P-Arylation of aryl halides by an environmentally compatible method

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Abstract

In this paper, palladium-DABCO complex supported on magnetic nanoparticles was successfully used as a new magnetically recoverable heterogeneous catalyst for the synthesis of arylphosphonates *via* P-arylation of different types of aryl halides (aryl iodides/bromides/chlorides and benzene boronic acid/sulfonate), with phosphite esters (triethyl/triphenyl/tri-*iso*-propyl/diethyl/diphenyl/di-*iso*-propyl phosphite) in neat water without using any additive. The heterogeneous catalyst was easily isolated from the reaction mixture by an external magnet and reused five times without significant degradation in its activity.

Keywords: Arylphosphonates. Hirao reaction. Heterogeneous catalyst. Magnetic nanoparticles. Palladium

Introduction

Arylphosphonates are valuable compounds in a variety of fields, especially as intermediates in organic synthesis,[1] in the preparation of biologically active materials,[2] and in designing fuel cell membranes and materials with special optical properties.[3] The widespread use of arylphosphonates in material sciences and biological chemistry caused a demand for improved protocols for P-arylation. The transition metal catalyzed cross-coupling reaction between aryl and vinyl bromides and diethylphosphite is the first and the most widely-used methods for the synthesis of arylphosphonates (Hirao reaction).[4,5] This classic method has been significantly modified and improved[6] in terms of type of the catalyst,[7,8] palladium source,[9] and reaction conditions[10,11] to meet the requirements of contemporary synthetic organic demands. Although the reported methods are suitable for certain syntheses, some of these procedures have one or more disadvantages such as the use of volatile and hazardous organic solvents,[12,13,14] the requirement for expensive ligands[15,16] and a microwave oven,[17,18] and severe problems related to the separation, recovery, and instability of the homogeneous catalysts. Thus, effort to elaborate greener variations of Hirao reaction for the preparation of arylphosphonates is highly desirable.

One way to have a greener process in organic synthesis is minimize the amount of waste formed by immobilization of homogeneous catalysts on an insoluble support. Heterogenization of homogeneous catalysts would simplify removal and reuse of the catalyst. Various solid supports such as metal oxides, zeolites, mesoporous and amorphous silica, carbon material and polymers have been used for heterogenization of homogeneous catalysts. Among the solid supports, magnetic nanoparticles (MNPs) serve as an attractive platform for catalyst immobilization because of their magnetic nature, which allows facile recovery and recycling of the catalyst and eliminates the requirement of catalyst filtration after completion of the reaction.[19-24] Moreover, MNPs have unique physical properties including high surface area, surface modification ability and excellent thermal and chemical stability.[25,26] In recent years, application of magnetically recoverable heterogeneous catalysts for different organic reactions such as reductions, oxidations, couplings, and multicomponent reactions has become increasingly popular and attracted considerable practical attention.[27,28] In contrast to the considerable success achieved in the field of magnetically separable nanocatalysts, the use of these kinds of catalysts for P-arylation remains unexplored.

Another approach to a green process is the replacement of volatile organic solvents by an environmentally benign reaction media such as water. Water is cheap, readily available, non-toxic, safe, non-flammable and sustainable. Apart from the economic and environmental benefits, water also exhibits unique physical and chemical activity that leads to unique selectivity compared with organic solvents. To the best of our knowledge, there are a few reports for the synthesis of arylphosphonates *via* P-arylation in water.[29-32] The reported methods mainly suffer from requiring inert atmosphere, microwave irradiation, high temperature, and tedious work-up procedures leading to copious amount of toxic wastes or using unstable dialkyl phosphites in water and therefore require an additive.

To benefit the valuable applications of MNPs and the unique properties of water as an environmentally benign reaction media, and in continue of our recent works on the development of new heterogeneous catalysts,[33-41] herein, we report palladium-DABCO (1,4-diazabicyclo[2.2.2]octane) complex supported on γ-Fe_2O_3 magnetic nanoparticles (Pd-DABCO-γ-Fe_2O_3) as a new heterogeneous catalyst for the synthesis of arylphosphonates in neat water without using any additive.

