Synthesis and Reactivity of (PCN^{Me}) Pincer Pd(II) Complexes

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Table of Contents

Abstract

New (PCN^{Me})Pd(II) complexes were synthesized and their properties were studied in various reactions. (PCN^{Me})Pd-Br was synthesized and employed as catalyst for Suzuki cross-coupling reactions of aryl halides (e.g. bromobenzene, 4-bromotoulene and 4-bromobenzaldehyde) with phenylboronic acids (e.g. phenylboronic acid, 4-formyl phenylboronic acid and p-tolyl boronic acid). High yields and high turnover numbers were achieved using catalyst loading of only 0.05 %. To gain a deeper insight into the mechanism of these coupling reactions, (PCN^{Me})Pd complexes bearing palladium carbon bonds were synthesized and its reactivity with aryl halides (or phenyl bromide) was studied. In kinetic experiments the influence of different additives on the reaction were analyzed to investigate their role in the CC coupling step.

List of abbreviations for (PCN^{Me})Pd(II) Complexes

(PCN^{Me})Pd-Cl	[1-((dimethylamino)methyl)-3-((di-*tert*-butylphosphino)methyl)benzene] palladium(II) chloride
(PCN^{Me})Pd-TFA	[1-((dimethylamino)methyl)-3-((di-*tert*-butylphosphino)methyl)benzene] palladium(II) Trifluoroacetate
(PCN^{Me})Pd-Br	[1-((dimethylamino)methyl)-3-((di-*tert*-butylphosphino)methyl)benzene] palladium(II) Bromide
(PCN^{Me})Pd-Ph	[1-((dimethylamino)methyl)-3-((di-*tert*-butylphosphino)methyl)benzene] Phenyl Palladium(II)
(PCN^{Me})Pd-NO_3	[1-((dimethylamino)methyl)-3-((di-*tert*-butylphosphino)methyl)benzene] palladium(II) Nitrate.
(PCN^{Me})Pd-I	[1-((dimethylamino)methyl)-3-((di-*tert*-butylphosphino)methyl)benzene] palladium(II) Iodide
(PCN^{Me})Pd-phenyl acetylide	[1-((dimethylamino)methyl)-3-((di-*tert*-butylphosphino)methyl)benzene] palladium(II) Phenyl acetylide

Introduction

Cross coupling reactions are considered one of the most useful and important in the field of organic chemistry where C-C and C-X (X= Heteroatom) bonds easy to form in presence of catalyst. Among the transition metal complexes, palladium complexes were employed as catalysts for Suzuki-Miyaura, Heck, Sonogashira and also Stille coupling reactions.[1]

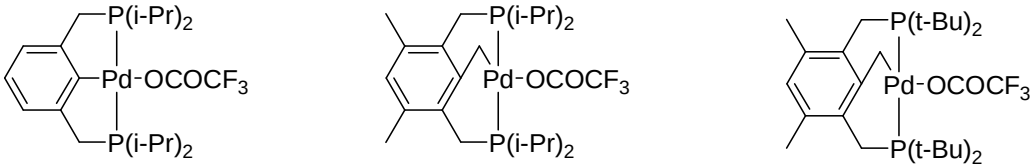
Many publications have been issued about the synthesis of new transition metal complexes with pincer ligands since Moulton and Shaw succeeded to cyclometallate transition metals like Iridium, Nickel, Palladium, Platinum, and Rhodium with the tridentate pincer type ligand (**1**).[2] After this work, Venanzi *et al.* used the analogous ligand (**2**) with palladium and nickel precursors to synthesize new pincer complexes.[3]

1 **2**

Scheme1. The structures of PCP pincer type ligand used by Shaw and Venanzi

Different structures of pincer ligands like PCP, SCS, SeCSe, NCN and PCN (where the abbreviations represent the attached atoms from the ligand to the central metal atom) were synthesized by changing the terminal atoms which attached to the arms. The tridentate coordination fashion with transition metals make the resulting complexes strong. Introducing different substituents to the terminal atoms (N, S and P) change the steric and electronic properties of these ligands. A new category of transition metal complexes was synthesized by cyclometallation with this different structure of pincer ligands.[4]

In 1997, David Milstein synthesized new PCP pincer Palladium complexes as shown in scheme 2. They were employed as catalysts for Heck reaction[5]; these complexes were thermally stable and are not sensitive to air and moisture. High turnover numbers were achieved especially with complex (**4)**.



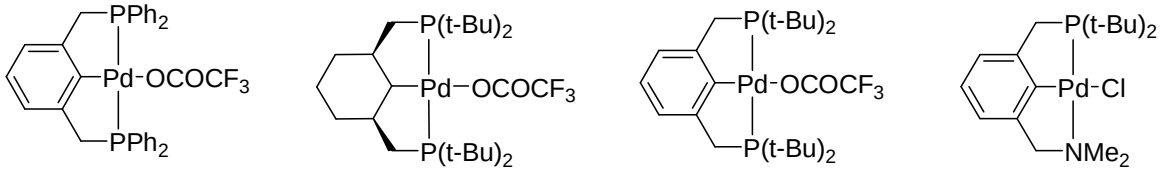
3 **4** **5**

Scheme2. Different structures of (PCP)Pd(II) complexes catalyzed Heck reaction by David Milstein

New pincer ligand with cyclic aliphatic backbone was synthesized by Sven Sjövall (in Wendt's group). Complexation with Pd(TFA)$_2$ produced complex **(7)**. The later complex was used as

catalyst for Heck reaction.[6]Gusev *et al.* used Sjövall's ligand to synthesize palladium and rhodium complexes.[7]

Complex **(6)** was used as a catalyst in Stille coupling reaction of trimethylphenyltin and aryl halide by Daniel Olsson.[8]The highest turnover number of 6.9×10^5 was achieved by catalyst loading 0.0001 % using bromobenzene as the aryl halide source and a heterogeneous mechanism including palladium particles was suggested. Complex **(7)** was used as catalyst for Suzuki coupling reaction of phenyl boronic acid with different aryl halides where metathesis mechanism including molecular Pd(II) species was suggested as a parallel mechanism to the conventional Pd(0)/Pd(II) mechanism for C-C bond formation step based on the negative mercury poisoning test and the kinetic experiments which were monitored using ^{31}P-NMR spectroscopy.[9]



6 **7** **8** **9**

Scheme3. The structures of (PCP)Pd(II) complexes which were synthesized in Wendt's group

Tridentate pincer type ligand was synthesized by Andre Fleckhaus[10] in Wendt's group, this ligand has a nitrogen atom bearing two methyl groups in one arm and phosphorus atom bear two *tert*-butyl groups on the other arm forming hemi-labile complexes with transition metals which opened the door to synthesize a new series of palladium complexes. The PCN^{Me} pincer ligand was reacted with $(MeCN)_2PdCl_2$ in presence of sodium bicarbonate as base to form (PCN^{Me})Pd-Cl **(9)** which was used as a precursor for synthesizing all palladium complexes in the present work. Using such kind of hemi-labile complexes could be useful for the metathesis mechanism of C-C bond formation step due to the weak binding nature of the nitrogen side arm to the palladium in comparison to the phosphorus side arm which facilitate the formation of the cross coupling product through opening the nitrogen side arm.

Project Aim

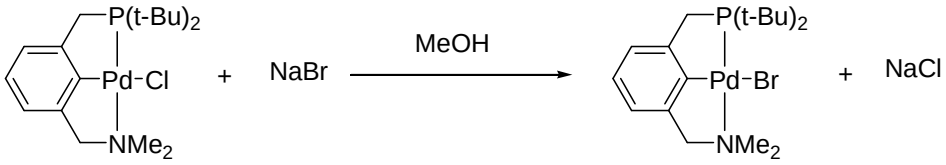
Synthesis of some (PCN^{Me})Pd(II) complexes and study the mechanism of the C-C bond formation step of Suzuki and Sonogashira cross-coupling reactions by the reaction of (PCN^{Me})Pd complexes bearing palladium carbon bonds with phenyl bromide. Also, Study the influence of different additives and investigate their role in the CC coupling step.

Results and discussions

Suzuki reaction catalyzed by (PCN^{Me})Pd-Br complex

In contrast to the previously synthesized (PCP)Pd-complexes in the group, (PCN^{Me})Pd-Br is a hemi labile complex containing nitrogen atom which binds weaker to the palladium in comparison to phosphorous atom. To check the difference in reactivity, (PCN^{Me})Pd-Br was

employed as catalyst for Suzuki reaction under the same reaction conditions as (PCP)Pd-complexes. The catalyst (PCN^{Me})Pd-Br was synthesized by ligand substitution reaction of (PCN^{Me})Pd-Cl with NaBr in methanol as shown below in scheme3.



Scheme4. Synthesis of (PCN^{Me})Pd-Br

(PCN^{Me})Pd-Br was used as a catalyst for Suzuki reaction of aryl halides (e.g. bromobenzene, 4-bromotoulene, and 4-bromobenzaldehyde) with Phenylboronic acids (e.g. Phenylboronic acid, 4-formyl, Phenylboronic acid, and p-Tolyl boronic acid). The products were not separated and isolated .The yields of these reactions were determined by GC analysis using 2-methylnaphthalene as internal standard. The ratio between the used aryl halides and phenyl boronic acids is 1:1.5 (mol: mol).The reactions were carried out at 160 °C for 24 h using potassium phosphate as base. The first experiment was carried out by loading 0.25 % of the catalyst and the yields were calculated after 5 h and 24 h as shown in Table1.

Table1. Suzuki reaction catalyzed by (PCN^{Me})Pd-Br (0.25 %)

Entry	**PhX**	**Ar-B(OH)$_2$**	**TON***	**Yield**	
				5 h	**24 h**
1	PhBr	Ph-B(OH)$_2$	308	70	77
2	PhBr	4-CH$_3$O-C$_6$H$_4$-B(OH)$_2$	140	33	35
3	PhBr	4-CHO-C$_6$H$_4$-B(OH)$_2$	20	4	5
4	4-CH$_3$-C$_6$H$_4$-Br	Ph-B(OH)$_2$	356	81	89
5	4-CH$_3$-C$_6$H$_4$-Br	4-CH$_3$O-C$_6$H$_4$-B(OH)$_2$	140	35	35
6	4-CH$_3$-C$_6$H$_4$-Br	4-CHO-C$_6$H$_4$-B(OH)$_2$	16	0	4
7	4-CHO-C$_6$H$_4$-Br	Ph-B(OH)$_2$	308	69	77
8	4-CHO-C$_6$H$_4$-Br	4-CH$_3$O-C$_6$H$_4$-B(OH)$_2$	160	0	40
9	4-CHO-C$_6$H$_4$-Br	4-CHO-C$_6$H$_4$-B(OH)$_2$	64	12	16

*[Prod]/ [Pd] (mol/mol)

From the previous results, Phenyl boronic acid achieved highest yields compared to the substituted phenyl boronic acids. The electron rich couple partner 4-tolyl bromide gave higher yield than the electron poor 4-bromobenzaldehyde and this is not expected.

