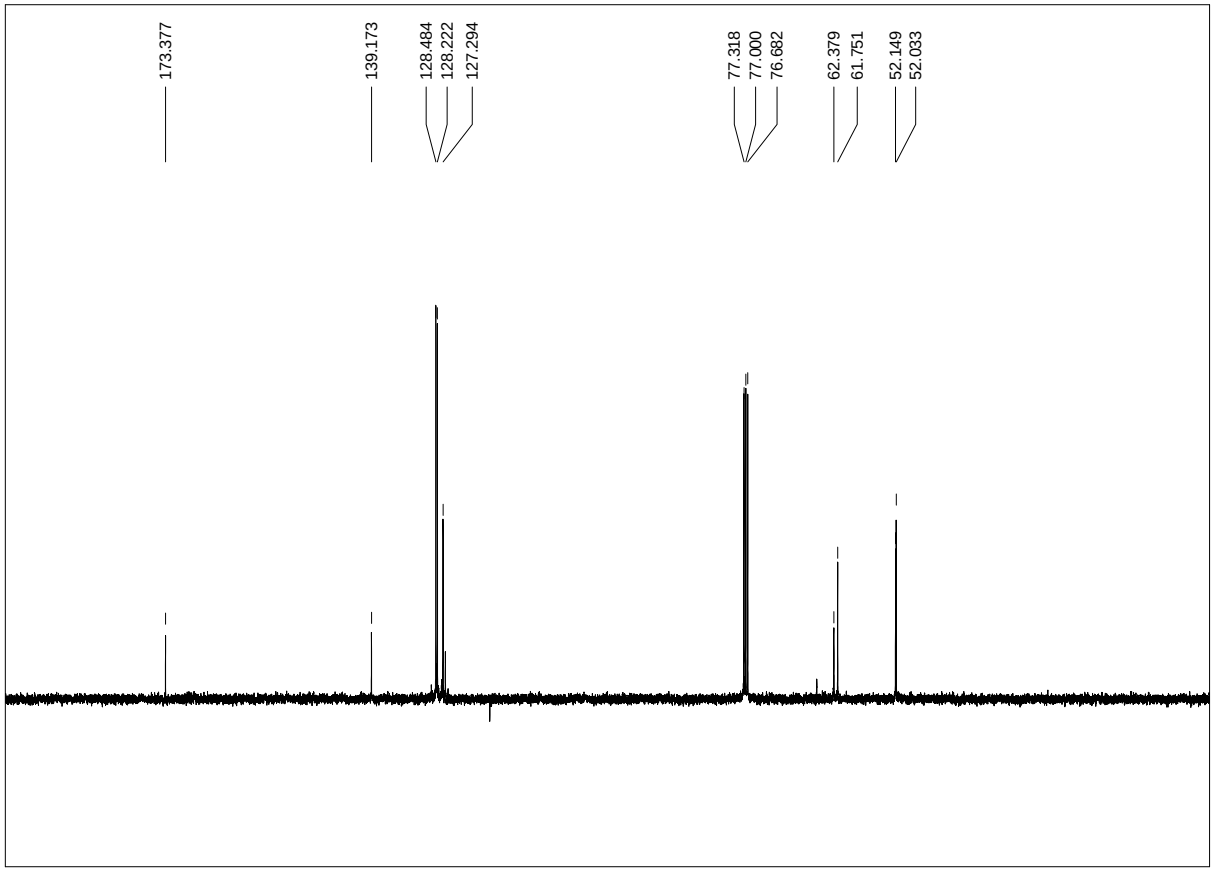

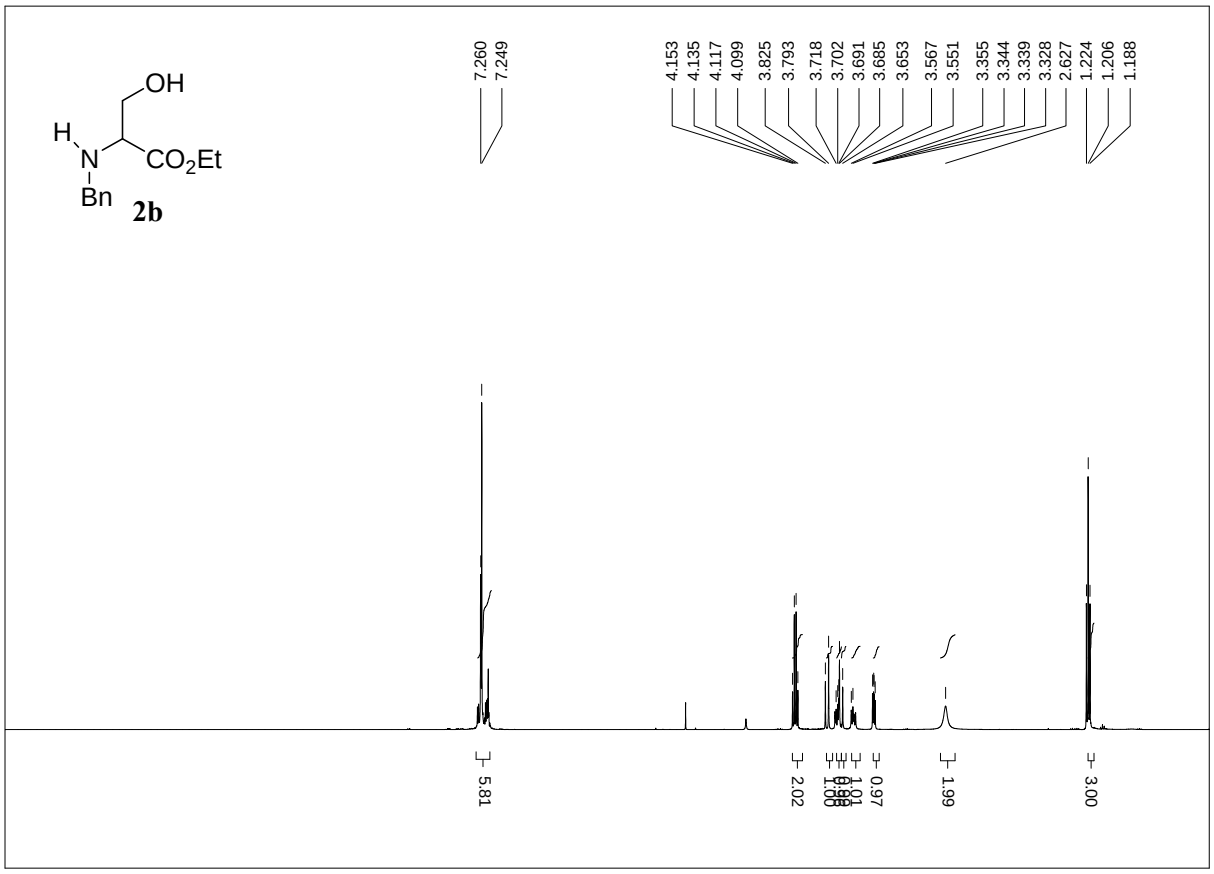

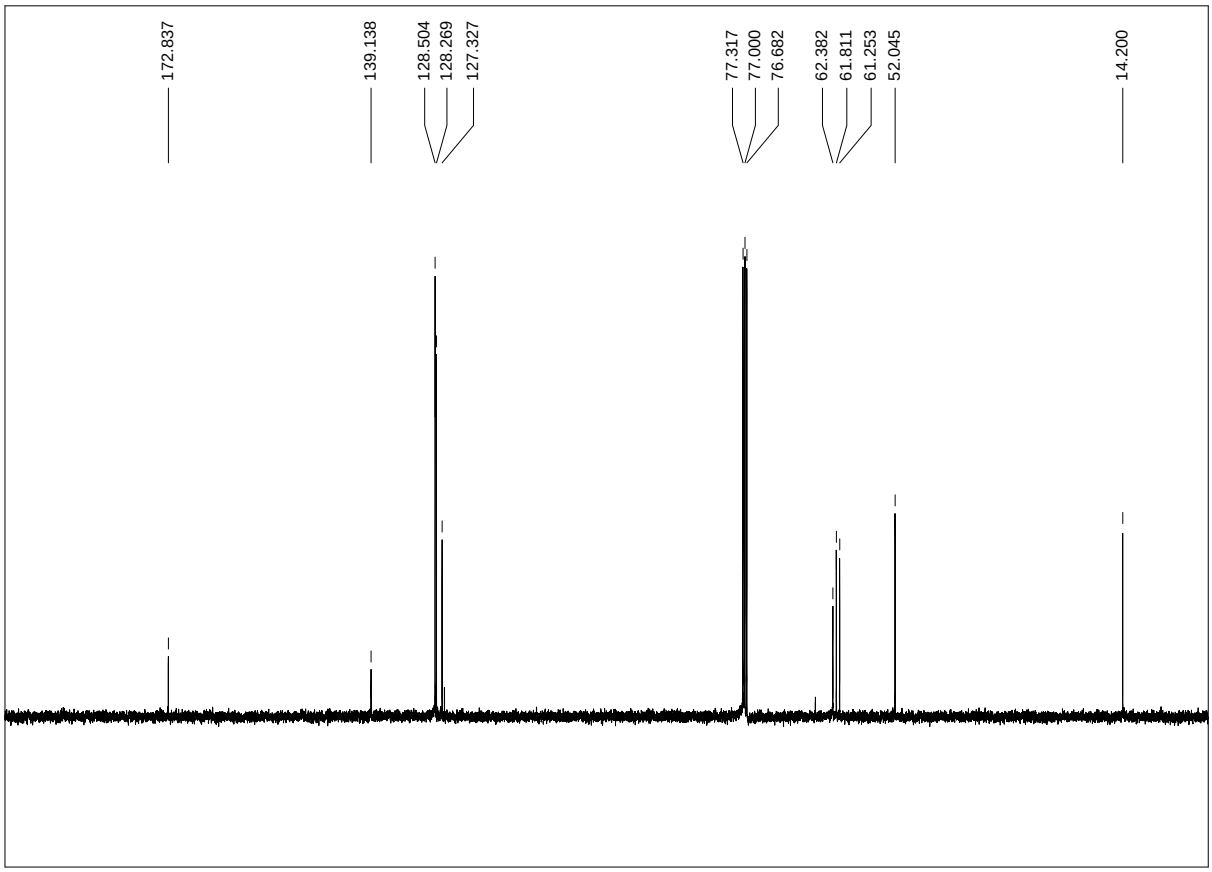

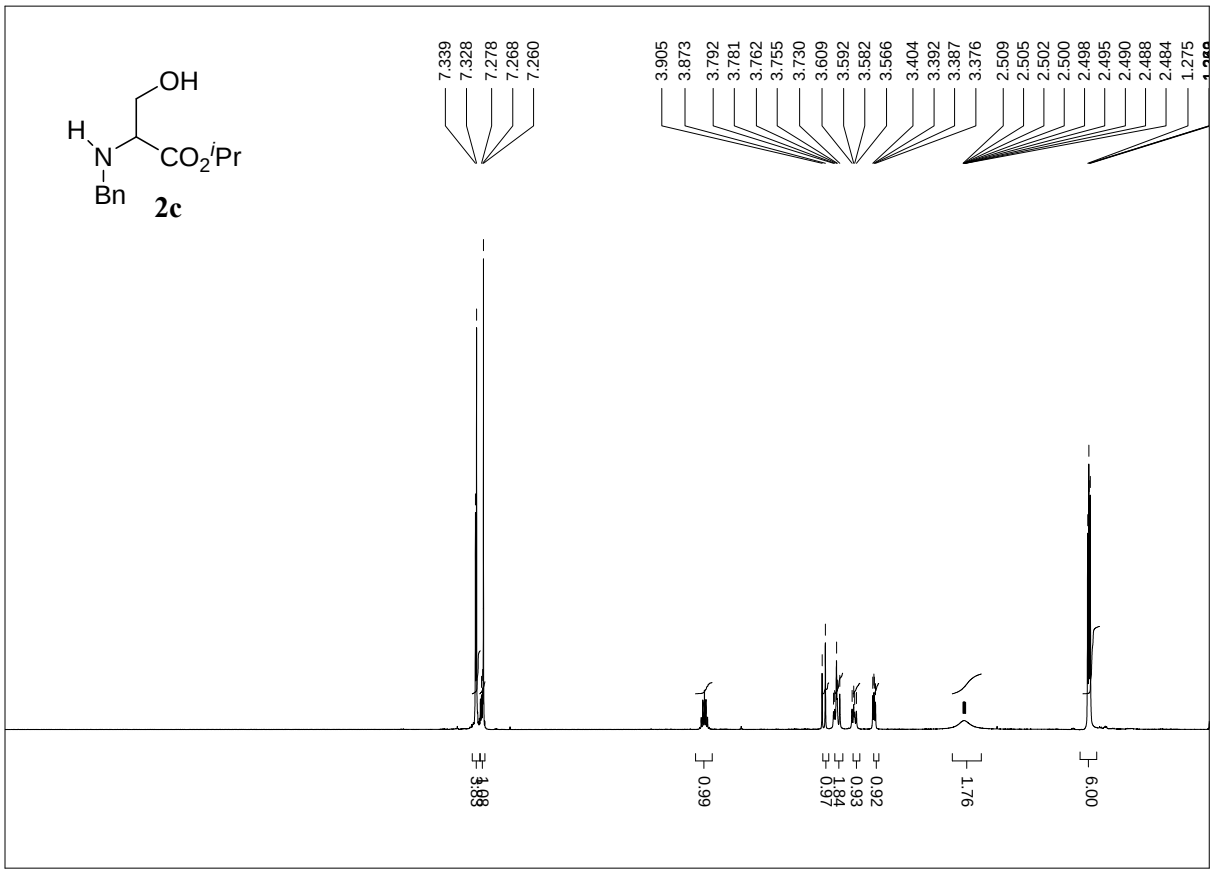

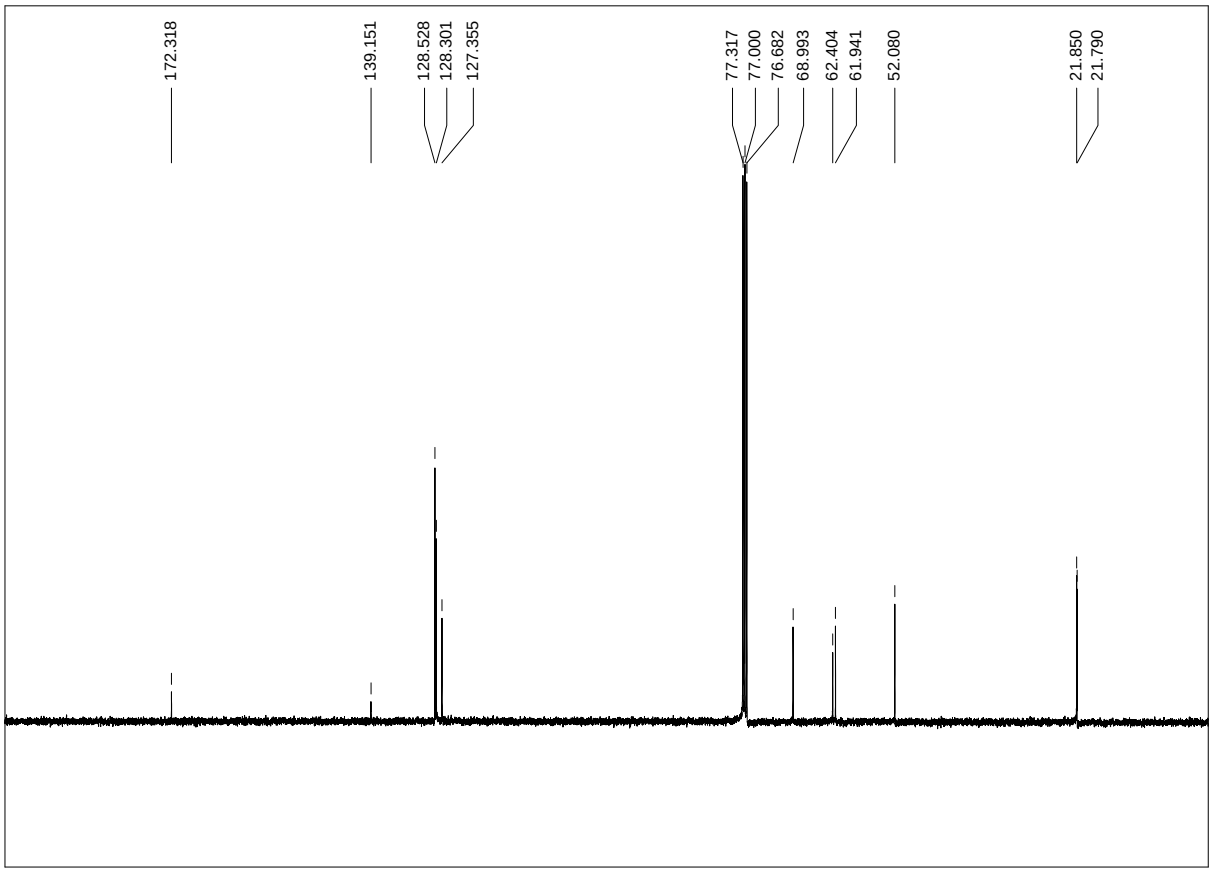

