Supplementary information for

How a grafting anchor tailors cellular uptake and *in vivo* fate of dendronized iron oxide nanoparticles

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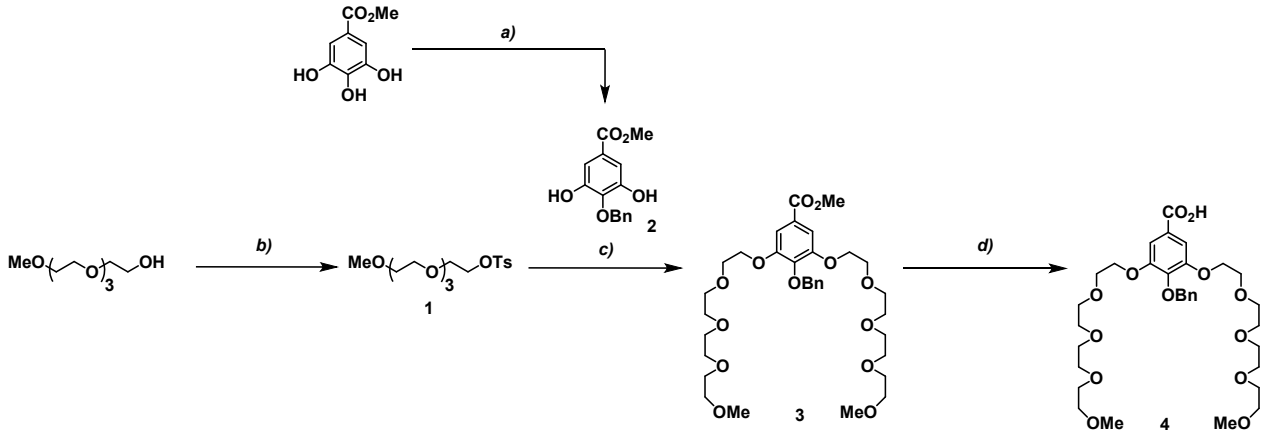
1) Synthesis ad characterization of Dendron D2-2P



Scheme S1 a) Benzyl bromide, $KHCO_3$, KI, DMF, 30°C, 4 days, 94%; b) TsCl, NaOH, THF/H_2O, r.t., 24h, 70%; c) K_2CO_3, KI, acetone, reflux, 24h, 75%; d) NaOH, MeOH/H_2O, reflux, 2h, 90%.

Compound 1: A solution of *para*-toluenesulfonyl chloride (22.3 g, 105 mM) in THF (35 mL) was added dropwise to a solution of tetraethyleneglycol monomethyl ether (20.0 g, 96 mM) and NaOH (6.7 g, 166 mM) in a mixture of THF/H_2O (135 mL/45 mL) kept at 0°C. After 1 hr stirring at 0°C, the reaction was allowed to warm to room temperature and stirred for 20 additional hours. The solution was then poured into 200 mL of brine and the volatiles were evaporated. The resulting mixture was extracted several times with CH_2Cl_2 and the combined organic layers were washed with brine, dried over $MgSO_4$ and filtered. The solvent was evaporated under reduced pressure and the crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH 98:2) to yield **1** (90.2 mmol., 94%). Pale yellow oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.73 (d, J = 1.5 Hz, 2H, Ar-2,6-*H*), 7.28 (d, J = 1.5 Hz, 2H, Ar-3,5-*H*), 4.11-4.08 (m, 2H, $ArSO_2OCH_2$), 3.64-3.47 (m, 14H, OCH_2CH_2O), 3.31 (s, 3H, OCH_3), 2.39 (s, 3H, $ArCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.9 (Ar-S), 133.2 (Ar-CH_3), 130.0 (Ar), 72.1 (PEG), 70.9 (PEG), 70.7 (PEG), 70.6 (PEG), 69.5 (PEG), 68.8 (PEG), 59.1 (OCH_3), 21.8 (CH_3). MS (MALDI-TOF) m/z calculated for $C_{16}H_{26}NaO_5S$: 385.14, obtained: 385.13.

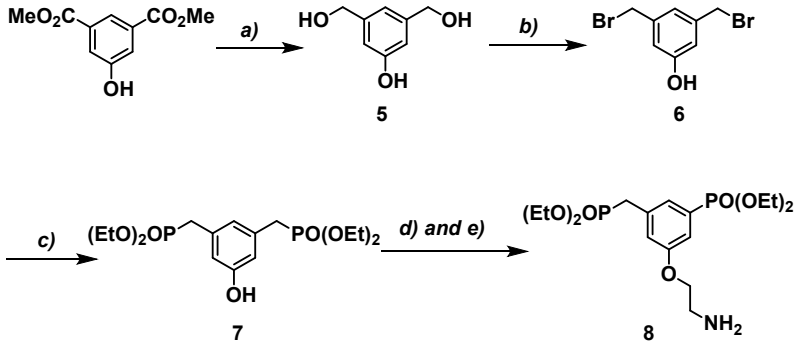
Compound 2: A solution of methyl gallate (20.0 g, 108.6 mmol), benzyl bromide (14.2 mL, 119.0 mmol, 1.1 equiv.), $KHCO_3$ (32.4 g, 324.0 mmol, 3.0 equiv.) and KI (0.1 g, 0.60 mmol) in DMF (100 mL) was stirred for 4 days at 30°C. The reaction mixture was then poured into 1 L of water and sulfuric acid was added until neutral pH was reached. The aqueous layer was extracted

3 times with CH_2Cl_2 (150 mL). The combined organic layers were washed three times with brine (50 mL), dried over $MgSO_4$ and filtered. The solvent was removed and the residue was purified by column chromatography (SiO_2, CH_2Cl_2 /MeOH 98:2) to provide a yellow oil, which was further washed with petroleum ether and afforded **2** (76.0 mmol, 70%). White foam. ^{1}H NMR (300 MHz, CD_3OD-*d*) δ 7.52 (d, J = 7.5 Hz, 2H, Ar^2-2,6-*H*), 7.31 (m, 3H, Ar^2-3,4,5-*H*), 7.13 (s, 2H, Ar^1-2,6-*H*), 5.18 (s, 2H, Ar^2OCH_2), 3.83 (s, 3H, $COOCH_3$); ^{13}C NMR (75 MHz, CD_3OD-*d*) δ 167.1 ($COOCH_3$), 150.5 (Ar-OH), 138.2 (Ar-O-CH_2), 137.2 (CH_2-Ar^{Bn}), 128.5 (Ar^{Bn}), 128.0 (Ar^{Bn}), 127.8 (Ar^{Bn}), 125.0 (Ar-$COOCH_3$), 108.8 (Ar), 73.8 (OCH_2), 51.2 ($COOCH_3$). MS (MALDI-TOF) m/z calculated for $C_{10}H_{12}NaO_5$: 225.20, obtained: 225.09.

Compound 3: A solution of **1** (26.9 g, 74.3 mmol, 2.2 equiv.), **2** (9.2 g, 33.4 mmol), K_2CO_3 (28.0 g, 200 mmol, 6.0 equiv.) and KI (0.6 g, 3.3 mM, 0.1 equiv.) in acetone (600 mL) was stirred 30 hrs at 65°C. The reaction mixture was filtered over Celite and the solvent was evaporated. The resulting crude product was diluted in CH_2Cl_2 (200 mL) and washed twice with an aqueous saturated solution of $NaHCO_3$ and with brine. After drying over $MgSO_4$, filtration and evaporation of the solvent, the crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH 95:5) to afford **3** (25.1 mmol, 75%). Colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.48 (d, J = 7.7 Hz, 2H, Ar^2-2,6-*H*), 7.28 (m, 5H, Ar^2-3,4,5-*H* and Ar^1-2,6-*H*), 5.12 (s, 2H, Ar^2OCH_2), 4.20-4.17 (t, J = 4.8 Hz, 4H, Ar^1OCH_2), 3.90 (s, 3H, $COOCH_3$), 3.88-3.85 (t, J = 4.8 Hz, 4H, OCH_2CH_2O), 3.74-3.69 (m, 4H, OCH_2CH_2O), 3.67-3.60 (m, 16H, OCH_2CH_2O), 3.54-3.50 (m, 4H, OCH_2CH_2O), 3.35 (s, 6H, $OCH_2CH_2OCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 166.9 ($COOCH_3$), 152.5 (Ar), 142.2 (Ar), 138.2 (CH_2-Ar^{Bn}), 128.2 (Ar^{Bn}), 128.0 (Ar^{Bn}), 127.8 (Ar^{Bn}), 125.3 (Ar-$COOCH_3$), 109.1 (Ar), 74.8 (OCH_2), 72.3 (PEG), 71.2 (PEG), 71.0 (PEG), 70.9 (PEG), 70.8 (PEG), 70.0 (PEG), 69.2 (PEG), 59.3 (OCH_3), 52.5 ($COOCH_3$). MS (MALDI-TOF) m/z calculated for $C_{33}H_{50}NaO_{13}$: 677.33, obtained: 677.03.

Compound 4: Sodium hydroxide (2.6 g, 63.5 mmol, 5 equiv.) was added to a solution of **3** (8.3 g, 12.7 mmol) in a mixture of MeOH/water 4/1 (150 mL). The reaction mixture was stirred 2 hrs at 70°C, concentrated *in vacuo* and hydrolyzed (200 mL). The pH was adjusted to 3 by addition of HCl 12 N and the aqueous solution was extracted with CH_2Cl_2 (3 x 100 mL). The combined organic phases were washed with brine and water, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude material was purified by column chromatography (SiO_2,

CH_2Cl_2/MeOH 95:5) to afford **4** (11.4 mM, 90%). Colourless oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, J = 7.8 Hz, 2H, Ar^2-2,6-*H*), 7.38 (s, 2H, Ar^1-2,6-*H*), 7.35-7.28 (m, 3H, Ar^2-3,4,5-*H*), 5.13 (s, 2H, Ar^2OCH_2), 4.20-4.16 (t, J = 4.8 Hz, 4H, Ar^1OCH_2), 3.87-3.82 (t, J = 4.8 Hz, 4H, OCH_2CH_2O), 3.74-3.69 (m, 4H, OCH_2CH_2O), 3.67-3.61 (m, 16H, OCH_2CH_2O), 3.54-3.50 (m, 4H, OCH_2CH_2O), 3.37 (s, 6H, $OCH_2CH_2OCH_3$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.6 (*C*OOH), 152.8 (Ar), 142.4 (Ar), 137.9 (CH_2-Ar^{Bn}), 128.2 (Ar^{Bn}), 128.0 (Ar^{Bn}), 127.8 (Ar^{Bn}), 124.8 (Ar-COOH), 109.2 (Ar), 74.8 (OCH_2), 72.3 (PEG), 71.2 (PEG), 71.0 (PEG), 70.9 (PEG), 70.8 (PEG), 70.0 (PEG), 69.2 (PEG), 59.1 (OCH_3). MS (MALDI-TOF) m/z calculated for $C_{32}H_{48}O_{13}$: 640.31, obtained: 640.24; calculated for $C_{29}H_{48}NaO_{13}$: 627.30, obtained: 627.13; calculated for $C_{29}H_{48}KO_{13}$: 643.27, obtained: 643.09.



Scheme S2 a) $LiAlH_4$ 1M in THF, THF, reflux, 3h, 94%; b) HBr in acetic acid 30%, Acetic acid, r.t. , 24h, 96%; c) $P(OEt)_3$, 160°C, 3h, 95%; d) Boc-2-bromoethylamine, K_2CO_3, KI, acetone, reflux, 16h, 76%; e) TFA, CH_2Cl_2, 0°C at r.t., overnight, 88%.

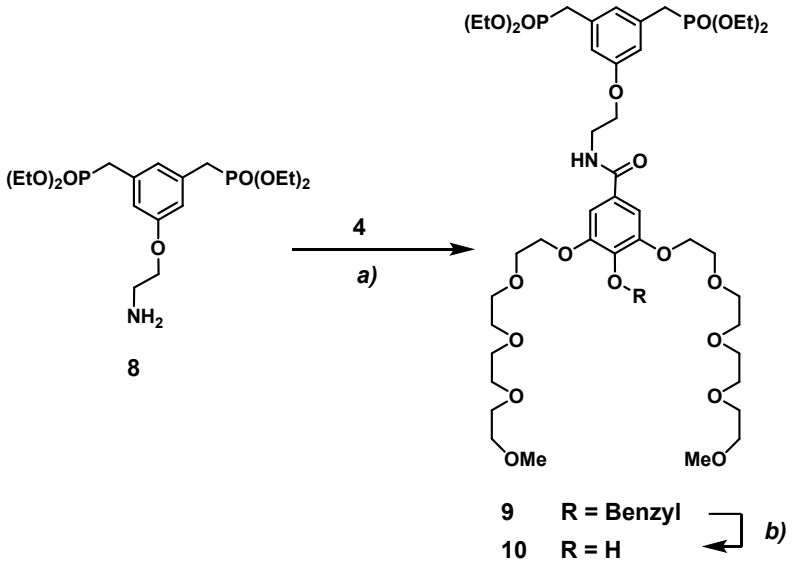
Compound 5: $LiAlH_4$ 0.5 M in THF (36.0 mmol, 1.8 equiv.) was added dropwise at 0°C to a solution of dimethyl 5-hydroxyisophtalate (4.20 g, 20.0 mmol) in anhydrous THF (21 mL). After 3 hrs stirring under reflux, the mixture was cooled to room temperature and acidified with H_2SO_4 (30 mL, 10%). The THF was evaporated under reduced pressure and the resulting aqueous phase was extracted several times (at least 6 times, TLC control) with ethyl acetate. The organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford **5** (18.8 mmol, 94%). White foam. ^{1}H NMR (300 MHz, CD_3OD-*d*) δ 6.82 (s, 1H, Ar-4-*H*), 6.71 (s, 2H, Ar-2,6-*H*), 4.52 (d, J = 5.8 Hz, 4H, $ArCH_2OH$); ^{13}C NMR (75 MHz, CD_3OD-*d*) δ 157.2 (Ar), 143.7 (Ar), 115.1 (Ar), 112.1 (Ar), 63.0 (CH_2OH). MS (MALDI-TOF) m/z calculated for $C_{10}H_{12}NaO_5$: 225.20, obtained: 225.09.

Compound 6: A solution of HBr 30% in acetic acid (36.0 mmol, 1.8 equiv.) was added dropwise at 0°C to a solution of **5** (2.00 g, 13.0 mmol) in acetic acid (21 mL). The mixture was stirred 24 hrs at room temperature, and then 80 mL of distilled water were added. A white precipitate was formed and the mixture was stirred for additional 10 minutes. The resulting aqueous phase was extracted 3 times with CH_2Cl_2 (200 mL) and the organic layer was washed with distilled water (2 x 120 mL), a saturated solution of sodium hydrogenocarbonate (2 x 120 mL), and with brine (80 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford **6** (12.5 mmol, 96%). White solid. Melting point: 93°C. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.99 (t, J = 1.3 Hz, 1H, Ar-4-*H*), 6.04 (d, J = 1.3 Hz, 2H, Ar-2,6-*H*), 5.38 (br s, 1H, O*H*), 4.40 (s, 4H, ArCH_2Br); ^{13}C NMR (75 MHz, $CDCl_3$) δ 155.8 (Ar), 140.0 (Ar), 122.2 (Ar), 116.2 (Ar), 32.7 (CH$_2$Br).

Compound 7: A solution of **6** (2.24 g, 8.0 mmol) in $P(OEt)_3$ (4.0 equiv., 5.0 mL) was stirred 2 hrs at 160°C. The excess of $P(OEt)_3$ was evaporated under reduced pressure at 70°C. The crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH 95:5) to afford **7** (7.6 mmol, 95%). White foam. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.82 (bs, 2H, Ar-2,6-*H*), 6.62 (bs, 1H, Ar-4-*H*), 3.99 (m, 8H, PO(OCH_2CH$_3$)$_2$), 3.49 (d, J = 21.9 Hz, 4H, ArCH_2P), 1.23 (t, J = 7.1 Hz, 12H, PO(OCH$_2$CH_3)$_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 157.9 (Ar), 132.6 (J = 10.6 Hz) (Ar), 122.4 (J = 6.7 Hz) (Ar), 115.8 (Ar), 62.5 (J = 6.6 Hz) (CH$_2$CH$_3$), 33.6 (J = 138.8 Hz) (CH-P), 16.5 (J = 5.2 Hz) (CH$_2$$CH_3$); ^{31}P NMR (81 MHz, $CDCl_3$) δ 26.72. MS (MALDI-TOF) m/z calculated for $C_{16}H_{29}O_7P_2$: 395.14, obtained: 394.96.