Experimental

2.1. General procedure for the synthesis of arylphosphonates catalyzed by Pd-DABCO-γ-Fe_2O_3 in neat water

Pd-DABCO-γ-Fe_2O_3 (2.5-3.6 mg, 0.07 or 0.1 mol%) was added to a stirring mixture of aryl halide (1 mmol), phosphite ester (2 mmol) and Et_3N (4 mmol) in water and heated at 100 ˚C. Progress of the reaction was monitored by TLC. After an appropriate time (Table 2), the reaction mixture was cooled to room temperature. The catalyst was separated using an external magnet, washed several times with ethyl acetate, dried and reused for a new run. The organic compound was extracted with ethyl acetate (3 × 10 mL) from aqueous layer and dried over anhydrous Na_2SO_4, filtered and concentrated in vacuum. The crude organic mixture was then purified by silica gel column chromatography using *n*-hexane/ethyl acetate (3/1) as eluent to obtain the desired product (Table 2).

Results and discussion

The designed Pd catalyst denoted as Pd-DABCO-γ-Fe_2O_3 were readily prepared *via* a 4-step procedure following our previously reported route[33] (Scheme 1): (1) synthesis of γ-Fe_2O_3 NPs by a chemical co-precipitation technique of ferric and ferrous ions in alkali solution; (2) functionalization of γ-Fe_2O_3 with 3-chloropropyl trimethoxysilane; (3) condensation of chloro-functionalized γ-Fe_2O_3 with DABCO and (4) complexation of DABCO functionalized γ-Fe_2O_3 with $Pd(OAc)_2$ in dry acetone.

Scheme 1

The catalytic activity of Pd-DABCO-γ-Fe_2O_3 was studied in the P-arylation reaction. At first, coupling reaction of iodobenzene (1 mmol) and triethylphosphite (2 mmol) in the presence of Pd-DABCO-γ-Fe_2O_3 (0.07 mol%) at 100 °C as a test model was investigated for optimizing reaction parameters such as the base, solvent and amount of the catalyst (Table 1). Among the examined bases, Et_3N showed the best results for this reaction in terms of reaction time and yield (Entries 1-4). A trace amount of the desired cross-coupling product was obtained after 24 h in the absence of a base (Entry 5). Study of the model reaction in different solvents such as, H_2O, DMF, toluene, EtOH, THF and under solvent-free conditions showed that the solvent had a crucial role in this coupling reaction. Water was found to be the best reaction medium (Entry 3). The yield of the product in a similar reaction at 80 °C was decreased to 57% (Entry 11). Coupling reactions did not take place in the absence of the catalyst even after 24 h (Entry 12). Only 43% of the product was achieved by decreasing the amount of the catalyst to 0.03% (Entry 13). When the reaction was carried out in the presence of lower amount of triethylphosphite, the yield of the desired product was decreased (Entry 14).

Table 1

On having the optimized reaction conditions (Table 1, Entry 3), the scope of the present catalytic system for the P-arylation of a range of aryl halides was extended. As shown in Table 2, the reaction of aryl iodide with various phosphite esters furnished the corresponding arylphosphonates in good to excellent yields without using any additive (Entries 1-6). The coupling of 4-iodoanisole with triethylphosphite using 0.1 mol% of Pd-DABCO-γ-Fe_2O_3 proceeded in 94% yield in 2.5 h (Entry 7). Moreover, bromobenzene and aryl bromides bearing the electron donating and electron withdrawing groups at the para position were reacted with triethylphosphite in 82-97% yields in 3-8 h (Entries 9-11 and 13). The methodology was also tolerant of sensitive functional groups such as carbonyls and styrene (Entries 14,15 and 23). Moreover, 1-chloro-4-iodobenzene and 1-bromo-4-chlorobenzene selectively furnished diethyl 4-chlorophenylphosphonate as the only product in 96 and 92% yields, respectively (Entries 8 and 12). Under the present reaction conditions, the coupling reaction of 1,4-diiodo and 1,4-dibromobenzene with triethylphosphite worked well to afford diethyl 4-iodophenylphosphonate and diethyl 4-bromophenylphosphonate in 92 and 94% yields, respectively (Entries 16 and 17). Both halogens in 1,4-diiodo and 1,4-dibromobenzene were replaced by twice amount of phosphite ester under the present reaction conditions (Entries 18 and 19). More importantly, the coupling reaction of aryl chlorides with triethylphosphite proceeded well in the presence of this catalytic system (Entries 20-22). This method was also applicable for some other aryl halides such as aryl tosylate, benzene boronic acid and vinyl bromide (Entries 24-26).

