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Article

Microwave Assisted Novel Efficient Pd-free Catalyst for Suzuki C-C Coupling Reaction

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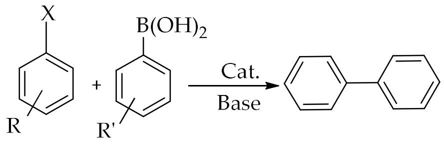
Abstract: Suzuki cross-coupling reaction has developed one of the furthermost effectual approaches for the synthesis of biaryls or substituted aromatic moieties from aryl halides and arylboronic acids with a palladium-catalyst in the past two era's. Herein, Pd-free layered double hydroxide containing nickel catalysts were prepared by co-precipitation method under ultrasonic irradiation and N_2 atmosphere with different molar ratios of Ni: Mg: Al and coded as (1NiLDHs-Dr), (1.5NiLDHs-Dr) and (2NiLDHs-Dr). A series of reduced catalysts under 5%H_2/N_2 at different temperatures were coded as 1NiLDHs-R200, 1.5NiLDHs-R200 and 2NiLDHs-R200. As-synthesized 2NiLDHs-Dr was the superlative catalyst when coupling different aryl halides with different boronic acids derivatives. Deep investigation of all catalysts was done using different techniques such as inductively coupled plasma optical emission spectroscopy (ICP-OES), x-ray photoelectron spectroscopy (XPS), powder x-ray diffraction (XRD), thermogravimetric analyses (TGA), Fourier transfer infrared (FTIR), scanning electron microscope (SEM) connected with energy dispersive x-ray (EDX) and N_2-physisorption at -196 °C. The results attained verified that α-$Ni(OH)_2$ was fashioned for 2NiLDHs-Dr catalyst and the enclosure of nickel ions in the cationic sheet of layered structure were responsible for the fascinating catalytic efficacy rather than the basic nature of material. The Ni-containing LDHs catalysts encourage forthcoming studies in Pd-free catalyzed C-C coupling reactions.

Keywords: Suzuki coupling reaction; Layered double hydroxides; Solid base catalyst, Microwave irradiation.

1. Introduction

Suzuki-Miyaura coupling reaction includes coupling an aromatic hydrocarbon or ethenyl boronic acid or boronic ester with aryl or ethenyl halides in the presence of a base (Scheme 1). It is generally carried out at temperatures range of 60 - 120 °C with generally excellent yield results when palladium was used in homogenous catalyzed system which is considered the most powerful and most applicable method for carbon - carbon bond formation. It is the backbone for biaryl and heterobiaryl compounds that are important in natural products, dyes, liquid crystals and dendrimers formation, ligands for catalysis and organic light-emitting polymers synthesis, pharmaceuticals and agrochemicals industries.



Scheme 1. General scheme for Suzuki-Miyaura reaction.

Furthermore, homogeneous catalysis is not preferably used due to the lack of reuse, the problem catalyst recycling leads to loss of noble metals and metals residual in the products and the purification becomes necessarily required especially when it use in pharmaceutical production. Therefore, there is needing to remove residual metals impurities in products and losing the expensive metals by palladium substitution, partially or totally, with cheap metals like non-noble metals. Also, heterogeneous catalysis is a promising option because it offers several advantages like high catalyst stability, the catalyst is easily removal from mixture of the reaction by simple filtration and reusing the catalyst many times with a frequent activity loss minimum.

Different types of transition metals were used to catalyze Suzuki coupling reaction. Volpe and co-workers [1] reported that a series of ceria catalysts used in Suzuki–Miyaura cross-coupling reaction between 4-iodotoluene and phenylboronic acid. The reaction was carried out at 150 °C, under N_2 atmosphere and DMF as the solvent which resulting in corresponding biphenyl in high selectivity percentage (Table 1, Entry 1).

Gold nanoparticles – graphene hybrids have been prepared by Li and his group [2]. They reported that the Au/graphene catalyst can act as efficient catalysts for the Suzuki reaction in water under aerobic conditions. They found the catalytic activity of gold nanoparticles – graphene hybrids which expressed as a value of selectivity was influenced by the size of the gold nanoparticles (Table 1, Entries 2,3).

Kim and co-workers [3] demonstrated that the Pt single atoms on thiolated multi-walled carbon nanotubes (Pt-S-MWNT) has a remarkably high activity and recyclability for the ligand-free Suzuki coupling reaction. Pt-S-MWNT showed a high activity in coupling process of iodoarene with methyl phenylboronic acid in presence of Cs_2CO_3 as base at 70 °C after 24 h (Table 1, Entry 4).

In 2008, Mao and co-workers developed an effective catalytic system from copper powder with K_2CO_3 as the base that was extremely effective catalyst for Suzukie Miyaura coupling reaction performed in polyethylene glycol 400 (PEG-400), which afforded almost quantitative coupling products of aryl iodides [4]. In the case of aryl bromides or chlorides, the coupling products could be obtained with moderate to good yields when using iodine as additive (Table 1, Entry 5).

Lipshutz and co-workers have used nickel on charcoal (Ni/C) [5] that worked as an effective heterogeneous catalyst for coupling chloroarenes and phenylboronic acids in presence triphenylphosphine ligand (PPh3) to give biphenyl products in good yields (Table 1, Entry 6). It was noticed little nickel was released from the charcoal during the coupling process, as established by ICP experiments. In 2008, the researchers group have reported a nickel-on-graphite (Ni/C_g) [6], as a safe and especially inexpensive material, which used to catalyze cross couplings with various boronic acids and aryl halides by bath heating or under Microwave (MW) conditions (Table 1, Entries 7, 8).

Wang and co-workers [7] have developed an efficient, simple and economic catalyst system for the Suzuki–Miyaura reaction of aryl iodides and bromides with aryl boronic acid without the need of phosphine ligands by using nickel–metal colloid supported on TBAB (tetra-n-butylammonium bromide). $Ni^{(0)}$/TBAB exhibited high activity for aryl bromides and iodides. In case of less reactive aryl chlorides, the phosphine ligand was required for more efficient reaction (Table 1, Entry 9).

In 2017, Willand and co-workers [8] improved procedure in the Suzuki Miyaura cross coupling reaction between N-BOC protected 3-iodoazetidine and a large variety of heteroaryl and arylboronic acids. The reaction was catalyzed by Nickel in the presence of NaHMDS as strong base and is promoted by microwave heating (Table 1, Entry 10). Furthermore, the N-protected azetidine can be further functionalized after deprotection.

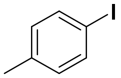
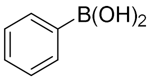
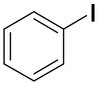
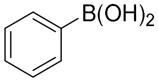
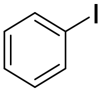
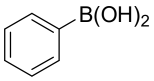
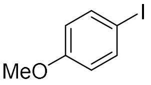
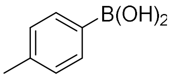
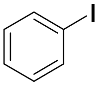
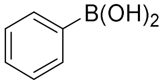
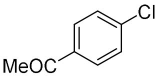
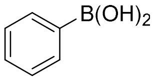
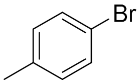
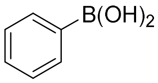
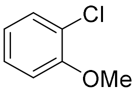
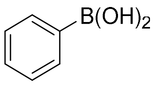
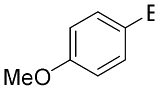
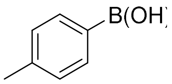
Guo and his co-workers [9] studied the effect of elevated pressure in the liquid phase on the Suzuki-Miyaura cross-coupling of aryl halides and aryl boronic acids using cheaper Fe(III), Co(II), and Ni(II) metal salts as catalysts. The yields were improved (Table 1, Entries 11-13) at 15 kbar but this procedure was disgraced with high loading of catalysts.

In 2003, Leadbeater and Marco [10] claimed that the Suzuki Miyaura coupling of boronic acids and aryl halides is possible without the need for a transition-metal catalyst. This methodology offers significant advantages since the use of transition metals leads to the generation of waste and has a number of hazards associated with it especially if this methodology used the water as solvent. The methodology was applicable to a wide range of aryl bromide substrates (Table 1, Entry 14), with good yields being obtained in the reaction with phenylboronic acid in presence of tetrabutylammonium bromide (TBAB) and Na_2CO_3 as base. The methodology has been proven that the reaction was indeed metal-free by using new glassware, apparatus, and reagents and analyzed the entire crude product mixture for palladium and other metals content. They found that there was no palladium down to below 0.1 ppm. Also, they found by using inductively coupled plasma atomic absorption (ICP-AA) spectroscopy none of the other metals were present in the product mixture in concentrations above the level of detection of the apparatus of 0.5 –1 ppm.

