Phosphine catalyzed Rauhut−Currier reaction of γ-alkyl allenoate and trapped by Diels-Alder reaction

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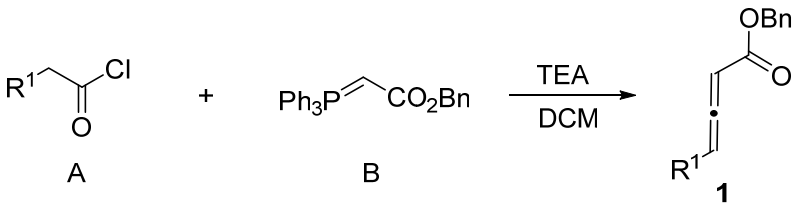
A. General information

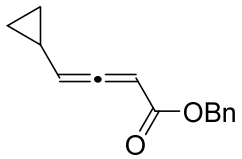
Unless otherwise specified, all reactions were carried out with dry solvents in anhydrous conditions. Solvents were dried by activated molecular sieve (3 Å). All chemicals were used without further purification as commercially available unless otherwise noted. Thin-layer chromatography (TLC) was performed on silica gel plates (60F−254) using UV-light (254 and 365 nm). Flash chromatography was conducted on silica gel (300 – 400 mesh). ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker AV400 MHz spectrometer. Chemical shifts were reported in parts per million (ppm). High resolution mass spectra (HRMS) were recorded on a Waters TOFMS GCT Premier using ESI ionization. Petroleum ether (PE) refers to the fraction with boiling point in the range 60 – 90 °C. Phosphine catalysts [1] and alkyl allenoate [2] was prepared by our laboratory and Maleimide [3] were prepared according to literature methods.

B. Preparation and analytical data of allenoate 1



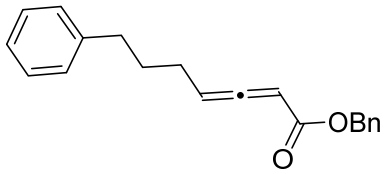
Under nitrogen atmosphere, to a solution of Wittig reagent **B** (5.25 mmol, 1.05 equiv.) and **TEA** (5 mmol, 1.0 equiv.) in DCM (15.0 mL) was added acyl chloride **A** (5.0 mmol, 1.0 equiv.) at 0 °C, and the resulting mixture was stirred at room temperature for 12 h. The mixture was concentrated and the residue was purified by flash column chromatography on silica gel (petroleum ether / ethyl acetate = 40 / 1) to afford the desired product **1**. The ^{1}H NMR spectra of known compounds were consistent with the literature reported. The analytical data of new compounds (**1i**, **1k**) were as follow.

Benzyl benzyl 4-cyclopropylbuta-2,3-dienoate (1i)



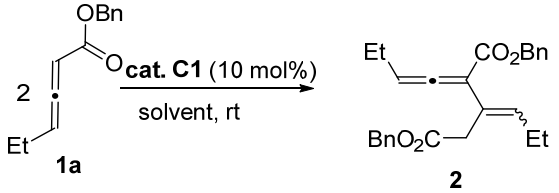
773.3 mg, yield, 72%, Colorless liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.36 (m, 4H), 7.35 – 7.32 (m, 1H), 5.72 (d, *J* = 6.1 Hz, 1H), 5.53 (dd, *J* = 7.3, 6.5 Hz, 1H), 5.21 (d, *J* = 12.5 Hz, 1H), 5.18 (d, *J* = 12.5 Hz, 1H), 1.43 – 1.30 (m, 1H), 0.85 – 0.77 (m, 2H), 0.51 – 0.44 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 212.9, 165.6, 136.0, 128.4, 128.0, 127.9, 100.1, 89.4, 66.3, 8.3, 7.2, 6.9; **IR** (KBr): 3032, 3006, 1958, 1720, 1631, 1258, 1150, 736, 697 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{14}H_{14}O_2$ $[M+H]^+$ = 215.1067, found = 215.1070.

Benzyl 7-phenylhepta-2,3-dienoate (1k)



1.03 g, yield, 71%; colorless liquid; It was an inseparable mixture with alkynoate. The ratio (allenoate : alkynoate:) was 1.62:1 from crude **^{1}H NMR**. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.25 (m, 7H), 7.23 – 7.13 (m, 3H), 5.66 (t, *J* = 5.50 Hz, 1.15 H, allenoate), 5.19 (d, *J* = 3.34 Hz, 2H), 3.34 – 3.33 (m, 1H, alkynoate), 2.76 – 2.64 (m, 2H), 2.28 – 2.13 (m, 2H), 1.89 – 1.74 (m, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 212.7 (allenoate), 168.7 (alkynoate), 166.0 (alkynoate), 141.8 (allenoate),141.6 (alkynoate), 136.0 (allenoate), 135.5 (alkynoate), 128.5 – 128.1 (m, mixture), 125.8, 95.2 (allenoate), 88.3 (allenoate), 83.5 (alkynoate), 71.8 (alkynoate), 67.1 (alkynoate), 66.4 (allenoate), 35.0 (allenoate), 34.7 (alkynoate), 30.2 (allenoate), 30.2 (alkynoate), 26.8 (allenoate), 26.1 (alkynoate), 18.2 (alkynoate); **IR** (KBr): 2937, 2859, 1959, 1720, 1631, 1455, 1363, 1150, 744, 698 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{20}H_{20}O_2$ $[M+H]^+$ = 293.1536, found = 293.1540.

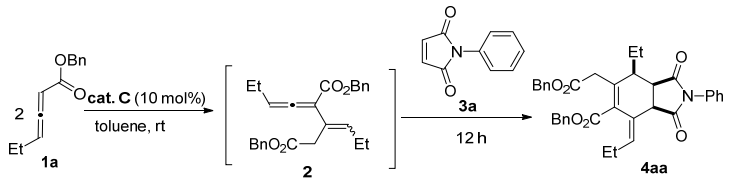
C. Synthesis and analytical data of the RC-adduct 2



To a dried seal tube with a magnetic stirring bar were added **1a** (0.4 mmol, 1.0 equiv.), toluene (10 mL) and catalyst **C1** (0.04 mmol, 0.1 equiv.) at aroom temperature. The tube was sealed and was stirred for 4 h until the consumption of **1a**. The reaction mixture was purified directly by flash column chromatography (PE / ethyl acetate = 10 / 1) to obtain compound **2** (40.5 mg, 50% yield) as a colorless liquid, which of the color got darkened slowly. Once **2** was obtained by flash column chromatography, NMR was test immediately. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 10H), 6.11 (t, *J* = 7.30 Hz, 1H), 5.61 (t, *J* = 6.40 Hz, 1H), 5.24 – 5.14 (m, 2H), 5.09 (d, *J* = 2.20 Hz, 2H), 3.40 – 3.26 (m, 2H), 2.20 – 2.12 (m, 2H), 2.10 – 2.02 (m, 2H), 1.03 – 0.96 (m, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 209.9, 170.8, 166.1, 136.3,136.2, 136.0, 128.4, 128.4, 128.1, 128.1, 127.9, 127.6, 123.7, 98.1, 66.3, 66.2, 35.4, 22.3, 21.5, 13.6, 13.0; **HRMS** (ESI-TOF): m/z calcd for $C_{26}H_{28}O_4$$[M+H]^+$ = 405.2060, found = 405.2060.

D. Optimization of the reaction conditions

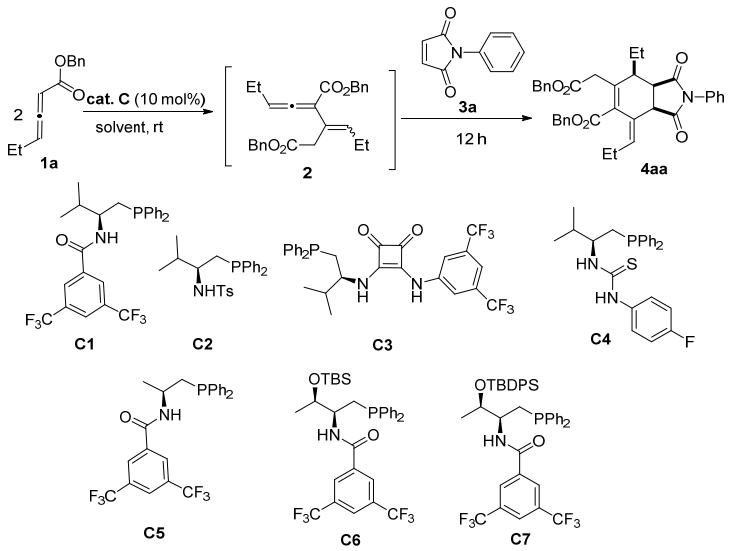
(a) Screening of commercial available catalysts (Table 1)



Entry	Catalyst	Yield (%) [b]	dr (%) [c]
1	DPPE	-	-
2	DPPP	-	-
3	Me_2PhP	13	>19:1
4	Cy_3P	-	-
5	Ph_3P	-	-
6	DMAP	-	-
7	DABCO	-	-

[a] Unless otherwise stated, the reaction was carried out using **1a** (0.2 mmol, 1.0 eq.) and 10 mol% of catalyst in toluene (2 mL) for 4 h at room tempreture, followed by the addition of **3a** (0.2 mmol, 1.0 eq.) and stirred for 12 h. [b] Isolated yields. [c] The dr value was determined by crude ^{1}H NMR.

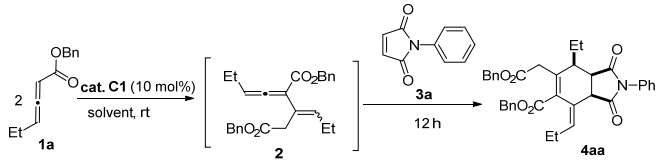
(b) Screening of bifunctional phoshine (Table 2)



Entry	Catalyst	Solvent	Ratio (**1a**/**3a**)	Yield (%) [b]	dr (%) [c]	ee (%) [d]
1	**C1**	toluene	1:1	40	>19:1	0
2	**C2**	toluene	1:1	14	>19:1	0
3	**C3**	toluene	1:1	19	>19:1	0
4	**C4**	toluene	1:1	27	>19:1	0
5	**C5**	toluene	1:1	30	>19:1	0
6	**C6**	toluene	1:1	14	>19:1	0
7	**C7**	toluene	1:1	14	>19:1	0

[a] Unless otherwise stated, the reaction was carried out using **1a** (0.2 mmol, 1.0 equiv.) and 10 mol% of catalyst in toluene (2 mL) for 4 h at room tempreture, followed by the addition of **3a** (0.2 mmol, 1.0 equiv.) and stirred for 12 h. [b] Isolated yields. [c] The dr value was determined by crude ^{1}H NMR. [d] The ee values was determined by HPLC analysis with a chiral stationary phase.

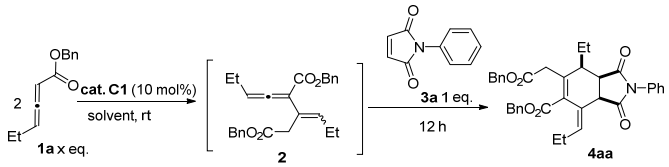
(c) Screening of reaction solvents (Table 3)



Entry	Solvent	Ratio (**1a**/**3a**)	Yield (%) [b]	dr (%)[c]	ee (%) [d]
1	toluene	1:1	40	>19:1	0
2	DCM	1:1	31	>19:1	0
3	EA	1:1	18	>19:1	0
4	MeCN	1:1	26	>19:1	0
5	THF	1:1	31	>19:1	0
6	acetone	1:1	24	>19:1	0
7	Et_2O	1:1	31	>19:1	0

[a] Unless otherwise stated, the reaction was carried out using **1a** (0.2 mmol, 1.0 equiv.) and 10 mol% of catalyst **C1** in solvent (2 mL) for 4 h at room tempreture, followed by the addition of **3a** (0.2 mmol, 1.0 equiv.) and stirred for 12 h. [b] Isolated yields. [c] The dr value was determined by crude ^{1}H NMR. [d] The ee values was determined by HPLC analysis with a chiral stationary phase.

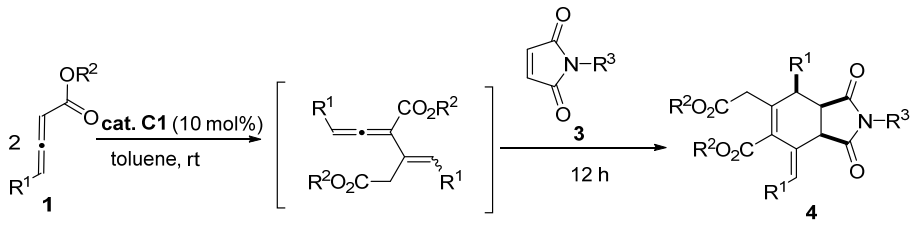
(d) Screening of the ratio of 1a/3a (Table 4)



Entry	Ratio (**1a**/**3a**)	Yield (%) [b]	dr (%) [c]
1	1:1	40	>19:1
2	1.5/1	43	>19:1
3	2:1	47	>19:1
4	2.5/1	62	>19:1
5	3:1	74	>19:1
6	3.5/1	79	>19:1
7	4:1	86	>19:1
8	4.5/1	94	>19:1
9	5:1	100	>19:1
10	1:1 [d]	24	>19:1

[a] Unless otherwise stated, the reaction was carried out using **1a** (x eq.) and 10 mol% of **C1** in toluene (2 mL) for 4 h at room tempreture, followed by the addition of **3a** (0.2 mmol, 1.0 equiv.) and stirred for 12 h. [b] Isolated yields. [c] The dr value was determined by crude ^{1}H NMR. [d] **1a** and **3a** was added together.

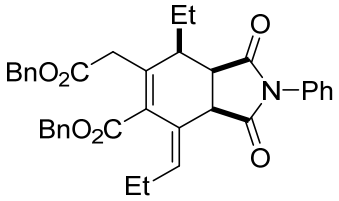
E. General procedure for the one pot two steps reaction



To a dried seal tube with a magnetic stirring bar were added allenoate **1** (1.0 mmol, 5.0 equiv.), toluene (2 mL) and catalyst **C1** (0.02 mmol, 0.1 equiv.) at room temperature. The tube was sealed and the mixture was stirred for 4 h. Then, Maleimide **3** (0.2 mmol, 1.0 equiv.) was added and was stirred for 12 h. After the completely consumption of **3** monitored by TLC, the mixture was purified directly by flash column chromatography (PE / ethyl acetate = 5 / 1) to afford compound **4**.

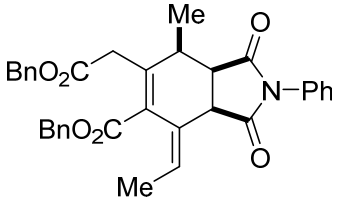
F. Analytical data of products 4

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-7-ethyl-1,3-dioxo-2-phenyl-4-propylidene-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4aa)



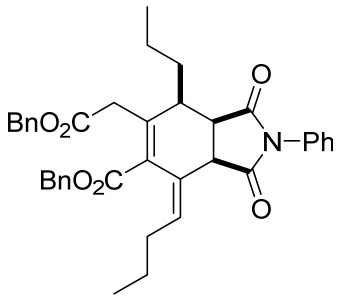
Yield: 116.0 mg, 100%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.29 (m, 13H), 7.15 (d, J = 8.14 Hz, 2H), 5.97 (t, J = 7.27 Hz, 1H), 5.23 – 5.09 (m, 2H), 5.08 – 4.98 (m, 2H), 3.89 (d, J = 16.64 Hz, 1H), 3.80 – 3.73 (m, 1H), 3.48 (d, J = 16.78 Hz, 1H), 3.44 (dd, J = 9.14, 5.10 Hz, 1H), 2.51 (q, J = 7.78 Hz, 1H), 2.04 – 1.93 (m, 1H), 1.93 – 1.86 (m, 2H), 1.77 – 1.68 (m, 1H), 1.03 (t, J = 7.27 Hz, 3H), 0.90 (t, J = 7.47 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ176.1, 175.4, 169.7, 166.5, 146.3, 135.6, 135.4, 135.3, 131.8, 130.5, 128.9, 128.5, 128.4, 128.2, 128.1, 126.5, 125.3, 66.7, 66.6, 48.1, 43.6, 43.4, 36.9, 23.1, 21.1, 13.3, 12.2; **IR** (KBr): 2964, 2832, 1712, 1597, 1363, 1184, 776, 749, 695 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{36}H_{35}NO_6$ $[M+H]^+$ = 578.2537, found = 578.2540.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-4-ethylidene-7-methyl-1,3-dioxo-2-phenyl-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4ba)



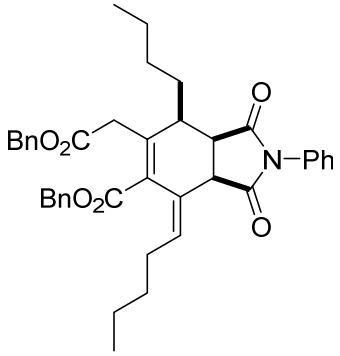
Yield: 83.1 mg,76%, pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 13H), 7.16 (d, *J* = 6.6 Hz, 2H), 6.09 (q, *J* = 7.3, 6.8 Hz, 1H), 5.25 – 5.11 (m, 2H), 5.06 (q, *J* = 12.3 Hz, 2H), 3.85 – 3.77 (m, 2H), 3.56 (d, *J* = 16.6 Hz, 1H), 3.28 (dd, *J* = 9.0, 5.2 Hz, 1H), 2.76 (p, *J* = 7.0 Hz, 1H), 1.54 (d, *J* = 7.1 Hz, 3H), 1.36 (d, *J* = 7.3 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.2, 175.4, 169.7, 166.4, 146.7, 135.7, 135.4, 131.8, 130.0, 129.0, 128.5, 128.5, 128.3, 128.2, 128.1, 126.6, 126.5, 66.7, 66.6, 47.9, 46.0, 36.5, 36.3, 15.2, 13.8; **IR** (KBr): 2948, 2832, 1711, 1597, 1363, 1184, 776, 736, 695 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{34}H_{31}NO_6$ $[M+H]^+$ = 550.2224, found = 550.2228.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-4-butylidene-1,3-dioxo-2-phenyl-7-propyl-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4ca)



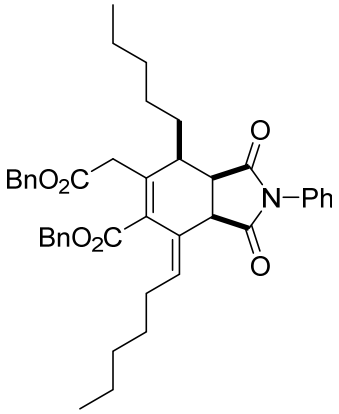
Yield: 111.3 mg, 92%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 13H), 7.16 (d, *J* = 6.6 Hz, 2H), 6.01 (t, *J* = 7.2 Hz, 1H), 5.21 (d, *J* = 12.4 Hz, 1H), 5.13 – 5.05 (m, 2H), 5.00 (d, *J* = 12.3 Hz, 1H), 3.92 (d, *J* = 16.6 Hz, 1H), 3.77 (d, *J* = 10.2 Hz, 1H), 3.46 (d, *J* = 16.7 Hz, 1H), 3.40 (dd, *J* = 9.2, 5.1 Hz, 1H), 2.61 (q, *J* = 7.6 Hz, 1H), 1.84 (q, *J* = 7.1 Hz, 3H), 1.62 (d, *J* = 10.2 Hz, 2H), 1.55 – 1.46 (m, 1H), 1.33 (d, *J* = 7.5 Hz, 2H), 0.90 (t, *J* = 7.2 Hz, 3H), 0.80 (t, *J* = 7.4 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.1, 175.4, 169.7, 166.6, 146.3, 135.7, 135.4, 133.6, 131.8, 130.7, 129.0, 128.5, 128.5, 128.3, 128.2, 128.2, 126.5, 125.8, 66.7, 66.6, 43.9, 41.9, 37.1, 31.7, 30.2, 22.1, 21.0, 14.1, 13.7; **IR** (KBr): 2958, 2930, 2871, 1712, 1597, 1499, 1371, 1180, 776, 749, 695 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{38}H_{39}NO_6$ $[M+H]^+$ = 606.2850, found = 606.2848.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-7-butyl-1,3-dioxo-4-pentylidene-2-phenyl-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4da)



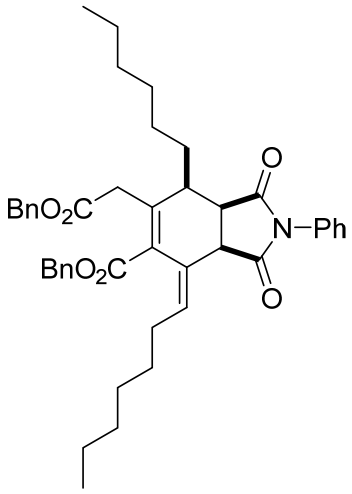
Yield: 112.4 mg, 88%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 13H), 7.16 (d, *J* = 6.7 Hz, 2H), 6.01 (t, *J* = 7.2 Hz, 1H), 5.23 – 5.09 (m, 2H), 5.09 – 4.98 (m, 2H), 3.93 (d, *J* = 16.6 Hz, 1H), 3.77 (d, *J* = 9.2 Hz, 1H), 3.46 (d, *J* = 16.6 Hz, 1H), 3.41 (dd, *J* = 9.2, 5.1 Hz, 1H), 2.59 (q, *J* = 7.6 Hz, 1H), 1.87 (q, *J* = 7.2 Hz, 3H), 1.65 (dd, *J* = 12.3, 6.5 Hz, 1H), 1.51 – 1.43 (m, 1H), 1.32 – 1.25 (m, 5H), 1.22 – 1.17 (m, 2H), 0.88 (t, *J* = 7.1 Hz, 3H), 0.81 (t, *J* = 7.2 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.1, 175.4, 169.7, 166.6, 146.4, 135.7, 135.4, 133.7, 131.8, 130.7, 129.0, 128.5, 128.5, 128.3, 128.2, 128.2, 126.5, 125.6, 66.7, 66.6, 43.9, 42.1, 31.0, 29.9, 29.4, 27.8, 22.7, 22.3, 13.9, 13.8; **IR** (KBr): 2956, 2858, 1712, 1597, 1499, 1455, 1371, 1179, 734, 695 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{40}H_{43}NO_6$ $[M+H]^+$ = 634.3163, found = 634.3170.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-4-hexylidene-1,3-dioxo-7-pentyl-2-phenyl-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylatebenzyl (4ea)



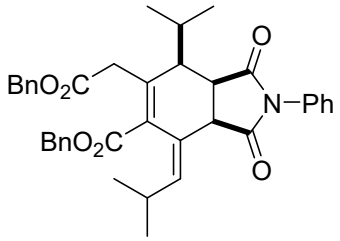
Yield: 114.7 mg, 86%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 13H), 7.17 (d, *J* = 6.7 Hz, 2H), 6.01 (t, *J* = 7.2 Hz, 1H), 5.23 – 5.09 (m, 2H), 5.08 – 4.98 (m, 2H), 3.92 (d, *J* = 16.6 Hz, 1H), 3.77 (d, *J* = 9.2 Hz, 1H), 3.47 (d, *J* = 16.7 Hz, 1H), 3.41 (dd, *J* = 9.1, 5.1 Hz, 1H), 2.59 (q, *J* = 7.5 Hz, 1H), 1.89 – 1.81 (m, 3H), 1.64 (d, *J* = 10.6 Hz, 1H), 1.48 (d, *J* = 8.8 Hz, 1H), 1.31 – 1.24 (m, 8H), 1.20 – 1.14 (m, 3H), 0.87 – 0.83 (m, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.1, 175.4, 169.7, 166.6, 146.4, 135.7, 135.4, 133.8, 131.8, 130.7, 129.0, 128.5, 128.5, 128.3, 128.2, 128.2, 126.5, 125.6, 66.7, 66.6, 43.9, 42.1, 31.8, 31.4, 29.7, 28.5, 28.0, 27.5, 22.4, 22.4, 13.9; **IR** (KBr): 2929, 2857, 1712, 1598, 1499, 1455, 1377, 1177, 749, 695 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{42}H_{47}NO_6$ $[M+H]^+$ = 662.3476, found = 662.3477.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-4-heptylidene-7-hexyl-1,3-dioxo-2-phenyl-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4fa)



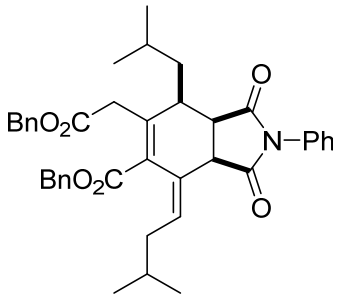
Yield: 135.2 mg, 98%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 13H), 7.17 (d, *J* = 6.7 Hz, 2H), 6.02 (t, *J* = 7.0 Hz, 1H), 5.23 – 5.10 (m, 2H), 5.09 – 4.98 (m, 2H), 3.98 – 3.88 (m, 1H), 3.77 (d, *J* = 9.2 Hz, 1H), 3.49 (d, *J* = 16.6 Hz, 1H), 3.42 (dd, *J* = 9.1, 5.1 Hz, 1H), 2.60 (q, *J* = 7.2 Hz, 1H), 1.87 (q, *J* = 7.4 Hz, 3H), 1.67 (d, *J* = 8.3 Hz, 1H), 1.51 – 1.43 (m, 1H), 1.27 (d, *J* = 4.6 Hz, 10H), 1.10 – 1.19 (m, 5H), 0.89 – 0.85 (m, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.1, 175.4, 169.7, 166.6, 146.4, 135.7, 135.4, 133.7, 131.8, 130.7, 128.9, 128.5, 128.4, 128.3, 128.2, 128.1, 126.5, 125.6, 66.7, 66.5, 43.9, 42.1, 31.6, 31.5, 29.8, 29.3, 28.9, 28.8, 28.1, 27.8, 22.5, 14.0, 14.0; **IR** (KBr): 2927, 2855, 1712, 1598, 1499, 1455, 1375, 1253, 1184, 735, 695 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{44}H_{51}NO_6$ $[M+H]^+$ = 690.3789, found = 690.3785.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-7-isopropyl-4-(2-methylpropylidene)-1,3-dioxo-2-phenyl-2, 3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4ga)



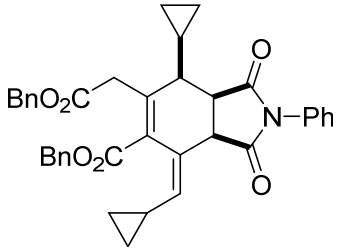
Yield: 83.2 mg, 69%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.26 (m, 11H), 7.24 – 7.22 (m, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 5.77 – 5.65 (m, 1H), 5.16 (d, *J* = 12.6 Hz, 1H), 5.04 (d, *J* = 12.6 Hz, 1H), 4.90 – 4.79 (m, 2H), 3.80 (dd, *J* = 12.0, 6.7 Hz, 1H), 3.70 (d, *J* = 9.2 Hz, 1H), 3.55 (dd, *J* = 8.9, 4.3 Hz, 2H), 2.39 (s, 1H), 2.25 – 2.23 (m, 6.6 Hz, 1H), 2.04 (s, 1H), 1.15 (d, *J* = 6.4 Hz, 3H), 0.94 (d, *J* = 6.4 Hz, 3H), 0.89 – 0.85 (m, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.2, 175.2, 169.5, 166.8, 145.2, 135.8, 135.4, 132.0, 131.8, 128.7, 128.5, 128.4, 128.3, 128.3, 128.2, 128.1, 128.0, 128.0, 126.7, 126.4, 124.7, 66.7, 66.4, 49.4, 43.8, 29.7, 26.9, 26.3, 23.3, 22.8, 21.9, 21.7; **IR** (KBr): 2958, 2869, 1712, 1597, 1499, 1366, 1153, 749, 695 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{38}H_{39}NO_6$ $[M+H]^+$ = 606.2850, found = 606.2854.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-7-isobutyl-4-(3-methylbutylidene)-1,3-dioxo-2-phenyl-2,3,3 a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4ha)



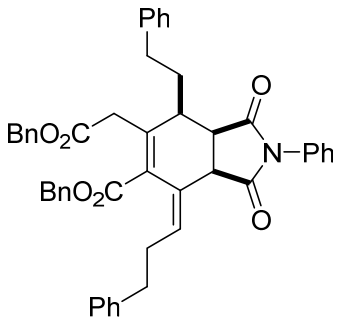
Yield: 92.1 mg, 73%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.30 (m, 13H), 7.16 (d, *J* = 6.6 Hz, 2H), 6.05 (t, *J* = 7.2 Hz, 1H), 5.21 (d, *J* = 12.4 Hz, 1H), 5.11 (d, *J* = 10.6 Hz, 1H), 5.08 (d, *J* = 10.5 Hz, 1H), 4.99 (d, *J* = 12.3 Hz, 1H), 3.88 (d, *J* = 16.6 Hz, 1H), 3.78 (d, *J* = 9.9 Hz, 1H), 3.49 (d, *J* = 16.7 Hz, 1H), 3.37 (dd, *J* = 9.1, 5.1 Hz, 1H), 2.73 – 2.63 (m, 1H), 1.74 (t, *J* = 7.2 Hz, 3H), 1.64 – 1.58 (m, 2H), 1.54 – 1.47 (m, 1H), 0.94 (d, *J* = 6.4 Hz, 3H), 0.84 (d, *J* = 6.4 Hz, 3H), 0.80 (dd, *J* = 6.6, 3.6 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.1, 175.5, 169.7, 166.6, 151.2, 146.3, 135.8, 135.5, 132.9, 131.9, 131.0, 129.1, 128.6, 128.5, 128.5, 128.3, 128.3, 126.6, 126.5, 119.7, 66.8, 66.7, 44.1, 39.7, 38.8, 37.1, 36.9, 28.3, 25.6, 22.8, 22.5, 22.3, 22.2; **IR** (KBr): 2955, 2832, 1712, 1592, 1363, 776 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{40}H_{43}NO_6$ $[M+H]^+$ = 634.3163, found = 634.3162.

Benzyl
(Z)-6-(2-(benzyloxy)-2-oxoethyl)-7-cyclopropyl-4-(cyclopropylmethylene)-1,3-dioxo-2-phenyl-2,3,3a, 4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4ia)



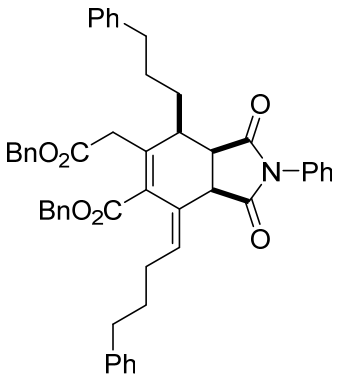
Yield: 121.2 mg, 100%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.27 (m, 13H), 7.17 – 7.13 (m, 2H), 5.35 (d, *J* = 10.0 Hz, 1H), 5.23 – 5.11 (m, 2H), 5.08 – 4.95 (m, 2H), 3.94 (d, *J* = 16.3 Hz, 1H), 3.80 – 3.71 (m, 2H), 3.45 (dd, *J* = 8.8, 4.6 Hz, 1H), 1.68 (dd, *J* = 10.9, 4.6 Hz, 1H), 1.53 (d, *J* = 5.4 Hz, 1H), 1.27 – 1.15 (m, 1H), 0.74 – 0.55 (m, 4H), 0.42 (d, *J* = 4.7 Hz, 2H), 0.22 (d, *J* = 15.2 Hz, 2H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.3, 175.5, 169.8, 166.9, 145.2, 138.4, 135.8, 135.5, 131.9, 130.2, 128.9, 128.4, 128.3, 128.1, 128.1, 128.1, 126.5, 124.2, 66.6, 66.6, 48.4, 47.6, 46.0, 36.6, 12.0, 10.1, 8.0, 7.4, 6.0, 4.3; **IR** (KBr): 3004, 2952, 1716, 1498, 1374, 1188, 751, 695(cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{38}H_{35}NO_6$ $[M+H]^+$ = 602.2537, found = 602.2540.

Benzyl
(Z)-6-(2-(benzyloxy)-2-oxoethyl)-1,3-dioxo-7-phenethyl-2-phenyl-4-(3-phenylpropylidene)-2,3,3a,4,7 ,7a-hexahydro-1H-isoindole-5-carboxylate (4ja)



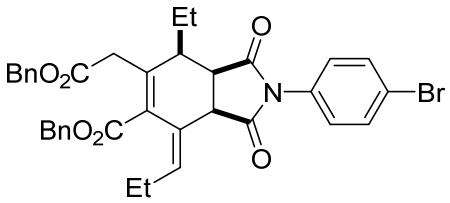
Yield: 98.3 mg, 72%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 (d, J = 7.7 Hz, 2H), 7.30 – 7.22 (m, 15H), 7.21 (s, 1H), 7.15 – 7.13 (m, 5H), 7.05 (d, J = 7.2 Hz, 2H), 5.92 (t, J = 7.2 Hz, 1H), 5.19 (d, J = 12.4 Hz, 1H), 5.09 (d, J = 12.4 Hz, 1H), 5.01 (d, J = 12.3 Hz, 1H), 4.94 (d, J = 12.3 Hz, 1H), 3.77 – 3.69 (m, 2H), 3.53 (d, J = 16.6 Hz, 1H), 3.43 (dd, J = 9.0, 5.1 Hz, 1H), 2.82 (t, J = 11.9 Hz, 1H), 2.64 – 2.51 (m, 3H), 2.45 – 2.37 (m, 1H), 2.32 – 2.24 (m, 1H), 2.23 – 2.17 (m, 2H), 1.95 – 1.87 (m, 1H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.9, 175.1, 169.6, 166.2, 146.6, 141.0, 141.0, 135.6, 135.4, 132.9, 131.8, 130.6, 129.0, 128.5, 128.5, 128.4, 128.3, 128.2, 128.2, 126.8, 126.6, 126.1, 125.9, 66.8, 66.6, 43.2, 41.3, 36.2, 34.8, 33.8, 31.1, 29.8; **IR** (KBr): 3062, 3028, 2935, 2833, 1712, 1598, 1498, 1365, 1184, 776, 738, 698 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{48}H_{43}NO_6$ $[M+H]^+$ = 730.3163, found = 730.3165.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-1,3-dioxo-2-phenyl-4-(4-phenylbutylidene)-7-(3-phenylpropyl)-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4ka)



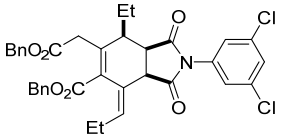
Yield: 155.7 mg, 95%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.27 (m, 13H), 7.23 – 7.21 (m, 4H), 7.17 – 7.08 (m, 8H), 6.00 (t, J = 7.0 Hz, 1H), 5.14 (d, J = 12.4 Hz, 1H), 5.06 – 5.01 (m, 2H), 4.97 (d, J = 12.2 Hz, 1H), 3.88 (d, J = 16.6 Hz, 1H), 3.72 (d, J = 9.2 Hz, 1H), 3.46 (d, J = 16.7 Hz, 1H), 3.38 (dd, J = 9.2, 5.1 Hz, 1H), 2.57 (dd, J = 12.2, 7.0 Hz, 2H), 2.50 – 2.46 (m, 2H), 1.91 – 1.86 (m, 2H), 1.84 – 1.75 (m, 1H), 1.74 – 1.66 (m, 1H), 1.63 – 1.57 (m, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.0, 175.3, 169.6, 166.4, 146.1, 141.9, 141.6, 135.6, 135.3, 133.4, 131.8, 130.7, 129.0, 128.5, 128.5, 128.3, 128.3, 128.2, 126.5, 126.0, 125.9, 125.8, 66.8, 66.6, 47.8, 43.8, 42.0, 35.9, 35.5, 30.5, 29.6, 29.4, 27.8; **IR** (KBr): 2935, 2857, 1716, 1631, 1497, 1372, 1181, 749, 697(cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{50}H_{47}NO_6$ $[M+H]^+$ = 758.3476, found = 758.3486.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-2-(4-bromophenyl)-7-ethyl-1,3-dioxo-4-propylidene-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4ab)



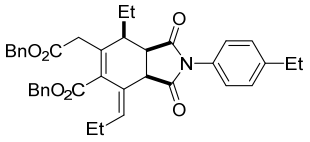
Yield: 130.9 mg, 100%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 (d, *J* = 8.7 Hz, 2H), 7.35 – 7.28 (m, 10H), 7.04 (d, *J* = 8.7 Hz, 2H), 5.91 (t, *J* = 7.3 Hz, 1H), 5.15 (d, *J* = 12.5 Hz, 2H), 5.06 – 4.96 (m, 2H), 3.84 – 3.72 (m, 2H), 3.57 (d, *J* = 16.7 Hz, 1H), 3.44 (dd, *J* = 9.0, 4.9 Hz, 1H), 2.46 (q, *J* = 7.8 Hz, 1H), 1.97 (dd, *J* = 13.5, 6.0 Hz, 1H), 1.90 (q, *J* = 7.4 Hz, 2H), 1.78 – 1.71 (m, 1H), 1.03 (t, *J* = 7.3 Hz, 3H), 0.91 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.8, 175.0, 169.7, 166.5, 146.0, 135.7, 135.6, 135.3, 132.1, 130.8, 130.5, 128.5, 128.5, 128.2, 128.2, 128.1, 125.3, 122.2, 66.8, 66.6, 48.5, 43.4, 36.4, 26.9, 23.1, 21.0, 13.3, 12.3; **IR** (KBr): 2965, 2875, 1712, 1600, 1489, 1370, 1070, 823, 735, 697 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{36}H_{34}BrNO_6$ $[M+H]^+$ = 656.1642, 658.1622, found = 656.1641, 658.1627.

