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Polystyrene Supported [N-(Alanine) Sulfonamide]/Palladium Chloride: Synthesis, Characterization, for Heck Coupling Reactions

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para-styrene sulfonyl chloride and (S)-(+)-alanine in the presence of KOH 1 M as a base, and $CHCl_3$ was used as solvent. The formation/presence of monomer was verified using FT-IR and ^{1}H NMR spectroscopy. Polystyrene [N-(alanine) sulfonamide] (PASS) was also prepared from the polymerization of [N-(alanine)] para-styrene sulfonamide (ASS) in the presence of AIBN (azoisobutyronitrile) under atmosphere of nitrogen. Polystyrene [N-(alanine) sulfonamide]/palladium chloride as a polymer-supported palladium complex was also prepared from the reaction of $PdCl_2(CH_3CN)_2$ with PASS in the presence of KOH 1 M. A green solid was consequently appeared. This catalyst was synthesized for the first time as a polymer-supported palladium and applied in Heck reactions.

Keywords: [N-(Alanine)] *para*-styrene sulfonamide, Polystyrene [N-(alanine) sulfonamide], Poly styrene [N-(alanine) sulfonamide]/ palladium chloride, Polymer-supported palladium, Heck reaction

INTRODUCTION

Transition metals have several coordination states. This property is suitable for the synthesis of catalysts to activate bonds through oxidative addition, to create bonds by intermolecular coupling, and to give products by reductive elimination. These metals play an important role as a catalyst in the organic synthesis. In heterogeneous catalysis [1], the catalyst is an inorganic solid which interacts with the reagents by a variety of sites on its surface, while in homogeneous catalysis[2], in most cases, the catalyst is a single metal molecule which are dissolved in the solvent of the reaction. Developments of coordination chemistry of transition metal complexes have gained significant importance because of their fascinating structures and enormous potential applications in pharmacy, biochemistry, industry, *etc*. [3]. During the last few decades, the coupling reactions have been widely used in synthetic organic chemistry [4-8]. The Heck and Suzuki coupling reactions are the methods utilized in constructing carbon-carbon bonds, particularly in the field of agrochemicals, pharmaceutical and materials science [9-11]. Among existing catalysts for the Mizoroki-Heck and Suzuki-Miyaura reactions, palladium complexes have played an important role because of their versatility and nontoxicity [12,13]. The most common ligands containing phosphine are air and moisture sensitive. In these ligands, sometimes P-C bond degradation at elevated temperatures occurs that leads to the decomposition of the catalyst [14]. In addition, many phosphine ligands are toxic and unrecoverable. In recent years, phosphine-free ligands including thioureas [15] bispyridines [16] and amino acids have been reported [17]. Developed knowledge about the π-acceptor ability of different groups of nitrogen and oxygen in amino acid could be of interest for the synthesis of new complexes and their applications in heterogeneous catalysis. Ligands containing nitrogen have been employed as a new class to demonstrate catalytic activity in Suzuki and Heck reactions [18-21]. Sulfonamides are important compounds which have been used in medicine. They possess interesting biological activities such as antimicrobial activity [22-24]. In this line, significant efforts have been also made to develop versatile polymers and palladium catalysts for coupling reactions [25,

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new series of sulfonamide derivatives for pharmaceutical chemistry and catalytic application. We have selected alanine as an amino acid and polystyrene structural parts to prepare a new sulfonamide structure due to the major importance of these group in coordination to metals and synthesis of novel complex-based sulfonamide drugs. Polystyrene sulfonamide derivative as a polymers-supported palladium is a useful catalyst for Heck reactions. Our previous report was related to palladium complex, its crystal structure and mixed ligands [27-29].

EXPERIMENTAL

Physical Measurements and Materials

Para-styrene sulfonic acid sodium salt, PCl_5, sodium hydroxide, AIBN (azoisobutyronitrile) and (S)-(+)-alanine were purchased from Sigma-Aldrich (USA) and were used without further purification. Fourier transform infrared (FT-IR) spectra of the prepared compounds were recorded at 400-4000 cm^{-1} region using KBr pellets on Shimadzu FT-IR 8400 spectrometer (Japan). ^1H NMR spectrum was recorded on a Brucker Ultrashield 400 MHz spectrometer using D_2O as solvent (German). The Pd analysis and loading test were carried out by inductively coupled plasma ICP_OES_730_ES_varian.

