ESI –Electronic Supplementary Information

A Case of Novel Catalytic Properties of Pyridyl-Bonded Pd-Catalysts in Cross-Couplings of Aryl halides with Phenyl boronic acid under aerobic conditions

Ridhima Aggarwal, Ritu Bala* and Tarlok Singh Lobana*

Department of Chemistry, Guru Nanak Dev University, Amritsar-143005, Punjab, India

General Details - s1

K_2CO_3 (2 mmol; 276 mg)

Phenyl boronic acid, $PhB(OH)_2$ (1.3 mM; 158.5 mg)

Bromobenzene (1 mM, 105 µL, 157 mg),

p-cyano-bromobenzene (1mM, 182 mg)

p-methoxy- bromobenzene (1mM, 187 mg)

p-methyl-bromobenzene (1mM, 171 mg)

Iodobenzene (1mM, 112 µL, 204 mg)

p-cyano-iodobenzene (1mM, 229 mg)

p-methoxy- iodobenzene (1mM, 234 mg)

p-methyl-iodobenzene (1mM, 218 mg)

[Pd(N,N,S-L- N^4H_2)Cl] (**1**) (10^{-2} mM. 3.9 mg)

[Pd(N,N,S-L-N^4HMe)Cl] (**2**), (10^{-2} mM. 4.1 mg)

[Pd(N,N,S-L-N^4HEt)Cl] (**3**) (10^{-2} mM. 4.24 mg)

[Pd(N,N,S-L-N^4HPh)Cl] (**4**) (10^{-2} mM. 4.7 mg)

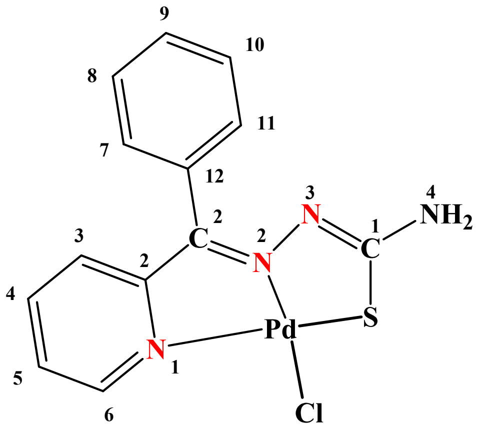
TON = no. of moles of product divided by no. of moles of catalyst

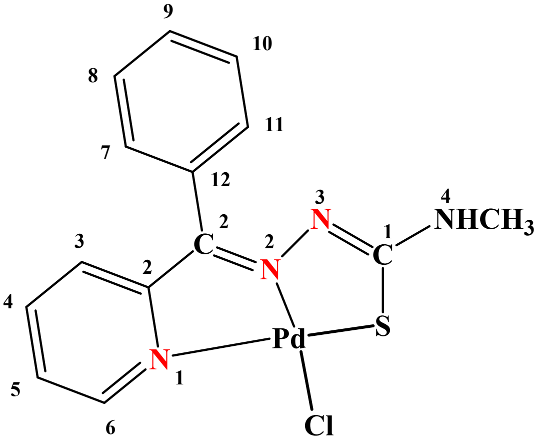
TOF = TON divided by time of reaction.

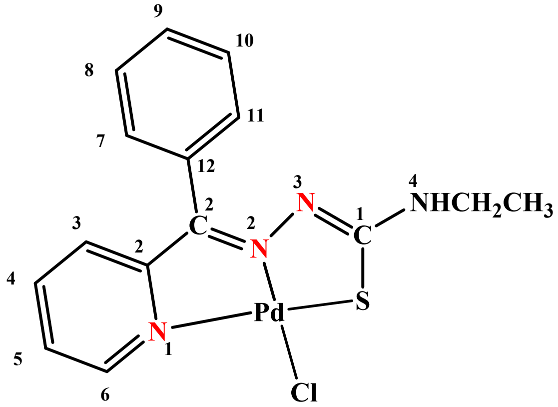
Mol wts. Cat **1** (H). 396.5, Cat **2**(Me). 410.5, Cat.**3**(Et), 424.5; Cat **4** (Ph), 472.5

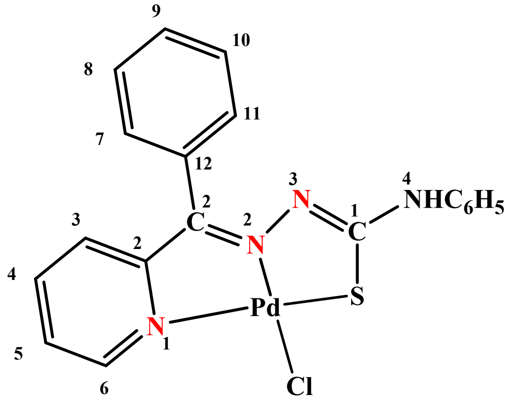
Mol Formula: $C_{13}H_{11}PdClN_4S$; $C_{14}H_{13}PdClN_4S$; $C_{15}H_{15}PdClN_4S$; $C_{19}H_{15}PdClN_4S$

Physical Properties of catalysts –s2

[Pd(N,N,S-L-N^4H_2)Cl] (**1**); Cat **1(H)**  	M. p. 220-224° C; colour: orange; Yield 72% M.F.: $C_{13}H_{11}N_4SPdCl$; MW: 396.5 Solubility: hot ethanol, CH_3CN, DMSO. IR (cm^{-1}) ν(N^4-H) 3451m; ν(C-H) 3131m; ν(C=N) 1595s; δ(N-H) 1618s; ν(C-N) 1059s; ν(C-S) 720w; ^1H NMR (δ ppm, DMSO-d_6): 8.57 (d, CH^6-py); 7.98 (td, CH^4-py); 7.86 (b, N^4H_2); 7.58 (t, CH^5-py); 7.50 (m, $C^{7,11}$-Ph), 7.47 (m, $C^{8,10}$-Ph); 6.94(d, CH^3-py).

[Pd(N,N,S-L-N^{4}HMe))Cl] (**2**); Cat **2(Me)**  	M. p. 260-264°C; colour: orange; Yield 76% MF: $C_{14}H_{13}N_4SPdCl$; MW: 410.5 Solubility: hot ethanol, CH_3CN and DMSO. IR (cm^{-1}) ν(N^4-H) 3414m, ν(C-H) 3021m; ν(C=N)1595s; δ(N-H) 1546m; ν(C-N) 1041s; ν(C-S) 787w; ^{1}H NMR (δ ppm, DMSO-d$_6$): 8.69 (b, N^{4}H); 8.62 (d, CH^6-py); 8.04 (td, CH^4-py); 7.62 (t, CH^{3,5}-py); 7.17 (m, C^2-Ph), 2.64 (s, -CH$_3$).