After one year, Leadbeater and co-workers [11] reported that when the Suzuki reaction is performed without the addition of a transition-metal catalyst but using commercially sodium carbonate as a base, palladium contaminants down to a level of 0.05 ppm are responsible for the formation of the biaryls (Table 1, Entries 15-17).

In order to investigate the possibility of catalyst-free Suzuki reaction, Yan and his co-workers reported in 2006 a novel and efficient method for coupling reaction of sodium tetraphenylborate with iodonium salts in acidic water [12]. This method was simple, mild, high-yielding, and more environmentally benign (Table 1, Entry 18). In the same year, Yan and his co-workers deeply investigated and they came to develop a greener procedure for catalyst- and solvent-free Suzuki coupling reaction of sodium tetraphenylborate with hypervalent iodonium salts that was carried out under microwave irradiation in the absence of a base [13]. This procedure provided a fast, simple and efficient method for preparation of biaryls with mild reaction conditions and good yields were obtained (Table 1, Entry 19).

Table 1. Survey on different catalysts for Suzuki coupling reaction.

	Aryl halide	Boronic acid direvative	Cat.	Base	Solvent	Conditions	t (h)	Yield (%)
1			HSA-CeO_2	K_2CO_3	DMF	150 °C, 0.1 MPa	3	89 Selectivity
2			Au–graphene (2-3 nm)	NaOH	H_2O	100 °C	4	85.8 Selectivity
3			Au–graphene (7.5 nm)	NaOH	H_2O	100 °C	4	11.2 Selectivity
4			Pt-S-MWNT	Cs_2CO_3	THF	70 °C	24	99.5
5			$Cu^{(0)}$	K_2CO_3	PEG-400	110 °C	12	99
6			Ni/C	K_3PO_4, LiBr	Dioxane	135 °C	18	92
7			Ni/C_g	K_3PO_4, LiBr	Dioxane	135 °C	9	87
8			Ni/C_g	K_3PO_4, LiBr	Dioxane	MW, 180 °C	42 min	87
9			$Ni^{(0)}$/ TBAB	Na_2CO_3	EtOH	80 °C	6	95

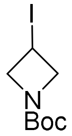
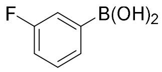
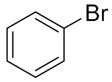
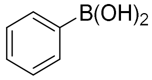
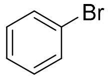
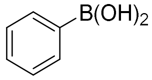
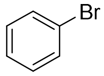
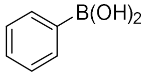
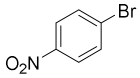
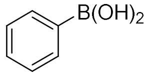
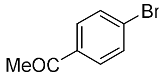
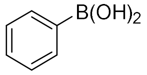
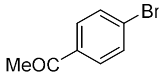
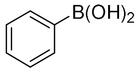
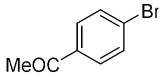
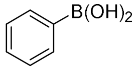
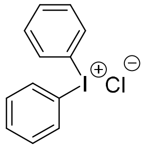
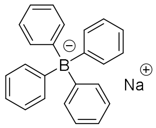
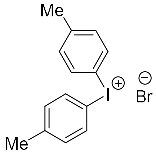
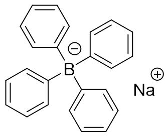
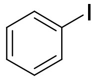
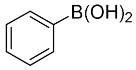
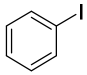
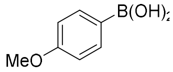
10			NiI_2	NaHMDS	iPrOH	MW, 80 °C	30 min	82
11			$NiCl_2$/ Ligand	KF/ KOH	THF	100 °C, 15 kbar	48	99

Table 1. *Cont.*

12			$CoCl_2$/ Ligand	KF/ KOH	THF	100 °C, 15 kbar	48	99
13			$FeCl_3$/ Ligand	KF/ KOH	THF	100, 15 kbar	48	97
14			Catalyst- free	Na_2CO_3, TBAB	H_2O	MW, 150 °C	5 min	99
15			Catalyst- free	Na_2CO_3, TBAB	H_2O	MW, 150 °C	5 min	98
16			Pd, 0.25 ppm	Na_2CO_3, TBAB	H_2O	MW, 150 °C	5 min	94
17			Pd, 0.25 ppm	K_2CO_3, TBAB	H_2O	MW, 150 °C	5 min	57
18			Catalyst- free	Base-free	H_2O / p-TsOH	50 °C	0.5	95
19			Catalyst- free	Base-free	Solvent-free	MW	3 min	95
20			LDH-Pt$^{(0)}$	K_3PO_4	Dioxane/ H_2O	100 °C	12	90
21			LDH-Rh$^{(0)}$	NaOAc	DME/ H_2O	100 °C	12-18	96

In period of ten years, a class of anionic clay is called layered double hydroxides (LDHs) or hydrotalcite (HTs) has attracted considerable interest from industrial and academic fields. LDHs are lamellar mixed hydroxides which have structured-layer and have hydroxide and carbonate ions intercalated in common, which usually restrict C-C coupling reactions. Mixed metal oxide could be obtained from these materials when subjected to thermal treatment and they can become a promising candidate for C-C coupling reactions. Furthermore, the separation is easier than before after the end of reaction, that way makes LDHs an important alternative to homogeneous catalysts because of the potential of its recycling [14]. Mg-Al-layered double hydroxide (LDH) has been used successfully as solid support for Suzuki reaction by Choudary and his co-workers. In the absence of ligand, LDH-Pt$^{(0)}$ [15] and LDH-Rh$^{(0)}$ [16] catalysts were prepared and utilized for Suzuki coupling of different aryl halides with a large number of arylboronic acids to give the corresponding biaryls in good to excellent yields (Table 1, Entries 20, 21). Carbon – carbon bond formation was investigated by our group using LDHs alone [17, 18] and supported on other materials such carbon nanotubes [19] and graphene oxides [20].

In this study we will present a simple generic protocol for the preparation of NiLDHs for Suzuki -Miyaura reaction. This has proven successful for biaryl products derived from different aryl halides and aryl boronic acids using microwave irradiation methodology. Herein we report the results of our investigation which showed that NiLDHs behave as a very efficient catalyst of the Suzuki reaction in a Pd and ligands-free.

Extensive survey about LDHs-containing nickel using as catalyst in Suzuki coupling reaction in absence of ligands has been done and to our knowledge no publications have been found.

2. Results

2.1. Elemental Chemical analysis (ICP-OES)

ICP analysis of NiLDHs-Dr samples was done to determine their chemical composition. The analysis showed that the MII/MIII molar ratio in the solid form of 1NiLDHs-Dr, 1.5NiLDHs-Dr and 2NiLDHs-Dr were 2.11, 2.17 and 2.28 respectively (Figure 1, Table 2). The molar ratios of NiLDHs-Dr samples indicate the efficiency of the preparation method because they are almost equal to the minimal molar composition of the as-synthesized Ni+Mg/Al molar ratio of 2 in the precipitate that prove also that LDHs phases are pure due to their stoichiometries formation is in the range $0.20 < x < 0.33$, i.e. MII/MIII ratios in the range 2–4 [21].

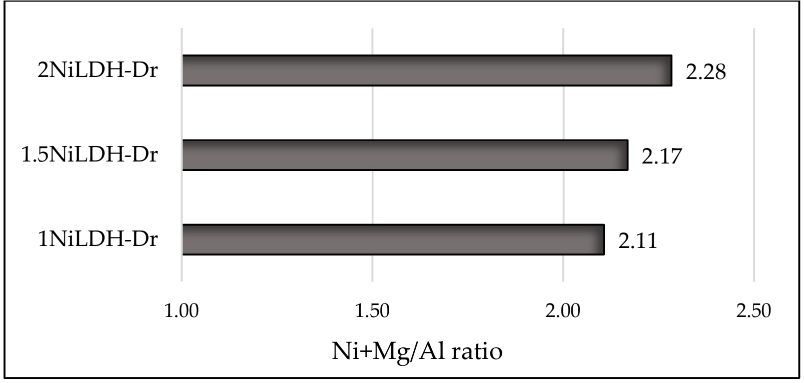


Figure 1. Representative graph for chemical analysis of ratio for NiLDHs-Dr.

2.2. X-ray photoelectron microscopy (XPS)

XPS investigation was conducted to gain further insight into the location and nature of the Ni species present in NiLDHs-Dr samples. Deconvoluted Ni 2p3/2 X-ray photoelectron spectra for 1NiLDHs-Dr, 1.5NiLDHs-Dr and 2NiLDHs-Dr samples are shown in Figure 2. All XPS spectra of samples have the same Ni species nature. Figure 2 shows the Ni 2p3/2 XPS spectrum from $Ni(OH)_2$ with the two obvious satellite intensities fit by broad peaks with binding energy at main line 852.0 eV (Table 2). The peaks have been deconvoluted into two contributions with binding energies at 855.8 eV and 861.4 eV respectively [22]. The first peak can be assigned to isolated Ni^{2+} species. It is interesting to note that the 2NiLDHs-Dr sample contained the highest amount of isolated Ni^{2+} species (97.7 %).