Benzyl Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-2-(3,5-dichlorophenyl)-7-ethyl-1,3-dioxo-4-propylidene-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4ac)



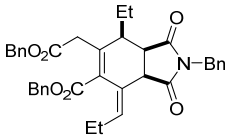
Yield: 128.2 mg, 99%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.28 (m, 11H), 7.24 (d, *J* = 1.8 Hz, 2H), 5.89 (t, *J* = 6.9 Hz, 1H), 5.17 – 5.09 (m, 2H), 5.06 – 4.98 (m, 2H), 3.81 – 3.70 (m, 2H), 3.64 (d, *J* = 16.8 Hz, 1H), 3.45 (dd, *J* = 9.2, 5.2 Hz, 1H), 2.49 – 2.40 (m, 1H), 1.94 (dd, *J* = 13.7, 6.3 Hz, 1H), 1.87 (q, *J* = 7.5 Hz, 2H), 1.79 – 1.92 (m, 1H), 1.04 (t, *J* = 7.3 Hz, 3H), 0.89 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.3, 174.6, 169.7, 166.4, 145.8, 136.0, 135.6, 135.3, 135.0, 133.6, 130.8, 128.6, 128.5, 128.5, 128.3, 128.3, 128.1, 128.0, 125.3, 125.2, 66.9, 66.6, 48.6, 43.4, 36.1, 29.7, 23.1, 21.1, 13.3, 12.3; **IR** (KBr): 2961, 2832, 1720, 1588, 1362, 1182, 777 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{36}H_{33}Cl_2NO_6$ $[M+H]^+$ = 646.1758, 648.1729, found = 646.1761, 648.1743.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-7-ethyl-2-(4-ethylphenyl)-1,3-dioxo-4-propylidene-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4ad)



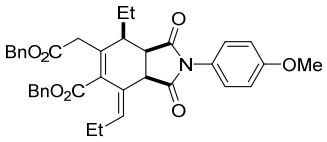
Yield: 110.3 mg, 91%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 10H), 7.19 (d, *J* = 8.3 Hz, 2H), 7.06 (d, *J* = 8.3 Hz, 2H), 5.97 (t, *J* = 7.3 Hz, 1H), 5.23 – 5.10 (m, 2H), 5.09 – 4.98 (m, 2H), 3.92 (d, *J* = 16.6 Hz, 1H), 3.75 (d, *J* = 10.0 Hz, 1H), 3.50 – 3.36 (m, 2H), 2.65 (q, *J* = 7.6 Hz, 2H), 2.51 (q, *J* = 7.8 Hz, 1H), 1.97 – 1.86 (m, 3H), 1.75 – 1.68 (m, 1H), 1.22 (t, *J* = 7.6 Hz, 3H), 1.02 (t, *J* = 7.4 Hz, 3H), 0.89 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.3, 175.5, 169.8, 166.6, 146.4, 144.7, 135.7, 135.4, 135.1, 130.5, 129.3, 128.5, 128.5, 128.2, 128.1, 126.3, 125.3, 66.7, 66.6, 43.6, 37.1, 29.7, 28.5, 23.1, 21.1, 15.3, 13.4, 12.3; **IR** (KBr): 2963, 2832, 1710, 1589, 1514, 1363, 776 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{38}H_{39}NO_6$ $[M+H]^+$ = 606.2850, found = 606.2856.

Benzyl (Z)-2-benzyl-6-(2-(benzyloxy)-2-oxoethyl)-7-ethyl-1,3-dioxo-4-propylidene-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4ae)



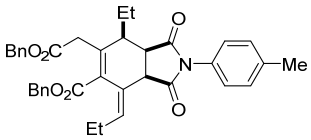
Yield: 119.8 mg, 100%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 11H), 7.26 – 7.22 (m, 2H), 7.20 – 7.19 (m, 3H), 5.83 (t, *J* = 7.3 Hz, 1H), 5.12 – 5.03 (m, 4H), 4.60 – 4.50 (m, 2H), 3.77 (d, *J* = 16.7 Hz, 1H), 3.62 – 3.56 (m, 1H), 3.29 – 3.22 (m, 2H), 2.37 (q, *J* = 7.1 Hz, 1H), 1.84 – 1.76 (m, 3H), 1.60 – 1.52 (m, 1H), 0.95 (t, *J* = 7.3 Hz, 3H), 0.82 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.7, 175.9, 169.8, 165.9, 147.0, 135.8, 135.7, 135.5, 135.1, 130.3, 128.5, 128.5, 128.4, 128.4, 128.2, 128.1, 128.0, 128.0, 127.7, 125.6, 66.7, 66.4, 48.4, 43.6, 42.9, 42.3, 36.7, 29.7, 23.1, 20.8, 13.3, 12.1; **IR** (KBr): 2962, 2832, 1702, 1657, 1588, 1362, 1155, 777 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{37}H_{37}NO_6$ $[M+H]^+$ = 592.2694, found = 592.2700.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-7-ethyl-2-(4-methoxyphenyl)-1,3-dioxo-4-propylidene-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4af)



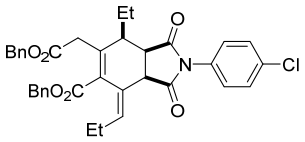
Yield: 117.9 mg, 97%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 10H), 7.05 (d, *J* = 8.93 Hz, 2H), 6.86 (d, *J* = 8.95 Hz, 2H), 5.95 (t, *J* = 7.28 Hz, 1H), 5.24 – 5.09 (m, 2H), 5.08 – 4.98 (m, 2H), 3.88 (d, *J* = 16.63 Hz, 1H), 3.79 (s, 3H), 3.74 (d, *J* = 9.94 Hz, 1H), 3.48 (d, *J* = 16.65 Hz, 1H), 3.42 (dd, *J* = 9.07, 5.03 Hz, 1H), 2.54 – 2.43 (m, 1H), 1.98 – 1.85 (m, 3H), 1.75 – 1.68 (m, 1H), 1.02 (t, *J* = 7.28 Hz, 3H), 0.89 (t, *J* = 7.47 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.3, 175.6, 169.7, 166.6, 159.3, 146.3, 135.7, 135.4, 135.2, 130.5, 128.5, 128.5, 128.2, 128.2, 128.1, 127.7, 125.4, 124.4, 114.3, 66.7, 66.6, 55.4, 43.5, 36.9, 29.6, 23.1, 21.1, 13.3, 12.3; **IR** (KBr): 2963, 2832, 1710, 1588, 1536, 1363, 1250, 1182, 777 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{37}H_{37}NO_7$ $[M+H]^+$ = 608.2643, found = 608.2646.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-7-ethyl-1,3-dioxo-4-propylidene-2-(p-tolyl)-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4ag)



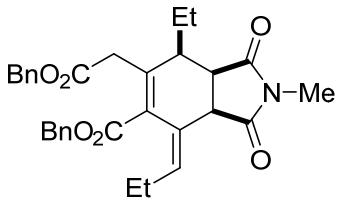
Yield: 104.5 mg, 88%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 10H), 7.17 (d, *J* = 8.19 Hz, 2H), 7.04 (d, *J* = 8.30 Hz, 2H), 6.01 – 5.94 (m, 1H), 5.21 (d, *J* = 12.47 Hz, 1H), 5.12 (d, *J* = 12.47 Hz, 1H), 5.08 (d, *J* = 12.33 Hz, 1H), 5.01 (d, *J* = 12.33 Hz, 1H), 3.91 (d, *J* = 16.63 Hz, 1H), 3.79 – 3.70 (m, 1H), 3.50 – 3.40 (m, 2H), 2.51 (q, *J* = 7.82 Hz, 1H), 2.35 (s, 3H), 1.99 – 1.86 (m, 3H), 1.78 – 1.68 (m, 1H), 1.02 (t, *J* = 7.27 Hz, 3H), 0.90 (t, *J* = 7.47 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.2, 175.5, 169.7, 166.5, 146.4, 138.5, 135.6, 135.4, 135.1, 130.5, 129.6, 129.1, 128.5, 128.4, 128.2, 128.1, 126.3, 125.3, 66.7, 66.6, 43.6, 37.0, 29.6, 23.1, 21.2, 21.1, 13.3, 12.2; **IR** (KBr): 2927, 2832, 1711, 1657, 1586, 1362, 1183, 777 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{37}H_{37}NO_6$$[M+H]^+$ = 592.2694, found = 592.2695.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-2-(4-chlorophenyl)-7-ethyl-1,3-dioxo-4-propylidene-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4ah)



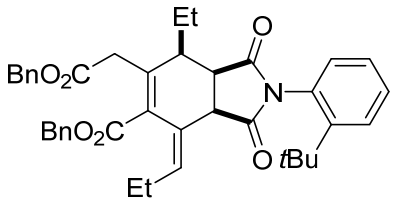
Yield: 115.4 mg, 94%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 12H), 7.09 (d, *J* = 8.70 Hz, 2H), 5.91 (t, *J* = 7.30 Hz, 1H), 5.21 (d, *J* = 12.37 Hz, 1H), 5.07 (d, *J* = 12.37 Hz, 1H), 5.04 (d, *J* = 12.25 Hz, 1H), 4.97 (d, *J* = 12.37 Hz, 1H), 3.82 – 3.72 (m, 2H), 3.57 (d, *J* = 16.66 Hz, 1H), 3.44 (dd, *J* = 9.01, 5.00 Hz, 1H), 2.45 (q, *J* = 7.77 Hz, 1H), 1.96 (dd, *J* = 13.51, 6.07 Hz, 1H), 1.89 (q, *J* = 7.42 Hz, 2H), 178 – 171 (m, 1H), 1.03 (t, *J* = 7.27 Hz, 3H), 0.90 (t, *J* = 7.47 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.9, 175.1, 169.7, 166.5, 146.0, 135.7, 135.6, 135.4, 134.2, 130.6, 130.3, 129.1, 128.5, 128.5, 128.2, 128.1, 127.8, 125.3, 66.8, 66.6, 48.5, 43.4, 43.3, 36.4, 23.1, 21.1, 13.4, 12.3; **IR** (KBr): 2964,2832, 1712, 1657, 1588, 1493, 1363,1182, 777(cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{36}H_{34}ClNO_6$$[M+H]^+$ = 612.2147, 613.2181, found = 612.2148, 613.2182.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-7-ethyl-2-methyl-1,3-dioxo-4-propylidene-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4ai)



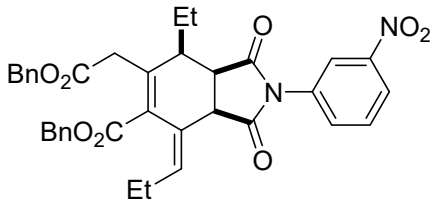
Yield: 110.8 mg, 100%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 10H), 5.90 (t, *J* = 7.21 Hz, 1H), 5.18 (d, *J* = 12.57 Hz, 1H), 5.10 (d, *J* = 12.56 Hz, 1H), 5.06 (d, *J* = 2.76 Hz, 2H), 3.88 (d, *J* = 16.70 Hz, 1H), 3.65 – 3.55 (m, 1H), 3.49 (d, *J* = 16.69 Hz, 1H), 3.25 (dd, *J* = 9.03, 5.44 Hz, 1H), 2.90 (s, 3H), 2.48 – 2.38 (m, 1H), 1.89 – 1.75 (m, 3H), 1.67 – 1.59 (m, 1H), 0.97 (t, *J* = 7.30 Hz, 3H), 0.85 (d, *J* = 7.49 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 177.0, 176.4, 169.7, 166.4, 146.4, 135.6, 135.5, 134.6, 130.7, 128.5, 128.4, 128.2, 128.1, 128.1, 128.0, 125.4, 66.8, 66.4, 43.6, 37.0, 29.7, 24.8, 23.1, 21.2, 13.3, 12.3; **IR** (KBr): 2956, 2832, 2716, 1709, 1592, 1362, 776 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{31}H_{33}NO_6[M+H]^+$ = 516.2381, found = 516.2383.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-2-(2-(tert-butyl)phenyl)-7-ethyl-1,3-dioxo-4-propylidene-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4aj)



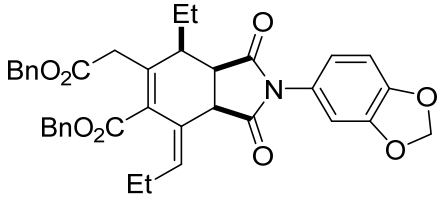
Yield: 33.4 mg, 26%, a pale yellow gel liquid; **^{1}H NMR** δ 7.48 (d, *J* = 8.08 Hz, 1H), 7.37 – 7.31 (m, 10H), 7.29 (d, *J* = 1.94 Hz, 1H), 7.23 (d, *J* = 7.51 Hz, 1H), 6.75 (d, *J* = 9.05 Hz, 1H), 5.70 (t, *J* = 7.28 Hz, 1H), 5.20 – 5.06 (m, 4H), 3.86 (d, *J* = 15.96 Hz, 1H), 3.78 (d, *J* = 9.53 Hz, 1H), 3.39 (dd, *J* = 9.28, 1.61 Hz, 1H), 3.17 (d, *J* = 15.96 Hz, 1H), 2.88 (dd, *J* = 9.01, 3.87 Hz, 1H), 1.88 – 1.80 (m, 3H), 1.55 – 1.46 (m, 1H), 1.04 (s, 9H), 0.98 (t, *J* = 7.38 Hz, 3H), 0.86 (t, *J* = 7.47 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 179.3, 177.0, 169.5, 165.8, 148.6, 147.9, 137.7, 135.7, 135.2, 131.7, 130.7, 129.7, 129.6, 128.5, 128.4, 128.4, 128.3, 128.2, 128.1, 127.4, 124.2, 66.8, 66.6, 49.1, 45.6, 44.0, 41.9, 35.1, 31.1, 29.7, 23.8, 23.2, 13.3, 12.2; **IR** (KBr): 2957, 2832, 2716, 1909, 1593, 1362, 776 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{40}H_{43}NO_6[M+H]^+$ = 634.3163, found = 634.3171.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-7-ethyl-2-(3-nitrophenyl)-1,3-dioxo-4-propylidene-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4ak)



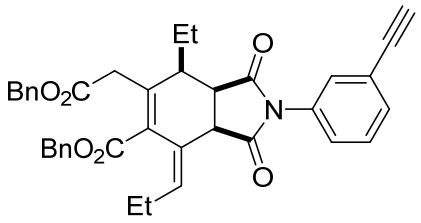
Yield: 127.7 mg, 100%, a pale yellow gel liquid; **^{1}H NMR** δ 8.27 (s, 1H), 8.19 (d, *J* = 8.02 Hz, 1H), 7.57 – 7.48 (m, 2H), 7.33 – 7.24 (m, 10H), 5.88 (t, *J* = 7.31 Hz, 1H), 5.21 – 5.08 (m, 2H), 5.07 – 4.98 (m, 2H), 3.81 (d, *J* = 9.02 Hz, 1H), 3.78 – 3.65 (m, 2H), 3.50 (dd, *J* = 8.99, 5.10 Hz, 1H), 2.44 (q, *J* = 8.15, 7.69 Hz, 1H), 2.06 – 1.95 (m, 1H), 1.94 – 1.86 (m, 2H), 1.84 – 1.75 (m, 1H), 1.07 (t, *J* = 7.25 Hz, 3H), 0.90 (t, *J* = 7.47 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.4, 174.8, 169.7, 166.4, 148.3, 145.7, 136.3, 135.6, 135.3, 132.9, 132.6, 130.8, 129.6, 128.5, 128.4, 128.2, 128.2, 128.1, 125.3, 123.0, 122.1, 66.9, 66.6, 49.0, 43.4, 43.3, 35.7, 29.6, 23.2, 21.1, 13.3, 12.3; **IR** (KBr): 2964, 2832, 1716, 1589, 1532, 1363, 1181, 776, 737, 698 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{36}H_{34}N_2O_8[M+H]^+$ = 623.2388, found = 623.2385.

Benzyl (Z)-2-(benzo[d][1,3]dioxol-5-yl)-6-(2-(benzyloxy)-2-oxoethyl)-7-ethyl-1,3-dioxo-4-propylidene-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4al)



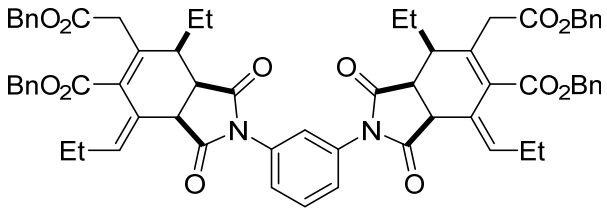
Yield: 121.6 mg, 98%, a pale yellow gel liquid; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.30 (m, 10H), 6.76 (d, *J* = 8.3 Hz, 1H), 6.67 (d, *J* = 2.1 Hz, 1H), 6.59 (dd, *J* = 8.3, 2.1 Hz, 1H), 5.98 (s, 2H), 5.94 (t, *J* = 7.2 Hz, 1H), 5.21 – 5.08 (m, 2H), 5.08 – 4.99 (m, 2H), 3.86 (d, *J* = 16.7 Hz, 1H), 3.73 (d, *J* = 9.6 Hz, 1H), 3.50 (d, *J* = 16.8 Hz, 1H), 3.41 (dd, *J* = 9.2, 5.1 Hz, 1H), 2.48 (q, *J* = 7.7 Hz, 1H), 1.98 – 1.91 (m, 1H), 1.91 – 1.85 (m, 2H), 1.75 – 1.68 (m, 1H), 1.02 (t, *J* = 7.3 Hz, 3H), 0.89 (t, *J* = 7.5 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.2, 175.5, 169.7, 166.5, 147.9, 147.6, 146.2, 135.6, 135.4, 135.3, 130.5, 128.5, 128.4, 128.2, 128.1, 125.3, 120.5, 108.2, 107.8, 101.6, 66.8, 66.6, 43.5, 43.3, 36.8, 26.9, 23.1, 21.1, 13.3, 12.3; **IR** (KBr): 2965, 2876, 2832, 1720, 1600, 1503 1353, 1245, 1037, 777, 738, 698(cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{37}H_{35}NO_8$ $[M+H]^+$ = 622.2435, found = 622.2441.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-7-ethyl-2-(3-ethynylphenyl)-1,3-dioxo-4-propylidene-2,3,3a, 4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4am)



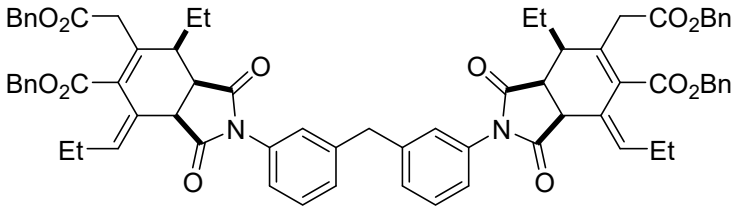
Yield: 128.1 mg, 100%, a pale yellow gel liquid; **^{1}H NMR** δ 7.45 (d, J = 7.70 Hz, 1H), 7.39 – 7.29 (m, 12H), 7.15 (d, J = 8.03 Hz, 1H), 5.93 (t, J = 7.55 Hz, 1H), 5.19 – 5.09 (m, 2H), 5.07 – 4.97 (m, 2H), 3.84 (d, J = 16.57 Hz, 1H), 3.75 (d, J = 9.08 Hz, 1H), 3.52 (d, J = 16.58 Hz, 1H), 3.45 – 3.40 (m, 1H), 2.48 (d, J = 7.03 Hz, 1H), 1.96 – 1.85 (m, 3H), 1.77 – 1.68 (m, 1H), 1.02 (t, J = 7.18 Hz, 3H), 0.88 (t, J = 7.50 Hz, 4H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.8, 175.1, 169.7, 166.5, 146.1, 135.6, 135.5, 135.4, 132.1, 131.9, 130.6, 130.2, 129.0, 128.5, 128.5, 128.2, 128.1, 127.1, 125.2, 123.1, 82.5, 78.2, 66.8, 66.6, 48.1, 43.5, 43.4, 36.7, 23.1, 21.1, 13.3, 12.3; **IR** (KBr): 2964, 2832, 1711, 1657, 1589, 1363, 776 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{38}H_{35}NO_6[M+H]^+$ = 602.2537, found = 602.2537.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-2-(3-(Z)-5-(2-(benzyloxy)-2-oxoethyl)-6-((benzyloxy)carbon yl)-4-ethyl-1,3-dioxo-7-propylidene-1,3,3a,4,7,7a-hexahydro-2H-isoindol-2-yl)phenyl)-7-ethyl-1,3-di oxo-4-propylidene-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4an)



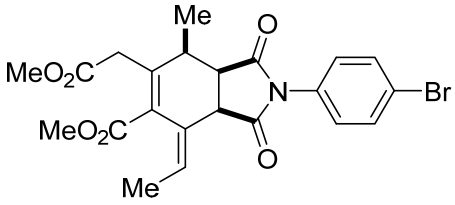
Yield: 205.9 mg, 96%, a pale yellow gel liquid; **^{1}H NMR** δ 7.34 – 7.27 (m, 22H), 7.14 (t, *J* = 9.28 Hz, 2H), 5.93 (t, *J* = 7.42 Hz, 2H), 5.21 – 5.09 (m, 4H), 5.08 – 4.97 (m, 4H), 3.86 (dd, *J* = 16.70, 7.79 Hz, 2H), 3.69 (dd, *J* = 8.85, 3.72 Hz, 2H), 3.47 (d, *J* = 16.61 Hz, 2H), 3.40 – 3.32 (m, 2H), 2.51 – 2.41 (m, 2H), 1.97 – 1.83 (m, 6H), 1.75 – 1.64 (m, 2H), 0.99 (t, *J* = 6.70 Hz, 6H), 0.88 (t, *J* = 7.45 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.5, 174.9, 169.7, 166.5, 146.2, 135.6, 135.4, 132.1, 130.5, 129.1, 128.5, 128.4, 128.2, 128.1, 128.1, 128.0, 126.2, 125.2, 124.0, 66.8, 66.5, 43.5, 43.5, 43.3, 36.8, 23.1, 21.0, 13.3, 12.2; **IR** (KBr): 2964, 2875, 2832, 1777, 1712, 1601, 1494, 1363, 1183, 776, 739, 697 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{66}H_{64}N_2O_{12}[M+H]^+$ = 1077.4532, found = 1077.4528.

Benzyl (Z)-6-(2-(benzyloxy)-2-oxoethyl)-2-(3-(3-(Z)-5-(2-(benzyloxy)-2-oxoethyl)-6-((benzyloxy)carbonyl)-4-ethyl-1,3-dioxo-7-propylidene-1,3,3a,4,7,7a-hexahydro-2H-isoindol-2-yl)benzyl)phenyl)-7-ethyl-1,3-dioxo-4-propylidene-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4ao)



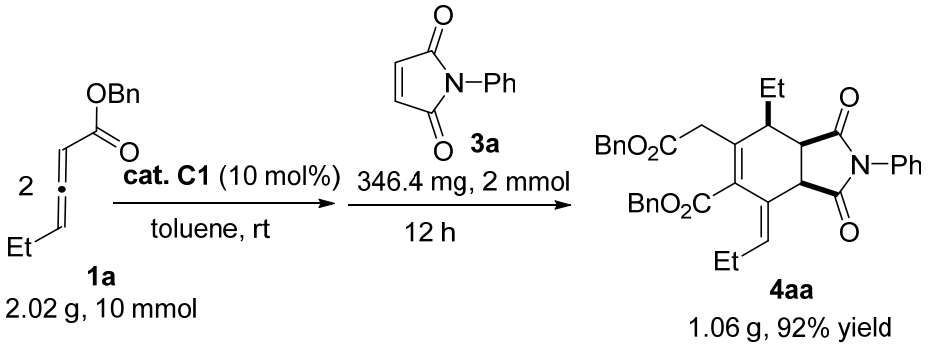
Yield: 211.6 mg, 91%, a pale yellow gel liquid; **^{1}H NMR** δ 7.34 – 7.26 (m, 20H), 7.14 (d, *J* = 8.36 Hz, 4H), 7.06 (d, *J* = 8.37 Hz, 4H), 5.98 – 5.93 (m, 2H), 5.22 – 5.08 (m, 4H), 5.07 – 4.98 (m, 4H), 3.97 (s, 2H), 3.89 (d, *J* = 16.58 Hz, 2H), 3.75 (d, *J* = 9.11 Hz, 2H), 3.49 – 3.39 (m, 4H), 2.49 (q, *J* = 7.70 Hz, 2H), 1.97 – 1.85 (m, 6H), 1.76 – 1.67 (m, 2H), 1.01 (t, *J* = 7.25 Hz, 6H), 0.89 (t, *J* = 7.47 Hz, 6H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 176.1, 175.4, 169.8, 166.5, 146.3, 140.7, 135.7, 135.4, 135.2, 130.5, 130.0, 129.5, 128.5, 128.5, 128.2, 128.2, 128.1, 126.5, 125.3, 66.7, 66.6, 43.6, 43.4, 41.1, 37.0, 26.9, 23.1, 21.1, 13.4, 12.3; **IR** (KBr): 2964, 2832, 1712, 1597, 1513, 1363, 1182, 776, 741 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{73}H_{70}N_2O_{12}[M+H]^+$ = 1167.5002, found = 1167.5002.

Methyl (Z)-2-(4-bromophenyl)-4-ethylidene-6-(2-methoxy-2-oxoethyl)-7-methyl-1,3-dioxo-2,3,3a,4,7,7a-hexahydro-1H-isoindole-5-carboxylate (4lb)



Yield: 128.1 mg, 100%, White solid; M.p. 106 – 107 °C (Petroleum ether/EtOAc); **^{1}H NMR** δ 7.57 (d, *J* = 8.66 Hz, 2H), 7.15 (d, *J* = 8.78 Hz, 2H), 6.06 (q, *J* = 6.86 Hz, 1H), 3.79 (d, *J* = 9.16 Hz, 1H), 3.74 (s, 3H), 3.66 (d, *J* = 6.42 Hz, 2H), 3.61 (s, 3H), 3.32 (dd, *J* = 9.08, 5.36 Hz, 1H), 2.81 – 2.64 (m, 1H), 1.62 (d, *J* = 7.18 Hz, 3H), 1.37 (d, *J* = 7.42 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 175.8, 175.1, 170.4, 167.1, 146.6, 132.2, 130.9, 129.9, 128.4, 128.1, 126.6, 122.4, 52.1, 52.0, 48.1, 46.0, 36.5, 35.8, 15.1, 13.9; **IR** (KBr): 2951, 2832, 1712, 1597, 1490, 1364, 1192, 1069, 1012, 816, 776, 796, 734 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{38}H_{35}NO_6[M+H]^+$ = 602.2537, 478.0683, found = 602.2537, 478.0695.

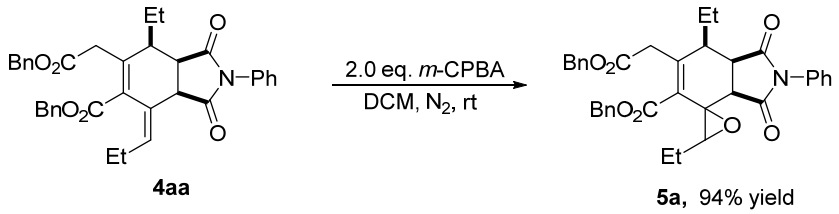
G. Gram-Scale Synthesis of 4aa



To a dried round-bottom flask with a magnetic stirring bar were added **1a** (10 mmol, 5.0 equiv.), toluene (20 mL) and catalyst **C1** (0.2 mmol, 0.1 equiv.) at room temperature. The resulting mixture was was stirred for 4 h, Then **3a** (2 mmol, 1.0 equiv.) was added and was stirred for 12 h until the consumption of 3a. The mixture was purified directly by flash column chromatography (PE / ethyl acetate = 5 / 1) to afford 1.06 g of **4aa** (92% yield).

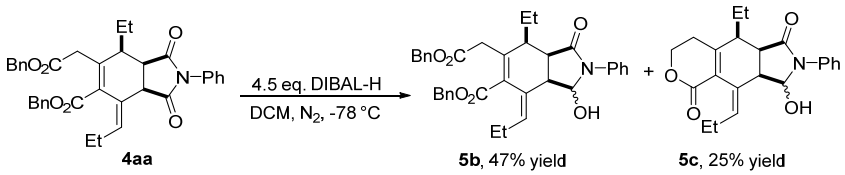
H. Transformations of 4aa

(a) Oxidation of compound 4aa



Under nitrogen atmosphere, compound **4aa** (115.6 mg, 0.2 mmol, 1.0 eq) was added to a 15 mL Schlenk tube, followed by adding 1 mL dry DCM, and 85% *m*-CPBA (69.0 mg, 0.4 mmol, 2.0 eq) was added at room temperature. The resulting mixture was stirred for 12 h. After the completely consumption of **4aa** monitored by TLC, the mixture was quenched by saturated $NaHCO_3$ aqueous (5 mL) and separated. The aqueous phase was extracted by DCM (10 mL×2), and the organic phase was combined, dried by Na_2SO_4 and filtered. The filtrate was concentrated under vacuum to remove solvent and the residue was purified by column chromatography on silica gel with PE / ethyl acetate = 5 / 1 as eluent to afford product **5a** (111.3 mg, 94%) as a pale yellow gel liquid. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 7.42 (dd, *J* = 11.27, 7.22 Hz, 3H), 7.36 – 7.30 (m, 10H), 7.20 (d, *J* = 7.22 Hz, 2H), 5.21 (d, *J* = 12.62 Hz, 1H), 5.09 (d, *J* = 12.74 Hz, 1H), 5.04 (d, *J* = 4.70 Hz, 2H), 3.65 – 3.58 (m, 1H), 3.53 – 3.44 (m, 3H), 2.88 (q, *J* = 7.64 Hz, 1H), 1.90 – 1.69 (m, 1H), 1.58 (dd, *J* = 8.83, 5.20 Hz, 2H), 1.20 – 1.12 (m, 1H), 0.96 – 0.90 (m, 6H), 0.90 – 0.80 (m, 1H); **^{13}C NMR** (101 MHz, DMSO-d_6) δ 175.6, 173.4, 169.1, 165.3, 135.8, 135.4, 132.0, 128.8, 128.4, 128.3, 128.0, 128.0, 127.8, 127.0, 66.3, 66.1, 62.6, 60.0, 41.3, 20.7, 12.0, 10.5; **IR** (KBr): 2968, 2832, 1715, 1597, 1499, 1186, 776, 749, 696 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{36}H_{35}NO_7$ $[M+H]^+$ = 594.2486, found = 594.2495.

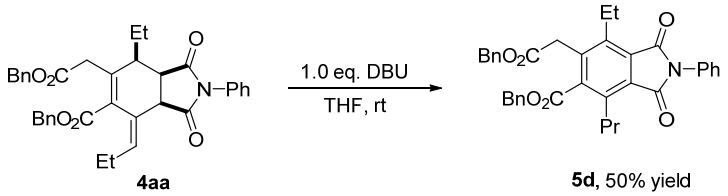
(b) Reduction of compound 4aa



Under nitrogen atmosphere, compound **4aa** (115.6 mg, 0.2 mmol, 1.0 eq) and anhydrous DCM (1 mL) was added into a 15 mL Schlenk tube, followed by dropwise addition of DIBAL-H (0.6 mL, 0.9 mmol, 1.5 M in toluene) at -78 °C over 30 min. The mixture was stirred at the same temperature. After 6 hours the compound **4aa** was consumed monitored by TLC, and the reaction was quenched by saturated potassium sodium tartrate solution and stirred until the mixture was clear. The mixture was extracted by DCM (10 mL×2), and the organic phase was combined, dried by Na_2SO_4 and filtered. The filtrate was concentrated under vacuum to remove solvent and the residue was purified by column chromatography on silica gel with PE / ethyl acetate = 3 / 1 to PE / ethyl acetate = 2 / 1 as eluent to afford product **5b** (55.7 mg, 47%) and product **5c** (18.2 mg, 25%) as a pale yellow gel liquid. Characterization data for **5b**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 8H), 7.25 – 7.18 (m, 7H), 5.63 – 5.52 (m, 2H), 5.19 – 5.03 (m, 4H), 3.92 (d, *J* = 13.24 Hz, 1H), 3.73 – 3.54 (m, 2H), 3.49 (dd, *J* = 8.97, 6.87 Hz, 1H), 3.26 (dd, *J* = 8.78, 3.34 Hz, 1H), 2.36 (dd, *J* = 14.98, 8.89 Hz, 1H), 2.17 – 2.10 (m, 1H), 1.92 – 1.80 (m, 3H), 1.04 (t, *J* = 7.27 Hz, 3H), 0.88 (t, *J* = 7.46 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 173.0, 170.8, 167.9, 149.7, 139.7, 135.5, 129.5, 129.4, 129.3, 129.2, 128.9, 128.8, 127.5, 126.9, 125.6, 84.5, 68.1, 67.4, 48.2, 45.2, 44.8, 36.2, 30.4, 24.0, 21.4, 14.1, 13.0; **IR** (KBr):2960, 2832, 1691, 1592, 1536, 1363, 776 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{36}H_{37}NO_6$ $[M+H]^+$ = 580.2694, found = 580.2702.