[Pd(N,N,S-L-N^4HEt)Cl] (3) ; Cat 3**(Et)** 	M. p. 280-284°C; colour: orange; Yield 75% MF:$C_{15}H_{15}N_4SPdCl$; MW: 424.5. Solubility: hot ethanol, CH_3CN and DMSO. IR (cm^{-1}) ν(N^4-H) 3400m, ν(C-H) 3156m; ν(C=N) 1579: δ(N-H) 1508m; ν(C-N) 1151s; ν(C-S) 756w; ^{1}H NMR (δ ppm, DMSO-d_6): 9.99 (b, N^4H); 8.95 (d, CH^6-py); 7.93 (td, CH^4-py); 7.70 (t, $CH^{3,5}$-py); 7.17 (m, C^2-Ph); 3.54 (m, -CH_2) 1.52 (m, -CH_3)

[Pd(N,N,S-L-N^4HPh)Cl] (**4**); Cat **4**(Ph) 	M. p. 288-290°C; colour: dark purple; Yield 77% MF: $C_{19}H_{15}N_4SPdCl$; MW: 472.5. Solubility: hot ethanol, CH_3CN and DMSO. IR (cm^{-1}) ν(N^4-H) 3189m, ν(C-H) 3162m; ν(C=N) 1585s: δ(N-H) 1546m; ν(C-N) 1180s; ν(C-S) 729w; ^{1}H NMR (δ ppm, DMSO-d_6): 10.21 (b, N^4H); 8.65 (d, CH^6-py); 8.06 (td, CH^4-py); 7.67 (t, $CH^{3,5}$-py); 7.58 (m, o- & p-H, N^4-Ph); 7.17 (m, C^2-Ph).

Screening of bases and temperatures (Table - **s1**).

Table **-s**1

Base Screening, 100° C			
Cycles	Base Variation	Time, h	Yield %
1	NaOH	2.5	80
1	KOH	2	83
1	Na_2CO_3	4.5	86
1	K_2CO_3	3	90
1	Cs_2CO_3	8	85

Temperature Screening				
Cycles	Base	Temperature (°C)	Time, h (per cycle)	Yield %
1	KOH	50	4.5	80
4	KOH	70	4.0	82
3	KOH	100	2.0	83
8	K_2CO_3	50	4	92

Cycle refers to completion of reaction, followed by successive in situ additions (aryl halide and phenyl boronic acid) for second, third etc cycles

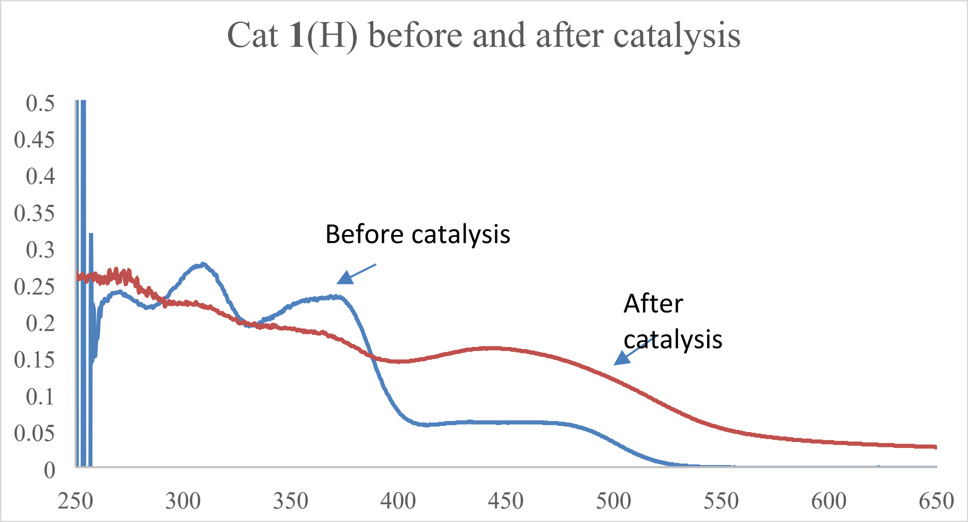
Reaction conditions: bromobenzene, 1 mmol; phenylboronic acid (1.3 mmol), Base (2 mmol), Cat **4**(Ph, (1 mol%)., Upto cycles 1-4, ethanol-water : 9 : 1 (10 mL) (v/v);

For 8 cycles : ethanol-water ratio, 18 : 2 (v/v)

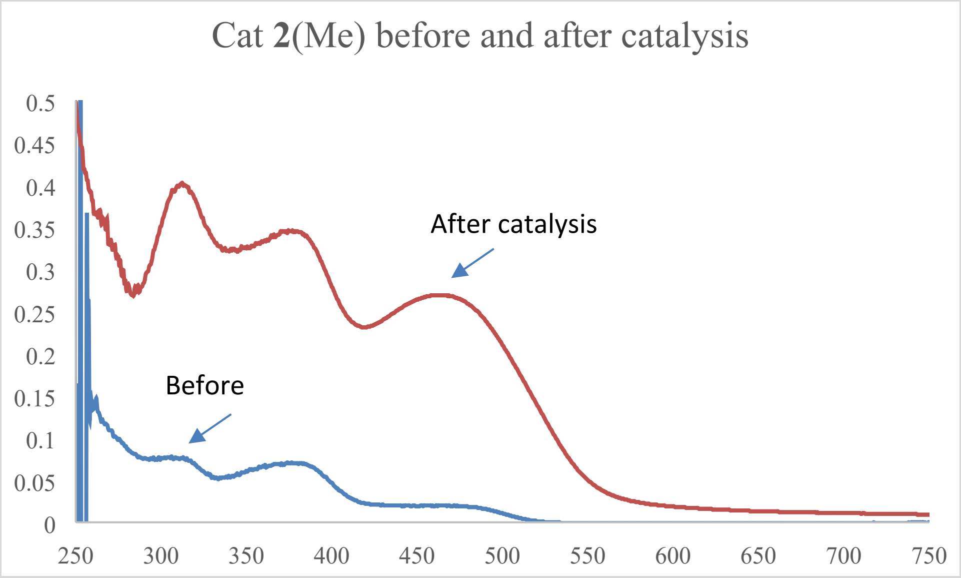
M.p. of catalysts after use – s3

Cat **1**(H): 219-222° C; Cat **2**(Me): 262-265° C; Cat **3**(Et): 273-276° C. Cat **4**(Ph): 284-288° C.

