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Method

The First Report on the Preparation of Peptide Nanofibers Decorated with Zirconium Oxide Nanoparticles: Applied as Versatile Catalyst for the Amination of Aryl Halides, Synthesis of Biaryl and Symmetrical Sulfides

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We have reported the preparation of peptide nanofibers decorated with zirconium oxide nanoparticles for the first time as a novel, non-toxic, inexpensive and recyclable catalyst for the amination of aryl halides, synthesis of biaryl and synthesis of symmetrical sulfides (*via* reaction of aryl halides with S_8 or 2-thiobarbituric acid as sulfur transfer reagents). The structure of the catalyst was studied by Fourier transform infrared spectroscopy (FT-IR), scanning electron microscopy (SEM), thermogravimetric analysis (TGA), atomic absorption spectroscopy (AAS), UV–visible absorption and Fluorescence Spectroscopy.

Introduction

Transition metal-catalyzed cross-coupling reaction has become a significant and well-known procedure for the formation of C-C, C-N and C-S bonds *via* combination of electrophilic and nucleophilic fragments. The formation of C-C, C-N and C-S bonds is very important and powerful tools for the preparation of a variety of biologically active, agrochemical and polymeric compounds.[1] In general, the catalysts that are chosen for cross coupling reactions are almost palladium, nickel and copper complexes.[2-6] These reactions often require harsh reaction conditions such as high temperature, high catalyst loading or specially designed phosphine ligands. These reactions often require harsh reaction conditions such as high temperature, high catalyst loading or specially designed phosphine ligands. To overcome these limitations, much attention has been paid to developing catalytic systems to minimize the environmental impact (E-factor) of the processes and efficient catalytic activity.

Zirconium compounds have been successfully applied for various reactions such as (1) carbon-carbon formation reactions, (2) carbon-heteroatom formation reactions, (3) synthesis of heterocycles, (4) one-pot multicomponent reactions, and (5) miscellaneous reactions [7]. Also, Roozbeh and co-workers reported that Ni-poly (N-vinyl-2-pyrrolidone)/TiO_2-ZrO_2 was an effective catalyst for coupling reactions of aromatic halides with phenylboronic acid. [8] Consequently, the key advances about zirconium-catalysed coupling reactions are paid more attention by us due to its wide distribution, low price and efficient catalytic activity. It is very difficult to directly catalyse coupling reaction by zirconium. Thus, it was highlighted how to take advantage of its characteristic properties to perform innovative and useful transformations.

A great attention toward nanoparticles has been apparent in the past decade because the high surface areas and their reactive surfaces make them successful supports in catalysis cross-coupling reactions.[9] The mostly and newly used nano-sized supports are boehmite,[10] MCM-41,[11] graphen oxide,[12] Fe_3O_4,[13] carbon nanotube[14] and nanofiber.[15] In the recent years, nanofibers have received considerable attention due to their environmentally friendly properties, pharmaceutical properties, degradability content, high specific surface area and high mechanical stability. Therefore, nanofibers are very promising candidates for catalyst supports. Nanofibers can be generated in numerous techniques such as drawing,[16] template synthesis,[17] electrospinning[18] and self-assembly.[19] Among these methods the self-assembling has gained increasing attention. Sufficient binding sites on nanofibers surface make them an ideal organic-based support for anchoring metal nanoparticles or the parent precursor metal ions. Hence, as a part of our research program directed toward the utility of peptide nanofiber, we decided to prepare ZrO nanoparticles immobilized on peptide nanofibers. This novel nanostructural material was applied as an effective catalyst for the amination of aryl halides, synthesis of biaryl and symmetrical sulfides.

Result and discussion

To the best of our knowledge, this is the first report for the green synthesis of peptide nanofibers decorated with zirconium oxide nanoparticles in aqueous solution. After converting of desired peptide into nanofiber using self-assembly procedure (that is recently reported by our group), [15] ZrO nanoparticles was immobilized on the surface of this nanostructural compound (Scheme 1).

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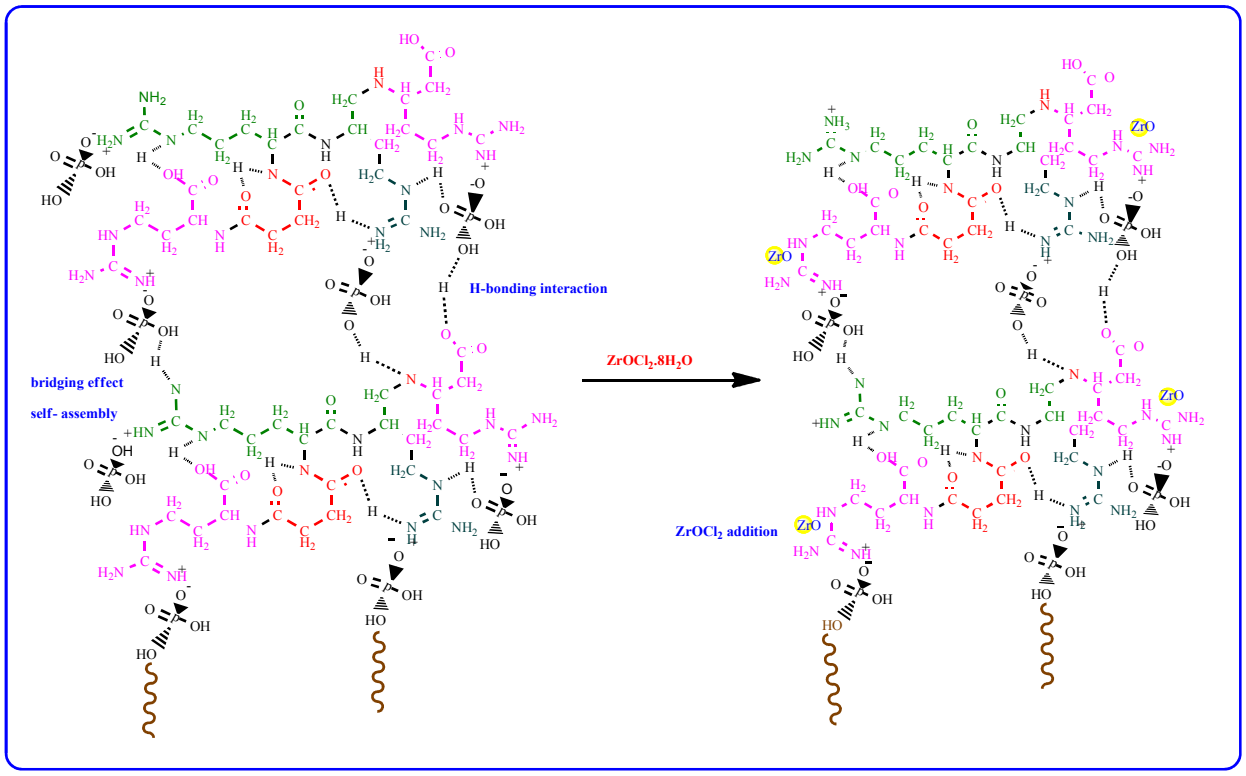

Scheme 1. Schematic synthesis of ZrO nanoparticles supported on the peptide nanofibers