Compound 8: (2-bromo-ethyl)carbamic acid tert-butyl ester (1.1 g, 4.95 mmol, 1.3 equiv.), K_2CO_3 (2.1 g, 15.2 mmol, 4 equiv.) and KI (0.1 g, 0.4 mmol, 0.1 equiv.) were added to a solution of **7** (1.5 g, 3.8 mmol) in acetone (40 mL). The mixture was stirred 48 hrs at 65°C, filtered over Celite and evaporated under reduced pressure. The resulting crude product was diluted in CH_2Cl_2 (100 mL) and washed twice with an aqueous saturated solution of $NaHCO_3$ and with brine. After drying over $MgSO_4$, filtration and evaporation of the solvent, the crude product was purified by column chromatography (SiO_2, CH_2Cl_2/MeOH 98/2 to 95/5) to afford (Boc-amino) derivative as white solid (76%). The compound (1.2 g, 2.2 mmol) was then dissolved in anhydrous CH_2Cl_2 (30 mL) at 0°C and trifluoroacetic acid (2 mL, 22.0 mmol, 10.0 equiv.) was added dropwise. The reaction mixture was stirred overnight at room temperature, and then the volatiles were

evaporated. The crude product was dissolved in CH_2Cl_2 (20 mL) and was washed with NaOH 1 N (2 x 10 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford **8** (1.9 mmol, 88%) as a white foam which was used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.72 (m, 3H, Ar-2,4,6-*H*), 5.25 (br s, 2H, $OCH_2CH_2NH_2$), 4.03-3.92 (m, 10H, $PO(OCH_2CH_3)_2$ and OCH_2CH_2NH), 3.10 (d, J = 21.7 Hz, 4H, $ArCH_2P$), 3.02 (m, 2H, OCH_2CH_2NH), 1.25 (t, J = 7.1 Hz, 12H, $PO(OCH_2CH_3)_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 159.0 (J = 2.8 Hz) (Ar), 133.1 (J = 6.0 Hz) (Ar), 123.8 (J = 6.8 Hz) (Ar), 114.5 (J = 5.0 Hz) (Ar), 70.0 (OCH_2), 62.1 (J = 7.0 Hz) (CH_2CH_3), 41.5 (CH_2NH_2), 33.5 (J = 138.2 Hz) (*C*H-P), 16.5 (J = 2.7 Hz) (CH_2CH_3); ^{31}P NMR (81 MHz, $CDCl_3$) δ 26.24. MS (MALDI-TOF) m/z calculated for $C_{18}H_{34}NO_7P_2$: 438.17, obtained: 438.18; calculated for $C_{18}H_{34}NaO_7P_2$: 460.17, obtained: 460.16.



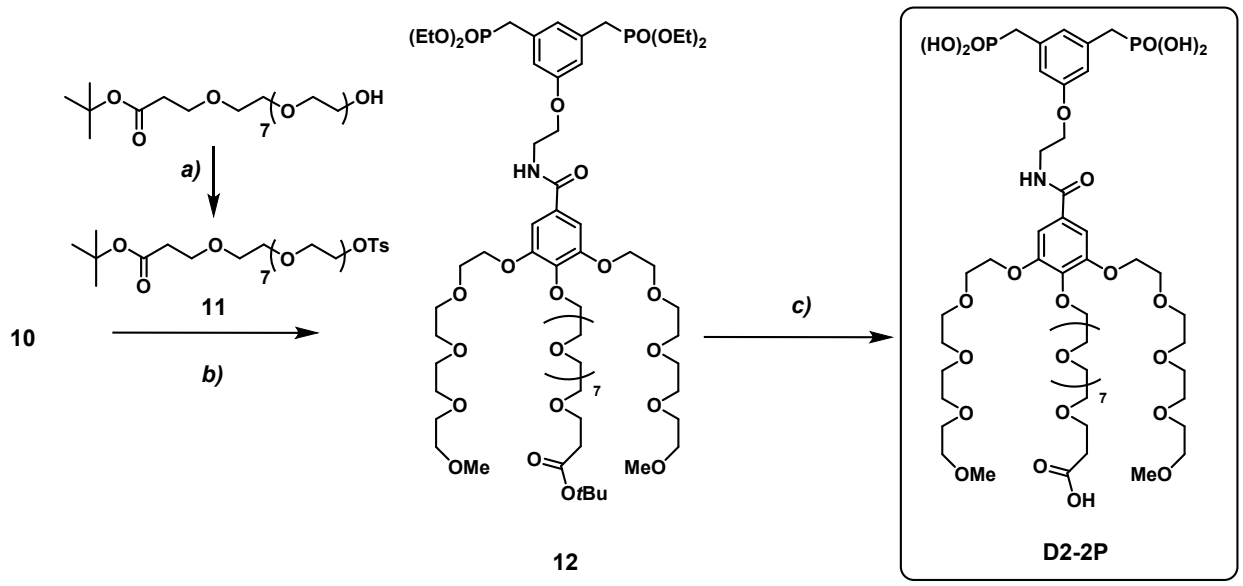
Scheme S3 a) compound **4**, BOP, DIPEA, CH_2Cl_2, r.t., 24h, 87%; b) Pd activated on Carbon 10%, H_2, EtOH, r.t., overnight, 70%.

Compound 9: BOP coupling reagent (1.3 equiv. per acid function) was added under argon to a solution **4** (1.0 equiv. per amine function) in distilled CH_2Cl_2. After 5 min of stirring, *N,N*-diisopropylethylamine (3 equiv. per amine function) and amine derivative **8** (1.0 equiv.) were added. The reaction mixture was stirred overnight at room temperature. CH_2Cl_2 (50 mL) was added and the organic layer was washed with a solution of sodium hydroxide 1 N (2 x 20 mL), HCl 1 N (2 x 20 mL), brine (2 x 20 mL) and water (2 x 20 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Starting from **4** (0.6 g, 1.4 mmol), **9** was obtained (1.2 mmol, 87%) as colourless oil after purification by column chromatography (SiO_2, CH_2Cl_2/MeOH

95:5). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, J = 7.7 Hz, 2H, Ar^3-2,6-*H*), 7.35-7.28 (m, 3H, Ar^3-3,4,5-*H*), 7.07 (s, 2H, Ar^2-2,6-*H*), 6.88 (t, J = 5.7 Hz, 1H, OCH_2CH_2NH), 6.85-6.78 (m, 3H, Ar^1-2,4,6-*H*), 5.07 (s, 2H, Ar^3OCH_2), 4.20-4.17 (t, J = 4.8 Hz, 4H, Ar^2OCH_2), 4.15-4.11 (t, J = 5.0 Hz, 2H, OCH_2CH_2NH), 4.08-3.96 (m, 8H, $PO(OCH_2CH_3)_2$), 3.88-3.78 (m, 6H, OCH_2CH_2NH and OCH_2CH_2O), 3.71-3.68 (m, 4H, OCH_2CH_2O), 3.65-3.58 (m, 16H, OCH_2CH_2O), 3.55-3.49 (m, 4H, OCH_2CH_2O), 3.35 (s, 6H, $OCH_2CH_2OCH_3$), 3.08 (d, J = 21.5 Hz, 4H, Ar^1CH_2P), 1.25 (t, J = 7.0 Hz, 12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2 (NH*C*O), 158.6 (J = 2.8 Hz) (Ar), 152.8 (Ar), 141.0 (Ar), 137.8 (Ar), 133.1 (J = 6.0 Hz) (Ar), 129.6 (Ar), 128.2 (Ar), 128.0 (Ar), 127.8 (Ar), 124.0 (J = 6.8 Hz) (Ar), 114.6 (J = 4.8 Hz) (Ar), 107.0 (Ar), 74.9 (OCH_2), 72.0 (PEG), 70.8 (PEG), 70.7 (PEG), 70.6 (PEG), 69.8 (PEG), 69.1 (PEG), 66.8 (OCH_2CH_2NH), 62.1 (J = 3.4 Hz) (CH_2CH_3), 58.9 (OCH_3), 39.5 ($CH_2NHCOAr$), 33.5 (J = 138.3 Hz) (*C*H-P), 16.5 (J = 2.7 Hz) (CH_2CH_3); ^{31}P NMR (81 MHz, $CDCl_3$) δ 26.08. MS (MALDI-TOF) m/z calculated for $C_{50}H_{79}NaNO_{19}P_2$: 1082.87, obtained: 1082.51.

Compound 10: compound **9** (0.40 g, 0.45 mmol) was dissolved in ethanol absolute (20 mL) and palladium activated on carbon 10% (0.5 equiv.) was added. The mixture was stirred under a hydrogen atmosphere at room temperature for 16 hrs. The crude mixture was filtered through a plug of Celite, concentrated and purified by column chromatography. Compound **10** was obtained (0.32 mmol, 70%) as colorless oil after purification by column chromatography (SiO_2, CH_2Cl_2/MeOH 95:5). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.50 (d, J = 7.7 Hz, 2H, Ar^3-2,6-*H*), 7.35-7.28 (m, 3H, Ar^3-3,4,5-*H*), 7.11 (s, 4H, Ar^2-2,6-*H*), 7.05 (t, J = 5.0 Hz, 2H, $Ar^2OCH_2CH_2NH$), 6.95 (d, J = 2.3 Hz, 2H, Ar^1-2,6-*H*), 6.69 (t, J = 2.4 Hz, 1H, Ar^1-4-*H*), 6.82-6.78 (m, 3H, Ar^2-2,4,6-*H*), 6.64 (t, J = 1.9 Hz, 1H, $Ar^1OCH_2CH_2NH$), 5.07 (s, 4H, Ar^3OCH_2), 4.20-4.17 (m, 14H, $Ar^2OCH_2CH_2O$, $Ar^1OCH_2CH_2NH$ and $Ar^2OCH_2CH_2NH$), 4.08-3.96 (m, 8H, $PO(OCH_2CH_3)_2$), 3.83-3.78 (m, 14H, $Ar^1OCH_2CH_2NH$, $Ar^2OCH_2CH_2NH$ and OCH_2CH_2O), 3.65-3.55 (m, 34H, OCH_2CH_2O), 3.55-3.48 (m, 8H, OCH_2CH_2O), 3.34 (s, 12H, $OCH_2CH_2OCH_3$), 3.08 (d, J = 22.0 Hz, 4H, Ar^1CH_2P), 1.23 (t, J = 7.0 Hz, 12H, $PO(OCH_2CH_3)_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 167.2 (NH*C*O), 159.8 (Ar), 152.5 (Ar), 141.0 (Ar), 137.8 (Ar), 136.5 (Ar), 133.1 (J = 6.0 Hz) (Ar), 129.5 (Ar), 128.2 (Ar), 128.0 (Ar), 127.8 (Ar), 124.0 (Ar), 114.8 (J = 4.8 Hz) (Ar), 107.8 (Ar), 107.0 (Ar), 106.0 (Ar), 74.9 (OCH_2), 72.0 (PEG), 70.8 (PEG), 70.7 (PEG), 70.6 (PEG), 69.8 (PEG), 69.1 (PEG), 66.8 (OCH_2CH_2NH), 62.1 (J = 3.4 Hz) (CH_2CH_3), 58.9 (OCH_3), 39.5 ($CH_2NHCOAr$), 33.3 (J = 138.0 Hz) (*C*H-P), 16.4 (J = 2.7 Hz) (CH_2CH_3); ^{31}P NMR (81 MHz,

$CDCl_3$) δ 26.18. MS (MALDI-TOF) m/z calculated for $C_{93}H_{169}NaN_3O_{34}P_2$: 1926.87, obtained: 1926.81.



Scheme S4 a) pTsCl, NEt_3, CH_2Cl_2, RT, 24h, 70%; b) compound **11**, K_2CO_3, KI, acetone, reflux, 16h, 90%; b) TMSBr, CH_2Cl_2, RT, overnight, 94%.

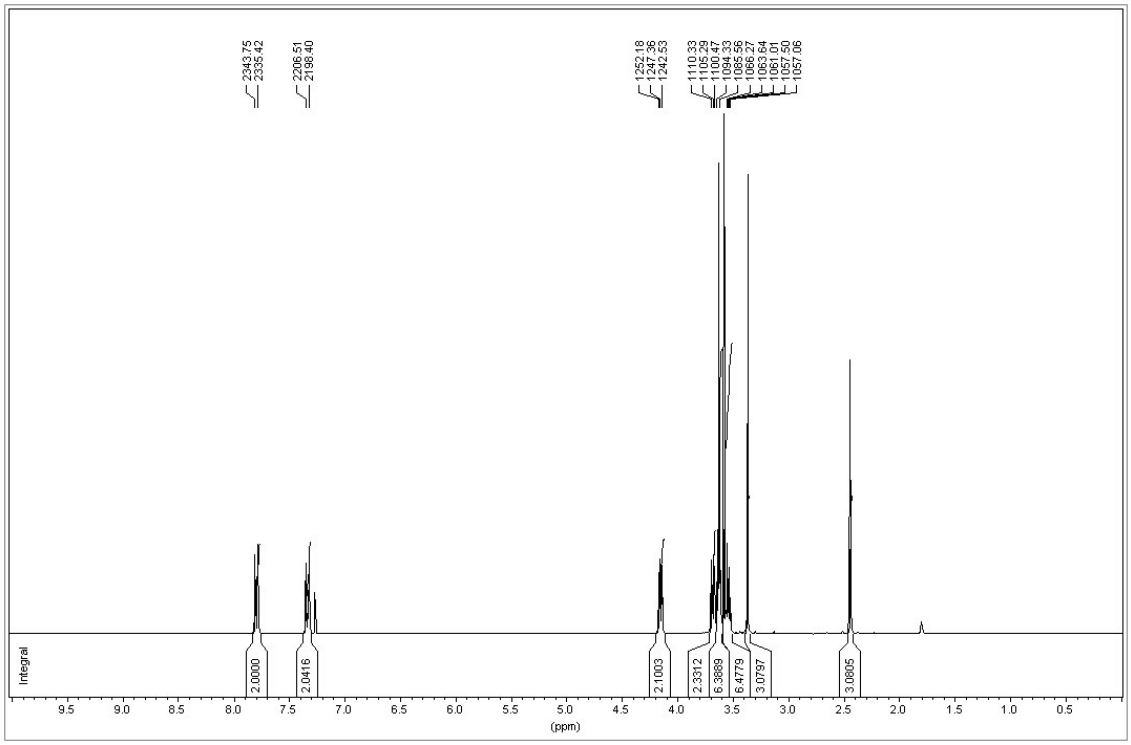
Compound 11: The synthesis and spectroscopic data of **11** are the same as those reported in the literature (Biomaterials **2011**, *32*, 8562-8573).

