Mechanochemistry allows carrying out sensitive organometallic reactions in air: Glove-box-and-Schlenk-line-free synthesis of oxidative addition complexes from aryl halides and palladium(0)

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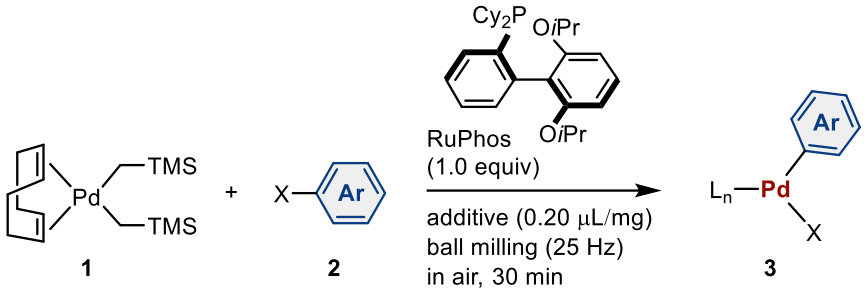
1. General and Materials.

The starting materials were obtained from commercial suppliers and used as received unless otherwise noted. Solvents were also purchased from commercial suppliers, and dried over molecular sieves (MS 4Å). All mechanochemical reactions were carried out using grinding vessels in a Retsch MM400 mill (Supplementary Figure 1). Both jars (1.5 mL or 25 mL) and balls (diameter: 3 mm or 10 mm) are made of stainless (Supplementary Figure 1). NMR spectra were recorded on JEOL JNM-ECX400P and JNM-ECS400 spectrometers (^{1}H: 392, 396 or 401 MHz, ^{13}C: 99 MHz, ^{31}P: 160 MHz). Tetramethylsilane (^{1}H), $CDCl_3$ (^{13}C) and H_3PO_4 (^{31}P) were employed as external standards, respectively. Multiplicity was recorded as follows: s = singlet, br, s = broad singlet, d = doublet, t = triplet, q = quartet, quin = quintet, sext = sextet, sep = septet, m = multiplet. Dibromomethane was used as an internal standard to determine NMR yields. High-resolution mass spectra were recorded at the Global Facility Center, Hokkaido University. Single crystal X-ray structural analyses were carried out on a Rigaku XtaLAB PRO MM007 diffractometer using graphite monochromated Cu-K_α radiation. The structure was solved by direct methods and expanded using Frontier techniques. Non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. All calculations were performed using Olex crystallographic software package except for refinement, which was performed using SHELXL.[1]

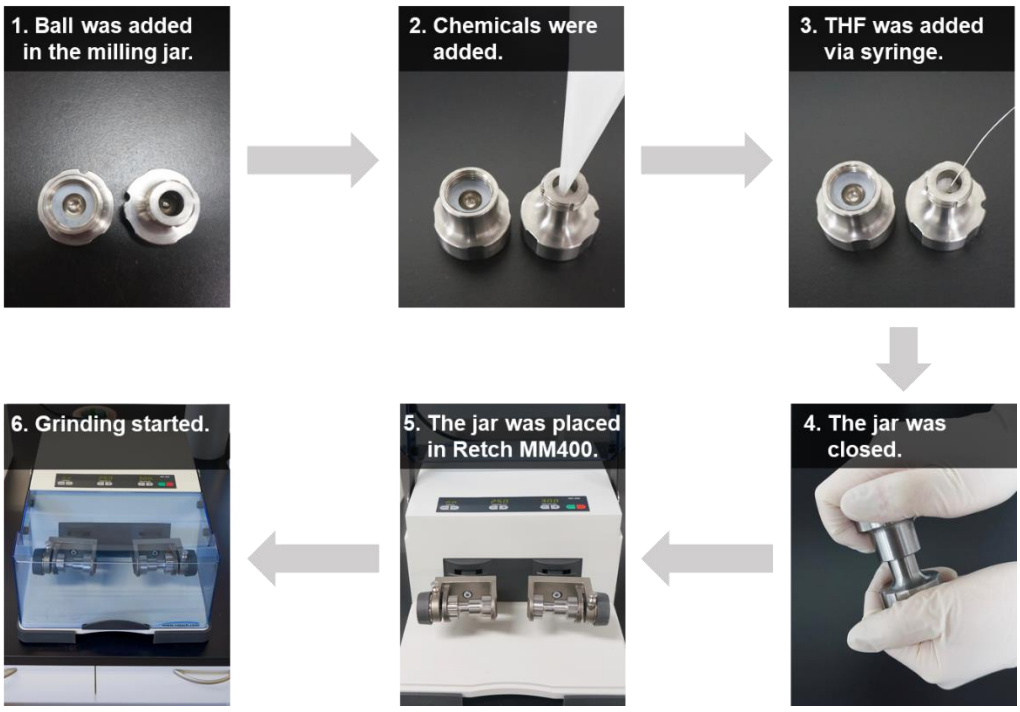
Supplementary Figure 1. Retsch MM400 mill (left) and ball milling vessels (right).

2. General Procedure for Synthesis of Palladium Oxidative Addition Complexes



$(COD)Pd(CH_2TMS)_2$ **1** was prepared by according to the procedure.[2] The material **1** is thermo-sensitive and must be stored at a temperature of –20 °C or lower to avoid decomposition, while the material can be stored out of glovebox and used in air.

$(COD)Pd(CH_2TMS)_2$ **1** (0.12 mmol), arylhalide **2** (0.12 mmol, 1.0 equiv), a phosphine ligand (0.12 mmol, 1.0 equiv) were placed in a ball milling vessel (stainless, 1.5 mL) loaded with one grinding ball (stainless, diameter: 3 mm), then THF (0.20 μL mg^{-1}) was added via syringe. After the vessel was closed in air without the purge with inert gas, the vessel was placed in the ball mill (Retch MM400, 30 min at 25Hz). After passing through a short silica gel column eluting with EtOAc, the crude mixture was concentrated, washed with pentane three times and dried under reduced pressure to afford the oxidative addition complex **3**.

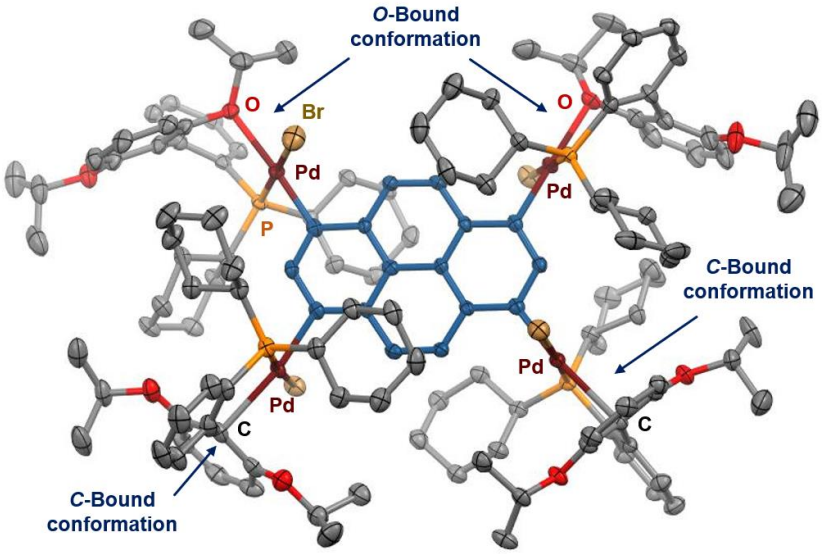


Supplementary Figure 2. How to set up the mechanochemical reactions.

3. Single Crystal X-Ray Analysis

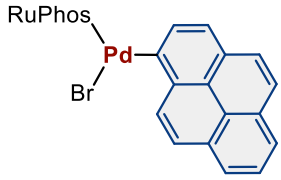
Supplementary Table 1. Summary of X-ray crystallographic data for **3v**.

CCDC number	1908179
Empirical Formula	$C_{141}H_{188}Br_4Cl_{10}O_8P_4Pd_4$
Formula Weight	3234.52
Crystal System	triclinic
Crystal Size / mm	0.18 × 0.17 × 0.02
a / Å	13.8478(2)
b / Å	18.2868(2)
c / Å	28.8141(2)
α / °	95.321(1)
β / °	96.590(1)
γ / °	92.188(1)
V / Å^3	7208.41(14)
Space Group	P-1
Z value	2
D_{calc} / g·cm^{-3}	1.490
Temperature / K	123
No. of Reflections	Total: 66930
Measured	27857 (R_{int} = 0.0455)
Residuals: R_1	5.38
(I > 2.00σ (*I*)) / %	
Residuals: wR_2	15.39
(All reflections) / %	
Goodness of Fit (GOF)	1.095
Maximum peak in Final Diff. Map / Å^3	1.71 e$^-$
Minimum peak in Final Diff. Map / Å^3	−1.67 e$^-$



Supplementary Figure 3. Single-crystal structure of **3v** (thermal ellipsoids set at 50% probability; hydrogen atoms and CH_2Cl_2 omitted for clarity).

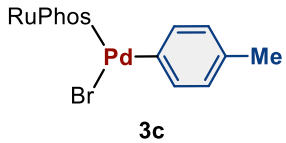
4. Characterization of Palladium Oxidative Addition Complexes



3a

The reaction was carried out with **1** (47.2 mg, 0.12 mmol), **2a** (33.5 mg, 0.12 mmol) and RuPhos (57.0 mg, 0.12 mmol). The product **3a** was obtained as an off-white solid by washing with hexane (79.5 mg, 0.093 mmol, 78% yield).

^{1}H NMR (392 MHz, $CDCl_3$, δ): –0.68––0.49 (m, 1H), 0.08–0.25 (m, 1H), 0.51–0.67 (m, 1H), 0.69–0.91 (m, 3H), 1.01 (d, J = 5.9 Hz, 3H), 1.13 (d, J = 6.3 Hz, 3H), 0.94–1.30 (m, 4H), 1.42 (d, J = 5.9 Hz, 3H), 1.46–1.56 (m, 4H), 1.61 (d, J = 5.9 Hz, 3H), 1.65–2.00 (m, 6H), 2.16–2.27 (m, 1H), 2.55 (t, J = 9.6 Hz, 1H), 4.65 (hept, J = 5.9 Hz, 1H), 4.75 (hept, J = 6.1 Hz, 1H), 6.66 (d, J = 8.2 Hz, 1H), 6.78 (d, J = 8.6 Hz, 1H), 6.88 (dd, J = 2.4, 7.4 Hz, 1H), 7.36 (t, J = 7.4 Hz, 1H), 7.44 (t, J = 7.6 Hz, 1H), 7.54 (t, J = 7.1 Hz, 1H), 7.74–7.94 (m, 7H), 8.02 (d, J = 7.8 Hz, 2H), 8.77 (d, J = 8.6 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.7 (CH_3), 22.1 (CH_3), 22.5 (CH_3), 24.9 (CH_2), 25.0 (CH_2), 26.2 (CH_2), 26.3 (CH_2), 26.4 (CH_2), 27.0 (CH_2), 27.1 (CH_2), 27.19 (CH_2), 27.23 (CH_2), 27.29 (CH_2), 27.33 (CH_2), 27.8 (CH_2), 29.8 (CH_2), 29.9 (CH_2), 32.8 (*C*H), 33.0 (*C*H), 34.7 (*C*H), 34.9 (*C*H), 70.2 (*C*H), 71.5 (*C*H), 106.8 (*C*H), 106.9 (*C*H), 109.61 (*C*), 109.65 (*C*), 123.4 (*C*H), 123.5 (*C*H), 123.7 (*C*H), 124.4 (*C*H), 124.67 (*C*), 124.74 (*C*), 125.1 (*C*H), 126.3 (*C*H), 126.4 (*C*H), 127.4 (*C*H), 127.9 (*C*), 130.5 (*C*H), 130.6 (*C*H), 131.3 (*C*), 131.4 (*C*), 132.0 (*C*H), 132.1 (*C*H), 133.9 (*C*H), 134.0 (*C*H), 134.5 (*C*), 134.6 (*C*H), 134.8 (*C*), 135.8 (*C*H), 136.71 (*C*), 136.73 (*C*), 137.7 (*C*), 145.1 (*C*), 145.3 (*C*), 160.1 (*C*), 160.4 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 32.0. HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{46}H_{52}BrNaO_2PPd$, 877.1825; found, 877.1817.

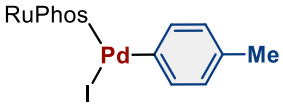


3c

The reaction was carried out with **1** (49.0 mg, 0.12 mmol), **2c** (20.1 mg, 0.12 mmol) and RuPhos (56.3 mg, 0.12 mmol). The product **3c** was obtained as an off-white solid (54.2 mg, 0.073 mmol, 62% yield).

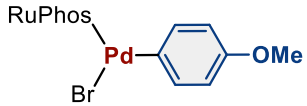
^{1}H NMR (396 MHz, $CDCl_3$, δ): 0.69–0.86 (m, 2H), 1.01 (d, J = 5.9 Hz, 6H), 1.06–1.29 (m, 6H), 1.37 (d, J = 5.9 Hz, 6H), 1.51–1.71 (m, 6H), 1.71–1.87 (m, 6H), 2.08–2.17 (m, 2H), 2.19 (s, 3H), 4.60 (hept,

J = 6.1 Hz, 2H), 6.64 (d, J = 8.7 Hz, 2H), 6.75 (d, J = 7.9 Hz, 2H), 6.86 (ddd, J = 1.3, 3.1, 7.4 Hz, 1H), 6.95 (dd, J = 1.8, 8.1 Hz, 2H), 7.33−7.38 (m, 1H), 7.41 (tt, J = 1.6, 7.3 Hz, 1H), 7.56−7.62 (m, 1H), 7.65 (t, J = 8.5 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 20.5 (CH_3) , 21.5 (CH_3), 22.1 (CH_3), 25.9 (CH_2), 26.7 (CH_2), 26.8 (CH_2), 27.1 (CH_2), 27.2 (CH_2), 27.4 (CH_2), 28.0 (CH_2), 33.4 (*C*H), 33.7 (*C*H), 70.6 (*C*H), 107.2 (*C*H), 111.5 (*C*), 126.1 (*C*H), 126.2 (*C*H), 127.9 (*C*H), 130.3 (*C*H), 130.4 (*C*H), 130.7 (*C*H), 132.2 (*C*H), 132.3 (*C*H), 132.4 (*C*), 133.2 (*C*), 133.6 (*C*), 134.4 (*C*H), 136.7 (*C*H), 136.8 (*C*H), 144.6 (*C*), 144.7 (*C*), 158.6 (*C*). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 31.1. HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{37}H_{50}BrNaO_2PPd$, 767.1665; found, 767.1634.



3d

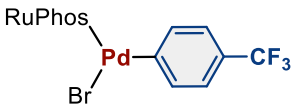
The reaction was carried out with **1** (47.8 mg, 0.12 mmol), **2d** (26.3 mg, 0.12 mmol) and RuPhos (56.0 mg, 0.12 mmol). The product **3d** was obtained as a yellow solid (72.0 mg, 0.091 mmol, 75% yield). ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.69−0.83 (m, 2H), 1.01 (d, J = 5.9 Hz, 6H), 1.05−1.27 (m, 6H), 1.39 (d, J = 6.3 Hz, 6H), 1.52−1.70 (m, 6H), 1.70−1.85 (m, 6H), 2.09−2.18 (m, 2H), 2.20 (s, 3H), 4.57 (hept, J = 5.9 Hz, 2H), 6.64 (d, J = 8.2 Hz, 2H), 6.73 (d, J = 8.2 Hz, 2H), 6.83 (ddd, J = 1.2, 3.1, 7.4 Hz, 1H), 6.92 (dd, J = 1.8, 8.0 Hz, 2H), 7.32−7.37 (m, 1H), 7.40 (tt, J = 0.8, 6.8 Hz, 1H), 7.57−7.62 (m, 1H), 7.63 (t, J = 8.4 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 20.5 (CH_3), 21.6 (CH_3), 22.1 (CH_3), 25.9 (CH_2), 26.7 (CH_2), 26.8 (CH_2), 27.1 (CH_2), 27.3 (CH_2), 27.9 (CH_2), 33.5 (*C*H), 33.7 (*C*H), 70.6 (*C*H), 107.5 (*C*H), 111.4 (*C*), 125.2 (*C*), 126.10 (*C*H), 126.15 (*C*H), 127.5 (*C*H), 130.3 (*C*H), 130.8 (*C*H), 131.9 (*C*), 132.3 (*C*H), 132.4 (*C*), 133.3 (*C*), 133.6 (*C*), 134.5 (*C*H), 138.00 (*C*H), 138.03 (*C*H), 144.4 (*C*), 144.6 (*C*), 158.9 (*C*). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 27.0. HRMS-ESI (m/z): $[M–I]^+$ calcd for $C_{37}H_{50}O_2PPd$, 663.2597; found, 663.2584.



3f

The reaction was carried out with **1** (48.3 mg, 0.12 mmol), **2f** (23.0 mg, 0.12 mmol) and RuPhos (56.1 mg, 0.12 mmol). The product **3f** was obtained as an off-white solid (52.0 mg, 0.068 mmol, 57% yield). ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.72−0.87 (m, 2H), 1.01 (d, J = 5.9 Hz, 6H), 1.06−1.30 (m, 6H), 1.37 (d, J = 5.9 Hz, 6H), 1.51−1.71 (m, 6H), 1.71−1.98 (m, 6H), 2.05−2.26 (m, 2H), 3.71 (s, 3H), 4.60 (hept,

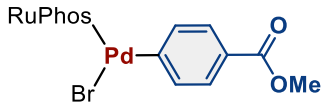
J = 5.9 Hz, 2H), 6.61 (d, J = 8.6 Hz, 2H), 6.65 (d, J = 8.6 Hz, 2H), 6.83−6.89 (m, 1H), 6.96 (d, J = 8.6 Hz, 2H), 7.32−7.48 (m, 2H), 7.59 (t, J = 7.2 Hz, 1H), 7.65 (t, J = 8.2 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.5 (*C*H_3), 22.1 (*C*H_3), 26.0 (*C*H_2), 26.8 (*C*H_2), 26.9 (*C*H_2), 27.1 (*C*H_2), 27.2 (*C*H_2), 27.5 (*C*H_2), 28.1 (*C*H_2), 33.5 (*C*H), 33.8 (*C*H), 55.1 (*C*H_3), 70.7 (*C*H), 107.3 (*C*H), 111.5 (*C*), 113.2 (*C*H), 122.8 (*C*), 126.2 (*C*H), 126.3 (*C*H), 130.4 (*C*H), 130.7 (*C*H), 132.3 (*C*H), 132.5 (*C*H), 133.2 (*C*), 133.6 (*C*), 134.5 (*C*H), 136.9 (*C*H), 137.0 (*C*H), 144.6 (*C*), 144.8 (*C*), 156.6 (*C*), 158.7 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 31.3. HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{37}H_{50}BrNaO_3PPd$, 783.1615; found, 783.1610.



3g

2g was distilled before the use. The reaction was carried out with **1** (46.4 mg, 0.12 mmol), **2g** (26.9 mg, 0.12 mmol) and RuPhos (55.9 mg, 0.12 mmol). The product **3g** was obtained as an off-white solid (57.5 mg, 0.072 mmol, 60% yield).

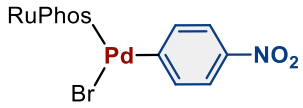
^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.63−0.77 (m, 2H), 1.02 (d, J = 6.3 Hz, 6H), 1.05−1.29 (m, 6H), 1.38 (d, J = 5.9 Hz, 6H), 1.48−1.86 (m, 12H), 2.03−2.17 (m, 2H), 4.61 (hept, J = 6.1 Hz, 2H), 6.66 (d, J = 7.8 Hz, 2H), 6.88 (ddd, J = 1.4, 3.1, 7.6 Hz, 1H), 7.15 (d, J = 8.2 Hz, 2H), 7.27 (d, J = 5.1 Hz, 2H), 7.34−7.41 (m, 1H), 7.44 (tt, J = 1.5, 7.5 Hz, 1H), 7.54−7.62 (m, 1H), 7.67 (t, J = 8.2 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.5 (*C*H_3), 22.1 (*C*H_3), 25.9 (*C*H_2), 26.6 (*C*H_2), 26.7 (*C*H_2), 27.0 (*C*H_2), 27.1 (*C*H_2), 27.4 (*C*H_2), 28.0 (*C*H_2), 33.5 (*C*H), 33.7 (*C*H), 70.9 (*C*H), 107.4 (*C*H), 110.86 (*C*), 110.90 (*C*), 122.7 (*C*H), 123.3 (*C*), 125.4 (*C*), 125.7 (*C*), 126.1 (*C*), 126.4 (*C*H), 126.5 (*C*H), 130.66 (*C*H), 130.70 (*C*H), 132.4 (*C*H), 132.5 (*C*H), 132.8 (*C*), 134.9 (*C*H), 137.40 (*C*H), 137.44 (*C*H), 143.0 (*C*), 144.4 (*C*), 144.6 (*C*), 159.0 (*C*) (observed complexity is due to C–P and C−F coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 31.4. HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{37}H_{47}BrF_3NaO_2PPd$, 821.1383; found, 821.1381.



3h

The reaction was carried out with **1** (46.2 mg, 0.12 mmol), **2h** (26.1 mg, 0.12 mmol) and RuPhos (60.0 mg, 0.12 mmol). The product **3h** was obtained as a pale yellow solid (69.1 mg, 0.088 mmol, 74% yield).

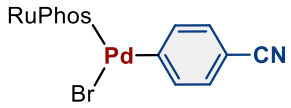
^{1}H NMR (401 MHz, $CDCl_3$, δ): 0.70−0.84 (m, 2H), 1.02 (d, J = 6.4 Hz, 6H), 1.05−1.30 (m, 6H), 1.38 (d, J = 6.0 Hz, 6H), 1.50−1.87 (m, 12H), 2.04−2.20 (m, 2H), 3.84 (s, 3H), 4.61 (hept, J = 5.9 Hz, 2H), 6.66 (d, J = 8.4 Hz, 2H), 6.84−6.91 (m, 1H), 7.21−7.31 (m, 2H), 7.40 (dt, J = 7.6, 22.8 Hz, 2H), 7.53 −7.62 (m, 3H), 7.66 (t, J = 8.4 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.4 (CH_3), 22.1 (CH_3), 25.9 (CH_2), 26.6 (CH_2), 26.7 (CH_2), 26.9 (CH_2), 27.1 (CH_2), 27.5 (CH_2), 28.0 (CH_2), 33.5 (*C*H), 33.8 (*C*H), 51.6 (CH_3), 70.9 (*C*H), 107.4 (*C*H), 111.0 (*C*), 111.1 (*C*), 125.1 (*C*), 126.36 (*C*H), 126.40 (*C*H), 127.0 (*C*H), 130.55 (*C*H), 130.64 (*C*H), 132.4 (*C*H), 132.5 (*C*H), 132.8 (*C*), 134.8 (*C*H), 137.31 (*C*H), 137.34 (*C*H), 144.3 (*C*), 144.5 (*C*), 146.9 (*C*), 158.9 (*C*), 168.0 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 31.2. HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{38}H_{50}BrNaO_4PPd$, 811.1564; found, 811.1570.



3i

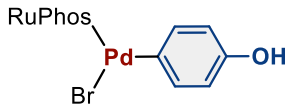
The reaction was carried out with **1** (47.6 mg, 0.12 mmol), **2i** (23.9 mg, 0.12 mmol) and RuPhos (57.5 mg, 0.12 mmol). The product **3i** was obtained as an off-white solid (66.4 mg, 0.086 mmol, 72% yield).

^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.72−0.88 (m, 2H), 1.03 (d, J = 6.3 Hz, 6H), 1.06−1.30 (m, 6H), 1.38 (d, J = 5.5 Hz, 6H), 1.49−1.64 (m, 2H), 1.64−1.86 (m, 10H), 2.03−2.16 (m, 2H), 4.62 (hept, J = 6.1 Hz, 2H), 6.67 (d, J = 8.6 Hz, 2H), 6.88 (ddd, J = 1.3, 2.8, 7.7 Hz, 1H), 7.35−7.42 (m, 3H), 7.45 (tt, J = 1.6, 7.4 Hz, 1H), 7.55−7.62 (m, 1H), 7.68 (t, J = 8.4 Hz, 1H), 7.79 (d, J = 8.6 Hz, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.4 (CH_3), 22.1 (CH_3), 25.9 (CH_2), 26.6 (CH_2), 26.7 (CH_2), 26.9 (CH_2), 27.0 (CH_2), 27.7 (CH_2), 28.1 (CH_2), 33.7 (*C*H), 34.0 (*C*H), 71.1 (*C*H), 107.5 (*C*H), 110.4 (*C*), 120.2 (*C*H), 126.58 (*C*H), 126.62 (*C*H), 130.7 (*C*H), 130.9 (*C*H), 132.0 (*C*), 132.4 (*C*), 132.5 (*C*H), 132.6 (*C*H), 135.3 (*C*H), 137.56 (*C*H), 137.60 (*C*H), 144.3 (*C*), 144.5 (*C*), 144.9 (*C*), 152.2 (*C*), 159.3 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 31.6. HRMS-ESI (m/z): $[M–Br]^+$ calcd for $C_{38}H_{50}BrNaO_4PPd$, 694.2291; found, 694.2292.



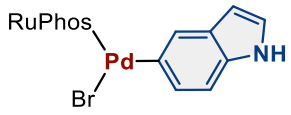
3j

The reaction was carried out with **1** (46.9 mg, 0.12 mmol), **2j** (21.8 mg, 0.12 mmol) and RuPhos (56.0 mg, 0.12 mmol). The product **3j** was obtained as an off-white solid (68.4 mg, 0.091 mmol, 76% yield). ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.67−0.82 (m, 2H), 1.02 (d, J = 5.8 Hz, 6H), 1.03−1.30 (m, 6H), 1.37 (d, J = 6.3 Hz, 6H), 1.48−1.64 (m, 2H), 1.65−1.84 (m, 10H), 2.01−2.16 (m, 2H), 4.56−4.67 (m, 2H), 6.66 (d, J = 8.5 Hz, 2H), 6.85−6.92 (m, 1H), 7.14−7.21 (m, 2H), 7.28−7.36 (m, 2H), 7.39 (t, J = 7.4 Hz, 1H), 7.45 (t, J = 7.4 Hz, 1H), 7.58 (t, J = 7.2 Hz, 1H), 7.67 (t, J = 8.3 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.5 (*C*H$_3$), 22.1 (*C*H$_3$), 25.9 (*C*H$_2$), 26.6 (*C*H$_2$), 26.7 (*C*H$_2$), 27.0 (*C*H$_2$), 27.1 (*C*H$_2$), 27.6 (*C*H$_2$), 28.1 (*C*H$_2$), 33.6 (*C*H), 33.9 (*C*H), 71.0 (*C*H), 106.5 (*C*), 107.4 (*C*H), 110.4 (*C*), 119.9 (*C*), 126.5 (*C*H), 126.6 (*C*H), 129.0 (*C*H), 129.2 (*C*H), 130.7 (*C*H), 130.8 (*C*H), 132.5 (*C*H), 132.6 (*C*H), 135.2 (*C*H), 138.3 (*C*H), 144.4 (*C*), 144.6 (*C*), 147.6 (*C*), 159.2 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 31.5, 32.6. HRMS-ESI (m/z): $[M–Br]^+$ calcd for $C_{37}H_{47}NaO_2PPd$, 674.2393; found, 674.2391.



3k

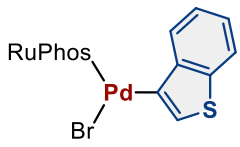
The reaction was carried out with **1** (47.2 mg, 0.12 mmol), **2k** (20.9 mg, 0.12 mmol) and RuPhos (56.4 mg, 0.12 mmol). The product **3k** was obtained as an off-white solid (31.3 mg, 0.042 mmol, 35% yield). ^{1}H NMR (396 MHz, $CDCl_3$, δ): 0.71−0.85 (m, 2H) , 1.01 (d, J = 6.3 Hz, 6H), 1.04−1.34 (m, 6H), 1.37 (d, J = 5.9 Hz, 6H), 1.49−1.96 (m, 12H), 2.06−2.23 (m, 2H), 4.59 (hept, J = 6.0 Hz, 2H), 6.48 (d, J = 8.7 Hz, 2H), 6.62 (d, J = 7.9 Hz, 2H), 6.80−6.90 (m, 3H), 7.33−7.47 (m, 2H), 7.55−7.61 (m, 1H), 7.64 (t, J = 8.5 Hz, 1H) (a proton of hydroxyl group cannot be detected). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.6 (*C*H$_3$), 22.1 (*C*H$_3$), 26.0 (*C*H$_2$), 26.8 (*C*H$_2$), 26.9 (*C*H$_2$), 27.1 (*C*H$_2$), 27.2 (*C*H$_2$), 27.6 (*C*H$_2$), 28.1 (*C*H$_2$), 33.6 (*C*H), 33.9 (*C*H), 70.6 (*C*H), 107.1 (*C*H), 110.00 (*C*), 115.1 (*C*H), 121.3 (*C*), 126.17 (*C*H), 126.21 (*C*H), 130.4 (*C*H), 130.7 (*C*H), 132.3 (*C*H), 132.4 (*C*H), 133.6 (*C*), 134.0 (*C*), 134.7 (*C*H), 136.7 (*C*H), 136.8 (*C*H), 144.8 (*C*), 144.9 (*C*), 152.9 (*C*), 158.9 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 31.6. HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{36}H_{48}BrNaO_3PPd$, 769.1458; found, 769.1442.



3l

The reaction was carried out with **1** (46.7 mg, 0.12 mmol), **2l** (23.6 mg, 0.12 mmol) and RuPhos (56.1 mg, 0.12 mmol). The product **3l** was obtained as an off-white solid by reprecipitation with CH_2Cl_2/hexane (45.8 mg, 0.060 mmol, 49% yield).