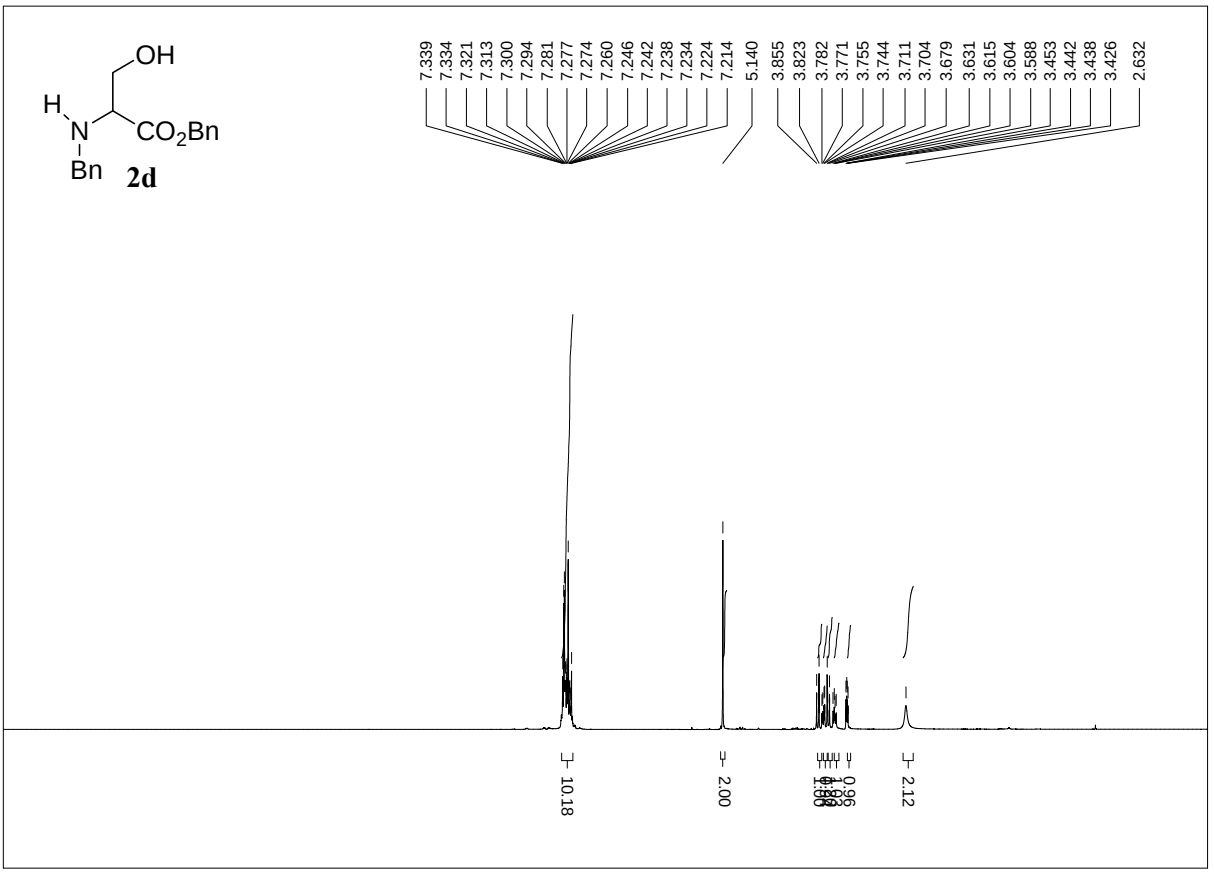

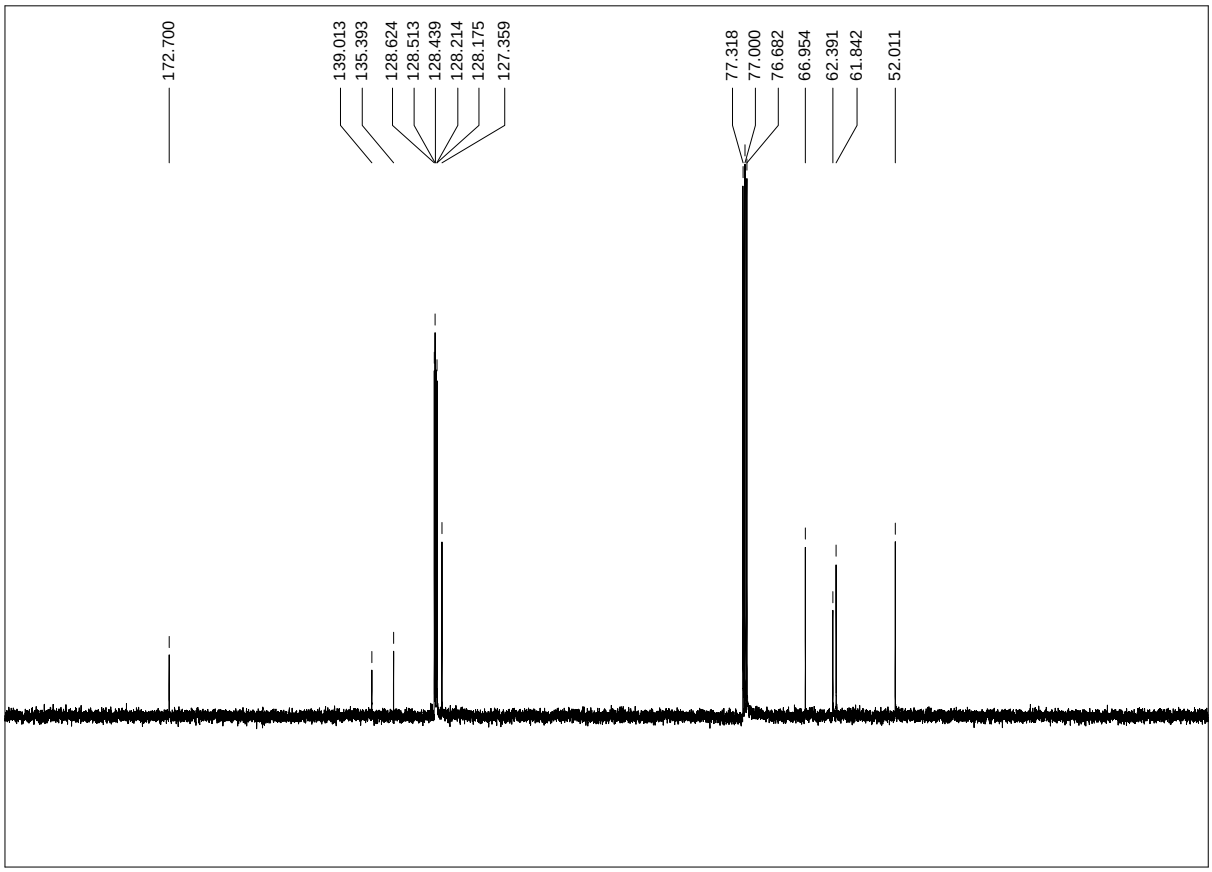

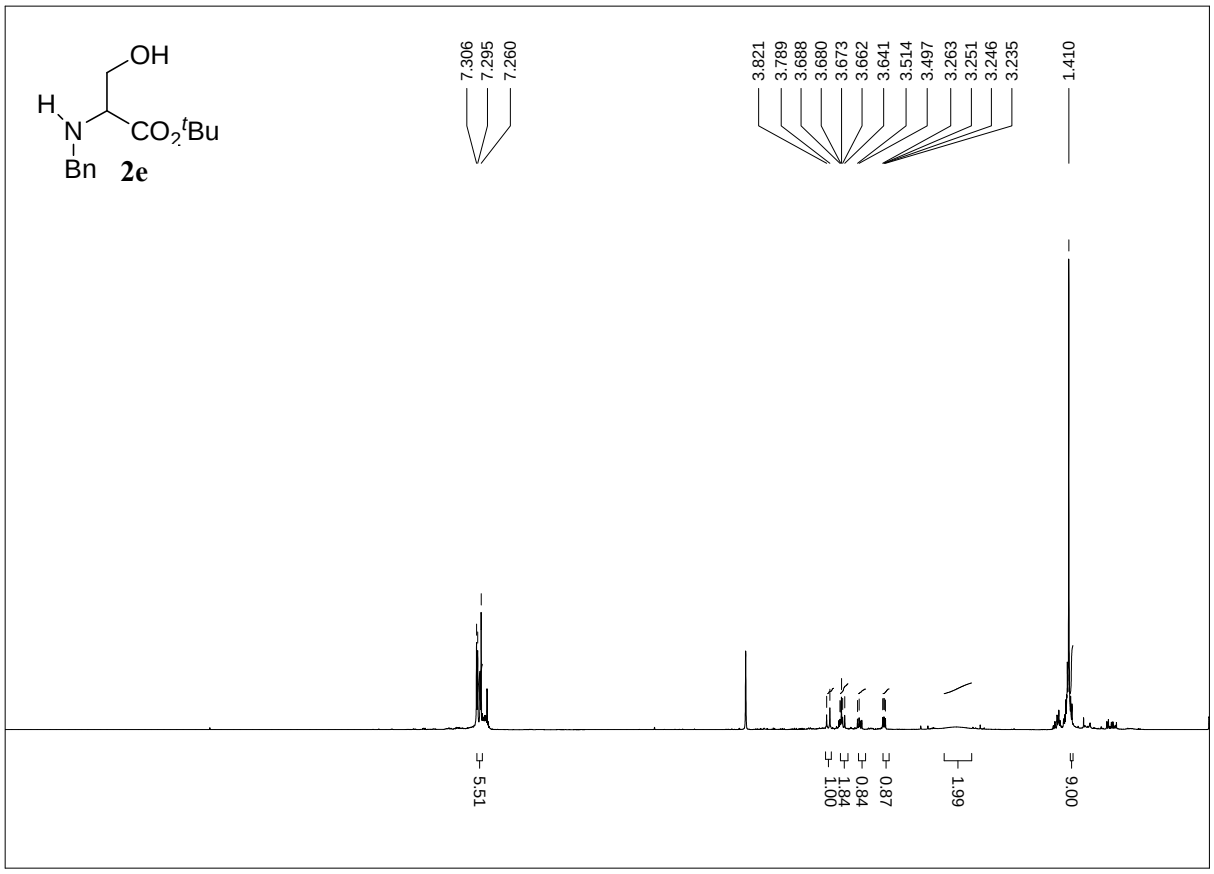

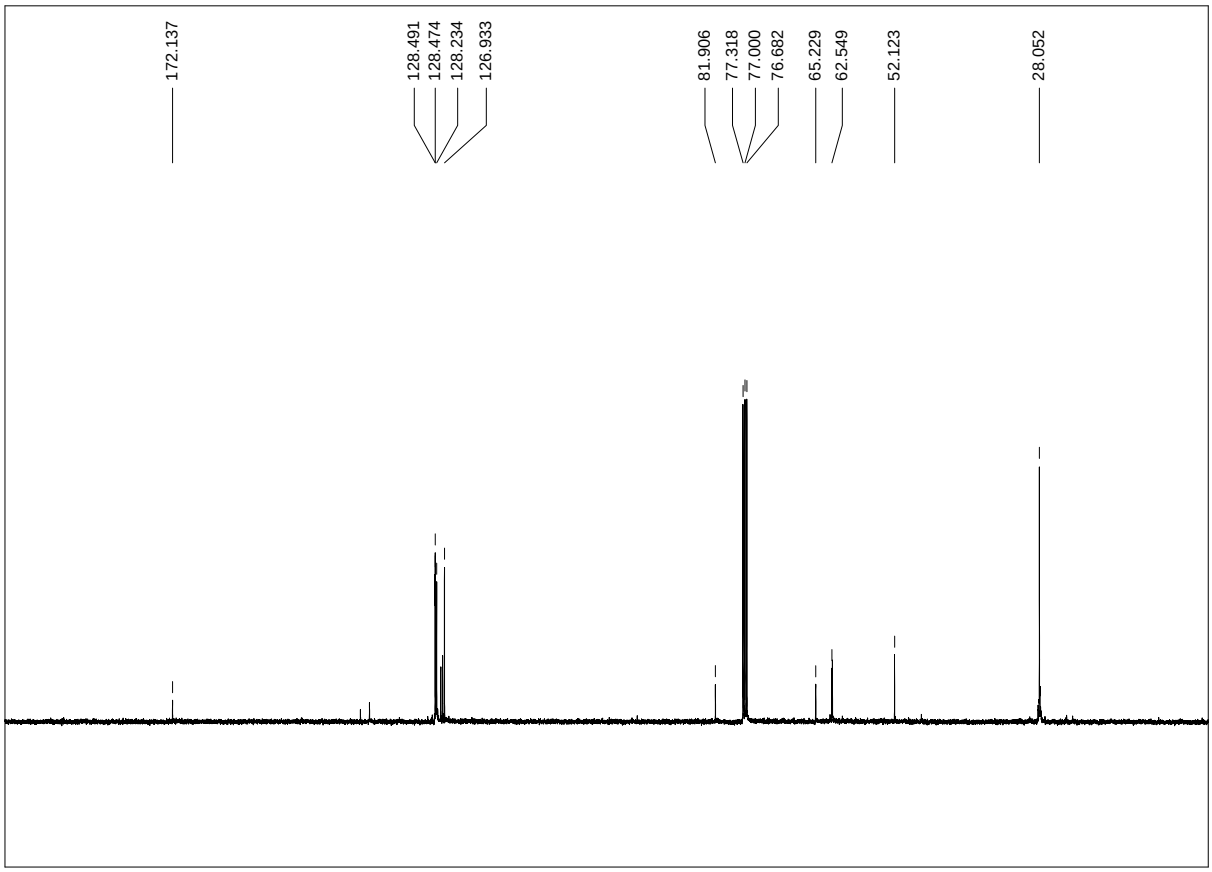

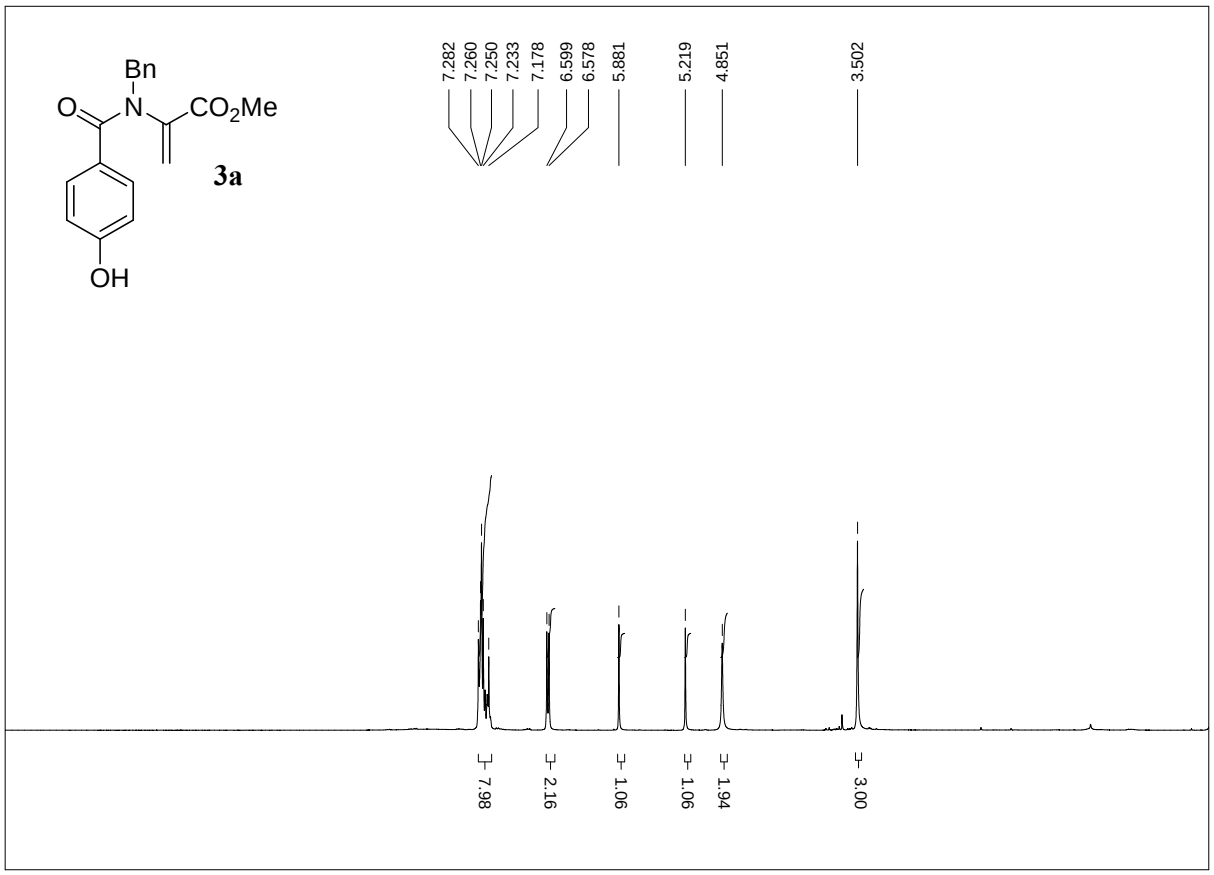