Table 2

The stability, durability, and reusability of the heterogeneous catalysts are important. Therefore, the recycling performance of Pd-DABCO-γ-Fe_2O_3 was studied in the P-arylation reaction of aryl iodide in water. Once the reaction was completed in the first run, the catalyst was recovered by an external magnet, followed by washing with ethyl acetate and dried under vacuum. The catalyst was carefully reused for a subsequent five cycles and resulted in 98, 98, 96, 92 and 83% yields of the desired product, respectively.

To determine whether the Pd catalyst is truly heterogeneous in nature in our catalytic system, a hot filtration test was performed. To do this, the solid catalyst was removed from the reaction mixture by an external magnet after the phosphonation of aryl iodide had run for 0.5 h (conversion 35%). The remaining solution was continually stirred at 100 ˚C. After 2 h, the analysis of the catalyst-free reaction showed no change in the progress of the reaction.

As a final point, in order to show the merit of the present method for the synthesis of arylphosphonates, we have compared our results with those reported in the literature for the synthesis of these important scaffolds in water (Table 3). These results indicate well the superior activity of Pd-DABCO-γ-Fe_2O_3 than those of other promoters especially for low catalyst loading and higher TON (mol of the product/mol of the catalyst) and TOF (TON/reaction time in h). Using a magnetically recyclable heterogeneous catalyst which works in pure water without requiring any additive [SDS (sodium dodecyl sulphate), TBAB (tetrabutylammonium bromide), Zn, *iso*-propanol] or activation by microwave irradiation are the other advantageous of the present method. It is worth to mention that Pd-DABCO-γ-Fe_2O_3 showed a high activity for C-P bond formation, when different phosphite esters (triphenyl/ tri-*iso*-propyl/ diethyl/ diphenyl/di-*iso*-propyl phosphite) were used in the reaction (Table 3, entry 1). Similar phosphite esters did not react with aryl halides in the presence of our previously reported catalyst (Pd-imino-Py-γ-Fe_2O_3) (Table 3, entry 2).

Table 3

Conclusion

In summary, we have successfully developed a new convenient protocol for the synthesis of aryl phosphonates by the P-arylation of aryl halides (aryliodides/ bromides/chlorides and benzene boronic acid/sulfonate) with different types of phosphite esters (triethyl/ triphenyl/ tri-*iso*-propyl/ diethyl/ diphenyl/di-*iso*-propyl phosphite) in neat water using Pd-DABCO-γ-Fe_2O_3 as a magnetically recyclable heterogeneous catalyst. Because of the utilization of (a) water as solvent without requiring any additive or activator, and (b) a small amount of a simply recyclable heterogeneous catalyst, this method is an environmentally friendly and sustainable reaction for carbon-phosphorus coupling.

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Supplementary data

Supplementary data containing the elemental analysis of the products related to this article is provided.

References

(1) Andaloussi, M.; Lindh, J.; Sävmarker, J.; JR Sjöberg, P.; Larhed, M. *Chem. A Eur. J.* **2009**, 15 (47), 13069.

(2) Demmer, C. S.; Krogsgaard-Larsen, N.; Bunch, L. *Chem. Rev.* **2011**, 111 (12), 7981.

(3) Kalek, M.; Ziadi, A.; Stawinski, J. *Org. lett.* **2008,** 10 (20), 4637.