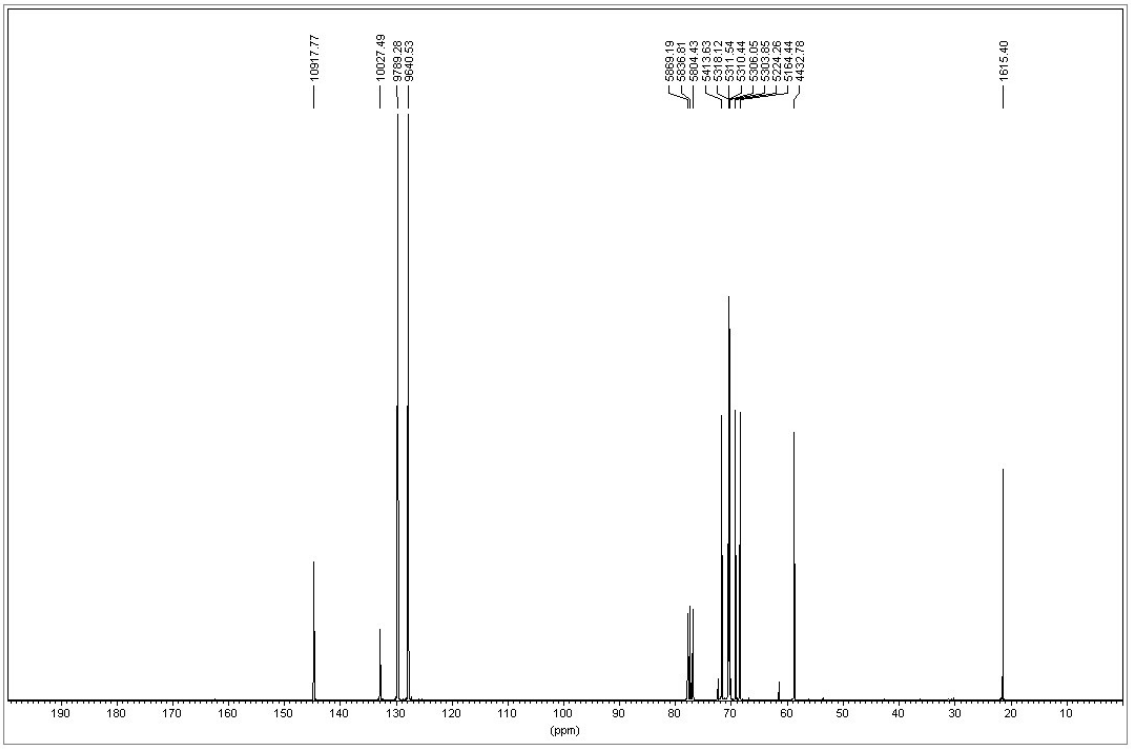
Compound 12: K_2CO_3 (3 equiv. per phenol) and KI (0.3 equiv. per tosyl) were added to an equimolar solution of phenol **10** and compound **11** (0.3 g, 0.31 mmol) in acetone (15 mL). The reaction mixture was stirred at 60°C during 24 hrs, filtered over Celite, evaporated under reduced pressure and the crude was diluted in CH_2Cl_2 (50 mL). The organic layer was washed twice with a saturated solution of $NaHCO_3$, then with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The compound **12** was obtained (0.28 mmol, 90%) as a colorless oil after purification by column chromatography (SiO_2, CH_2Cl_2/MeOH 90:10). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.10 (s, 2H, Ar^2-2,6-*H*), 6.87 (t, *J* = 5.1 Hz, 1H, $Ar^1OCH_2CH_2NH$), 6.80 (t, 1H, *J* = 2.0 Hz, Ar^1-2-*H*), 6.76 (q, 2H, *J* = 2.0 Hz, Ar^1-4,6-*H*), 4.22-4.15 (m, 6H, $Ar^2OCH_2CH_2O$), 4.12 (t, 2H, *J* = 5.1 Hz, $Ar^1OCH_2CH_2NH$), 4.05-3.95 (m, 8H, *J* = 7.0 Hz, $PO(OCH_2CH_3)_2$), 3.85-3.75 (m, 8H, $Ar^1OCH_2CH_2NH$ and OCH_2CH_2O), 3.70-3.50 (m, 54H, OCH_2CH_2O), 3.33 (s, 6H, $OCH_2CH_2OCH_3$), 3.07 (d, *J* = 21.7 Hz, 4H, Ar^1CH_2P), 2.48 (t, 2H, *J* = 6.6 Hz, $Ar^2OCH_2CH_2COOC(CH_3)_3$), 1.42 (s, 9H, $Ar^2OCH_2CH_2COOC(CH_3)_3$), 1.22 (t, *J* = 7.0 Hz, 12H,

PO(OCH_2CH_3)$_2$); ^{13}C NMR (75 MHz, $CDCl_3$) δ 170.9 (*C*OO(CH_3)$_3$), 167.1 (NH*C*O), 157.5 (Ar), 152.4 (Ar), 141.6 (Ar), 133.2 (*J* = 6.0 Hz) (Ar), 129.4 (Ar), 124.1 (Ar), 114.6 (*J* = 5.0 Hz) (Ar), 107.3 (Ar), 80.4 (*C*(CH_3)$_3$), 72.2 (PEG), 71.9 (PEG), 70.7 (PEG), 70.6 (PEG), 70.55 (PEG), 70.5 (PEG), 70.4 (PEG), 70.3 (PEG), 69.7 (PEG), 69.1 (PEG), 66.8 (O*C*$H_2$$CH_2$NH), 66.6 (*C*$H_2$$CH_2$COO), 62.1 (*J* = 7.0 Hz) (*C*$H_2$$CH_3$), 58.9 (O*C*$H_3$), 39.6 (*C*$H_2$NHCOAr), 35.2, (*C*$H_2$COO), 33.8 (*J* = 137.8 Hz) (*C*H-P), 27.9 (C(*C*H_3)$_3$), 16.4 (*J* = 6.0 Hz) (CH_2*C*H_3); ^{31}P NMR (81 MHz, $CDCl_3$) δ 26.06. MS (MALDI-TOF) m/z calculated for $C_{66}H_{117}NaNO_{29}P_2$: 1472.72, obtained: 1472.65.

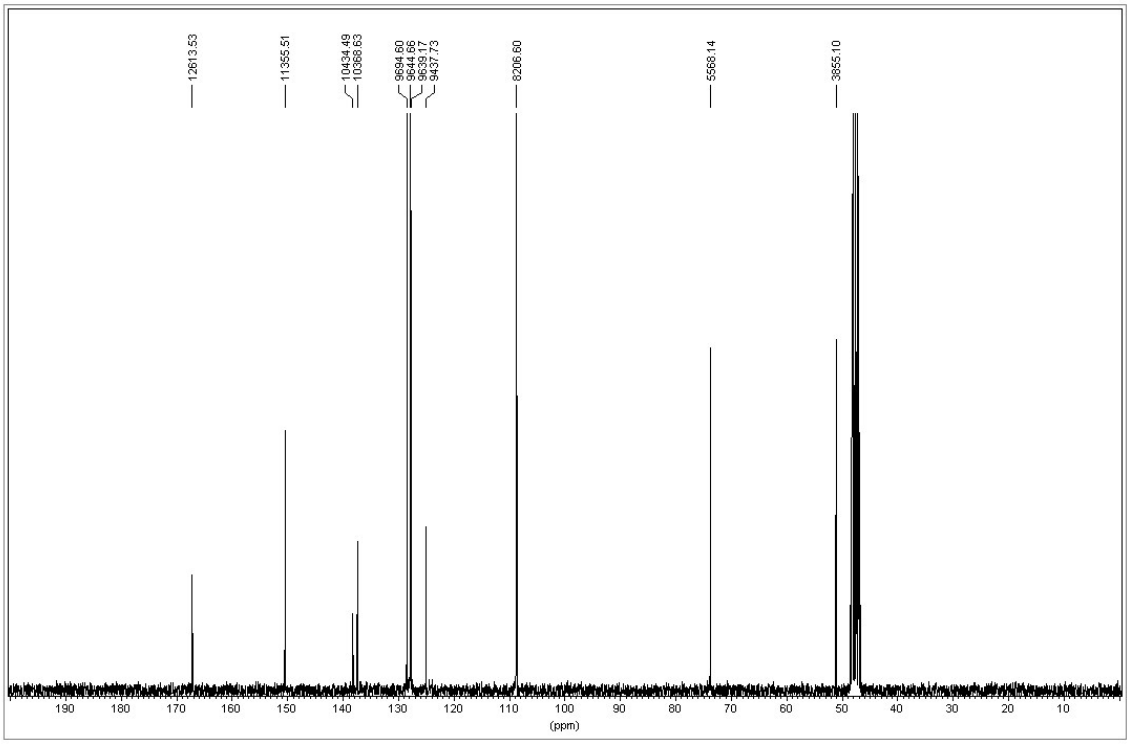
D2-2P: dendron **D2-2P** was synthesized following the Mc Kenna procedure (see reference 5). TMSBr (0.55 mL, 3 mmol, 30 equiv., 10.0 equiv. per ethyl phosphonate and t-butyl ester function) was added dropwise to a solution of compound **12** (0.2 g, 0.14 mmol) in CH_2Cl_2 at 0°C. After stirring overnight at room temperature, the volatiles were evaporated and MeOH was added to the crude product, and then evaporated. The phosphonic acid **D2-2P** was obtained without further purification (0.13 mmol, 94%) as an orange oil. ^{1}H NMR (300 MHz, CD_3OD) δ 7.28 (s, 2H, Ar^2-2,6-*H*), 6.92-6.86 (m, 3H, Ar^1-2,4,6-*H*), 4.35-4.20 (m, 8H, Ar^{2}O*C*$H_2$$CH_2$O and Ar^{1}O*C*$H_2$$CH_2$NH), 3.92-3.82 (m, 8H, Ar^{1}OCH_2*C*H_2NH and O$CH_2$$CH_2$O), 3.80-3.53 (m, 54H, O$CH_2$$CH_2$O), 3.38 (s, 6H, O$CH_2$$CH_2$O*C*$H_3$), 3.18 (d, *J* = 21.8 Hz, 4H, Ar^{1}CH_2P), 2.62 (t, 2H, *J* = 6.0 Hz, Ar^{2}OCH_2*C*H_2COOH); ^{13}C NMR (75 MHz, CD_3OD) δ 172.2 (*C*OOH), 167.1 (NH*C*O), 158.8 (Ar), 152.3 (Ar), 141.0 (Ar), 134.8 (*J* = 6.0 Hz) (Ar), 128.8 (Ar), 123.8 (Ar), 114.3 (Ar), 106.4 (Ar), 72.2 (PEG), 71.7 (PEG), 70.4 (PEG), 70.25 (PEG), 70.15 (PEG), 70.1 (PEG), 70.0 (PEG), 69.95 (PEG), 69.4 (PEG), 68.8 (PEG), 66.3 (O*C*$H_2$$CH_2$NH), 66.1 (*C*$H_2$$CH_2$COO), 57.8 (O*C*$H_3$), 50.8, 39.6 (*C*$H_2$NHCOAr), 34.6 (*C*$H_2$COO), 33.6 (*J* = 134.5 Hz) (*C*H-P); ^{31}P NMR (81 MHz, CD_3OD) δ 25.19. MS (MALDI-TOF) m/z calculated for $C_{54}H_{94}NO_{29}P_2$: 1282.53, obtained: 1282.46; calculated for $C_{54}H_{93}NaNO_{29}P_2$: 1304.53, obtained: 1304.45.

Compound 1 (^{1}H and ^{13}C, $CDCl_3$)

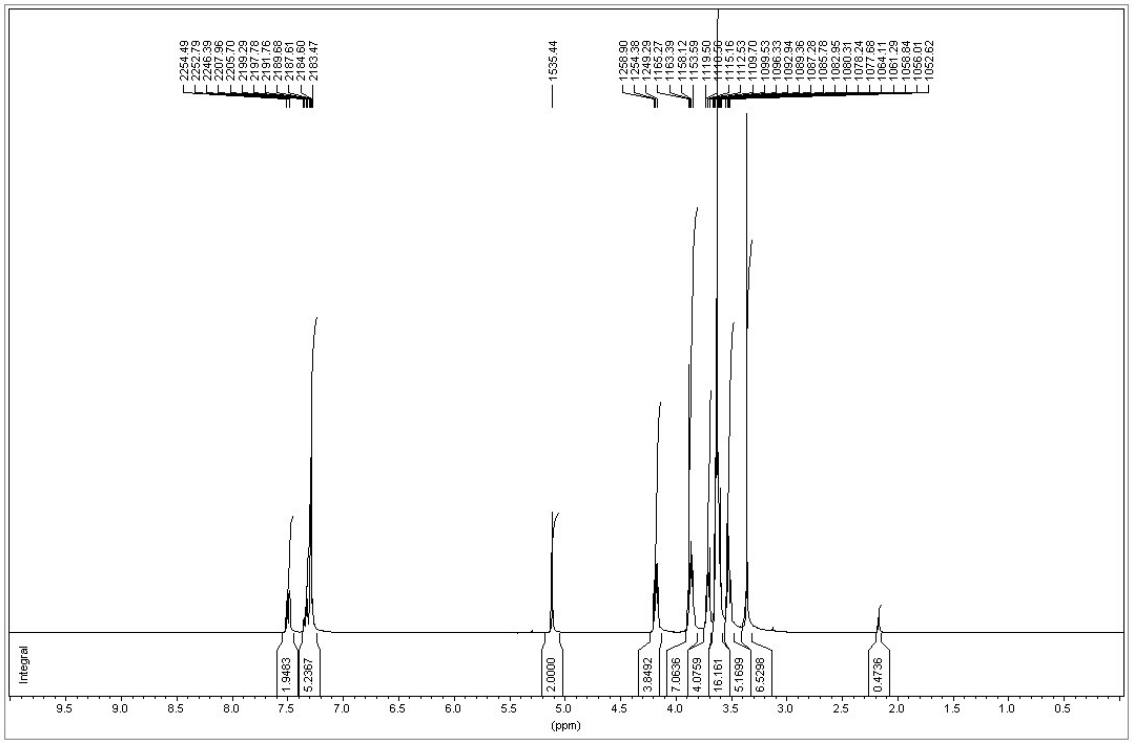


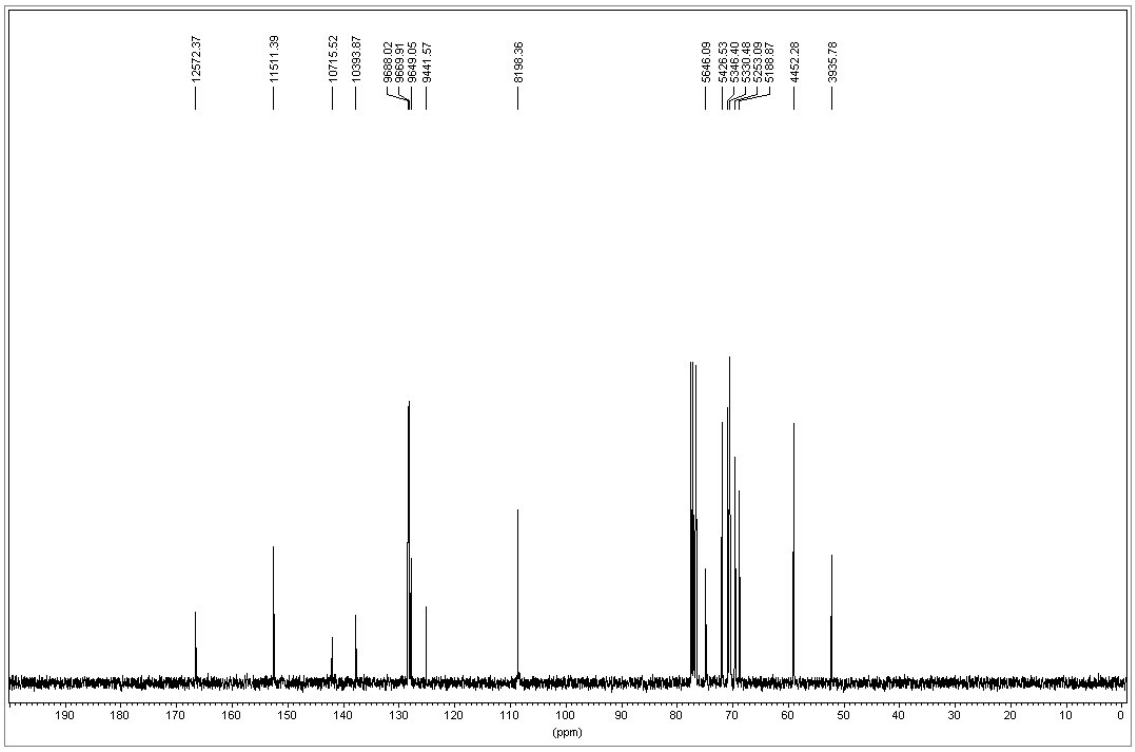


Compound 2 (^{13}C, CD_3OD)

