Enhanced Catalyst Recovery in an Aqueous Copper Free Sonogashira Cross-Coupling Reaction

Daniel Rosario-Amorin,*[a,b] Manuel Gaboyard,[c] Rodolphe Clérac,[d,e] Sylvain Nlate,*[a,b] Karine Heuzé*[a, b]

- SUPPORTING INFORMATION (9 pages) -

Table of contents Page

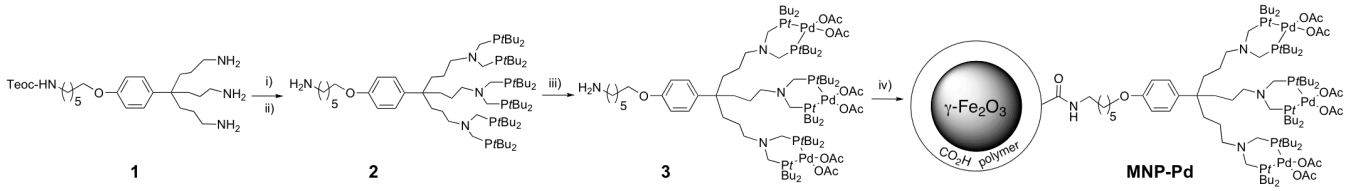


Figure S1. Synthesis of superparamagnetic nanoparticles supported diphosphino palladium complex **MNP-Pd**. **1** has been synthesize according to the previous procedure.[1] Reagents and conditions: i) HCHO, $HPtBu_2$, MeOH, toluene, 12 h, 70°C to RT; ii) Bu_4NF, THF, 5 h, 60°C; iii) $Pd(OAc)_2$, CH_2Cl_2, 20 min, RT; iv) Carboxyl Adembead® 300 nm, CHMC, MeOH/H_2O (1/2), Triton X-405, 16h, RT.

Entry	Base	Conversion (%)
1	$CsCO_3$	32
2	K_2CO_3	41
3	K_3PO_4	55
4	tBuOK	52
5	tBuONa	80
6	KOH	64
7	NaOH	80
8	LiOH	89

Table S1. Coupling reactions between bromobenzene (259 μmol) and phenylacetylene (388 μmol) with **3**-Cy (1 mol% Pd), base (777 μmol), in MeOH, at 70°C, for 15 h. Conversions were obtained by GC.

[1] Rosario-Amorin, D.; Wang, X.; Gaboyard, M.; Clérac, R.; Nlate, S.; Heuzé, K. *Chem. Eur. J.* **2009**, *15*, 12636-12643.

All reactions were performed under a nitrogen atmosphere in standard glassware. The starting materials were obtained commercially and used without further purification. The solvents were dried according to standard procedures and saturated with nitrogen. The ^{1}H, ^{13}C, and ^{31}P NMR spectra were recorded on the following spectrometers: Bruker DPX 200 FT NMR spectrometer (^{1}H: 200.16, ^{13}C: 50.33, ^{31}P: 81.02 MHz), Bruker AC 250 FT NMR spectrometer (^{1}H: 250.13, ^{13}C: 62.90 MHz), and Bruker Avance 300 FT NMR spectrometer (^{1}H: 300.13, ^{13}C: 75.46, ^{31}P: 121.49 MHz). Chemicals shifts are reported in parts per million (δ) against referenced solvent signals. MALDI-TOF spectra were performed by CESAMO (Bordeaux, France) on a Voyager mass spectrometer (Applied Biosystems). The instrument is equipped with a pulsed N_2 laser (337 nm) and a time-delayed extracted-ion source. Spectra were recorded in positive-ion mode by using a reflectron and with an accelerating voltage of 20 kV. The elemental analyses were performed with ThermoFischer Flash EA1112. GC spectra were recorded with a Varian star 3900 gas chromatograph equipped with a fused-silica capillary column heated gradually to 250°C (from 40°C, rate 10°C min^{-1}) with He as vector gas at a column head pressure of 10 psi. An FID detector was used. Yields were calculated by an integration of product peaks (Star chromatography workstation 5.50) after determination of the response coefficient of each product versus each bromoarene reagent. For column chromatography, Merck silica gel 60 (230–400 mesh) was used. Synthesis of **1** has been previously described.[1]