(4) Hirao, T.; Masunaga, T.; Yamada, N.; Ohshiro, Y., Agawa, T. *Bull. Chem. Soc. Jpn.* **1982**, 55 (3), 909.

(5) Jablonkai, E.; Keglevich, G. *Org. Prep. Proced. Int.* **2014**, 46 (4), 281.

(6) Jablonkai, E.; Keglevich, G. *Current Green Chem.* **2015**, 2 (4), 379.

(7) Zhang, H. Y.; Sun, M.; Ma, Y. N.; Tian, Q. P.; Yang, S. D. *Org. Biomol. Chem.* **2012,** 10 (48), 9627.

(8) Stankevič, M.; Włodarczyk, A. *Tetrahedron* **2013,** 69 (1), 73.

(9) Matsumura, M.; Dong, Y.; Kakusawa, N.; Yasuike, S. *Chem. Pharm. Bull.* **2015,** 63 (2), 130.

(10) Goossen, L. J.; Dezfuli, M. K., *Synlett* **2005**, (3), 445.

(11) Jablonkai, E.; Keglevich, G. *Tetrahedron Lett.* **2013,** 54 (32), 4185.

(12) Kalek, M.; Jezowska, M.; Stawinski, J. *Adv. Synth. Catal.* **2009,** 351 (18), 3207.

(13) Xu, K.; Hu, H.; Yang, F.; Wu, Y. *Eur. J. Org. Chem.* **2013,** 2013 (2), 319.

(14) Kohler, M.C.; Sokol, J. G.; Stockland Jr. R.A. *Tetrahedron Lett.* **2009**, 50 (4), 457.

(15) Bloomfield, A. J.; Herzon, S. B. *Org. lett.* **2012,** 14 (17), 4370.

(16) Deal, E. L.; Petit, C.; Montchamp, J. L. *Org. lett.* **2011,** 13 (12), 3270.

(17) Brahmachari, G. *ChemTexts* **2015,** 1 (15), 1.

(18) Keglevich, G.; Jablonkai E.; Balázs, L. B. *RSC Adv*. **2014**, 4 (43), 22808.

(19) Sobhani, S.; Mesbah Falatooni, Z.; Honarmand, M. *RSC Adv.* **2014,** 4 (30), 15797.

(20) Sobhani, S.; Honarmand, M. *Appl. Catal. A: Gen.* **2013,** 467, 456.

(21) Sobhani, S.; Pakdin-Parizi, Z.; Nasseri, R. *J. Chem. Sci*. **2013,** 125 (5), 975.

(22) Sobhani, S.; Pakdin-Parizi, Z. *RSC Adv.* **2014,** 4 (25), 13071.

(23) Sobhani, S., Ghasemzadeh, M. S.; Honarmand, M. *Catal. Lett.* **2014,** 144 (9), 1515.

(24) Sobhani, S.; Vahidi, Z.; Zeraatkar, Z.; Khodadadi, S. *RSC Adv.* **2015,** 5 (46), 36552.

(25) Liu, Y. H., Deng, J.; Gao, J. W.; Zhang, Z. H. *Adv. Synth. Catal.* **2012,** 354 (2-3), 441.

(26) Dyal, A.; Loos, K.; Noto, M.; Chang, S. W.; Spagnoli, C.; Shafi, K. V.; Ulman, A.; Cowman, M.; Gross, R. A. *J. Am. Chem. Soc.* **2003,** 125 (7), 1684.

(27) Polshettiwar, V.; Luque, R.; Fihri, A.; Zhu, H.; Bouhrara, M.; Basset, J.-M. *Chem. Rev.* **2011,** 111 (5), 3036.

(28) Lima, C. G.; Silva, S.; Goncalves, R. H.; Leite, E. R.; Schwab, R. S.; Corrêa, A. G.; Paixão, M. W. *ChemCatChem* **2014,** 6 (12), 3455.

(29) Zhang, X.; Liu, H.; Hu, X.; Tang, G.; Zhu, J.; Zhao, Y. *Org. lett.* **2011,** 13 (13), 3478.