Synthesis of Compounds

Preparation of *para*-styrene sulfonyl chloride. To prepare the monomer, first, *para*- styrene sulfonyl chloride was synthesized by the reaction of 5.00 g of *para*-styrene sulfonic acid sodium salt with 7.50 g of PCl_5, as chlorination agent. The product was separated from inorganic materials by chloroform and ice water. The chloroform was evaporated from the Para- styrene sulfonyl chloride. Experimental details are described in Ref. [30].

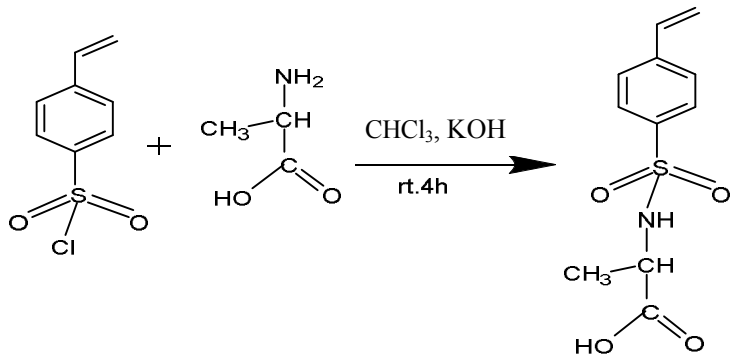
Preparation of N-(alanine)-*para*-styrene sulfonamide (ASS). The synthetic method for the preparation of ASS with chemical formula ($C_{11}H_{13}NO_4S$) is as follows: In a 100 ml round-bottomed flask, equipped with a magnetic stirrer, 4.86 g para styrene sulfonyl chloride (24 mmol) in 50 ml $CHCl_3$ as a solvent and 2.14 g (S)-(+)-alanine (24 mmol) were placed. Then, 2.4 ml KOH 1M was slowly added. The reaction mixture was stirred for 4 h at room temperature. After the reaction time, the solvent was evaporated and ASS as the product was obtained. The obtained product was washed 3 times with water and analyzed without further purification. (Yield 5.20 g, 85.0%; m.p.: 123 °C). FT-IR (KBr, cm^{-1}): 3267(s), 3096(m), 3001(m), 2941(m), 2737(m), 1712(s), 1651(m), 1595(m), 1425(s), 1344(s), 1228(s), 1157(s), 1091(m), 1053(m), 1012(m), 848(m). ^1H NMR (D_2O, ppm): 1.42(CH_3), 3.97(CH), 4.70(NH) 5.42 (CH in vinyl), 5.92(CH in vinyl), 6.77(CH in vinyl), 7.59(CH Benzene) 7.75(CH Benzene), 9.96(COOH).

Preparation of polystyrene2-alanine sulfonamide (PASS). 0.1 mol monomer, 50 ml THF as a solvent and 0.05 mol AIBN (azoisobutyronitrile) as an initiator were placed in a round-bottomed flask, equipped with a reflux condenser, atmosphere of nitrogen and a magnetic stirrer. The reaction mixture was refluxed at 80 °C for 10 h. After the reaction time, the solvent was evaporated. The polymer was washed with water and dried with $MgSO_4$. The FT-IR and ^1H NMR spectra confirmed that the polymer has been synthesized.

IR (KBr, cm^{-1}): 3269(m), 3125(m), 3080(m), 3003(m), 2993(m), 2937(m), 2885(m), 1716(s), 1660(m) 1597(m), 1456(m), 1411(s), 1361(s), 1305(s), 1232(m), 1172(s), 1112(m), 1014m, 848m. ^1H NMR (DMSO-d_6, ppm): 1.37(CH_3), 1.79(CH_2), 2.09(CH), 3.63(CH), 4.00(NH), 7.71 (CH Benzene), 7.68(CH Benzene), 9.96(COOH).

Preparation of polymer-supported palladium. The synthetic method for the preparation of the palladium(II) complex is as follows; 0.09 g $PdCl_2$ (0.5 mmol) and CH_3CN (50 ml) were placed in a 100 ml round-bottomed flask, equipped with a reflux condenser and a magnetic stirrer. The mixture was stirred and warmed to 70 °C to give a light orange solution. Then, 0.13 g ligand (0.5 mmol) and potassium hydroxide solution 0.5 M (1 ml) were added. The reaction mixture was refluxed for 12. Then, a green solid appeared. The green solution was filtered and washed with CH_3CN (3 × 10 ml). The IR and ^1H NMR spectra confirmed that the complex has been synthesized. In order to determine the Pd content of the catalyst, it was treated with 30 ml mixture of concentrated HCl and H_2SO_4 (1:1). Then, it was filtered. The filtrate, with distilled water, was diluted to 50 ml and subjected to ICP determination using calibration curve method.