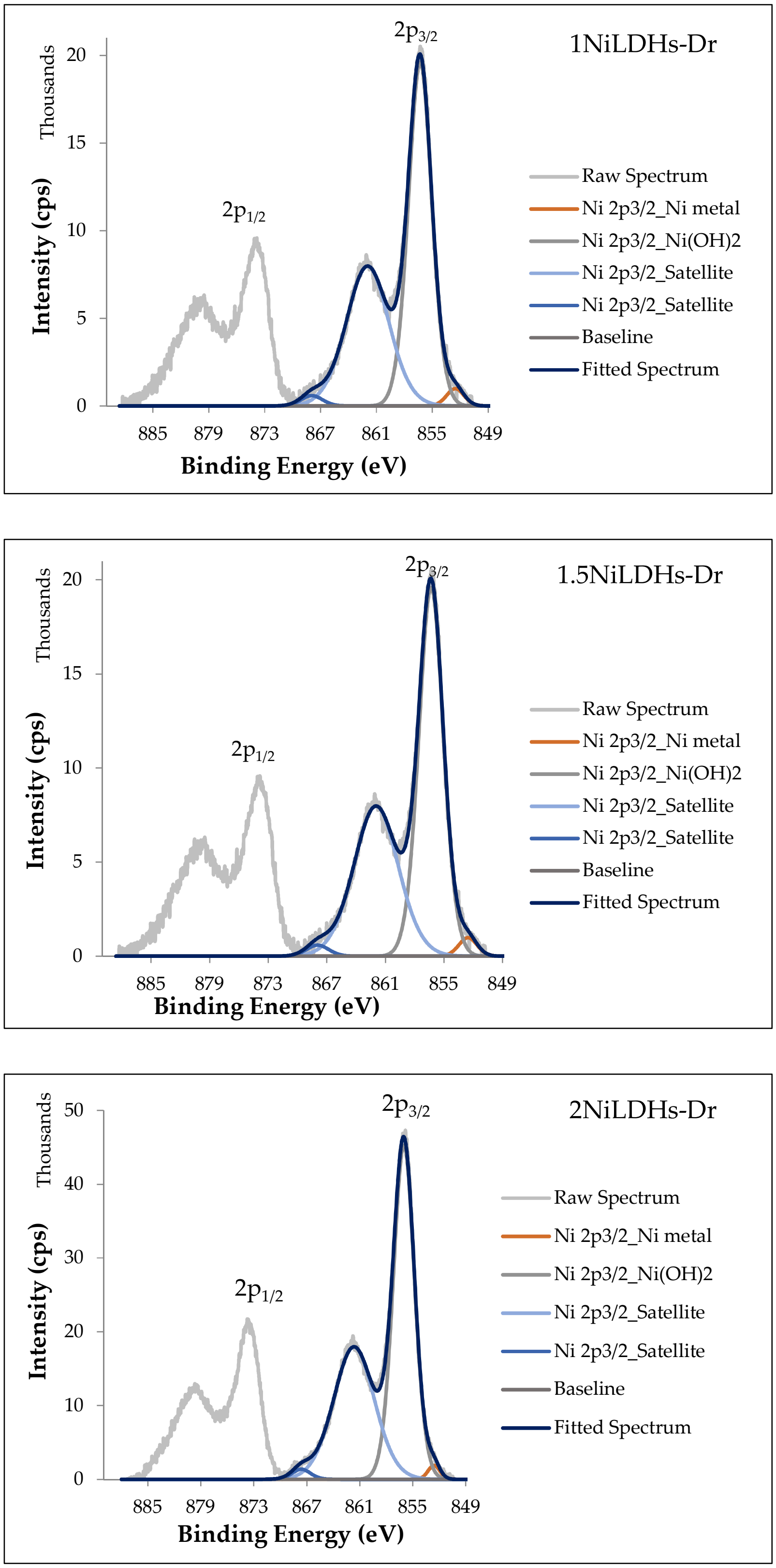


Figure 2. Deconvoluted Ni 2p3/2 XPS spectra for NiLDHs-Dr samples.

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2.3. Basic properties of NiLDHs-Dr

The strength of basic sites and their amounts were measured using acid–base titration and the Hammett indicator methods. Since the catalysts are considered have basic properties, the number of moles of basic sites were calculated and it was found in order of 1NiLDHs-Dr > 1.5NiLDHs-Dr > 2NiLDHs-Dr. Where the base strength of 1NiLDHs-Dr, 1.5NiLDHs-Dr and 2NiLDHs-Dr are found in range of pK_{BH+} = 11.1 – 12.7 (Table 7). There is no change in colors of catalysts filtrate which mean there are no leachable basicity from all the catalysts. The reduction in basic sites upon substitution of Mg^{2+} ions by Ni^{2+} ions in the NiLDHs samples could be credited to the departure of Lewis basic sites or formation of new phase structure of α-$Ni(OH)_2$, which is less basic than brucite β-$Ni(OH)_2$ phase [23].

Table 2. Elemental chemical, XPS data and basic properties of NiLDHs-Dr samples.

	Ni+Mg/Al		**Basic strength mmol/g**	**Ni^{2+} isolated species sample**	
	Solution	**Soild**		**Binding energy (eV)**	**%**
1NiLDH-Dr	2.0	2.11	0.333	856.1	96.4
1.5NiLDH-Dr	2.0	2.17	0.173	855.6	96.5
2NiLDH-Dr	2.0	2.28	0.073	855.8	97.7

2.4. X-ray diffraction (XRD)

X-ray diffraction pattern of prepared NiLDHs-Dr are shown in Figure 3. It is sharp high intensity signals at low 2θ values and weak signals at high 2θ values. It is signing that LDH structure was successfully attained, where the sample has the three characteristic XRD reflections of LDH. The reflection peaks are presented in Table 3. Full width at half maximum (FWHM) of the most intense peak was used to deduce the size (D) of crystallite/ particle using Debye-Scherrer's equation: $D = 0.9 \lambda / \beta \cos \theta$. The crystallite size of different NiLDHs-Dr are 40.67, 50.92 and 67.73 nm for 1NiLDHs-Dr, 1.5NiLDHs-Dr and 2NiLDHs-Dr, respectively. The crystallite sizes of NiLDHs-Dr increase with the increase of Ni content. Usually, Ni could be represented either in β-$Ni(OH)_2$ (strictly packed brucite type layers in which Ni^{2+} is in the middle of hydroxyl octahedral structure), and α-$Ni(OH)_2$ (NiLDHs) of foremost attention due to its tunable assembly (oxidation state, interlayer species, interlayer distance) [21, 24]. The obvious growth in the crystallite size and the intensity of diffraction pattern of the layered structure of the 2NiLDHs-Dr (of high Ni content) without substantial shift in the peak position endorse the α-$Ni(OH)_2$ creation.

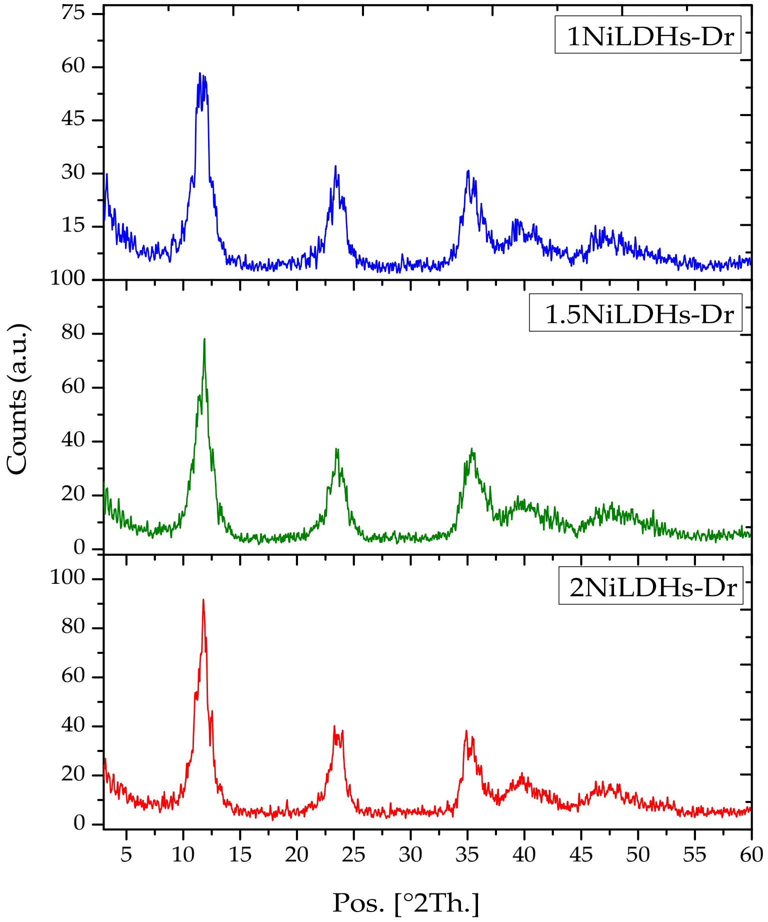

Figure 3. XRD patterns of different NiLDHs-Dr.

