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Flavonoid-Alkylphospholipid Conjugates Elicit Dual Inhibition of Cancer Cell Growth and Lipid Accumulation

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Figure S1: UV spectral recording of **I-d** (13 µM) and **II-c** (12 µM) in organic solvent MeOH/CH_2Cl_2 (A) and in a buffer solution with increasing concentration of sodium dodecyl sulfate (SDS) (B).

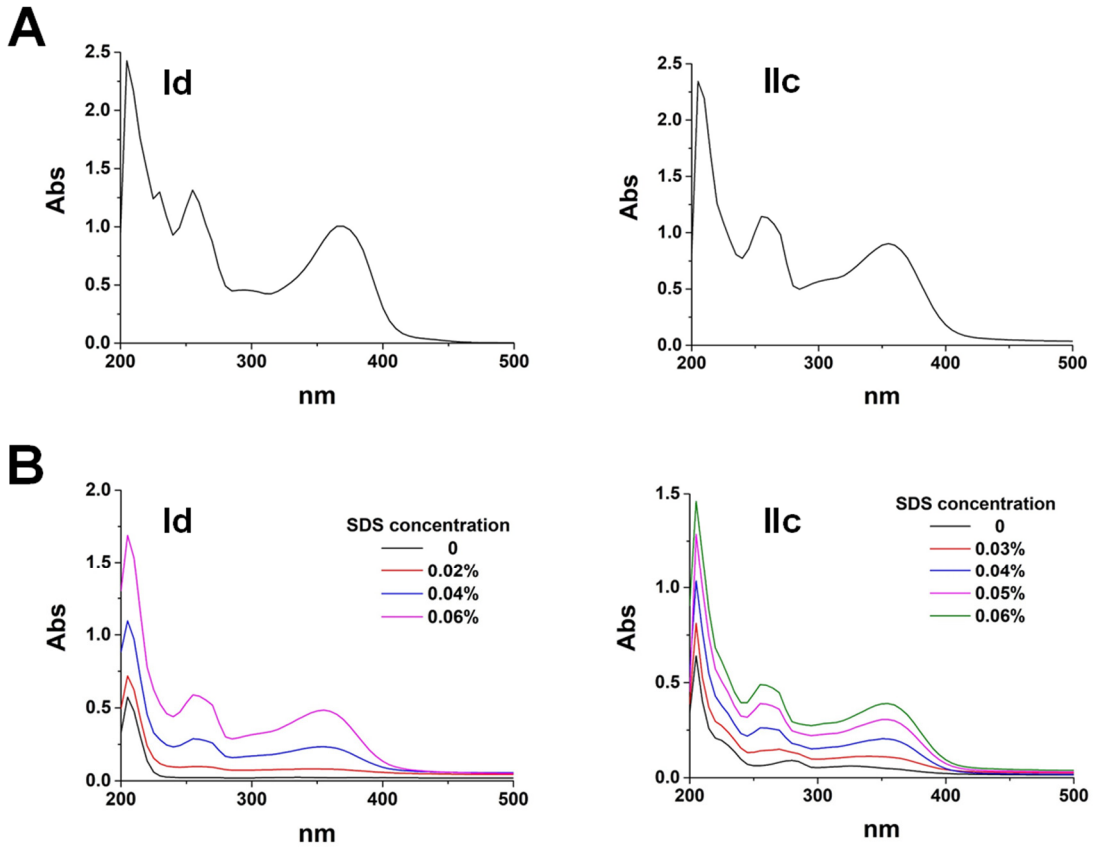
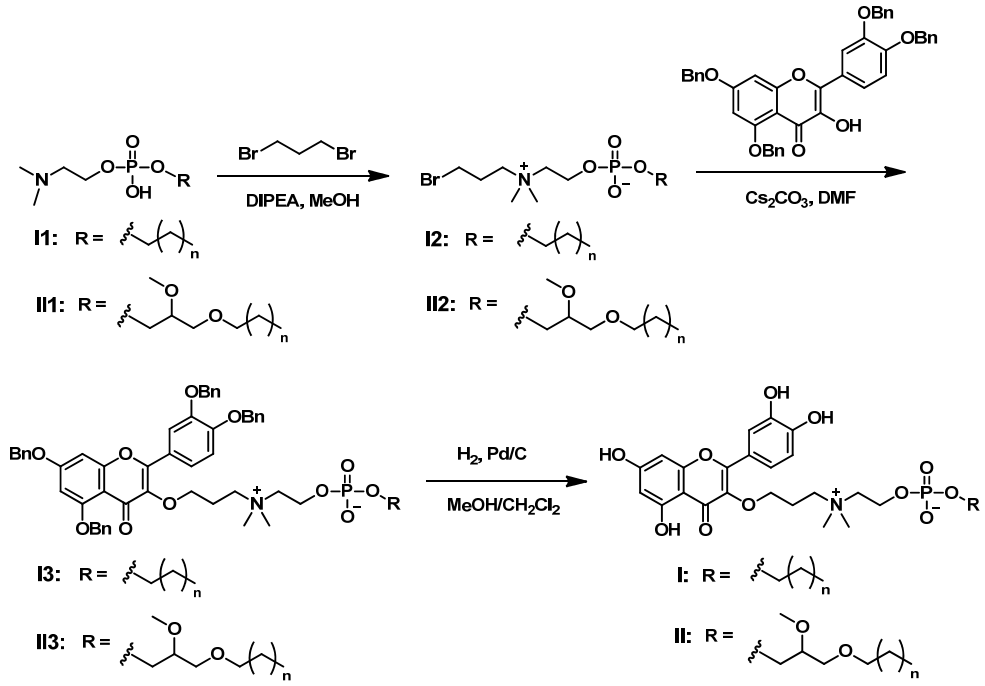


Table S1. Synthesis of quercetin-alkylphospholipid conjugates **I** and **II**.



Entry	n	Comp.	Yield (%)	Comp.	Yield (%)	Comp.	Yield (%)
1	10	**I2a**	79	**I3a**	61	**Ia**	98
2	12	**I2b**	75	**I3b**	61	**Ib**	95
3	14	**I2c**	79	**I3c**	71	**Ic**	95
4	16	**I2d**	81	**I3d**	64	**Id**	97
5	10	**II2a**	77	**II3a**	61	**IIa**	79
6	12	**II2b**	69	**II3b**	59	**IIb**	83
7	14	**II2c**	67	**II3c**	66	**IIc**	77
8	16	**II2d**	75	**II3d**	70	**IId**	81

Table S2. Antiproliferation activity of quercetin-alkylphospholipid conjugates **I** and **II** on different cancer cells

No	Comp.	IC_{50} (μM)[a]			
		HepG2	Hep3B	Panc-1	SKOV3
1	**I-a**	>50	>50	>50	>50
2	**I-b**	25±1	41±1	36±4	26±3
3	**I-c**	20±1	33±1	18±1	25±1
4	**I-d**	9.8±1.1	16±1	8.9±0.2	19±1
5	**II-a**	>50	>50	49±2	47±1
6	**II-b**	21±1	31±2	20±1	15±1
7	**II-c**	13±1	20±2	10±2	18±1
8	**II-d**	20±1	27±2	20±1	18±2
9	Quercetin	72±1	>100	61±1	>100
10	Miltefosine	>50	35±2	20±1	>50
11	Edelfosine	>50	24±1	12±2	>50

[a] IC_{50} represents the concentration of a compound that is required for 50% inhibition of cancer cell growth.

General

All the reagents were purchased from Adamas-beta or Energy Chemical. Solvents were purchased from a local supplier and used without further purification beside THF. THF was distilled from sodium and benzophenone. All compounds were purified by performing flash chromatography on silica gel (200–300 mesh). ^{1}H-NMR and ^{13}C-NMR spectra were recorded on Agilent DD2 400-MR or DD2 600-MR. The chemical shifts were recorded in parts per million (ppm) with tetramethylsilane as the internal reference. The ESI-MS was recorded on a Waters Acquity SQ Detector mass spectrometer. The high resolution of ESI-MS was recorded on a Bruker SolariX 7.0T mass spectrometer. All MS analysis samples were prepared as solutions in methanol. UV spectral was recorded on Agilent Technologies Cary 60 UV-Vis. Analytical HPLC runs were performed on Agilent Technologies 1260 Infinity using columns packed with Inertsil® hypersil C8 4.6×250mm (method 1) and Inertsil® ODS-3 5mm 4.6×250mm (method 2) produced by GL sciences Inc, with 1260 VWD VL, wavelength 370 nm. All the samples were dissolved in DMSO (contain 1% TFA). The mobile phase was consisted of a gradient elution of MeOH (contain 0.1% TFA) and H_2O. Elution system was the mixture of MeOH/H_2O from 10/90 to 100/0 in 20 min and then kept 100/0 in 25 min. The flow rate was 1.0 mL/min. Temperature was 30 °C. Compounds of **I1** and **II1** were synthesized following the reference of previous report.[1]

Synthesis of compound I and II

*General procedure of synthesis of **I2***

To a solution of **I1** (0.5 mmol) in MeOH (10 mL) was added 1,3-dibromopropane (1.0 g, 10.0 eq) and diisopropylethylamine (260 mg, 4.0 eq), the mixture was stirred at 50 ºC for 48 h. Then the solvent was removed and the residue was purified by column gel chromatograph to afford product.

I2a: 79%, white solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.27 (m, 2H), 3.79-3.82 (m, 4H), 3.70 (m, 2H), 3.56 (t, 2H, *J* = 6.4 Hz), 3.36 (s, 6H), 2.42 (m, 2H), 1.58 (m, 2H), 1.26 (m, 18H), 0.88 (t, 3H, *J* = 6.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 65.74, 65.68, 64.21, 58.84, 52.00, 31.90, 31.12, 31.05, 29.69, 29.65, 29.53, 29.34, 29.26, 25.94, 22.66, 14.09. MS (ESI, *m/z*): 458.4, 460.4 $[M + H]^+$.

I2b: 75%, white solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.28 (m, 2H), 3.77-3.84 (m, 4H), 3.67-3.71 (m, 2H), 3.56 (t, 2H, *J* = 6.0 Hz), 3.36 (s, 6H), 2.42 (m, 2H), 1.57-1.58 (m, 2H), 1.26 (m, 22H), 0.88 (t, 3H, *J* = 6.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 65.84, 64.26, 58.92, 52.00, 31.90, 31.09, 31.01, 29.72, 29.66, 29.56, 29.35, 29.20, 25.95, 22.66, 14.09. MS (ESI, *m/z*): 486.5, 488.5 $[M + H]^+$.

I2c: 79%, white solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.27 (m, 2H); 3.77-3.83 (m, 4H); 3.68-3.72 (m, 2H); 3.56 (t, 2H, *J* = 6.4 Hz); 3.36 (s, 6H); 2.42 (m, 2H); 1.57-1.60 (m, 2H); 1.26 (m, 26H); 0.88 (t, 3H, *J* = 6.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 65.68, 65.62, 64.14, 58.82, 51.93, 31.86, 31.11, 31.04, 29.69, 29.61, 29.52, 29.30, 29.24, 25.92, 22.62, 14.05. MS (ESI, *m/z*): 514.5, 516.5 $[M + H]^+$.

I2d: 81%, white solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.29 (m, 2H); 3.78-3.83 (m, 4H);

3.68-3.72 (m, 2H); 3.55 (t, 2H, J = 6.0 Hz); 3.36 (s, 6H); 2.41 (m, 2H); 1.57-1.60 (m, 2H); 1.25 (m, 30H); 0.88 (t, 3H, J = 6.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 65.67, 65.61, 64.18, 58.82, 51.96, 31.88, 31.12, 31.05, 29.70, 29.67, 29.62, 29.52, 29.31, 29.25, 25.93, 22.64, 14.06. MS (ESI, *m/z*): 542.5, 544.5 $[M + H]^+$.

*General procedure of synthesis of **I3***

I2 (0.1 mmol), quercetin (99.3 mg, 1.5 eq) and Cs_2CO_3 (65 mg, 2.0 eq) were suspended in DMF (5 mL) and the mixture was stirred at room temperature overnight. Then the solvent was removed and the residue was purified by column gel chromatograph to afford product.

I3a: 61%, yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.62 (d, 1H, J = 8.4 Hz), 7.28-7.50 (m, 21H), 7.06 (d, 1H, J = 8.4 Hz), 6.41 (s, 1H), 6.35 (s, 1H), 5.18 (s, 2H), 5.17 (s, 2H), 5.14 (s, 2H), 4.98 (s, 2H), 4.27 (m, 2H), 3.88 (m, 2H), 3.65-3.79 (m, 6H), 3.23 (s, 6H), 2.09 (m, 2H), 1.48-1.52 (m, 2H), 1.12-1.26 (m, 18H), 0.84 (t, 3H, J = 6.8 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 173.55, 162.81, 159.58, 158.50, 153.08, 151.22, 148.26, 139.71, 137.08, 136.57, 136.17, 135.51, 128.72, 128.62, 128.54, 128.43, 127.93, 127.54, 127.36, 127.30, 126.86, 123.10, 123.02, 115.05, 113.86, 109.58, 97.88, 93.68, 71.80, 70.69, 70.40, 68.77, 65.85, 65.81, 63.70, 58.87, 51.80, 31.90, 30.93, 30.86, 29.70, 29.53, 29.36, 25.84, 23.78, 22.67, 14.12. MS (ESI, *m/z*): 1040.8 $[M + H]^+$.

I3b: 61%, yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.62 (d, 1H, J = 8.4 Hz), 7.28-7.53 (m, 21H), 7.06 (dd, 1H, J_1 = 8.4 Hz, J_2 = 2.4 Hz), 6.44 (s, 1H), 6.40 (s, 1H), 5.21 (s, 4H), 5.17 (s, 2H), 5.01 (s, 2H), 4.27 (m, 2H), 3.89 (m, 2H), 3.66-3.80 (m, 6H), 3.26

(s, 6H), 2.09 (m, 2H), 1.53 (m, 2H), 1.16-1.25 (m, 22H), 0.86 (t, 3H, J = 6.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 173.55, 162.83, 159.58, 158.54, 153.09, 151.16, 148.24, 139.69, 137.05, 136.53, 136.16, 135.48, 128.74, 128.58, 128.46, 127.99, 127.95, 127.56, 127.36, 127.29, 126.82, 123.02, 122.96, 115.00, 113.79, 109.59, 97.89, 93.68, 71.73, 70.69, 70.41, 68.73, 65.69, 64.04, 63.74, 58.83, 51.78, 31.92, 31.01, 30.94, 29.73, 29.54, 29.38, 25.88, 23.76, 22.69, 14.15. MS (ESI, *m/z*): 1068.8 $[M + H]^+$.

I3c: 71%, yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.61 (d, 1H, J = 8.4 Hz), 7.26-7.54 (m, 21H); 7.07 (d, 1H, J = 8.4 Hz); 6.45 (s, 1H); 6.40 (s, 1H); 5.20 (s, 4H); 5.16 (s, 2H); 5.02 (s, 2H); 4.27 (m, 2H); 3.90 (m, 2H); 3.74-3.82 (m, 6H); 3.25 (s, 6H); 2.10 (m, 2H); 1.52-1.55 (m, 2H); 1.16-1.23 (m, 26H); 0.86 (t, 2H, J = 6.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 173.50, 162.86, 159.64, 158.55, 153.09, 151.25, 148.35, 139.75, 137.08, 136.57, 136.19, 135.54, 128.72, 128.55, 128.42, 127.97, 127.93, 127.51, 127.37, 127.29, 126.82, 123.13, 122.98, 115.22, 113.96, 109.67, 97.97, 93.81, 71.83, 70.79, 70.43, 68.80, 65.62, 65.56, 64.13, 63.78, 58.81, 51.78, 31.89, 31.06, 30.98, 29.70, 29.64, 29.52, 29.33, 25.89, 23.81, 22.65, 14.09. MS (ESI, *m/z*): 1096.9 $[M + H]^+$.

I3d: 64%, yellow solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.61 (d, 1H, J = 8.4 Hz); 7.26-7.50 (m, 21H); 7.06 (d, 1H, J = 8.8 Hz); 6.42 (s, 1H); 6.36 (s, 1H); 5.18 (s, 2H); 5.17 (s, 2H); 5.14 (s, 2H); 4.99 (s, 2H); 4.28 (m, 2H); 3.88 (m, 2H); 3.71-3.79 (m, 6H); 3.23 (s, 6H); 2.09 (m, 2H); 1.49-1.52 (m, 2H); 1.12-1.28 (m, 30H); 0.86 (t, 2H, J = 6.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 173.58, 162.87, 159.65, 158.56, 153.14, 151.30, 148.35, 139.77, 137.13, 136.62, 136.21, 135.57, 128.74, 128.65, 128.57, 128.44, 127.97, 127.55, 127.40, 127.34, 126.91, 123.10, 115.20, 113.97, 109.65, 97.97, 93.79,

71.87, 70.77, 70.44, 68.83, 65.87, 64.19, 63.78, 58.94, 51.85, 31.93, 30.96, 30.91, 29.78, 29.74, 29.68, 29.57, 29.37, 25.88, 23.83, 22.69, 14.12. MS (ESI, *m/z*): 1125.0 $[M + H]^+$.

General procedure of synthesis of ***I***

I3 (0.1 mmol) and Pd/C (20 mg) was suspended in MeOH/CH_2Cl_2 (5 mL, 1:1) and the mixture was stirred at room temperature under hydrogen atmosphere for 4 h. Then the solid was filtered off and the filtrate was collected. After evaporation, the residue was washed by ethyl acetate to afford the product.

Ia: 98%, yellow solid. HPLC: t_R = 21.762 min (Method 1, purity 97.90 %), t_R = 22.654 min (Method 2, purity 97.51 %). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.67 (s, 1H), 11.57 (br, 1H), 11.23 (br, 1H), 9.58 (br, 1H), 7.74 (s, 1H), 7.19 (d, 1H, *J* = 8.4 Hz), 6.88 (d, 1H, *J* = 8.4 Hz), 6.41 (s, 1H), 6.20 (s, 1H), 4.12 (m, 2H), 3.96 (m, 2H), 3.68-3.70 (m, 2H), 3.59 (m, 4H), 3.12 (s, 6H), 2.16 (m, 2H), 1.46-1.48 (m, 2H), 1.15-1.30 (m, 18H), 0.84 (t, 3H, *J* = 6.8 Hz). ^{13}C-NMR (100 MHz, DMSO-d_6): δ 178.01, 164.85, 161.60, 157.11, 156.79, 149.42, 146.34, 136.42, 120.85, 119.70, 116.38, 115.96, 104.39, 99.01, 94.08, 70.20, 69.26, 64.89, 64.83, 62.75, 61.30, 58.63, 52.08, 31.72, 30.87, 30.80, 29.49, 29.47, 29.45, 29.28, 29.14, 25.86, 23.55, 22.52, 14.38. MS (ESI, *m/z*): 680.6 $[M + H]^+$. HRMS: calcd for $C_{34}H_{51}NO_{11}P^+$, $[M + H]^+$, 680.3194; found, 680.3169.

Ib: 95%, yellow solid. HPLC: t_R = 22.617 min (Method 1, purity 96.48 %), t_R = 23.478 min (Method 2, purity 96.49 %). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.68 (br, 1H), 11.71 (br, 1H), 11.00 (br, 1H), 9.50 (br, 1H), 7.76 (s, 1H), 7.19 (d, 1H, J = 8.0 Hz), 6.88 (d, 1H, J = 8.4 Hz), 6.41 (s, 1H), 6.19 (s, 1H), 4.11 (m, 2H), 3.97 (m, 2H), 3.58-3.70

(m, 6H), 3.11 (s, 6H), 2.17 (m, 2H), 1.45-1.47 (m, 2H), 1.16-1.22 (m, 22H), 0.85 (t, 3H, J = 6.4 Hz). ^{13}C-NMR (100 MHz, DMSO-d_6): δ 177.95, 164.92, 161.54, 157.00, 156.73, 149.37, 146.23, 136.35, 120.82, 119.73, 116.30, 115.95, 104.29, 98.99, 94.05, 69.22, 64.94, 64.88, 62.64, 61.31, 58.70, 52.02, 31.74, 30.84, 30.78, 29.52, 29.48, 29.29, 29.18, 25.86, 23.54, 22.55, 14.40. MS (ESI, *m/z*): 708.6 $[M + H]^+$. HRMS: calcd for $C_{36}H_{55}NO_{11}P^+$, $[M + H]^+$, 708.3507; found, 708.3485.

Ic: 95%, yellow solid. HPLC: t_R = 23.187 min (Method 1, purity 97.07 %), t_R = 24.157 min (Method 2, purity 97.94 %). ^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.63 (s, 1H), 11.39 (br, 1H), 9.67 (br, 1H), 7.71, (s, 1H), 7.19 (d, 1H, *J* = 8.0 Hz), 6.89 (d, 1H, *J* = 8.4 Hz), 6.40 (s, 1H), 6.19 (s, 1H), 4.16 (m, 2H), 3.96 (m, 2H), 3.72-3.74 (m, 2H), 3.61 (m, 4H), 3.13 (s, 6H), 2.17 (m, 2H), 1.47-1.51 (m, 2H), 1.15-1.21 (m, 26H), 0.84 (t, 3H, *J* = 6.4 Hz). ^{13}C-NMR (100 MHz, DMSO-d_6): δ 178.00, 164.93, 161.59, 156.99, 156.77, 149.40, 146.22, 136.45, 120.87, 119.88, 116.31, 116.01, 104.36, 99.03, 94.06, 69.27, 65.07, 65.02, 62.89, 61.58, 58.78, 51.95, 31.72, 30.83, 30.76, 29.49, 29.28, 29.14, 25.83, 23.56, 22.52, 14.36. MS (ESI, *m/z*): 736.6 $[M + H]^+$. HRMS: calcd for $C_{38}H_{59}NO_{11}P^+$, $[M + H]^+$, 736.3820; found, 736.3794.

Id: 97%, yellow solid. HPLC: t_R = 25.641 min (Method 1, purity 96.51 %), t_R = 26.438 min (Method 2, purity 97.22 %). ^{1}H-NMR (400 MHz, CD_3OD): δ 7.56 (s, 1H), 7.40 (d, 1H, *J* = 8.0 Hz), 6.94 (d, 1H, *J* = 8.4 Hz), 6.35 (s, 1H), 6.17 (d, 1H, *J* = 1.6 Hz), 4.27 (m, 2H), 4.00-4.02 (m, 2H), 3.84-3.89 (m, 2H), 3.63-3.67 (m, 4H), 3.18 (s, 6H), 2.19 (m, 2H), 1.56-1.62 (m, 2H), 1.22-1.35 (m, 30H), 0.89 (t, 3H, *J* = 6.8 Hz). ^{13}C-NMR (100 MHz, DMSO-d_6): δ 178.12, 164.76, 161.63, 156.88, 156.80, 149.37, 146.06,

136.63, 120.90, 120.41, 116.14, 104.50, 99.04, 94.09, 69.33, 65.87, 62.98, 61.97, 59.28, 51.69, 31.72, 30.58, 30.54, 29.47, 29.43, 29.19, 29.13, 25.67, 23.57, 22.52, 14.38. MS (ESI, *m/z*): 764.7 $[M + H]^+$. HRMS: calcd for $C_{40}H_{63}NO_{11}P^+$, $[M + H]^+$, 764.4133; found, 764.4104..

*General procedure of synthesis of **II2***

To a solution of **II1** (0.5 mmol) in MeOH (10 mL) was added 1,3-dibromopropane (1.0 g, 10.0 eq) and diisopropylethylamine (260 mg, 4.0 eq). The mixture was stirred at 50 ºC for 48 h. Then the solvent was removed and the residue was purified by column gel chromatograph to afford the product.

II2a: 77%, white waxy solid.^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.33 (s, 2H), 3.84-3.97 (m, 4H), 3.69-3.72 (m, 2H), 3.49-3.58 (m, 6H), 3.43-3.49 (m, 2H), 3.41 (t, 2H, *J* = 6.8 Hz), 3.36 (s, 6H), 2.42 (m, 2H), 1.53-1.55 (m, 2H), 1.26 (s, 18H), 0.88 (t, 3H, *J* = 6.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 79.60, 79.52, 71.79, 70.10, 65.05, 64.28, 58.98, 57.79, 51.98, 31.89, 29.67, 29.64, 29.53, 29.34, 26.06, 25.90, 22.66, 14.10. MS (ESI, *m/z*): 546.5, 548.5 $[M+H]^+$.

