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Preparation of a Nafion–Teflon bimembrane-supported palladium catalyst and its use in the Heck reaction

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Abstract—A novel palladium catalyst supported on the Nafion membrane, reinforced with poly(tetrafluoroethylene) fiber, has been prepared. The catalyst exhibits high activity and stability in the Heck arylation reactions of aryl iodides with olefins and Sonogashira couplings with phenylacetylene, and can be readily recovered and reused twenty times without significant loss of activity.

Palladium catalyzed coupling of aryl and vinyl halides with olefins, known as Heck reactions has become a reliable way for Csp^2–Csp^2 bond formation.[1] During the past two decades, the Heck coupling reaction has witnessed great success in the areas of natural products, high-performance materials, and biologically active compounds.[2,3] Typical conditions include the use of various palladium species and phosphine ligands. However, many employed phosphines are air- and moisture-sensitive and can be converted to phosphine oxide species, which poison the catalysts leading to loss of the catalytic ability. Hence, the high cost of the catalyst and the metal contamination of the product remain to be surmounted. The search for recyclable catalysts with low leaching level of metals has been constantly recognized as one of the prime concerns from both academic and industrial perspectives.[4,5]

Various supported catalysts are useful approaches toward this goal. The linchpin of the strategies relies on the immobilization of the ligand onto a functionalized polymer backbone through covalent binding. In comparison to homogenous solution conditions, polymer-bound catalysis can facilitate the catalyst separation from the reaction mixture, simplify catalysts recovery and recycling, and eventually be prospective to meet the tendency of green chemistry. Many papers have appeared describing polymer-supported Heck reactions.[6] Recent examples include an oligo(ethyleneglycol)-bound palladacycle[7] and chitosan-based palladium catalyst.[8] While there have been many advances in this area, new recyclable catalyst systems seem to be constant desiderata.[9]

Nafion-H®, developed by DuPont in the early 1960s, is a perfluorinated ion-exchange polymer containing tetrafluoroethylene and perfluorovinyl ether units terminated with a –SO_3H group. The high chemical and thermal stability, in addition to its high mechanical strength, make it ideal for use as a support.[10] Indeed, acting as an excellent support, a few cationic metal complexes have been successfully immobilized onto the Nafion motif,[11] and in several instances exhibited catalytic activities comparable to homogeneous conditions.[12] However, metal complex attached to Nafion by ion exchange can seldom be reused without loss of activities. On the other hand, the precursor of Nafion-H, named as Nafion-F that is terminated with a sulfuryl fluoride group, provides the potential to combine an NH_2-bearing ligand via a sulfamide binding. Intrigued by the relative inertness to corrosive environments, we expect such kind of polymer-supported ligands and the resulted palladium catalysts to be air stable. Herein, we wish to describe the first use of a Teflon-reinforced Nafion membrane (∼0.003 in. thick, 0.3 mmol/g, Gore product) as support for diphenylphosphine ligand, the preparation of the palladium catalyst **4**, and its use for the Heck reactions.

The preparation of (2-cyanoethyl)diphenylphosphine **1** was achieved with a slightly modified method[13] by conjugate addition of the sodium salt of diphenylphosphine

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Keywords: Palladium catalyst; Nafion film; Heck reaction; Sonogashira couplings.

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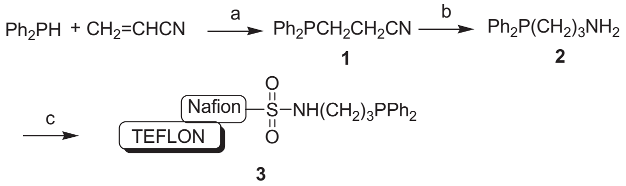
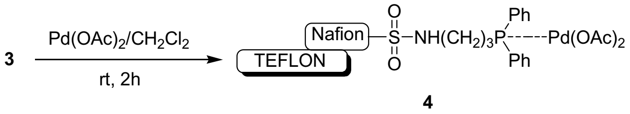


Scheme 1. Reagents and conditions: (a) 50% aq NaOH, 55 °C, 1 h; (b) $LiAlH_4$, Et_2O, reflux, 1 h; (c) Teflon–Nafion-F resin, DMF/H_2O, aq Na_2CO_3, MW (250 W), 10 min.