Characterization of supported ZrO nanoparticles on the peptide nanofiber

To assess the coordination of ZrO with peptide nanofiber, we performed FT-IR, UV Visible analysis, fluorescence spectroscopy, SEM, TGA, and atomic absorption spectroscopy (AAS). In order to study the binding mode of the peptide nanofiber to metal, the IR spectrum of the free peptide nanofiber was compared with the corresponding peptide nanofiber decorated with ZrO. The band at 1643 cm^{-1} is characteristic of bending vibration of N–H group's in the peptide. Reducing this frequency to 1636 cm^{-1} is due to coordination of nitrogen to zirconium[20] (Figure 1). UV-Vis and fluorescence properties of peptide nanofiber, metallic salt and peptide nanofiber decorated with ZrO using water as solvent is also presented in Figure 2. In the peptide nanofiber and ZrONP-PNF, π-π* transitions of imine bond at 250-300 nm were studied. It can be seen that the visible spectra of the ZrONP-PNF show higher absorption than the free peptide nanofiber and alone metallic salt, this fact can be illustrated because of the coordination of metal ion to the peptide nanofiber. [21]

The fluorescence properties of peptide nanofiber and ZrONP-PNF were studied at room temperature in H_2O (Fig. 3). It is interesting that the ZrONP-PNF shows a higher intensity than that of the free peptide nanofiber. However in the absence of metal ions, the fluorescence of the peptide nanofiber is perhaps quenched by the occurrence of a photoinduced electron transfer (PET) process because of the presence of lone pairs of donor atoms in the ligand. The complexation of zirconium ions with PNF probably prevents PET process; therefore, the fluorescence intensity can significantly be increase *via* this coordination. [22]

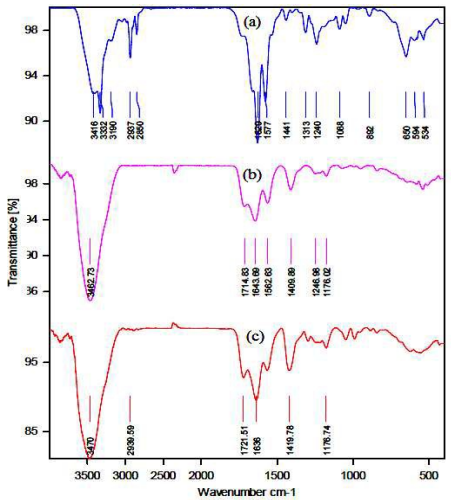

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Fig. 1. FT-IR spectra of peptide powder (a) the peptide nanofiber solution (b) ZrO nanoparticles supported on peptide nanofiber (c).

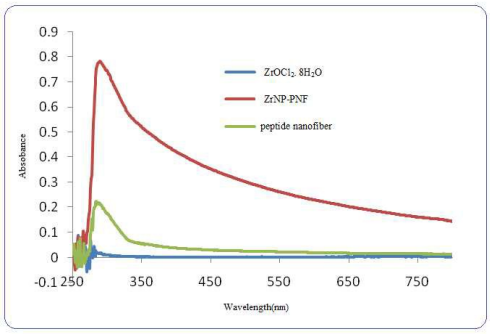


Fig. 2. UV-Visible absorption spectra for $ZrOCl_2.8H_2O$, peptide nanofiber and ZrONP-PNF

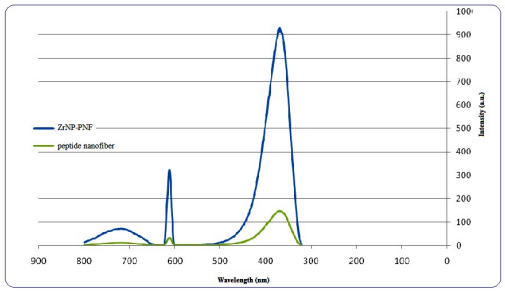
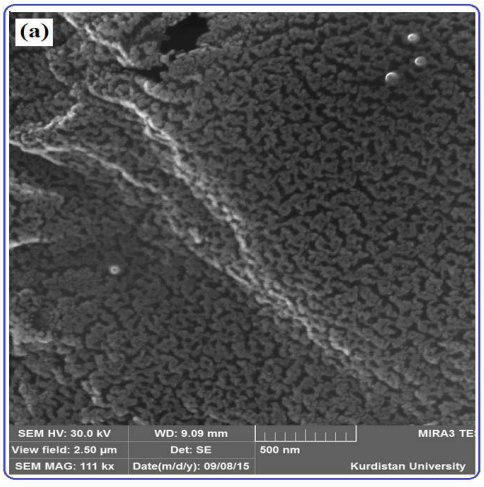
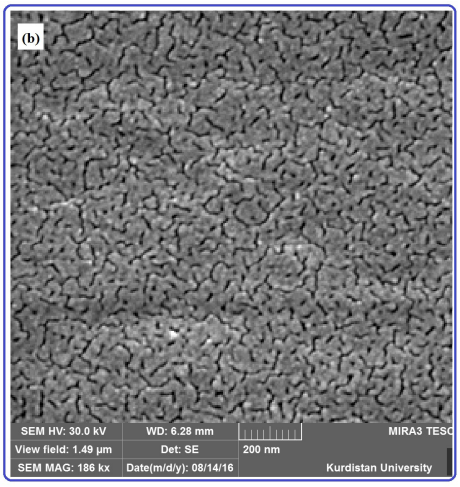
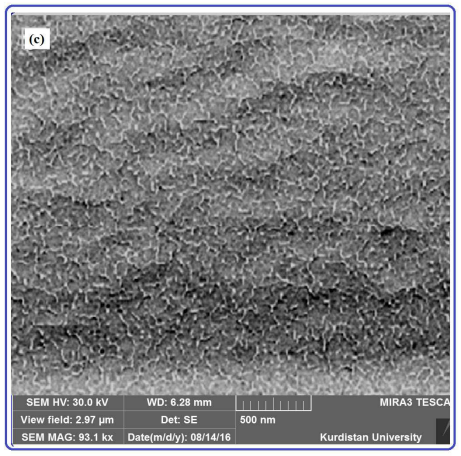


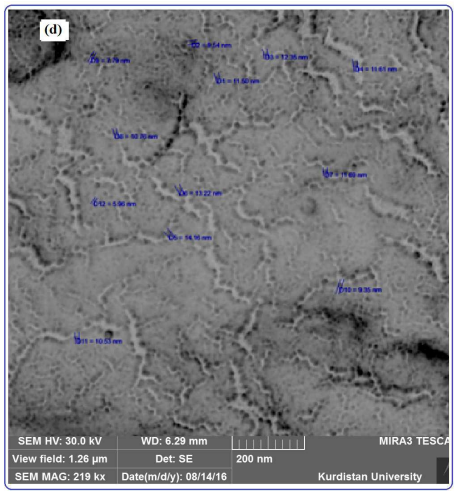
Fig 3. Fluorescence spectra of peptide nanofiber and ZrONP-PNF

SEM images of the zirconium oxide immobilized on the peptide nanofibers. Fig 4 (b and c) show that nanofibers with preserved morphology after the addition of ZrO, also (d and e) indicate the distribution of zirconium oxide nanoparticles on the nanofiber without agglomeration.









