Tunable Palladium-FibreCats for Aryl Chloride Suzuki Coupling with Minimal Metal Leaching

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A very convenient general method was developed for making tunable polypropylene-supported Pd complexes of electron-rich and bulky monodentate ligands such as Q-Phos, t-Bu$_3$P, (Me$_2$NC$_6$H$_4$)P(t-Bu)$_2$ (A^{ta}-Phos), and IPr-carbene as well as bidentate ligands such as BINAP, dppf, and dippf in 4−8% Pd loading. These catalysts have been utilized for Suzuki coupling of aryl chlorides and bromides with product conversions up to 100%. Minimal metal leaching has been observed in many cases. Many of these catalysts were recycled a few times in model systems with an undetected amount of Pd leaching.

Introduction

During the last two decades, Suzuki coupling has emerged as one of the most sought out name reactions in the area of synthetic organic chemistry.[1] This is fundamentally due to its commercial importance in the pharmaceutical and fine chemical industries for devising complex molecules via Pd-catalyzed coupling.[2] The use of bulky, electron-rich ligands such as t-Bu$_3$P, X-Phos, Q-Phos, Ad$_2$P(n-Bu), t-Bu$_2$P(O)H, and N-heterocyclic carbenes in the presence of Pd(OAc)$_2$, Pd$_2$dba$_3$, or [π-allylPdCl]$_2$ precursors, or fully formed catalysts, such as (D^{t}BPF)PdCl$_2$, (A^{ta}-Phos)$_2$PdCl$_2$ [A^{ta}-Phos = Me$_2$NC$_6$H$_4$)P(t-Bu)$_2$], Pd(t-Bu$_3$P)$_2$, and [Pd(μ-Br)(t-Bu$_3$P)]$_2$ for aryl chloride coupling is one of the recent breakthroughs in accelerating the rapid developments in the area of cross-coupling.[3]

While the use of homogeneous catalysts in Suzuki coupling is increasing in the pharmaceutical processes, metal contamination of the product poses a major concern; hence resolving this has become a “holy grail”. To address these concerns, numerous academic and industrial groups have investigated the immobilization of palladium on various supports such as: carbon, perovskites, silicates, zeolites, ionic liquids, and polymers.[4] Recently “ossification” has been used as a new immobilization technique in Suzuki coupling.[5] Although some of these are potentially attractive process technologies, the catalyst systems are mostly limited to the coupling of less challenging substrates such as aryl iodides and bromides. A couple of years ago, we reported the syntheses of the first examples of Ph$_3$P-supported polypropylene-based FibreCats with different Pd precursors for simple Suzuki coupling reactions.[6] We also synthesized and characterized the first example of a novel tunable supported catalyst, FibreCat-1032, and explored its applications in non-routine substrates such as chloroacetophenone and bromothiophene.[6] Subsequently Sauer et.al., from Abbott, successfully explored the potential of FibreCat-1032 in microwave-assisted Suzuki coupling of activated aryl/heteroaryl bromides and chlorides with electron-rich, electron-neutral, and electron-poor aryl boronic acids.[7] Very recently Prasad of Novartis used Johnson Matthey’s polypropylene-based thiol (SMOPEX-111) as the support to anchor Pd(OAc)$_2$ and demonstrated its application in coupling of relatively less challenging aryl bromides in the Heck and Suzuki coupling with very low levels of Pd.[8] The catalyst was recycled four times in a Suzuki coupling reaction of aryl bromides with no activity loss, and very minimal Pd leaching was observed.[8]

In order to expand the scope and generality of the catalyst synthesis[6] and to address the coupling of more challenging aryl

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(1) Suzuki Coupling Publications/(Patents): 2000−2007 ∼3300/(415) 1990−1999 ∼3500/(16); 1980−1989 ∼2/(0).

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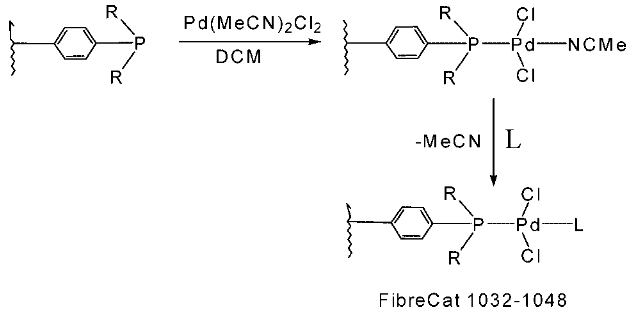
Scheme 1. General Synthetic Route to Pd-Based Tunable FibreCat



chloride substrates (C−X bond dissociation enthalpy: Ph−I = 67 kcal/mol; Ph−Br = 84 kcal/mol; Ph−Cl = 97.1 kcal/mol)[9] and electron-donating and bulky aryl bromides, we herein report the synthesis, characterization, and catalysis of the next-generation tunable Pd-based FibreCats, with varying steric and electronic properties of the ligands. This paper also reports the relative activities, robustness, and recycling characteristics of these catalysts from a process chemistry point of view, allowing organic chemists to choose the right catalyst for a given substrate.

Results and Discussion

Unlike in the case of the conventional polystyrene beads technology, FibreCat supports are functionalized polyethylene or polypropylene (more advanced) with a typical dimension of 0.2−2 mm length. These polymers are obtained by grafting vinyl monomers onto a preirradiated polyolefin with the aid of an electron beam.[10] The fibers are designed in such a way to have excellent functional group accessibility, mechanical stability, easy filterability, and superior chemical stability in various solvents.[11] The conventional beads undergo swelling by a solvent, where the substrate has to go through the beads by diffusion. Conversely, the functional groups on the FibreCat are readily accessible to the substrate without any major diffusion process.[11b] The “fiber technology” allows the catalyst to be more robust.