II2b: 69%, white waxy solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.33 (m, 2H), 3.85-3.96 (m, 4H), 3.69-3.72 (m, 2H), 3.49-3.57 (m, 6H), 3.43-3.47 (m, 2H), 3.41 (t, 2H, *J* = 6.8 Hz), 3.36 (s, 6H), 2.42 (m, 2H), 1.54 (t, 2H, *J* = 5.6 Hz), 1.26 (s, 22H), 0.88 (t, 3H, *J* = 6.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 79.68, 79.61, 71.78, 70.21, 65.01, 64.32, 58.89, 57.78, 51.95, 31.88, 29.62, 29.52, 29.32, 26.06, 25.90, 22.64, 14.08. MS (ESI, *m/z*): 574.6, 576.4 $[M+H]^+$, 596.6, 598.6 $[M+Na]^+$.

II2c: 67%, white waxy solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.31 (s, 2H), 3.78-3.95 (m, 5H), 3.62-3.66 (m, 2H), 3.51-3.59 (m, 5H), 3.44-3.48 (m, 4H), 3.41 (t, 2H, *J* = 6.8 Hz), 3.31 (s, 6H), 2.42 (m, 2H), 1.55 (t, 2H, *J* = 6.4 Hz), 1.26 (s, 26H), 0.88 (t, 3H, *J* = 6.8 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 79.58, 79.50, 71.80, 70.09, 65.09, 64.25, 58.98, 57.80, 52.02, 31.89, 29.69, 29.55, 29.48, 29.33, 26.07, 25.91, 22.65, 14.08. MS (ESI, *m/z*): 602.6, 604.6 $[M+H]^+$.

II2d: 75%, white waxy solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 4.33 (s, 2H), 3.84-3.97 (m, 4H), 3.66-3.70 (m, 2H), 3.46-3.58 (m, 6H), 3.42-3.46 (m, 4H), 3.41 (t, 2H, *J* = 6.4 Hz), 3.34 (s, 6H), 2.87 (s, 1H), 2.42 (m, 2H), 1.53-1.56 (m, 2H), 1.25 (s, 30H), 0.88 (t, 3H, *J* = 6.0 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 79.41, 79.33, 71.76, 70.04, 65.15, 59.63, 57.75, 52.05, 43.43, 31.89, 29.71, 29.66, 29.57, 29.33, 26.07, 22.64, 14.06. MS (ESI, *m/z*): 630.7, 632.7 $[M+H]^+$.

*General procedure of synthesis of **II3***

II2 (0.1 mmol), quercetin (99.3 mg, 1.5 eq) and Cs_2CO_3 (65 mg, 2.0 eq) were suspended in DMF (5 mL) and the mixture was stirred at room temperature overnight. After that, the solvent was removed and the residue was purified by column gel chromatograph to afford product.

II3a: 61%, yellow waxy solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.60 (d, 1H, *J* = 8.4 Hz), 7.33-7.55 (m, 21H), 7.08 (d, 1H, *J* = 8.4 Hz), 6.52 (s, 1H), 6.46 (s, 1H), 5.27 (s, 2H), 5.24 (s, 2H), 5.20 (s, 2H), 5.09 (s, 2H), 4.31 (m, 2H), 3.78-3.96 (m, 7H), 3.66 (m, 2H), 3.45-3.56 (m, 5H), 3.37 (t, 2H, *J* = 6.8 Hz), 3.24 (s, 6H), 2.22 (t, 1H, *J* = 8.0 Hz), 2.06

(m, 2H), 1.51 (t, 2H, *J* = 6.0 Hz), 1.23 (s, 18H), 0.87 (t, 3H, *J* = 6.0 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 173.54, 162.88, 159.66, 158.57, 153.15, 151.27, 148.36, 139.74, 137.08, 136.59, 136.17, 135.54, 128.72, 128.56, 128.42, 127.94, 127.51, 127.37, 127.30, 126.85, 123.13, 122.98, 115.23, 113.97, 109.66, 97.97, 93.82, 79.73, 79.65, 71.82, 71.65, 70.79, 70.67, 70.44, 68.82, 64.73, 64.68, 64.20, 63.91, 58.84, 57.80, 51.77, 31.88, 29.61, 29.50, 29.31, 26.03, 23.76, 22.64, 14.08. MS (ESI, *m/z*): 1128.9 $[M+H]^+$, 1150.8 $[M+Na]^+$.

II3b: 59%, yellow waxy solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.60 (d, 1H, *J* = 8.4 Hz), 7.32-7.55 (m, 15H), 7.08 (d, 1H, *J* = 8.8 Hz), 6.51 (s, 1H), 6.46 (s, 1H), 5.26 (s, 2H), 5.23 (s, 2H), 5.19 (s, 2H), 5.08 (s, 2H), 4.32 (s, 2H), 3.79-3.95 (m, 8H), 3.66 (s, 2H), 3.45-3.56 (m, 4H), 3.37 (t, 2H, *J* = 7.6 Hz), 3.24 (s, 6H), 2.04 (m, 2H), 1.52-1.55 (m, 2H), 1.21-1.27 (m, 22H), 0.87 (t, 3H, *J* = 6.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 173.66, 162.92, 159.64, 158.58, 153.27, 151.28, 148.34, 139.71, 137.05, 136.56, 136.14, 135.52, 128.72, 128.61, 128.56, 127.95, 127.53, 127.36, 127.29, 126.88, 123.08, 122.99, 115.19, 113.92, 109.60, 97.98, 93.79, 79.61, 79.54, 71.81, 71.68, 70.77, 70.74, 70.46, 68.78, 64.80, 64.15, 63.92, 58.80, 57.79, 51.74, 50.34, 31.88, 29.67, 29.62, 29.50, 29.32, 26.01, 23.70, 22.65, 14.08. MS (ESI, *m/z*): 1157.1 $[M+H]^+$.

II3c: 66%, yellow waxy solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.61 (d, 1H, *J* = 8.0 Hz), 7.26-7.53 (m, 21H), 7.05 (d, 1H, *J* = 8.8 Hz), 6.42 (s, 1H), 6.38 (s, 1H), 5.20 (s, 2H), 5.17 (s, 2H), 5.15 (s, 2H), 5.00 (s, 2H), 4.38 (m, 2H), 3.78-3.96 (m, 5H), 3.40-3.51 (m, 5H), 3.40-3.51 (m, 4H), 3.33 (t, 2H, *J* = 6.8 Hz), 3.27 (s, 6H), 2.11 (m, 2H), 1.48-1.49 (m, 2H), 1.22 (m, 26H), 0.87 (t, 3H, *J* = 5.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 173.60,

162.92, 159.67, 158.60, 153.24, 151.27, 148.36, 139.71, 137.07, 136.57, 136.14, 135.53, 128.73, 128.58, 128.44, 127.99, 127.95, 127.53, 127.36, 127.29, 126.86, 123.11, 122.92, 115.24, 113.97, 109.66, 98.00, 93.83, 79.73, 79.66, 71.81, 71.67, 70.81, 70.67, 70.47, 68.78, 64.71, 64.66, 64.23, 64.01, 58.80, 57.82, 51.82, 33.88, 32.70, 31.89, 29.68, 29.63, 29.52, 29.33, 28.53, 28.00, 26.04, 23.75, 22.65, 14.09. MS (ESI, *m/z*): 1184.9 $[M+H]^+$.

II3d: 70%, yellow waxy solid. ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.62 (d, 1H, *J* = 8.4 Hz), 7.27-7.54 (m, 21H), 7.07 (d, 1H, *J* = 8.4 Hz), 6.49 (s, 1H), 6.43 (s, 1H), 5.23 (s, 2H), 2.22 (s, 2H), 5.18 (s, 2H), 5.06 (s, 2H), 4.32 (s, 2H), 3.91-3.94 (m, 4H), 3.87 (m, 2H), 3.78 (m, 2H), 3.36-3.53 (m, 4H), 3.33 (t, 2H, *J* = 6.8 Hz), 3.22 (s, 6H), 2.05 (m, 2H), 1.49 (m, 2H), 1.21-1.25 (m, 30H), 0.87 (t, 3H, *J* = 6.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$): δ 173.53, 162.88, 159.66, 158.57, 153.15, 151.26, 148.36, 139.74, 137.07, 136.58, 136.17, 135.54, 128.72, 128.56, 128.42, 127.97, 127.94, 127.51, 127.37, 127.29, 126.84, 123.13, 122.96, 115.23, 113.97, 109.66, 97.97, 93.82, 79.75, 79.67, 71.81, 71.66, 70.79, 70.70, 70.44, 68.82, 64.65, 64.06, 63.92, 58.83, 57.80, 51.74, 50.09, 33.88, 31.88, 29.62, 29.52, 29.32, 26.04, 23.75, 22.65, 14.09. MS (ESI, *m/z*): 1213.0 $[M+H]^+$.

*General procedure of synthesis of **II***

II3 (0.1 mmol) and Pd/C (20 mg) was suspended in MeOH/CH_2Cl_2 (5 mL, 1:1). The mixture was stirred at room temperature under hydrogen atmosphere for 4 h. After the solid was filtered off, the filtrate was collected and evaporated. Then the residue was washed by ethyl acetate to afford product.

IIa: 79%, yellow solid. HPLC: t_R = 22.734 min (Method 1, purity 96.87 %), t_R = 23.486 min (Method 2, purity 96.74 %).^{1}H-NMR (600 MHz, DMSO-d_6): δ 12.66 (s, 1H), 11.37 (s, 1H), 11.20 (s, 1H), 9.58 (s, 1H), 7.72 (s, 1H), 7.20 (d, 1H, *J* = 8.4 Hz), 6.88(d, 1H, *J* = 8.4 Hz), 6.40 (s, 1H), 6.19 (s, 1H), 4.14 (m, 2H), 3.96-3.97 (m, 2H), 3.69-3.77 (m, 2H), 3.58-3.60 (m, 3H), 3.40-3.42 (m, 3H), 3.27-3.31 (m, 6H), 3.12 (s, 6H), 2.17 (m, 2H), 1.40 (m, 2H), 1.19-1.23 (m, 18H), 0.84 (t, 3H, *J* = 6.6 Hz). ^{13}C-NMR (150 MHz, DMSO-d_6): δ 178.04, 164.78, 161.61, 157.10, 156.80, 149.43, 146.32, 136.45, 120.85, 119.77, 116.31, 115.99, 104.44, 99.00, 94.08, 79.50, 79.45, 71.04, 70.31, 69.30, 64.36, 62.82, 61.36, 58.71, 57.45, 52.04, 31.72, 29.60, 29.44, 29.29, 29.14, 26.01, 23.55, 22.52, 14.38. MS (ESI, *m/z*): 768.7 $[M+H]^+$, 790.6 $[M+Na]^+$. HRMS: calcd for $C_{38}H_{58}NNaO_{13}P^+$, $[M+Na]^+$, 790.3527; found, 790.3538.

IIb: 83%, yellow solid. HPLC: t_R = 23.207 min (Method 1, purity 96.17 %), t_R = 24.179 min (Method 2, purity 96.04 %).^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.69 (s, 1H), 11.59 (s, 1H), 10.93 (s, 1H), 9.51 (s, 1H), 7.74 (s, 1H), 7.21 (d, 1H, *J* = 8.0 Hz), 6.88 (d, 1H, *J* = 8.4 Hz), 6.41 (s, 1H), 6.19 (s, 1H), 4.12 (s, 2H), 3.98 (s, 2H), 3.67-3.74 (m, 2H), 3.58 (s, 4H), 3.39-3.42 (m, 8H), 3.11 (s, 6H), 2.18 (m, 2H), 2.00 (m, 2H), 1.40 (m, 2H), 1.21 (m, 22H), 0.85 (t, 3H, *J* = 6.0 Hz). ^{13}C-NMR (150 MHz, DMSO-d_6): δ 178.04, 164.80, 161.62, 157.00, 156.80, 149.39, 146.19, 136.51, 120.88, 120.01, 116.24, 116.06, 104.44, 99.02, 94.08, 79.46, 79.41, 71.06, 70.25, 69.33, 64.52, 62.96, 61.66, 58.78, 57.47, 51.92, 51.18, 31.72, 29.60, 29.48, 29.46, 29.31, 29.14, 26.01, 23.58, 22.52, 14.37. MS (ESI, *m/z*): 796.8 $[M+H]^+$, 818.9 $[M+Na]^+$. HRMS: calcd for $C_{40}H_{63}NO_{13}P^+$, $[M+H]^+$, 796.4054; found, 796.4032.

IIc: 77%, yellow solid. HPLC: t_R = 23.675 min (Method 1, purity 97.88 %), t_R = 24.639 min (Method 2, purity 97.89 %).^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.69 (s, 1H), 11.56 (br, 1H), 10.92 (s, 1H), 9.52 (br, 1H), 7.74 (s, 1H), 7.21 (d, 1H, *J* = 8.0 Hz), 6.88 (d, 1H, *J* = 8.0 Hz), 6.41 (s, 1H), 6.18 (s, 1H), 4.12 (m, 2H), 3.97 (m, 2H), 3.66-3.75 (m, 3H), 3.59 (m, 4H), 3.40-3.41 (m, 3H), 3.30 (m, 4H), 3.11 (s, 6H), 2.18 (m, 2H), 1.40 (m, 2H), 1.21 (d, 26H), 0.85 (t, 3H, *J* = 6.8 Hz). ^{13}C-NMR (150 MHz, DMSO-d_6): δ 178.04, 164.80, 161.62, 157.02, 156.80, 149.40, 146.21, 136.50, 120.86, 119.97, 116.25, 116.04, 104.44, 99.01, 94.07, 79.46, 79.42, 71.05, 70.26, 69.32, 64.47, 62.92, 61.60, 58.76, 57.46, 55.33, 51.94, 31.72, 29.60, 29.31, 29.13, 26.01, 23.56, 22.52, 14.36. MS (ESI, *m/z*): 824.7 $[M+H]^+$, 846.6 $[M+Na]^+$. HRMS: calcd for $C_{42}H_{66}NNaO_{13}P^+$, $[M+Na]^+$, 846.4175; found, 846.4164.

IId: 81%, yellow solid. HPLC: t_R = 24.388 min (Method 1, purity 95.10 %), t_R = 25.355 min (Method 2, purity 95.85 %).^{1}H-NMR (400 MHz, DMSO-d_6): δ 12.71 (s, 1H), 11.70 (br, 1H), 10.94 (br, 1H), 9.55 (br, 1H), 7.76 (s, 1H), 7.21 (d, 1H, *J* = 8.0 Hz), 6.88 (d, 1H, *J* = 8.0 Hz), 6.41 (s, 1H), 6.18 (s, 1H), 4.11 (m, 2H), 3.97 (m, 2H), 3.71 (m, 2H), 3.51-3.58 (m, 6H), 3.29-3.41 (m, 4H), 3.11 (s, 6H), 2.18 (m, 2H), 1.39 (s, 2H), 1.21 (d, 30H), 0.85 (t, 3H, *J* = 6.8 Hz). ^{13}C-NMR (150 MHz, DMSO-d_6): δ 178.04, 164.82, 161.62, 156.98, 156.80, 149.39, 146.17, 136.51, 120.87, 120.04, 116.23, 116.06, 104.44, 99.02, 94.07, 79.46, 79.41, 71.06, 70.26, 69.33, 64.52, 62.98, 61.71, 58.78, 57.46, 51.89, 51.17, 31.73, 29.61, 29.33, 29.14, 26.02, 23.57, 22.52, 14.35. MS (ESI, *m/z*): 852.8 $[M+H]^+$. HRMS: calcd for $C_{44}H_{71}NO_{13}P^+$, $[M+H]^+$, 852.4637; found, 852.4657. calcd for $C_{44}H_{70}NNaO_{13}P^+$, $[M+Na]^+$, 874.4455; found, 874.4477.

UV spectral recording in organic solvent and phosphate buffer

The test samples were prepared in methanol/dichloromethane (1:2). The concentration of **Id** and **IIc** in the solvent was 13 μM and 12 μM, respectively. The UV spectra was recorded on Agilent Technologies Cary 60 UV-Vis.

To 0.1 mg of the compound was added 2.0 mL of 100 mM phosphate buffer (pH = 7.4) and mixed by vortex. After that, the mixture was allowed to stand for 1 minute. The supernatant was used for UV recording. Then the detergent sodium dodecyl sulfate (SDS) was added and the UV spectra of the samples with different concentrations of SDS were recorded.

Cell culture

Human liver cancer HepG2 cell and ovarian cancer SKOV3 cells were purchased from Cell Resource Centre, IBMS, CAMS/PUMC. Human liver cancer Hep3B cell were purchased from China Center for Type Culture Collection, Wuhan University. Human pancreatic cancer Panc-1 cells were the gifts from Prof. Huaizhi Wang (Institute of Hepatopancreatobiliary Surgery, Southwest Hospital, Chongqing). HepG2 and Hep3B cells were grown in Dulbecco's modified eagle's medium (DMEM) (HyClone) supplemented with 10% fetal bovine serum (FBS). Panc-1 cells were grown in Roswell Park Memorial Institute 1640 (RPMI 1640) (GIBCO) supplemented with 10% FBS. SKOV3 cells were grown in McCoy's 5A (GIBCO) supplemented with 10% FBS. All cells were incubated at a humidified atmosphere containing 5% CO_2 at 37 °C.

Reagents and Antibodies

MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) was purchased from Adamas. The annexin V-FITC/ Propidium Iodide (PI) apoptosis detection kit was purchased from Sangon Biotech (Shanghai, China). Oil Red O and haematoxylin were purchased from Sangon Biotech (Shanghai, China). The BCA Protein Assay Kit was purchased from EnoGene (Nanjing, China). Kits for determining triglyceride (TG) was purchased from Applygen Technologies Inc (Beijing, China). The primary antibodies including Bcl-2 antibody, HSF1 rabbit mAb, HSP70 rat mAb, HSP27 rabbit mAb, eIF4E rabbit mAb, PARP antibody, LXR-β rabbit mAb and PPARγ rabbit mAb were all obtained from Cell Signaling Technology (Danvers, MA, USA). The AKT antibody was purchased from EnoGene (Nanjing, China). The β-actin rabbit antibody and goat anti-rat (HRP) secondary antibody were purchased from Bioss (Beijing, China). The goat anti-rabbit (HRP) secondary antibody was purchased from Sino Biological Inc. (Beijing, China). The cell lysis buffer, primary antibody dilution buffer and ECL kit were purchased from Beyotime (Shanghai, China).

Cell growth inhibition assay

HepG2, Hep3B and SKOV3 cells were seeded into a 96-well plate at 10000 cells per well, while Panc-1 cells at 5000 cells per well, and allowed to adhere overnight. Then the culture medium was removed and replaced with fresh media alone as control or containing various concentrations of the compounds. After indicated treatment in 72h, the number of viable cells remained was determined by MTT colorimetric assay at 490 nm. All experiments were done in triplicate and repeated three independent times.

The IC_{50} value were calculated with the software program SPSS 22.0.

Lactate dehydrogenase (LDH) assay.

The LDH assay was measured by using commercial LDH kit (Cytotoxicity Assay Kit, Beyotime). The cancer cells were seeded 10,000 cells per well in 96-well plates, respectively. 24 hours later, the culture medium was removed and replaced with fresh media (1% FBS) alone or containing the test compounds. After 1h treatment, the plates were centrifuged for 5 minutes in a multiwell plate centrifuge (400 g), and 120 μL supernatant of each well was transferred to a new 96-well plate. The LDH reaction mixture was freshly prepared according to the manufacturer's protocol and 60 μL of this mixture was added to each well of the plates containing blank, control, or cells in culture. The plate was incubated at 25 °C for 30 min. Control was performed with release agent and blank medium, and set as 100% and 0% LDH release, respectively. The relative LDH release is defined by the ratio of LDH released over total LDH in the cells. All samples were performed in triplicate.

Apoptosis and necrosis assay on flow cytometry

The cancer cells were seeded in 6-well plates (2.5×10^5 cells/well) and allowed to adhere and proliferate overnight. Culture medium was then removed and fresh media containing the compound was added. After 48 hours treatment, the cells were harvested and washed with cold PBS. The samples were pelleted again through centrifugation and resuspended in binding buffer. Annexin-V/FITC and propidium iodide (PI) was then added to the cells and the samples were incubated for 15 minutes at room temperature.

After staining, flow cytometry was performed on Fluorescence Activated Cell Sorting (Beckman Coulter). Each sample was performed in triplicate.

Western blotting analysis

The cancer cells after being treated by the compounds for 48h were lysed in lysis buffer. A total of 10-50 μg protein were quantified and loaded into the 10% SDS-PAGE gel. After electrophoresis, the proteins in the gel were transferred to a PVDF membrane. Then the membrane was blocked in 5% (w/v) skim milk in TBS-T for 1 h and incubated with the primary antibodies at 4 °C overnight. The membrane was washed with TBS-T and incubated with HRP-conjugated secondary antibody for 1 h. Specific proteins were detected using an ECL kit.

Oil red O staining

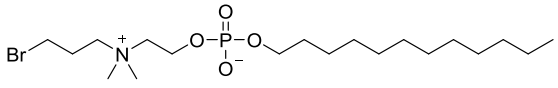
HepG2 cells were grown at an initial density of 2×10^5 cells/well on glass coverslips in 12-well plates and treated with different concentrations of compounds for 48 h. Cells were then washed three times with PBS and fixed with 4% paraformaldehyde for 30 min. After fixation, cells were washed with PBS and stained with freshly diluted Oil Red O working solution (0.5% Oil Red O in isopropanol: H_2O = 3:2) for 1 h at room temperature. Then cells were washed again with PBS several times to remove excess stain. Cell nuclei were stained with haematoxylin for 30 seconds and washed with ddH_2O. The stained samples were observed using a microscope (Leica, DMi8, Germany).

Measurements of cellular triglyceride (TG) content in HepG2 Cells

HepG2 cells were grown at an initial density of 2×10^5 cells/well in a 12-well plate and treated with different concentrations of compounds for 48 h. Cells were washed three times with PBS and were lysed in RIPA buffer, then the supernatant was collected. The intracellular TG levels were measured using enzymatic colorimetric assay kits and the protein concentrations were determined using the bicinchoninic acid (BCA) method. Intracellular TG contents were normalized to cellular protein content. All results were presented as the mean ± SD. Data analysis was performed using the IBM SPSS 22.0 software package for Windows (SPSS, Chicago, IL, USA). Statistical differences were analyzed by one-way ANOVA, followed by Fisher's least significant difference (LSD's) multiple comparison test. Statistical significance was shown as * $p < 0.05$, ** $p < 0.01$, and *** $p < 0.001$.