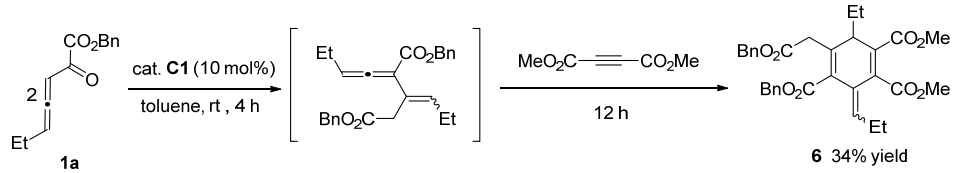
Characterization data for **5c**: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 (t, *J* = 7.73 Hz, 2H), 7.23 – 7.16 (m, 3H), 5.69 (t, *J* = 7.36 Hz, 1H), 5.54 (dd, *J* = 13.36, 6.68 Hz, 1H), 4.49 (dd, *J* = 11.08, 4.52 Hz, 1H), 4.38 – 4.29 (m, 1H), 3.74 (d, *J* = 13.38 Hz, 1H), 3.58 – 3.52 (m, 1H), 3.32 (dd, *J* = 8.31, 2.88 Hz, 1H), 2.80 – 2.66 (m, 1H), 2.54 (d, *J* = 15.96 Hz, 1H), 2.33 (t, *J* = 7.25 Hz, 2H), 2.18 – 2.06 (m, 1H), 2.02 – 1.89 (m, 2H), 1.11 (t, *J* = 7.06 Hz, 3H), 1.03 (t, *J* = 7.48 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 172.0, 163.6, 162.0, 139.5, 136.1, 128.7, 126.7, 125.5, 122.9, 83.6, 65.6, 47.5, 44.7, 43.5, 26.2, 24.0, 20.3, 13.3, 12.6; **IR** (KBr): 2963, 1692, 1658, 1596, 1363, 776 (cm^{-1}); **HRMS** (ESI-TOF): m/z calcd for $C_{22}H_{25}NO_4$ $[M+H]^+$ = 368.1856, found = 368.1861.

(c) Aromatization of compound 4aa



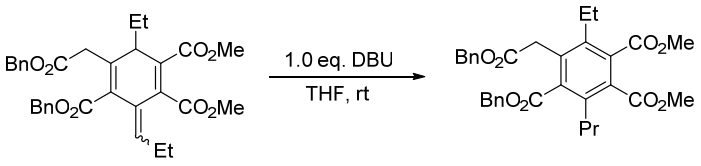
To a dried seal tube with a magnetic stirring bar were added **4aa** (0.2 mmol, 1.0 equiv.), THF (1 mL) and DBU (0.2 mmol, 1 equiv.) at room temperature. The resulting mixture was stirred untill **4aa** was consumed monitored by TLC. The reaction mixture was concentrated under vacuum to remove solvent and the residue was purified by flash column chromatography (PE / ethyl acetate = 5 / 1) to afford product **5d** (57.6 mg, 50%) as a white solid.; M.p. 82 – 83°C (Petroleum ether/EtOAc); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49 (t, *J* = 7.68 Hz, 2H), 7.40 (d, *J* = 7.72 Hz, 5H), 7.38 – 7.31 (m, 6H), 7.29 (d, *J* = 7.62 Hz, 2H), 5.29 (s, 2H), 5.05 (s, 2H), 3.79 (s, 2H), 3.16 (q, *J* = 7.55 Hz, 2H), 2.94 – 2.86 (m, 2H), 1.55 (s, 3H), 1.18 (t, *J* = 7.48 Hz, 3H), 0.84 (t, *J* = 7.30 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.4, 168.0, 142.5, 141.5, 138.3, 136.7, 134.7, 129.3, 129.1, 129.0, 128.8, 128.7, 128.5, 128.4, 128.3, 128.1, 126.7, 67.7, 67.1, 35.3, 31.3, 24.6, 21.1, 14.5, 14.3; **IR** (KBr):2962, 2832, 1713, 1593, 1363, 1172, 776, 741; **HRMS** (ESI-TOF): m/z calcd for $C_{36}H_{35}NO_6$ $[M+H]^+$ = 576.2381, found = 576.2390.

I. Diels-Alder reaction of the allenoate RC-adduct with DMAD



To a dried seal tube with a magnetic stirring bar were added **1a** (1.0 mmol, 5.0 equiv.), toluene (2 mL) and catalyst **C1** (0.02 mmol, 0.1 equiv.) at room temperature. The tube was sealed and the mixture was stirred for 4 h, Then DMAD (0.2 mmol, 1.0 equiv.) was added and was stirred for 12 h until consumption of DMAD monitored by TLC. The mixture was purified directly by flash column chromatography (PE / ethyl acetate = 5 / 1) to afford **6** (37.2 mg, 34%) as a pale yellow gel liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 10H), 5.72 (t, *J* = 7.52 Hz, 1H), 5.23 (d, *J* = 12.28 Hz, 1H), 5.13 (d, *J* = 12.18 Hz, 1H), 5.07 (d, *J* = 6.27 Hz, 2H), 3.91 (s, 3H), 3.80 (d, *J* = 15.71 Hz, 1H), 3.75 (s, 3H), 3.57 (t, *J* = 5.07 Hz, 1H), 3.23 (d, *J* = 15.71 Hz, 1H), 2.04 – 1.95 (m, 2H), 1.89 – 1.80 (m, 1H),

1.79 – 1.69 (m, 1H), 0.92 (t, *J* = 7.41 Hz, 3H), 0.77 (t, *J* = 7.47 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.3, 167.8, 165.4, 140.6, 138.0, 135.6, 135.1, 128.6, 128.4, 128.3, 128.1, 128.1, 127.4, 126.9, 66.9, 66.7, 52.5, 52.2, 43.5, 38.1, 27.0, 22.8, 13.4, 9.3; **IR** (KBr):2953, 2878, 1735, 1631, 1455, 1363, 777, 751, 698; **HRMS** (ESI-TOF): m/z calcd for $C_{32}H_{34}O_8$ $[M+H]^+$ = 547.2326, found = 547.2328.



6 **7**

To a dried seal tube with a magnetic stirring bar were added **6** (0.2 mmol, 1 equiv.), THF (1 mL) and DBU (0.2 mmol, 1 equiv.) atroom temperature. The tube was sealed and the mixture was stirred until compound **6a** was consumed monitored by TLC. The reaction mixture was concentrated under vacuum to remove solvent and the residue was purified by flash column chromatography (PE / ethyl acetate = 5 / 1) to afford product **7** (54.7 mg, 50%) as a pale yellow gel liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 5.40 Hz, 2H), 7.32 (d, *J* = 5.87 Hz, 6H), 7.26 (d, *J* = 5.82 Hz, 2H), 5.23 (s, 2H), 5.02 (s, 2H), 3.84 (d, *J* = 6.06 Hz, 6H), 3.70 (s, 2H), 2.65 (q, *J* = 7.73 Hz, 2H), 2.54 – 2.48 (m, 2H), 1.43 (q, *J* = 7.69 Hz, 2H), 1.10 (t, *J* = 7.61 Hz, 3H), 0.73 (t, *J* = 7.30 Hz, 3H); **^{13}C NMR** (101 MHz, $CDCl_3$) δ 169.6, 168.5, 168.5, 139.6, 137.8, 136.3, 135.5, 134.8, 132.0, 129.0, 128.6, 128.6, 128.4, 128.2, 128.1, 67.4, 66.8, 52.4, 35.7, 33.3, 24.7, 23.7, 14.9, 14.2; **IR** (KBr):2956, 2874, 1735, 1631, 1455, 1363, 1079, 751, 698; **HRMS** (ESI-TOF): m/z calcd for $C_{32}H_{34}O_8$ $[M+H]^+$ = 547.2326, found = 547.2333.

J. X-Ray crystallographic analysis of 4lb

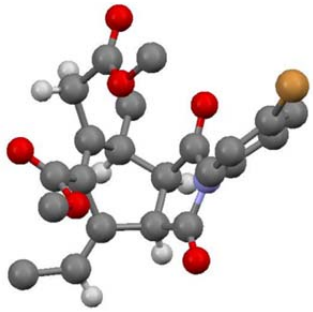


Figure 1. X-ray structure of **4lb**

The title compound was recrystallized from hexane/DCM, by slow evaporation of solvent.

Table 1. Crystal data and structure refinement for **4lb**

Empirical formula	C22 H22 Br N O6	
Formula weight	474.32	
Temperature	296 K	
Wavelength	0.71073 Å	
Crystal system	monoclinic	
Space group	C 2/c	
Unit cell dimensions	a = 26.095(4) Å	α= 90.
	b = 9.3443 Å	β= 125.058(2) (4).
	c = 21.347 (4) Å	γ = 90.
Volume	4260.9(10) $Å^3$	
Z	8	
Density (calculated)	1.479 Mg/m^3	
Absorption coefficient	1.965 mm^{-1}	
F(000)	1944	
Crystal size	0.180 x 0.160 x 0.140 mm^3	
Theta range for data collection	1.907 to 27.475°.	
Index ranges	-33<=h<=33, -12<=k<=12, -27<=l<=27	
Reflections collected	19336	
Independent reflections	4870 [R(int) = 0.0408]	
Completeness to theta = 25.242°	100.0 %	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4870/ 0 / 275	
Goodness-of-fit on F^2	1.041	
Final R indices [I>2sigma(I)]	R1 = 0.0388, wR2 = 0.0966	
R indices (all data)	R1 = 0.0648, wR2 = 0.1082	
Largest diff. peak and hole	0.412 and -0.449 e.$Å^{-3}$	

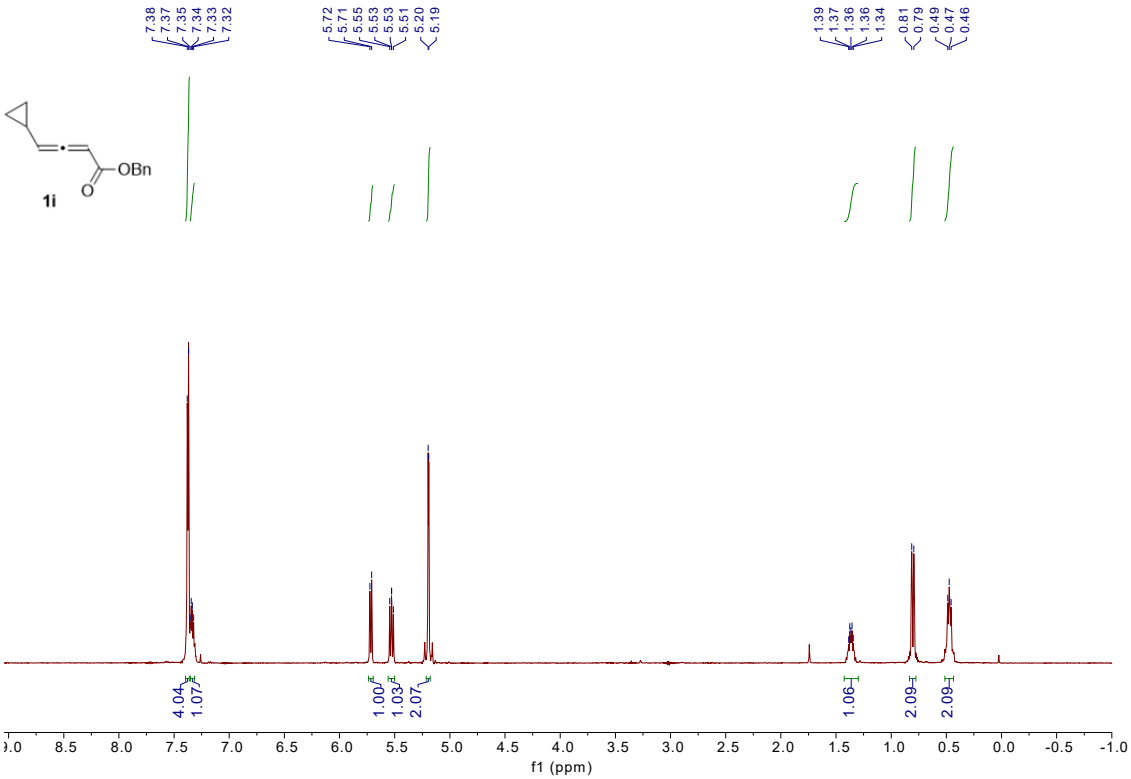
K.References

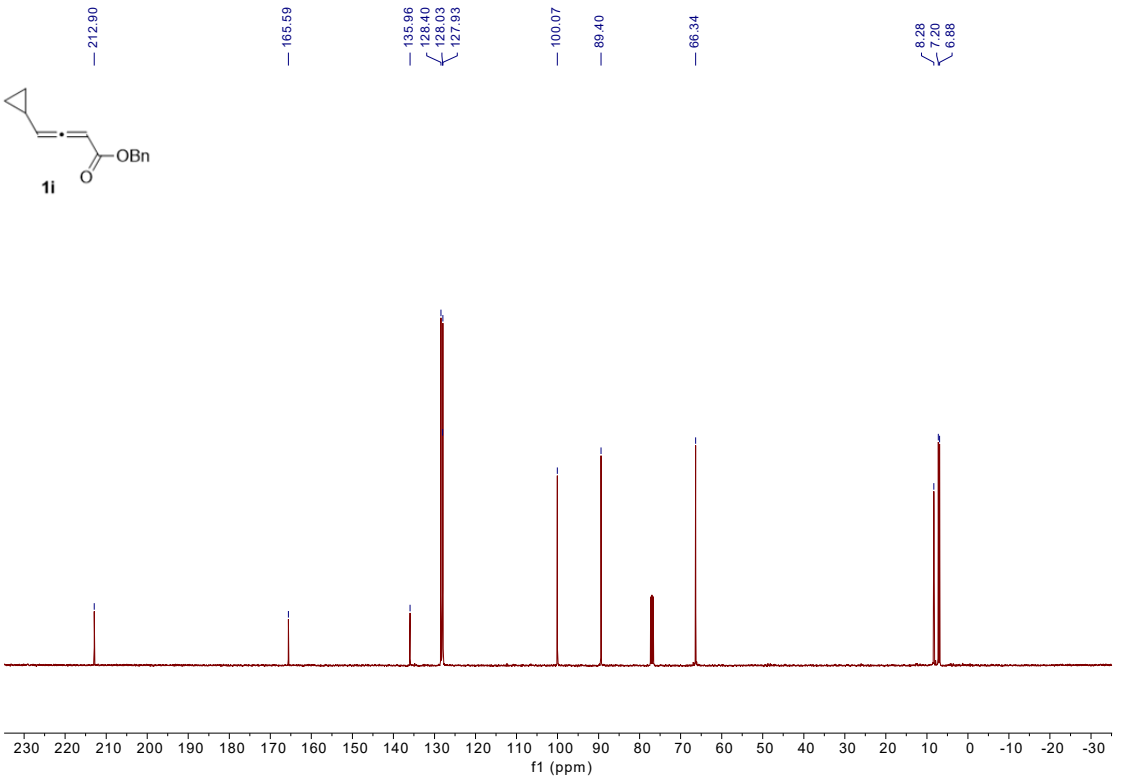
[1] Y. Gao, J. Zhang, W. Shan, W. Fei, J. Yao and W. Yao, *Org. Lett*., **2021**, *23*, 6377–6381.

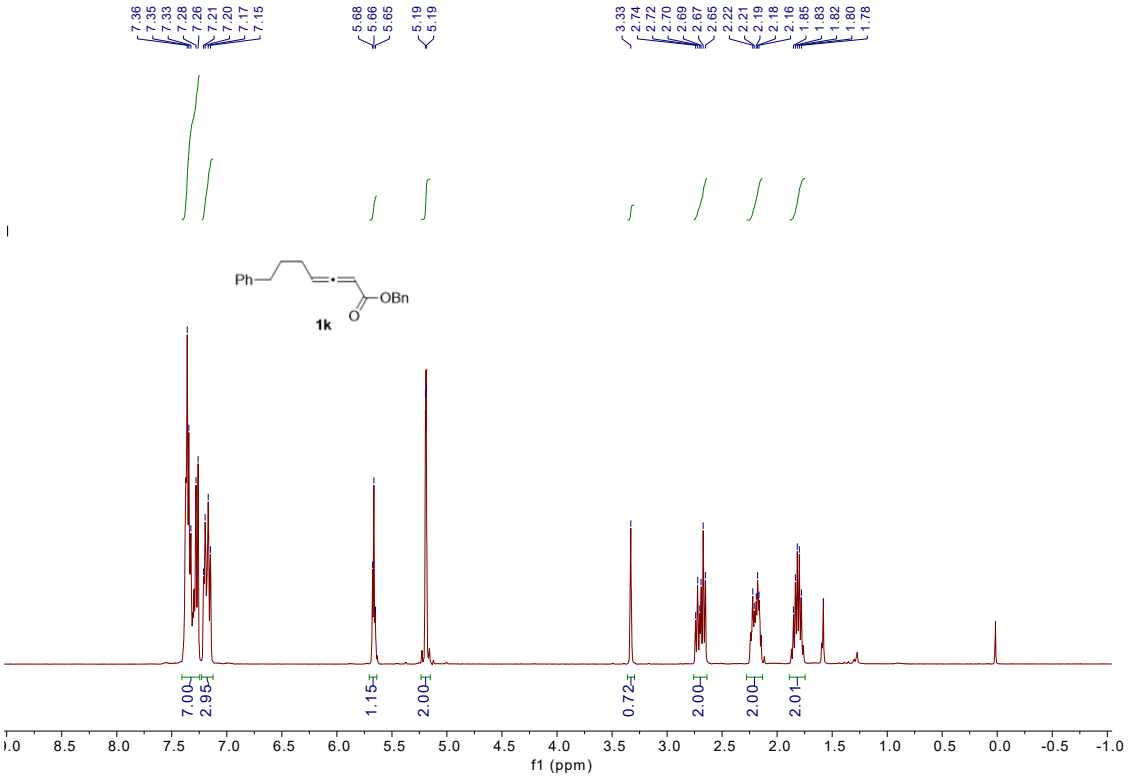
[2] W. Fei, P. Xu, J. Hou and W. Yao, *Chem. Commun.,* **2020**, *56*, 11669–11672.

[3] (a) M. Skrifvars and H.-W. Schmidt, *Syn. comm.,* **2006**, *25*, 1809–1815; (b) H. Wang, Y. Wei, Y. Li, S. Long, L.-J. Sun, S. Li and Y.-W. Lin, *Org. Lett*., **2022**, *24*, 6494–6498.

L. NMR Spectra



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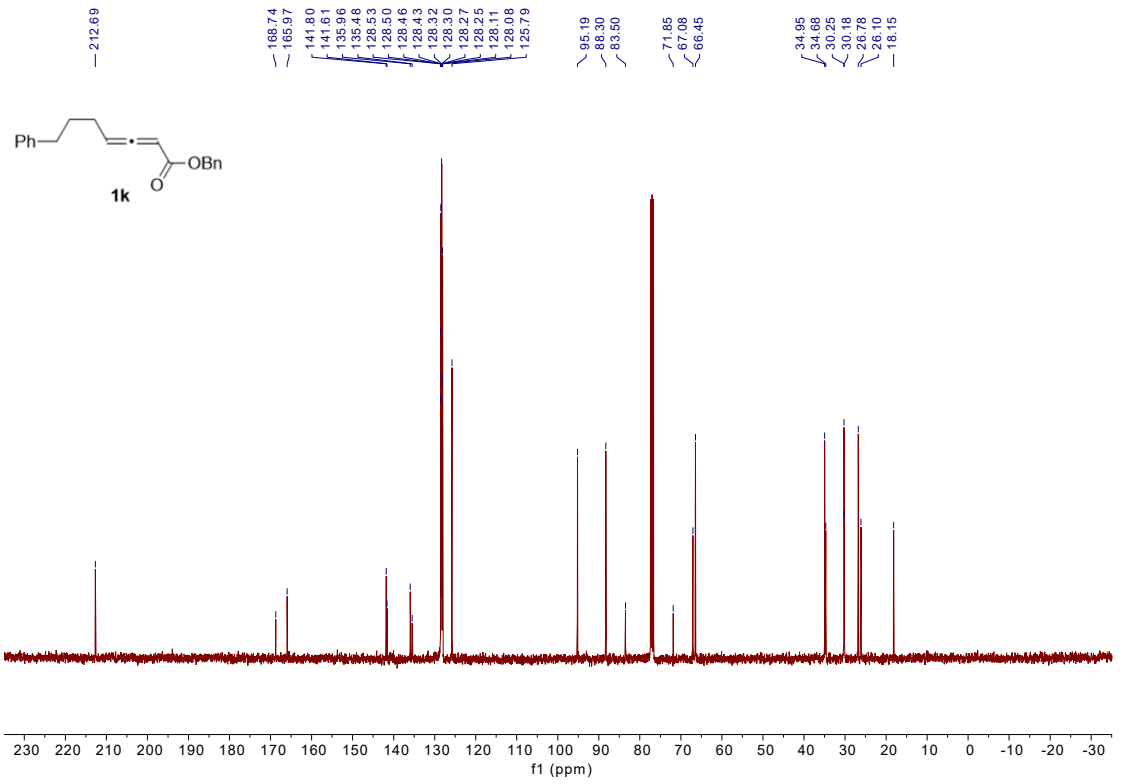
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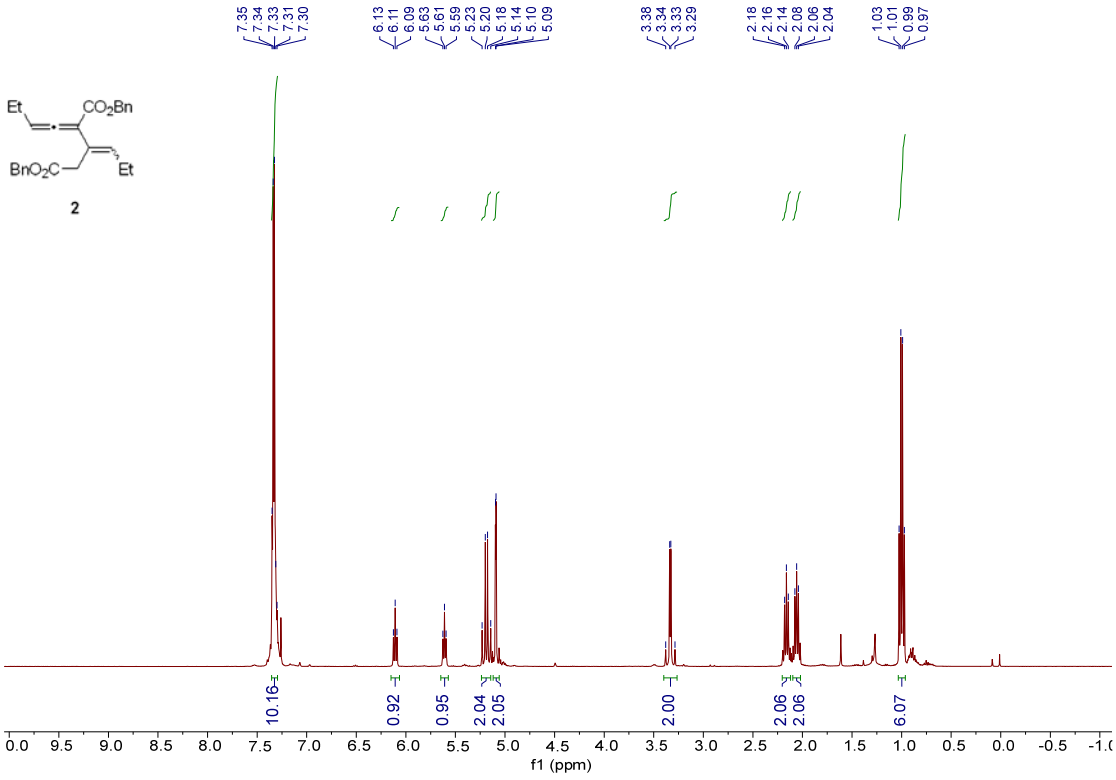
f1 (ppm)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1.01
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CO2Bn
BnO2C
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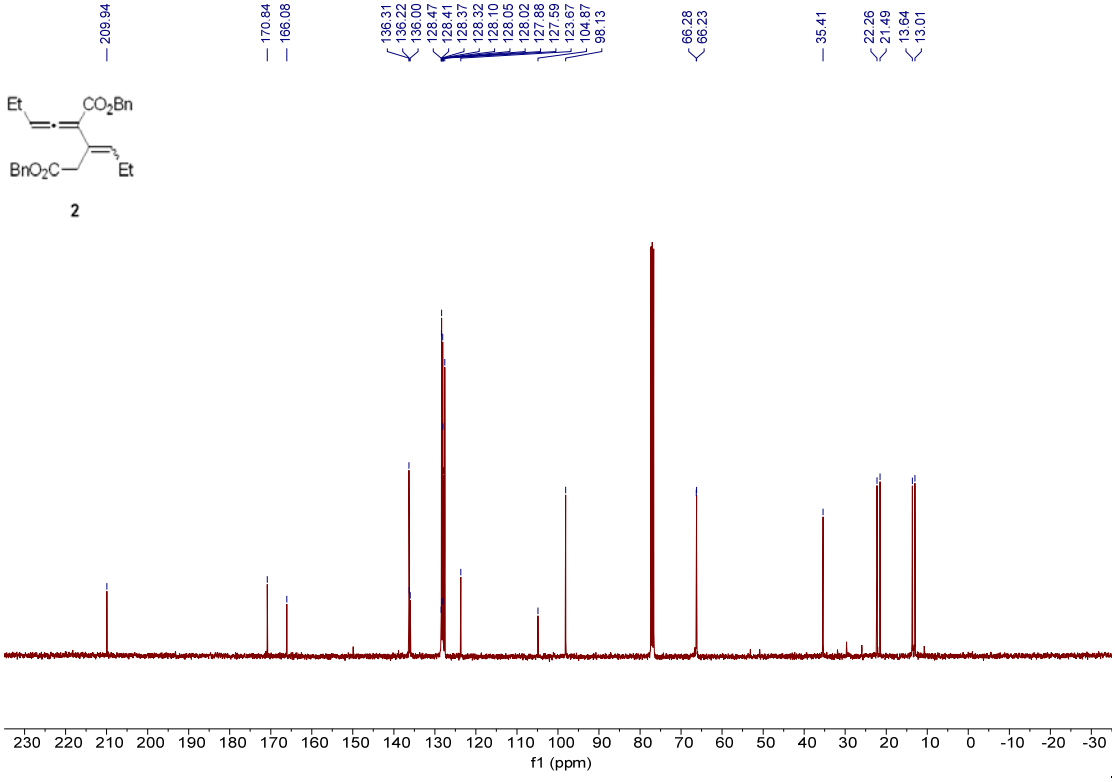
f1 (ppm)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Et
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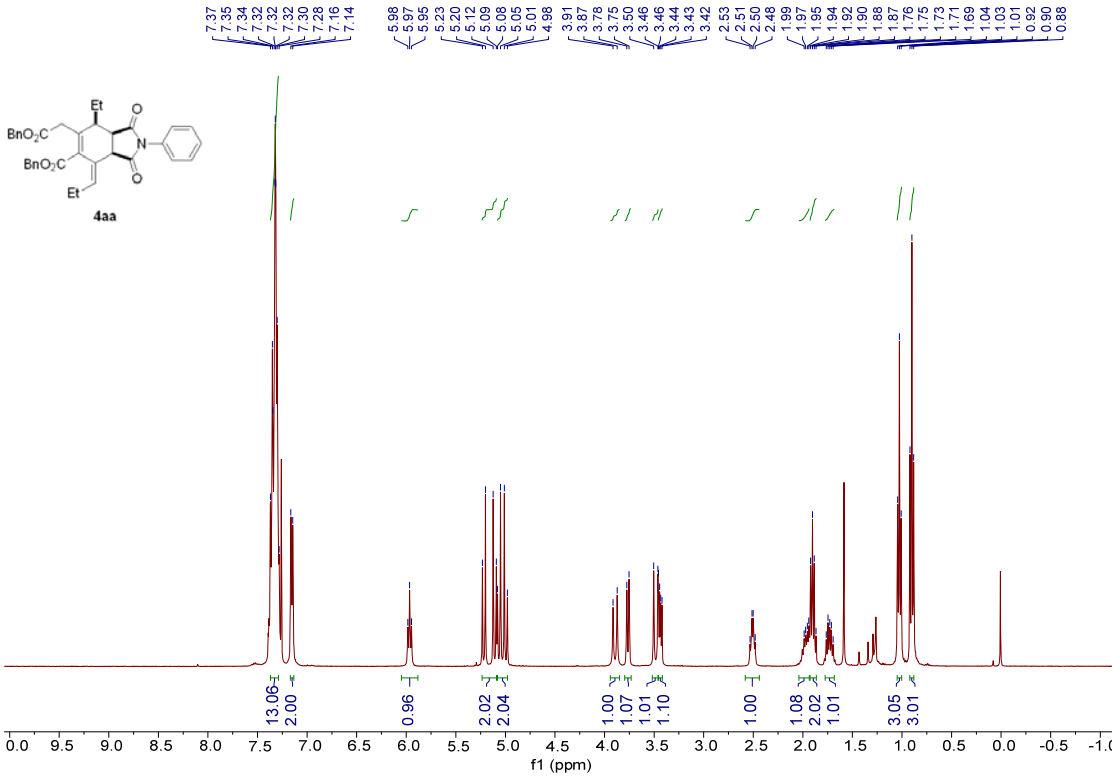
f1 (ppm)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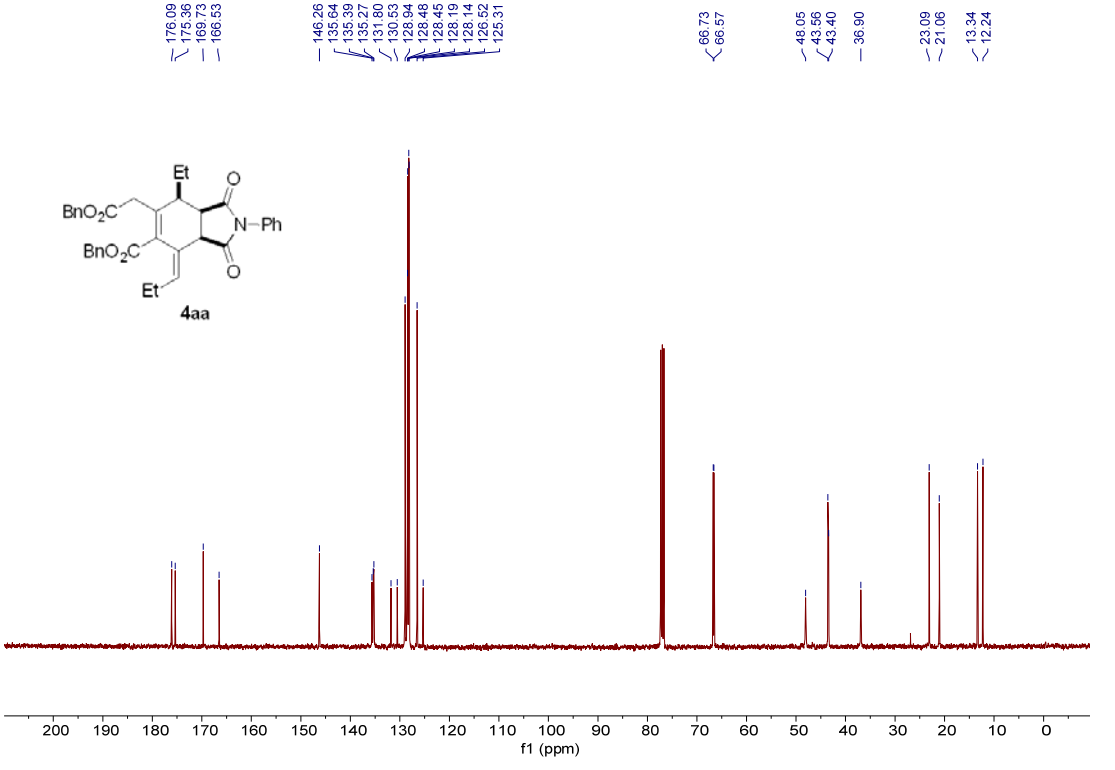
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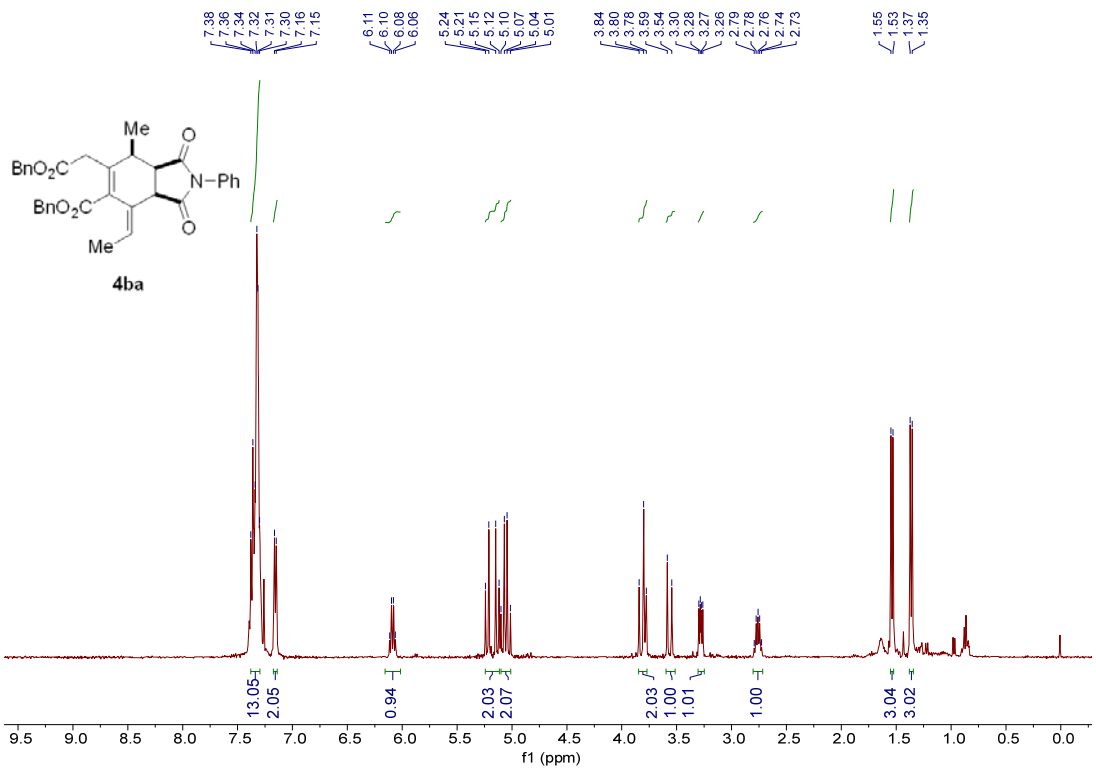
f1 (ppm)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5.10
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3.27
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1.53
1.37
1.35
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BnO2C
BnO2C
N–Ph
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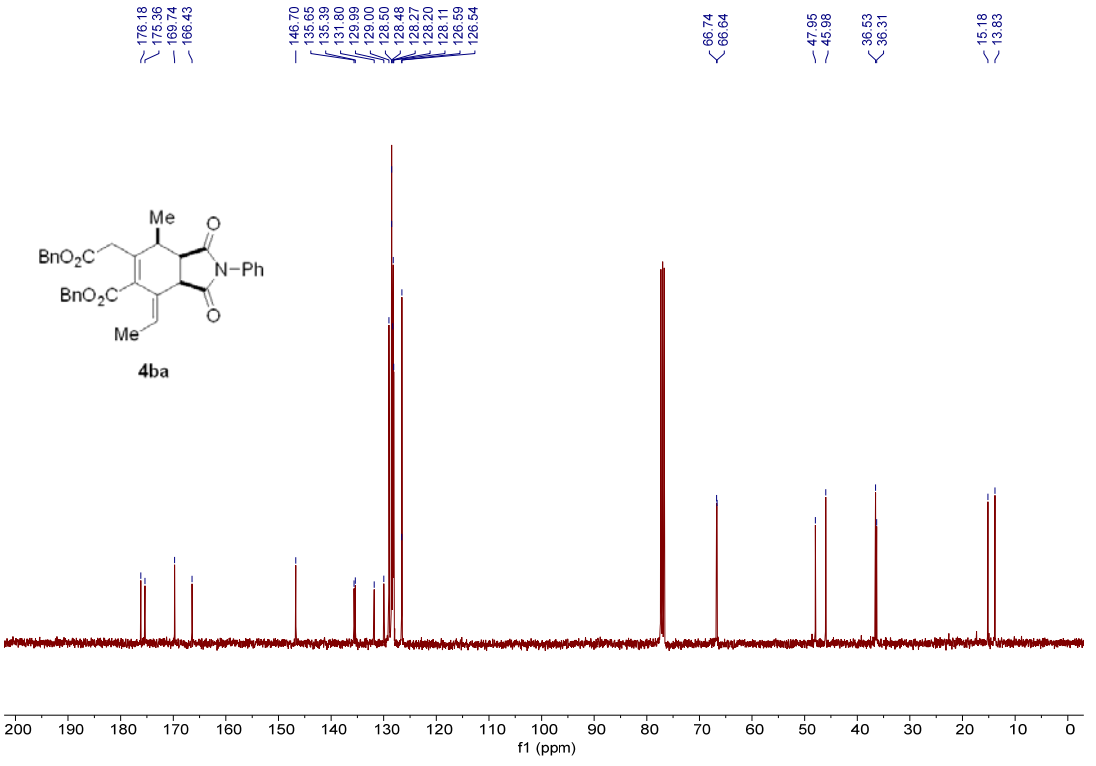
f1 (ppm)