IR (KBr, cm^{-1}): 3100(m), 3050(m), 2991(m), 2935(m), 2881(m), 1714(s), 1659(m), 1592(m), 1453(m), 1409(s),



Scheme 1. The reaction involving synthesis of ASS

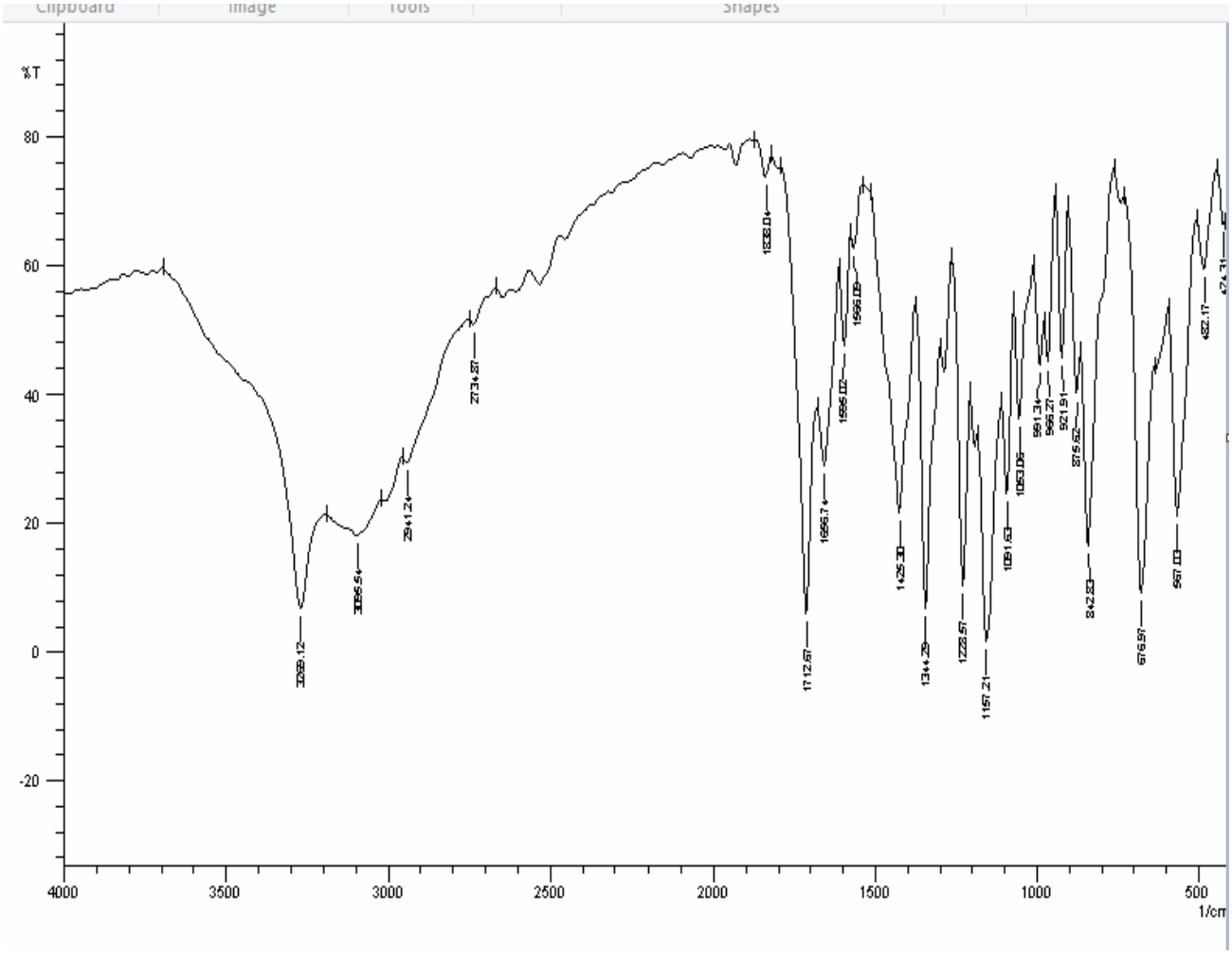


Fig. 1. The experimental FT-IR of ASS.

