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Biological Activities of NHC Pd(II) Complexes Based on Benzimidazolylidene N-heterocyclic Carbene (NHC) Ligands Bearing Aryl Substituents

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1. Synthesis of Benzimdazolium Salts 1

A round bottom flask was charged with 5,6-dimethylbenzimidazole or benzimidazole (30 mmol), potassium hydroxide (30 mmol, 1.68 g) and ethanol (30 ml) and stirred at room temperature for 1 h. Then, 2-bromoethyl methyl ether (30 mmol, 4.17 g) was added slowly and the resulting mixture was refluxed at 80°C for 24–48 h. After the reaction was complete, the reaction mixture was cooled down to room temperature and the solvent was removed under reduced pressure. The white precipitate obtained was washed with DCM (20 to 30 ml) and filtered through filter paper. DCM was removed under reduced pressure and the crude product was dried under vacuum [1].

1-(2-methoxyethyl)-1H-benzo[d]imidazole (**1a**) Yield: 94%, $C_{10}H_{12}N_2O$, M= 176.22 g mol^{-1}, $\nu_{(CN)}$= 1446.43 cm^{-1}, ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 3.23 (s, 3H, $CH_{3(4')}$), 3.63 (s, 2H, $H_{2'}$), 4.24 (s, 2H, $H_{1'}$), 7.20 (s, 1H, H_7), 7.35 (s, 1H, H_6), 7.60 (s, 1H, H_5), 7.73 (s, 1H, H_4), 7.92 (s, 1H, H_2). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 45.03 ($C_{1'}$), 59.07 ($C_{4'}$), 70.68 ($C_{2'}$), 109.64 ($C_{4,7}$), 120.17 (C_5), 122.23 (C_6), 122.52 (C_8), 123.0 (C_9), 143.63 (C_2).

1-(2-methoxyethyl)-5,6-dimethyl-1H-benzo[d]imidazole (**1b**) Yield: 98%, $C_{12}H_{16}N_2O$, M= 204.27 g mol^{-1}, M.p. 218.2 °C, $\nu_{(CN)}$= 1434.30 cm^{-1}, ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.31 (s, 3H, $CH_{3(a,b)}$), 3.21 (s, 3H, $CH_{3(4')}$), 3.60 (s, 2H, $H_{2'}$), 4.17 (s, 2H, $H_{1'}$), 7.08 (s, 1H, H_7), 7.48 (s, 1H, H_4), 7.77 (s, 1H, H_2). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 19.19 (C_a), 19.55 (C_b), 43.87 ($C_{1'}$), 58.0 ($C_{4'}$), 69.71 ($C_{2'}$), 108.65 ($C_{4,7}$), 119.26 ($C_{5,6}$), 129.85 (C_8), 130.92 (C_9), 141.87 (C_2).

2. Synthesis of Benzimdazolium Salts 2

A mixture of 2-methoxyethyl benzimidazole **1** (1 mmol) and the corresponding benzyl bromide or chloride (1.2 mmol) in DMF (4 ml) was stirred at 70°C for 24–48 h. Then, the white precipitate was washed with diethyl ether (2 × 10 ml) and stirred for a few hours. The solid was dried under vacuum [54].

2-methoxyethyl-3-(2,3,4,5,6-penthamethylbenzyl) benzimidazolium chloride **(2a)** Yield: 93%, $C_{22}H_{29}N_2OCl$, M= 372.94 g mol^{-1}, M.p. 199.1 °C, $\nu_{(CN)}$= 1557.72 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.23 (s, 6H, $CH_{3(a,e)}$), 2.26 (s, 9H, $CH_{3(b,c,d)}$), 3.27 (s, 3H, $CH_{3(4')}$), 3.86 (t, 2H, $H_{2'}$), 4.94 (t, 2H, $H_{1'}$), 5.76 (s, 2H, $H_{1''}$), 7.39 (d, 1H, H_7), 7.48 (t, 1H, H_6), 7.57 (t, 1H, H_5), 7.88 (d, 1H, H_4), 10.56 (s, 1H, H_2). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 17.00 ($C_{a,e}$), 17.06 ($C_{b,d}$) 17.34 (C_c), 47.89 ($C_{1'}$), 47.93 ($C_{1''}$), 58.95 ($C_{4'}$), 70.50 ($C_{2'}$), 113.11 (C_7), 114.33 (C_4), 124.75 (C_5), 126.97 (C_6), 131.19 (C_8), 132.47 (C_9), 133.58 ($C_{3'',5'',7''}$), 134.01 ($C_{4'',6''}$), 137.42 ($C_{2''}$), 142.98 (C_2). Anal. Calc. for $C_{22}H_{29}N_2OCl$ (%): C 63.31, H 7.00, N 6.71. Found (%): C 63.22, H 7.01, N 6.88.

2-methoxyethyl-3-(2,4,6-trimethylbenzyl)benzimidazolium chloride **(2b)** Yield: 96%, $C_{20}H_{25}N_2OCl$, M= 344.88 g mol^{-1}, M.p. 246.7 °C, $\nu_{(CN)}$= 1555.39 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.30 (s, 3H, $CH_{3(b)}$), 2.33 (s, 6H, $CH_{3(a,c)}$), 3.32 (s, 3H, $CH_{3(4')}$), 3.92 (t, 2H, $H_{2'}$), 4.91 (t, 2H, $H_{1'}$), 5.83 (s, 2H, $H_{1''}$), 6.94 (s, 2H, $H_{4'',6''}$), 7.29 (d, 1H, H_7), 7.46 (t, 1H, H_6), 7.57 (t, 1H, H_5), 7.87 (d, 1H, H_4), 11.06 (s, 1H, H_2). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 20.17 ($C_{a,c}$), 21.08 (C_b), 47.14 ($C_{1'}$), 47.76 ($C_{1''}$), 59.0 ($C_{4'}$), 70.28 ($C_{2'}$), 113.35 (C_7), 114.11 (C_4), 125.02 (C_5), 127.04 (C_6), 130.21 ($C_{4'',6''}$), 131.60 (C_8), 132.31 (C_9), 137.97 ($C_{3'',5'',7''}$), 139.78 ($C_{2''}$), 143.67 (C_2). Anal. Calc. for $C_{20}H_{25}N_2OCl$ (%): C, 61.70; H, 6.47; N, 7.20. Found (%): C, 61.58; H, 6.54; N, 7.12.

2-methoxyethyl-3-(3,5-dimethylbenzyl)benzimidazolium bromide **(2c)** Yield: 92%, $C_{19}H_{23}N_2OBr$, M= 375.31 g mol^{-1}, M.p. 311.1 °C. $\nu_{(CN)}$= 1560.26 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.28 (s, 6H, $CH_{3(a,b)}$), 3.36 (s, 3H, $CH_{3(4')}$), 3.98 (t, 2H, $H_{2'}$), 4.89 (t, 2H, $H_{1'}$), 5.73 (s, 2H, $H_{1''}$), 6.96 (s, 1H, $H_{5''}$), 7.06 (s, 2H, $H_{3'',7''}$), 7.55 (m, 3H, $H_{5,6,7}$), 7.82 (d, 1H, H_4), 11.40 (s, 1H, H_2). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 21.28 ($C_{b,d}$), 47.98 ($C_{1'}$), 51.74 ($C_{1''}$), 59.22 ($C_{4'}$), 70.54 ($C_{2'}$), 113.45 (C_7), 114.14 (C_4), 126.07 ($C_{3'',5'',7''}$), 127.02 ($C_{5,6}$), 130.99 (C_8), 131.04 (C_9), 132.34 ($C_{2''}$), 139.16 ($C_{4'',6''}$), 142.62 (C_2). Anal. Calc. for $C_{19}H_{23}N_2OBr$ (%): C, 60.81; H, 6.18; N, 7.46. Found (%): C, 60.88; H, 6.30; N, 7.59.

2-methoxyethyl-3-(4-methylbenzyl)benzimidazolium bromide **(2d)** Yield: 90%, $C_{18}H_{21}N_2OBr$, M= 361.28 g mol^{-1}, M.p. 302.5 °C. $\nu_{(CN)}$= 1557.32 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.29 (s, 3H, $CH_{3(a)}$), 3.35 (s, 3H, $CH_{3(4')}$), 3.95 (t, 2H, $H_{2'}$), 4.87 (t, 2H, $H_{1'}$), 5.83 (s, 2H, $H_{1''}$), 7.10 (s, 2H, $H_{4'',6''}$), 7.29 (d, 2H, $H_{3'',7''}$), 7.52 (d, 1H, H_7), 7.58 (d, 1H, H_6), 7.61 (d, 1H, H_5), 7.86 (d, 1H, H_4), 11.24 (s, 1H, H_2). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 21.18 (C_a), 47.87 ($C_{1'}$), 51.31 ($C_{1''}$), 59.12 ($C_{4'}$), 70.09 ($C_{2'}$), 113.55 (C_7), 114.10 (C_4), 127.05 ($C_{5,6}$), 128.38 ($C_{3'',4'',6'',7''}$), 129.98 (C_8), 130.93 (C_9), 132.20 ($C_{2''}$), 139.21 ($C_{5''}$), 142.79 (C_2). Anal. Calc. for $C_{18}H_{21}N_2OBr$ (%): C, 68.24; H, 6.68; N, 8.84. Found (%): C, 68.19; H, 6.75; N, 8.93.

2-methoxyethyl-3-(2,3,4,5,6-penthamethylbenzyl)-5,6-dimethylbenzimidazolium chloride **(2e)** Yield: 97%, $C_{24}H_{33}N_2OBr$, M= 400.99 g mol^{-1}, M.p. 132.3 °C. $\nu_{(CN)}$= 1558.0 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.19 (s, 6H, $CH_{3(c,g)}$), 2.21 (s, 6H, $CH_{3(d,f)}$), 2.22 (s, 3H, $CH_{3(e)}$), 2.31 (s, 3H, $CH_{3(a)}$), 2.36 (s, 3H, $CH_{3(b)}$), 3.21 (s, 3H, $CH_{3(4')}$), 3.78 (t, 2H, $H_{2'}$), 4.83 (t, 2H, $H_{1'}$), 5.59 (s, 2H, $H_{1''}$), 7.21, (s, 1H, H_7), 7.56 (s, 1H, H_4), 10.01 (s, 1H, H_2). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 16.99 ($C_{c,g}$), 17.02 ($C_{d,f}$), 17.31 (C_e), 20.66 (C_a), 20.80 (C_b), 47.36 ($C_{1'}$), 47.70 ($C_{1''}$), 58.93 ($C_{4'}$), 70.52 ($C_{2'}$), 112.66 (C_7), 113.85 (C_4), 124.28 (C_8), 129.73 (C_9), 130.95 ($C_{5''}$), 133.58 ($C_{3'',7''}$), 134.00 ($C_{4'',6''}$) 137.05 ($C_{2''}$), 137.19 (C_6), 137.37 (C_5), 141.38 (C_2). Anal. Calc. for $C_{24}H_{33}N_2OCl$ (%): C, 64.71; H, 7.47. N, 6.29; Found (%): C, 64.65; H, 7.39; N, 6.31.

2-methoxyethyl-3-(2,4,6-trimethylbenzyl)-5,6-dimethylbenzimidazolium chloride **(2f)** Yield: 94%, $C_{22}H_{29}N_2OCl$, M= 372.94 g mol^{-1}, M.p. 241.2 °C, $\nu_{(CN)}$= 1554.12 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.30 (s, 12H, $CH_{3(b,c,d,e)}$), 2.38 (s, 3H, $CH_{3(a)}$), 3.29 (s, 3H, $CH_{3(4')}$), 3.87 (s, 2H, $H_{2'}$), 4.81 (s, 2H, $H_{1'}$), 5.74 (s, 2H, $H_{1''}$), 6.92 (s, 2H, $H_{4'',6''}$), 6.99 (s, 1H, H_7), 7.53 (s, 1H, H_4), 10.81 (s, 1H, H_2). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 20.11 ($C_{c,e}$), 20.63 (C_d), 20.79 (C_a), 21.07 (C_b), 46.71 ($C_{1'}$), 47.48 ($C_{1''}$), 58.98 ($C_{4'}$), 70.36 ($C_{2'}$), 112.92 (C_7), 113.54 (C_4), 125.14 (C_6), 129.68 (C_5), 130.12 ($C_{4'',6''}$), 130.83 ($C_{5''}$), 137.05 ($C_{2''}$), 137.96 ($C_{3'',7''}$), 139.70 ($C_{5,6}$), 142.32 (C_2). Anal. Calc. for $C_{22}H_{29}N_2OCl$ (%): C, 63.31; H, 7.00; N, 6.71. Found (%): C, 63.44; H, 7.09; N, 6.74.

2-methoxyethyl-3-(3,5-dimethylbenzyl)-5,6-dimethylbenzimidazolium bromide **(2g)** Yield: 89%, $C_{21}H_{27}N_2OBr$, M= 403.4 g mol^{-1}, M.p. 267.6 °C. $\nu_{(CN)}$= 1563.49 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.22 (s, 6H, $CH_{3(c,d)}$), 2.31 (s, 3H, $CH_{3(a)}$), 2.35 (s, 3H, $CH_{3(b)}$), 3.29 (s, 3H, $CH_{3(4')}$), 3.89 (t, 2H, $H_{2'}$), 4.73 (t, 2H, $H_{1'}$), 5.59 (s, 2H, $H_{1''}$), 6.90 (s, 1H, $H_{5''}$), 6.95 (s, 2H, $H_{3'',7''}$), 7.22 (s, 1H, H_4), 7.47 (s, 1H, H_7), 11.05 (s, 1H, H_2). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 20.68 (C_a), 20.72 (C_b), 21.24 ($C_{c,d}$), 47.54 ($C_{1'}$), 51.19 ($C_{1''}$), 59.14 ($C_{4'}$), 70.28 ($C_{2'}$), 112.95 (C_7), 113.54 (C_4), 125.70 ($C_{3'',5'',7''}$), 129.55 (C_8), 130.82 (C_9), 132.59 ($C_{2''}$), 137.21 ($C_{5,6}$), 139.07 ($C_{4'',6''}$), 141.81 (C_2). Anal. Calc. for $C_{21}H_{27}N_2OBr$ (%): C, 62.53; H, 6.75; N, 6.95. Found (%): C, 62.59; H, 6.79; N, 7.13.

2-methoxyethyl-3-(4-methylbenzyl)-5,6-dimethylbenzimidazolium bromide **(2h)** Yield: 87%, $C_{20}H_{25}N_2OBr$, M= 389.3 g mol^{-1}, M.p. 256.8 °C, $\nu_{(CN)}$= 1559.72 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.32 (s, 3H, $CH_{3(c)}$), 2.37 (s, 3H, $CH_{3(a)}$), 2.41 (s, 3H, $CH_{3(b)}$), 3.36 (s, 3H, $CH_{3(4')}$), 3.95 (t, 2H, $H_{2'}$), 4.78 (t, 2H, $H_{1'}$), 5.72 (s, 2H, $H_{1''}$), 7.18 (d, 2H, $H_{4'',6''}$), 7.31 (d, 2H, $H_{3'',7''}$), 7,36 (d, 1H, H_4), 7.53 (s, 1H, H_7), 11.23 (s, 1H, H_2). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 20.67 (C_a), 20.71 (C_b), 21.20 (C_c), 47.54 ($C_{1'}$), 51.04 ($C_{1''}$), 59.16 ($C_{4'}$), 70.24 ($C_{2'}$), 113.0 (C_7), 113.52 (C_4), 128.19 ($C_{8,9}$), 129.98 ($C_{3'',4'',6'',7''}$), 130.77 ($C_{2''}$), 137.22 ($C_{5''}$), 139.14 ($C_{5,6}$), 141.78 (C_2). Anal. Calc. for $C_{20}H_{25}N_2OBr$ (%): C, 69,65; H, 7.31; N, 8.12. Found (%): C, 69.77; H, 7.43; N, 8.24.

2-methoxyethyl-3-(4-tert-buthylbenzyl)-5,6-dimethylbenzimidazolium bromide **(2i)** Yield 74%, $C_{23}H_{31}N_2OBr$, M= 431.4 g mol^{-1}, M.p. 255.4 °C. $\nu_{(CN)}$= 1559.06 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.29 (s, 9H, $CH_{3(c,d,e)}$), 2.40 (s, 3H, $CH_{3(a)}$), 2.43 (s, 3H, $CH_{3(b)}$), 3.38 (s, 3H, $CH_{3(4')}$), 3.98 (t, 2H, $H_{2'}$), 4.79 (t, 2H, $H_{1'}$), 5.73 (s, 2H, $H_{1''}$), 7.34 (s, 1H, H_4), 7.42 (s, 4H, $H_{3'',4'',6'',7''}$), 7.53 (s, 1H, H_7), 11.27 (s, 1H, H_2). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 20.68 (C_a), 20.71 (C_b), 31.19 ($C_{c,d,e}$), 34.68 ($C_{8'}$), 47.54 ($C_{1'}$), 50.86 ($C_{1''}$), 59.16 ($C_{4'}$), 70.29 ($C_{2'}$), 112.94 (C_7), 113.52 (C_4), 126.27 ($C_{4'',6''}$), 127.98 ($C_{3'',7''}$), 129.54 (C_8), 129.83

(C_9), 130.76 ($C_{2''}$), 137.22 ($C_{5,6}$), 141.81 (C_2), 152.33 ($C_{5''}$). Anal. Calc. for $C_{23}H_{31}N_2OBr$ (%): C, 64.03; H, 7.24; N, 6.49. Found (%): C, 64.11; H, 7.30; N, 6.61.

3. Synthesis of Palladium Complexes

3.1. Synthesis of Palladium PEPPSI Complexes

A pressure tube was charged with benzimidazolium salt **2** (1 mmol), palladium chloride (1 mmol, 0.18 g), potassium carbonate (4.34 mmol, 0.6 g) and pyridine (3 ml). The mixture was stirred at 80°C for 12 h. After the end of the reaction, the mixture was cooled down to room temperature, then diluted with DCM and filtered through a silica column, eluting with dichloromethane. The DCM was removed under reduced pressure and the crude product was washed with hexane (2 × 10 ml) to remove excess pyridine and dried under vacuum. The yellow solid was crystallized from DCM/hexane (1: 3) for further purification [2]

Dichloro[2-(methoxyethyl)-3-(2,3,4,5,6-pentamethylbenzyl) benzimidazole-2-ylidene]pyridinepalladium(II) **(3a)** Yield: 88%, $C_{27}H_{33}N_3OCl_2Pd$, M= 592.9 g mol^{-1}, M.p. 243.9 °C. $\nu_{(CN)}$= 1447.16 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.25 (s, 6H, $CH_{3(a,e)}$), 2.32 (s, 6H, $CH_{3(b,d)}$), 2.34 (s, 3H, $CH_{3(c)}$), 3.38 (s, 3H, $CH_{3(4')}$), 4.23 (t, 2H, $H_{2'}$), 5.13 (t, 2H, $H_{1'}$), 6.26 (s, 2H, $H_{1''}$), 6.44 (d, 1H, H_4), 6.97 (t, 1H, H_5), 7.18 (t, 1H, H_6), 7.39 (t, 2H, $H_{3''',5'''}$), 7.54 (d, 1H, H_7), 7.81 (t, 1H, $H_{4'''}$), 8.98 (d, 2H, $H_{2''',6'''}$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 16.92 ($C_{a,e}$), 17.29 (C_c), 17.49 ($C_{b,d}$), 48.61 ($C_{1'}$), 51.15 ($C_{1''}$), 59.21 ($C_{4'}$), 71.98 ($C_{2'}$), 111.28 ($C_{4,7}$), 122.67 ($C_{3''',5'''}$), 123.02 ($C_{5,6}$), 124.45 ($C_{4'',6''}$), 127.80 ($C_{5''}$), 133.14 ($C_{8,9}$), 134.7 ($C_{3'',7''}$), 135.9 ($C_{4'''}$), 138.1 ($C_{2''}$), 151.2 ($C_{2''',6'''}$), 163.27 (C_2). Anal. Calc. for $C_{27}H_{33}N_3OCl_2Pd$ (%): C, 54.70; H, 5.61; N, 7.09. Found (%): C, 54.78; H, 5.73; N, 7.21. HR-MS(ESI), m/z= 468,1243 $[M+Na+H]^+$ (Calc. for $C_{22}H_{28}N_2OPdNa$: 468,1217).

Dichloro[2-(methoxyethyl)-3-(2,4,6-trimethylbenzyl)benzimidazole-2-ylidene]pyridinepalladium(II) **(3b)** Yield: 82%, $C_{25}H_{29}N_3OCl_2Pd$, M= 564.9 g mol^{-1}, M.p. 215.5 °C. $\nu_{(CN)}$= 1448.80 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.26 (s, 9H, $CH_{3(a,b,c)}$), 3.28 (s, 3H, $CH_{3(4')}$), 4.14 (t, 2H, $H_{2'}$), 5.04 (t, 2H, $H_{1'}$), 6.11 (s, 2H, $H_{1''}$), 6.39 (d, 1H, H_4), 6.86 (s, 2H, $H_{4'',6''}$), 6.89 (t, 1H, H_5), 7.10 (t, 1H, H_6), 7.31 (t, 2H, $H_{3''',5'''}$), 7.47 (d, 1H, H_7), 7.72 (t, 1H, $H_{4'''}$), 8.91 (d, 2H, $H_{2''',6'''}$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm)

Dichloro[2-(methoxyethyl)-3-(3,5-dimethylbenzyl)benzimidazole-2-ylidene]pyridinepalladium(II) **(3c)** Yield: 88%, $C_{24}H_{27}N_3OCl_2Pd$, M= 550.8 g mol^{-1}, M.p. 205.5 °C. $\nu_{(CN)}$= 1445.58 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.21 (s, 6H, $CH_{3(a,b)}$), 3.30 (s, 3H, $CH_{3(4')}$), 4.16 (m, 2H, $H_{2'}$), 5.03 (d, 2H, $H_{1'}$), 5.99 (m, 2H, $H_{1''}$), 6.86 (s, 1H, H_4), 7.05 (m, 2H, $H_{5,6}$), 7.15, (s, 2H, $H_{3'',7''}$), 7.19 (s, 1H, $H_{5''}$), 7.28 (m, 2H, $H_{3''',5'''}$), 7.48 (d, 1H, H_7), 7.70 (m, 1H, $H_{4'''}$), 8.95 (m, 2H, $H_{2''',6'''}$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 21.27 ($C_{a,b}$), 48.76 ($C_{1'}$), 53.31 ($C_{1''}$), 59.20 ($C_{4'}$) 71.69 ($C_{2'}$), 111.22 (C_7), 111.52 (C_4), 123.09 ($C_{3''',5'''}$), 124.56 ($C_{5,6}$), 125.86 ($C_{3'',7''}$), 129.82 ($C_{5''}$), 134.25 (C_8), 134.82 (C_9), 135.90 ($C_{2''}$), 138.07 ($C_{4'''}$), 138.41 ($C_{4'',6''}$), 152.05 ($C_{2''',6'''}$), 163.37 (C_2). Anal. Calc. for $C_{24}H_{29}N_3OCl_2Pd$ (%): C, 52.33; H, 4.94; N, 7.63. Found (%): C, 52.39; H, 5.01; N, 7.95. HR-MS(ESI), m/z= 571,6105 $[M+Na-H]^+$ (Calc. for $C_{24}H_{27}N_3OCl_2PdNa$: 571,0385); m/z= 426,0798 $[M+Na+H]^+$ (Calc. for $C_{19}H_{22}N_2OPdNa$: 426,0786).

Dichloro[2-(methoxyethyl)-3-(4-methylbenzyl)benzimidazole-2-ylidene]pyridinepalladium(II) **(3d)** Yield: 86%, $C_{23}H_{25}N_3OCl_2Pd$, M= 536.8 g mol^{-1}, M.p. 200.7 °C. $\nu_{(CN)}$= 1446.03 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.10 (s, 3H, $CH_{3(a)}$), 3.30 (s, 3H, $CH_{3(4')}$), 4.16 (s, 2H, $H_{2'}$), 5.02 (m, 2H, $H_{1'}$), 6.06 (s, 2H, $H_{1''}$), 7.0 (m, 3H, $H_{4,5,6}$), 7.10 (t, 2H, $H_{3'',7''}$), 7.28 (m, 2H, $H_{4'',6''}$), 7.38 (dd, 2H, $H_{3''',5'''}$), 7.48 (d, 1H, H_7), 7.70 (m, 1H, $H_{4'''}$), 8.97 (m, 2H, $H_{2''',6'''}$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 21.21 (C_a), 48.92 ($C_{1'}$), 53.54 ($C_{1''}$), 59.19 ($C_{4'}$), 71.40 ($C_{2'}$), 111.32 (C_7), 111.54 (C_4), 123.04 ($C_{3''',5'''}$), 124.59 ($C_{5,6}$), 128.02 ($C_{3'',7''}$), 129.50 ($C_{4'',6''}$), 131.80 ($C_{8,9}$), 134.22 ($C_{5''}$), 136.04 ($C_{2''}$), 137.89 ($C_{4'''}$), 152.66 ($C_{2''',6'''}$), 163.09 (C_2). Anal. Calc. for $C_{23}H_{25}N_3OCl_2Pd$ (%): C, 51.46; H, 4.69; N, 7.83. Found (%): C, 51.54; H, 4.76; N, 7.95%. HR-MS(ESI), m/z= 467,1327 $[M+2H]^+$ (Calc. for $C_{23}H_{25}N_3OPd$: 467,1189); m/z= 464,1175 $[M-H]^+$ (Calc. for $C_{23}H_{25}N_3OPd$: 464,0954).

