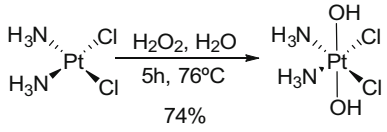
Supplementary material

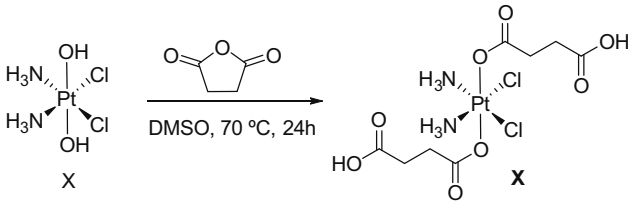
Synthesis of PtBC

Synthesis of c,c,t-[Pt(NH3)$_2$Cl$_2$(OH)$_2$]



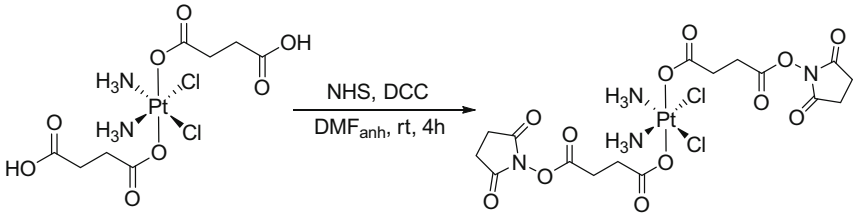
To a suspension of cis-platin (1.3 g, 4.3 mmol) in 35.8 mL Milli Q water, hydrogen peroxide 30% (35.8mL) was added. The resulting pale-yellow suspension was heated to 76°C for 5 h under reflux and in absence of light. Afterwards, the mixture is let to cool down to room temperature overnight under continuous stirring. The obtained suspension was then left in the fridge for 3 h. The precipitated yellow crystals were then isolated by filtration and washed with ice cold water, ethanol and ether, affording the final product as a granular crystalline yellow solid (1.063g, 3.1 mmol, 74% yield) IR *ν*: 3,783 (m), 3,694 (w), 3,661 (w), 3,579 (w), 3,515 (s), 3,258 (s), 2,989 (s), 2,722 (s), 2,508 (w), 2,445 (m), 2,445 (m), 22,74 (s), 2,107 (s), 1,813 (s), 1,585 (s), 1,488 (m), 1,356 (s), 1,037 (s), 964 (s), 904 (s), 557 (s), 452 cm^{-1} (s).

Synthesis of disuccinic cisplatin



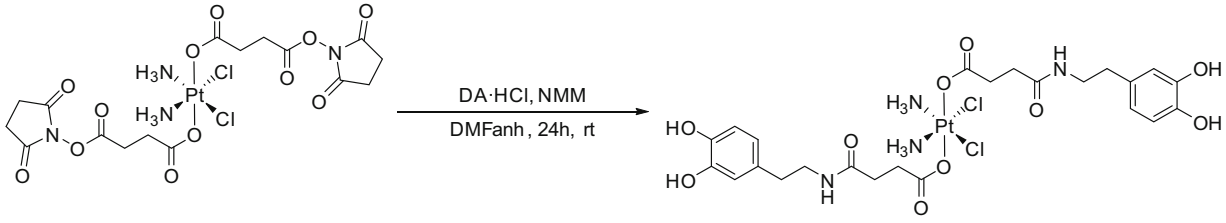
Oxoplatin (561.2 mg, 1.68 mmol) and succinic anhydride (674 mg, 6.74 mmol) were suspended in anhydrous DMSO (2mL). The resulting suspension was then heated to 76°C in darkness for 24 h. The resulting clear yellow solution was lyophilized to remove the solvent. The viscous residue was then sonicated with ethyl acetate to yield a light-yellow solid in suspension. The precipitate was then filtrated and washed with ice cold acetone, yielding the final DSCP product as a light-yellow powder (686mg, 1.283 mmol, 76% Yield). ^{1}H NMR (360 MHz, DMSO-d_6) δ 12.07 (bs, 2H^4), 6.48 (bs, 6H^1), 2.41–2.28 (m, 8H^3).; IR (KBr) *ν*: 3,467 (m), 3,278 (s), 3,081 (s), 3,933 (w), 2,631 (m), 1,734 (s), 1,709 (m), 1,684 (s), 1,661 (s), 1,630 (s), 1,581 (m), 1,551 (w), 1,425 (m), 1,390 (m), 1,346 (s), 1,294 (s), 1,265 (w), 1,210 (s), 1,180 (s), 1,014 (s), 956 (s), 799 (w), 713 (w), 671 (s), 592 (m), 481 (s) cm^{-1}

Synthesis of succinic acid-NHS



DSCP (0.5 g, 0.93 mmol), DCC (0.58 g, 2.8 mmol), and NHS (0.43 g, 3.75 mmol) were dissolved in anhydrous DMF (4 mL) under Ar in darkness. The resulting solution was then stirred overnight. The resulting slurry mixture was stored in the freezer for 4 h. The resultant white precipitate, dicyclohexylurea (DCU), was removed by filtration. Subsequent to this, a large amount of ethyl acetate was poured into the filtrate and sonicated to obtain an off-white precipitate, which was washed with cold ether and dried to yield the activated ester succinic acid-NHS (0.407 mg, 0.58 mmol, 62%). ^{1}H NMR (360 MHz, DMSO- d_6) δ 6.47 (s, 6H^1), 2.85–2.76 (m, 12H^{2,4,5}), 2.64 (t, $J_{3,2}$ = 6.8 Hz, 4H^3).

Synthesis of complex PtBC



The activated ester succinic acid-NHS (130 mg, 0.19 mmol) and dopamine hydrochloride (84 mg, 0.37 mmol) were dissolved in anhydrous DMF (0.6 mL). Triethylamine (TEA, 26 µL, 1.2 mmol) was then added to the solution. As a result, the milky suspension changed to a clear yellow solution. The resulting solution was then left stirring for 24 h. The reaction was stopped and transferred to a flask filled with toluene. The solvent mixture was then removed under reduced pressure to yield a brownish residue. The reaction crude is then purified by reverse phase open column chromatography with a gradient from 5:95 to 40:60 methanol:-water in volume. Lyophilization of the collected fractions yielded the final PtBc prodrug as a clear yellow powder (85 mg, 0.106 mmol, 57% yield). ^{1}H NMR (400 MHz, Methanol-d_4) δ 6.70 (d, $J_{10,14}$ = 8.0 Hz, 1H^{10}), 6.67 (d, $J_{13,14}$ = 2.1 Hz, 1H^{13}), 6.55 (dd, $J_{14,10}$ = 8.0, $J_{14,13}$ = 2.1 Hz, 1H^{14}), 3.37–3.35 (m) 2.67 (t, $J_{8,7}$ = 6.5 2H^8), 2.62 (t, $J_{3,2}$ = 6.7 Hz, 2H^3), 2.44 (t, $J_{2,3}$ = 6.7 Hz, 2H^2). ^{13}C NMR (101 MHz, MeOD) δ 181.0 (s, C^2), 173.9(s, C^6), 144.8 (s, C^{11}), 143.3 (s, C^9), 130.8 (s, C^{12}), 119.7 (s, C^{14}), 115.5 (s, C^{10}), 115.0 (s, C^{13}), 41.1 (s, C^7), 34.5 (s, C^8), 31.3 (s, C^3), 31.1 (s, C^2); IR ν: 3,609 (w), 3,219 (s), 2,939 (w), 1,716 (w), 1,678 (w), 1,620 (s), 1,558 (s) 1,527 (s), 1,442 (m), 1,328 (s), 1,283 (s), 1,198 (s), 1,115 (s), 958 (s), 872 (m), 796 (s), 683 (m) cm^{-1}; HRMS (ESI+) m/z: [M+H]$^+$ Calcd. for $C_{24}H_{34}Cl_2N_4O_{10}Pt$ 805,1361; found 805,1353 and [M + Na]$^+$ Calcd. for $C_{24}H_{34}Cl_2N_4O_{10}Pt$ 827, 1,180; found 827, 1,166.