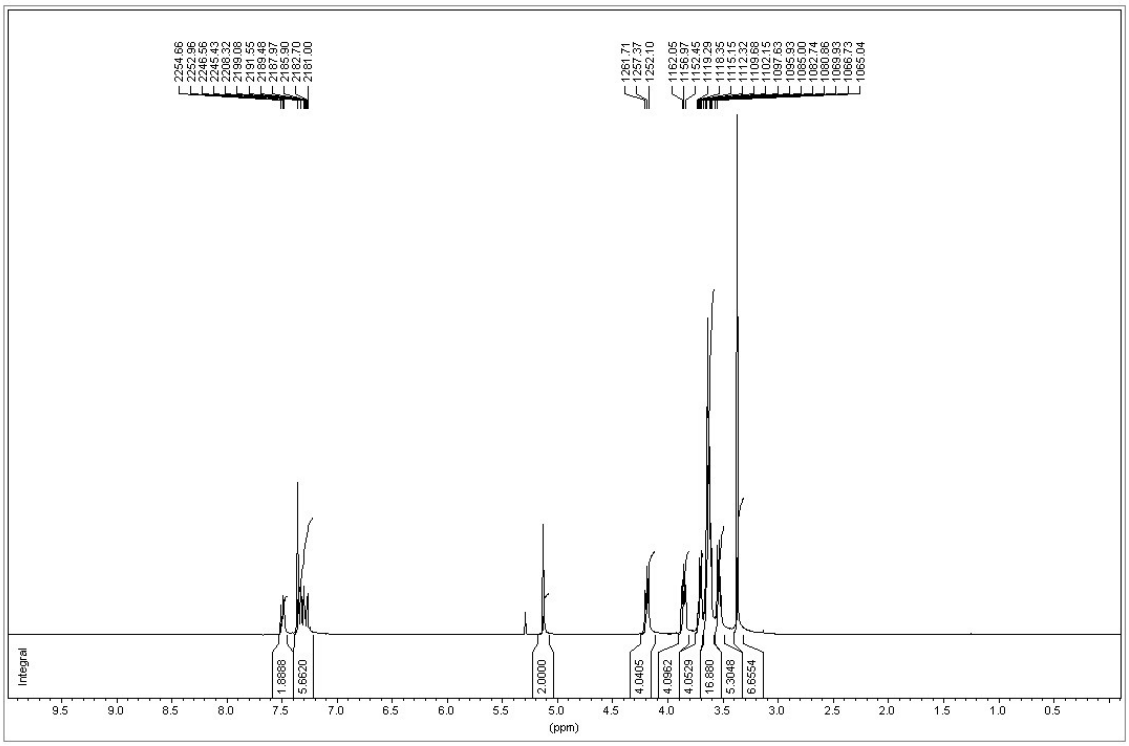


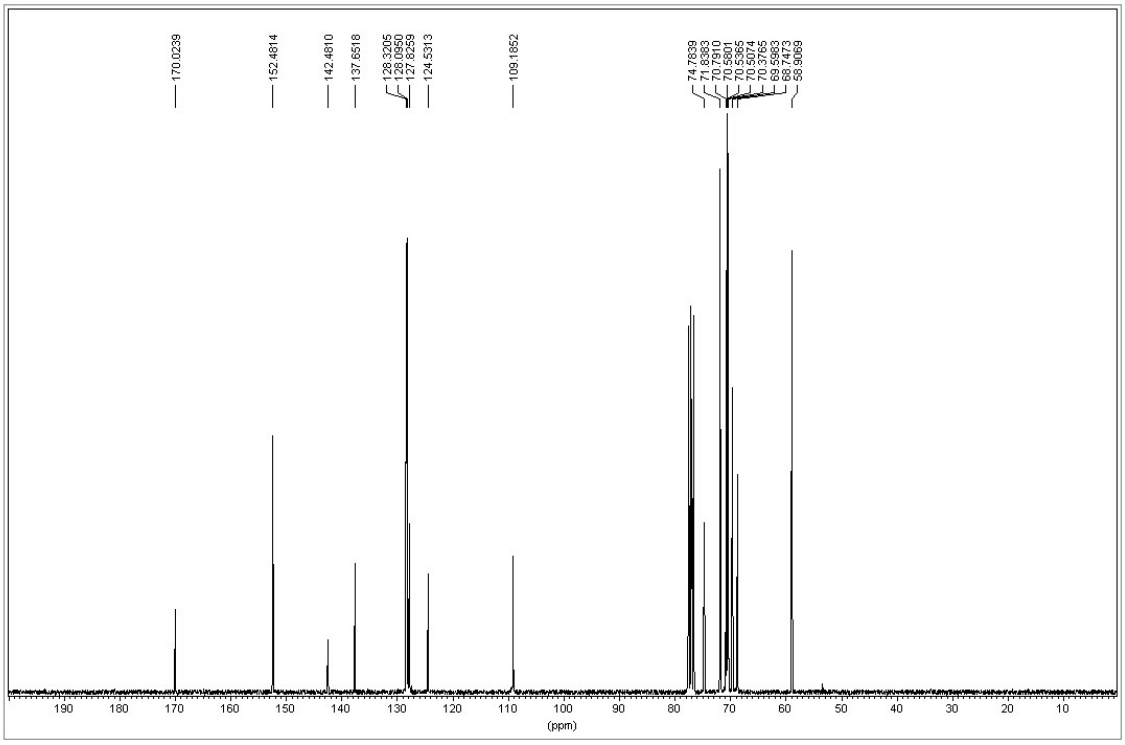
Compound 3 (^{1}H and ^{13}C, $CDCl_3$)



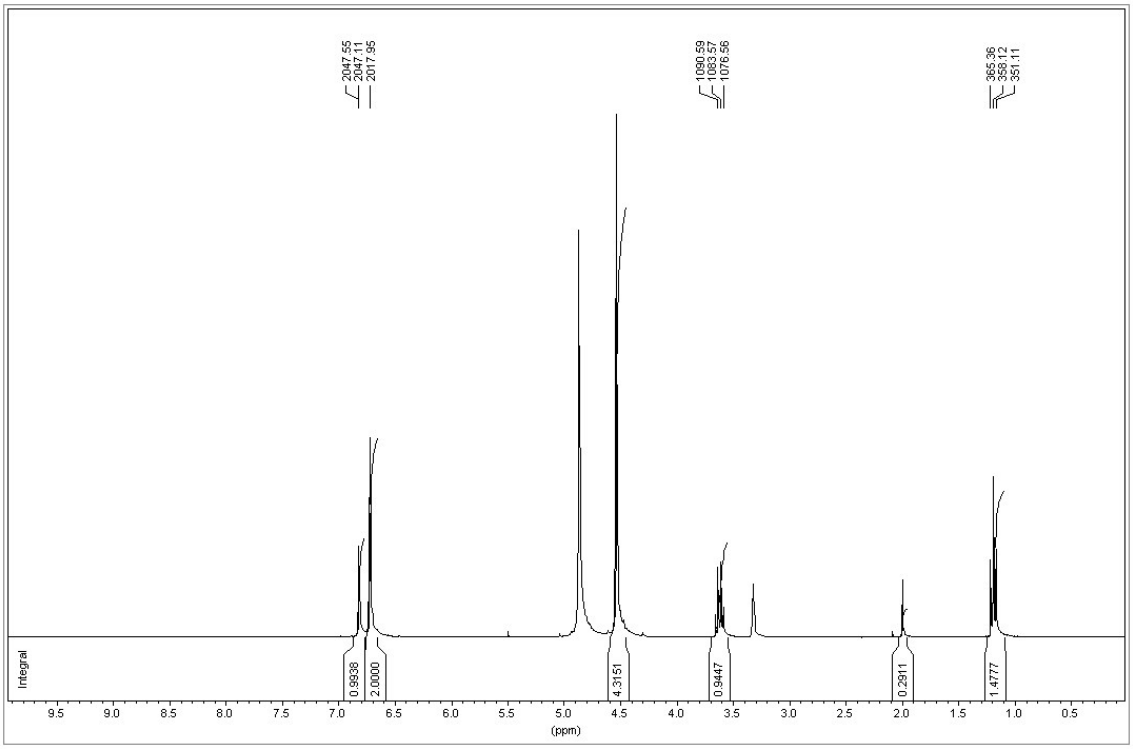


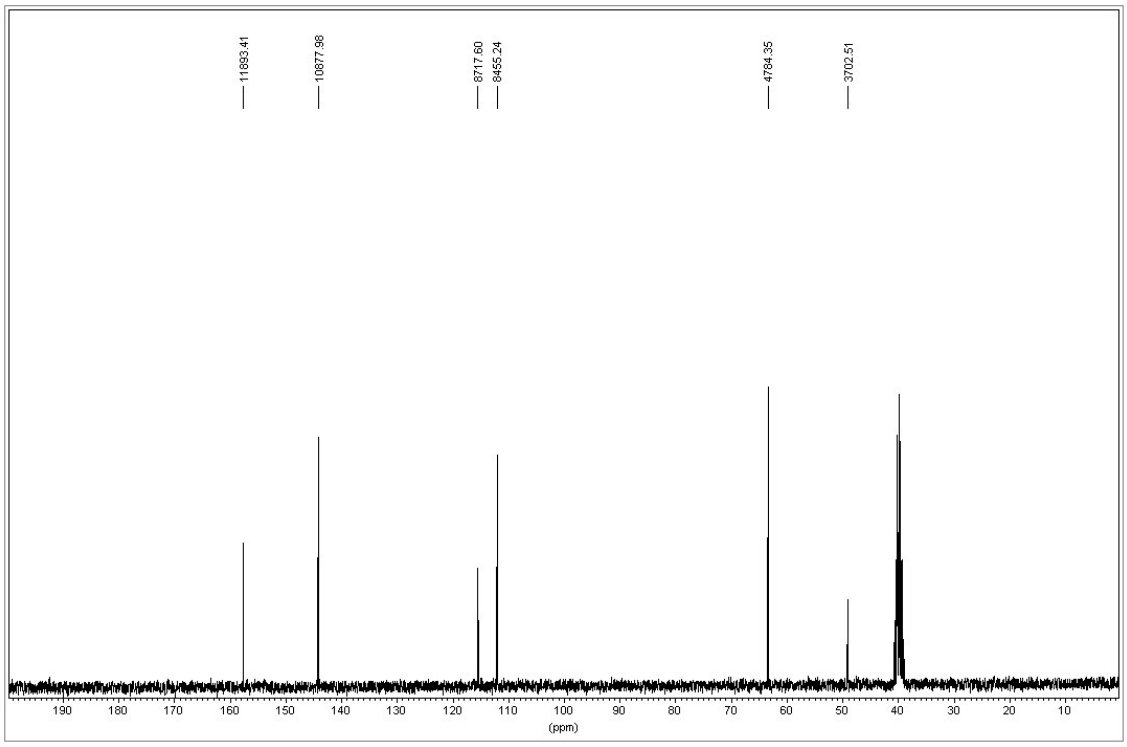
Compound 4 (^{1}H and ^{13}C, $CDCl_3$)



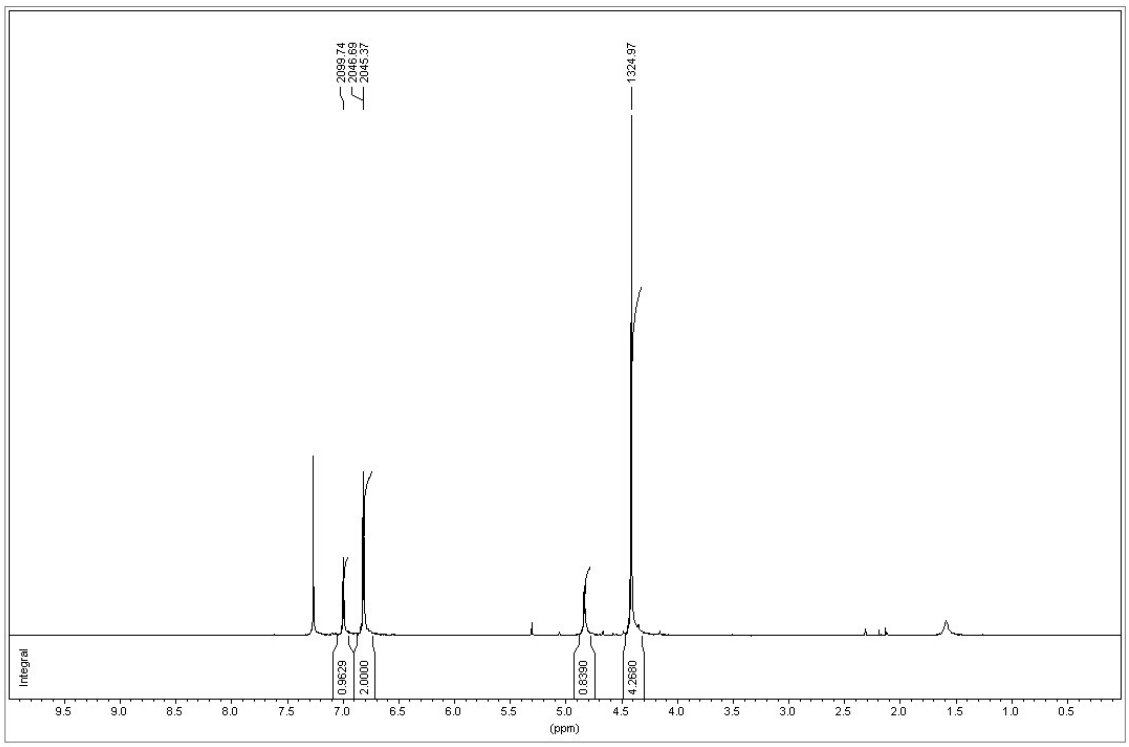


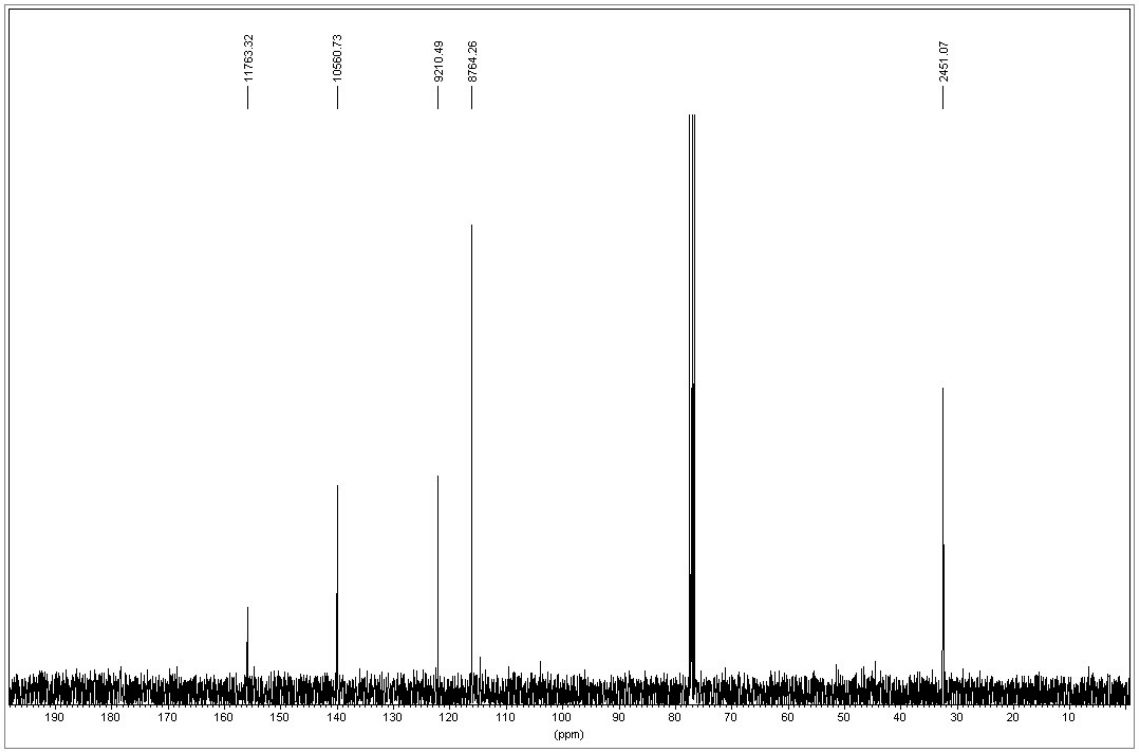
Compound 5 (^{1}H and ^{13}C, CD_3OD)