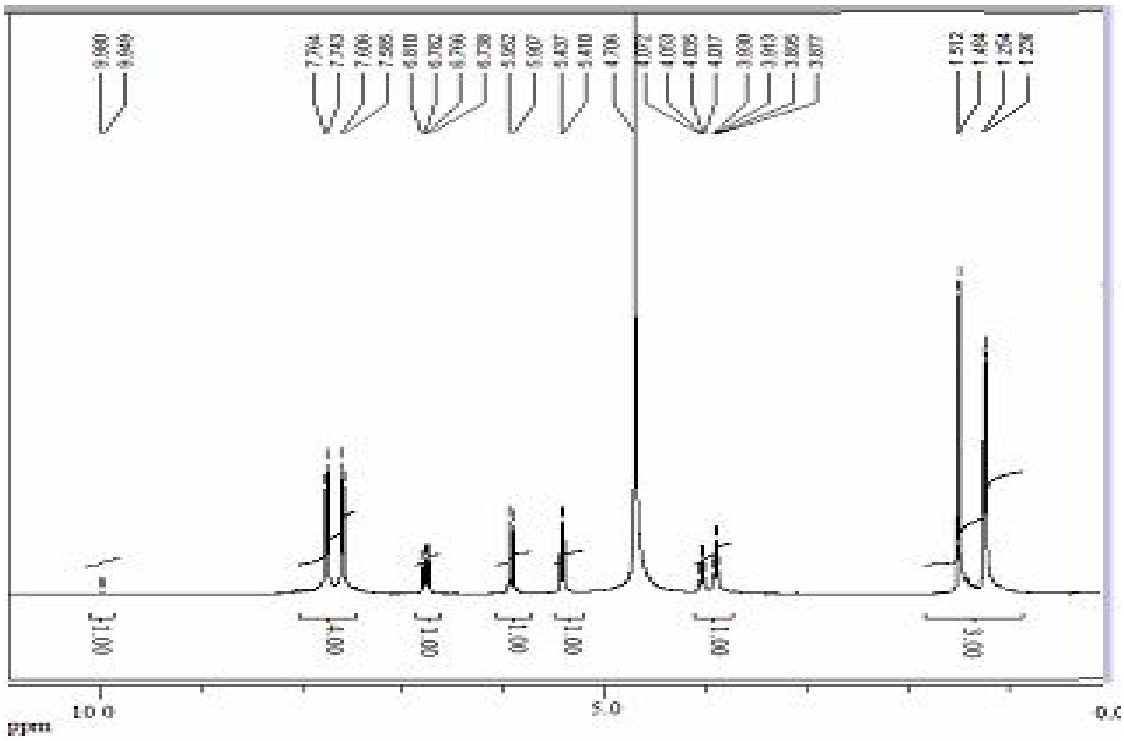
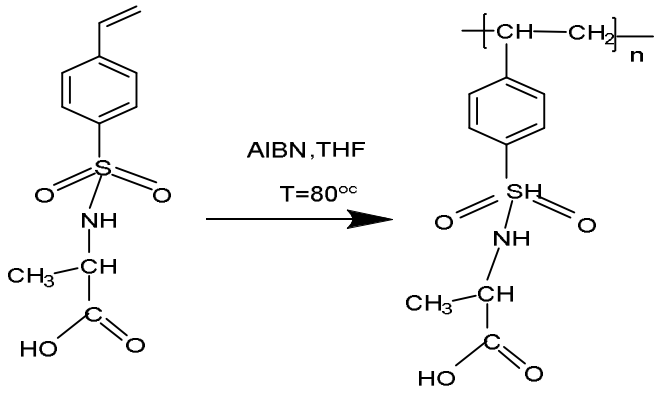


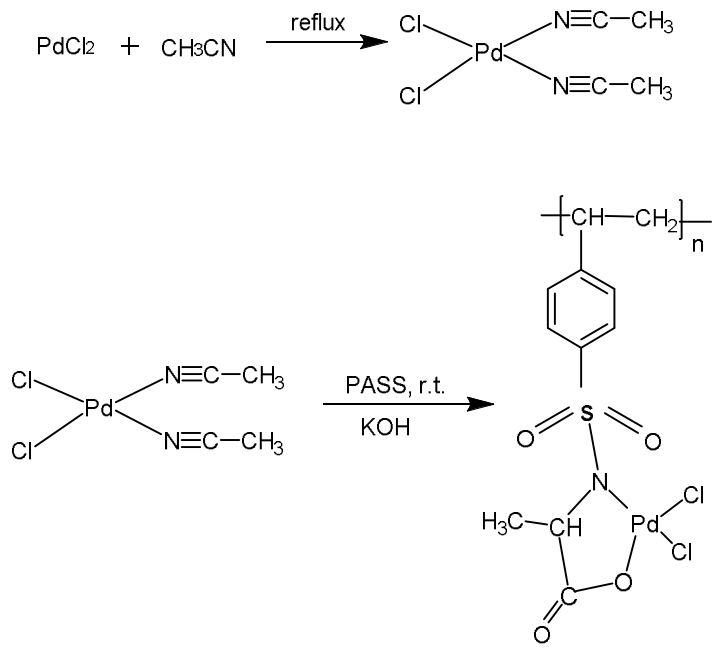
Fig. 2. The experimental ^{1}H NMR of ASS.