S2Synthesis and characterization of pPtBC NPs

Complex PtBC (10.0 mg, 0.013 mmol) was dissolved in 6 mL of a 1:1 mixture ethanol:MilliQ water. Sodium periodate (5.3 mg, 0.024 mmol) was dissolved in 0.4 mL of MilliQ water. The sodium periodate solution was then added drop wise to complex PtBC solution, while heated to 30°C. Addition was carried out with a syringe pump, addition was carried over a period of 1 h (6.7 µl/min) under vigorous stirring (1,500 rpm). The reaction was then allowed to evolve for 3 h heated at 30°C and under dark. The product was then isolated by centrifugation (10 min at 12,000 rpm) and washed multiple times with ethanol and water and resuspended in water for storing, yielding pPtBC NPs as a brown turbid suspension in a 3.0 mg yield. IR (KBr) ν: 3,256 (s), 1,638 (s), 1,564 (s), 1,438 (w), 1,338 (w), 1,258 (s), 1,173 (w), 1,022 (m), 876 (w), 771 (m), 725 (s), 541 (w), 514 (s) cm^{-1}; Z-Ave (H_2O) 214.2 ± 0.8 nm; PDI (H_2O) 0.07 ± 0.02; ζ-pot −37.1 ± 0.95 mV; ICP-MS Pt (%(w/w)) calcd. 24% found 17%

S3Synthesis and characterization of NDGA-NPs

NDGA (20.0 mg, 0.066 mmol) was dissolved in 28 ml of a 1:1 mixture ethanol:MilliQ water. Sodium periodate (28.2 mg, 0.132 mmol) was dissolved in 4 mL of MilliQ water. The sodium periodate solution was then added drop wise to the PtBc solution. Addition was carried out with a syringe pump, and addition was carried over a period of 1 h (66.7 µl/min) under vigorous stirring (1,500 rpm). The reaction was then allowed to evolve for 3 h under dark. The product was then isolated by centrifugation (10 min at 12,000 rpm) and washed multiple times with ethanol and water and resuspended in water for storing, yielding 4.5 mg of the pNDGA NPs as a brown turbid suspension. IR (KBr) ν: 3,414 (s), 2,960 (s), 2,929 (s), 2,876 (w), 1,725 (m), 1,663 (s), 1631 (w), 1,504 (s), 1,443 (s), 1,380 (s), 1,279 (s), 1,230 (w), 1,108 (w), 871 (m), 819 (w) cm^{-1}; Z-Ave (H_2O) 234.6 ± 0.5 nm; PDI (H_2O) 0.087 ± 0.022; ζ-pot −28.7 ± 0.5 mV.

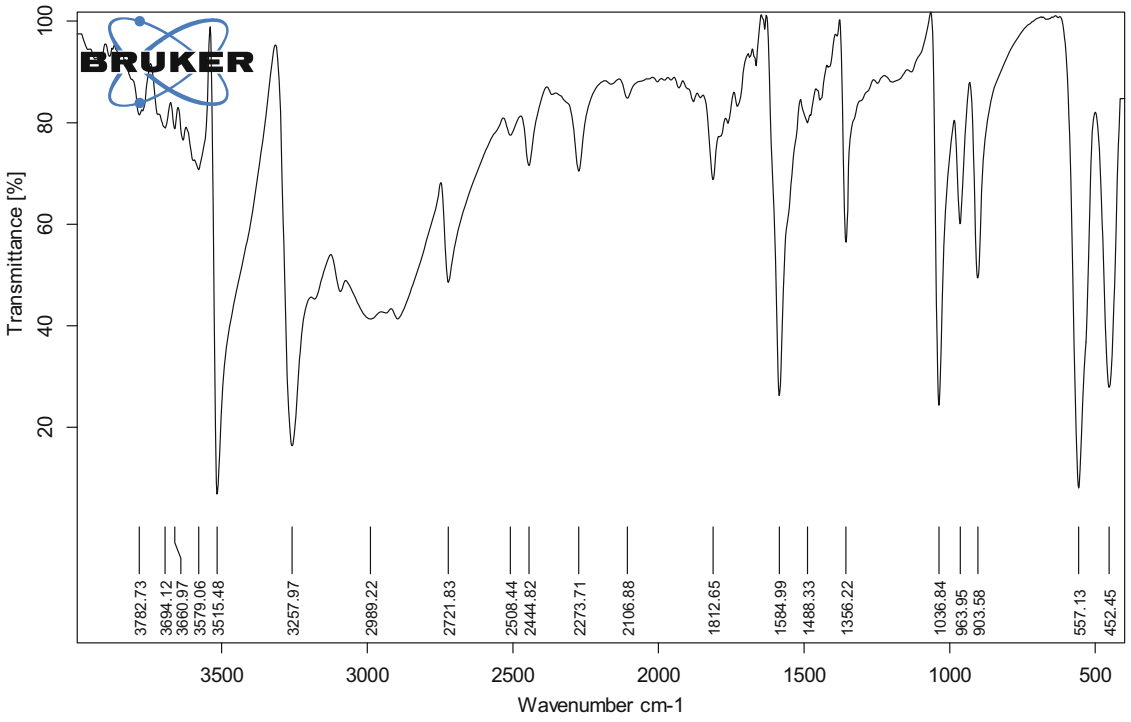


Figure S1: FTIR of *c,c,t-[Pt(NH3)$_2$Cl$_2$(OH)$_2$]*.