Dichloro[2-(methoxyethyl)-3-(2,3,4,5,6-pentamethylbenzyl)-5,6-dimethylbenzimidazole-2-ylidene]pyridinepalladium(II) **(3e)** Yield: 81%, $C_{29}H_{37}N_3OCl_2Pd$, M= 620,9 g mol^{-1}, M.p. 206.5 °C. $\nu_{(CN)}$= 1449.03 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.02 (s, 3H, $CH_{3(e)}$), 2.15 (s, 6H, $CH_{3(c,g)}$), 2.22 (s, 9H, $CH_{3(a,d,f)}$), 2.24 (s, 3H, $CH_{3(b)}$), 3.30 (s, 3H, $CH_{3(4')}$), 4.12 (t, 2H, $H_{2'}$), 4.96 (t, 2H, $H_{1'}$), 6.04 (s, 2H, $H_{1''}$), 6.18

(s, 1H, H_4), 7.18 (s, 1H, H_7), 7.27 (d, 2H, $H_{3''',5'''}$), 7.70 (t, 1H, $H_{4'''}$), 8.83 (d, 2H, $H_{2''',6'''}$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 16.89 ($C_{c,g}$), 17.24 (C_e), 17.52 ($C_{d,f}$), 20.19 (C_a), 20.44 (C_b), 48.35 ($C_{1'}$), 50.43 ($C_{1''}$), 59.23 ($C_{4'}$), 71.91 ($C_{2'}$), 111.29 (C_7), 111.60 (C_4), 124.36 ($C_{3''',5'''}$), 128.22 (C_8), 131.80 (C_9), 133.03 ($C_{4'',6''}$), 133.27 ($C_{5''}$), 134.10 ($C_{5,6}$), 134.76 ($C_{3'',7''}$), 135.68 ($C_{2''}$), 137.96 ($C_{4'''}$), 151.15 ($C_{2''',6'''}$), 160.88 (C_2). Anal. Calc. for $C_{29}H_{37}N_3OCl_2Pd$ (%): C, 56.09; H, 6.01; N, 6.77. Found (%): C, 56.15; H, 6.10; N, 6.91. HR-MS(ESI), m/z= 494,1506 $[M+Na+H]^+$ (Calc. for $C_{24}H_{32}N_2OPdNa$: 494,1525).

Dichloro[2-(methoxyethyl)-3-(2,4,6-trimethylbenzyl)-5,6-dimethylbenzimidazole-2-ylidene]pyridinepalladium(II) **(3f)** Yield: 79%, $C_{27}H_{33}N_3OCl_2Pd$, M= 592.9 g mol^{-1}, M.p. 208.9 °C. $\nu_{(CN)}$= 1410.35 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.03 (s, 3H, $CH_{3(a)}$), 2.22 (s, 3H, $CH_{3(b)}$), 2.26 (s, 6H, $CH_{3(c,e)}$), 2.26 (s, 3H, $CH_{3(d)}$), 3.29 (s, 3H, $CH_{3(4')}$), 4.13 (t, 2H, $H_{2'}$), 4.96 (t, 2H, $H_{1'}$), 6.01 (s, 2H, $H_{1''}$), 6.19 (s, 1H, H_4), 6.85 (s, 2H, $H_{4'',6''}$), 7.19 (s, 2H, $H_{3''',5'''}$), 7.29 (t, 1H, H_7), 7.71 (t, 1H, $H_{4'''}$), 8.89 (d, 2H, $H_{2''',6'''}$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 20.20 (C_a), 20.42 (C_b), 20.79 ($C_{c,e}$), 21.07 (C_d), 48.30 ($C_{1'}$), 49.54 ($C_{1''}$), 59.24 ($C_{4'}$), 71.94 ($C_{2'}$), 111.36 (C_7), 111.46 (C_4), 124.44 ($C_{3''',5'''}$), 127.88 ($C_{4'',6''}$), 129.48 (C_8) 131.99 (C_9), 133.01 ($C_{5,6}$), 134.15 ($C_{5''}$), 138.06 ($C_{3'',7''}$), 138.39 ($C_{4'''}$), 138.89 ($C_{2''}$), 151.25 ($C_{2''',6'''}$), 161.15 (C_2). Anal. Calc. for $C_{27}H_{33}N_3OCl_2Pd$ (%): C, 54.70; H, 5.61; N, 7.09. Found (%): C, 54.75; H, 5.69; N, 7.21. HR-MS(ESI), m/z= 637,5322 $[M+2Na]^+$ (Calc. for $C_{27}H_{33}Cl_2N_3OPdNa_2$: 637,0831); m/z= 489,1196 $[M+2Na+H]^+$ (Calc. for $C_{22}H_{28}N_2OPdNa_2$: 489,1110); m/z= 468,1246 $[M+Na+H]^+$ (Calc. for $C_{22}H_{28}N_2OPdNa$: 468,1217).

Dichloro[2-(methoxyethyl)-3-(3,5-dimethylbenzyl)-5,6-dimethylbenzimidazole-2-ylidene]pyridinepalladium(II) **(3g)** Yield: 87%, $C_{26}H_{31}N_3OCl_2Pd$, M= 578.9 g mol^{-1}, M.p. 233.5 °C. $\nu_{(CN)}$= 1445.47 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.23 (s, 3H, $CH_{3(a)}$), 2.28 (s, 6H, $CH_{3(c,d)}$), 2.33 (s, 3H, $CH_{3(b)}$), 3.39 (s, 3H, $CH_{3(4')}$), 4.22 (t, 2H, $H_{2'}$), 5.01 (t, 2H, $H_{1'}$), 5.99 (m, 2H, $H_{1''}$), 6.85 (s, 1H, H_4), 6.93 (s, 1H, $H_{5''}$), 7.20 (s, 2H, $H_{3'',7''}$), 7.30 (s, 1H, H_7), 7.33 (m, 2H, $H_{3''',5'''}$), 7.76 (m, 1H, $H_{4'''}$), 9.02 (m, 2H, $H_{2''',6'''}$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 20.35 ($C_{a,b}$), 21.27 ($C_{c,d}$), 48.63 ($C_{1'}$), 53.16 ($C_{1''}$), 59.23 ($C_{4'}$), 71.37 ($C_{2'}$), 111.42 (C_7), 111.60 (C_4), 124.52 ($C_{3''',5'''}$), 125.75 ($C_{3'',7''}$), 129.65 ($C_{5''}$), 132.19 (C_8), 133.03 (C_9), 134.50 ($C_{5,6}$), 135.01 ($C_{2''}$), 137.88 ($C_{4'''}$), 138.28 ($C_{4'',6''}$), 152.67 ($C_{2''',6'''}$), 160.82 (C_2). Anal. Calc. for $C_{26}H_{31}N_3OCl_2Pd$ (%): C, 53.95; H, 5.40; N, 7.26. Found (%): C, 54.01; H, 5.48; N, 7.33. HR-MS(ESI), m/z= 1102,3491 $[2M+4Na]^+$ (Calc. for $C_{52}H_{58}N_6O_2Pd_2Na_4$: 1102,2282); m/z= 507,0180 $[M]^+$ (Calc. for $C_{26}H_{31}N_3OPd$: 507,1502); m/z= 509,0369 $[M+2H]^+$ (Calc. for $C_{26}H_{31}N_3OPd$: 509,1506).

Dichloro[2-(methoxyethyl)-3-(4-methylbenzyl)-5,6-dimethylbenzimidazole-2-ylidene]pyridinepalladium(II) **(3h)** Yield: 75%, $C_{25}H_{29}N_3OCl_2Pd$, M= 564.9 g mol^{-1}, M.p. 225.6 °C. $\nu_{(CN)}$= 1445.91 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.21 (s, 3H, $CH_{3(c)}$), 2.25 (s, 6H, $CH_{3(a,b)}$), 3.32 (s, 3H, $CH_{3(4')}$), 4.14 (t, 2H, $H_{2'}$), 4.95 (t, 2H, $H_{1'}$), 6.04 (m, 2H, $H_{1''}$), 7.10 (m, 2H, $H_{3'',7''}$), 7.19 (s, 1H, H_4), 7.22 (s, 1H, H_7), 7.36 (m, 2H, $H_{4'',6''}$), 7.40 (m, 2H, $H_{3''',5'''}$), 7.68 (m, 1H, $H_{4'''}$), 8.96 (m, 2H, $H_{2''',6'''}$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 20.27 ($C_{a,b}$), 21.21 (C_c) 48.45 ($C_{1'}$), 53.0 ($C_{1''}$), 59.24 ($C_{4'}$), 71.59 ($C_{2'}$), 111.45 (C_7), 111.61 (C_4), 124.53 ($C_{3''',5'''}$), 127.85 ($C_{3'',7''}$), 129.45 ($C_{4'',6''}$), 132.19 (C_8), 132.74 (C_9), 134.46 ($C_{5,6}$), 138.01 ($C_{5''}$), 151.29 ($C_{2''}$), 152.05 ($C_{4'''}$), 152.66 ($C_{2''',6'''}$), 161.04 (C_2). Anal. Calc. for $C_{25}H_{29}N_3OCl_2Pd$ (%): C, 53.16; H, 5.17; N, 7.44. Found (%): C, 53.22; H, 5.24; N, 7.53. HR-MS(ESI), m/z= 560,3253 $[M-3H]^+$ (Calc. for $C_{25}H_{29}N_3OPdCl_2$: 560,0488); m/z= 415,0857 $[M+H]^+$ (Calc. for $C_{20}H_{24}N_2OPd$: 415,1002); m/z= 440,0926 $[M+Na+2H]^+$ (Calc. for $C_{20}H_{24}N_2OPdNa$: 440,1056).

Dichloro[2-(methoxyethyl)-3-(4-tert-butylbenzyl)-5,6-dimethylbenzimidazole-2-ylidene]pyridinepalladium(II) **(3i)** Yield: 79%, $C_{28}H_{35}N_3OCl_2Pd$, M= 606.9 g mol^{-1}, M.p. 174.8 °C. $\nu_{(CN)}$= 1448.41 cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.22 (s, 9H, $CH_{3(c,d,e)}$), 2.15 (s, 3H, $CH_{3(a)}$), 2.25 (s, 3H, $CH_{3(b)}$), 3.31 (s, 3H, $CH_{3(4')}$), 4.15 (t, 2H, $H_{2'}$), 4.96 (t, 2H, $H_{1'}$), 5.99 (m, 2H, $H_{1''}$), 6.76 (m, 1H, H_4), 7.19 (s, 2H, $H_{3'',7''}$), 7.26 (m, 2H, $H_{4'',6''}$), 7.31 (s, 1H, H_7), 7,43 (d, 2H, $H_{3''',5'''}$), 7.69 (s, 1H, $H_{4'''}$), 8.96 (m, 2H, $H_{2''',6'''}$). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 20.22 ($C_{a,b}$), 31.33 ($C_{c,d,e}$), 34.57 ($C_{8'}$), 48.47 ($C_{1'}$), 52.91 ($C_{1''}$), 59.24 ($C_{4'}$), 71.61 ($C_{2'}$), 111.51 (C_7), 111.60 (C_4), 124.52 ($C_{3''',5'''}$), 125.71 ($C_{4'',6''}$), 127.68 ($C_{3'',7''}$), 132.17 (C_8), 132.77 (C_9), 134.46 ($C_{5,6}$), 138.00 ($C_{2''}$), 151.29 ($C_{4'''}$), 152.06 ($C_{5''}$), 1152.66 ($C_{2''',6'''}$), 161.02 (C_2). Anal. Calc. for $C_{28}H_{35}N_3OCl_2Pd$ (%): C, 55.41; H, 5.81; N, 6.92. Found (%): C, 55.47; H, 5.87; N, 7.03. HR-MS(ESI), m/z= 455,1254 $[M-H]^+$ (Calc. for $C_{23}H_{30}N_2OPd$: 455,1315).

3.2. Synthesis of Palladium Triphenylphosphine Complexes

A solution of the palladium-PEPPSI complexes **3** (1 mmol) and PPh_3 (1.2 mmol, 0.314 g) in dried dichloromethane (30 ml) were stirred at room temperature for 48 h. The solvent of the solution was evaporated under reduced pressure and the white product obtained was washed with hexane (20 ml) and then recrystallized in a DCM/hexane mixture [2].

Dichloro[2-(methoxyethyl)-3-(2,3,4,5,6-pentamethylbenzyl)benzimidazole-2-ylidene]triphenylphosphine palladium(II) **(4a)** Yield: 49%, $C_{40}H_{43}N_2OCl_2PPd$, M= 776.1 g mol^{-1}, M.p. 290.5 °C. $\nu_{(CN)}$= 1389.93 cm^{-1}. [Found: C, 62.01; H, 5.69; N, 3.75. Calc. for $C_{40}H_{43}N_2Cl_2OPPd$: C, 61.90; H, 5.58; N, 3.61 %]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.89 (s, 6H, $CH_{3(a,e)}$), 2.12 (s, 6H, $CH_{3(b,d)}$), 2.21 (s, 3H, $CH_{3(c)}$), 3.03 (s, 3H, $CH_{3(4')}$), 3.42 (s, 1H, $H_{2'}$), 3.81 (m, 2H, $H_{1',2'}$), 4.31 (m, 1H, $H_{1'}$) 4.61 (m, 1H, $H_{1''}$), 4.91 (d, 1H, $H_{1''}$), 5.79 (d, 1H, H_4), 6.42 (d, 1H, H_5), 6.70 (t, 1H, H_6), 6.99 (t, 1H, H_7), 7.15-7.52 (m, 15H, H_{ph}). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 16.88 ($C_{a,e}$), 17.31 ($C_{b,c,d}$), 48.64 ($C_{1'}$), 51.42 ($C_{1''}$), 58.75 ($C_{4'}$), 70.73 ($C_{2'}$), 111.16 (C_7), 111.42 (C_4), 122.59 (C_6), 123.08 (C_5), 126.75, 128.51 and 128.62 (C_{ph}), 131.24 ($C_{4'',5'',6''}$), 133.14 ($C_{3'',7''}$), 134.47 ($C_{8,9}$), 135.36 ($C_{1''',1''',1''''}$), 136.48 ($C_{2''}$), 174.06 (C_2). ^{31}P NMR ($CDCl_3$, 162 MHz) δ (ppm) 26.7 (P_{PPh3}). HRMS (ESI): [M-2Cl+Na+H^-]$^-$, Found 730,2054. [$C_{40}H_{43}N_2OPPd$+Na+H^-] requires 730,2128; [M+Na+2H^-], (m/z) found 467,1352 [$C_{22}H_{28}N_2OPd$+Na+2H^-]$^-$ requires 467,1138.

Dichloro[2-(methoxyethyl)-3-(2,4,6-trimethylbenzyl)benzimidazole-2-ylidene] triphenylphosphine palladium (II) **(4b)** Yield: 45%, $C_{38}H_{39}N_2Cl_2OPPd$, M= 748 g mol^{-1}, M.p. 271.3 °C. ν(CN)= 1434.98 cm^{-1}. [Found: C, 61.09; H, 5.31; N, 3.79. requires $C_{38}H_{39}N_2Cl_2OPPd$: C, 61.01; H, 5.26; N, 3.74 %]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm): 2.01 (s, 6H, $CH_{3(a,c)}$), 2.29 (s, 3H, $CH_{3(b)}$), 3.06 (s, 3H, $CH_{3(4')}$), 3.87 (m, 2H, $H_{2'}$), 4.49 (m, 1H, $H_{1'}$), 4.70 (m, 2H, $H_{1',1''}$), 5.79 (d, 1H, $H_{1''}$), 5.89 (d, 1H, H_4), 6.44 (d, 1H, H_5), 6.80 (t, 1H, H_6), 6.84 (s, 2H, $H_{4'',6''}$), 7.08 (t, 1H, H_7), 7.22-7.57 (m, 15H, H_{ph}). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 20.77 ($C_{a,c}$), 21.05 (C_b), 48.70 ($C_{1'}$), 49.88 ($C_{1''}$), 58.69 ($C_{4'}$), 70.80 ($C_{2'}$), 111.12 (C_7), 111.30 (C_4), 122.77 (C_6) , 123.09 (C_5), 126.41 ($C_{4'',6''}$), 128.49 and 128.60 (C_{ph}), 129.55 ($C_{8,9}$), 131.24 ($C_{5''}$), 134.10 ($C_{3'',7''}$), 135.70 ($C_{1''',1''',1''''}$), 139.02 ($C_{2''}$), 174.18 (C_2). ^{31}P NMR ($CDCl_3$, 162 MHz) δ (ppm) 26.6 (P_{PPh3}). HRMS (ESI): [M-2Cl+Na+H^-]$^-$, found 702,1861. $C_{38}H_{39}N_2OPPd$+Na+H^- requires 702,1815.

Dichloro[2-(methoxyethyl)-3-(3,5-dimethylbenzyl)benzimidazole-2-ylidene]triphenylphosphine palladium(II) **(4c)** Yield: 42%, $C_{37}H_{37}N_2Cl_2OPPd$, M= 734 g mol^{-1}, M.p. 300.2 °C. $\nu_{(CN)}$= 1432.38 cm^{-1}. [Found: C, 60.61; H, 5.14; N, 3.94. requires $C_{37}H_{37}N_2Cl_2OPPd$: C, 60.54; H, 5.08; N, 3.82 %]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.16 (s, 6H, $CH_{3(a,b)}$), 3.06 (s, 3H, $CH_{3(4')}$), 3.87 (m, 2H, $H_{2'}$), 4.06 (m, 1H, $H_{1'}$), 4.65 (m, 2H, $H_{1',1''}$), 6.05 (m, 1H, $H_{1''}$), 6.68 (d, 1H, H_4), 6.80 (s, 1H, H_5), 6.93 (t, 1H, H_6), 7.07 (t, 3H, $H_{3'',5'',7''}$), 7.20 (s, 1H, H_7), 7.14-7.49 (m, 15H, C_{ph}). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 21.17 ($C_{a,b}$), 49.07 ($C_{1'}$), 53.45 ($C_{1''}$), 58.57 ($C_{4'}$), 70.47 ($C_{2'}$), 111.48 ($C_{4,7}$), 122.92 (C_7), 123.07 (C_4), 126.32 ($C_{3'',7''}$), 128.42 ($C_{5''}$), 130.13 and 131.17 (C_{ph}), 133.63 ($C_{8,9}$), 134.31 ($C_{4'',6''}$), 136.18 ($C_{1''',1''',1''''}$), 138.39 ($C_{2''}$), 174.10 (C_2). ^{31}P NMR ($CDCl_3$, 162 MHz) δ (ppm) 25.4 (P_{PPh3}). HRMS (ESI): [M-2Cl+Na+H^-]$^-$, found 686,1545. $C_{37}H_{37}N_2OPPd$+Na+H^- requires 686,1776.

Dichloro[2-(methoxyethyl)-3-(4-methylbenzyl)benzimidazole-2-ylidene]triphenylphosphine palladium(II) **(4d)** Yield: 40%, $C_{36}H_{35}N_2Cl_2OPPd$, M= 720 g mol^{-1}, M.p. 236.4 °C. $\nu_{(CN)}$= 1434.71 cm^{-1}. [Found: C, 60.11; H, 5.03; N, 4.04. requires $C_{36}H_{35}N_2Cl_2OPPd$: C, 60.06; H, 4.90; N, 3.89 %]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.26 (s, 3H, $CH_{3(a)}$), 3.09 (s, 3H, $CH_{3(4')}$), 3.88 (t, 2H, $H_{2'}$), 4.43 (m, 2H, $H_{1'}$), 4.73 (m, 2H, $H_{1''}$), 6.19 (m, 2H, $H_{5,6}$), 6.77 (m, 2H, $H_{4,7}$), 7.01 (s, 4H, $H_{3'',4'',6'',7''}$), 7.20-7.55 (m, 15H, H_{ph}). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 21.17 (C_a), 48.96 ($C_{1'}$), 53.07 ($C_{1''}$), 58.67 ($C_{4'}$), 70.42 ($C_{2'}$), 111.48 (C_7), 111.70 (C_4), 122.91 (C_6), 123.02 (C_5), 128.50 ($C_{3'',7''}$), 129.43 ($C_{4'',6''}$), 131.13 and 132.05 (C_{ph}), 133.64 (C_8), 133.83 (C_9), 134.27 ($C_{5''}$), 135.94 ($C_{1''',1''',1''''}$), 138.20 ($C_{2''}$), 174.16 (C_2). ^{31}P NMR ($CDCl_3$, 162 MHz) δ (ppm) 26.0 (P_{PPh3}). HRMS (ESI): [M-2Cl+Na+H^-]$^-$, found 671,1496. $C_{36}H_{35}N_2OPPd$+Na+H^- requires 671,1420.

Dichloro[2-(methoxyethyl)-3-(2,4,6-trimethylbenzyl)-5,6-dimethylbenzimidazole-2-ylidene]triphenylphosphine palladium(II) **(4e)** Yield: 48%, $C_{40}H_{43}N_2Cl_2OPPd$, M= 776.1 g mol^{-1}, M.p. 294.6 °C. $\nu_{(CN)}$= 1435.95 cm^{-1}. [Found: C, 61.97; H, 5.63; N, 3.69. requires $C_{40}H_{43}N_2Cl_2OPPd$: C, 61.90; H, 5.58; N, 3.61 %]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.88 (s, 3H, $CH_{3(d)}$), 1.93 (s, 6H $CH_{3(c,e)}$), 2.15 (s, 3H, $CH_{3(b)}$), 2.23 (s, 3H, $CH_{3(a)}$), 3.01 (s, 3H, $CH_{3(4')}$), 3.76 (m, 1H, $H_{2'}$), 3.85 (m, 1H, $H_{2'}$), 4.32 (m, 1H, $H_{1'}$), 4.52 (m, 1H, $H_{1'}$), 4.59 (m, 1H, $H_{1''}$), 6.29 (m, 1H, $H_{1''}$), 6.77 (s, 2H, $H_{4'',6''}$), 6.95 (s, 1H, H_4), 7.19 (s, 1H, H_7), 7.16-7.48 (m, 15H, H_{ph}). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 20.19 (C_a), 20.43 (C_b), 20.74 ($C_{c,e}$),

21.03 (C_d), 48.37 ($C_{1'}$), 49.66 ($C_{1''}$), 58.73 ($C_{4'}$), 70.69 ($C_{2'}$), 111.16 (C_7), 111.49 (C_4), 126.70 ($C_{4'',6''}$), 128.47 and 128.58 (C_{ph}), 129.34 ($C_{8,9}$), 131.17 ($C_{5,6}$), 131.97 ($C_{5''}$), 132.76 ($C_{3'',7''}$), 134.21 ($C_{1''',1'''',1'''''}$), 138.92 ($C_{2''}$), 171.84 (C_2). RMN ^{31}P ($CDCl_3$, 162 MHz) δ (ppm): 26.7 (P_{PPh3}). HRMS (ESI): [M-2Cl+Na+2H$^-$]$^-$, found 731,4385. $C_{40}H_{43}N_2OPPd$+Na+2H$^-$ requires 731,2206; [M+Na+H$^-$]$^-$, (m/z) found 468,1233. [$C_{22}H_{30}N_2OPd$+Na+H$^-$]$^-$ requires 468,1369.

Dichloro[2-(methoxyethyl)-3-(3,5-dimethylbenzyl)-5,6-dimethylbenzimidazole-2-ylidene]triphenylphosphine palladium(II) **(4f)** Yield: 42%, $C_{39}H_{41}N_2Cl_2OPPd$, M= 762.1 g mol^{-1}, M.p. 297.6 °C. $\nu_{(CN)}$= 1434.39 cm^{-1}. [Found: C, 61.56; H, 5.49; N, 3.77. requires $C_{39}H_{41}N_2Cl_2OPPd$: C, 61.47; H, 5.42; N, 3.68 %]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.16 (s, 3H, $CH_{3(a)}$), 2.23 (s, 6H, $CH_{3(c,d)}$), 2.28 (s, 3H, $CH_{3(b)}$), 3.09 (s, 3H, $CH_{3(4')}$), 3.82 (m, 2H, $H_{2'}$), 4.12 (m, 1H, $H_{1'}$), 4.65 (m, 2H, $H_{1,1''}$), 6.02 (m, 1H, $H_{1''}$), 6.51 (s, 1H, H_4), 6.86 (s, 1H, H_7), 7.11 (s, 3H, $H_{3'',5'',7''}$), 7.21-7.55 (m, 15H, H_{ph}). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 20.29 ($C_{a,b}$), 21.16 ($C_{c,d}$), 48.79 ($C_{1'}$), 52.95 ($C_{1''}$), 58.58 ($C_{4'}$), 70.39 ($C_{2'}$), 111.53 (C_7), 111.57 (C_4), 126.10 ($C_{3'',5'',7''}$), 128.38 and 129.95 (C_{ph}), 131.05 ($C_{8,9}$), 132.04 ($C_{5,6}$), 132.64 ($C_{4'',6''}$), 134.33 ($C_{1''',1'''',1'''''}$), 138.26 ($C_{2''}$), 171.83 (C_2). ^{31}P NMR ($CDCl_3$, 162 MHz) δ (ppm) 25.5 (P_{PPh3}). HRMS (ESI): [M-2Cl+Na+H$^-$]$^-$, found 715,1841. $C_{39}H_{41}N_2OPPd$+Na+H$^-$ requires 715,1893.

Dichloro[2-(methoxyethyl)-3-(4-methylbenzyl)-5,6-dimethylbenzimidazole-2-ylidene]triphenylphosphine palladium(II) **(4g)** Yield: 40%, $C_{38}H_{39}N_2Cl_2OPPd$, M= 748 g mol^{-1}, M.p. 300.6 °C. $\nu_{(CN)}$= 1434.60 cm^{-1}. [Found: C, 61.06; H, 5.32; N, 3.83. requires $C_{38}H_{39}N_2Cl_2OPPd$: C, 61.01; H, 5.26; N, 3.74 %]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 2.17 (s, 3H, $CH_{3(c)}$), 2.27 (s, 6H, $CH_{3(a,b)}$), 3.10 (s, 3H, $CH_{3(4')}$), 3.85 (m, 2H, $H_{2'}$), 4.45 (m, 2H, $H_{1'}$), 4.64 (m, 1H, $H_{1''}$), 6.02 (m, 1H, $H_{1''}$), 6.54 (m, 1H, H_4), 7.01 (m, 2H, $H_{3'',7''}$), 7.06 (m, 1H, H_7), 7.19 (m, 2H, $C_{4'',6''}$), 7.21-7.53 (m, 15H, H_{ph}). ^{13}C NMR ($CDCl_3$, 100 MHz) δ (ppm) 20.27 ($C_{a,b}$), 21.17 (C_c), 48.62 ($C_{1'}$), 52.86 ($C_{1''}$), 58.70 ($C_{4'}$), 70.34 ($C_{2'}$), 111.52 (C_7), 111.63 (C_4), 128.38 ($C_{3'',7''}$), 129.35 ($C_{4'',6''}$), 130.02 and 131.08 (C_{ph}), 132.10 (C_8), 132.16 (C_9), 132.25 ($C_{5,6}$), 132.65 ($C_{5''}$), 134.30 ($C_{1''',1'''',1'''''}$), 137.97 ($C_{2''}$), 171.83 (C_2). ^{31}P NMR ($CDCl_3$, 162 MHz) δ (ppm) 25.2 (P_{PPh3}). HRMS (ESI): [M-2Cl+Na+H$^-$] found 701,1779. $C_{38}H_{39}N_2OPPd$+Na+H$^-$ requires 701,1737.