***p*-$NH_2(CH_2)_6O(C_6H_4)C\{CH_2CH_2CH_2N(CH_2P$*t*$Bu_2)_2\}_3$ (2):**

A mixture of di(*tert*-butyl)phosphine (2.5 g, 17.1 mmol) and paraformaldehyde (514 mg, 17.1 mmol) in MeOH/toluene (2/1, 15 mL) was stirred under inert atmosphere at 70°C for 10 min. A solution of **1** (1.49 g, 2.84 mmol) in MeOH/toluene (2/1, 10 mL) was added, and the mixture stirred at 70°C for 10 min and then at room temperature for 12 h. The solvent was removed under reduced pressure and tetrabutylammonium fluoride 1 M in THF (28 mL, 28 mmol) was added and the mixture stirred at 60°C for 5 h. The solvent was removed under reduced pressure and the residue diluted in dichoromethane (30 mL). Organic layer was washed several time with water (4 x 10 mL), dried over anhydrous $MgSO_4$. Solvent was removed under reduced pressure to afford **2** as a white powder (1.75 g, 46%)

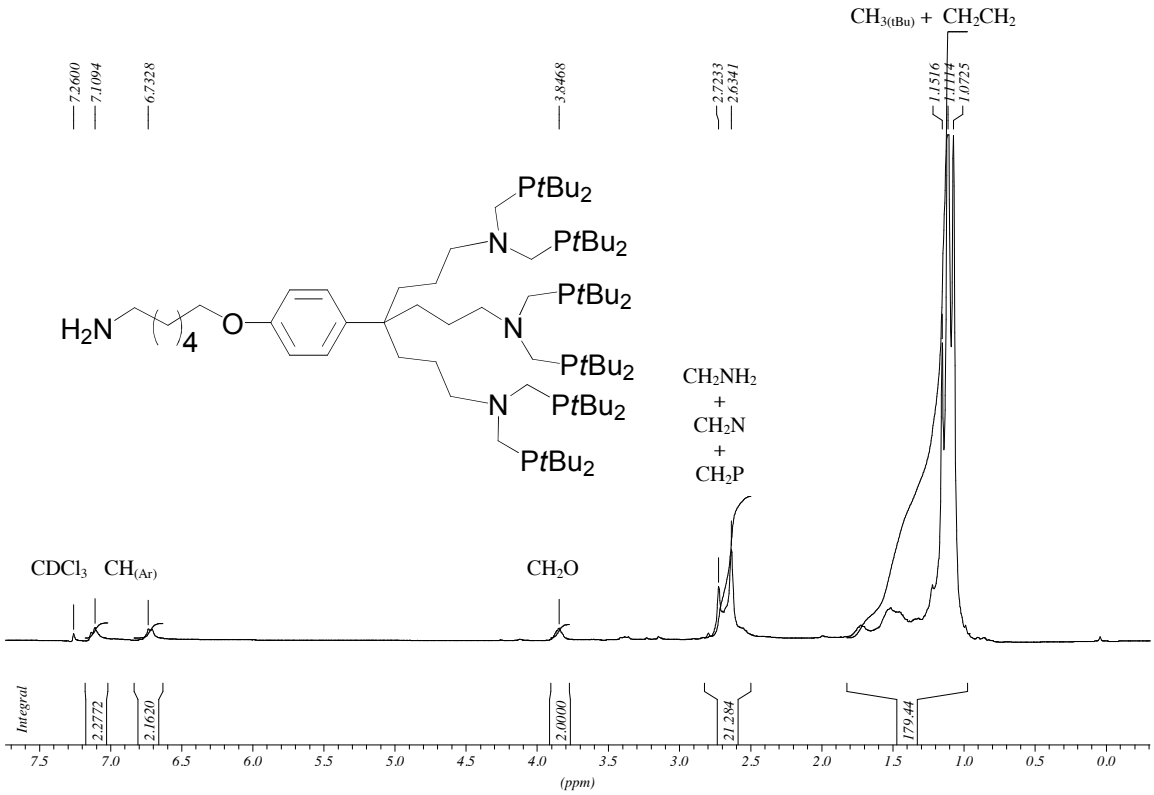
^{1}H NMR ($CDCl_3$): δ = 7.12 (d, 2H, CH_{ar}, J=8.3 Hz), 6.74 (d, 2H, CH_{ar}, J=8.3 Hz), 3.85 (t, 2H, CH_2O, J=6.0 Hz), 2.73 (m, 6H, CH_2NCH_2P) 2.64 (m, 14H, NCH_2P, + C$H_2$$NH_2$), 1.7-1.1 (m, 128H, $CH_{3(tBu)}$ + CH_2); ^{13}C NMR ($CDCl_3$) δ: 156.6 (1C, *C*O_{ar}), 139.2 (1C, $C_{q(ar)}$), 127.6 (2C,