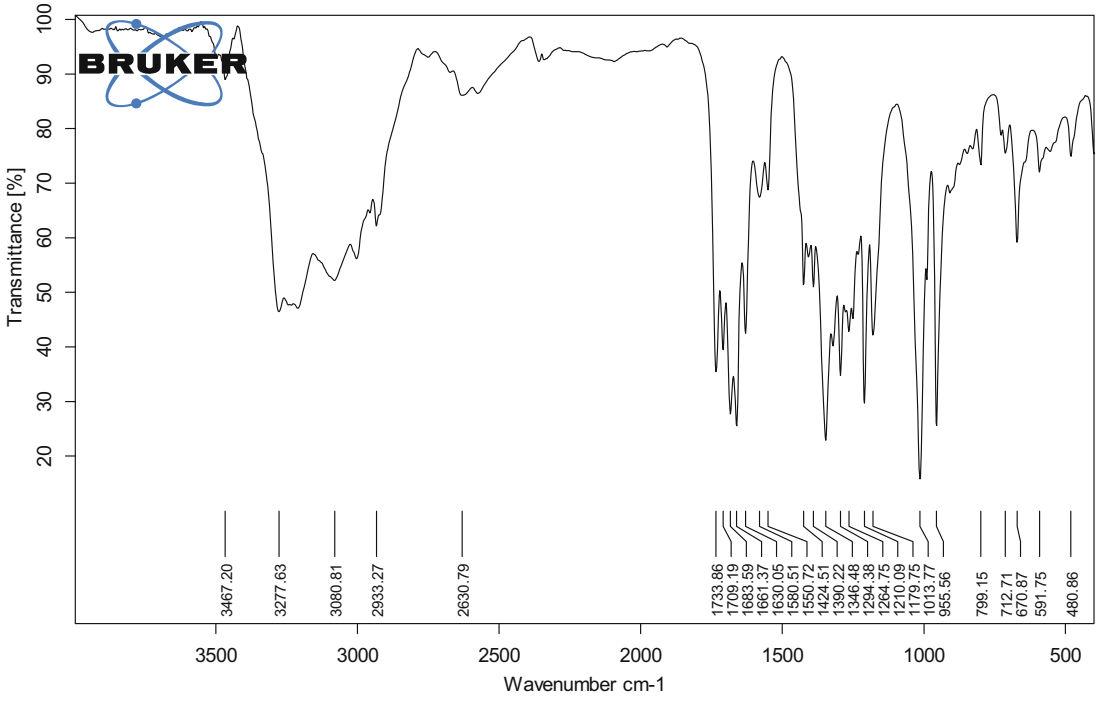


Figure S2: FTIR of *Disuccinic cisplatin.*

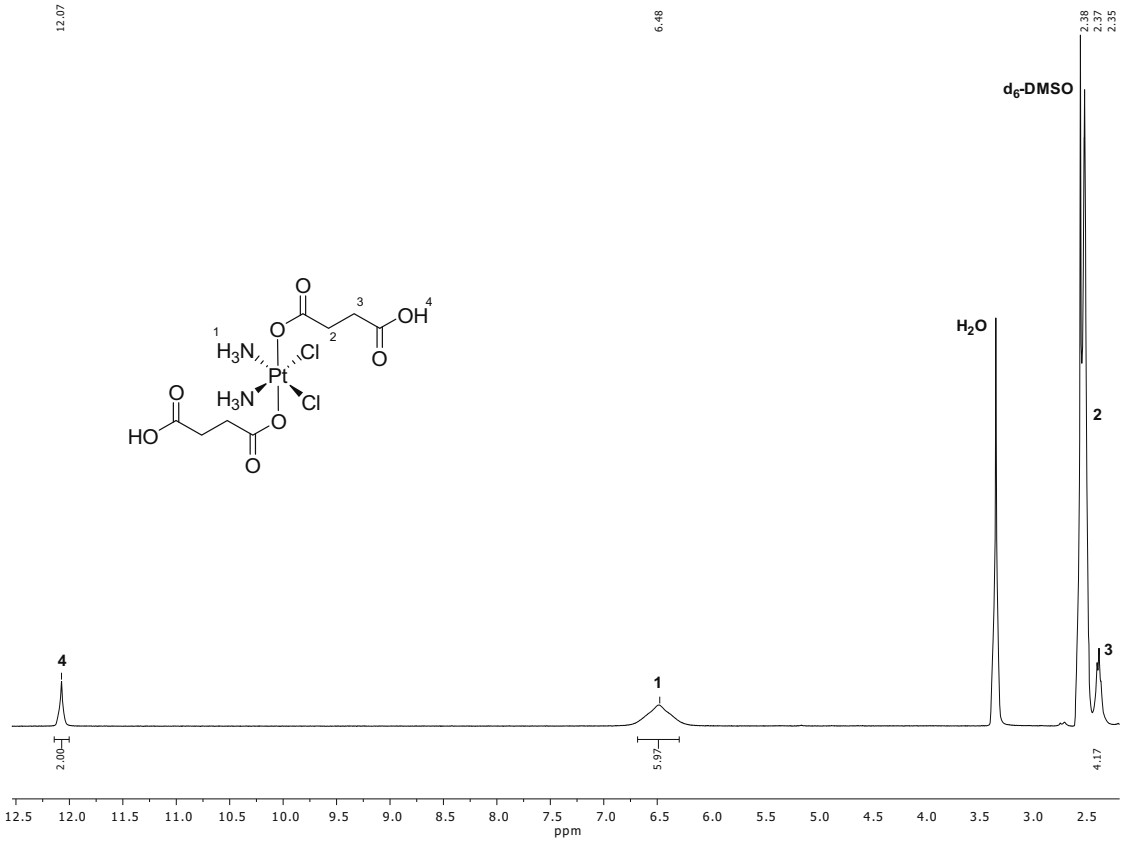


Figure S3: ^{1}H-NMR of *Disuccinic cisplatin.*

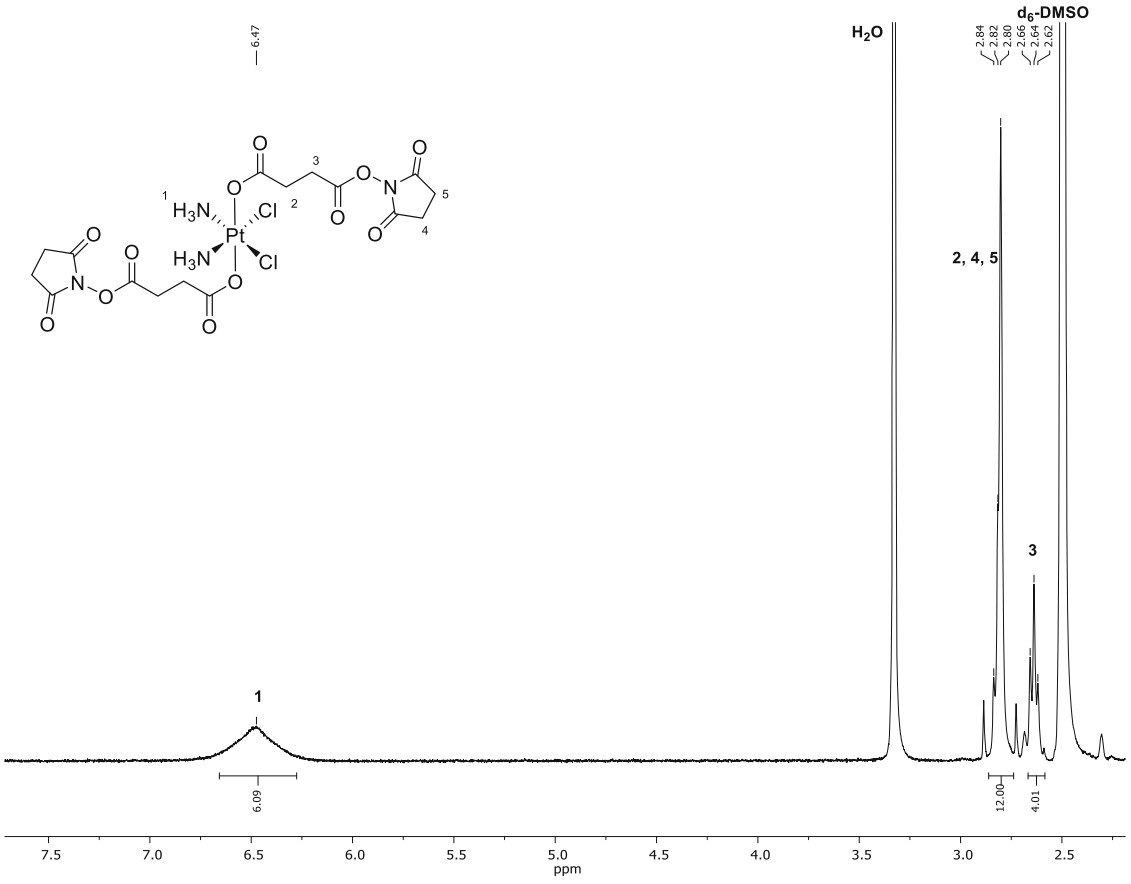