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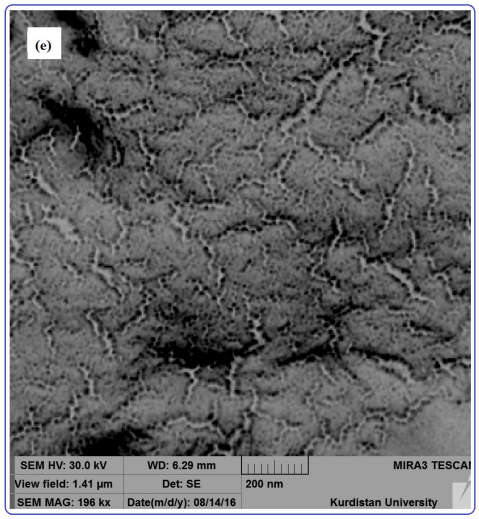


Fig. 4 (a) SEM image of the surface of the woven nanofibers (b, c, d and e) SEM image of the surface of the woven nanofibers decorated with ZrO nanoparticles

Atomic absorption spectroscopy (AAS) was employed to determine the exact amount of ZrO immobilized on peptide nanofiber that was found to be 1.6× 10^{-4} mol g^{-1}. The thermal behavior of ZrO immobilized on peptide nanofiber was investigated by thermogravimetric analysis from room temperature to 500 °C (TGA) (Fig. 5). The first step from room temperature to 140 °C shows a ~4% weight loss due to loss of adsorbed water and organic solvents. The second step between 140 and 240 °C shows a ~12% weight loss of the total solid catalyst. Differential thermogravimetric analysis (DTA) of catalyst reveals that a peak at 160 °C, which is related to the start a decomposition process; also this curve shows an exothermic peak at 420 °C.

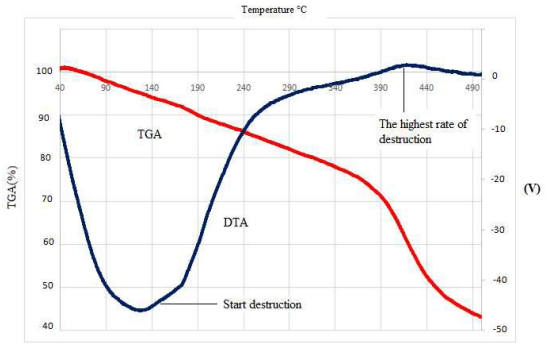
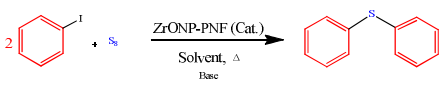


Fig. 5 TGA curve of ZrO immobilized on peptide nanofiber

Catalytic studies

After preparation and characterization of ZrO nanoparticles supported on peptide nanofiber, catalytic activity of this compound was investigated for the coupling reaction of aniline, ammonia, phenyl boronic acid, S_8, and 2- thiobarbituric with aryl halides. In general, all reactions were very clean, and the desired products were obtained in high yields under normal atmospheric conditions. Initially, we examined coupling reactions of iodobenzene with S_8 in the presence of ZrO-woven nanofiber, and various parameters were optimized to improve the reaction further. The results are summarized in Table 1.

Table 1 Optimization of the reaction conditions for the C-S coupling using iodobenzene and S_8 as sulfur transfer agent.[a]



Entry	Cat (µl)	Solvent	Temp. (ºC)	base	Time (h)	Yield (%)[b]
1	200	DMSO	120	KOH	1.5	90
2	200	PEG	120	KOH	1.5	N.R
3	200	DMF	120	KOH	1.5	79
4	200	H_2O	120	KOH	1.5	N.R
5	200	Toluene	120	KOH	1.5	N.R
6	200	DMSO	120	Et_3N	1.5	N.R
7	200	DMSO	120	KF	1.5	N.R
8	200	DMSO	120	K_2CO_3	1.5	17
9	200	DMSO	120	Na_2CO_3	1.5	Trace
10	100	DMSO	120	KOH	1.5	39
11	200	DMSO	100	KOH	2	90
11	200	DMSO	80	KOH	2	44

[a]Reaction conditions: iodobenzene (1 mmol), S_8 (1 mmol), ZrONP-PNF solution (µL), base (4 mmol).

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According to the results shown in Table 1, it was found that the base and solvent significantly affected the yield of the desired product. The best solvents for this system were found to be DMSO and DMF (Table 1, entries 1, 3). Furthermore, among organic and inorganic bases, KOH was effective base for this reaction. In addition, the reaction yield and reaction rate increased by rising the reaction temperature and the amount of woven nanofiber templated ZrO nanoparticles. It should be mentioned when we examined the temperature of 120 °C, the yield did not change. Increasing temperature of 120 °C decreases the reaction time, but did not increase the yield of diphenyl sulfide (Table 1, entry 1). Thus, we preferred to choose 100 °C. Finally, the best results were obtained with iodobanzane (1 mmol), S_8 (1 mmol), and KOH (4 mmol) in the presence of catalytic amounts of woven nanofiber ZrO (200 µl) in DMSO as solvent at 100 °C (Table 1). By these optimal conditions we studied the coupling reaction of different aryl halides including electron drawing and electron-donating groups to produce the corresponding symmetrical sulfides in moderate to excellent yields (results are summarized in Table 2). Experimental results show that halide derivatives with different functional groups, such as OCH_3, CF_3, Me, NO_2 and etc. provide good to excellent yields. As can be seen, aryl chlorides were not as reactive as aryl bromides and iodides. In the case of aryl halide with a free hydroxy group the reaction proceeded without the need of a protecting group and the desired product was obtained in good yield. It should be noted in some cases the product in the presence of electron-with drawing substituent's has shorter reaction time than electron-donating substituent's ones.

In order to investigate the selectivity of described method; the reaction of 1-bromo-4-chloro benzene as dihalogenated aryl halide wit S_8 was also investigated that the bromide showed more reactivity (Table 2, entry 8). This selectivity allows remaining an active halide site for further functionalization.

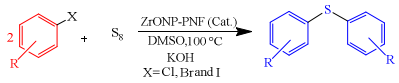

Table 2. Synthesis of symmetrical sulfides *via* reaction of S_8 and aryl/alkyl halides catalyzed by peptide nanofibers decorated with ZrO nanoparticles (ZrONP-PNF) in DMSO.[a]

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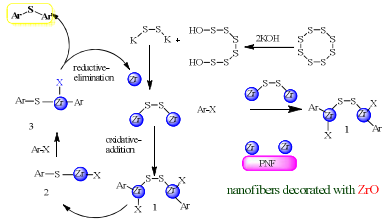
[a]Reaction conditions: aryl halides (1 mmol), S_8 (1 mmol), ZrONP-PNF (200 µL), KOH (4 mmol) and DMSO (2 mL). [b]Isolated yield.

The proposed mechanism for the synthesis of sulfides on the basis of previous reports[23] has been depicted in Scheme 2. Initially S_8 reacts with KOH to give potassium disulfide then peptide nanofibers decorated with ZrO nanoparticle react with potassium disulfide to give zirconium disulfide, which adds to aryl halide *via* oxidative addition reaction to produce intermediate **1**. Reductive elimination then occurred to form intermediate. **2**. After that, aryl halide reacts with intermediate **2** by oxidative addition to generate compound **3**, which can undergo reductive elimination to produce diphenyl sulfide and Zr (Scheme 2).

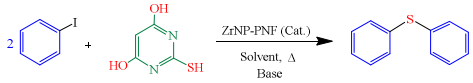


Scheme 2. Proposed mechanisms for the synthesis of symmetrical sulfides *via* reaction of aryl halides and S_8 catalyzed by peptide nanofibers decorated with ZrO nanoparticles.

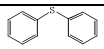
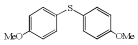
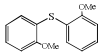
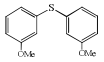
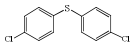
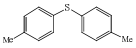
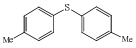
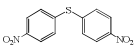
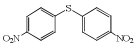
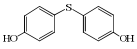
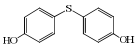
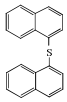
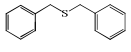
A second portion of this work involves the application of our protocol to the synthesis of symmetrical sulfides from reaction of aryl halide and 2- thiobarbituric acid as a novel sulfur transfer reagent.