CH_{ar}), 113,7 (2C, CH_{ar}), 67.7 (1C, CH_2O), 57.1 (3C, CH_2NCH_2P), 53.0 (6C, CH_2P) 42.7 (2C, $C_{ar}C_q$ + CH_2NH_2), 35.8 (3C, CH_2C_q), 31.6 (d, 12C, $C_{q(tBu)}$), 29.8 (d, 36C, $CH_{3(tBu)}$), 29.9-26.0 (4C, CH_2), 19.6 (3C, CH_2); ^{31}P NMR ($CDCl_3$): δ = 12.8; MS (MALDI-TOF): m/z (%): [M+Na] (100%) calc. 1350.06, found 1349.45

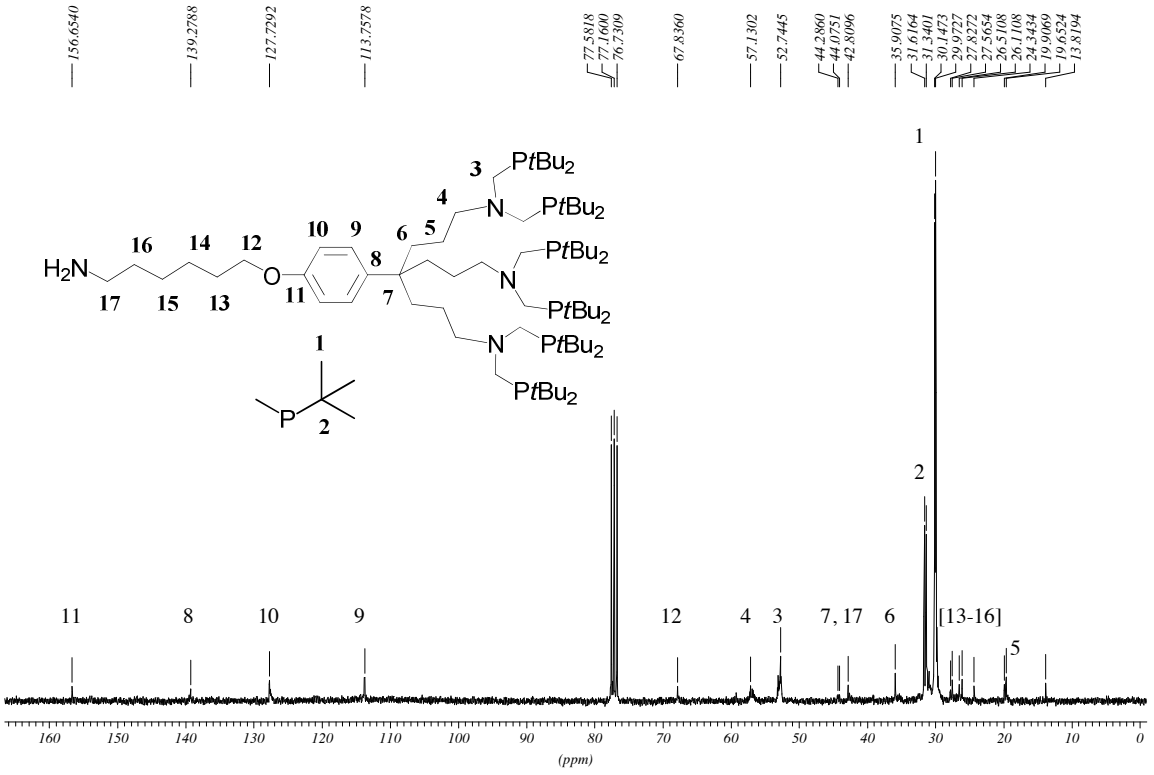
_p_-$NH_2(CH_2)_6O(C_6H_4)C\{CH_2CH_2CH_2N(CH_2P$*t*$Bu_2)_2Pd(OAc)_2\}_3$ (3):

A mixture of **2** (1.6 g, 1.2 mmol) and palladium diacetate (811 mg, 3.6 mmol) was stirred in CH_2Cl_2 (15 mL) at room temperature under inert atmosphere for 20 min. Then the mixture reaction was evaporated and the product dried under vacuum to give **3** as a dark brown powder (2.4 g, quant.).