^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.62 (br, s, 1H), 0.78−1.32 (m, 12H), 1.40 (d, J = 5.9 Hz, 6H), 1.46−1.86 (m, 12H), 1.98 (br, s, 1H), 2.07−2.24 (m, 2H), 4.56−4.69 (m, 2H), 6.29 (t, J = 2.4 Hz, 1H), 6.67 (dd, J = 8.0, 22.1 Hz, 2H), 6.88 (ddd, J = 1.3, 3.2, 7.5 Hz, 1H), 6.97 (t, J = 2.7 Hz, 1H), 6.94−7.05 (m, 2H), 7.17 (d, J = 1.6 Hz, 1H), 7.32−7.45 (m, 2H), 7.56−7.62 (m, 1H), 7.65 (t, J = 8.4 Hz, 1H), 7.88 (s, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.4 (*C*H_3), 21.6 (*C*H_3), 22.2 (*C*H_3), 25.9 (*C*H_2), 26.0 (*C*H_2), 26.5 (*C*H_2), 26.6 (*C*H_2), 26.8 (*C*H_2), 26.9 (*C*H_2), 27.0 (*C*H_2), 27.1 (*C*H_2), 27.3 (*C*H_2), 27.7 (*C*H_2), 28.2 (*C*H_2), 28.3 (*C*H_2), 30.9 (*C*H), 32.9 (*C*H), 33.2 (*C*H), 34.1 (*C*H), 34.3 (*C*H), 70.3 (*C*H), 70.9 (*C*H), 100.8 (*C*H), 106.9 (*C*H), 107.6 (*C*H), 109.3 (*C*H), 112.03 (*C*), 112.06 (*C*), 121.7 (*C*), 122.5 (*C*H), 126.07 (*C*H), 126.13 (*C*H), 126.9 (*C*H), 127.0 (*C*H), 128.46 (*C*), 128.49 (*C*), 130.2 (*C*H), 130.46 (*C*H), 130.49 (*C*H), 130.7 (*C*H), 132.3 (*C*H), 132.4 (*C*H), 133.5 (*C*), 133.8 (*C*), 134.2 (*C*H), 144.6 (*C*), 144.8 (*C*), 158.2 (*C*), 158.7 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 31.2. HRMS-ESI (m/z): $[M-Br]^+$ calcd for $C_{38}H_{49}NO_2PPd$, 688.2550; found, 688.2527.

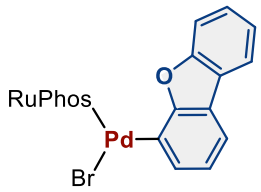


3m

The reaction was carried out with **1** (46.6 mg, 0.12 mmol), **2m** (25.9 mg, 0.12 mmol) and RuPhos (55.9 mg, 0.12 mmol). The product **3m** was obtained as an off-white solid (73.6 mg, 0.094 mmol, 78% yield).

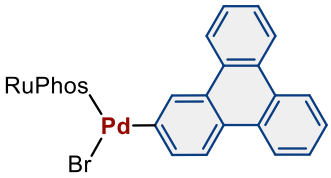
^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.66 (br, s, 1H), 0.77−0.93 (m, 1H), 0.95−1.30 (m, 12H), 1.34−1.45 (m, 6H), 1.47−1.85 (m, 11H), 1.93 (br, s, 1H), 2.12 (br, s, 2H), 4.63 (br, s, 2H), 6.68 (dd, J = 8.2, 18.0 Hz, 2H), 6.89 (ddd, J = 1.4, 3.1, 7.6 Hz, 1H), 7.10 (d, J = 5.1 Hz, 1H), 7.17−7.24 (m, 2H), 7.33−7.49 (m, 4H), 7.59 (t, J = 6.7 Hz, 1H), 7.66 (t, J = 8.4 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.4 (*C*H_3), 21.5 (*C*H_3), 22.1 (*C*H_3), 25.9 (*C*H_2), 26.8 (*C*H_2), 27.1 (*C*H_2), 27.2 (*C*H_2), 27.7 (*C*H_2), 28.0 (*C*H_2), 28.3 (*C*H_2), 33.0 (*C*H), 33.3 (*C*H), 33.9 (*C*H), 34.2 (*C*H), 70.5 (*C*H), 71.1 (*C*H), 107.2 (*C*H), 107.7 (*C*H),

111.7 (*C*), 119.7 (*C*H), 123.0 (*C*H), 124.5 (*C*H), 126.2 (*C*H), 126.23 (*C*H), 130.0 (*C*), 130.4 (*C*H), 130.7 (*C*H), 130.89 (*C*H), 130.93 (*C*H), 132.4 (*C*H), 132.5 (*C*H), 132.8 (*C*), 133.1 (*C*), 133.67 (*C*H), 133.71 (*C*H), 134.4 (*C*H), 135.5 (*C*), 139.3 (*C*), 139.4 (*C*), 144.4 (*C*), 144.6 (*C*), 158.3 (*C*), 158.9 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 31.2. HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{38}H_{48}BrNaO_2PPdS$, 809.1401; found, 809.1218.



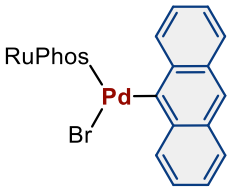
3n

The reaction was carried out with **1** (46.9 mg, 0.12 mmol), **2n** (29.7 mg, 0.12 mmol) and RuPhos (56.0 mg, 0.12 mmol). The product **3n** was obtained as an off-white solid (50.2 mg, 0.061 mmol, 51% yield). ^{1}H NMR (392 MHz, $CDCl_3$, δ): –0.22––0.03 (m, 1H), 0.20–0.41 (m, 1H), 0.79–1.40 (m, 18H), 1.41–1.85 (m, 10H), 1.86–2.24 (m, 3H), 2.30–2.42 (m, 1H), 4.55–4.76 (m, 2H), 6.58 (d, *J* = 8.5 Hz, 1H), 6.69 (d, *J* = 8.5 Hz, 1H), 6.86 (d, *J* = 6.7 Hz, 1H), 7.00–7.15 (m, 2H), 7.18–7.27 (m, 1H), 7.29–7.39 (m, 2H), 7.43 (d, *J* = 8.1 Hz, 2H), 7.49 (d, *J* = 7.2 Hz, 1H), 7.57 (t, *J* = 7.2 Hz, 1H), 7.77 (t, *J* = 8.3 Hz, 1H), 7.85 (d, *J* = 7.6 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.7 (CH_3), 21.9 (CH_3), 22.0 (CH_3), 22.5 (CH_2), 25.4 (CH_2), 25.6 (CH_2), 26.1 (CH_2), 26.3 (CH_2), 26.5 (CH_2), 26.7 (CH_2), 26.8 (CH_2), 26.9 (CH_2), 27.0 (CH_2), 27.1 (CH_2), 27.3 (CH_2), 27.5 (CH_2), 28.1 (CH_2), 29.41 (CH_2), 29.44 (CH_2), 33.0 (*C*H), 33.3 (*C*H), 35.1 (*C*H), 35.3 (*C*H), 70.2 (*C*H), 70.9 (*C*H), 106.3 (*C*H), 106.8 (*C*H), 108.1 (*C*), 113.3 (*C*H), 115.5 (*C*), 115.6 (*C*H), 120.5 (*C*H), 121.5 (*C*), 121.7 (*C*H), 122.7 (*C*H), 125.3 (*C*), 125.8 (*C*H), 126.28 (*C*H), 126.34 (*C*H), 130.6 (*C*H), 130.8 (*C*H), 132.1 (*C*H), 132.2 (*C*H), 134.7 (*C*H), 136.1 (*C*H), 145.3 (*C*), 145.5 (*C*), 155.8 (*C*), 159.9 (*C*), 160.0 (*C*), 161.0 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 36.2, 37.4. HRMS-ESI (m/z): $[M–Br]^+$ calcd for $C_{42}H_{50}O_3PPd$, 739.2548; found, 739.2547.



3o

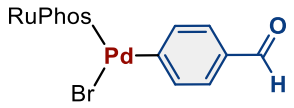
The reaction was carried out with **1** (48.1 mg, 0.12 mmol), **2o** (37.1 mg, 0.12 mmol) and RuPhos (56.3 mg, 0.12 mmol). The product **3o** was obtained as an off-white solid (98.3 mg, 0.11 mmol, 92% yield). ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.62−0.77 (m, 1H), 0.90−1.36 (m, 6H), 1.02 (d, J = 5.9 Hz, 3H), 1.11 (d, J = 5.9 Hz, 3H), 1.46 (d, J = 5.9 Hz, 6H), 1.50−1.85 (m, 12H), 1.98−2.23 (m, 3H), 4.63−4.75 (m, 2H), 6.74 (q, J = 6.8 Hz, 2H), 6.90−6.95 (m, 1H), 7.38 (t, J = 6.3 Hz, 1H), 7.45 (t, J = 7.1 Hz, 1H), 7.51−7.64 (m, 6H), 7.70 (t, J = 8.4 Hz, 1H), 8.20 (d, J = 8.6 Hz, 1H), 8.30 (s, 1H), 8.51−8.63 (m, 4H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.5 (CH_3), 21.6 (CH_3), 22.3 (CH_3), 26.0 (CH_2), 26.1 (CH_2), 26.7 (CH_2), 26.8 (CH_2), 27.0 (CH_2), 27.1 (CH_2), 27.3 (CH_2), 28.0 (CH_2), 28.2 (CH_2), 28.4 (CH_2), 33.2 (*C*H), 33.5 (*C*H), 34.1 (*C*H), 34.4 (*C*H), 70.7 (*C*H), 71.2 (*C*H), 107.3 (*C*H), 108.0 (*C*H), 111.9 (*C*), 120.8 (*C*H), 122.8 (*C*H), 123.0 (*C*H), 123.1 (*C*H), 123.3 (*C*H), 126.1 (*C*H), 126.2 (*C*), 126.3 (*C*H), 126.39 (*C*H), 126.43 (*C*H), 126.7 (*C*H), 126.8 (*C*H), 128.7 (*C*), 129.0 (*C*), 129.66 (*C*), 129.74 (*C*), 130.5 (*C*H), 130.56 (*C*), 130.64 (*C*H), 130.7 (*C*H), 130.8 (*C*H), 132.5 (*C*H), 132.7 (*C*H), 132.8 (*C*), 133.1 (*C*H), 134.6 (*C*H), 136.1 (*C*), 137.49 (*C*H), 137.52 (*C*H), 144.6 (*C*), 144.7 (*C*), 158.4 (*C*), 159.0 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 31.2. HRMS-ESI (m/z): $[M–Br]^+$ calcd for $C_{48}H_{54}O_2PPd$, 799.2914; found, 799.2904.



3p

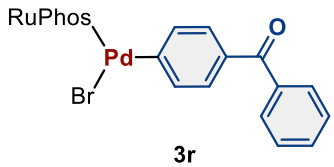
The reaction was carried out with **1** (47.5 mg, 0.12 mmol), **2p** (31.1 mg, 0.12 mmol) and RuPhos (56.0 mg, 0.12 mmol). The product **3p** was obtained as a yellow solid (77.7 mg, 0.094 mmol, 78% yield). ^{1}H NMR (392 MHz, $CDCl_3$, δ): −0.43−−0.26 (m, 2H), 0.50 (q, J = 13.1 Hz, 2H), 0.72−0.85 (m, 2H), 0.97 (q, J = 12.3 Hz, 2H), 1.06 (d, J = 6.3 Hz, 6H), 1.26−1.57 (m, 12H), 1.50 (d, J = 5.9 Hz, 6H), 1.58 −1.74 (m, 2H), 4.72 (hept, J = 6.1 Hz, 2H), 6.71 (d, J = 8.6 Hz, 2H), 6.84 (ddd, J = 1.0, 2.7, 7.6 Hz, 1H), 7.27−7.36 (m, 5H), 7.38−7.48 (m, 2H), 7.72−7.80 (m, 2H), 7.87 (t, J = 8.6 Hz, 1H), 7.95 (s, 1H), 8.66−8.73 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.7 (CH_3), 22.3 (CH_3), 25.5 (CH_2), 26.3 (CH_2),

26.4 (CH_2), 26.6 (CH_2), 26.7 (CH_2), 26.9 (CH_2), 27.0 (CH_2), 34.2 (*C*H), 34.5 (*C*H), 70.8 (*C*H), 106.7 (*C*H), 109.0 (*C*H), 109.1 (*C*H), 122.4 (*C*H), 122.8 (*C*H), 124.3 (*C*H), 126.30 (*C*H), 126.35 (*C*H), 127.7 (*C*H), 129.9 (*C*H), 130.6 (*C*H), 131.7 (*C*), 131.8 (*C*H), 131.9 (*C*H), 134.7 (*C*H), 135.8 (*C*), 136.2 (*C*), 136.3 (*C*H), 137.20 (*C*), 137.24 (*C*), 142.21 (*C*), 142.25 (*C*), 145.1 (*C*), 145.3 (*C*), 161.0 (*C*). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 31.7. HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{44}H_{52}BrNaO_2PPd$, 853.1824; found, 853.1819.



3q

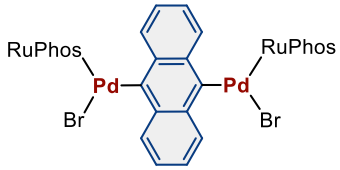
The reaction was carried out with **1** (46.8 mg, 0.12 mmol), **2q** (22.5 mg, 0.12 mmol) and RuPhos (56.1 mg, 0.12 mmol). The product **3q** was obtained as an off-white solid (71.7 mg, 0.095 mmol, 79% yield). ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.70−0.83 (m, 2H), 1.03 (d, J = 6.3 Hz, 6H), 1.05−1.31 (m, 6H), 1.39 (d, J = 6.3 Hz, 6H), 1.50−1.86 (m, 12H), 2.04−2.20 (m, 2H), 4.62 (hept, J = 5.9 Hz, 2H), 6.67 (d, J = 8.2 Hz, 2H), 6.88 (ddd, J = 1.5, 3.2, 7.5 Hz, 1H), 7.36−7.50 (m, 6H), 7.59 (t, J = 7.1 Hz, 1H), 7.67 (t, J = 8.2 Hz, 1H), 9.83 (s, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.4 (CH_3), 22.0 (CH_3), 25.9 (CH_2), 26.6 (CH_2), 26.7 (CH_2), 26.9 (CH_2), 27.1 (CH_2), 27.5 (CH_2), 28.0 (CH_2), 33.6 (*C*H), 33.8 (*C*H), 70.9 (*C*H), 107.4 (*C*H), 110.72 (*C*), 110.74 (*C*), 126.4 (*C*H), 126.5 (*C*H), 126.9 (*C*H), 130.6 (*C*H), 132.3 (*C*), 132.4 (*C*H), 132.5 (*C*H), 132.6 (*C*), 135.0 (*C*H), 137.98 (*C*H), 138.01 (*C*H), 144.3 (*C*), 144.5 (*C*), 151.3 (*C*), 159.0 (*C*), 192.7 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 31.4. HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{37}H_{48}BrNaO_3PPd$, 781.1458; found, 781.1458.



3r

The reaction was carried out with **1** (47.3 mg, 0.12 mmol), **2r** (31.7 mg, 0.12 mmol) and RuPhos (57.0 mg, 0.12 mmol). The product **3r** was obtained as an off-white solid (61.8 mg, 0.074 mmol, 61% yield). ^{1}H NMR (396 MHz, $CDCl_3$, δ): 0.72−0.87 (m, 2H), 1.02 (d, J = 5.9 Hz, 6H), 1.05−1.28 (m, 6H), 1.39 (d, J = 5.9 Hz, 6H), 1.51−1.84 (m, 12H), 2.07−2.19 (m, 2H), 4.62 (hept, J = 6.0 Hz, 2H), 6.68 (d, J = 8.7 Hz, 2H), 6.88 (ddd, J = 1.4, 3.2, 7.7 Hz, 1H), 7.29−7.47 (m, 8H), 7.53 (tt, J = 1.6, 7.5 Hz, 1H), 7.56−7.62 (m, 1H), 7.68 (t, J = 5.1 Hz, 1H), 7.73−7.78 (m, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.5

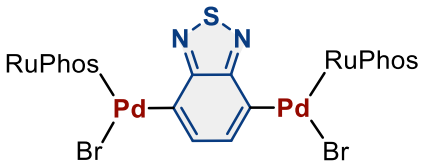
(CH_3), 22.0 (CH_3), 25.8 (CH_2), 26.6 (CH_2), 26.7 (CH_2), 27.0 (CH_2), 27.1 (CH_2), 27.5 (CH_2), 28.0 (CH_2), 33.5 (*C*H), 33.8 (*C*H), 70.9 (*C*H), 107.4 (*C*H), 110.97 (*C*), 111.01 (*C*), 126.38 (*C*H), 126.43 (*C*H), 127.8 (*C*H), 127.9 (*C*H), 129.8 (*C*H), 130.6 (*C*H), 130.7 (*C*H), 131.6 (*C*H), 132.37 (*C*H), 132.42 (*C*H), 132.5 (*C*), 132.7 (*C*), 134.8 (*C*H), 137.2 (*C*H), 137.3 (*C*H), 138.4 (*C*), 144.4 (*C*), 144.5 (*C*), 147.5 (*C*), 158.9 (*C*), 197.0 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 31.3. HRMS-ESI (m/z): $[M+Na]^+$ calcd for $C_{43}H_{52}BrNaO_3PPd$, 857.1773; found, 857.1756.



3s

The reaction was carried out with **1** (779.1 mg, 2.0 mmol), **2s** (336.2 mg, 1.0 mmol) and RuPhos (933.3 mg, 2.0 mmol). The product **3s** was obtained as an orange solid (1.261 g, 0.85 mmol, 85% yield).

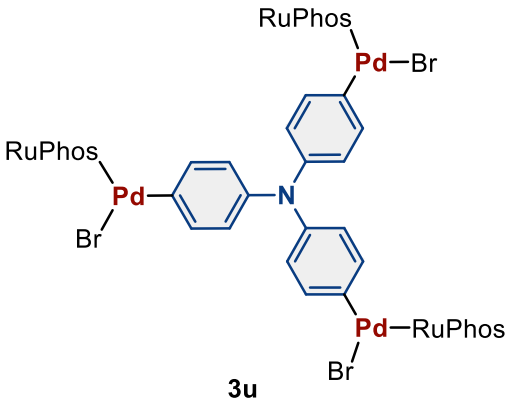
^{1}H NMR (392 MHz, $CDCl_3$, δ): –0.44––0.22 (m, 4H), 0.37−0.54 (m, 4H), 0.69−0.83 (m, 4H), 0.84−0.98 (m, 4H), 1.04 (d, J = 5.8 Hz, 12H), 1.18−1.60 (m, 36H), 1.71−1.85 (m, 4H), 4.70 (quin, J = 5.8 Hz, 4H), 6.68 (d, J = 8.5 Hz, 4H), 6.78−6.83 (m, 2H), 7.17 (dd, J = 3.1, 6.3 Hz, 4H), 7.23−7.29 (m, 2H), 7.34 (t, J = 6.7 Hz, 2H), 7.41 (t, J = 7.2 Hz, 2H), 7.78 (t, J = 8.1 Hz, 2H), 8.57 (dd, J = 3.1, 6.3 Hz, 4H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.7 (CH_3), 22.6 (CH_3), 26.0 (CH_2), 26.6 (CH_2), 26.7 (CH_2), 26.8 (CH_2), 26.95 (CH_2), 26.99 (CH_2), 27.7 (CH_2), 34.7 (CH_2), 35.0 (CH_2), 71.0 (*C*H), 107.3 (*C*H), 111.1 (*C*), 121.9 (*C*H), 126.1 (*C*H), 130.1 (*C*H), 130.3 (*C*H), 131.8 (*C*H), 132.0 (*C*H), 134.5 (*C*H), 135.5 (*C*H), 136.7 (*C*), 137.5 (*C*), 145.2 (*C*), 160.7 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 31.4 (s). HRMS-ESI (m/z): $[M–Br]^+$ calcd for $C_{74}H_{94}BrO_4P_2Pd_2$, 1401.3906; found, 1401.3888.



3t

The reaction was carried out with **1** (93.5 mg, 0.24 mmol), **2t** (35.3 mg, 0.12 mmol) and RuPhos (112.1 mg, 0.12 mmol). The product **3t** was obtained as a yellow solid (146.9 mg, 0.10 mmol, 85% yield).

^{1}H NMR (392 MHz, $CDCl_3$, δ): −0.59 (q, J = 12.7 Hz, 2H), 0.16 (q, J = 12.9 Hz, 2H), 0.66 (q, J = 12.4 Hz, 2H), 0.80−1.95 (m, 56H), 1.99−2.11 (m, 2H), 2.20−2.35 (m, 2H), 2.44−2.53 (m, 2H), 4.57 (quin, J = 5.8 Hz, 2H), 4.69 (quin, J = 6.0 Hz, 2H), 6.54 (d, J = 8.5 Hz, 2H), 6.62 (s, 2H), 6.77 (d, J = 8.1 Hz, 2H), 6.85 (d, J = 6.3 Hz, 2H), 7.33 (t, J = 7.4 Hz, 2H), 7.40 (t, J = 7.4 Hz, 2H), 7.54 (t, J = 7.4 Hz, 2H), 7.65 (t, J = 8.3 Hz, 2H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.5 (CH_3), 21.6 (CH_3), 22.2 (CH_3), 22.8 (CH_3), 25.7 (CH_2), 26.0 (CH_2), 26.3 (CH_2), 26.56 (CH_2), 26.62 (CH_2), 26.7 (CH_2), 27.3 (CH_2), 27.4 (CH_2), 27.6 (CH_2), 27.8 (CH_2), 30.2 (CH_2), 31.8 (*C*H), 32.1 (*C*H), 34.8 (*C*H), 35.1 (*C*H), 70.0 (*C*H), 72.0 (*C*H), 106.4 (*C*H), 107.9 (*C*H), 106.4 (*C*H), 107.9 (*C*H), 110.90 (*C*), 110.91 (*C*), 123.1 (*C*), 126.05 (*C*H), 126.10 (*C*H), 130.3 (*C*H), 130.9 (*C*H), 132.3 (*C*), 132.4 (*C*), 134.3 (*C*), 134.8 (*C*H), 144.9 (*C*), 145.1 (*C*), 158.9 (*C*), 160.2 (*C*), 160.4 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 35.4. HRMS-ESI (m/z): $[M–Br]^+$ calcd for $C_{66}H_{88}BrN_2O_4P_2Pd_2S$, 1359.3214; found, 1359.3198.

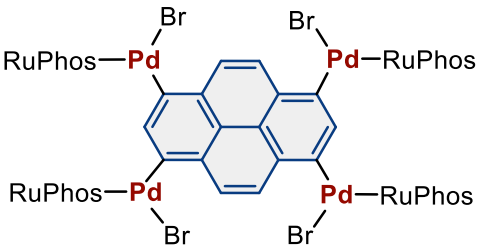


3u

The reaction was carried out with **1** (140.1 mg, 0.36 mmol), **2u** (57.8 mg, 0.12 mmol) and RuPhos (168.1 mg, 0.36 mmol). The product **3u** was obtained as an orange solid (240.4 mg, 0.11 mmol, 91% yield).

^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.64−0.82 (m, 6H), 0.95−1.30 (m, 36H), 1.35 (d, J = 2.7 Hz, 9H), 1.37 (d, J = 2.9 Hz, 9H), 1.45−1.92 (m, 33H), 2.20 (q, J = 10.5 Hz, 6H), 4.53−4.64 (m, 6H), 6.62 (dd, J =

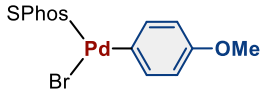
2.2, 8.5 Hz, 6H), 6.68−6.76 (m, 6H), 6.78−6.97 (m, 11H), 7.14 (d, J = 8.5 Hz, 1H), 7.32−7.45 (m, 6H), 7.59 (t, J = 7.0 Hz, 3H), 7.67 (td, J = 4.0, 8.3 Hz, 3H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.6 (*C*H$_3$), 22.0 (*C*H$_3$), 25.9 (*C*H$_2$), 26.8 (*C*H$_2$), 26.9 (*C*H$_2$), 27.2 (*C*H$_2$), 27.3 (*C*H$_2$), 27.5 (*C*H$_2$), 27.9 (*C*H$_2$), 33.4 (*C*H), 33.6 (*C*H), 70.4 (*C*H), 70.6 (*C*H), 106.97 (*C*H), 107.01 (*C*H), 110.68 (*C*), 110.72 (*C*), 111.0 (*C*), 111.1 (*C*), 112.4 (*C*), 122.7 (*C*H), 123.5 (*C*H), 123.6 (*C*H), 124.6 (*C*), 126.1 (*C*H), 126.19 (*C*H), 126.23 (*C*H), 127.4 (*C*), 130.3 (*C*H), 130.5 (*C*H), 130.7 (*C*H), 130.8 (*C*H), 131.3 (*C*H), 132.2 (*C*H), 132.27 (*C*H), 132.33 (*C*H), 132.4 (*C*H), 133.4 (*C*), 133.7 (*C*), 133.8 (*C*), 134.1 (*C*), 134.6 (*C*H), 134.9 (*C*H), 136.56 (*C*H), 136.60 (*C*H), 137.2 (*C*H), 137.3 (*C*H), 143.2 (*C*), 144.0 (*C*), 144.8 (*C*), 144.9 (*C*), 145.9 (*C*), 147.5 (*C*), 158.8 (*C*), 159.0 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 31.5, 31.6, 32.4, 32.7. HRMS-ESI (m/z): $[M–Br]^+$ calcd for $C_{108}H_{141}Br_2NO_6P_3Pd_3$, 2120.5480; found, 2120.5469.



3v

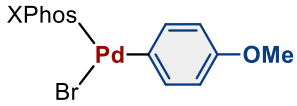
The reaction was carried out with **1** (124.7 mg, 0.32 mmol), **2v** (41.5 mg, 0.08 mmol) and RuPhos (149.3 mg, 0.32 mmol). The product **3v** was obtained as an orange solid (137.5 mg, 0.05 mmol, 61% yield).

^{1}H NMR (392 MHz, $CDCl_3$, δ): −0.40—0.25 (m, 3H), 0.32−0.69 (m, 8H), 0.72−1.37 (m, 62H), 1.42−2.01 (m, 55H), 2.29−2.54 (m, 8H), 4.50−4.62 (m, 4H), 4.70−4.83 (m, 4H), 6.54−6.65 (m, 4H), 6.82−6.95 (m, 8H), 7.01−7.13 (m, 2H), 7.25−7.40 (m, 8H), 7.48−7.61 (m, 8H), 8.36−8.45 (m, 4H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 21.47 (*C*H$_3$), 22.05 (*C*H$_3$), 25.84 (*C*H$_2$), 26.60 (*C*H$_2$), 26.72 (*C*H$_2$), 26.95 (*C*H$_2$), 27.08 (*C*H$_2$), 27.52 (*C*H$_2$), 28.04 (*C*H$_2$), 33.53 (*C*H), 33.80 (*C*H), 70.90 (*C*H), 107.41 (*C*H), 110.97 (*C*), 111.01 (*C*), 126.38 (*C*H), 126.43 (*C*H), 127.84 (*C*H), 127.89 (*C*H), 129.81 (*C*H), 130.61 (*C*H), 130.68 (*C*H), 131.57 (*C*H), 132.37 (*C*H), 132.42 (*C*H), 132.52 (*C*), 132.73 (*C*), 134.85 (*C*H), 137.23 (*C*H), 137.27 (*C*H), 138.38 (*C*), 144.36 (*C*), 144.54 (*C*), 147.46 (*C*), 158.92 (*C*), 197.00 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 28.8, 29.2, 29.3, 30.4. HRMS-ESI (m/z): $[M]^+$ calcd for $C_{136}H_{178}Br_4O_8P_4Pd_4$, 2809.5383; found, 2809.5324.



3w

The reaction was carried out with **1** (46.8 mg, 0.12 mmol), **2f** (22.4 mg, 0.12 mmol) and SPhos (49.4 mg, 0.12 mmol). The product **3w** was obtained as an off-white solid (37.2 mg, 0.053 mmol, 44% yield). ^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.60−0.73 (m, 2H), 1.01−1.31 (m, 7H), 1.51−1.82 (m, 9H), 1.83−1.98 (m, 2H), 2.17 (q, J = 11.4 Hz, 2H), 3.72 (s, 3H), 3.78 (s, 6H), 6.59−6.69 (m, 4H), 6.83−6.88 (m, 1H), 6.94 (dd, J = 2.0, 8.7 Hz, 2H), 7.42 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 7.4 Hz, 1H), 7.65 (t, J = 6.7 Hz, 1H), 7.79 (t, J = 8.3 Hz, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 25.9 (CH_2), 27.0 (CH_2), 27.2 (CH_2), 27.4 (CH_2), 27.5 (CH_2), 27.7 (CH_2), 34.1 (*C*H), 34.4 (*C*H), 55.1 (CH_3), 55.9 (CH_3), 106.1 (*C*H), 107.97 (*C*), 108.00 (*C*), 113.4 (*C*H), 121.9 (*C*), 126.7 (*C*H), 126.8 (*C*H), 131.3 (*C*H), 131.4 (*C*H), 131.6 (*C*H), 131.7 (*C*H), 135.8 (*C*H), 136.7 (*C*H), 136.8 (*C*H), 144.2 (*C*), 156.8 (*C*), 160.4 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 34.3, 35.2. HRMS-ESI (m/z): $[M-Br]^+$ calcd for $C_{33}H_{42}O_3PPd$, 623.1919; found, 623.1904.



3x

The reaction was carried out with **1** (46.9 mg, 0.12 mmol), **2f** (22.4 mg, 0.12 mmol) and XPhos (57.2 mg, 0.12 mmol). The product **3x** was obtained as a pale-yellow solid (29.6 mg, 0.038 mmol, 44% yield).