Scheme 1 summarizes the general synthetic route for the next-generation FibreCats. These Pd(II) complexes are tuned by (i) changing the R group on P and (ii) changing the second ligand, L, on Pd. We have been successful in making two sets of catalysts using FC-1029 and FC-1039 starting materials. All these complexes are air-stable and easy to handle. We have done full elemental analyses of the FC-1029 series (FC-1032−1048) and found that the elements add up to ca. 100%. Therefore, for the FC-1039 series we have done only the Pd assay. Earlier we had shown that tuning was also possible by changing the Pd precursors: Pd$_2$dba$_3$, Pd(OAc)$_2$, (π-allylPdCl)$_2$, Pd(C$_6$H$_5$CN)$_2$Cl$_2$, and Pd(MeCN)$_2$Cl$_2$.[6] However, such tuning does not make any significant activity change, as the ligand is the most important component for improving the catalyst activity.

Table 1. New Generation FibreCats Developed for Applications in Suzuki Coupling[a]

R	L	% Pd	code	color
Ph	MeCN	8.31	FC-1029	orange
	t-Bu$_3$P	4.47	FC-1032	yellow
	Q-Phos	6.34	FC-1033	brown
	PhP(t-Bu)$_2$	4.62	FC-1034	orange
	dppf	4.64	FC-1035	orange
	BINAP	4.85	FC-1036	orange
	dippf	5.23	FC-1037	red
	IPr carbene	6.96	FC-1038	red
	(Me$_2$NC$_6$H$_4$)P(t-Bu)$_2$	4.37	FC-1034A	gold
Cy	MeCN	9.61	FC-1039	red
	t-Bu$_3$P	5.76	FC-1042	gold
	Q-Phos	6.61	FC-1043	brown
	PhP(t-Bu)$_2$	6.48	FC-1044	gold
	dppf	5.61	FC-1045	gold
	BINAP	6.63	FC-1046	gold
	dippf	7.47	FC-1047	red
	(Me$_2$NC$_6$H$_4$)P(t-Bu)$_2$	4.33	FC-1048	gold

[a] The abbreviations of the ligands are given in the Supporting Information.

Table 2. Benchmarking the Catalytic Activities of Supported Systems with Pd(OAc)$_2$/2Ph$_3$P in EtOH−Water (1:1) Solvent and Na$_2$CO$_3$ Base for the Coupling of *p*- Bromoanisole with PhB(OH)$_2$

catalyst	entry	loading (mol %)	rxn time (h)	rxn temp (°C)	yield[a] (%)	TON	TOF (h^{-1})
FC-1032	1	1.0	4	75	100 (94)		
	2	0.5	4	75	100 (95)		
	3	0.5	6	22	68 (52)		
	4	0.25	2	75	88 (72)	352	176
	5	0.25	4	75	95 (82)		
FC-1039	6	1.0	4	75	100 (94)		
	7	0.5	4	75	100 (94)		
	8	0.5	6	22	72 (61)		
	9	0.25	2	75	100 (94)	400	200
	10	0.25	4	75	100 (93)		
FC-1029	11	1.0	4	75	100 (94)		
	12	0.5	4	75	100 (95)		
	13	0.5	6	22	79 (69)		
	14	0.25	2	75	100 (94)	400	200
	15	0.25	4	75	100 (95)		
Pd-Smopex-111	16	1.0	4	75	100 (94)		
	17	0.5	4	75	100 (95)		
	18	0.5	6	22	78 (69)		
	19	0.25	2	75	92 (78)	368	184
	20	0.25	4	75	100 (94)		
Pd(OAc)$_2$/2Ph$_3$P	21	1.0	4	75	100 (94)		
	22	0.5	1	75	5 (−)		
	23	0.5	2	75	20 (−)		
	24	0.5	4	75	100 (94)	200	50

[a] Number in parentheses refers to the isolated yield.

Having successfully synthesized several examples of FibreCats with different ligands (Table 1), we mostly explored their activities in Suzuki coupling of activated, unactivated, and neutral aryl chlorides/bromides. Typically FC-1039 and its derivatives are expected to be more active than FC-1029 and its derivatives, as FC-1039 contains a bulky electron-rich Cy$_2$P group instead of a Ph$_2$P group on the fiber.

During the second tuning, L on the Pd has been altered to a wide variety of commercially available bulky electron-rich ligands such as Q-Phos (Johnson Matthey, Strem, Aldrich), t-Bu$_3$P (FMC, Strem, Digital), t-Bu$_2$PPh (Johnson Matthey), (Me$_2$NC$_6$H$_4$)P(t-Bu)$_2$ (Johnson Matthey), iPr-carbene (Strem), and bidentate ligands such as dppf (Johnson Matthey), BINAP (Strem, Digital), and dippf (Johnson Matthey). This tuning process makes this class of supported catalysts unique for carrying out relatively challenging coupling reactions.

