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Towards applications of metal–organic frameworks in catalysis: C–H direct activation of benzoxazole with aryl boronic acids using $Ni_2(BDC)_2(DABCO)$ as an efficient heterogeneous catalyst†

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A crystalline porous metal–organic framework $Ni_2(BDC)_2(DABCO)$ was synthesized and characterized by X-ray powder diffraction (XRD), scanning electron microscopy (SEM), transmission electron microscopy (TEM), thermogravimetric analysis (TGA), Fourier transform infrared (FT-IR), atomic absorption spectrophotometry (AAS), and nitrogen physisorption measurements. The $Ni_2(BDC)_2(DABCO)$ could be used as an efficient heterogeneous catalyst for the nickel-catalyzed direct heterocycle C–H arylation reactions between azoles and arylboronic acids forming 2-arylbenzoxazoles as the principal product. This approach avoids the use of hazardous aryl halides as well as the formation of halide byproducts in the synthesis of aryl-substituted benzoxazoles. The $Ni_2(BDC)_2(DABCO)$ exhibited significantly higher catalytic activity than that of other Ni-MOFs such as $Ni_3(BTC)_2$, Ni(HBTC)(BPY), and that of some common nickel salts such as $NiCl_2$, $Ni(NO_3)_2$, Ni_2SO_4, and $Ni(OAc)_2$. To the best of our knowledge, application of $Ni_2(BDC)_2(DABCO)$ in the field of catalysis as well as the C–C cross coupling reaction *via* direct C–H functionalization using a nickel heterogeneous catalyst have not previously been reported in the literature.

1. Introduction

Metal-mediated C-arylation of heterocycle compounds through direct C–H activation has recently attracted significant attention as a shorter and more efficient synthetic approach than the conventional cross-coupling methods.[1,2] The direct functionalization of C–H bonds would avoid or minimize the preparation of prefunctionalized starting materials, thus improving atom-economics and environmental aspects of the synthetic schemes.[3–5] Enormous effort has been devoted to achieve C–C bond formation through direct C–H functionalization, employing palladium-, rhodium-, ruthenium-, or iridium-based catalyst systems.[6–13] Daugulis and Do previously demonstrated a significant breakthrough in the copper-catalyzed direct heterocycle C–H arylation reaction of various heteroarenes with haloarenes using copper salts as catalysts.[2,14,15] Recently, nickel-based catalysts have emerged as promising candidates for organic transformations through direct C–H activation. Miura and co-workers discovered that the combination of $NiBr_2$ and nitrogen-containing compounds such as 2,2′-bipyridine or 1,10-phenanthroline as ligands could offer high activity for the direct coupling of azole derivatives and organoboronic acids.[16] This protocol avoids the use of hazardous aryl halides as well as the formation of halide byproducts. Lei and co-workers demonstrated a novel oxidative arylation of cyclic ethers with arylboronic acid employing $Ni(acac)_2$ as the catalyst precursor in the presence of triphenylphosphine (PPh_3) as the ligand and di-*tert*-butyl peroxide as the oxidant.[17] For the development of greener processes, however, heterogeneous catalysts should be targeted in terms of the ease of handling, simple workup, recyclability and reusability.[18]

Metal–organic frameworks (MOFs) have emerged as a new class of porous materials with potential applications in several fields including gas separation and storage, sensors and luminescence, drug storage and delivery, templated low-dimensional material preparation, and catalysis.[19–24] Although the application of MOFs in catalysis has been investigated only for the past few years, several MOFs have been used as heterogeneous catalysts for a variety of organic transformations, ranging from carbon–carbon to carbon–heteroatom forming reactions.[25–37] However, nickel-based MOFs as catalysts for organic transformations have been rarely reported in the

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literature. Kim and co-workers previously demonstrated that nickel nanoparticles embedded in the pores of a mesoporous MOF could be used as a catalyst for the hydrogenolysis of nitrobenzene or the hydrogenation of styrene.[38] Similarly, Chou and co-workers reported that nickel nanoparticles supported on MOF-5 exhibited high activity in the hydrogenation reaction of crotonaldehyde.[39] Recently, Jiang and co-workers employed a nickel(salphen)-based MOF as a heterogeneous catalyst for the synthesis of cyclic carbonates.[40] In this work, we report the nickel-catalyzed direct heterocycle C–H arylation reaction between azoles and arylboronic acids using $Ni_2(BDC)_2(DABCO)$ as an efficient heterogeneous catalyst. The Ni-MOF catalyst could be facilely isolated from the reaction mixture and could be reused without a significant degradation in activity. To the best of our knowledge, the application of $Ni_2(BDC)_2(DABCO)$ in the field of catalysis as well as the C–C cross coupling reaction *via* direct C–H functionalization using a nickel heterogeneous catalyst have not previously been reported in the literature.