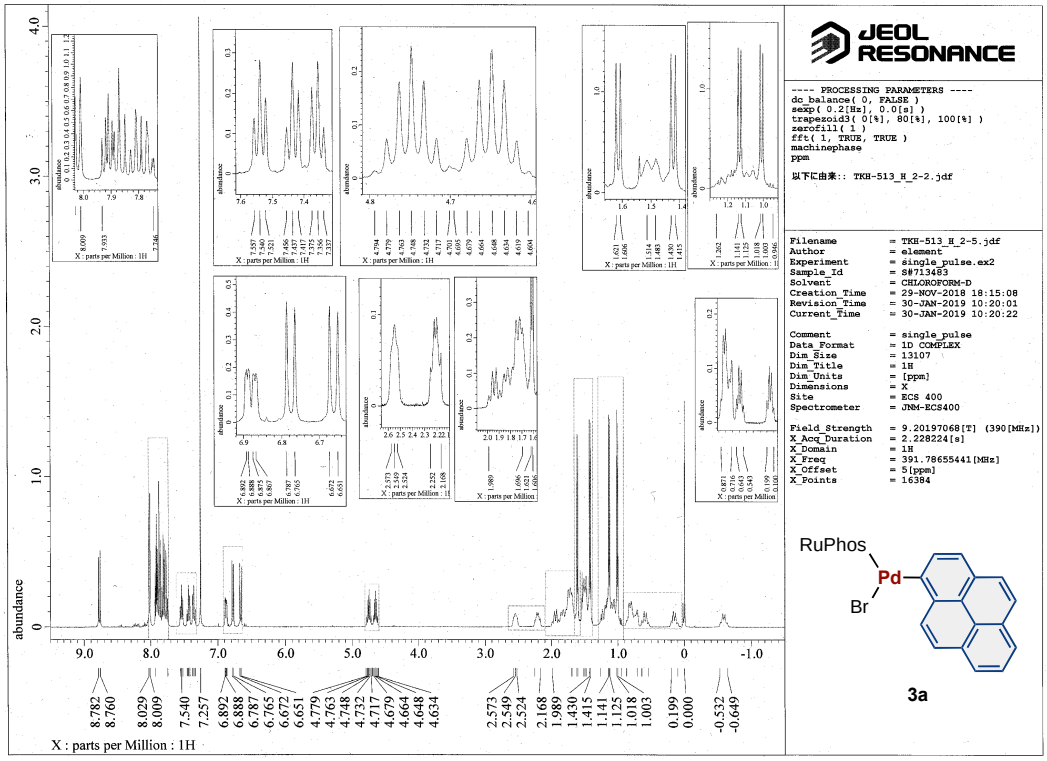
^{1}H NMR (392 MHz, $CDCl_3$, δ): 0.60−0.75 (m, 2H), 0.90 (d, J = 6.7 Hz, 6H), 1.05−1.29 (m, 8H), 1.39 (d, J = 7.2 Hz, 6H), 1.59 (d, J = 6.7 Hz, 6H), 1.62−1.85 (m, 8H), 1.91−2.01 (m, 2H), 2.22 (q, J = 11.4 Hz, 2H), 2.44 (sep, J = 6.5 Hz, 2H), 3.12 (sep, J = 6.7 Hz, 1H), 3.70 (s, 3H), 6.61 (d, J = 8.5 Hz, 2H), 6.85−6.92 (m, 3H), 7.13 (s, 2H), 7.38−7.44 (m, 2H), 7.64−7.71 (m, 1H). ^{13}C NMR (99 MHz, $CDCl_3$, δ): 24.1 (CH_3), 24.4 (CH_3), 24.6 (CH_3), 25.5 (CH_3), 25.8 (CH_2), 27.2 (CH_2), 27.3 (CH_2), 27.5 (CH_2), 27.6 (CH_2), 28.2 (CH_2), 31.4 (*C*H), 34.1 (*C*H), 35.0 (*C*H), 35.3 (*C*H), 55.2 (CH_3), 113.5 (*C*H), 121.6 (*C*), 124.6 (*C*H), 125.56 (*C*), 125.60 (*C*), 126.68 (*C*H), 126.73 (*C*H), 130.3 (*C*H), 131.8 (*C*H), 133.3 (*C*H), 133.4 (*C*H), 134.3 (*C*), 134.6 (*C*), 136.38 (*C*H), 136.42 (*C*H), 147.4 (*C*), 147.6 (*C*), 149.1 (*C*), 155.8 (*C*), 156.7 (*C*) (observed complexity is due to C–P coupling). ^{31}P NMR (160 MHz, $CDCl_3$, δ): 26.7. HRMS-ESI (m/z): $[M-Br]^+$ calcd for $C_{40}H_{56}OPPd$, 689.3119; found, 689.3118.

5. References

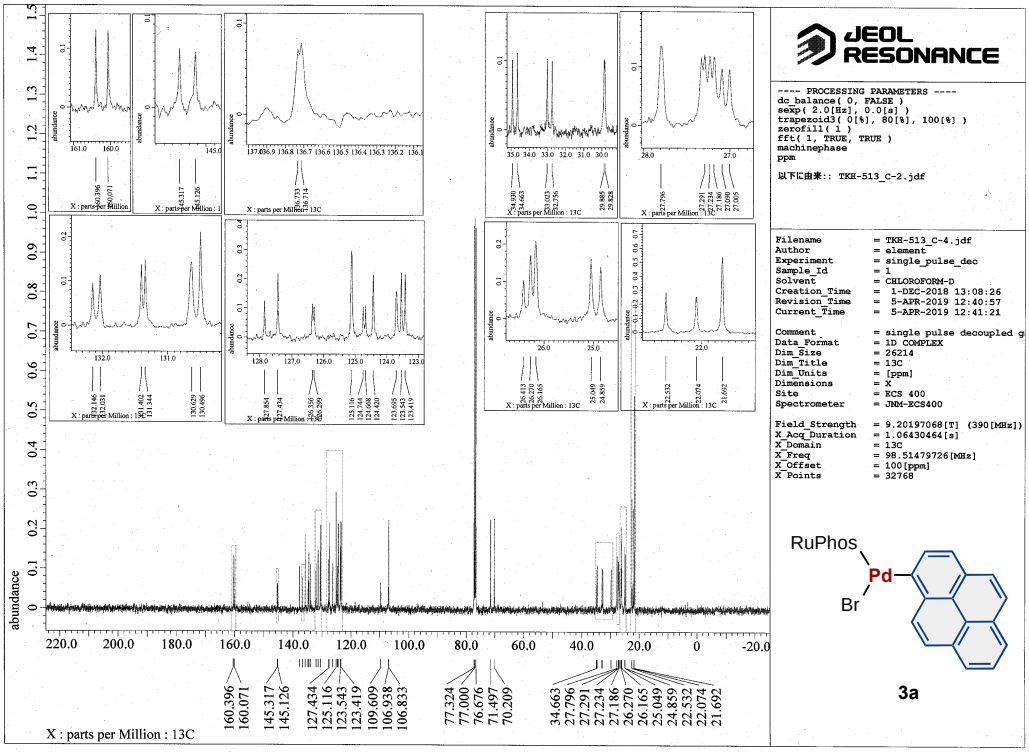
1) Sheldrick, G. M. *Acta Crystallogr*., *Sect*. *A* **2008**, *64*, 112.

2) Kubota, K.; Dai, P.; Pentelute, B. L.; Buchwald, S. L. *J. Am. Chem. Soc.* **2018**, *140*, 3128−3133.

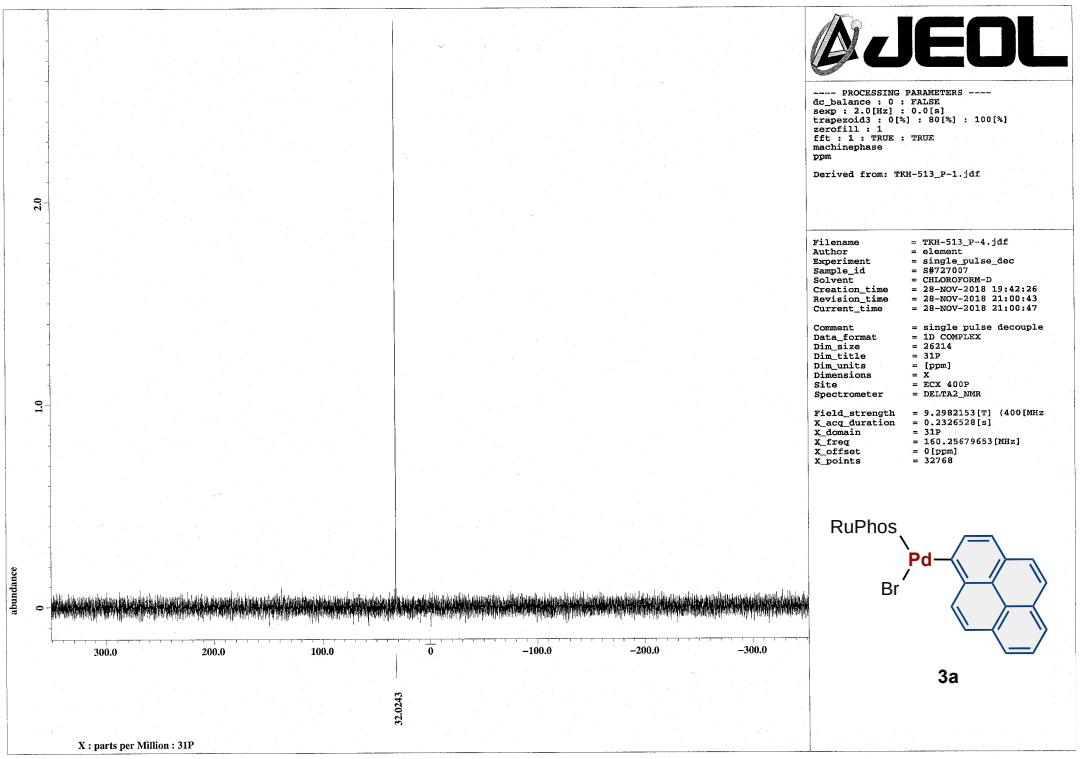
6. NMR Spectra



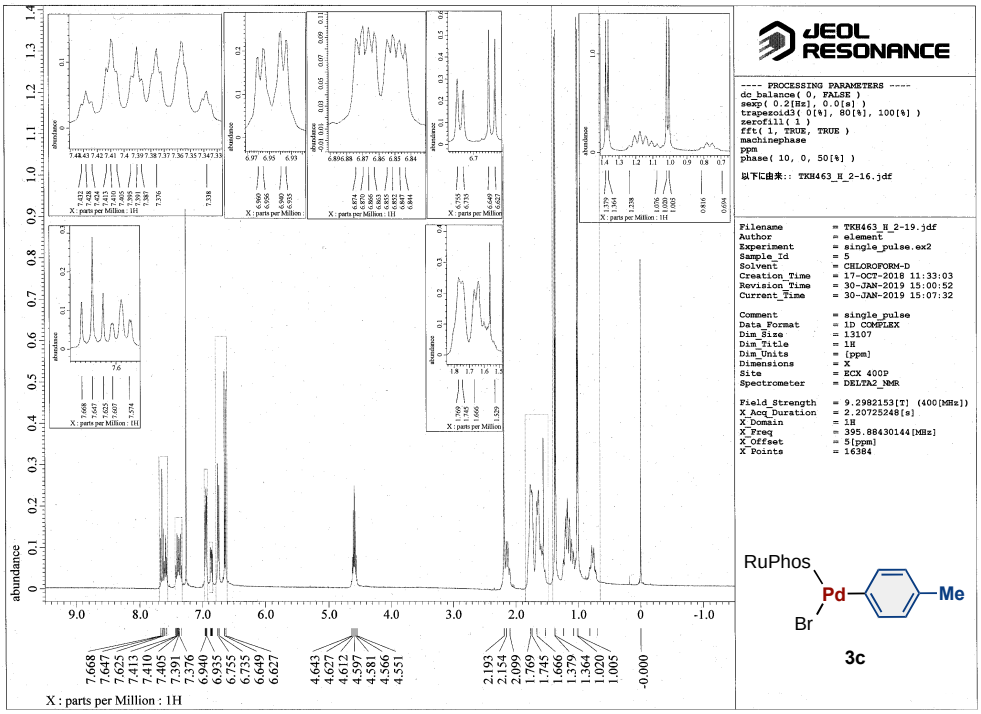
Supplementary Figure 4. ^{1}H NMR spectrum of **3a**.



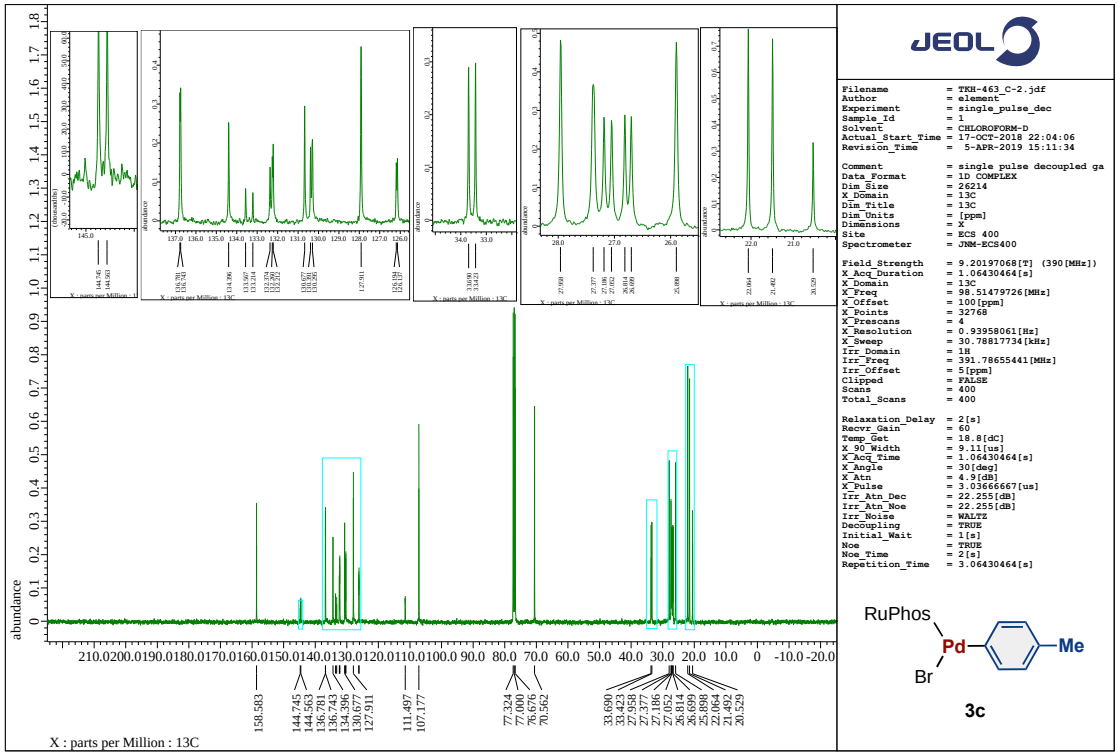
Supplementary Figure 5. ^{13}C NMR spectrum of **3a**.



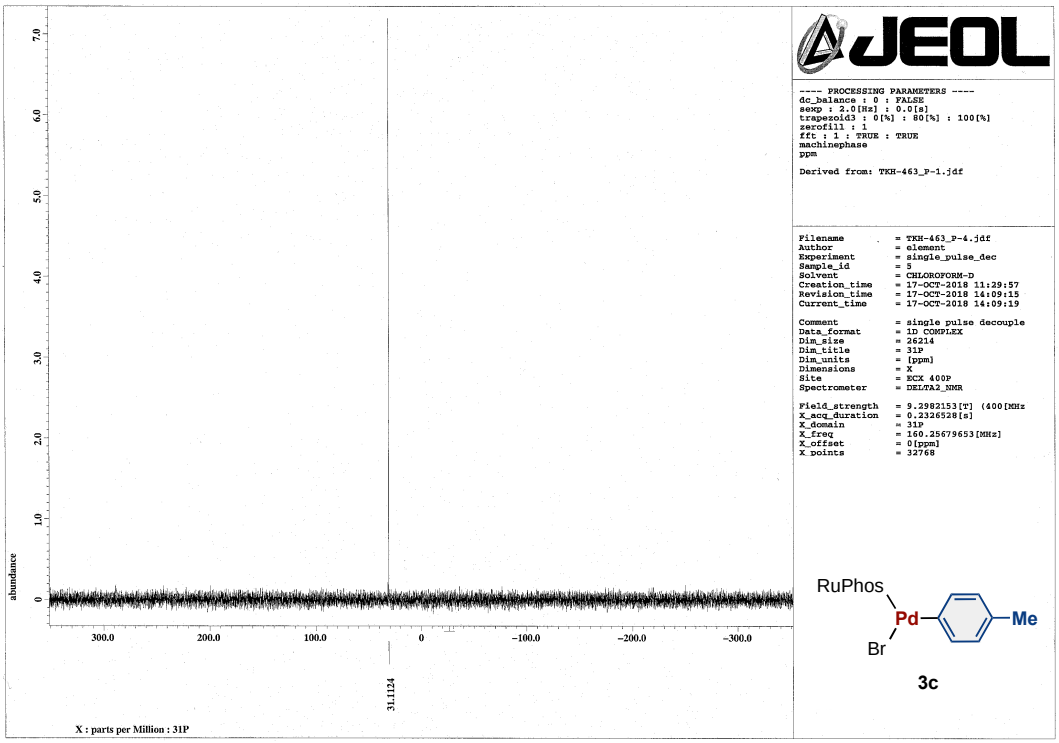
Supplementary Figure 6. ^{31}P NMR spectrum of **3a**.



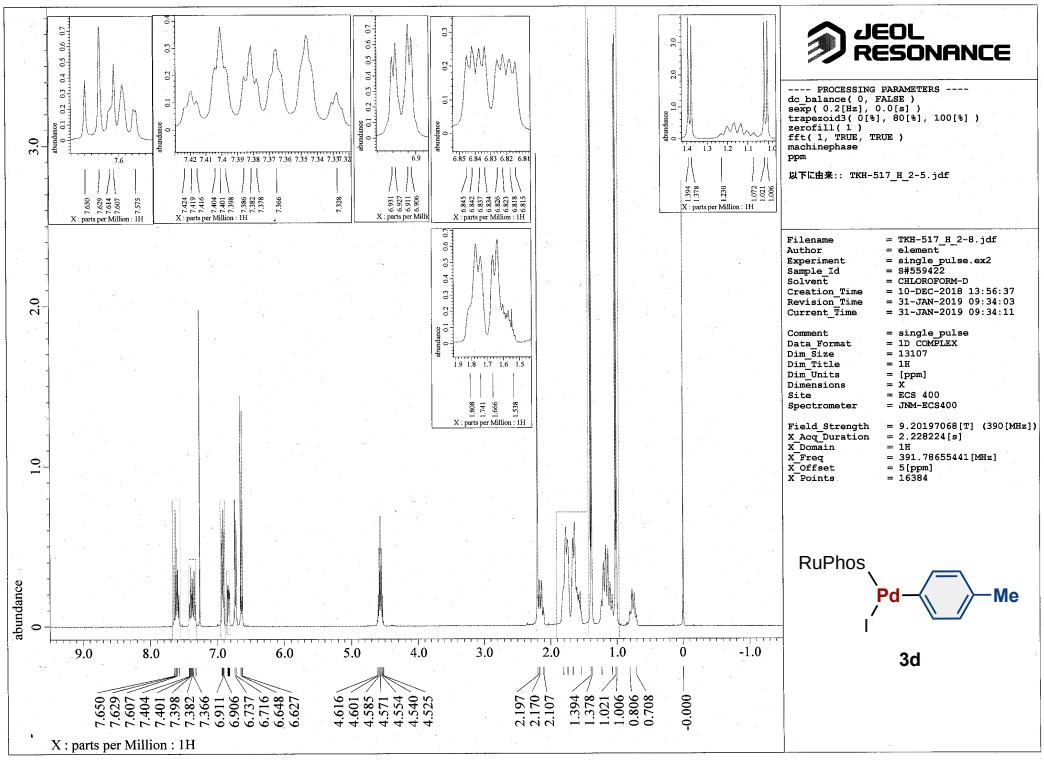
Supplementary Figure 7. ^{1}H NMR spectrum of **3c**.



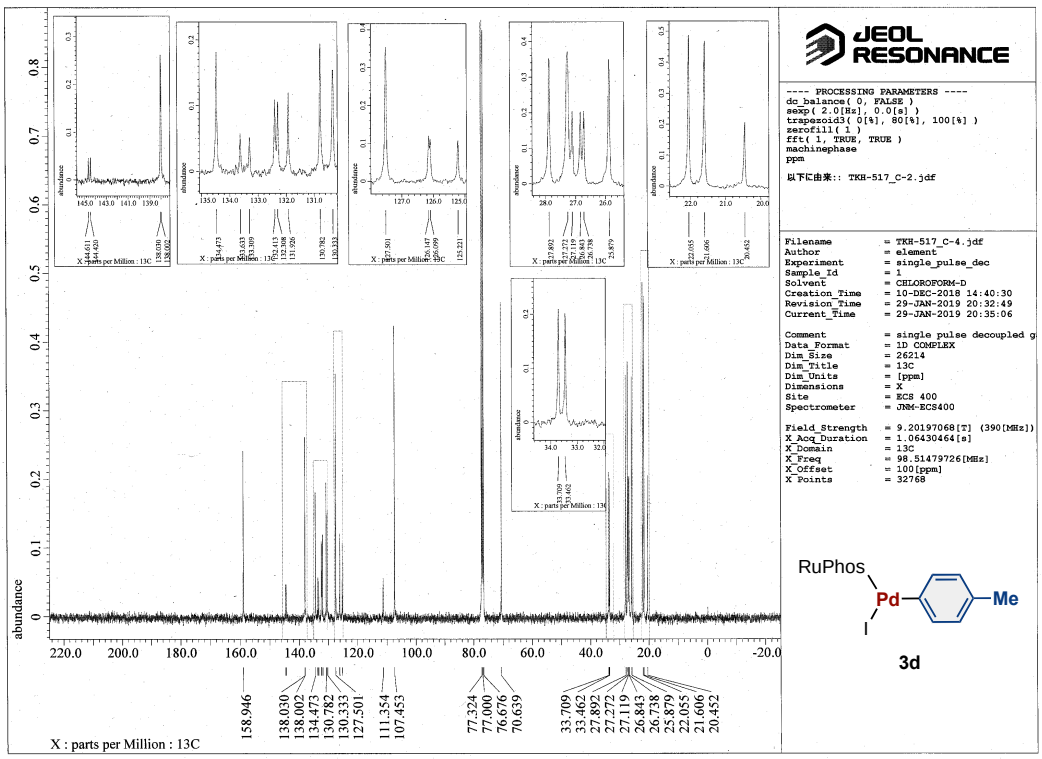
Supplementary Figure 8. ^{13}C NMR spectrum of **3c**.



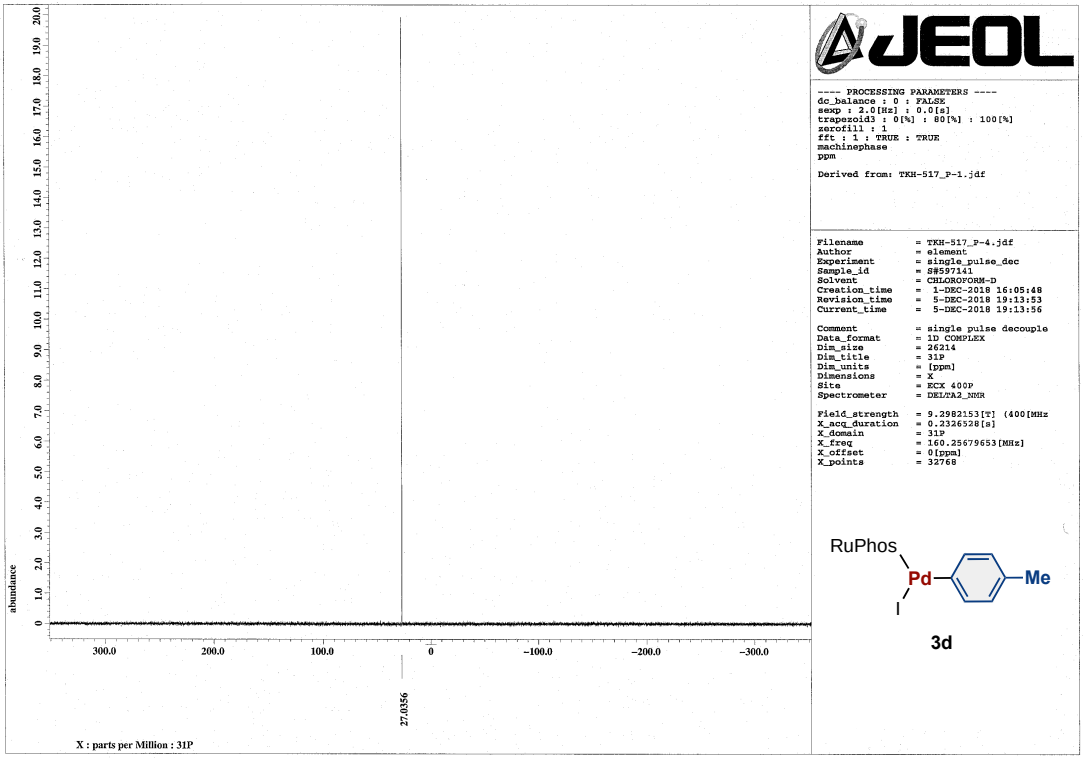
Supplementary Figure 9. ^{31}P NMR spectrum of **3c**.



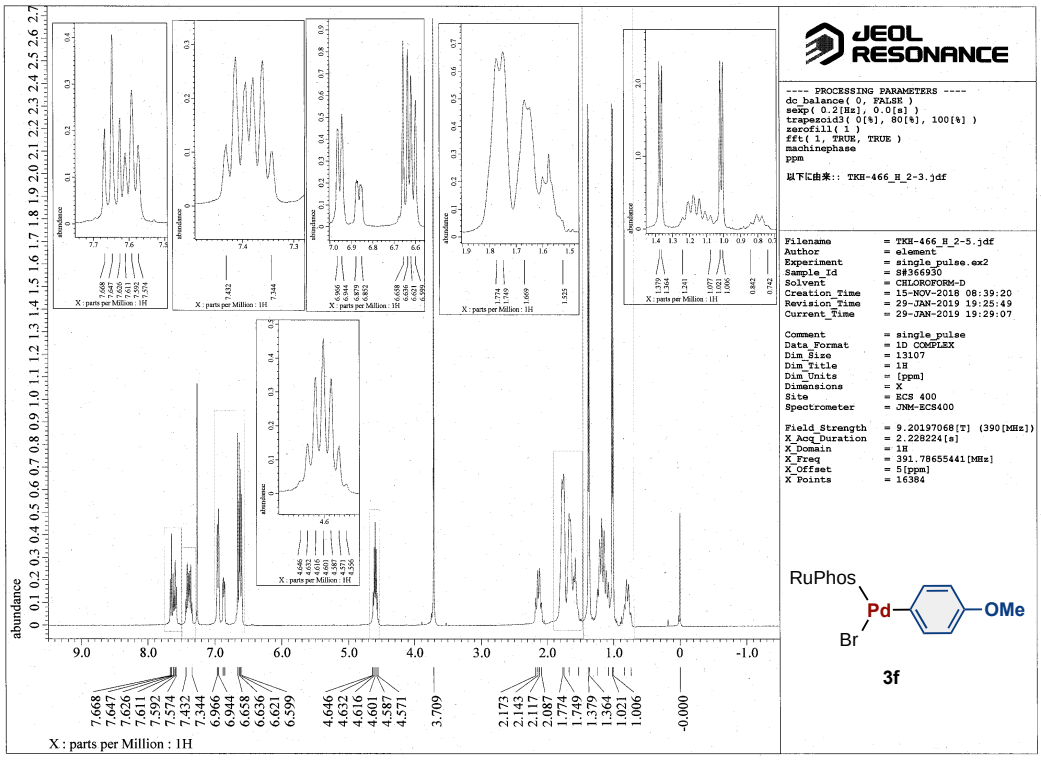
Supplementary Figure 10. ^{1}H NMR spectrum of **3d**.



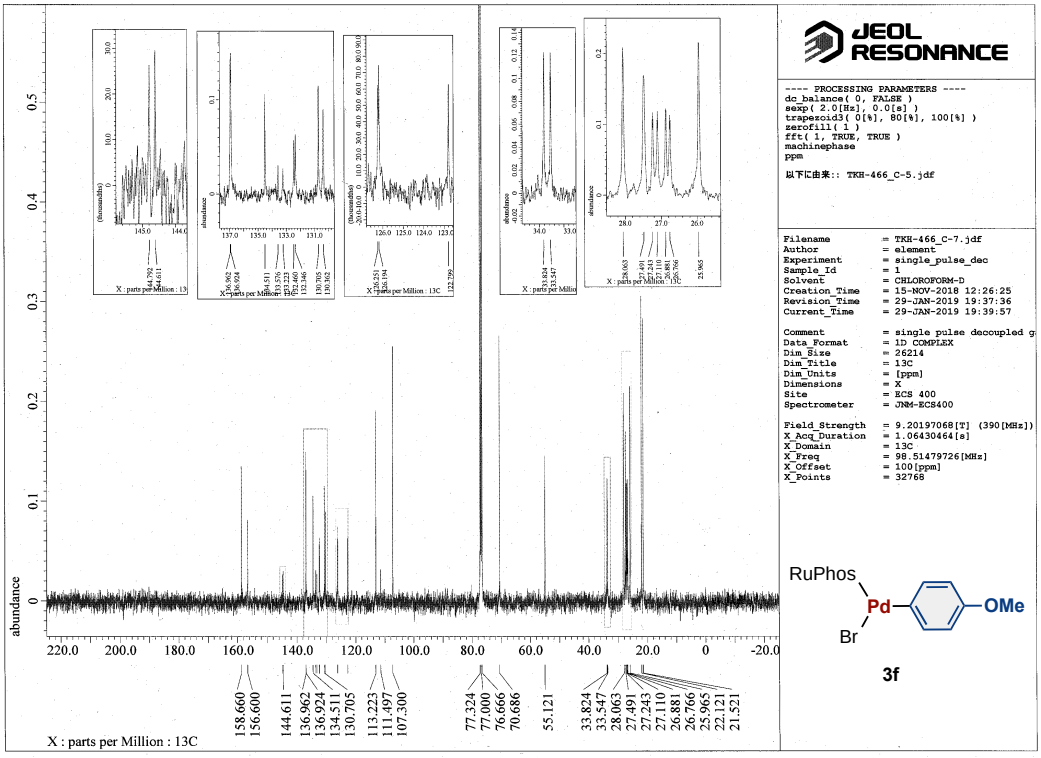
Supplementary Figure 11. ^{13}C NMR spectrum of **3d**.