Scheme 2.

to acrylonitrile and subsequent reduction with $LiAlH_4$ in 81% and 70% yields, respectively.[14] The attachment of the biphenylphosphine ligand to the polymer membrane was accomplished through the sulfonamido linkage under microwave heating condition by using Na_2CO_3 as the base and DMF as the solvent to provide the Nafion-bound diphenylphosphino ligand **3** (Scheme 1).[15]

The supported palladium catalyst was generated by complexion of **3** with a palladium source. Two palladium compounds, that is, palladium acetate and di(μ-chloro)bis(η^3-allyl)dipalladium(II), were examined and both were effective for Heck reactions. Since palladium acetate is much cheaper, it has been applied throughout the present research. The supported catalyst **4** was obtained as a yellowish solid (Scheme 2) by stirring a mixture of the bound ligand **3** and $Pd(OAc)_2$ in dichloromethane.[16] The palladium content was determined to be 0.665 wt % by Graphite Furnace Atomic Absorption (GFAA) analysis.

It was found that catalyst **4** was effective for the coupling of aryl iodides with alkenes (Heck reactions) and also with alkynes (Sonogashira couplings) at 100 °C using Et_3N as the base and acetonitrile as the medium. An attractive feature was the low catalyst loading (0.5 mol %) required. In the absence of a base, the reaction did not proceed, indicating that it was indispensable to the procedure. After screening a range of usual inorganic and organic bases, triethylamine was the most appropriate. By exploring the scope of the solvent, it was found that the Teflon–Nafion bimembrane swelled well in acetonitrile and satisfactory results were obtained.

Catalyst **4** was tested for its efficacy in the coupling reactions of aryl iodides with alkenes or alkynes.[17] The results are summarized in Table 1. It is shown that all of the aryl iodides employed could be coupled with alkenes or alkynes to give the products in good yields. If the formation of *E*/*Z* isomers was possible, the exclusive

Table 1. Heck reactions and Sonogashira couplings catalyzed by **4**[a]

$$\mathrm{Ar{-}I} + \begin{matrix}\mathrm{CH_2{=}CH{-}X} \\ \text{or } \mathrm{CH{\equiv}C{-}Ph}\end{matrix} \longrightarrow \begin{matrix}\mathrm{Ar{-}CH{=}CH{-}X} \\ \text{or } \mathrm{Ar{-}C{\equiv}C{-}Ph}\end{matrix}$$

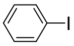
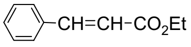
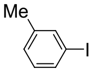
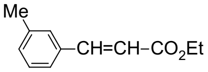
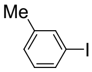
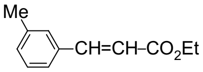
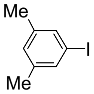
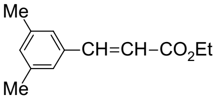
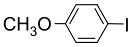
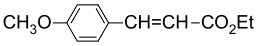
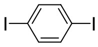
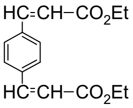
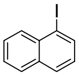
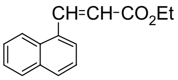
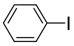
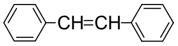
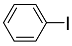
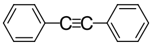
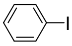
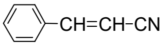
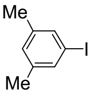
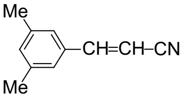
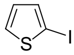
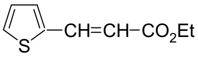
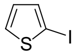
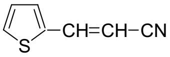
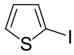
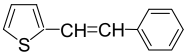
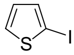
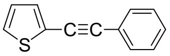
Entry	Aryl iodide	Alkene or alkyne	Time (h)	Product	Yield (%)[b]
1		$CH_2{=}CH{-}CO_2Et$	16		96
2		$CH_2{=}CH{-}CO_2Et$	24		84
3		$CH_2{=}CH{-}CO_2Et$	24		86[c]
4		$CH_2{=}CH{-}CO_2Et$	20		97[d]
5		$CH_2{=}CH{-}CO_2Et$	24		87
6		$CH_2{=}CH{-}CO_2Et$	48		96[e]
7		$CH_2{=}CH{-}CO_2Et$	16		98[f]
8		$C_6H_5CH{=}CH_2$	18		82

Table 1 (*continued*)

Entry	Aryl iodide	Alkene or alkyne	Time (h)	Product	Yield (%)[b]
9		$C_6H_5C{\equiv}CH$	18		89
10		$CH_2{=}CH\text{–}CN$	24		90
11		$CH_2{=}CH\text{–}CN$	30		85
12		$CH_2{=}CH\text{–}CO_2Et$	15		92
13		$CH_2{=}CH\text{–}CN$	15		93[g]
14		$C_6H_5CH{=}CH_2$	20		80
15		$C_6H_5C{\equiv}CH$	15		90

[a] Reagents and conditions: alkene or alkyne (1.5 equiv), Et_3N (2.0 equiv), 0.8 mol % **4**, CH_3CN, 100 °C.