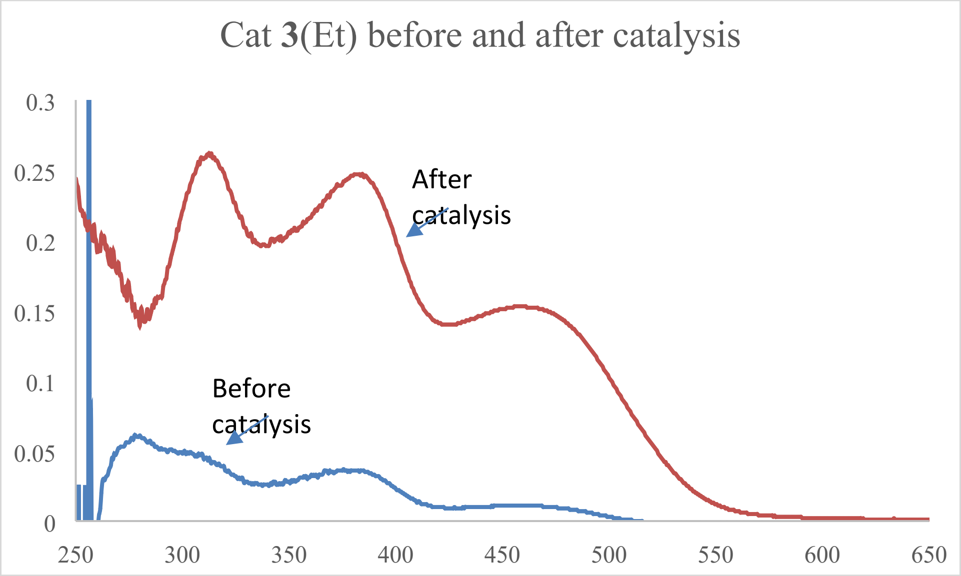
UV-vis spectra of Catalysts before and after use – s4.



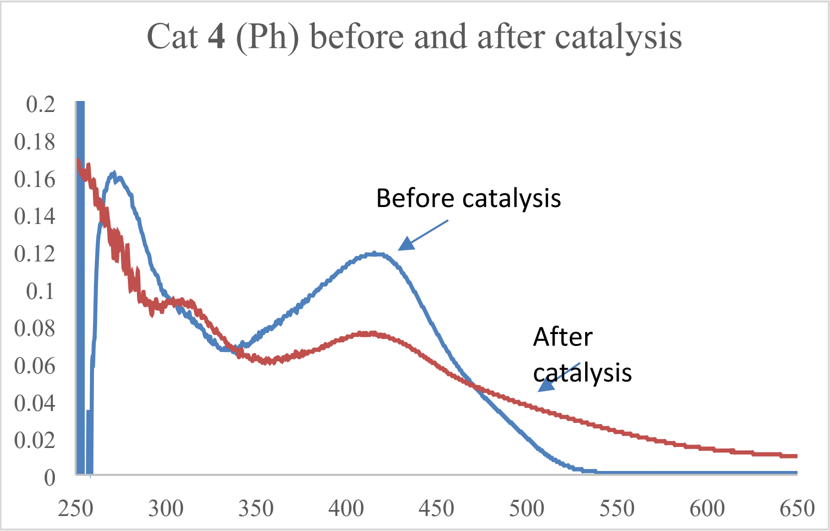
Uv-vis spectra of Cat **1**(H) before and after use (nm)



Uv-vis spectra of Cat **2**(Me) before and after use (nm)



Uv-vis spectra of Cat **3**(Et) before and after use (nm)



Uv-vis spectra of Cat **4**(Ph) before and after use (nm)

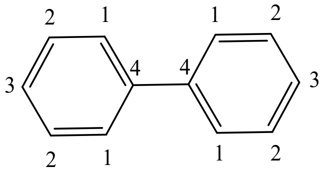
Details of Isolation of diaryl products –s5

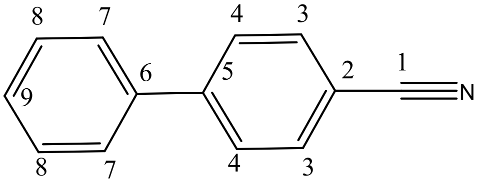
The progress of each catalytic reaction was monitored initially after 15 minutes and later periodically until the reaction was complete (For this an aliquot amount was used by doing a mini work up in eppendorf tube, to which small amount of ethyl acetate and water were added. The di-aryl product goes to the ethyl acetate layer, and is checked using TLC method}. After completion of first cycle, further addition of reactants (aryl halide and phenylboronic acid) was made and reaction monitored as above until the cycle is complete. In this way, the reactions were continued for eight cycles. The reaction mixture was allowed to cool at room temperature and then transferred to the tubes of an electric centrifuge machine, which was operated at 4000 rpm for 30 minutes. After centrifugation, the mother liquor was transferred to a 250 mL RB flask (First) and a fresh lot of ethanol and water mixture (18:2, v/v) was used for centrifugation. The mother liquor was again transferred to the first RB flask and the process was repeated for the third time. In this way the maximum di-aryl product was extracted from centrifuge tubes.

Now to this first RB flask, 20-25 mL each of ethyl acetate and water was added for creating two separate layers: ethyl acetate organic layer and aqueous layer containing ethanol. The contents were stirred for about 2 hours and the entire mixture was transferred to a 250 mL separating funnel in which two layers are visible. The upper ethyl acetate layer contains di-aryl product, and the lower aqueous layer may contain soluble inorganic salts. This upper ethyl acetate layer is passed through a glass funnel (contains anhydrous Na_2SO_4 on a cotton plug), and collected into a new 250 mL RB flask (Second). The aqueous layer is transferred into the first RB flask for second extraction using 20-25 mL each of ethyl acetate and water. The extraction was repeated for the third time. From second and third extractions, the ethyl acetate layers were passed each time through the same separating funnel and organic layers collected into the second RB flask. The ethyl acetate layer containing di-aryl and any other product or impurity, was distilled (use a bead to offset bumping) until a solid product at the bottom of flask was clearly visible (The ethyl acetate recovered can be reused for extractions).