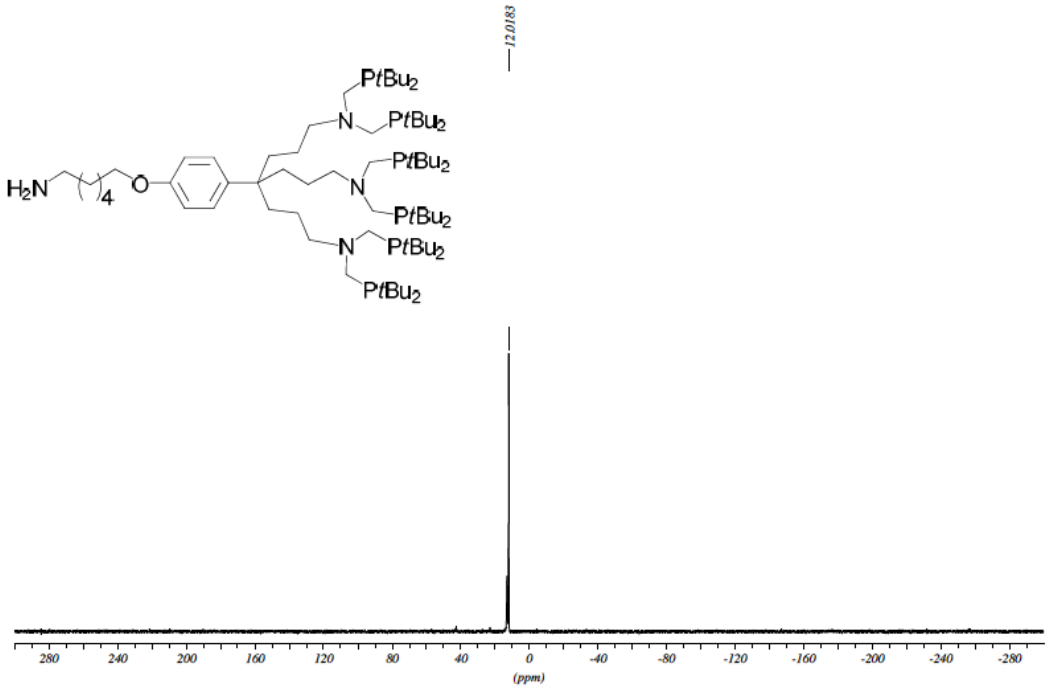
^{1}H NMR (CD_2Cl_2) : δ = 7.12 (broad d, 2H, C*H*$_{ar}$, J=8 Hz), 6.78 (broad d, 2H, C*H*$_{ar}$ J=8 Hz), 3.82 (t, 2H, C*H*$_2$O, J=6.3 Hz), 2.74-2.51 (m, 20H, NC*H*$_2$P + C*H*$_2$NCH$_2$P + C*H*$_2$NH$_2$), 1.92 (s, 18H, C*H*$_{3(OAc)}$), 1.9-1.2 (m, 128H, $CH_{3(tBu)}$ + CH_2); ^{13}C NMR (CD_2Cl_2): δ = 127.1 (2C, CH_{ar}), 114,0 (2C, CH_{ar}), 68.1 (1C, CH_2O), 63.9 (3C, CH_2NCH_2P), 49.6 (6C, CH_2P) 43.5 (2C, $C_{ar}C_q$ + CH_2NH_2), 38.4 (6C, $CH_{3(OAc)}$), 35.2 (3C, CH_2C_q), 30.4 (d, 48C, $C_{q(tBu)}$+ $CH_{3(tBu)}$), 29.9-24.0 (4C, CH_2), 20.1 (3C, CH_2); ^{31}P RMN (CD_2Cl_2): δ = 36.5; Elemental analysis calc (%) for $C_{88}H_{174}N_4O_{13}P_6Pd_3$.10 H_2O : C 46.4, H 8.5, N 2.5; found C 46.7, H 7.9, N 2.6.