Dichloro[2-(methoxyethyl)-3-(4-tert-butylbenzyl)-5,6-dimethylbenzimidazole-2-ylidene]triphenylphosphine palladium(II) **(4h)** Yield: 44%, $C_{41}H_{45}N_2Cl_2OPPd$, M= 790.1 g mol^{-1}, M.p. 237.3 °C. $\nu_{(CN)}$= 1434.60 cm^{-1}. [Found: C, 62.41; H, 5.86; N, 3.67. requires $C_{38}H_{39}N_2Cl_2OPPd$: C, 62.33; H, 5.74; N, 3.55 %]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ (ppm) 1.17 (s, 9H, $CH_{3(c,d,e)}$), 2.10 (s, 3H, $CH_{3(a)}$), 2.21 (s, 3H, $CH_{3(b)}$), 3.03 (s, 3H, $CH_{3(4')}$), 3.81 (m, 2H, $H_{2'}$), 4.36 (m, 2H, $H_{1'}$), 4.56 (m, 1H, $H_{1''}$), 5.97 (m, 1H, $H_{1''}$), 6.49 (s, 1H, H_4), 7.0 (s, 1H, H_7), 7.14 (m, 4H, $H_{3'',4'',6'',7''}$), 7.16-7.47 (m, 15H, H_{ph}). ^{13}C NMR($CDCl_3$, 100 MHz) δ (ppm) 20.28 ($C_{a,b}$), 31.26 ($C_{c,d,e}$), 34.54 ($C_{8'}$), 48.70 ($C_{1'}$), 53.45 ($C_{1''}$), 58.71 ($C_{4'}$), 70.36 ($C_{2'}$), 111.57 (C_7), 111.66 (C_4), 125.58 ($C_{3'',7''}$), 128.4 ($C_{4'',6''}$), 129.30, 130.06 and 130.58 (C_{ph}), 131.09 (C_8), 132.10 (C_9), 132.27 ($C_{5,6}$), 132.66 ($C_{2''}$), 134.32 ($C_{1''',1'''',1'''''}$), 151.27 ($C_{5''}$), 171.88 (C_2). ^{31}P NMR ($CDCl_3$, 162 MHz) δ (ppm) 25.4 (P_{PPh3}). HRMS (ESI): [M-2Cl+Na+2H$^-$]$^-$, found 744,9729. $C_{41}H_{45}N_2OPPd$+Na+2H$^-$ requires 744,2240.

4. Biological Activities

4.1. Anticancer Cytotoxicity Activities

The property of the compounds against cancer cells was performed using 3-(4,5-dimethylthiazolyl-2)-2,5-diphenyltetrazolium bromide (MTT) assays against MDA-MB-231 and MCF7 cells according to previously mentioned techniques [3,4]. 96-well plates (Corning, USA) were used for culturing the cells in at a density of 5 × 10^5 cells per well in 200 μL medium and allowed for overnight staying. The compounds were used for treating the cells using various concentrations (10, 5, 2.5, or 1 μg mL^{-1}) then allowed for 48 h incubation. Then each well was received 20 μL of MTT after that the cells were further incubated for 2 h at 37 °C. At the last, the media was removed from each well and replaced by 200 μL 0.1% HCL-MeOH in order to dissolve the crystal of formazan salt. The OD value was read at 490 nm on a microplate reader (Thermo MULTISCAN FC, China). The control cells were treated only with MeOH. The relative cell viability was calculated using the following formula:

Relative cell viability (%) = × OD treated C/OD control 100%

4.2. Antimicrobial Assays

E. coli (ATCC® 10418) and MRSA (ATCC® 3359) were cultivated on nutrient agar plates (HiMedia, India), while potato dextrose agar (HiMedia, India) was used for culturing *C. albicans* (ATCC® 90028) for 24 h at 35°C. For the evaluation the antimicrobial activities of compoundsdisc diffusion assay was applied according to the previous methods [4]. Microorganisms were suspended in sterilized normal saline (0.9%) and the turbidity was adjusted to 0.5 OD using a spectrophotometer (Labomed Inc., USA). Then sterile swab cotton was used for making the inoculum at the surface of the agar plates. Ten µL of compounds at concentration (50 µg/disc) were added to sterile blank discs (6 mm). Commercial tetracycline discs (30 µg per disc) were used as positive controls and methanol as a negative control for comparison. The plates were incubated at 35 °C for 24 h. The diameters of the zones of inhibition produced by the compounds on the test isolates were measured in mm.

4.3. Leishmania Major Cell Isolation, Culture Conditions, and Assays

During the year 2016, L. *major* promastigotes were obtained from indoor male patient and then kept in Schneider's *Drosophila* medium (Invitrogen, USA) at 26°C. Liquid nitrogen was used for parasite cryopreservation with concentration of 3×10^6 parasites mL^{-1}. [5]

L. major promastigotes were cultured in completed RPMI 1640 medium (Invitrogen, USA) for assessing compounds activity. hemocytometer was used for counting the promastigotes then a concentration of 10^6 cells mL^{-1} were cultured on 96-wells plates to yield (200 µL/well). Different concentrations of compounds and control positive AmB (50, 16.6, 5.5, 1.8, 0.6 or 0.2 µg mL^{-1}) were added. While DMSO (1%) was used as negative control. After 72 h incubation at 26 °C. MTT colorimetric assay used for assessing viable promastigotes. ELISA reader (FLUOstar OPTIMA spectrophotometer) at 570 nm was used for obtaining % inhibition of compounds. After that IC_{50} values obtained from triplicate reading [5].

Female BALB/c mice of 45 – 60 days were used for macrophages collection from their peritoneal cavity according to the method described previously [6]. About 5×10^4 cells/well were seeded on 96-well plates in phenol red-free RPMI 1640 medium with 10% FBS for 4 h at 37°C in a 5% CO_2 atmosphere for enhancing the attaching of the cells. Then the medium was removed and followed by washing of the cells with phosphate buffered saline (PBS). Then, a 200 µL solution containing *L. major* promastigotes (at a ratio of 10 promastigotes: 1 macrophage in RPMI 1640 medium with 10% FBS) for each well. The infection and differentiation of amastigotes occurred after 6 h incubation at 37 °C. Then, the infected macrophages were washed with PBS and overlaid with fresh phenol red-free RPMI 1640 medium containing the compounds and control positive AmB (at the final concentrations of 50, 16.6, 5.5, 1.8, 0.6 or 0.2 mL^{-1}) and the cells were incubated for 72 h. DMSO (1%) was used as negative control. Microscopes were used for the evaluation of infected macrophages percentage [5].

4.4. Toxoplasma Gondii Cell Line, Culture Conditions, and Assay

RH tachyzoites strain of *T. gondii* was obtained from Dr. S. El-Ashram (China Agricultural University, Bejing, China) were cultivated using Vero cell line (ATCC® CCL81™, USA). Activity assessment of the compounds was achieved as described previously [7]. Vero cells were seeded in 96-well plates (5×10^3 cells/well in 200 µL RPMI 1640 medium). Then, RPMI 1640 medium with 2% FBS containing tachyzoites (RH strain) of *T. gondii* at a ratio of 5 (parasites): 1 (Vero cells) was added. After incubation at 37 °C and 5% CO_2 for 5 h, the cells were washed with PBS, and then the compounds and atovaquone (ATO) control positive (at final concentrations of 50, 16.6, 5.5, 1.8, 0.6 or 0.2 µg mL^{-1}) were added, and then the cells were allowed for incubation at 37 °C in a humidified 5% CO_2 atmosphere for 72 h. The negative control was treated only with DMSO (1%). Inverted photomicroscope was used for the examination of the and % inhibition was determined and followed by IC_{50} values calculation [8].

4.5. In Vitro Cytotoxicity Assay

Cytotoxicity assessment of the compounds was done by using MTT colorimetric assay as mentioned by OECD guidelines [9]. Ninety six well plates were used for culturing Vero (5×10^3 cells/well/200 μL) for overnight at completed RPMI 1640 medium with 10% FBS and 5% CO_2 at 37 °C. The cells were washed with PBS and treated with the test compounds for 72 h with different concentrations (50, 16.6, 5.5, 1.8, 0.6 or 0.2 μg mL^{-1}) in medium with 10% FBS. The cells those only treated with complete media was used as negative control. Then the supernatant was discarded and 50 μL of RPMI 1640 medium containing 14 μL MTT (5 mg mL^{-1}) was added and allowed for 5 h incubation at room temperature. Followed by discarding the media and MTT while 200 μL DMSO was added for enhancing the solubility of the formazan. A FLUOstar OPTIMA spectrophotometer was used for colorimetric analysis (λ = 540 nm). Cytotoxic effects were expressed by the CC_{50} values (concentrations that caused a 50% reduction in viable cells). Then CC_{50} values were obtained from triplicate reading [5,8].

Complex 3a

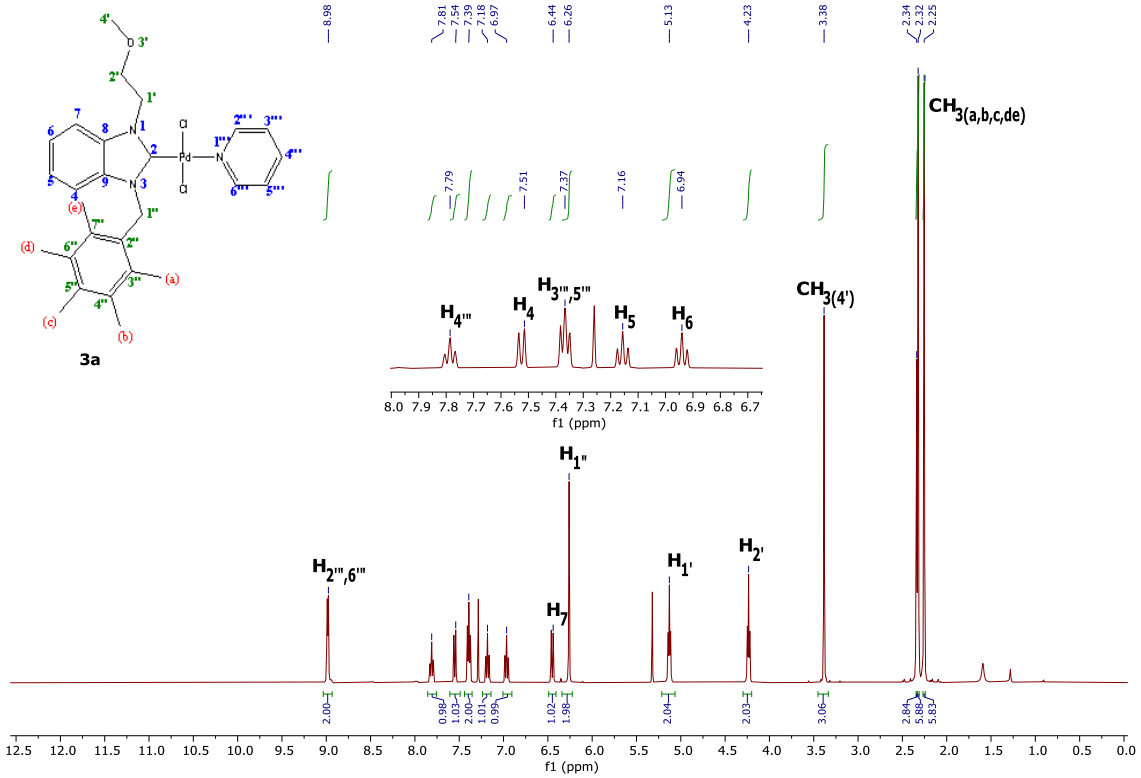


Figure S1. [1]H NMR spectrum of complex 3a in $CDCl_3$.

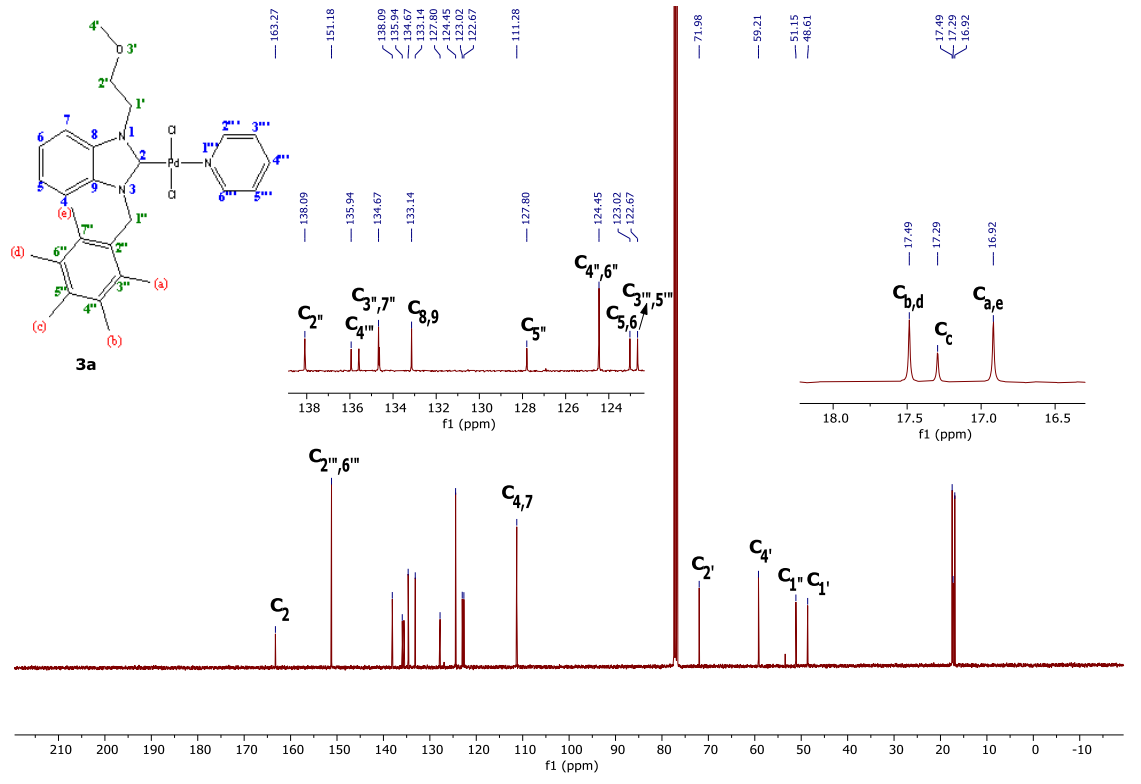


Figure S2. [13]C NMR spectrum of complex 3a in $CDCl_3$.

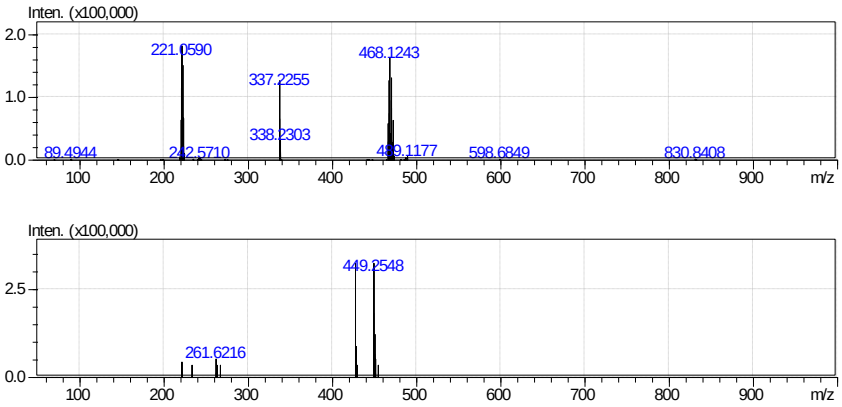


Figure S3. HRMS spectra of complex 3a.

Complex 3b

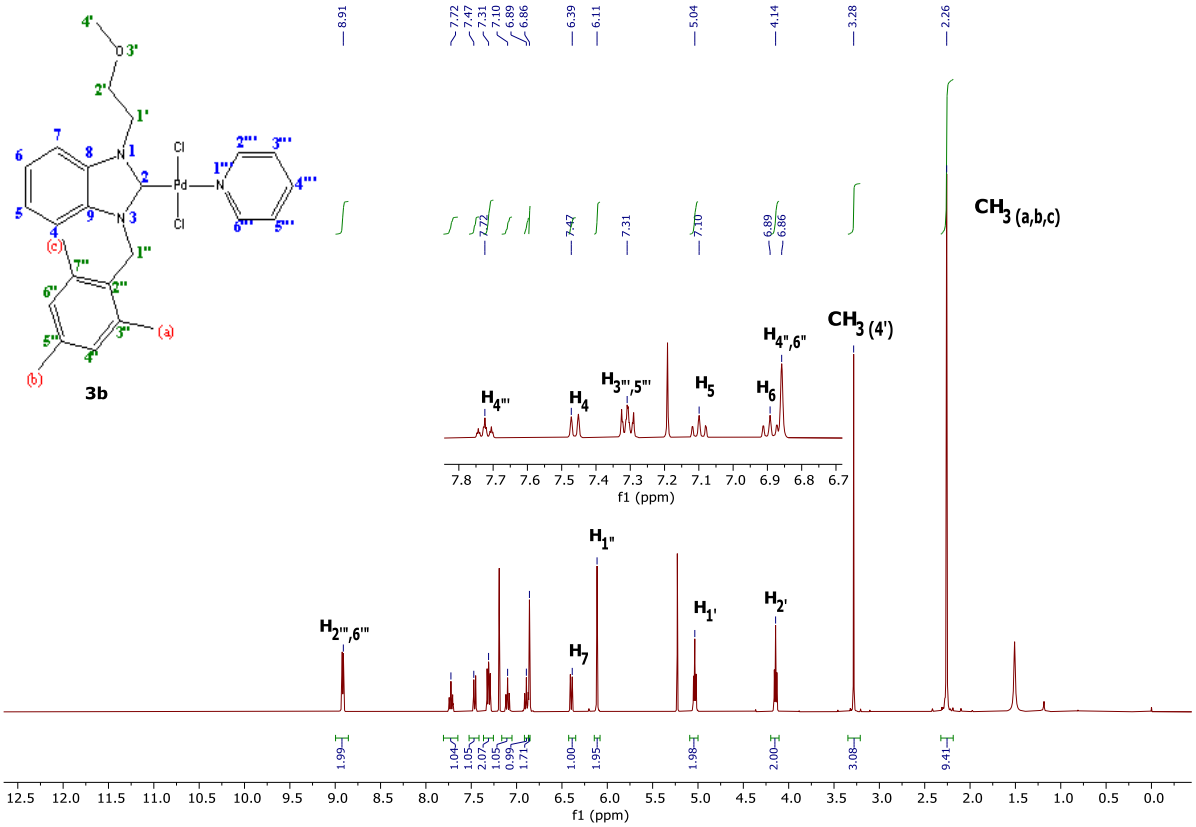


Figure S4. ^{1}H NMR spectrum of complex 3b in $CDCl_3$.

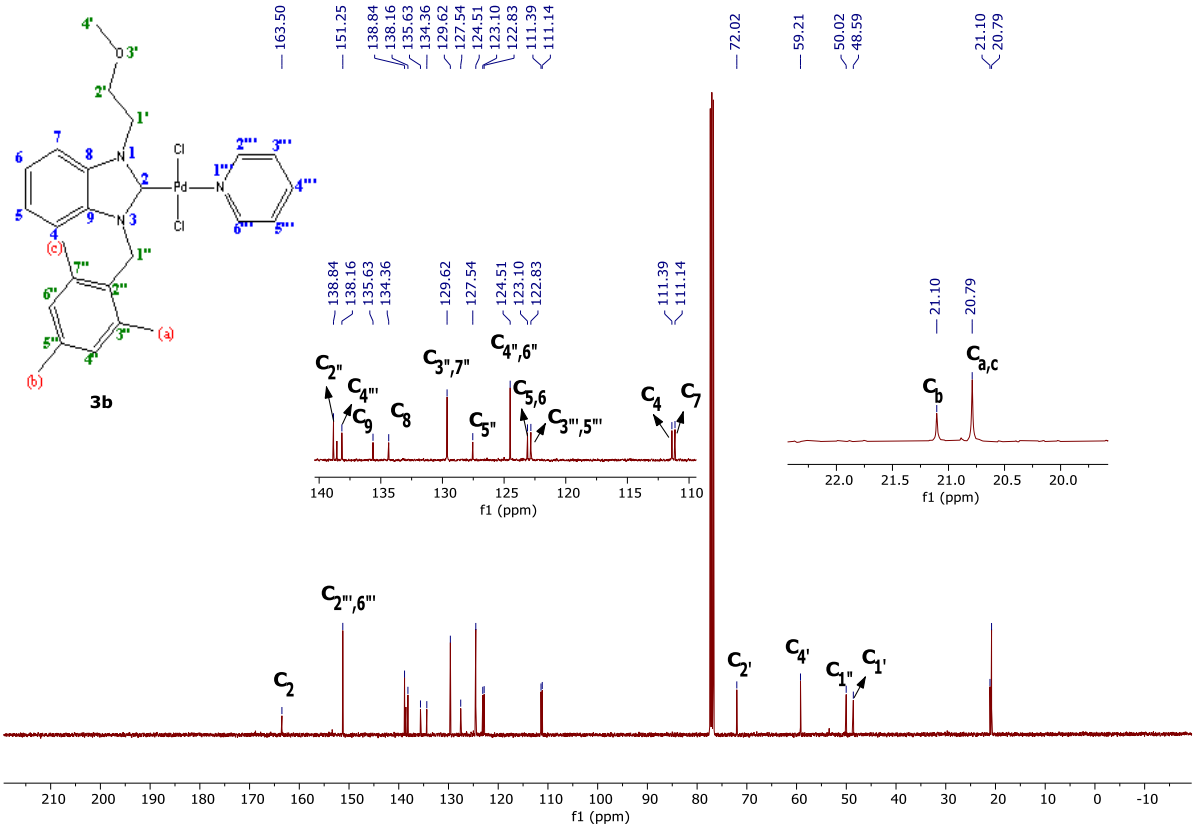


Fig S5. ^{13}C NMR spectrum of complex 3b in $CDCl_3$.

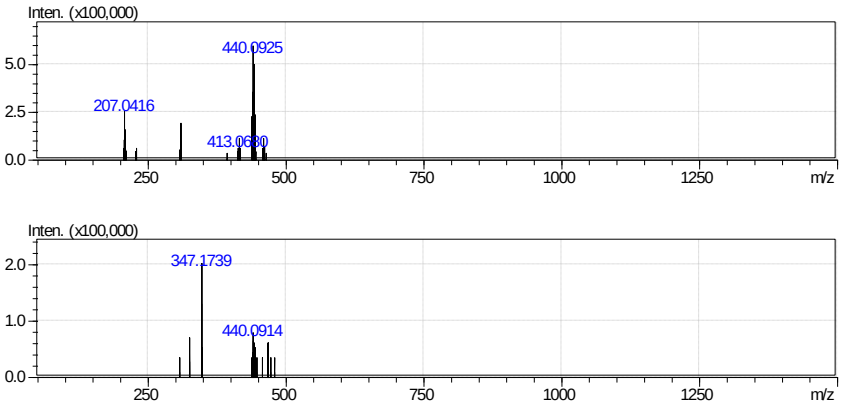


Figure S6. HRMS spectra of complex 3b.

Complex 3c

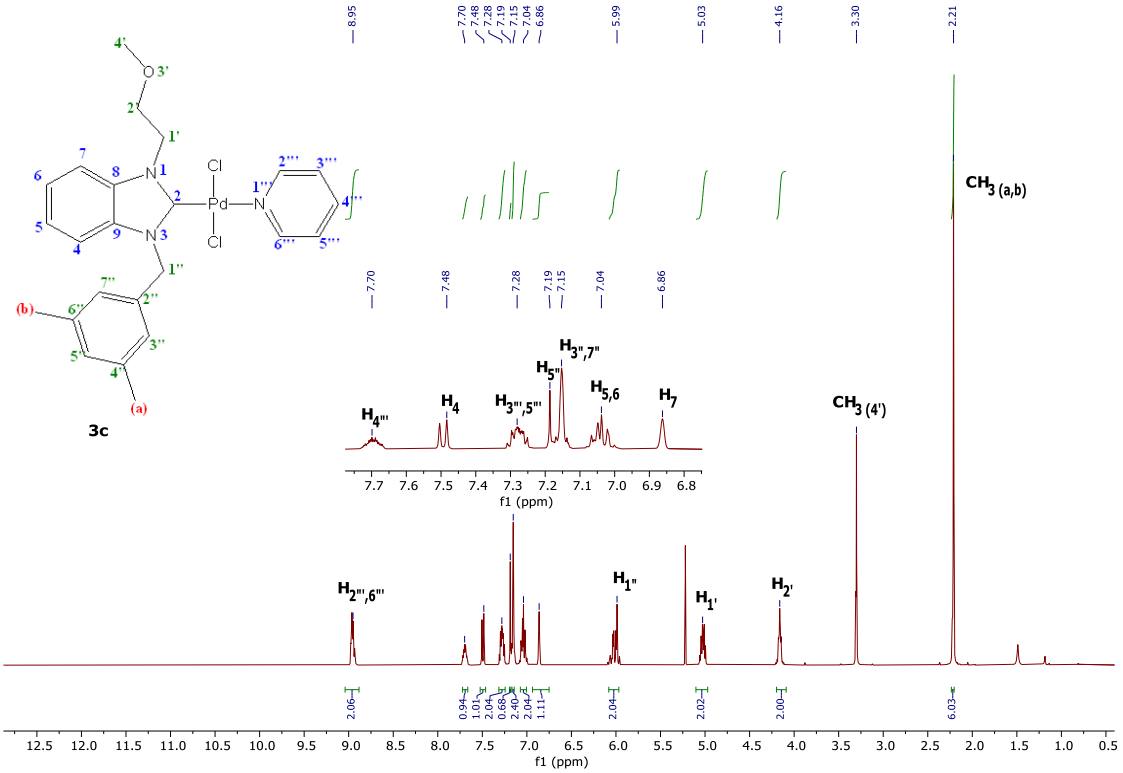


Figure S7. ^{1}H NMR spectrum of complex 3c in $CDCl_3$.