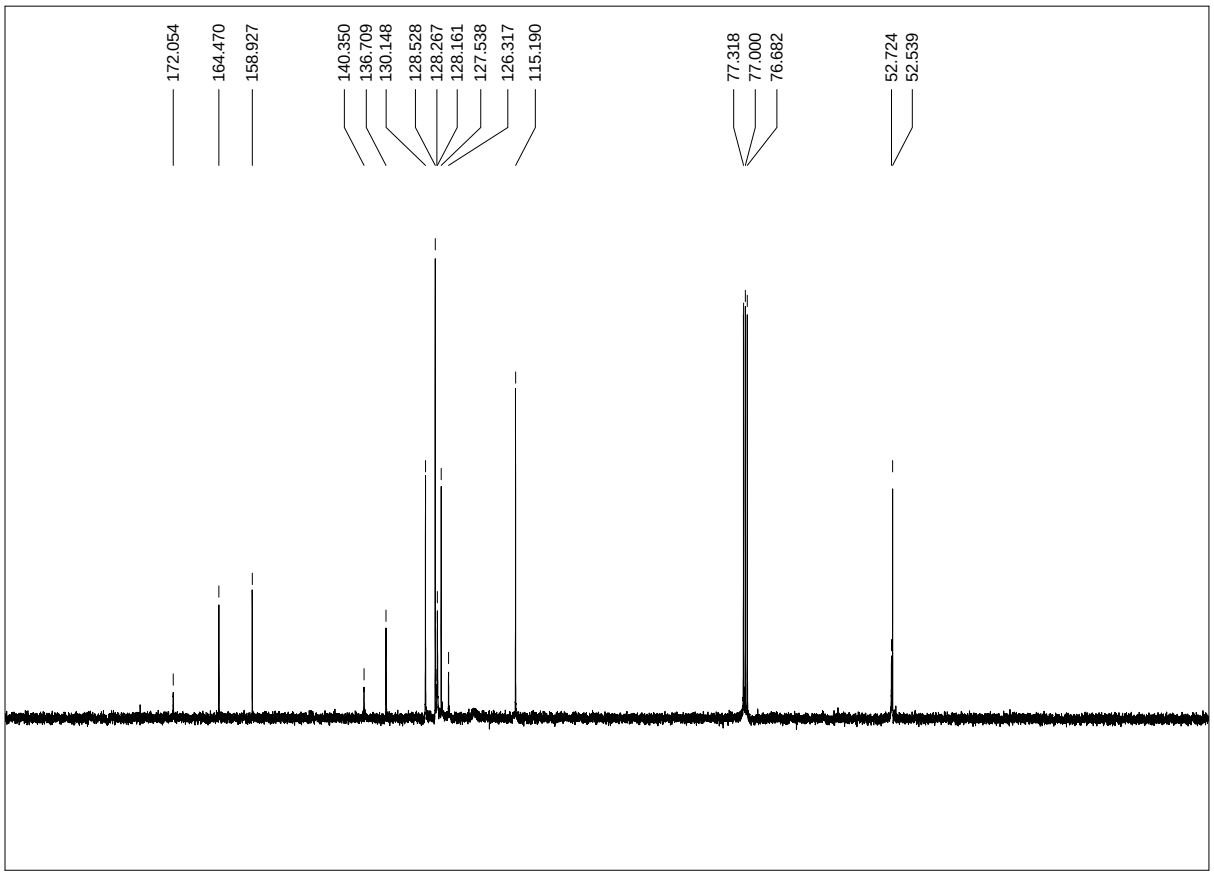

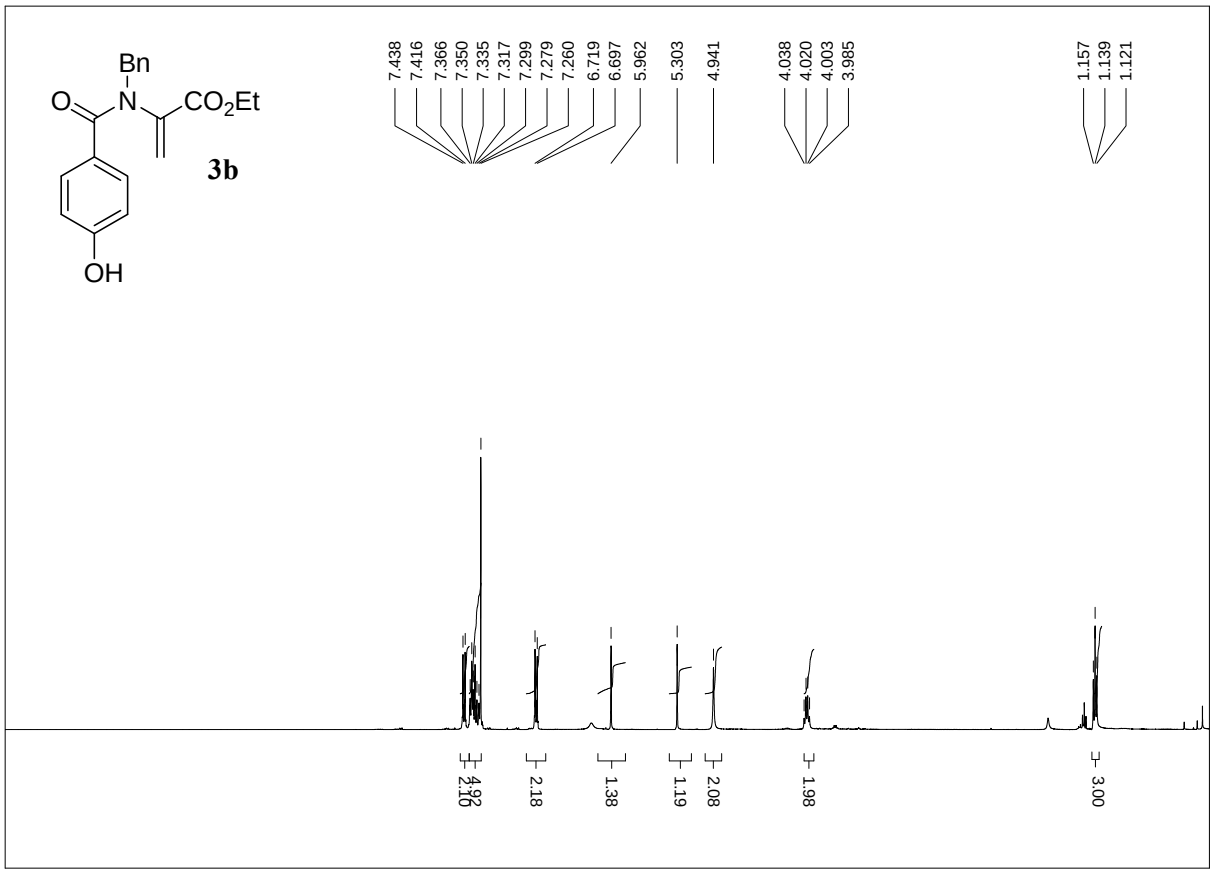

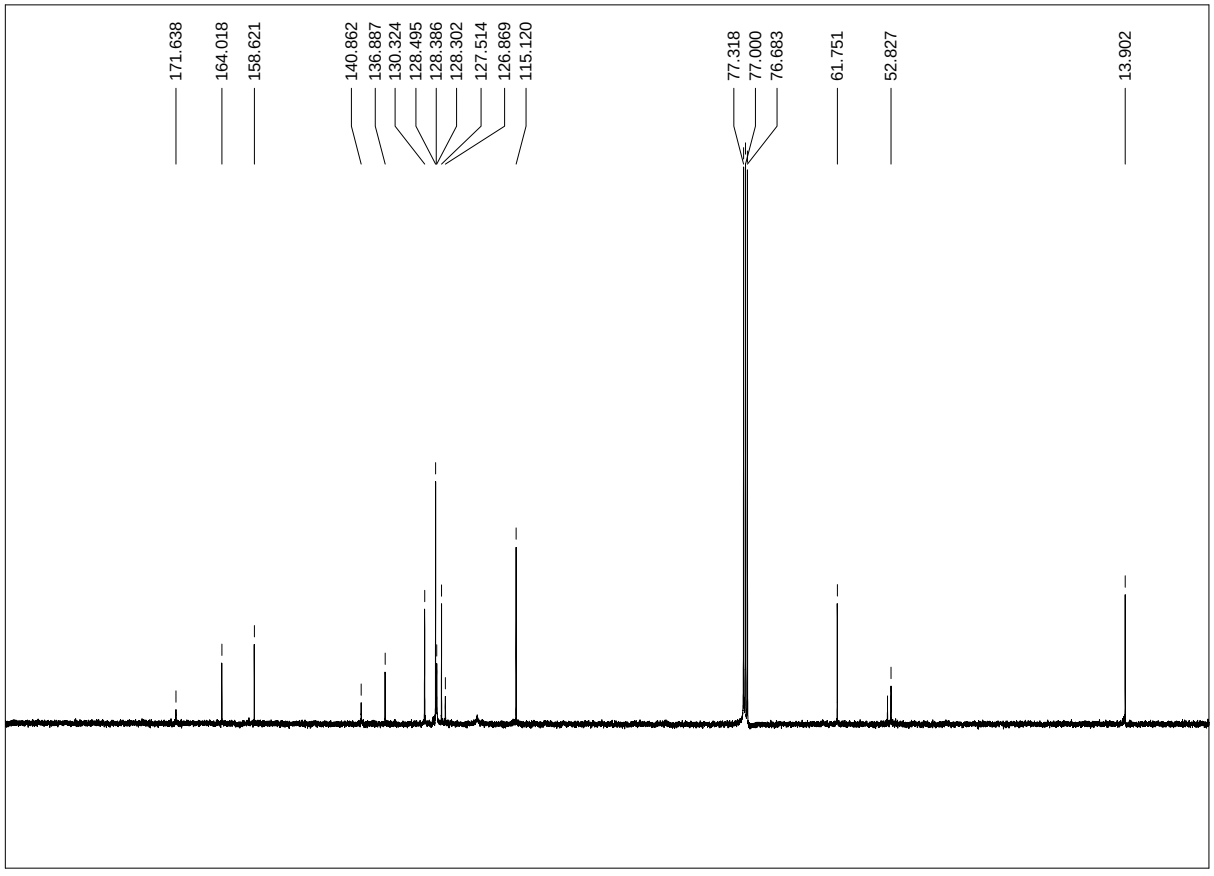

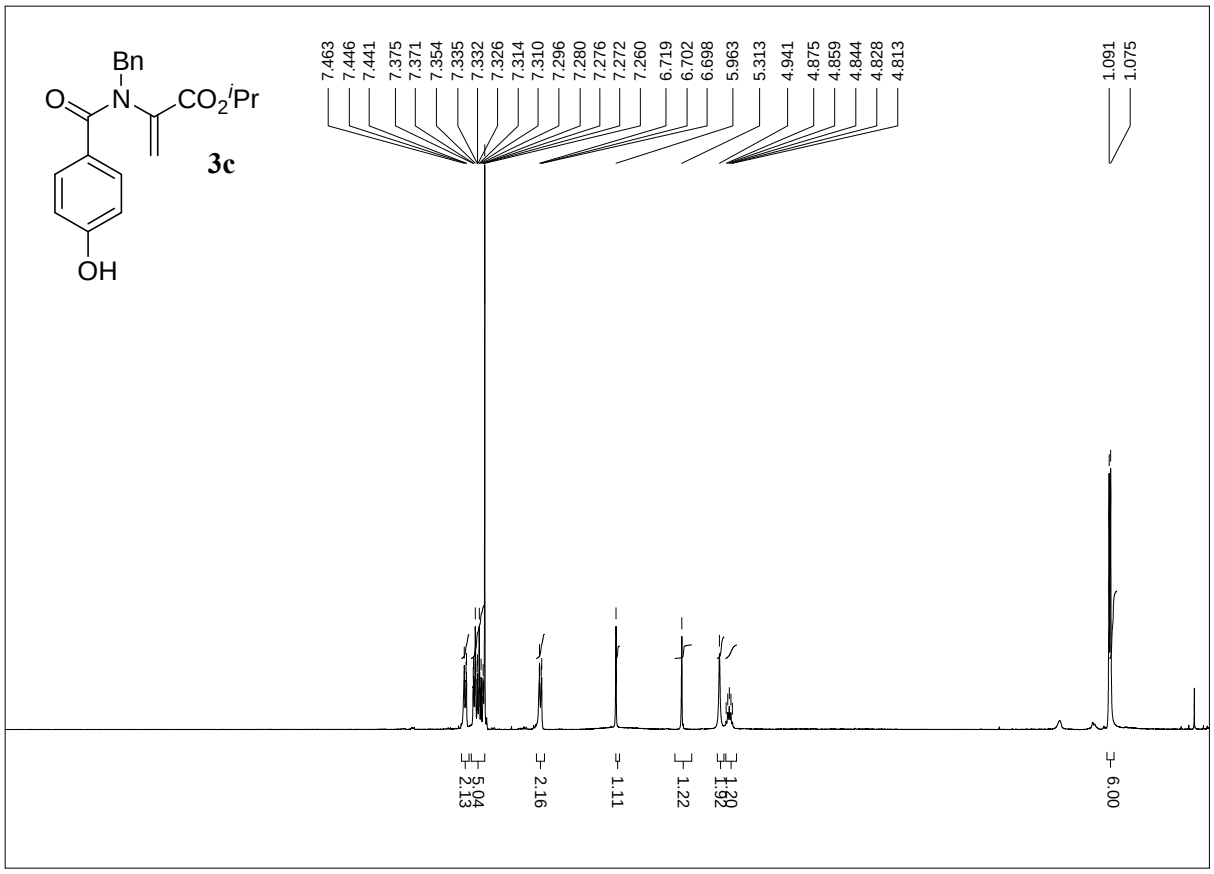