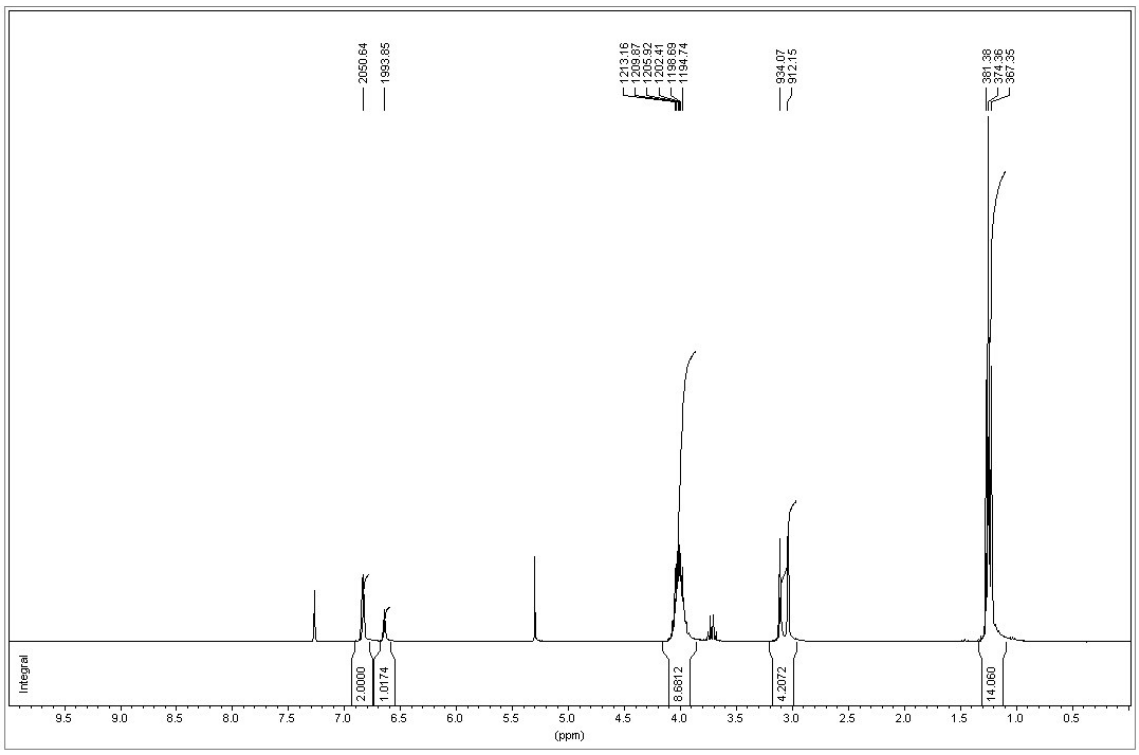


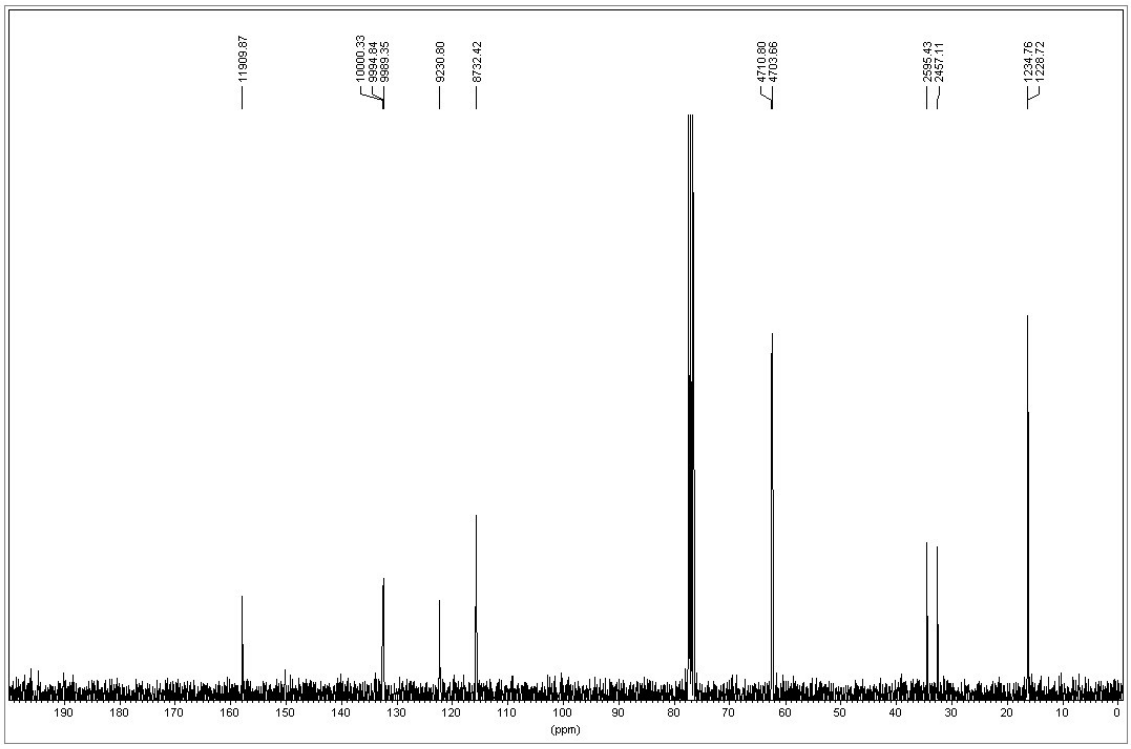
Compound 6 (^{1}H and ^{13}C, $CDCl_3$)





Compound 7 (^{1}H, ^{13}C and ^{31}P, $CDCl_3$)

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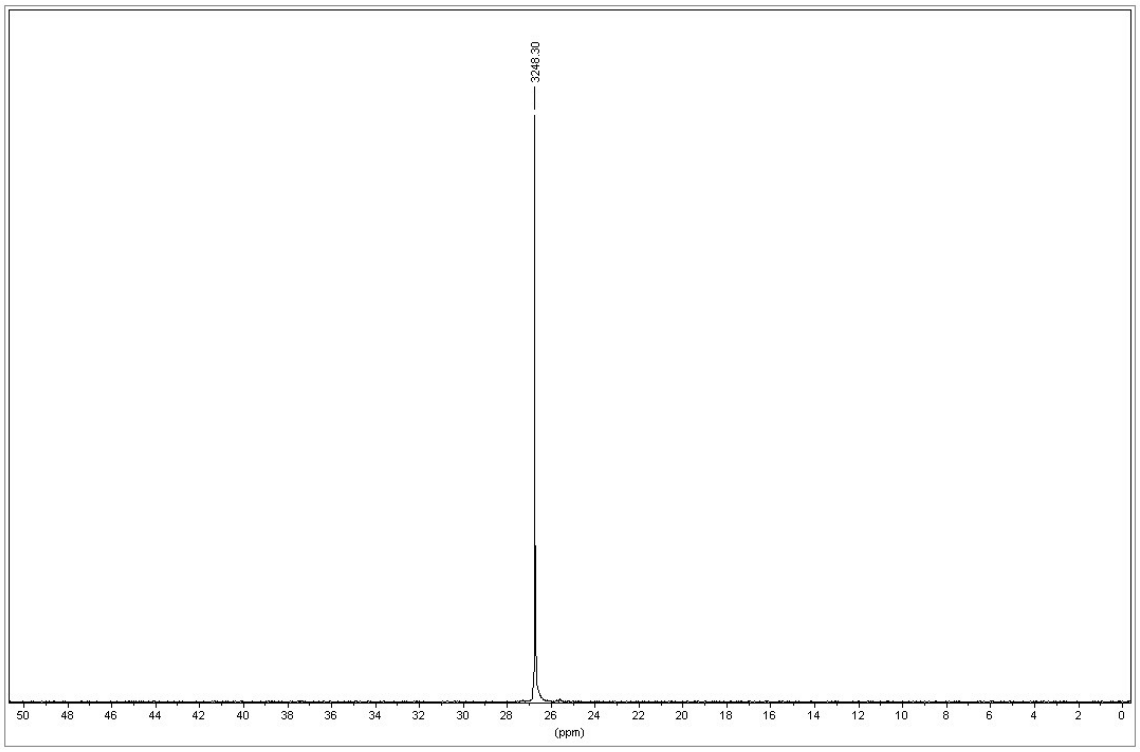
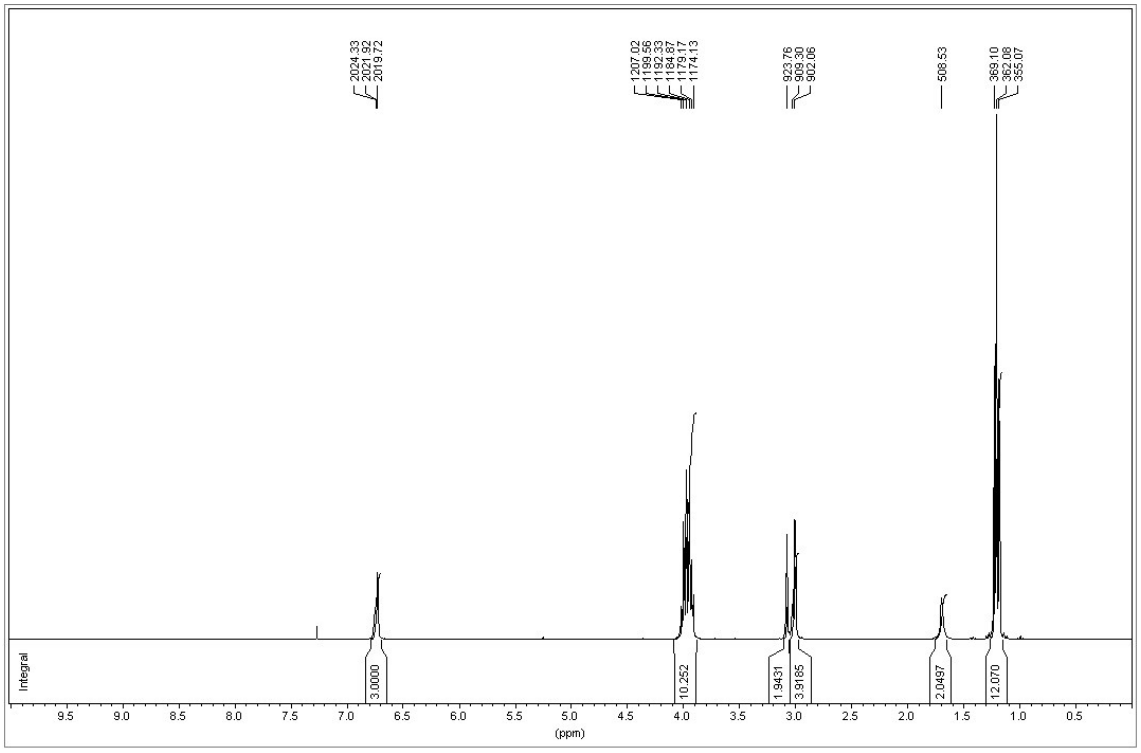
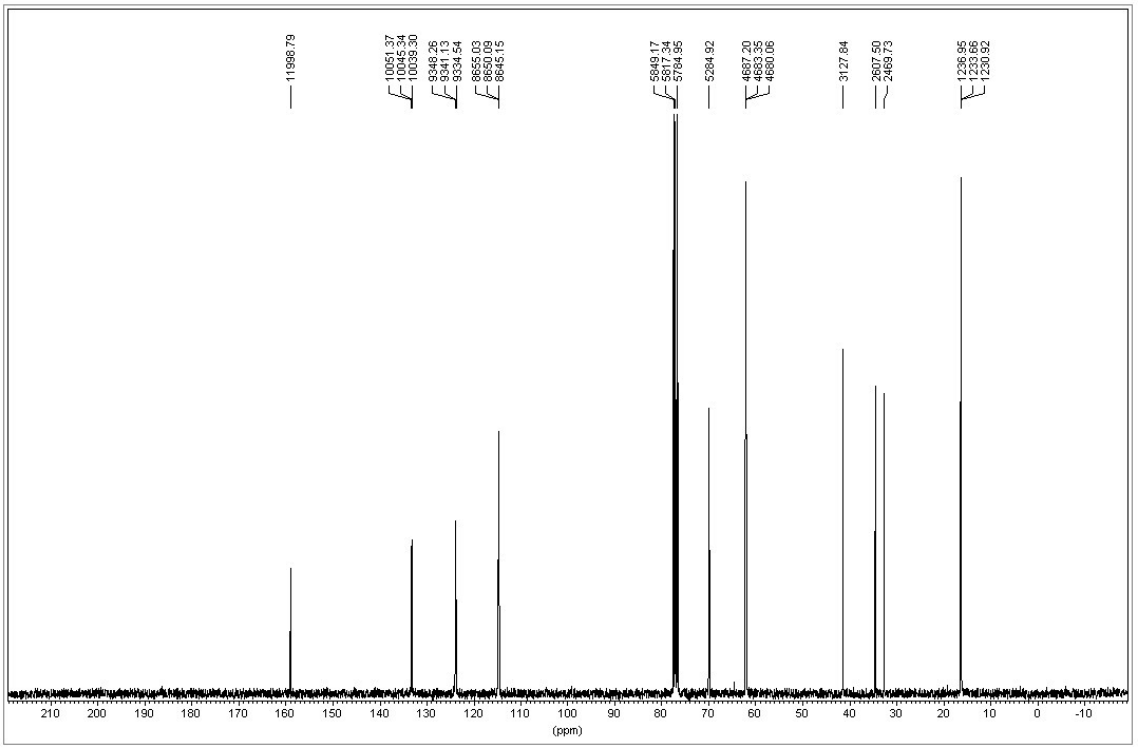
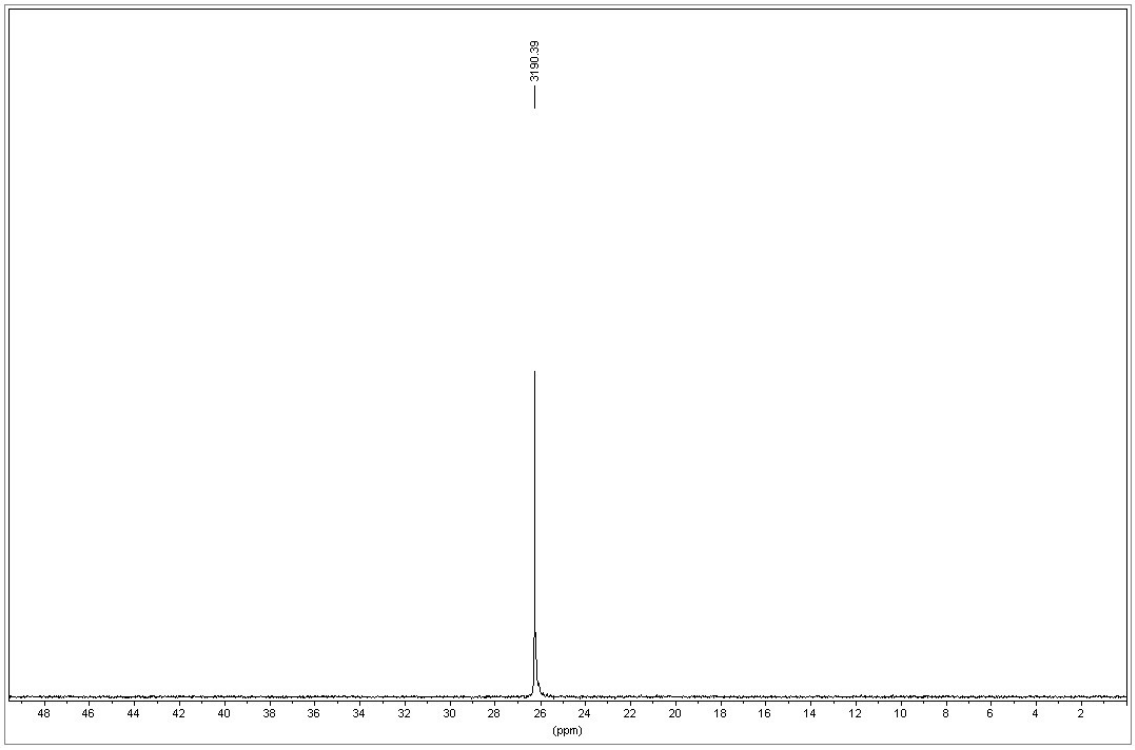
9969.35
9230.80
8732.42
4710.80
4703.86
2595.43
2457.11
1234.76
1228.72
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
(ppm)