Figure S4: ^{1}H-NMR *succinic acid-NHS.*

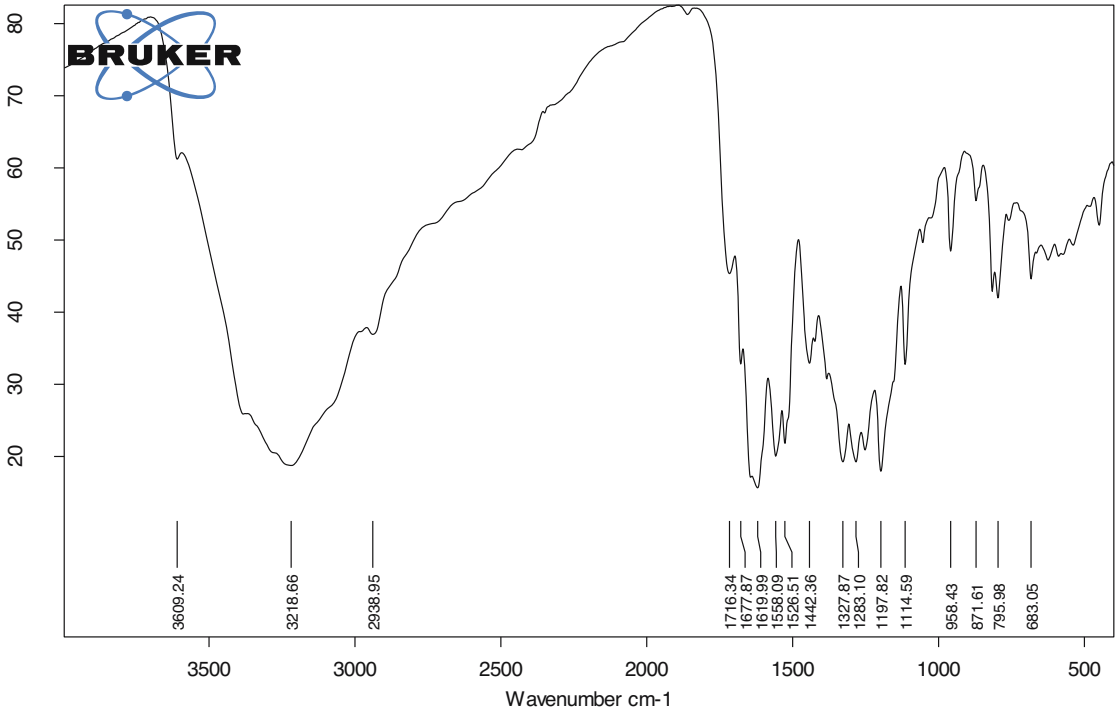


Figure S5: FTIR of complex PtBC.

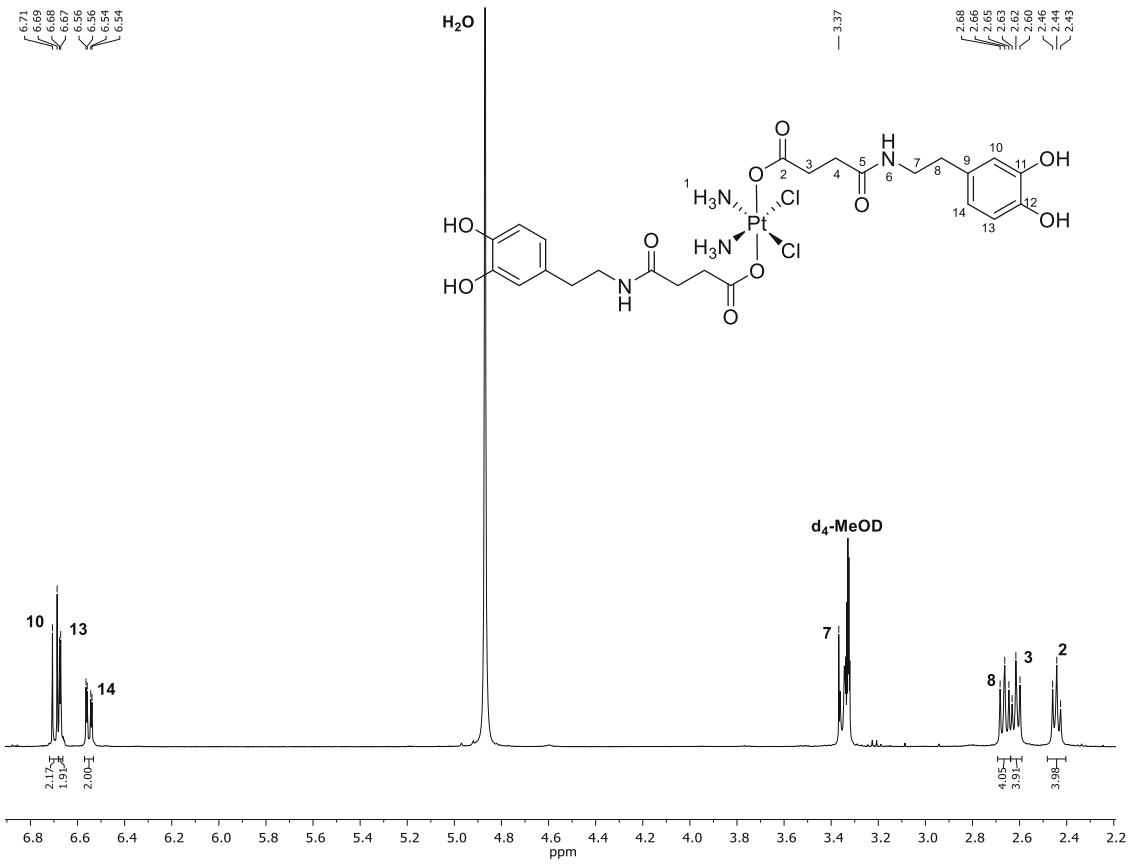


Figure S6: ^{1}H-NMR of complex PtBC.