Table 2 summarizes the relative activities of different classes of FibreCat for a model system such as *p*-bromoanisole with PhB(OH)$_2$ in ethanol−water using K$_2$CO$_3$ base. The classical homogeneous *in situ* system Pd(OAc)$_2$/2Ph$_3$P has also been used

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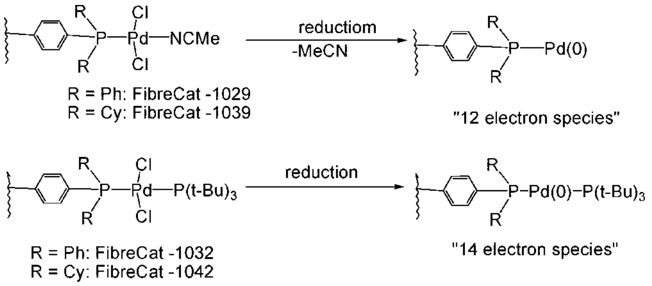
Scheme 2. Proposed Pd(0) Species in the Oxidative Addition Step



as a benchmark. All the supported catalysts such as FC-1029, FC-1039, Pd-Smopex-111, and FC-1032 have been found to be more active than the homogeneous systems even at lower catalyst loadings and lower reaction temperatures, although at 1 mol % loading no difference in reactivities was observed when the reaction temperature was 75 °C. The better selectivity of the supported systems in comparison to the *in situ* system for the Suzuki coupling of *p*-bromoacetophenone with Ph-$B(OH)_2$ was earlier demonstrated from our laboratory.[6] Interestingly, even at RT all the supported systems gave 70−80% conversion to products within 6 h at 0.5 mol % catalyst loading. FC-1029 and FC-1039 gave 100% conversion with about 95% isolated yields even at 0.25 mol % loading within 2 h at 75 °C in an EtOH−water system. At this loading, both Pd-SMOPEX-111 and FC-1032 were slightly less active than FC-1029 and FC-1039. The relatively lower reactivity of Pd-SMOPEX-111 is understandable as the ligand, thiol, is less electron-rich in comparison to the phosphine-based ligands on the FibreCat. If the same hypothesis is correct, one should expect FC-1032 to be more active than FC-1029 and FC-1039 at lower catalyst loading, as it contains a bulkier electron-rich ligand, t-Bu_3P. Similarly $Pd(OAc)_2$ with 2 equiv of Ph_3P in theory should be at least equally active as FC-1029. Therefore, we believe that the relatively higher activities of FC-1029, FC-1039, and even Pd-SMOPEX in the coupling of simple aryl bromides could be due to the fact that these catalysts presumably form a low-coordinated "12-electron Pd(0) species" during the oxidative addition step, while FC-1032 and $Pd(OAc)_2/2Ph_3P$ could potentially give a "14-electron species" (see Scheme 2). However, for challenging substrates, such as aryl chlorides and sterically hindered or heteroaryl aryl bromides, bulky electron-rich ligand based systems, such as FC-1042 and FC-1048, are required to facilitate the oxidative addition and subsequent reductive elimination. This is understandable, as the oxidative addition step of an activated Ar−Br is more facile in comparison to Ar−Cl due to its lower C−Br bond dissociation energy.[9]

Table 3 shows the superior activity of the new generation FibreCats (e.g., FC-1042) in the coupling of 4-chloropyridine with $PhB(OH)_2$. As expected, FC-1029, FC-1039, and Pd-SMOPEX 111 are not very suitable for coupling aryl chlorides effectively. Although FC-1032 has been reported to be effective for coupling of certain heteroaryl chlorides,[7] it has not been very effective for 4-chloropyridine, on the basis of the results from Table 3.

Table 4 shows the generality of the Suzuki coupling of a variety of activated, neutral, and unactivated aryl bromides in KF base, based on the prescreen results (Table 3, entry 13). Interestingly, for the coupling of a very easy substrate such as *p*-bromoacetophenone, FC-1029 gave 100% conversion and 100% selectivity (Table 4, entry 4) within 2 h, while more active catalysts such as FC-1032 gave lower conversions under identical conditions.[12] However, with a longer reaction period, the yields were improved with FC-1032. This observation once again suggests that for activated substrates Ph_3P-based catalysts are active enough. For several of the unactivated aryl bromides, next-generation catalysts such as FC-1032, FC-1042, and FC-1044, were required with ca. 1% catalyst loadings. This is based on our earlier observation that FC-1029 was not very suitable for coupling of more challenging aryl bromides such as bromothiophene.[6]

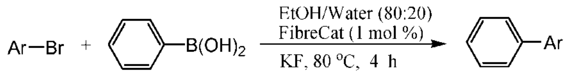
The results listed in Table 5 are very interesting. Model substrates such as electron-donating, sterically hindered and

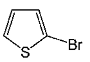
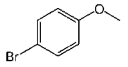
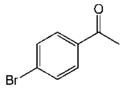
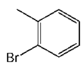
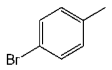
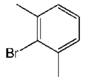
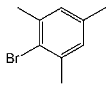
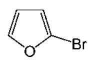
Table 3. Relative Superior Activity of New Generation Catalysts in the Coupling of 4-Chloropyridine with $PhB(OH)_2$ in $EtOH-H_2O$ (1:1) Solvent and K_2CO_3 Base at 75 °C

catalyst	entry	loading (mol %)	time (h)	yield^a (%)
FC-1032	1	2	8	11
	2	3	15	70
FC-1039	3	2	8	25
	4	3	15	36
FC-1042	5	2	8	41
	6	3	15	100 (93)
FC-1029	7	2	8	16
	8	3	15	16
Pd-Smopex 111	9	2	8	
	10	3	15	6
FC-1034A	11	2	8	59
	12	3	15	100 (92)^b
	13^b	3	4	100 (94)

[a] Yield in parentheses refers to the isolated yield. [b] KF was used as a base.

Table 4. Suzuki Coupling of Aryl Bromides



entry	substrate	catalyst	leaching (ppm)	yield (*)
1		FC-1042	0.01	100 (92)^a
2		FC-1042	< 0.01	96 (89)
3		FC-1032	< 0.01	100 (89)
4		FC-1029		100^b
5		FC-1044	< 0.01	100 (95)^a
6		FC-1044	< 0.01	100 (97)^a
7		FC-1044	<0.01	97 (88)^a
8		FC-1044	<0.01	91 (88)^a
9		FC-1042	<0.01	99^{b,c}

[a] Reaction time = 4 h. [b] Reaction time = 2 h. [c] The starting material is very volatile; hence isolated yield is low. [d] Isolated yield.