4ba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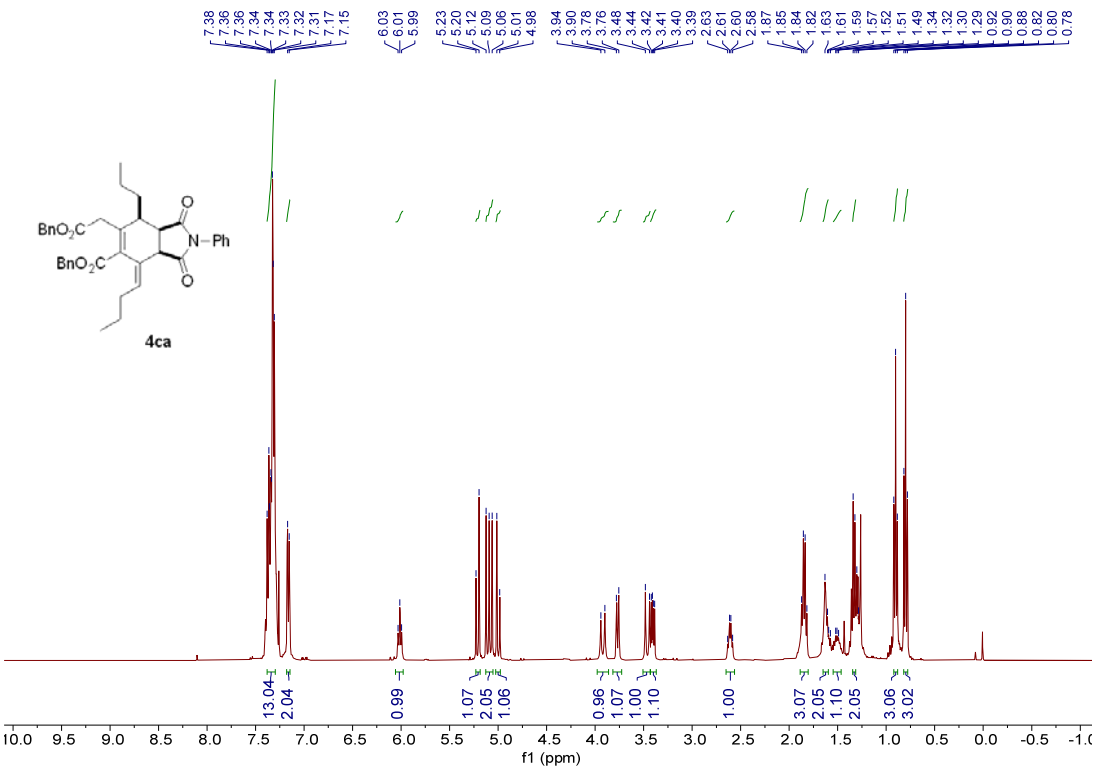
BnO2C
N–Ph
Me
f1 (ppm)

4ba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1.87 1.85 1.84 1.82 1.63 1.61 1.59 1.57 1.52 1.51 1.49 1.34 1.32 1.30 1.29 0.92 0.90 0.88 0.82 0.80 0.78
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BnO2C
N–Ph
O
O
O
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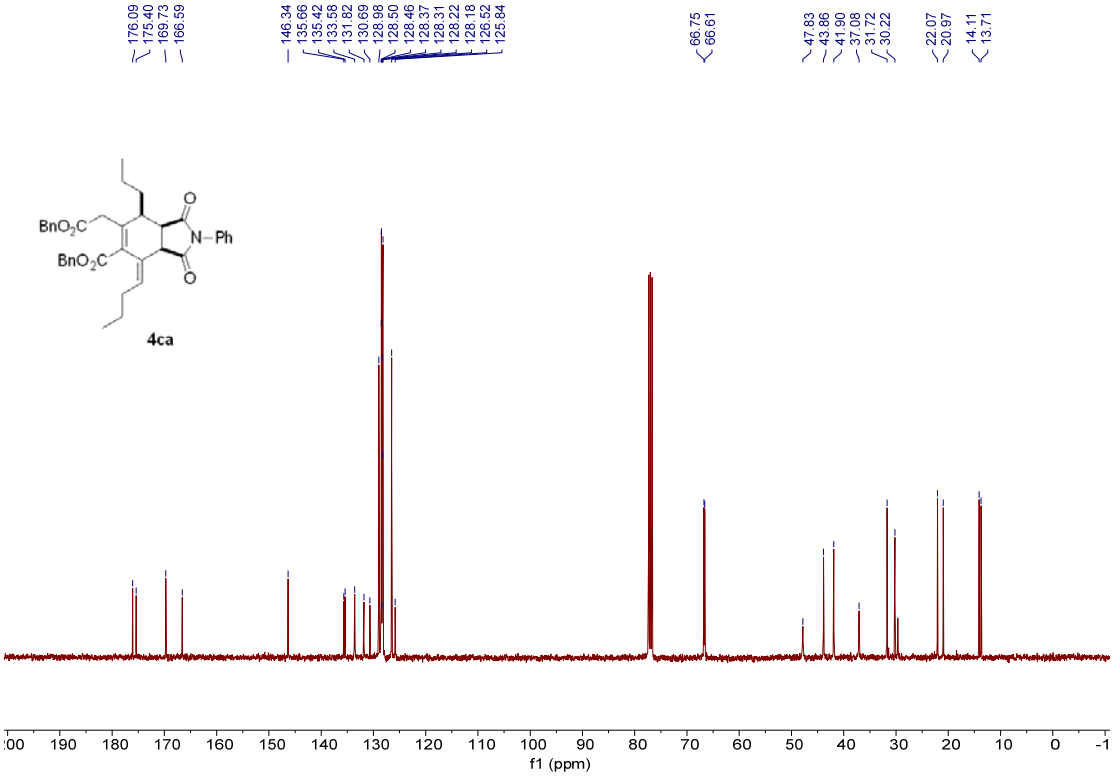
f1 (ppm)


176.09 175.40 169.73 166.59
146.34 135.66 135.42 133.58 131.82 130.69 128.98 128.50 128.46 128.37 128.31 128.22 128.18 126.52 125.84
66.75 66.61
47.83 43.86 41.90 37.08 31.72 30.22
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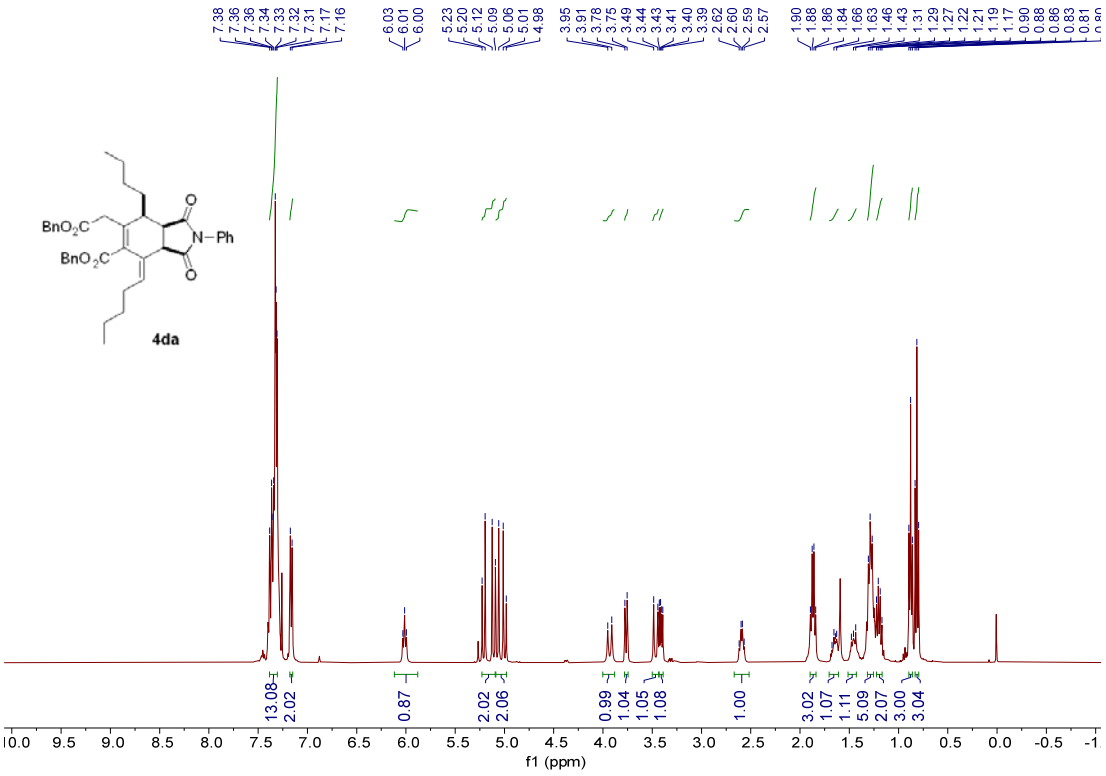
BnO2C
BnO2C
N–Ph
O
O
O
4ca
f1 (ppm)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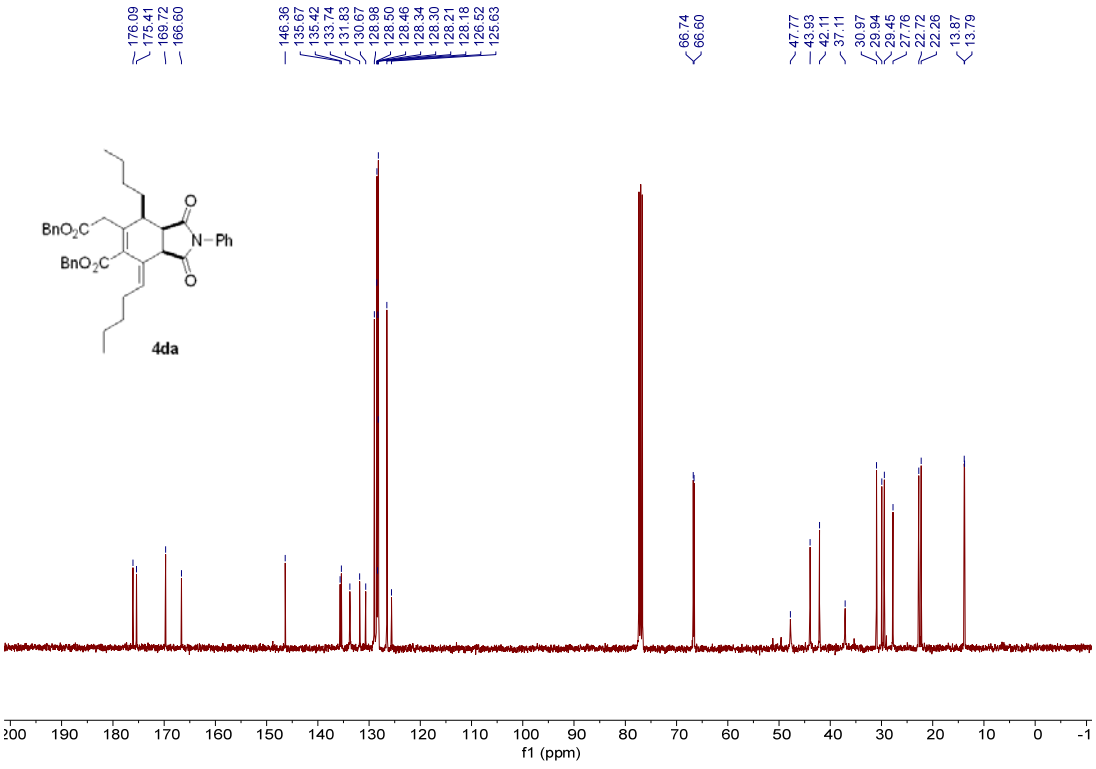
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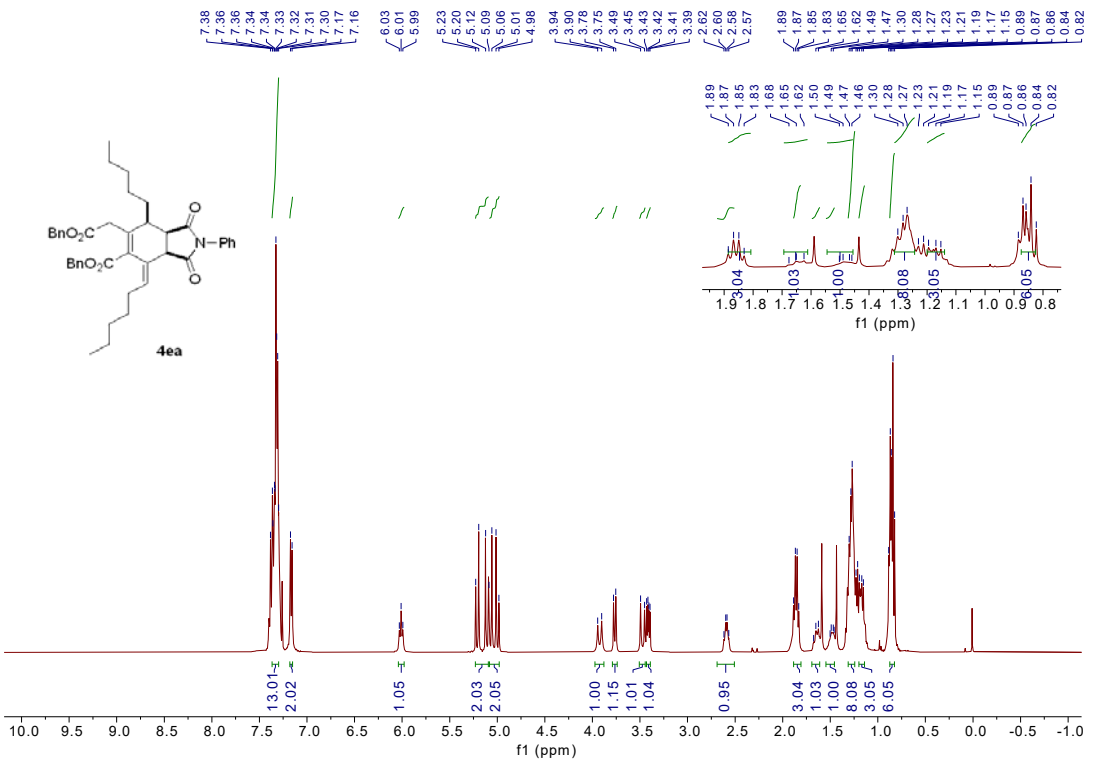
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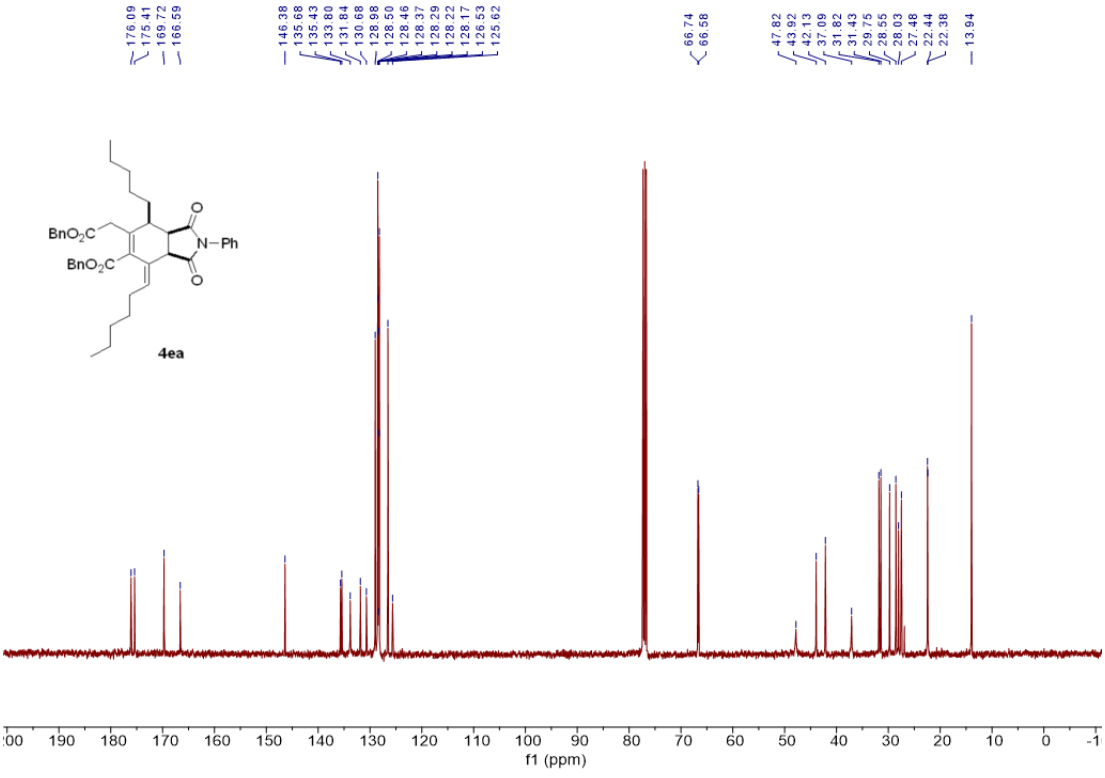
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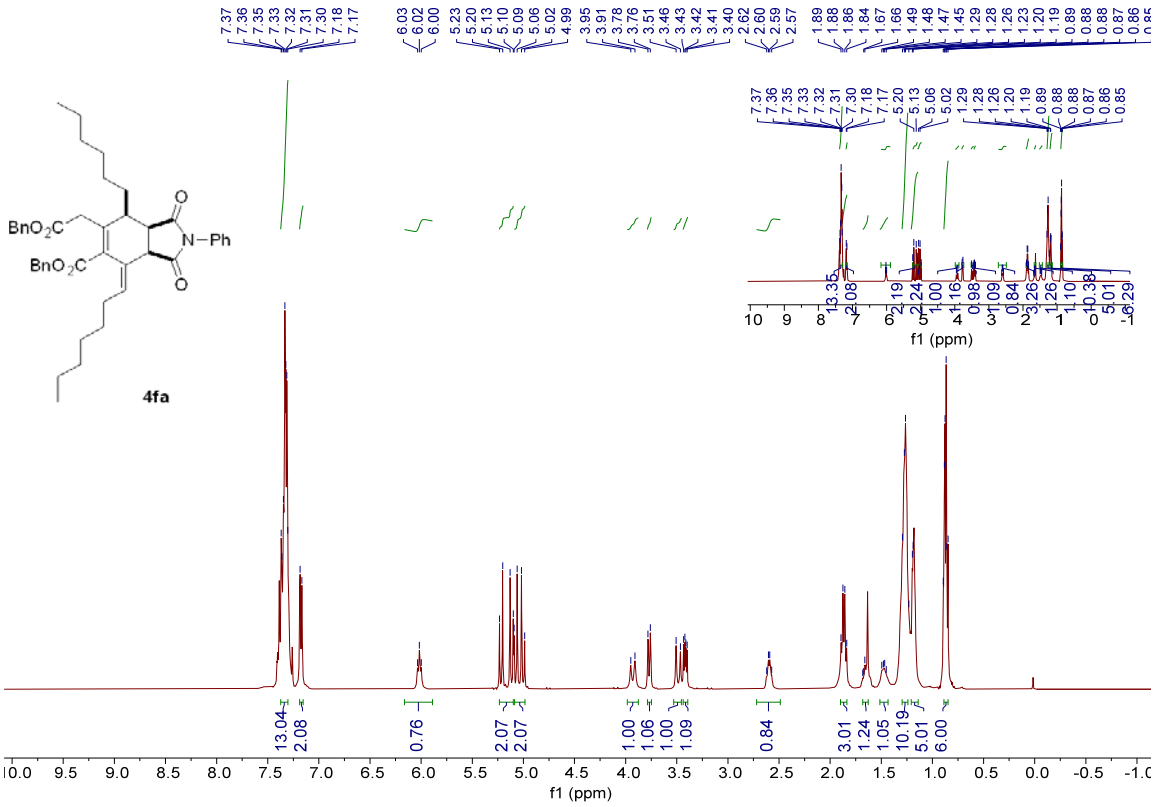
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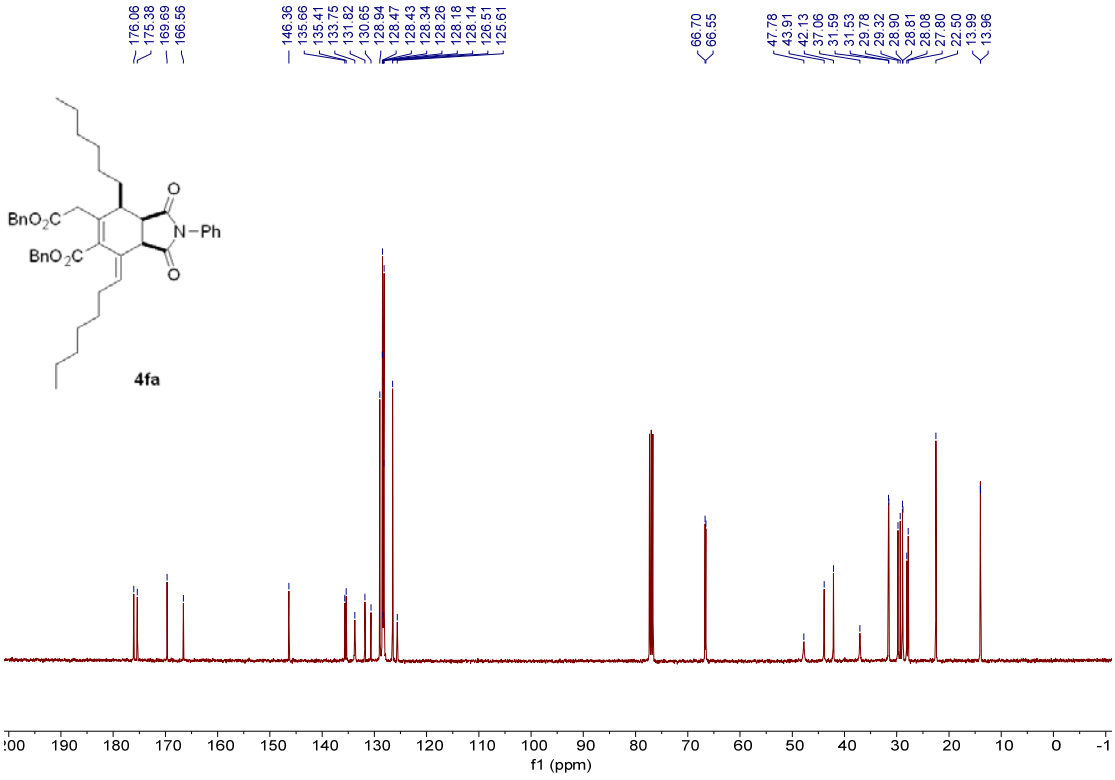
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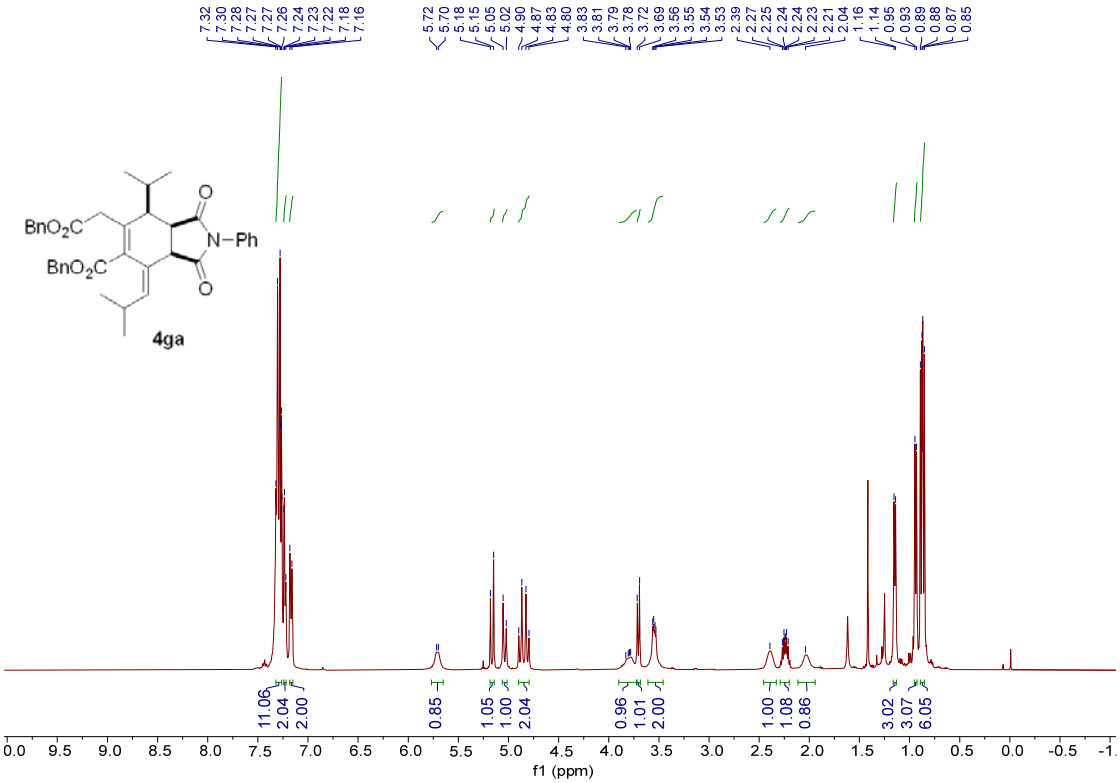
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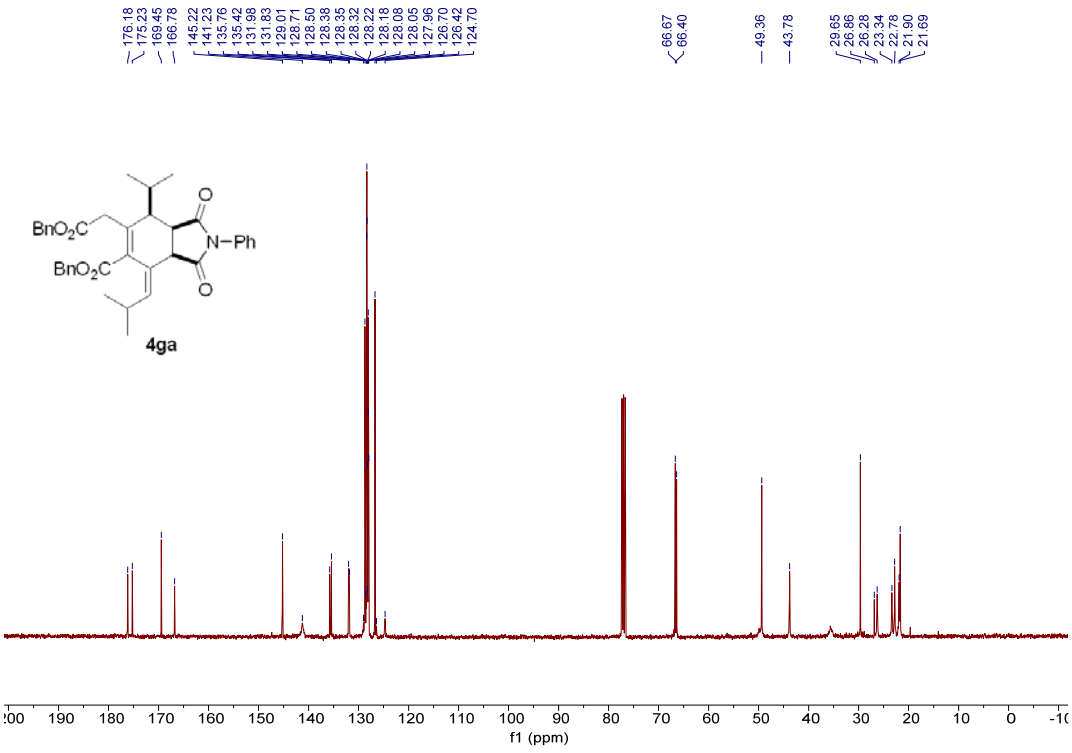
5.72 5.70 5.18 5.15 5.05 5.02 4.90 4.87 4.83 4.80 3.83 3.81 3.79 3.78 3.72 3.69 3.56 3.55 3.54 3.53 2.39 2.27 2.25 2.24 2.24 2.23 2.21 2.04 1.16 1.14 0.95 0.93 0.89 0.88 0.87 0.85
BnO2C
BnO2C
N−Ph
O
O
O
4ga
11.06 2.04 2.00 0.85 1.05 1.00 2.04 0.96 1.01 2.00 1.00 1.08 0.86 3.02 3.07 6.05
f1 (ppm)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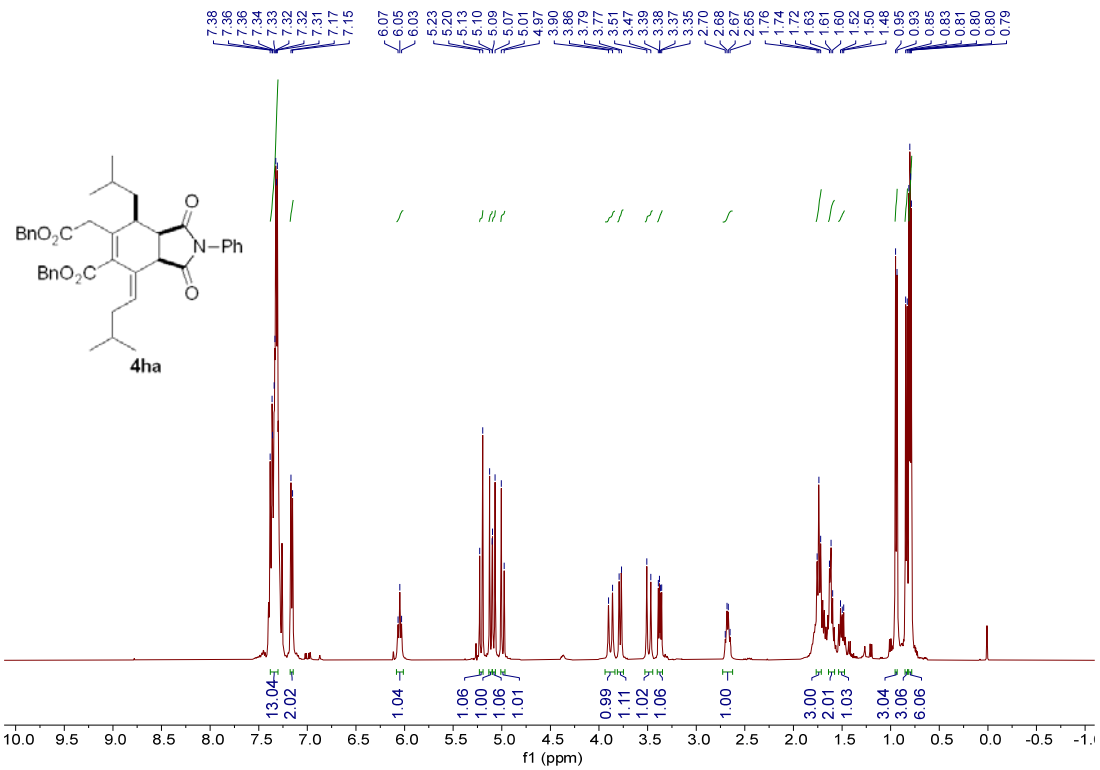
66.67 66.40 49.36 43.78 29.65 26.86 26.28 23.34 22.78 21.90 21.69
BnO2C
BnO2C
N−Ph
O
O
O
4ga
f1 (ppm)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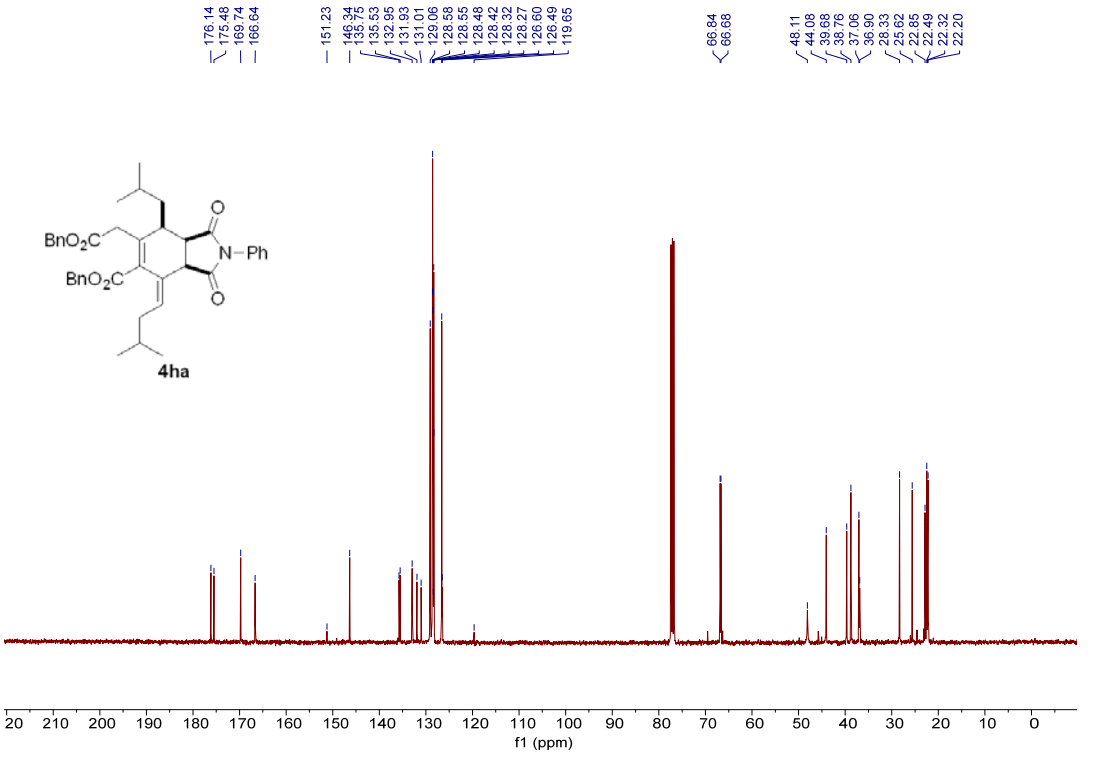
f1 (ppm)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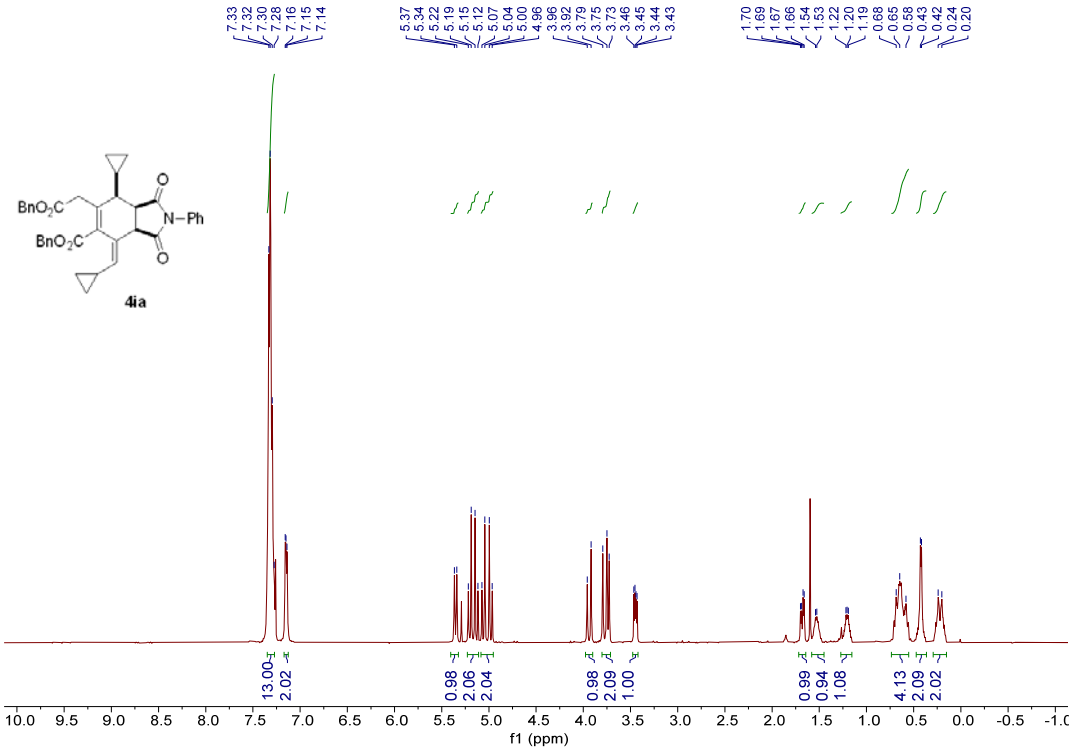
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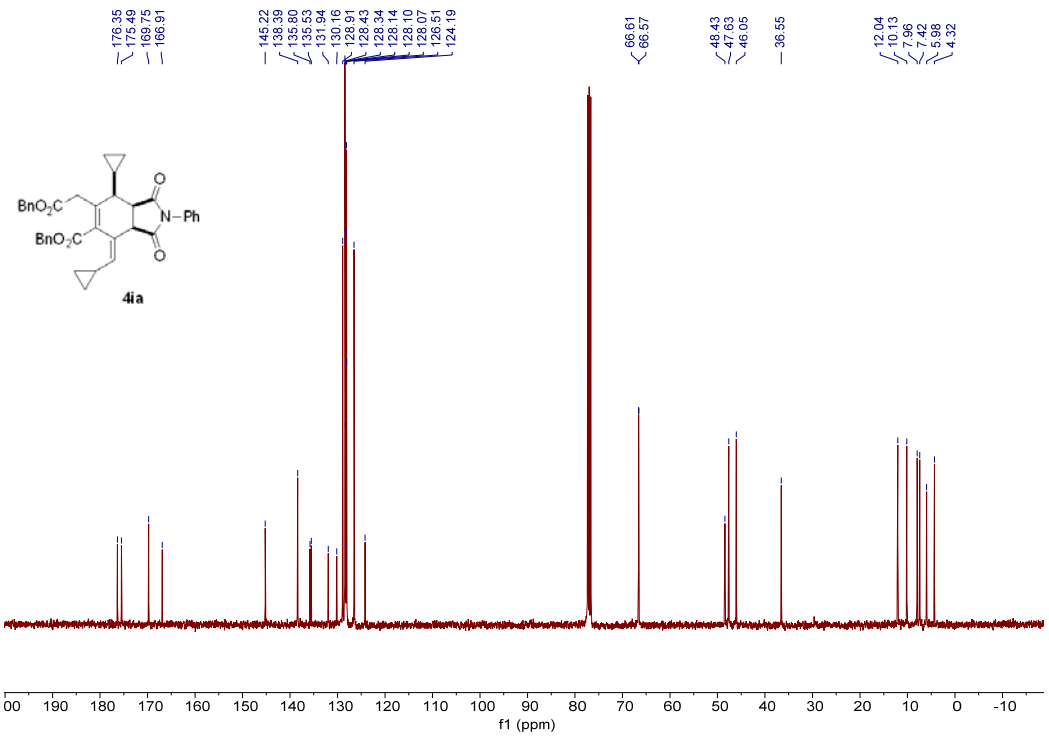
7.15
7.14
5.37
5.34
5.22
5.19
5.15
5.12
5.07
5.04
5.00
4.96
3.96
3.92
3.79
3.75
3.73
3.46
3.45
3.44
3.43
1.70
1.69
1.67
1.66
1.54
1.53
1.22
1.20
1.19
0.68
0.65
0.58
0.43
0.42
0.24
0.20
BnO2C
BnO2C
N–Ph
O
O
O
4ia
13.00
2.02
0.98
2.06
2.04
0.98
2.09
1.00
0.99
0.94
1.08
4.13
2.09
2.02
f1 (ppm)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166.91
145.22
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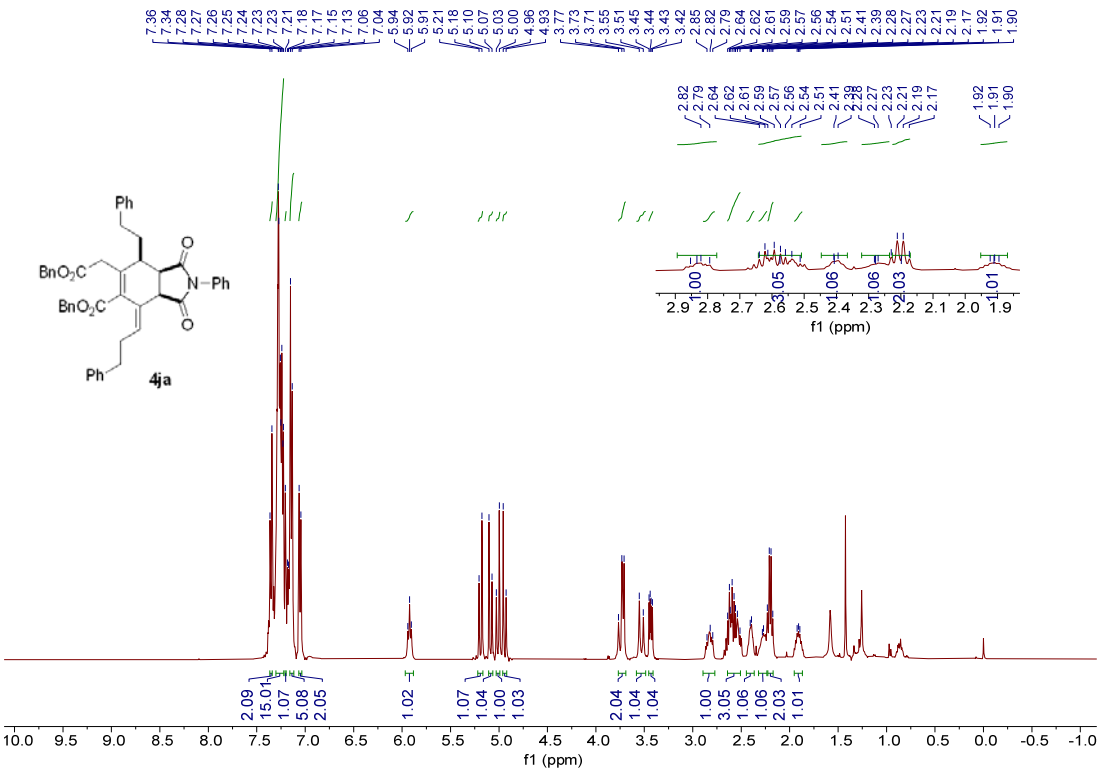
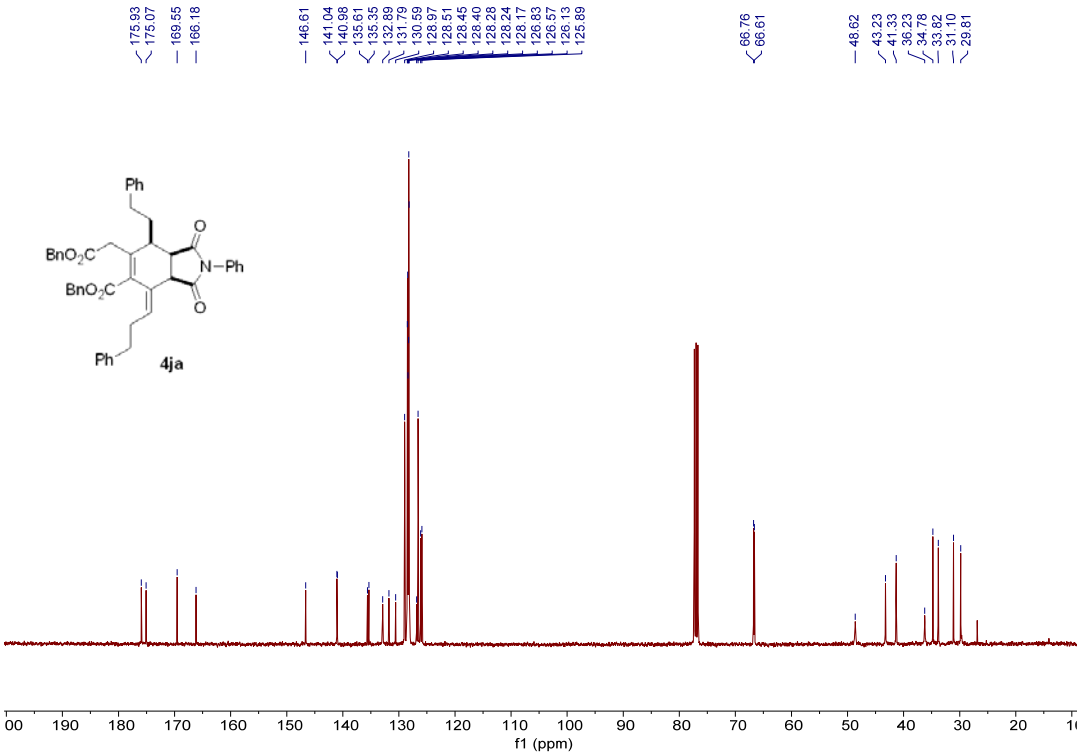
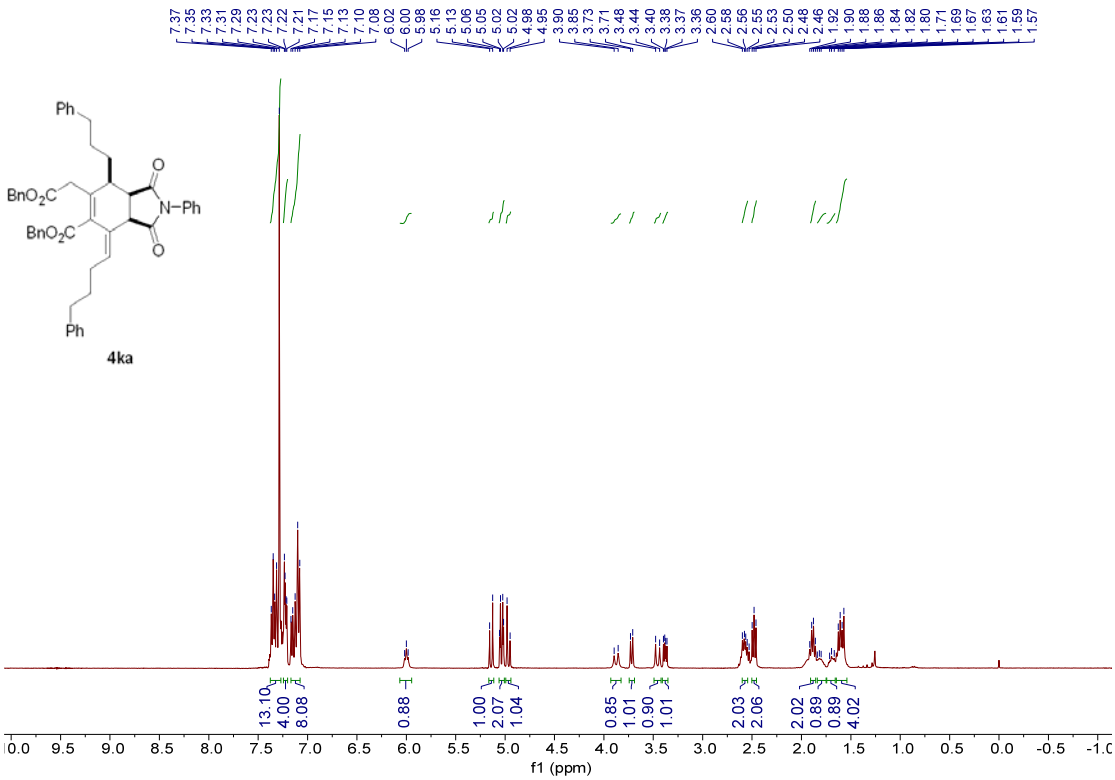
135.80
135.53
131.94
130.16
128.91
128.43
128.34
128.14
128.10
128.07
126.51
124.19
66.61
66.57
48.43
47.63
46.05
36.55
12.04
10.13
7.96
7.42
5.98
4.32
BnO2C
BnO2C
N–Ph
O
O
O
4ia
f1 (ppm)