Table 3. XRD data for different NiLDHs-Dr

1NiLDHs-Dr			**1.5NiLDHs-Dr**			**2NiLDHs-Dr**		
Pos. [°2Th.]	d-spacing [Å]	Crystallite Size [nm]	Pos. [°2Th.]	d-spacing [Å]	Crystallite Size [nm]	Pos. [°2Th.]	d-spacing [Å]	Crystallite Size [nm]
11.86	7.459		12.08	7.326		11.85	7.471	
23.91	3.722	40.67	23.47	3.791	50.92	23.47	3.791	67.73
34.79	2.579		35.02	2.562		35.44	2.533	

2.5. Thermogravimetric analysis (TGA)

Thermogravimetric analysis of NiLDHs-Dr are shown in Figure 4. The thermograms of 1NiLDHs-Dr, 1.5NiLDHs-Dr and 2NiLDHs-Dr were analyzed to obtain information about percentage weight loss at different temperatures. The results of these analyses are presented in Table 4. In the 1NiLDHs-Dr and 2NiLDHs-Dr thermograms, they show five stages of weight loss while 1.5NiLDHs-Dr shows only four stages. The analysis of all stages could be put into three main categories. First range of weight loss (37-110 °C) is attributed to the loss of water molecules at the surface by desorption process and the dehydration of the sample. The second range of weight loss (180 - 220 °C) which is attributed to loss interlayer water molecules. At the third range of weight loss (250 – 350 °C) which is attributed to the removal of OH^- groups and decarbonation of carbonate anions present in the interlayer space of LDHs that leading to the formation of metal oxides [25].

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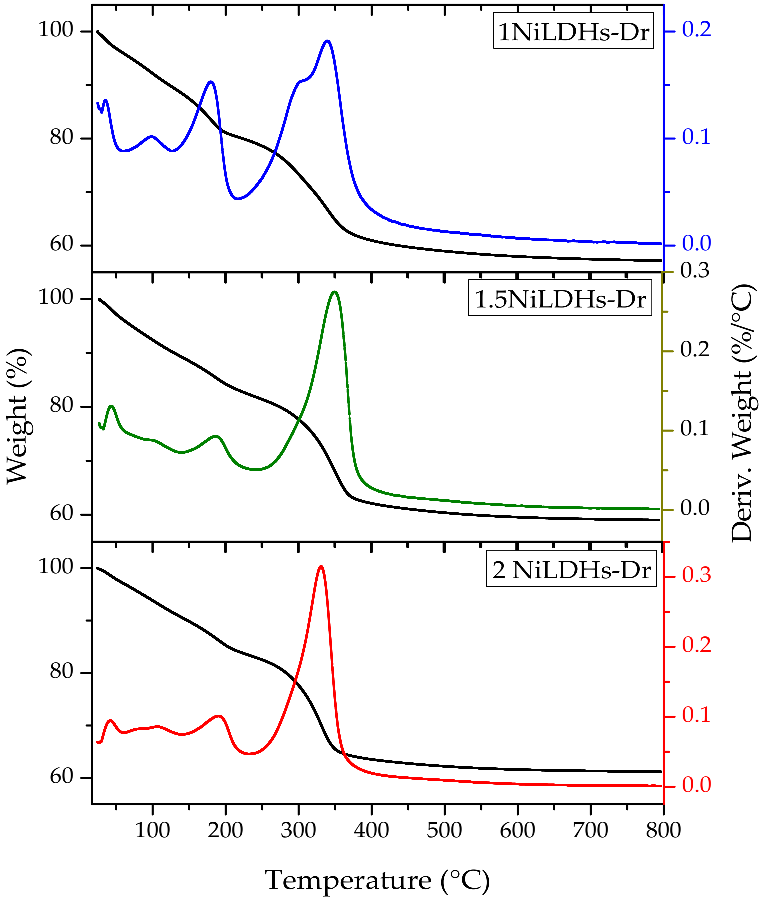

Figure 4. TGA of NiLDHs-Dr.

Table 4. TGA data for NiLDHs-Dr samples.

	Temperature ℃ / Weight loss %		
Weight loss steps	**1NiLDHs-Dr**	**1.5NiLDHs-Dr**	**2NiLDHs-Dr**
1	36.7 / 1.7	44.8 / 2.1	40.6 / 1.3
2	98.3 / 6	100.6 / 5.5	81.0 / 3.3
3	180.9 / 8.9	185.2 / 6.8	107.0 / 2.2
4	300.8 / 10.2	349.9 / 17.3	189.9 / 6.9
5	340.2 / 6.6		331.2 / 16.3

2.6. Fourier-transform infrared spectroscopy (FT-IR)

Figure 5 shows the FTIR spectra of 1NiLDHs-Dr, 1.5NiLDHs-Dr and 2NiLDHs-Dr samples which they have similar IR bands. The signal at 3400 cm^{-1} is the O-H stretching band, arising from interlayer water molecules and metal-hydroxyl groups [26]. The small band centered around 1600 cm^{-1} can be ascribed to the bending vibration of water. Additionally, the band at 1350 cm^{-1} can be assigned to the vibration of interlayer CO_3^{2-} and NO_3^- anions. The broad peak at 630 cm^{-1} can be assigned to the M–O, O–M–O, and M–O–M (M =Al, Mg and Ni) vibrations.

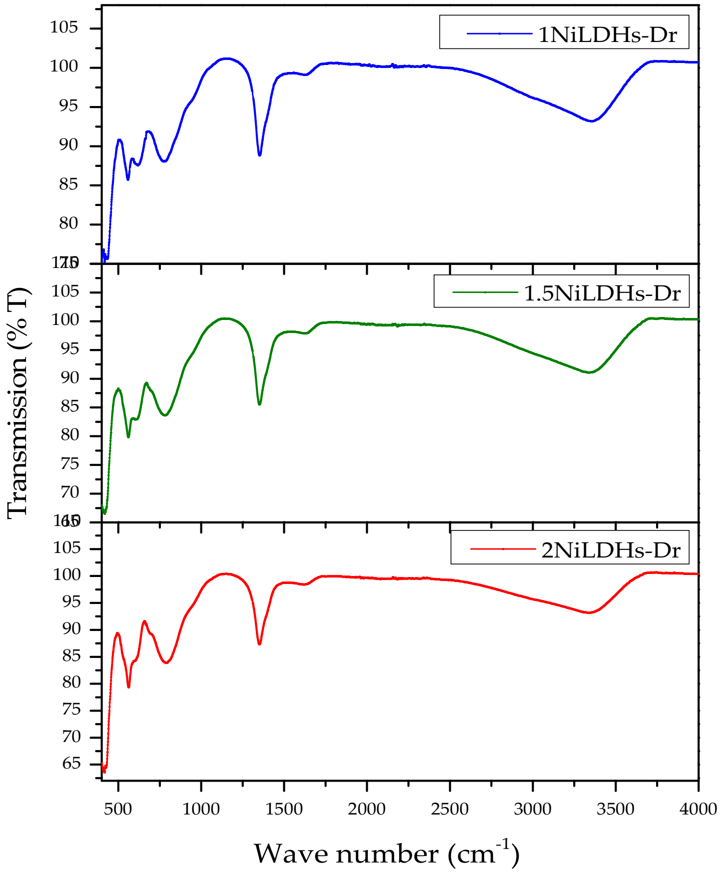

Figure 5. FTIR spectra of NiLDHs-Dr samples.

2.7. N_2 physisorption

Figure 6 show that nitrogen adsorption/desorption isotherm of all samples are type IV according to IUPAC classification [27]. The hysteresis loops in the isotherms indicate the mesoporous nature of NiLDHs-Dr. Hysteresis shapes are attributed to the presence of cylindrical, slit and blind hole pores according to Sing et al [28]. BET surface area for NiLDHs-Dr catalysts have no obvious trend (Table 5). The pore volume and average pore radius decline with growing of Ni content. The formation of α-$Ni(OH)_2$ greatly affect the pore nature by possible aggregation.

Table 5. Textural properties of different NiLDHs-Dr from N_2-physisorption.