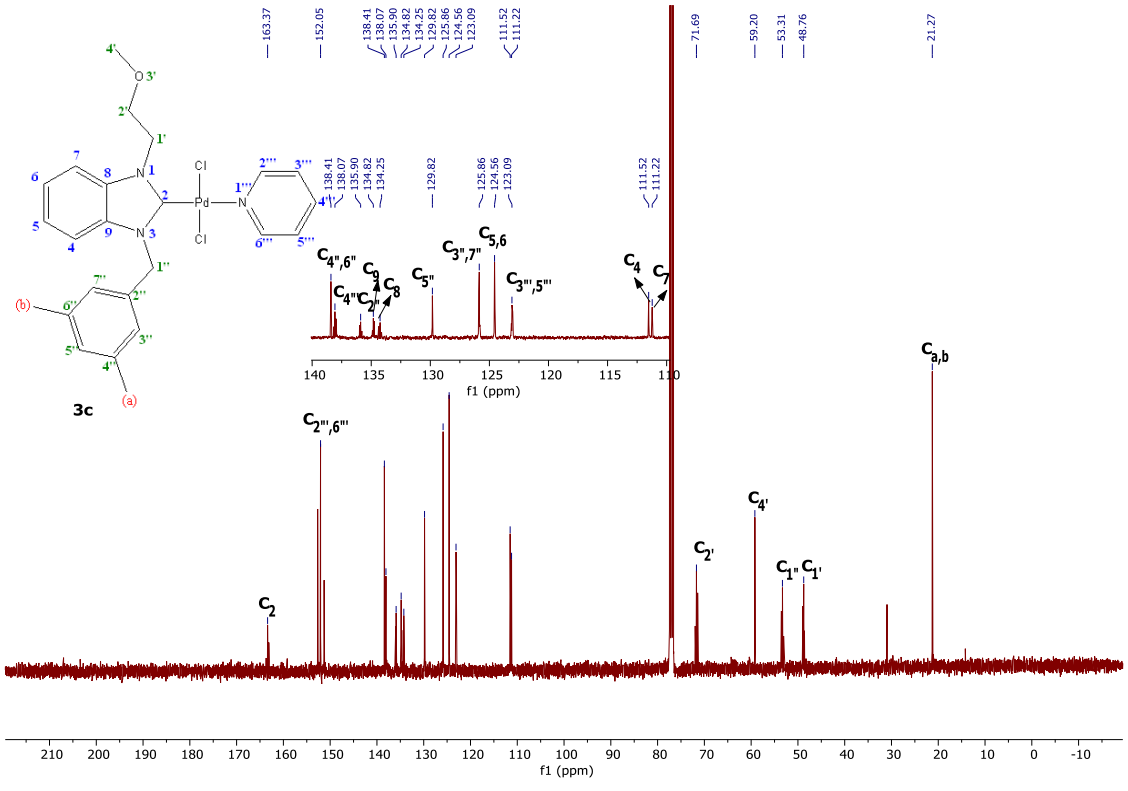


Figure S8. ^{13}C NMR spectrum of complex 3c in $CDCl_3$.

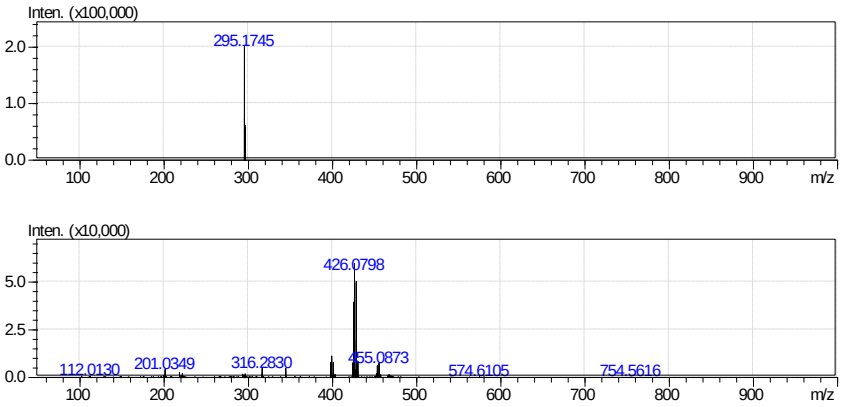


Figure S9. HRMS spectrum of complex 3c.

Complex 3d

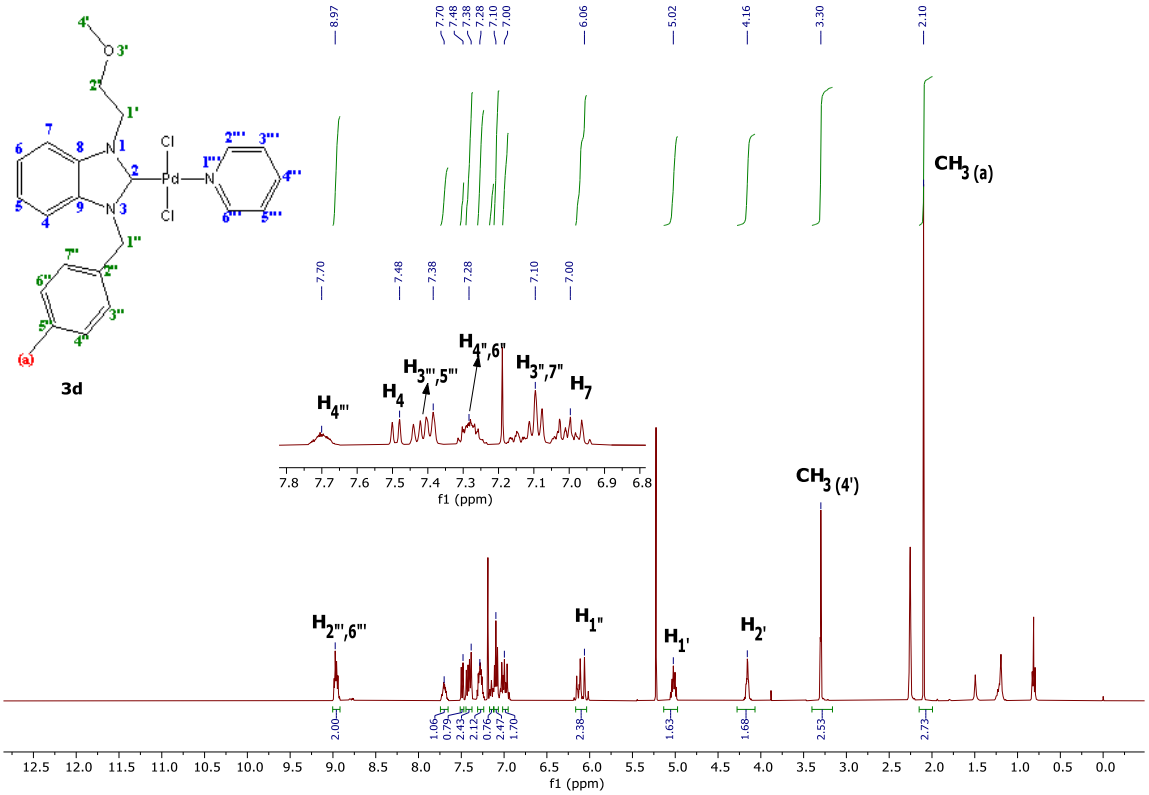


Figure S10. ^{1}H NMR spectrum of complex 3d in $CDCl_3$.

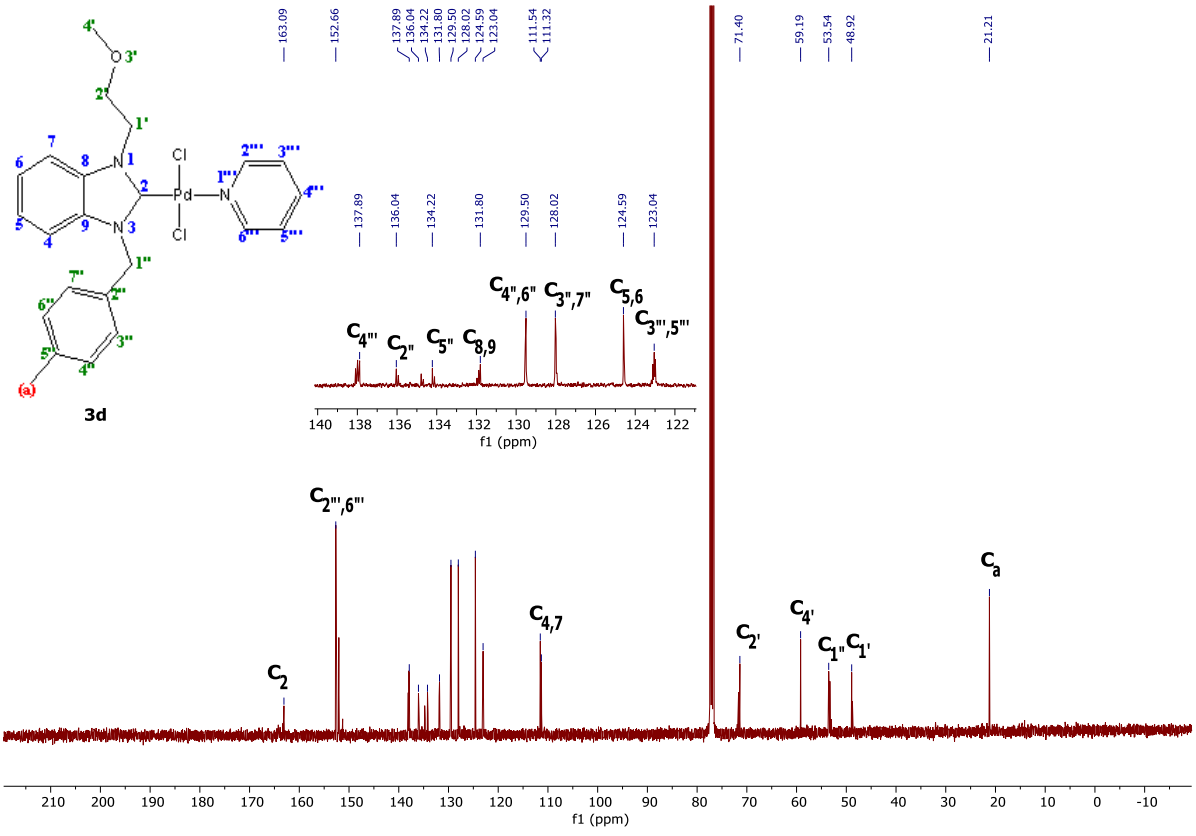


Fig S11. ^{13}C NMR spectrum of complex 3d in $CDCl_3$.

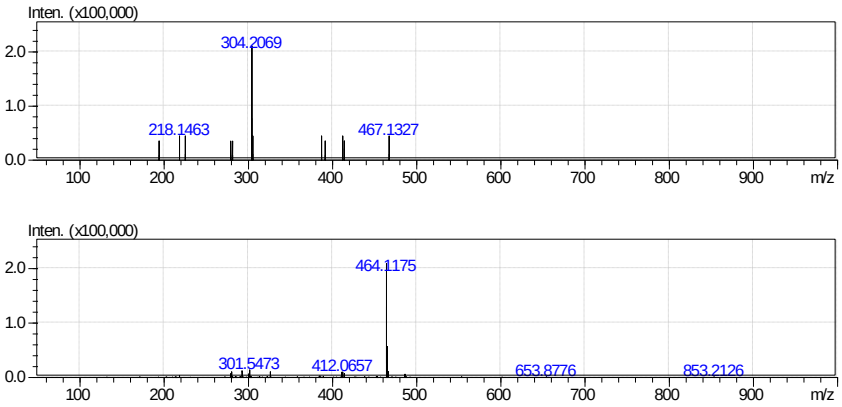


Figure S12. HRMS spectra of complex 3d.

Complex 3e

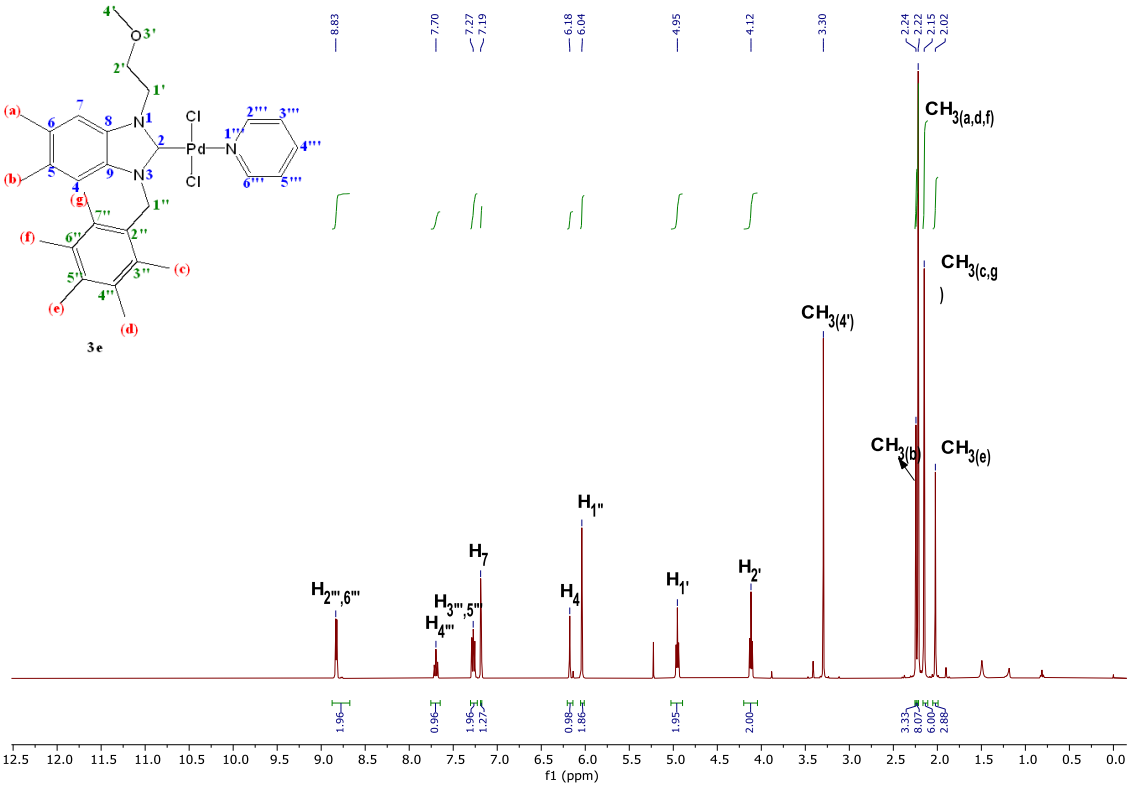


Figure S13. ^{1}H NMR spectrum of complex 3e in $CDCl_3$.

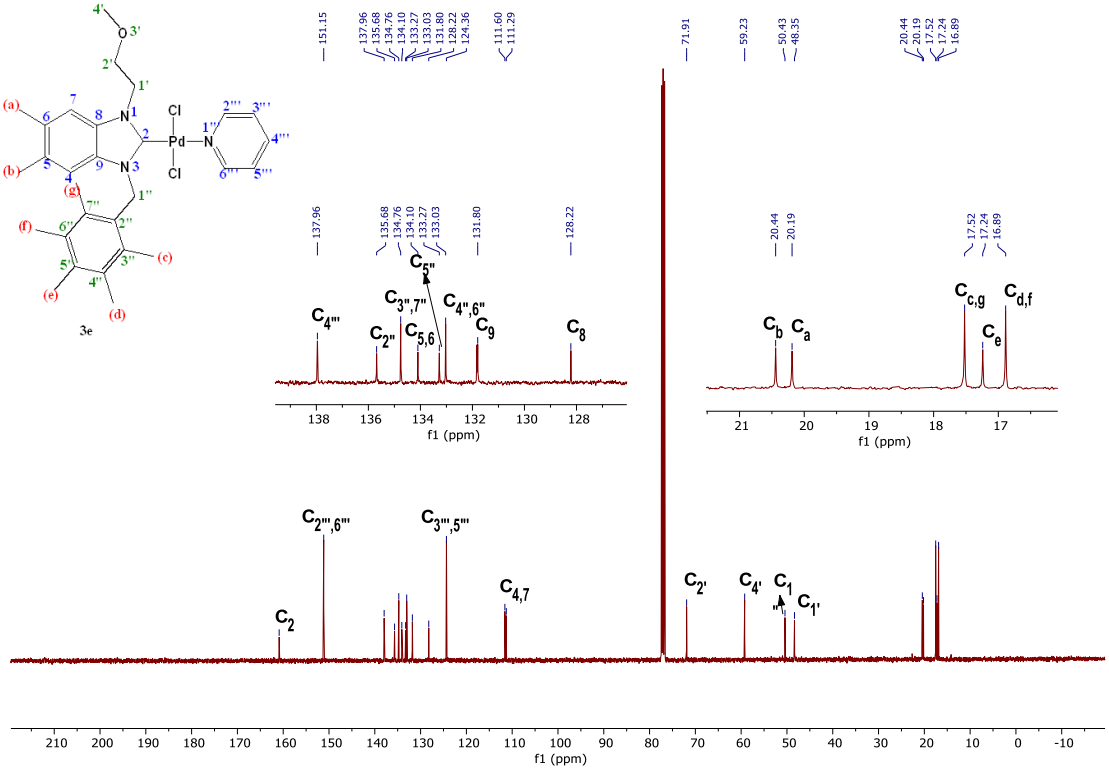


Figure S14. ^{13}C NMR spectrum of complex 3e in $CDCl_3$.

Complex 3f

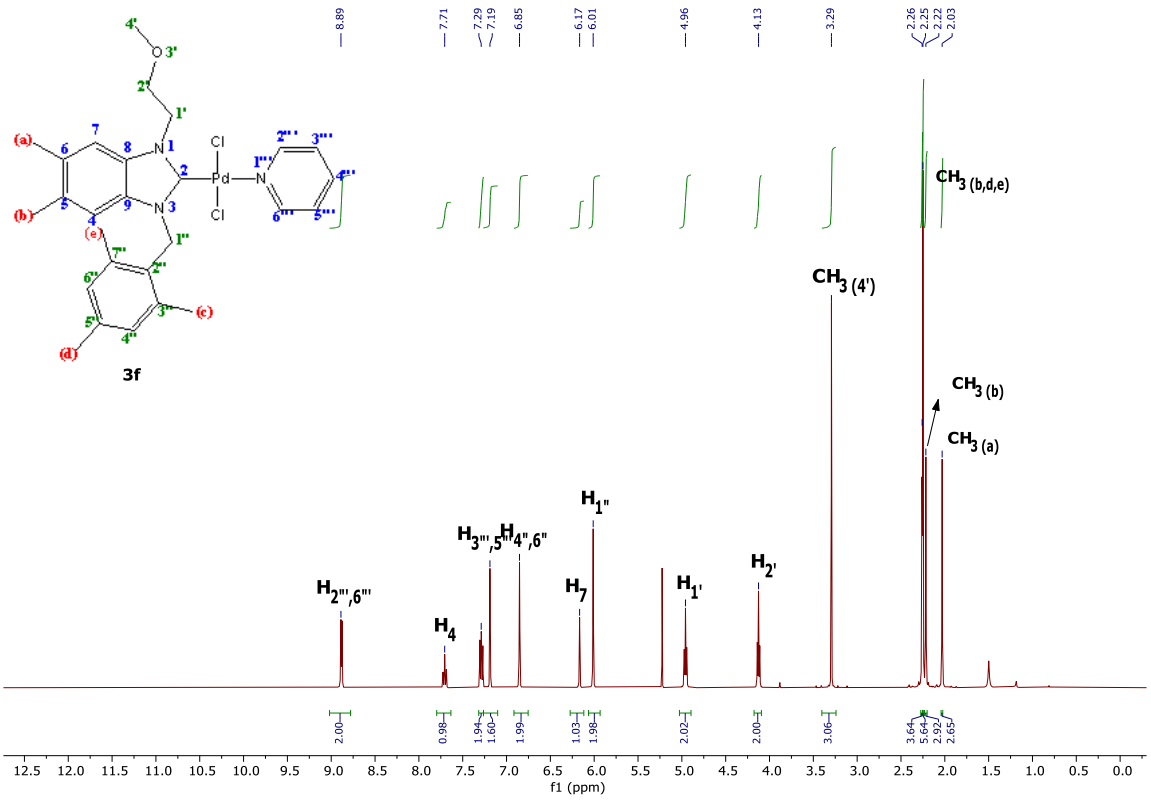


Figure S15. ^{1}H NMR spectrum of complex 3f in $CDCl_3$.

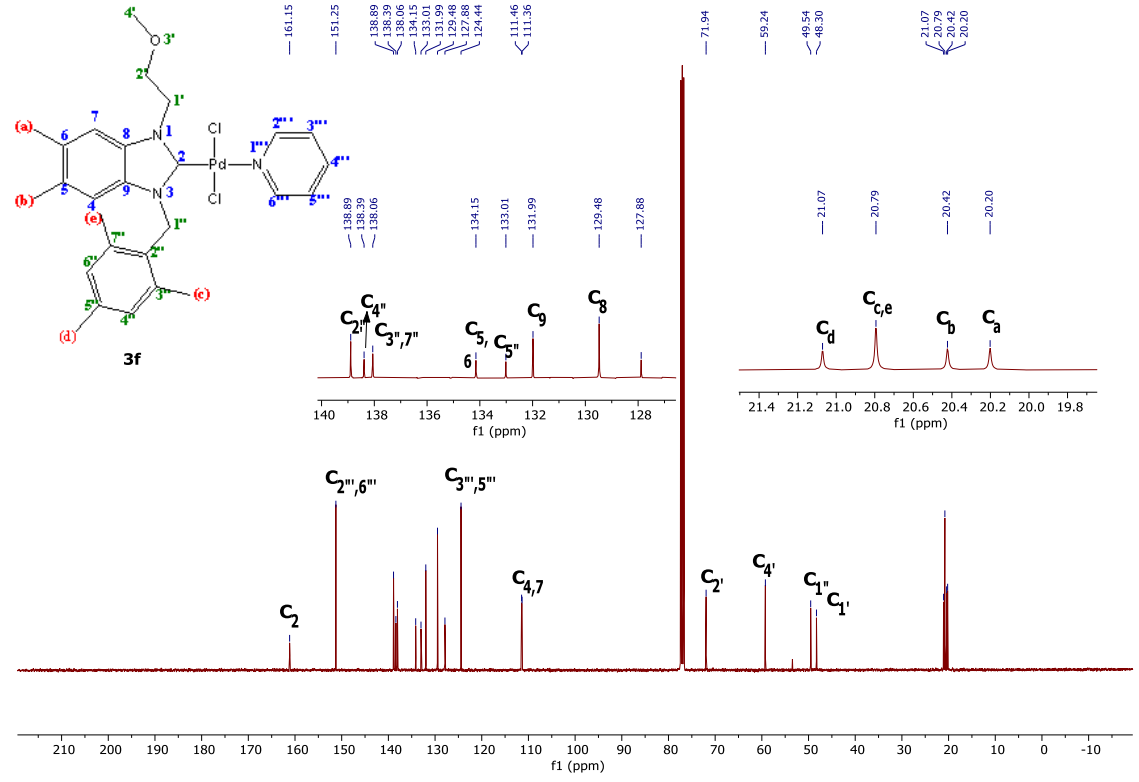


Figure S16. ^{13}C NMR spectrum of complex 3f in $CDCl_3$.

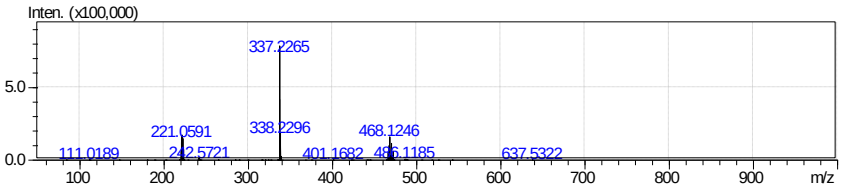


Figure S17. HRMS spectra of complex 3f.

Complex 3g

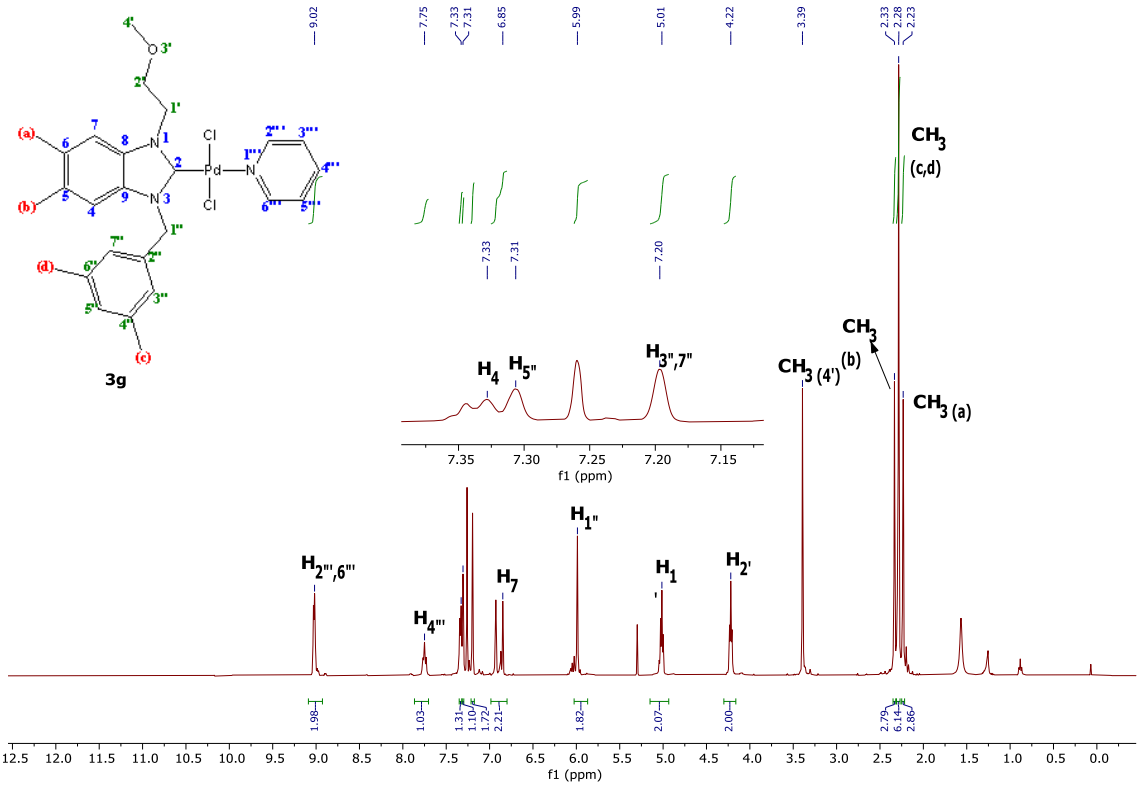


Figure S18. ^{1}H NMR spectrum of complex 3g in $CDCl_3$.