Decreasing the amount of the loading catalyst led to a decrease in the yield of the cross coupling product as shown in table 2. The highest yield was achieved with the electron poor substituted aryl halide 4-formyl bromobenzene and the electron rich p-tolyl boronic acids.

Table2. Suzuki reaction catalyzed by (PCN^{Me})Pd-Br (0.05 %)

Entry	PhX	Ar-$B(OH)_2$	TON*	Yield%	
				5 h	24 h
1	PhBr	Ph-$B(OH)_2$	1040	46	52
2	PhBr	4-CH_3-C_6H_4-$B(OH)_2$	740	35	37
3	PhBr	4-CHO-C_6H_4-$B(OH)_2$	100	4	5
4	4-CH_3-C_6H_4-Br	Ph-$B(OH)_2$	1000	48	50
5	4-CH_3-C_6H_4-Br	4-CH_3-C_6H_4-$B(OH)_2$	720	34	36
6	4-CH_3-C_6H_4-Br	4-CHO-C_6H_4-$B(OH)_2$	----	0	0
7	4-CHO-C_6H_4-Br	Ph-$B(OH)_2$	920	42	46
8	4-CHO-C_6H_4-Br	4-CH_3-C_6H_4-$B(OH)_2$	1080	53	54
9	4-CHO-C_6H_4-Br	4-CHO-C_6H_4-$B(OH)_2$	200	8	10

Reaction of the coupling partner phenyl boronic acid with three different aryl halides was carried out to check the reactivity of the substituted aryl halide toward the cross coupling reaction. In case of bromobenzene the yield is not the absolute value for the cross coupling product since the homo coupling and the cross coupling is the same in this case (biphenyl). In the case of 4-formyl bromobenzene, the electron withdrawing group CHO makes the aryl halide more electrophilic and highly reactive to couple with phenyl boronic acid. This gave a high yield in comparison to the electron donating group CH_3 in case of p-tolyl bromobenzene as shown in table3.

Table3. Suzuki reaction catalyzed by (PCN^{Me})Pd-Br (0.05 %) (phenyl boronic acid & different aryl halides)

Entry	PhX	Yield%			
		15 min	1h	5h	24h
1	PhBr	29	38	48	49
2	4-CH_3-C_6H_4-Br	29	33	36	36

3	4-CHO-C_6H_4-Br	26	32	49	47

Reaction of phenyl boronic acid with p-tolyl bromide in presence of additives was studied. As shown in table 4, sodium bromide increased the yield but not so much and in case of copper acetate there is no cross coupling reaction and this is may be due transmetalation between copper acetate and (PCN^{Me})Pd-Br to produce (PCN^{Me})Pd-acetate and copper bromide.

Table4. Suzuki reaction catalyzed by (PCN^{Me})Pd-Br (0.05 %) (Phenyl boronic acid & p-tolyl bromide) with additives

Entry	**Additives**	**Yield %**	
		1 h	**18 h**
1	No additives	33	42
2	Copper acetate	0	0
3	Sodium bromide	0	48
4	Iron bromide	34	41
5	Silver acetate	10	10
6	Cobalt (II) chloride.$6H_2O$	35	43
7	Chromium (III) chloride	23	28
8	Nickel (II) chloride	36	39
9	IMesAu(I)-Cl	17	17

In case of IMesAu(I)-Cl only 17 % of the cross coupling product was observed after 1h and there was no change after 18 h and this may be due deactivation of the catalyst.

Different concentrations of the additives which achieved good yields in the previous experiments were studied as shown in table 5

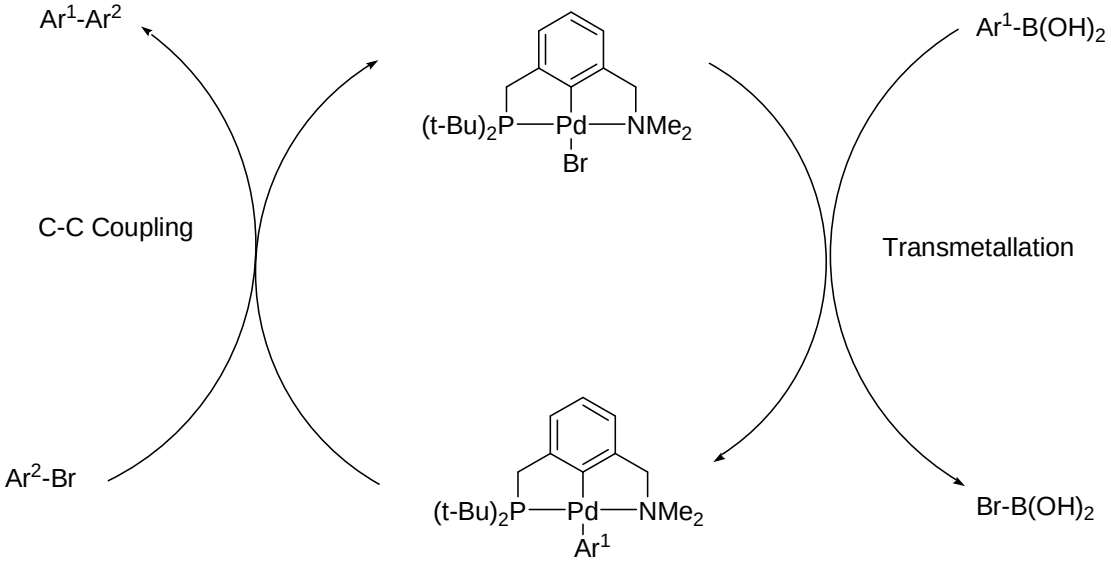
Table5. Suzuki reaction catalyzed by (PCN^{Me}) Pd-Br (0.05 %) (Phenyl boronic acid & p-tolyl bromide) with different concentrations of the additives

Entry	**Additives**	**Con.**	**Yield %**	
			1 h	**18 h**
1	No additives		32	40

2	Sodium bromide	0.1 equiv.	28	36
3	Cobalt (II) chloride.6H_2O	0.1 equiv.	34	41
4	Nickel (II) chloride	0.1 equiv.	33	41
5	Sodium bromide	0.5 equiv.	33	43
6	Cobalt (II) chloride.6H_2O	0.5 equiv.	0	36
7	Nickel (II) chloride	0.5 equiv.	35	41
8	Sodium bromide	1 equiv.	32	39
9	Cobalt (II) chloride.6H_2O	1 equiv.	40	47
10	Nickel (II) chloride	1 equiv.	0	0

Using additives did not affect so much the yield except in the case of Cobalt (II) chloride.6H_2O. The effect of Cobalt (II) chloride.6H_2O in these reactions is not clear. One can suggest that it act as a co-catalyst. In case of 1 equivalent of Nickel (II) chloride, the vial was opened during the heating process and the products were evaporated.

The suggested catalytic cycle for cross coupling reaction between phenyl boronic acids and aryl halides starts by transmetalation between (PCN^{Me})Pd-Br complex and phenyl boronic acid to form (PCN^{Me})Pd-Ph which reacts with aryl halide to form the cross coupling product and generate the catalyst as shown in scheme 5. The same the catalytic cycle was suggested by Daniel Olsson with (PCP)Pd(II) complex due to the fact there is no difference in reactivity between both catalysts as approximately the same amount of yields of cross coupling products were obtained under the same reaction conditions.



Scheme5. Suggested catalytic cycle for Suzuki reaction using (PCN^{Me})Pd-Br as catalyst

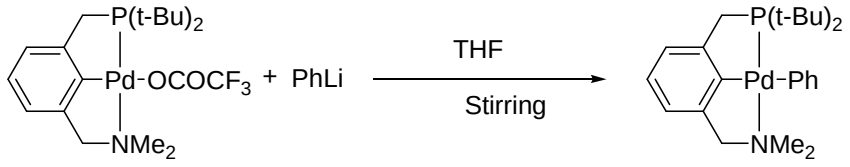
To understand the mechanism of formation of cross coupling product, the phenyl complex should be synthesized and reacted with aryl halide.

Synthesis and study the reactivity of (PCN^{Me})Pd–Ph

To give more insight about C-C bond formation, the air stable (PCN^{Me})Pd–Ph was synthesized

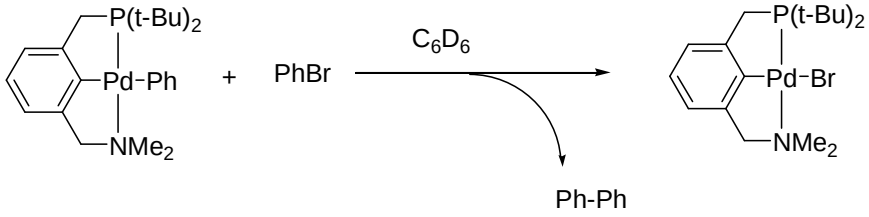
Synthesis of (PCN^{Me})Pd–Ph

(PCN^{Me})Pd-Ph was synthesized by the reaction of (PCN^{Me})Pd-TFA with phenyl lithium as shown in scheme 6. Unfortunately, the desired product was contaminated by (PCN^{Me}) Pd -Cl and the later complex was formed due to the lithium chloride which was present in phenyl lithium. The phenyl complex was decomposed on TLC plate. So, the crude product was used to study the Carbon-Carbon bond formation step.



Scheme6. Synthesis of (PCN^{Me})Pd-Ph

Kinetic experiments were carried out using the crude product which was contaminated by 22% of (PCN^{Me})Pd-Cl to study the reactivity of the phenyl complex toward cross-coupling reaction specially to study C-C bond formation step.