Iodobenzene and 2- thiobarbituric acid were chosen as model substrates to optimize the reaction conditions, and several parameters such as amount of catalyst, base, solvent, and temperature under normal atmospheric conditions was screened (Table 3).

Table 3 Optimization of the reaction conditions for the C-S coupling using Iodobenzene and 2- thiobarbituric acid as sulfur transfer agent.[a]



Entry	Cat (µl)	Solvent	Temp. (ºC)	base	Yield (%)[b]
1	300	DMSO	130	KOH	82
2	300	PEG	130	KOH	N.R
3	300	DMF	130	KOH	17
4	300	H_2O	130	KOH	N.R
5	300	Toluene	130	KOH	N.R
6	300	DMSO	130	Et_3N	N.R
7	300	DMSO	130	K_2CO_3	N.R

Entry	Ar-X	product	Time (h)	Yield (%)[b]	Mp (°C)
1			2	90	Oil [28]
2			4	85	Oil [28]
3			15	65	Oil [28]
4			8	88	Oil[29]
5			6.5	92	Oil[30]
6			7	87	Oil[31]
7			9	85	Oil [32]
8			5	78	Oil[33]
9			6.5	75	Oil [34]
10			7.5	71	Oil[34]
11			3	79	Oil [35]
12			2	70	149-150[36]
13			2.5	65	149-150[36]
14			10	60	150-153[37]
15			12	55	150-153[37]
16			7	80	156-158[38]
17			1	80	43-46[39]

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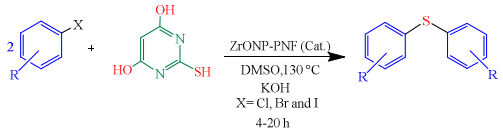
8	300	DMSO	140	KOH	85
9	200	DMSO	130	KOH	54
10	300	DMSO	100	KOH	27
11	200	DMSO	80	KOH	N.R

[a]Reaction conditions: iodobenzene (1 mmol), 2- thiobarbituric acid (1 mmol), ZrONP-PNF (μL), base (7 mmol). [b]Isolated yield. Reaction time: 24 h.

Firstly, the effect of solvents was investigated and it was observed that the desired product was not obtained in PEG, H_2O and Toluene (Table 3, entries 2, 4 and 5). However, the reaction readily proceeded in DMSO and DMF (Table 3). Among various bases that was screened (e.g., KOH, K_2CO_3 and Et_3N), KOH was the most effective one in DMSO. The reaction when conducted at 100 °C, the observed yield was very low (Table 3, entries 9). It should be mentioned when we examined the temperature of 140 °C, the yield only increased 3 percent (Table 3, entries 8) in comparison with 130 °C (small change in yield was observed). Thus, the ideal temperature for the reaction was found to be 130 °C. Finally, the amount of catalyst was also screened, and 300 μL of woven nanofiber templated ZrO nanoparticles was found to be optimal value, a lower yield and longer reaction time was observed when the amount of the catalyst was decreased (Table 3, entry 9).Under optimized conditions (Table 3), we studied the coupling reaction of various aryl halides with 2-thiobarbituric acid. This protocol efficiently cross coupled aryl halides having electron withdrawing group (e.g., NO_2, Cl and CF_3) with 2-thiobarbituric acid to produce the corresponding aryl sulfides in excellent yields whereas in the presence of electron donating group (4-OMe) a slight decrease in the yield of the diaryl sulfide (Table 4) was observed. It should be noted the coupling reaction of 1-bromo-4-nitrobanzane, 1-chloro-4-nitrobenzene led to the desired product without nitrobenzene converted to amino benzene sulfides. This protocol was also applied for the cross-coupling reaction between of 1-bromo-4-chlorobenzene as dihalogenated aryl halide with 2-thiobarbituric acid to investigate the selectivity of this procedure which the bromide showed more reactivity than the chloride group (Table 4, entry 8).



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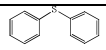
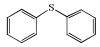
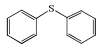
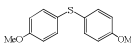
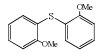
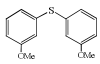
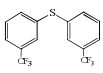
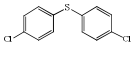
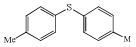
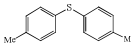
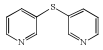
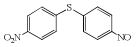
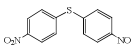
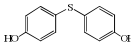
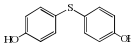
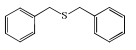
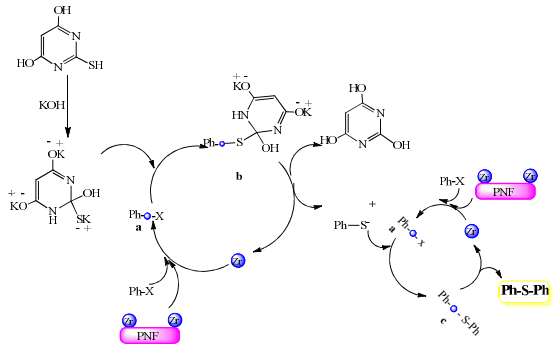
Entry	Ar-X	product	Yield (%)[b]	Time (h)	Mp (°C)
1			82	24	Oil [28]
2			78	24	Oil [28]
3			23	24	Oil [28]
4			70	24	Oil [29]
5			50	24	Oil [30]
6			72	24	Oil [31]
7			68	24	Oil [32]
8			75	24	Oil [33]
9			65	24	Oil [34]
10			62	24	Oil [34]
11			80	10	149-150 [35]
12[c]			50	6	149-150 [36]
13[d]			35	8	150-153 [36]
14			25	24	150-153 [37]
15			10	24	150-153 [37]
16			60	4	43-46 [39]

[a]Reaction conditions: aryl halides (1 mmol), 2-thiobarbituric acid (1 mmol), ZrONP-PNF (300 µL), KOH (7 mmol) and DMSO (2 mL). [b]Isolated yield. [c, d]The reaction was carried out for 4h.

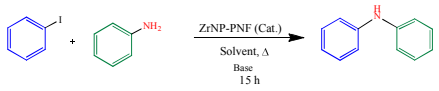
The mechanism of this reaction is suggested as outlined in Scheme 3. It is assumed that 2-thiobarbituric acid reacts with KOH to produce the potassium thiolate. Next, the aryl halid caused the oxidative addition of zirconium to produce intermediate ***a***. The intermediate ***a*** reacts with the potassium thiolate to produce intermediate ***b***, which is transformed into thiol anion in the presence of KOH, then thiol anion reacts with intermediate ***a*** by oxidative addition to form compound ***c***, which undergoes reductive elimination to produce corresponding sulfide and releases ZrO nanoparticles that start another catalytic cycle.



Scheme 3. Proposed mechanisms for the synthesis of symmetrical sulfides *via* reaction of aryl halides and 2-thiobarbituric acid catalyzed by peptide nanofibers decorated with ZrO nanoparticles.

The reactivity of woven nanofiber templated ZrO nanocatalyst, also examined for cross-coupling reaction between aryl halides and aniline or aqueous ammonia. To identify optimum reaction conditions, we first investigated the C-N cross-coupling of aniline and iodobenzene in the presence of woven nanofiber templated ZrO nanoparticles. Selected results from our screening experiments are summarized in Table 5.