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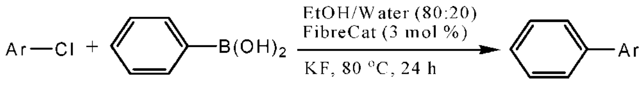
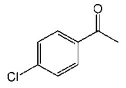
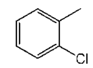
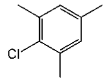
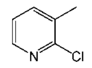
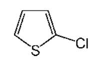
(12) Table 2, entry 3: FC-1032 gave only 56% conversion in 2 h when K_2CO_3 base was used, while FC-1029 gave 100% conversion (entry 4) under identical conditions.

Table 5. Suzuki Coupling of Aryl Chlorides



entry	substrate	catalyst	leaching (ppm)	yield (*)
1		FC-1044	< 0.01	96 (93)
2		FC-1045	< 0.01	89 (70)
3		FC-1043	< 0.01	93 (89)
4		FC-1044	< 0.01	87 (75)
5		FC-1042	N/T	98 (94)[a]

[a] N/T = not tested. [b]Isolated yield. [c]DMF solvent at 120 °C.

heterocyclic aryl chlorides have been effectively coupled with $PhB(OH)_2$ to achieve very good product conversion using the new generation catalysts. Incorporation of bulky electron-rich ligands such as Q-Phos, $PhP(t\text{-}Bu)_2$, $(t\text{-}Bu)_3P$, and dippf indeed seem to have a profound influence in increasing the activity of the catalyst. However, the activities of these catalysts might be lower than that of the homogeneous systems containing these ligands (L) alone, but higher than that of Ph_3P- or Cy_3P-based homogeneous systems. It is also worth mentioning that a fully formed complex of Q-Phos has never been isolated before.[13] Hence this method is quite powerful and unique in tuning a supported catalyst appropriately to match the steric and electronic properties of the substrate.

To our knowledge there are not many effective supported catalyst systems available to perform the Suzuki coupling of aryl chlorides. However, it is worth mentioning that a Merrifield resin-supported Buchwald ligand was effective in carrying out C−N and Suzuki couplings with very limited examples of aryl chlorides such as *p*-chlorotoluene and 2,5-dimethylchlorobenzene, although coupling was done *in situ* using $Pd(OAc)_2$ or Pd_2dba_3 precursors.[14] No studies on the Pd leaching were reported in their investigation.

Previously Buchmeiser and Wurst studied the Heck coupling of activated and neutral aryl chlorides such as chloroacetophenone and chlorobenzene with styrene (96% and 89% conversion, respectively) at high temperature (140 °C).[15] Reetz also reported a Heck coupling of chlorobenzene with styrene at 155 °C using Pd/Al_2O_3.[16] Nevertheless, their method is impractical, as the yield is only 40% under these conditions. Our portfolio of FibreCats allows us to carry out coupling of a wide variety of aryl chlorides such as: 2-chloro-3-methylpyridine, 2-chlorothiophene, chloromesitylene, *o*-chlorotoluene, and chloroacetophenone in high yields (Table 5). We are optimistic that these catalysts could be utilized in several other examples of aryl chlorides and challenging aryl bromides.

Table 6. Recycling of Catalysts Used in the Coupling of Bromoanisole with Phenyl Boronic Acid in EtOH−H_2O Solvent and K_2CO_3 Base at 70 °C for 4 h

entry	catalyst	loading (mol %)	cycle	yield[a]	leaching (ppm)
1	FC-1032	1	1	100 (94)	<1.0
			2	100 (92)	<1.0
			3	100 (93)	5.0
			4	95 (87)	10.0
2	FC-1039	0.5	1	100 (93)	<1.0
			2	98 (91.5)	<1.0
			3	94 (88)	1.0
			4	16	20.0
3	FC-1029	0.5	1	100 (94)	0.0
			2	100 (91)	<1.0
			3	92 (88)	1.0
			4	26	30.0
4	Pd Smopex-111	1	1	100 (92)	not detected
			2	100 (91)	<1.0
			3	77 (65)	1.0
			4	5	65.0

[a] Isolated yield in parentheses.

Leaching and Reusability. An ideal supported homogeneous catalyst should demonstrate its application for higher activity without undergoing any leaching and therefore should give very good recyclablilty. To our knowledge, there is no such “dream supported catalyst” available today for coupling of a wide variety of substrates including aryl chlorides. The “three-phase test” conducted on several of the known systems indicates that the catalysis in many cases takes place in a homogeneous or pseudohomogeneous manner.[4e,j,17] When catalysis is conducted with such catalysts, using substrates with several heterocyclic atoms, some leaching can be expected for many supported systems; however, the extent of leaching may depend on how well the “release and capture mechanism” occurs in that system. In this study we have not done any detailed mechanistic investigation as to whether the catalysis occurs heterogeneously or homogenously, as the focus of this paper was to establish the generality of the tunablity of the catalysts for coupling of relatively challenging aryl halides with minimal leaching. Our *in situ* ^{31}P NMR studies of the reaction mixture involving FC-1032 or FC-1042 did not show any trace amount of the free ligand even after scanning the solution overnight using a 400 MHz NMR.

As shown in Table 4, entries 1−3 and 5−9, and Table 5, entries 1−4, we have tested the Pd leaching in several cases and observed practically no Pd leaching including the simple thiophene and pyridine cases. In some cases the catalysts turned black, although in many cases they retained their original yellow or yellowish-brown color. The color change and degradation of the catalyst are very much dependent on the substrate and the reaction conditions.