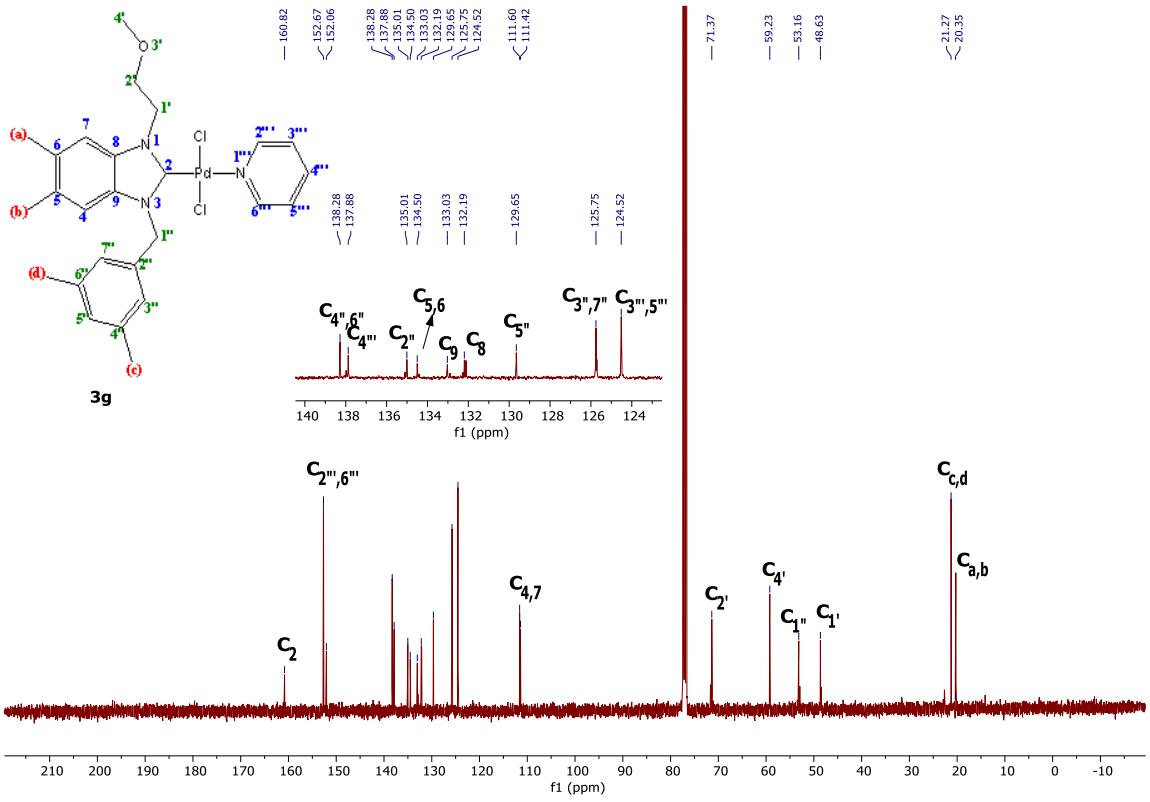


Figure S19. ^{13}C NMR spectrum of complex 3g in $CDCl_3$.

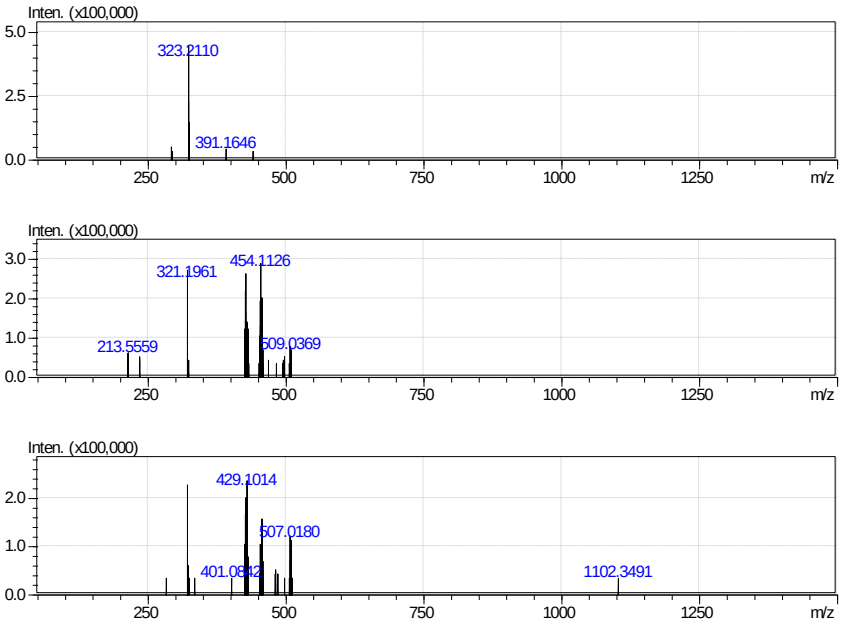


Figure S20. HRMS spectra of complex 3g.

Complex 3h

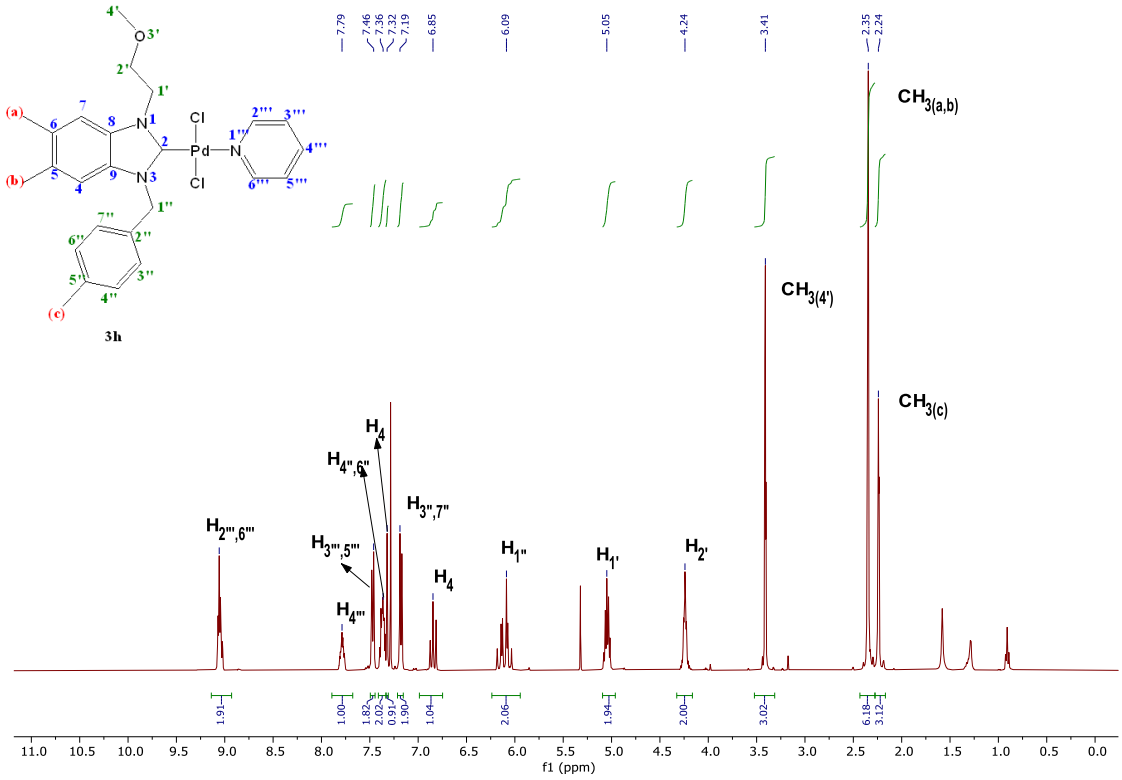


Figure S21. ^{1}H NMR spectrum of complex 3h in $CDCl_3$.

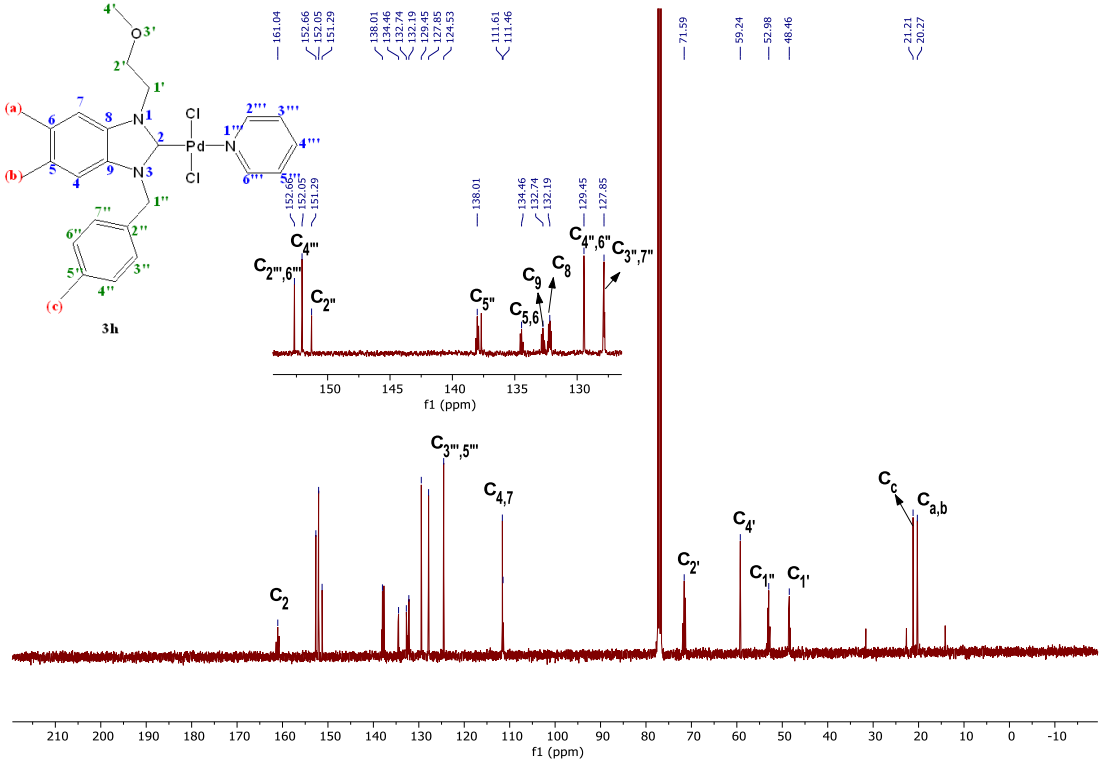


Figure S22. ^{13}C NMR spectrum of complex 3h in $CDCl_3$.

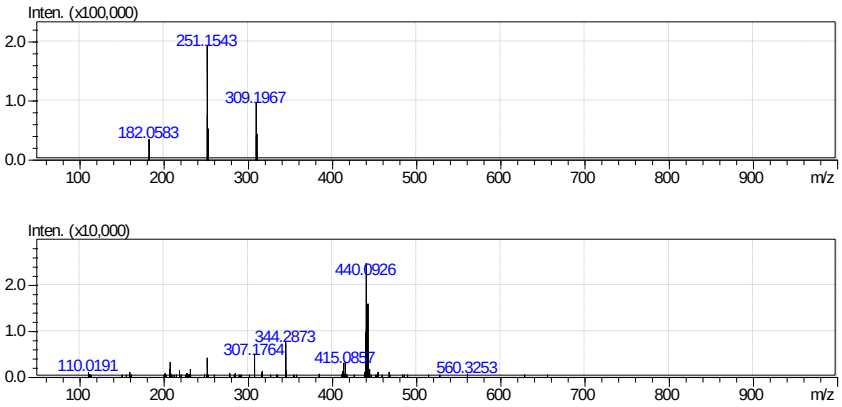


Figure S23. HRMS spectra of complex 3h.

Complex 3i

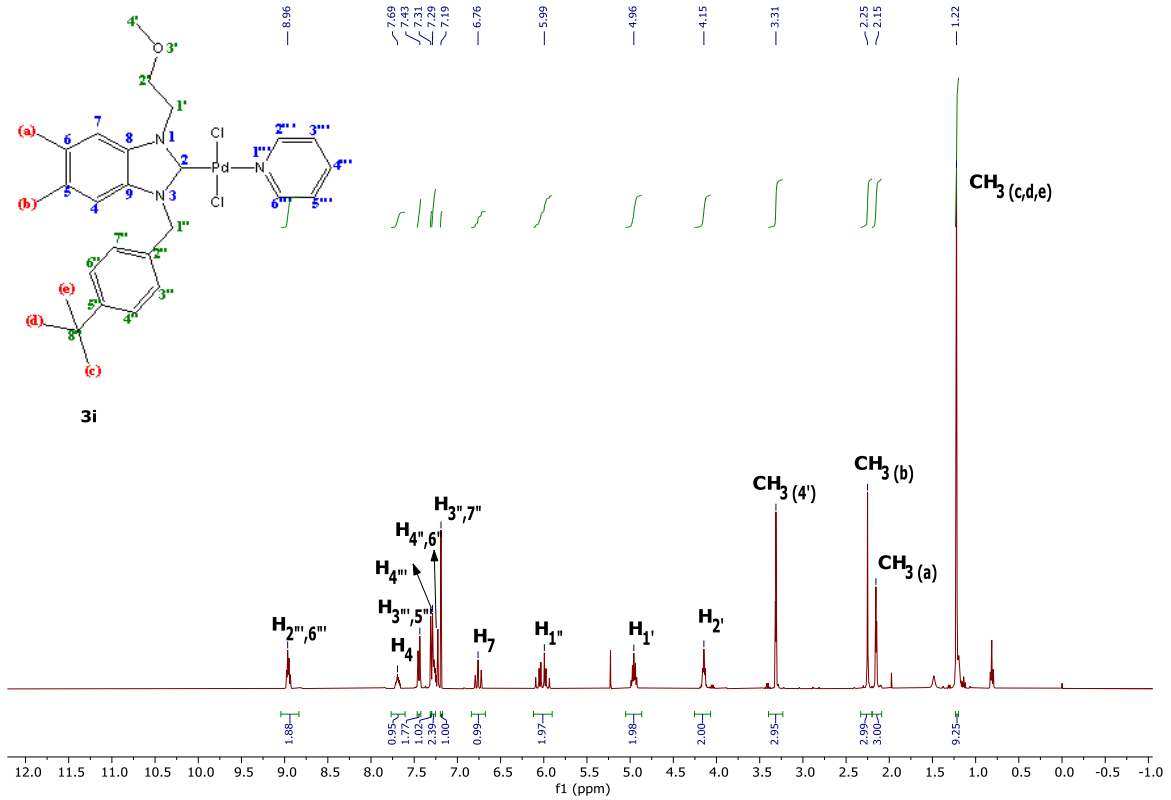


Figure S24. ^{1}H NMR spectrum of complex 3i in $CDCl_3$.

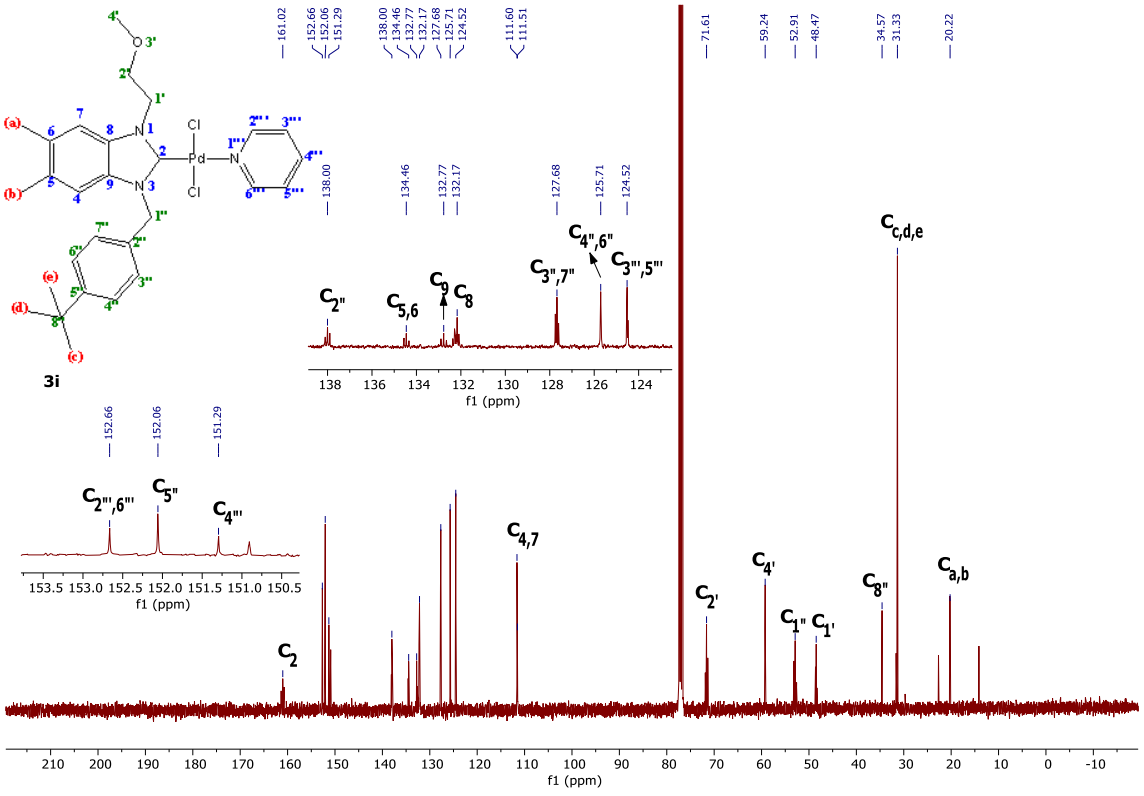


Figure S25. ^{13}C NMR spectrum of complex 3i in $CDCl_3$.

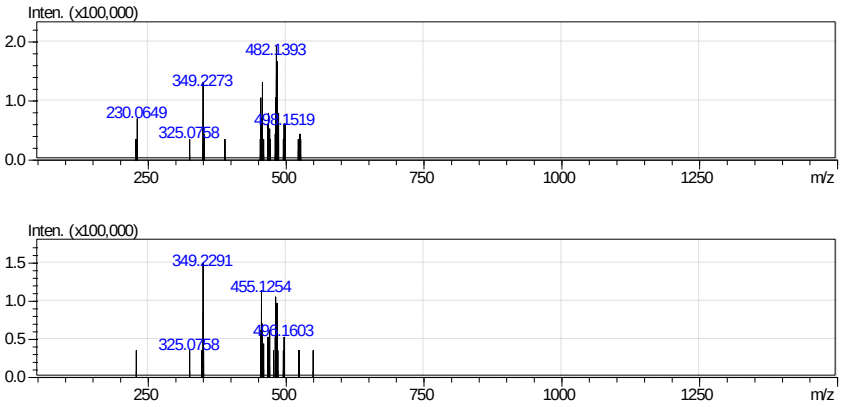


Figure S26. HRMS spectra of complex 3h.

Complex 4a

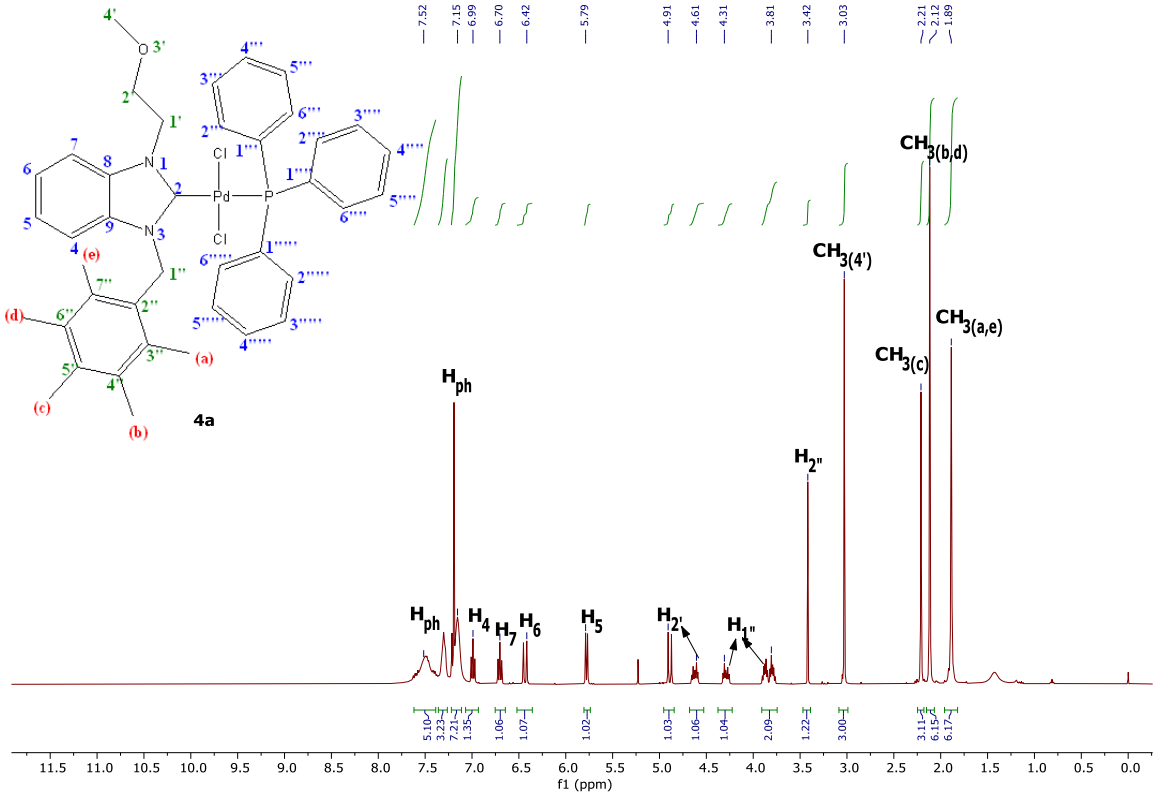


Figure S27. ^{1}H NMR spectrum of complex 4a in $CDCl_3$.

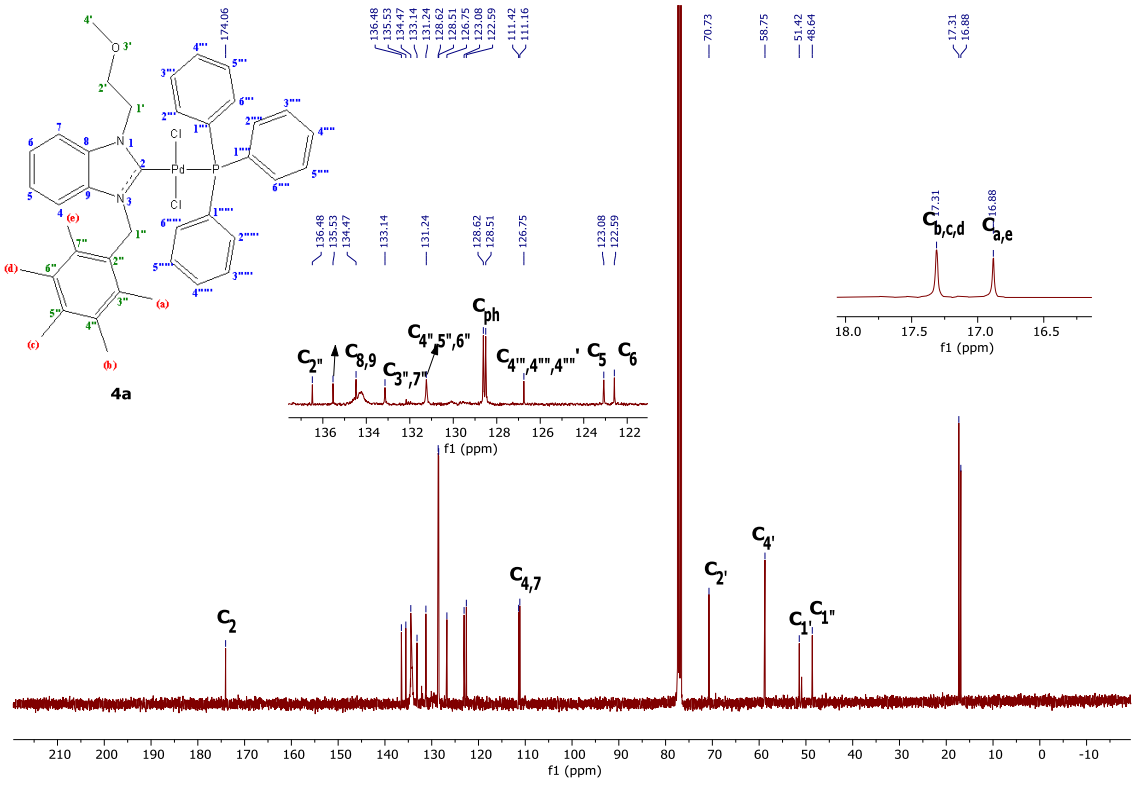


Figure S28. ^{13}C NMR spectrum of complex 4e in $CDCl_3$.