Reference

1. North, E. J.; Osborne, D. A.; Bridson, P. K.; Baker, D. L.; Parrill, A. L. *Bioorg. Med. Chem*. 2009, **17**, 3433–3442.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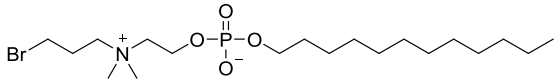

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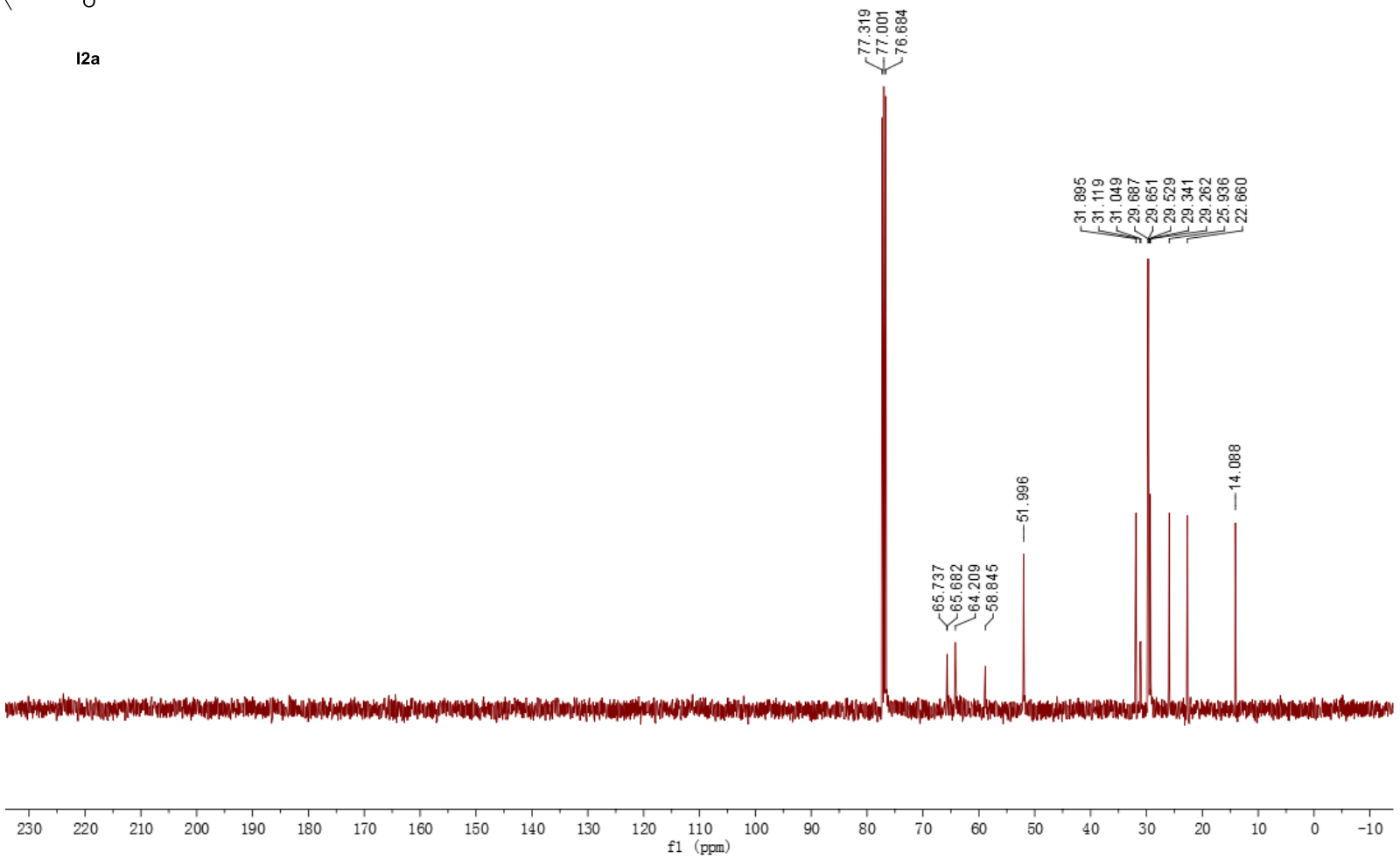
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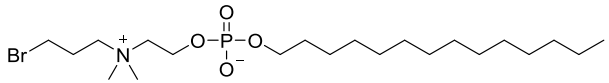

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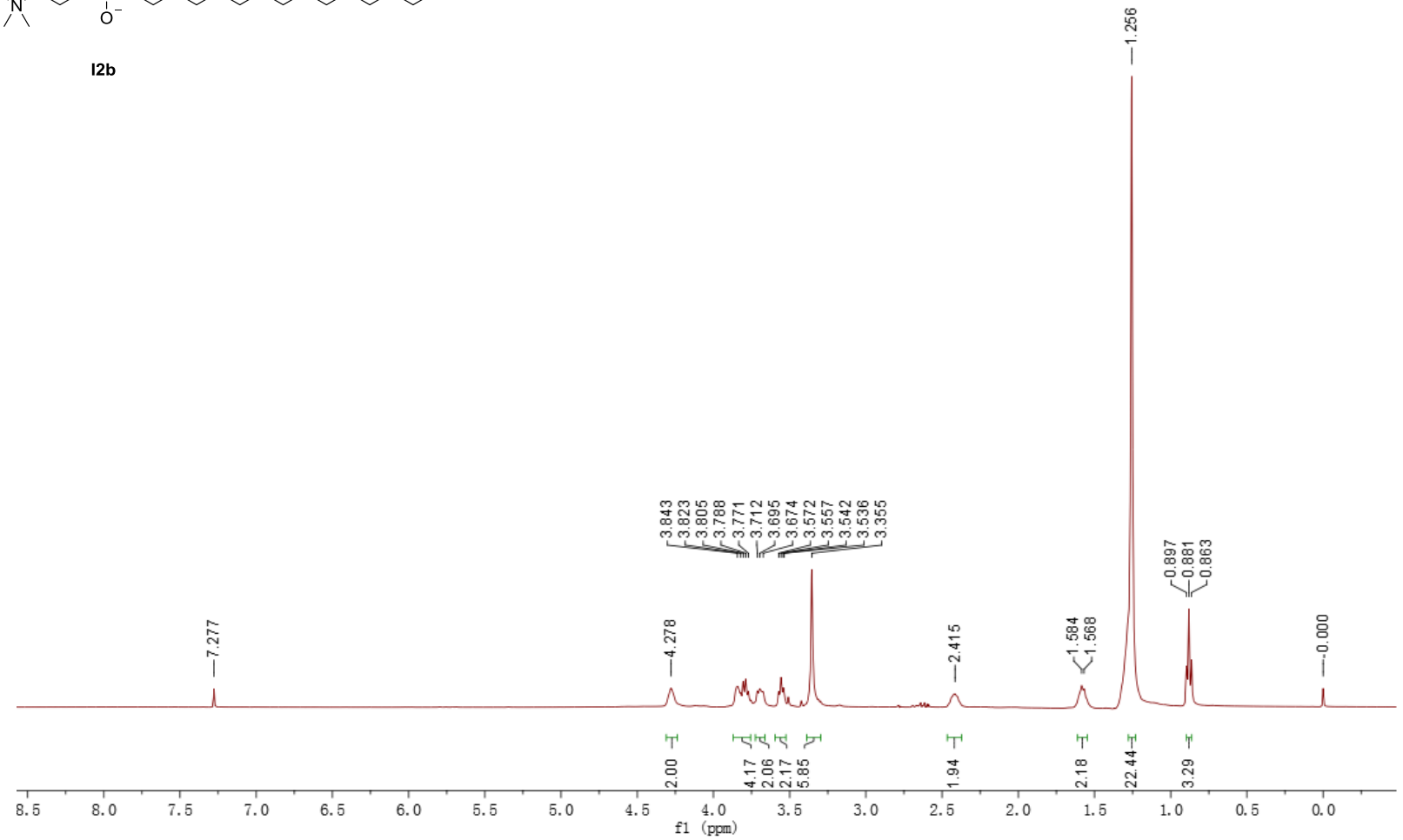
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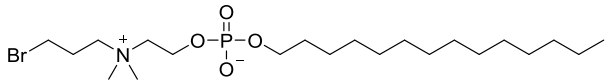
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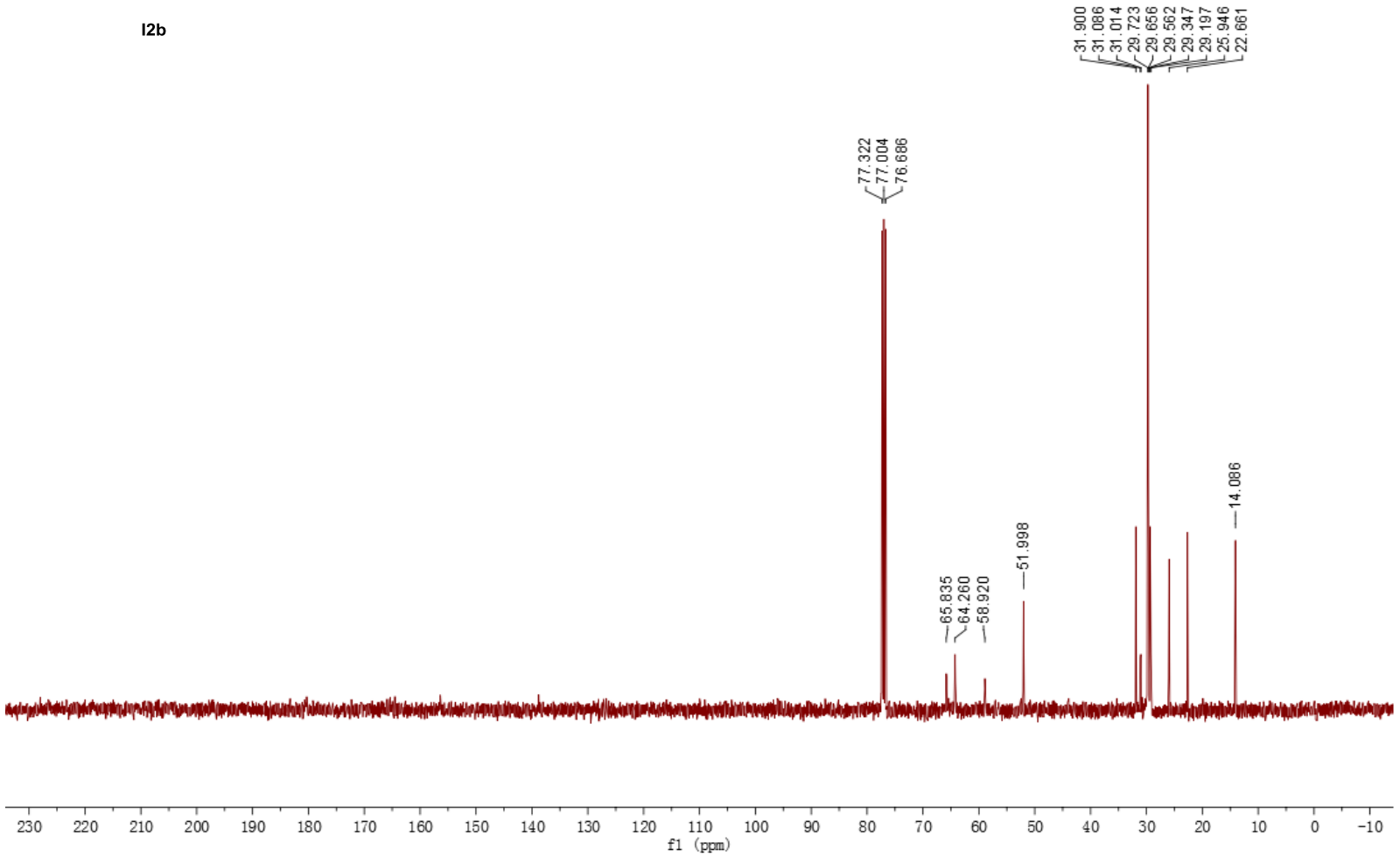
I2b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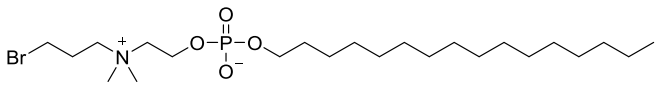
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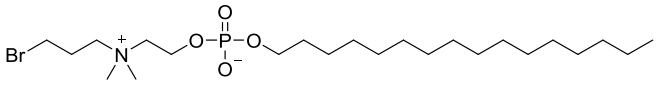
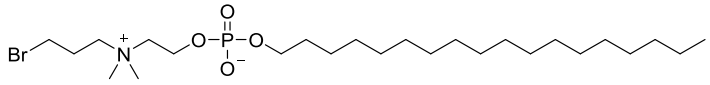
3.00
f1 (ppm)



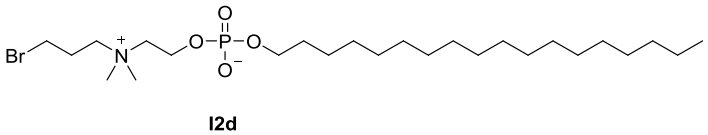
I2c

31.865
31.112
31.040
29.686
29.610
29.522
29.305
29.235
25.925
22.625
77.331
77.013
76.695
65.681
65.621
64.140
58.816
51.927
14.052
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



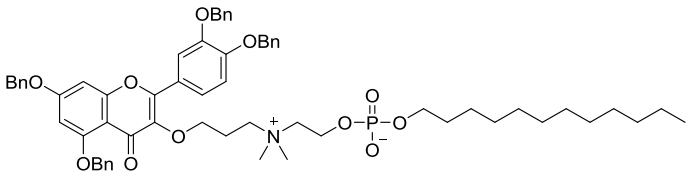
I2d

1.254
3.831
3.815
3.798
3.782
3.723
3.705
3.685
3.566
3.551
3.537
3.363
7.265
4.288
2.413
1.603
1.587
1.570
0.896
0.880
0.863
0.000
1.96
4.05
1.90
1.93
5.71
1.94
2.01
30.00
3.27
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

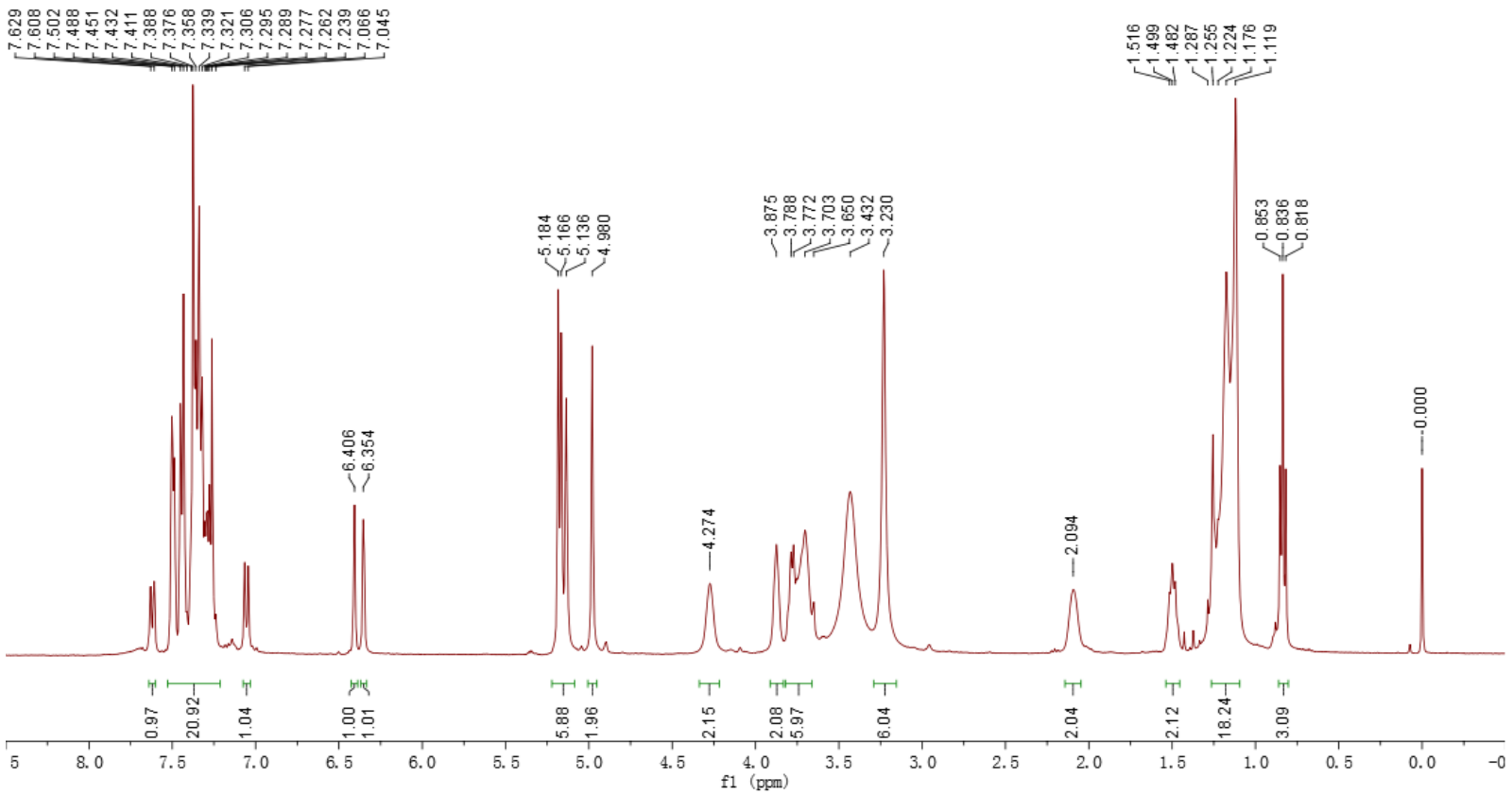

Br
N
O
P
O
O
O

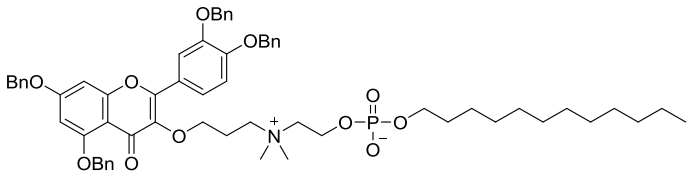
I2d

77.316
76.999
76.681
31.876
31.123
31.052
29.697
29.672
29.617
29.521
29.314
29.254
25.927
22.637
14.062
65.667
65.608
64.180
58.817
51.955
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OBn
OBn
BnO
O
OBn
O
O
O
N
O
P
O
O
O

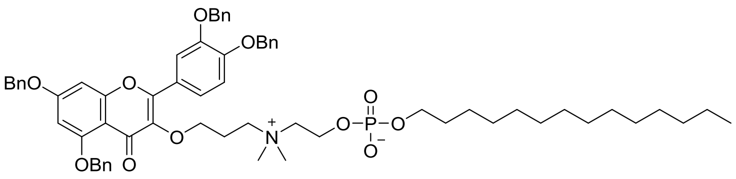
I3a


7.629
7.608
7.502
7.488
7.451
7.432
7.411
7.388
7.376
7.358
7.339
7.321
7.306
7.295
7.289
7.277
7.262
7.239
7.066
7.045
6.406
6.354
5.184
5.166
5.136
4.980
4.274
3.875
3.788
3.772
3.703
3.650
3.432
3.230
2.094
1.516
1.499
1.482
1.287
1.255
1.224
1.176
1.119
0.853
0.836
0.818
0.000
0.97
20.92
1.04
1.00
1.01
5.88
1.96
2.15
2.08
5.97
6.04
2.04
2.12
18.24
3.09
f1 (ppm)


OBn
OBn
BnO
O
O
O
O
P
O
O
N
OBn
O

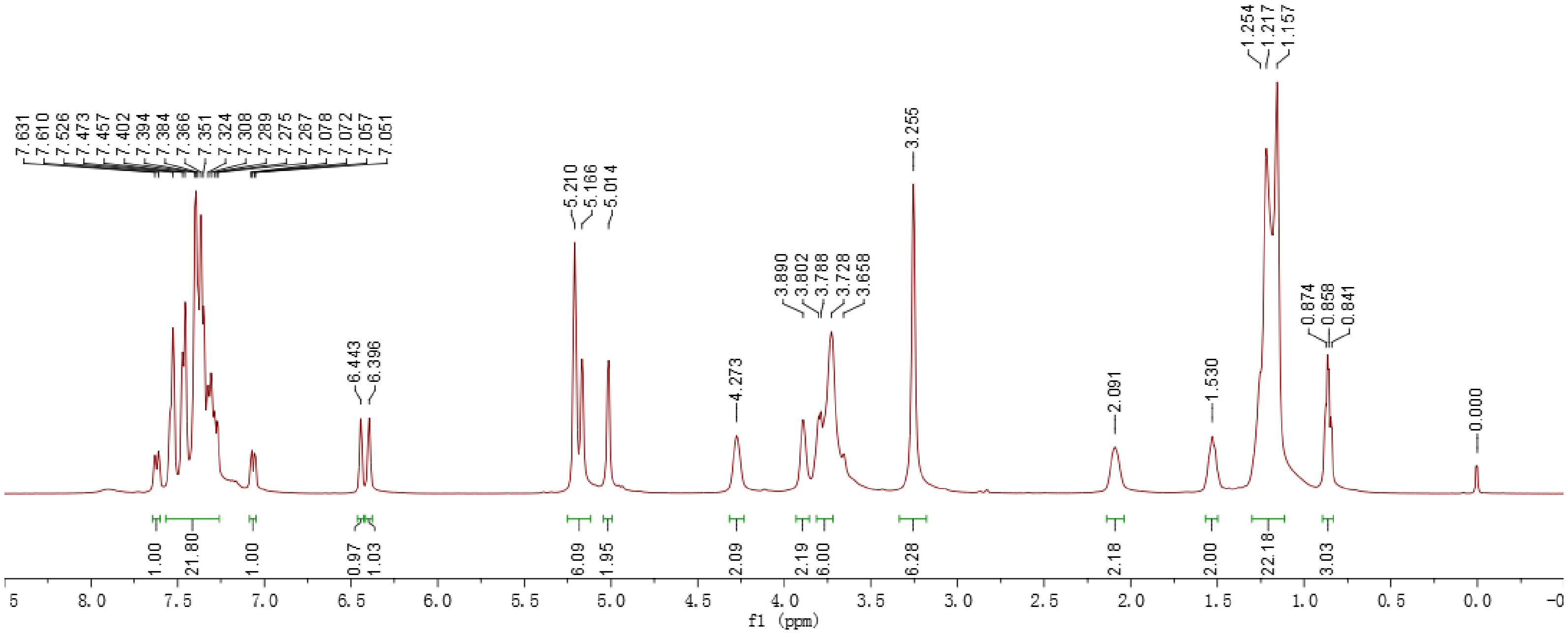
I3a

77.332
77.015
76.697
71.797
70.687
70.395
68.771
65.854
65.806
63.705
58.867
128.715
128.619
128.544
128.427
127.929
127.535
127.359
127.305
126.862
123.100
123.015
173.547
162.812
159.585
158.505
153.081
151.225
148.260
139.714
137.085
136.571
136.169
135.514
115.049
113.859
109.578
97.879
93.685
51.798
31.903
30.932
30.860
29.705
29.526
29.363
25.837
23.776
22.669
14.119
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

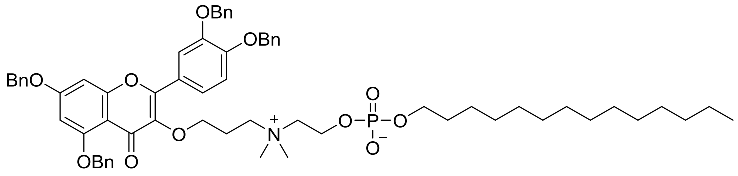


OBn
OBn
BnO
O
O
OBn
O
N
O
P
O
O
O

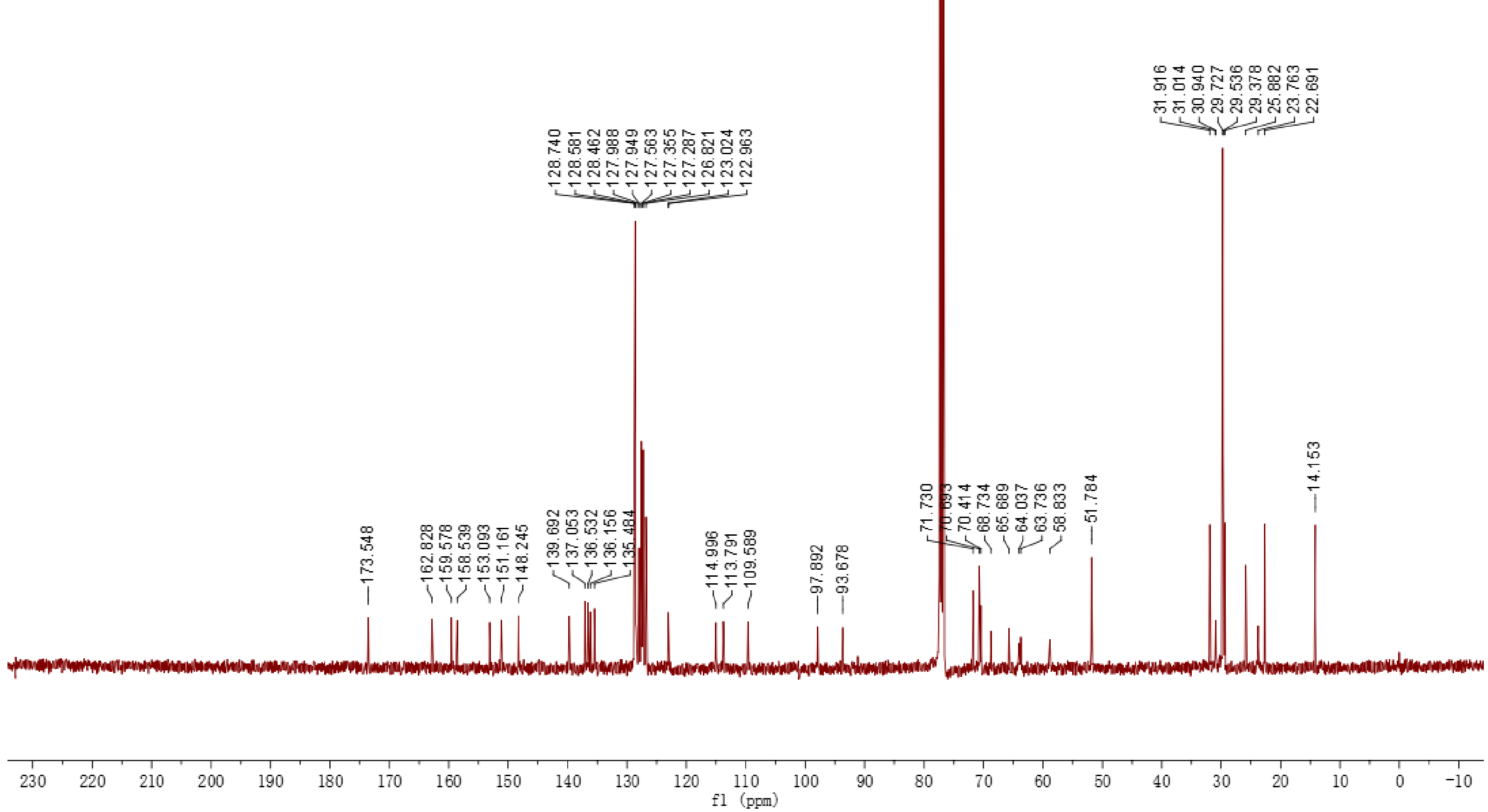
I3b

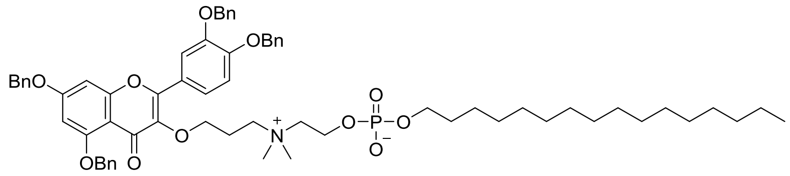


7.631
7.610
7.526
7.473
7.457
7.402
7.394
7.384
7.366
7.351
7.324
7.308
7.289
7.275
7.267
7.078
7.072
7.057
7.051
6.443
6.396
5.210
5.166
5.014
4.273
3.890
3.802
3.788
3.728
3.658
3.255
2.091
1.530
1.254
1.217
1.157
0.874
0.858
0.841
0.000
1.00
21.80
1.00
0.97
1.03
6.09
1.95
2.09
2.19
6.00
6.28
2.18
2.00
22.18
3.03
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