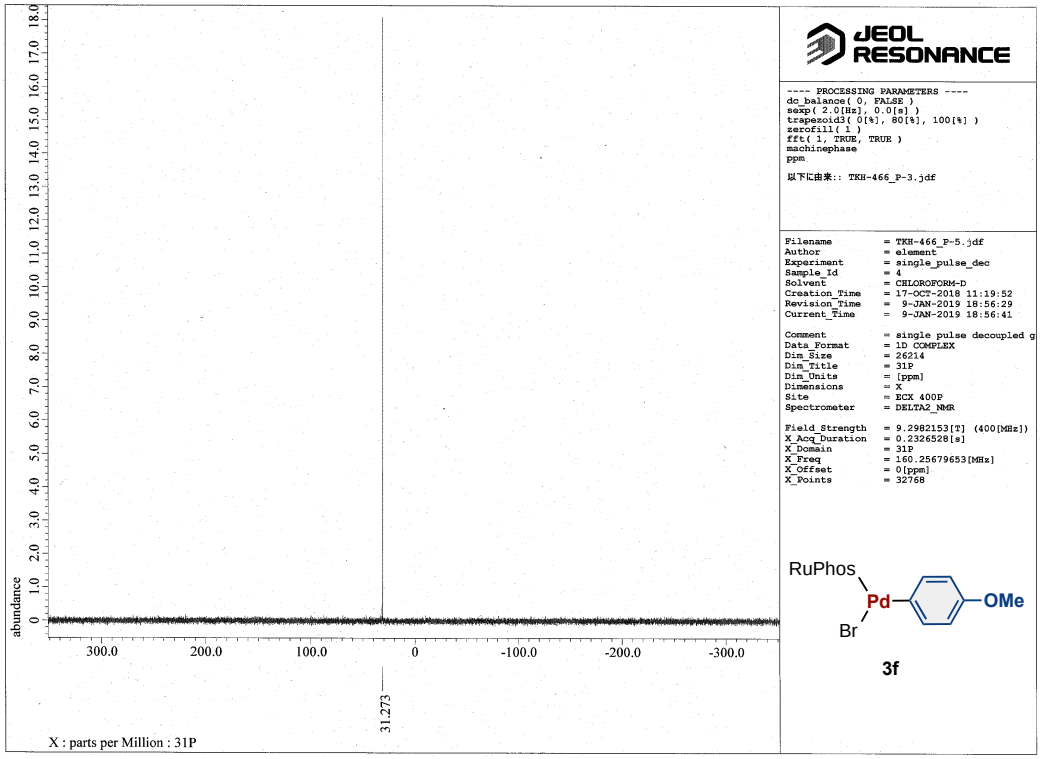
Supplementary Figure 12. ^{31}P NMR spectrum of **3d**.



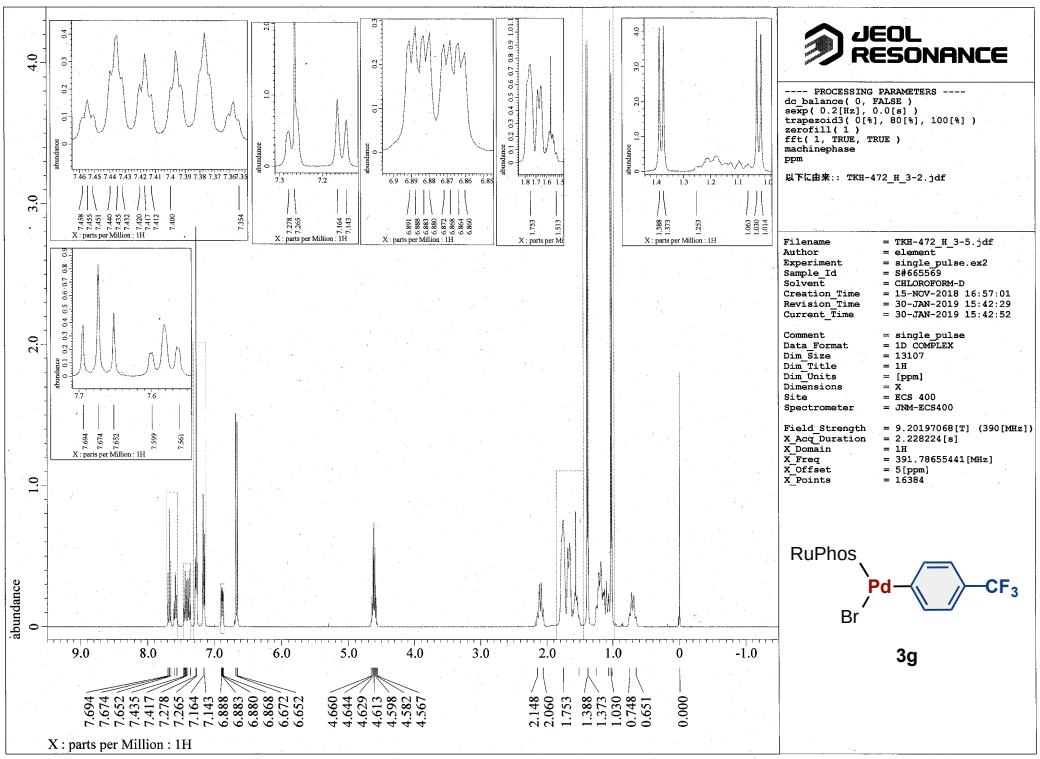
Supplementary Figure 13. ^{1}H NMR spectrum of **3f**.



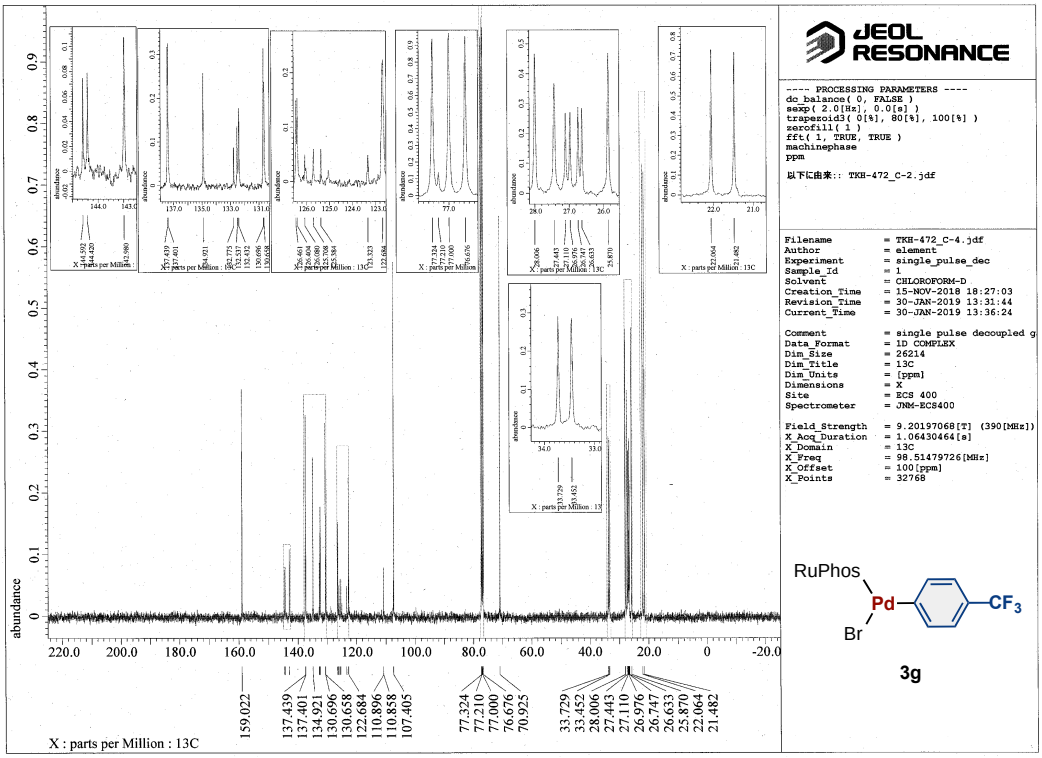
Supplementary Figure 14. ^{13}C NMR spectrum of **3f**.



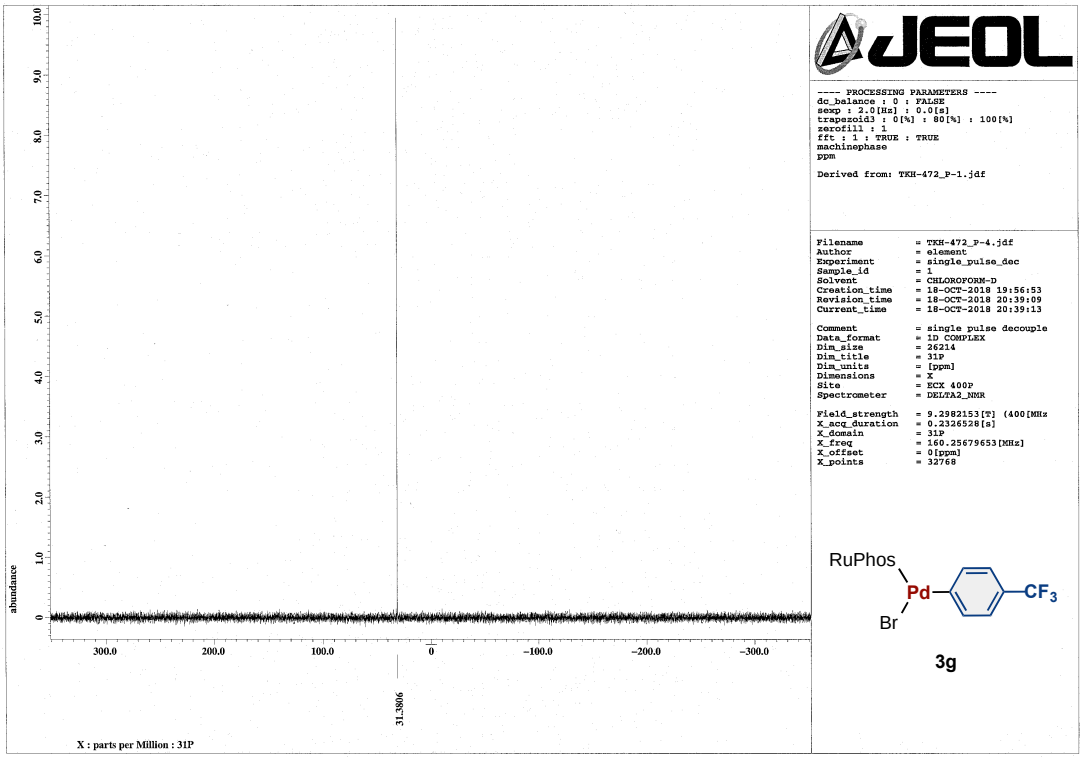
Supplementary Figure 15. ^{31}P NMR spectrum of **3f**.



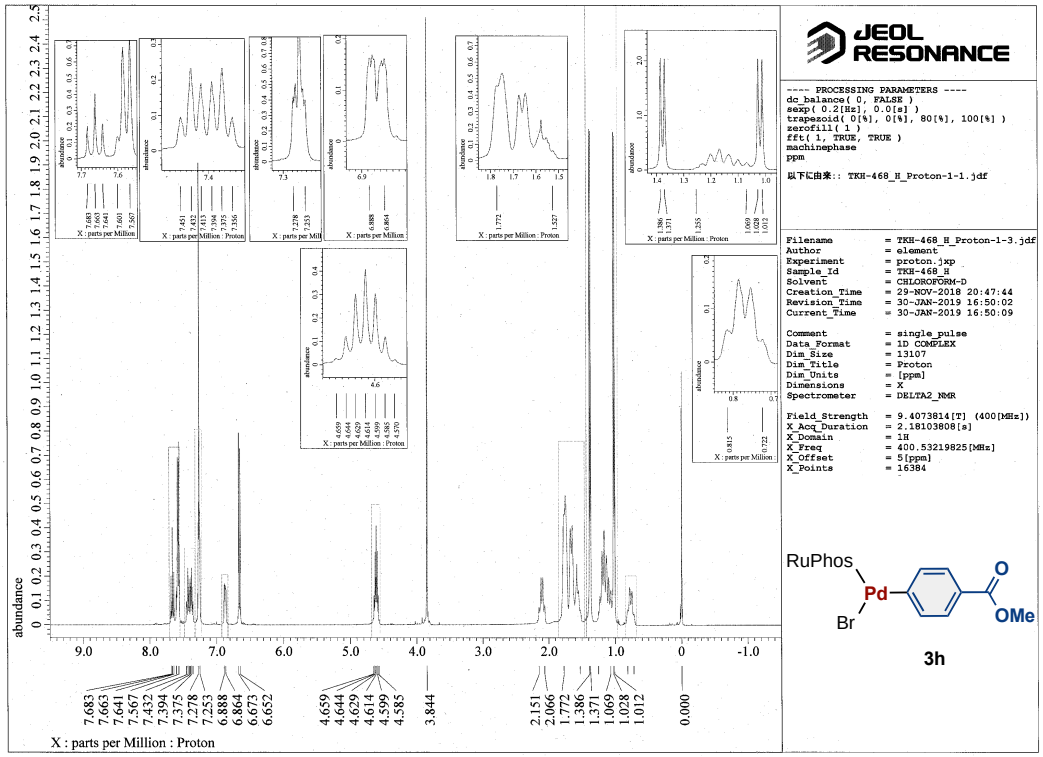
Supplementary Figure 16. ^{1}H NMR spectrum of **3g**.



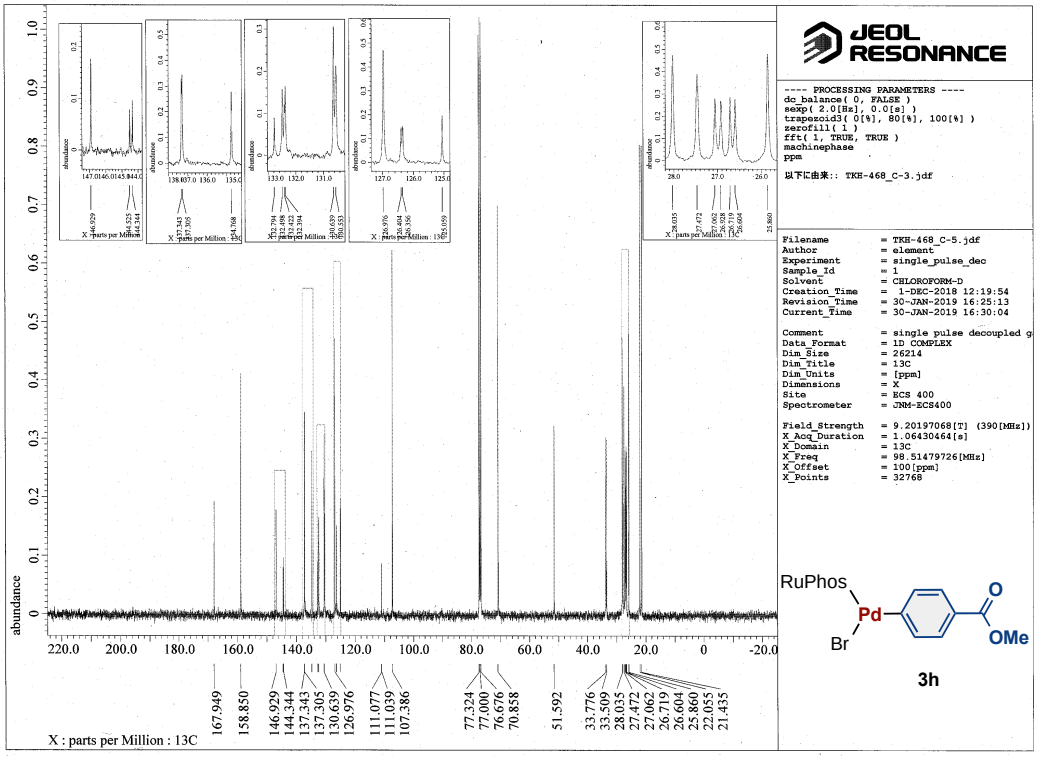
Supplementary Figure 17. ^{13}C NMR spectrum of **3g**.



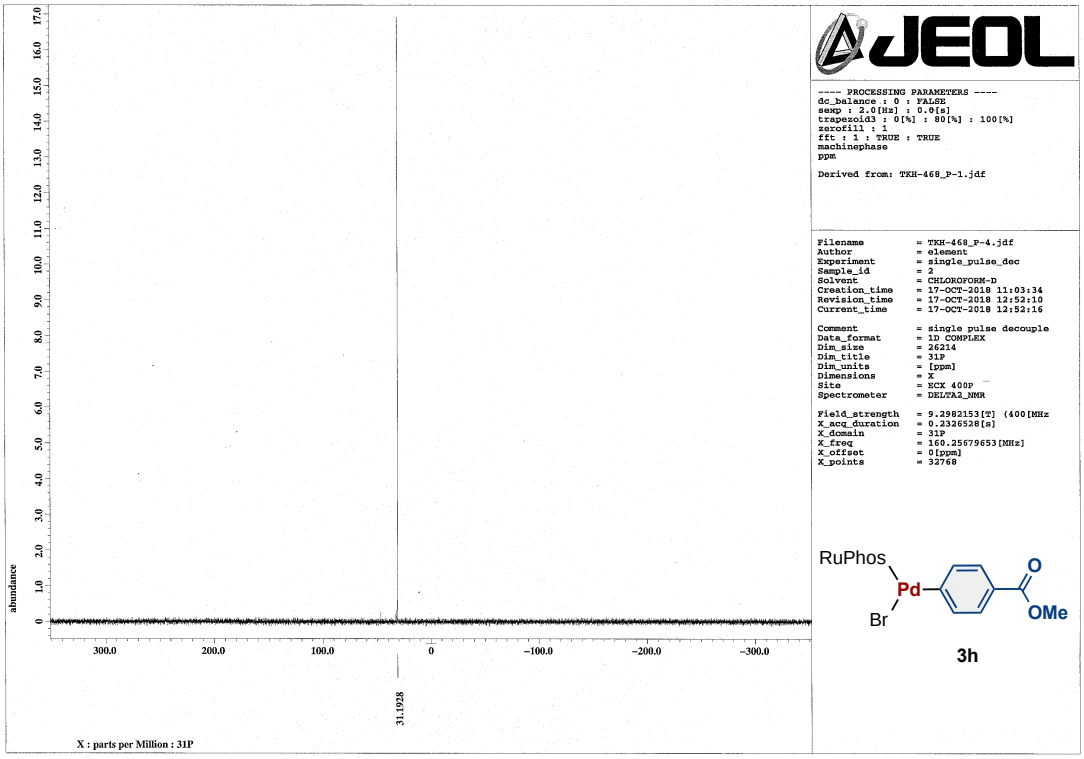
Supplementary Figure 18. ^{31}P NMR spectrum of **3g**.



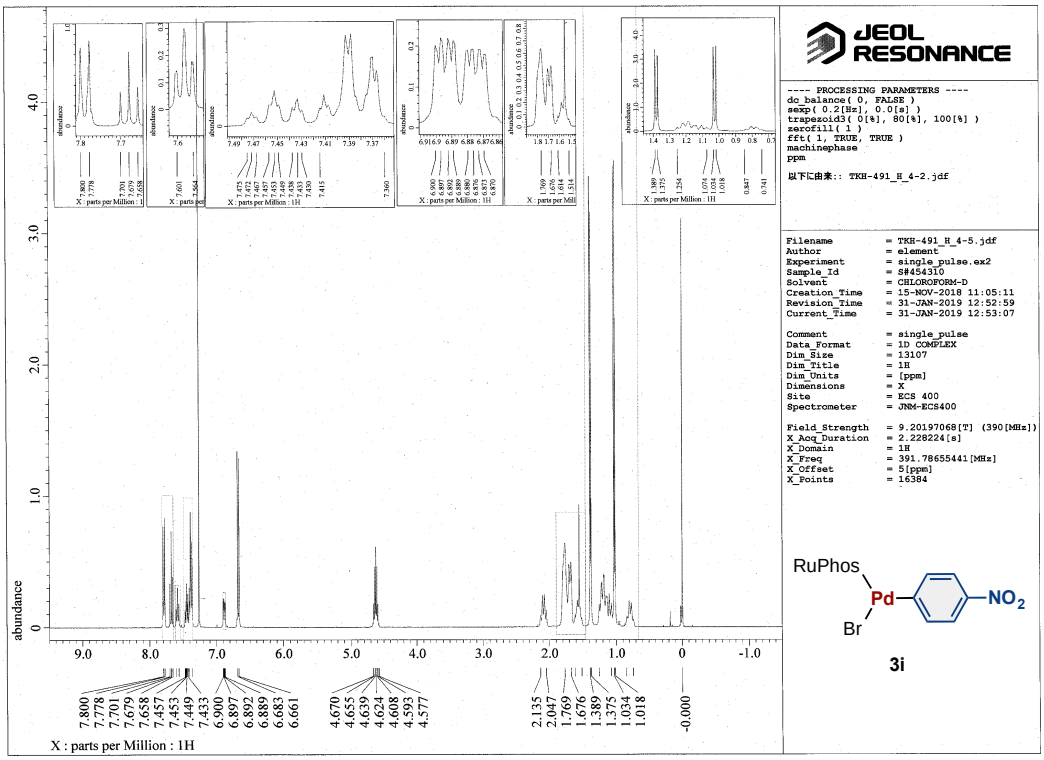
Supplementary Figure 19. ^{1}H NMR spectrum of **3h**.



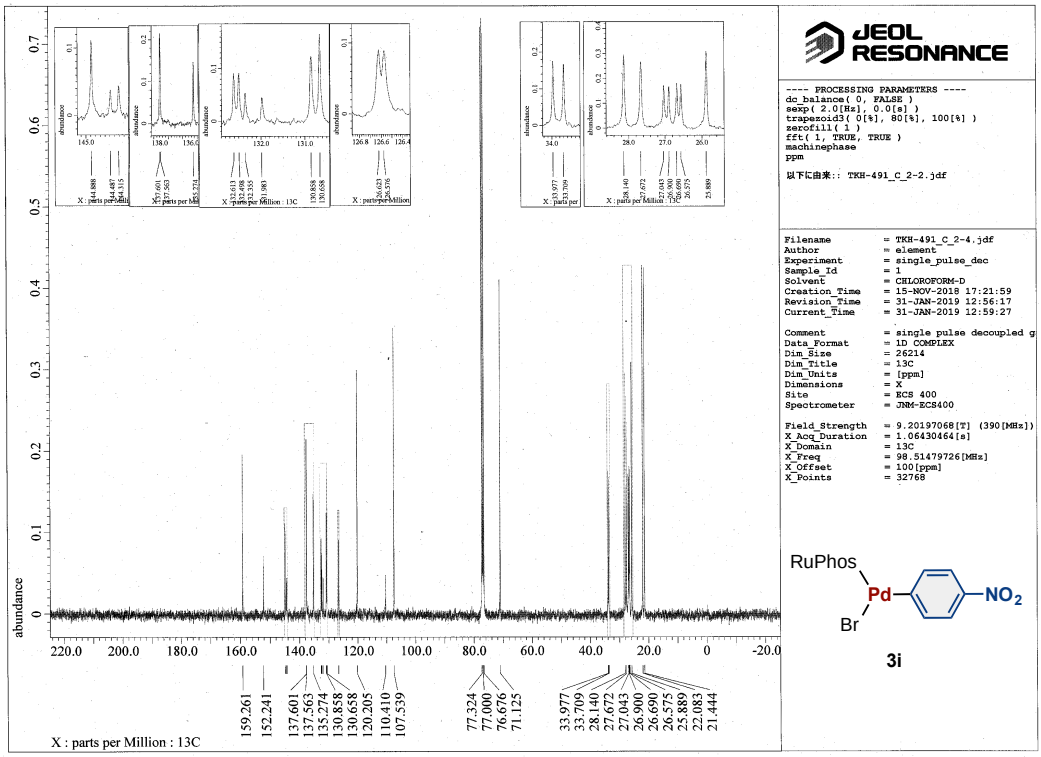
Supplementary Figure 20. ^{13}C NMR spectrum of **3h**.



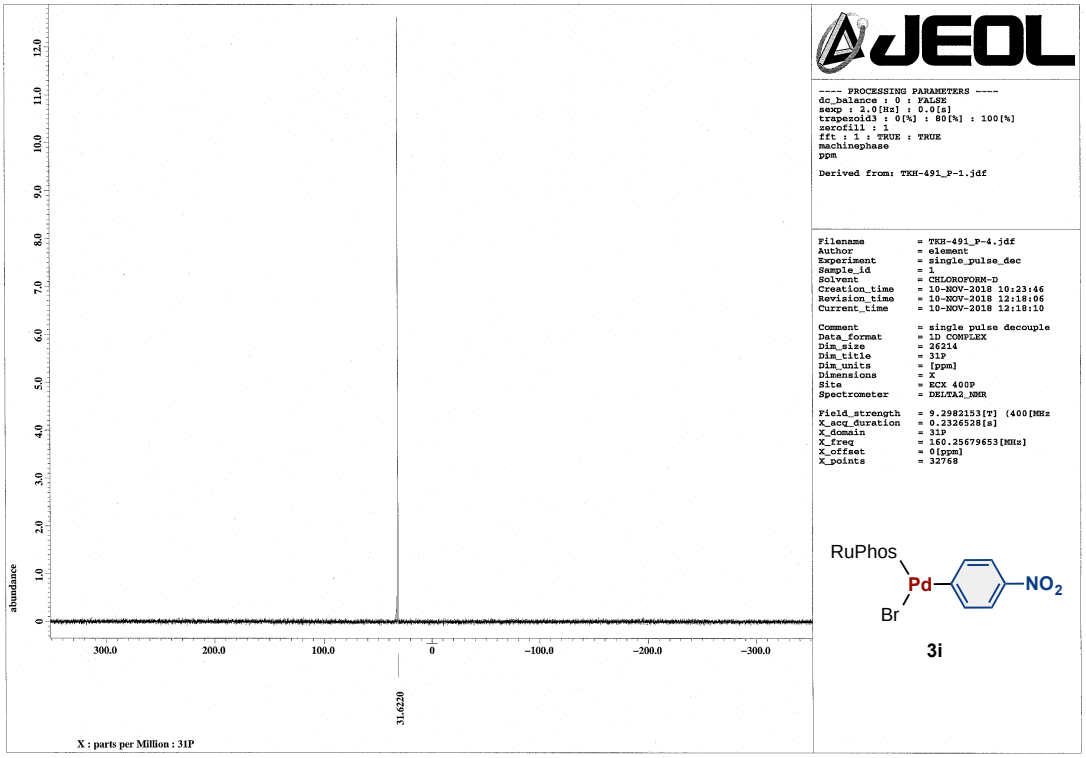
Supplementary Figure 21. ^{31}P NMR spectrum of **3h**.



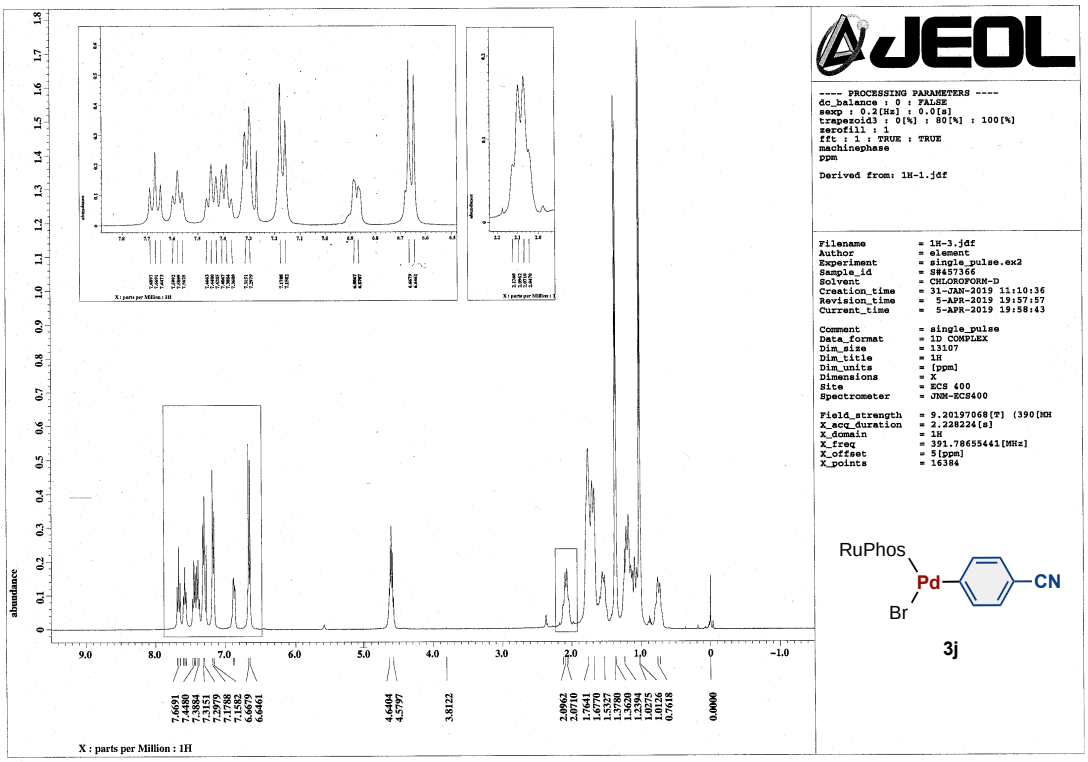
Supplementary Figure 22. ^{1}H NMR spectrum of **3i**.