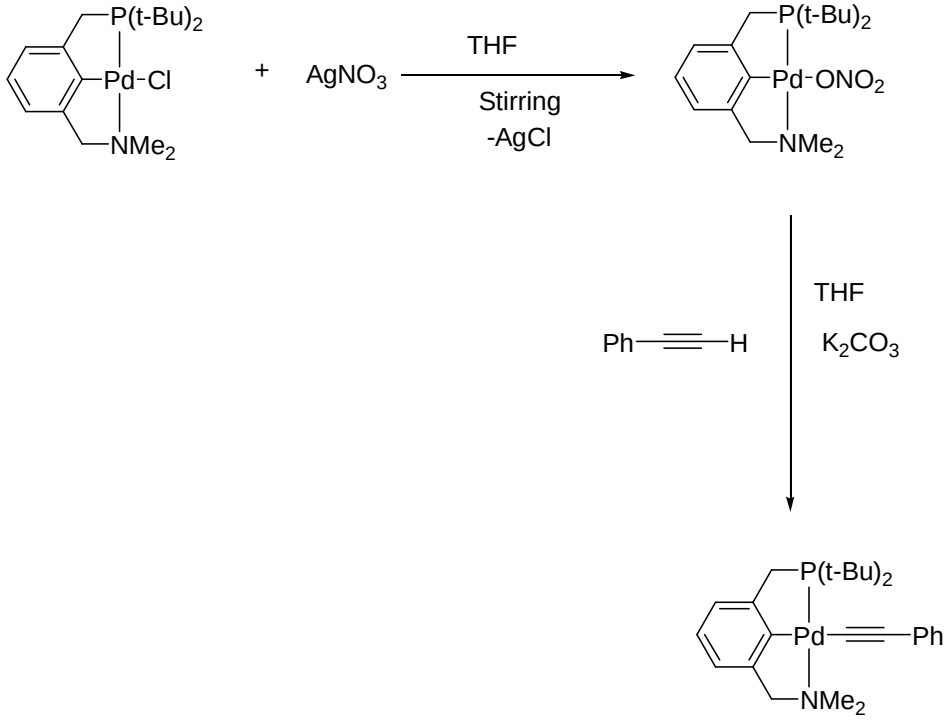
Scheme7. Reaction of crude (PCN^{Me})Pd-Ph with bromobenzene

The reaction was run at 50 ^{o}C but no reaction occurred for 20 h then the temperature was raised to 100 ^{o}C. After 3h, 6% conversion of the phenyl complex to (PCN^{Me})Pd-Br was recorded by monitoring the reaction using ^{1}H- and ^{31}P-NMR and the biphenyl was formed. 49 % conversion was recorded after 65 h and 55% was recorded after 89h. The long time of the reaction beside the presence of (PCN^{Me})Pd-Cl as impurity make the mechanistic evaluation for this reaction so difficult since the role of the chloride complex is not clear. Therefore, to find the new model to study the mechanism of C-C bond formation step, (PCN^{Me})Pd-Phenylacetylide was synthesized in fairly good yield and high purity.

Synthesis and study the reactivity of (PCN^{Me})Pd–Phenylacetylide

Synthesis of (PCN^{Me})Pd–Phenylacetylide

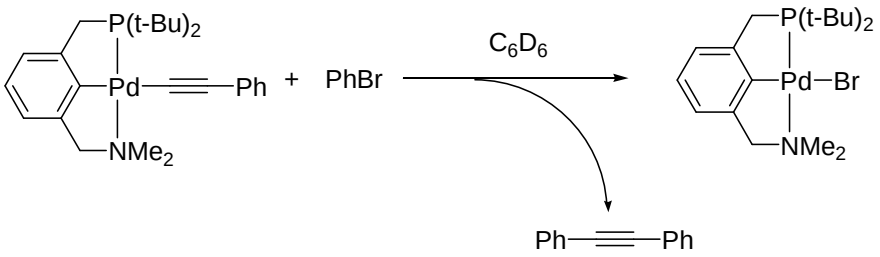
(PCN^{Me})Pd-Phenylacetylide was synthesized by ligand substitution reaction starting from (PCN^{Me})Pd-Cl as shown in scheme 8 with $AgNO_3$ to give (PCN^{Me})Pd-NO_3[11], the weaker coordinating NO_3 is more reactive toward phenyl acetylene in presence of Potassium carbonate. The driving force for the last reaction is formation of the strong Pd-C_{sp} bond.



Scheme8. Synthesis of (PCN^{Me})Pd-phenyl acetylide from (PCN^{Me})Pd-Cl

Crystallization of the product from hexane at -20 ^{o}C did not lead to the pure product. The desired product was contaminated with yellowish impurity. To get rid of the yellowish impurity, the crude (PCN^{Me})Pd–Phenylacetylide was dissolved in hexane, activated carbon was added to trap any impurities, and the solution was kept overnight then was filtrated using Celite® to give colorless solution which evaporated to give white solids. Colorless crystals were obtained by slow evaporation of hexane at room temperature.

Reaction of (PCN^{Me})Pd-phenyl acetylide with Bromobenzene



Scheme9. Reaction of (PCN^{Me})Pd-phenyl acetylide with bromobenzene

First kinetic experiment was performed using the crude (PCN^{Me})Pd-Phenylacetylide containing the yellowish impurity with 10 equivalents of PhBr as shown in scheme 9, the experiment was run at 50 ^{o}C and there was no reaction for more than 16 h. so, the temperature was increased to 100 ^{o}C, 60 % conversion was recorded by monitoring the reaction by ^{1}H- and ^{31}P-NMR after 4 h at 100 ^{o}C the reaction was fast but there was doubt about the purity of the used phenyl acetylide complex.

The experiment was repeated using the well purified (PCN^{Me})Pd-Phenylacetylide . It showed slow progress for the reaction and this confirmed that impurities catalyzed the reaction in the first experiment due to the presence of high amounts of impurities which were trapped later by using activated carbon. Due to the fact that ^{1}H- and ^{31}P-NMR spectra for the impurities and the desired product is the same, one can conclude that the impurities might be Pd(0).

(PCN^{Me})Pd-Phenylacetylide reacted with 10 equivalents of both bromobenzene and (PCN^{Me})Pd-Br at 50 ^{o}C, full conversion of the Phenylacetylide complex to the bromide was recorded within 30 minutes and the cross coupling product was observed. Decreasing the temperature could be useful to study the kinetic of the reaction.

To know the role of (PCN^{Me})Pd–Br in C-C bond formation in Sonogashira reaction, (PCN^{Me})Pd-Phenylacetylide reacted with 10 equivalent of bromobenzene using C_6D_6 as solvent in presence of (PCN^{Me})Pd-Br. An array of ^{1}H-NMR experiments were set to reduce the experimental errors in comparison to the previous experiments.

(1) An array of ^{1}H-NMR experiment was run at room temperature to follow the reaction between (PCN^{Me})Pd-Phenylacetylide and10 equivalents of both bromobenzene and (PCN^{Me})Pd–Br for 3h. Consumption of (PCN^{Me})Pd–Phenylacetylide and formation of (PCN^{Me}) Pd –Br were calculated according to the integrated area of ^{1}H-NMR peak for the singlet (CH_2) attached to the nitrogen atom over time, the cross coupling product was observed . The reaction is 1st order in [(PCN^{Me})Pd–Phenylacetylide] as shown in figure1. The reaction rate is only dependant on this compound. All other reactants are present in a large excess.

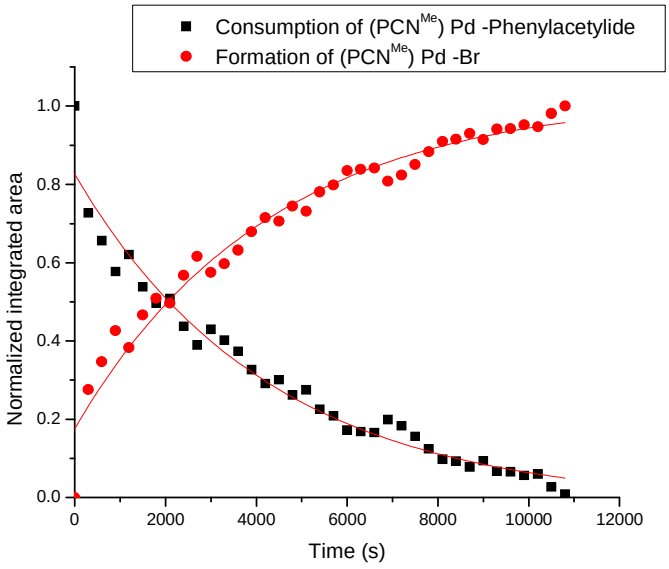


Figure1. Consumption of (PCN^{Me}) Pd-phenyl acetylide and formation of (PCN^{Me}) Pd-Br as were calculated from the integrated peak area from array ^{1}H-NMR.

(2) Second array of ^{1}H-NMR experiment was run at 50 ^{o}C to follow the reaction between (PCN^{Me}) Pd -Phenylacetylide and10 equivalents of bromobenzene in presence of 1 equivalent of (PCN^{Me}) Pd –Br. Consumption of (PCN^{Me}) Pd –Phenylacetylide and formation of (PCN^{Me}) Pd –Br were calculated according to the integrated area of ^{1}H-NMR peak for the singlet (CH_2) attached to the nitrogen atom over time. After 12 h at 50 ^{o}C there was no much conversion to the bromide complex. So, the temperature was raised to 100 ^{o}C. Full conversion was recorded during 4h and the cross coupling product was observed.

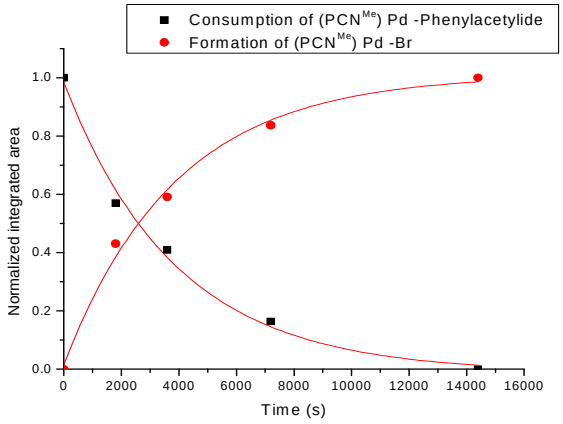


Figure2. Consumption of (PCN^{Me})Pd-phenyl acetylide and formation of (PCN^{Me})Pd-Br as were calculated from the integrated peak area from ^{1}H-NMR at 100^{o}C.

Study the effect of using additives

To get a deeper insight into the C-C coupling reaction, the influence of various additives was studied. The phenyl acetylide complex was reacted with 10 equivalents of bromobenzene in presence of 2 equivalents of potassium carbonate, Triethyl amine, palladium (II) acetate and

mixture of palladium (II) acetate and Triethyl amine. Also, the reaction was carried out in presence of 10 equivalents of tetra butyl ammonium bromide, cuprous iodide, and sodium bromide as shown in table 7.