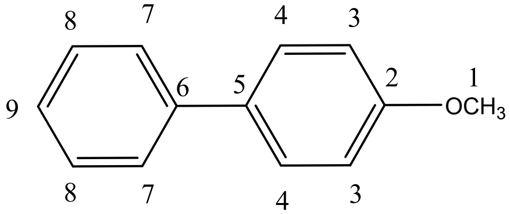
To the crude product left in the second RB flask, after distillation of ethyl acetate, an adequate amount of chloroform is added followed by the slow addition of silica gel to this RB flask, to make a slurry with uniform distribution of silica gel. Prepare a column by fixing cotton plug at the bottom of the column just above the knob to support the silica gel (60-120 mesh). Gently, tap the column for uniform packing. The slurry made above is now poured into the column followed by a gentle tapping of the column to settle the slurry in silica column by ensuring no air bubble is left in the slurry. Now, add n-hexane into the column to elute the sample. The first fraction collected in a 100 mL flask is used for determining the by-product or second product which may be an impurity. The fractions in a series of 250 mL (or higher volume flasks) contain the main product. Both types of products after distilling off n-hexane were identified using TLC method. In case of synthesis of substituted di-aryl product, there is possibility of di-phenyl product owing to the homo coupling of phenyl boronic acid. This di-phenyl being non-polar is eluted in the first fraction followed by other fractions which may contain substituted di-aryl products. The catalyst which is left in the centrifugal tubes is removed with the help of acetonitrile alone or using a mixture of acetonitrile and ethyl acetate. The catalyst goes into the used solvents and evaporation of these solvents gave a solid catalyst which was studied using m.p. and UV-visible spectrum

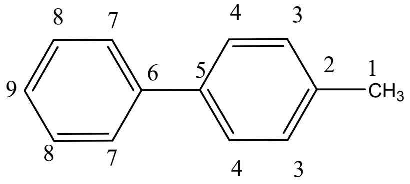
Characterization data of diaryl products - s6

 **[Ref S1]**	M.p. 68-70°C, MF: $C_{12}H_{10}$, MW: 154 ^{1}H NMR (500 MHz, CDCl$_3$): δ (ppm) 7.6 (d, *J* = 7.4 Hz, 4H, C^1-H), 7.54 (t, *J* = 7.3 Hz, 4H, C^2-H), 7.44(t, *J* = 7 Hz, 2H, C^3-H). ^{13}C NMR (125 MHz, CDCl$_3$): δ (ppm) 141.2 (-C^4), 128.2 (-C^2), 127.3 (-C^1), 127.2 (-C^3).

	M.p. 84-86°C, MF: $C_{13}H_9N$, MW: 179 ^{1}H NMR (500 MHz, CDCl$_3$): δ (ppm) 7.73 (dd, *J* = 20.8, 8.2 Hz, 4H, C^{3,4}-H), 7.62 (d, *J* = 7.7 Hz, 2H, C^7-

[**Ref. S2]**	H), 7.51 (t, *J* = 7.5 Hz, 2H, C^{8}-H), 7.45 (t, *J* = 7.3 Hz, 1H, C^{9}-H) ^{13}C NMR (125 MHz, CDCl$_3$): δ (ppm) 145.7 (-C^{5}), 139.2 (-C^{6}), 132.6 (-C^{3}), 129.1 (-C^{8}), 128.6 (-C^{7}), 127.7 (-C^{9}), 127.2 (-C^{4}), 118.9 (-C^{1}), 110.9 (-C^{2})

 [**Ref S1**]	M.p. 88-91°C, MF: $C_{13}H_{12}O$, MW: 184 ^{1}H NMR (500 MHz, CDCl$_3$): δ (ppm) 7.56 (d, *J* = 12 Hz, 2H, C^{7}-H), 7.54 (d, *J* = 3Hz, 2H, C^{4}-H), 7.41 (t, *J* = 7.5 Hz, 2H, C^{8}-H), 7.30 (t, *J* = 7.3 Hz, 1H, C^{9}-H), 6.98 (d, *J* = 8.7 Hz, 2H, C^{3}-H), 3.84 (s, 3H, C^{1}-H) ^{13}C NMR (125 MHz, CDCl$_3$): δ (ppm) 159.1 (-C^{2}), 140.8 (-C^{6}), 133.8 (-C^{5}), 128.7 (-C^{4}), 128.2 (-C^{8}), 126.7 (-C^{9}), 126.6 (-C^{7}), 114.2 (-C^{3}), 55.4 (-C^{1})

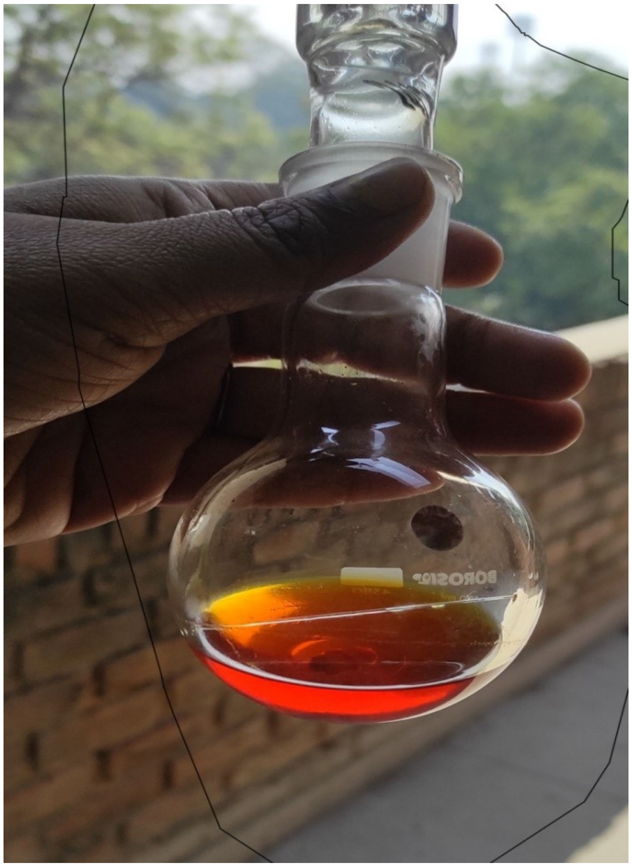
 [Ref **s1**]	M.p. 44-45°C, MF: $C_{13}H_{12}$, MW: 168 ^{1}H NMR (500 MHz, CDCl$_3$): δ (ppm) 7.50 (d, *J* = 7.8 Hz, 2H, C^{7}-H), 7.42 (d, *J* = 8 Hz, 2H, C^{8}-H), 7.35 (t, *J* = 7.7 Hz, 1H, C^{9}-H), 7.25 (t, *J* = 7.3 Hz, 1H, C^{4}-H),

	7.18 (d, $J = 7.6$ Hz, 2H, C^3-H), 2.32 (s, 3H, C^1-H) ^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) 140.1 (-C^6), 137.3 (-C^5), 135.9 (-C^2), 128.7 (-C^3), 128.4 (-C^8), 127.6 (-C^7), 125.9 (-C^9), 125.8 (-C^4), 20.1 (-C^1)

Ref. **s1**. H. Yan, P. Chellan, T. Li, J. Mao, K. Chibale and G. S. Smith, Cyclometallated Pd(II) thiosemicarbazone complexes: new catalyst precursors for Suzuki-coupling reactions, Tetrahedron Lett., 2013, 54, 154–157. doi.org/10.1016/j.tetlet.2012.10.115.