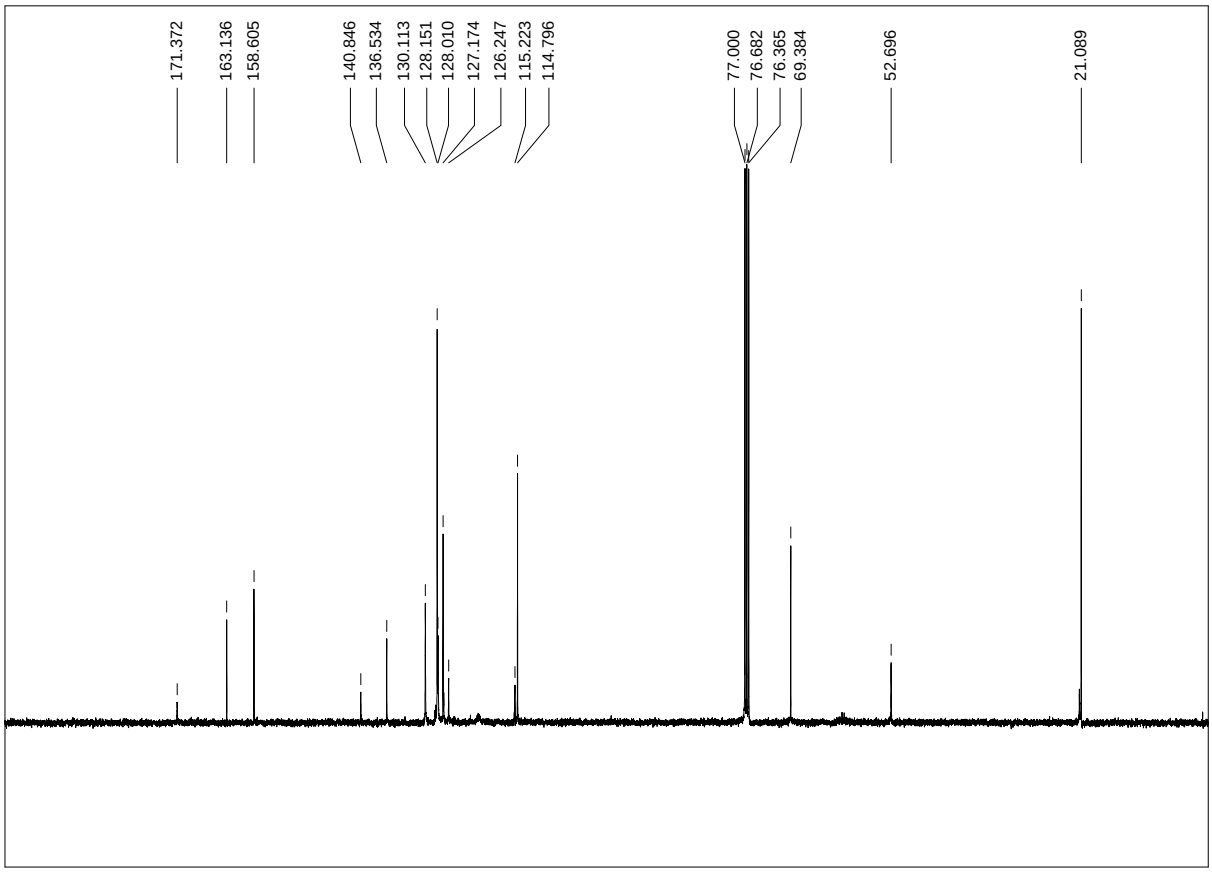

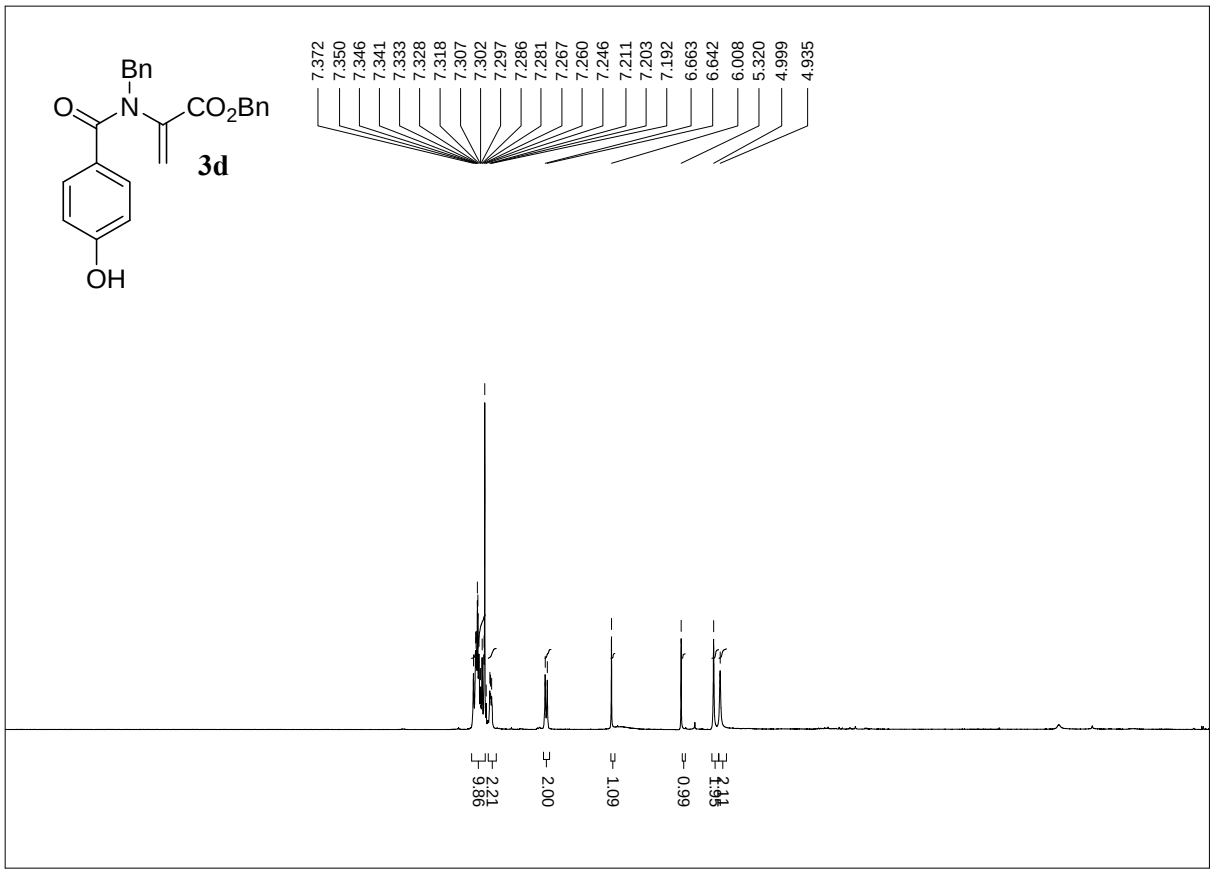

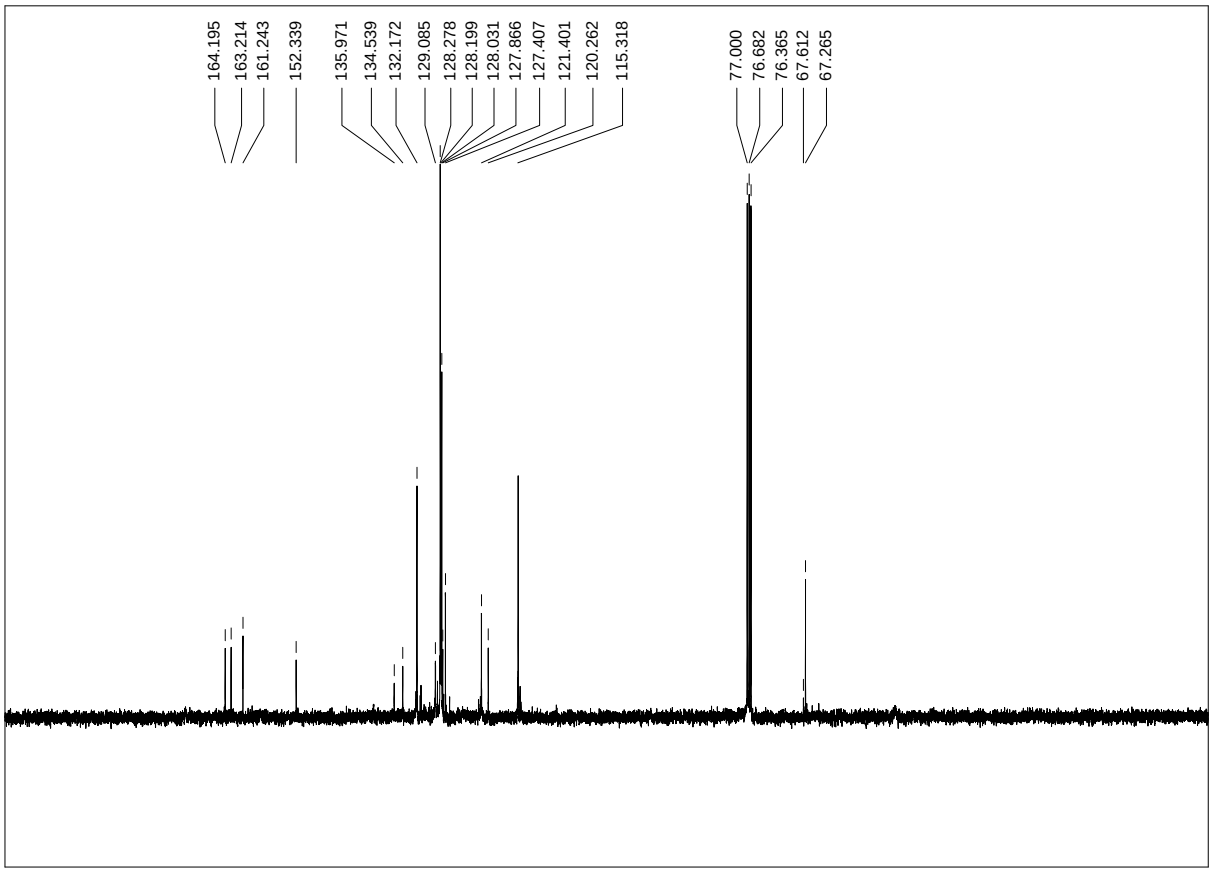

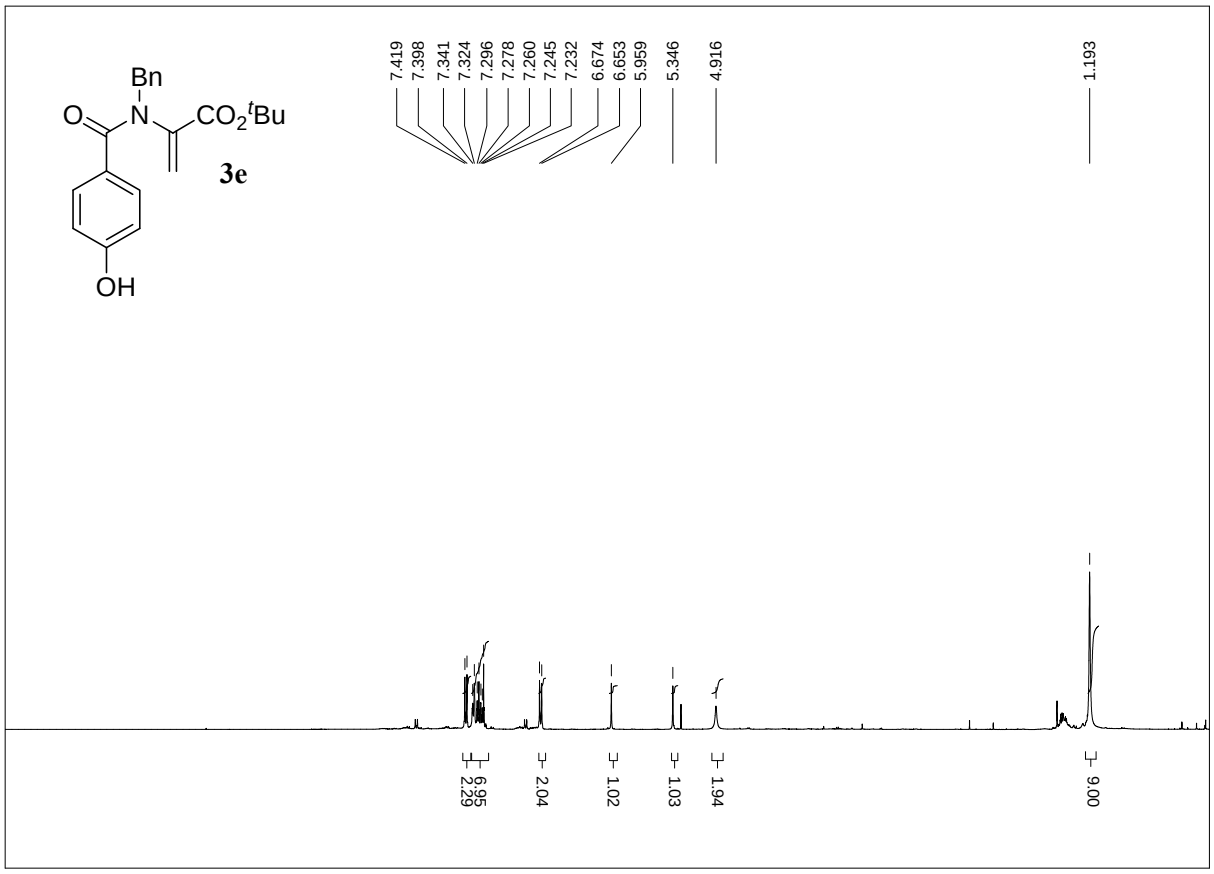

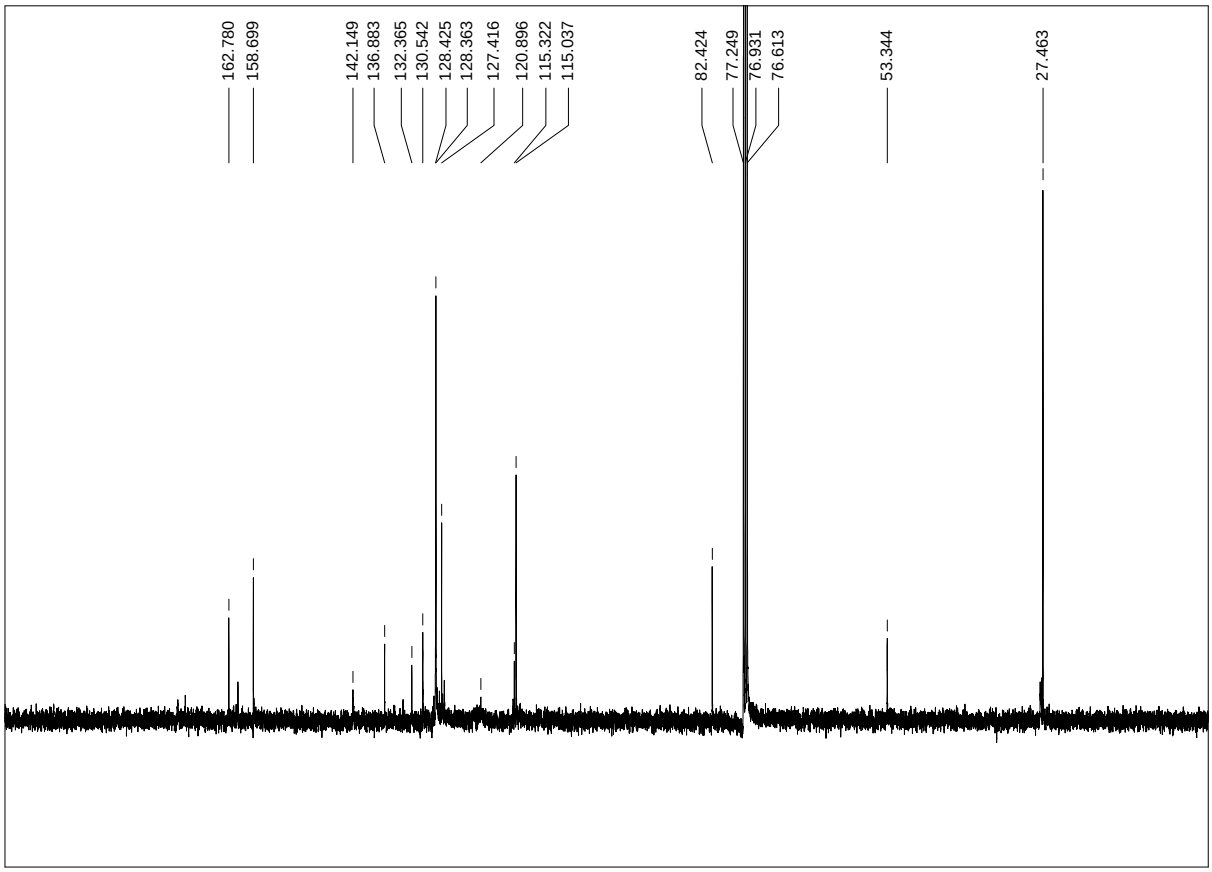