Table 5 Optimization of the reaction conditions for the C-N cross coupling reaction using iodobenzen and aniline.[a]



Entry	Cat (µl)	Solvent	Temp. (ºC)	base	Yield (%)[b]
1	300	DMSO	130	KOH	80
2	300	PEG	130	KOH	N.R
3	300	DMF	130	KOH	N.R
4	300	H_2O	130	KOH	N.R

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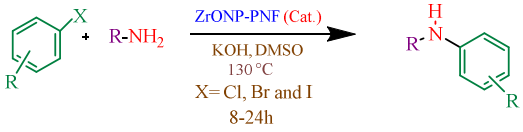
5	300	DMSO	130	Et_3N	N.R
6	300	DMSO	130	-	N.R
7	300	DMSO	140	KOH	76
8	200	DMSO	130	KOH	77
9	300	DMSO	100	KOH	55
10	200	DMSO	80	KOH	19

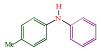
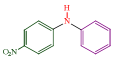
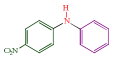
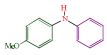
[a]Reaction conditions: iodobenzene (1 mmol), aniline (3 mmol), ZrONP-PNF (µL), base (4 mmol).

It was found that when the reaction proceeded at 80 °C, the observed yield was very low and when the temperature was increased to 130 °C, a yield of 90% could be obtained but when we examined temperature 140, the yield significantly decreased. The decrease is due to the composition of side products, thus the ideal temperature for the reaction was found to be 130 °C. Without base addition, the reaction in DMSO proceeded ineffectively (Table 5, entry 6), whereas the reactions in the presence of KOH in DMSO resulted in high conversion of starting materials to diphenyl amine. Also the influence of the amount of catalyst on the yield of the product was evaluated. It was observed that 300 µL of woven nanofiber templated ZrO nanoparticles was the optimum value for this transformation.

Eventually, the best result was achieved when the reaction was pursued at 130 °C using 300 µL of woven nanofiber templated ZrO nanoparticles in the presence of KOH in DMSO.

Table 6. Synthesis of aniline derivatives *via* reaction of R-NH_2 and aryl halides catalyzed by peptide nanofiber decorated with ZrO nanoparticles (ZrONP-PNF) in DMSO.[a]



Entry	Ar-X	Amine	Product	Time (h)	Yield (%)[b]	Mp (°C)
1				15	80	53[40]
2				18	78	53[40]
3				18	68	90[41]
4[c]				14	75	Oil[41]
5[d]				8	70	135-136[41]
6[e]				10	68	135-136[42]
7				18	68	Oil[43]
8				18	72	103-105[44]
9		NH_3		24	70	Oil[45]
10		NH_3		24	45	56–59[46]
11		NH_3		24	69	146-148[47]

[a]Reaction conditions: aryl halide (1 mmol), aniline (3 mmol), ZrONP-PNF (µL), KOH 4 mmol.

As shown in (Table 6), the expected products were obtained in moderate to high yields. It was shown that aryl halides with electron-withdrawing groups reacted more quickly than the aryl halides with electron-releasing groups (Table 4, entries 4–6).

The proposed mechanism for this transformation has been illustrated in Schemes 4 based of previous reports.[24] Initially aryl halide reacts with ZrO by oxidative addition to form intermediate ***(a)***, then the intermediate ***(a)*** reacts with amine in the presence of KOH to produce intermediate ***(b)***, then intermediate ***(b)*** *via* reductive elimination afford to aniline or secondary amine and releases zirconium oxide nanoparticle.

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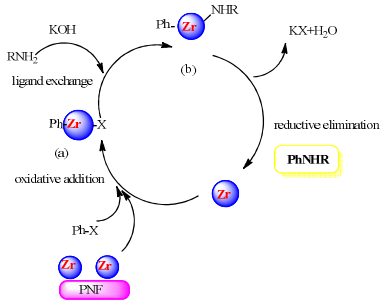


Scheme 4. Proposed mechanism for the synthesis of secondary amine *via* reaction of R-NH_2 and aryl halides catalyzed by peptide nanofiber decorated with ZrO nanoparticles.

Finally, the C-C cross-coupling reactions of triphenyltin chloride and/or phenyl boronic acid with aryl halides were studied (Table 7). Triphenyltin chloride and iodobenzene were used as model reaction, and various parameters were optimized (Table 7).

Table 7 Optimization of the reaction conditions for the C-C coupling using iodobenzene and triphenyltin chloride.[a]

Entry	Cat (µl)	Solvent	Temp. (ºC)	base	Yield (%)[b]
1	400	DMSO	110	KOH	80
2	400	PEG	110	KOH	N.R
3	400	DMF	110	KOH	N.R
4	400	H_2O	110	KOH	N.R
5	400	DMSO	110	Na_2CO_3	N.R
6	400	DMSO	110	K_2CO_3	N.R
7	400	DMSO	130	KOH	70
8	300	DMSO	110	KOH	66
9	300	DMSO	80	KOH	33

[a]Reaction conditions: iodobenzene (1 mmol), phenyl boronic acid (1.2 mmol), ZrONP-PNF (µL), base (3 mmol).

As shown in (Table 7), the nature of the base and solvent affects the yield of the desired product. Among screened solvents and bases, DMSO and KOH both gave the better yield compared with other solvents and bases. The ideal temperature for the reaction was found to be 110°C. When the reaction conducted at the temperature of 130 for the identical amount of time, we faced a decrease in yield. Therefore, we preferred to choose 110 temperature.

Also, the reaction yield and reaction rate increased *via* increasing the amount of the catalyst.

Utilizing these conditions, various aryl halides reacted with triphenyltin chloride and/or phenyl boronic acid to give the corresponding biaryl. Importantly, aryl halide derivatives bearing electron-donating as well as electron- withdrawing substituents efficiently provided the desired products; also, iodobenzenes was found to be a more reactive substrate than bromo- and chlorobenzenes.

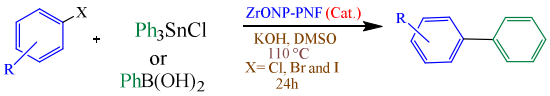
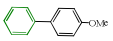
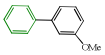
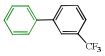
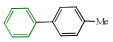
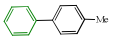
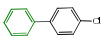
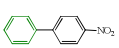
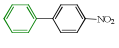
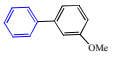


Table 8 Synthesis of biphenyles *via* reaction of triphenyltin chloride or phenyl boronic acid with aryl halides catalyzed by peptide nanofiber decorated with ZrO nanoparticles (ZrONP-PNF) in DMSO.[a]

Entry	Ar-X	Phenyl reagent	product	Yield [b] (%)	Mp (°C)
1		Ph_3SnCl		80	63-66[48]
2		Ph_3SnCl		70	63-66[48]
3		Ph_3SnCl		65	86-90[49]
4		Ph_3SnCl		50	30-32[50]
5		Ph_3SnCl		85	Oil[51]
6		Ph_3SnCl		65	27[51]
7		Ph_3SnCl		55	44-46[52]
8		Ph_3SnCl		48	44-46[52]
9		Ph_3SnCl		80	69-70[52]
10		Ph_3SnCl		78	113-115[53]
11		Ph_3SnCl		75	113-115[53]
12		Phenyl boronic acid		70	Oil[51]