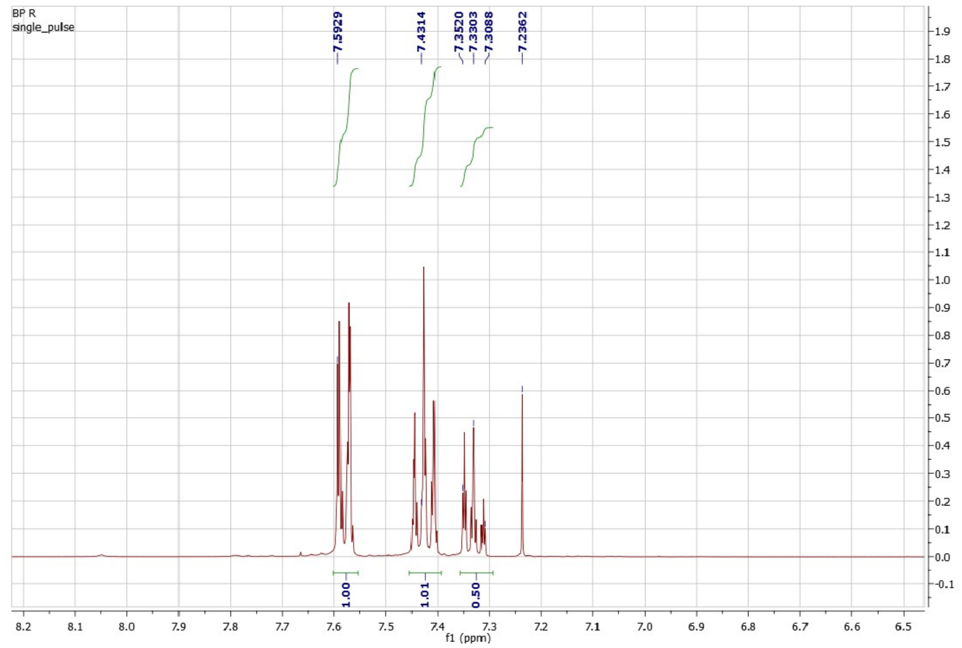
Ref. **-s2 :** A. Aschenaki, F. Ren, J. Liu, W. Zheng, Q. Song, W. Jia, J. J. Bao and Y. Li, Preparation of a magnetic and recyclable superparamagnetic silica support with a boronic acid group for immobilizing Pd catalysts and its applications in Suzuki reactions, RSC Adv, 2021,11, 33692-33702. DOI: 10.1039/d1ra04892a.