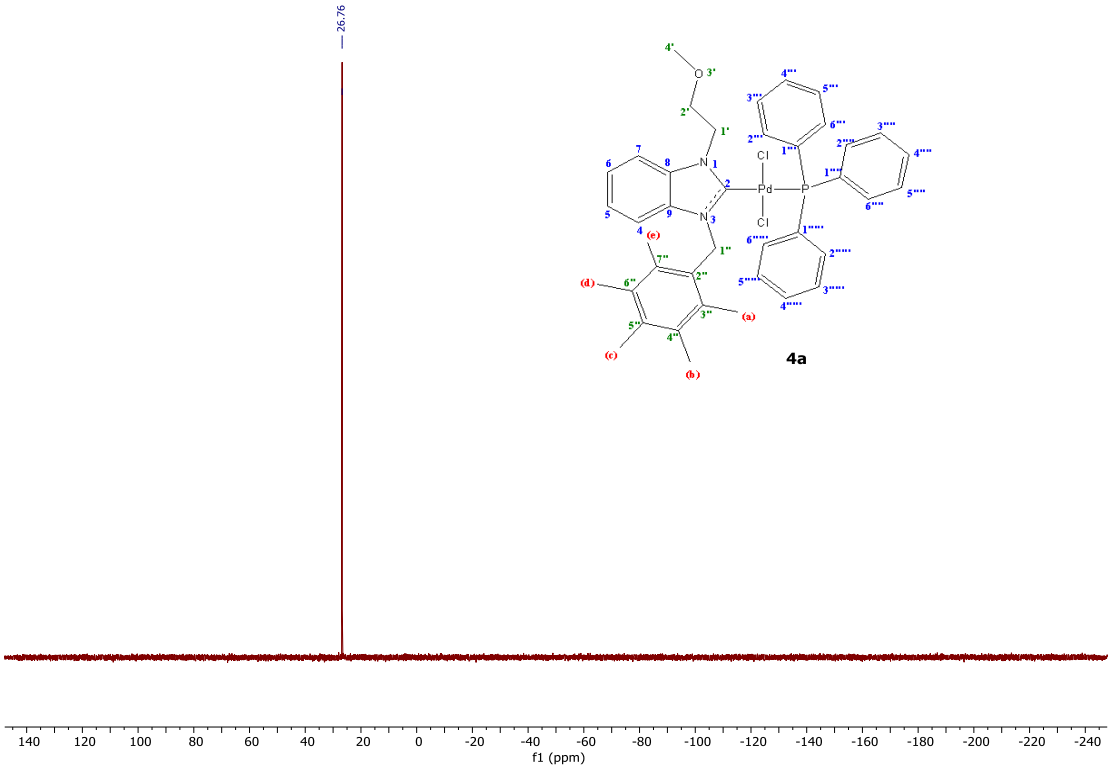


Figure S29. ^{31}P NMR spectrum of complex 4a in $CDCl_3$.

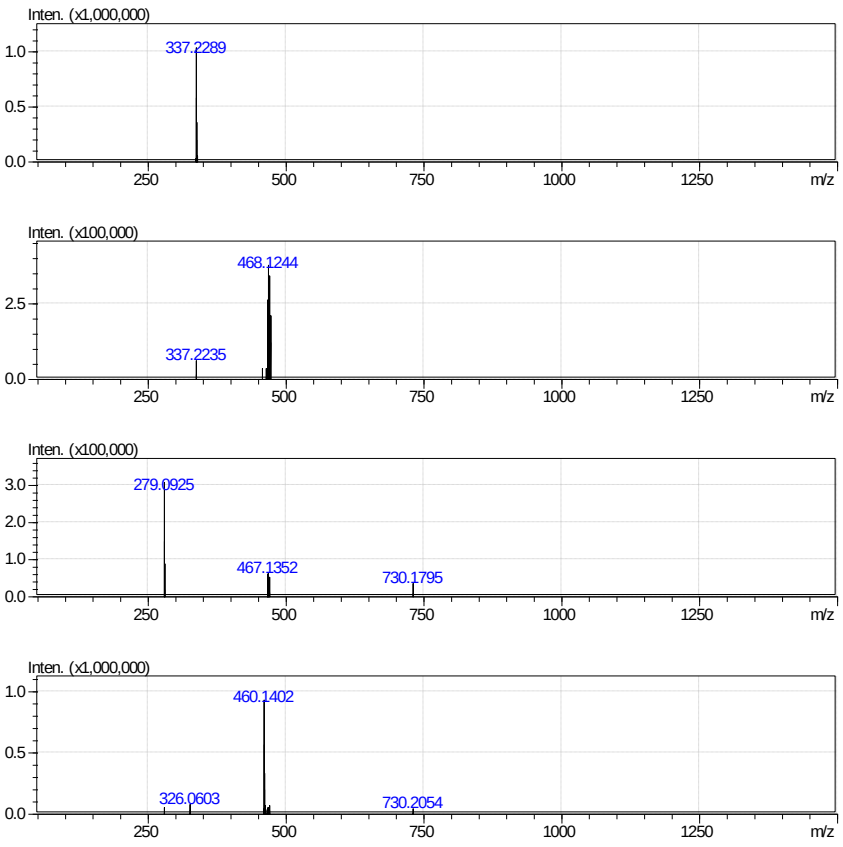


Figure S30. HRMS spectra of complex 4a.

Complex 4b

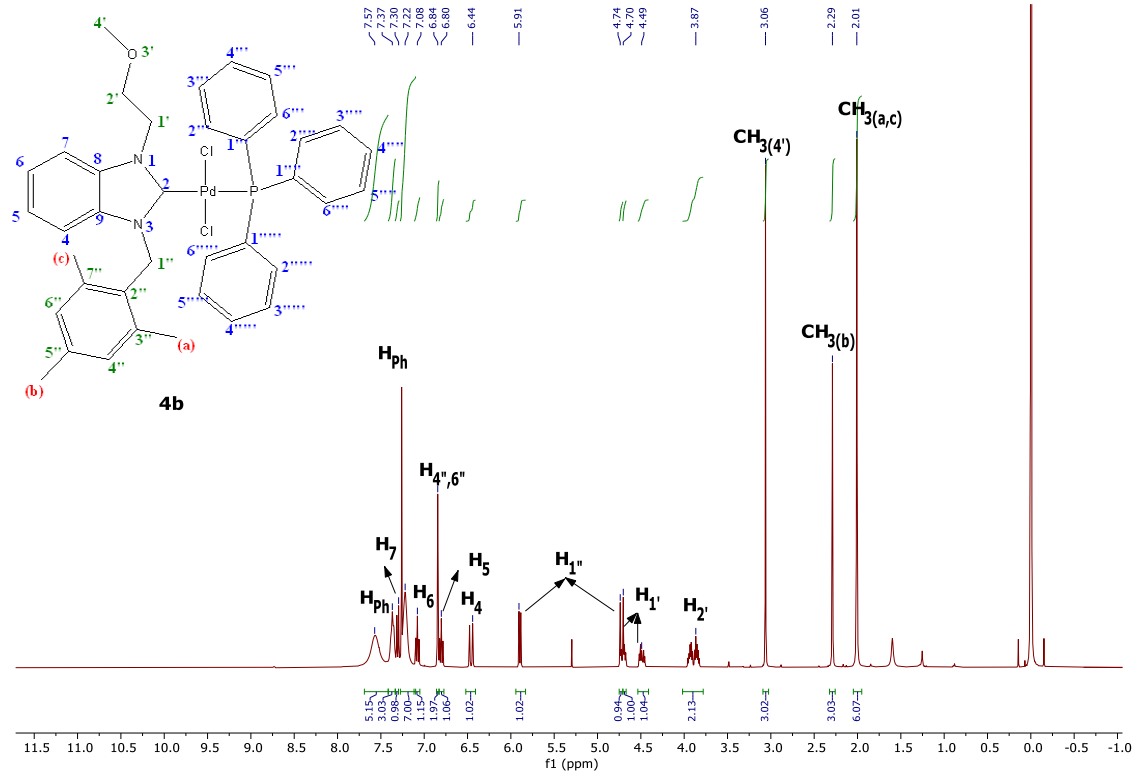


Figure S31. ^{1}H NMR spectrum of complex 4b in $CDCl_3$.

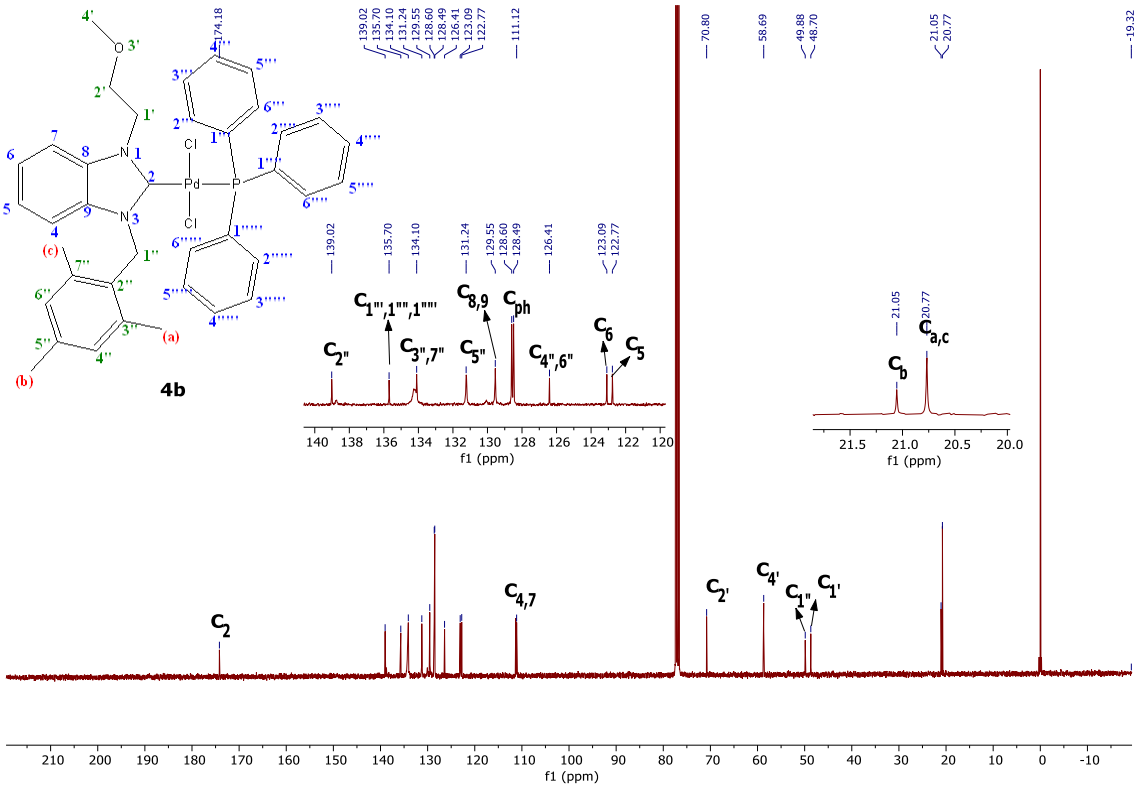


Figure S32. ^{13}C NMR spectrum of complex 4b in $CDCl_3$.

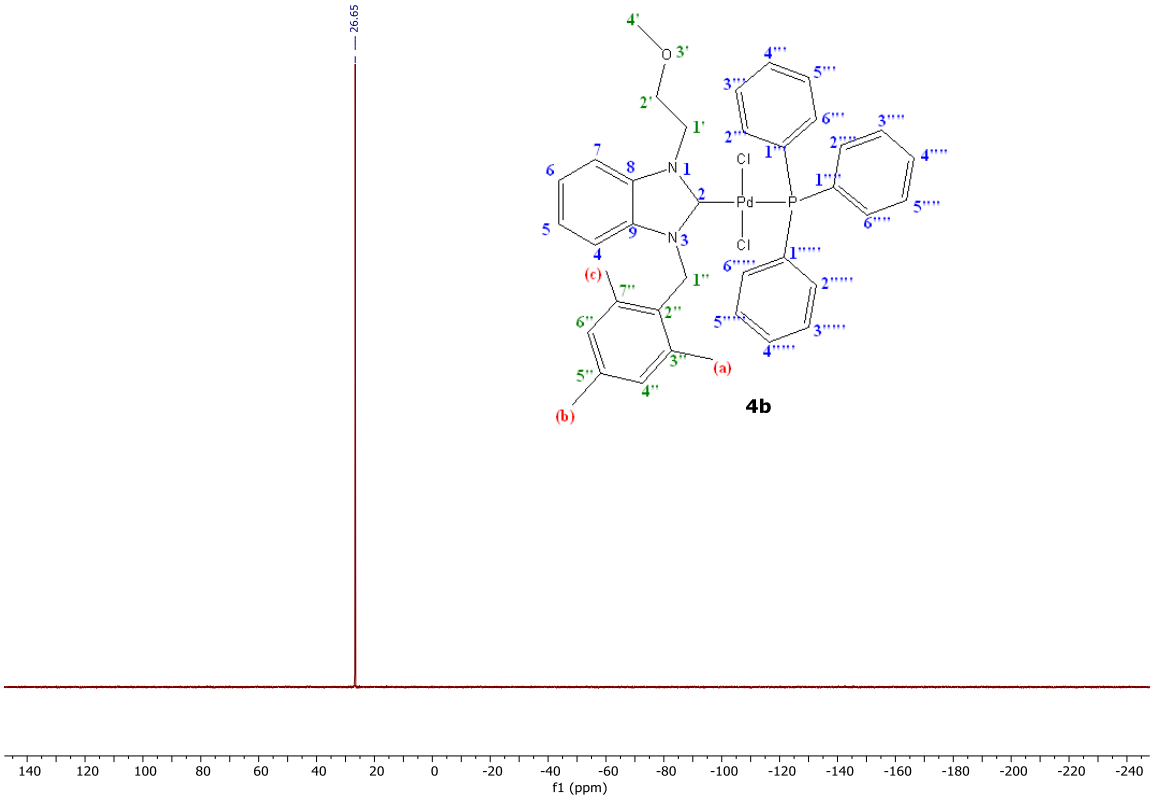
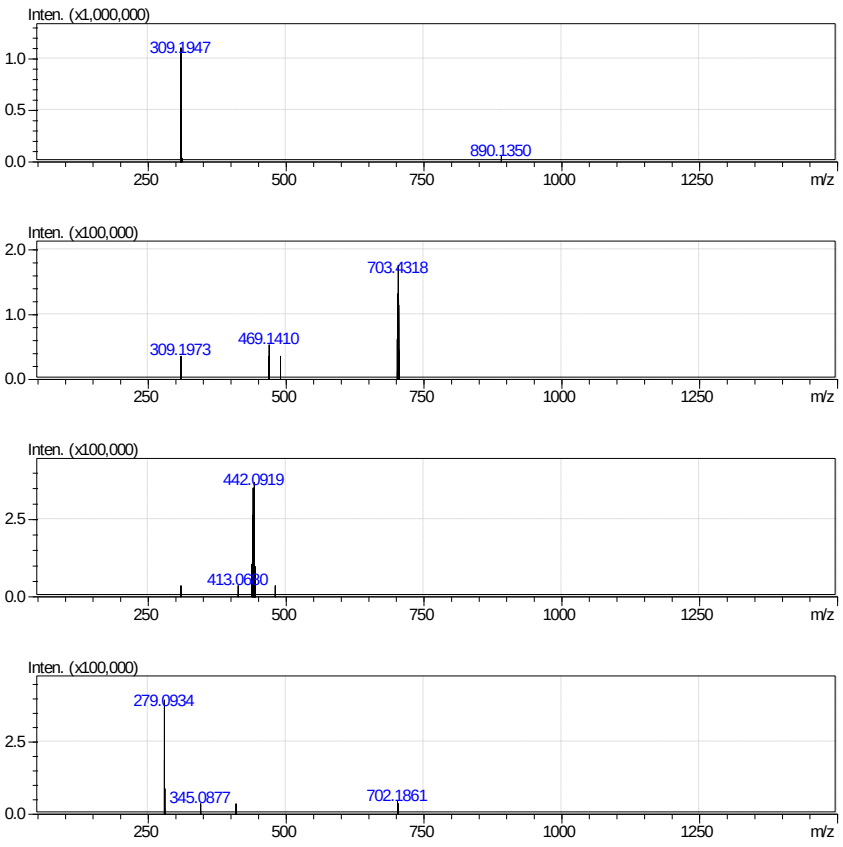


Figure S33. ^{31}P NMR spectrum of complex 4b in $CDCl_3$.



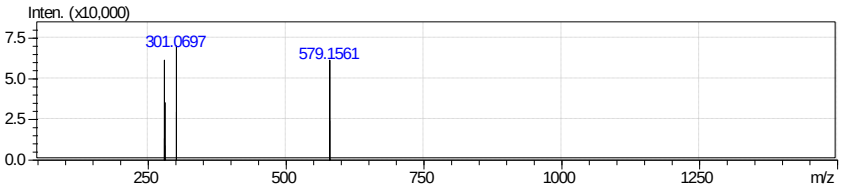


Figure S34. HRMS spectra of complex 4b.

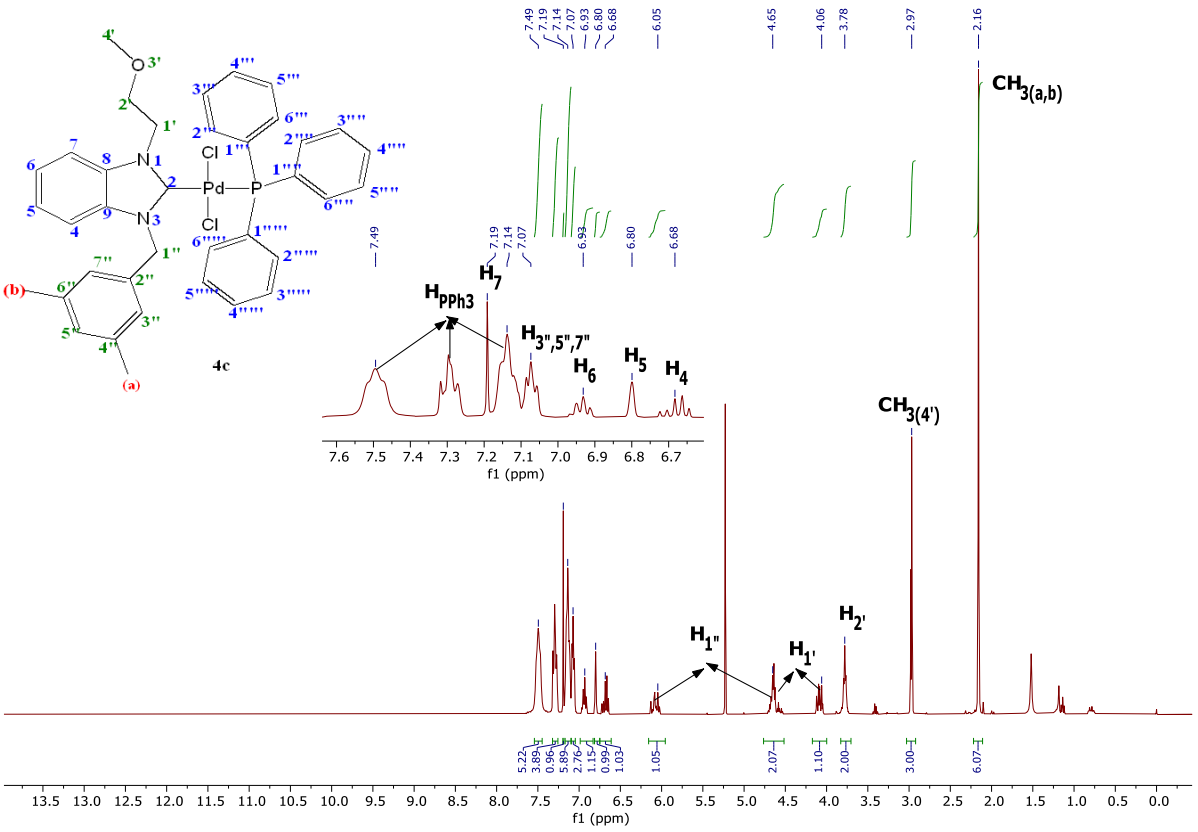


Figure S35. ^{1}H NMR spectrum of complex 4c in $CDCl_3$.

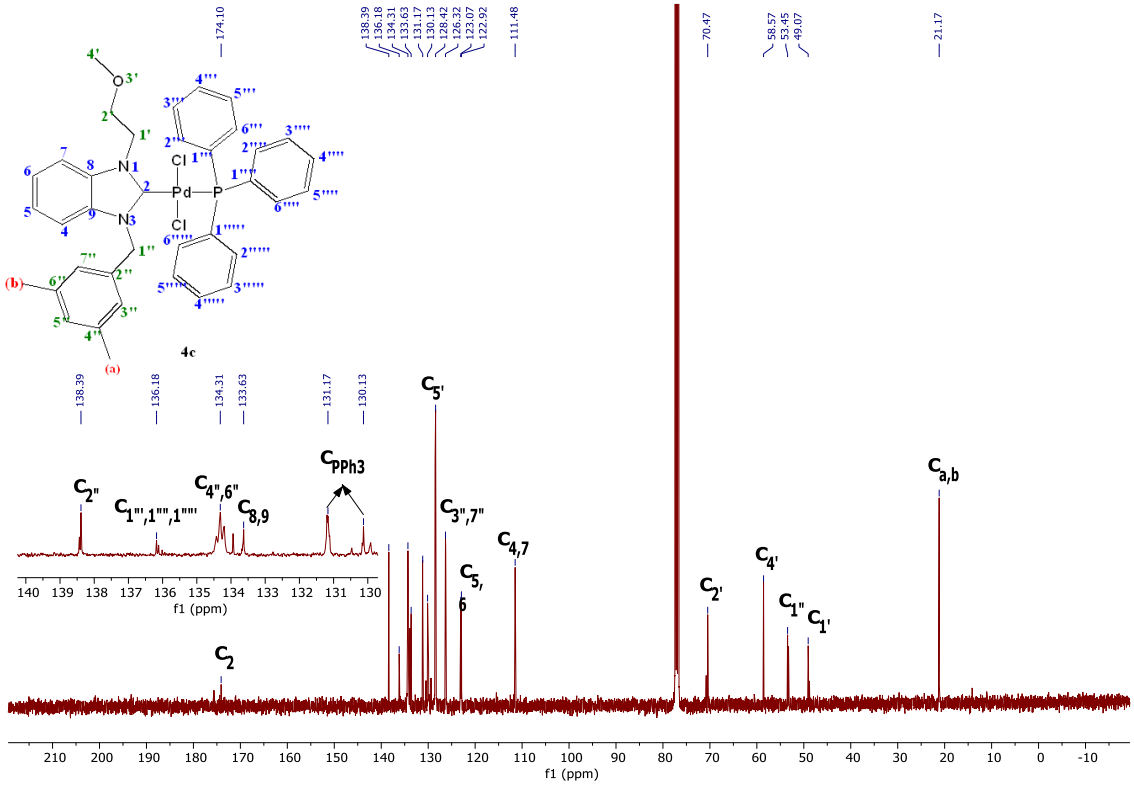


Figure S36. ^{13}C NMR spectrum of complex 4c in $CDCl_3$.

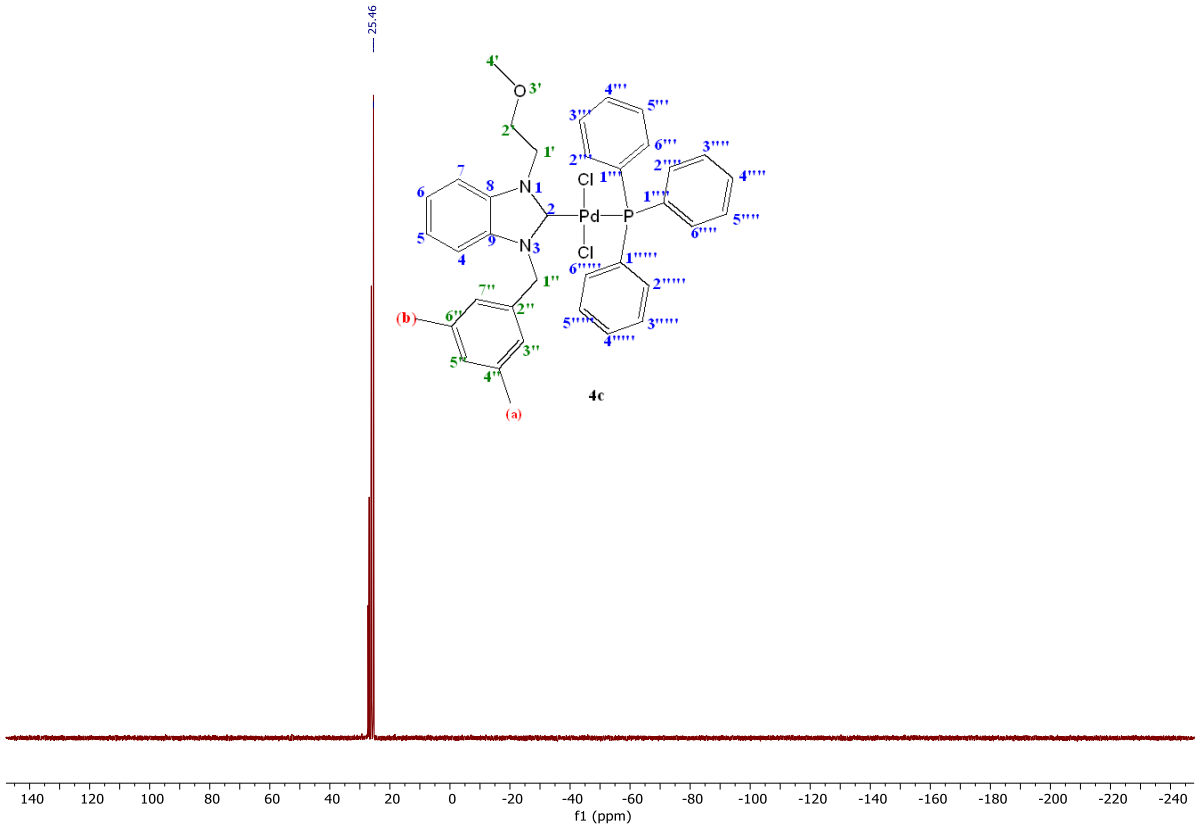


Figure S37. ^{31}P NMR spectrum of complex 4c in $CDCl_3$.