(30) Rummelt, S. M.; Ranocchiari, M.; van Bokhoven, J. A. *Org. lett.* **2012,** 14 (8), 2188.

(31) Xu, K.; Yang, F.; Zhang, G.; Wu, Y. *Green Chem.* **2013,** 15 (4), 1055.

(32) Iranpoor, N.; Firouzabadi, H.; Rajabi Moghadam, K.; Motavalli, S. *RSC Adv*. **2014,** 4 (99), 55732.

(33) Sobhani, S.; Pakdin-Parizi, Z. *Appl. Catal. A: Gen*. **2014,** 479, 112.

(34) Sobhani, S.; Ramezani, Z. *RCS Adv.* **2016,** 6 (35), 29237.

(35) Sobhani, S.; Zeraatkar, Z. *Appl. Organometal. Chem.* **2016,** 30 (1), 12.

(36) Sobhani, S.; Pakdin Parizi, Z.; Razavi, N. *Appl. Catal. A: Gen.* **2011,** 409-410, 162.

(37) Sobhani, S.; Bazrafshan, M.; Arabshahi Delluei, A.; Pakdin Parizi, Z. *Appl. Catal. A: Gen.* **2013,** 454, 145.

(38) Sobhani, S.; Jahanshahi, R. *New J. Chem.* **2013,** 37 (4), 1009.

(39) Sobhani, S.; Zarifi, F. *Chin. J. Catal.* **2015,** 36 (4), 555.

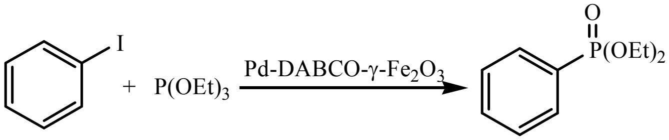
(40) Sobhani, S.; Zarifi, F. *RSC Adv.* **2015,** 5 (117), 96532.

(41) Sobhani, S.; Mesbah Falatooni, Z.; Asadi, S.; Honarmand, M. *Catal. Lett.* **2016,** 146 (1), 255.

(42) Ballester, J.; Gatignol, J.; Schmidt, G.; Alayrac, C.; Gaumont, A. C.; Taillefer, M. Chem. Cat. Chem. **2014**, 6 (6), 1549.

(43) Hartmann, M.; Hipler, U.C.; Hulbig, K. Zeitschrift fuer Chemie. **1976**, 16 (8), 487.

Table 1 P-arylation of aryl iodide with triethylphosphite catalyzed by Pd-DABCO-γ-Fe_2O_3 under different reaction conditions



Entry	Catalyst (mol%)	Base	Solvent	Time (h)	Isolated Yield[a] (%)
1	0.07	K_2CO_3	H_2O	2	84
2	0.07	KOH	H_2O	4	93
3	0.07	Et_3N	H_2O	1	98
4	0.07	(*iso*-Pr)$_3$N	H_2O	5	92
5[b]	0.07	-	H_2O	24	Trace
6	0.07	Et_3N	DMF	6	64
7	0.07	Et_3N	toluene	3	53
8	0.07	Et_3N	EtOH	3	52
9	0.07	Et_3N	THF	3	29
10	0.07	Et_3N	-	4	63
11[c]	0.07	Et_3N	H_2O	4	57
12[d]	-	Et_3N	H_2O	24	-
13	0.03	Et_3N	H_2O	2	43
14[e]	0.07	Et_3N	H_2O	2	86

[a] Reaction conditions: iodobenzene (1 mmol), triethylphosphite (2 mmol, except for entry 14), base (4 mmol, except for entry 5), Pd-DABCO-γ-Fe_2O_3 (except for entry 12), 100 ˚C (except for entry 11).

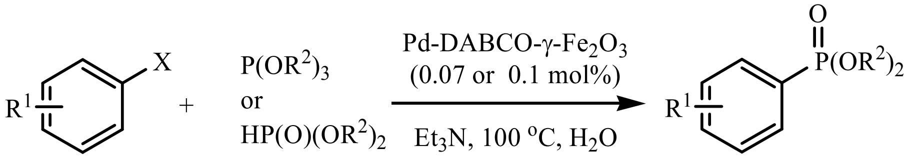
[b] No base.