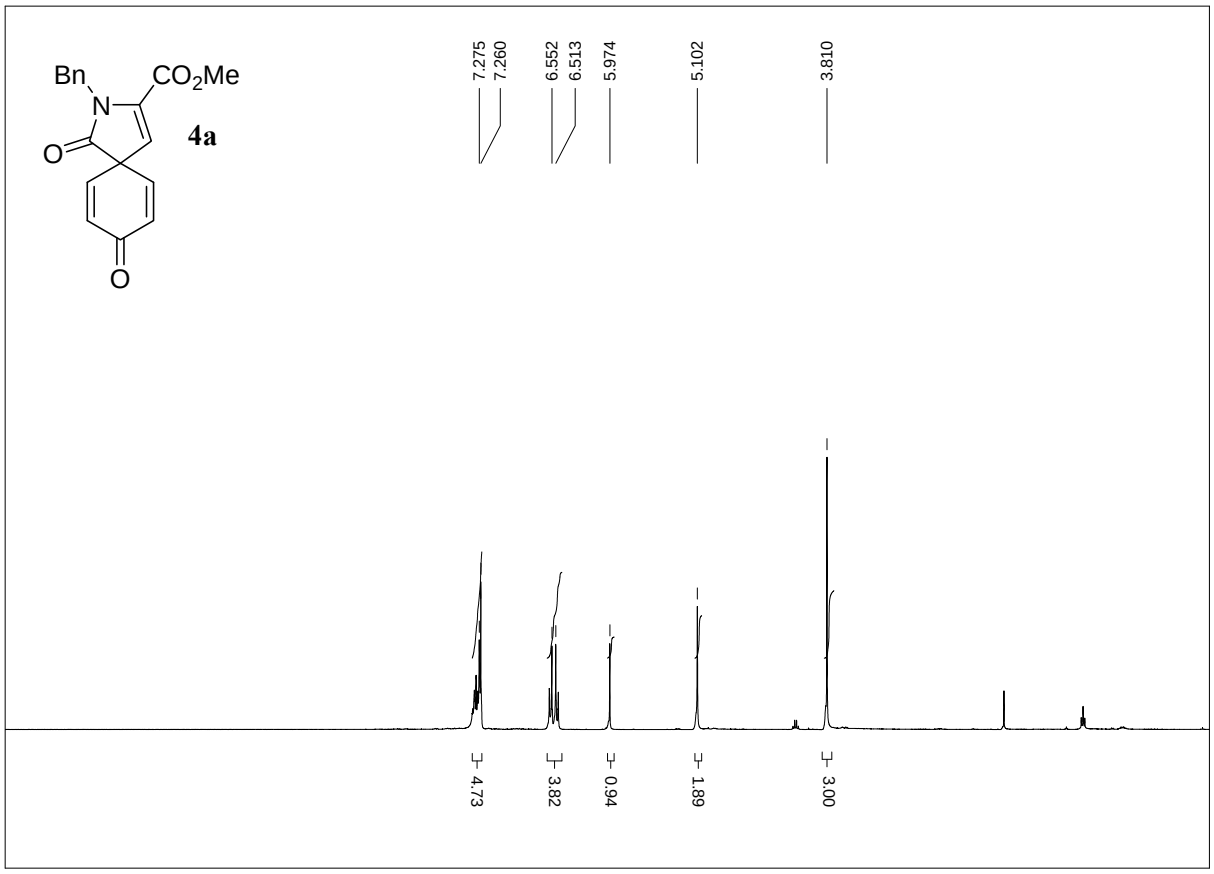

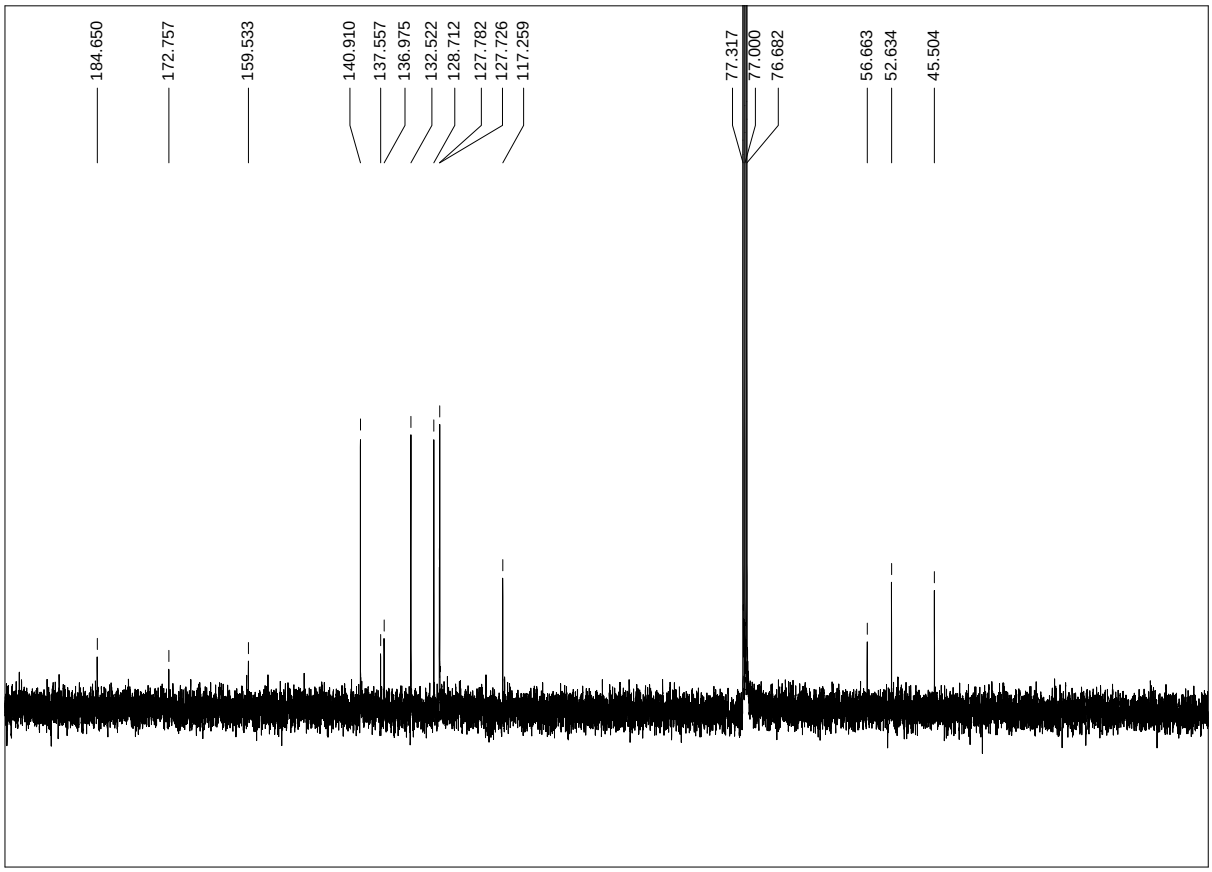

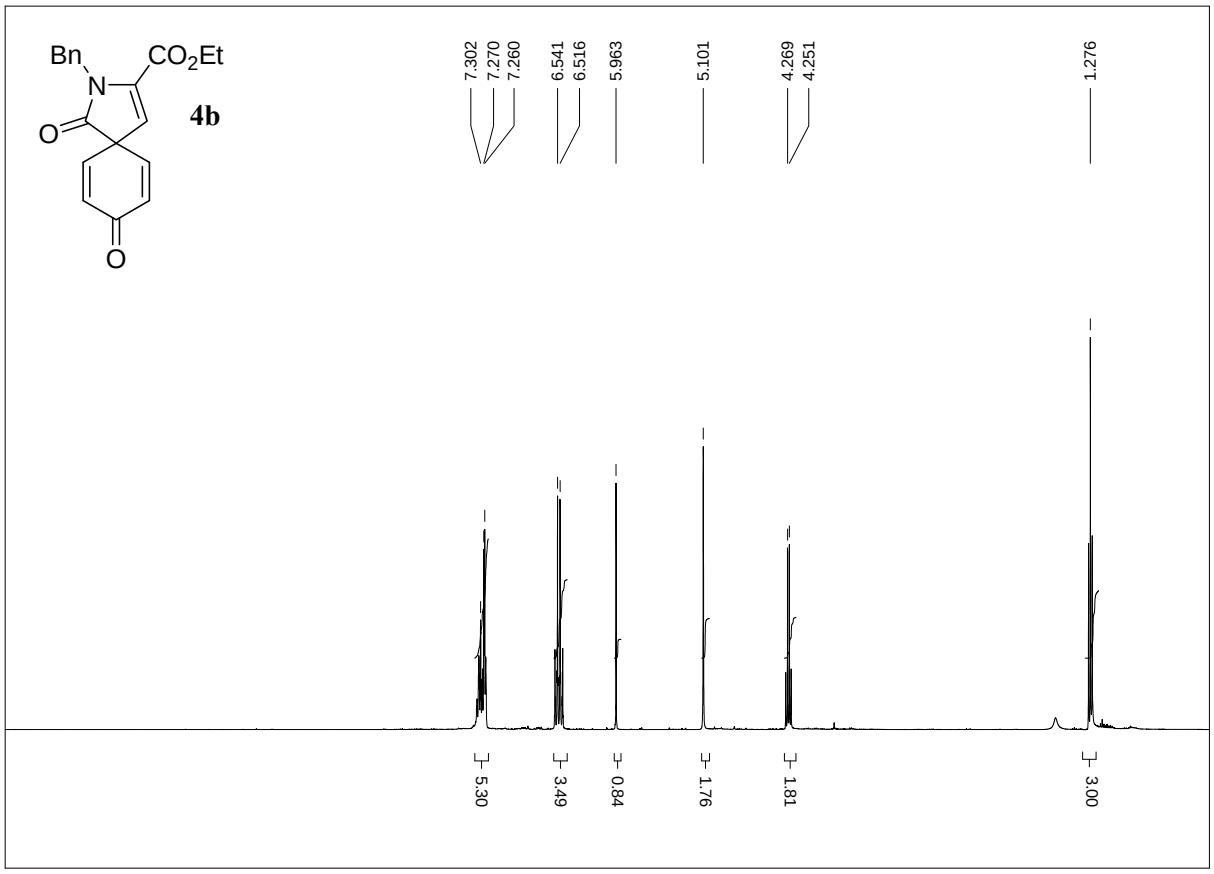

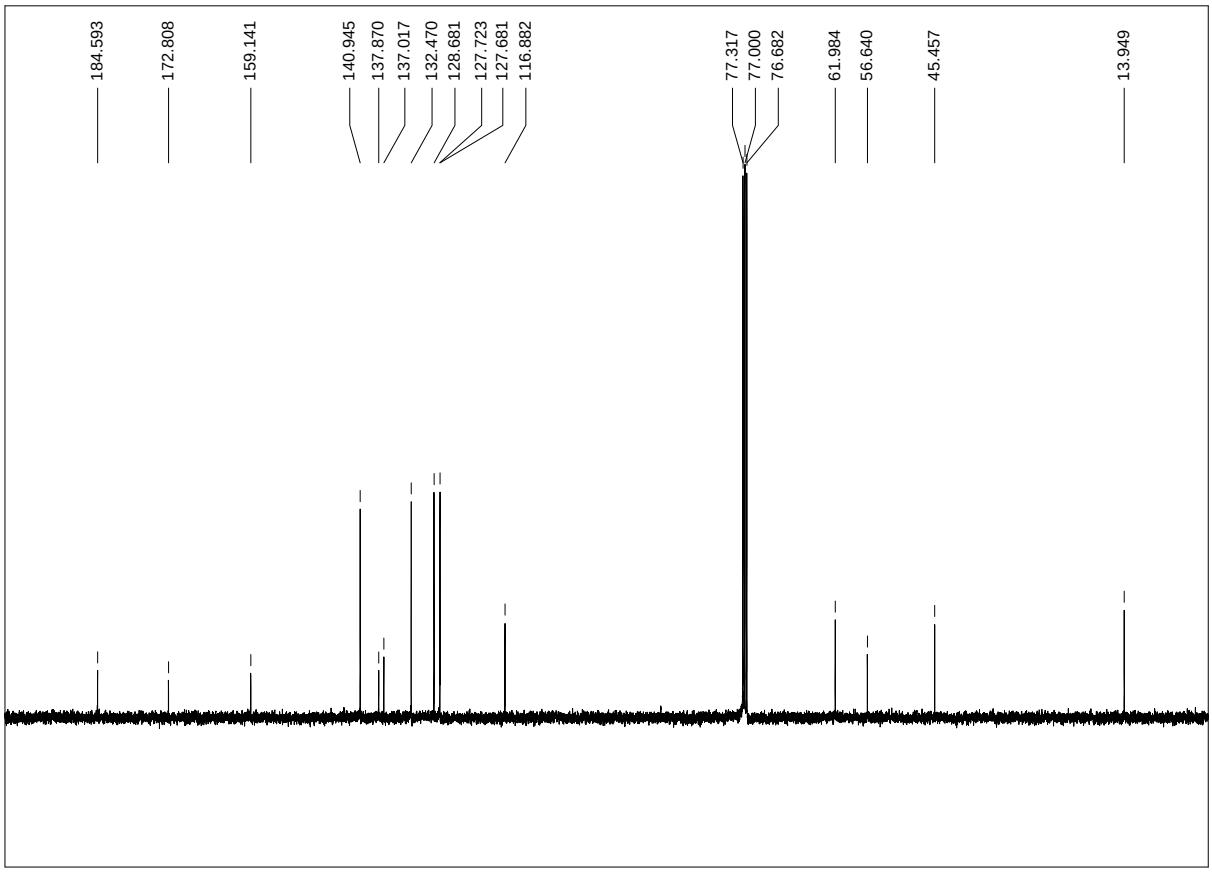

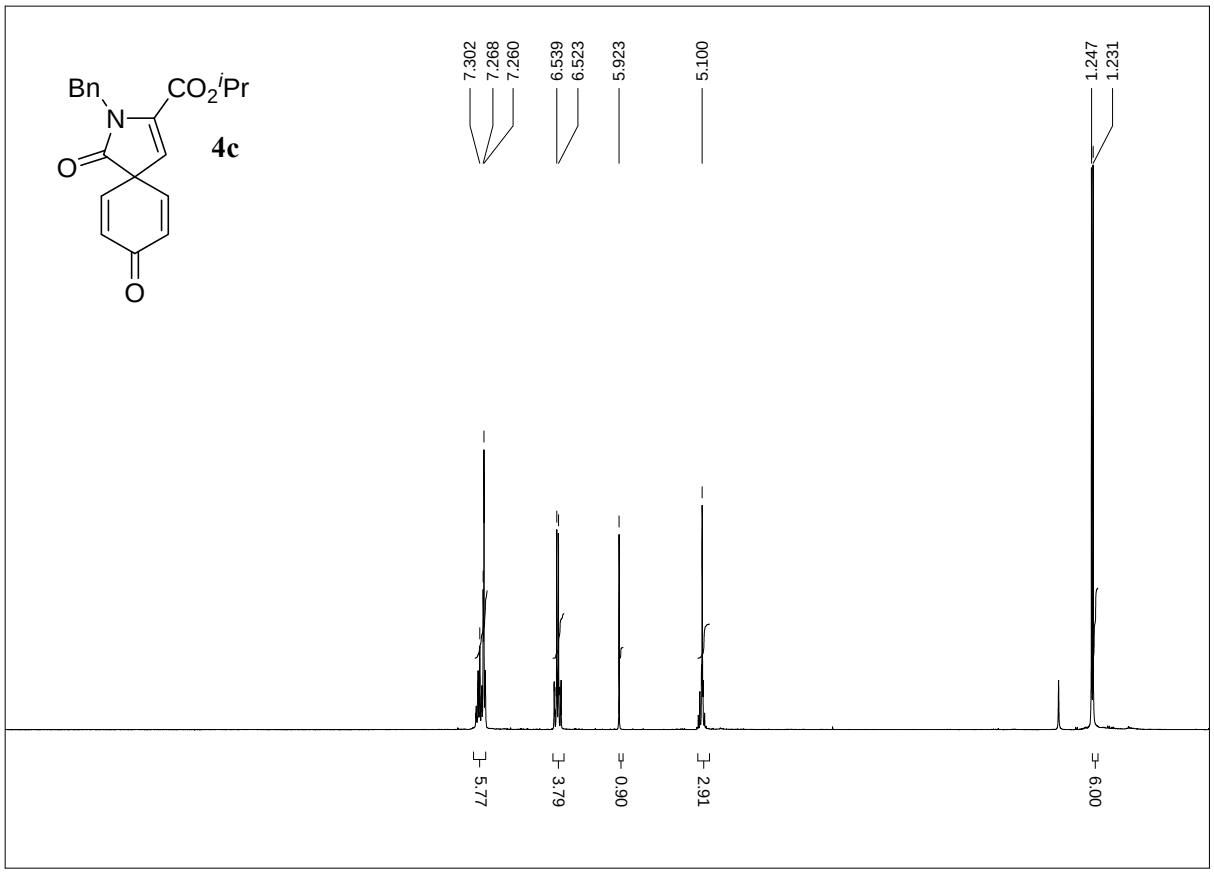