2. Experimental

2.1. Materials and instrumentation

All reagents and starting materials were obtained commercially from Sigma-Aldrich and Merck, and were used as received without any further purification unless otherwise noted. Nitrogen physisorption measurements were conducted using a Micromeritics 2020 volumetric adsorption analyzer system. Samples were pretreated by heating under vacuum at 150 °C for 3 h. A Netzsch Thermoanalyzer STA 409 was used for thermogravimetric analysis (TGA) with a heating rate of 10 °C min^{-1} under a nitrogen atmosphere. X-ray powder diffraction (XRD) patterns were recorded using a Cu Kα radiation source on a D8 Advance Bruker powder diffractometer. Scanning electron microscopy studies were conducted on a S4800 Scanning Electron Microscope (SEM). Transmission electron microscopy studies were performed using a JEOL JEM 1400 Transmission Electron Microscope (TEM) at 100 kV. The $Ni_2(BDC)_2(DABCO)$ sample was dispersed on holey carbon grids for TEM observation. Elemental analysis with atomic absorption spectrophotometry (AAS) was performed on an AA-6800 Shimadzu. Fourier transform infrared (FT-IR) spectra were obtained on a Nicolet 6700 instrument, with samples being dispersed on potassium bromide pellets.

Gas chromatographic (GC) analysis was performed using a Shimadzu GC 2010-Plus equipped with a flame ionization detector (FID) and an SPB-5 column (length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.25 μm). The temperature program for GC analysis heated samples from 120 to 130 °C at 40 °C min^{-1}, then heated them from 130 to 180 °C at 40 °C min^{-1} and held them at 180 °C for 0.5 min, then heated them from 180 to 280 °C at 50 °C min^{-1} and held them at 280 °C for 2 min. The inlet and detector temperatures were set to a constant value of 280 °C. *n*-Hexadecane was used as an internal standard to calculate reaction conversions. GC-MS analysis was performed using a Hewlett Packard GC-MS 5972 with a RTX-5MS column (length = 30 m, inner diameter = 0.25 mm, and film thickness = 0.5 μm). The temperature program for GC-MS analysis heated samples from 60 to 280 °C at 10 °C min^{-1} and held them at 280 °C for 2 min. The inlet temperature was set to a constant value of 280 °C. MS spectra were compared with the spectra in the NIST library.

2.2. Synthesis of the metal–organic framework $Ni_2(BDC)_2(DABCO)$

In a typical preparation, a solid mixture of H_2BDC (H_2BDC = 1,4-benzenedicarboxylic acid; 0.332 g, 2 mmol), DABCO (DABCO = 1,4-diazabicyclo[2.2.2]octane; 0.112 g, 1 mmol), and $Ni(NO_3)_2{\cdot}6H_2O$ (0.58 g, 2 mmol) was dissolved in DMF (DMF = *N*,*N*′-dimethylformamide; 15 ml). The resulting solution was distributed among two 20 ml vials. The vials were then heated at 100 °C in an isothermal oven for 48 h. After cooling the vials to room temperature, the solid product was removed by decanting with the mother liquor and washed in DMF (3 × 10 ml) for 3 days. Solvent exchange was carried out with methanol (3 × 10 ml) at room temperature for 3 days. The material was then evacuated under vacuum at 140 °C for 6 h, yielding 0.385 g of $Ni_2(BDC)_2(DABCO)$ in the form of green crystals (69% yield).

2.3. Catalytic studies

The $Ni_2(BDC)_2(DABCO)$ was used as a catalyst for the nickel-catalyzed coupling of benzoxazole and arylboronic acids to achieve phenylbenzoxazole derivatives. In a typical experiment, a pre-determined amount of $Ni_2(BDC)_2(DABCO)$ was added to the flask containing a mixture of benzoxazole (0.119 g, 1 mmol), phenylboronic acid (0.244 g, 2 mmol), K_3PO_4 (0.532 g, 2 mmol), 2,2′-bipyridine (0.031 g, 0.2 mmol) as ligand, and *n*-hexadecane (0.1 ml) as internal standard in *N*,*N*-dimethylacetamide (DMAc) (5 ml). The catalyst concentration was calculated based on the molar ratio of nickel/benzoxazole. The reaction mixture was stirred at 100 °C for 180 min. The reaction conversion was monitored by withdrawing aliquots from the reaction mixture at different time intervals, quenching with an aqueous NaOH solution (5%, 1 ml), drying over anhydrous Na_2SO_4, analyzing by GC with reference to *n*-hexadecane, and further confirming the product identity by GC-MS. To investigate the recyclability of the $Ni_2(BDC)_2(DABCO)$, the catalyst was filtered from the reaction mixture after the experiment, washed with copious amounts of DMF, dried at 140 °C under vacuum for 6 h, and reused if necessary. For the leaching test, the catalytic reaction was stopped after 30 min, analyzed by GC, and filtered to remove the solid catalyst. The reaction solution was then stirred for a further 150 min. The reaction progress, if any, was monitored by GC as previously described.