Table7. Reaction of (PCN^{Me})Pd–Phenylacetylide complex with bromobenzene in presence of additives

Entry	Additives	Equivalent	Time(h)	Temperature(^{o}C)
1	K_2CO_3	2	18	100
2	Et_3N	2	18	100
3	Pd(II)acetate	2	18	100
4	Pd(II)acetate + Et_3N	2	2	100
5	NaBr	10	48	100
6	NBu_4Br	10	28	100
7	CuI	10	20	50

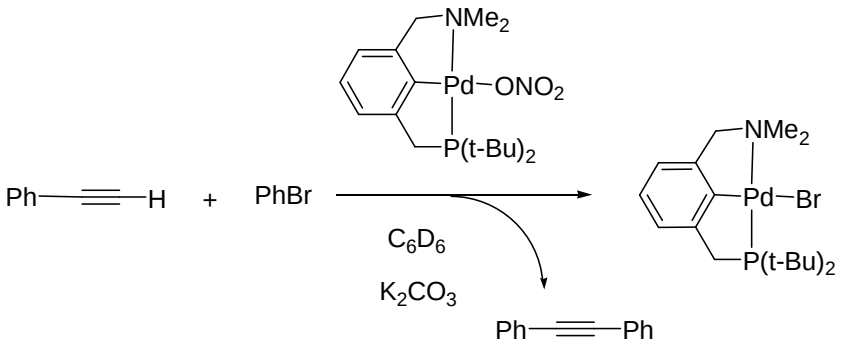
- Without using additives, 22 % conversion of the phenyl acetylide complex to the bromide was determined by measuring ^{1}H- and ^{31}P-NMR after 21 h. the cross coupling product (diphenyl acetylene) was observed from ^{1}H- NMR spectra and was compared with ^{1}H-NMR spectra for diphenyl acetylene as a reference for more accuracy .
- With potassium carbonate there was no reaction for more than 18 h while in case of Triethyl amine, 17 % conversion of the phenyl acetylide complex to the bromide was determined by measuring ^{1}H- and ^{31}P-NMR after 18 h and the cross coupling product was observed.
- With palladium (II) acetate, the phenyl acetylide complex was completely converted after 2h at 100 ^{o}C to 57% of the bromide complex and 43% of another complex which shows ^{31}P-NMR peak at δ 90.10 ppm. After 18 h this complex was converted to the bromide complex. The fast consumption of the phenyl acetylide complex is an indication that palladium (II) acetate catalyzed the reaction.
- With mixture of palladium (II) acetate and Triethyl amine, the phenyl acetylide complex was completely converted to the bromide complex after 2 h at 100 ^{o}C. Triethyl amine accelerated the formation of the cross-coupling product.
- With sodium bromide, the cross coupling product was formed after 48 h at 100 ^{o}C.
- With Tetra butyl ammonium bromide, full conversion of the Phenylacetylide to the bromide was achieved after more than 28 h at 100 ^{o}C. In comparison to sodium bromide, Tetra butyl ammonium bromide was totally soluble in the used solvent (C_6D_6).

In the last two reactions, the amount of the cross coupling product which was formed approximately the same in comparison with the experiment without additives.

- With cuprous iodide, 10% conversion of the phenyl acetylide complex to (PCN^{Me})Pd-I after 1 h at 50 ^{o}C and for full conversion the reaction was kept for more 20 h. There was no cross-coupling product which indicates that transmetalation occurred between cuprous iodide and the pincer palladium complex.

Reaction between (PCN^{Me})Pd-Phenylacetylide and methyl trifluoromethanesulfonate was studied at room temperature. Methyl triflate was suggested instead of bromobenzene due to its high reactivity. As soon as the reactants were mixed together in the glovebox, 43 % conversion of the Phenylacetylide complex to (PCN^{Me})Pd-OSO_2CF_3 was determined by measuring ^{1}H- and ^{31}P-NMR. The cross coupling product (Methyl phenyl acetylene) was observed. Studying the kinetic of this system was excluded because it's difficult to mix the reactant outside glovebox.

Catalytic reaction was carried out using (PCN^{Me})Pd-NO_3 (1 mol%) as a catalyst in presence of potassium carbonate as base at 100^{o}C as shown in scheme 10



Scheme10. Reaction of phenyl acetylene and bromobenzene in presence of (PCN^{Me})Pd-NO_3 as catalyst.

The cross coupling product was determined using ^{1}H-NMR and this confirm that reaction between phenyl acetylene and bromobenzene run catalytically.

Conclusion

- (PCN^{Me})Pd-Br was used as catalyst for Suzuki coupling reaction with high turnover number and very good yields were calculated using GC analysis in absence and presence of additives.
- To give a deeper insight about the C-C bond formation, (PCN^{Me})Pd-Phenylacetylide was synthesized and was reacted with bromobenzene in presence and absence additives. Formation of the cross coupling product was confirmed from ^{1}H-NMR spectra. Since no palladium black was formed, the heterogeneous catalysis was excluded. One would suggest that Pd(0) catalyzed the formation of cross coupling product by oxidative addition of bromobenzene to form Pd(II) species then transmetalation with (PCN^{Me})Pd-Phenylacetylide to form the cross coupling product and (PCN^{Me})Pd-Br.

Future work

- (PCN^{Me})Pd-(p-tolyl) acetylide should be synthesized and react with phenyl bromide in presence and absence of additives. It will be easy to integrate the singlet peak of the methyl group instead of the unclear aromatic peak of the cross coupling product in case of (PCN^{Me})Pd-Phenylacetylide. Therefore, the yield of the cross coupling product will be accurately determined.

- Mercury poison test should be carried out.

Experimental Section

General considerations

Air sensitive experiments were carried out using Schlenk line, glove box or high vacuum line techniques. The used solvents were transferred to the reaction flask under nitrogen atmosphere after collecting from solvent dispenser machine. All deuterated solvents and reagents were purchased from Sigma-Aldrich and used as received. J. Young NMR- tubes which used for kinetic experiments were rinsed with aqua regia, water and acetone and then oven dried before use. ^{1}H- and ^{31}P-NMR spectra were recorded on a Varian Unity INOVA (499.77 MHz for 1H) spectrometer. Chemical shifts are given in ppm downfield from TMS using the residual ^{1}H-NMR solvent peak as internal reference and H_3PO_4 (^{31}P δ 0) as external reference.

Synthesis of (PCN^{Me})Pd-TFA

(0.109 g, 0.25 m mol) of (PCN^{Me})Pd-Cl was dissolved in 10 ml benzene and (0.057 g, 0.26 m mol) Silver trifluoroacetate was added , the solution was stirred for 1 h then was filtered and the resulted solution was evaporated to give the product as a yellow solids. Yield: 116 mg (91 %).

^{1}H-NMR (C_6D_6): δ 6.95 (dd, *J* = 8.0, 6.9 Hz, 1H), 6.79 (d, *J* = 7.5 Hz, 1H), 6.61 (d, *J* = 7.5 Hz, 1H), 3.25 (s, 2H), 2.74 (d, *J* = 9.4 Hz, 2H), 2.40 (d, *J* = 2.1 Hz, 6H), 1.14 (d, *J* = 14.1 Hz, 18H). ^{31}P {^{1}H} NMR (C_6D_6): δ 90.88 (s).

Synthesis of (PCN^{Me})Pd-Ph

(0.512 g, 0.1 m mol) (PCN^{Me})Pd-TFA was dissolved in 5 ml THF and (0.1 ml, 0.2 mmol) PhLi solution (1.9 M / Dibutyl ether) was added, the reaction mixture was stirred for 2 h under nitrogen atmosphere. The solvent was evaporated and pentane was used to dissolve the product and was filtrated using Celite® inside glove box and the filtrate was crystallized at -20 ^{o}C. ^{1}H-, ^{31}P-NMR measurement confirmed presence of two different Pd-Complexes as it's shown below:

(PCN^{Me})Pd-Ph (80 %): ^{1}H-NMR (C_6D_6): δ 8.01(d, *J* = 7.3 Hz, 2H), 7.39 (t, *J* = 7.1 Hz, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.13 (d, *J* = 6.4 Hz, 1H), 6.91 (d, *J* = 6.4 Hz, 1H), 3.60 (s, 2H), 3.24 (d, *J* = 8.8 Hz, 2H), 2.12 (d, *J* = 1.7 Hz, 6H), 1.16 (d, *J* = 13.5 Hz, 18H). ^{31}P {1H} NMR (C_6D_6): δ 92.29 (s).

(PCN^{Me})Pd-Cl (20 %): ^{1}H-NMR (C_6D_6): δ 6.99 (t, *J* = 6.9 Hz, 1H), 6.88 (d, *J* = 7.5 Hz, 1H), 6.69 (d, *J* = 7.4 Hz, 1H), 3.42 (s, 2H), 2.90 (d, *J* = 9.3 Hz, 2H), 2.55 (d, *J* = 1.7 Hz, 6H), 1.29 (d, *J* = 14.0 Hz, 18H). ^{31}P {1H} NMR (C_6D_6): δ 93.80 (s).

Cross-Coupling reaction using crude (PCN^{Me})Pd-Ph contaminate by (PCN^{Me})Pd-Cl

(0.007 g , 0.015 mmol) of crude (PCN ^{Me})Pd-Ph containing 30% mmol of (PCN ^{Me})Pd-Cl was dissolved in 0.5 ml C_6D_6 and 10 equivalent of phenyl bromide (16 µl, 0.15 mmol) was added using J. Young NMR tube at 50 ^{o}C and the reaction was monitored by measuring ^{1}H-, ^{31}P-NMR spectra.

Suzuki reaction catalyzed by (PCN^{Me})Pd-Br complex

Synthesis of (PCN^{Me})Pd-Br

(0.434 g, 1 mmol) (PCN^{Me}) Pd-Cl was dissolved in 20 ml Methanol and the solution was stirred for 4 h. The solvent was evaporated and the solid was dissolved in Benzene and filtrated through Celite. The solvent was evaporated to give yellow crystals. Yield: 0.471 g (99 %).

^{1}H-NMR (C_6D_6): δ 7.00 (t, *J* = 7.4 Hz, 1H), 6.90 (d, *J* = 7.4 Hz, 1H), 6.70 (d, *J* = 7.3 Hz, 1H), 3.43 (s, 2H), 2.93 (d, *J* = 9.4 Hz, 2H), 2.58 (d, *J* = 2.1 Hz, 6H), 1.30 (d, *J* = 14.0 Hz, 18H). ^{31}P {^{1}H} NMR (C_6D_6): δ 94.92 (s).