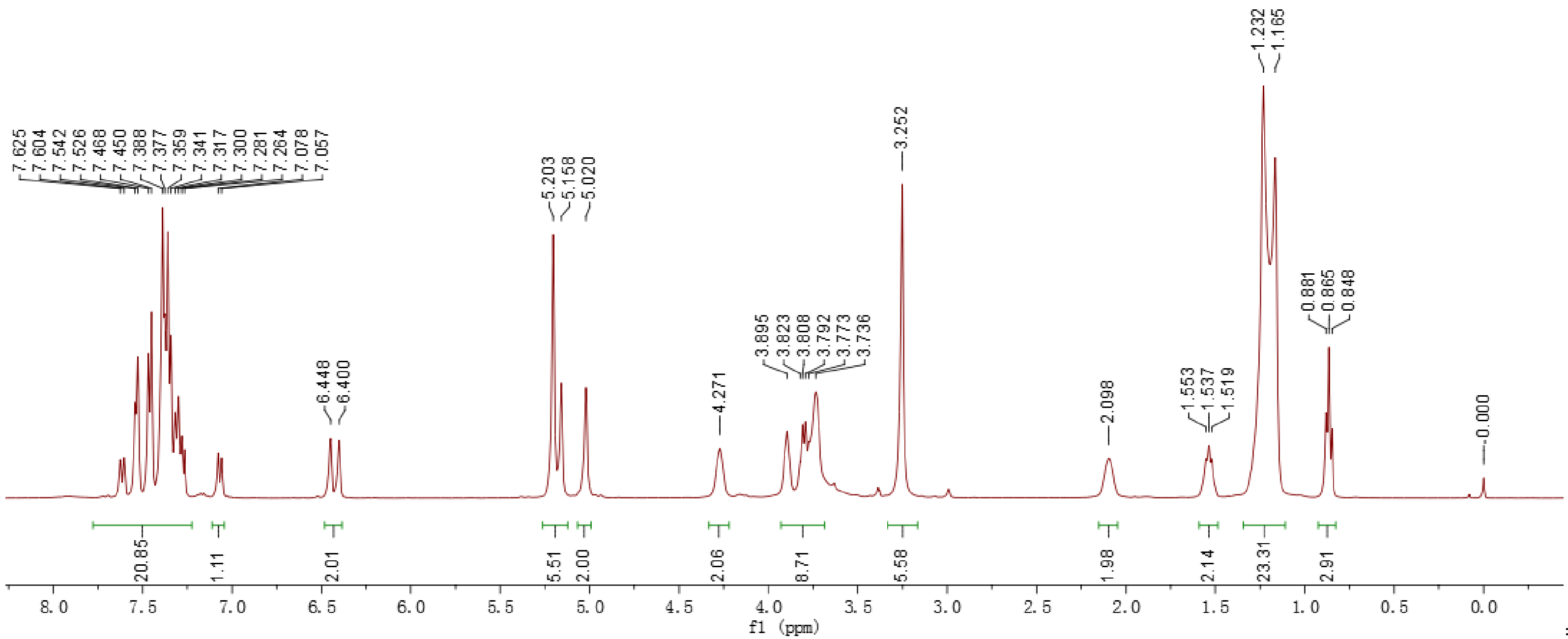

OBn
OBn
BnO
O
O
N
+
O
P
O
O
O
O
−
OBn
O

I3b

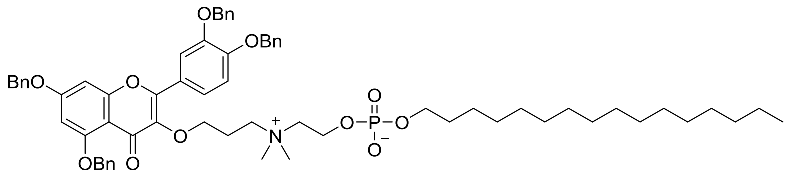

173.548
162.828
159.578
158.539
153.093
151.161
148.245
139.692
137.053
136.532
136.156
135.484
128.740
128.581
128.462
127.988
127.949
127.563
127.355
127.287
126.821
123.024
122.963
114.996
113.791
109.589
97.892
93.678
71.730
70.693
70.414
68.734
65.689
64.037
63.736
58.833
51.784
31.916
31.014
30.940
29.727
29.536
29.378
25.882
23.763
22.691
14.153
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)



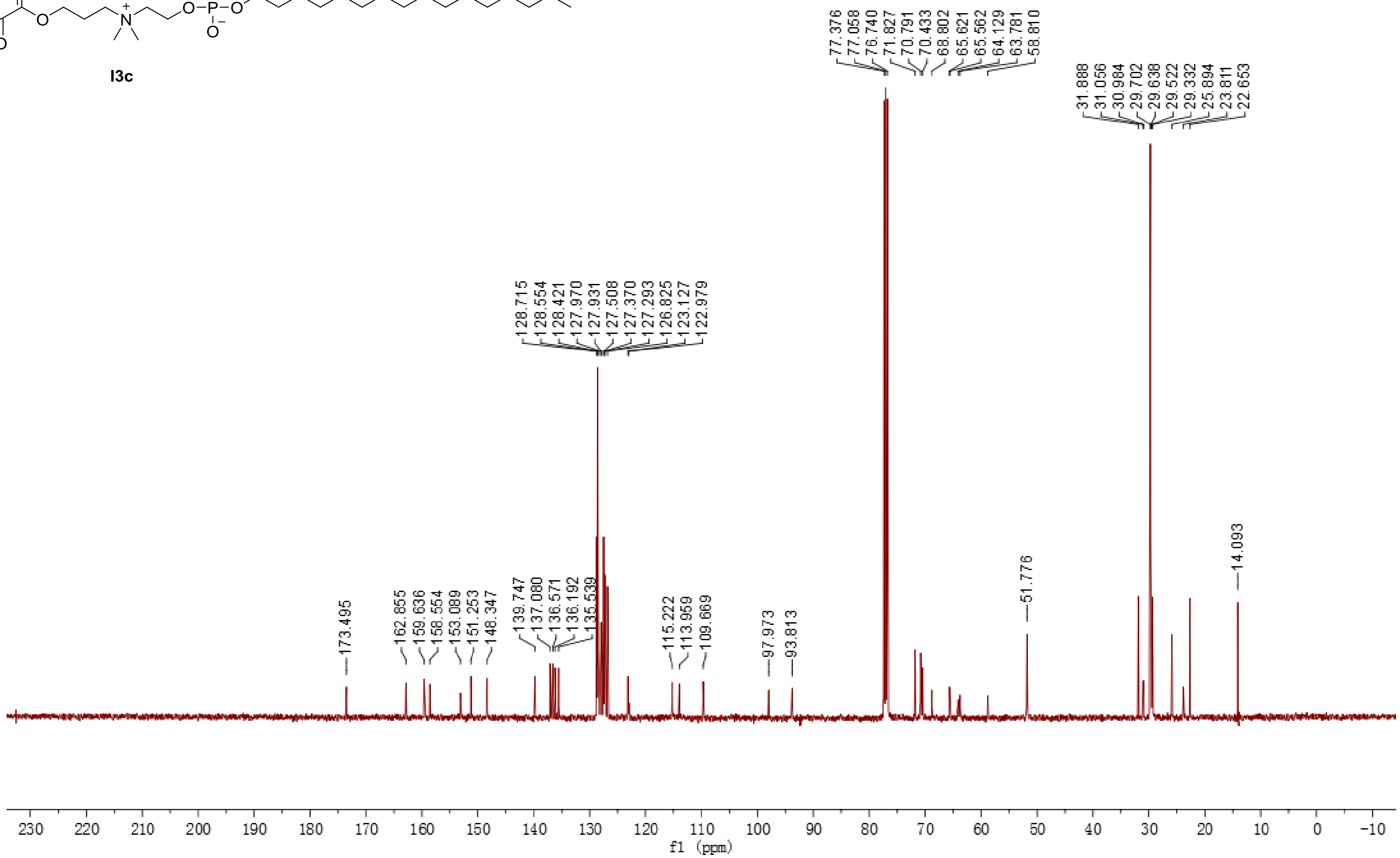
I3c

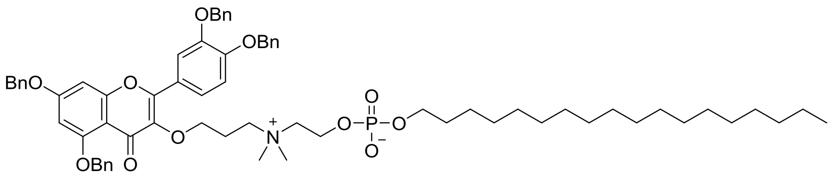


7.625
7.604
7.542
7.526
7.468
7.450
7.388
7.377
7.359
7.341
7.317
7.300
7.281
7.264
7.078
7.057
6.448
6.400
5.203
5.158
5.020
4.271
3.895
3.823
3.808
3.792
3.773
3.736
3.252
2.098
1.553
1.537
1.519
1.232
1.165
0.881
0.865
0.848
0.000
20.85
1.11
2.01
5.51
2.00
2.06
8.71
5.58
1.98
2.14
23.31
2.91
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

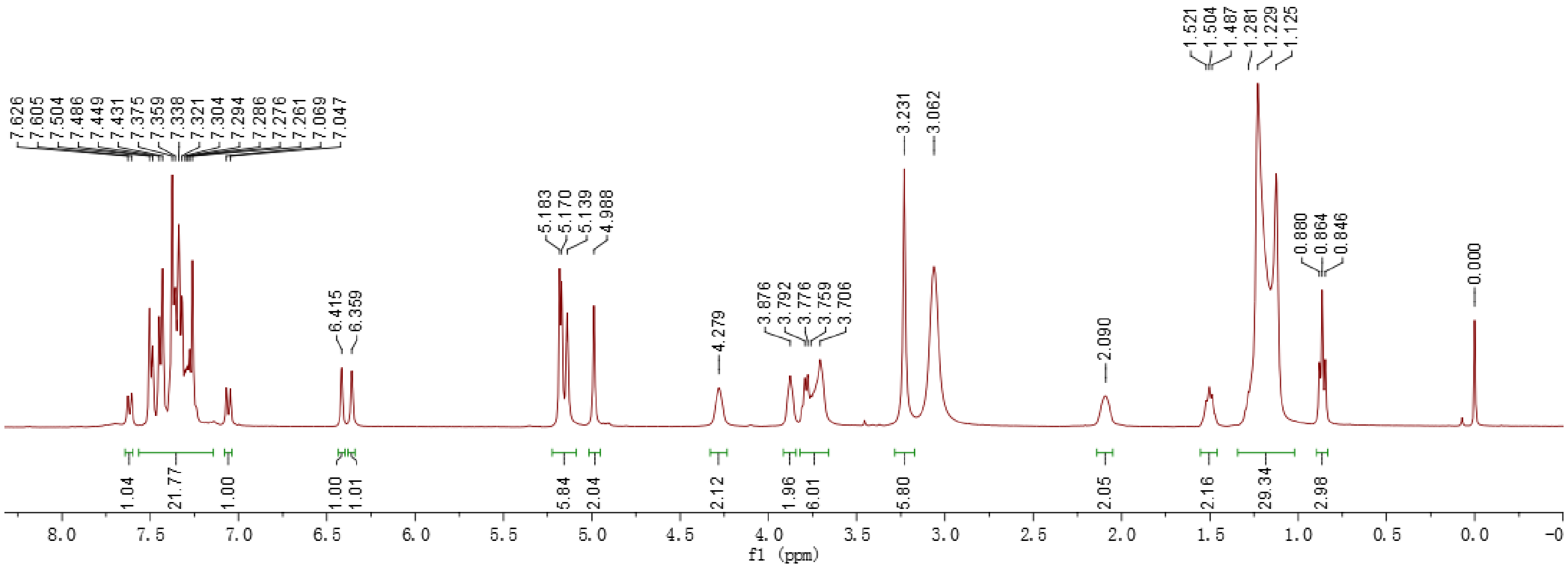

OBn
OBn
BnO
OBn
O
O
O
O
N
O
P
O
O
O

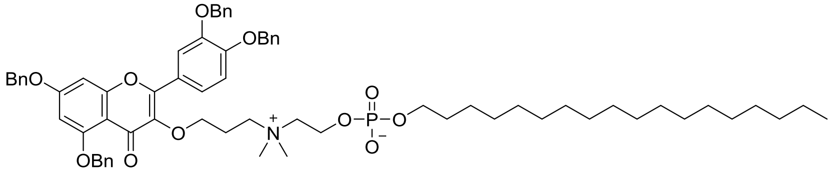
I3c


77.376
77.058
76.740
71.827
70.791
70.433
68.802
65.621
65.562
64.129
63.781
58.810
31.888
31.056
30.984
29.702
29.638
29.522
29.332
25.894
23.811
22.653
128.715
128.554
128.421
127.970
127.931
127.508
127.370
127.293
126.825
123.127
122.979
173.495
162.855
159.636
158.554
153.089
151.253
148.347
139.747
137.080
136.571
136.192
135.539
115.222
113.959
109.669
97.973
93.813
51.776
14.093
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

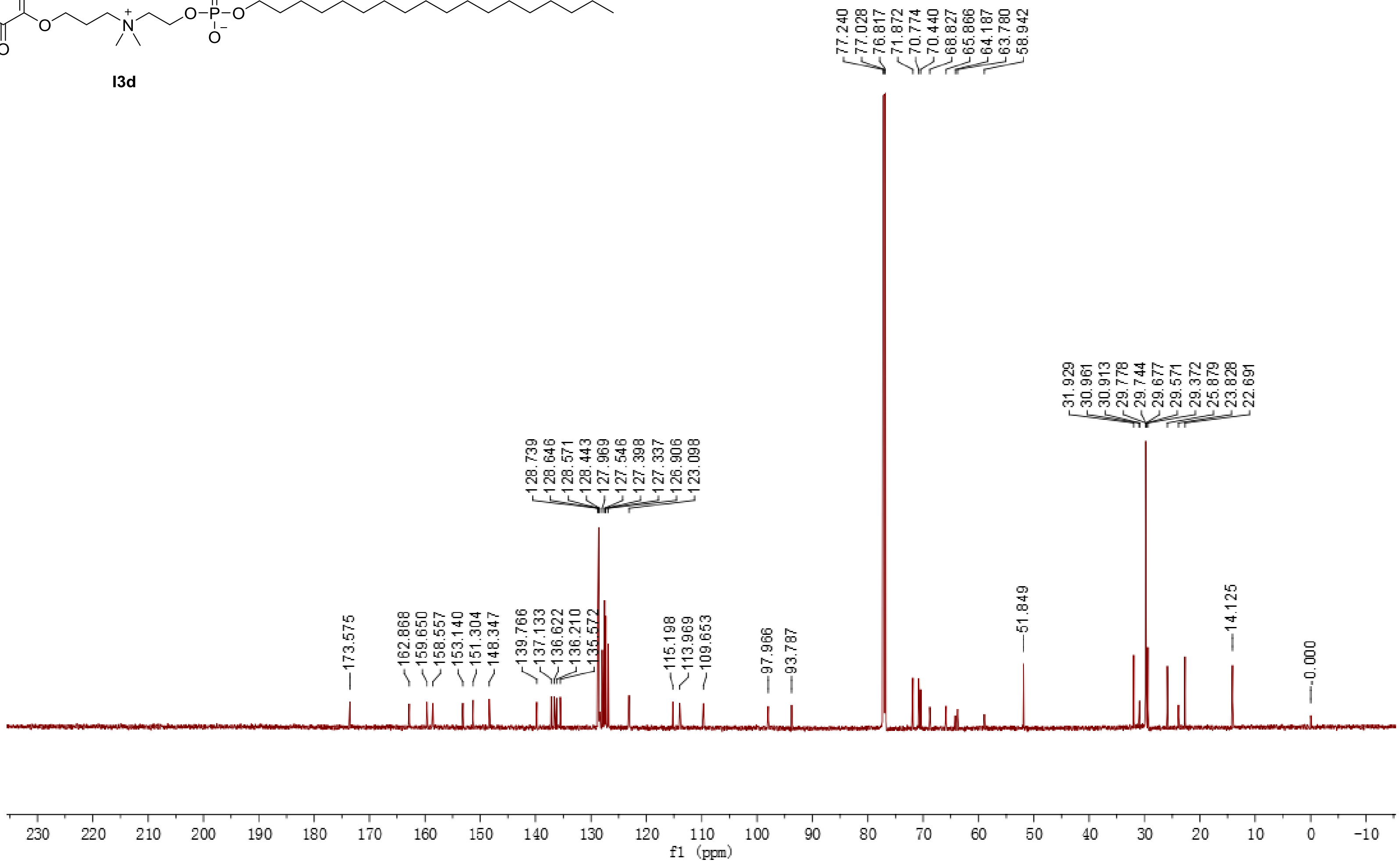

OBn
OBn
BnO
O
OBn
O
O
N
O
P
O
O

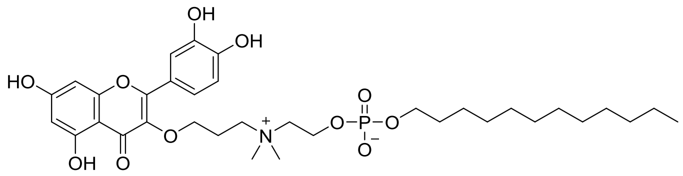
I3d


7.626
7.605
7.504
7.486
7.449
7.431
7.375
7.359
7.338
7.321
7.304
7.294
7.286
7.276
7.261
7.069
7.047
6.415
6.359
5.183
5.170
5.139
4.988
4.279
3.876
3.792
3.776
3.759
3.706
3.231
3.062
2.090
1.521
1.504
1.487
1.281
1.229
1.125
0.880
0.864
0.846
0.000
1.04
21.77
1.00
1.00
1.01
5.84
2.04
2.12
1.96
6.01
5.80
2.05
2.16
29.34
2.98
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

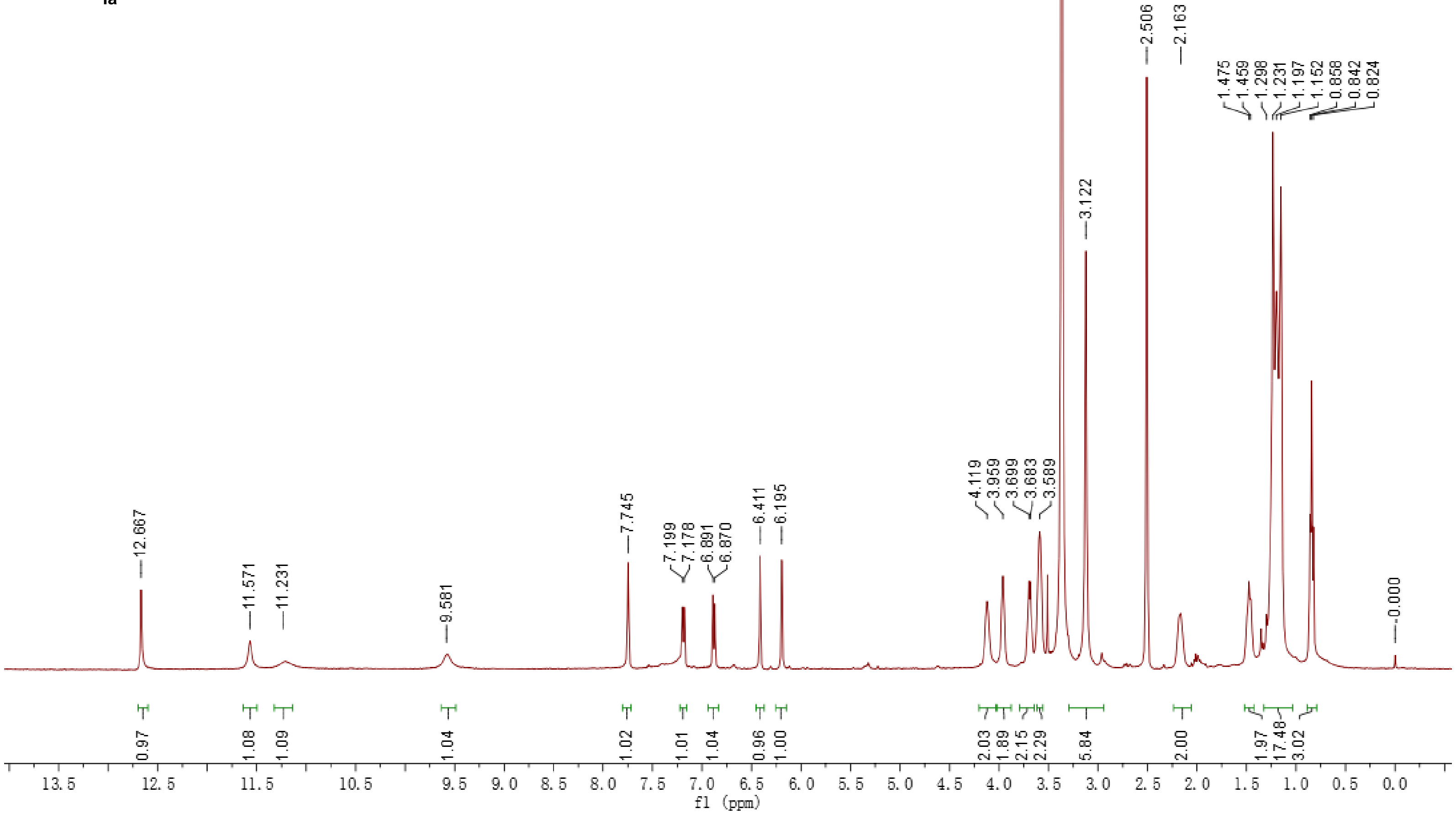

OBn
OBn
BnO
O
O
N
O
P
O
O
O
OBn
O

I3d


77.240
77.028
76.817
71.872
70.774
70.440
68.827
65.866
64.187
63.780
58.942
31.929
30.961
30.913
29.778
29.744
29.677
29.571
29.372
25.879
23.828
22.691
128.739
128.646
128.571
128.443
127.969
127.546
127.398
127.337
126.906
123.098
173.575
162.868
159.650
158.557
153.140
151.304
148.347
139.766
137.133
136.622
136.210
135.572
115.198
113.969
109.653
97.966
93.787
51.849
14.125
-0.000
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