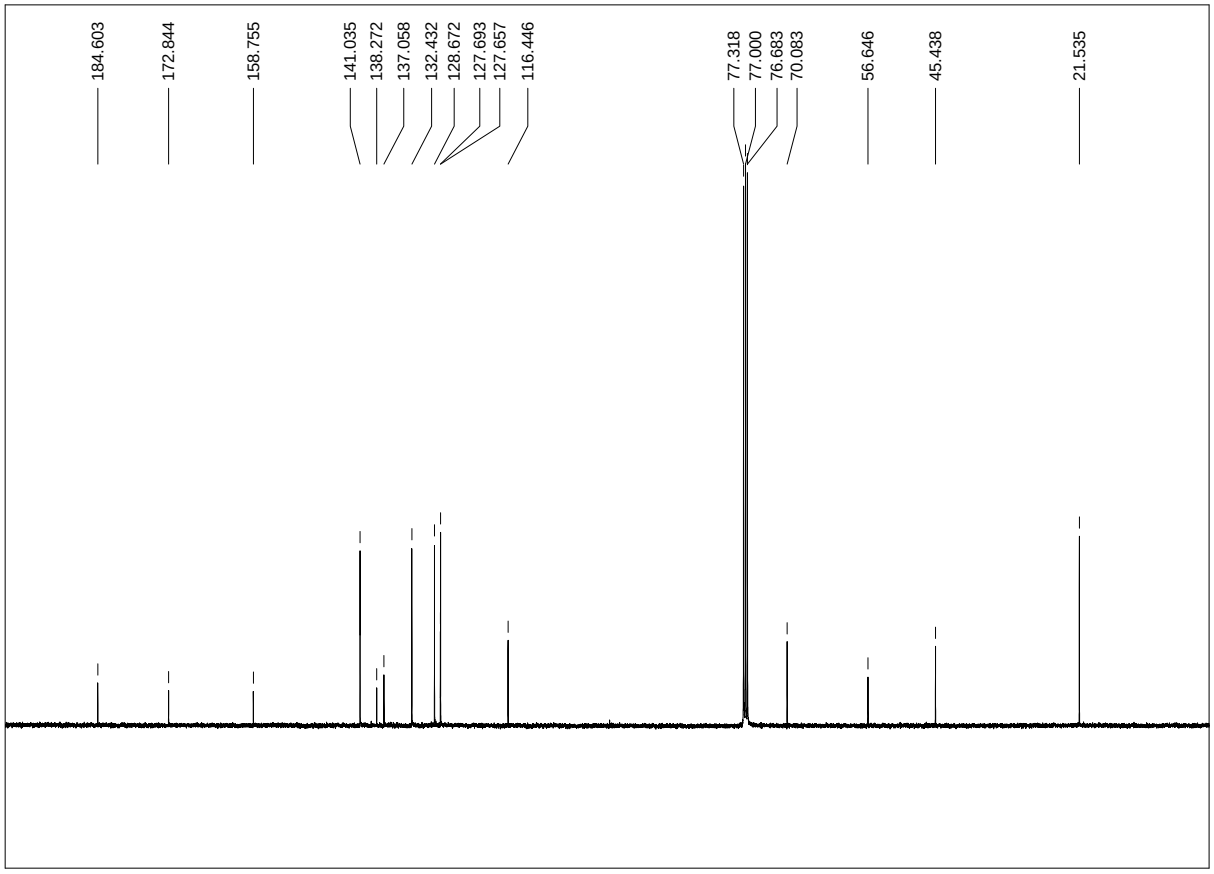

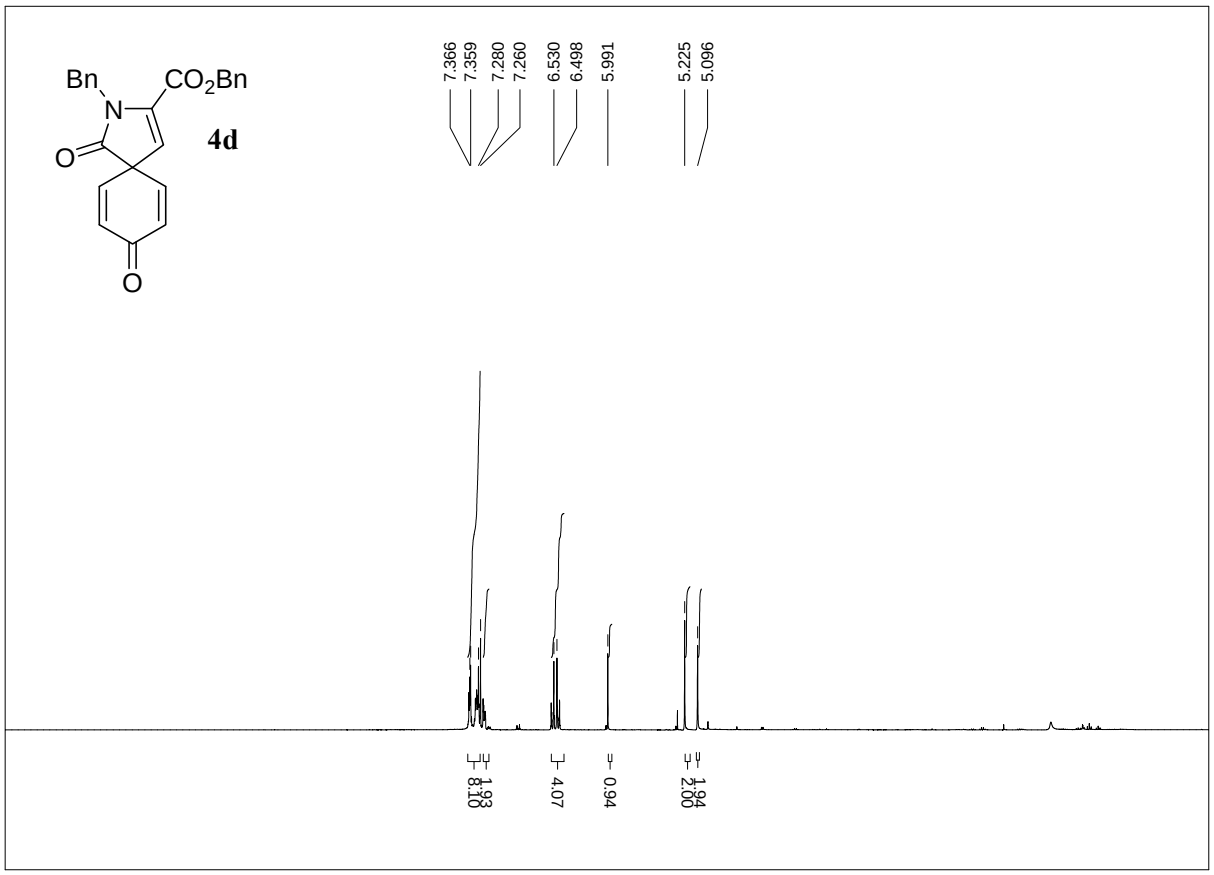

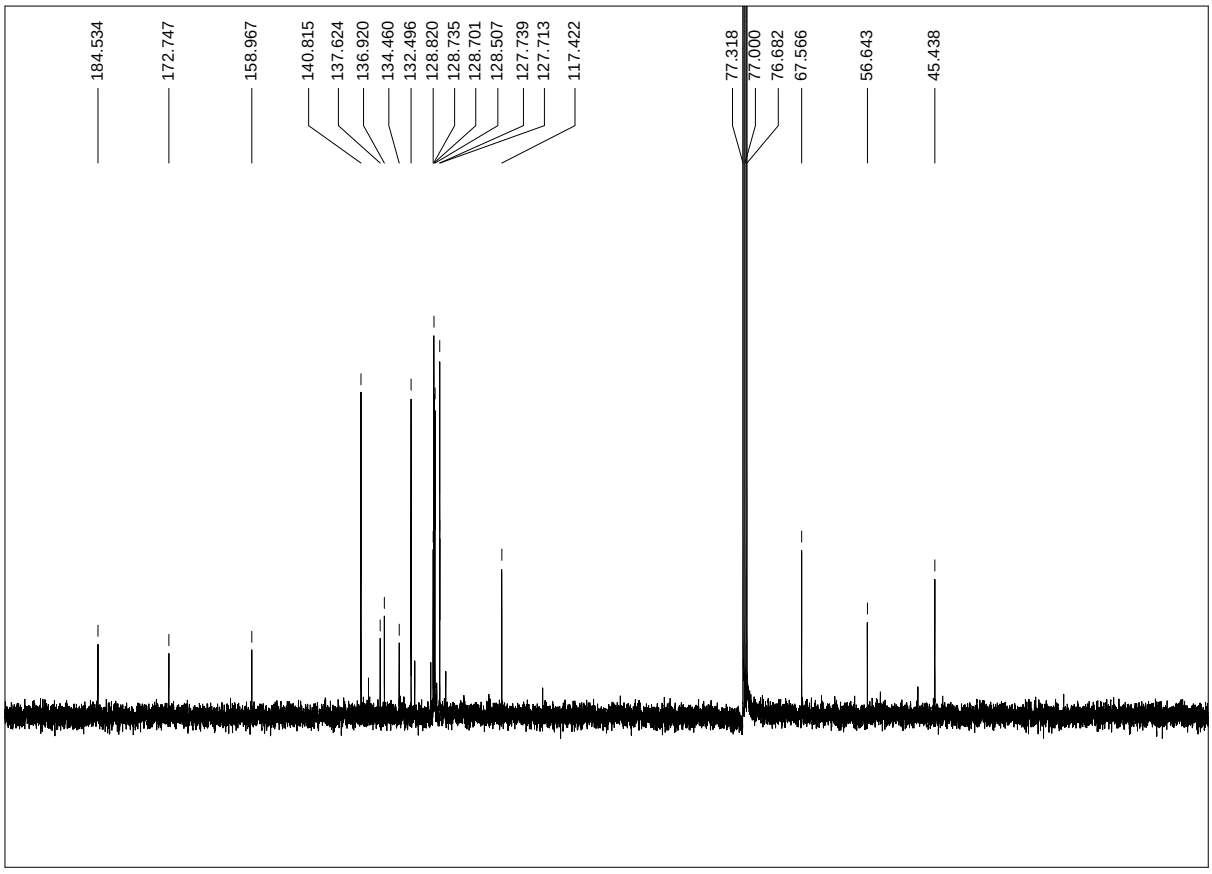

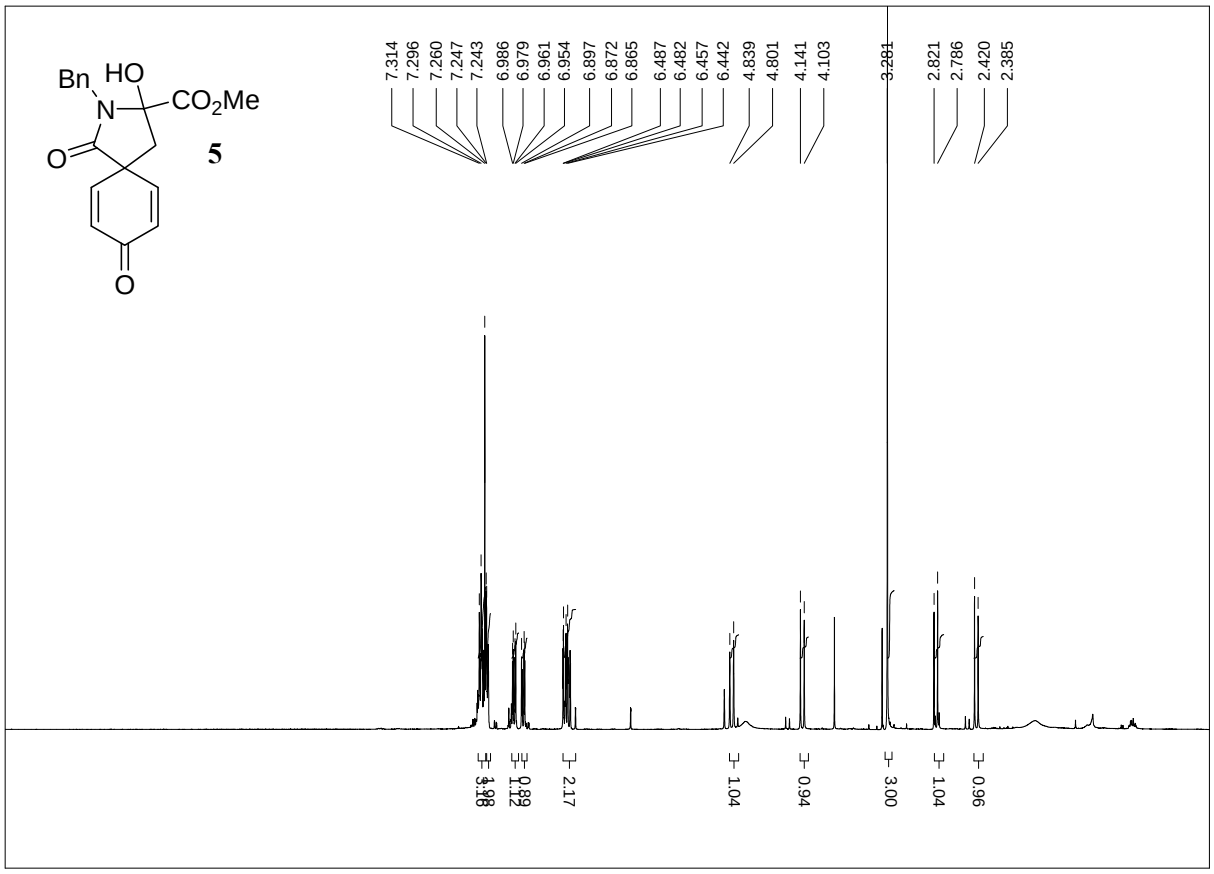

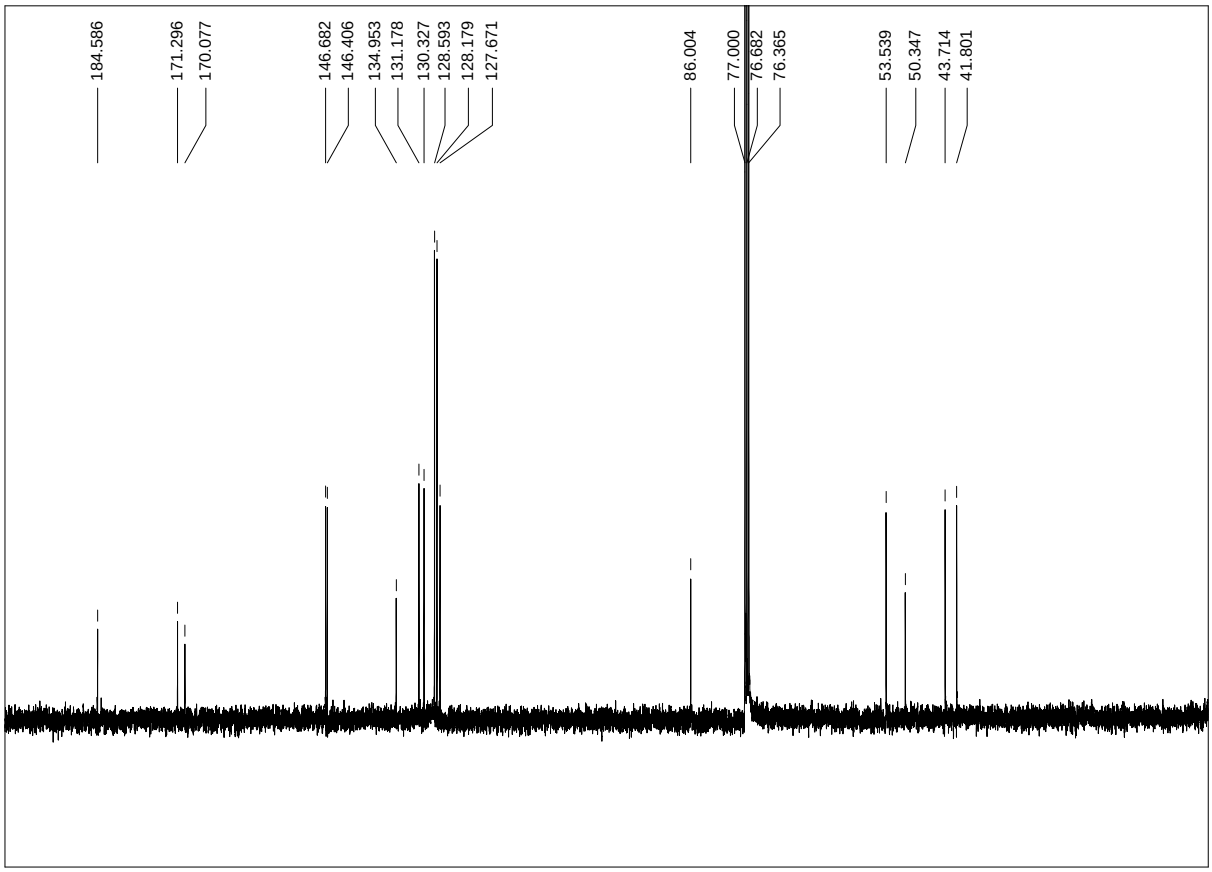