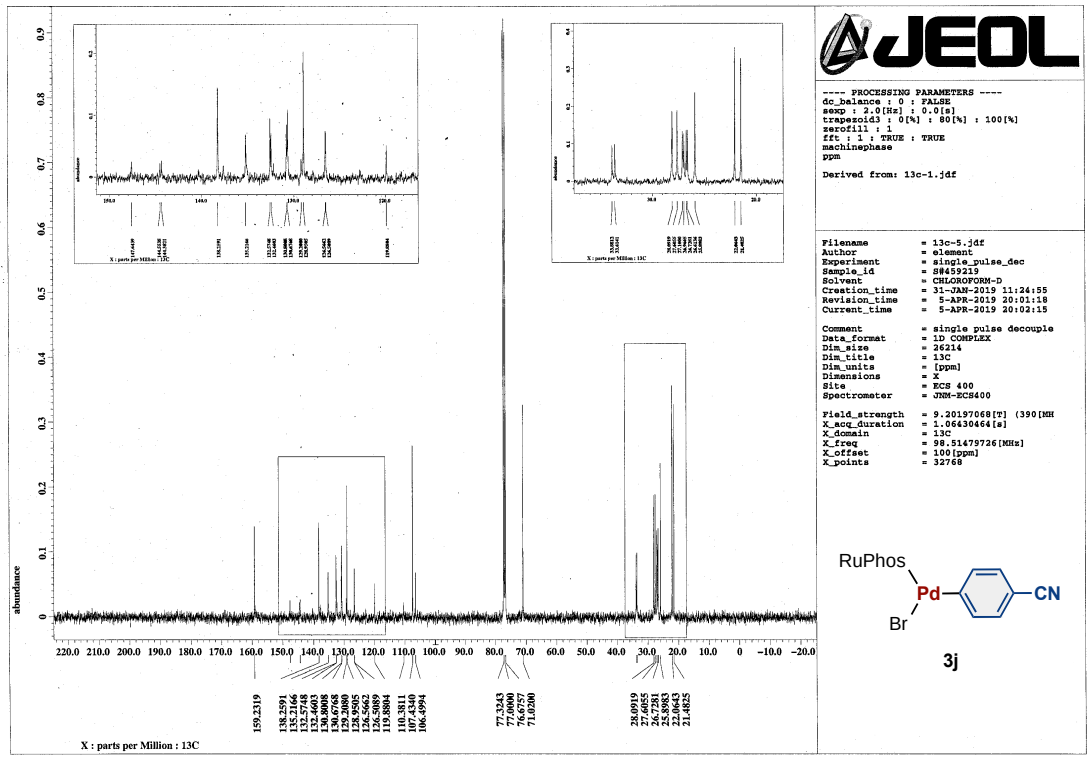
Supplementary Figure 23. ^{13}C NMR spectrum of **3i**.



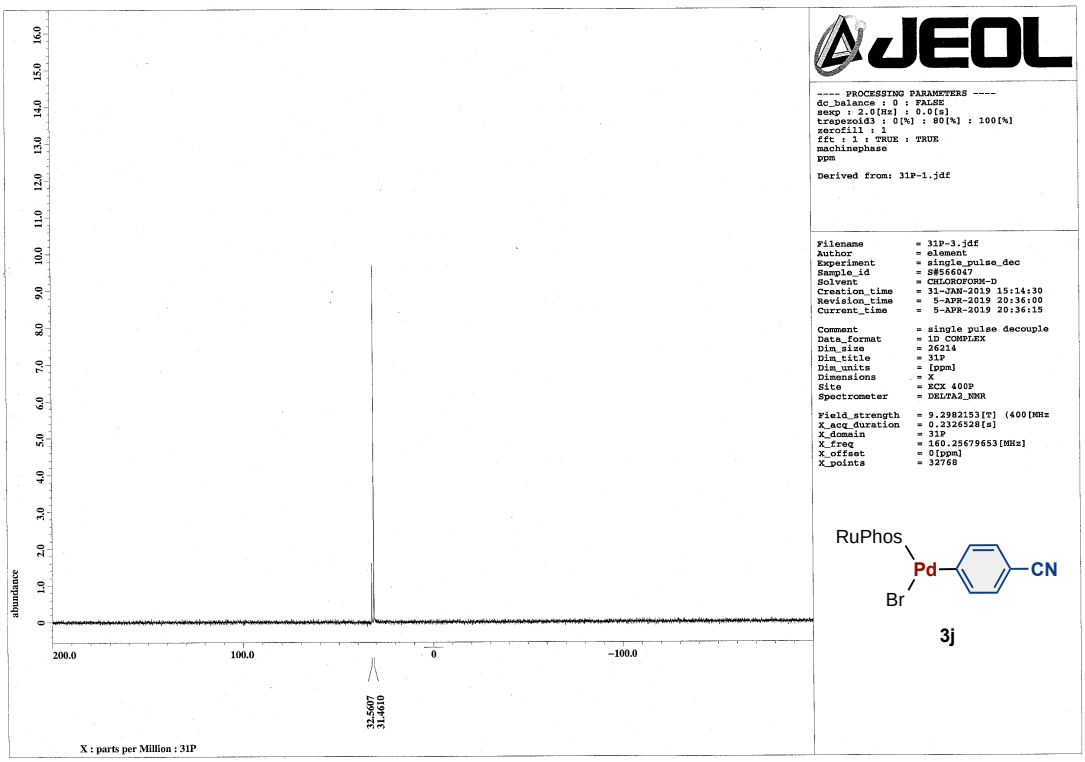
Supplementary Figure 24. ^{31}P NMR spectrum of **3i**.



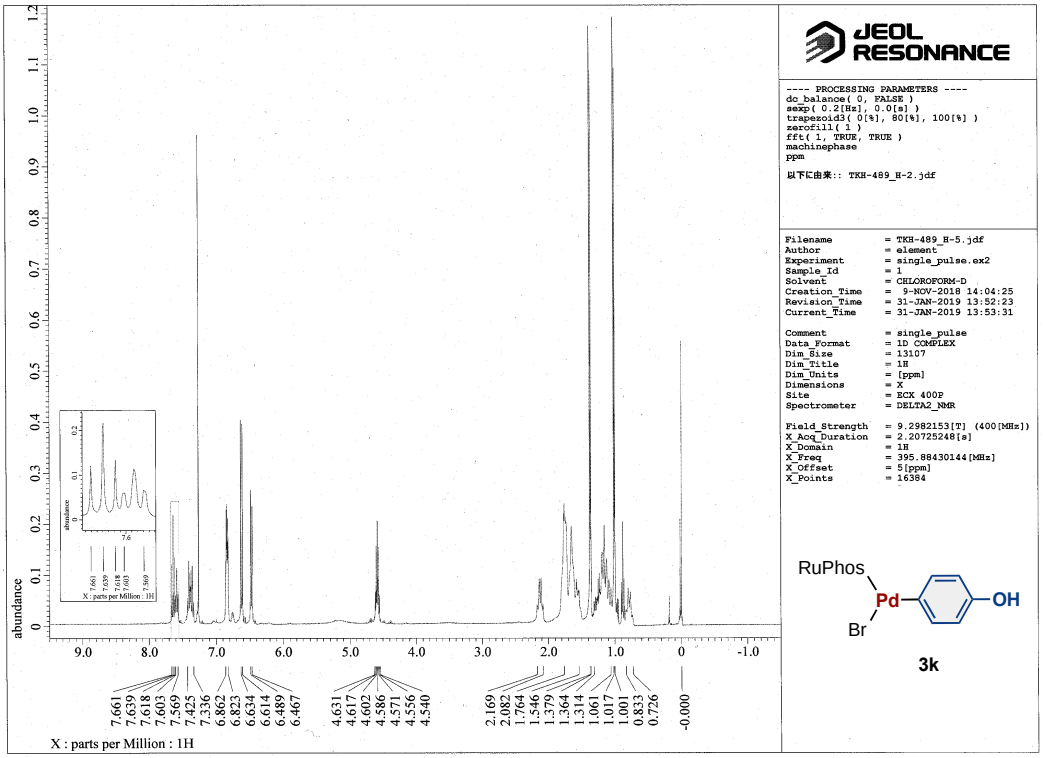
Supplementary Figure 25. ^{1}H NMR spectrum of **3j**.



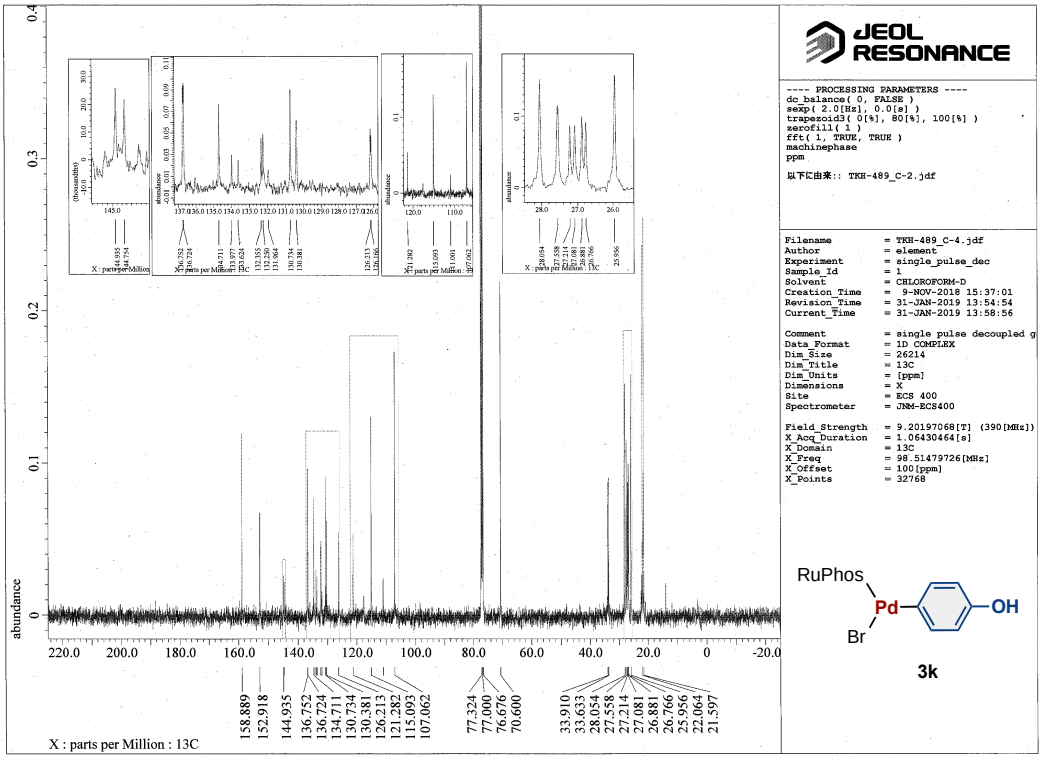
Supplementary Figure 26. ^{13}C NMR spectrum of **3j**.



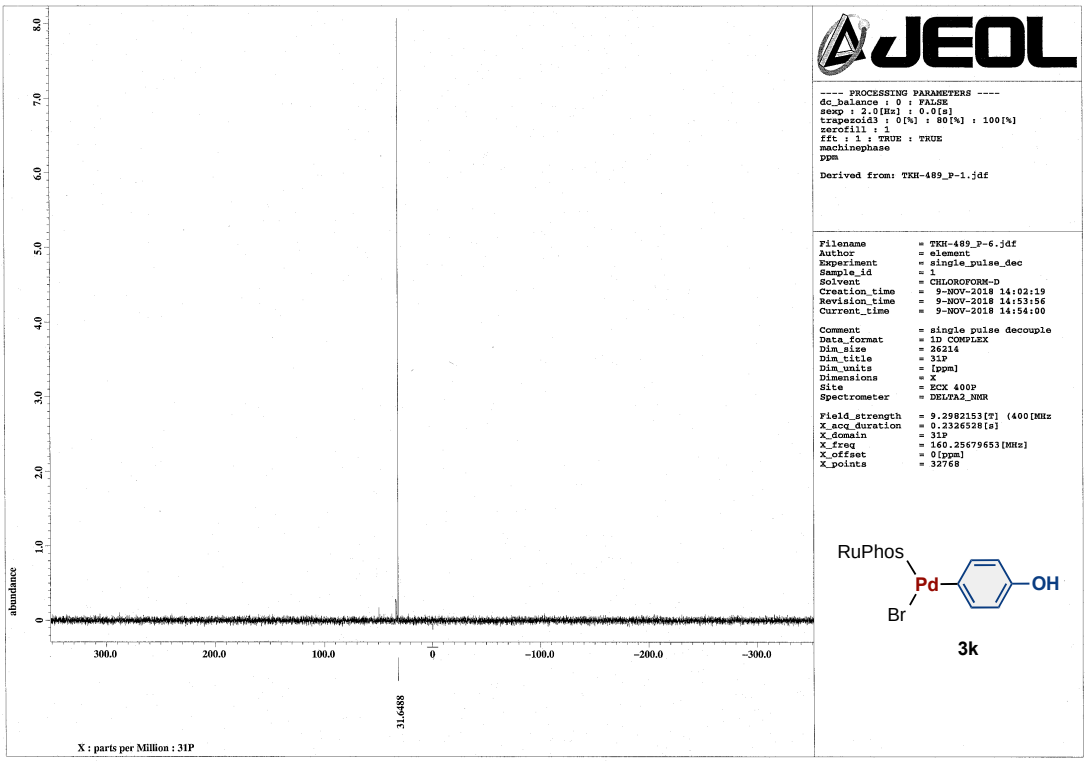
Supplementary Figure 27. ^{31}P NMR spectrum of **3j**.



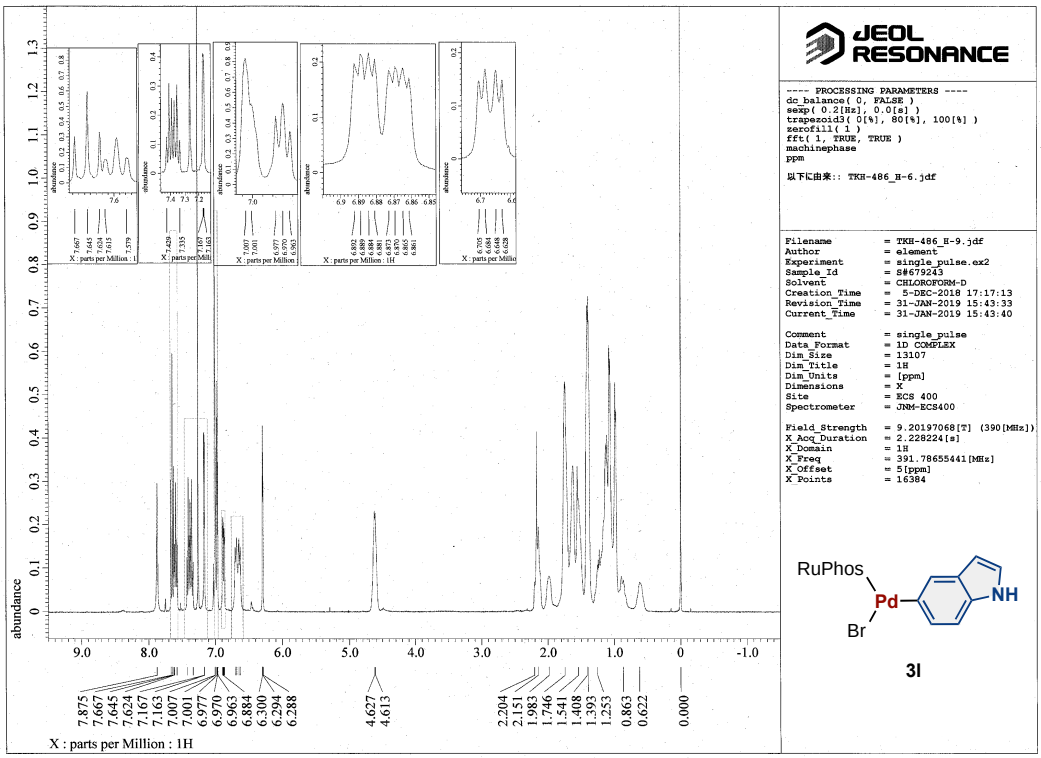
Supplementary Figure 28. ^{1}H NMR spectrum of **3k**.



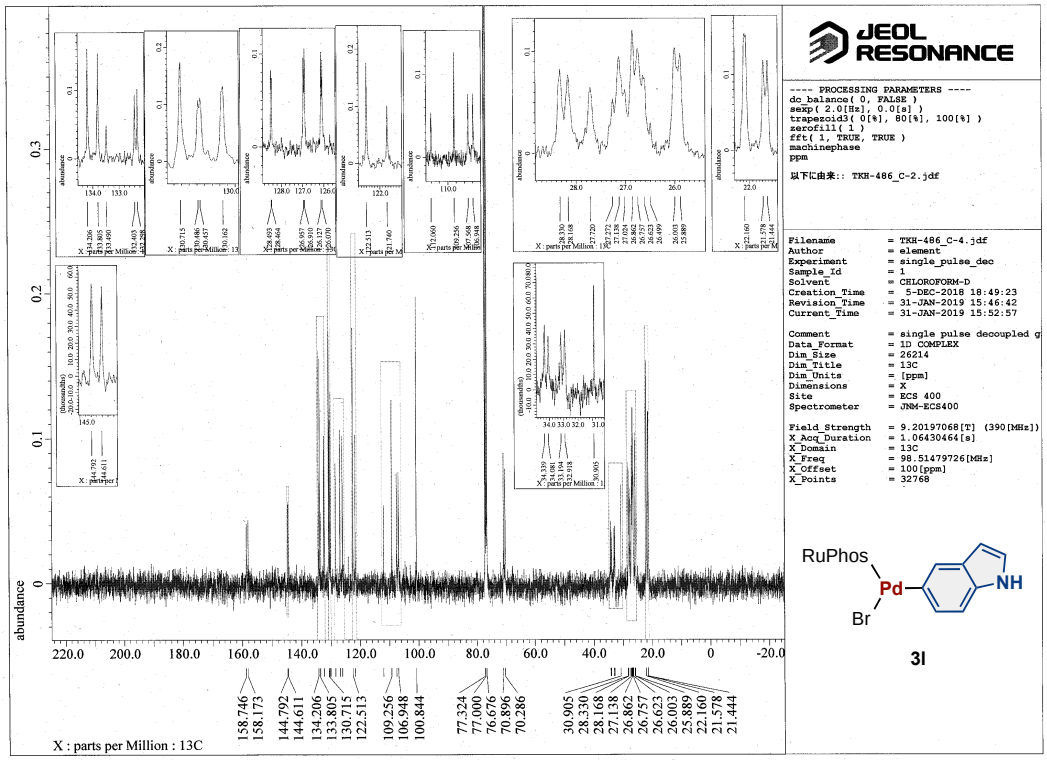
Supplementary Figure 29. ^{13}C NMR spectrum of **3k**.



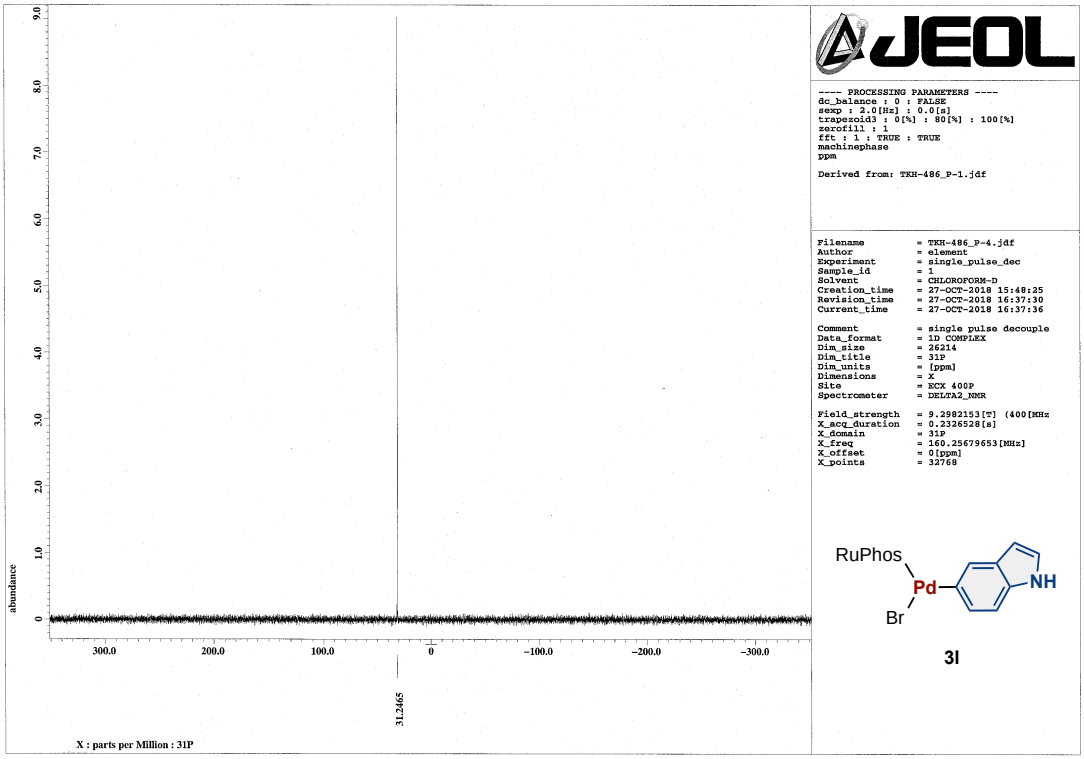
Supplementary Figure 30. ^{31}P NMR spectrum of **3k**.



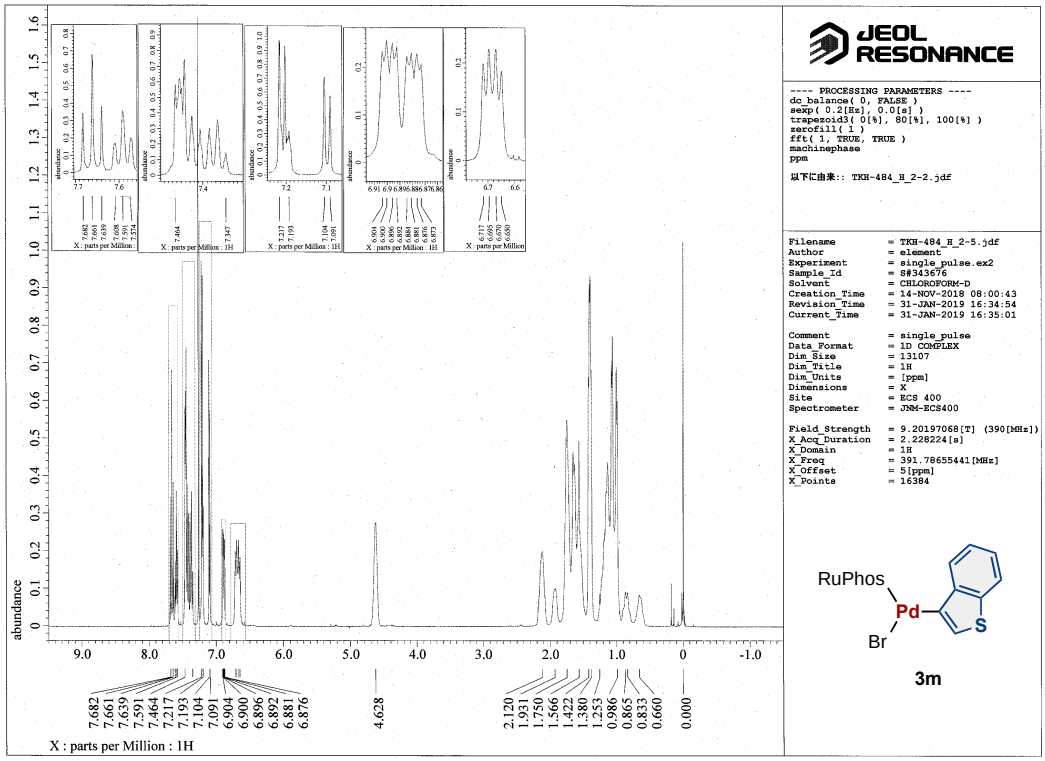
Supplementary Figure 31. ^{1}H NMR spectrum of **3l**.



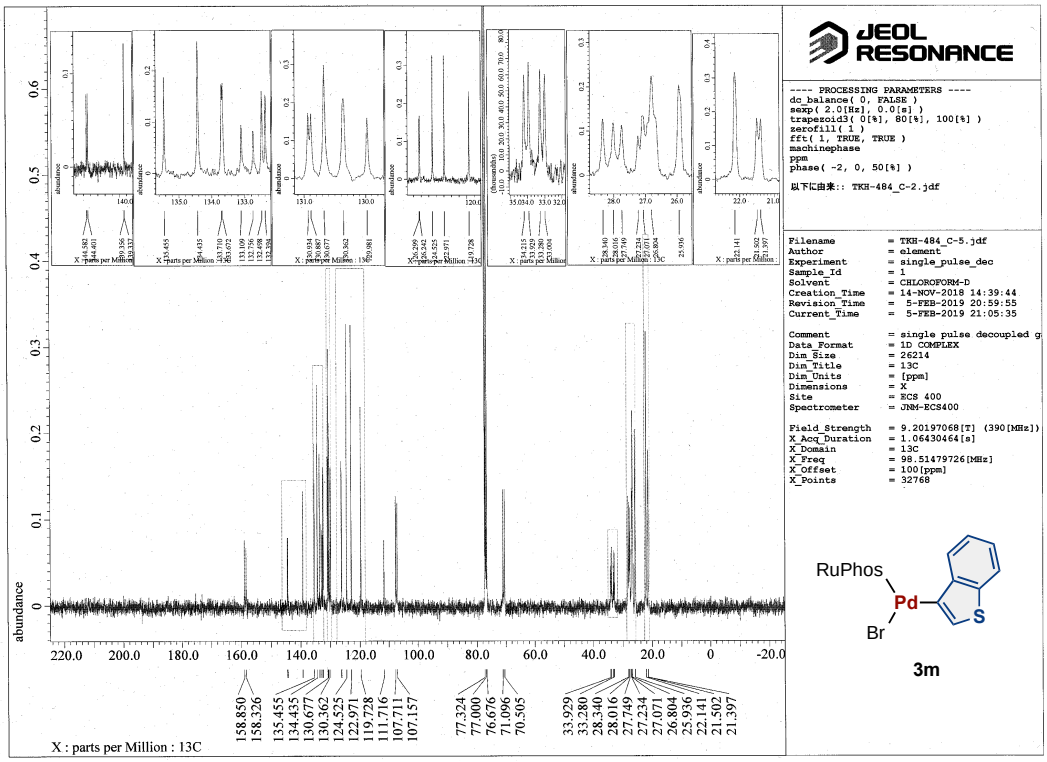
Supplementary Figure 32. ^{13}C NMR spectrum of **3l**.



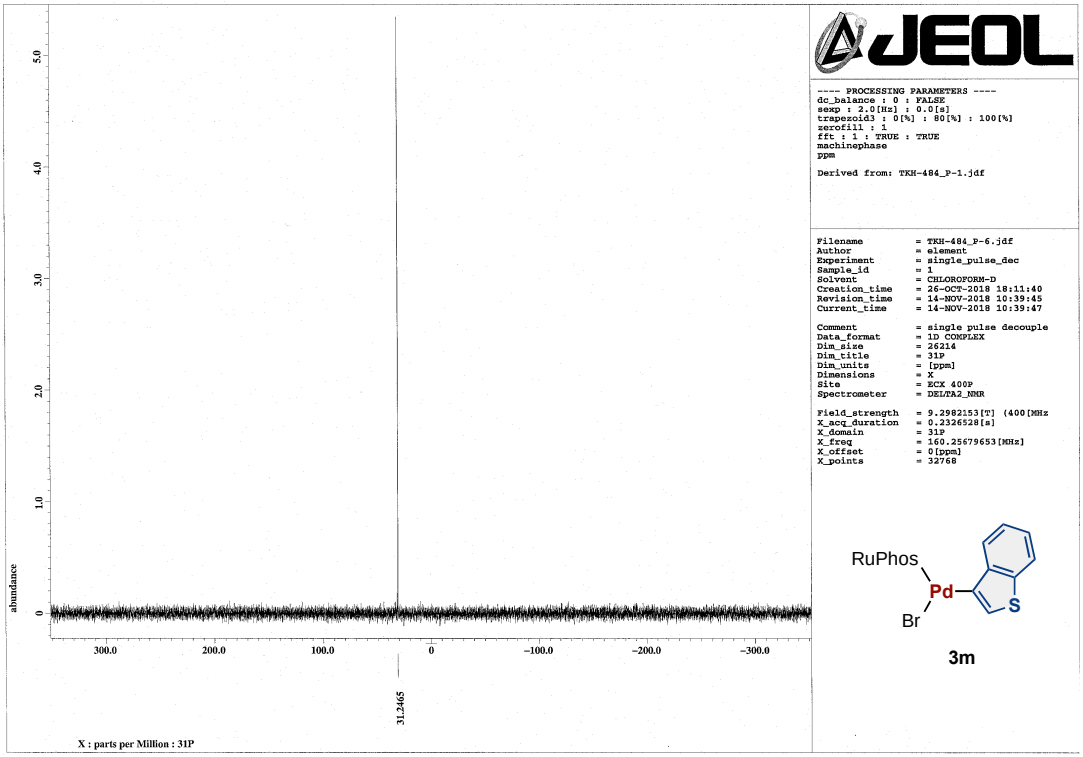
Supplementary Figure 33. ^{31}P NMR spectrum of **3l**.