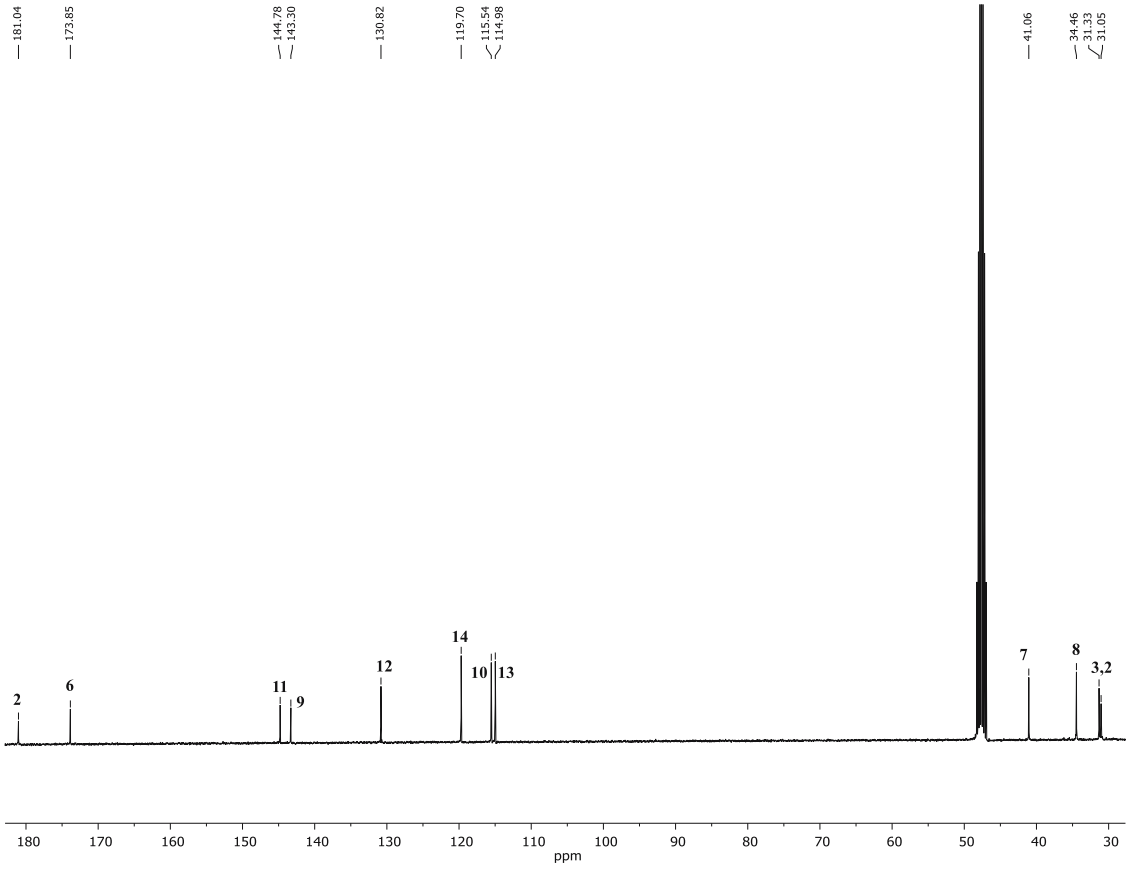


Figure S7: ^{13}C-NMR of complex PtBC.

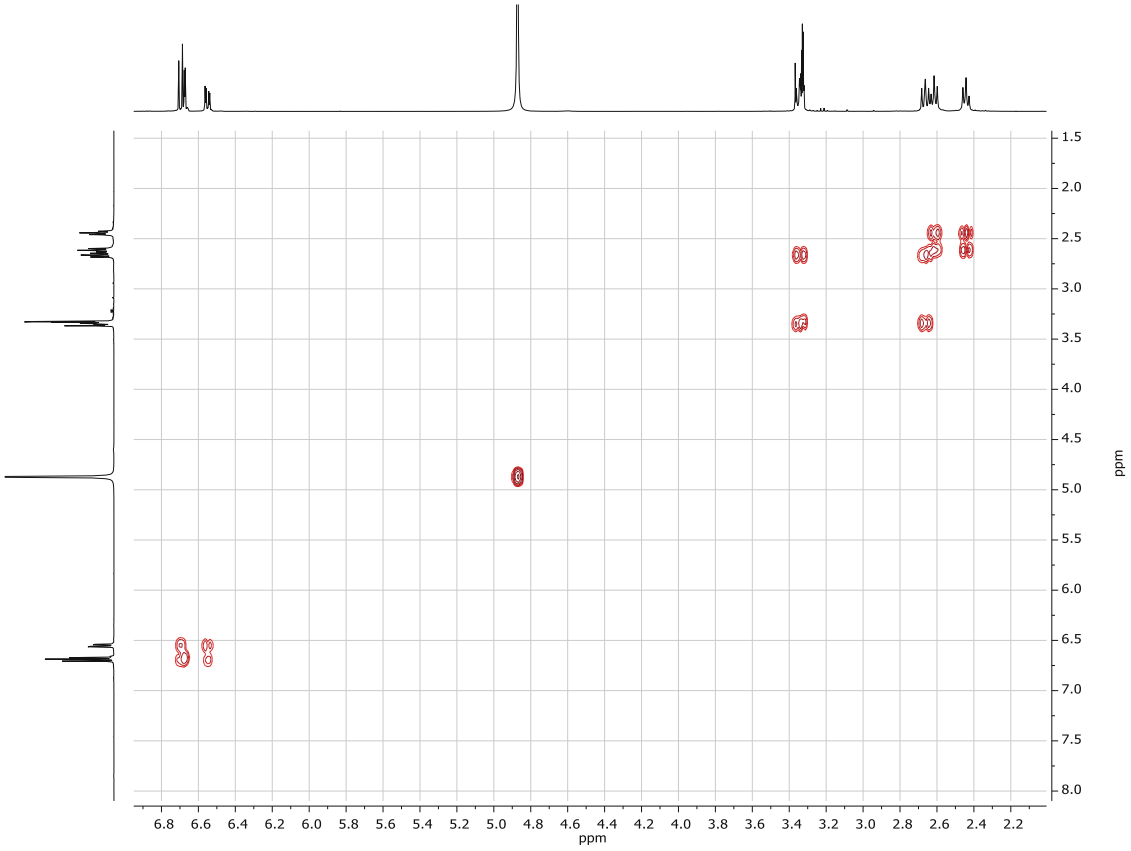


Figure S8: COSY NMR of complex PtBC.

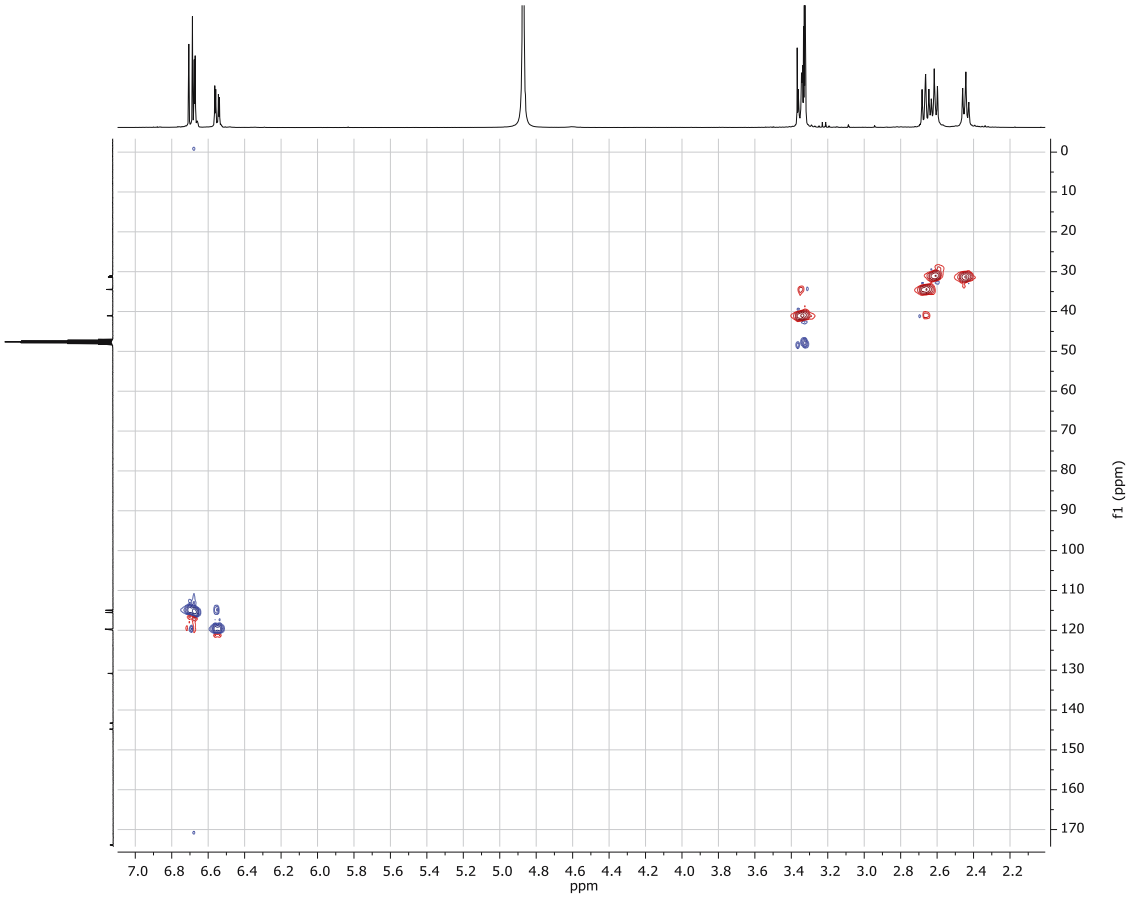


Figure S9: HSQC NMR of complex PtBC.