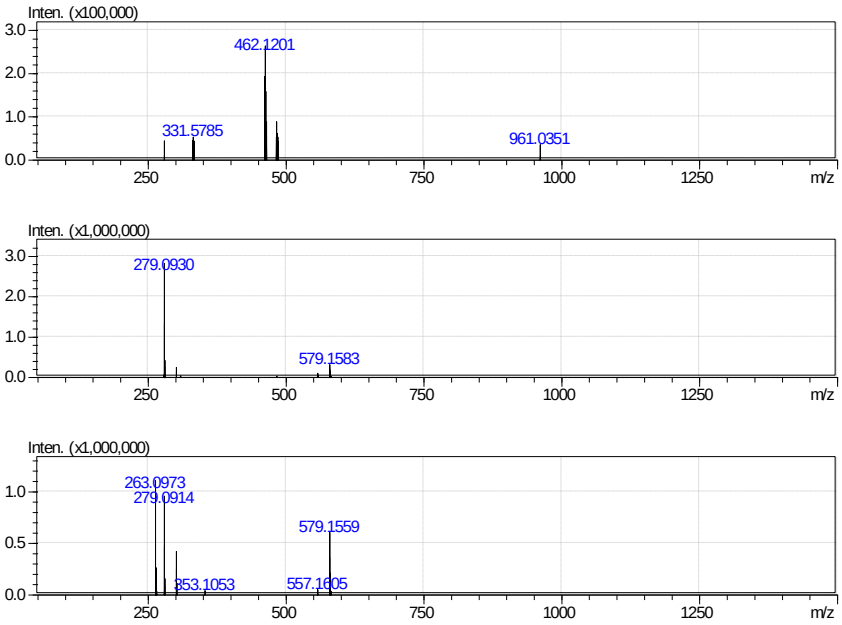


Figure S38. HRMS spectra of complex 4c.

Complex 4d

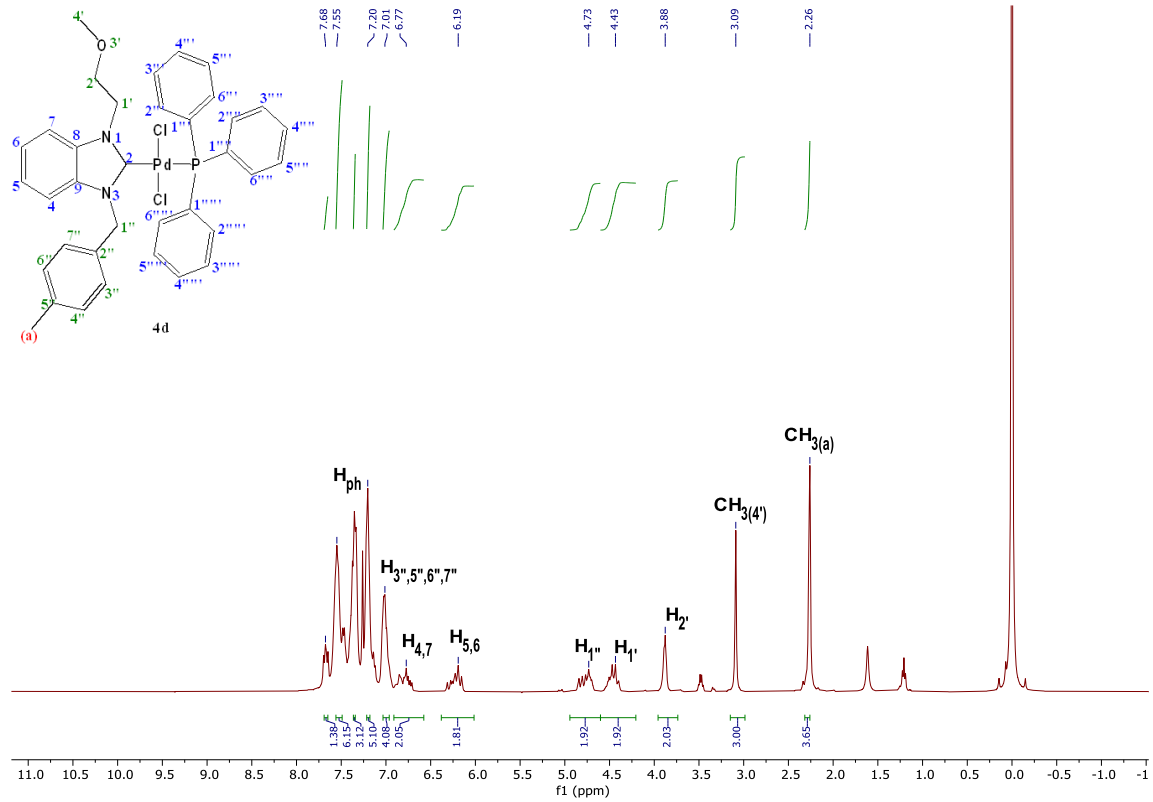


Figure S39. ^{1}H NMR spectrum of complex 4d in $CDCl_3$.

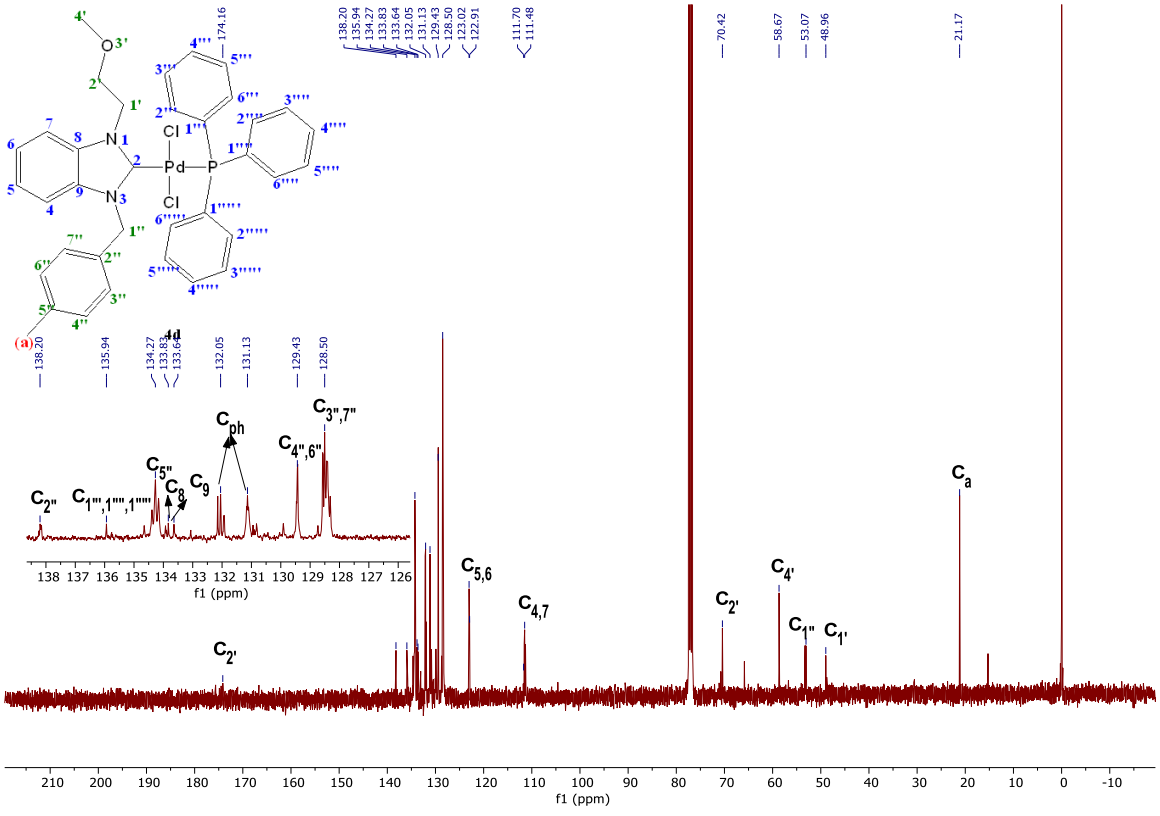


Figure S40. ^{13}C NMR spectrum of complex 4d in $CDCl_3$.

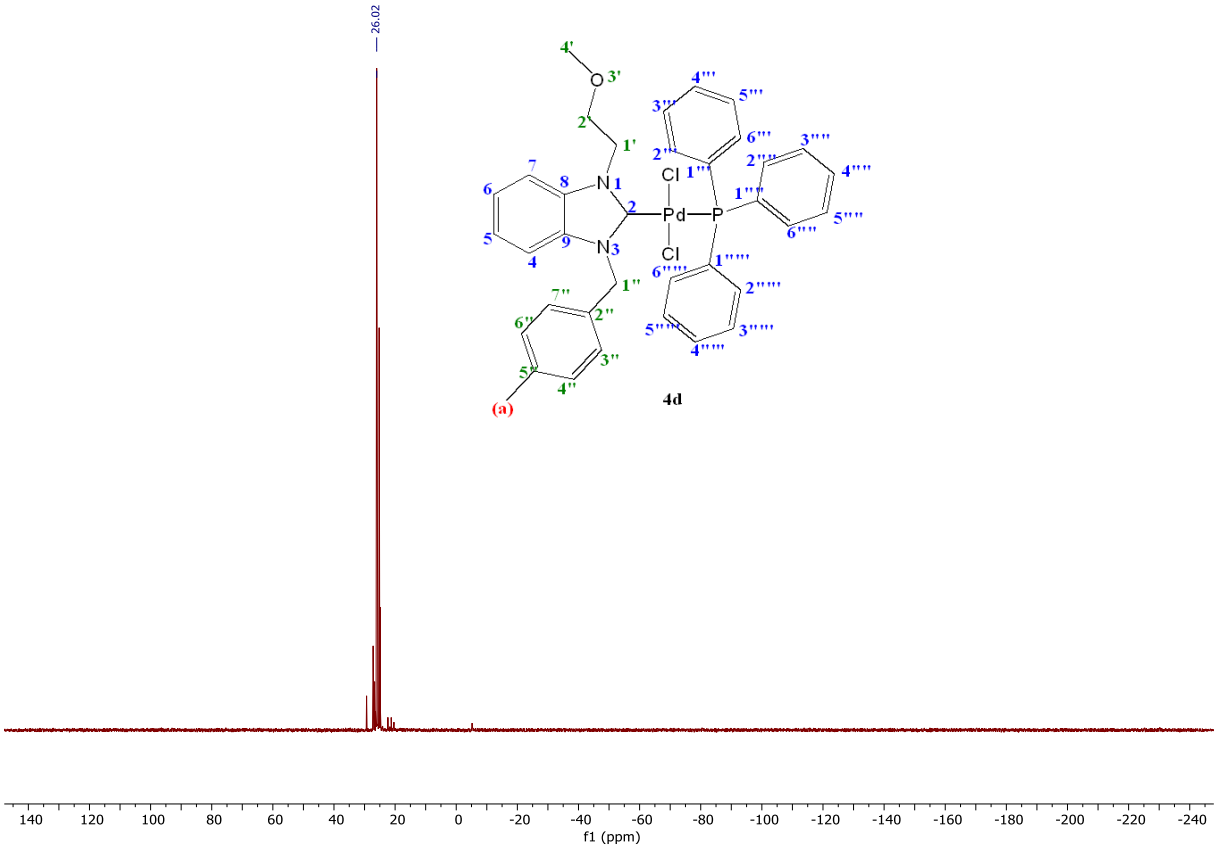


Figure S41. ^{31}P NMR spectrum of complex 4d in $CDCl_3$.

Complex 4e

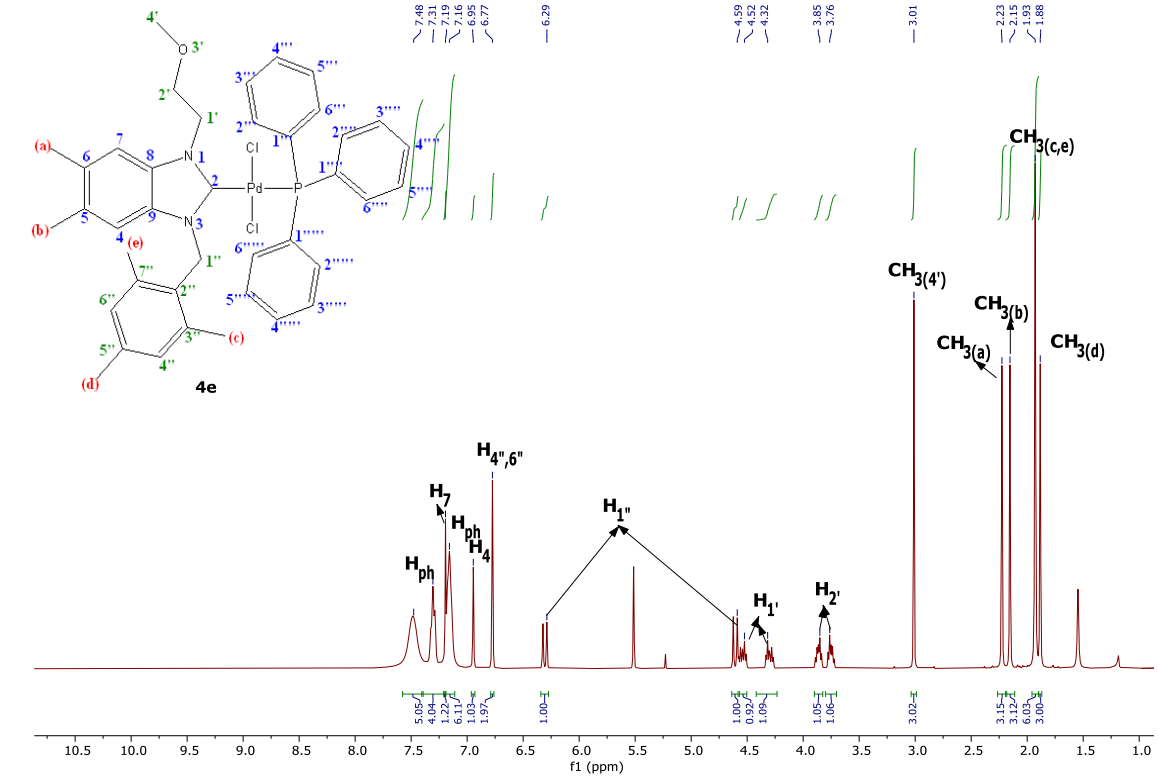


Figure S42. ^{1}H NMR spectrum of complex 4e in $CDCl_3$.

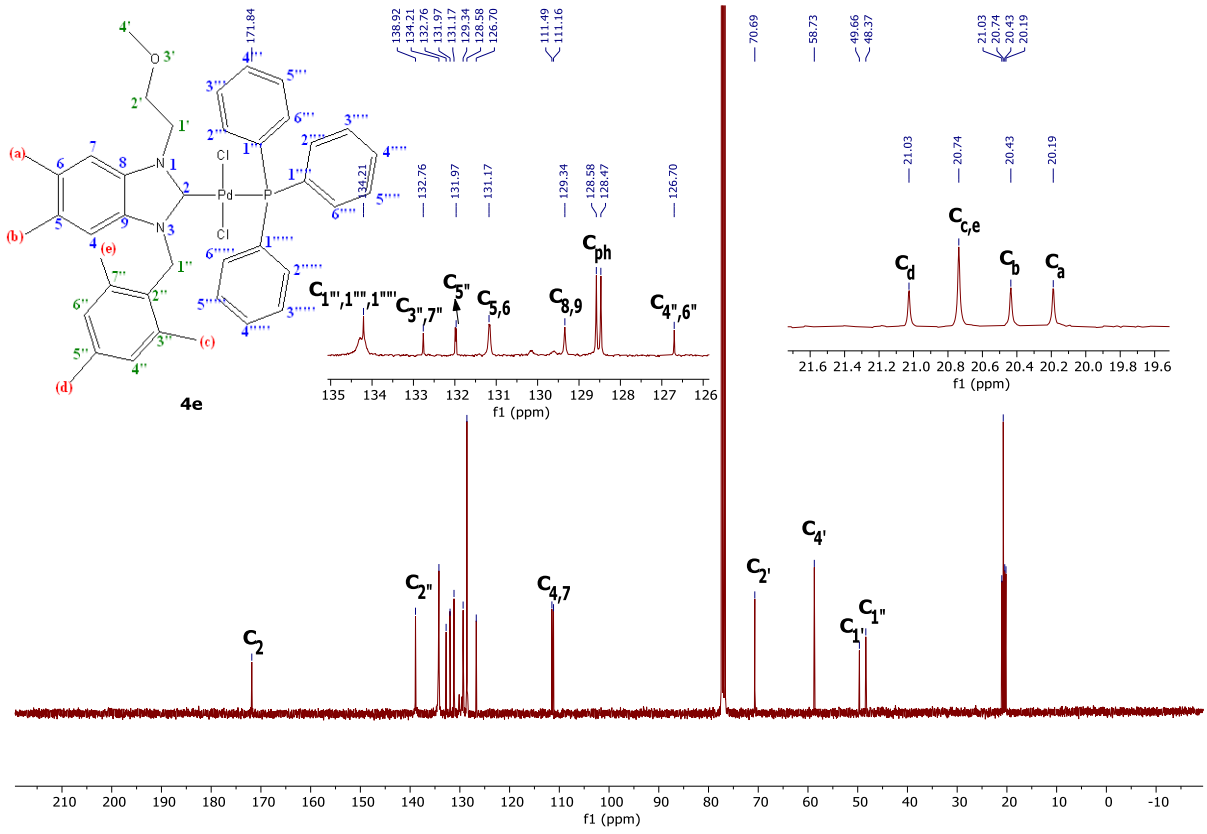


Figure S43. ^{13}C NMR spectrum of complex 4e in $CDCl_3$.

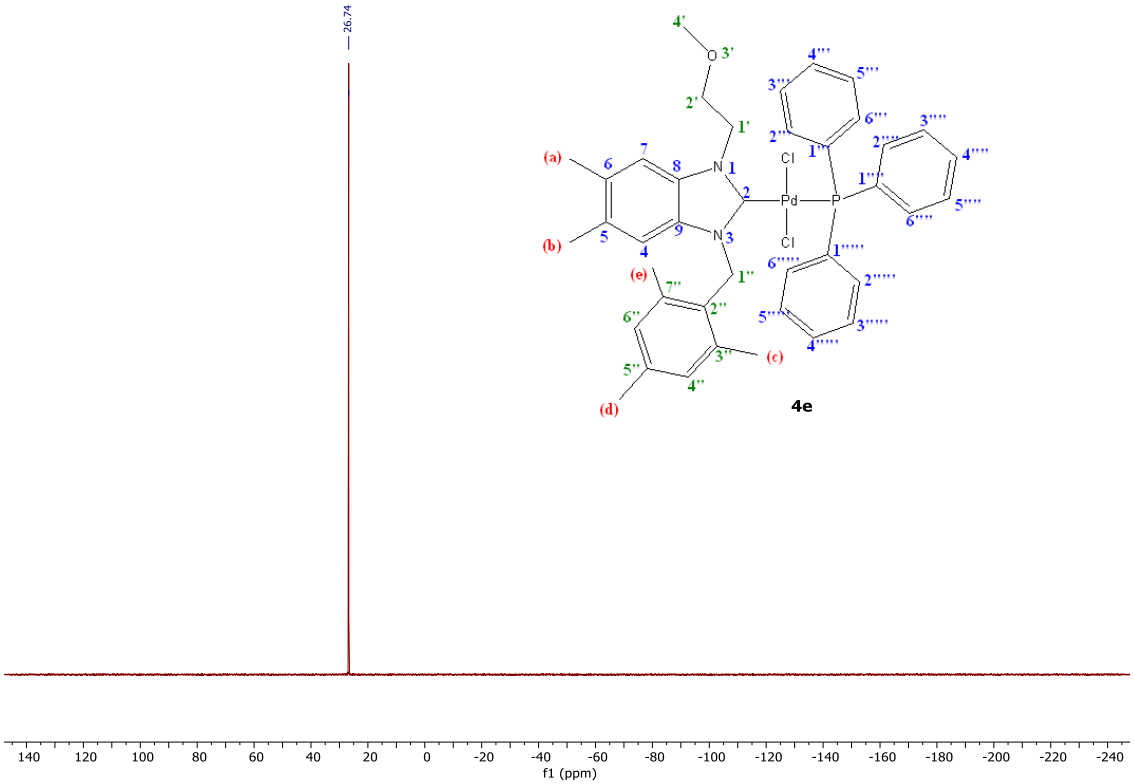
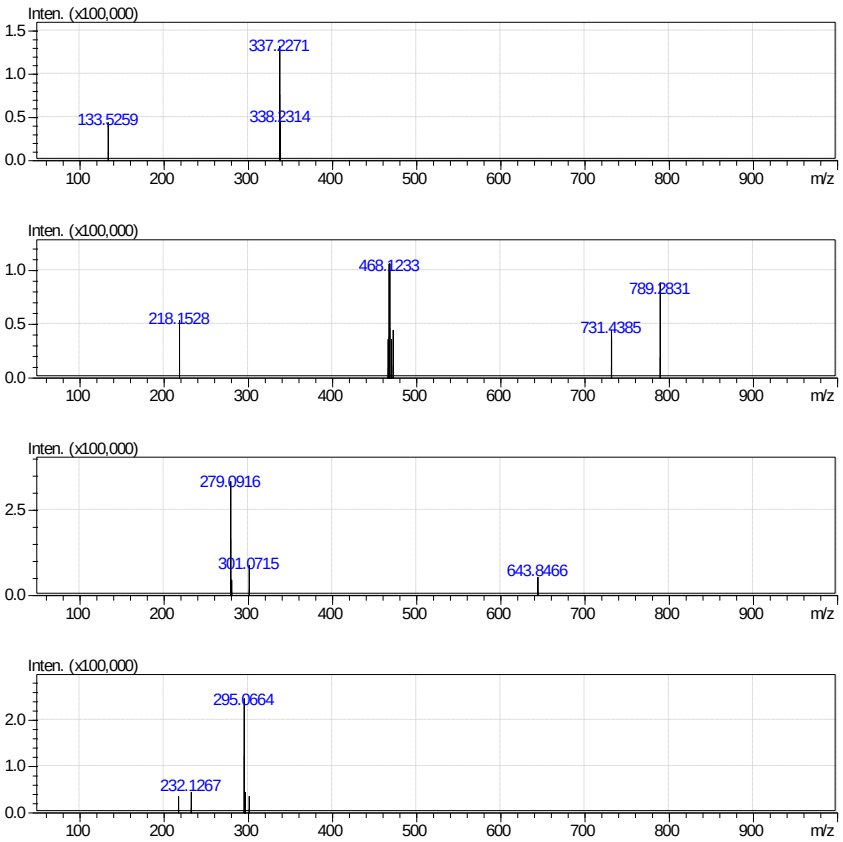


Figure S44. ^{31}P NMR spectrum of complex 4e in $CDCl_3$.



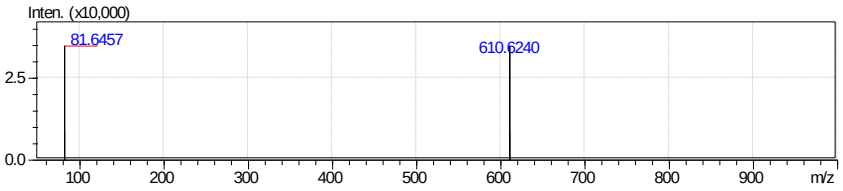


Figure S45. HRMS spectra of complex 4b.

Complex 4f

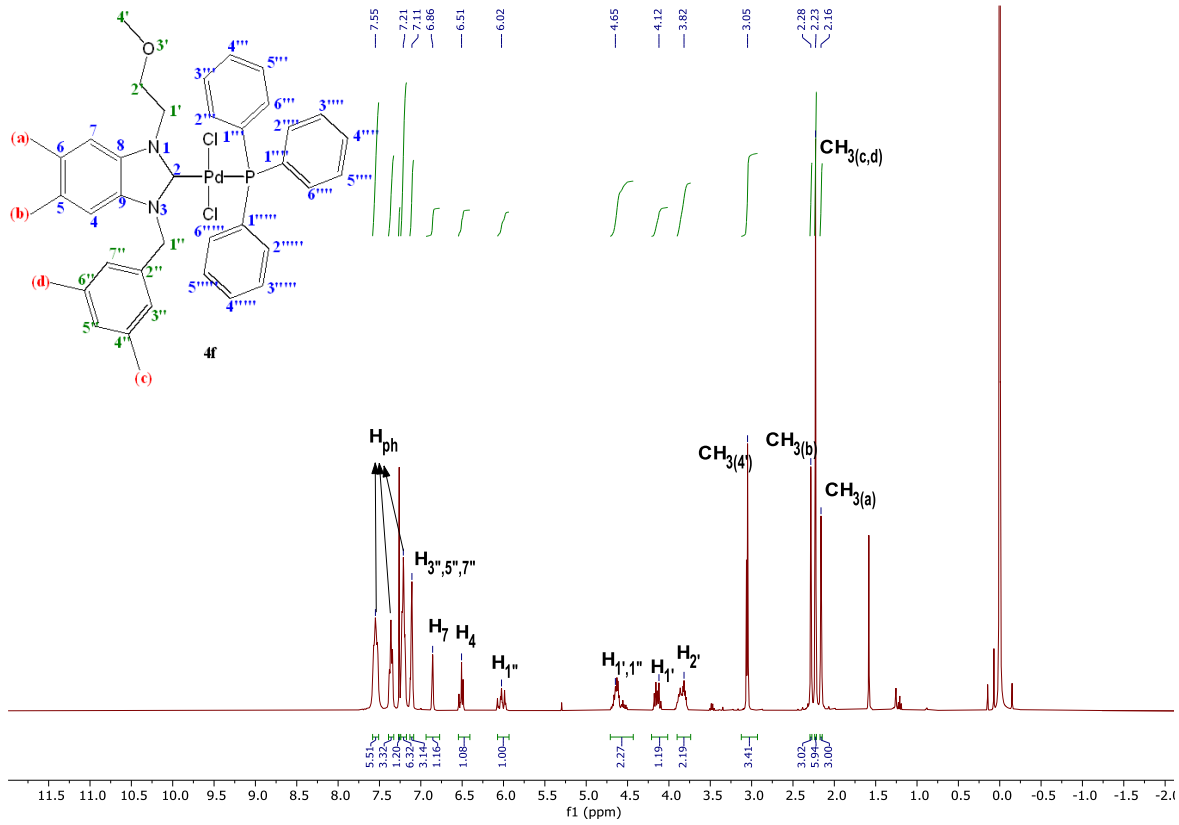


Figure S46. ^{1}H NMR spectrum of complex 4f in $CDCl_3$.