3248.30
50 48 46 44 42 40 38 36 34 32 30 28 26 24 22 20 18 16 14 12 10 8 6 4 2 0
(ppm)

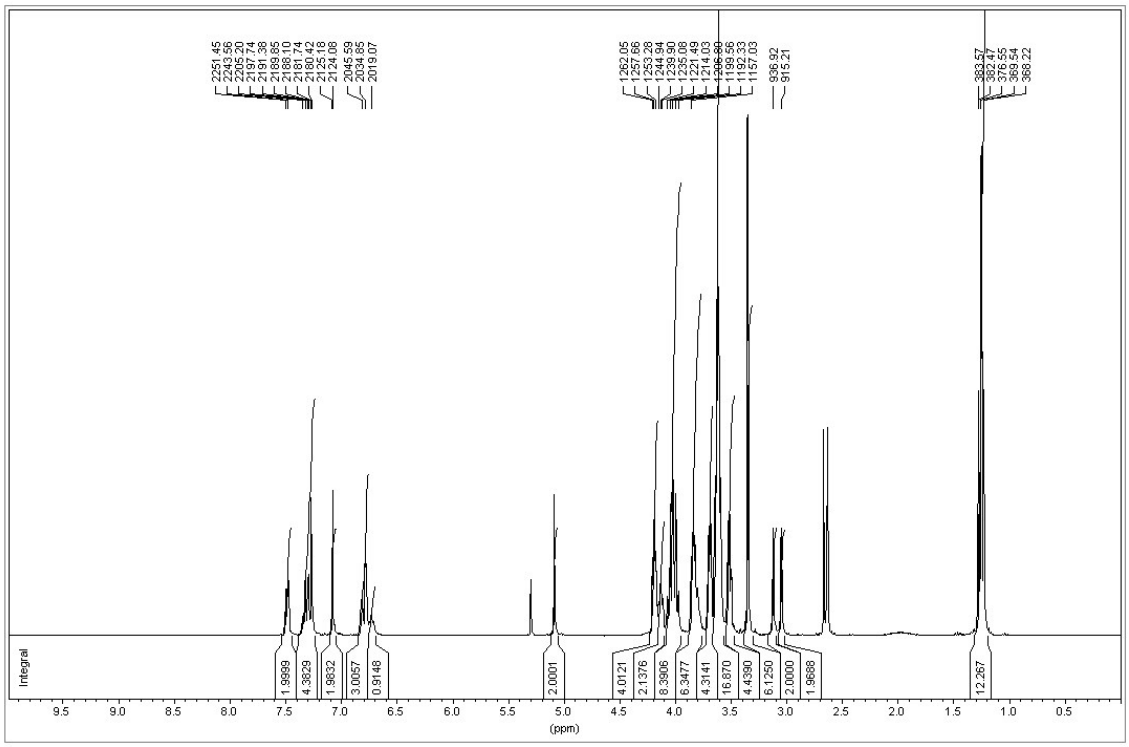
Compound 8 (^{1}H, ^{13}C and ^{31}P, $CDCl_3$)

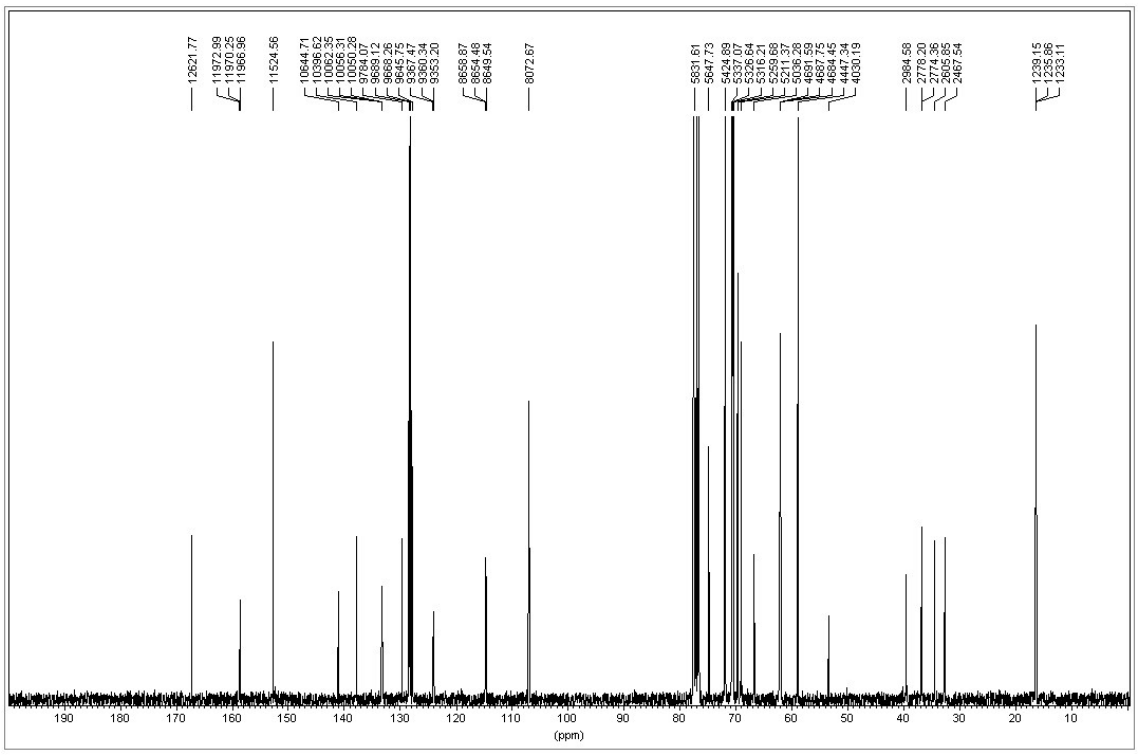






Compound 9 (^{1}H, ^{13}C and ^{31}P, $CDCl_3$)

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11966.96
11524.56
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10095.62
10062.35
10056.31
10050.28
9784.07
9669.12
9665.26
9648.75
9367.47
9360.34
9353.20
8658.87
8654.48
8649.54
8072.67
5831.61
5647.73
5424.89
5337.07
5336.64
5316.21
5259.68
5211.37
5036.28
4691.59
4687.75
4684.45
4447.34
4030.19
2984.58
2778.20
2774.36
2695.85
2467.54
1239.15
1235.86
1233.11
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170
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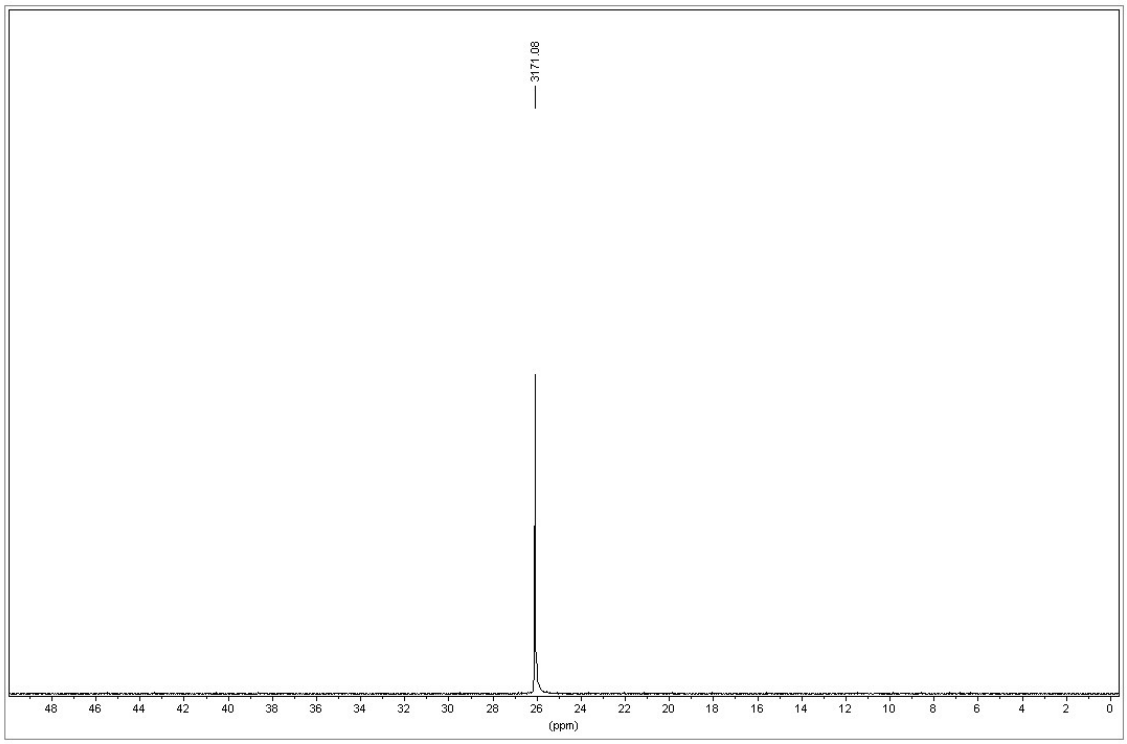
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
(ppm)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36
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32
30
28
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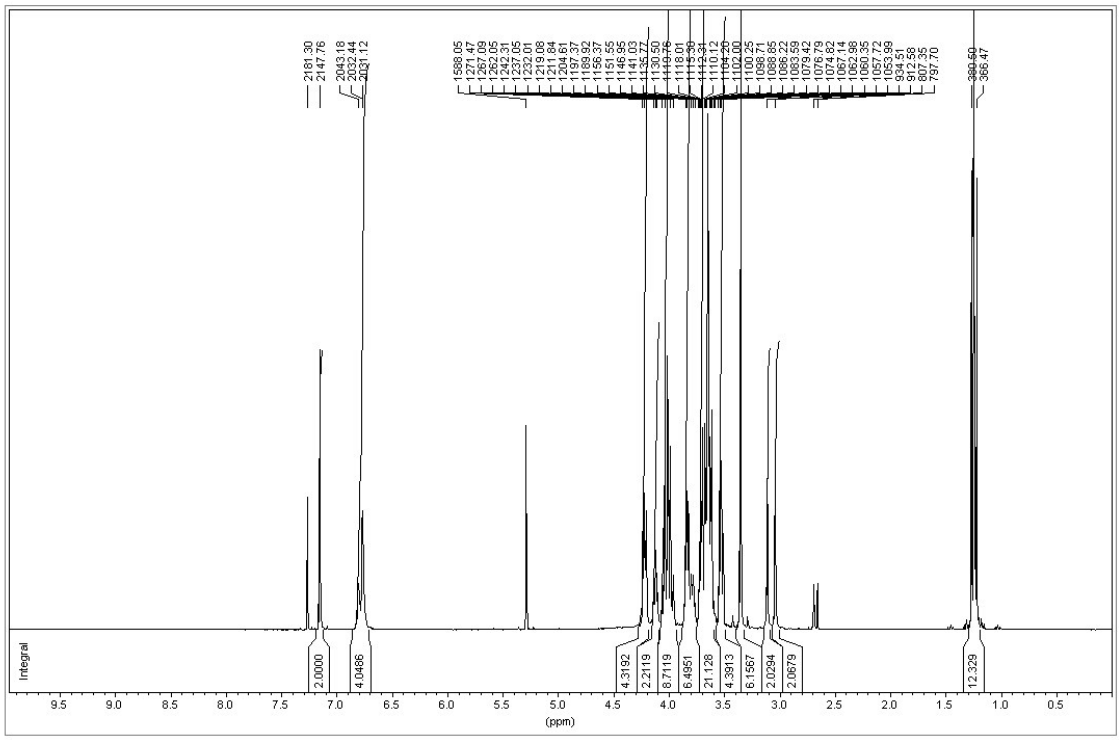
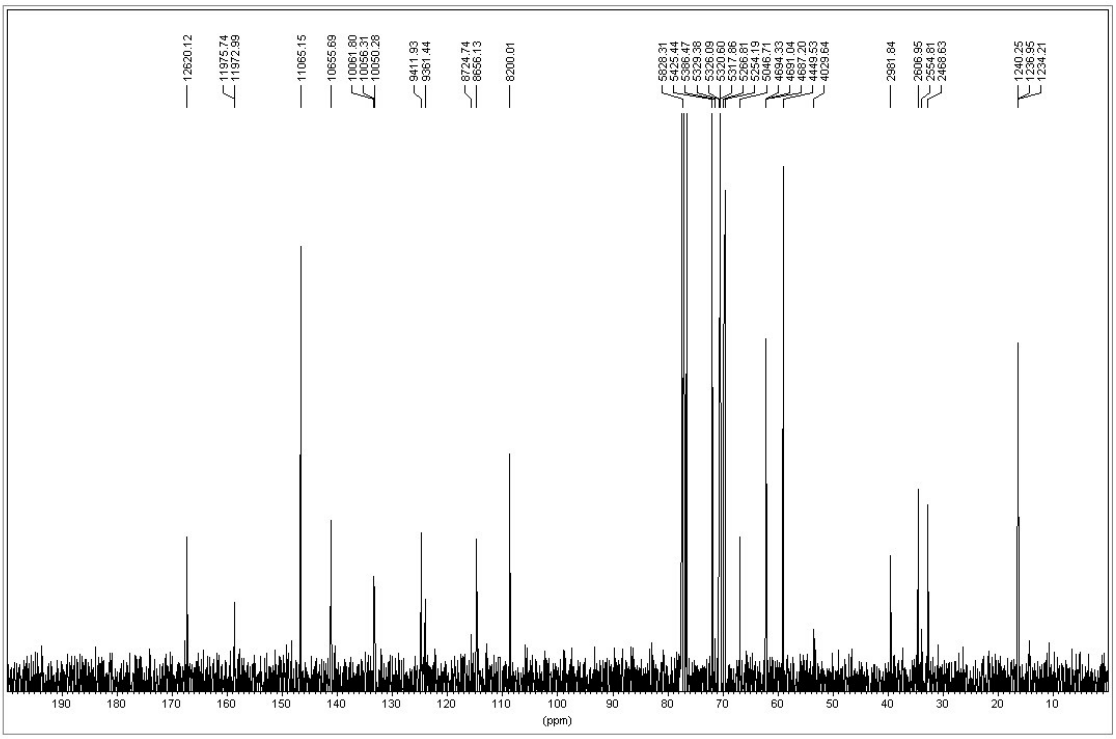
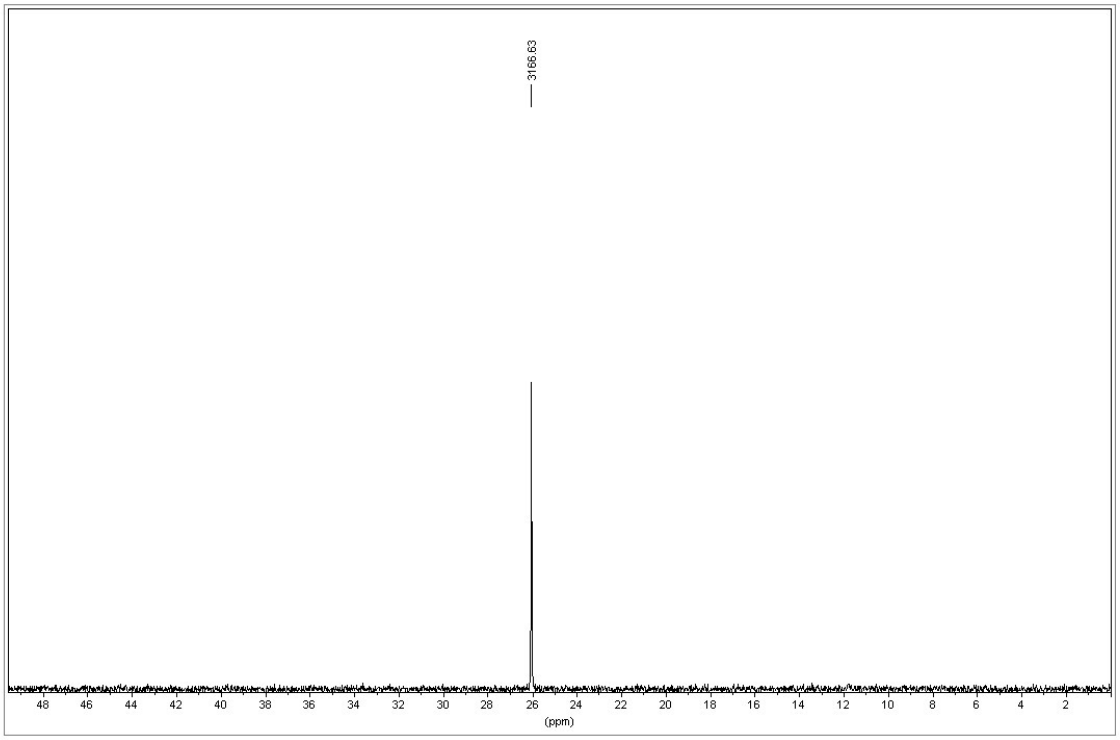
22
20
18
16
14
12
10
8
6
4
2
0
(ppm)