[c] Temperature = 80 ˚C.

[d] No catalyst.

[e] Triethylphosphite (1.5 mmol).

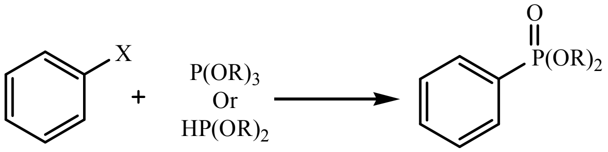
Table 2 P-arylation of various aryl halides with different phosphite esters catalyzed by Pd-DABCO-γ-Fe_2O_3



Entry	Aryl halide	Phosphite ester	Time (h)	Isolated Yield (%)	Ref.
1	C_6H_5I	$P(OEt)_3$	1	98	32
2	C_6H_5I	$HP(O)(OEt)_2$	4	82	32
3	C_6H_5I	$P(OPh)_3$	5	83	42
4	C_6H_5I	$HP(O)(OPh)_2$	6	76	42
5	C_6H_5I	P(O-*iso*-Pr)$_3$	4	96	32
6	C_6H_5I	HP(O)(O-*iso*-Pr)$_2$	2	77	32
7[b]	4-$MeOC_6H_4I$	$P(OEt)_3$	2.5	94	32
8	4-ClC_6H_4I	$P(OEt)_3$	2	96	32
9[b]	C_6H_5Br	$P(OEt)_3$	3	97	32
10[b]	4-$MeOC_6H_4Br$	$P(OEt)_3$	8	91	32
11	4-MeC_6H_4Br	$P(OEt)_3$	6	83	32
12	4-ClC_6H_4Br	$P(OEt)_3$	5	92	32
13	4-$NO_2C_6H_4Br$	$P(OEt)_3$	4	82	32
14	4-$CH_3COC_6H_4Br$	$P(OEt)_3$	7	52	42
15	4-$CH_2=CHC_6H_4Br$	$P(OEt)_3$	3	67	43
16	4-IC_6H_4I	$P(OEt)_3$	4	92	42
17[b]	4-BrC_6H_4Br	$P(OEt)_3$	3	94	32
18[c]	4-IC_6H_4I	$P(OEt)_3$	13	74	4
19[c]	4-BrC_6H_4Br	$P(OEt)_3$	15	74	4
20	C_6H_5Cl	$P(OEt)_3$	5	96	32
21	4-MeC_6H_4Cl	$P(OEt)_3$	6	94	32
22	4-$O_2NC_6H_4Cl$	$P(OEt)_3$	5	81	32
23	4-$H_3CCOC_6H_4Cl$	$P(OEt)_3$	8	51	42
24[b]	C_6H_5OTs	$P(OEt)_3$	8	72	32
25[b]	$C_6H_5B(OH)_2$	$P(OEt)_3$	6	51	32
26	$C_6H_5CH=CHBr$	$P(OEt)_3$	7	73	32

[a] Reaction conditions: aryl halide (1 mmol), phosphite ester (2 mmol, except for entries 18 and 19), Et_3N (4 mmol, except for entries 18 and 19), Pd-DABCO-γ-Fe_2O_3 (0.07 mol%, except for entries 7,9,10, 17, 24 and 25), 100 °C.
[b] 0.1 mol% Pd-DABCO-γ-Fe_2O_3.
[c] Triethylphosphite (4 mmol), Et_3N (8 mmol).

Table 3 Comparison of the present method with those reported in water as reaction media.