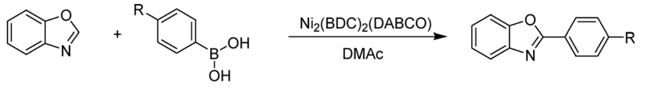
3. Results and discussion

3.1. Catalyst synthesis and characterization

In this work, the $Ni_2(BDC)_2(DABCO)$ was synthesized in a yield of 69% by a solvothermal method, according to a slightly modified literature procedure.[41] The Ni-MOF was then characterized by several techniques. Elemental analysis by AAS indicated a nickel loading of 3.55 mmol g^{-1}. The X-ray diffraction patterns of the $Ni_2(BDC)_2(DABCO)$ (Fig. S1†) exhibited the presence of very sharp peaks, being consistent with the theoretical patterns from the single crystal data previously reported in the literature.[42,43] The SEM micrograph of the Ni-MOF showed the formation of a crystalline powder (Fig. S2†). As expected, the TEM observation of the $Ni_2(BDC)_2(DABCO)$ revealed that a porous structure was obtained (Fig. S3†). However, the pore structure of the Ni-MOF was more apparently complex than that of conventionally used microporous and mesoporous materials due to the bent BDC linker molecules and the type of guest molecules in the pores. Nitrogen physisorption measurements indicated that the $Ni_2(BDC)_2(DABCO)$ is a well-defined crystalline microporous material, with a median pore width of 6.112 Å being detected (Fig. S4†). Our results are consistent with previous reports.[42] Calculations from nitrogen adsorption/desorption isotherm data showed that a Langmuir surface area and BET surface area of 2006 m^2 g^{-1} and 1473 m^2 g^{-1}, respectively, were achieved for the material (Fig. S5†). TGA result indicated that the Ni-MOF was stable up to over 200 °C (Fig. S6†). FT-IR spectra of the $Ni_2(BDC)_2(DABCO)$ exhibited a significant difference as compared to those of the H_2BDC and the DABCO linkers, revealing the deprotonation of –COOH groups in the H_2BDC upon the reactions with nickel cations (Fig. S7†).[41]

3.2 Catalytic studies

The $Ni_2(BDC)_2(DABCO)$ was assessed for its catalytic activity in the C–H arylation of benzoxazole with phenylboronic acid to form 2-phenylbenzoxazole as the principal product (Scheme 1). Initial studies addressed the effect of temperature on the reaction conversion of benzoxazole to 2-phenylbenzoxazole. The coupling reaction was carried out in DMAc, at a benzoxazole : phenylboronic acid molar ratio of 1 : 2, using two equivalents of K_3PO_4 as a base, in the presence of 10 mol% $Ni_2(BDC)_2(DABCO)$ catalyst and 20 mol% of 2,2′-bipyridine as a ligand, at 80 °C, 90 °C, 100 °C, and 120 °C. Aliquots were withdrawn from the reaction mixture at different time intervals and analyzed by GC, giving kinetic data during the course of the reaction. It was observed that the reaction proceeded with difficulty at 80 °C, affording a conversion of 23% after 180 min. As expected, increasing the reaction temperature resulted in a significant enhancement in the reaction rate, with 61% and 75% conversions being achieved after 180 min for the reactions carried out at 90 °C and 100 °C, respectively (Fig. 1). From the experimental point of view, it should be noted that carrying out the $Ni_2(BDC)_2(DABCO)$-catalyzed coupling reaction at 120 °C led to the significant decomposition of benzoxazole. Indeed, Liu and co-workers also carried out the direct coupling reaction of azoles with boronic acids using a mixture of 5 mol% $Pd(OAc)_2$ and 10 mol% $Cu(OAc)_2$ as a bimetallic catalytic system in the temperature range of 80–100 °C.[44] However, Miura and co-workers previously employed $NiBr_2$ as a catalyst and nitrogen-containing compounds such as 2,2′-bipyridine or 1,10-phenanthroline as ligands for the direct coupling of benzoxazole with 4-methylphenylboronic acid, and demonstrated that a high yield could be obtained at 120 °C.[16]



R: -Cl, F, H, C_2H_5, COOH, CHO

Scheme 1 The direct heterocycle C–H arylation reactions between azoles and arylboronic acids using $Ni_2(BDC)_2(DABCO)$ as a catalyst.