Ia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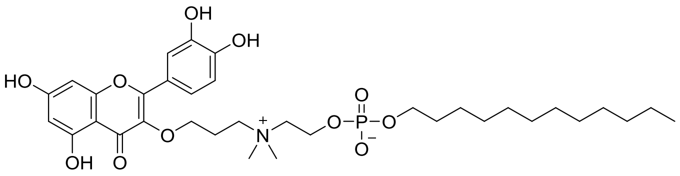
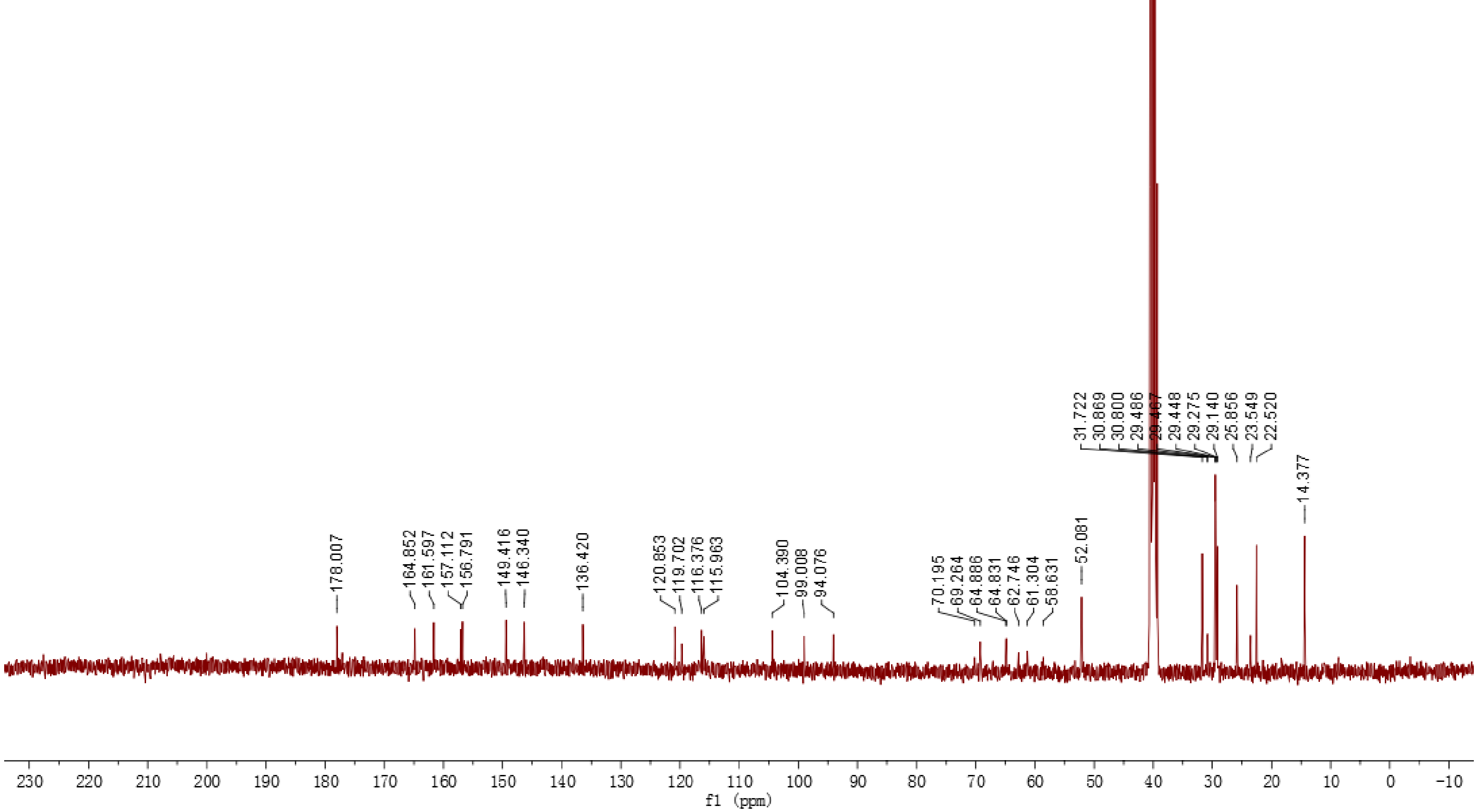
11.231
9.581
7.745
7.199
7.178
6.891
6.870
6.411
6.195
4.119
3.959
3.699
3.683
3.589
3.122
2.506
2.163
1.475
1.459
1.298
1.231
1.197
1.152
0.858
0.842
0.824
-0.000
0.97
1.08
1.09
1.04
1.02
1.01
1.04
0.96
1.00
2.03
1.89
2.15
2.29
5.84
2.00
1.97
17.48
3.02
13.5 12.5 11.5 10.5 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)


OH
OH
HO
O
O
N
O
P
O
O
O
OH
O

Ia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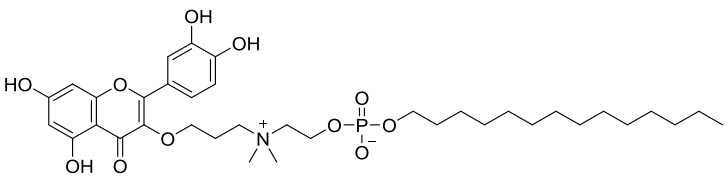
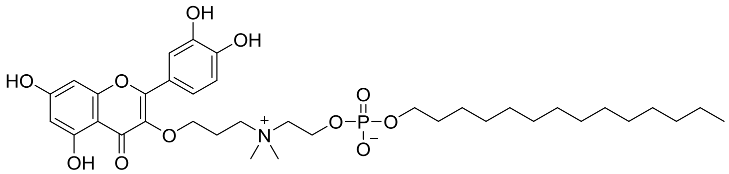
161.597
157.112
156.791
149.416
146.340
136.420
120.853
119.702
116.376
115.963
104.390
99.008
94.076
70.195
69.264
64.886
64.831
62.746
61.304
58.631
52.081
31.722
30.869
30.800
29.486
29.467
29.448
29.275
29.140
25.856
23.549
22.520
14.377
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

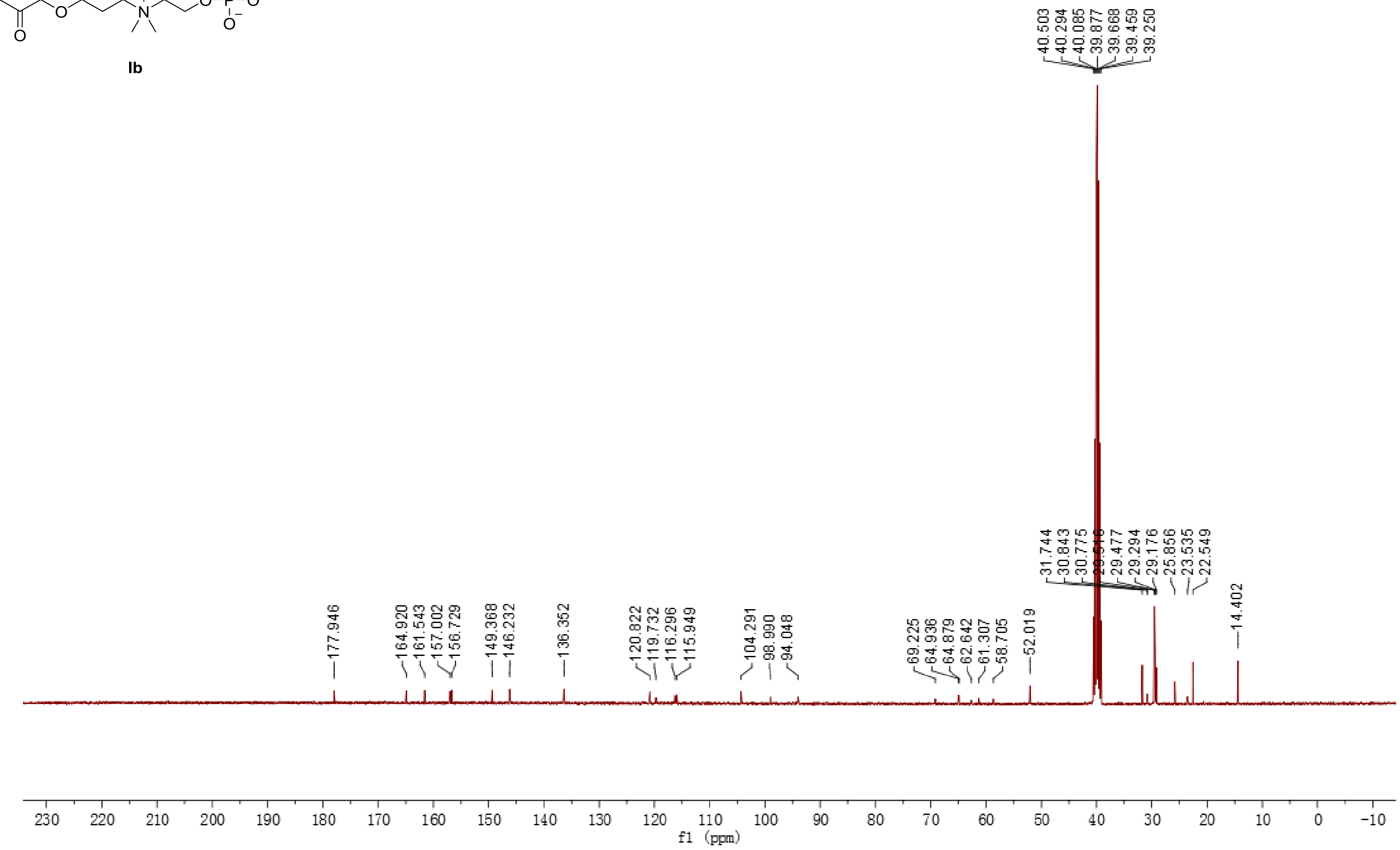

OH
OH
HO
O
O
OH
O
N+
O
P
O
O
O-

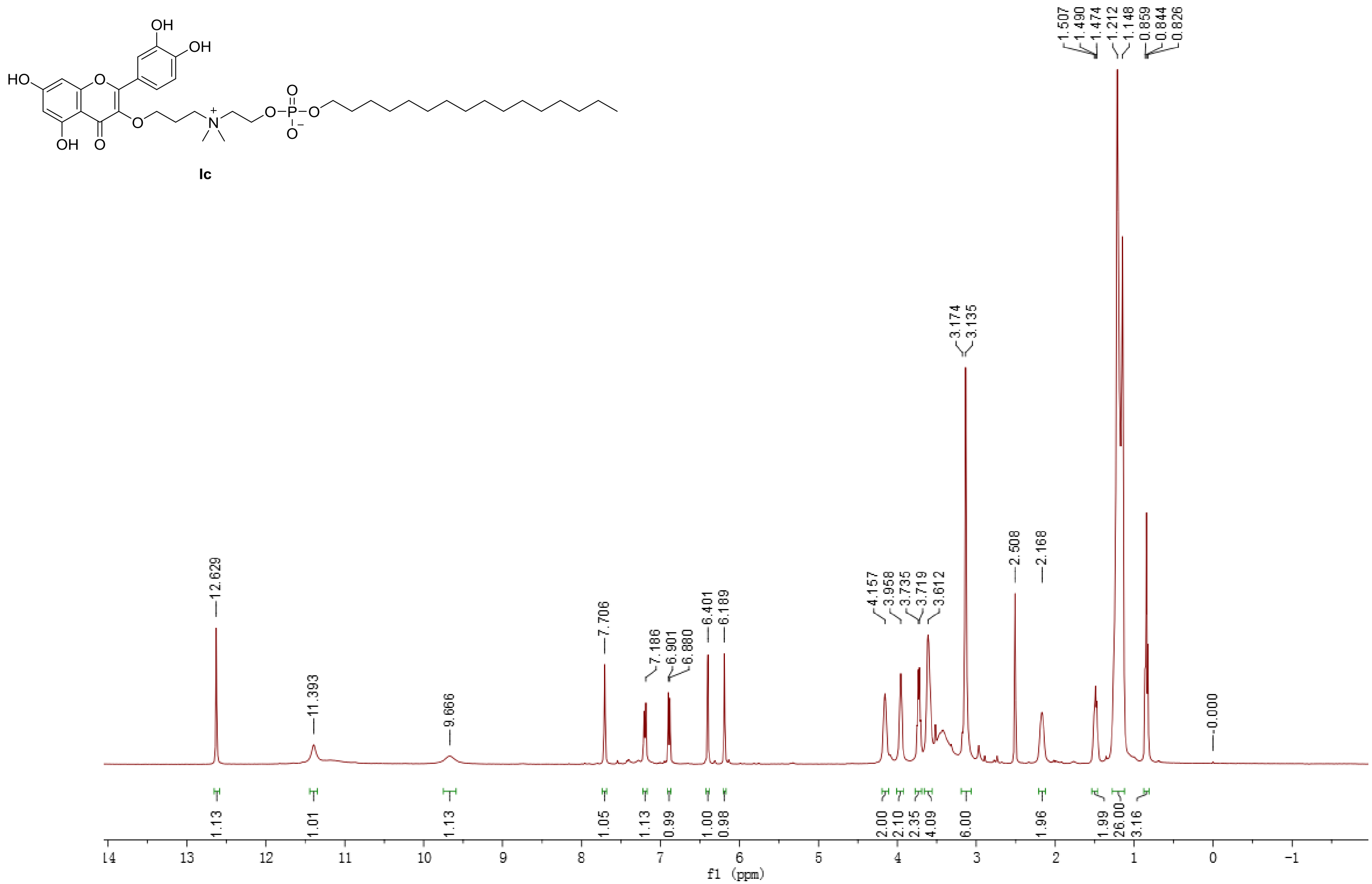
Ib

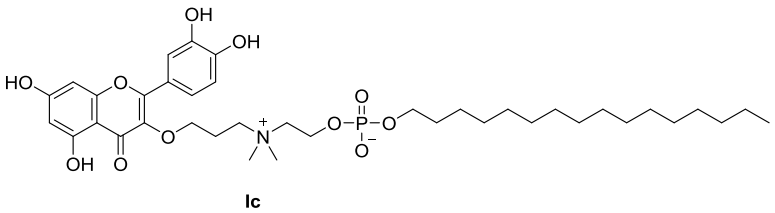
12.684
11.714
10.999
9.496
7.758
7.204
7.184
6.890
6.869
6.414
6.191
4.107
3.969
3.704
3.689
3.672
3.656
3.578
3.322
3.114
2.502
2.172
1.471
1.455
1.220
1.156
0.864
0.849
0.832
0.000
1.13
1.04
1.17
1.22
1.00
1.11
0.99
0.96
1.02
1.99
1.99
2.07
3.72
5.14
2.01
2.10
20.78
2.87
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



Ib

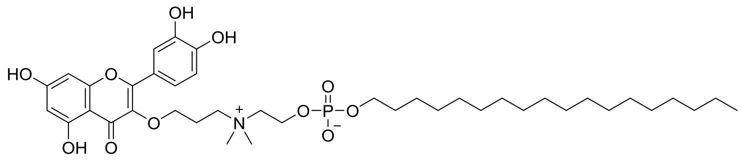

40.503
40.294
40.085
39.877
39.668
39.459
39.250
177.946
164.920
161.543
157.002
156.729
149.368
146.232
136.352
120.822
119.732
116.296
115.949
104.291
98.990
94.048
69.225
64.936
64.879
62.642
61.307
58.705
52.019
31.744
30.843
30.775
29.477
29.294
29.176
25.856
23.535
22.549
14.402
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OH
OH
HO
O
O
O
O
P
O
O
N
OH
O
Ic
1.507
1.490
1.474
1.212
1.148
0.859
0.844
0.826
3.174
3.135
2.508
2.168
12.629
11.393
9.666
7.706
7.186
6.901
6.880
6.401
6.189
4.157
3.958
3.735
3.719
3.612
-0.000
1.13
1.01
1.13
1.05
1.13
0.99
1.00
0.98
2.00
2.10
2.35
4.09
6.00
1.96
1.99
26.00
3.16
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

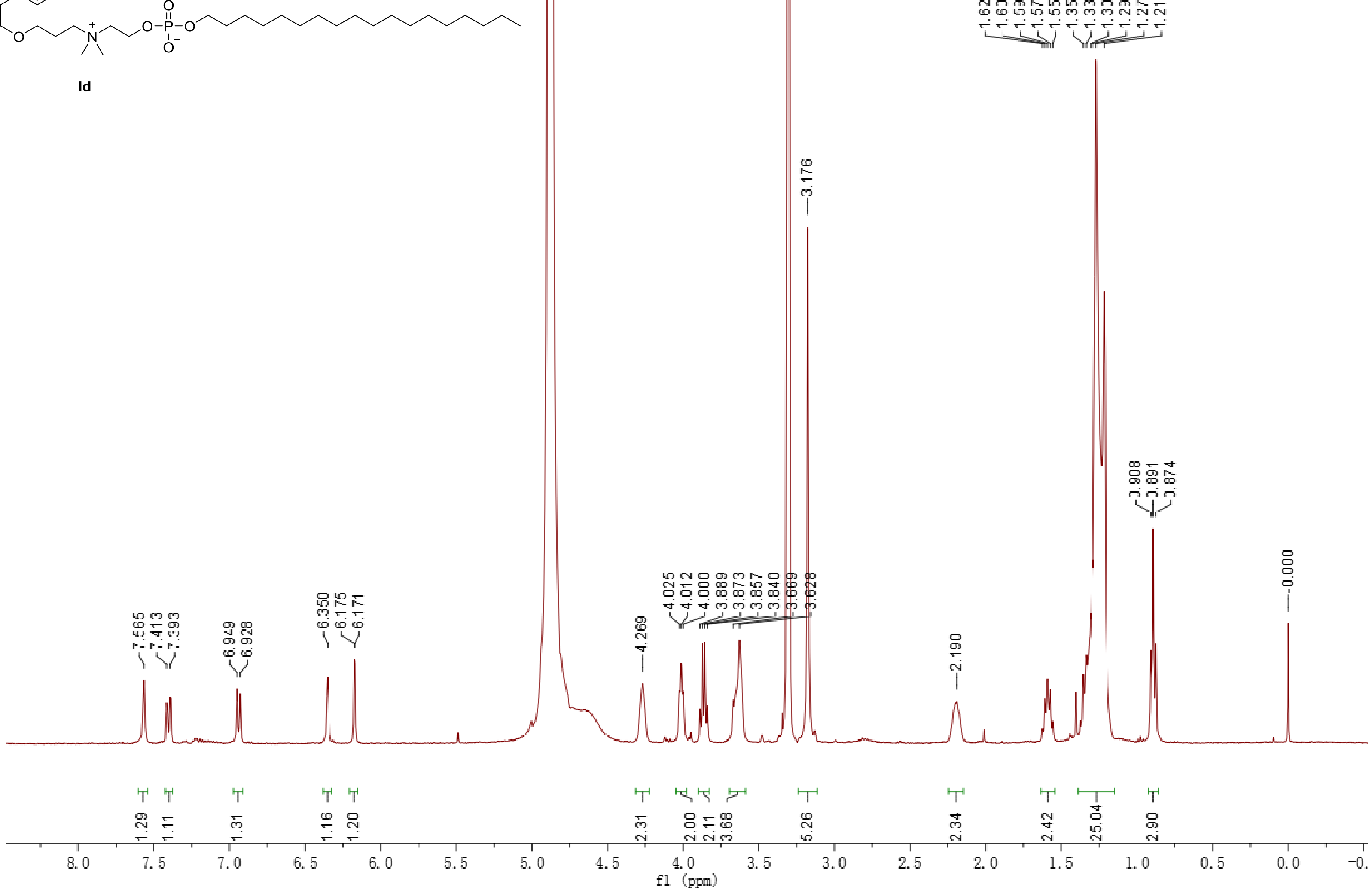

OH
OH
HO
O
OH
O
O
N
O
P
O
O
O

Ic

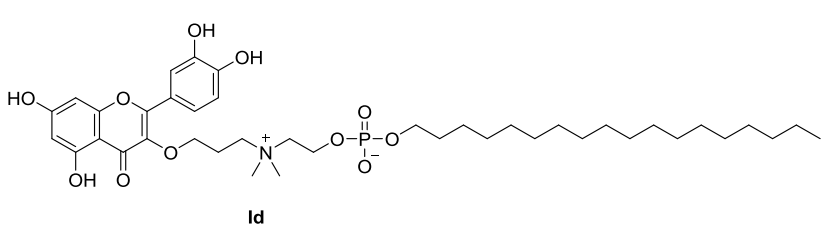
40.587
40.379
40.170
39.752
39.544
39.335
30.833
30.765
29.488
29.278
29.141
25.830
23.563
22.521
177.998
164.933
161.588
156.989
156.773
149.395
146.222
136.452
120.872
119.882
116.313
116.014
104.362
99.030
94.063
69.268
65.074
65.016
62.894
61.577
58.776
51.948
14.358
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



Id



7.565
7.413
7.393
6.949
6.928
6.350
6.175
6.171
4.269
4.025
4.012
4.000
3.889
3.873
3.857
3.840
3.669
3.628
3.176
2.190
1.625
1.609
1.591
1.572
1.556
1.353
1.334
1.304
1.295
1.271
1.216
0.908
0.891
0.874
0.000
1.29
1.11
1.31
1.16
1.20
2.31
2.00
2.11
3.68
5.26
2.34
2.42
25.04
2.90
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.
f1 (ppm)


OH
OH
HO
O
O
OH
O
N
O
P
O
O
O

Id

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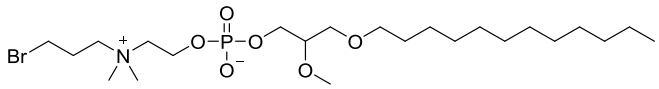
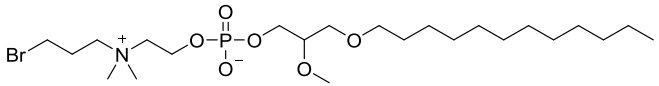
161.634
156.885
156.798
149.374
146.063
136.632
120.905
120.406
116.145
104.497
99.045
94.091
69.326
65.870
62.978
61.969
59.281
51.692
31.719
30.582
30.538
29.469
29.432
29.192
29.130
25.669
23.567
22.520
14.377
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



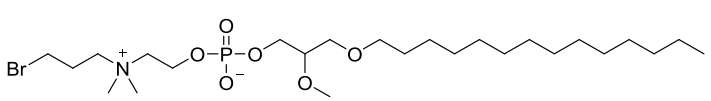
II2a

7.268
4.332
2.868
2.419
1.547
1.532
1.257
0.897
0.881
0.865
0.000
3.968
3.953
3.941
3.896
3.884
3.869
3.853
3.845
3.723
3.706
3.686
3.576
3.561
3.552
3.535
3.490
3.452
3.428
3.411
3.393
3.359
2.04
4.24
2.14
5.91
6.00
2.14
1.92
1.83
18.44
3.00
f1 (ppm)


Br
N
O
P
O
O
O
O

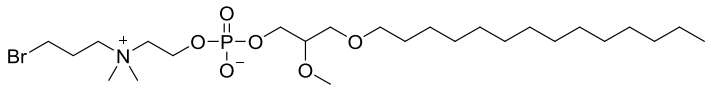
II2a

31.891
29.669
29.636
29.529
29.335
26.062
25.905
22.662
14.103
79.599
79.522
71.788
70.100
65.051
64.285
58.977
57.790
51.979
f1 (ppm)