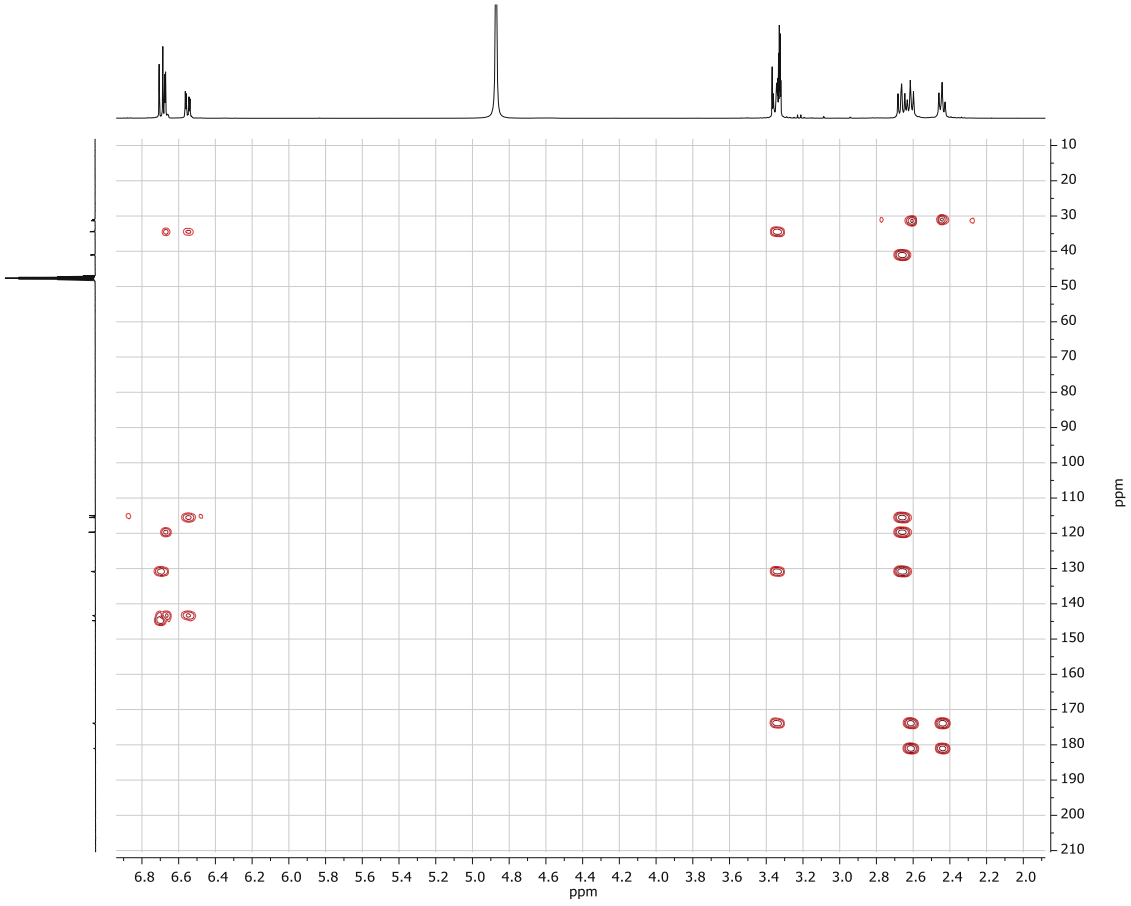


Figure S10: HMBC NMR of complex PtBC.

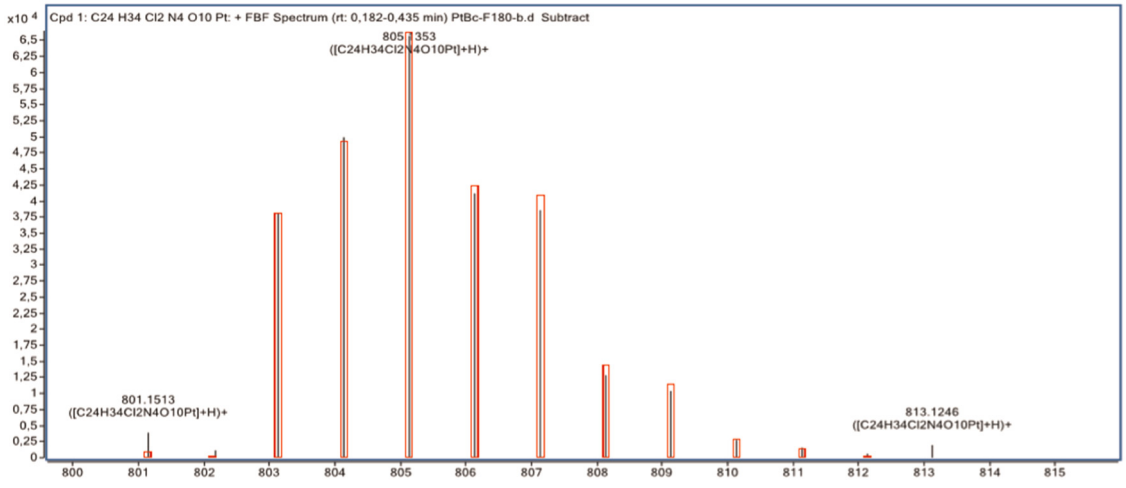


Figure S11: HRMS $[M+H]^+$ of complex PtBC.

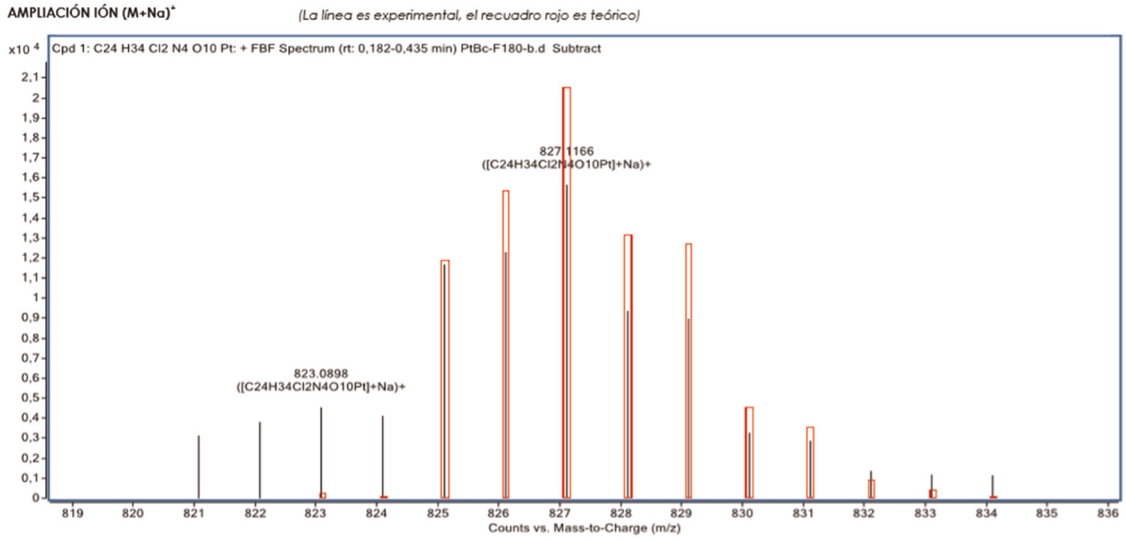


Figure S12: HRMS $[M+Na]^+$ of complex PtBC.