	BET surface areas (m^2 /g)	Pore volume (cm^3 /g)	Av. Pore radius (Å)	C-constant
1NiLDHs-Dr	68.28	0.14	22.71	14.27
1.5NiLDHs-Dr	57.33	0.09	19.84	10.24
2NiLDHs-Dr	58.03	0.08	18.97	5.95

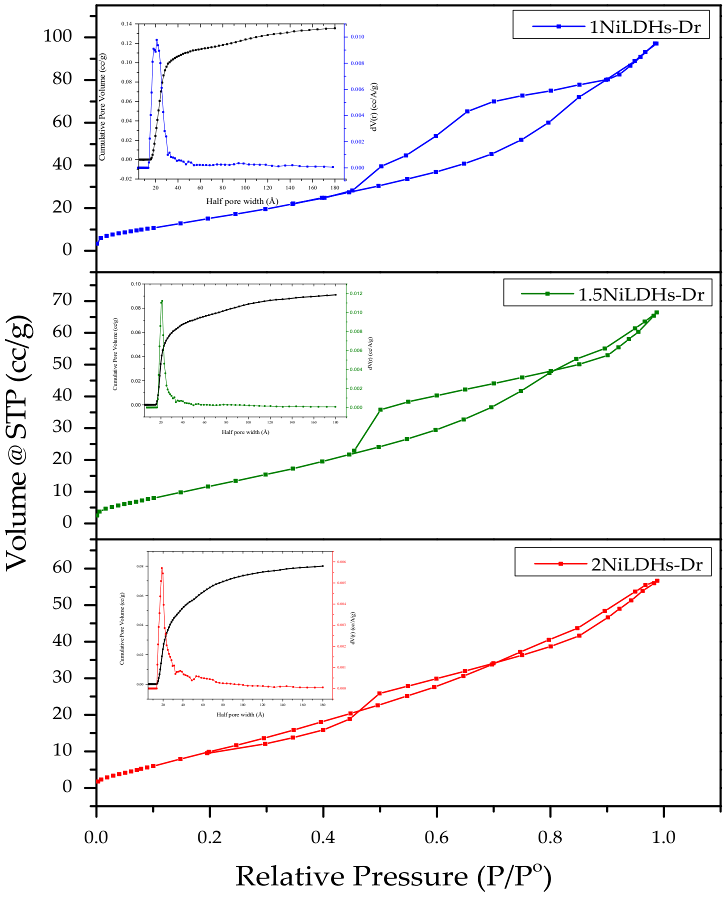

Figure 6. N_2 isotherms and Pore size distribution (inset) patterns of different ratio for NiLDHs-Dr.

2.8. Scanning electron microscopy (SEM-EDX)

The SEM images of NiLDHs-Dr ravel out the morphology which stacked platelets shape. Figure 7 shows that the layered flakes are clearer in 1NiLDHs-Dr than the other Ni- containing materials. It seems that isomorphic substitution of Mg^{2+} ions by Ni^{2+} ions in the cationic sheet and the nucleation of α-$Ni(OH)_2$ phase of relatively larger crystallite size as evidenced by XRD data analysis resulted in the distinct thickness progress of the flakes. 2NiLDHs-Dr, of high Ni-content disclosed accumulated gloomy like stacked sheets as a result of α-$Ni(OH)_2$ foundation.

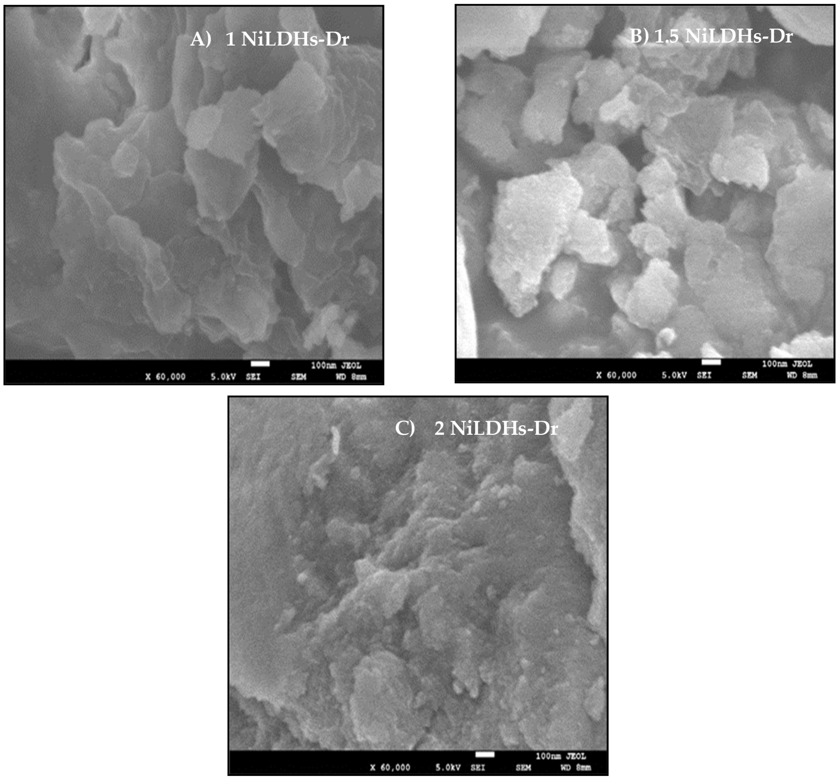

Figure 7. SEM images of all the examined NiLDHs-Dr catalysts.

2.10. Catalytic activity

The activity of different forms of NiLDHs catalysts was tested in the Suzuki coupling reaction, which has widely used for the synthesis of biaryl and heterobiaryl compounds [29]. Suzuki coupling reaction of aryl iodides and bromides carried out with high yields mostly in the presence of a good catalyst, base and solvent. The discovery of dedicated tool, catalyst composition, and other reaction conditions to achieve the highest possible product's yield, for the Suzuki coupling reaction should be extensively studied. In the present work Suzuki reaction was performed using different chemical compositions of reduced and dried forms of NiLDHs catalysts in presence of K_3PO_4 as base [15] and dioxane – water (5:1) as solvents [30] under microwave irradiation (800W) for 15 min. reaction time. It was found that the Suzuki coupling reaction provided the highest % product yield (~35%) using 2NiLDH-Dr in comparison to 2NiLDHs-R200 and the other forms of 1NiLDHs and 1.5NiLDHs catalysts (Figure 8).

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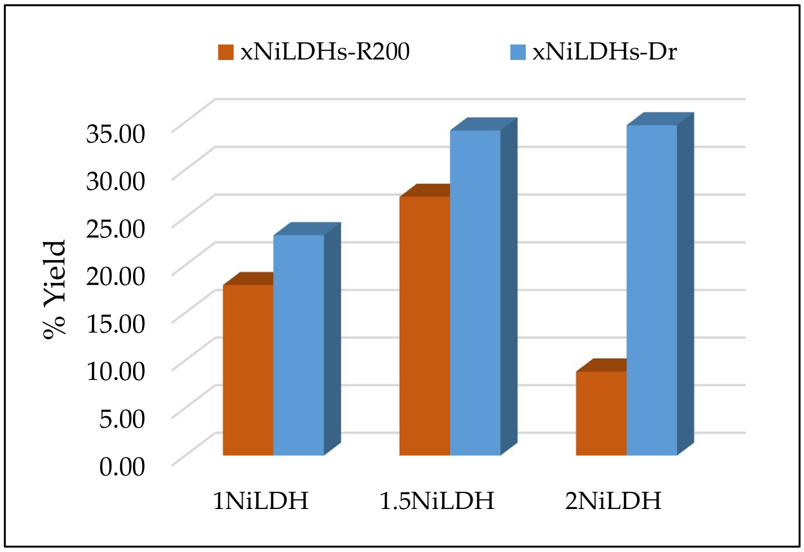

Figure 8. % product yield utilizing different NiLDHs catalyst composition in reduced and dried forms; reaction conditions: 100 mg of catalyst, 1 mmol of iodobenzene, 1.5 mmol of 4-tolylboronic acid, 2 mmol K_3PO_4 and 2 mL of dioxane/H_2O (5:1), 800W, 200°C and 15 min.

In order to investigate the effect of reduction temperature on the possible improvement of catalytic activity, the excellent catalyst (2NiLDHs-Dr) was reduced at 300 and 450 °C prior to be used for Suzuki reaction. Figure 9 revealed that the reduced samples over 400 °C have almost the same activity as 2NiLDHs-Dr when used in coupling of iodobenzene with 4-tolylboronic acid.