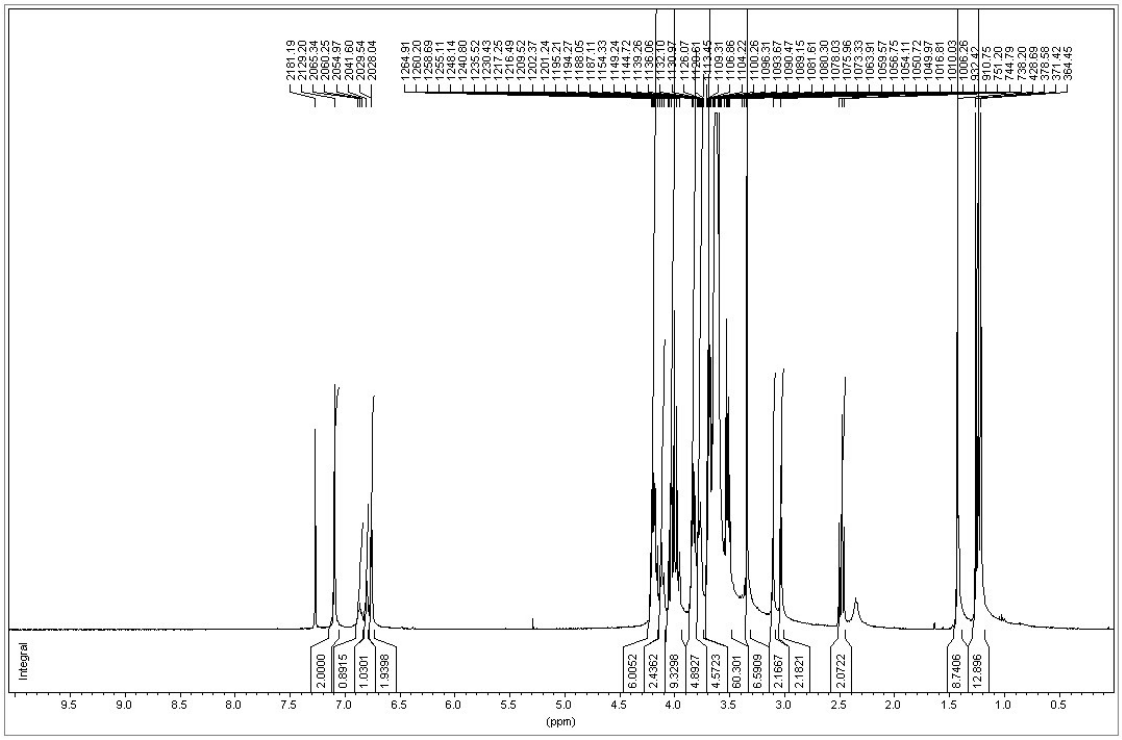
Compound 10 (^{1}H, ^{13}C and ^{31}P, $CDCl_3$)

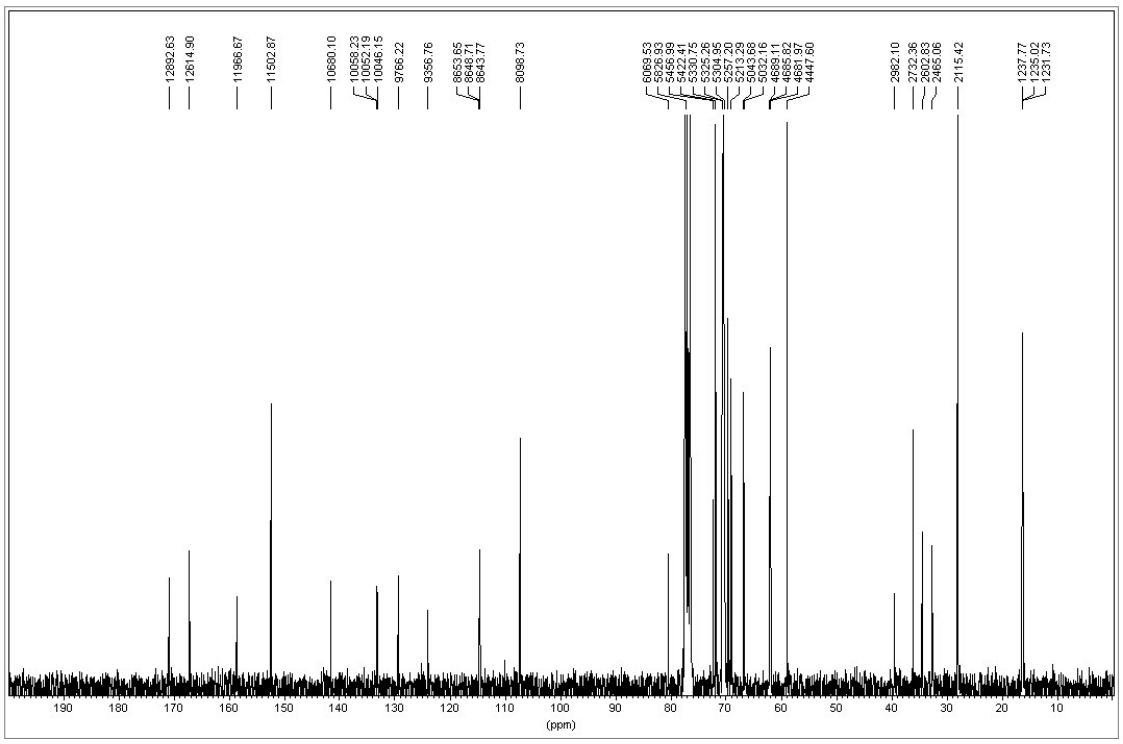






Compound 12 (^{1}H, ^{13}C and ^{31}P, $CDCl_3$)

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10052.19
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9766.22
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8847.71
8843.77
8098.73
6069.53
5826.93
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5422.41
5330.75
5325.26
5304.95
5257.20
5213.29
5043.68
5007.15
4639.11
4685.02
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4447.60
2982.10
2732.36
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2465.06
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1235.02
1231.73
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70
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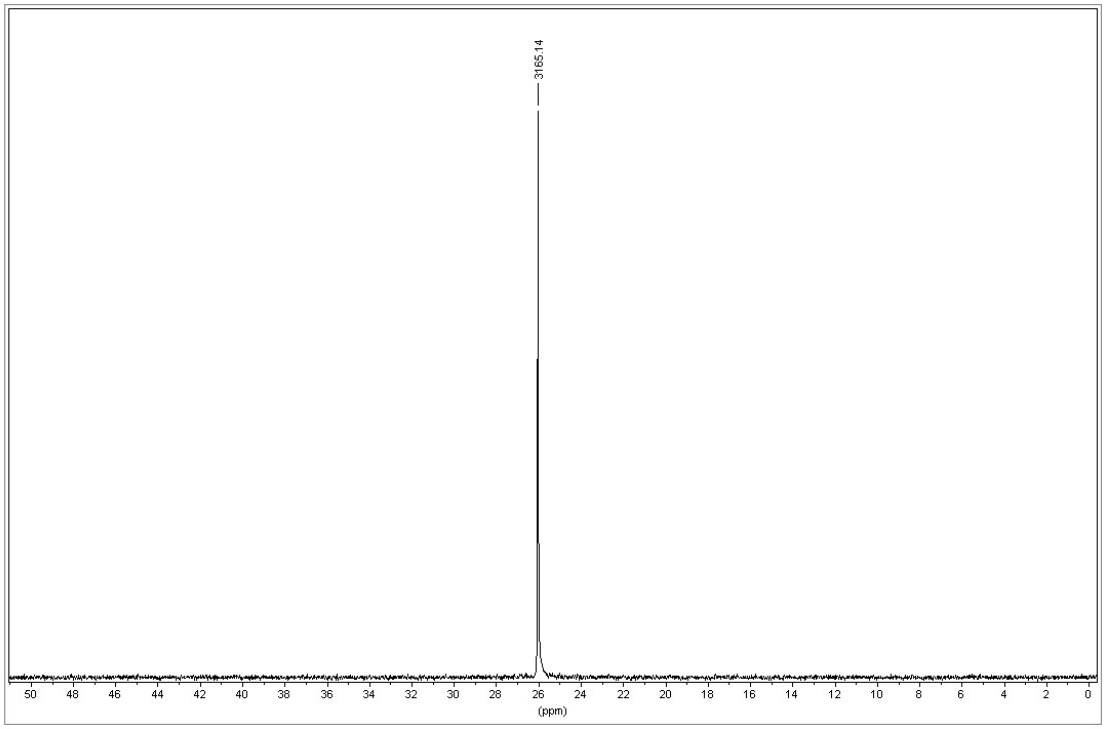
10
(ppm)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30
28
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24
22
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18
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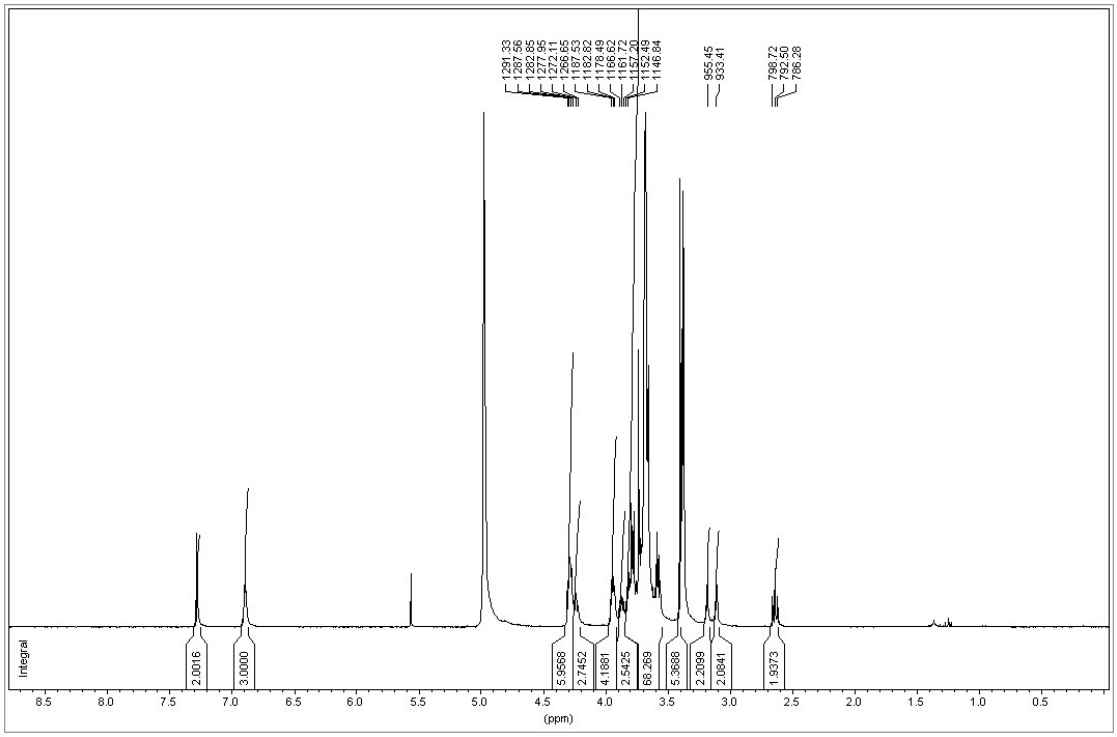
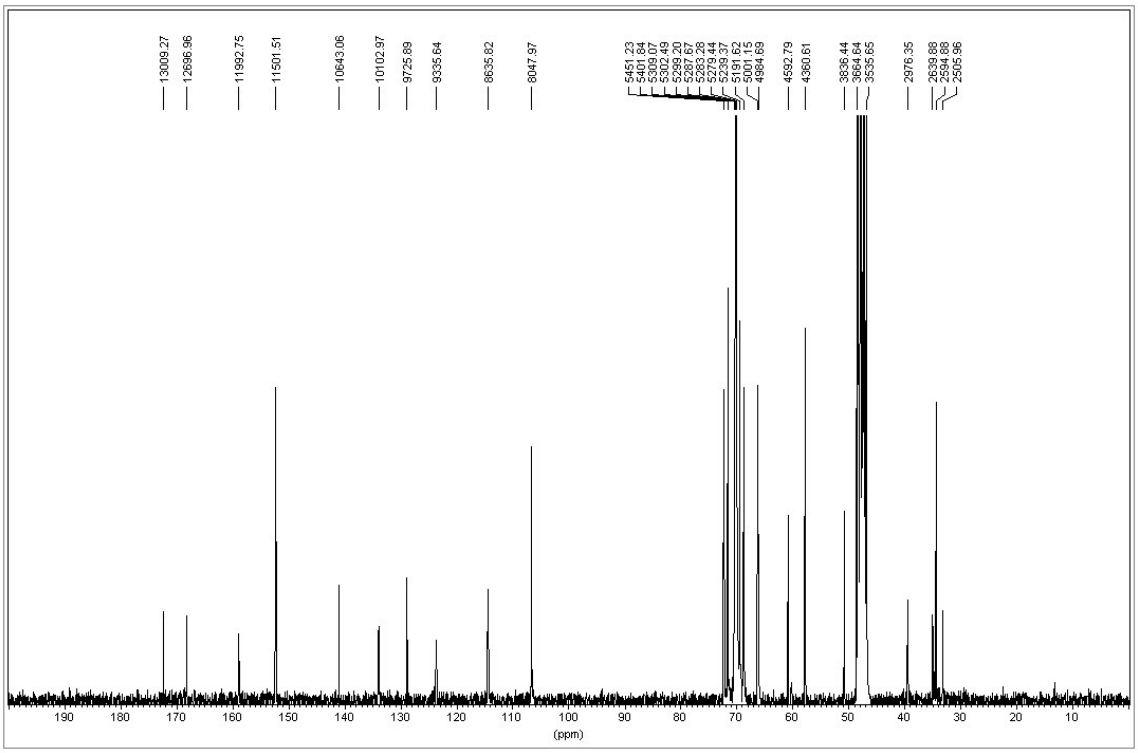
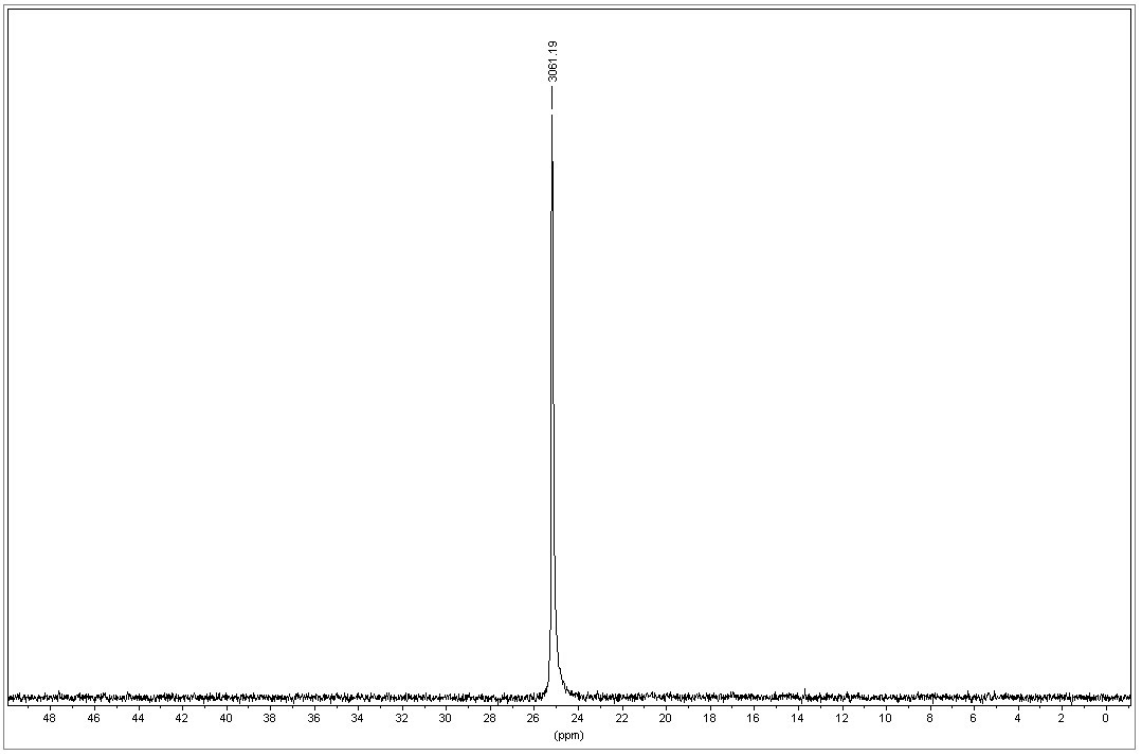
8
6
4
2
0
(ppm)