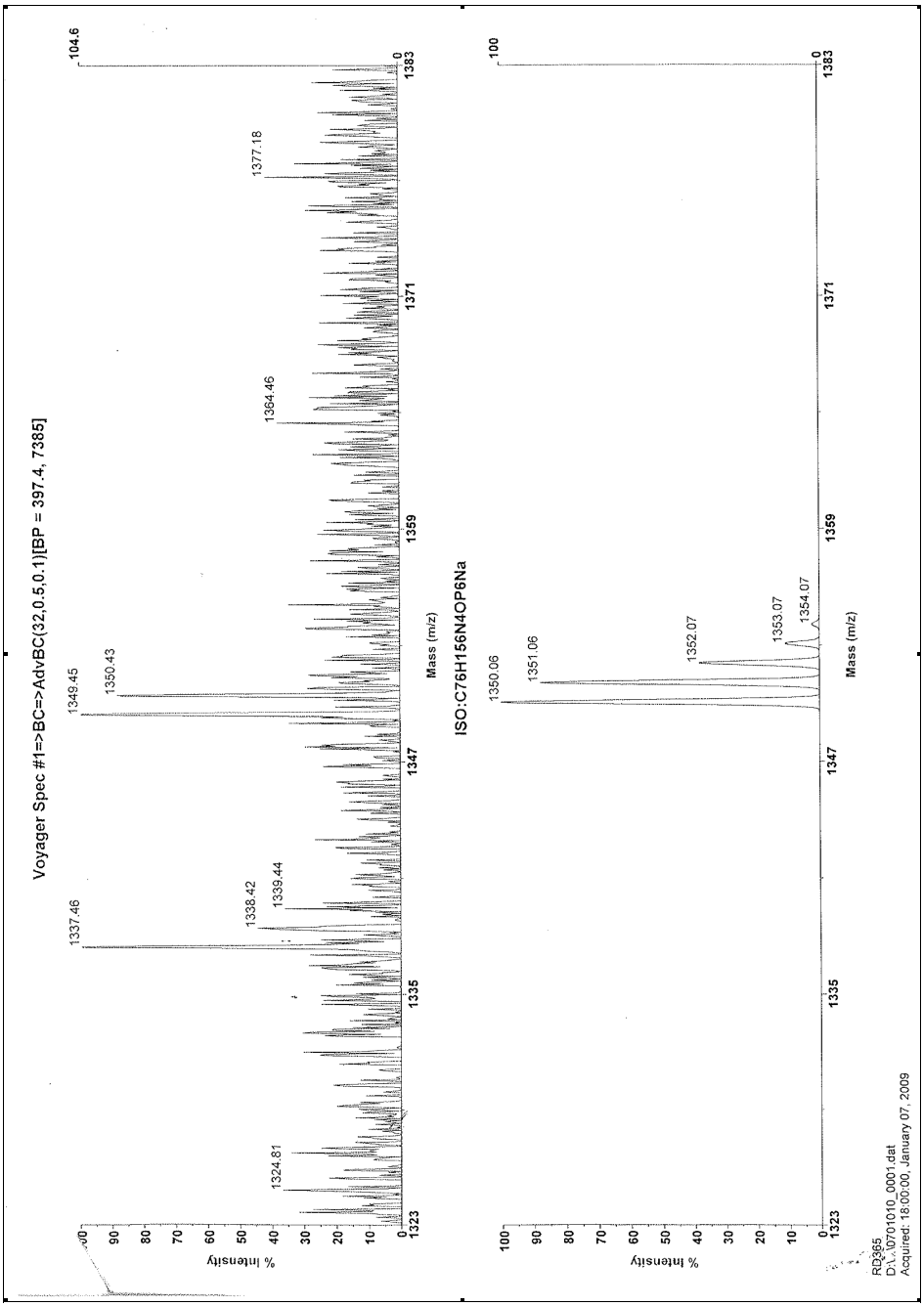
^{1}H NMR spectra of 2



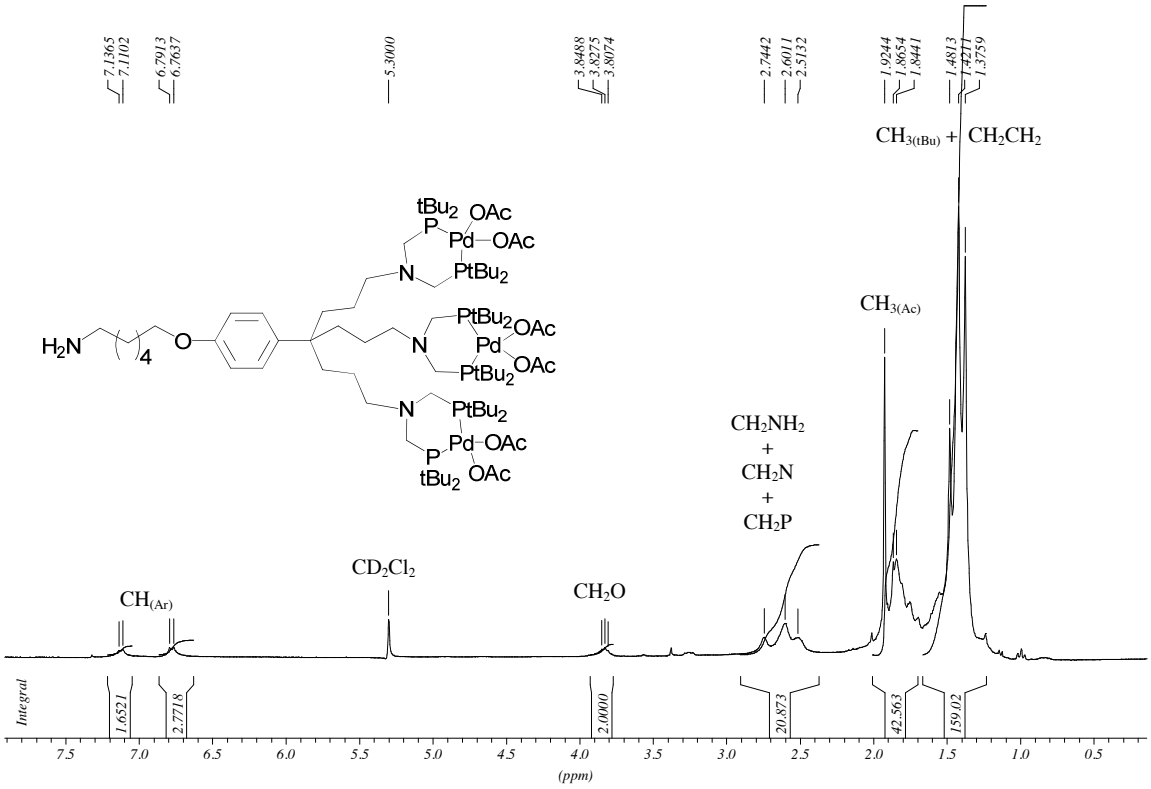