Scheme 2. The reaction involving synthesis of polystyrene [N-(alanine) sulfonamide]

1358(s), 1302(s), 1229(m), 1170(s), 1111(m), 1010m, 842m. ^{1}H NMR (DMSO-d_6, ppm): 1.30(CH_3), 1.73(CH_2), 2.09(CH), 3.68(CH), 7.68(CH Benzene), 7.98(CH Benzene).

General procedure for Heck reaction. A round bottom flask was charged with aryl halide (15 mmol), olefins (15 mmol) using DMF as a solvent (100 ml), Then Na_2CO_3 as base (15 mmol) and catalyst (0.5 mol%) were added. The stirring solution was refluxed at 100 °C for 12 h. After the required time, the reaction mixture was cooled to room



Scheme 3. Synthesis of polymer-supported palladium (poly-pd)

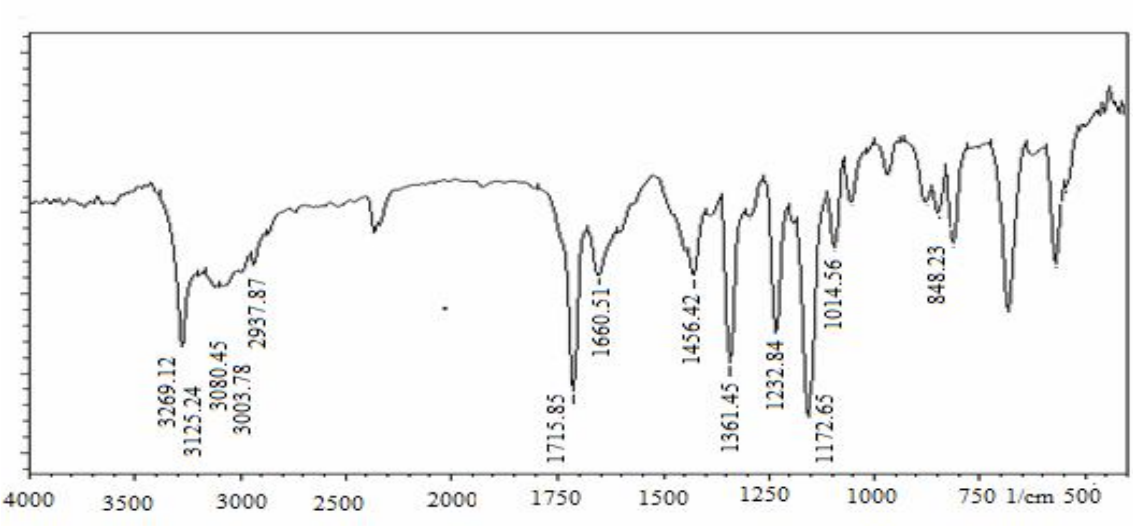


Fig. 3. FT-IR of polystyrene [N-(alanine) sulfonamide] (PASS).

temperature. The palladium catalyst was separated from the mixture by filtration. The solution was diluted with water (30 ml) and the product was extracted with ethyl acetate (3 × 10 ml). Then, the product was concentrated under reduced pressure. The organic layer recrystallizes with ethanol and water (1:1).