[b] Isolated yields.

[c] $[PdCl(\eta^3\text{-}C_3H_5)]_2$ was used instead of $Pd(OAc)_2$.

[d] When the catalyst was reused for second, third, fourth and fifth cycle, yields of 90%, 86% 85% and 80% were obtained, respectively.

[e] 3.0 equiv of alkene were employed.

[f] E:Z = 30:1.

[g] E:Z = 2:1.

or predominant product was the trans isomer by inspection of their olefinic H–H coupling constants. The scope of the reaction was investigated using a variety of unsaturated substrates, including ethyl acrylate (entries 1–7 and 12), acrylonitrile (entries 10, 11, and 13), styrene (entries 8 and 14), and phenylacetylene (entries 9 and 15). In all of these reactions, the supported catalyst **4** provided very high catalytic activities. However, our efforts on employing aryl bromides as the substrates produced less success, reflecting the substrate scope of the present protocol. The utility of supported $[PdCl(\eta^3\text{-}C_3H_5)]_2$ was also verified by the coupling of 3-iodotoluene with ethyl acrylate (entry 3). Notably, the reactions with 2-iodothiophene were also successfully achieved (entries 12–15). This could provide a useful way for introduction of an unsaturated group on the thiophene ring.

Experimentally, catalyst **4** was readily recovered from the reaction mixture by filtration, and the product was isolated following the usual aqueous workup. Since the potentiality to recycle the catalyst containing expensive metals is of considerable significance in rendering the method green, the recovered catalyst **4** was reused with the coupling between 5-iodoxylene and ethyl acrylate as a model reaction (entry 4). Recycling of the catalyst involved a simple filtration and washing. As shown by entry 4 in Table 1, the catalyst provided sufficient activity until the fifth consecutive reaction. Less than 0.1% Pd leaching into the products was observed. Addition of traces of palladium source (here: $Pd(OAc)_2$) could retrieve the catalytic activities. Another merit of the method lay in the fact that the ligand proved to be insensitive to moisture and air, and amenable to survive under the reaction conditions for up to 20 times.

In summary, we have designed a kind of diphenylphosphino ligand attached to the surface of a Teflon–Nafion bimembrane and demonstrated its utility in the Heck reactions and Sonogashira reactions. Under the optimum conditions, the respective arylated products have been produced in high to excellent yields. To the best of our awareness, it represents an unprecedented example of Nafion-supported catalyst, via covalent bond, for palladium-catalyzed cross-coupling reaction. Of particular note are the exceptional stability of the ligand and the recyclability of the catalyst. The catalyst has also been successfully applied in other coupling reactions like Suzuki cross-couplings. These will be reported separately in due course.

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14. Freshly distilled acrylonitrile (1.80 g, 33.9 mmol) was added slowly to a stirred mixture of diphenylphosphine (3.80 g, 20.4 mmol), 50% aq NaOH (0.1 mL) and acetonitrile (5 mL). The mixture was stirred for 1 h at 55 °C. The yellow solution was extracted with benzene (3×10 mL) and the organic layer was separated and dried over Na_2SO_4. Removal of the solvent left yellow oil which was extracted into ether (50 mL) under reflux. Vacuum evaporation afforded 3.91 g of (2-cyanoethyl)diphenylphosphine (yield: 81%). IR (neat): 3057, 2250, 1591, 1481, 1438, 1184, 1118 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): 1.61 (m, 2H, PCH_2), 2.63 (m, 2H, CH_2CN), 7.51–7.75 (m, 10H, $2C_6H_5$) ppm.