General procedures for Suzuki Cross coupling reaction

A small vial was charged with (10µL, 1 x10^{-7} mol) of 1x10^{-2} M stock solution of (PCN^{Me})Pd-Br in toluene, aryl halide (2 x10^{-4} mol), arylboronic acid (3 x10^{-4} mol), Potassium phosphate (4 x 10^{-4} mol),2-methylnapthalene as internal standard and toluene (2 ml). The vial was sealed and heated at 160^{o}C for 24h. After 5h and also after 24h the vial was removed from the heating plate, cooled and opened for sample withdrawal. 5-10 drops of the reaction mixture were taken out and added to an extraction mixture containing 0.8 ml Et_2O and 0.8 ml 1M HCl (aq). The organic layer was separated and sealed in a GC-vial. The yields were calculated from the integral area of the product and the integral area of the internal standard.

Detailed procedures for Suzuki Cross coupling reaction

Different series of cross- coupling reactions were carried out using three different aryl halides with three different phenyl boronic acids in presence of (PCN^{Me})Pd-Br as catalyst.

Entry	**Ar-X**	**Ar-B(OH)$_2$**	**Catalyst loading (% mol)**	
1	Ph-Br	Ph-B(OH)$_2$	0.25	0.05
2	Ph-Br	4-CH$_3$-B(OH)$_2$	0.25	0.05
3	Ph-Br	4-CHO-C$_6$H$_4$-B(OH)$_2$	0.25	0.05
4	CH$_3$-C$_6$H$_4$-Br	Ph-B(OH)$_2$	0.25	0.05
5	CH$_3$-C$_6$H$_4$-Br	4-CH$_3$-B(OH)$_2$	0.25	0.05
6	CH$_3$-C$_6$H$_4$-Br	4-CHO-C$_6$H$_4$-B(OH)$_2$	0.25	0.05
7	CHO-C$_6$H$_4$-Br	Ph-B(OH)$_2$	0.25	0.05
8	CHO-C$_6$H$_4$-Br	4-CH$_3$-B(OH)$_2$	0.25	0.05
9	CHO-C$_6$H$_4$-Br	4-CHO-C$_6$H$_4$-B(OH)$_2$	0.25	0.05

Suzuki Cross coupling reaction in presence of additives

Cross- coupling reactions of Phenyl boronic acid & p-Tolyl bromide catalyzed by (PCN^{Me})Pd-Br complex were carried out in presence of the following additives:

Additives	Concentration	Amount
Copper acetate	1×10^{-4} mol	0.0182 g
Sodium bromide	1×10^{-4} mol	0.0103 g
Iron bromide	1×10^{-4} mol	0.0216 g
Silver acetate	1×10^{-4} mol	0.0167 g
Cobalt (II) chloride.$6H_2O$	1×10^{-4} mol	0.0238 g
Nickel (II) chloride	1×10^{-4} mol	0.0129 g
Chromium(III)chloride	1×10^{-4} mol	0.0159 g
Au(NHC)-Cl complex	1×10^{-4} mol	0.0537 g
Lithium bromide	1×10^{-4} mol	0.0087 g
Sodium iodide	1×10^{-4} mol	0.0149 g
Potassium bromide	1×10^{-4} mol	0.0119 g
Cuprous iodide	1×10^{-4} mol	0.191 g

Also 0.1, 0.5 and 1 equivalents of Sodium bromide, Cobalt (II) chloride hexahydrate and Nickel (II) chloride were used.

Synthesis of (PCN^{Me})Pd-NO_3

(0.434 g, 1 mmol) (PCN^{Me})Pd-Cl was dissolved in 50 ml dry THF then (0.178 g, 1.05 mmol) $AgNO_3$ was added , the reaction mixture was stirred for 2 days at room temperature then the solvent was evaporated and the solid was dissolved in benzene and the resulting solution was filtered to get rid from silver chloride and the solvent was evaporated again. Yield: 392 mg (85 %).

^{1}H-NMR (C_6D_6): δ 6.93 (t, *J* = 6.9 Hz, 1H), 6.77 (d, *J* = 7.1 Hz, 1H), 6.58 (d, *J* = 7.5 Hz, 1H), 3.23 (s, 2H), 2.72 (d, *J* = 9.3 Hz, 2H), 2.36 (d, *J* = 2.1 Hz, 6H), 1.12 (d, *J* = 14.1 Hz, 18H). ^{31}P {^{1}H} NMR (C_6D_6): δ 90.93 (s).

Synthesis of (PCN^{Me})Pd-phenyl acetylide

(0.461 g, 1 mmol) (PCN^{Me}) Pd-NO_3 and (0.178 g, 5 mmol) K_2CO_3 were dissolved in 50 ml dry THF and (0.204 g, 2 mmol) of phenyl acetylene was added then the reaction mixture was stirred

for 1 day at room temperature then the solvent was evaporated and the solid was dissolved in benzene and was filter and the solvent was evaporated again the resulting solid was dissolved in Hexane to give yellow solution and then was mixed with charcoal and filtrate to get rid from Pd(0) and then was evaporated to give white solid which was crystallized as colorless crystals by slow evaporation of hexane.

^{1}H-NMR (C_6D_6): δ 7.72 (dd, *J* = 8.2, 1.2 Hz, 2H), 7.19 (d, *J* = 1.7 Hz, 1H), 7.17 (d, *J* = 3.4 Hz, 2H), 7.07 (td, *J* = 7.5, 1.2 Hz, 1H), 7.03 (m, 1H), 6.83 (d, *J* = 7.2 Hz, 1H), 3.57 (s, 2H), 3.13 (d, *J* = 9.1 Hz, 2H), 2.69 (d, *J* = 2.0 Hz, 6H), 1.33 (d, *J* = 13.9 Hz, 18H). ^{31}P {^{1}H} NMR (C_6D_6): δ 98.46 (s).

Reaction of (PCN^{Me})Pd-phenyl acetylide with Bromobenzene

General procedures

(0.005 g, 0.01 mmol) of (PCN^{Me})Pd-phenyl acetylide was dissolved in 0.5 ml C_6D_6 in J. Young NMR tube then 10 equivalent of Bromobenzene was added and the reaction was heated to 50 ^{o}C for 16 h then the temperature was increased to 100 ^{o}C and the reaction was monitored by measuring ^{1}H- and ^{31}P-NMR.

Array NMR experiments

(1) (0.005 g, 0.01 mmol) of (PCN^{Me})Pd- phenyl acetylide was mixed with 10 equivalents of (PCN^{Me})Pd-Br in J. Young NMR tube , 0.5 ml C_6D_6 was added then 10 equivalents of Bromobenzene was added. The reaction was monitored by measuring ^{1}H- NMR as array at room temperature for 3h.
(2) (0.005 g, 0.01 mmol) of (PCN^{Me})Pd- phenyl acetylide was mixed with 1 equivalent of (PCN^{Me})Pd-Br in J. Young NMR tube , 0.5 ml C_6D_6 was added then 10 equivalents of Bromobenzene was added. The reaction was monitored by measuring ^{1}H- NMR as array at 50 ^{o}C for 12 h. Then the reaction mixture was heated to 100 ^{o}C to 4h.

Reaction of (PCN^{Me})Pd-phenyl acetylide with Bromobenzene in presence of additives

(0.005 g, 0.01 mmol) of (PCN^{Me})Pd- phenyl acetylide was dissolved in 0.5 ml C_6D_6 in J.Young NMR tube then 10 equivalent of Bromobenzene was added and the additives was added and the reaction was heated to 100 ^{o}C . The reaction was monitored by measuring ^{1}H- and ^{31}P-NMR.

The used additives:

(1) Potassium carbonate (3 mg, 0.02 mmol)
(2) Triethyl amine (3 µl, 0.02 mmol)
(3) Pd (II) acetate (5 mg, 0.02 mmol)
(4) Pd (II) acetate (5 mg, 0.02 mmol) in presence of Triethyl amine (3 µl, 0.02 mmol)
(5) Sodium bromide (10 mg, 0.1 mmol)

(6) Cuprous iodide (19 mg, 0.1 mmol)
(7) Tetra butyl ammonium bromide (11 µl, 0.1 mmol)

The catalytic reaction

A small vial was charged with (3 mg, 5µ mol) (PCN^{Me})Pd-NO_3, (80 µl, 0.75 mmol) Bromobenzene, (55 µl, 0.5 mmol) Phenyl acetylene, (0.138g, 1 mmol) Potassium carbonate and C_6D_6 (0.8 ml). The vial was sealed and heated at 100 ^oC. After 15 h the vial was removed from the hot plate and left to cool at room temperature then ^1H- and ^{31}P-NMR was measured.

Reaction of (PCN^{Me})Pd-phenyl acetylide with methyl trifluoromethanesulfonate

(0.005 g, 0.01 mmol) of (PCN^{Me})Pd- phenyl acetylide was dried under high vacuum then 2 drops of methyl trifluoromethanesulfonate was added to the J. Young NMR tube inside the glove box and 0.5 ml of C_6D_6 was added. The reaction was monitored by measuring ^1H- and ^{31}P-NMR.