Entry	Phosphite ester	X	Catalyst (mol%)	Conditions	Time (h)	Yield (%)	TON	TOF (h^{-1})	Ref.
1	$P(OEt)_3$, $HP(O)(OEt)_2$, $P(OPh)_3$, $HP(O)(Ph)_2$, P(O-*iso*-Pr)$_3$, HP(O)(O-*iso*-Pr)$_2$	I, Br, Cl OTs, $B(OH)_2$	Pd-DABCO-γ-Fe_2O_3 [0.07 or 0.1]	H_2O, Et_3N, 100 °C	1-15	51-98	510-1400	85-1400	this work
2	$P(OEt)_3$	I, Br, Cl OTs, $B(OH)_2$	Pd-imino-Py-γ-Fe_2O_3 [0.1]	H_2O, Et_3N, 100 °C	1-15	57-98	570-980	38-980	34
3	$HP(O)Ph_2$	I, Br, Cl	Pd/C [1]	H_2O, K_2CO_3, Microwave, 180 °C	1	18-87	18-87	18-87	30
4	HP(O)(O-*iso*-Pr)$_2$, $HP(O)(Ph)_2$ HP(O)(O-*iso*-Pr)$_2$	I, Br, Cl	Palladacycle (II)[a] [1] Palladacycle (I)/X-Phos[b] [1]	H_2O, TBAB, KF, reflux, *iso*-PrOH, N_2	16	53-99 35-99 65-99	53-99 35-99 65-99	3.3-6.1 2.1-6.1 4.0-6.1	31
5	$HP(O)(Ph)_2$,	I, Br	$NiCl_2.6H_2O$ [10 and 20]	H_2O, Zn, 2,2'-bipyridine, 70 °C	15 and 24	75-97	3.7-9.7	0.1-0.6	29
6	$P(OEt)_3$	I, Br, Cl, OTs, $B(OH)_2$	Pd-2-ATP-γ-Fe_2O_3 [0.1]	H_2O, SDS, 100 °C	1.5-15	48-97	480-970	32-646.6	35

7	$P(OEt)_3$ $P(O\text{-}iso\text{-}Pr)_3$	I, Br, Cl	$PdCl_2$ [4.4]	H_2O, TBAB, *n*-Pr_3N, 100 °C	1.5-6	65-99	14.7-22.5	1.7-15	32

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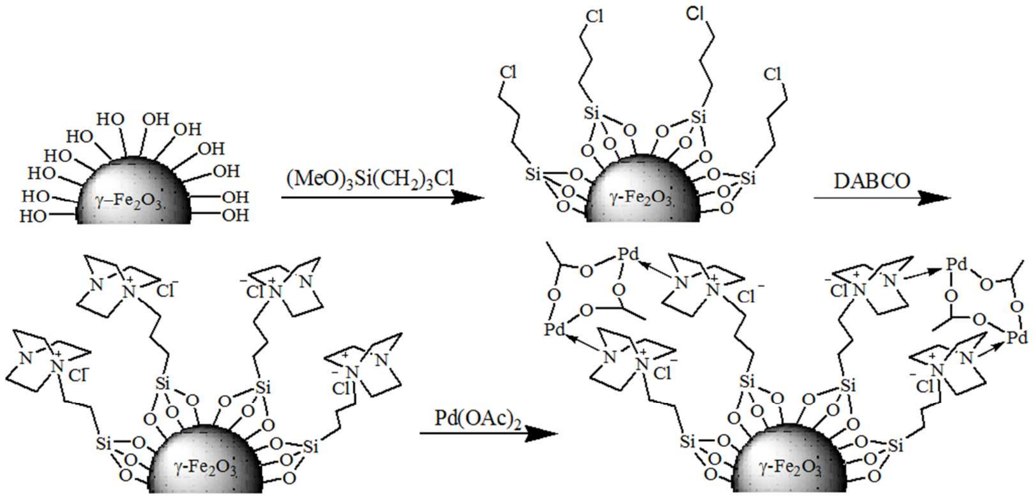
[a]Cyclopalladated ferrocenylimine.

[b]2-(Dicyclohexylphosphanyl)-2,4,6-tri-*iso*-propyl-1,1-biphenyl.

[c]TON = mol of the product/mol of the catalyst.

[d]TOF = TON/reaction time in h.



Scheme 1 Synthesis of Pd-DABCO-γ-Fe_2O_3