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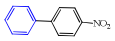
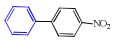
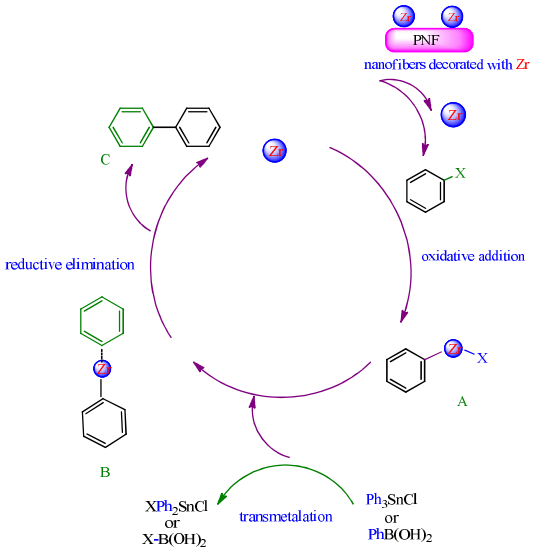
Entry	Ar-X	Phenylating agent	product	Yield (%)[b]	Mp (°C)
13		Phenyl boronic acid		68	113-115 [53]
14		Phenyl boronic acid		65	113-115 [53]

[a]Reaction conditions: aryl halide (1 mmol), phenyl boronic acid (1.2 mmol), triphenyltin chloride (0.5 mmol), ZrONP-PNF (400 µL), KOH (3 mmol), reaction time: 24 h.

The proposed mechanism for described-above cross-coupling reaction has been outlined in Scheme 5. We hypothesize that aryl halide reacts with zirconium to give intermediate ***A***, followed by trans metalation and reductive elimination to give the coupling product and restore the catalytically active zirconium species.



Scheme 5 Proposes mechanism for the synthesis biphenyl *via* reaction of triphenyltin chloride or phenyl boronic acid with aryl halides catalyzed by peptide nanofibers decorated with ZrO nanoparticles

There is an increasing pressure on chemical and pharmaceutical industries to decrease chemical waste and advance the selectivity and effectiveness of synthetic processes. For the development of recoverable and recyclable catalysts, it is necessary to implement green chemistry principles. In this aim, we investigated the recoverability and reusability of the ZrO nanoparticle supported on the peptide nanofiber for the synthesis of sulfides *via* reaction of iodobenzene with S_8 over four successive runs. Reaction was performed in DMSO at 130 °C, using 1 mmol iodobenzene, 1 mmol S_8 and KOH 4 mmol in the presence of ZrONP-PNF (200 µl), upon completion of the reaction, the mixture was cooled down to room temperature. Then 20 mL of ethyl acetate was added to the reaction mixture, which led to the precipitation of ZrONP-PNF. The resulting precipitate was washed twice with ethyl acetate (2 x 10 mL), dried and applied for the next run. It was found that ZrONP-PNF could be reused at least four times without a significant loss of its catalytic activity.

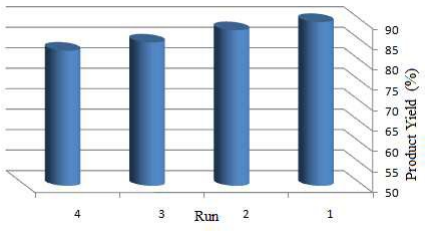


Fig. 6 Catalyst recycling study for the synthesis of diphenyl sulfide.

Finally, in order to assess the present protocol with respect to other reported methods for the synthesis of symmetrical sulfides *via* reaction of aryl halides and alkyl halide with S_8 the catalytic performance of the zirconium oxide immobilized on the peptide nanofiber was compared with some of the previously reported catalysts (Table 9). This catalyst leads to good reaction time and higher yield than the previously reported catalysts. More importantly, compared with other catalysts, ZrONP-PNF is easily prepared and can be reused at least four times without any significant loss of its catalytic activity.

Table 9. Comparison of ZrONP-PNF for the synthesis of diphenyl sulfide *via* reaction of S_8 and iodobenzene with previously reported procedures.

Entry	Catalyst	Yield (%)[a]	Time (h)	Ref.
1	MCM-41-2N-CuI	88	24	25
2	Nano copper oxide	94	20	26
3	Copper oxide particles	92	21	27
5	CoI_2 (dppe) /Zn	98	10	4
6	Indium	96	24	5
7	ZrONP-PNF	90	2	This work

[a]Isolated yields.

Conclusions

In summary, we have described the first peptide nanofibers decorated with zirconium oxide nanoparticles that catalyzed C-N, C-S and C-C cross-coupling reactions under mild reaction conditions in excellent yields. Peptide nanofibers can provide multiple functions such as support, ligand and the high surface area for the immobilization of ZrO nanoparticles, which is resulting the high catalytic activity in described reactions. This new coupling reaction

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underlines the potential of using zirconium oxide nanoparticles as a very user-friendly, inexpensive and efficient catalyst for the cross coupling of carbon-heteroatom and carbon-carbon bonds. In addition, this nanocatalyst can be easily recovered and reused for subsequent run for at least 4 times with less deterioration in its catalytic activity.

Experimental section

Materials

All reagents and solvents used in this work were purchased from Sigma-Aldrich, Fluka or Merck Chemical Companies and used without further purification.

Instrumentation

NMR spectra were acquired on a Bruker Avance III 400 MHz. Melting points were measured with an Electrothermal 9100 apparatus. The particles size and morphology were investigated by a JEOL JEM-2010 scanning electron microscopy (SEM), on an accelerating voltage of 200 kV. Varian Cary 300 Bio UV-Vis, Vertex 70 Fourier transformed infrared and Varian Cary spectrofluoremeter were used for UV-Vis, FT-IR and fluorescence spectral analysis.

Preparation of peptide nanofiber (PNF)

Peptide nanofiber (PNF) has been prepared based on our newly reported procedure.[15]

Synthesis of ZrO nanoparticle supported on the peptide nanofiber (ZrONP-PNF)

Peptide 30.14 mg (0.04 mmol) was dissolved in 0.2 mL doubly distilled water and 0.8 mL phosphate buffer solution (pH 8) was added. Then 32 mg (0.31 mmol) of succinic anhydride was added to the peptide solution. The solution was sonicated for a few minutes. This mixture was stirred overnight at 80 °C. In the next step $ZrOCl_2.8H_2O$ (3.2 mg, 0.01 mmol) was added to reaction mixture and stirred for 12 hour at 80 °C, to obtain ZrONP-PNF quantitatively.

General procedure for the sulfides synthesis using S_8

A round bottom flask was charged with of 1 mmol of S_8, aryl halide (1 mmol), KOH (4 mmol), 200 µL of the solution containing ZrO nanoparticle decorated on nanofibers and DMSO (2 mL). Then the reaction mixture was stirred at 100 °C. The progress of reaction was monitored by TLC. After reaction completion, the mixture was extracted with ethyl acetate (2×20 mL). The organic extract was washed twice with water, and then dried with anhydrous Na_2SO_4, filtered, and the solvent was evaporated to achieve corresponding sulfide. In order to obtain high pure sulfide, the crude product was purified by preparative TLC.

General procedure for the sulfides synthesis using 2-thiobarbituric acid

A round bottom flask was charged with of 1 mmol of 2-thiobarbituric acid, aryl halide (1 mmol), KOH (7 mmol), solution containing ZrO nanoparticle decorated on nanofibers (300 µL) and DMSO (2 mL). Then reaction mixture was stirred at 130 °C. The progress of reaction was monitored by TLC. After reaction completion, the mixture was extracted with ethyl acetate (2×20 mL). The organic extract was washed twice with water and dried over anhydrous Na_2SO_4, then filtered and the solvent was evaporated to achieve corresponding sulfide. In order to obtain high pure sulfide, the crude product was purified by preparative TLC.