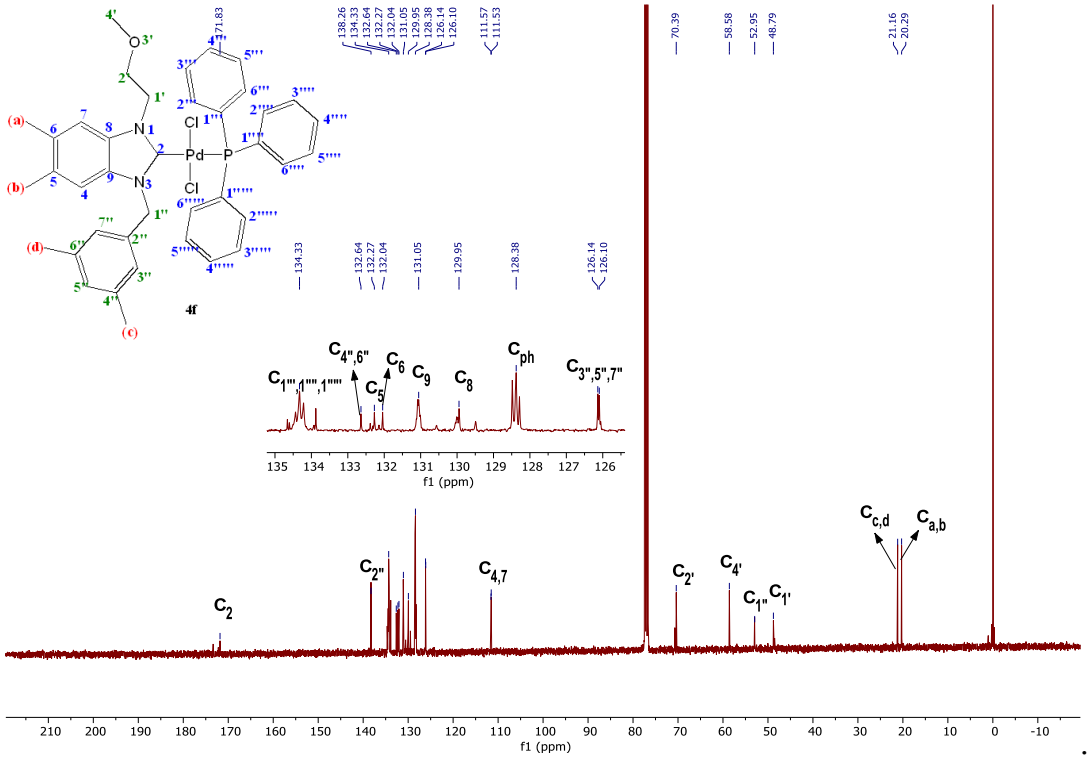


Figure S47. ^{13}C NMR spectrum of complex 4f in $CDCl_3$.

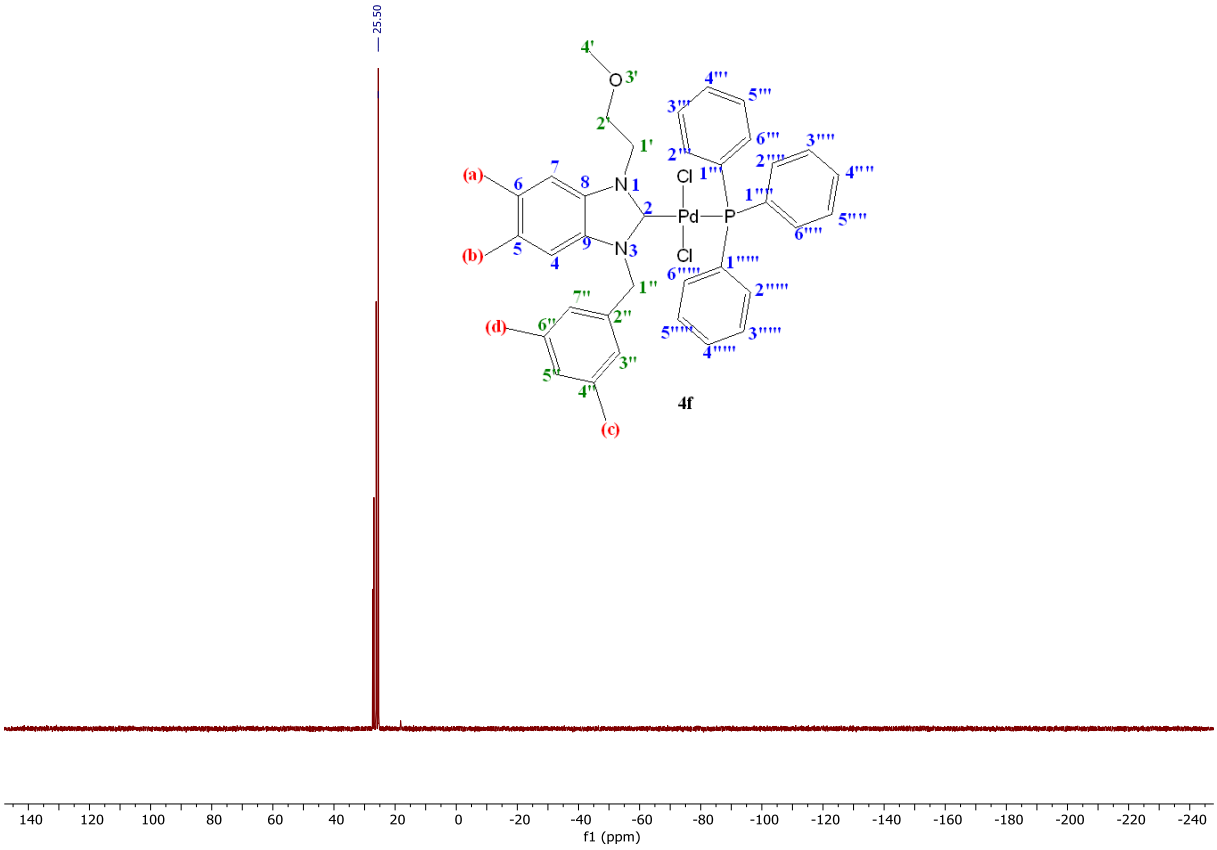


Figure S48. ^{31}P NMR spectrum of complex 4f in $CDCl_3$.

Complex 4g

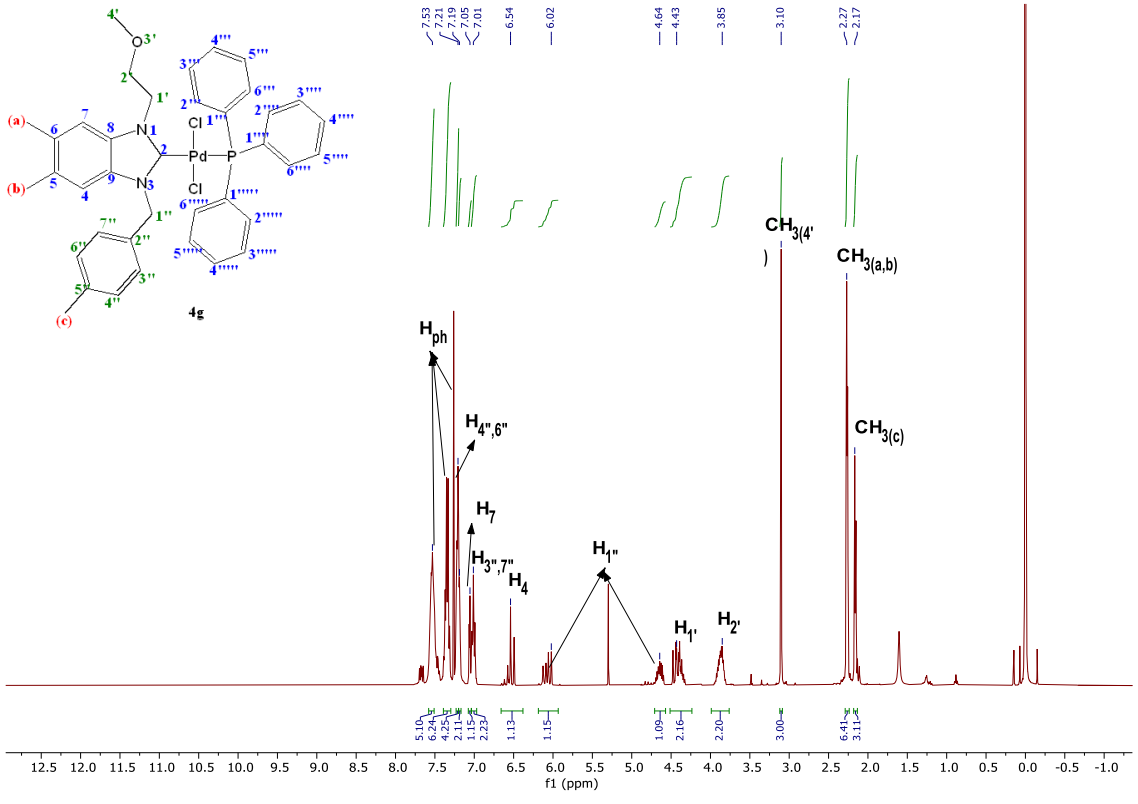


Figure S49. ^{1}H NMR spectrum of complex 4g in $CDCl_3$.

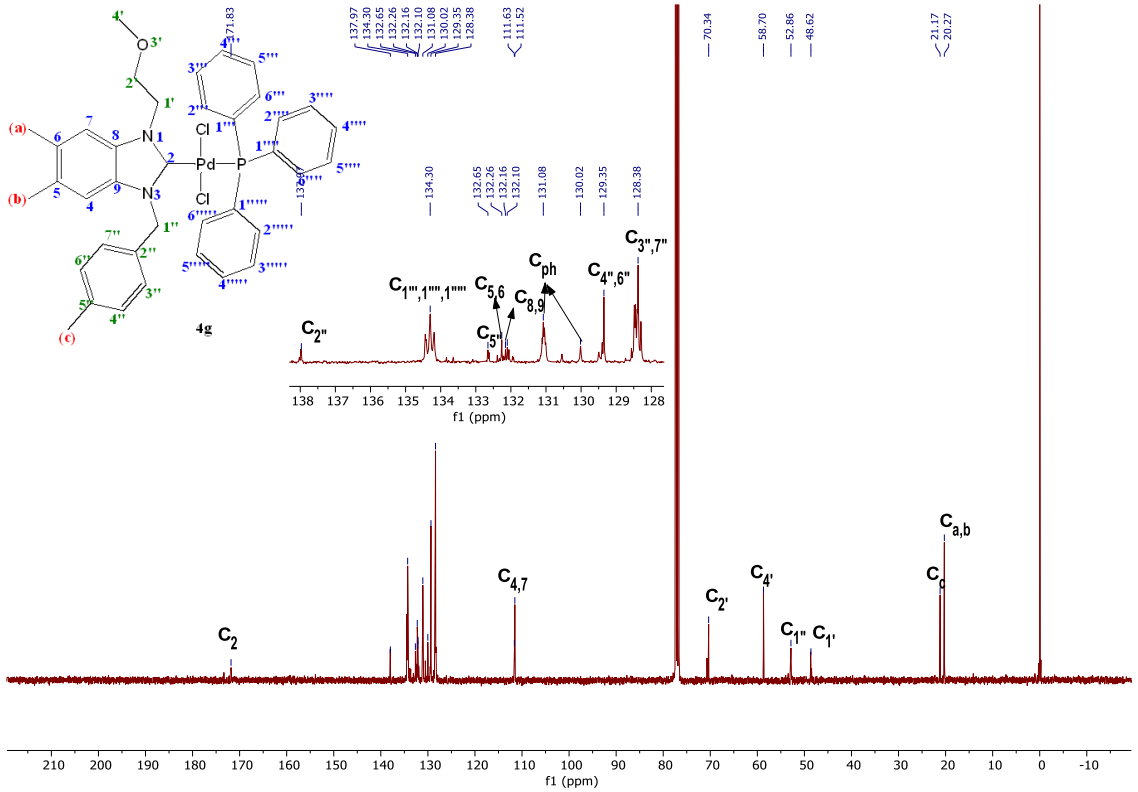


Figure S50. ^{13}C NMR spectrum of complex 4g in $CDCl_3$.

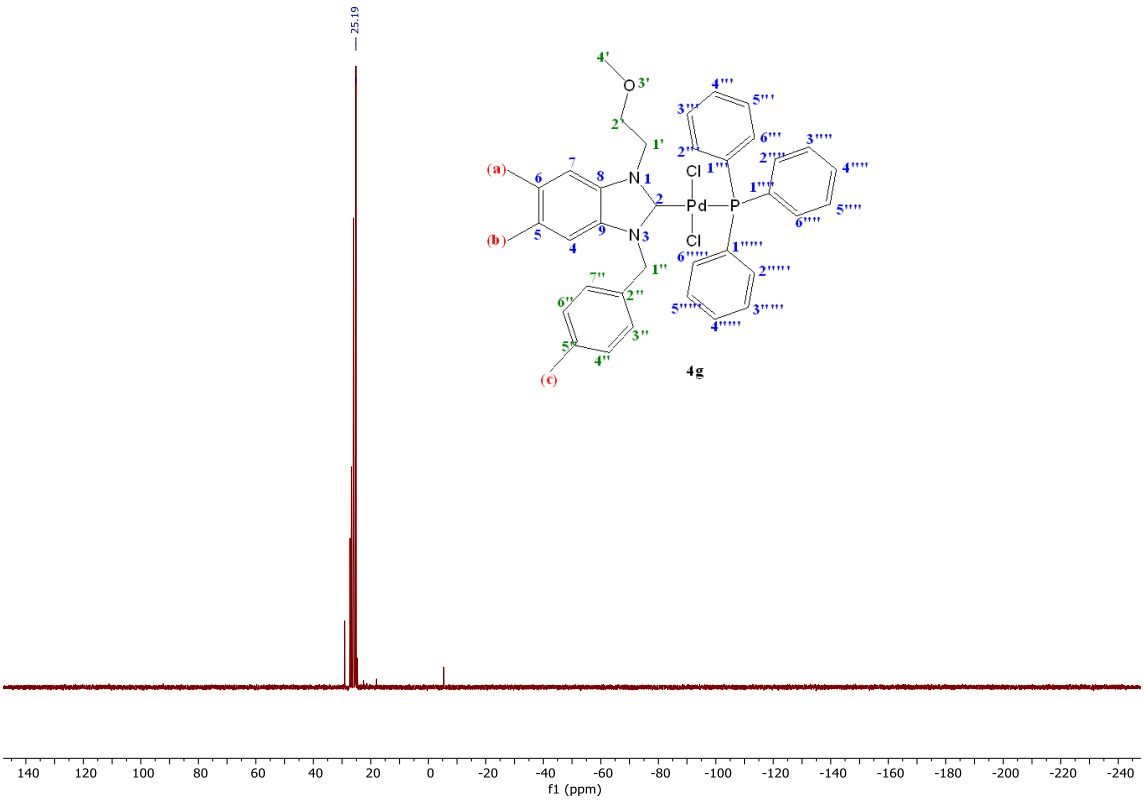


Figure S51. ^{31}P NMR spectrum of complex 4g in $CDCl_3$.

Complex 3h

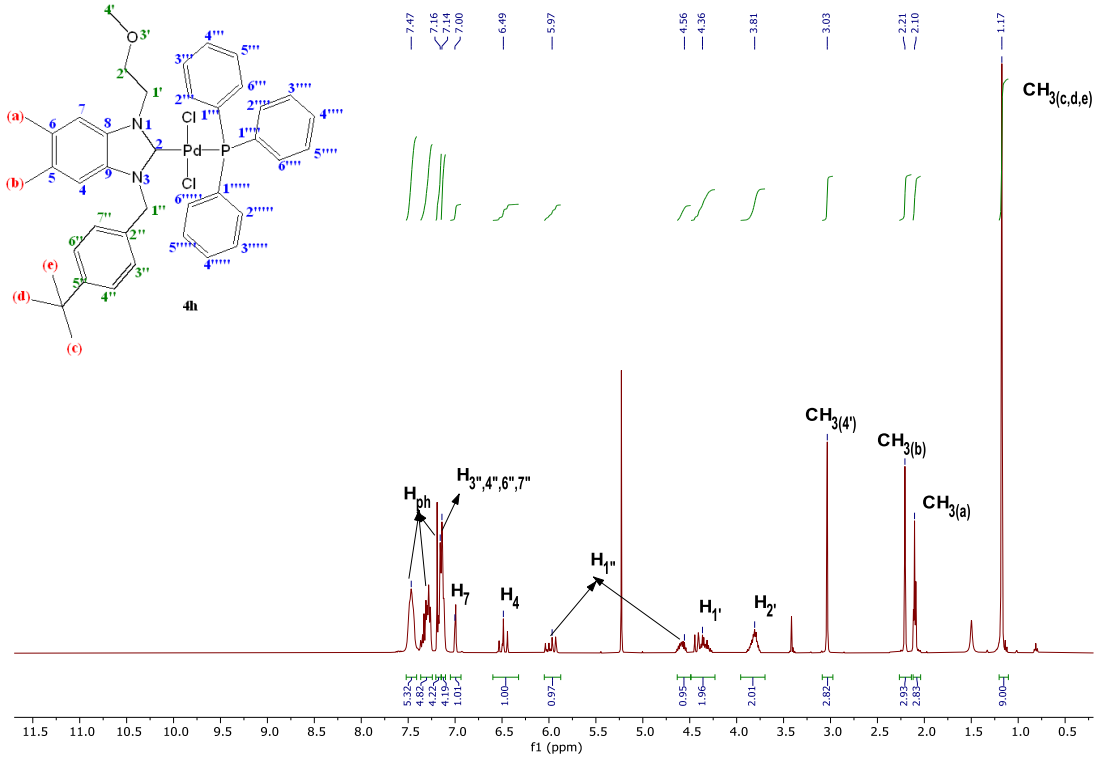


Figure S52. ^{1}H NMR spectrum of complex 4h in $CDCl_3$.

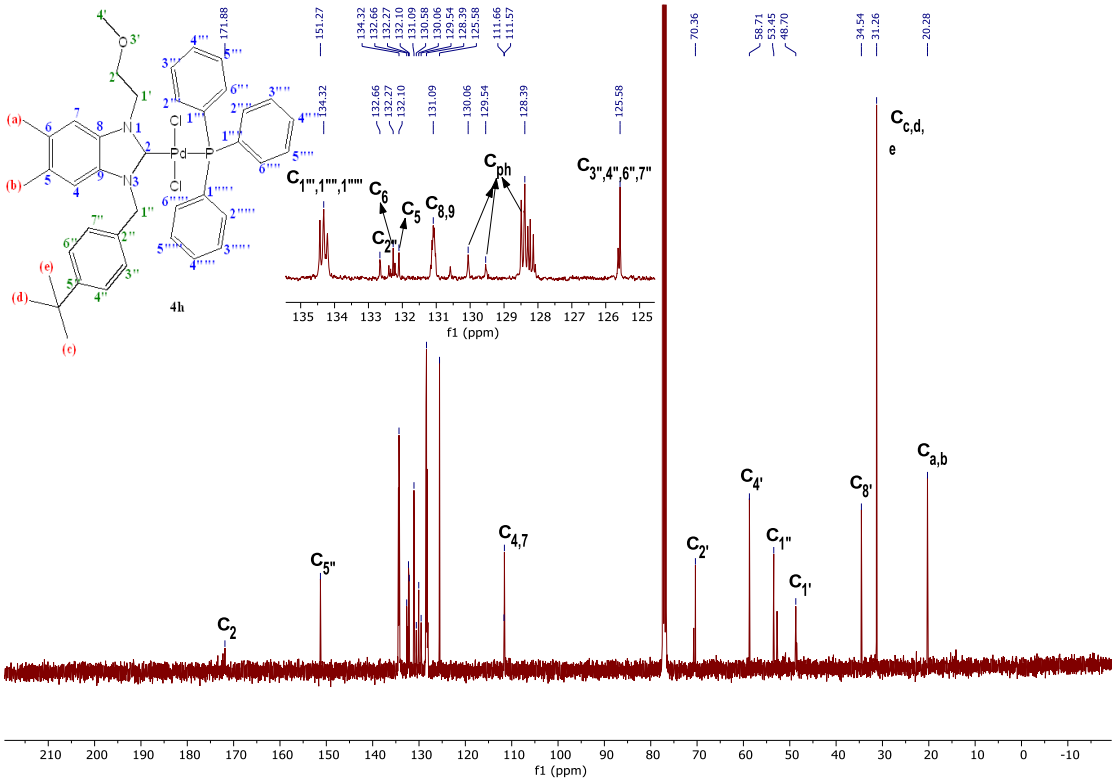


Figure S53. ^{13}C NMR spectrum of complex 4h in $CDCl_3$.

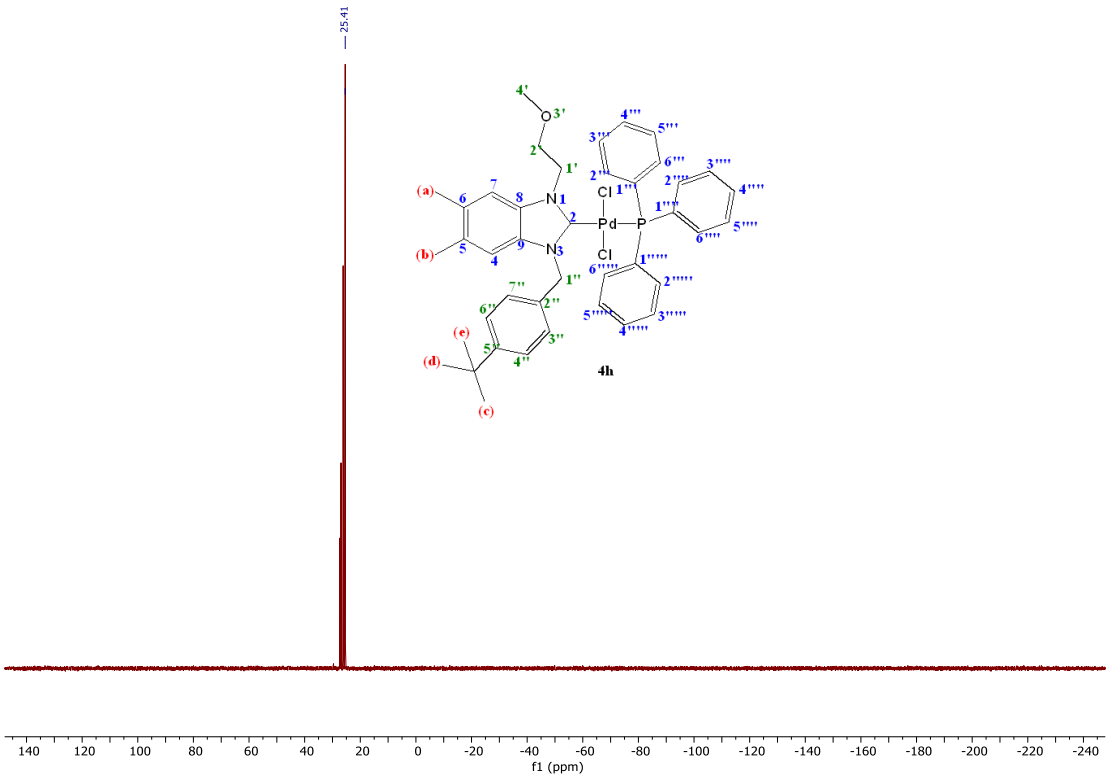


Figure S54. ^{31}P NMR spectrum of complex 4h in $CDCl_3$.

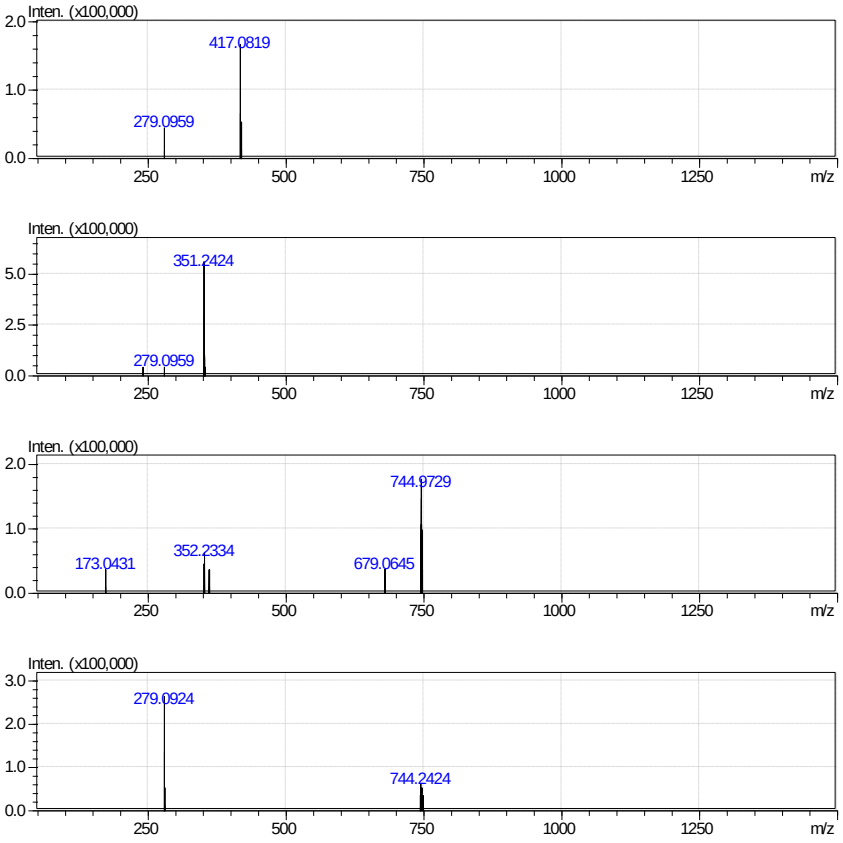


Figure S55. HRMS spectra of complex 4h.

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