Therefore, 2NiLDHs-Dr was the superlative catalyst that selected to explore the optimization conditions for Suzuki coupling reaction. The next parameter has been studied was the reaction time. According to Figure 10, 60 min was perfect time for coupling iodobenzene with 4-tolylboronic acid that gave almost 100 % of 4-methyl biphenyl. Studying the effect of catalyst's mass at 50, 100 and 150 mg showed that there is no significant difference between 50 and 150 mg, they depicted almost the same performance (Figure 11).

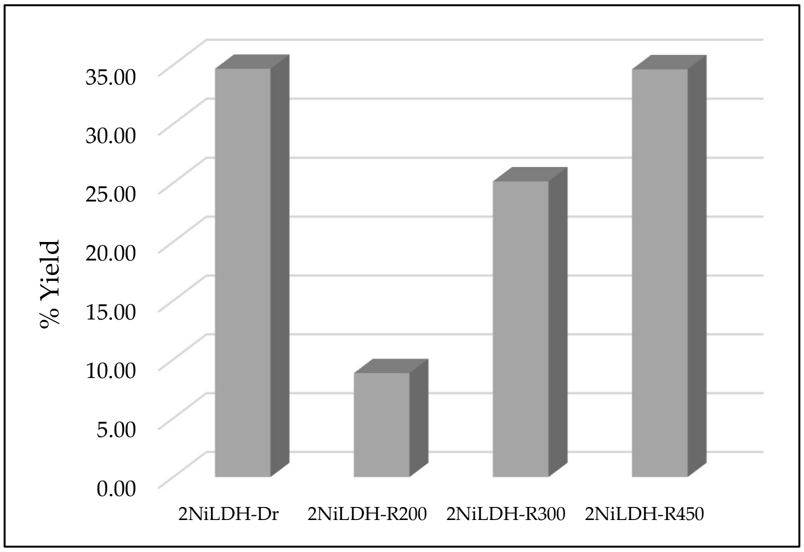

Figure 9. % product yield utilizing reduced 2NiLDHs catalyst at different temperatures; reaction conditions: 100 mg of catalyst, 1 mmol of iodobenzene, 1.5 mmol of 4-tolylboronic acid, 2 mmol K_3PO_4 and 2 mL of dioxane/H_2O (5:1), 800W, 200°C and 15 min.

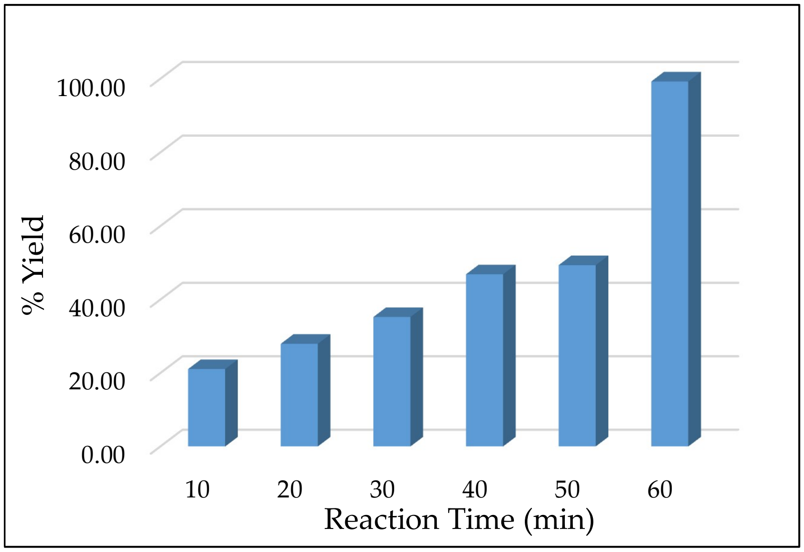

Figure 10. Effect of reaction time on the catalytic performance of 2NiLDHs-Dr; reaction conditions: 50 mg of catalyst, 1 mmol of iodobenzene, 1.5 mmol of 4-tolylboronic acid, 2 mmol K_3PO_4 and 2 mL of dioxane/H_2O (5:1), 800W and 200°C.

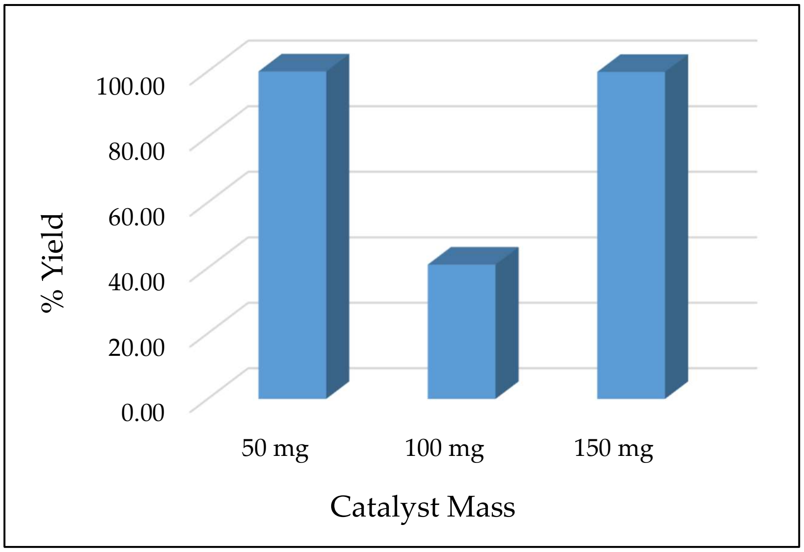

Figure 11. Effect of mass of 2NiLDHs-Dr catalyst on the product's %yield; reaction conditions: 1 mmol of iodobenzene, 1.5 mmol of 4-tolylboronic acid, 2 mmol K_3PO_4 and 2 mL of dioxane/H_2O (5:1), 800W, 200°C and 60 min.

Figure 12 and Table 6 show that the 2NiLDHs-Dr catalyst displays a high percentage yield for 4-tolyl boronic acid (entry 1,2 and 3,4), an increase by 6.7 and 2.4-fold when compared to the results obtained for phenyl boronic acid with iodobenzene and bromobenzene, respectively [31]. Opposite trend was noticed with chlorobenzene, % yield for 4-tolyl boronic acid (entry 5,6) decreased by 1.7-fold compared to results obtained for phenyl boronic acid [30, 32]. In previous studies, coupling iodobenzene with phenyl boronic acid showed high percentage yield than coupling with 4-tolyl boronic acid [16]. While some studies in literature [15] agreed with our results. In case of bromobenzene, it showed high percentage yield with 4-tolyl boronic acid but Choudary's group [15] showed that phenyl boronic acid has better yield than 4-tolyl boronic acid. Coupling with 4-tolyl boronic acid shows the order Ar-I > Ar-Br > Ar-Cl which agreed with other studies [3, 33, 34].

Table 6. Different reactants that were used in Suzuki reaction utilizing 2NiLDHs-Dr catalyst.

Entry	Aryl halide	Boronic acid	Product	% Yield
1				99.98
2				14.94
3				76.35
4				31.63
5				13.42
6				23.47

Reaction conditions: 50 mg of catalyst, 1 mmol of aryl halide, 1.5 mmol of bronic acid, 2 mmol of K_3PO_4, 2 mL of dioxane/H_2O (5:1). Microwave irradiation = 800 W, 200 °C; temperature ramped to that stated and held there for 60 min.

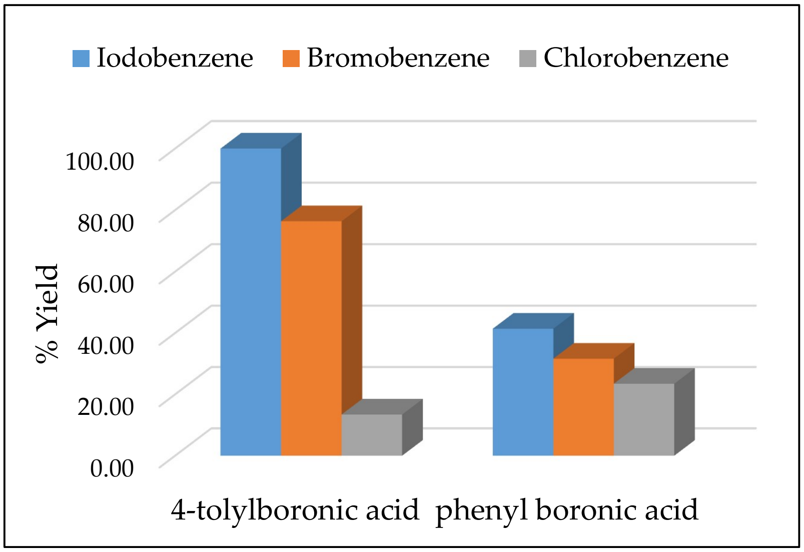

Figure 12. % yield of different products utilizing 2NiLDHs-Dr; reaction conditions:50 mg of catalyst, 1 mmol of iodobenzene, 1.5 mmol of 4-tolylboronic acid, 1.5 mmol of phenylboronic acid, 2 mmol of K_3PO_4, 2 mL of dioxane/H_2O (5:1). Microwave irradiation = 800 W, 200 °C; temperature ramped to that stated and held there for 60 min.