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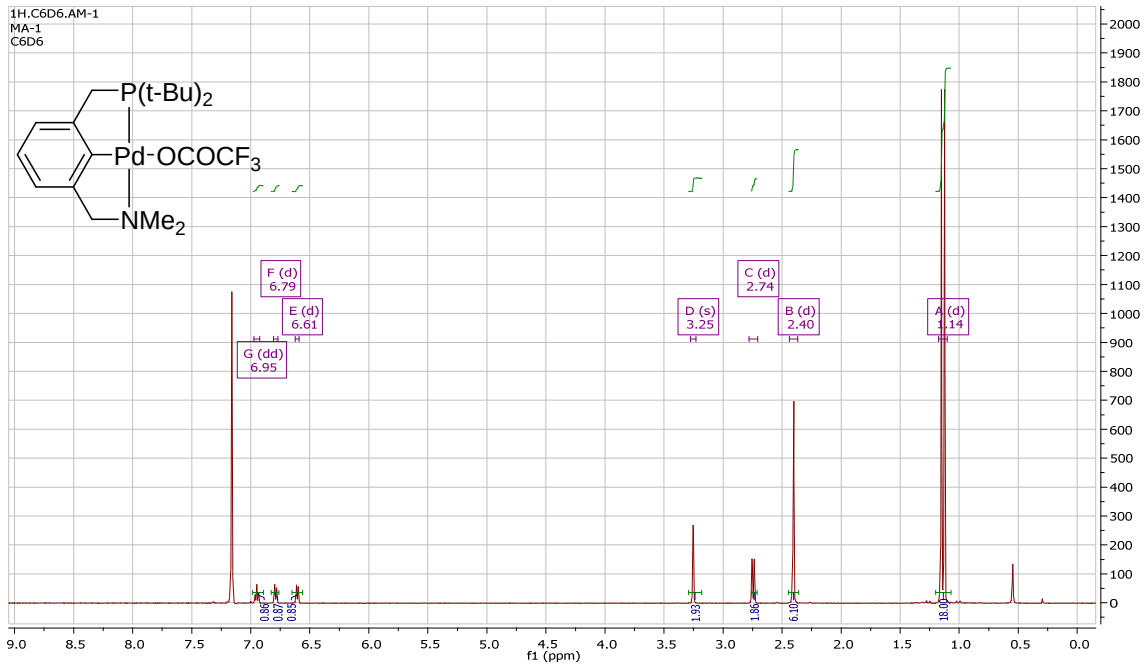
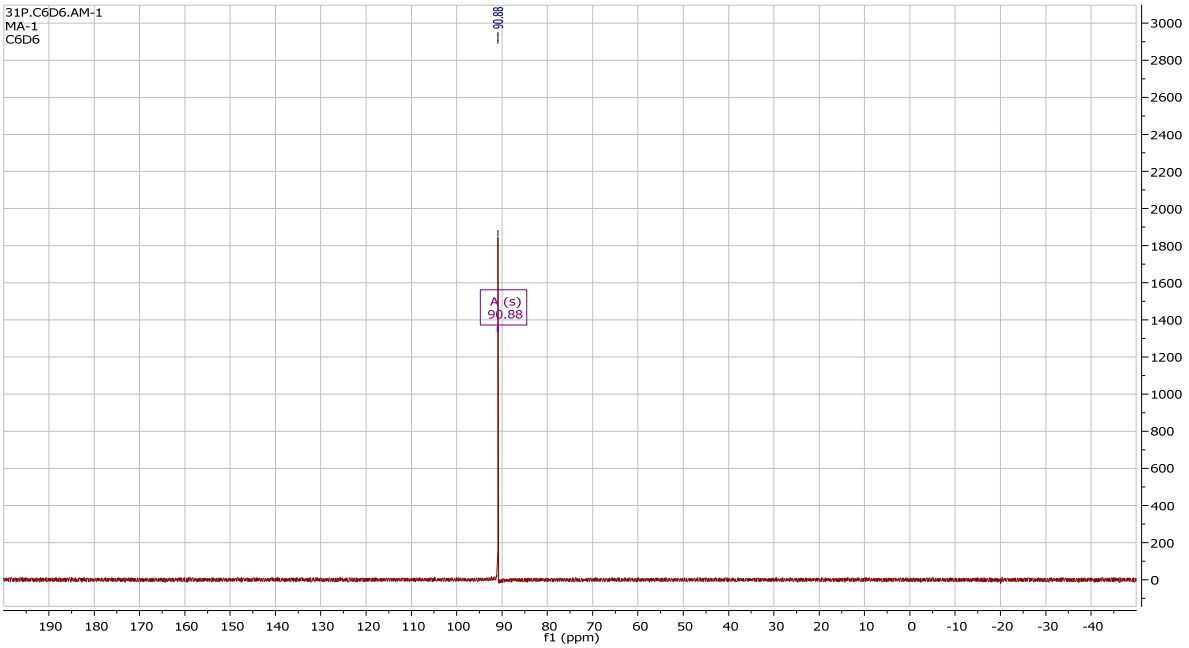
Appendix 1

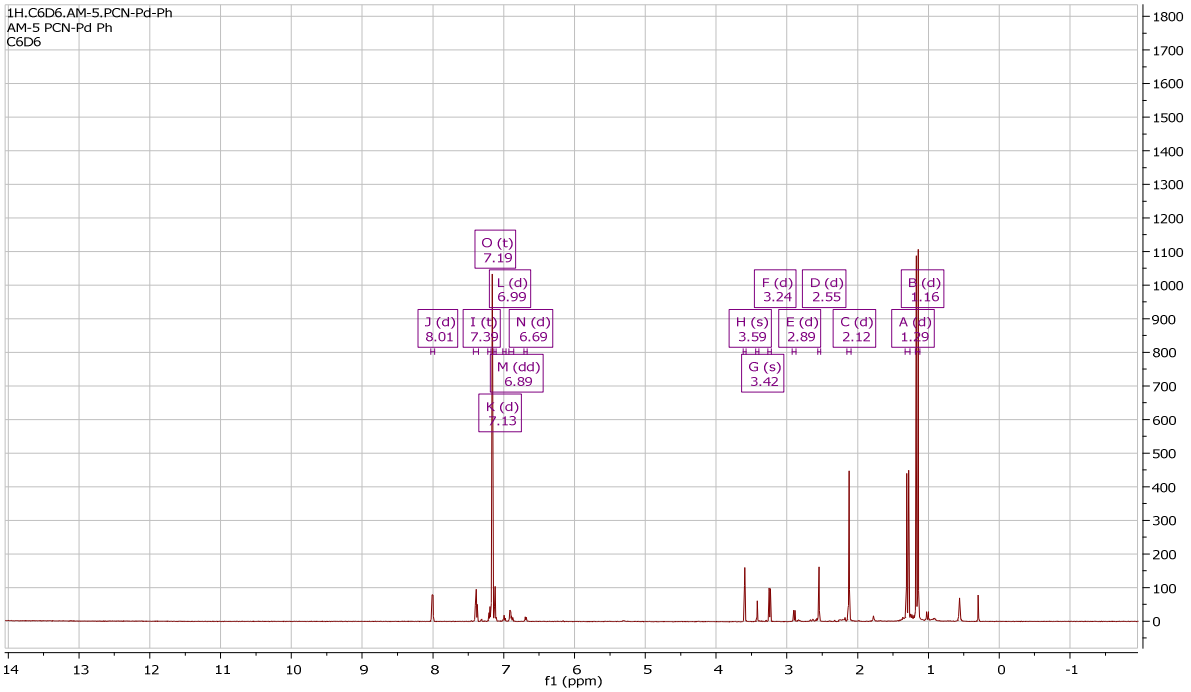
^{1}H- and ^{31}P-NMR for (PCN^{Me})Pd-complexes