RESULTS AND DISCUSSION

Preparation of monomer [N-(alanine)] *para*-styrene

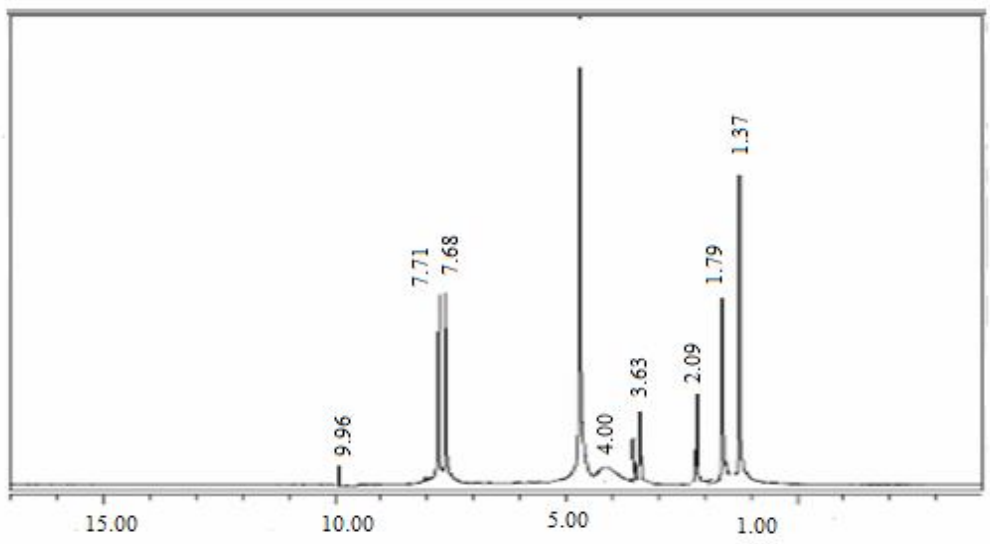


Fig. 4. [1]H NMR of polystyrene [*N*-(alanine) sulfonamide] (PASS).

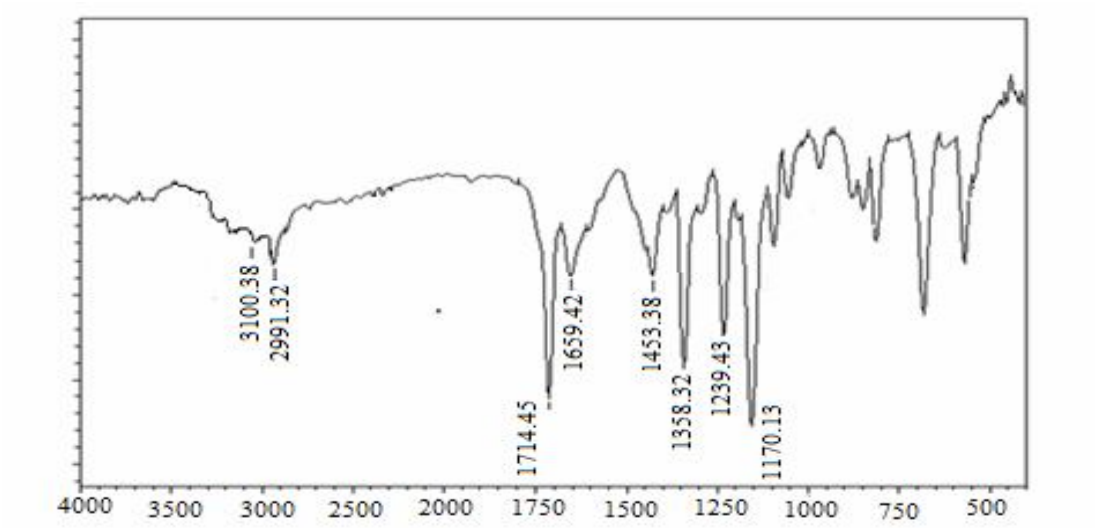


Fig. 5. FT-IR of polymer-supported palladium as a catalyst.

sulfonamide (ASS). Alanine *para*-styrene sulfonamide (ASS) was synthesized from the reaction of para-styrene sulfonyl chloride and (S)-(+)-alanine. ASS were prepared by method shown in Scheme 1. The new monomer was characterized by FT- IR, and [1]H NMR spectroscopy (data in the experimental section).

Spectroscopic characterization of ASS. The experimental FT-IR of ASS are reported in the experimental section (Fig. 1). The C-H stretching frequencies of aromatic can be observed in the range of 3100-3000 cm^{-1} is shown at 3096 cm^{-1}. The aliphatic C-H stretching frequencies are also appeared below 3000 cm^{-1} . The C= C stretching vibration in the range of 1650-1430 cm^{-1} and the C-H bending bands are appeared in the regions 1275-1000 cm^{-1} (in-plane C-H