General procedure for the synthesis of *N*-arylation

The reaction was conducted at 130 °C in DMSO (3 ml) with 3 mmol of amine, 1 mmol of aryl halid, 4 mmol of KOH and 300 µL of a solution containing ZrO nanoparticle decorated on nanofibers. The progress of reaction was monitored by TLC. After reaction completion, the mixture was cooled to room temperature and was extracted with ethyl acetate (2 x 20 mL). The organic layer was washed twice with water and dried with anhydrous Na_2SO_4, then filtered and the solvent was evaporated to achieve corresponding aryl amine. In order to obtain high pure aryl amine, the crude product was purified by preparative TLC.

General procedure for the synthesis of biaryl

A round bottom flask was charged with an aryl halid (1 mmol), phenyl boronic acid (1.2 mmol) or triphenyltin chloride (0.5 mmol), KOH (3 mmol), ZrO nanoparticle supported on peptide nanofiber (ZrONP-PNF) (400 µl) and DMSO (3 mL). The reaction mixture was then stirred at 130°C under atmospheric conditions. Reaction progress was monitored by TLC. Upon the reaction completion, mixture was cooled down to room temperature, then filtered, and extracted with ethyl acetate. The combined organic layer was dried over Na_2SO_4, filtered, and purified by preparative tin layer chromatography using *n*-hexane/ethyl acetate as eluent.

Selected spectral data

4, 4'-Dimethoxy diphenyl sulfide: [29]

^{1}H NMR ($CDCl_3$, 400 MHz): δ= 7.36 (d, *J* = 6.8 Hz, 4H), 6.76 (d, *J*=7.2 Hz, 4H), 3.63 (s, 6H).

3, 3'-Dimethoxy diphenyl sulfide: [31]

^{1}H NMR ($CDCl_3$, 400 MHz): δ= 7.76-7.73(m, 1H), 7.58-7.54(m, 1H), 7.4(d, J=6.4 Hz, 1H), 7.14(d, J=6 Hz, 1H), 4.26(s, 3H).

Bis(3-(Trifluoromethyl)phenyl)sulfane:[32]

^{1}H NMR ($CDCl_3$, 400 MHz): δ= 7.90-7.77(m, 4H), 7.58-7.40 (m, 4H); MS (EI, m/z): 322.1.

4,4'-Dichloro diphenyl sulfide: [33]

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^{1}H NMR ($CDCl_3$, 400 MHz): δ =7.57-7.56(m, 4H), 7.55-7.51(m, 4H).

Dip-tolyl sulfide: [34]

^{1}H NMR ($CDCl_3$, 400 MHz): δ= 7.37-7.35 (d, *J* = 6.4 Hz, 2H), 7.17-7.15(d, *J* = 7.6 Hz, 2H), 2.37(s, 3H); MS (EI, m/z): 215.2.

Bis-(3-pyridyl) sulfide: [35]

^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.63(s, 1H), 8.57(d, *J*= 4, 1H), 7.73-7.71(m, 1H), 7.36-7.32(m, 1H).

4, 4'-Dinitro diphenyl sulfide: [36]

^{1}H NMR($CDCl_3$, 400 MHz): δ= 8.25 (d, *J*=9.2 Hz, 2H), 7.76-7.71 (m, 2H) 7.66 (d, *J*= 9.2, 2H) 7.58-7.54(m, 2H).

4, 4'- Thiodiphenol: [37]

^{1}H NMR (DMSO, 400 MHz): δ= 7.33 (d, *J*=8.8 Hz, 4H), 6.73 (d, *J*=8.8 Hz, 4H); ^{13}C NMR (DMSO, 100 MHz): δ= 167.5, 132.2, 132.1, 129.2.

4-Nitro-*N*-phenylaniline: [42]

^{1}H NMR (400MHz, $CDCl_3$): δ=8.17-8.15 (d, *J*=8 Hz, 2H), 7.45-7.40 (t, *J*=8.8Hz, 2H), 7.25-7.22 (m, 3H), 6.99-6.97 (d, *J*=10Hz, 2H), 6.36 (br s, 1H).

***N*-(2-Methoxyphenyl) aniline:** [43]

^{1}HNMR ($CDCl_3$, 400 MHz): δ= 7.75 (t, *J* = 6.8 Hz, 1H), 7.58-7.49 (m, 7H), 6.95-6.88 (m, 1H) 5.9(s, 1H), 4.26 (s, 3H).

***N*-(4-Methoxyphenyl) aniline:** [44]

^{1}HNMR ($CDCl_3$, 400 MHz): δ =7.80-7.58 (m, 4H), 7.51-7.48 (m, 2H), 7.40-7.29 (m, 1H), 5.51 (s, 1H), 3.91 (s, 3H)

***p*-Anisidine:** [46]

^{1}H NMR (400 MHz, $CDCl_3$): δ= 6.88 (dd, *J* = 6.4, 2.0 Hz, 2H), 6.66 (dd, *J* = 6.4, 2.0 Hz, 2H) 3.78 (s, 3H), 3.44 (s, br, 2H).

Biphenyl: [48]

^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.65-7.62 (m, 2H), 7.50-7.46 (m, 2H), 7.39-7.37(m, 1H).

4-Methoxybiphenyl: [49]
^{1}H NMR ($CDCl_3$, 400 MHz): δ = 7.60-7.56 (m, 4H), 7.47(t, *J* = 7.8 Hz, 2H), 7.35(t, *J* = 7.4 Hz, 1H), 7.03(d, *J* = 8.8 Hz, 2H), 3.9(s, 3H).

4-Methylbiphenyl: [52]

^{1}H NMR (400 MHz, $CDCl_3$): δ= 7.66 (d, *J* = 7.2 Hz, 2H), 7.56 (d, *J* = 8.0 Hz, 2H), 7.53–7.46 (2H, m), 7.45 (1H, t, *J* = 7.2 Hz), 7.29 (d, *J* = 7.6 Hz, 2H), 2.44 (3H, s).

4-Chloro-biphenyl: [52]
^{1}H NMR (400 MHz, $CDCl_3$): δ =7.62–7.60 (m, 2H), 7.58–7.55 (m, 2H), 7.51–7.42 (m, 4H), 7.42–7.38 (m, 1H)

4-Nitro-biphenyl: [53]

^{1}H NMR (400 MHz, DMSO): *δ*= 8.33 (d, *J*= 8.8 Hz, 2H), 8.08 (d, *J* = 8.8 Hz, 2H), 7.81 (d, *J* = 8.8 Hz, 2H), 7.57-7.47 (m, 3H). ^{13}C NMR (100 MHz, DMSO): δ= 147.1, 147.1, 138.2, 129.7, 128.3, 127.8, 127.7, 124.5.