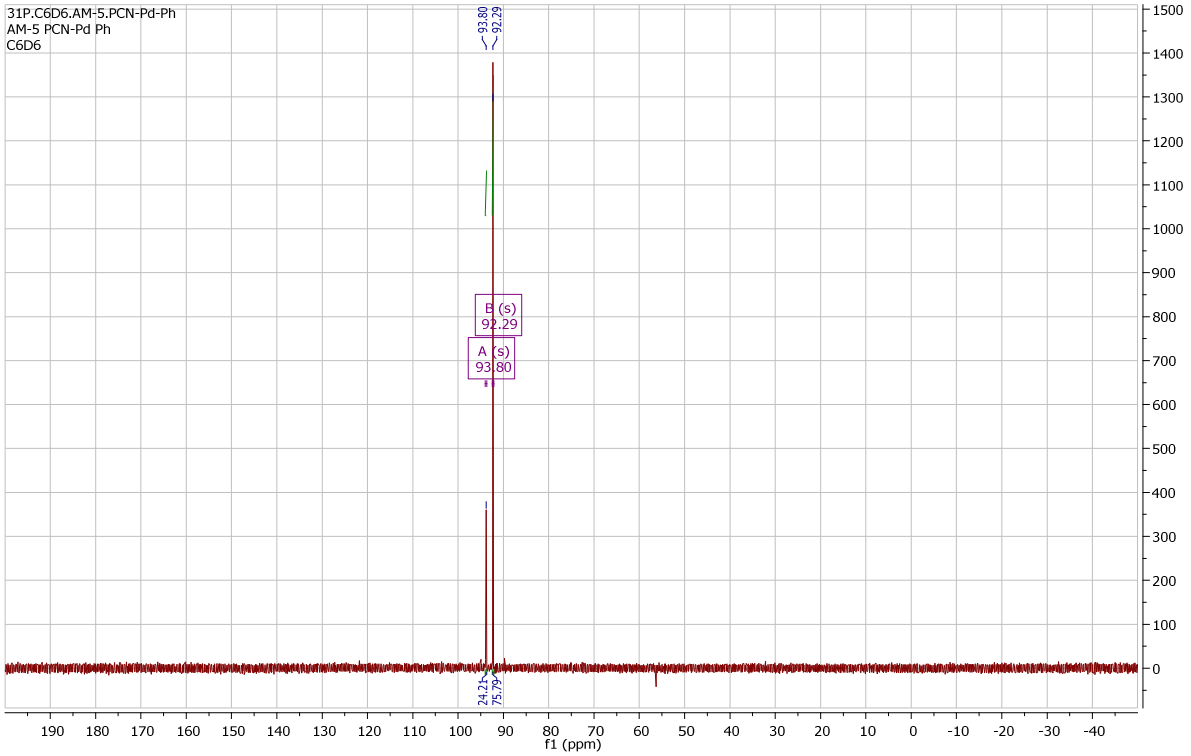
^{1}H- NMR for (PCN) Pd-TFA



^{31}P- NMR for (PCN) Pd-TFA



^{1}H-NMR for (PCN) Pd-Ph contaminated by (PCN) Pd-Cl



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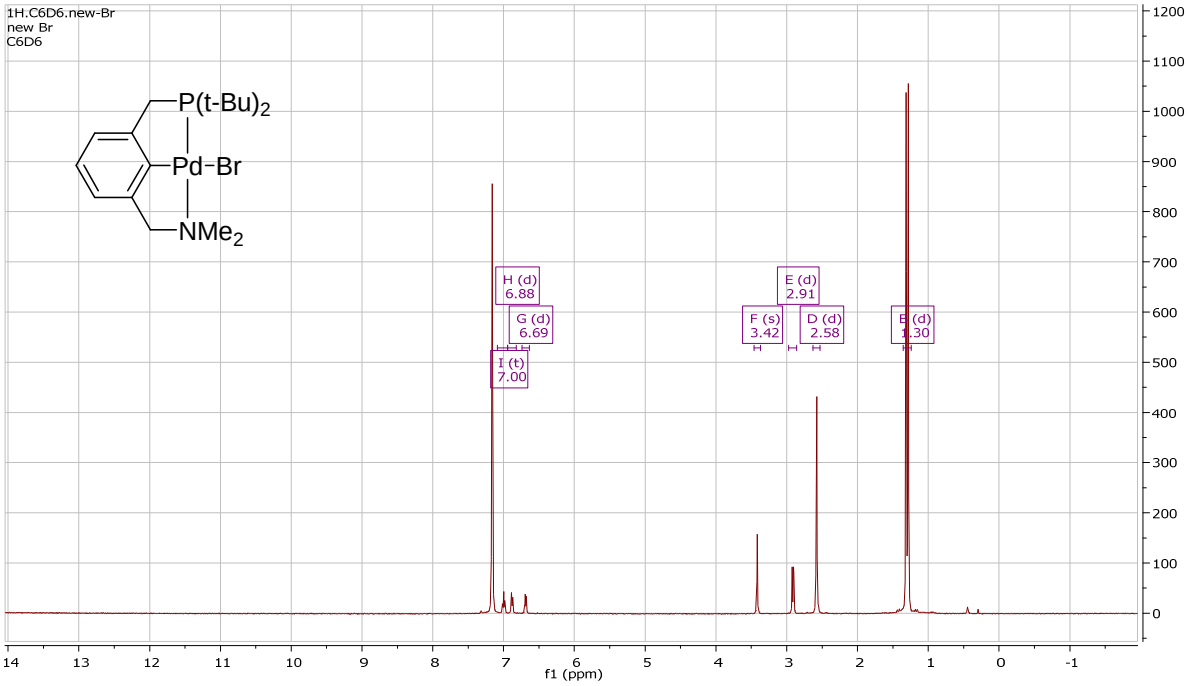
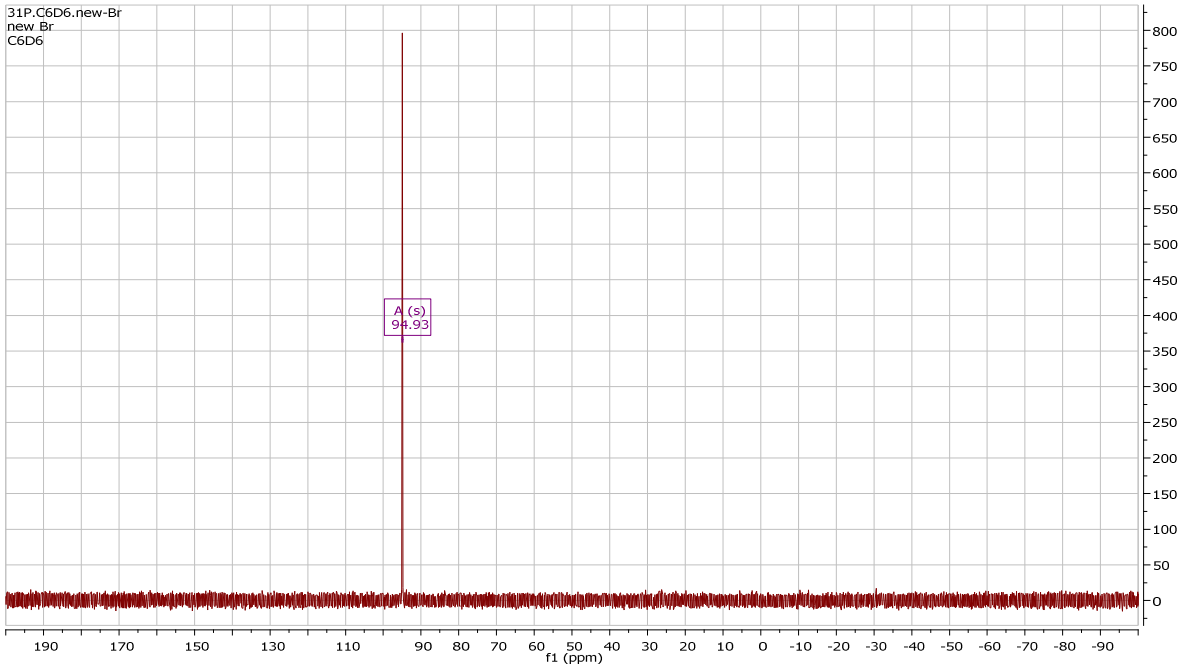
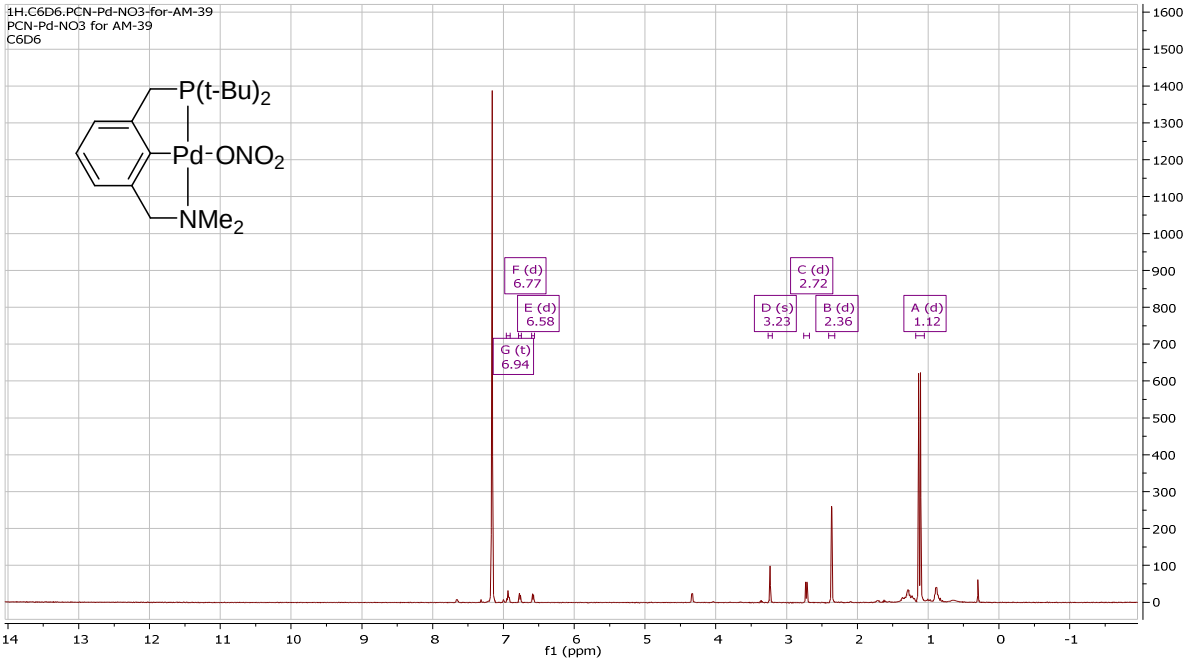