We have studied the recyclability and leaching of a few selected catalysts for a few substrates. The results obtained for bromoanisole and bromopyridine are summarized in Tables 6 and 7, respectively. Among the first-generation catalyst, FC-1032 seems to be more robust, as it was recycled up to four times with very little leaching. For bromopyridine, next-generation catalysts such as FC-1042 and FC-1044A are more robust on the basis of the minimal leaching even after the fourth

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(13) (a) Yamashita, M.; Hartwig, J. F. *J. Am. Chem. Soc.* **2004**, *126*, 5344–5345, and references therein. (b) Kataoka, N.; Shelby, Q.; Stambuli, J. P.; Hartwig, J. F. *J. Org. Chem.* **2002**, *67*, 5553–5566.

(14) Parrish, C. A.; Buchwald, S. L. *J. Am. Chem. Soc.* **2001**, *66*, 3820–27. See also references for supported catalysts in aryl iodide and bromide coupling.

(15) Buchmeiser, M. R.; Wurst, K. *J. Am. Chem. Soc.* **1999**, *121*, 11101–11107.

(16) Reetz, M. T.; Lohmer, G. *Chem. Commun.* **1996**, *584*, 1921–1922.

(17) Davies, I. W.; Matty, L.; Hughes, D. L.; Reider, P. J. *J. Am. Chem. Soc.* **2001**, *123*, 10139.

Table 7. Recycling of 2-Bromopyridine with Phenyl Boronic Acid in EtOH−H_2O in K_2CO_3 for 15 h

entry	catalyst	loading (mol %)	cycle	yield[a]	leaching (ppm)
1	FC-1032	3	1	100 (92)	<1
			2	90 (82)	<1
			3	60	<1
			4	58	<1
2	FC-1042	3	1	100 (92)	<1
			2	100 (94)	<1
			3	91 (82)	<1
			4	82	<1
3	FC-1034A	3	1	100 (94)	<1
			2	100(91)	<1
			3	100 (91)	<1
			4	96 (88)	<1

[a] Isolated yield in parentheses.

cycle with no activity loss. Depending on the conditions and substrate, we did see discoloration of the catalysts in certain cases.

It is worth mentioning that Churruca et al. successfully recyled FC-1029 catalyst (also known as FC-1026) up to five times in the α-ketone arylation reaction after the simple treatment of the discolored catalyst.[18]

We expect simple bidentate ligands, such as dppf and BINAP, to be more robust catalysts due to the fact that bidentate ligands allow more cross-linked systems, although we have not done any detailed studies. However, we could not make a robust catalyst using the dtbpf ligand, although dtbpf$PdCl_2$ is one of the best catalyst systems for aryl chloride coupling.[3k,19] The surface characterization of these complexes was also carried out in some detail.[20]

We could not make a direct comparison of the activities of the tunable FibreCats with their corresponding homogeneous systems, as the mixed Pd complexes are not available or easy to synthesize. FibreCats are indeed superior in minimizing the metal contamination in the products on the basis of our results on the model substrates. Results from our earlier studies reveal that first-generation FibreCats are equally active as the respective homogeneous system with better selectivity when model substrates have been used.[6]

Conclusion

We have been able to develop a reasonably robust process for a new class of tunable polypropylene-supported catalysts for carrying out Suzuki coupling reactions of a variety of substrates. The FC-1029 and -1039 platform allows us to incorporate new ligands of varying electronic and steric properties, thereby making them tunable. Minimal leaching or activity loss was observed in many cases. However, substrates and reaction conditions may have a profound influence on leaching. To our knowledge these are some of the best supported systems available in the literature in the area of Suzuki couplings. As expected, a higher catalyst loading was required for Ar−Cl versus Ar−Br, although the systems were not fully optimized. Our preliminary studies show that some of these catalysts such as FC-1032 are good for reductive carbonylation reactions with practically no metal leaching. Detailed work on the use of various boronic acids as well as the use of these catalysts in other coupling reactions such as Sonogashira coupling, and Heck coupling are in progress. As mentioned in the Introduction, more work in this area should be encourgaged to solve the metal contamination issues in pharmaceutical and fine chemical industries.

Experimental Section

General Procedures. All the reactions were carried out in an inert atmosphere using a Schlenk line in conjunction with a Radleys carousel 12 place reaction station.[21] The solvents and substrates were obtained from Alfa Asear/Aldrich and were used without further purification. The FibreCats used in the study were synthesized as new products using a procedure analogous to what is reported in the literature earlier by our group.[6] A typical procedure is given below. The supported ligands used for making the FC-1029 and FC-1039 series are listed as FCS-110 and FC-111, respectively, and are commercially available through Johnson Matthey Catalysis and Chiral Technologies upon request. All of the used catalysts are also currently commercially available at Johnson Matthey, Catalysts and Chiral Technology, 2001 Nolte Drive, West Deptford, NJ 08066, in the form of kits. FC-1029, Pd-SMOPEX-111, and FC-1032 are available in kilogram quantities. The coupled products in most cases yielded between 80% and 100% for both bromo and chloro substrates under varying conditions.

Elemental analyses were done at Robertson Microlit, P.O. Box 927, Madison, NJ 07940, while NMR spectra were recorded using a Bruker 400 MHz spectrometer.