Compound D2-2P (^{1}H, ^{13}C and ^{31}P, CD_3OD)







2) Characterization of the nanoparticles NP10@OA

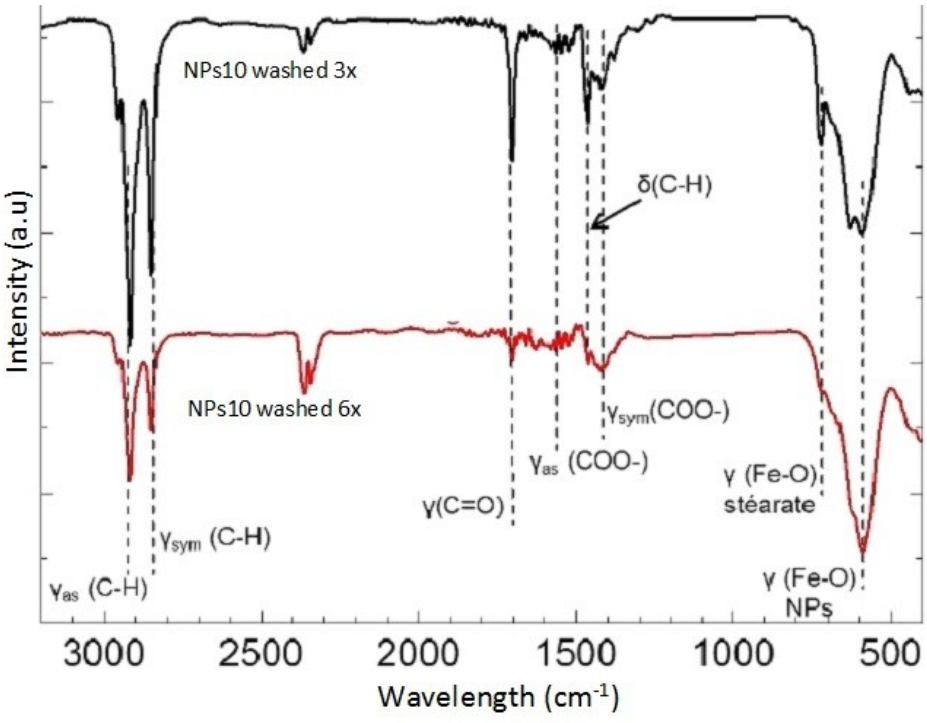


Figure S1 FTIR profiles of NP10@OA washed 3 and 6 times by precipitation/redispersing technique.

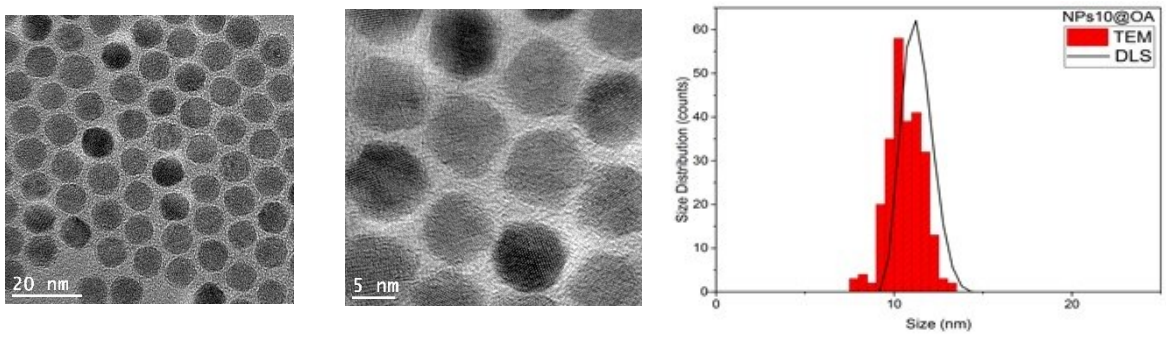


Figure S2: TEM images of NS10@AO at 20nm zoom (left) and at high resolution (middle); DLS and TEM size distribution of NPs10@OA (right).

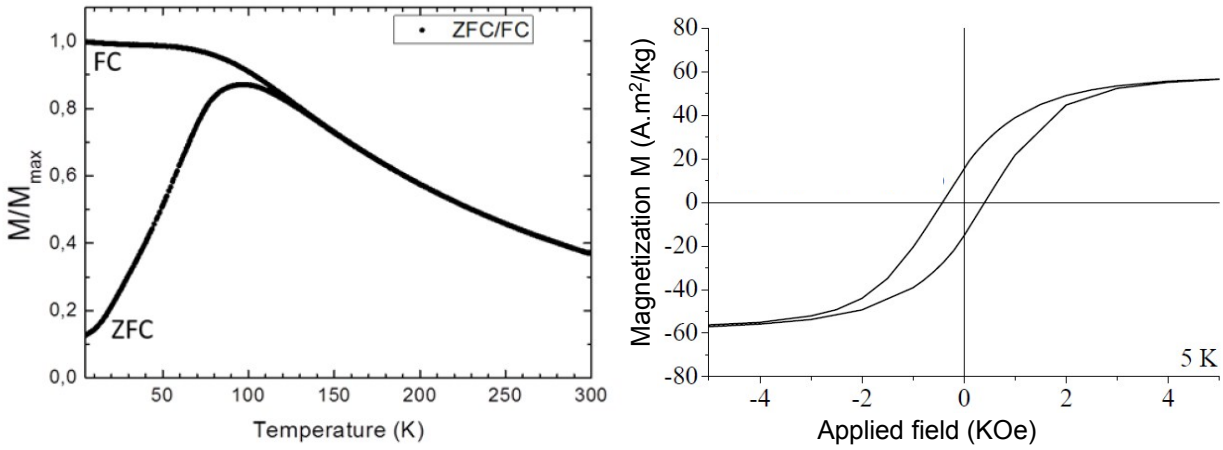


Figure S3: Temperature dependence of ZFC and FC magnetization (left) and hysteresis loop recorded at 5K (right) for NPs10@OA sample.

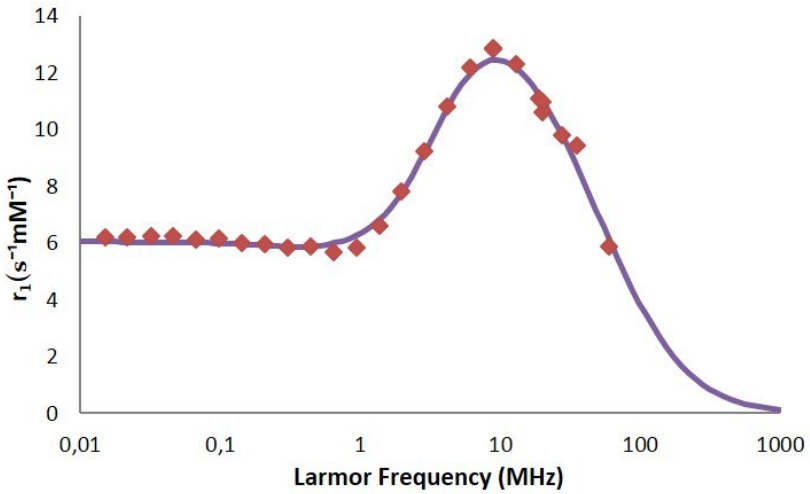


Figure S4: Relaxation evolution with Larmor frequency of NPs10@OA (dots) and the theoretical simulation according to superparamagnetic theory (line).

Table S1: Size distribution by volume and Zeta potential before and after Alexa495 grafting on dendronized NPs at pH = 7.4.

	NPs10@D2	NPs10@D2-2P	NPs10@D2_Alexa495	NPs10@D2-2P_Alexa495
d^{DLS} (nm)	17 ± 1.5	14 ± 1.1	18 ± 0.9	21 ± 2.3
PDI	0.33	0.29	0.20	0.37
Zeta potential (mV)	–16.9	–18.5	–11.5	–15

3) *In vitro* supplementary data

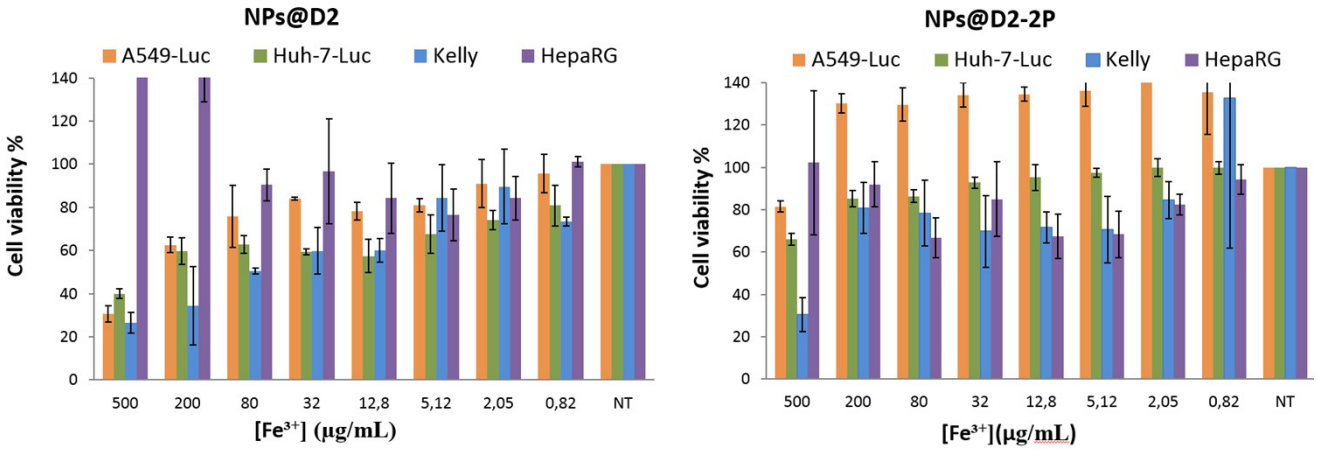


Figure S5 MTT cell viability results obtained for cells transfected with NPs10@D2 or NPS10@D2-2P after 48h incubation.

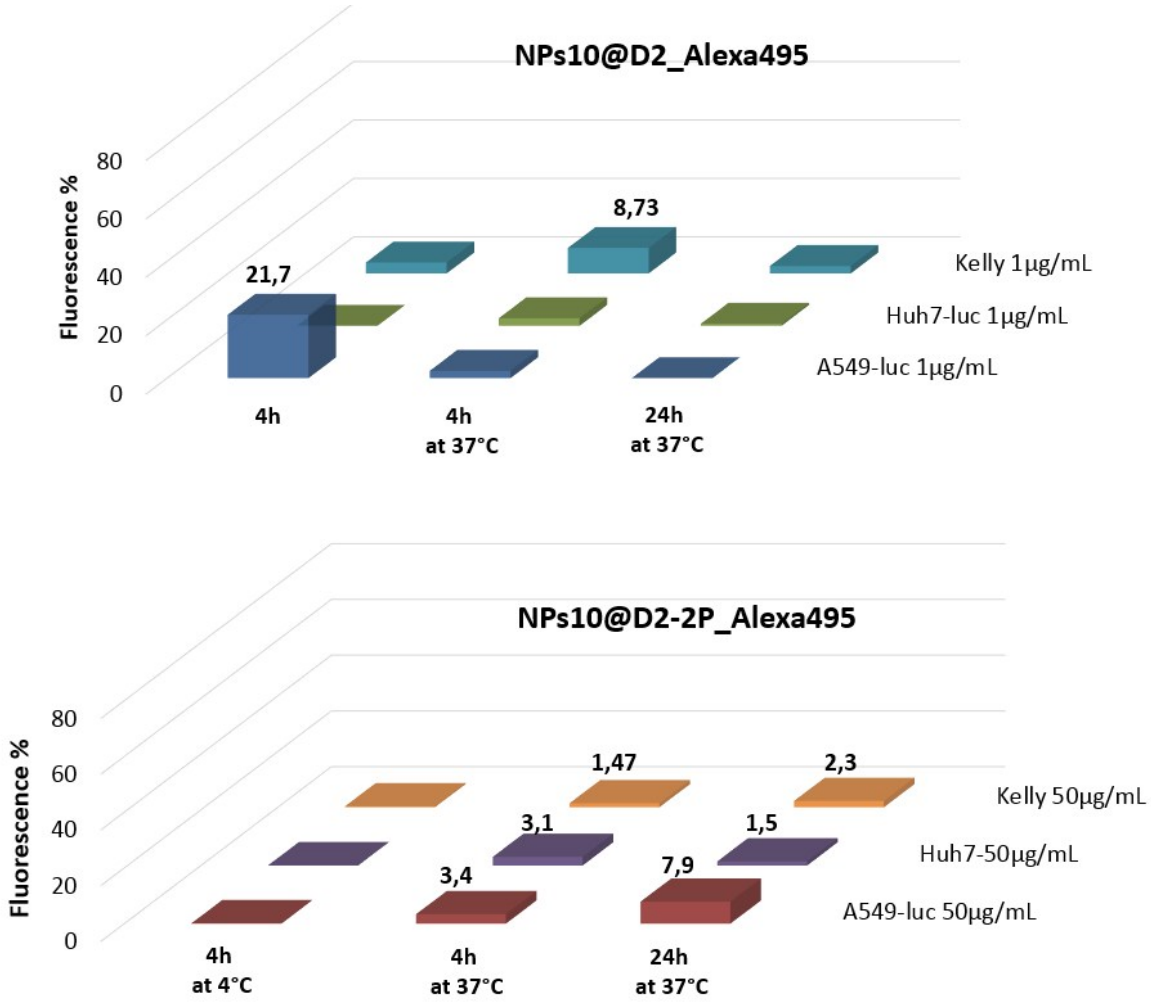


Figure S6: Flow cytometric analysis of A549-luc, Huh7-luc and Kelly cells incubated at different temperatures and times, with different concentrations of Alexa495 labeled NPs10@D2 (1 µg/mL) and NPs10@D2-2P (50 µg/mL).