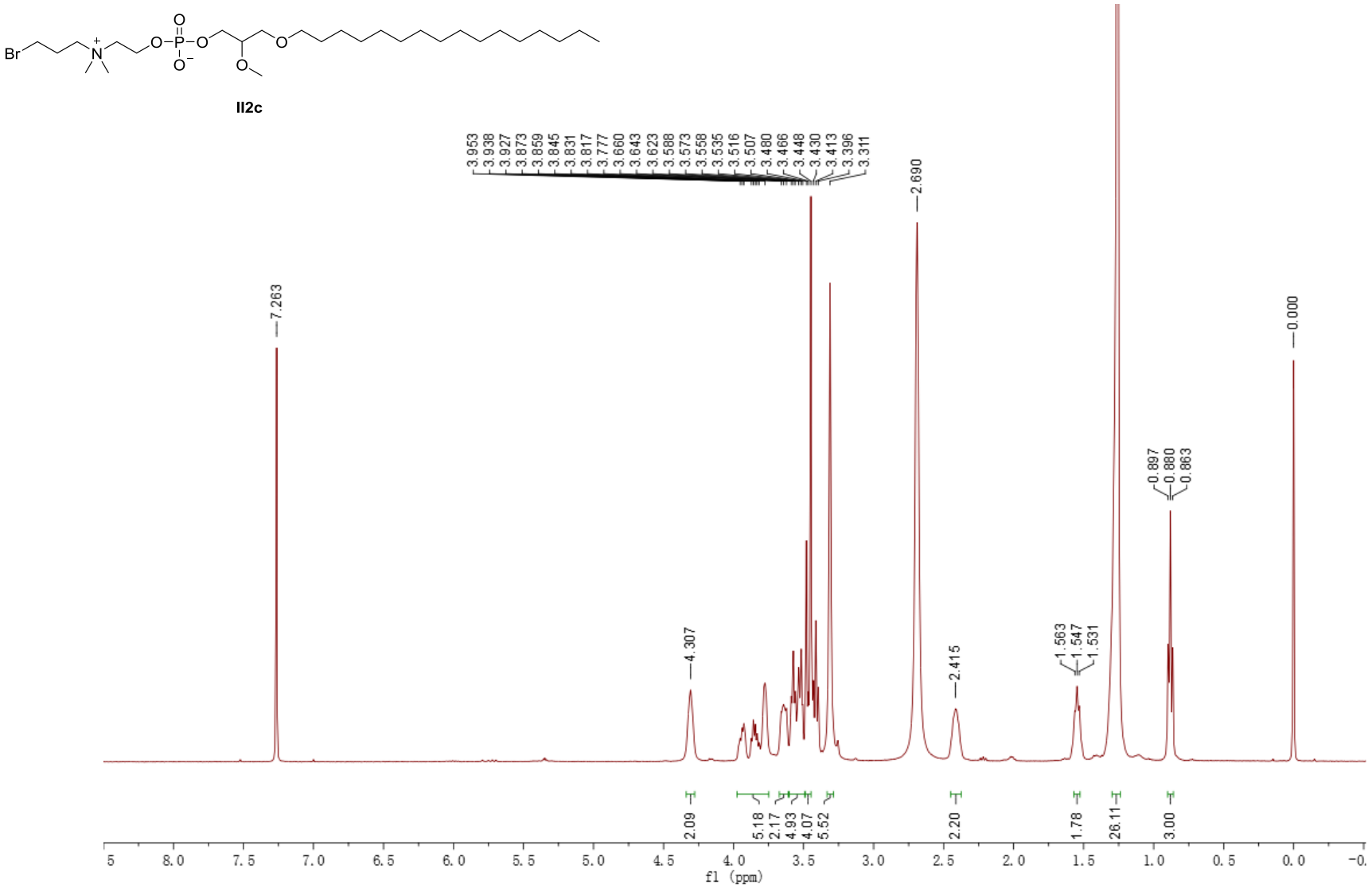
II2b

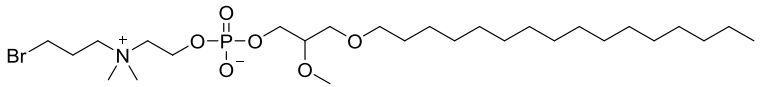
7.262
3.964
3.951
3.938
3.927
3.896
3.882
3.854
3.724
3.707
3.686
3.572
3.558
3.547
3.530
3.488
3.471
3.427
3.410
3.393
3.358
4.334
2.853
2.420
1.559
1.544
1.528
1.256
0.896
0.880
0.863
0.000
1.71
4.14
1.66
3.99
1.66
1.88
4.64
0.28
2.49
1.77
22.37
3.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



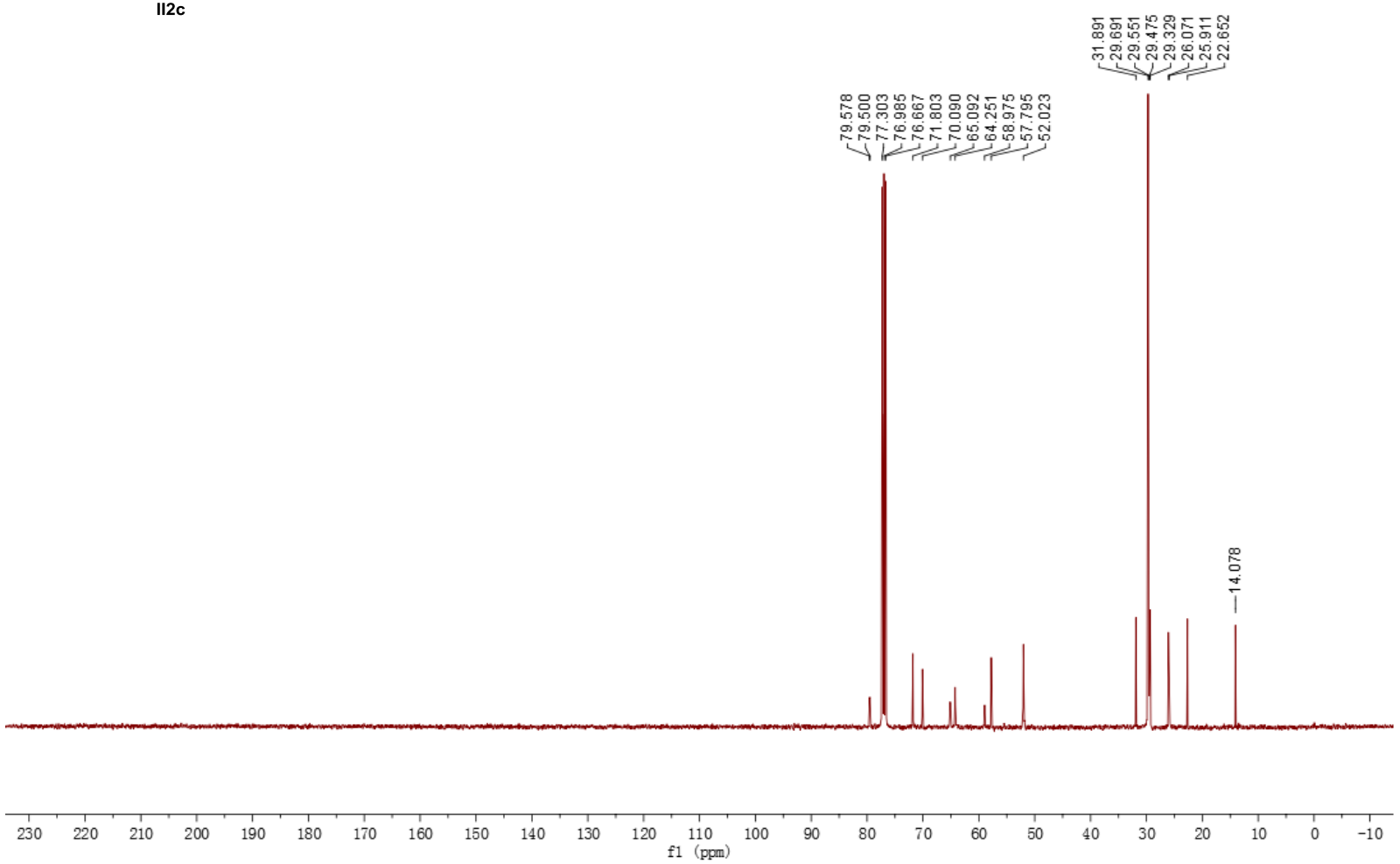
II2b

31.879
29.624
29.516
29.319
26.058
25.896
22.644
14.075
71.779
70.206
65.014
64.320
58.887
57.775
51.946
79.685
79.607
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
O
O
P
O
O
O
O
O
+
N
−
II2c
3.953
3.938
3.927
3.873
3.859
3.845
3.831
3.817
3.777
3.660
3.643
3.623
3.588
3.573
3.558
3.535
3.516
3.507
3.480
3.466
3.448
3.430
3.413
3.396
3.311
7.263
4.307
2.690
2.415
1.563
1.547
1.531
0.897
0.880
0.863
0.000
2.09
5.18
2.17
4.93
4.07
5.52
2.20
1.78
26.11
3.00
5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



II2c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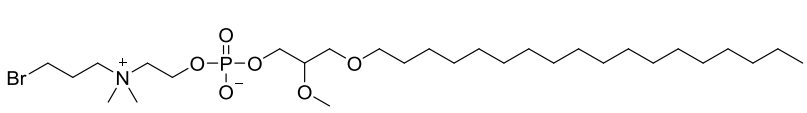
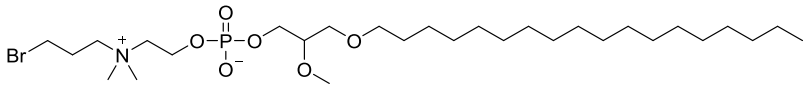
79.500
77.303
76.985
76.667
71.803
70.090
65.092
64.251
58.975
57.795
52.023
31.891
29.691
29.551
29.475
29.329
26.071
25.911
22.652
14.078
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


Br
N
O
P
O
O
O
O
O

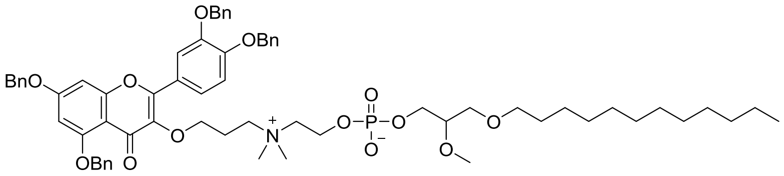
Il2d

7.268
4.332
3.968
3.953
3.941
3.896
3.884
3.869
3.853
3.845
3.723
3.706
3.686
3.576
3.561
3.552
3.535
3.490
3.452
3.428
3.411
3.393
3.359
2.868
2.419
1.547
1.532
1.257
0.897
0.881
0.865
0.000
2.04
4.24
2.14
5.91
6.00
2.14
1.92
1.83
18.44
3.00
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)

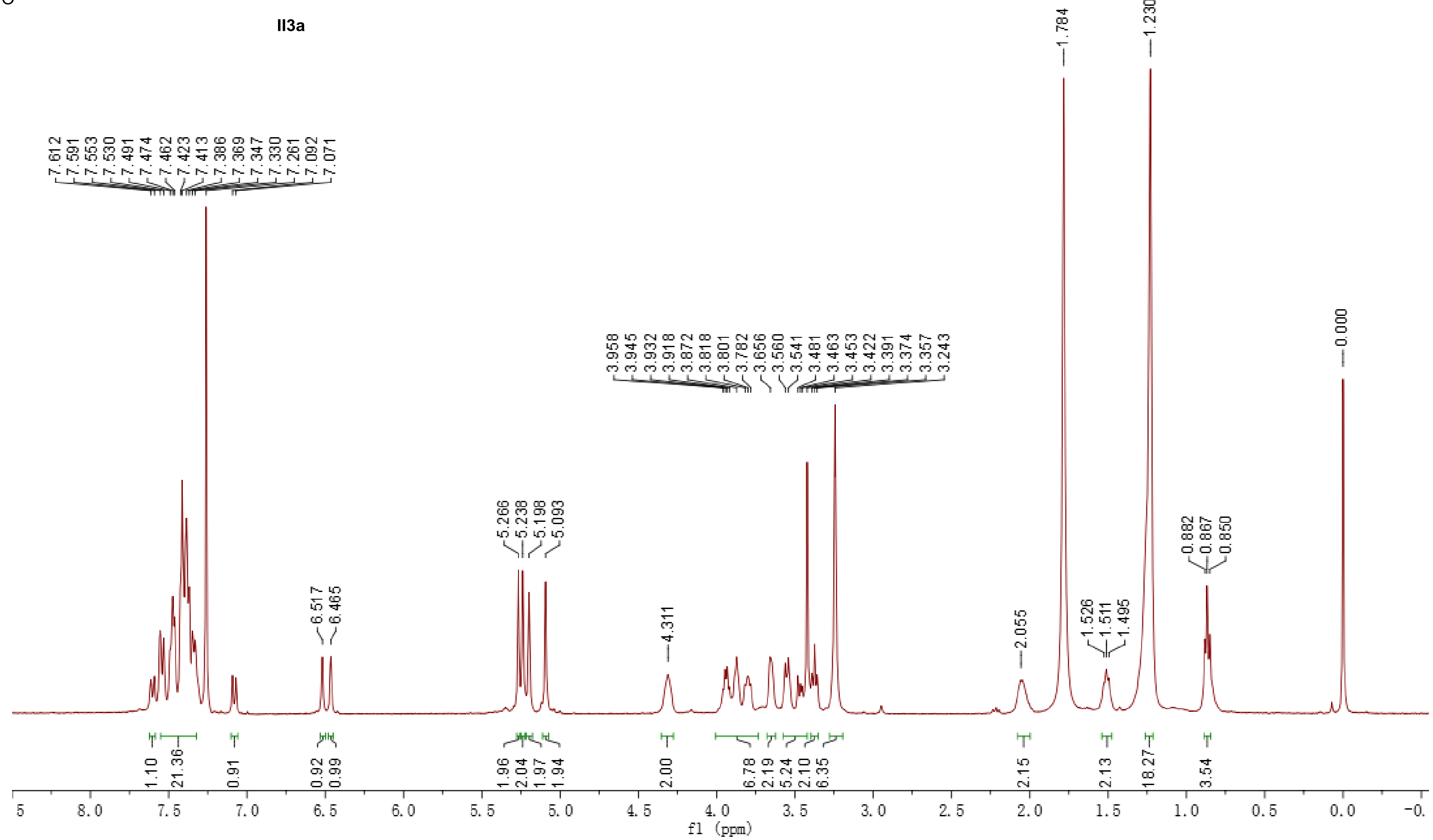


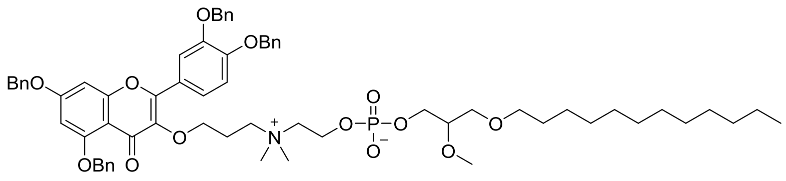
II2d

79.407
79.329
77.309
76.674
71.764
70.044
65.148
59.633
57.751
52.050
31.889
29.706
29.658
29.574
29.329
26.071
22.645
43.431
14.062
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

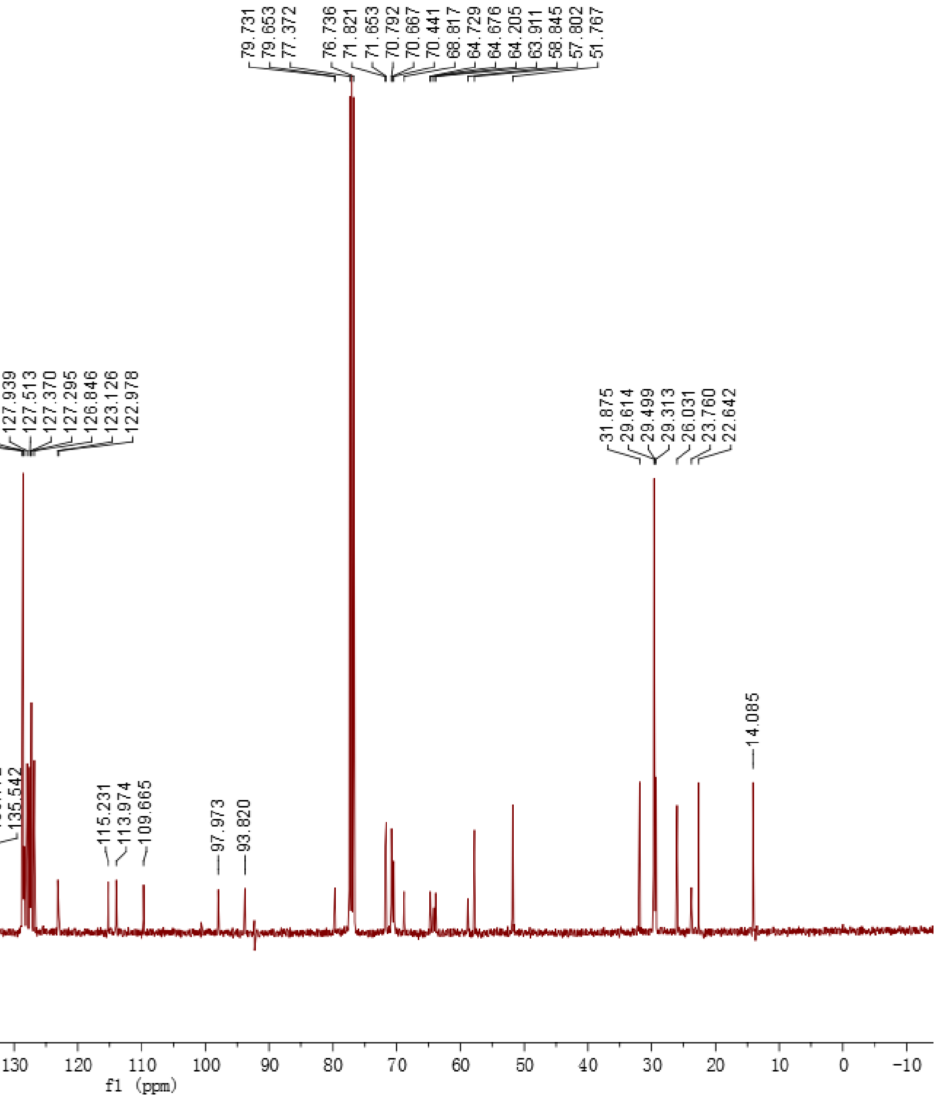

OBn
OBn
BnO
O
O
OBn
O
N
O
P
O
O
O
O
O
O

II3a


1.784
1.230
7.612
7.591
7.553
7.530
7.491
7.474
7.462
7.423
7.413
7.386
7.369
7.347
7.330
7.261
7.092
7.071
3.958
3.945
3.932
3.918
3.872
3.818
3.801
3.782
3.656
3.560
3.541
3.481
3.463
3.453
3.422
3.391
3.374
3.357
3.243
0.000
5.266
5.238
5.198
5.093
0.882
0.867
0.850
6.517
6.465
4.311
2.055
1.526
1.511
1.495
1.10
21.36
0.91
0.92
0.99
1.96
2.04
1.97
1.94
2.00
6.78
2.19
5.24
2.10
6.35
2.15
2.13
18.27
3.54
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


OBn
OBn
BnO
OBn

II3a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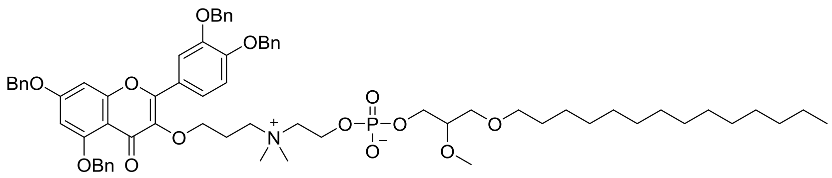
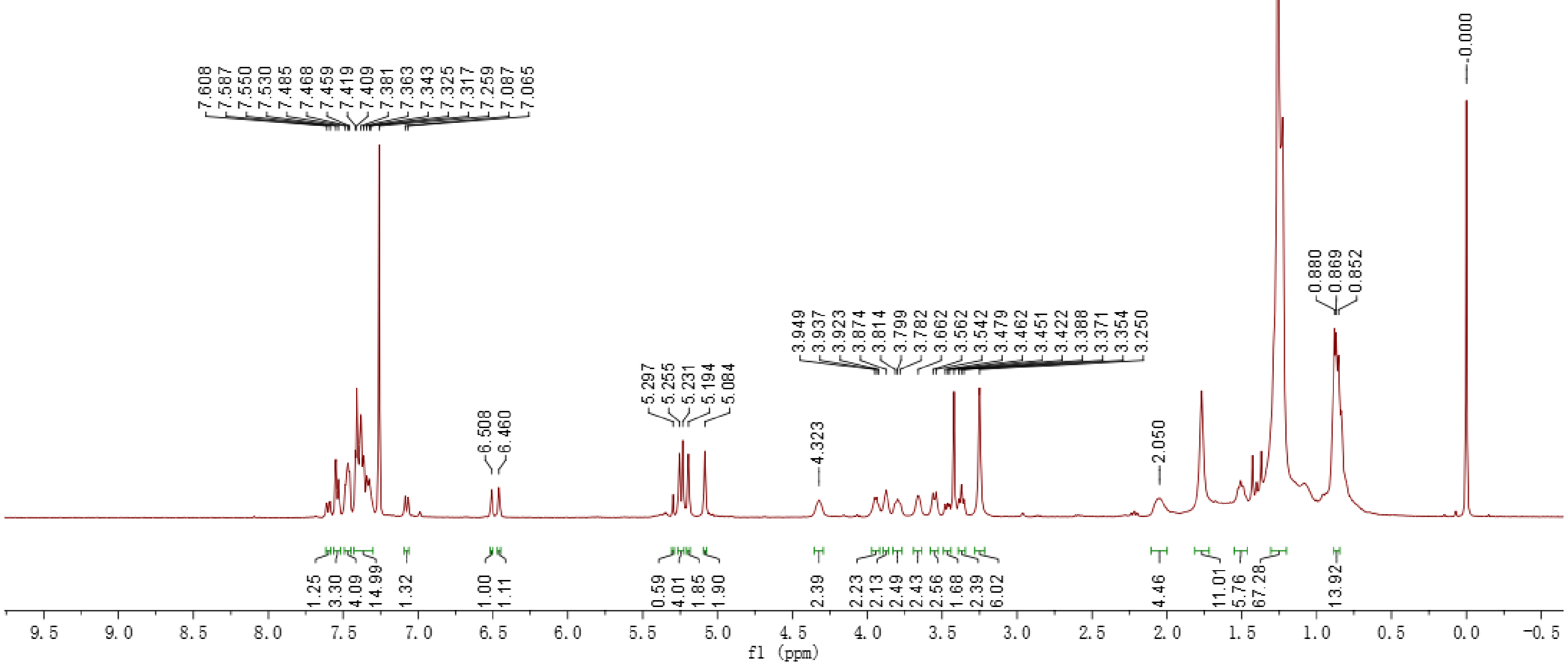
76.736
71.821
71.653
70.792
70.667
70.441
68.817
64.729
64.676
64.205
63.911
58.845
57.802
51.767
128.719
128.560
128.424
127.939
127.513
127.370
127.295
126.846
123.126
122.978
31.875
29.614
29.499
29.313
26.031
23.760
22.642
14.085
173.537
162.877
159.656
158.568
153.154
151.268
148.356
139.738
137.078
136.588
136.172
135.542
115.231
113.974
109.665
97.973
93.820
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