Synthesis of FibreCat-1034 as a Typical Example. In a general procedure commercially available FC-1029[6] with a loading of 0.82 mmol/g (25.1 g; 20.6 mmol of Pd) was taken in a 500 mL Schlenk flask with a Teflon stir bar and was degassed three times using N_2 and vacuum cycles. To this was added anhy CH_2Cl_2 (189 mL) by cannula while stirring under N_2. The flask was then cooled to ca. 0 °C using an ice bath, and a freshly prepared solution of phenyl-di-*tert*-butylphosphine (4.84 g; 21.8 mmol) in CH_2Cl_2 (33 mL) was added under strict inert conditions over a period of 10 min by cannula. The mixture was slowly warmed to room temperature over a period of 6 h. The reaction mixture was filtered on a coarse frit and washed five times with 100 mL portions of CH_2Cl_2 to obtain a colorless filtrate. The free-flowing yellow fiber was dried in a 40 °C vacuum oven overnight to obtain 25.2 g of FC-1034. Using an analogous procedure, other FibreCats were also synthesized. The samples were submitted for elemental analysis, which are listed in the Supporting Information.

Procedure for Catalyst Screenings. In a standard screening experiment, Radley's carousel (model: RTC-B-519) test tube was loaded with the appropriate FibreCat catalyst (1−3 mol %), aryl halide solution (100 mg of substrate in 1 mL of solvent), boronic acid solution (1.05 mol of $PhB(OH)_2$/mol substrate in 1 mL of

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(18) (a) Churruca, F.; SanMartin, R.; Tellitu, I.; Domínguez, E. *Tetrahedron Lett.* **2003**, *44*, 5925–5929. (b) Churruca, F.; SanMartin, R.; Carril, M.; Tellitu, I.; Domínguez, E. *Tetrahedron* **2004**, *60*, 2393–2408.

(19) (a) Grasa, G.; Colacot, T. *Org. Lett.* **2007**, *9*, 5489–5492. (b) Grasa, G.; Colacot, T. J. *Org. Process. Res. Dev.* **2008**, *12*, 522–529.

(20) Currently we have full elemental analyses for these complexes of FC-1029 series (see Supporting Information). Preliminary solid state ^{31}P NMR data of the FibreCat samples were obtained with the help of Prof. Mark Smith, Warwick University. FibreCat-1029 was used as a standard. FibreCat-1029 gave a single broad peak at 30−35 ppm, with associated spinning side-bands. This is assigned to be polymer-bound−PPh_2 complexed to Pd(II). For FibreCat-1032 the main peak for−PPh_2 is shifted to ca. 20 ppm (presumably due to trans effect of the P^tBu_3 ligand displacing MeCN) in addition to a new peak at ca. 40 ppm. The area for the second peak is smaller than that of−PPh_2, suggesting incomplete substitution with the bulky *t*-Bu_3P ligand. As expected, where the added ligand contains only aryl substituents, as is the case for BINAP (FibreCat-1036), separate resonances are not resolved. For FibreCat-1039, containing the polymer-bound Cy_2P− ligand, only one ^{31}P resonance is expected, but two are observed, at 25 and 45 ppm. This suggests that a significant proportion of the Cy_2P−ligands have been oxidized to−$P(O)Cy_2$ or that many of the−PCy_2 groups remain unreacted with Pd. The presence of these additional sites further complicates the spectral interpretation for FibreCat-1045 and -1046. Therefore detailed solid state NMR and surface characterization studies are required.

(21) http://www.radleys.com/pages/products/carousel12.shtml.

solvent), base solution (e.g., KF, K_2CO_3, 3 mol equiv in 1 mL of nanopure water), and an additional 2 mL of solvent (DMF or EtOH). The Radley's tubes were then degassed five times and kept under a nitrogen blanket. The carousel was heated to 80−120 °C for a 2−24 h period with vigorous stirring using magnetic stir bars. When the reaction was over, the tubes were cooled to RT, and approximately 1−1.5 mL of the reaction mixture was removed using a syringe and filtered into a GC vial using a disposable nylon frit (0.45 μm) attached to a syringe to remove any solids (catalyst or precipitated product). The sample was then analyzed using a Perkin-Elmer Autosystem XL gas chromatograph with an FID detector. A Varian 5CB column (30 m length, 0.25 mm diameter) with a temperature program (70 °C, hold for 1 min; 20 °C $\min^{-1}$ to 280 °C, hold for 3 min) was used for a run time of 15 min. The crude GC yields of the products were obtained by comparing their GC peaks with that of the authentic commercial samples.

The products, which are not commercially available, were isolated in >80% yield and fully characterized by elemental assays, ^{1}H NMR, ^{13}C NMR, and GC-MS, while commercially available products were isolated to check their yield and purity by elemental assay, in addition to comparing their ^{1}H NMR spectrum with that of the authentic samples.

In all cases, the crude reaction mixture was stirred with DCM (20 mL) and water (10 mL) for 5 min. The organic layer was then separated via gravity and stirred with anhydrous sodium sulfate for 30 min to remove any remaining water. The mixtures were then filtered to remove any catalyst and sodium sulfate. In the case of solid products such as phenylacetophenone and phenylanisole, after extraction and filtration the solvent was removed by a Rotovap to obtain a solid. The solid was redissolved in a minimum amount of ethanol, followed by slow addition of water to obtain a white precipitate. The solid was filtered and dried at 45 °C in a vacuum oven to obtain analytically pure material. The details of the isolation of the products are given below.