4ja
f1 (ppm)


4ja
f1 (ppm)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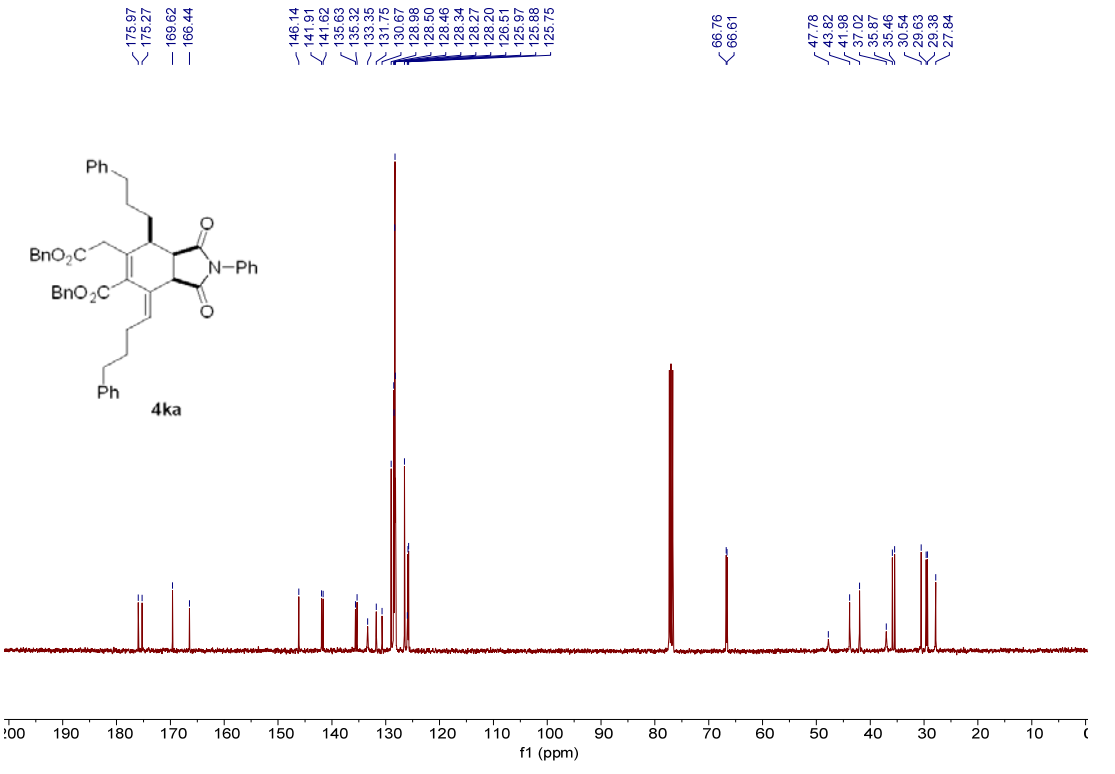
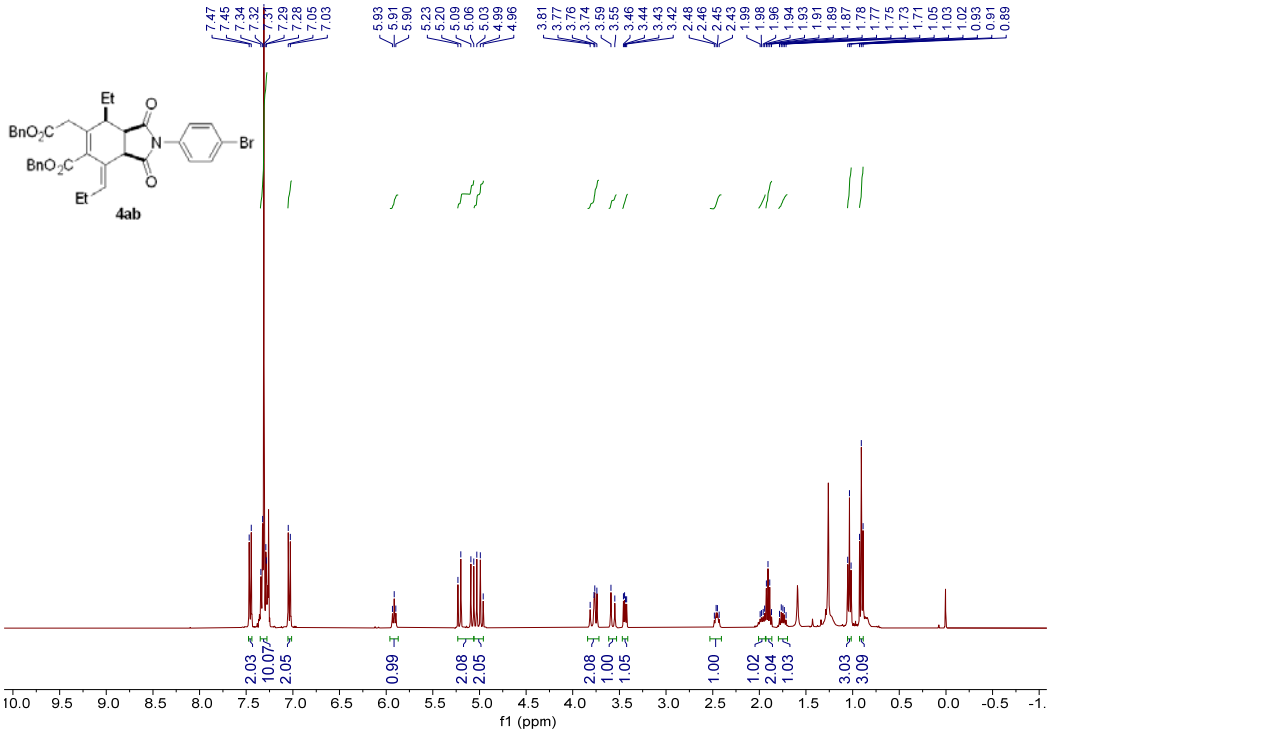
Ph
BnO2C
BnO2C
N–Ph
O
O
O
Ph
4ka
13.10 4.00 8.08 0.88 1.00 2.07 1.04 0.85 1.01 0.90 1.01 2.03 2.06 2.02 0.89 0.89 4.02
f1 (ppm)