    Reduction: To a suspension of $LiAlH_4$ (1.0 g, 26.4 mmol) in dry ether (50 mL) was added dropwise a solution of 2-(cyanoethyl)diphenylphosphine in dry ether (50 mL) at 0 °C with stirring under N_2. The mixture was heated to reflux for 24 h. After cooling to 0 °C, 4 mL of degassed water was added carefully to quench the reaction. The precipitate was filtered and the organic layer was separated and dried over Na_2SO_4. Evaporation of the solvent in vacuo yielded the ligand **2** (2.80 g, 70%) as a colorless viscous liquid. IR (film): 3069, 3051, 2929, 2855, 1585, 1481, 1435, 1026 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): 1.23 (br, 2H, NH_2), 1.55 (m, 2H, PCH_2), 2.05 (m, 2H, CH_2), 2.75 (t, 7.0 Hz, 2H, NCH_2), 7.25–7.45 (m, 10H, $2C_6H_5$) ppm. ^{31}P NMR (500 MHz, $CDCl_3$): −15.4 ppm.
15. Procedure for attachment of **2** onto the bimembrane: 3-(diphenylphosphino)propylamine **2** (0.24 g, 1 mmol) was dissolved in DMF (10 mL), then the Teflon-Nafion-F membrane (0.5 g, 0.3 mmol/g, 0.15 mmol) and 15 mL of water were sequentially added. The mixture was adjusted to about pH 11 by slow addition of aq Na_2CO_3. The vial was heated under selected microwave conditions (~250 W output) for two times, each for 10 min. After irradiation, the polymer was taken out by filtration, washed successively with degassed water, acetone and ether, and dried in vacuo at 50 °C to give the supported ligand **3**, which was characterized by IR analysis. The loading value was determined to be 0.314 mmol/g by nitrogen elemental analysis.
16. Preparation of the supported catalyst **4**: a vial was charged with the Nafion-bound diphenylphosphino ligand **3** and 20 mL of dichloromethane. $Pd(OAc)_2$ (5 mg, 0.022 mmol) was added in one portion to the resulted suspension at ambient temperature, and the mixture was stirred at room temperature for an additional 2 h. The polymer was taken out from the mixture by filtration, washed successively with dichloromethane, ethanol and acetone to ensure exclusive removal of the unbound metal. Drying at 50 °C in vacuum afforded the supported catalyst **4** as a yellowish solid. The palladium content was determined to be 0.665 wt % by Graphite Furnace Atomic Absorption (GFAA) analysis.
17. General procedure for Heck arylation reactions: The reaction was carried out at 100 °C for 15–48 h under N_2 in CH_3CN by using 1.0 equiv of aryl halide, 1.5 equiv of alkene, 2.0 equiv of Et_3N and the indicated amount of catalyst **4** (0.665 wt % of palladium). After cooling to room temperature, the polymer was filtrated and washed successively with CH_3CN for reuse. The mixture was then diluted with water and extracted with ether. The combined organic layers were washed with brine, dried with Na_2SO_4, filtered, and then evaporated to dryness. The crude product was purified by flash column chromatography to afforded the pure product. The Nafion-bound catalyst can be recycled several times. Addition of catalytic amount of palladium sources refresh the catalytic activities and the ligand itself proves to be extremely stable even after using for 20 cycles.

    The selected spectroscopic data for the coupled products are as follows:

    Ethyl *trans*-cinnamate (entry 1). IR (film) 2931, 1737, 1495, 1451, 1361, 1230, 1029, 954 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): 1.34 (t, 7.1 Hz, 3H, CH_3), 4.27 (q, 7.1 Hz, 2H, CH_2), 6.44 (d, 16.0 Hz, 1H, =CH), 7.26–7.53 (m, 5H, C_6H_5), 7.69 (d, 16.0 Hz, 1H, =CH) ppm. ^{13}C NMR (100 MHz, $CDCl_3$): 20.80, 64.90, 123.19, 126.52, 127.98, 128,51, 134.11, 136.27, 170.71 ppm.

    trans-Stilbene (entry 8). IR (KBr): 3020, 1497, 1450, 966, 764 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): 7.10 (d, 16.5 Hz, 2H, 2 =CH), 7.25–7.59 (m, 10H, $2C_6H_5$). ^{13}C NMR (100 MHz, $CDCl_3$): 126.43, 127.31, 128.60, 129.01, 138.01 ppm.

    Ethyl *trans*-3-(2-thienyl)acrylate (entry 12). IR (film): 2985, 1742, 1611, 1427, 1237, 841 cm^{-1}. ^1H NMR (500 MHz, $CDCl_3$): 1.32 (t, 7.1 Hz, 3H, CH_3), 4.24 (q, 7.1 Hz, 2H, CH_2), 6.23 (d, 15.7 Hz, 1H, =CH), 6.78–7.36 (m, 3H), 7.77 (d, 15.7 Hz, 1H, =CH). ^{13}C NMR (100 MHz, $CDCl_3$): 21.19, 61.38, 121.70, 125.34, 126.10, 127.01, 130.57, 139.55, 171.26 ppm.