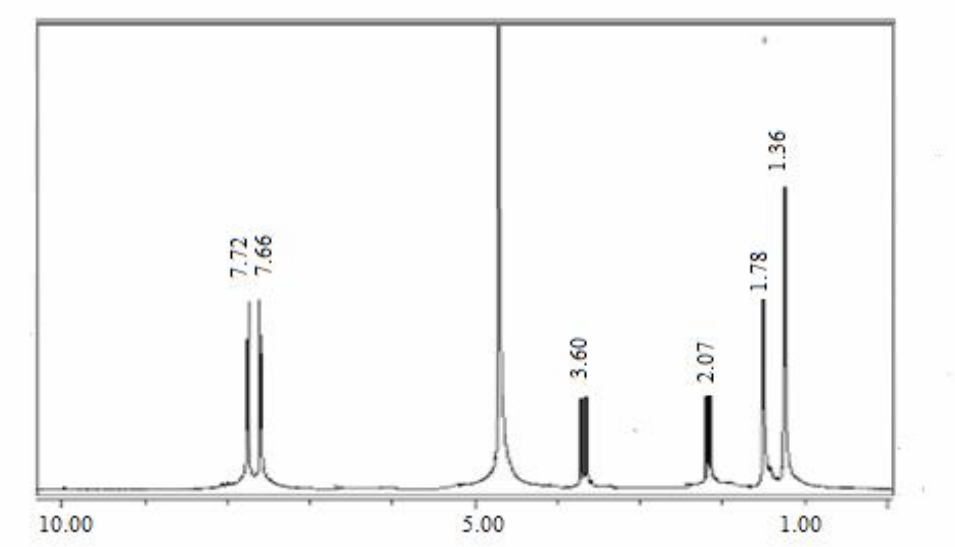
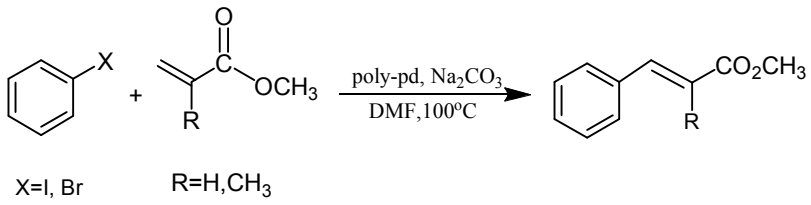


Fig. 6. ^{1}H NMR of polymer-supported palladium as a catalyst.

Table 1. Optimization of Reaction Condition for Heck Reaction Catalyzed by Polymer Supported Palladium

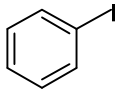
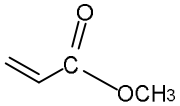
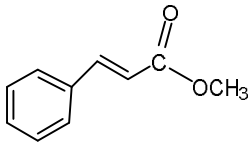
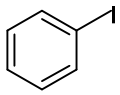
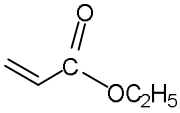
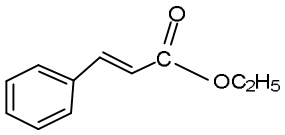
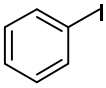
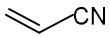
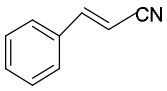
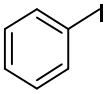
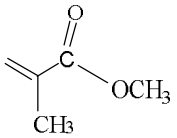
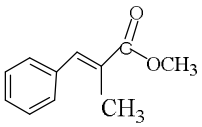
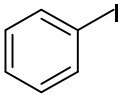
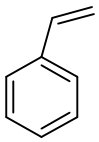
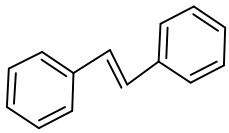
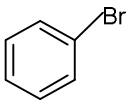
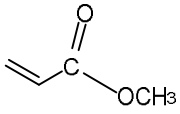
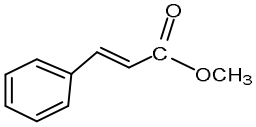
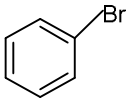
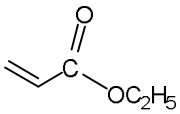
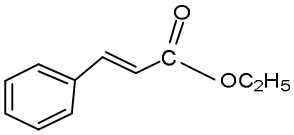
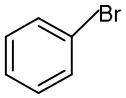
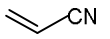
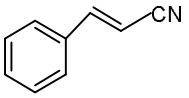
Entry[a]	Solvent	Cat (mol%)	T (°C)	Yield (%)[b]
1	DMF	0.5	80	81
2	DMF	0.5	100	99
3	DMF	0.25	100	85
4	DMF	1.00	100	99
5	DMF/H_2O	0.5	100	82

[a]Reaction conditions: iodo benzene (15 mmol), methyl acrylate (15 mmol), Na_2CO_3 (15 mmol), for 12 h. [b]Isolated yield.