Snice the Suzuki coupling reaction is important in pharmaceutical industries, obtaining the biphenyl compounds with no residual of Ni, or at least not above the legal limit, which is the case in different metals catalyzed Suzuki reaction, the product mixture of Suzuki reaction was analyzed by

ICP to test if there is Ni leaching. The results should be agreed with Permitted Daily Exposure (PDE) of Ni which is 22 ppm parenteral, 6 ppm inhalation and 220 oral [35]. Fortunately, the Ni is not leachable at all (0 ppm) in product mixture which makes 2NiLDHs-Dr catalyst is a sustainable and promising candidate for Suzuki coupling reaction. It seems that the inclusion of Ni ions in the cationic sheet of layered material fix a comfortable octahedral coordination that resist Ni ions depletion.

2.11. Reusability of 2NiLDHs-Dr

The potential of reusability of a catalyst is an important key in catalytic activity assessment. Therefore, coupling reaction of iodobenzene with 4-methyl tolylboronic acid was repeated four times using the regenerated 2NiLDHs-Dr. The catalyst was removed after the reaction under vacuum filtration using membrane filter 0.45 µm to prevent losing of catalyst mass, washed with water to dissolve the remain K_3PO_4 then with ethanol to dissolved any organic contaminations after that dried overnight at 80 °C. The recovered catalyst is reused several times under the same optimum conditions that reached to in catalytic activity test section. The drop observed in the catalytic activity of 2NiLDHs-Dr catalyst from the 2nd time of being used which could be attributed to temporary poisoning by organic contaminants, the mass losing of the catalyst and/or to the change in the crystal structure of the catalyst under the operating conditions. Checking for mass losing of 2NiLDHs-Dr, Ni existence in the filtrate was determined by ICP-OES and it was found that 1.7±0.05 ppm (2.9×10^{-5} mol) from reused 2NiLDHs-Dr losing in reaction mixture in every cycle which was not happened with fresh catalyst but agreed with PDE [35]. The Ni leaching after reusing the catalyst could be attributed to washing procedure or to presence the K_3PO_4 and tolylboronic acid that might induced the Ni leaching which was proved before by Fang and his co-workers in 2011 in case of Pd leaching [36].

FT-IR spectrum proved presence of contaminated organic moieties that adsorbed on surface of reused 2NiLDHs-Dr (Figure 13) where the absorption band at 1647 cm-1 indicated to C= C of benzene ring. Also, FT-IR showed that the crystal structure has been changed by the appeared band at 3642 cm-1 that indicated to OH stretching of Ni(OH)2 and by disappeared band at 1356 cm-1 and 788 cm-1 which indicated to CO32- and M-O-M, respectively. The decay in catalytic activity indicate that the activity of this catalyst attributed to Ni more than to basicity nature of the catalyst.

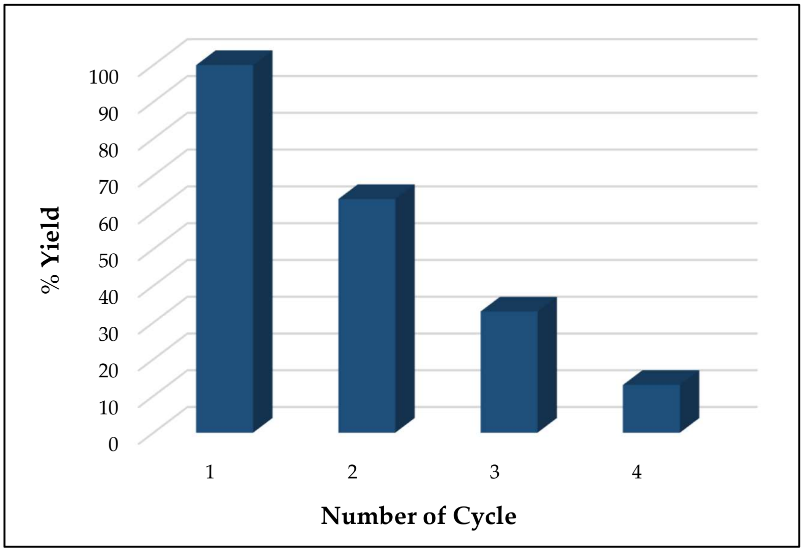

Figure 12. Reusability of 2NiLDHs-Dr catalyst, reaction conditions in every cycle: 1 mmol of iodobenzene, 1.5 mmol of 4-tolylboronic acid, 2 mmol K_3PO_4 and 2 mL of dioxane/H_2O (5:1), 800W, 200°C and 60 min.

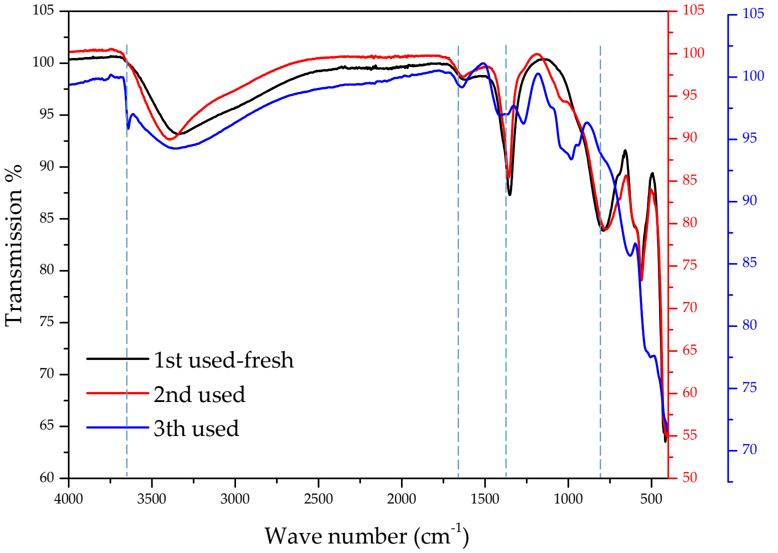

Figure 13. FT-IR spectra of fresh and reused 2NiLDHs-Dr catalyst.

3. Experimental Details

3.1. Materials

$Al(NO_3)_3$. $9H_2O$, $Ni(NO_3)_2.6H_2O$ and Iodobenzene were purchased from Fluka. $Mg(NO_3)_2.6H_2O$ was purchased from Koch-Light. Chlorobenzene and Na_2CO_3 were purchased from BDH, England. Bromobenzene was purchased from MCIB, USA. NaOH was purchased from Riedel-de Haën. 4-Tolylboronic acid, 97% was purchased from Acros Organics. Pre-coated TLC sheets silica gel 60 F-254 from Merck to monitor the reaction process.

3.2. Preparation of NiLDHs

NiLDHs with molar ratio 1:1:1, 1:0.5:1.5 and 1:0:2 of Al: Mg: Ni (with constant molar ratio of $M^{(II)}/M^{(III)}$ by 2:1) synthesized using co-precipitation method. At 50 °C in sonicated bath, mixture of $Al(NO_3)_3$, $Mg(NO_3)_2$ and $Ni(NO_3)_2$ as a SLOUTION A was added simultaneously with a mixture of 1.0 mol of NaOH and 0.5 mol of Na_2CO_3 as a SOLUTION B in a beaker contained reservoir solution of 0.02 M NaOH. The mixture of prepared NiLDHs mixed by mechanical stirrer (Figure 12).

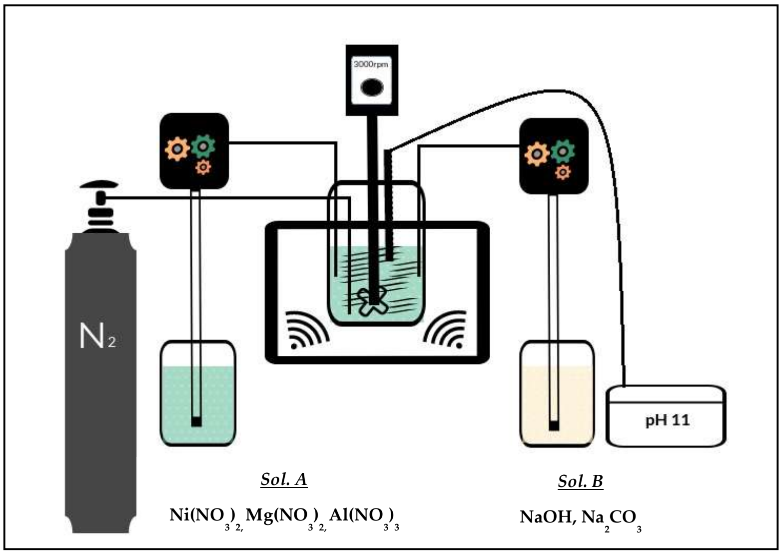

Figure 12. Schematic drawing of the co-precipitation for NiLDHs-Dr.

pH was fixed at 11 by controlling the flow rate of solutions A and B. After the end of precipitation process, the mixture was washed until pH reached to 7 or showed no Na^+ ions were contained by ICP-AES. Then, the mixture was filtered, dried in oven at 80 °C for 20 hours and it was coded as 1NiLDHs-Dr, 1.5NiLDHs-Dr and 2NiLDHs-Dr depending to anticipated molar content of Ni.