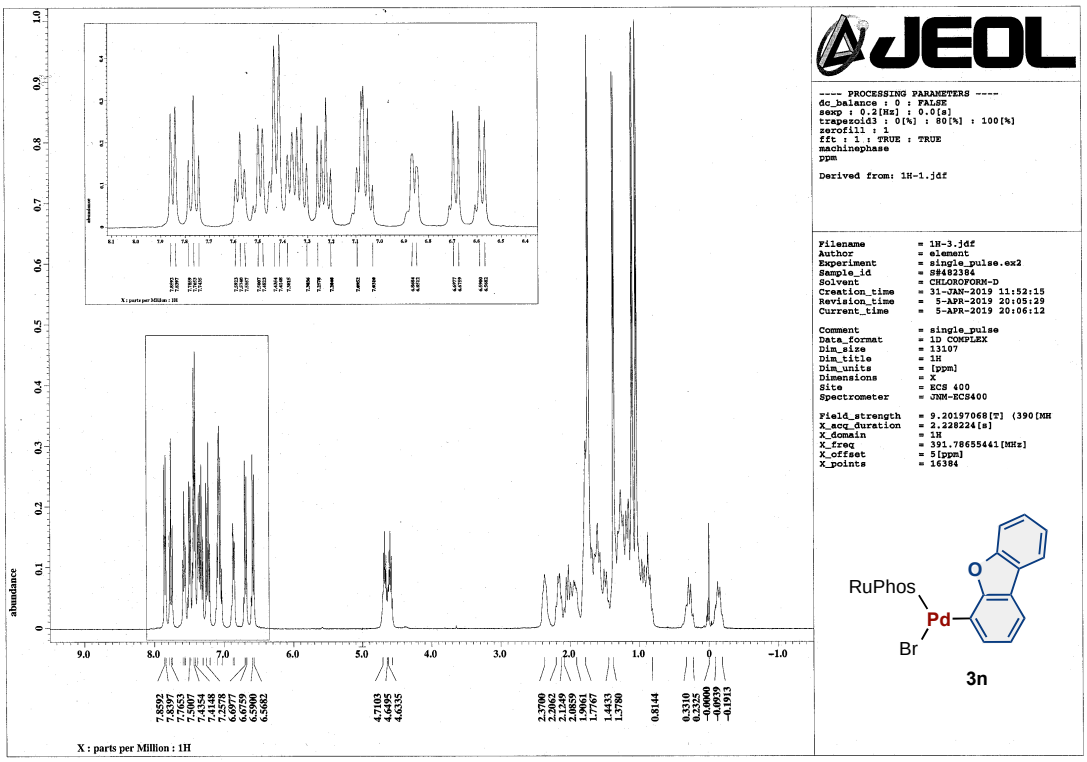
Supplementary Figure 34. ^{1}H NMR spectrum of **3m**.



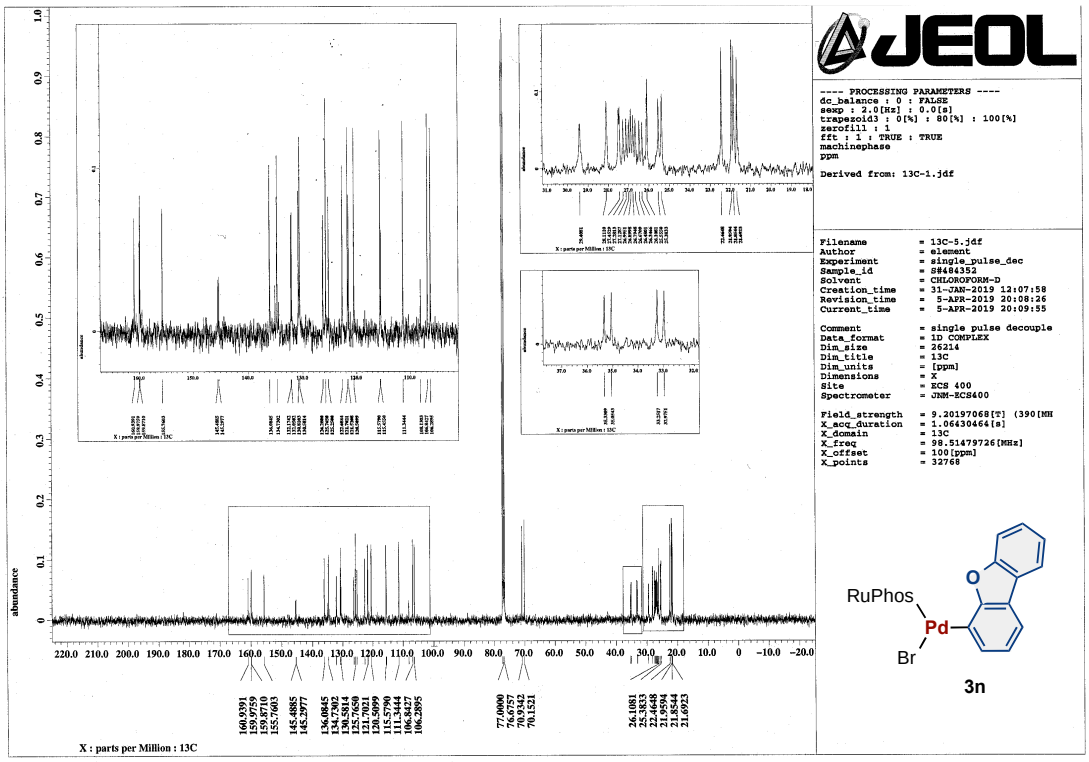
Supplementary Figure 35. ^{13}C NMR spectrum of **3m**.



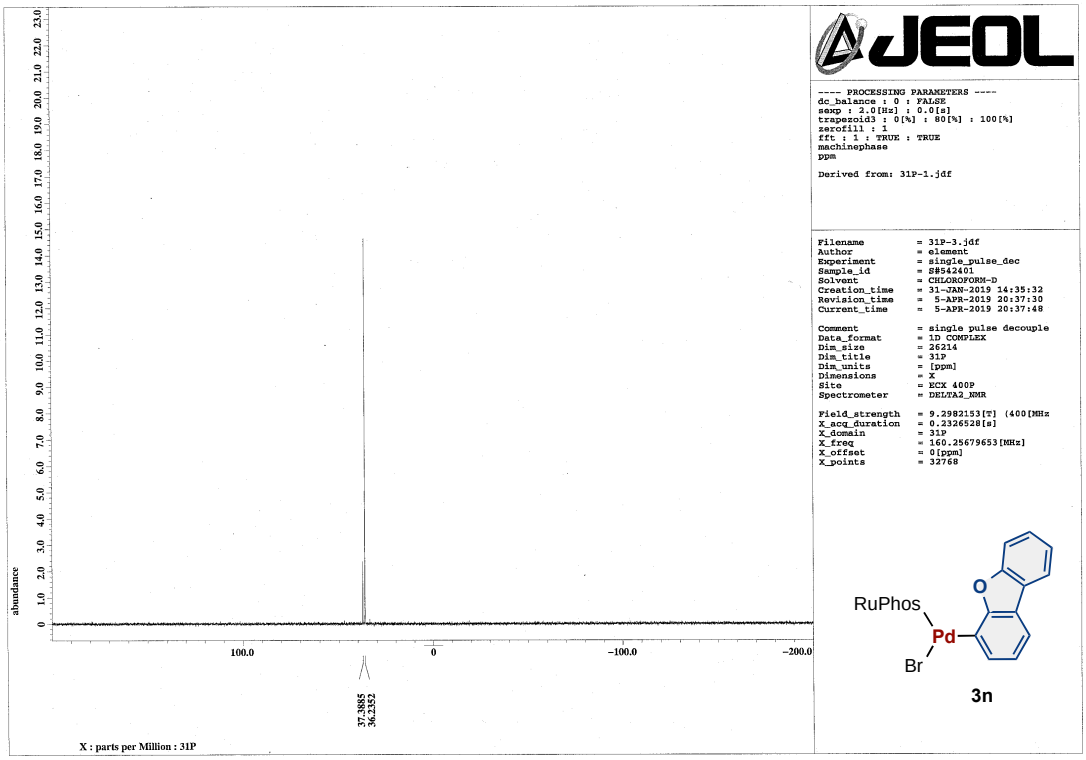
Supplementary Figure 36. ^{31}P NMR spectrum of **3m**.



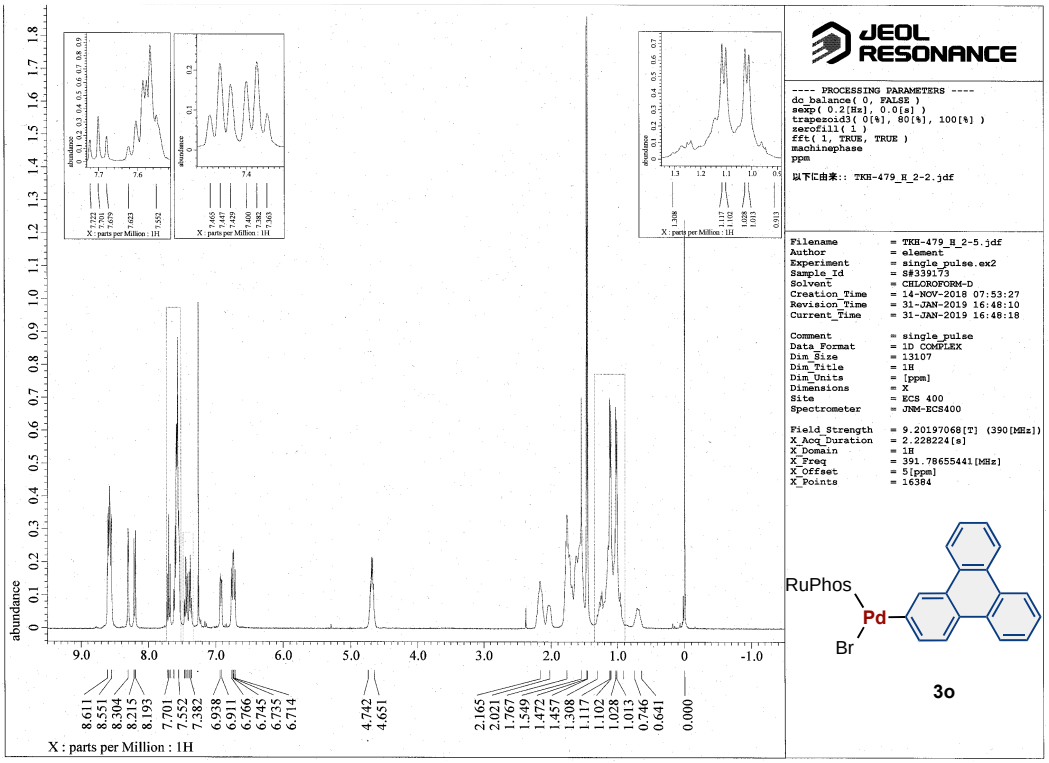
Supplementary Figure 37. ^{1}H NMR spectrum of **3n**.



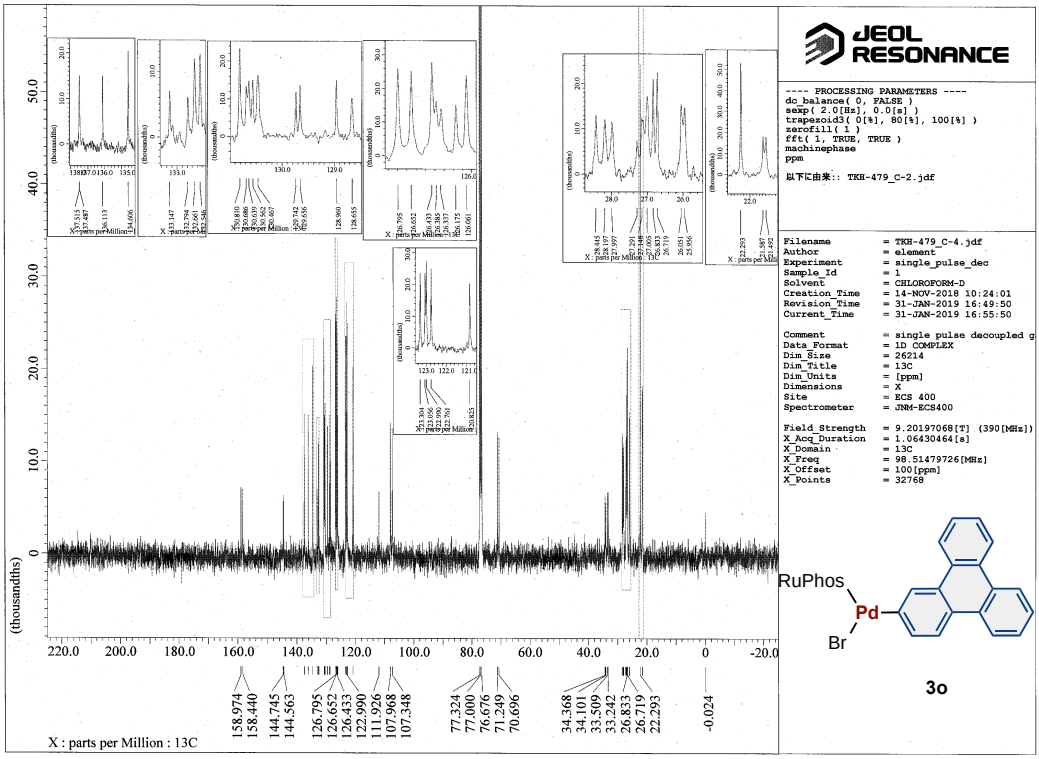
Supplementary Figure 38. ^{13}C NMR spectrum of **3n**.



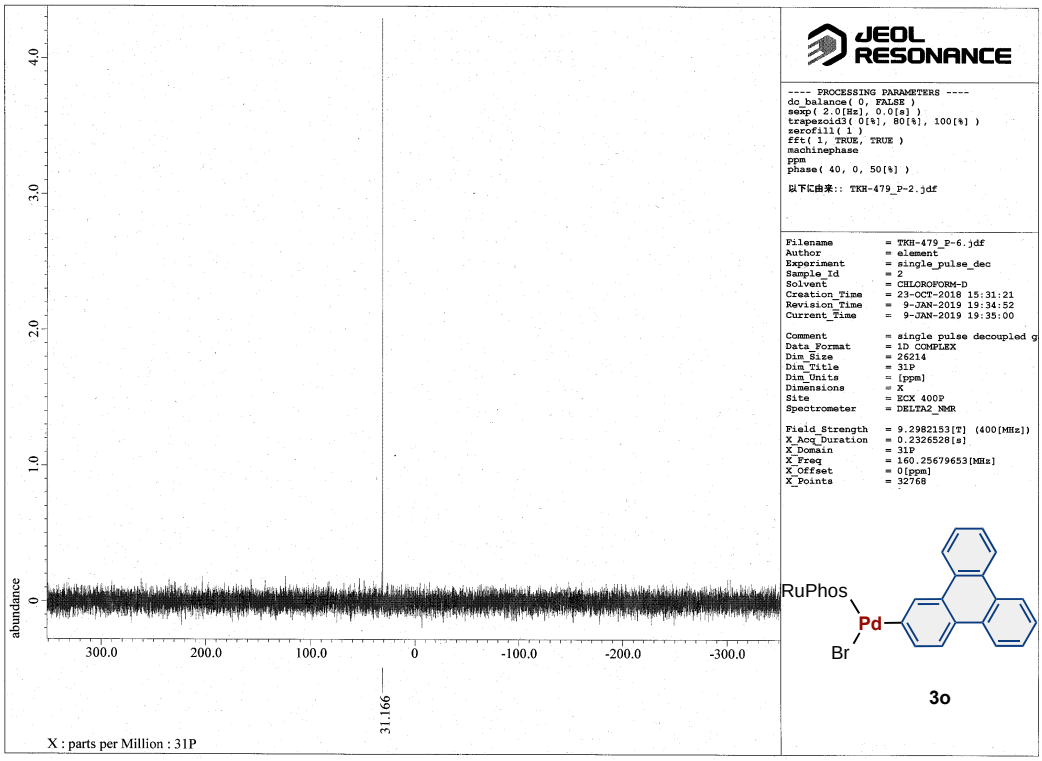
Supplementary Figure 39. ^{31}P NMR spectrum of **3n**.



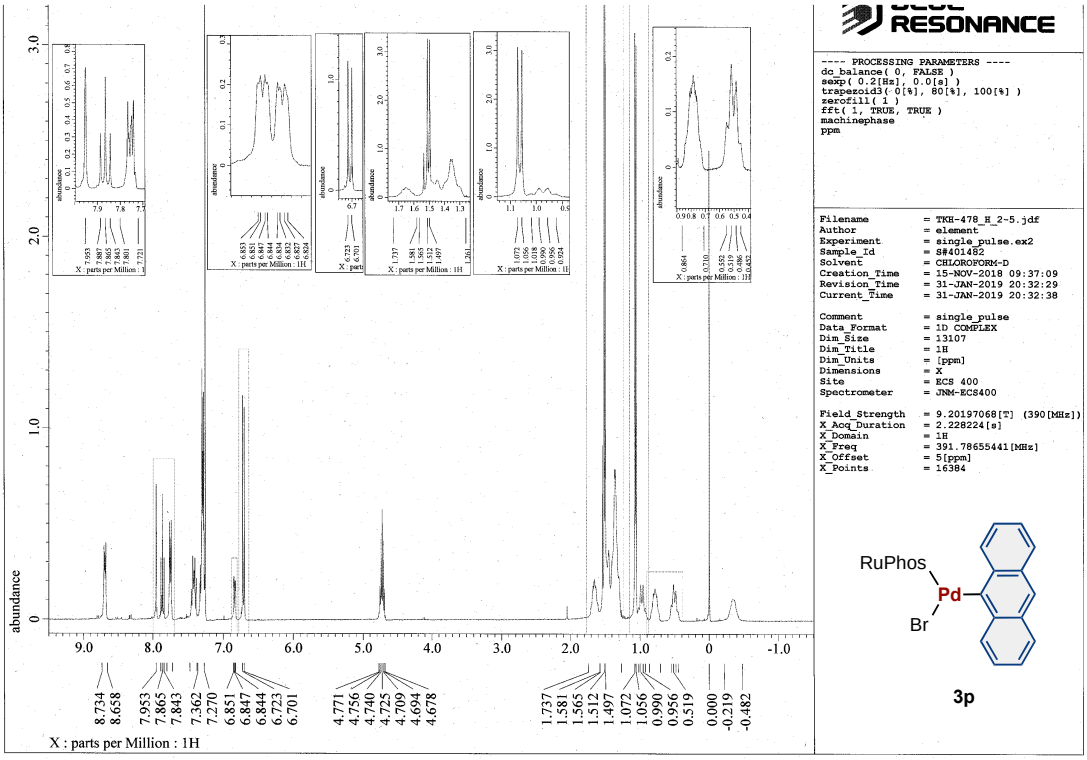
Supplementary Figure 40. ^{1}H NMR spectrum of **3o**.



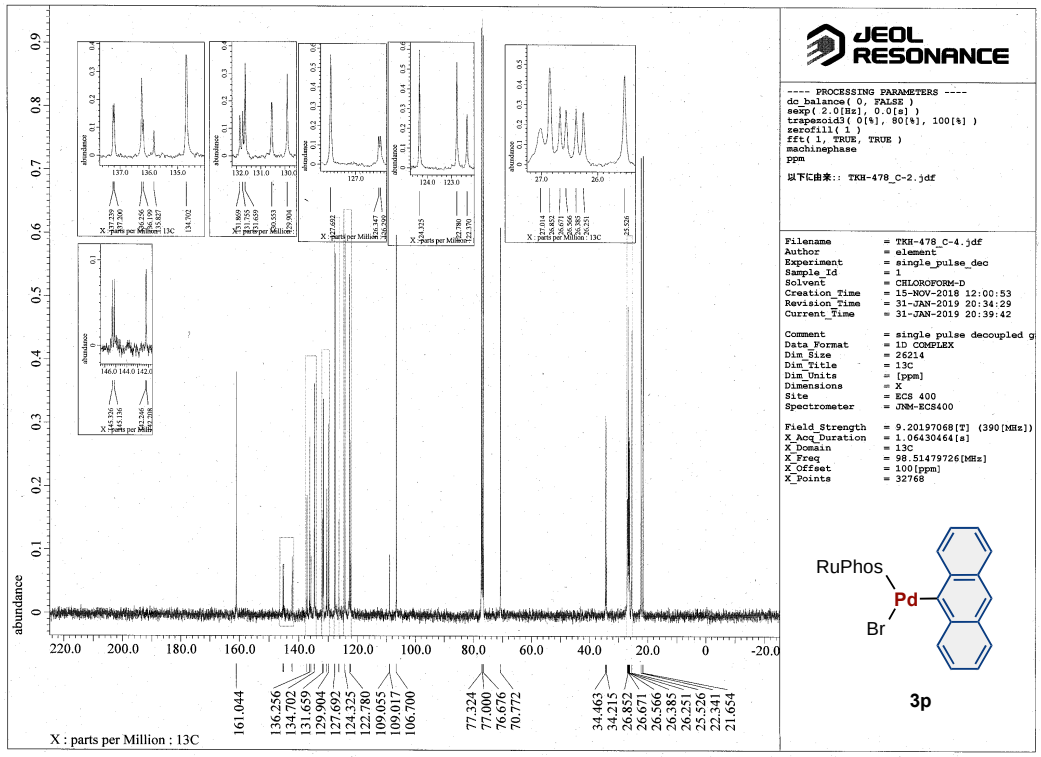
Supplementary Figure 41. ^{13}C NMR spectrum of **3o**.



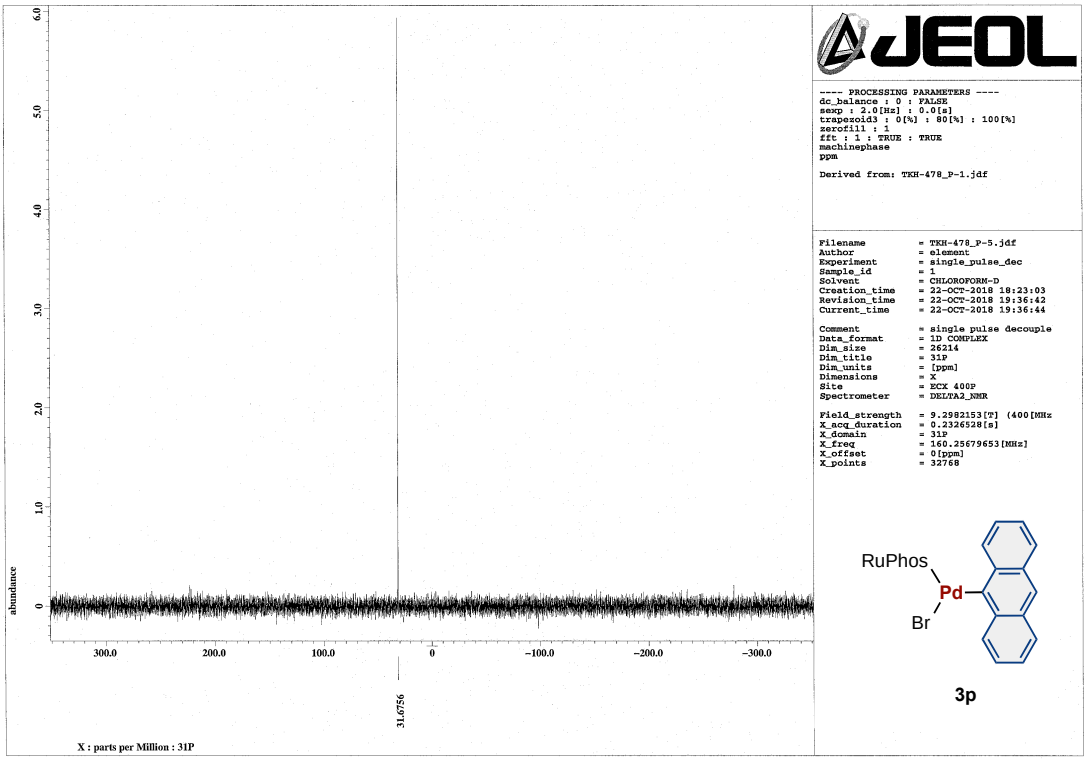
Supplementary Figure 42. ^{31}P NMR spectrum of **3o**.



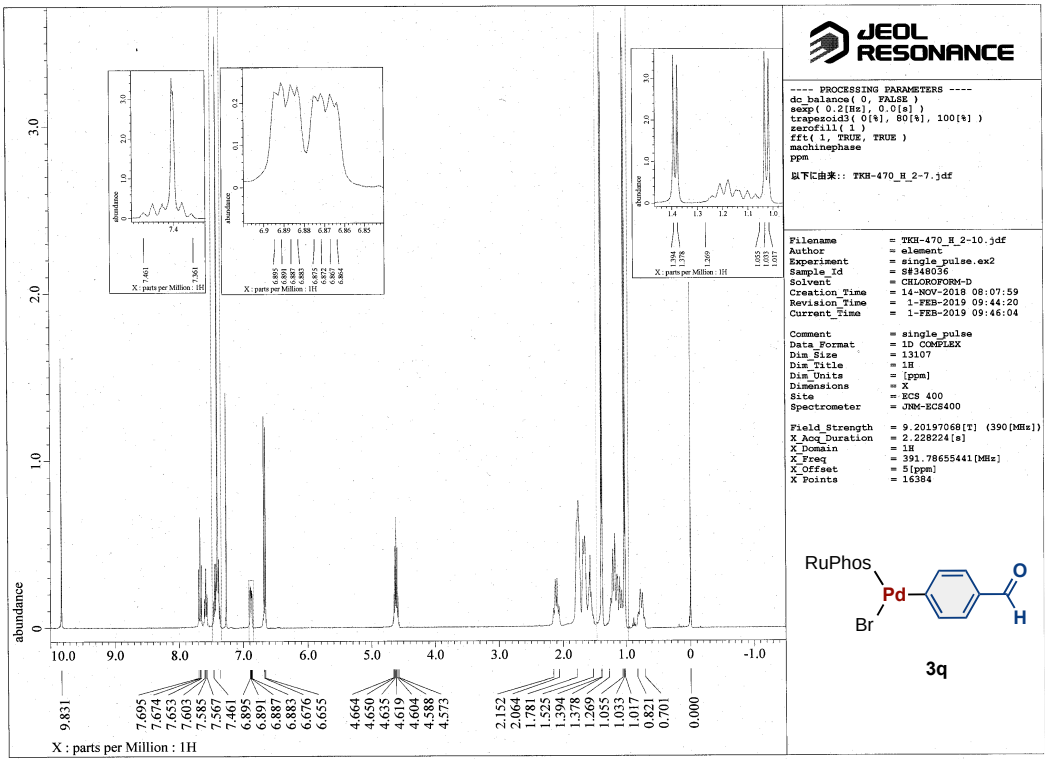
Supplementary Figure 43. ^{1}H NMR spectrum of **3p**.



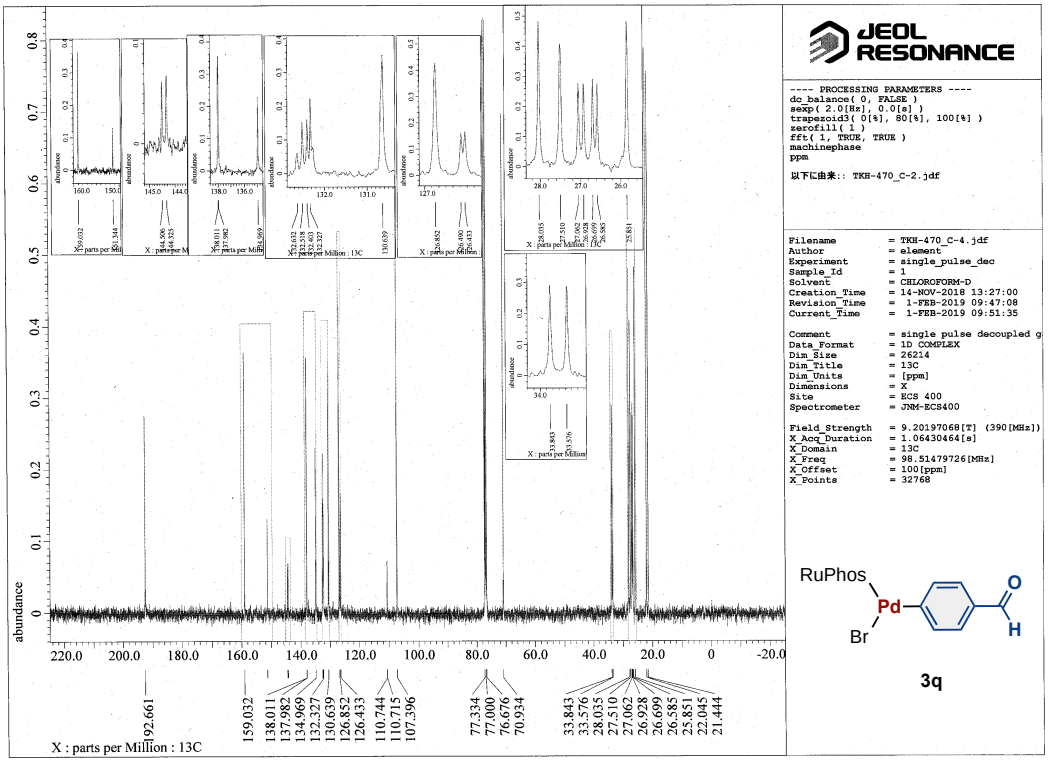
Supplementary Figure 44. ^{13}C NMR spectrum of **3p**.