Scheme 4. Condition of the Heck reaction

Table 2. Heck Coupling of Aryl Halides with Olefins Catalyzed by (Poly-pd)

Entry[a]	Aryl halide	Olefin	Product	Yield (%)[b]
1				98
2				97
3				96
4				95
5				93
6				81
7				79
8				77

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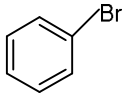
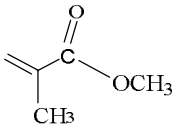
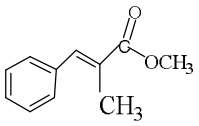
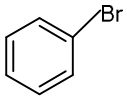
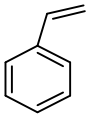
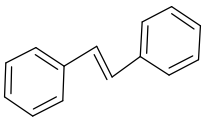
9				75
10				73

[a]Reaction conditions: aryl halide (15 mmol), olefin (15 mmol), Na_2CO_3 (15 mmol), DMF (100 ml), catalyst (0.5 mol%), for 12 h, at 100 °C under air. [b]Isolated yields.

bend). In addition, the stretching mode of NH group is appeared at 3267 cm^{-1}. In the following discussion, sulfonamides absorb strongly at 1370-1335 and 1170-1155 cm^{-1}. The symmetrical and asymmetrical stretching modes of O=S=O are observed at 1157 cm^{-1} and 1338 cm^{-1}, respectively. The C=O stretching frequency is observed at 1712 cm^{-1}.

Observed and calculated ^{1}H NMR chemical shifts. The experimental ^{1}H NMR spectrum of the compound are reported in experimental section (Fig. 2). The ^{1}H NMR spectrum of the ASS was recorded in D_2O as solvent with TMS as internal standard at 400 MHz.

Preparation of Polystyrene [N-(Alanine) Sulfonamide] and Polymer-supported Palladium

The synthetic routes of polystyrene [N-(alanine) sulfonamide] and Polystyrene [N-(alanine) sulfonamide]/ palladium chloride, reported in experimental section, are shown in Schemes 2 and 3 (data in the experimental section).

Spectroscopic Characterization of PASS and Polymer-supported Palladium (poly-pd)

The FT-IR spectra of PASS and polystyrene supported palladium (poly-pd) are listed in the experimental section. The vibrational bands present at 3269 cm^{-1} and 3003 cm^{-1} are respectively assigned to ν(N-H) and ν(COOH) for PASS (Fig. 3). These bands disappear for polymer-supported palladium, because PASS has been deprotonated (Fig. 5).

The frequency range of 3080 cm^{-1} and 2937 cm^{-1} are assigned to $\nu(C\text{-}H)_{Ar}$ of aromatic ring and $\nu(C\text{-}H)_{Ai}$ groups, respectively. The FT-IR spectra of polymer-supported palladium show a slight positive shift, indicating that palladium is attached to nitrogen and oxygen of alanine. The ^{1}H NMR spectra of PASS and polymer-supported palladium in DMSO-d_6 solution are listed in the experimental section. The ^{1}H NMR spectrum of PASS showed a broad singlet at 4.00 ppm for -NH group and 9.96 ppm for -COOH group (Fig. 4). These signals are absence in the spectrum of polymer-supported, indicating the removal of -COOH and -NH protons and formation of the Pd-O and Pd-N bonds. (Fig. 6). Determination of Pd content was performed on catalyst followed by ICP analysis. The Pd content of the catalyst was 0.10 mmol g^{-1}.

Heck Reactions

The performance of coupling reactions was investigated in a variety of parameters. In order to optimize the reaction condition, we applied different temperatures (80 °C, 100 °C), solvent (DMF and DMF/H_2O) and amounts of catalyst (0.25, 0.5, 1 mol%) in the presence of base. We found that using Na_2CO_3 as a base, DMF as a solvent, and 0.5 mol% catalyst at 100 °C provides the highest yield. The result is shown in Table 1.

After optimizing, with this new class polymer-supported palladium, we investigated to apply it for the construction of C-C bond *via* cross-coupling reactions various aryl halides and olefins were used as substrate for coupling Heck

reaction (Scheme 4). The results are given in Table 2.

CONCLUSIONS

To verify the effective functioning of polymer-supported palladium as the economical and highly efficient catalyst in organic synthesis, we applied polystyrene derivative-supported palladium as the catalyst in the Heck reaction. The Heck reaction occurred using iodo- and bromobenzene with olefins as substrates in the presence of Na_2CO_3 as base and DMF as solvent at 100 °C for 12 h (Table 2). The Heck coupling reactions represent a powerful method for the C-C bond formation. In conclusion, the new palladium(II) complex, as a polymer-supported palladium, was evaluated for the first time as catalyst for the Heck reaction under low catalyst loading (0.5 mol%) which can be easily separated. The heterogeneous catalyst was recycled without any loss in its properties.

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