Homogeneous reaction mixturen– **Figure - s1**

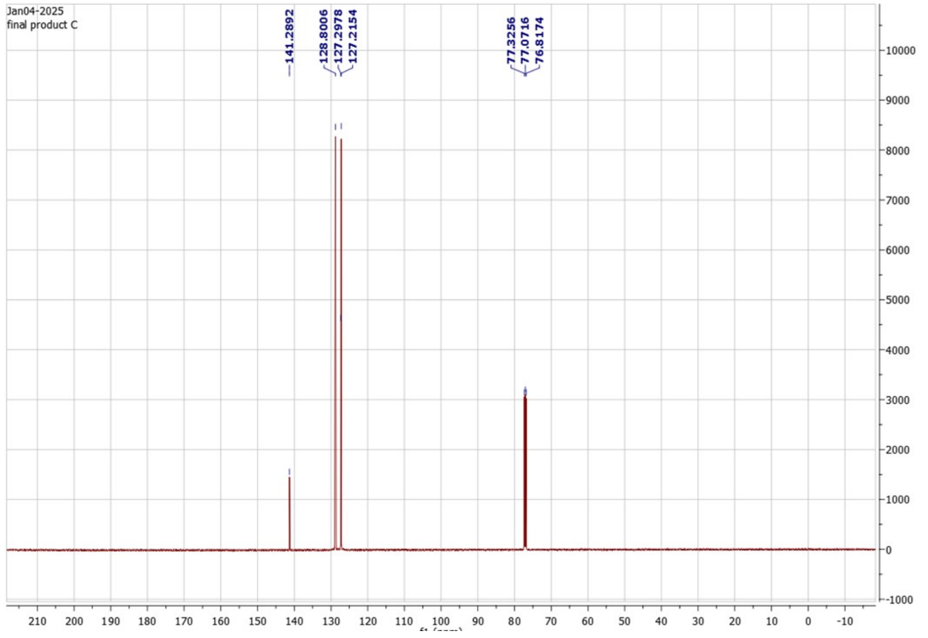


^{1}H and ^{13}C NMR of biaryl products – s7

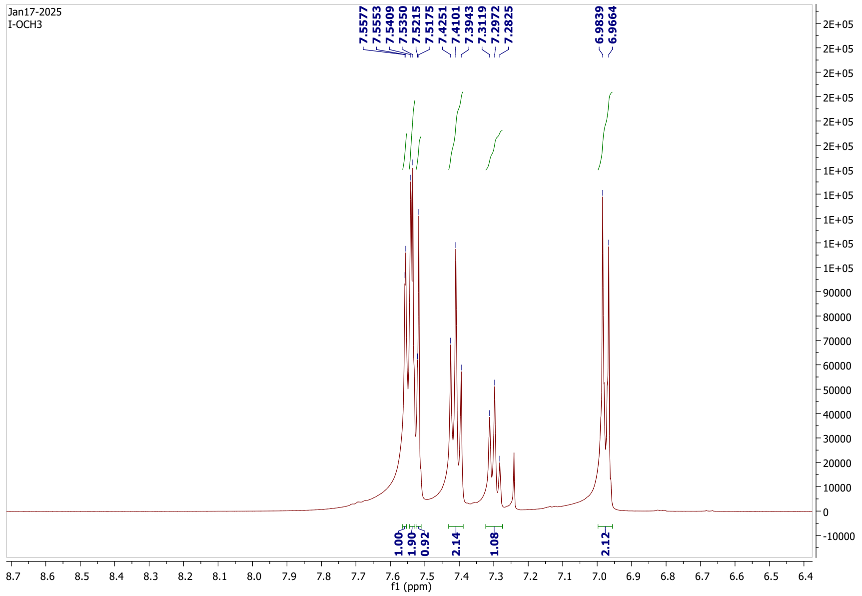
^{1}H NMR of biphenyl

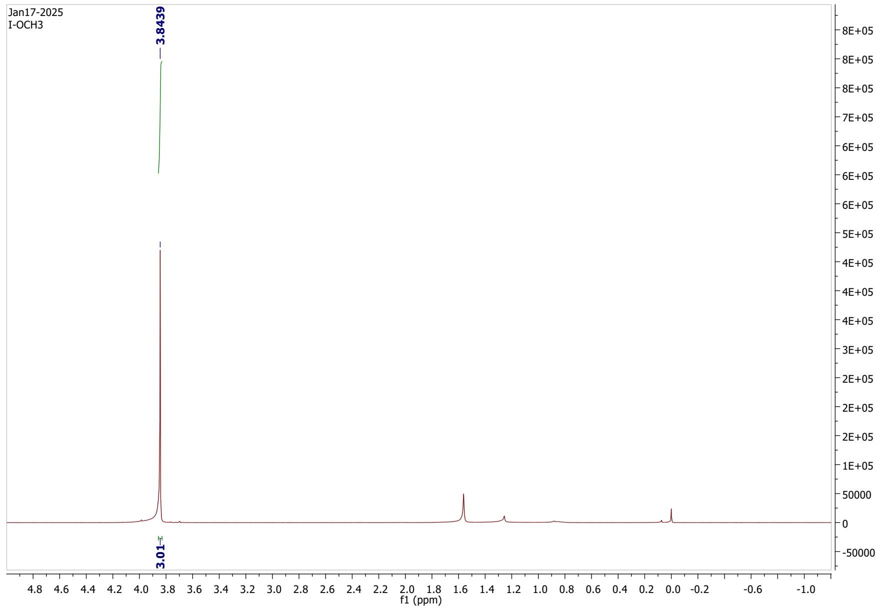


^{13}C NMR of biphenyl

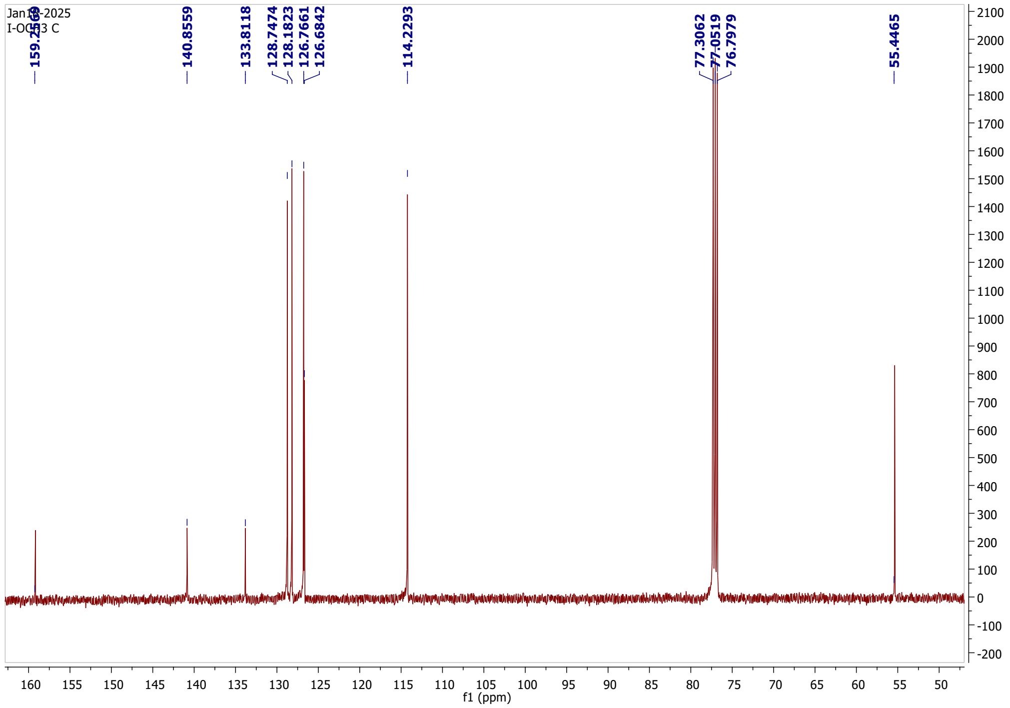


^{1}H NMR of 4-methoxy biphenyl

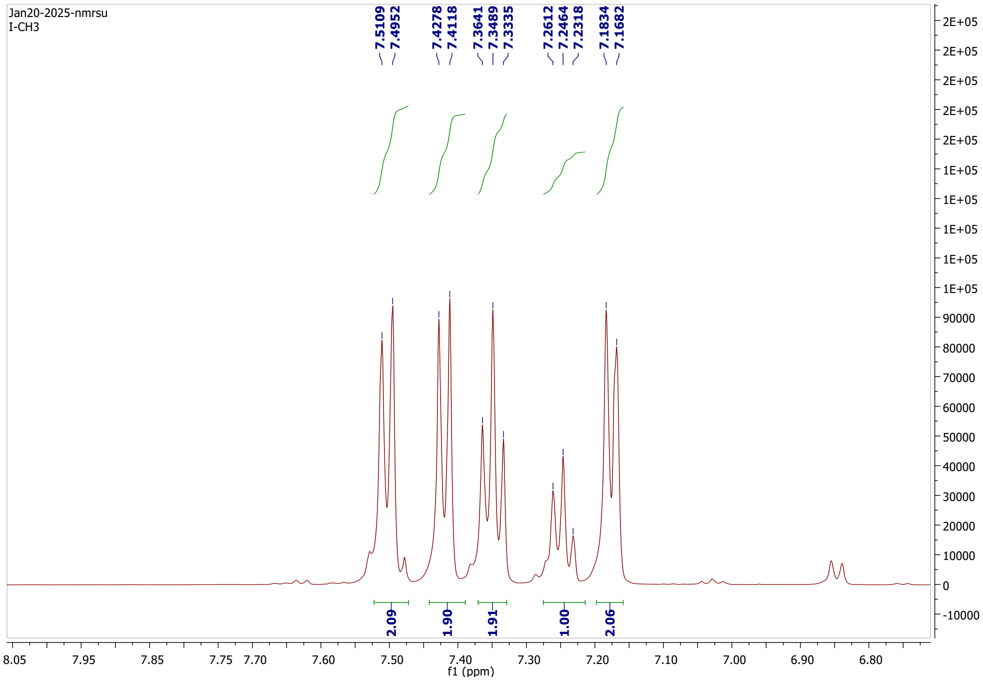


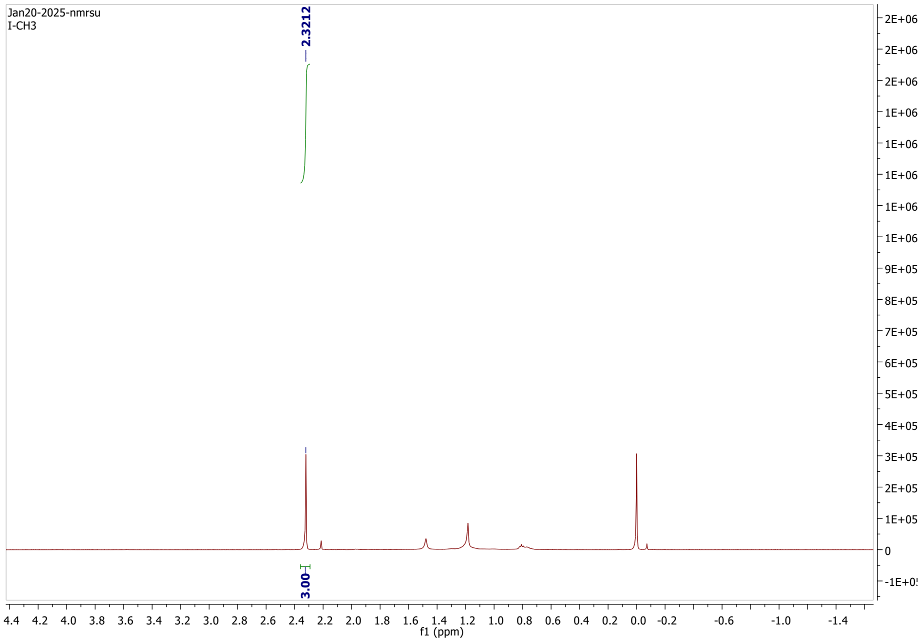