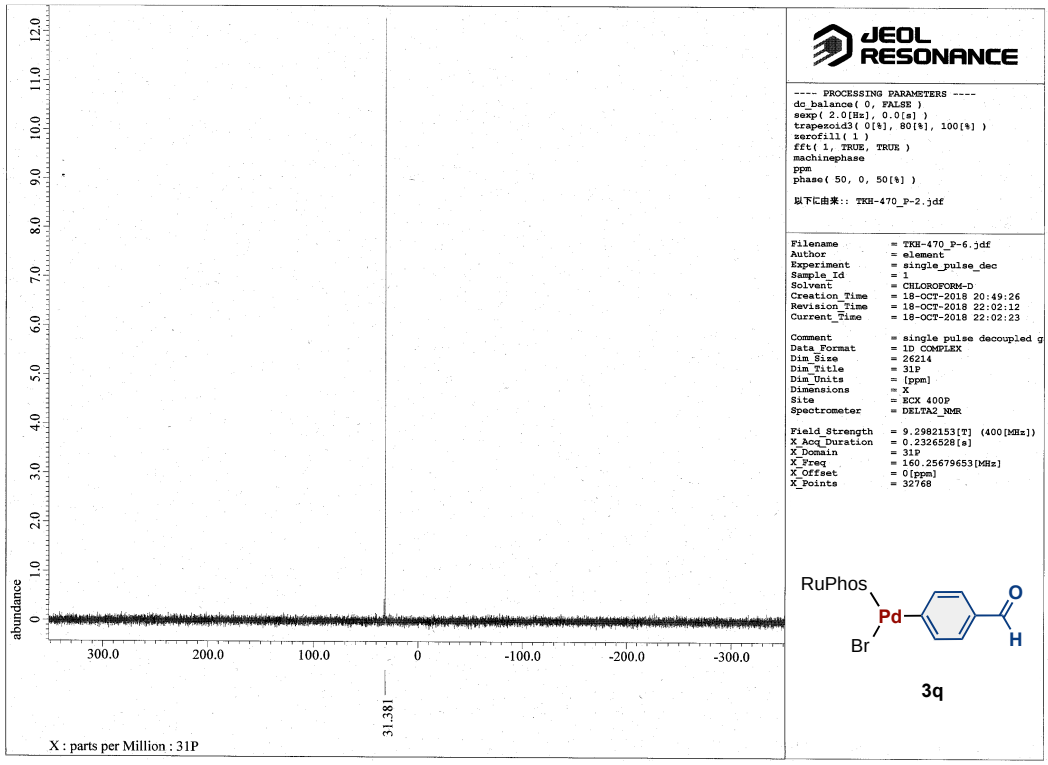
Supplementary Figure 45. ^{31}P NMR spectrum of **3p**.



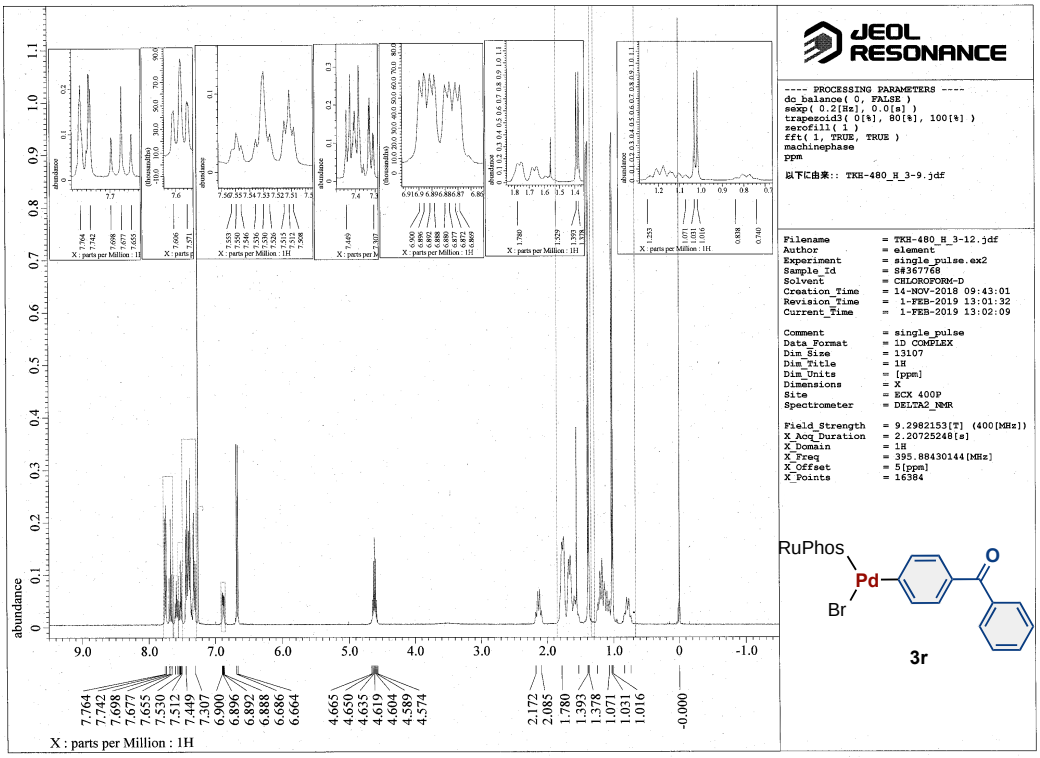
Supplementary Figure 46. ^{1}H NMR spectrum of **3q**.



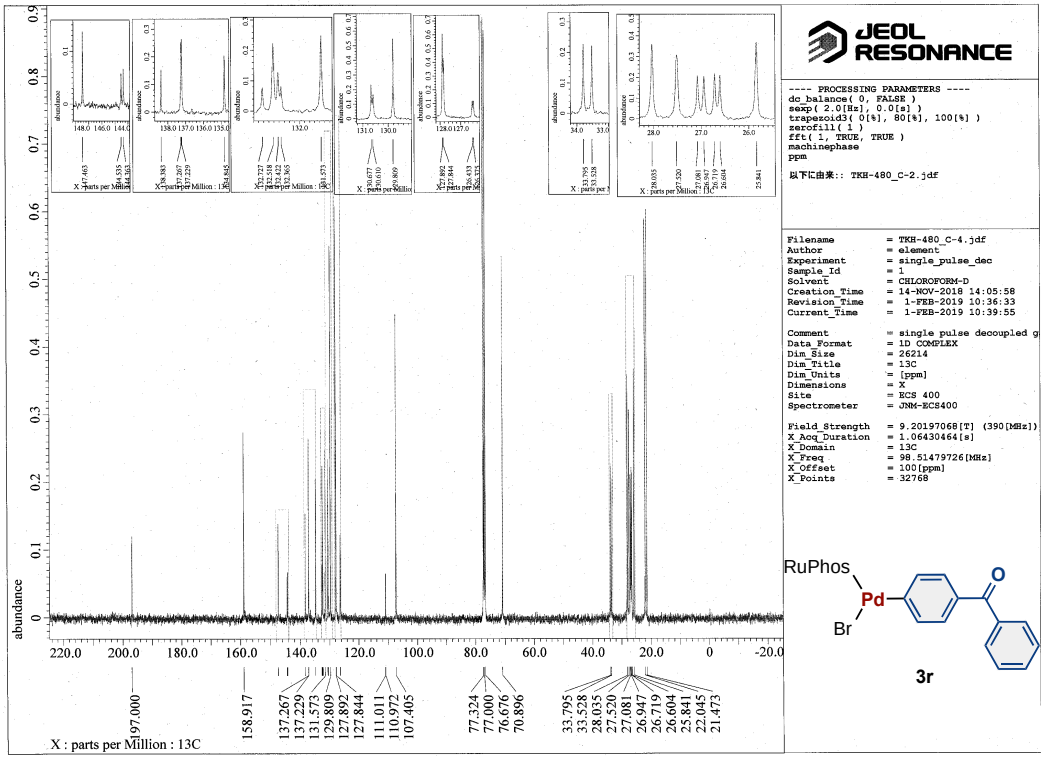
Supplementary Figure 47. ^{13}C NMR spectrum of **3q**.



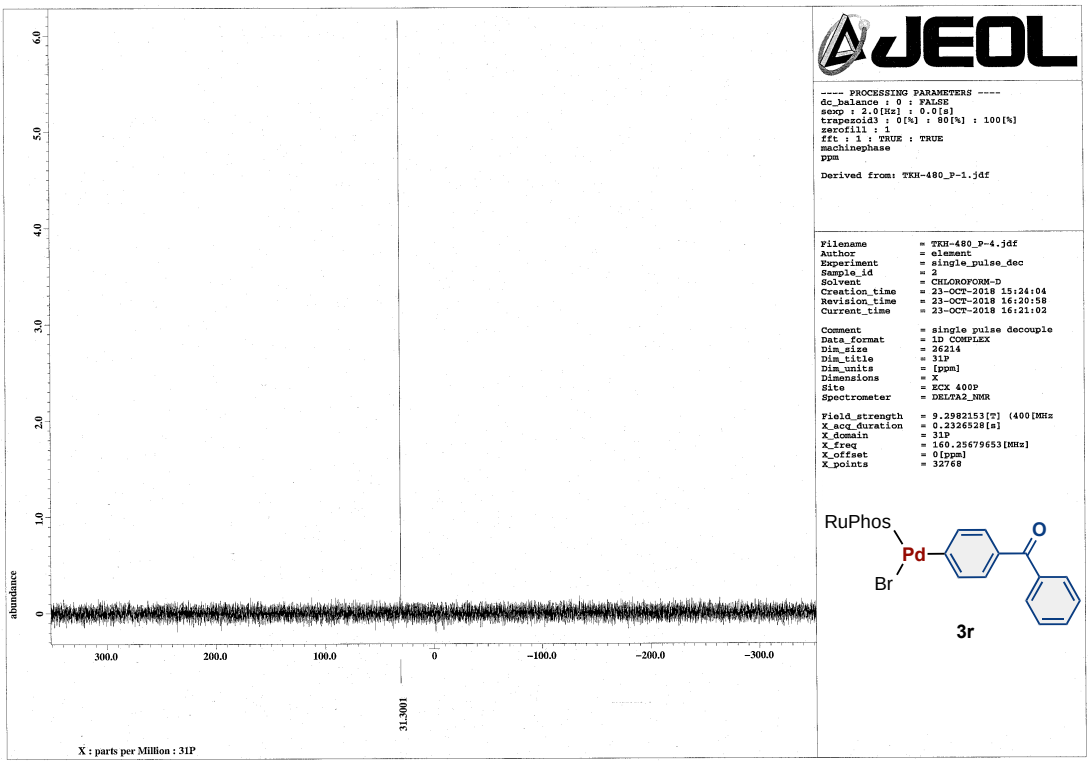
Supplementary Figure 48. ^{31}P NMR spectrum of **3q**.



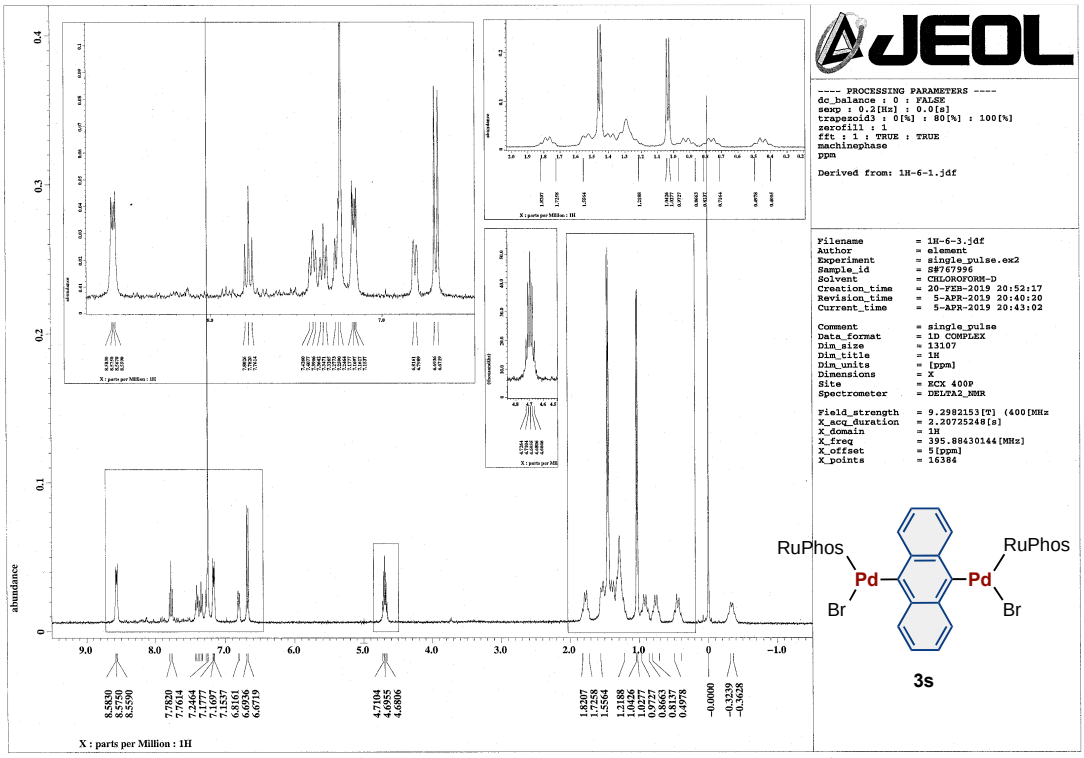
Supplementary Figure 49. ^{1}H NMR spectrum of **3r**.



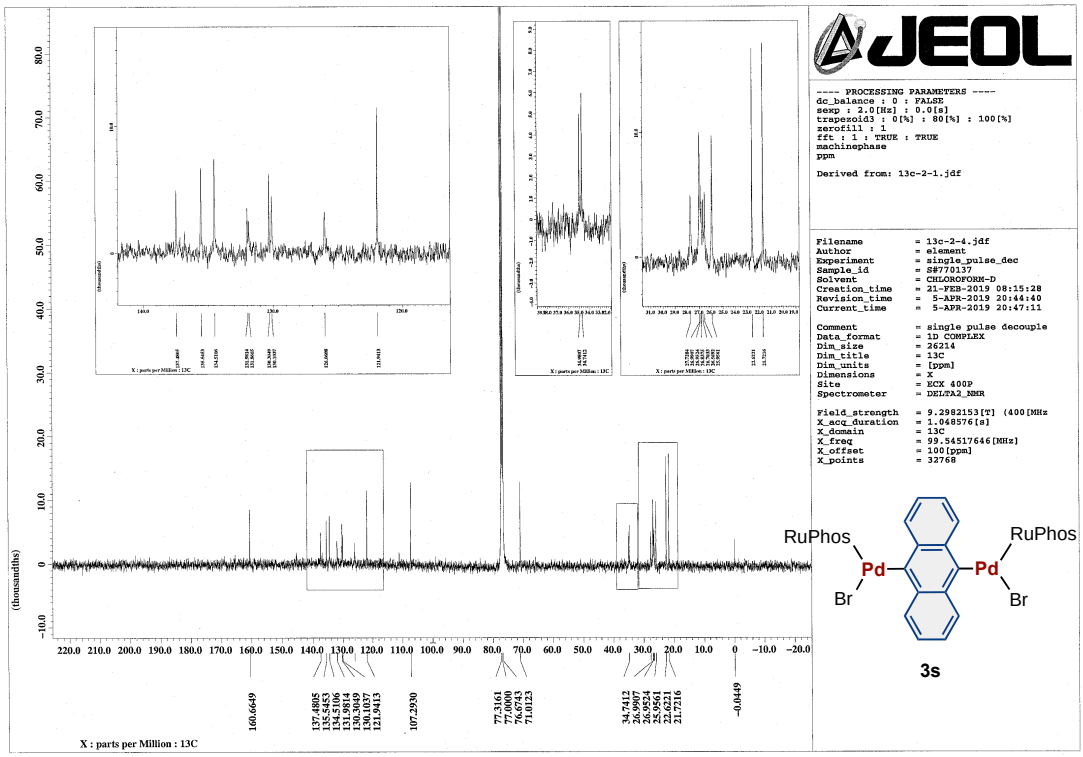
Supplementary Figure 50. ^{13}C NMR spectrum of **3r**.



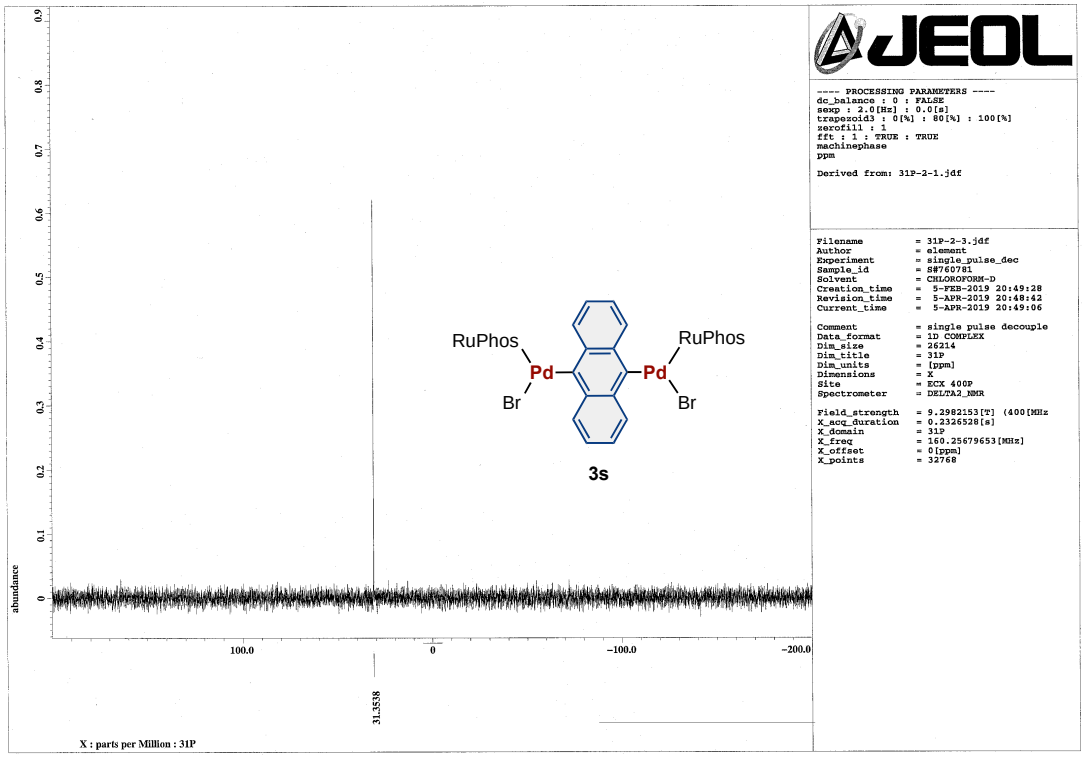
Supplementary Figure 51. ^{31}P NMR spectrum of **3r**.



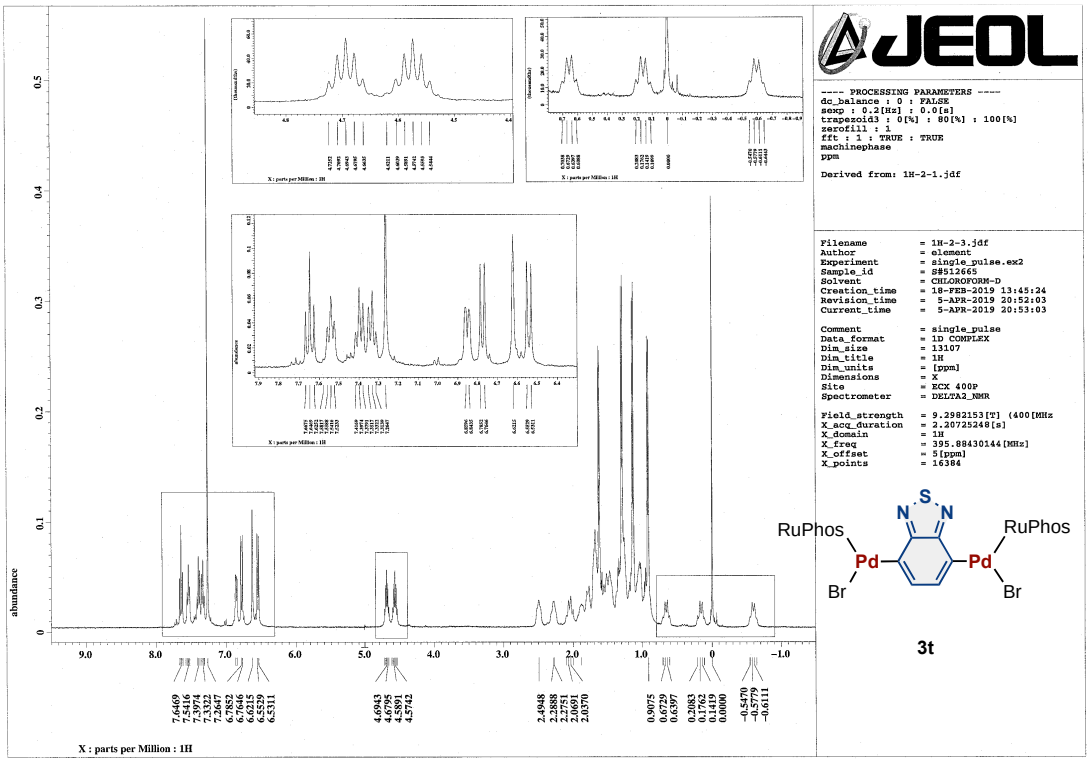
Supplementary Figure 52. ^{1}H NMR spectrum of **3s**.



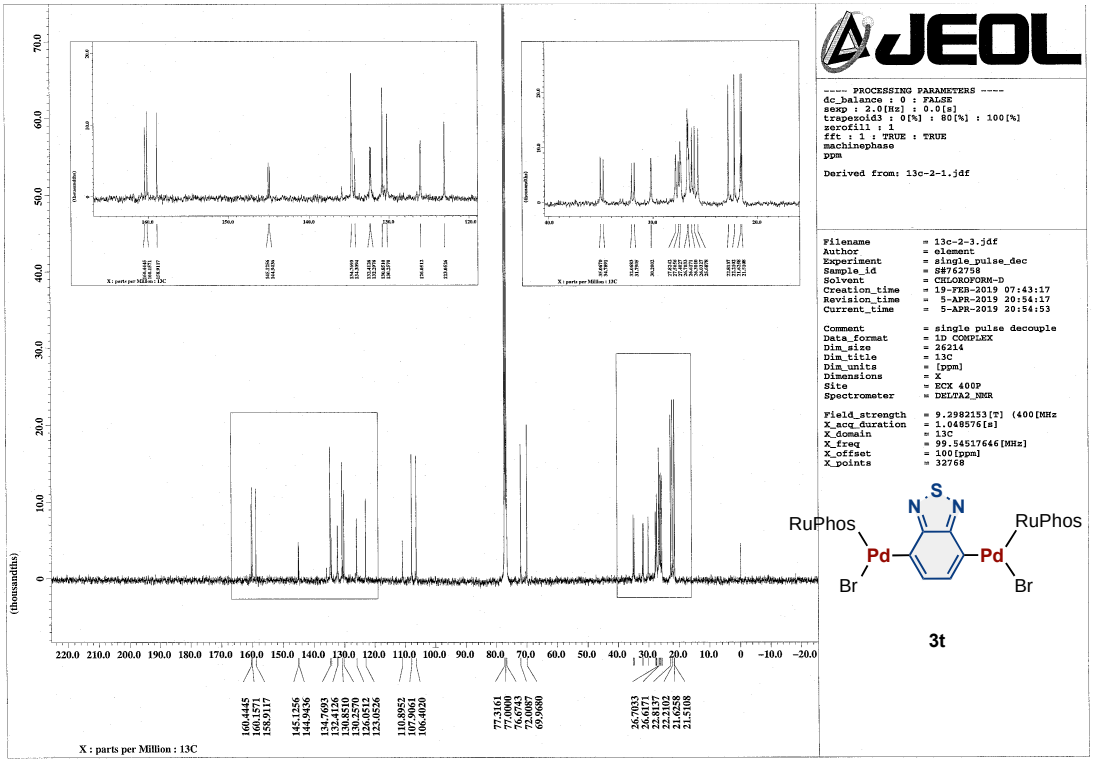
Supplementary Figure 53. ^{13}C NMR spectrum of **3s**.



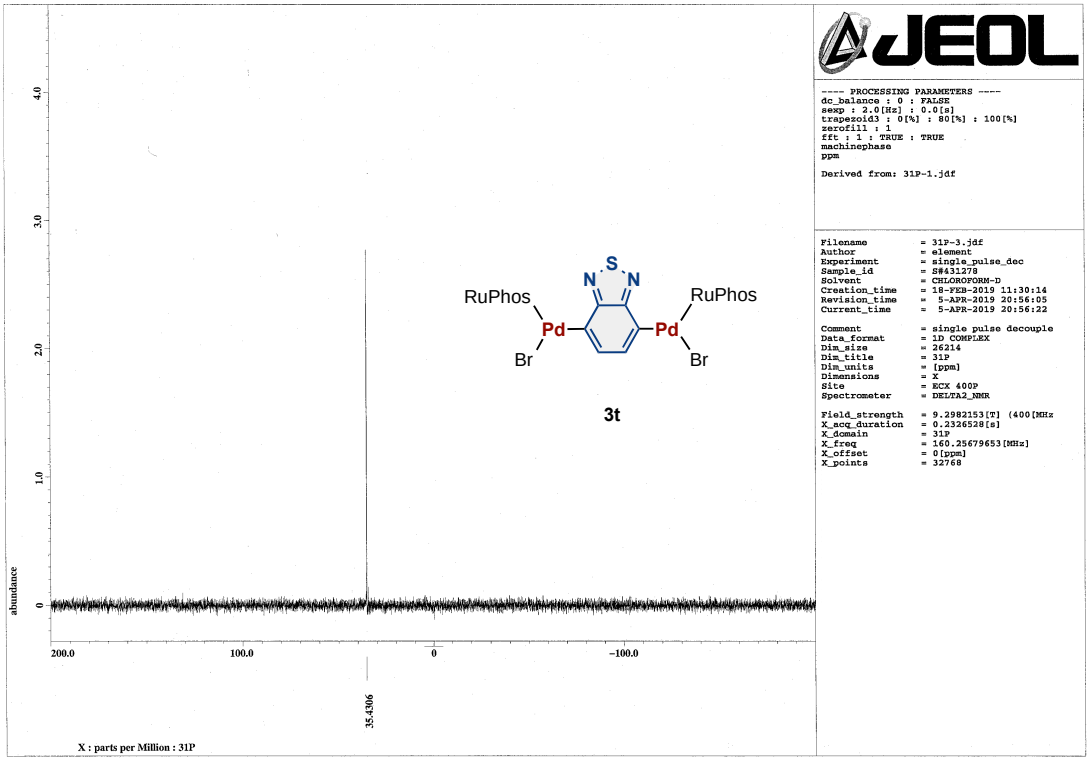
Supplementary Figure 54. ^{31}P NMR spectrum of **3s**.



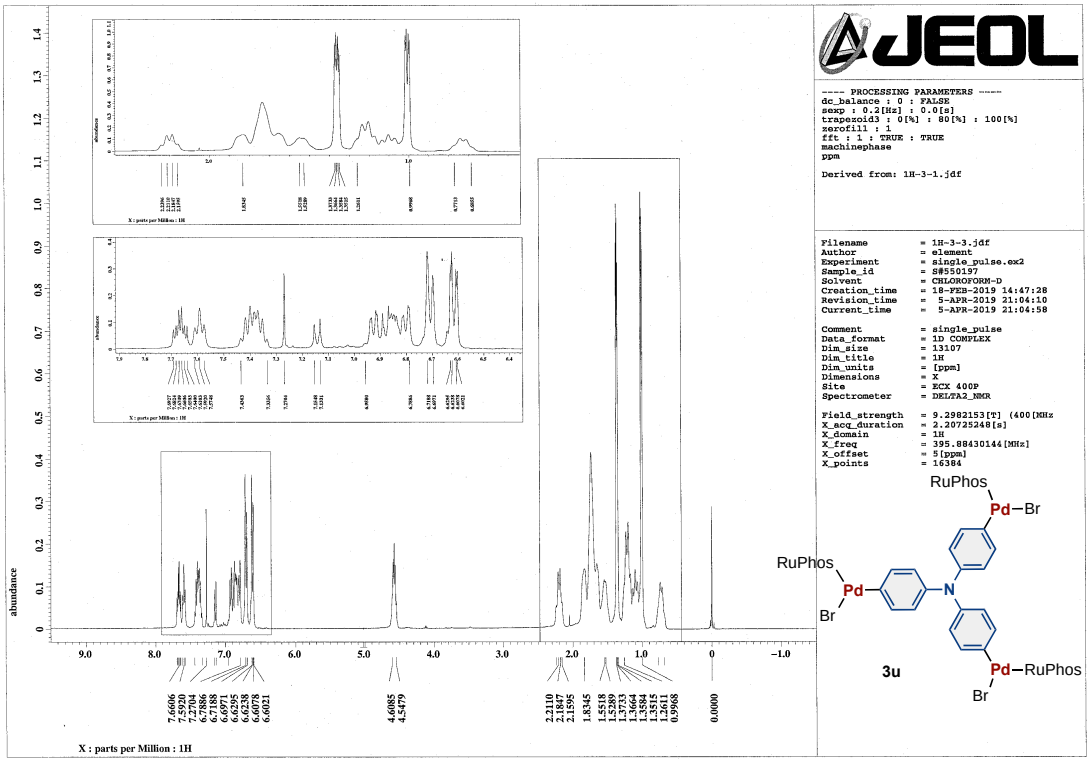
Supplementary Figure 55. ^{1}H NMR spectrum of **3t**.