3.3 Preparation of reduced NiLDHs

Hydrogen reduction of NiLDHs-Dr for different chemical compositions at temperature 200 °C were carried out in a U-shaped quartz reactor. The reduction of NiLDHs-Dr was occurred in 5% H_2 / N_2 atmosphere with flow 90 ml/min. for 3h using CHEMBET 3000, Quantachrome, USA. After reduction, the samples coded as 1NiLDHs-R200, 1.5NiLDHs-R200 and 2NiLDHs-R200. The chemical composition of 2NiLDHs reduced also under the same previous atmosphere and conditions at different temperature - 300 and 450 °C - and coded as 2NiLDHs-R300 and 2NiLDHs-R450.

3.4. Measurements and Characterization

Determination of strength of basic sites in deferent ratio NiLDHs was done qualitatively by Hammett indicators [37]. 25 mg of NiLDHs was shaking with 1 mL of Hammett indicator solution 0.1 % in methanol and left to equilibrate 2 h. The changing color of NiLDHs was then noted. The base strength is qualitatively determining as stronger than the weakest indicator which exhibits a color change and weaker than the strongest indicator which exhibits no color change. The Hammett indicators that listed in Table 7 were used. To determine the basicity for NiLDHs quantitatively, titration method was used with benzoic acid [37, 38]. 150 mg of NiLDHs was stirred in 2 mL, 0.1 mg/mL of toluene solution of phenolphthalein for 30 min then titrated with 0.01 M of toluene solution of benzoic acid. The total basicity was determined from molarity and the consumed volume of titrant. The leachable basicity [37] was also determined by shaking 500 mg of NiLDHs in 50 mL water for 1h at room temperature. After that, the NiLDHs was separated by centrifuge then 5 mL, 0.1 mg/mL of methanol solution of phenolphthalein was added to the filtrate then was titrated with 0.01 M of methanol solution of benzoic acid.

Inductively Coupled Plasma Optical Emission Spectroscopy (ICP-OES) was performed using PerkinElmer Optima 7000 DV. ICP-OES data were used to determine the molecular formula of the samples. The better selected wavelengths were 309.271 nm for Al, 227.022 nm for Ni and 279.077 nm for Mg.

The X-ray photoelectron spectroscopy (XPS) measurements were carried out by using a SPECS GmbH X-ray photoelectron spectrometer. Prior to analysis, the samples were degassed under vacuum inside the load lock for 16 h. The binding energy of the adventitious carbon (C 1s) line a 284.6 eV was used for calibration, and the positions of other peaks were corrected according to the position of the C 1s signal.

Powder X-ray diffraction (XRD) measurements were carried out using a Bruker diffractometer (Bruker D8 advance target, Karlsruhe, Germany) at room temperature. The patterns were obtained using Cu Kα1 and a monochromator (λ = 1.5405Å) at 40 kV and 40 mA, with 2θ varying between 2° and 80°.X'Pert HighScore Plus software was used to analyze the spectra. The crystallite size of NiLDH was calculated using Scherrer equation:

$$d\ (nm) = \frac{0.9\ \times\ \lambda}{B\ \times Cos(\theta)}$$

where d is the average crystallite size of the NiLDH under investigation, λ is wavelength of the X-ray beam used, 0.9 is the Scherrer constant, B is the full width at half maximum (FWHM) of diffraction peak and θ is the diffraction angle.

Fourier transfer infrared (FTIR) spectroscopy in transmission mode was performed using a PerkinElmer UATR Two FT-IR spectrometer. The measurements were carried out in the wavenumber range 4000 −400 cm^{-1} with 4 cm^{-1} resolution.

Thermogravimetric analysis (TGA) runs were carried out on TA instrument apparatus (model TGA-Q500). In each run 6-10 mg was placed in the TGA pan and heated to 800 °C at a heating rate of 10 °C min^{-1} and an N_2 atmosphere (flow rate of 40 ml min^{-1}).

High resolution field emission (FEG quanta 250) scanning electron microscope (SEM) connected with Energy Dispersive X-Ray (EDX) detector which allows the chemistry of NiLDHs to be investigated on the sub-micron scale.

Texture properties of the prepared samples were determined from nitrogen adsorption/desorption Isotherms measurements at 77 K using a model NOVA3200e automated gas sorption system (Quantachrome, USA). Prior to the measurement, each sample was degassed for 6 h at 200 ◦C. The specific surface area, SBET, was calculated by applying the Brunauer–Emmett–Teller (BET) equation [39]. Pore size distribution over the mesopore range was generated by the Barrett–Joyner–Halenda (BJH) [40] analysis of the desorption branches, and values of the average pore size were calculated.

Gas chromatography analyses were done by using BRUKER SCION 456-GC-MS with BR-1 capillary column (30 m, 0.25 mm ID, 0.25 um).

Table 7. List of Hammett indicators that were used to determine basic sites.

No.	Hammett Indicators	pKa	pH Range	Changing Color	
				Acidic	Basic
1	Thymol blue (First change)	1.5	1.2 – 2.8	Red	Yellow
2	Methyl yellow	3.3	2.9 – 4.0	Red	Yellow
3	Methyl red	5.1	4.2 – 6.2	Red	Yellow
4	Bromothymol blue	7.0	6.0 – 7.6	Yellow	Blue
5	Thymol blue (Second change)	8.9	8.0 – 9.6	Yellow	Blue
6	Phenolphthalein	9.4	8.3 – 10.0	Colorless	Pink
7	Tropaeolin-0	11.9	11.1 – 12.7	Yellow	Orange

3.5. Experimental Procedure for Suzuki reaction

4-tolylboronic acid (1.5 mmol, 204 mg), potassium phosphate (2 mmol, 533 mg), catalyst (50 mg) and 1,4-dioxane/water (5:1, 2 mL) were put in a Teflon vessel. After iodobenzene (1 mmol, 111μL) was added, the vessel was sealed with a Teflon cover and put into the microwave oven (Milestone ETHOS 1). The reaction mixture was rapidly heated to 200 °C by setting the microwave irradiation to 800 W. After the reaction reached 200 °C, taking 10 min, it was held for 60 min. After the reaction mixture was cooled to room temperature, it was washed with Ethanol, filtered by passing through

Celite and dried from water moisture over Mg_2SO_4. Analyzing the filtrate by GC–MS to determine the yield of the desired product using biphenyl as internal standard (1×10^{-2} M in Ethanol).

4. Conclusion

In this study, Ni-layered double hydroxides (NiLDHs) were prepared by co-precipitation method under ultrasonic irradiation. Isomorphic substitution of Mg^{2+} by Ni^{2+} ions was proved by XRD. All the investigated NiLDHs catalysts exhibited capable catalytic activity towards Suzuki carbon-carbon homocoupling reaction. The dried as-synthesized 2NiLDHs-Dr was highly efficient comparing to other synthesized/treated catalysts. The results obtained claimed that the catalytic efficacy was correlated to Ni-content more than the basicity of the catalysts. Different aryl halide and boronic acid derivatives were used in catalytic activity test and coupling iodobenzene with 4-methyl boronic acid gave the highest percent yield. The reusability test of the catalyst showed a pronounced decay in catalytic activity after first use as a result of Ni leaching, loss of catalyst by filtration and active site contamination. Pd-free catalyst with high catalytic efficacy towards Suzuki C-C homocoupling was attained and vital enhancement for better re-usability is currently under investigation.

Physical and spectral data of the titled compounds (Supplementary Materials).
4-methylbiphenyl
1H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.58 (q, 2H), 7.46 – 7.50 (t, 2H), 7.39 – 7.43 (t, 2H), 7.29 – 7.33 (t, 1H), 7.21 – 7.25 (t, 2H), 2.39 (s, 3H)); 13C NMR (400 MHz, $CDCl_3$) δ 141.21, 138.40, 137.05, 129.51, 129.47, 128.74, 127.00, 77.38, 77.07, 76.75, 21.12.

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