II3b



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7.587
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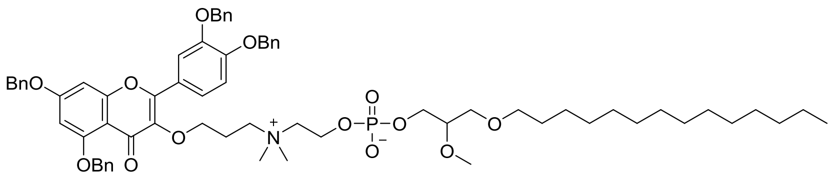
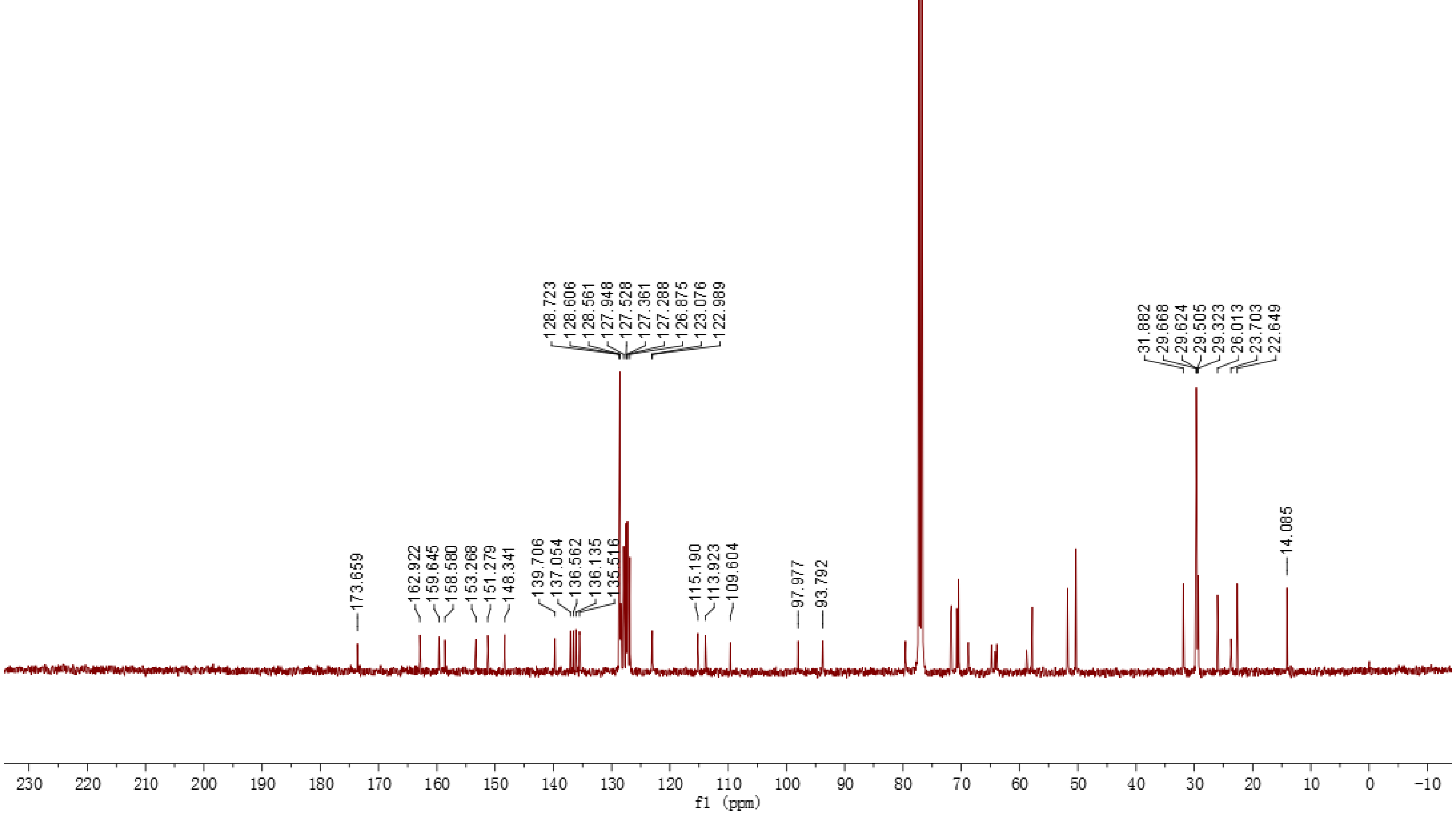
7.530
7.485
7.468
7.459
7.419
7.409
7.381
7.363
7.343
7.325
7.317
7.259
7.087
7.065
6.508
6.460
5.297
5.255
5.231
5.194
5.084
4.323
3.949
3.937
3.923
3.874
3.814
3.799
3.782
3.662
3.562
3.542
3.479
3.462
3.451
3.422
3.388
3.371
3.354
3.250
2.050
1.767
1.508
1.491
1.257
1.226
0.880
0.869
0.852
-0.000
1.25
3.30
4.09
14.99
1.32
1.00
1.11
0.59
4.01
1.85
1.90
2.39
2.23
2.13
2.49
2.43
2.56
1.68
2.39
6.02
4.46
11.01
5.76
67.28
13.92
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)



II3b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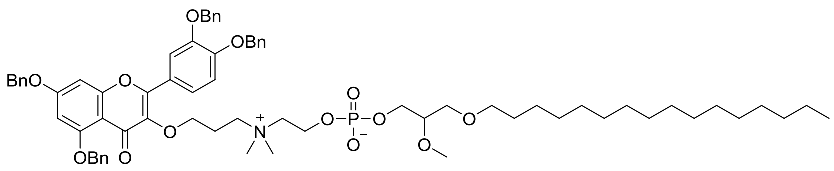
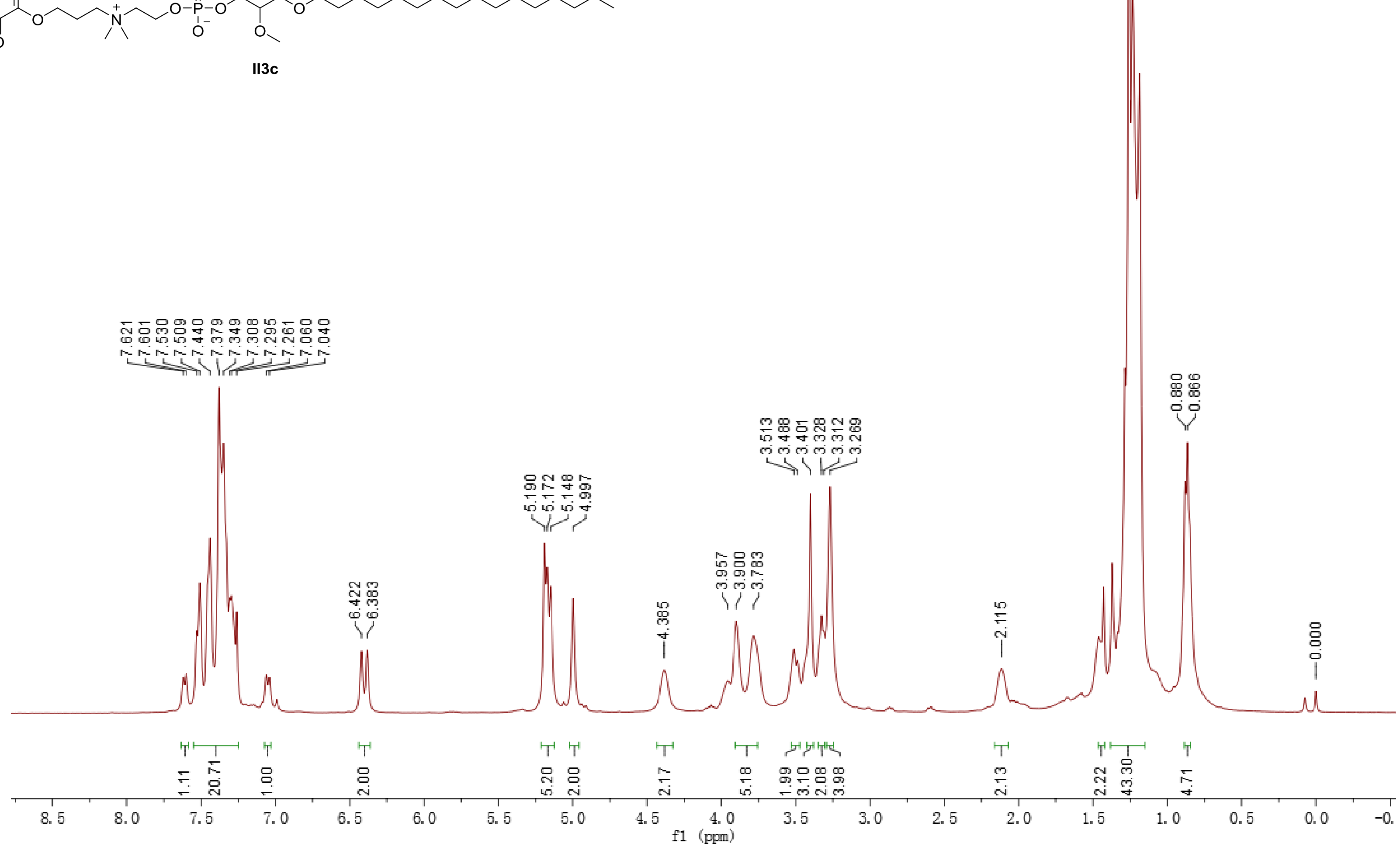
79.535
77.346
76.710
71.812
71.679
70.771
70.741
70.462
68.777
64.804
64.148
63.919
58.804
57.794
51.743
50.344
128.723
128.606
128.561
127.948
127.528
127.361
127.288
126.875
123.076
122.989
31.882
29.668
29.624
29.505
29.323
26.013
23.703
22.649
14.085
173.659
162.922
159.645
158.580
153.268
151.279
148.341
139.706
137.054
136.562
136.135
135.516
115.190
113.923
109.604
97.977
93.792
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



II3c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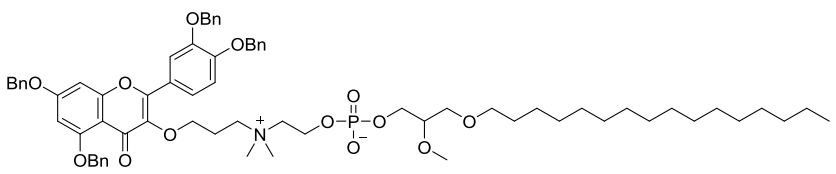
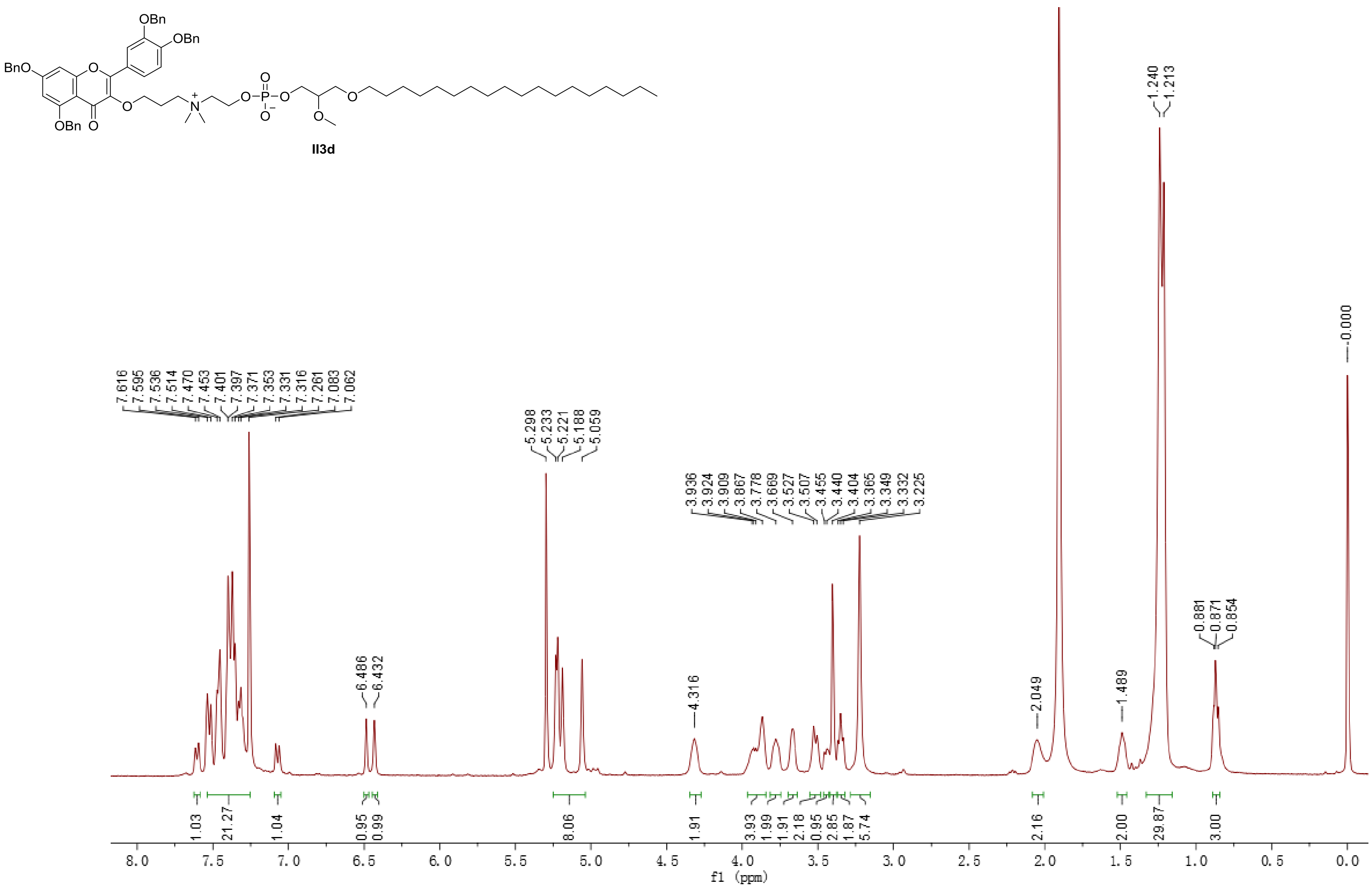
7.440
7.379
7.349
7.308
7.295
7.261
7.060
7.040
6.422
6.383
5.190
5.172
5.148
4.997
4.385
3.957
3.900
3.783
3.513
3.488
3.401
3.328
3.312
3.269
2.115
1.463
1.428
1.373
1.334
1.286
1.233
1.187
0.880
0.866
0.000
1.11
20.71
1.00
2.00
5.20
2.00
2.17
5.18
1.99
3.10
2.08
3.98
2.13
2.22
43.30
4.71
8.5 8.0 7.5 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.
f1 (ppm)


OBn
OBn
BnO
O
OBn
O
O
N
O
P
O
O
O
O

II3c

33.876
32.699
31.888
29.678
29.627
29.517
29.326
28.529
28.005
26.041
23.746
22.653
128.733
128.578
128.442
127.994
127.953
127.533
127.362
127.287
126.857
123.109
122.919
173.599
162.923
159.670
158.600
153.238
151.273
148.362
139.714
137.067
136.571
136.143
135.530
115.239
113.970
109.659
98.002
93.832
79.733
79.658
71.808
71.673
70.813
70.667
70.472
68.783
64.712
64.657
64.234
64.010
58.803
57.819
51.815
14.089
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


OBn
OBn
BnO
OBn
O
II3d
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7.536
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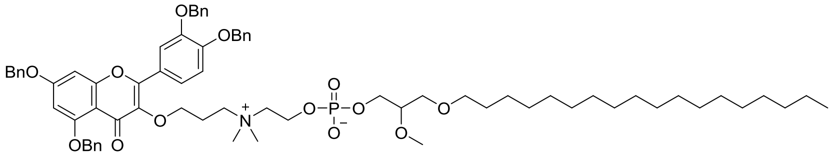
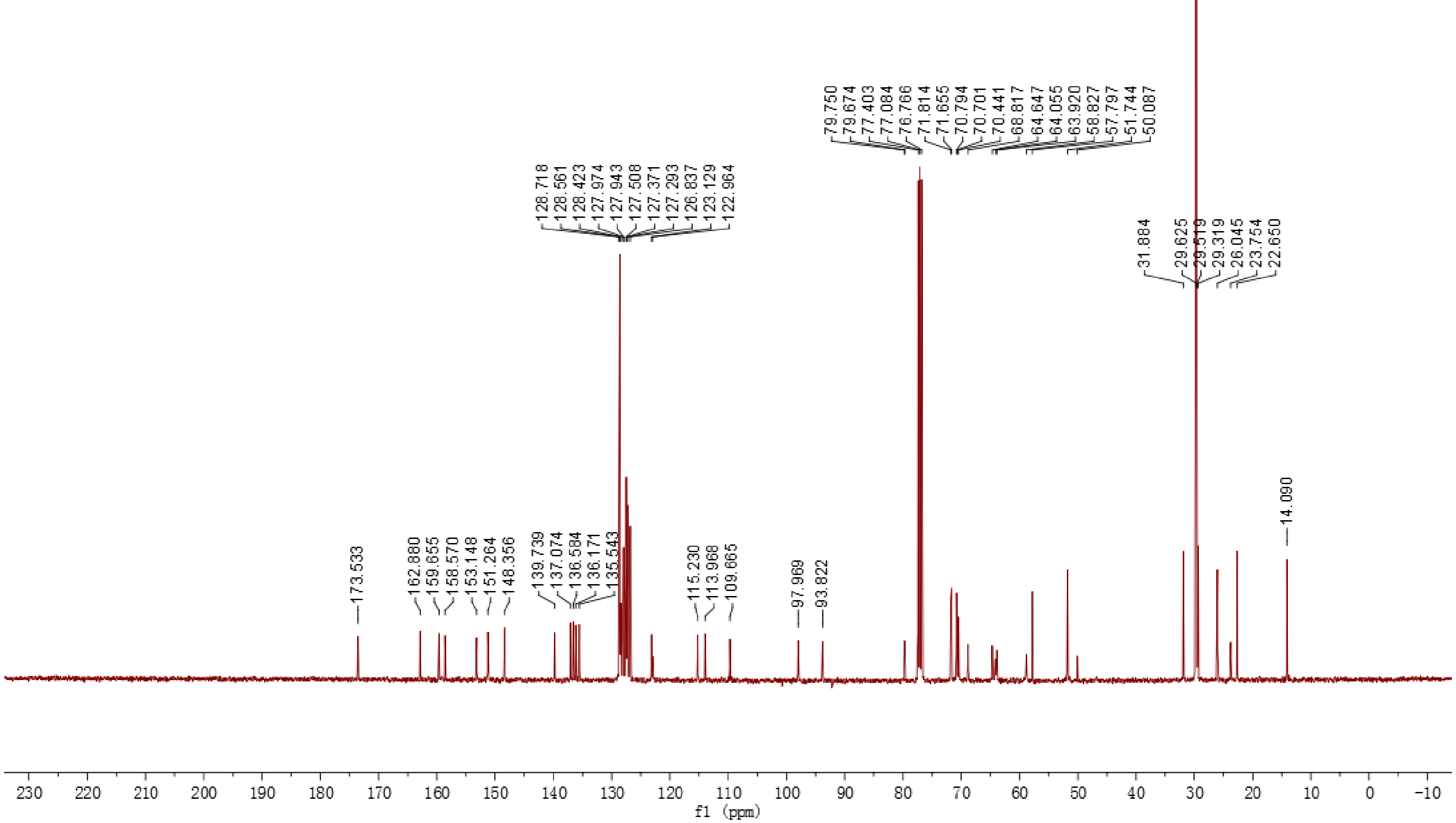
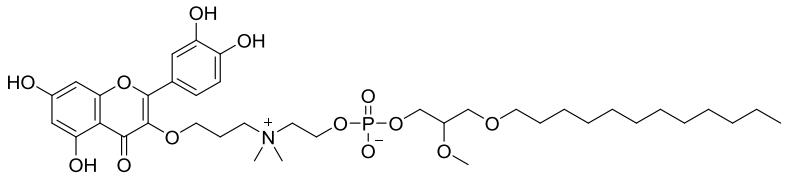
7.470
7.453
7.401
7.397
7.371
7.353
7.331
7.316
7.261
7.083
7.062
6.486
6.432
5.298
5.233
5.221
5.188
5.059
4.316
3.936
3.924
3.909
3.867
3.778
3.669
3.527
3.507
3.455
3.440
3.404
3.365
3.349
3.332
3.225
2.049
1.489
1.240
1.213
0.881
0.871
0.854
-0.000
1.03
21.27
1.04
0.95
0.99
8.06
1.91
3.93
1.99
1.91
2.18
0.95
2.85
1.87
5.74
2.16
2.00
29.87
3.00
f1 (ppm)

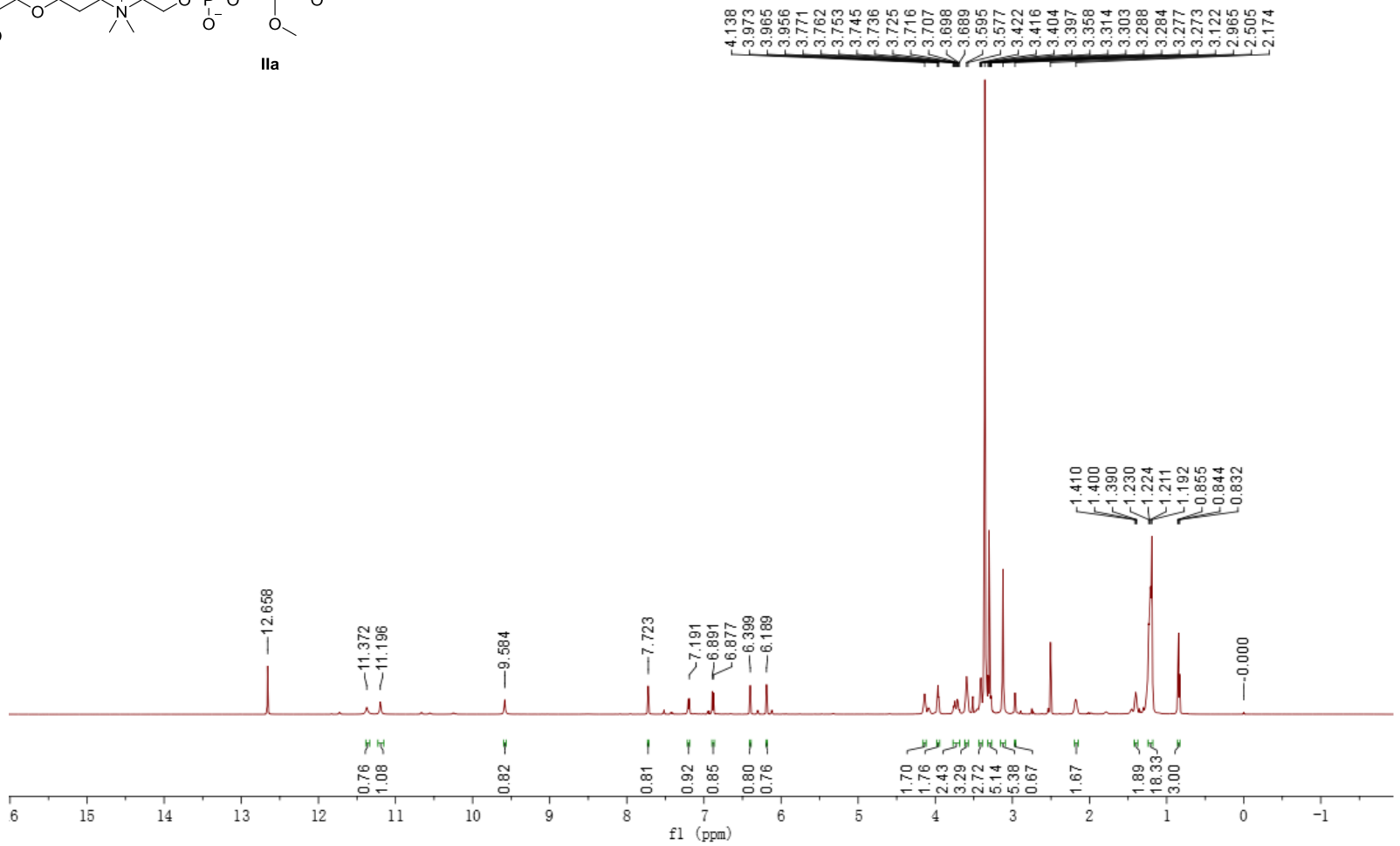

OBn
OBn
BnO
OBn
O
O
N
P

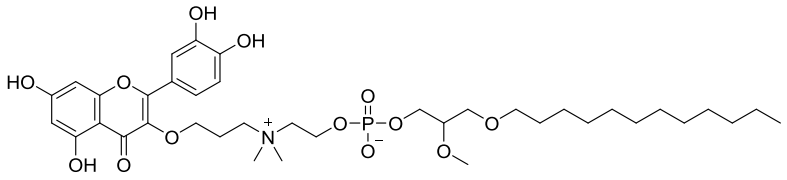
II3d


79.750
79.674
77.403
77.084
76.766
71.814
71.655
70.794
70.701
70.441
68.817
64.647
64.055
63.920
58.827
57.797
51.744
50.087
128.718
128.561
128.423
127.974
127.943
127.508
127.371
127.293
126.837
123.129
122.964
31.884
29.625
29.519
29.319
26.045
23.754
22.650
14.090
173.533
162.880
159.655
158.570
153.148
151.264
148.356
139.739
137.074
136.584
136.171
135.543
115.230
113.968
109.665
97.969
93.822
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