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References

1) E. Sperotto, G.P. van Klink, J.G. de Vries and G. van Koten, *Tetrahedron*., 2010, **66**, 9009.
2)A. Ghaderi, *Tetrahedron.,* 2016, **72**, 4758.
3)A. Rostami, A. Rostami and A. Ghaderi, *J. Org. Chem.*, 2016, **80**, 8694.
4)A. Rostami, A. Rostami, A. Ghaderi and M.A. Zolfigol, *RSC Adv.*, 2015, **5**, 37060.
5)A. Aghayee, M.A. Zolfigol, H. Keypour, M. Yarie and L. Mohammadi, *Appl. Org. Chem.,* 2016, **8**, 612.
6)Y. Liu, C. Long, L. Zhao and M.X. Wang, *Org. Lett.*, 2016, **18**, 5078.
7) Z.H. Zhang, and T.S. Li, *Curr. Org. Chem*., 2009, **13**, 1.
8) L.P. Mo, and Z.H. Zhang, *Curr. Org. Chem*., 2011, **15**, 3800.
9)M. Faraji, Y. Yamini and M. Rezaee, *J. Iran. Chem. Soc.,* 2010, **7**, 1.
10)A. Ghorbani-Choghamarani and B. Tahmasbi, *New.J.Chem*., 2016, **40**, 1205.
11) M. Nikoorazm, A. Ghorbani- Choghamarani and M. Khanmoradi, *RSC Adv.,* 2016, **2**, 56549.
12)A. Sengupta, C. Su, C. Bao, C.T. Nai and K.P. Loh, *ChemCatChem.,* 2014, **6**, 2507.
13)M. Mokhtary, *J. Iran. Chem. Soc.*, 2016, **13**, 1827.
14)S. Rayati and Z. Sheybanifard, *J. Iran. Chem. Soc.*, 2016, **13**, 541.
15) A. Ghorbani-Choghamarani and Z. Taherinia, *RSC. Adv*., 2016, **6**, 59410.
16) S. Amrinder, S. Nain, C.W. Joanna, A. Cristina and S. Metin, *Appl. Phys. Lett*., 2006, **89**, 183105.
17) C. R. Martin, *Chem. Mater*, 1996, **8**, 1739.
18) J.M. Deitzel, J. Kleinmeyer, J.K. Hirvonen and T.N.C. Beck, *Polymer*., 2001, **42**, 8163.
19) G.M. Whitesides and B. Grzybowski, *Science*., 2002, **295**, 2418.
20) R.M. Ahmed, E.I. Yousif, H.A. Hasan and M.J. Al-Jeboori, *Scientific World J.,* 2013*,* **2013.**
21) A. Barakat, M. Al-Noaimi, M. Suleiman, A.S. Aldwayyan, B. Hammouti, T.B. Hadda and I. Warad, *Int. J. Mol. Sci.,* 2013, **14**, 23941.
22) C. Anitha, C.D. Sheela, P. Tharmaraj and R. Shanmugakala, int. j. inorg. chem., 2013, **2013.**
23) H.Y. Chen, W.T. Peng, Y.H. Lee, Y.L. Chang, Y.J. Chen, Y.C. Lai and H.Y. Chen, *Organometallics*., 2013*,* **32**, 5514.
24) X. Guo, H. Rao, H. Fu, Y. Jiang and Y.G. Zhao, Synth Catal., 2006, 348, 2197.
25) M. Cai, R. Yao, C. Lin and H. Zhao, *J. Mol. Catal. A*: *Chem*., 2014, **395**, 349.
26) K.H. Reddy, V.P. Reddy, A.A. Kumar, G. Kranthi and Y.V.D. Nageswar, *Beilstein. J. Org. Chem.,* 2011, **7**, 886.
27) K. H.V. Reddy, V. Prakash Reddy, J. Shankar, B. Madhav, B. S. P. Anil Kumar and Y. V. D. Nageswar, *Tetrahedron Lett*., 2011, **52**, 2679.

View Article Online
DOI: 10.1039/C7NJ00628D

28) V. Prakash Reddy, K. Swapna, A. Vijay Kumar and K. Rama Rao, ***JOC***., 2009, **74**, 3189.
29) M.A. Ferna´ndez-Rodrı´guez and J.F. Hartwig, *J. Org. Chem.,* 2009, **74**, 1663.
30) F. Ke, Y. Qu, Z. Jiang, Z. Li, D. Wu, X. Zhou, *Org. Lett*., 2011, **13**, 454.
31) C. Savarin, J. Srogl, L.S. Liebeskind, *Org. Lett.,* 2002, **4,** 4309.
32)M. Cai, R. Yao, L., Chen and H. Zhao*, J. Mol. Catal. A: Chem*., 2014, **395**, 349.
33) T. Isobe and T. Ishikawa, *J. Org. Chem.,* 1999, **64**, 5832.
34) X. Ku, H. Huang, H. Jiang and H. Liu, *J. Comb. Chem.,* 2009, **11**, 338.
35) H. J. Xu, Y. F. Liang, Z. Y. Cai, H. X. Qi, C. Y. Yang and Y. S. Feng, *J. Org. Chem*., 2011, **76**, 2296.
36)V.S. Pilyugin, S.L. Kuznetsova, Y. E. Sapozhnikov, G.E. Chikisheva, G.V. Kiseleva, T.P. Vorob'eva, E.V. Klimakova, N.A. Sapozhnikova, R.D. Davletov and Z. B, Galeeva, *Russ. J. Gen. Chem.,* 2008, **78**, 446.
37) (a)F. Mohanazadeh, H. Veisi, A. Sedrpoushan, M.A. Zolfigol, F. Golmohammad, S. Hemmati and M. Hashemi, *J. Sulfur. Chem.,* 2014, **35**, 7.(b) (http://www.chemspider.com)
38)C. Combellas, S. Dellerue, G. Mathey and A. Thiebault,. *Tetrahedron. Lett*. 1997, **38**, 539.
39) T. Miyazaki, M. Katayama, S. Yoshimoto, Y. Ogiwara and N. Sakai, *Tetrahedron Lett*., 2016, *57*, 676.
40) C. Desmarets, R. Schneider and Y. Fort, *J. Org. Chem.,* 2002, **67**, 3029.
41) M.A. Carroll and R.A. Wood, Tetrahedron*.,* 2007, **63**, 11349.
42) D. Ma, Q. Cai and H. Zhang, *Org. Lett*., 2003, **5,** 2453.
43)H. Rao, H. Fu, Y. Jiang and Y. Zhao, *J. Org. Chem*., 2005, **70**, 8107.
44) H. Zhang, Q. Cai and D. Ma*, J. Org. Chem.,* 2005*,* **70***,* 5164.
45) A. Cors, S.M. Bonesi and R. Erra-Balsells, *Tetrahedron Lett*., 2008, **49**, 1555.
46) K. G. Thakur, K. S. Srinivas, K. Chiranjeevi and G. Sekar, Green Chem., 2011, 13, 2326.
47) M.S. Yusubov, T.V. Funk, K. Chi, E. Cha, G.H. Kim, A. Kirschning and V.V. Zhdankin, *J. Org. Chem*., 2008, **73**, 295.
48)P. Puthiaraj, P. Suresh and K. Pitchumani, *Green Chem.,* 2014, **16**, 2865.
49) H. Rao, H. Fu, Y. Jiang and Y. Zhao, *J. Org. Chem*., 2005, **70**, 8107.
50) C.L. Sun, H. Li, D.G. Yu, M. Yu, X. Zhou, Z.Y. Lu and Z.J. Shi, *Nat. Chem.*, 2010, **2**, 1044.
51) Y. Chen, H. Peng, Y.X. Pi, T. Meng, Z.Y. Lian, M.Q. Yan and G.A. Yu, *Org Biomol Chem*., 2015, **13**, 3236.
52) Y. Y. Peng, J. Liu, X. Lei and Z. Yin, *Green Chem*., 2010, **12**, 1072.
53) A. Ghorbani-Choghamarani and H. Rabiei, *Tetrahedron. Lett*., 2016**, 57**, 159.