2-Phenylthiophene (Table 4, entry 1). Reaction yielded product, 2-phenylthiophene, in high purity by GC (>99%). The CH_2Cl_2 extract was removed under vacuum, and product, as a solid, was left to dry overnight in a vacuum oven at 50 °C under a gentle nitrogen sweep to obtain a 92% yield. Anal. Calcd for $C_{10}H_8S$: C, 74.96; H, 5.03. Found: C, 74.69; H, 4.97. ^{1}H NMR (CD_2Cl_2): δ (ppm) 7.63 (m, 2H, ortho-Ph), 7.40 (m, 2H, meta-Ph), 7.36 (m, 1H, para-Ph), 7.31 (m, 2H, thiophene), 7.11 (m, 1H, thiophene). **Table 5**, entry 5: Reaction yielded product, 2-phenylthiophene, in high purity (98%). Solvent was removed under vacuum, and the solid product was left to dry overnight in a vacuum oven at 50 °C under a nitrogen sweep. Anal. Calcd for $C_{10}H_8S$: C, 74.96; H, 5.03. Found: C, 75.28; H, 5.04. ^{1}H NMR was identical to the product reported above.

4-Phenylanisole (Table 4, entry 2). Reaction yielded product, 4-methoxybiphenyl, in >95% purity by GC. Solvent was removed, and the resulting solid, was left to dry overnight in a fume hood. Since the coupled product contained a small amount of starting material, it was recrystallized in ethanol−water (89% yield). Anal. Calcd for $C_{13}H_{12}O$: C, 84.75; H, 6.57. Found: C, 84.94; H, 6.3. ^{1}H NMR (CD_2Cl_2): δ (ppm) 7.56 (m, 4 H, ortho-Ar), 7.43 (m, 2 H, Ph), 7.31 (m, 1H, para-Ph), 7.01 (m, 2H, anisole), 3.85 (s, 3H, $-OCH_3$).

4-Phenylaceophenone (Table 4, entry 3). Reaction yielded product, 4-acetylbiphenyl, in high purity (>99% by GC) with 89% isolated yield. Anal. Calcd for $C_{14}H_{12}O$: C, 85.68; H, 6.16. Found: C, 85.47; H, 6.17. ^{1}H NMR (CD_2Cl_2): δ (ppm) 8.04 (m, 2 H, phenyl), 7.73 (m, 2H, tolyl), 7.67 (m, 2H, phenyl), 7.50 (m, 2H, tolyl), 7.41 (m, 1H, phenyl), 2.62 (s, 3H, CH_3). **Table 5**, entry 1: Reaction yielded product, 4-acetylbiphenyl, in high purity (>95%) by GC. Solvent was removed and product was left to dry overnight in a fume hood. About 10 mL of ethanol was added to the solid to extract any starting materials. The remaining solid was filtered onto a 30 mL fritted funnel under vacuum. To the filtrate, 50 mL of distilled water was added slowly to crash out any dissolved product. This was again collected onto the same frit and dried overnight in a vacuum oven at 50 °C to obtain 93% yield of the product. Anal. Calcd for $C_{14}H_{12}O$: C, 85.68; H, 6.16. Found: C, 85.43; H, 6.31. ^{1}H NMR was identical to the product reported above.

2-Phenyltoluene (Table 4, entry 5). Reaction yielded product, 2-phenyltoluene, in high purity (>99% by GC). Solvent was removed and product, as a solid, was left to dry overnight in a vacuum oven at 50 °C under a nitrogen sweep. Product was isolated in 95% yield. Anal. Calcd for $C_{13}H_{12}$: C, 92.81; H, 7.19. Found: C, 92.84; H, 7.26. ^{1}H NMR (CD_2Cl_2): δ (ppm) 7.45 (m, 2H, phenyl), 7.37 (t, 3H, phenyl), 7.30 (m, 2H, tolyl), 7.26 (m, 2H, tolyl), 2.30 (s, 3H, CH_3). **Table 5**, entry 2: Reaction yielded product, 2-phenyltoluene, in 88% yield by GC. After extraction and concentration the solution was run through a column of silica gel using hexane as eluent. The fractions containing the product were concentrated and then dried in a vacuum oven overnight at 55 °C under a very slow stream of nitrogen. Product was isolated in 70% yield. Anal. Calcd for $C_{13}H_{12}$: C, 92.81; H, 7.19. Found: C, 92.59; H, 7.26. ^{1}H NMR was found to be identical to what is reported above.

4-Phenyltoluene (Table 4, entry 6). Reaction yielded product, 4-phenyltoluene, in high purity (>99%) by GC. Solvent was removed, and the resulting solid was left overnight in a vacuum oven at 50 °C under nitrogen to obtain a 97% yield. Anal. Calcd for $C_{13}H_{12}$: C, 92.81; H, 7.19. Found: C, 92.85; H, 7.32. ^{1}H NMR ($CDCl_3$): δ (ppm) 7.55 (m, 2H, ortho-phenyl), 7.47 (m, 2H, ortho-tolyl), 7.40 (m, 2H, meta-phenyl), 7.30 (t, 1H, para-phenyl), 7.23 (d, 2H, meta-tolyl), 2.38 (s, 3H, CH_3).

2-Phenyl-*m*-xylene (Table 4, entry 7). Reaction yielded product, 2-phenyl-*m*-xylene, in very good purity (>97%) by GC. Solvent was removed by vacuum, and the product (colorless oil) was left to dry overnight in a vacuum oven at 50 °C under a nitrogen sweep. Product was isolated in 88% yield. Anal. Calcd for $C_{14}H_{14}$: C, 92.26; H, 7.74. Found: C, 91.94; H, 7.95. ^{1}H NMR (CD_2Cl_2): δ (ppm) 7.44 (m, 2H, ArH), 7.35 (t, 1H, phenyl), 7.14 (m, 3H, ArH), 7.11 (d, 2H, ArH), 2.02 (s, 6H, CH_3). MS: (EI-MS) *m/z* 182 [M^+].