175.97 175.27 169.62 166.44 146.14 141.91 141.62 135.63 135.32 133.35 131.75 130.67 128.98 128.50 128.46 128.34 128.27 128.20 126.51 125.97 125.88 125.75 66.76 66.61 47.78 43.82 41.98 37.02 35.87 35.46 30.54 29.63 29.38 27.84
Ph
BnO2C
BnO2C
N–Ph
O
O
O
Ph
4ka
f1 (ppm)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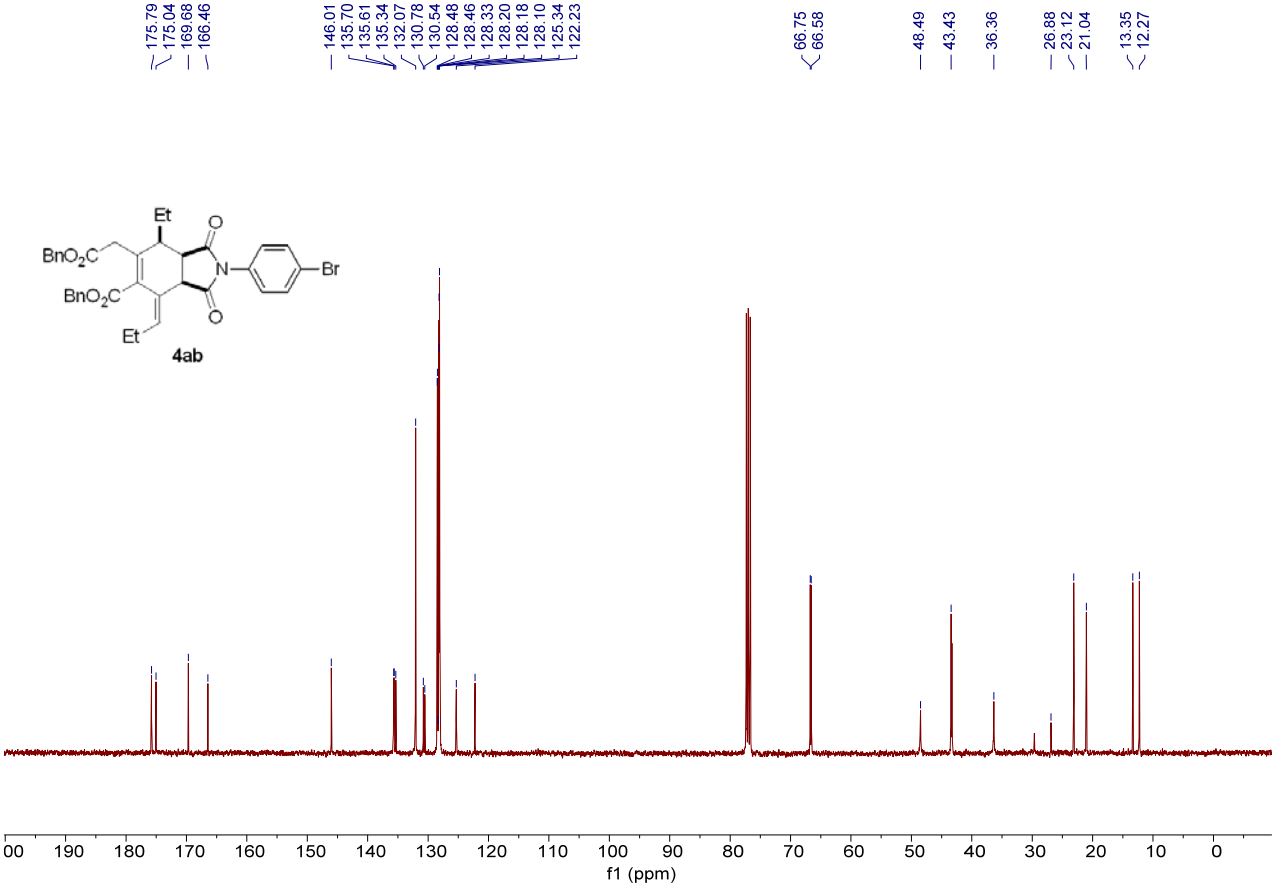
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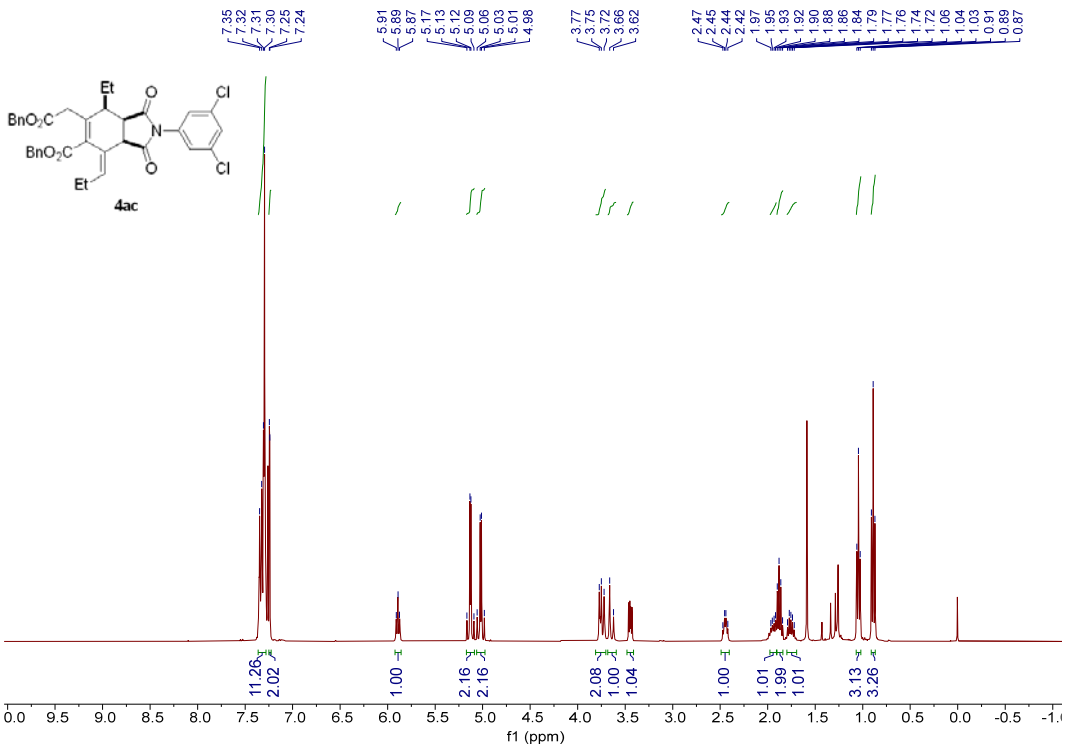
f1 (ppm)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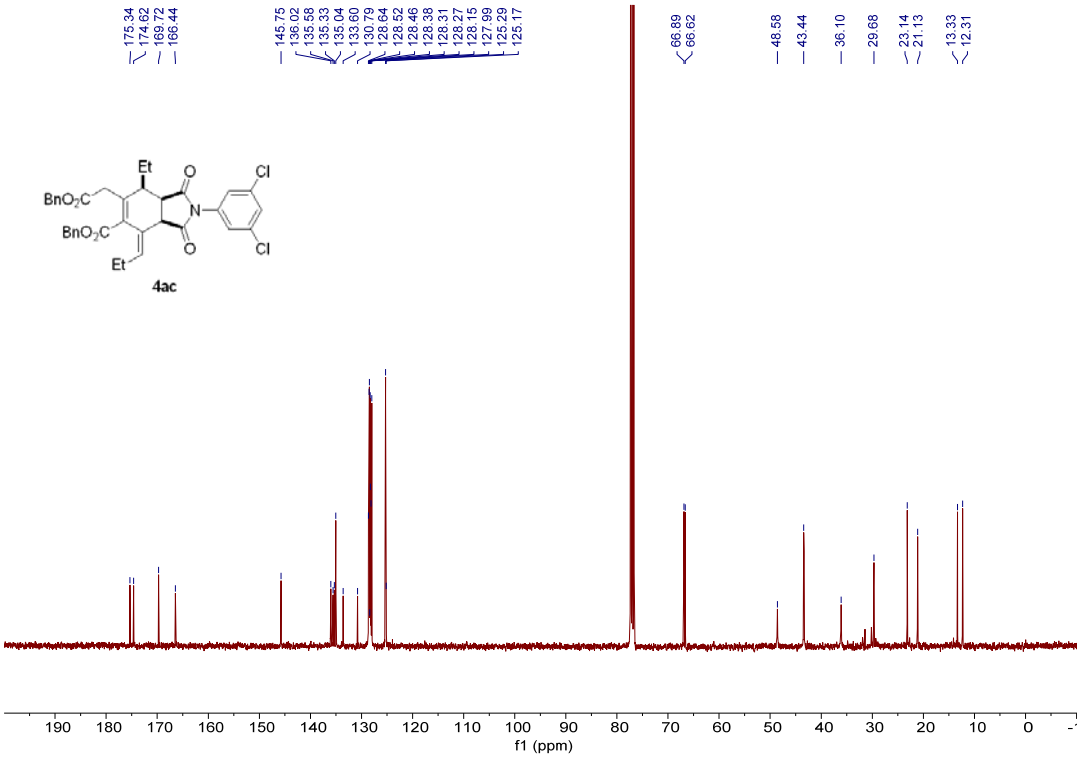
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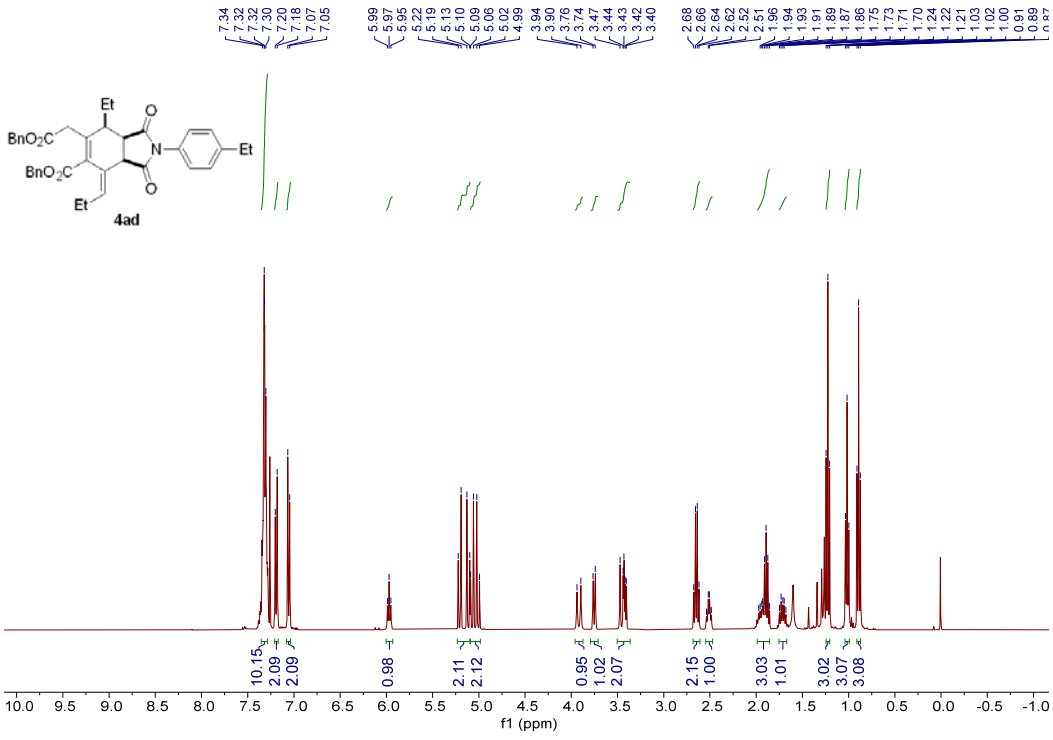
f1 (ppm)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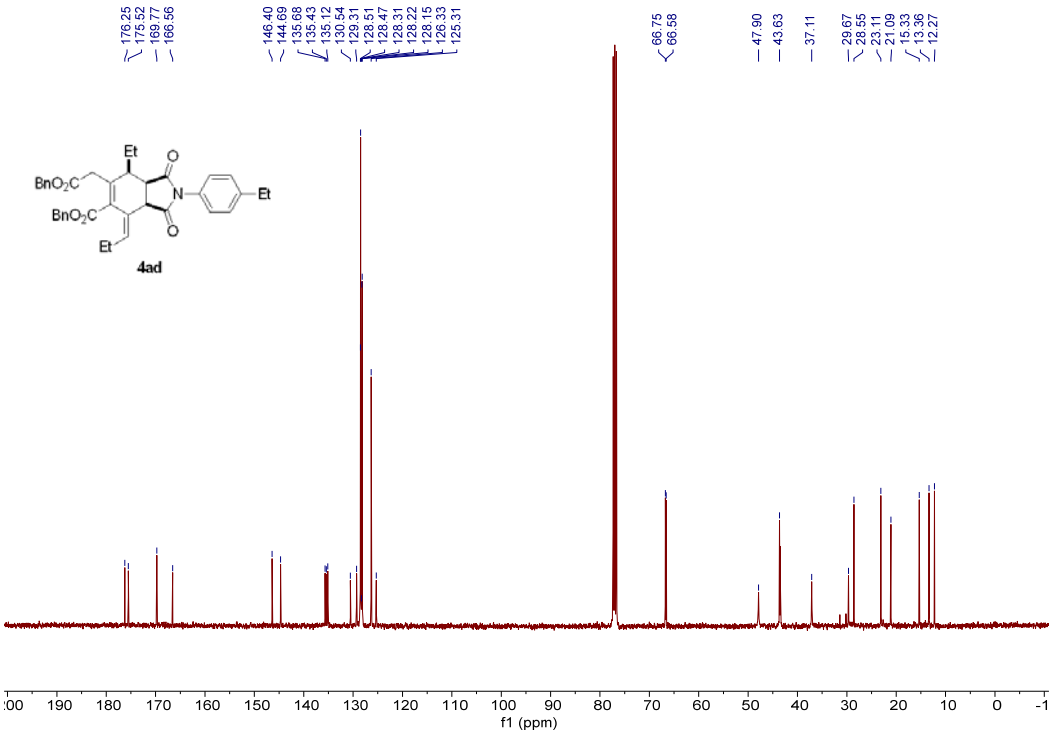
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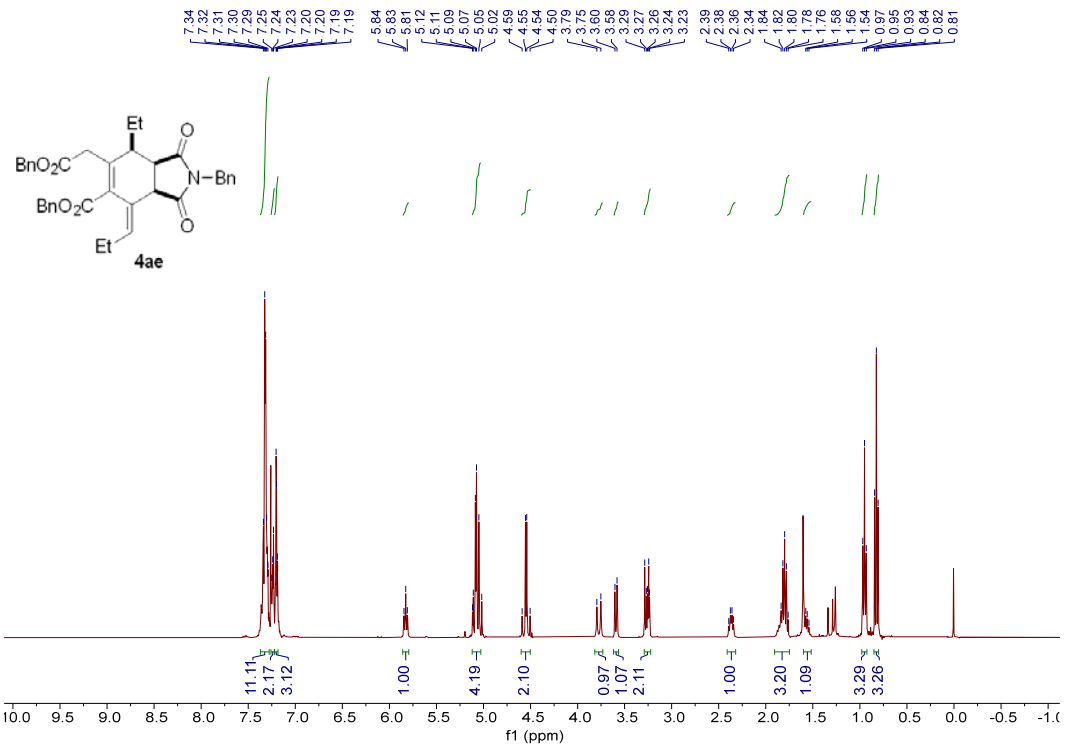
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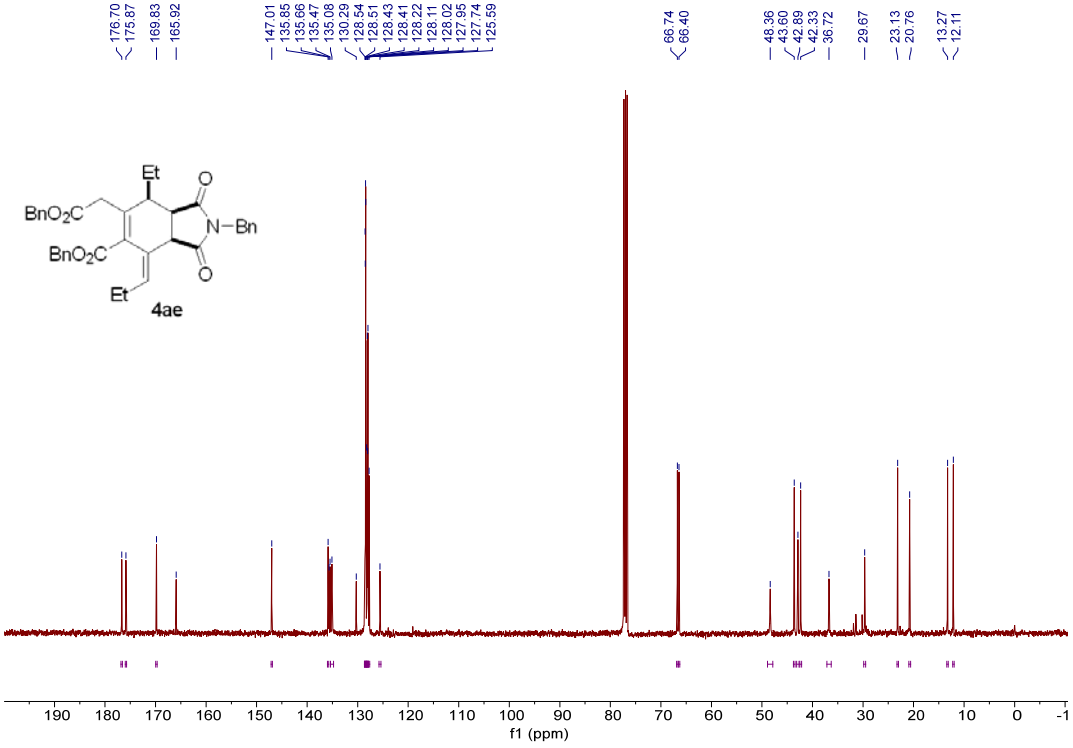
f1 (ppm)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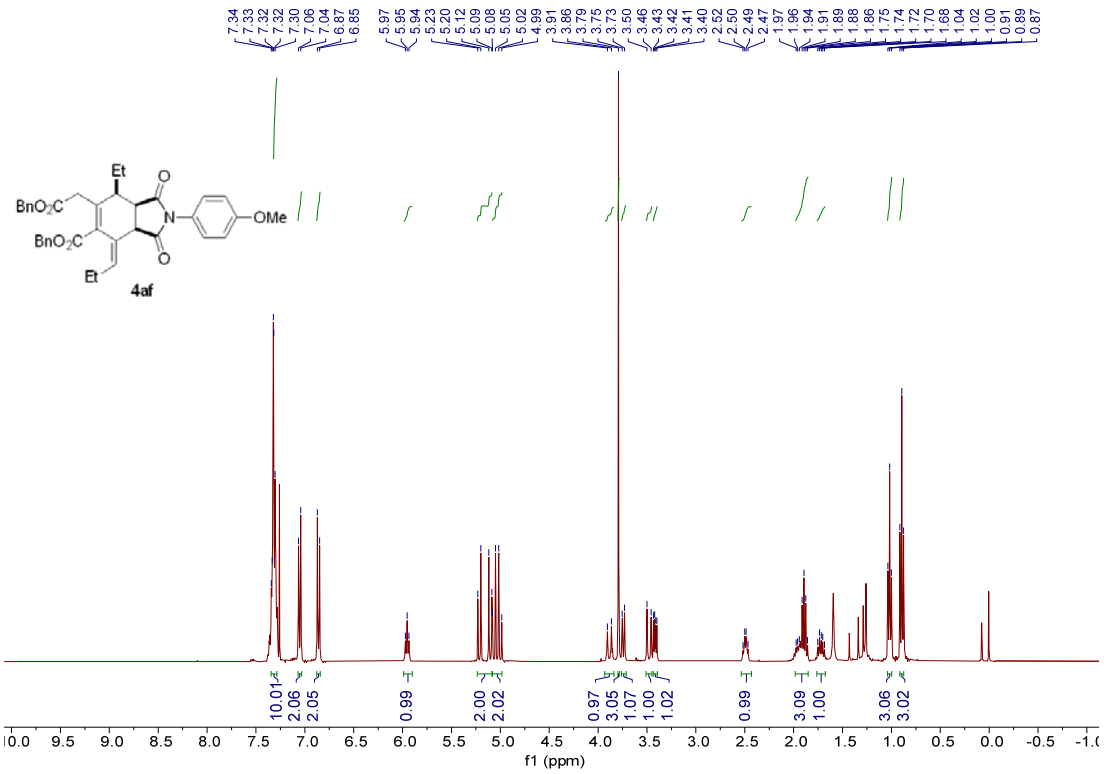
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Et
BnO2C
BnO2C
Et
O
N
OMe
O
4af
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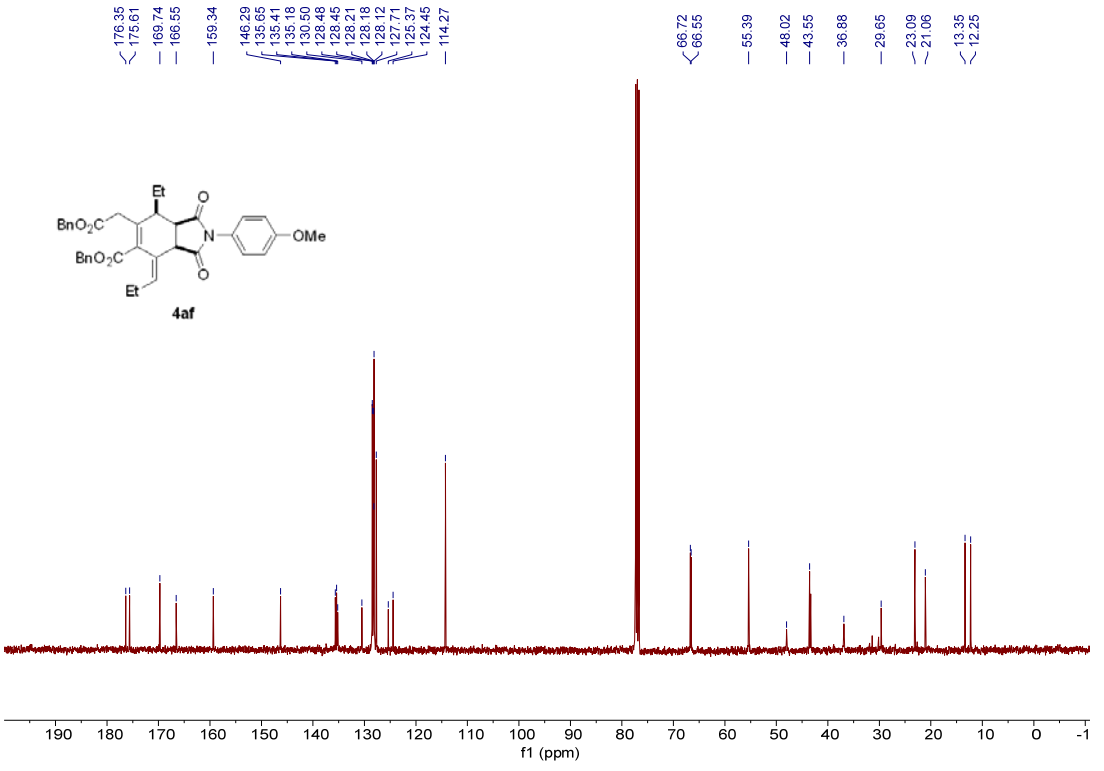
f1 (ppm)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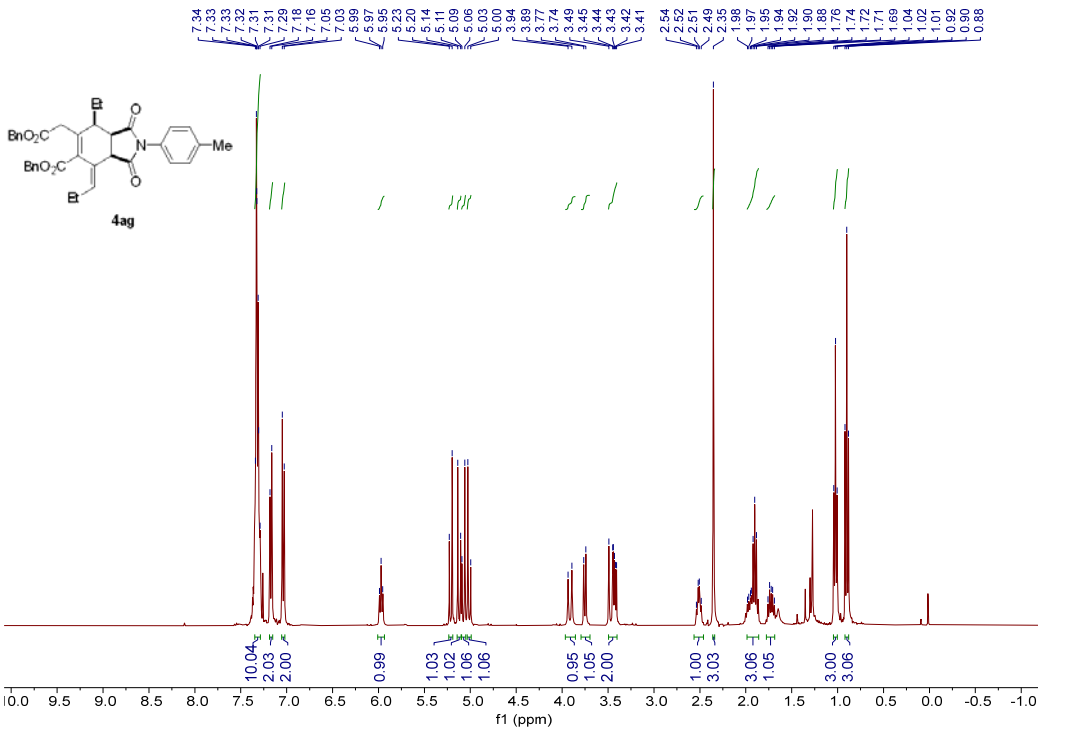
Et
BnO2C
BnO2C
Et
O
N
OMe
O
4af
f1 (ppm)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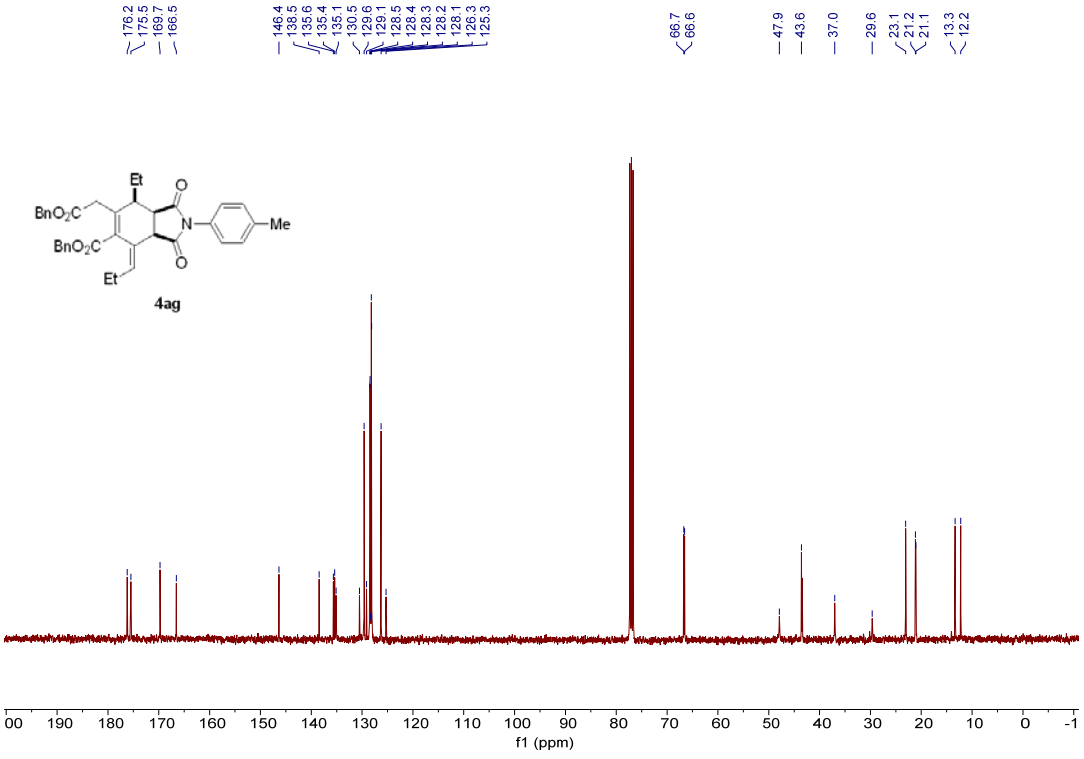
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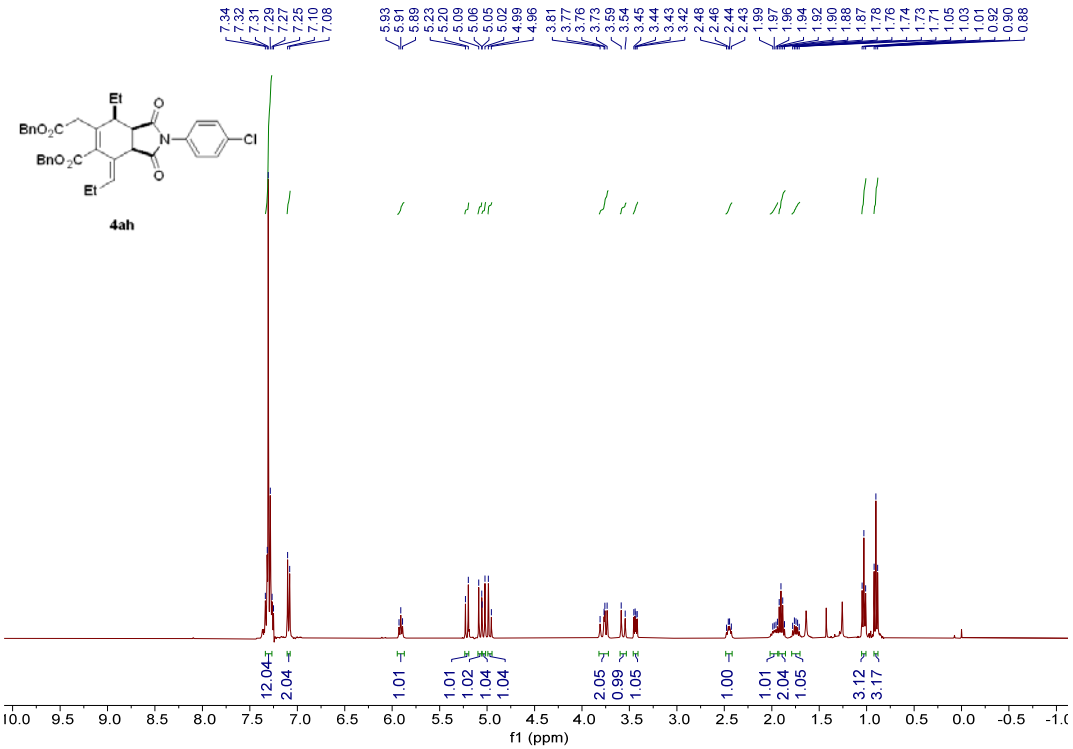
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5.09
5.06
5.05
5.02
4.99
4.96
3.81
3.77
3.76
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3.45
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3.43
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2.48
2.46
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2.43
1.99
1.97
1.96
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1.90
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1.87
1.78
1.76
1.74
1.73
1.71
1.05
1.03
1.01
0.92
0.90
0.88
Et
BnO2C
BnO2C
Et
O
N
O
Cl
4ah
12.04
2.04
1.01
1.01
1.02
1.04
1.04
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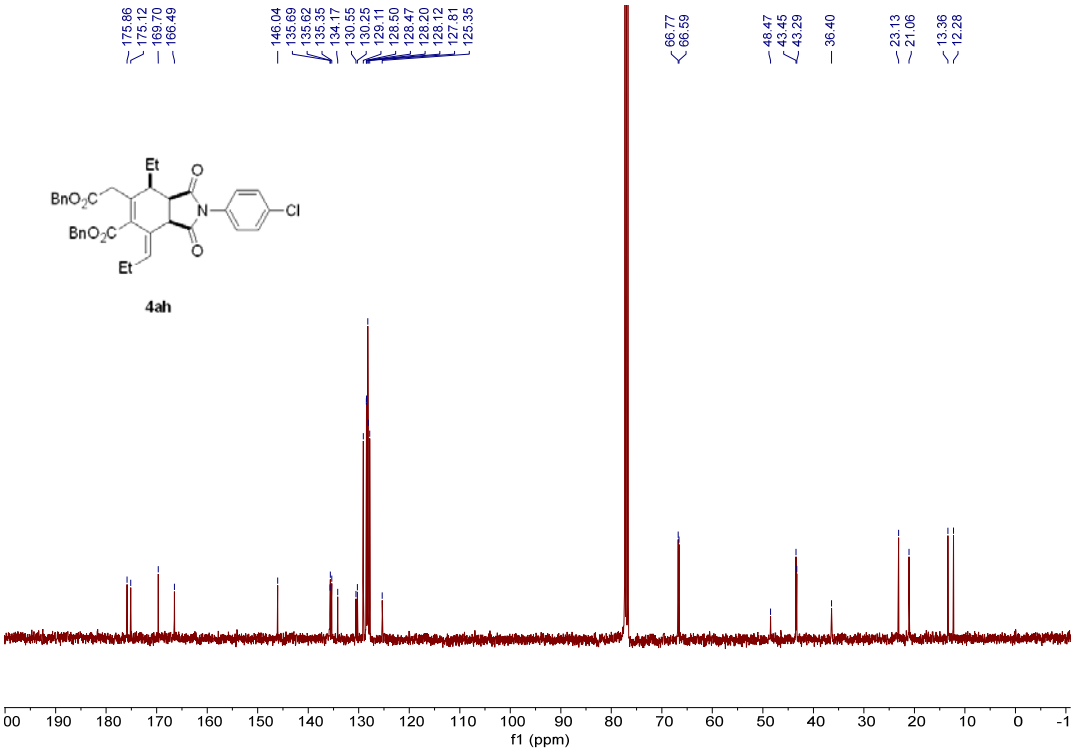
0.99
1.05
1.00
1.01
2.04
1.05
3.12
3.17
f1 (ppm)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128.12
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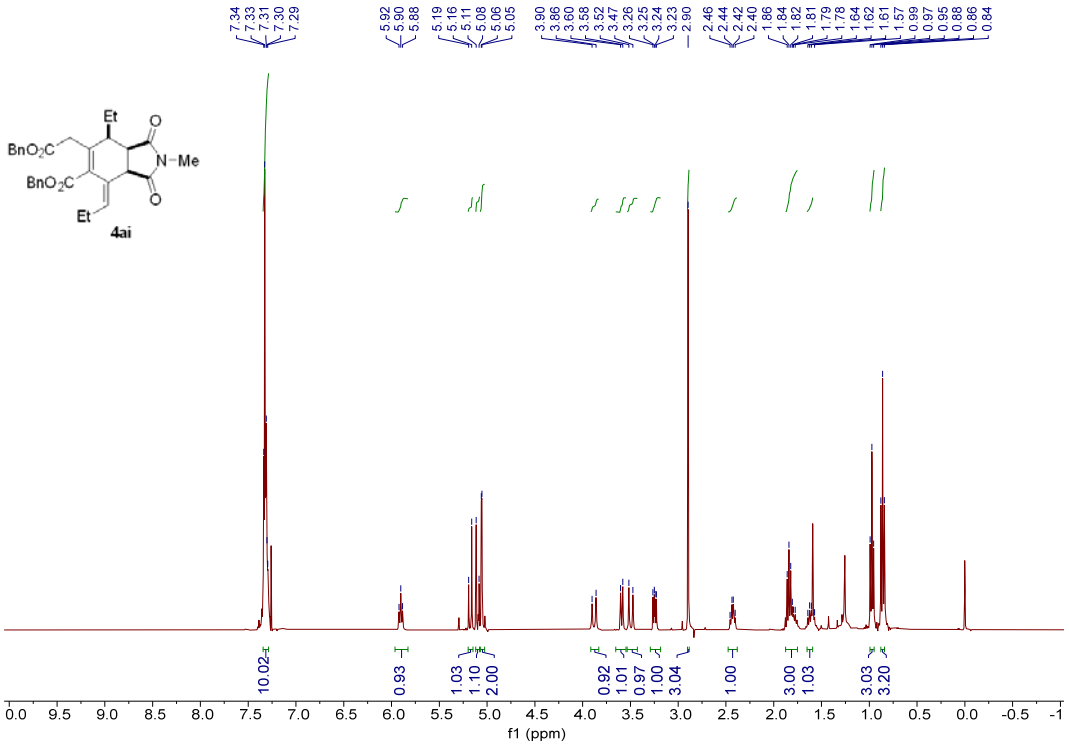
48.47
43.45
43.29
36.40
23.13
21.06
13.36
12.28
Et
BnO2C
BnO2C
Et
O
N
O
Cl
4ah
f1 (ppm)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7.33
7.31
7.30
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5.06
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3.26
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2.90
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2.44
2.42
2.40
1.86
1.84
1.82
1.81
1.79
1.78
1.64
1.62
1.61
1.57
0.99
0.97
0.95
0.88
0.86
0.84
Et
O
N−Me
BnO2C
BnO2C
Et
O
4ai
10.02
0.93
1.03
1.10
2.00
0.92
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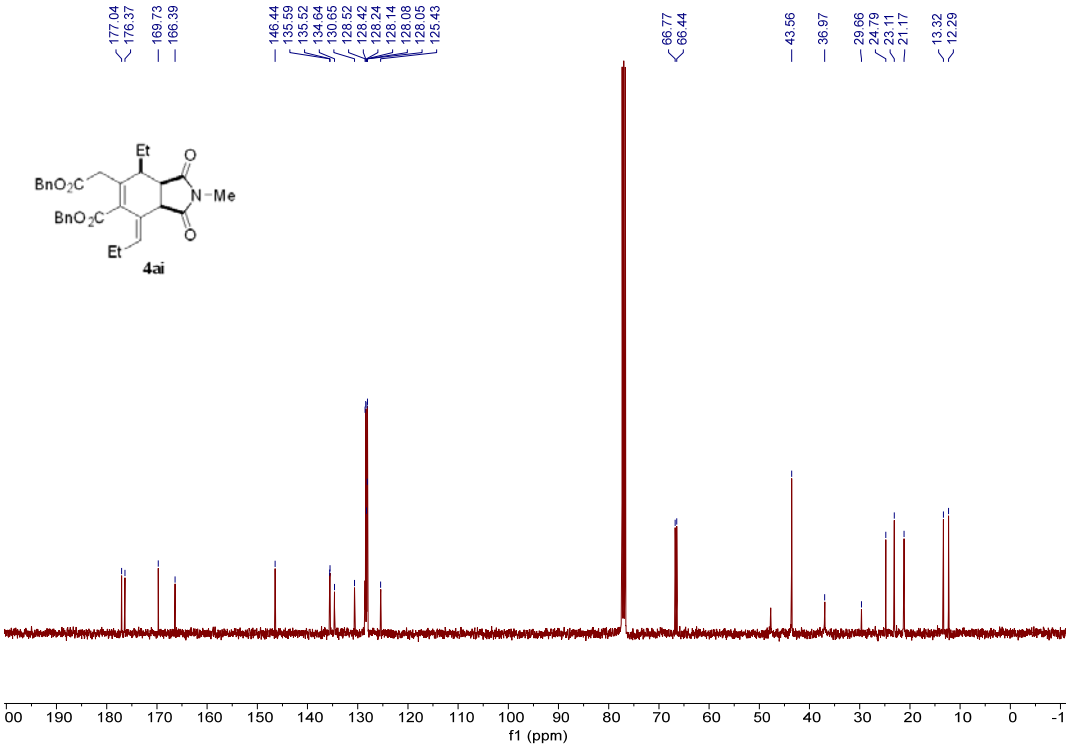
0.97
1.00
3.04
1.00
3.00
1.03
3.03
3.20
f1 (ppm)


177.04
176.37
169.73
166.39
146.44
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128.52
128.42
128.24
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128.08
128.05
125.43
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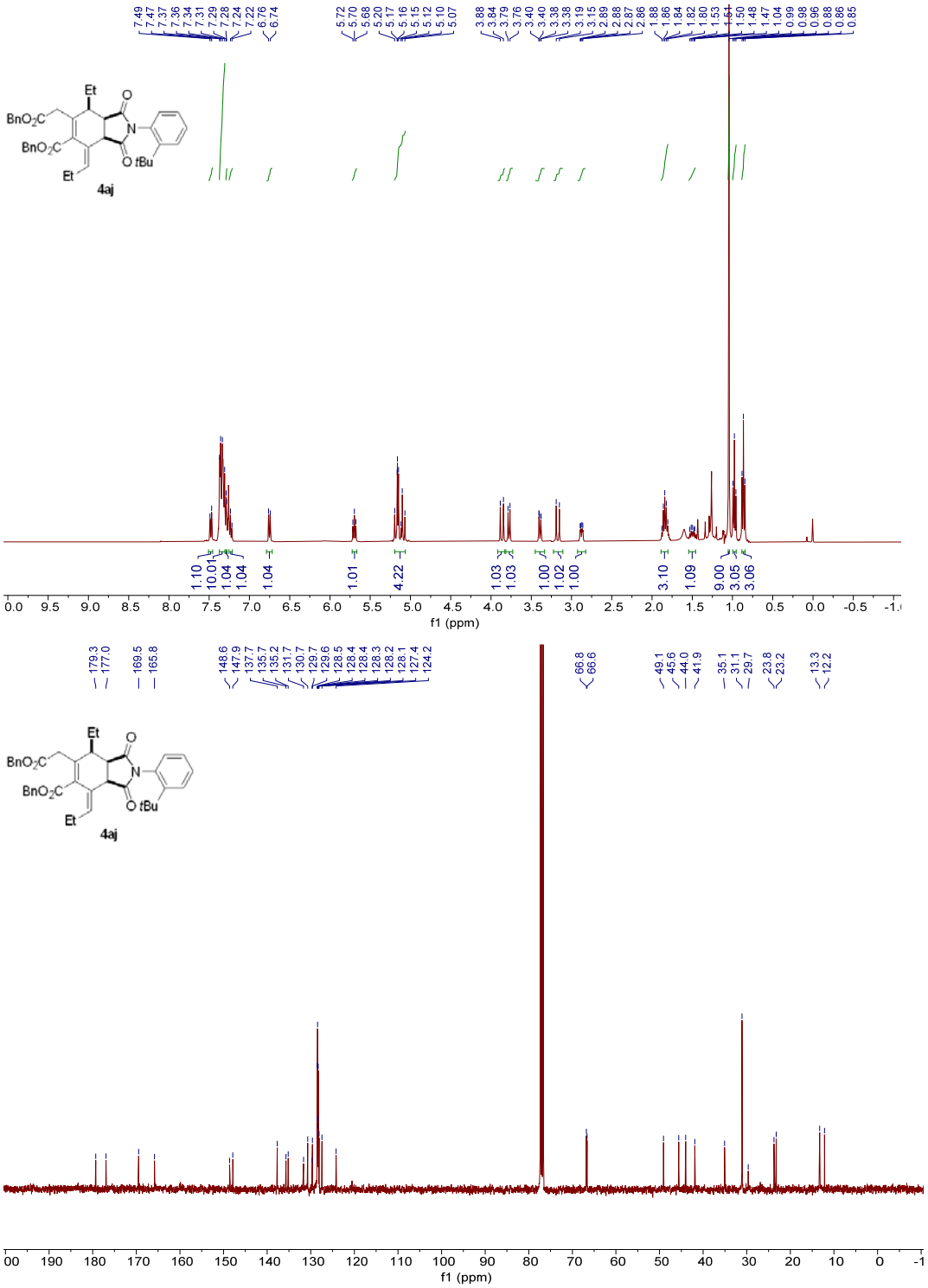
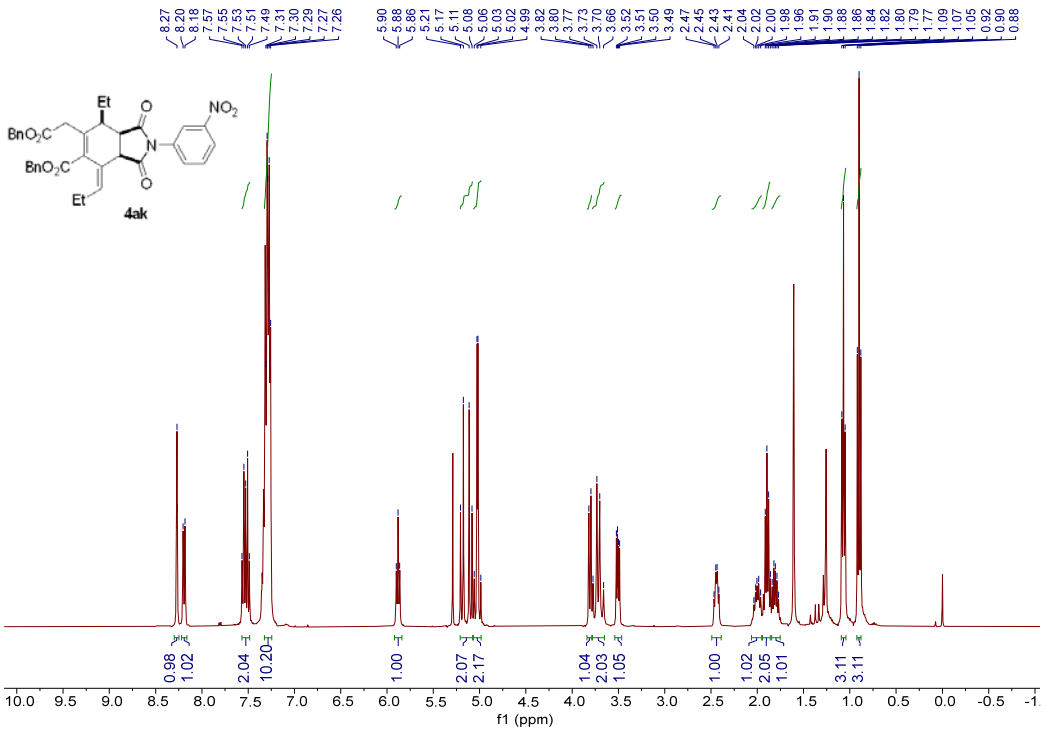
66.44
43.56
36.97
29.66
24.79
23.11
21.17
13.32
12.29
Et
O
N−Me
BnO2C
BnO2C
Et
O
4ai
f1 (ppm)