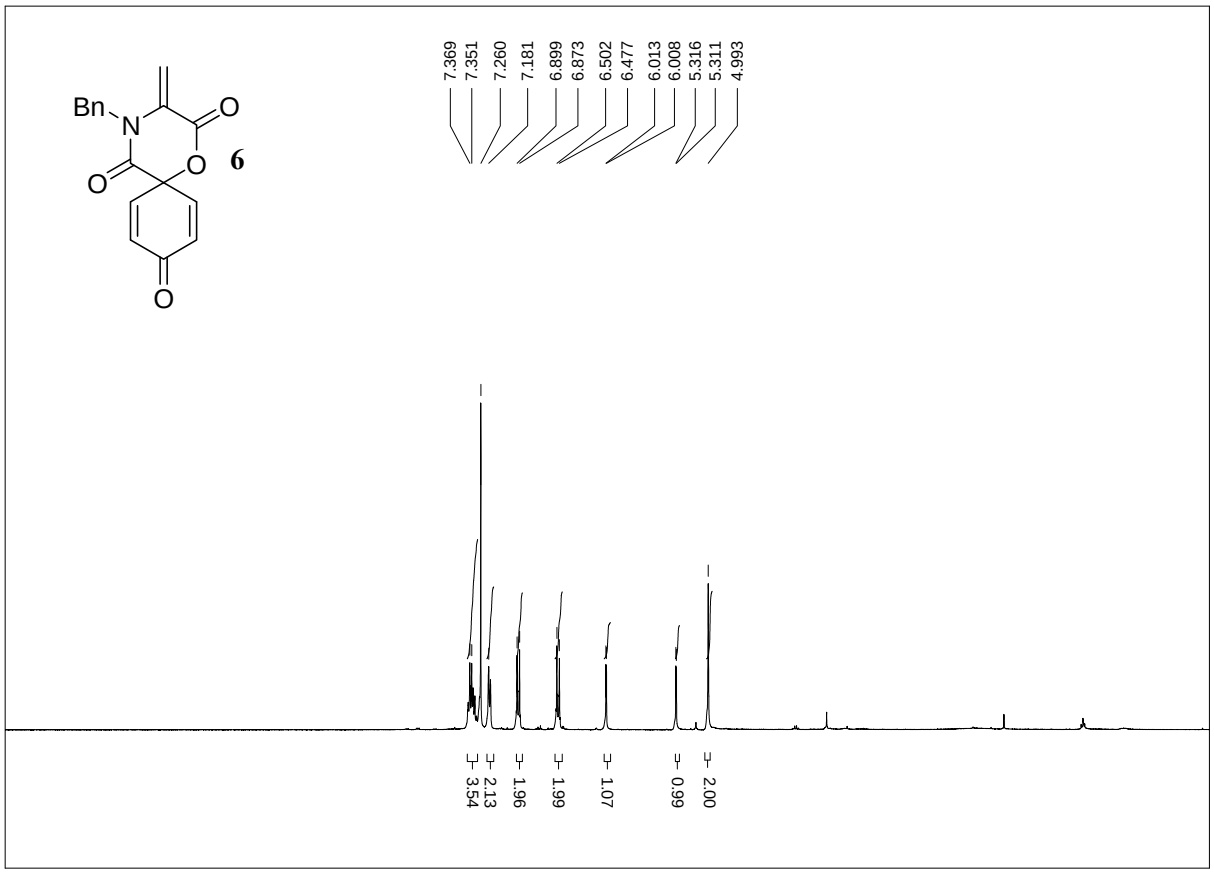

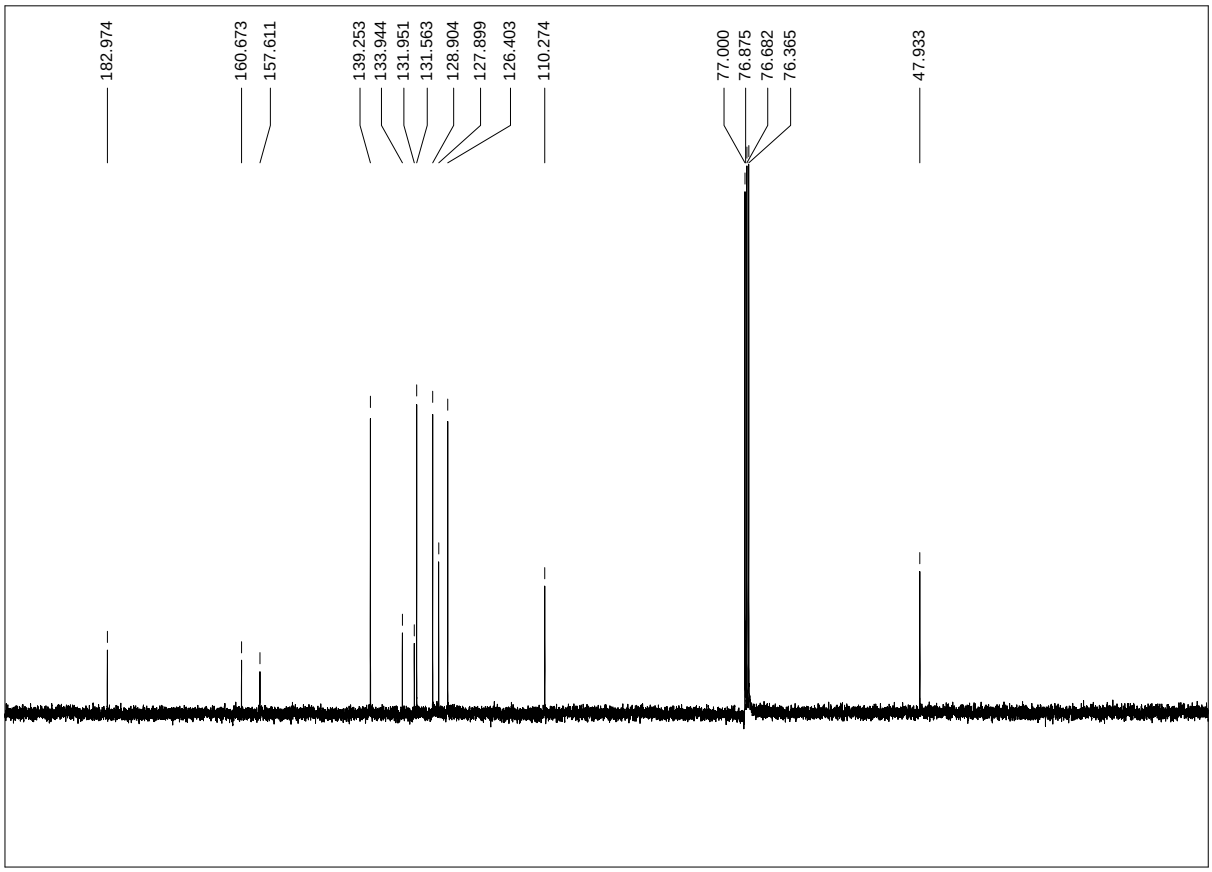

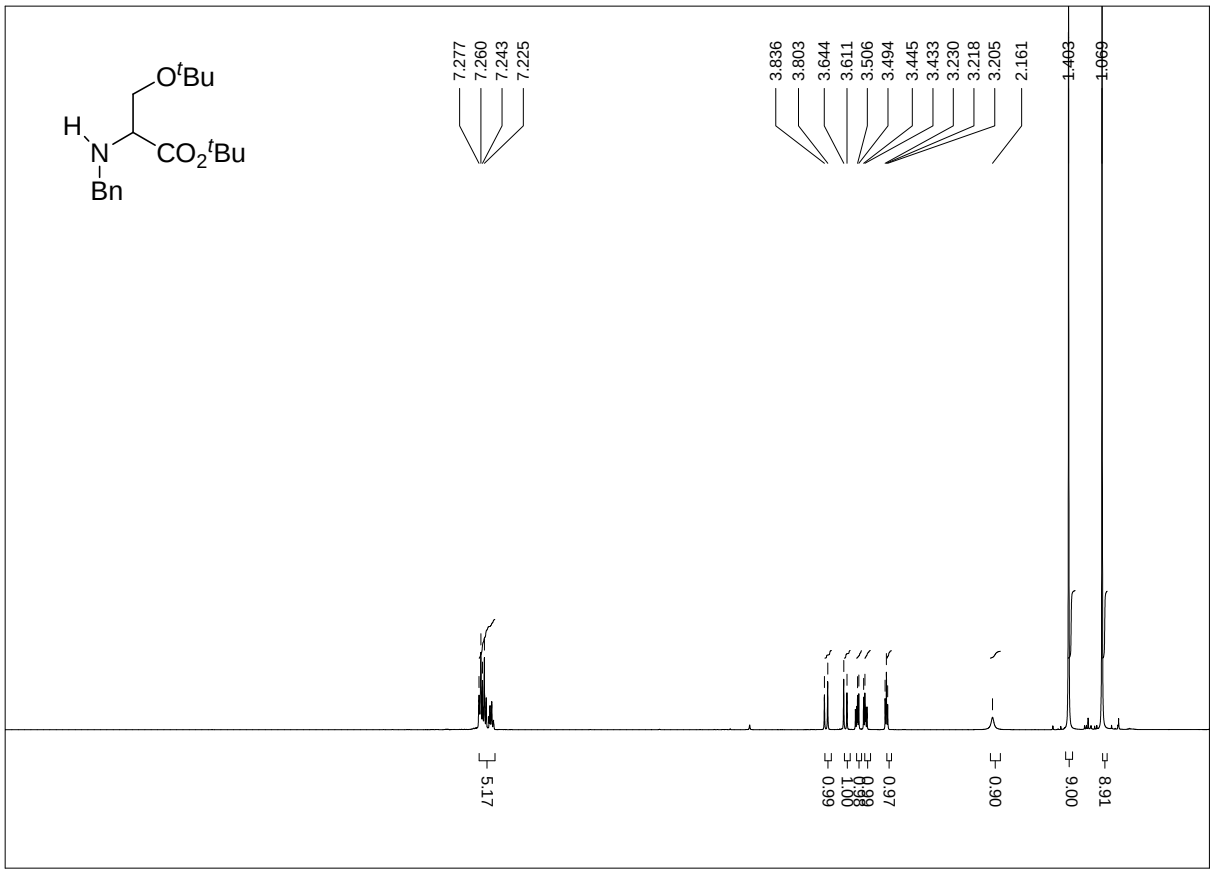

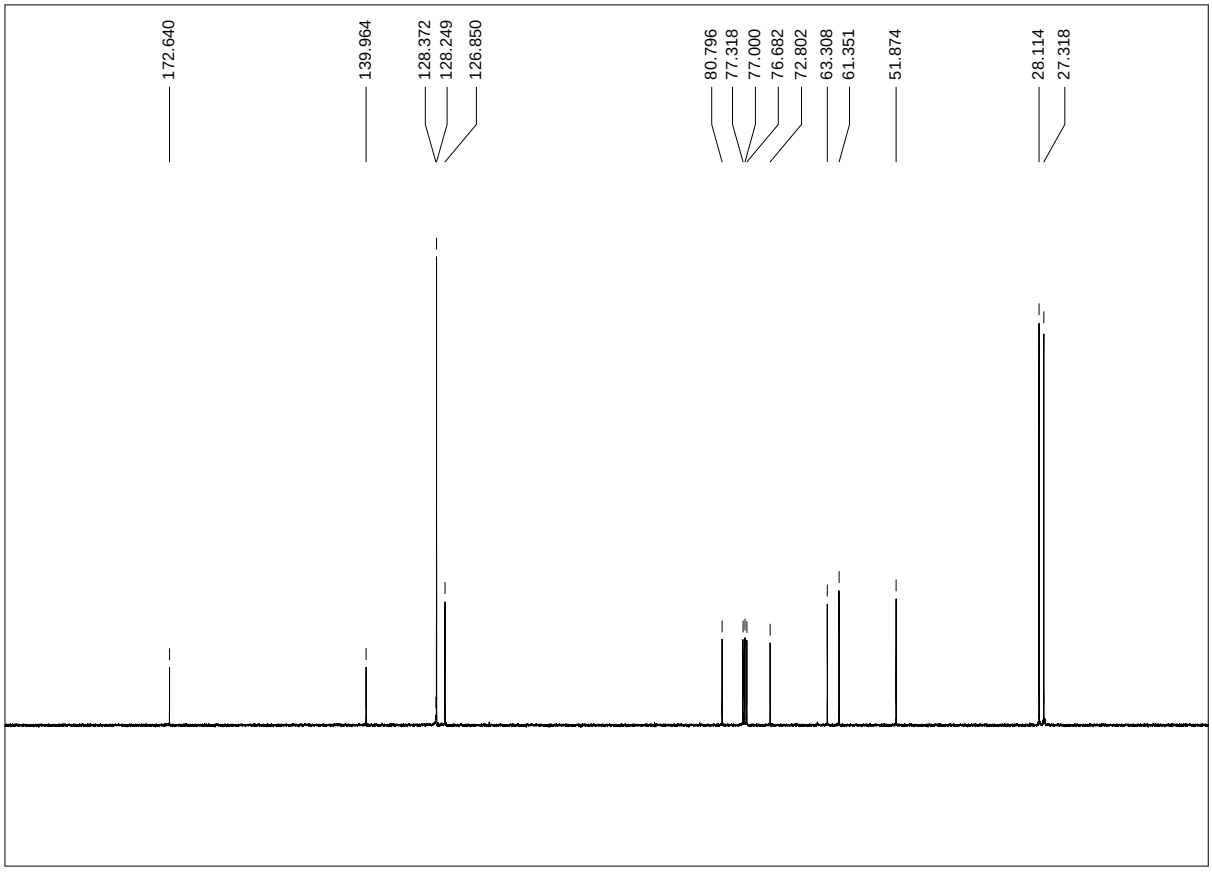