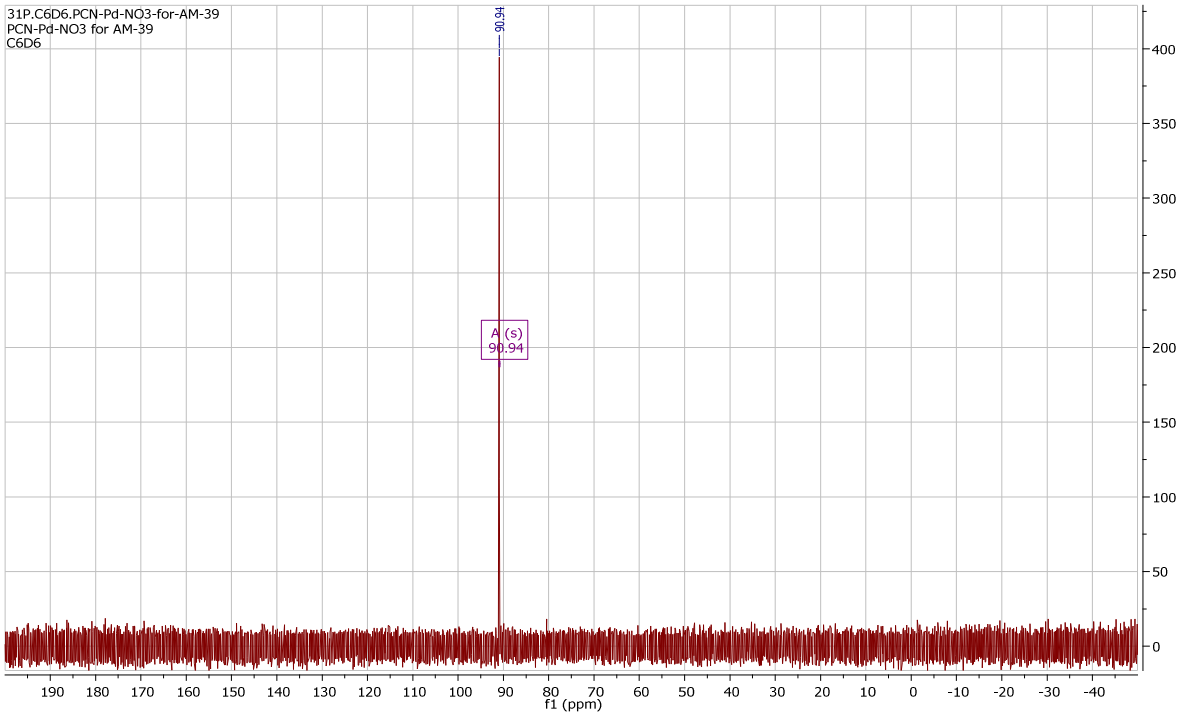
^{1}H-NMR for (PCN) Pd-Br



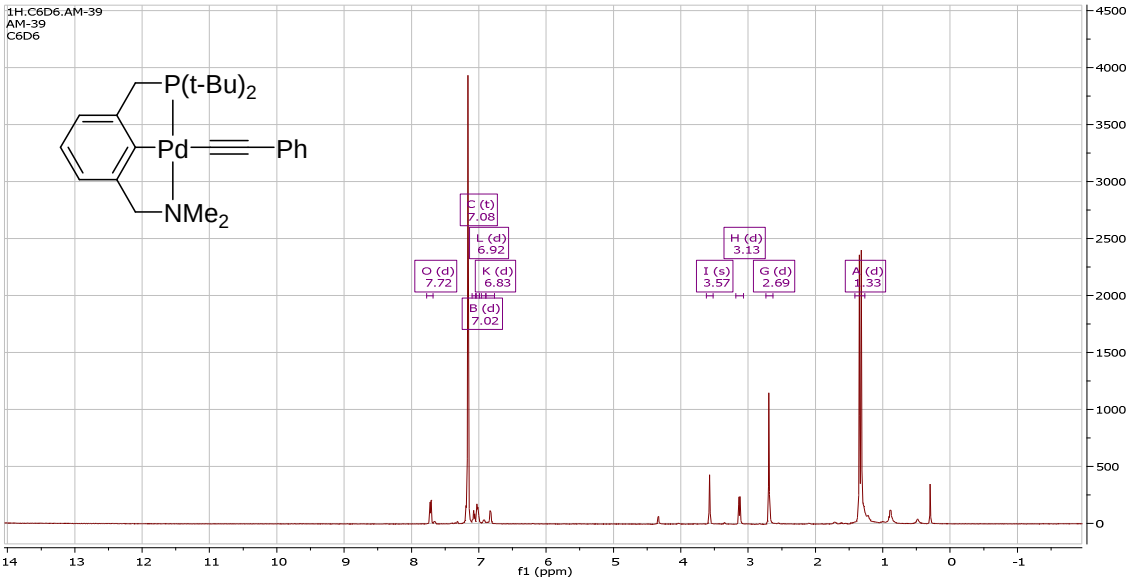
^{31}P-NMR for (PCN) Pd-Br



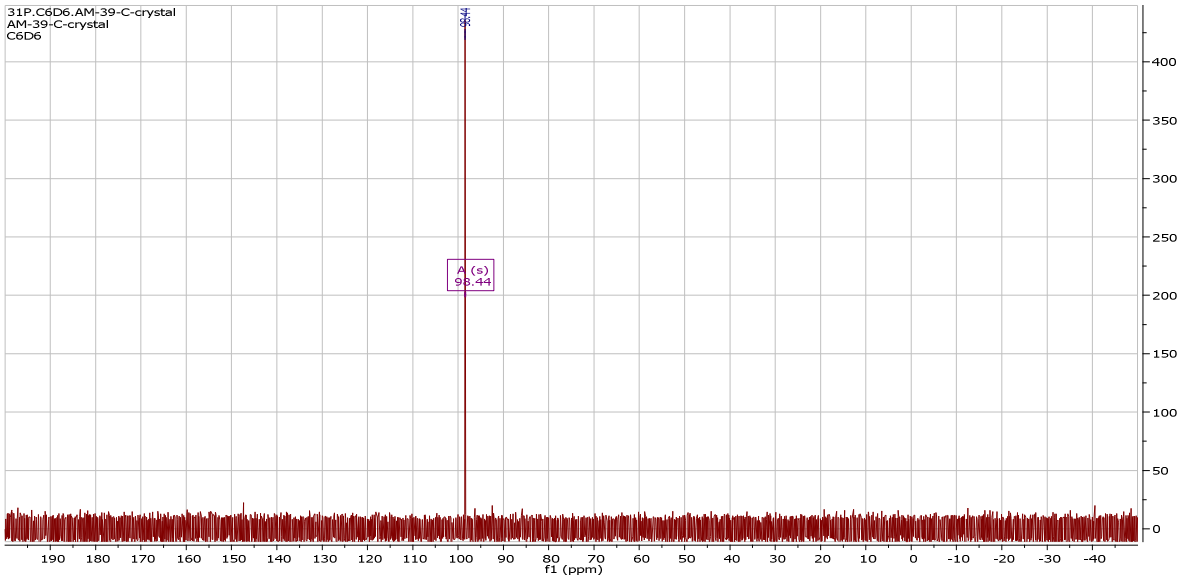
^{1}H-NMR for (PCN) Pd-NO_3



^{31}P-NMR for (PCN) Pd-NO_3



^{1}H-NMR for (PCN) Pd-Phenylacetylide



^{31}P-NMR for (PCN) Pd-Phenylacetylide

Appendix 2

X-ray crystallographic for (PCN^{Me})Pd-complexes

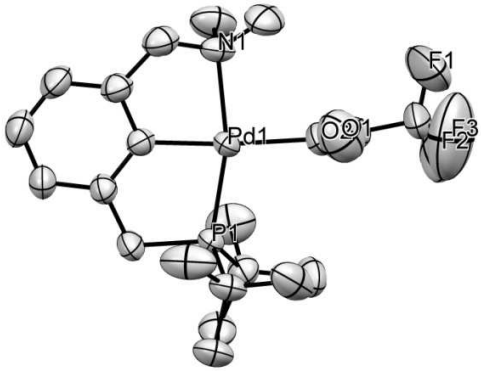


Figure 1. Perspective view (ORTEP) of (PCN^{Me})Pd-TFA complex. Hydrogen atoms have been deleted for clarity

Crystal data	
Chemical formula	$C_{24}H_{24}F_3NPO_2PPd$
M_r	552.81
Crystal system, space group	Triclinic, P-1
a, *b*, *c* (Å)	7.8868(3), 10.7285(5), 14.6768(7)
α, β, γ (°)	106.375(4), 97.885(3), 93.039(3)
V (Å³)	1174.71
Z	2
Crystal size (mm)	0.25 x 0.14 x 0.08
Data collection, Refinement	
Diffractometer	Oxford Diffraction CCD
μ (mm^{-1})	26.42
Radiation source	Mo *K*α
No. of independent reflections	5625
R_{int}	0.0468
S	1.053
R_1, wR^2 (I > 2σ(I))	0.0482, 0.1410

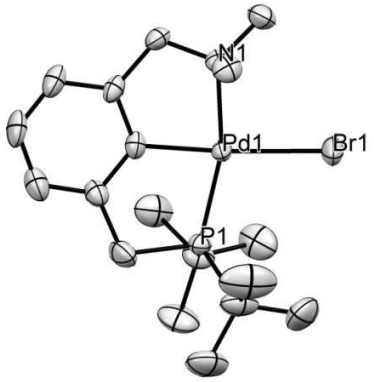


Figure 2. Perspective view (ORTEP) of (PCN^{Me})Pd-Br complex. Hydrogen atoms have been deleted for clarity

Crystal data	
Chemical formula	$C_{18}H_{30}BrNPPPd$
M_r	477.71
Crystal system, space group	Triclinic, P-1
a, *b*, *c* (Å)	16.6384(5), 10.4228(3), 12.3767(4)
β (°)	108.018(3)
V (Å³)	2041.09(11)
Z	4
Crystal size (mm)	0.30 x 0.20 x 0.18
Data collection, Refinement	
Diffractometer	Oxford Diffraction CCD
μ (mm^{-1})	26.42
Radiation source	Mo *K*α
No. of independent reflections	5042
R_{int}	0.0803
S	1.052
R_1, wR^2 ($I > 2\sigma(I)$)	0.0545, 0.1416

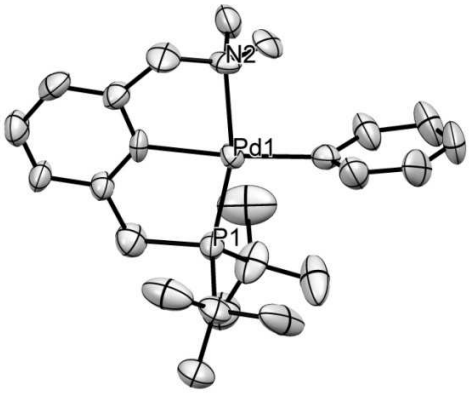


Figure 3. Perspective view (ORTEP) of (PCN^{Me})Pd-Ph. Hydrogen atoms have been deleted for clarity

Crystal data	
Chemical formula	$C_{24}H_{36}NPPPd$
M_r	475.91
Crystal system, space group	Triclinic, P1
a, *b*, *c* (Å)	7.8909(3), 11.1290(3), 14.3585(4)
α, β, γ (°)	103.174(3), 98.611(3), 96.949(3)
V (Å³)	1198.04(6)
Z	2
Crystal size (mm)	0.12 x 0.10 x 0.04
Data collection, Refinement	
Diffractometer	Oxford Diffraction CCD
μ (mm^{-1})	26.42
Radiation source	Mo *K*α
No. of independent reflections	9635
R_{int}	0.0315
S	1.081
R_1, wR^2 (I > 2σ(I))	0.0314, 0.0724

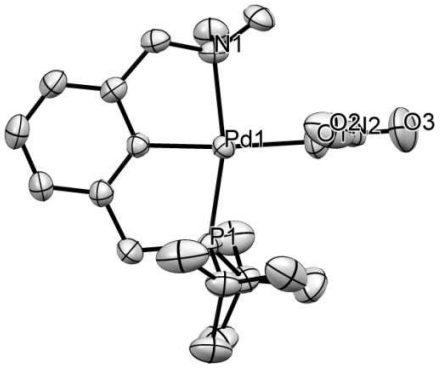


Figure 4. Perspective view (ORTEP) of (PCN^{Me})Pd-NO_3. Hydrogen atoms have been deleted for clarity

Crystal data	
Chemical formula	$C_{18}H_{31}N_2O_3PPPd$
M_r	460.82
Crystal system, space group	Monoclinic, Cc
a, *b*, *c* (Å)	17.6654(4), 7.8345(2), 34.8490(9)
β (°)	107.445(3)
V (Å³)	4601.2(2)
Z	10
Crystal size (mm)	0.30 x 0.14 x 0.14
Data collection, Refinement	
Diffractometer	Oxford Diffraction CCD
μ (mm^{-1})	26.42
Radiation source	Mo *K*α
No. of independent reflections	10109
R_{int}	0.0282
S	1.242
R_1, wR^2 (I > 2σ(I))	0.0407, 0.0801

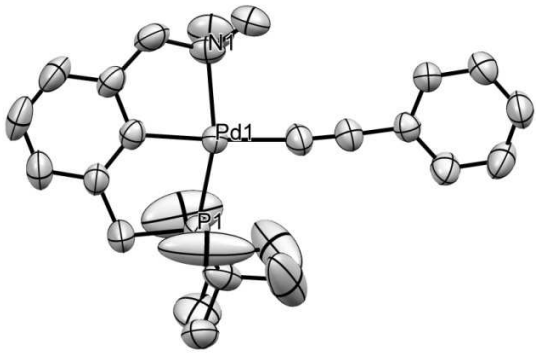


Figure 5. Perspective view (ORTEP) of (PCN^{Me})Pd-Phenyl acetylide. Hydrogen atoms have been deleted for clarity

Crystal data	
Chemical formula	$C_{26}H_{36}NPPPd$
M_r	499.93
Crystal system, space group	Orthorhombic, Pbca
a, *b*, *c* (Å)	14.9116(8), 16.5301(7), 20.8655(8)
$\alpha = \beta = \gamma$ (°)	90
V (Å³)	5143.1(4)
Z	8
Crystal size (mm)	0.60 x 0.40 x 0.20
Data collection, Refinement	
Diffractometer	Oxford Diffraction CCD
μ (mm^{-1})	26.42
Radiation source	Mo *K*α
No. of independent reflections	5396
R_{int}	0.1903
S	1.031
R_1, wR^2 ($I > 2\sigma(I)$)	0.0692, 0.1845