^{13}C NMR of 4-methoxy biphenyl

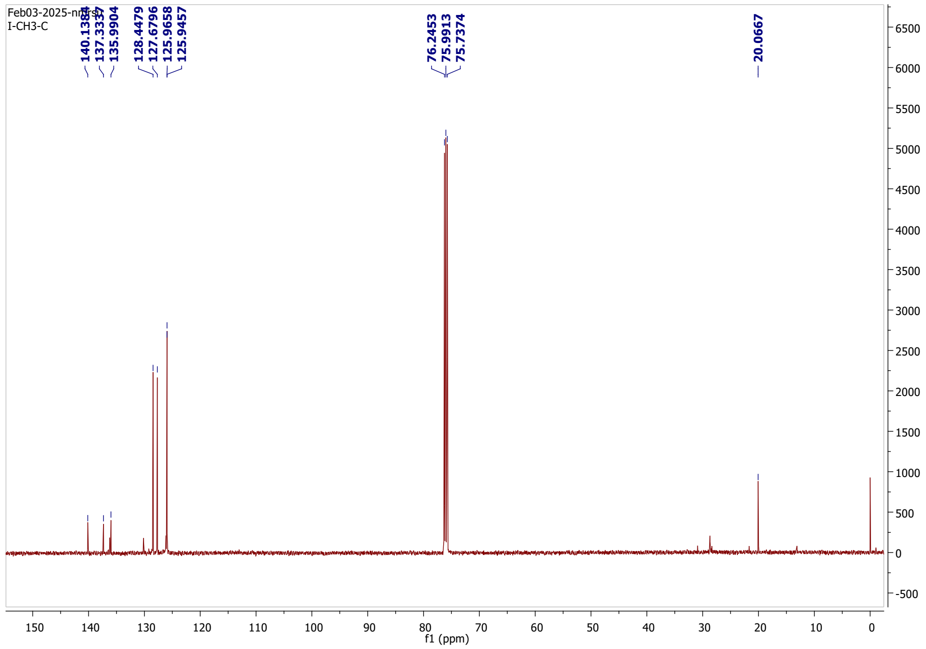


^{1}H NMR of 4-methyl biphenyl

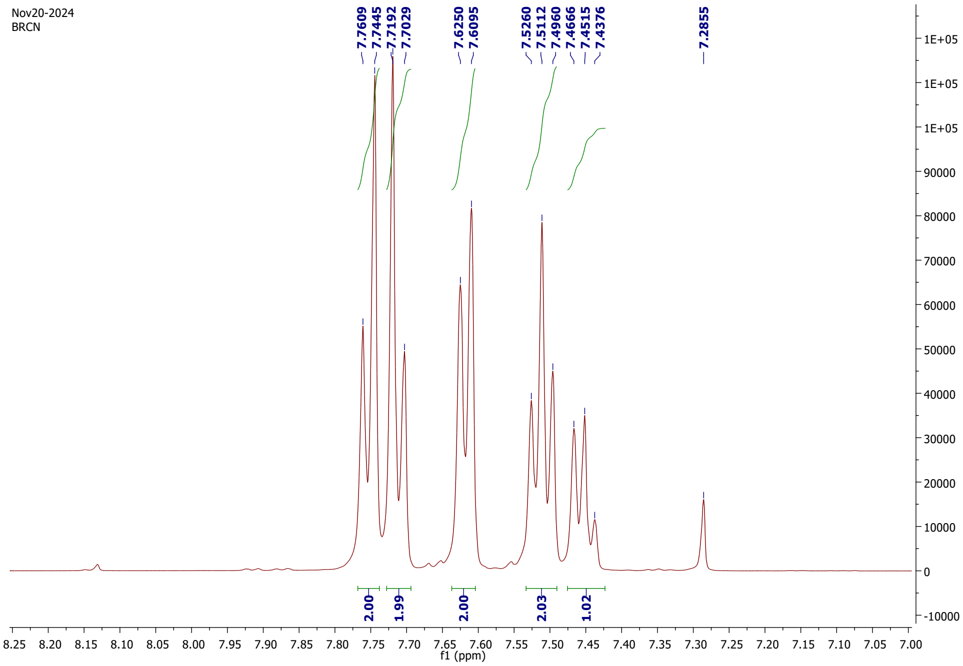


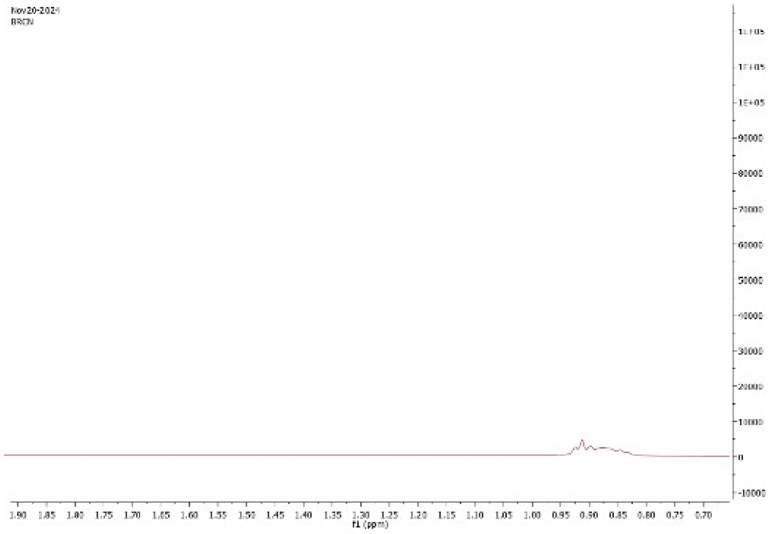


^{13}C NMR of 4-methyl biphenyl

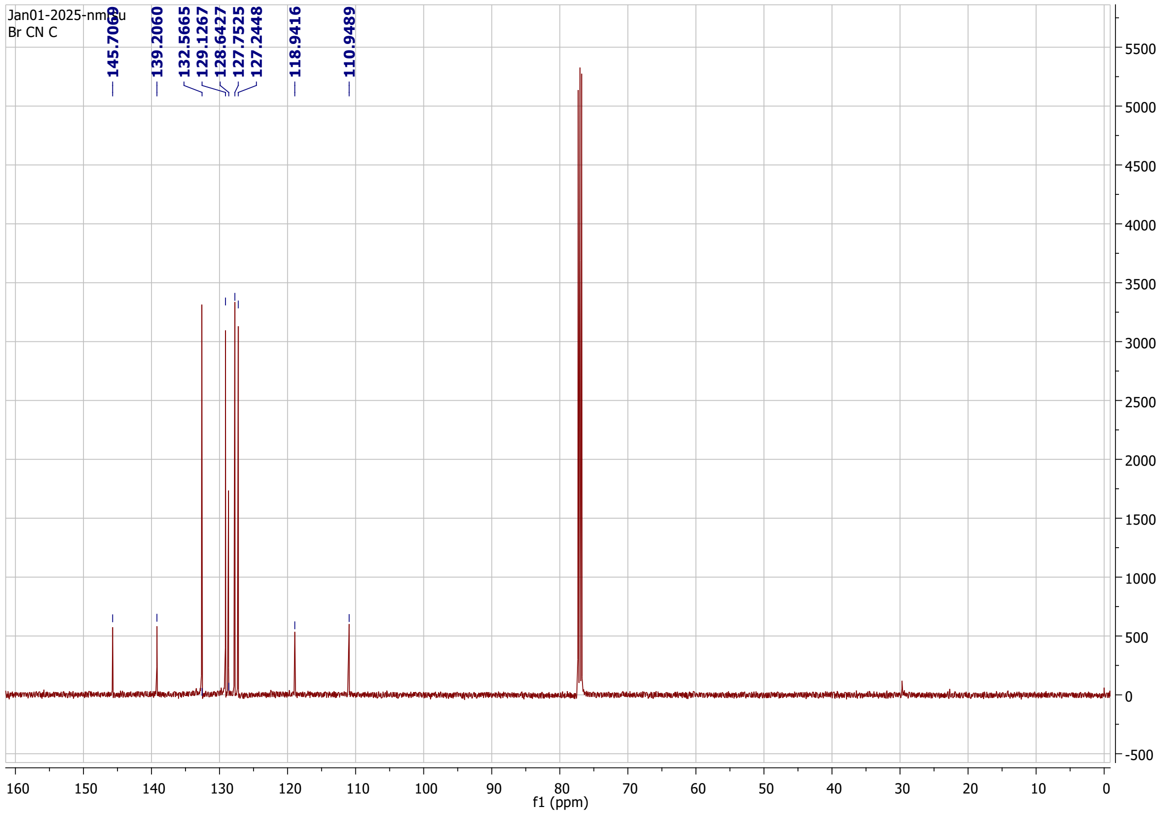


^{1}H NMR of 4-cyano biphenyl



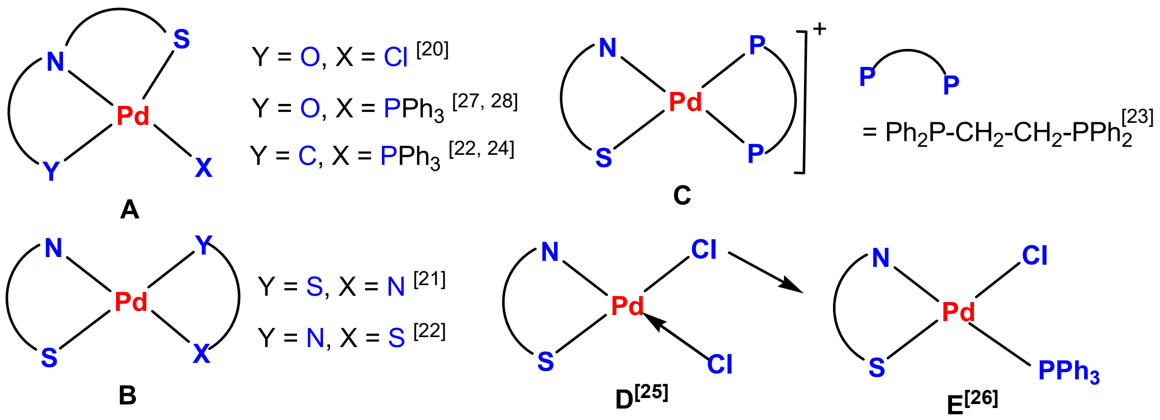


^{13}C NMR of 4-cyano biphenyl



Cores of catalysts –s8

Thiosemicarbazone based Pd catalysts, reported in literature, have central coordination cores (A-E) : {Pd(Y,N,S)X}(Y=O, C; X= Cl, PPh_3) (**mode A**),[20,22,24,27,28] $\{Pd(N,S)_2\}$ **(mode B)**,[21,22] $[Pd(N,S)(P,P)]^+$(**mode C**), [23] dimeric $[Pd_2(N,S)_2(\mu\text{-}Cl)_2\ )]$ (**mode D**- half shown) and $[Pd(N,S)(Cl)(PPh_3)]$ (**mode E**)[26] but none of which have pyridyl group bonded to Pd.



Types of coordination cores of catalysts