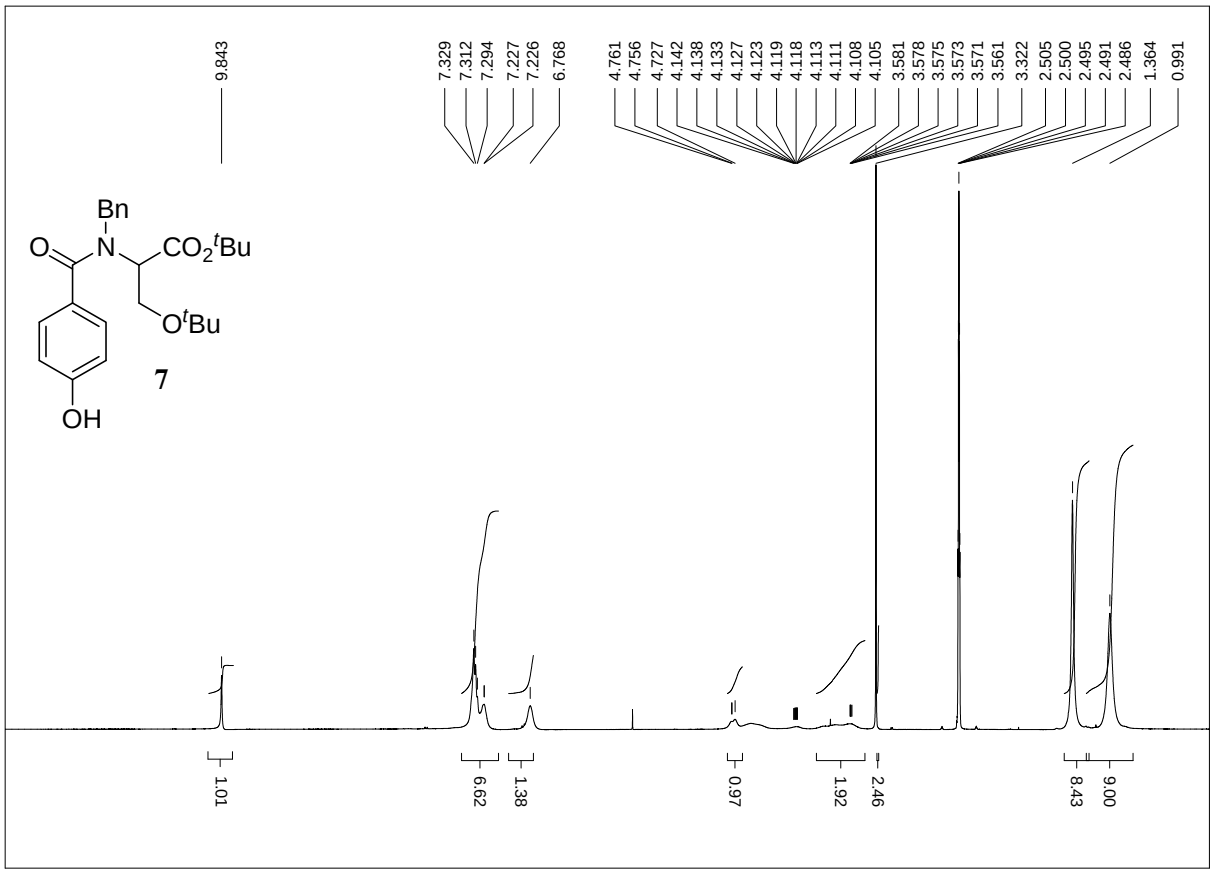

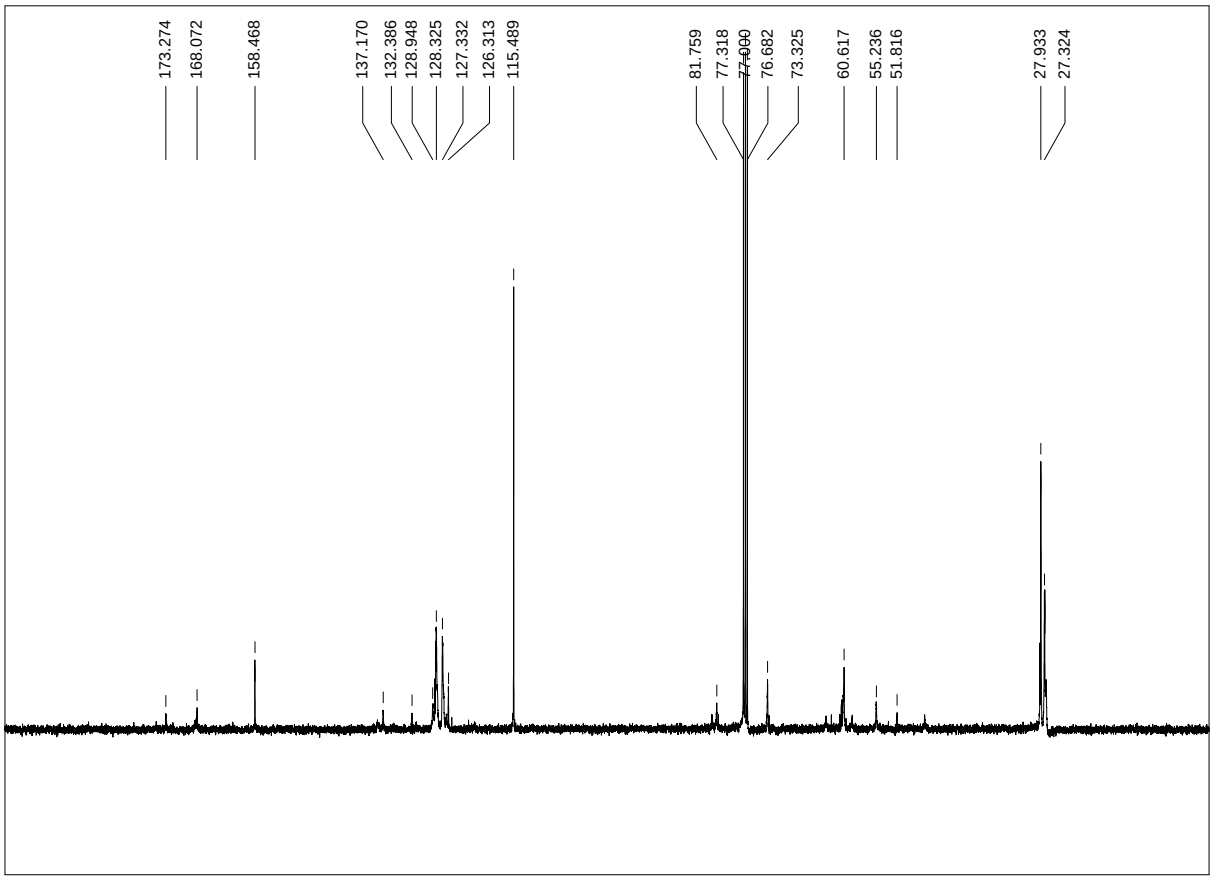

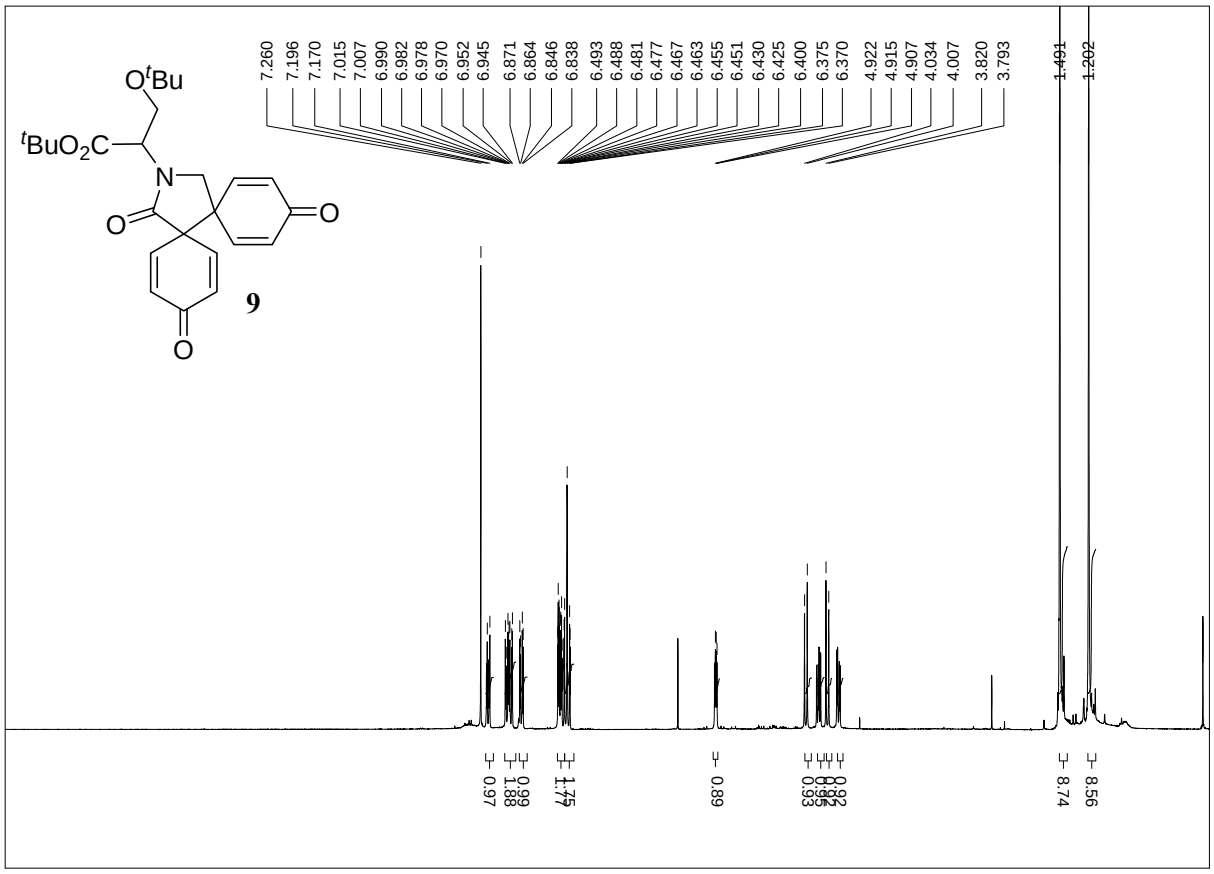

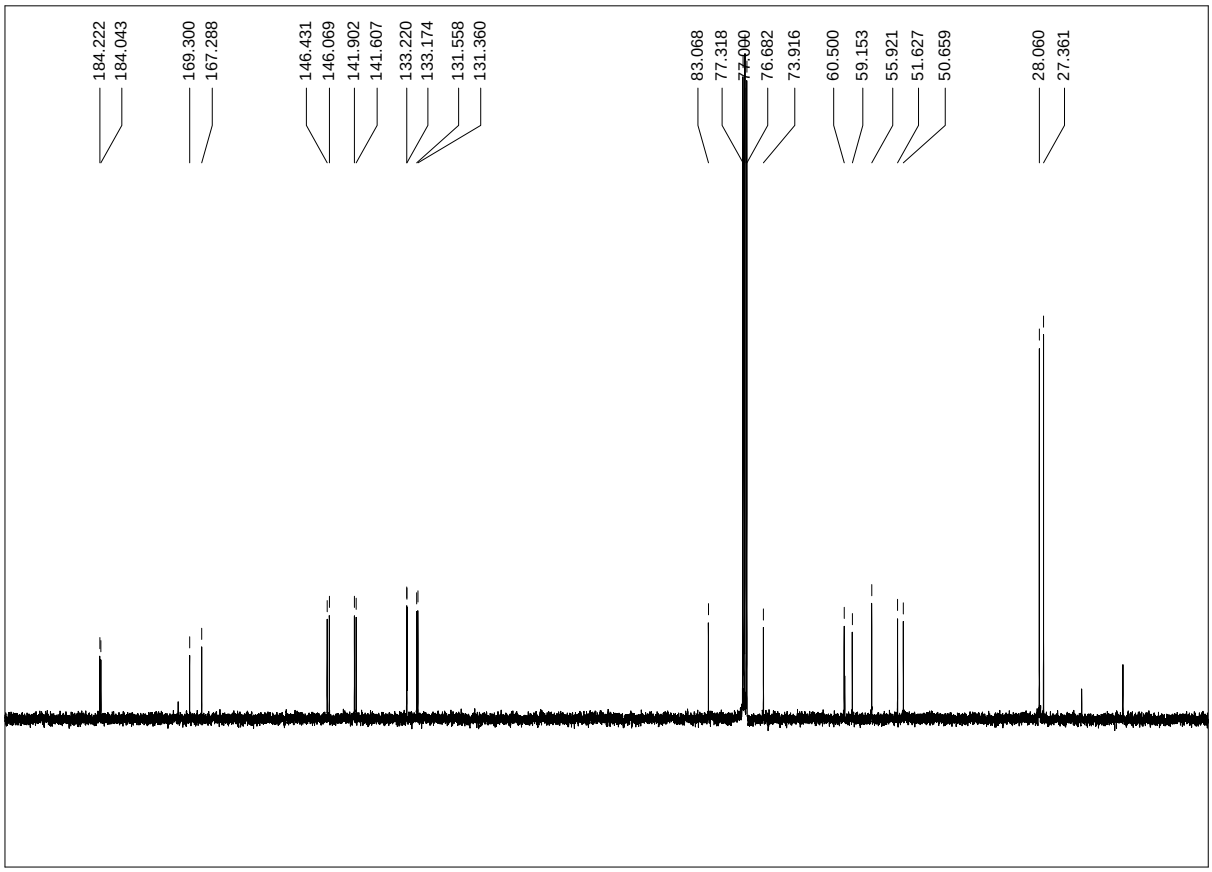

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