^{13}C NMR spectra of 2



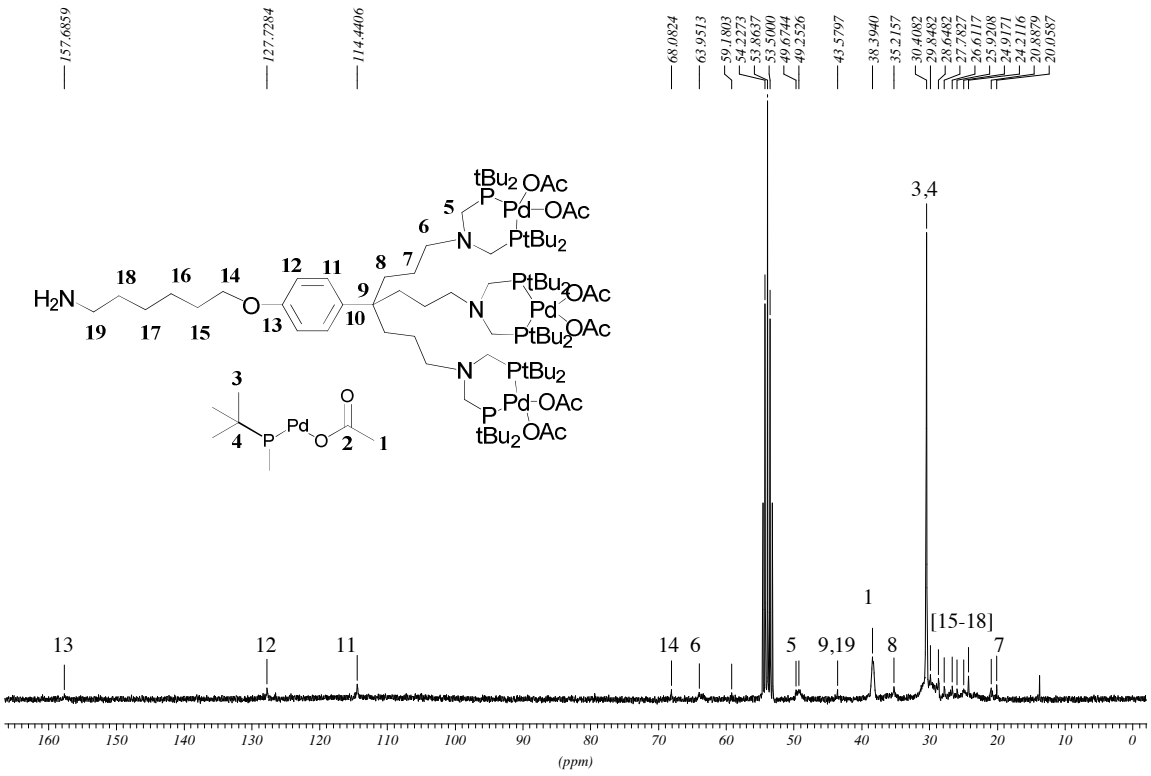
^{31}P NMR spectra of 2



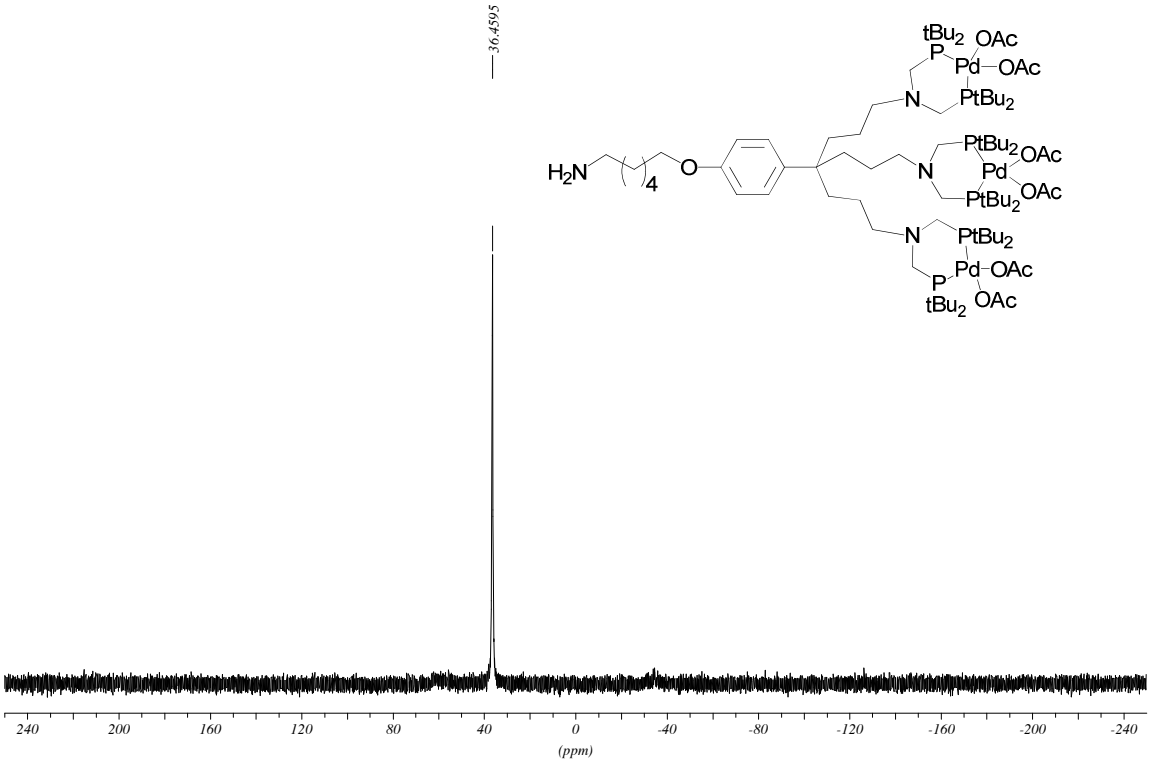
MALDI-TOF spectra of 2



^{1}H NMR spectra of 3



^{13}C NMR spectra of 3



^{31}P NMR spectra of 3