4aj
f1 (ppm)
4aj
f1 (ppm)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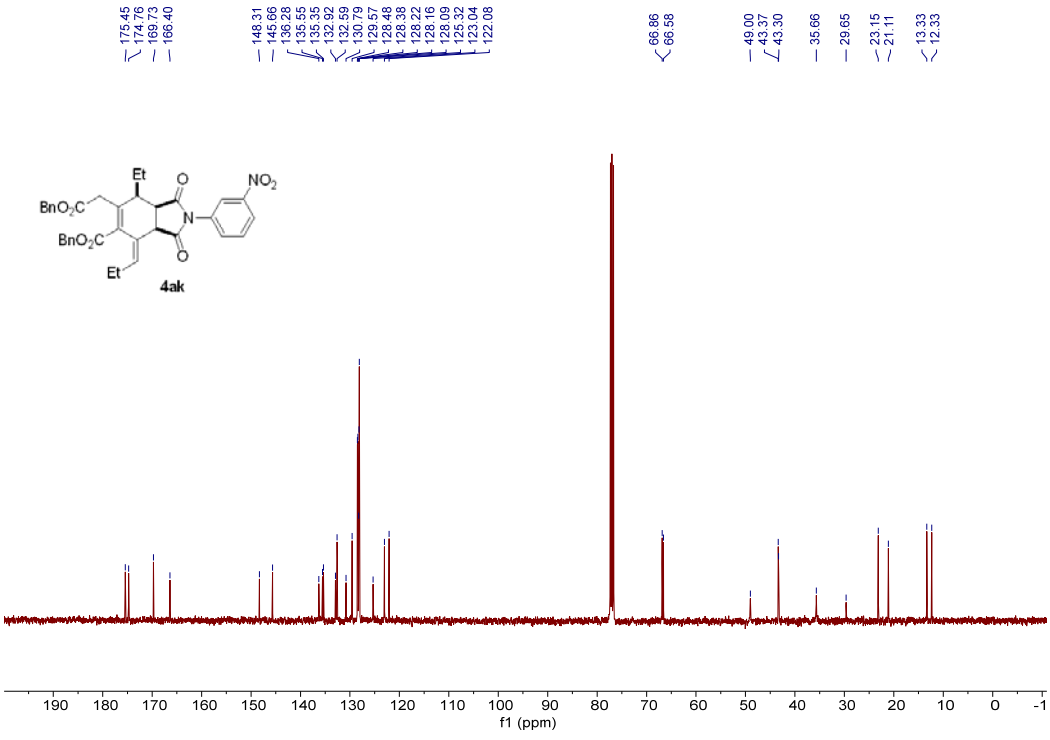
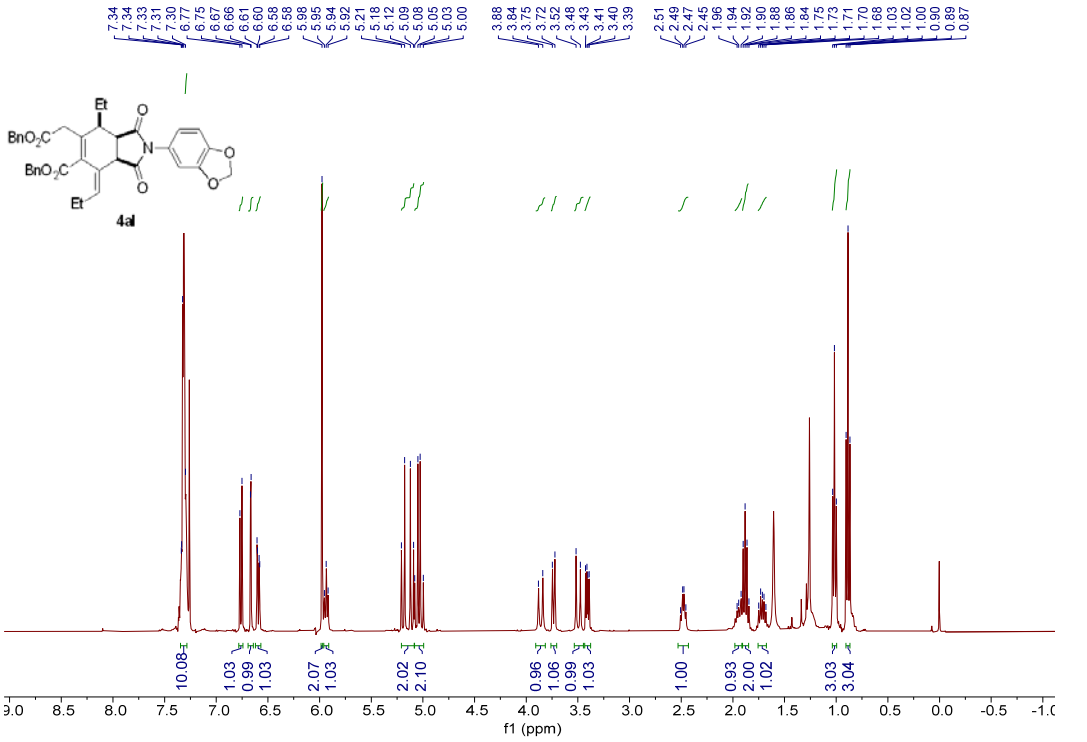
5.90 5.88 5.86 5.21 5.17 5.11 5.08 5.06 5.03 5.02 4.99
3.82 3.80 3.77 3.73 3.70 3.66 3.52 3.51 3.50 3.49
2.47 2.45 2.43 2.41 2.04 2.02 2.00 1.98 1.96 1.91 1.90 1.88 1.86 1.84 1.82 1.80 1.79 1.77 1.09 1.07 1.05 0.92 0.90 0.88
Et
O
NO2
BnO2C
BnO2C
N
O
Et
4ak
0.98 1.02 2.04 10.20 1.00 2.07 2.17 1.04 2.03 1.05 1.00 1.02 2.05 1.01 3.11 3.11
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 -0.5
f1 (ppm)


175.45 174.76 169.73 166.40
148.31 145.66 136.28 135.55 135.35 132.92 132.59 130.79 129.57 128.48 128.38 128.22 128.16 128.09 125.32 123.04 122.08
66.86 66.58
49.00 43.37 43.30
35.66
29.65
23.15 21.11
13.33 12.33
Et
O
NO2
BnO2C
BnO2C
N
O
Et
4ak
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)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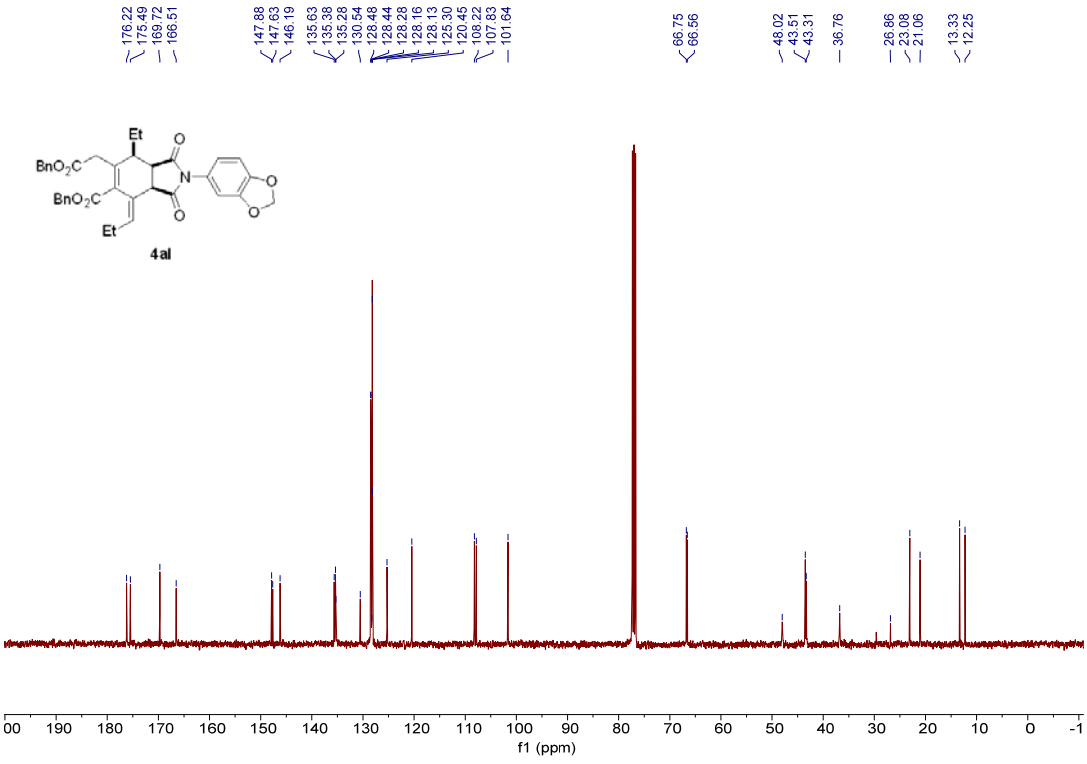
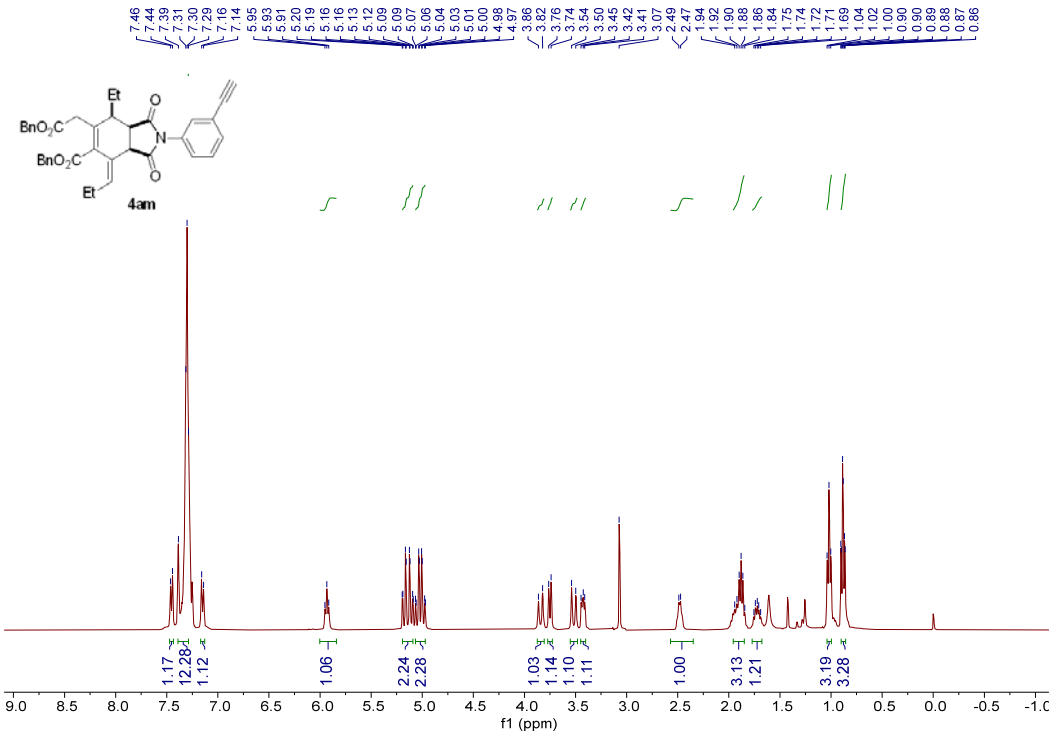
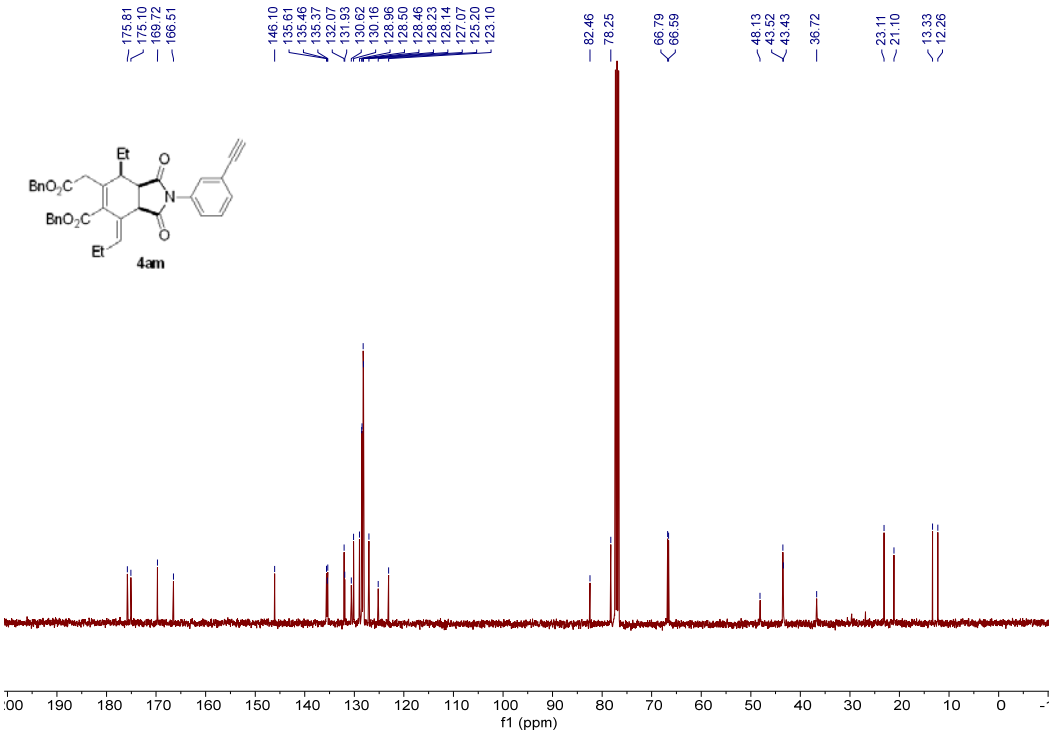
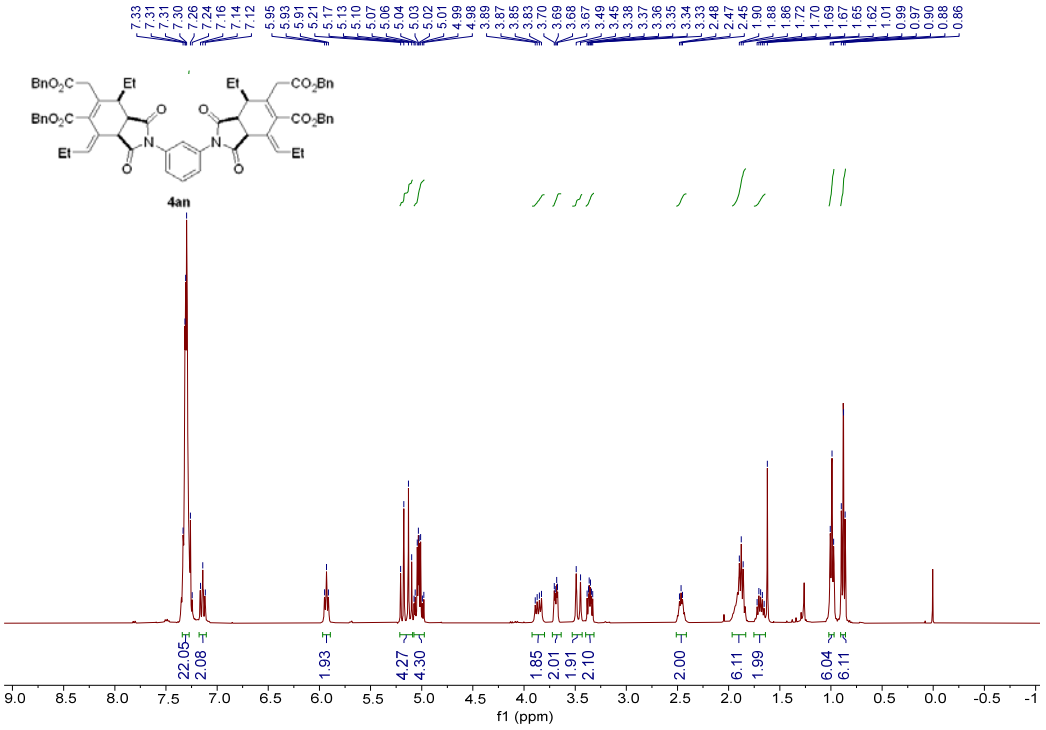
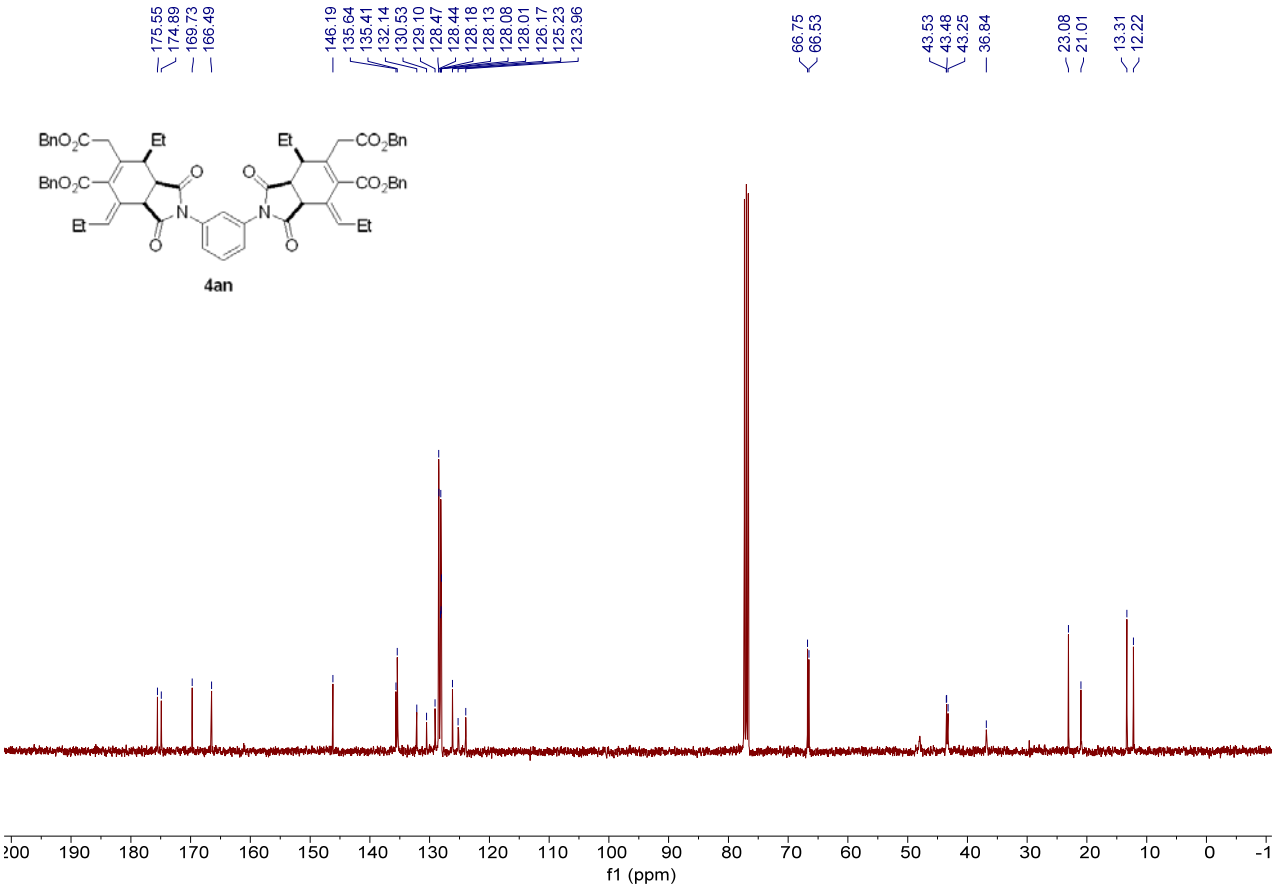
Et
BnO2C
BnO2C
Et
4al
10.08 1.03 0.99 1.03 2.07 1.03 2.02 2.10 0.96 1.06 0.99 1.03 1.00 0.93 2.00 1.02 3.03 3.04
f1 (ppm)


176.22 175.49 169.72 166.51 147.88 147.63 146.19 135.63 135.38 135.28 130.54 128.48 128.44 128.28 128.16 128.13 125.30 120.45 108.22 107.83 101.64 66.75 66.56 48.02 43.51 43.31 36.76 26.86 23.08 21.06 13.33 12.25
Et
BnO2C
BnO2C
Et
4al
f1 (ppm)


4am
f1 (ppm)


4am
f1 (ppm)


7.33 7.31 7.31 7.30 7.26 7.24 7.16 7.14 7.12 5.95 5.93 5.91 5.21 5.17 5.13 5.10 5.07 5.06 5.04 5.03 5.02 5.01 4.99 4.98 3.89 3.87 3.85 3.83 3.70 3.69 3.68 3.67 3.49 3.45 3.38 3.37 3.36 3.35 3.34 3.33 2.48 2.47 2.45 1.90 1.88 1.86 1.72 1.70 1.69 1.67 1.65 1.62 1.01 0.99 0.97 0.90 0.88 0.86
4an
22.05 2.08 1.93 4.27 4.30 1.85 2.01 1.91 2.10 2.00 6.11 1.99 6.04 6.11
f1 (ppm)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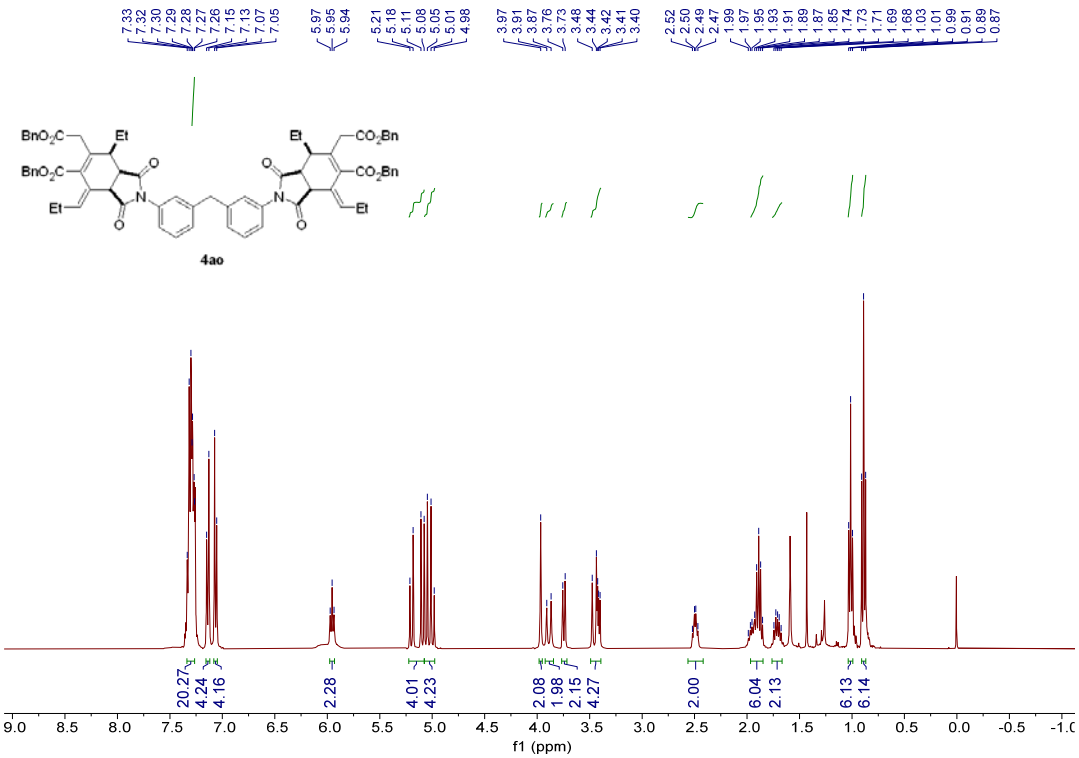
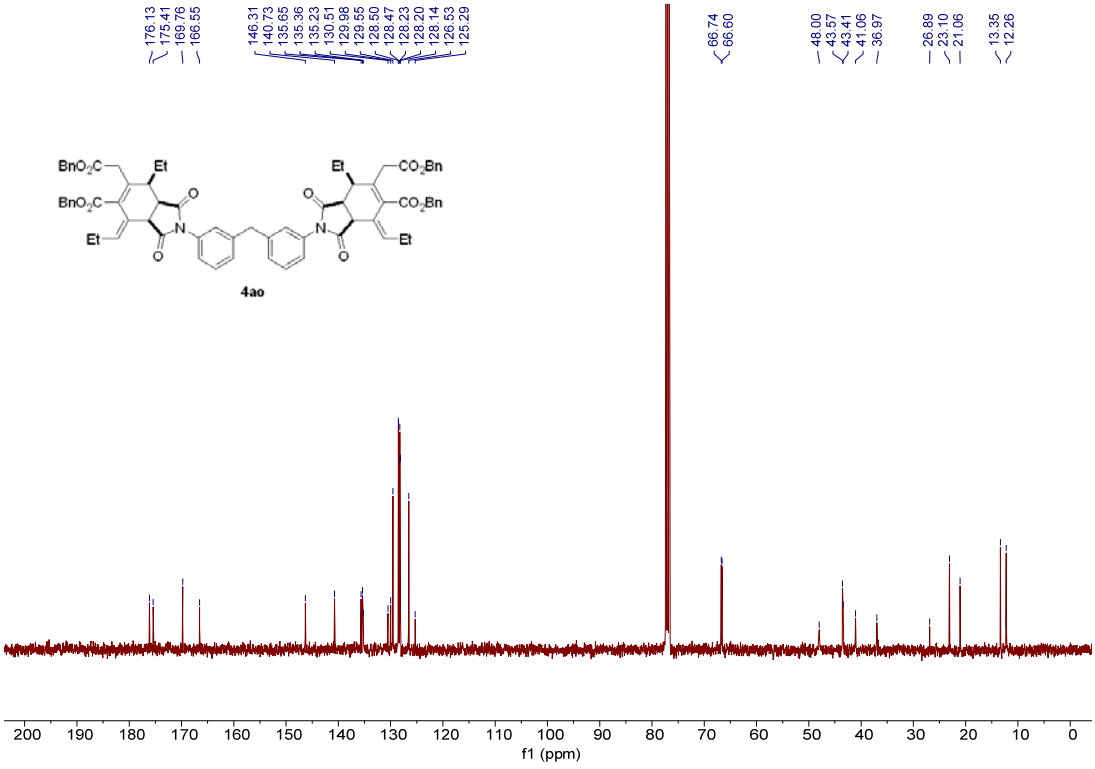
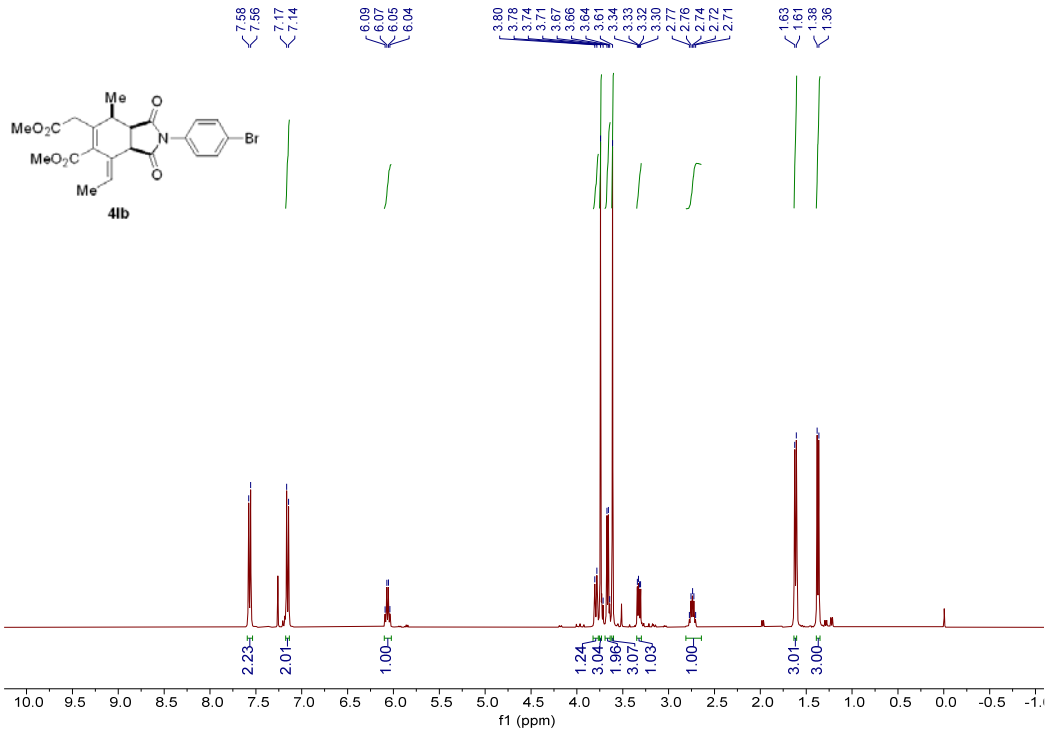
4an
f1 (ppm)


7.33 7.32 7.30 7.29 7.28 7.27 7.26 7.15 7.13 7.07 7.05
5.97 5.95 5.94
5.21 5.18 5.11 5.08 5.05 5.01 4.98
3.97 3.91 3.87 3.76 3.73 3.46 3.44 3.42 3.41 3.40
2.52 2.50 2.49 2.47 1.99 1.97 1.95 1.93 1.91 1.89 1.87 1.85 1.74 1.73 1.71 1.69 1.68 1.03 1.01 0.99 0.91 0.89 0.87
BnO2C
Et
CO2Bn
4ao
20.27 4.24 4.16 2.28 4.01 4.23 2.08 1.98 2.15 4.27 2.00 6.04 2.13 6.13 6.14
f1 (ppm)