OH
OH
HO
O
O
OH
O
N
O
P
O
O
O
O

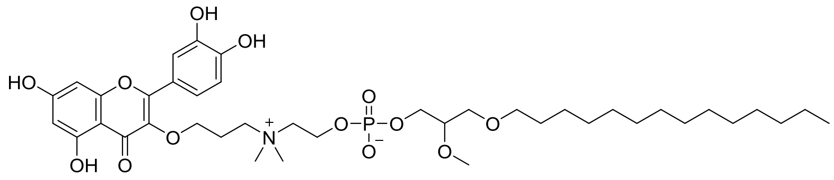
IIa


4.138
3.973
3.965
3.956
3.771
3.762
3.753
3.745
3.736
3.725
3.716
3.707
3.698
3.689
3.595
3.577
3.422
3.416
3.404
3.397
3.358
3.314
3.303
3.288
3.284
3.277
3.273
3.122
2.965
2.505
2.174
1.410
1.400
1.390
1.230
1.224
1.211
1.192
0.855
0.844
0.832
12.658
11.372
11.196
9.584
7.723
7.191
6.891
6.877
6.399
6.189
-0.000
0.76
1.08
0.82
0.81
0.92
0.85
0.80
0.76
1.70
1.76
2.43
3.29
2.72
5.14
5.38
0.67
1.67
1.89
18.33
3.00
6
15
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

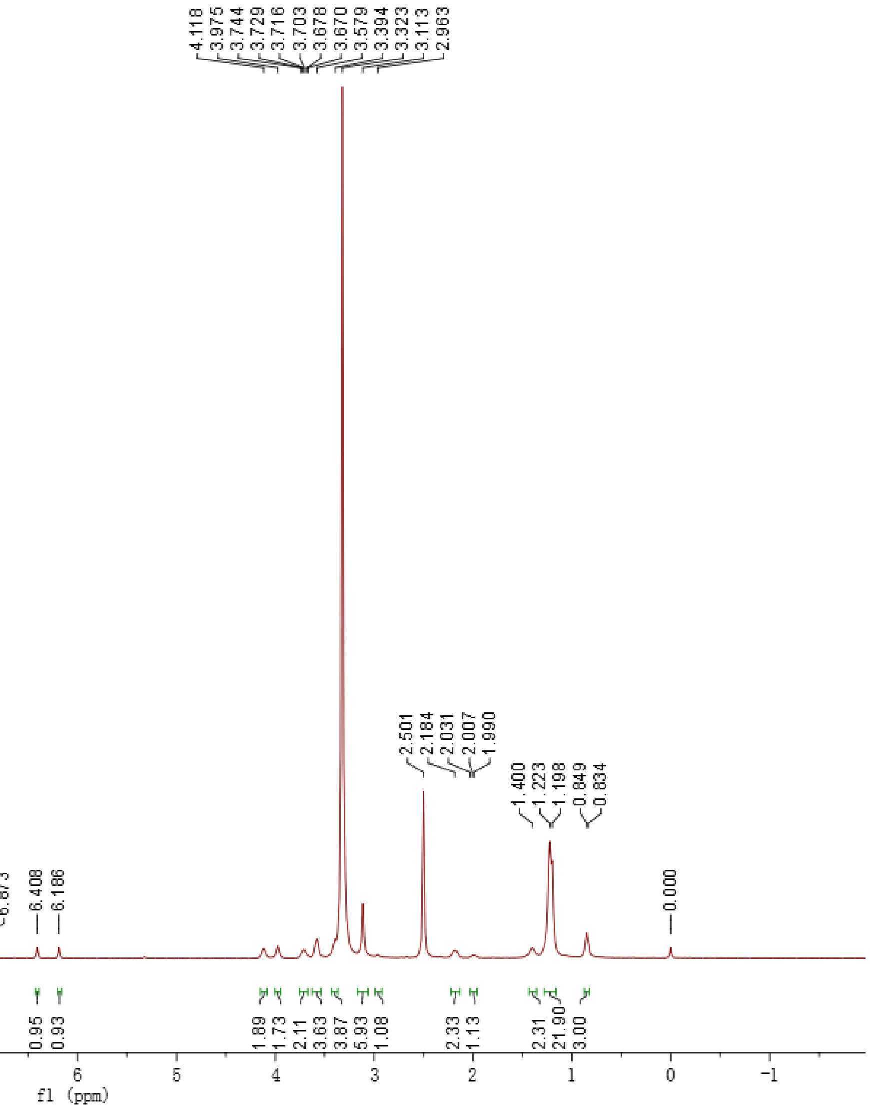

OH
OH
HO
O
O
OH
O
N
O
P
O
O
O
O
O

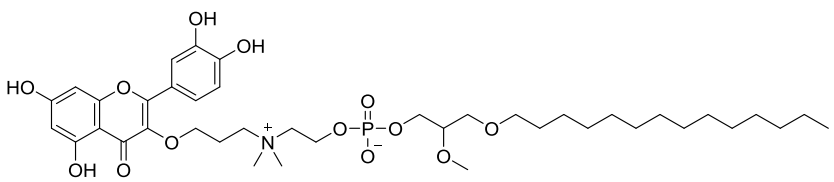
IIa

178.038
164.779
161.613
157.105
156.803
149.427
146.319
136.453
120.846
119.767
116.306
115.990
104.437
98.996
94.079
79.499
79.450
71.035
70.307
69.299
64.360
62.820
61.362
58.706
57.446
52.045
40.363
39.529
31.720
29.597
29.442
29.294
29.138
26.011
23.554
22.521
14.375
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



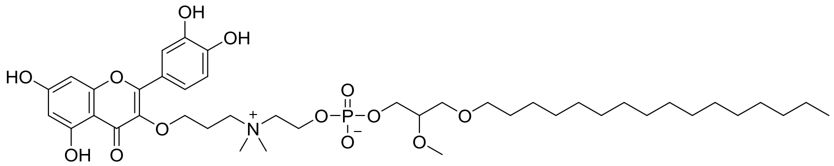
IIb


4.118
3.975
3.744
3.729
3.716
3.703
3.678
3.670
3.579
3.394
3.323
3.113
2.963
2.501
2.184
2.031
2.007
1.990
1.400
1.223
1.198
0.849
0.834
12.689
11.591
10.929
9.512
7.745
7.221
7.201
6.894
6.873
6.408
6.186
0.000
0.81
0.88
1.04
0.94
0.83
1.21
1.06
0.95
0.93
1.89
1.73
2.11
3.63
3.87
5.93
1.08
2.33
1.13
2.31
21.90
3.00
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
f1 (ppm)

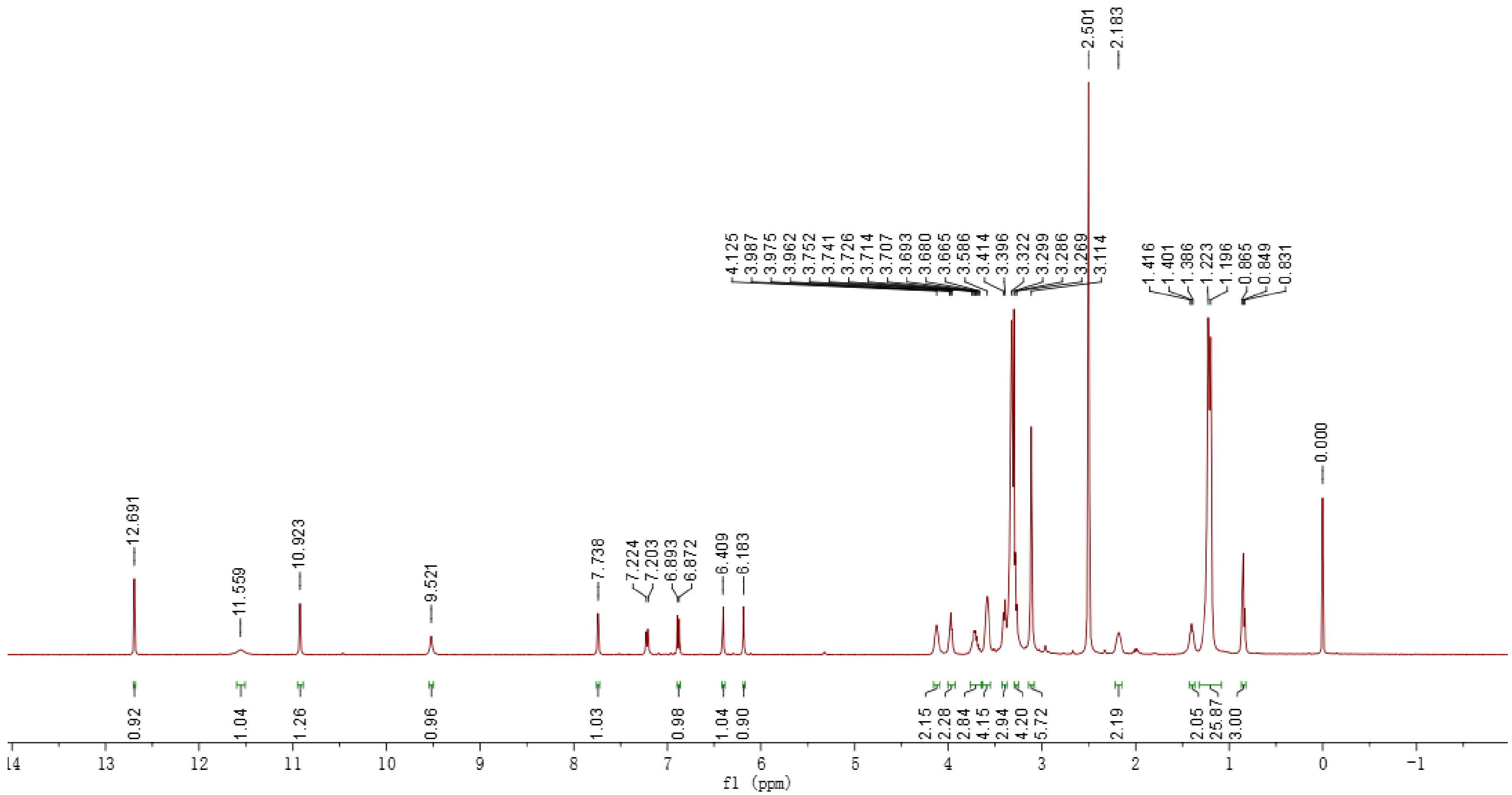

OH
OH
HO
O
O
OH
O
N
O
P
O
O
O
O
O

IIb

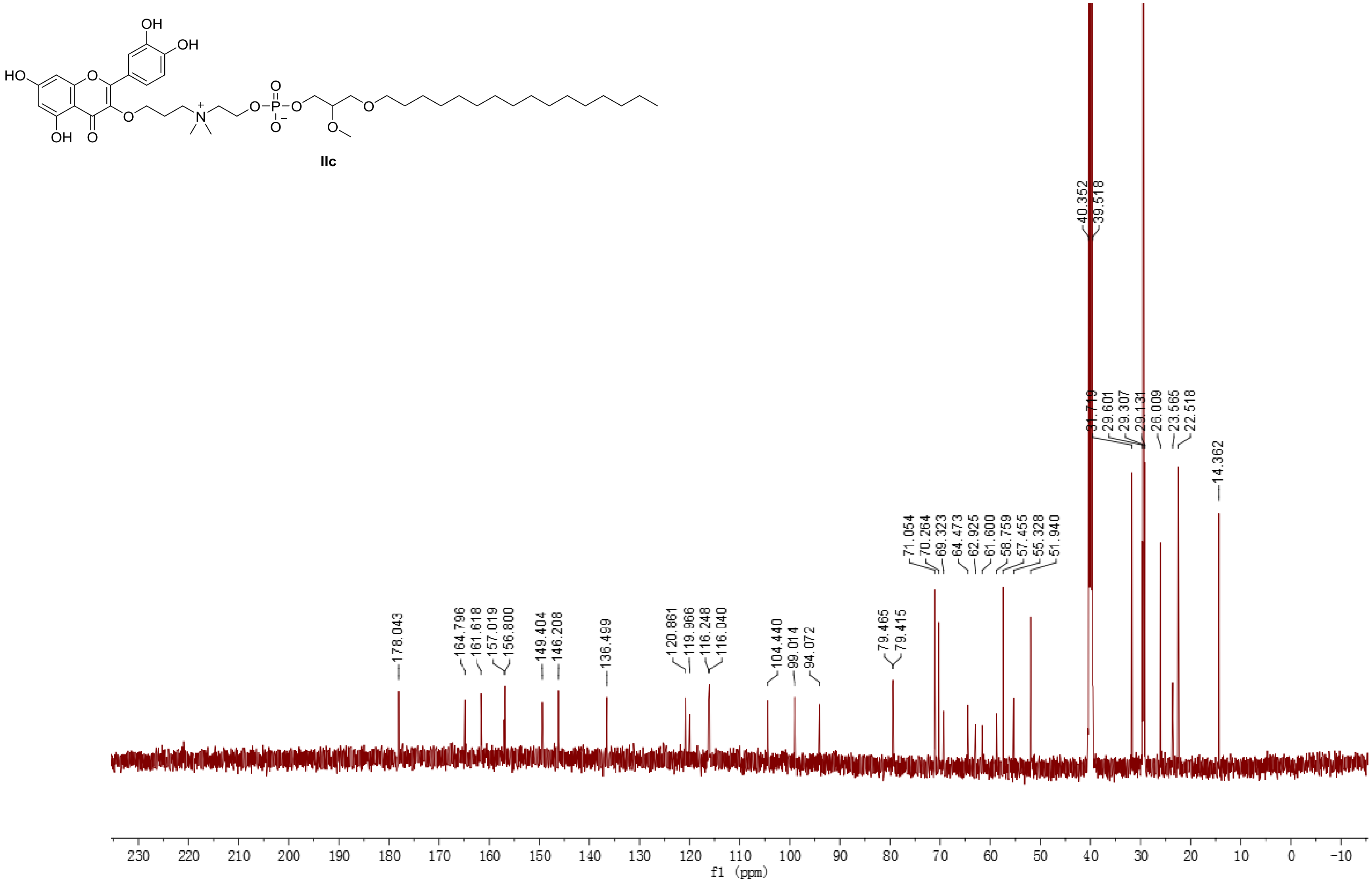
178.045
164.804
161.617
156.995
156.797
149.393
146.187
136.510
120.875
120.008
116.243
116.059
104.444
99.016
94.075
79.459
79.408
71.061
70.250
69.332
64.523
62.964
61.665
58.776
57.466
51.919
51.181
40.370
39.536
31.724
29.605
29.479
29.457
29.309
29.142
26.012
23.582
22.524
14.372
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)



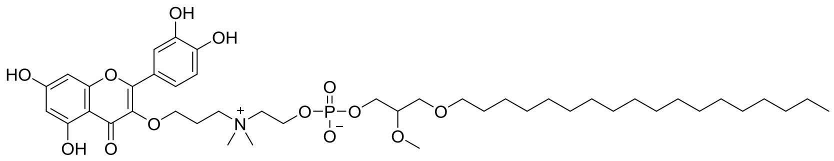
IIc



12.691
11.559
10.923
9.521
7.738
7.224
7.203
6.893
6.872
6.409
6.183
4.125
3.987
3.975
3.962
3.752
3.741
3.726
3.714
3.707
3.693
3.680
3.665
3.586
3.414
3.396
3.322
3.299
3.286
3.269
3.114
2.501
2.183
1.416
1.401
1.386
1.223
1.196
0.865
0.849
0.831
0.000
0.92
1.04
1.26
0.96
1.03
0.98
1.04
0.90
2.15
2.28
2.84
4.15
2.94
4.20
5.72
2.19
2.05
25.87
3.00
f1 (ppm)

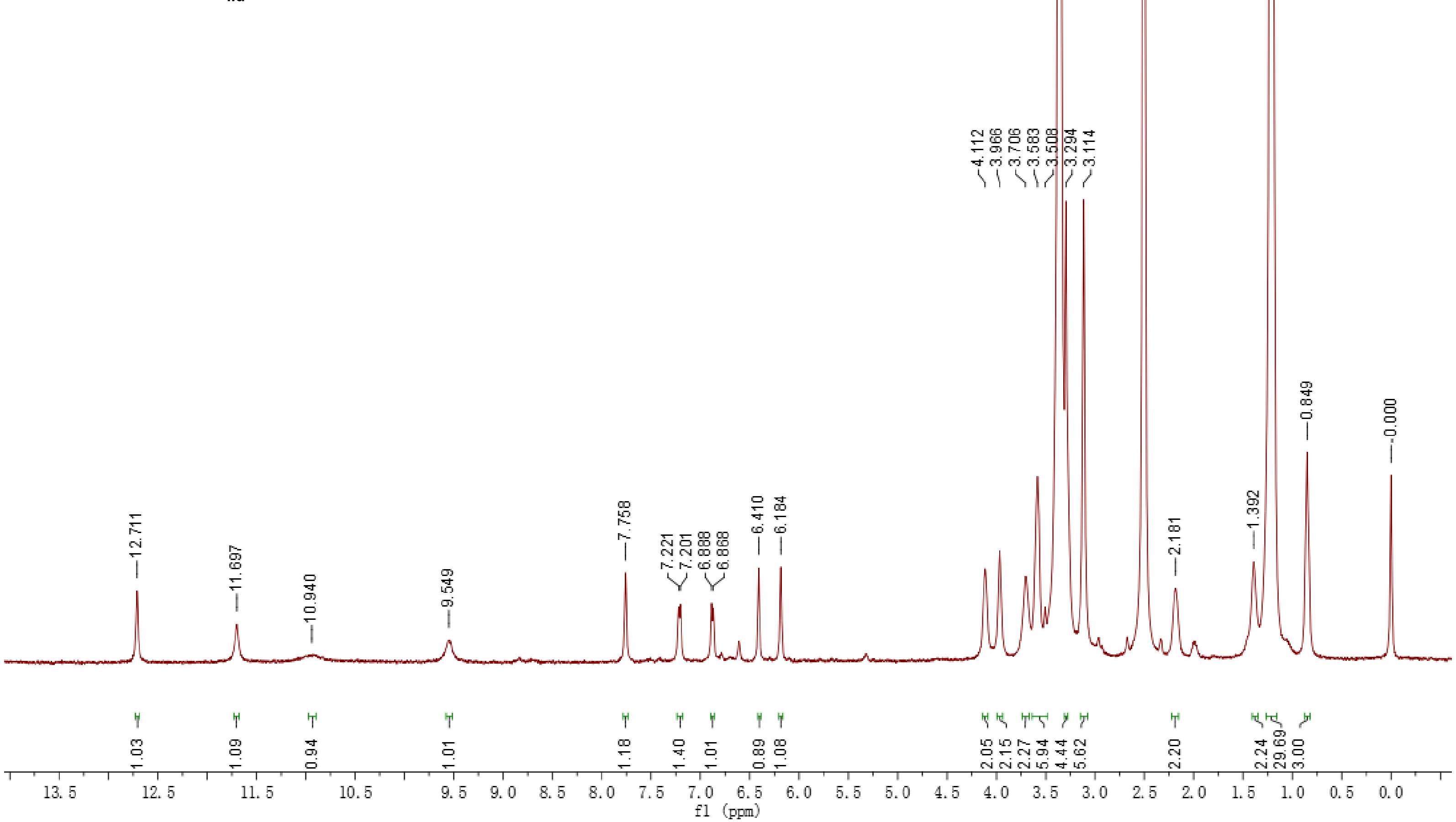

OH
OH
HO
O
O
O
OH
O
N
+
O
P
O
O
O
−
O
O
O
40.352
39.518
31.719
29.601
29.307
29.131
26.009
23.565
22.518
14.362
71.054
70.264
69.323
64.473
62.925
61.600
58.759
57.455
55.328
51.940
178.043
164.796
161.618
157.019
156.800
149.404
146.208
136.499
120.861
119.966
116.248
116.040
104.440
99.014
94.072
79.465
79.415
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

IIc

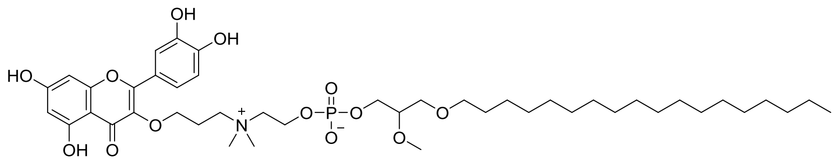


OH
OH
HO
OH
O
O
O
+
N
O
P
O
O
O
O
O
O

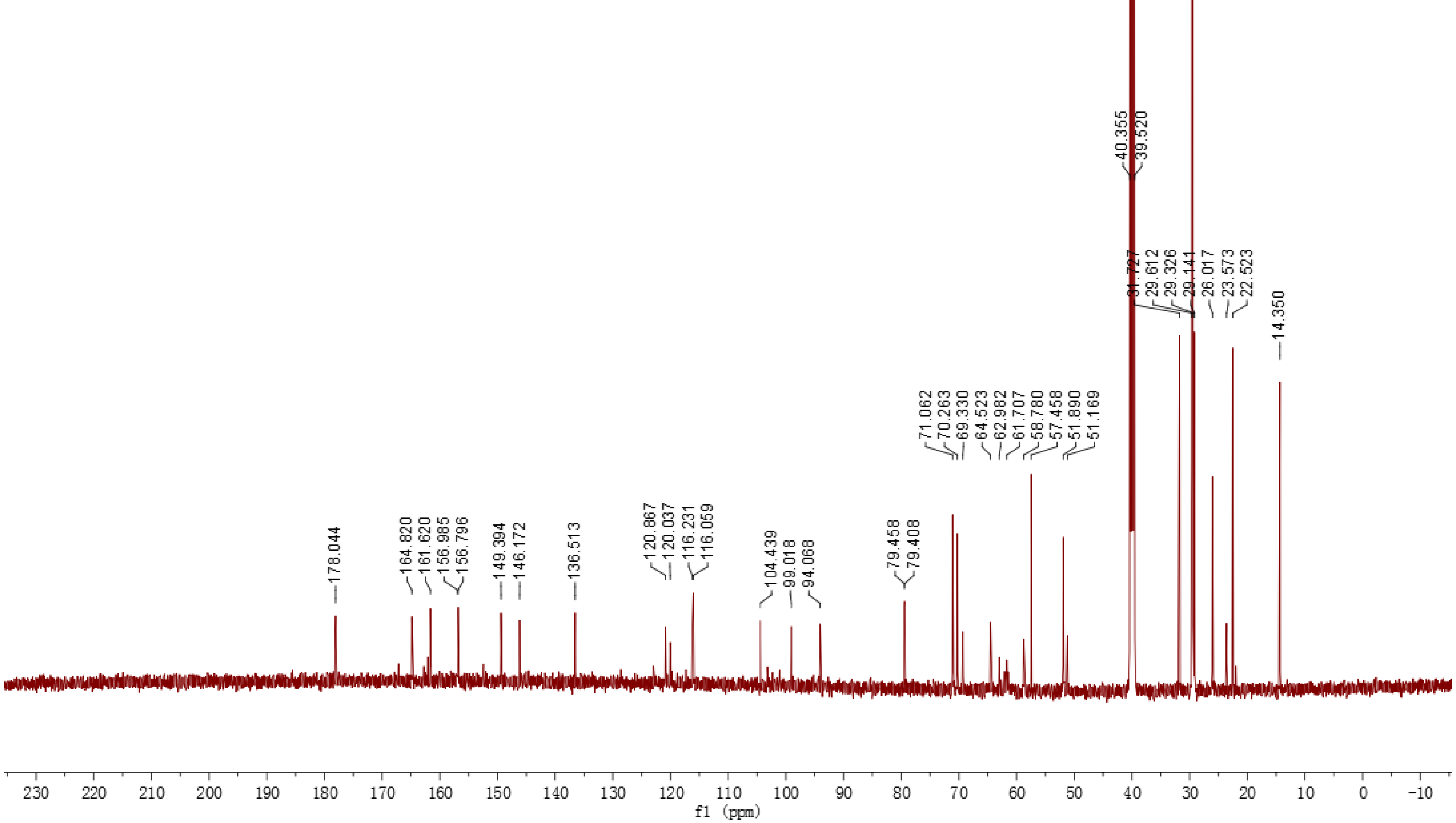
IId



4.112
3.966
3.706
3.583
3.508
3.294
3.114
0.849
-0.000
12.711
11.697
10.940
9.549
7.758
7.221
7.201
6.888
6.868
6.410
6.184
2.181
1.392
1.03
1.09
0.94
1.01
1.18
1.40
1.01
0.89
1.08
2.05
2.15
2.27
5.94
4.44
5.62
2.20
2.24
29.69
3.00
13.5
12.5
11.5
10.5
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)



IId


178.044
164.820
161.620
156.985
156.796
149.394
146.172
136.513
120.867
120.037
116.231
116.059
104.439
99.018
94.068
79.458
79.408
71.062
70.263
69.330
64.523
62.982
61.707
58.780
57.458
51.890
51.169
40.355
39.520
31.727
29.612
29.326
29.141
26.017
23.573
22.523
14.350
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)