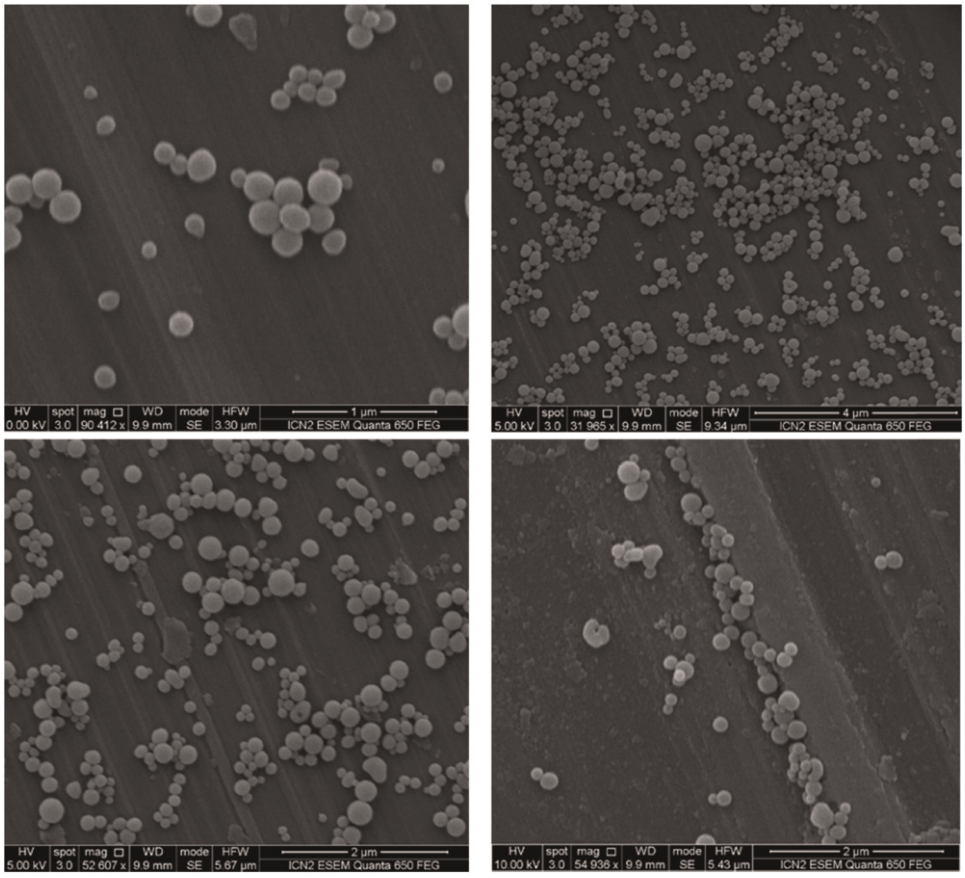


Figure S13: SEM imaging of pPtBC NPs.

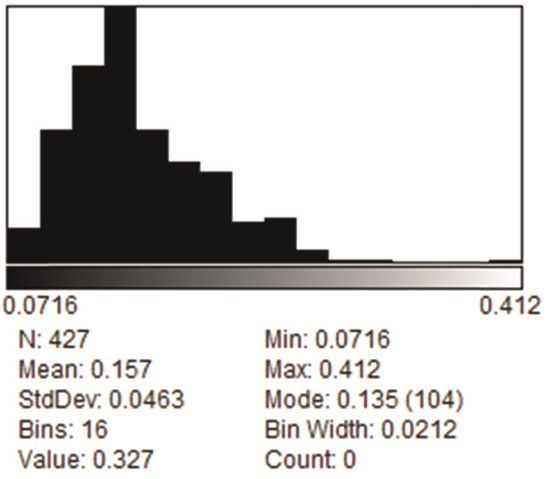


Figure S14: ImageJ histogram distribution of pPtBC NPs.

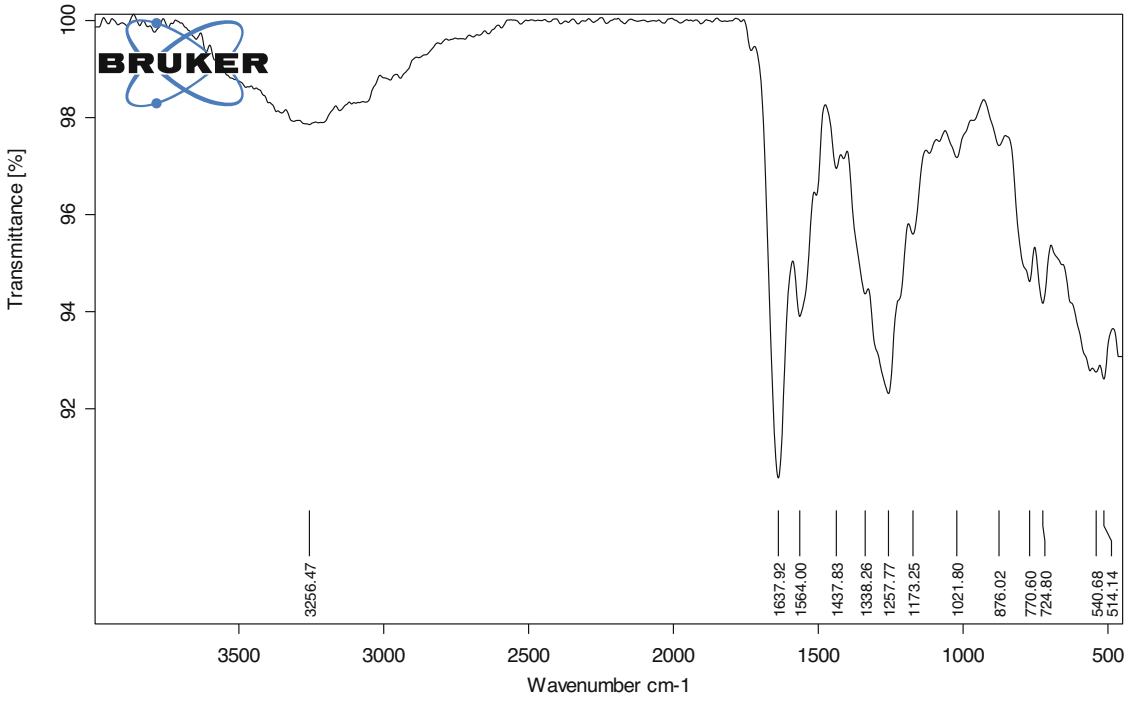


Figure S15: FTIR of pPtBC NPs.