176.13 175.41 169.76 166.55
146.31 140.73 135.65 135.36 135.23 130.51 129.98 129.55 128.50 128.47 128.23 128.20 128.14 126.53 125.29
66.74 66.60
48.00 43.57 43.41 41.06 36.97
26.89 23.10 21.06
13.35 12.26
BnO2C
Et
CO2Bn
4ao
f1 (ppm)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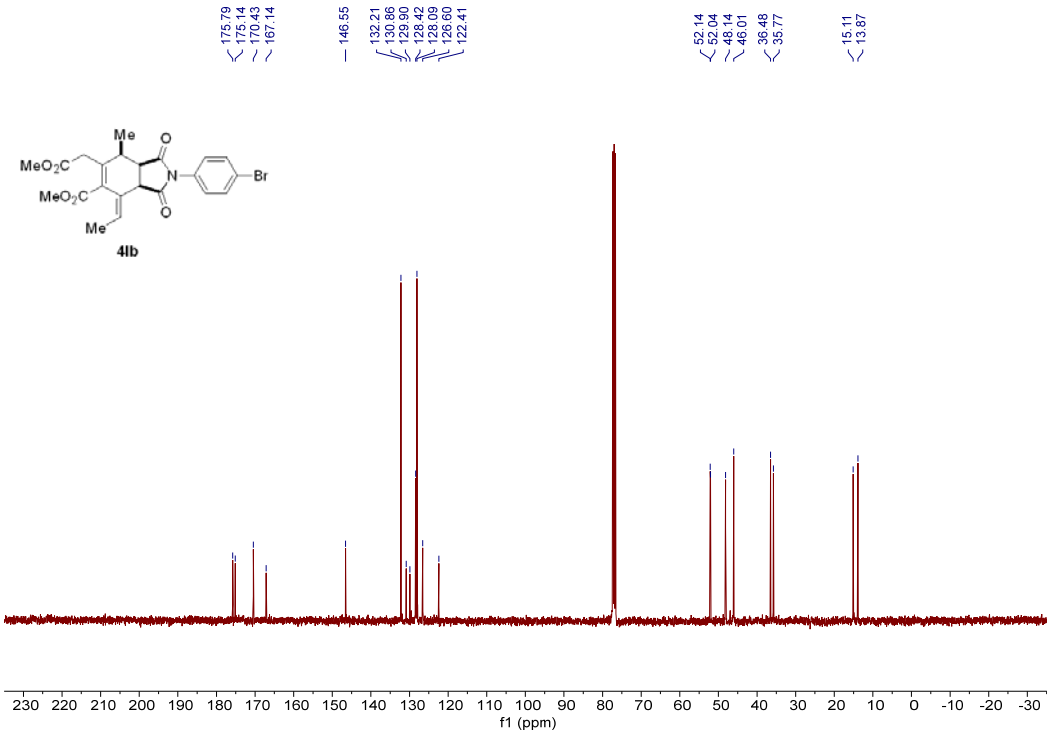
7.56
7.17
7.14
6.09
6.07
6.05
6.04
3.80
3.78
3.74
3.71
3.67
3.66
3.64
3.61
3.34
3.33
3.32
3.30
2.77
2.76
2.74
2.72
2.71
1.63
1.61
1.38
1.36
Me
MeO2C
MeO2C
Me
O
N
O
Br
4lb
2.23
2.01
1.00
1.24
3.04
1.96
3.07
1.03
1.00
3.01
3.00
f1 (ppm)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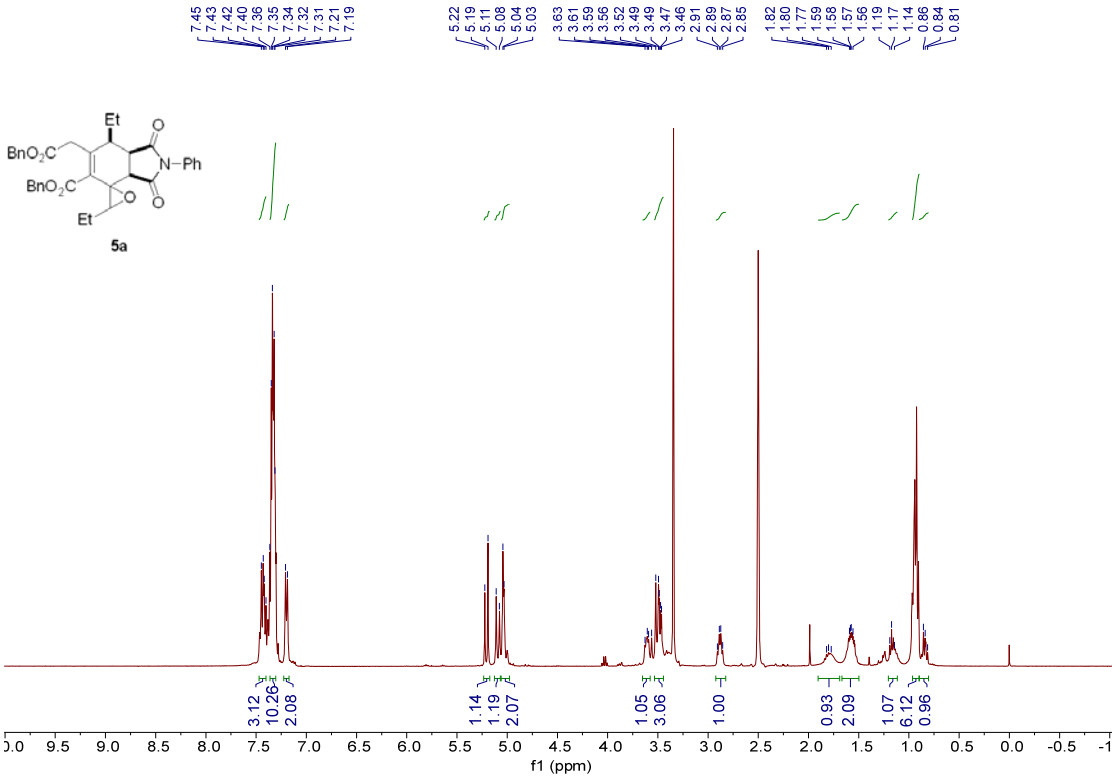
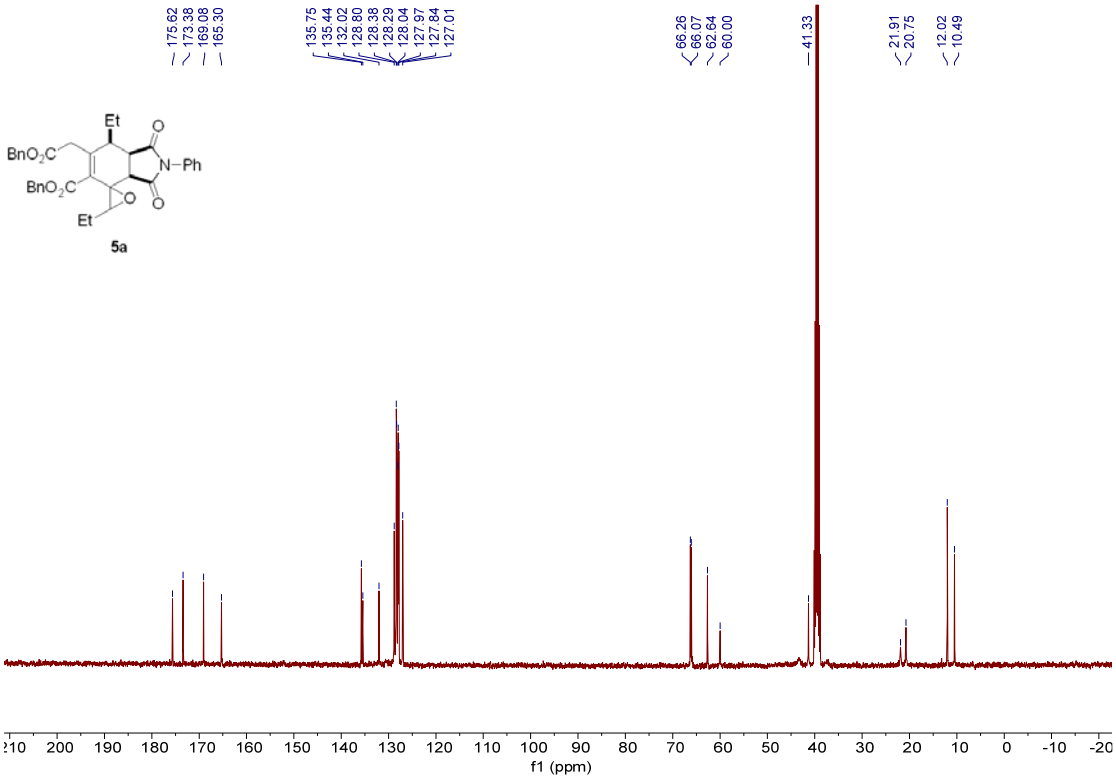
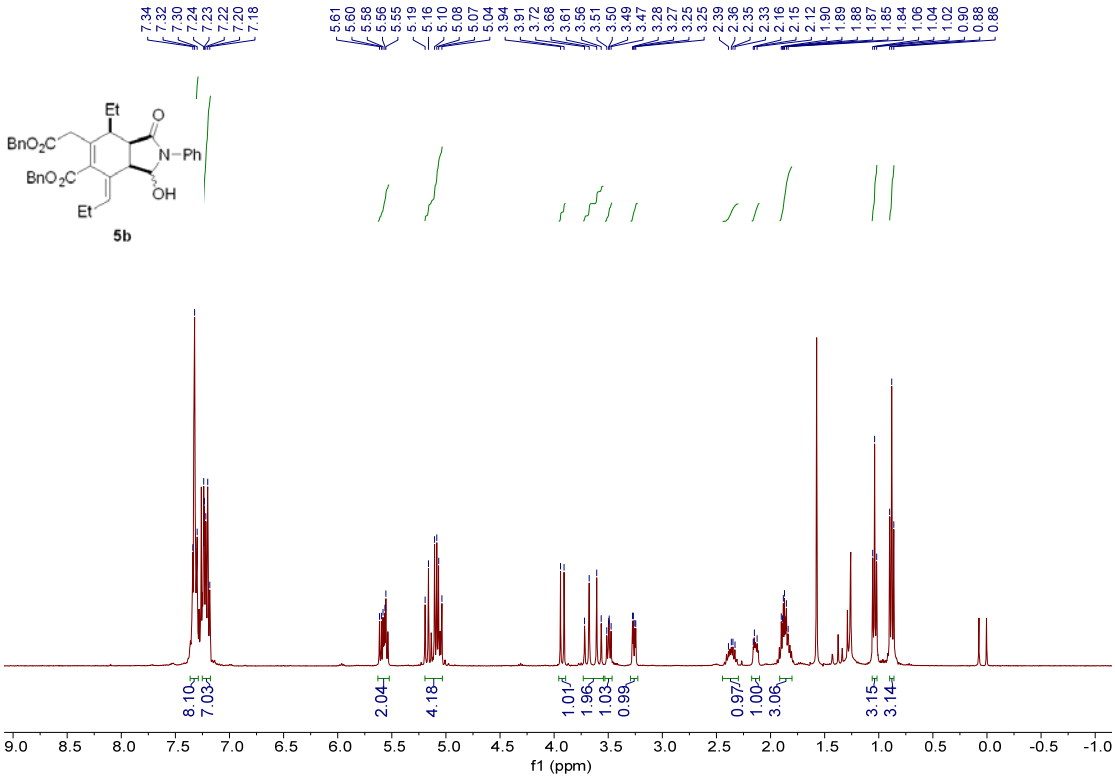
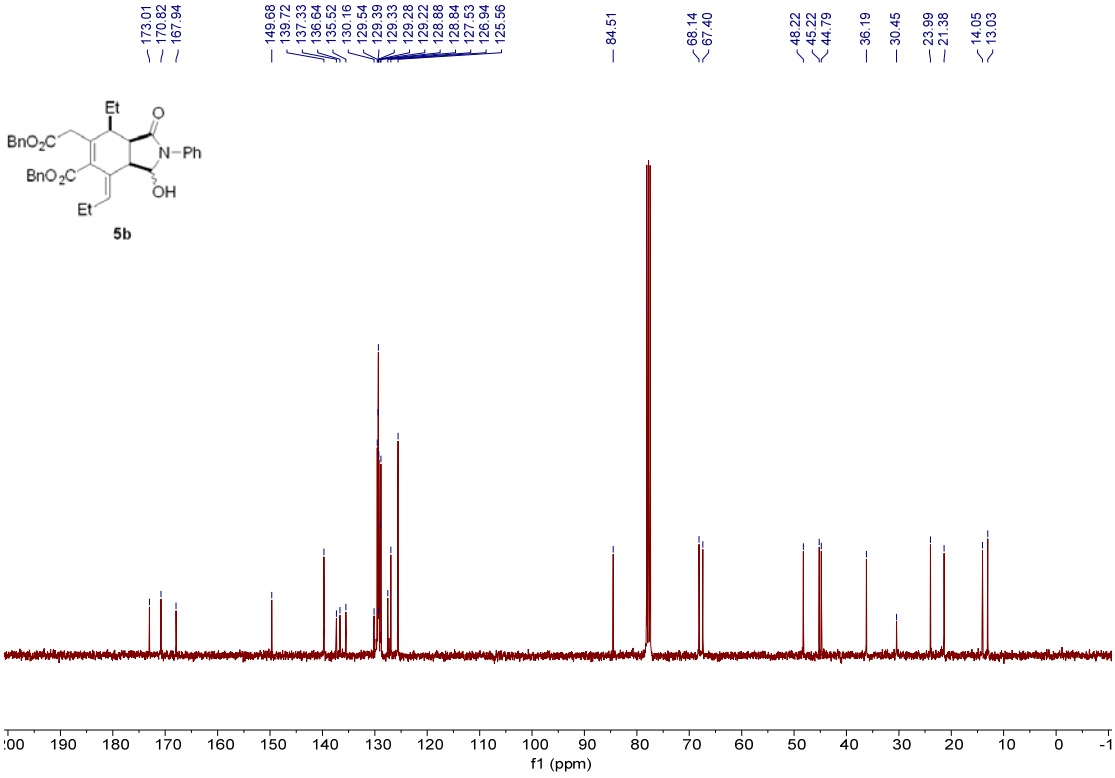
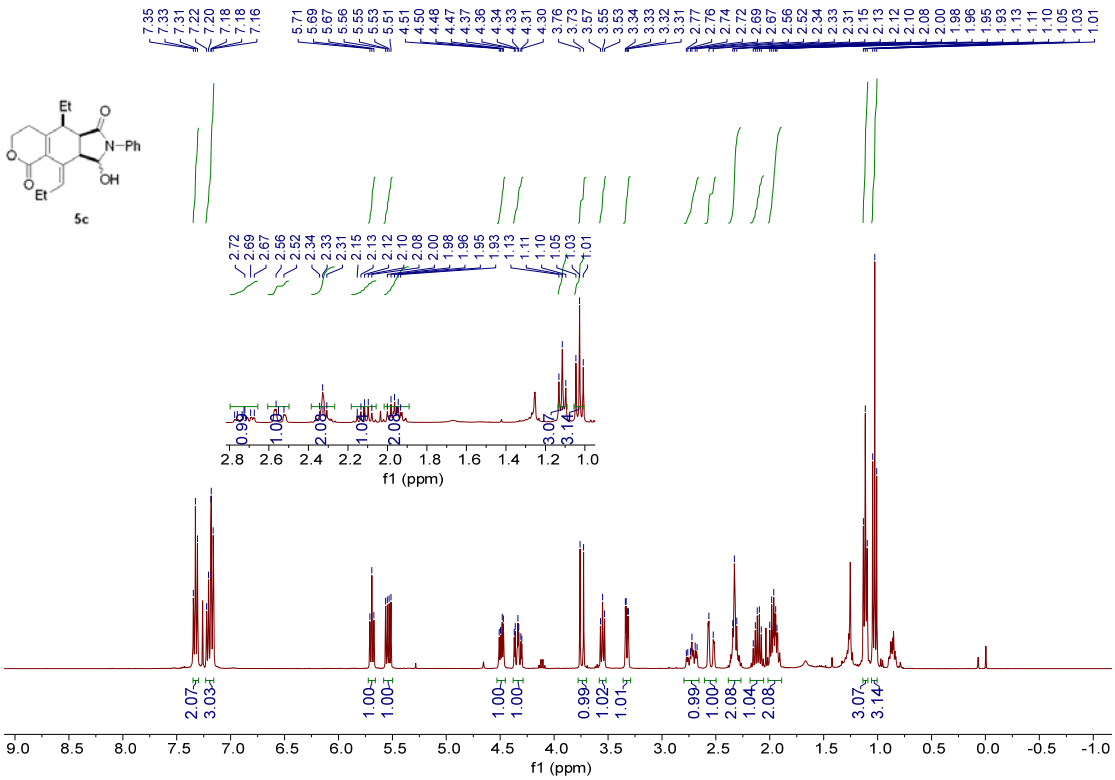
175.14
170.43
167.14
146.55
132.21
130.86
129.90
128.42
128.09
126.60
122.41
52.14
52.04
48.14
46.01
36.48
35.77
15.11
13.87
Me
MeO2C
MeO2C
Me
O
N
O
Br
4lb
f1 (ppm)

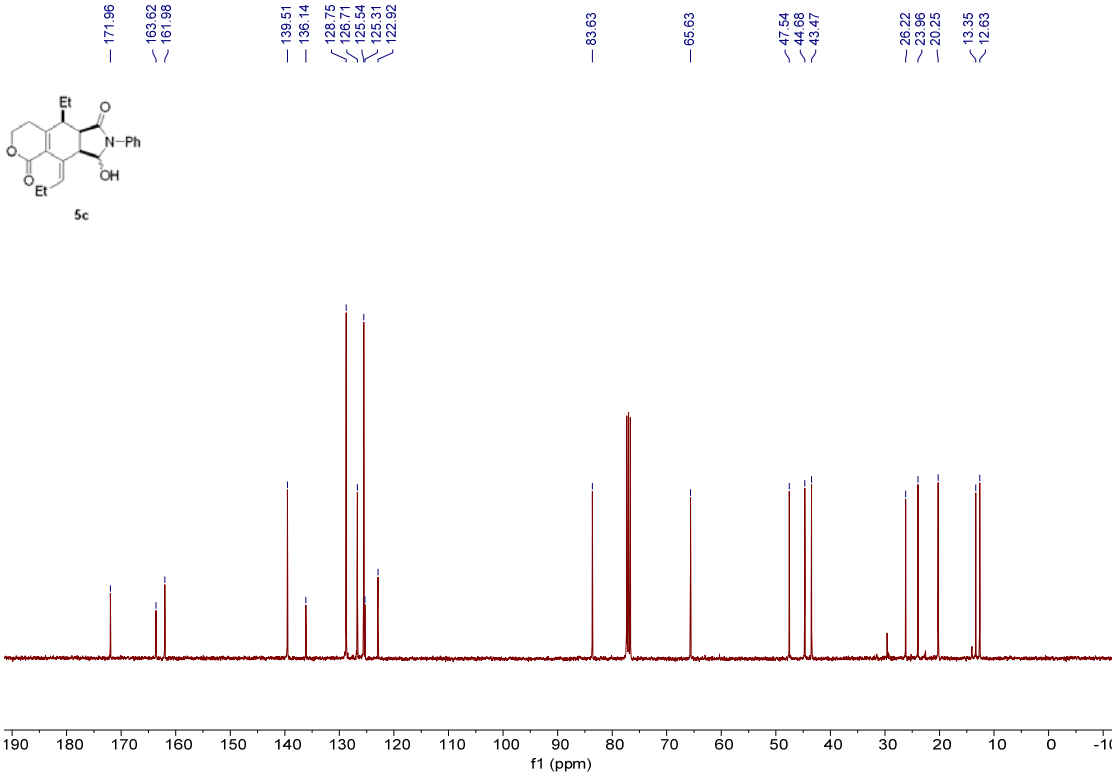

7.45
7.43
7.42
7.40
7.36
7.35
7.34
7.32
7.31
7.21
7.19
5.22
5.19
5.11
5.08
5.04
5.03
3.63
3.61
3.59
3.56
3.52
3.49
3.49
3.47
3.46
2.91
2.89
2.87
2.85
1.82
1.80
1.77
1.59
1.58
1.57
1.56
1.19
1.17
1.14
0.86
0.84
0.81
Et
O
BnO2C
N–Ph
BnO2C
O
Et
O
5a
3.12
10.26
2.08
1.14
1.19
2.07
1.05
3.06
1.00
0.93
2.09
1.07
6.12
0.96
f1 (ppm)

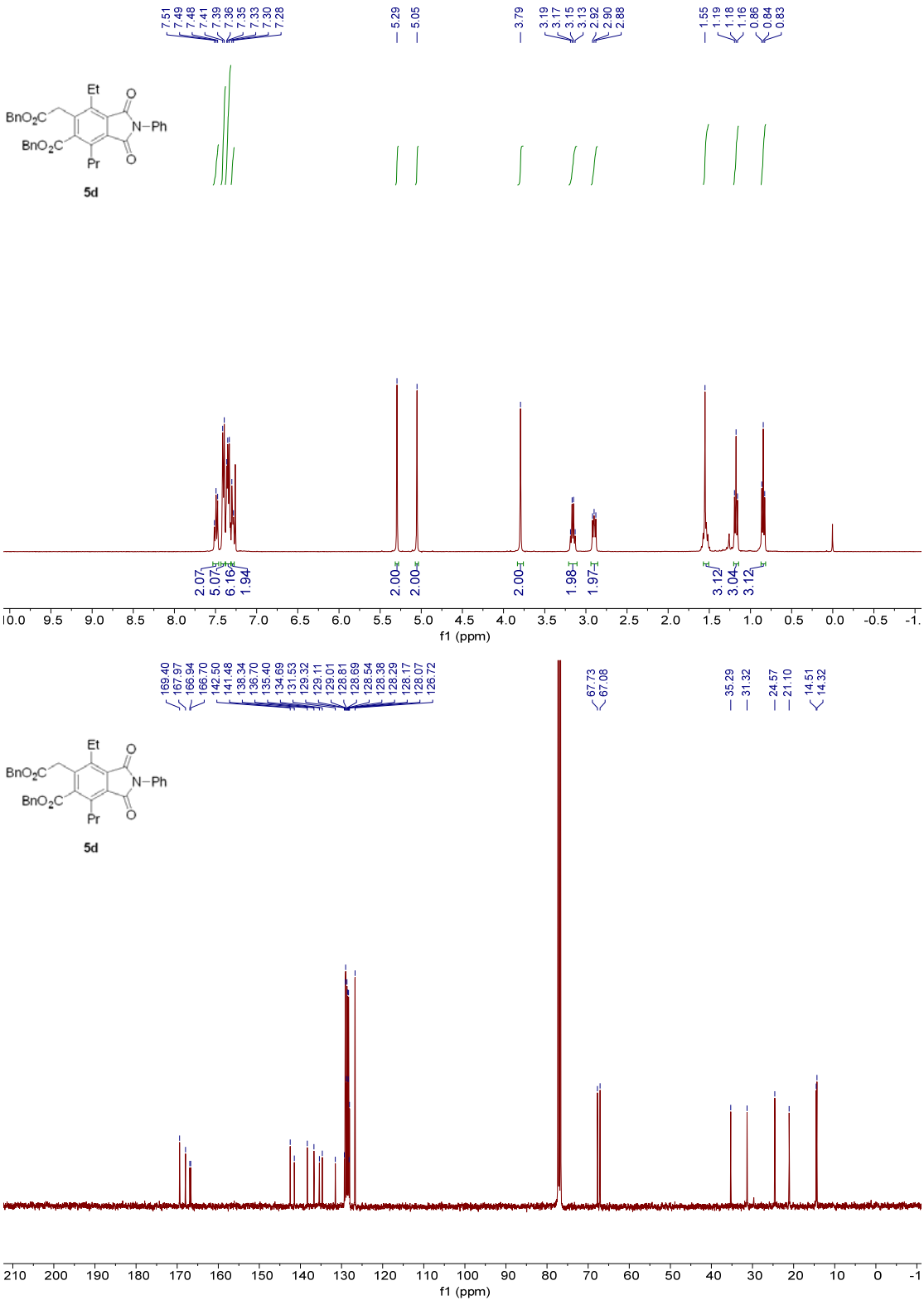

175.62
173.38
169.08
165.30
135.75
135.44
132.02
128.80
128.38
128.29
128.04
127.97
127.84
127.01
66.26
66.07
62.64
60.00
41.33
21.91
20.75
12.02
10.49
Et
O
BnO2C
N–Ph
BnO2C
O
Et
O
5a
f1 (ppm)


7.34 7.32 7.30 7.24 7.23 7.22 7.20 7.18
5.61 5.60 5.58 5.56 5.55 5.19 5.16 5.10 5.08 5.07 5.04 3.94 3.91 3.72 3.68 3.61 3.56 3.51 3.50 3.49 3.47 3.28 3.27 3.25 2.39 2.36 2.35 2.33 2.16 2.15 2.12 1.90 1.89 1.88 1.87 1.85 1.84 1.06 1.04 1.02 0.90 0.88 0.86
Et
O
BnO2C
N–Ph
BnO2C
OH
Et
5b
8.10 7.03 2.04 4.18 1.01 1.96 1.03 0.99 0.97 1.00 3.06 3.15 3.14
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 -0.5 -1.0
f1 (ppm)


173.01 170.82 167.94
149.68 139.72 137.33 136.64 135.52 130.16 129.54 129.39 129.33 129.28 129.22 128.88 128.84 127.53 126.94 125.56
84.51
68.14 67.40
48.22 45.22 44.79
36.19
30.45
23.99 21.38
14.05 13.03
Et
O
BnO2C
N–Ph
BnO2C
OH
Et
5b
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -1
f1 (ppm)


7.35 7.33 7.31 7.22 7.20 7.18 7.16
5.71 5.69 5.67 5.56 5.55 5.53 5.51
4.51 4.50 4.48 4.47 4.37 4.36 4.34 4.33 4.31 4.30
3.76 3.73 3.57 3.55 3.53 3.34 3.33 3.32 3.31
2.77 2.76 2.74 2.72 2.69 2.67 2.56 2.52 2.34 2.33 2.31 2.15 2.13 2.12 2.10 2.08 2.00 1.98 1.96 1.95 1.93 1.13 1.11 1.10 1.05 1.03 1.01
Et
O
N–Ph
OH
O
O
Et
5c
2.72 2.69 2.67 2.56 2.52 2.34 2.33 2.31 2.15 2.13 2.12 2.10 2.08 2.00 1.98 1.96 1.95 1.93 1.13 1.11 1.10 1.05 1.03 1.01
0.95 1.08 2.08 1.08 2.05 3.07 3.14
2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0
f1 (ppm)
2.07 3.03 1.00 1.00 1.00 1.00 0.99 1.02 1.01 0.99 1.00 2.08 1.04 2.08 3.07 3.14
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 -0.5 -1.0
f1 (ppm)


171.96 163.62 161.98 139.51 136.14 128.75 126.71 125.54 125.31 122.92 83.63 65.63 47.54 44.68 43.47 26.22 23.96 20.25 13.35 12.63
Et
O
N–Ph
OH
O
O
Et
5c
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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7.41
7.39
7.36
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7.33
7.30
7.28
5.29
5.05
3.79
3.19
3.17
3.15
3.13
2.92
2.90
2.88
1.55
1.19
1.18
1.16
0.86
0.84
0.83
Et
BnO2C
BnO2C
N–Ph
Pr
5d
2.07
5.07
6.16
1.94
2.00
2.00
2.00
1.98
1.97
3.12
3.04
3.12
f1 (ppm)
169.40
167.97
166.94
166.70
142.50
141.48
138.34
136.70
135.40
134.69
131.53
129.32
129.11
129.01
128.81
128.69
128.54
128.38
128.29
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128.07
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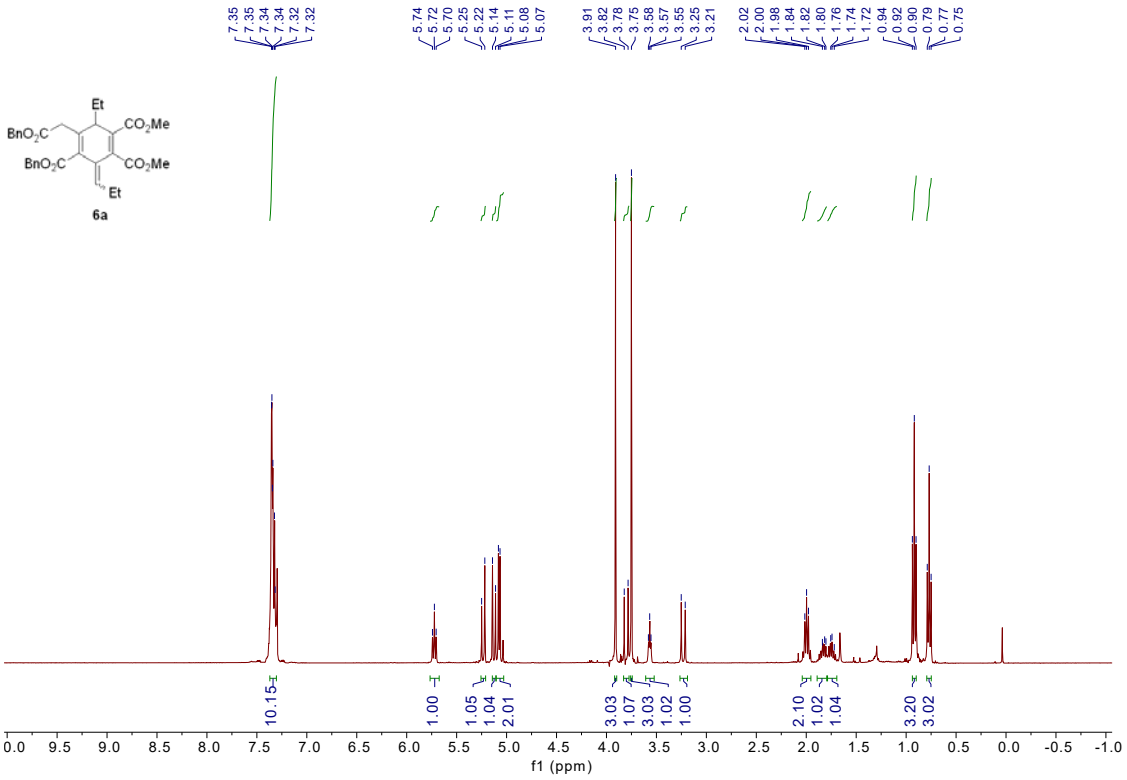
67.73
67.08
35.29
31.32
24.57
21.10
14.51
14.32
f1 (ppm)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7.34
7.34
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7.32
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5.25
5.22
5.14
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5.08
5.07
3.91
3.82
3.78
3.75
3.58
3.57
3.55
3.25
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1.98
1.84
1.82
1.80
1.76
1.74
1.72
0.94
0.92
0.90
0.79
0.77
0.75
Et
BnO2C
CO2Me
BnO2C
CO2Me
Et
6a
10.15
1.00
1.05
1.04
2.01
3.03
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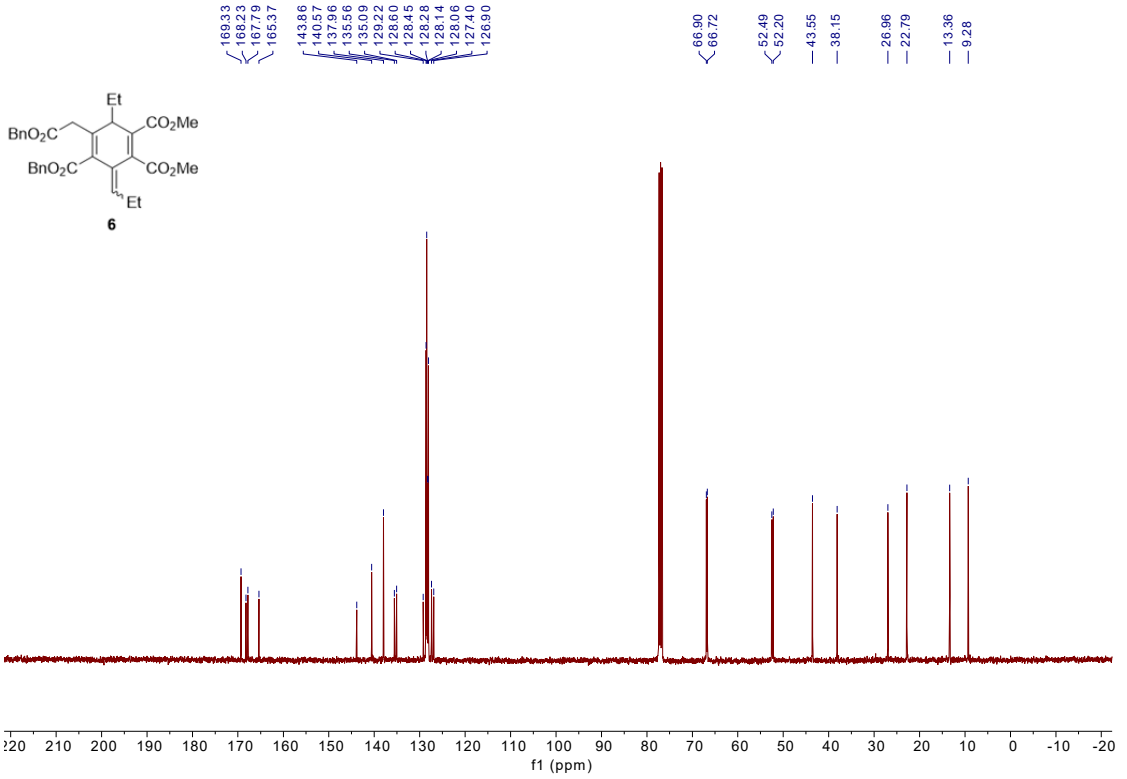
1.02
1.04
3.20
3.02
f1 (ppm)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143.86
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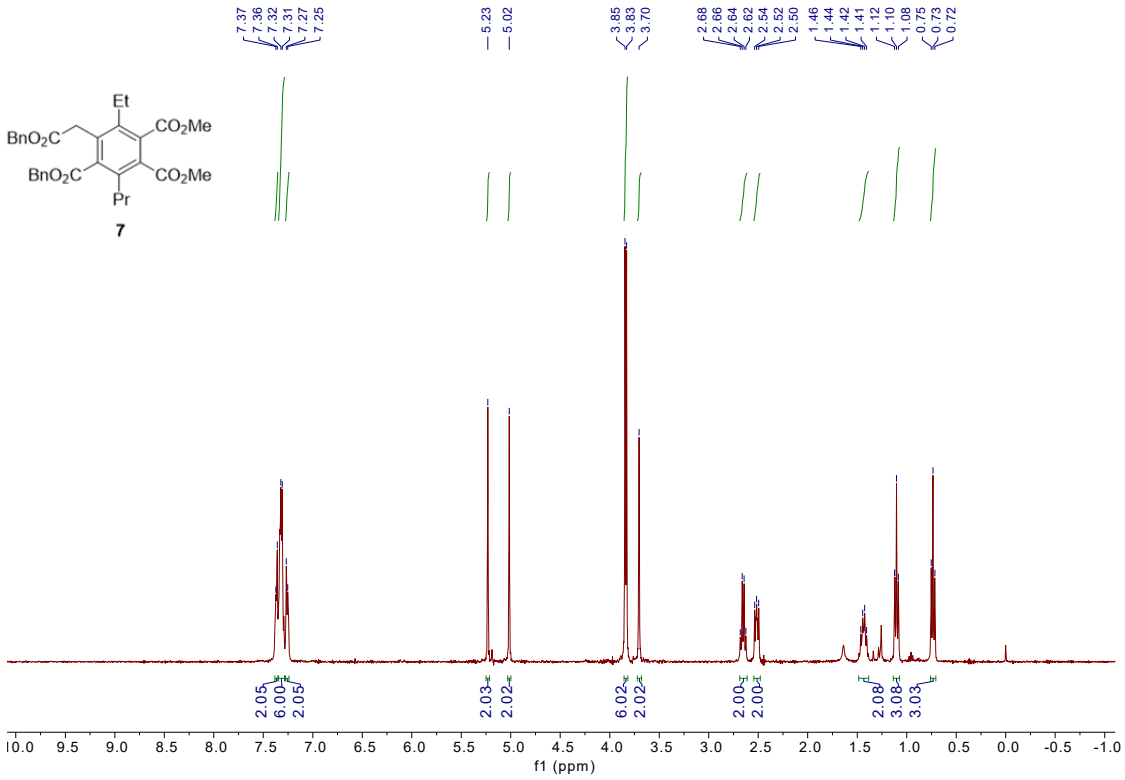
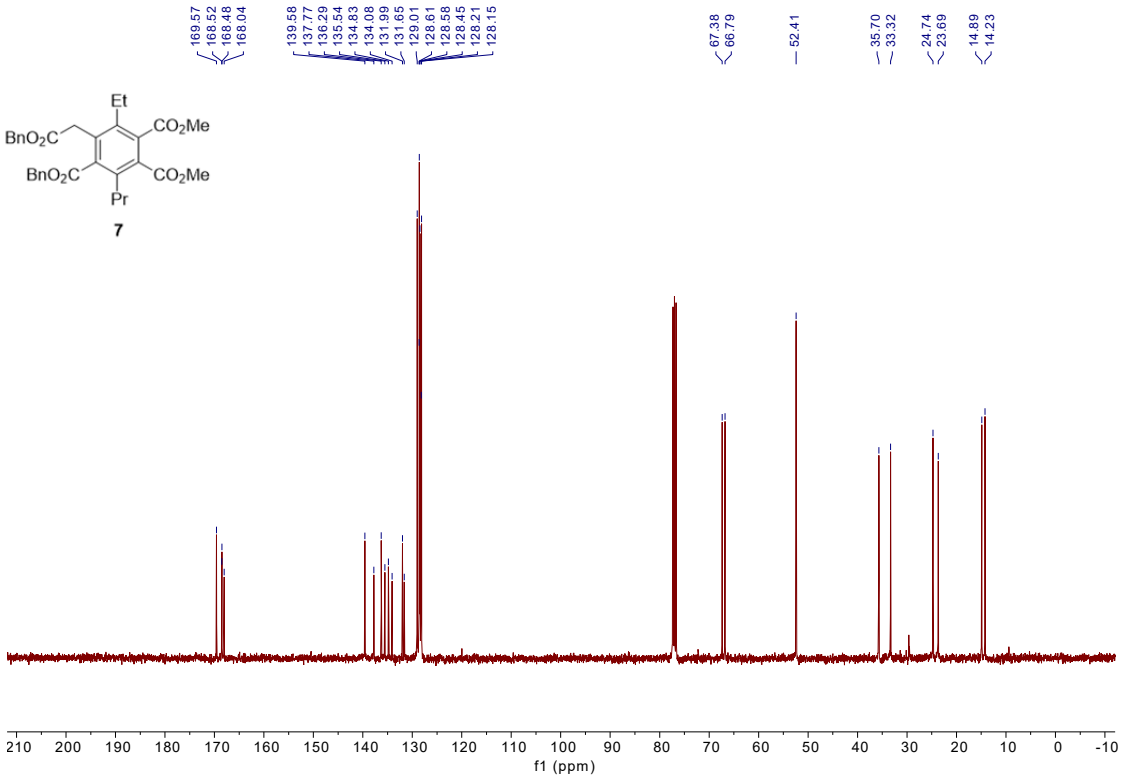
137.96
135.56
135.09
129.22
128.60
128.45
128.28
128.14
128.06
127.40
126.90
66.90
66.72
52.49
52.20
43.55
38.15
26.96
22.79
13.36
9.28
Et
BnO2C
CO2Me
BnO2C
CO2Me
Et
6
f1 (ppm)


7.37
7.36
7.32
7.31
7.27
7.25
5.23
5.02
3.85
3.83
3.70
2.68
2.66
2.64
2.62
2.54
2.52
2.50
1.46
1.44
1.42
1.41
1.12
1.10
1.08
0.75
0.73
0.72
Et
BnO2C
CO2Me
BnO2C
CO2Me
Pr
7
2.05
6.00
2.05
2.03
2.02
6.02
2.02
2.00
2.00
2.08
3.08
3.03
f1 (ppm)


169.57
168.52
168.48
168.04
139.58
137.77
136.29
135.54
134.83
134.08
131.99
131.65
129.01
128.61
128.58
128.45
128.21
128.15
67.38
66.79
52.41
35.70
33.32
24.74
23.69
14.89
14.23
Et
BnO2C
CO2Me
BnO2C
CO2Me
Pr
7
f1 (ppm)