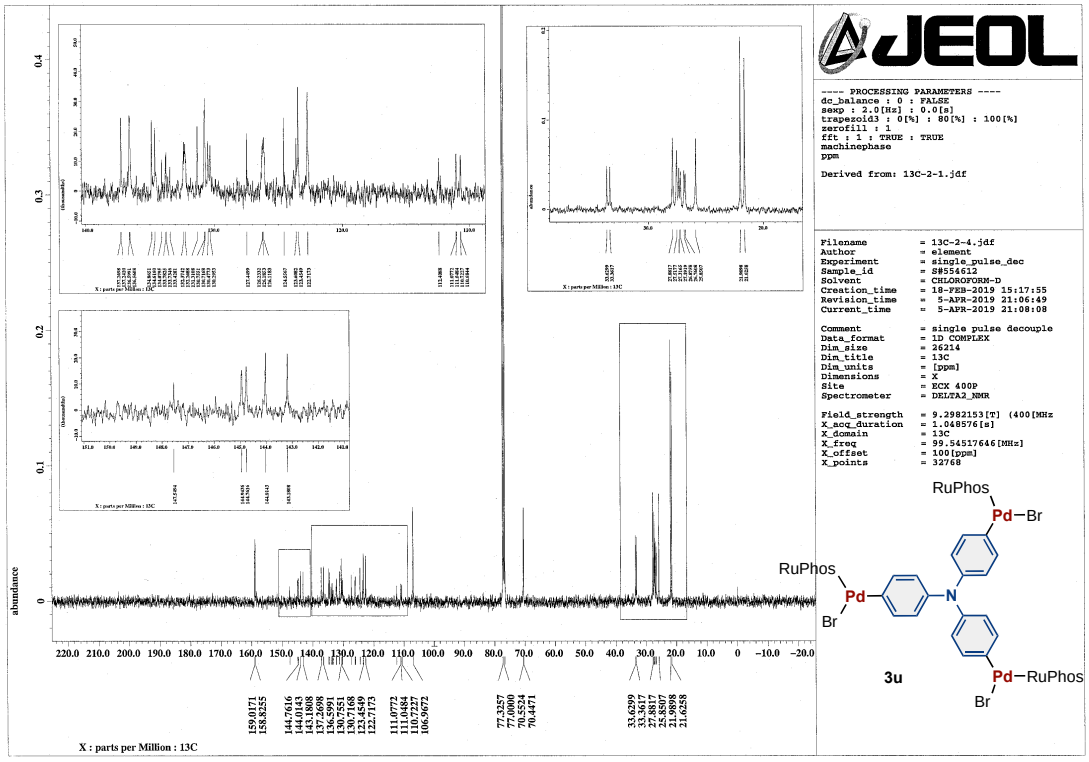
Supplementary Figure 56. ^{13}C NMR spectrum of **3t**.



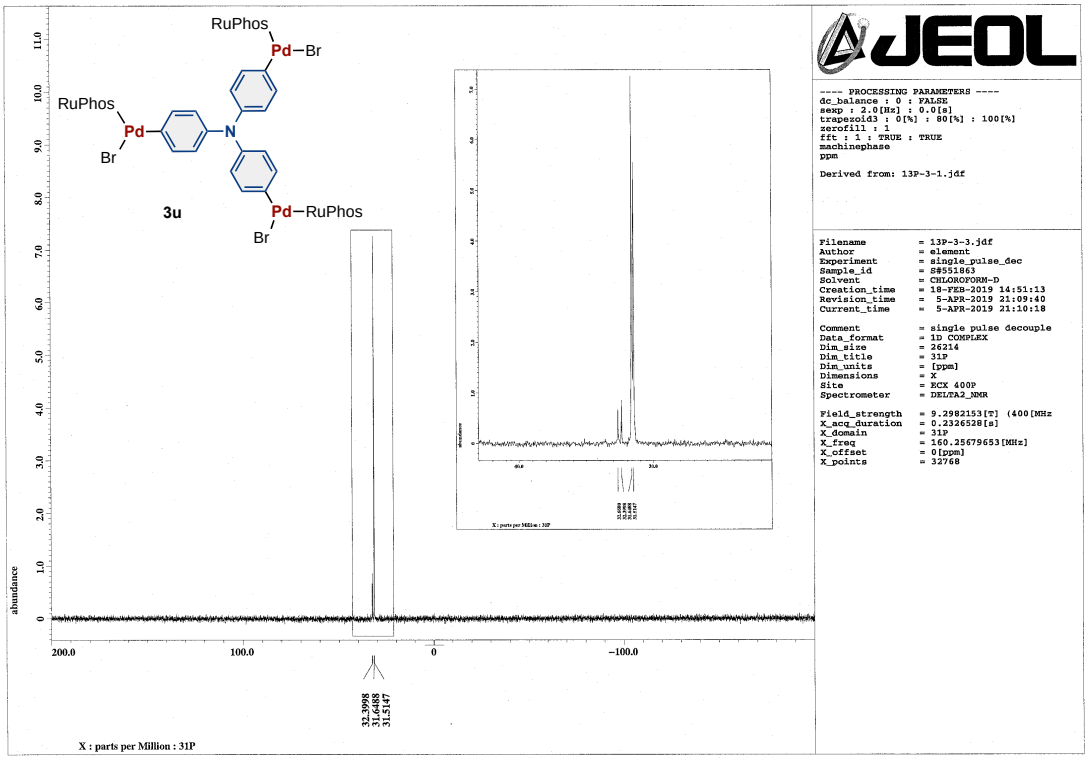
Supplementary Figure 57. ^{31}P NMR spectrum of **3t**.



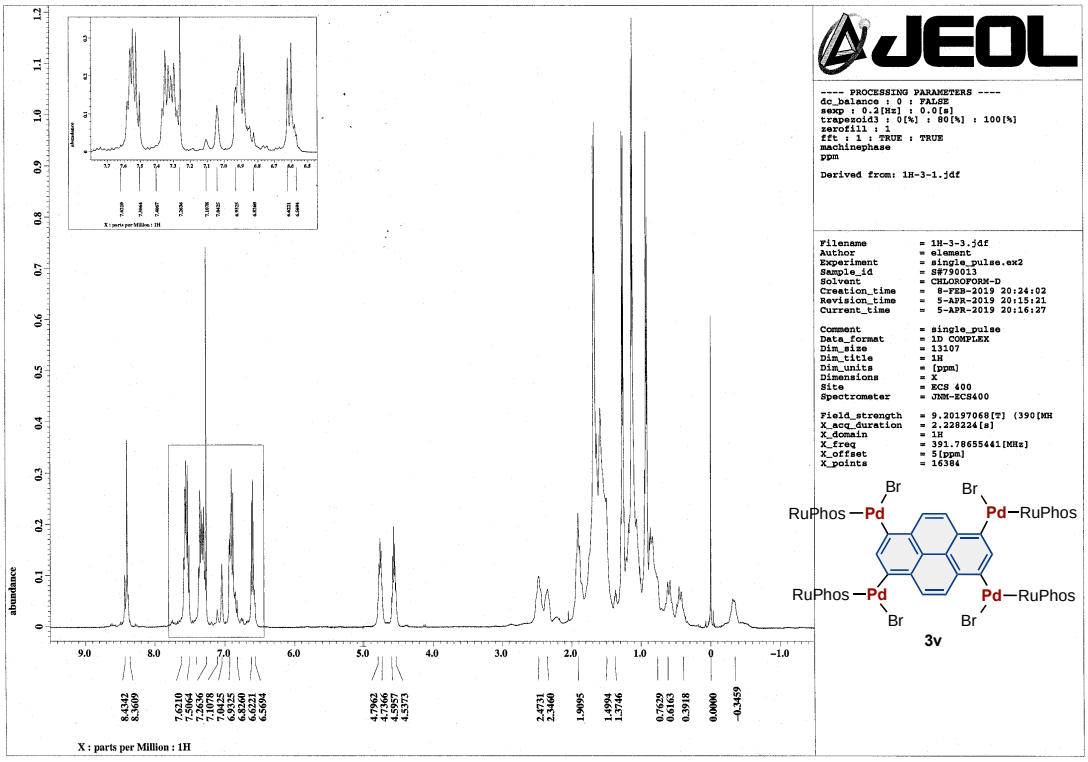
Supplementary Figure 58. ^{1}H NMR spectrum of **3u**.



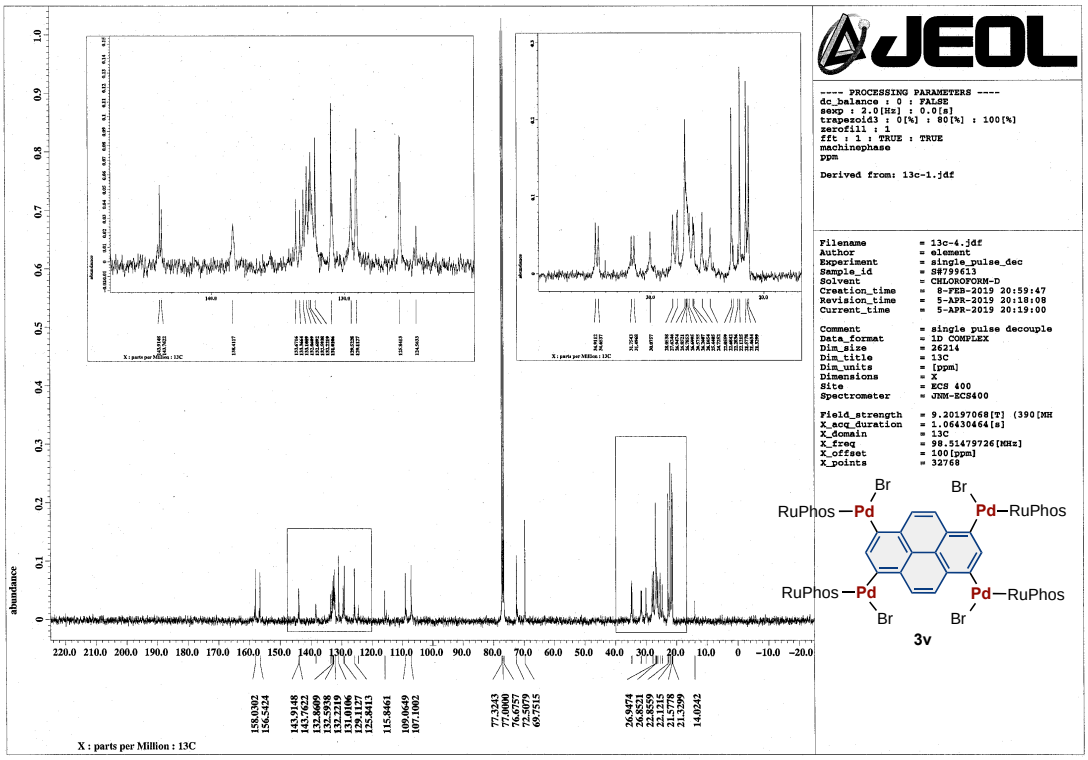
Supplementary Figure 59. ^{13}C NMR spectrum of **3u**.



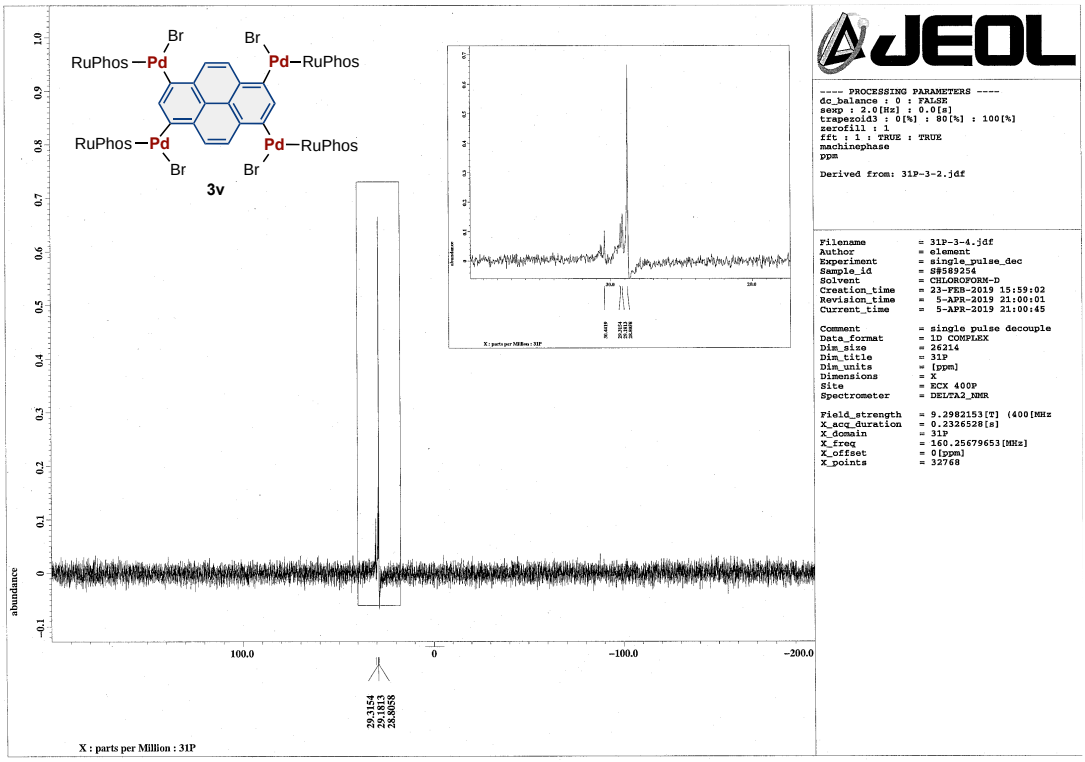
Supplementary Figure 60. ^{31}P NMR spectrum of **3u**.



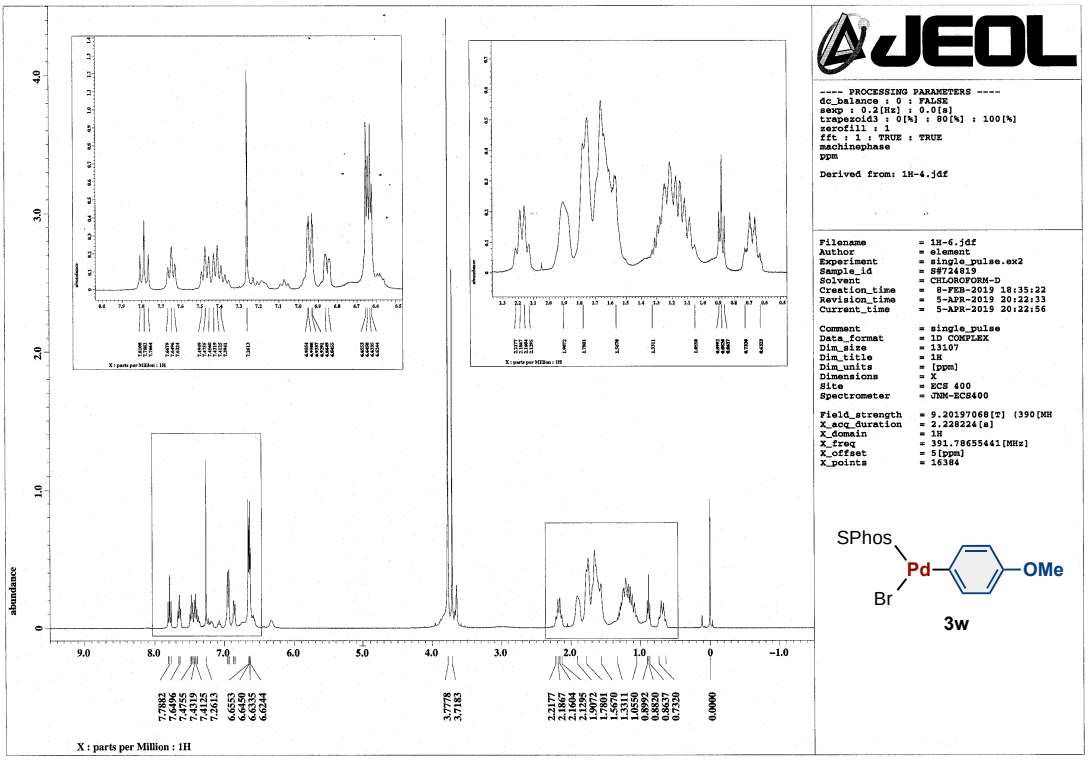
Supplementary Figure 61. ^{1}H NMR spectrum of **3v**.



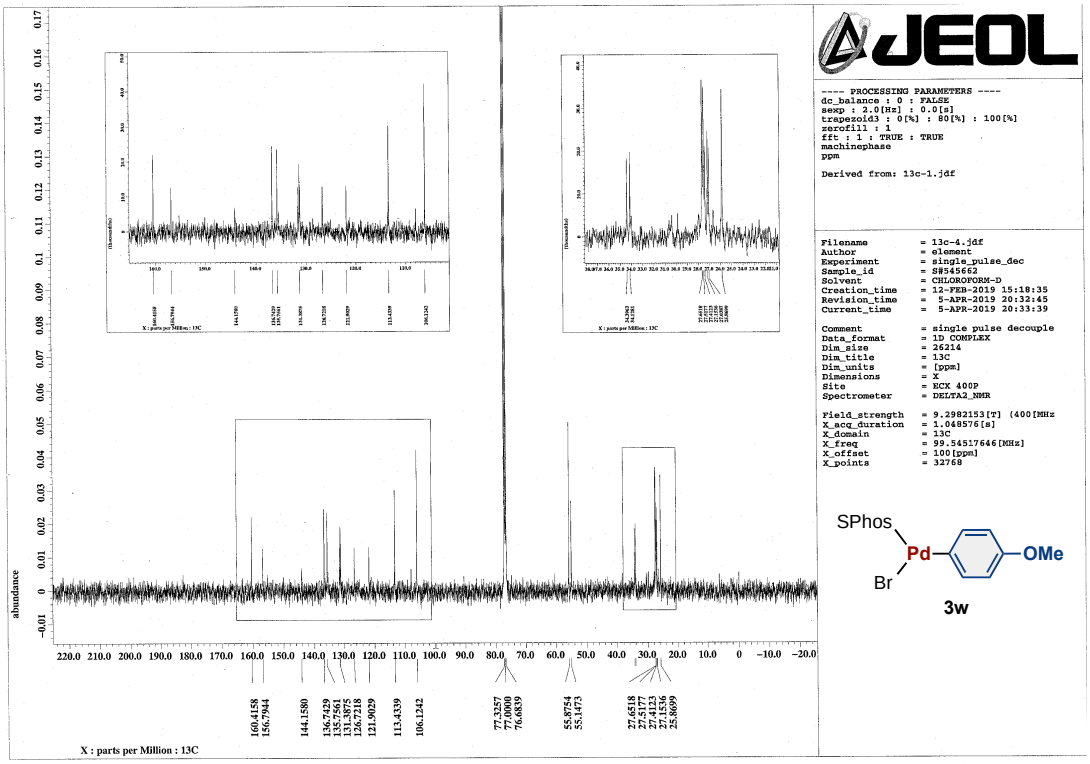
Supplementary Figure 62. ^{13}C NMR spectrum of **3v**.



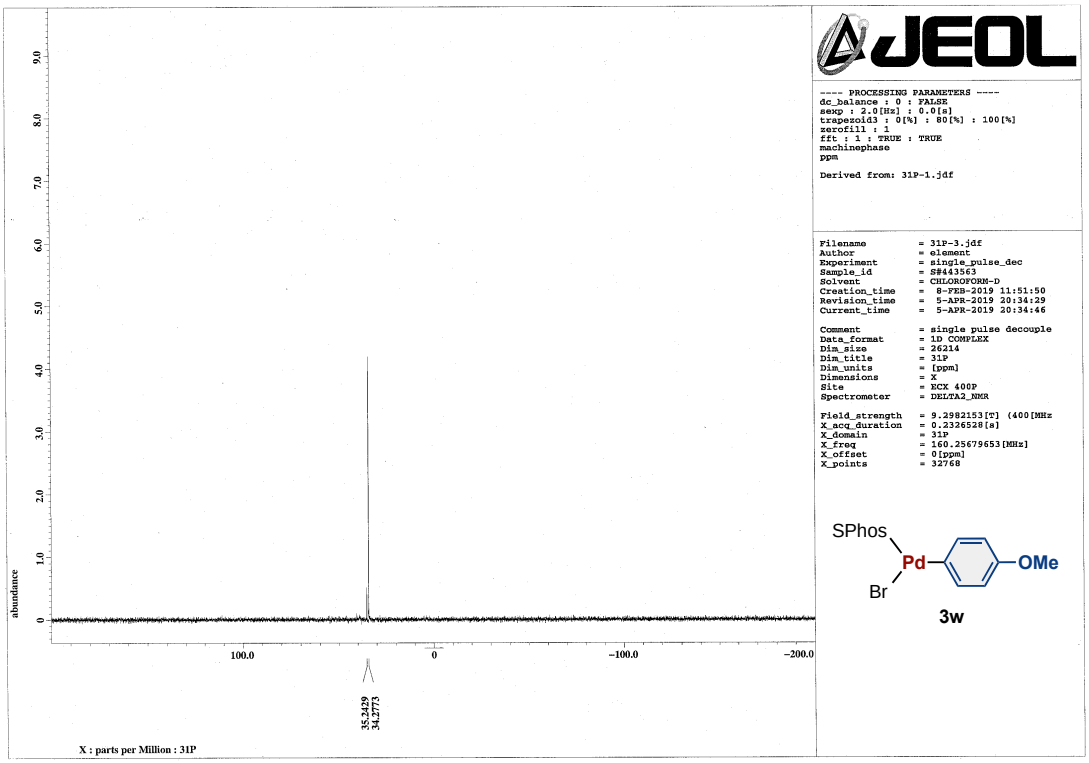
Supplementary Figure 63. ^{31}P NMR spectrum of **3v**.



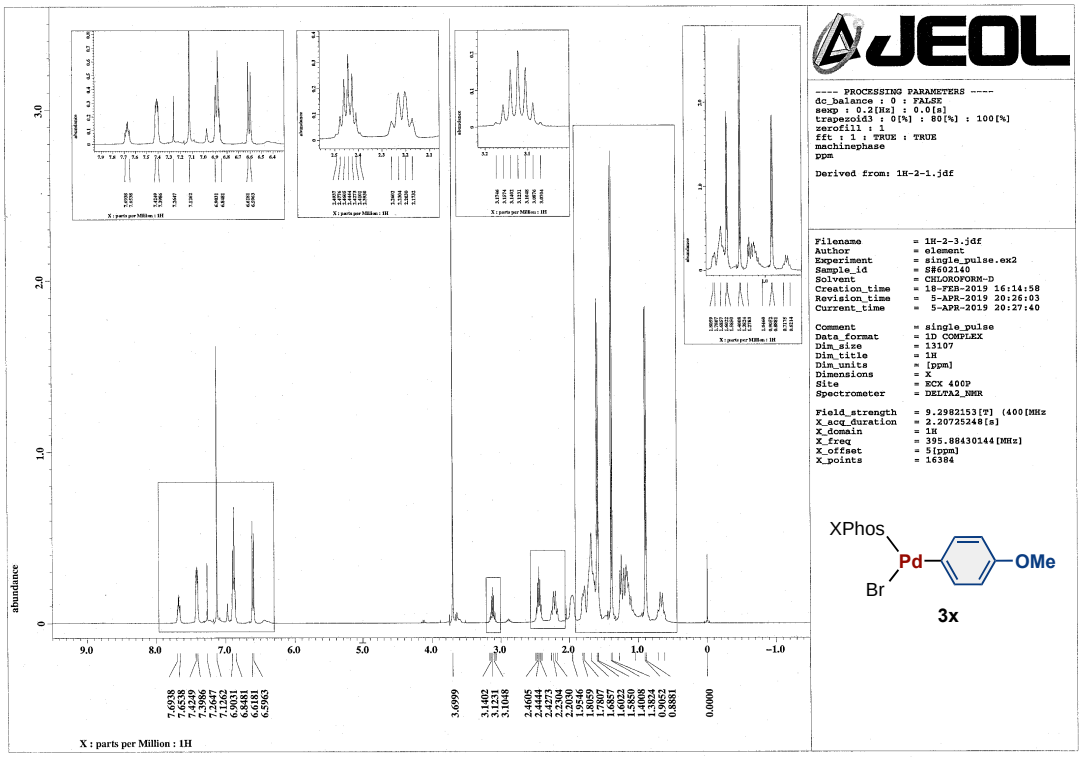
Supplementary Figure 64. ^{1}H NMR spectrum of **3w**.



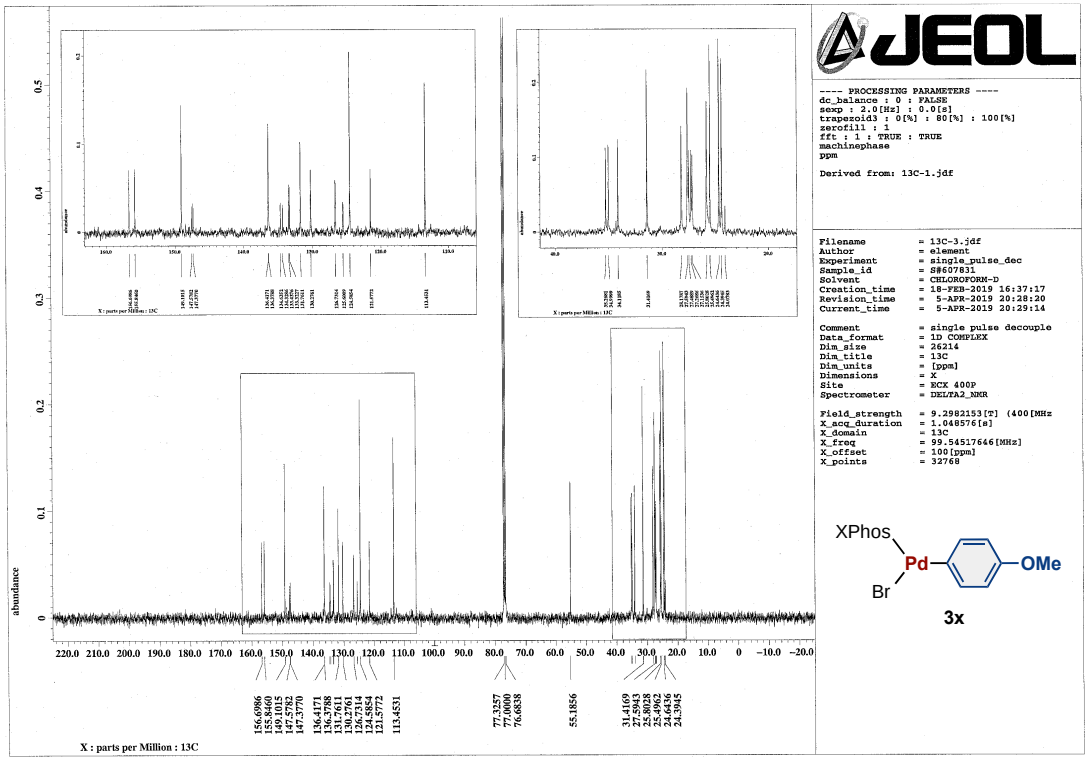
Supplementary Figure 65. ^{13}C NMR spectrum of **3w**.



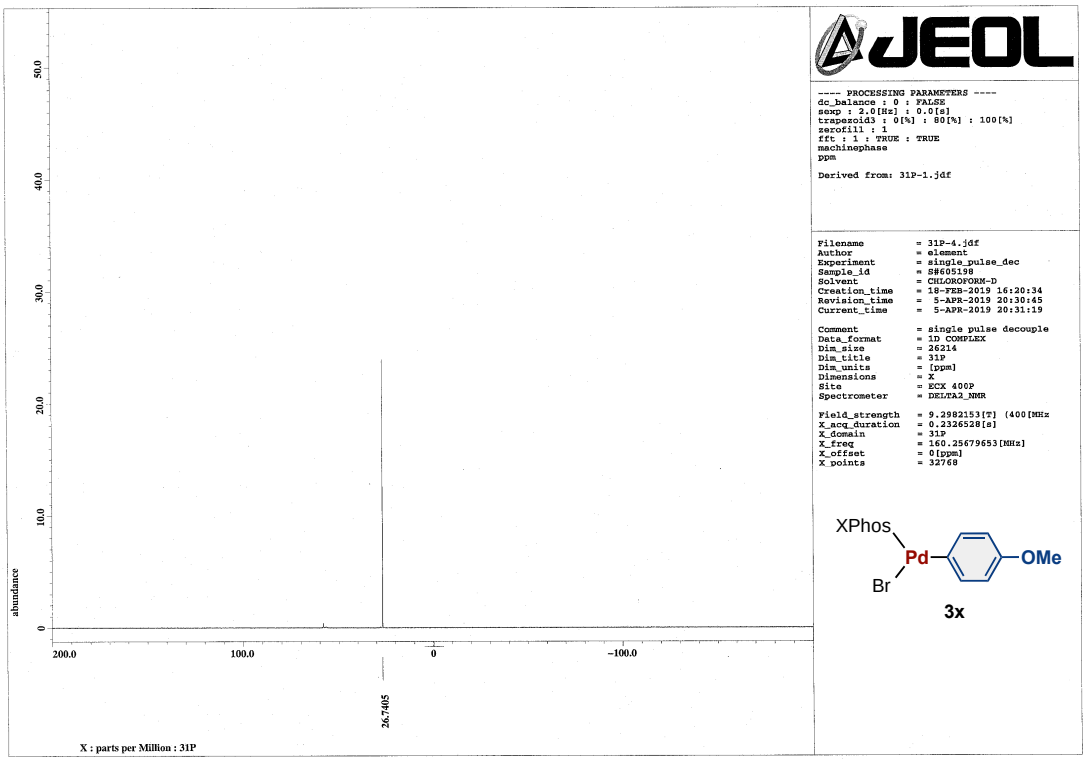
Supplementary Figure 66. ^{31}P NMR spectrum of **3w**.



Supplementary Figure 67. ^{1}H NMR spectrum of **3x**.



Supplementary Figure 68. ^{13}C NMR spectrum of **3x**.



Supplementary Figure 69. ^{31}P NMR spectrum of **3x**.