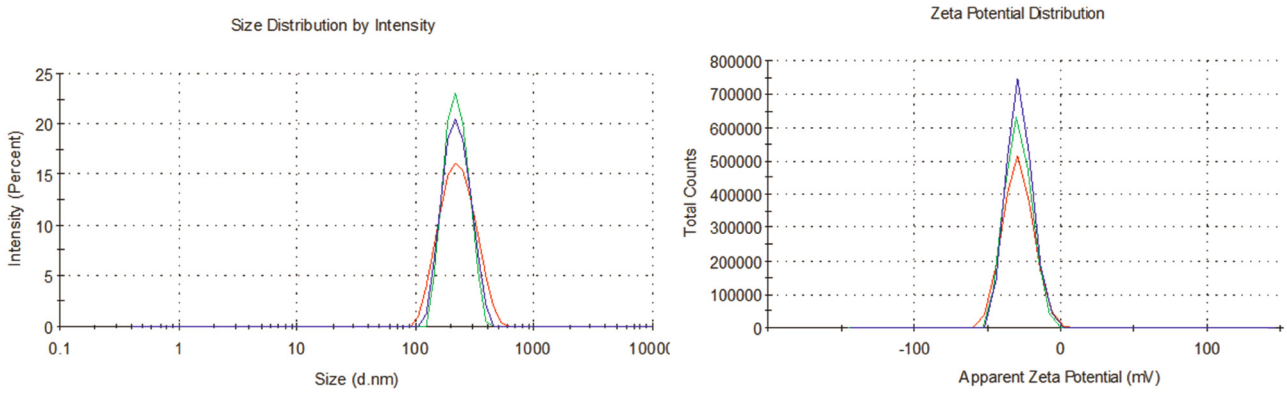


Figure S16: (i) DLS size distribution and (ii) ζ-potential of pNDGA NPs.

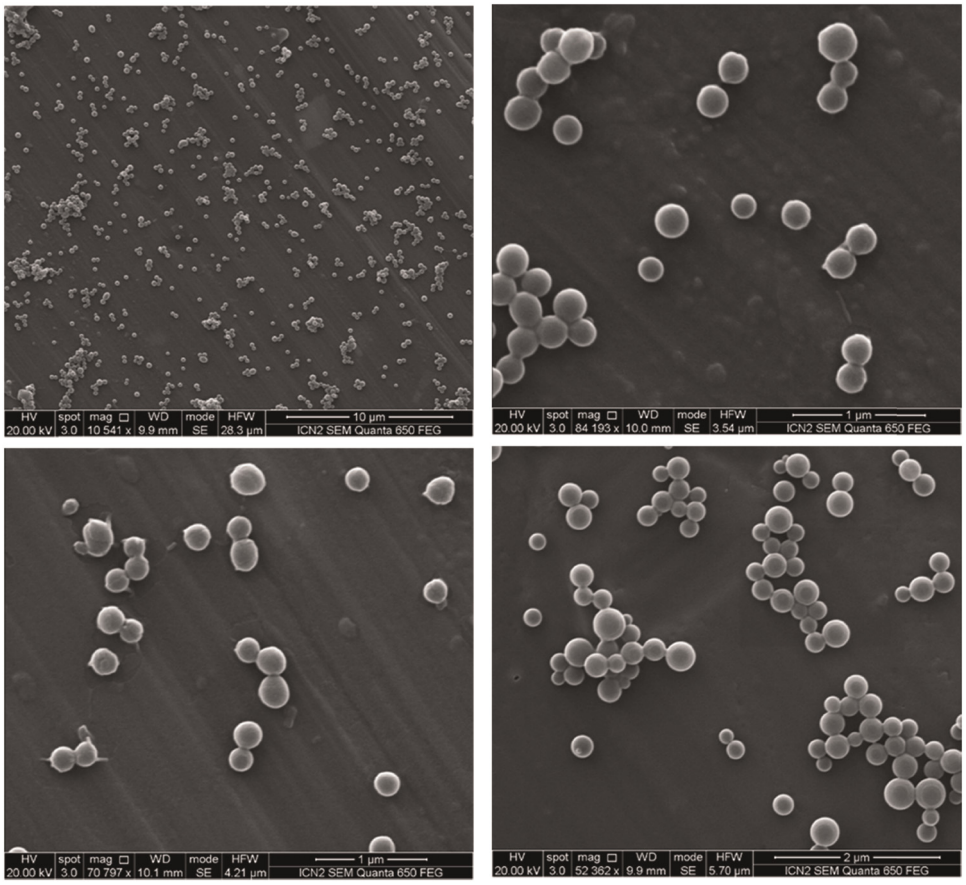


Figure S17: SEM imaging of pNDGA NPs.

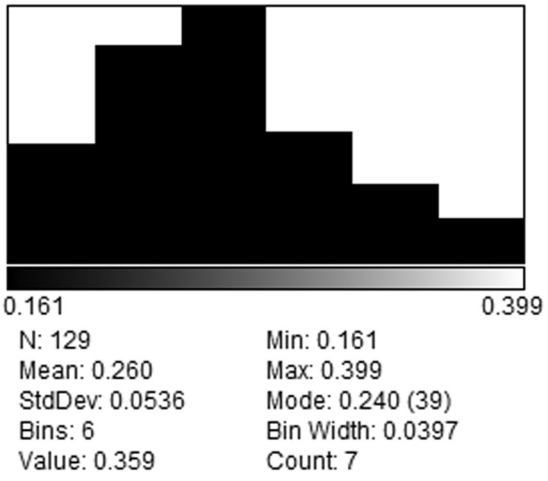


Figure S18: ImageJ histogram distribution of pNDGA NPs.

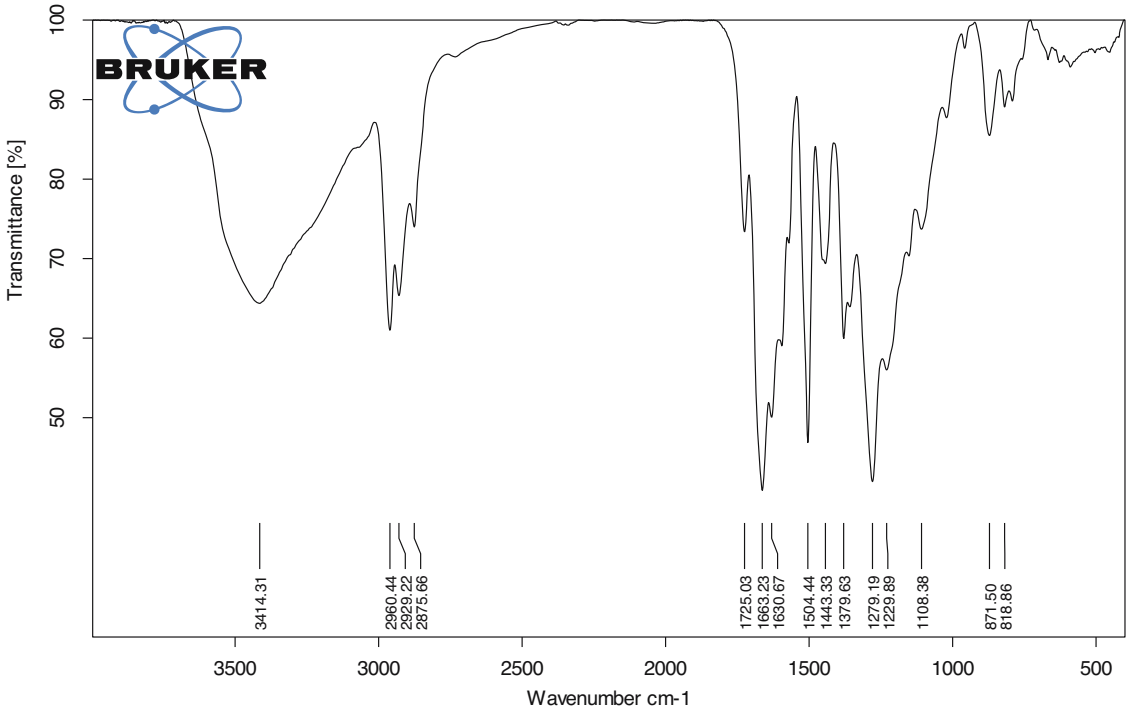


Figure S19: FTIR of pNDGA NPs.