2-Phenylmesitylene (Table 4, entry 8). Reaction yielded product, 2-phenylmesitylene, 87% purity by GC. Solvent was removed by vacuum, and the oily product was left to dry overnight in a vacuum oven at 55 °C under nitrogen. Product was isolated in 88% yield. Anal. Calcd for $C_{15}H_{16}$: C, 91.78; H, 8.22. Found: C, 91.68; H, 8.43. ^{1}H NMR (CD_2Cl_2): δ (ppm) 7.43 (m, 2H, ArH), 7.34 (t, 1H, ArH), 7.14 (d, 2H, ArH), 6.94 (s, 2H, ArH), 2.32 (s, 3H, CH_3), 1.99 (s, 6H, CH_3). MS: (EI-MS) *m/z* 196 [M^+]. **Table 5, entry 3:** Reaction product, 2-phenylmesitylene, was 85% pure (conversion) by GC. After extraction and concentration of the solution the product was isolated using column chromatography using hexane as the mobile phase. The fractions containing the product were concentrated and then dried in a vacuum oven overnight at 50 °C under a slow stream of nitrogen. Product was isolated in 89% yield. Anal. Calcd for $C_{15}H_{16}$: C, 91.78; H, 8.22. Found: C, 91.63; H, 8.40. ^{1}H NMR and MS were identical to what was reported for the isolated product above.

2-Phenyl-3-methylpyridine (Table 5, entry 4). Reaction yielded product, 3-methyl-2-phenylpyridine, in 88% yield by GC. After extraction and concentration the solution was run through a column of silica gel using 90% hexane−10% ethyl acetate as the mobile phase. The fractions containing the product were concentrated under vacuum and then dried in a vacuum oven overnight at 50 °C under nitrogen. Product was isolated in 75% yield. Anal. Calcd for $C_{12}H_{11}N$: C, 85.17; H, 6.55; N, 8.28. Found: C, 84.98; H, 6.36; N, 7.99. ^{1}H NMR (CD_2Cl_2): δ (ppm) 8.50 (d, 1H, ArH), 7.61 (d, 1H, ArH), 7.53 (d, 2H, ArH), 7.45 (t, 2H, ArH), 7.42 (t, 1H, ArH), 7.20 (t, 1H, ArH), 2.35 (s, 3H, CH_3). MS: (EI-MS) *m/z* 169 [M^+].

2-Phenylfuran (Table 4, entry 9). Reaction yielded product, 2-phenylfuran, in high purity (99%) by GC. Elemental analysis, ^{1}H NMR, and ^{13}C NMR were used to confirm the purity and to characterize the product. Anal. Calcd for $C_{10}H_8O$: C, 83.31; H, 5.59. Found: C, 81.55; H, 5.54. ^{1}H NMR (CD_2Cl_2): δ (ppm) 7.72 (d, 2H, ArH), 7.53 (d, 1H, ArH), 7.43 (t, 2H, ArH), 7.30 (t, 1H, ArH), 6.71 (d, 1H, ArH), 6.53 (t, 1H, ArH).

Recycling Experiment. Leaching and Recycling: Reaction of Bromoanisole with Phenyl Boronic Acid. In a typical recycling experiment, Radley's six-flask carousel was loaded with a base (e.g., K_2CO_3, 4.14 g, 3 mol), $PhB(OH)_2$ (1.3 g, 1.07 mol), and the catalysts (e.g., FibreCat-1032 120 mg, 0.5 mol %) and was degassed for 10 min using vacuum and nitrogen. To this was added a solution (100 mL in the case of ethanol−water solvent system, 50 mL of ethanol solution followed by 50 mL of water) of the substrate (e.g., *p*-bromoanisole, 1.8 g, 1 mol) using a manual syringe in the case of Radley's, and the mixture was heated to the desired temperature (75 °C) for a specified period of time (2 h). The reaction mixture was cooled to RT, extracted with 100 mL of dichloromethane in the case of the ethanol−water system, and filtered using a Whatman filter paper to separate the catalyst. The filtrate containing organic and aqueous layers was separated by gravity. The organic layer was dried on anhydrous sodium sulfate and then divided into two halves. The half on solvent evaporation using a Rotovap gave 0.84 g of pure product (94% yield). The other half of the organic layer and aqueous extracts were submitted to Johnson Matthey's ISO certified analytical laboratory for % Pd (ppm) by the "wet-ash" method for dissolving oragnometallic compounds for analysis by ICP. After heating to remove as much solvent as possible, the sample was digested with various mineral acids, i.e., sulfuric, hydrochloric, and nitric, to obtain an aqueous solution. Once a clear solution was obtained, the sample was submitted to ICP for analysis. In ICP a suitable internal standard was added to the sample. An analytical curve for Pd was constructed from working standards that are prepared from gravimetrically analyzed stocks. The detection limit in this matrix is estimated to be below 0.5 ppm, and a standard at 1 ppm typically returns a value within 0.1 ppm of the standard value when the instrument is checked for accuracy.

The catalyst on the filter paper was washed with water (10 mL) followed by acetone (5 mL) and dichloromethane (20 mL) properly to remove any impurities. It was dried in an oven for 20 min at 50 °C and under vacuum and used for the next reaction, retaining its original color.

Recycling of the reaction of 2-bromopyridine with $PhB(OH)_2$ (Table 7) was also performed in a similar way.

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Note Added after ASAP Publication. In the version of this paper published on the Web on Oct 4, 2008, there were errors in references 9, 10, and 19 as well as a column head in Table 2. The version published on Oct 9, 2008, is correct.

Supporting Information Available: The definitions of the various ligands, complete elemental assay of the first set of FibreCats, proton NMR data of the commercially available products, as well as the ^{1}H and ^{13}C NMR and MS data of the unknown compounds are available free of charge via the Internet at http://pubs.acs.org.

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