For liquid-phase organic transformations using solid catalysts, the effect of different solvents on the reaction rate is normally an important issue that should be seriously considered.[45,46] In the first example of the C–H arylation reaction between benzoxazole and 4-methylphenylboronic acid using $NiBr_2$ as the catalyst, Miura and co-workers demonstrated that DMAc offered better performance for the reaction compared to other solvents such as dimethyl sulfoxide (DMSO), DMF, and *N*-methyl-2-pyrrolidone (NMP).[16] Itami and co-workers reported that 1,4-dioxane offered better performance compared to toluene, dimethoxyethane (DME), DMF, and NMP for the $Ni(OAc)_2$-catalyzed C–H arylation reaction of azoles with haloarenes.[47,48] It was therefore decided to investigate the effect of different solvents on the reaction conversion, having used DMAc, DMF, DEF, NMP, toluene, DMSO, and 1,4-dioxane as the reaction solvent. The coupling reaction was carried out at 100 °C using the reagent molar ratio of 1 : 2, in the presence of 10 mol% $Ni_2(BDC)_2(DABCO)$ catalyst with two equivalents of K_3PO_4 as the base and 20 mol% of 2,2′-bipyridine as the ligand. It was found that toluene and DMSO were completely ineffective for the reaction, with no trace amount of the product being detected. 1,4-Dioxane was also unsuitable for the reaction, affording only 11% conversion after 180 min. DEF and NMP offered better performance than 1,4-dioxane, with 27% and 18% conversions, respectively, being observed after 180 min. The $Ni_2(BDC)_2(DABCO)$-catalyzed coupling reaction carried out in

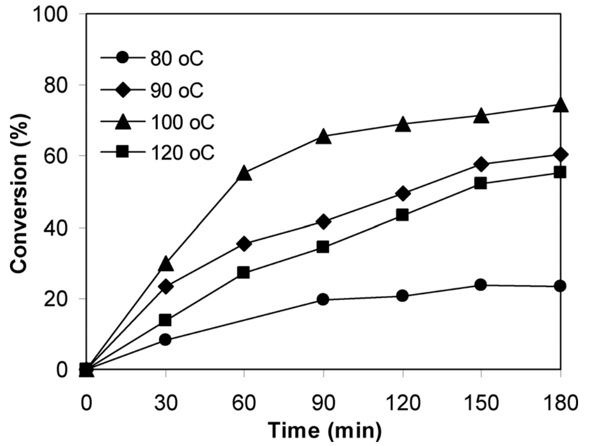


Fig. 1 Effect of temperature on reaction conversion.

DMF could offer 60% conversion after 180 min. Among these solvents, DMAc exhibited the best performance, and should be the solvent of choice for the C–H arylation of benzoxazole and phenylboronic acid using the $Ni_2(BDC)_2(DABCO)$ catalyst (Fig. 2). Moreover, it was found that increasing the benzoxazole : phenylboronic acid molar ratio to 1 : 2.5 could improve the reaction conversion to 86% after 180 min (Fig. 3).

With these results in mind, we then decided to investigate the effect of catalyst concentration on the reaction conversion. The coupling reaction was carried out at 100 °C in DMAc, using the reagent molar ratio of 1 : 2.5, in the presence of two equivalents of K_3PO_4 as the base or 20 mol% of 2,2′-bipyridine as the ligand, with 5 mol%, 7.5 mol%, or 10 mol% catalyst. It was found that the C–H arylation reaction between benzoxazole and phenylboronic acid using 10 mol% $Ni_2(BDC)_2(DABCO)$ catalyst could proceed readily to 86% conversion after 180 min. As expected, decreasing the catalyst concentration to 7.5 mol% resulted in a drop in the reaction rate, with 73% conversion being obtained. The coupling reaction using 5 mol% could still afford 65% conversion after 180 min. It should be noted that no reaction occurred in the absence of the $Ni_2(BDC)_2(DABCO)$ catalyst, confirming the necessity of using the Ni-MOF as catalyst for the direct heterocycle C–H arylation reaction between azoles and arylboronic acids (Fig. 4). Indeed, in the first example of the Ni-catalyzed C–H arylation reaction between benzoxazole and 4-methylphenylboronic acid, up to 10 mol% $NiBr_2$ was employed as catalyst.[16] Lei and co-workers previously reported the oxidative arylation of cyclic ethers with arylboronic acids using 10 mol% $Ni(acac)_2$ catalyst in the presence of triphenylphosphine (PPh_3) as the ligand and di-*tert*-butyl peroxide as the oxidant.[17] Moreover, Liu and co-workers successfully performed the direct coupling reaction of azoles with boronic acids using a mixture of 5 mol% $Pd(OAc)_2$ and 10 mol% $Cu(OAc)_2$ as a bimetallic catalytic system.[44] The $Ni_2(BDC)_2(DABCO)$ catalyst concentrations used in the arylation of benzoxazole with phenylboronic acid *via* C–H activation in this study were therefore comparable to those in the literature.

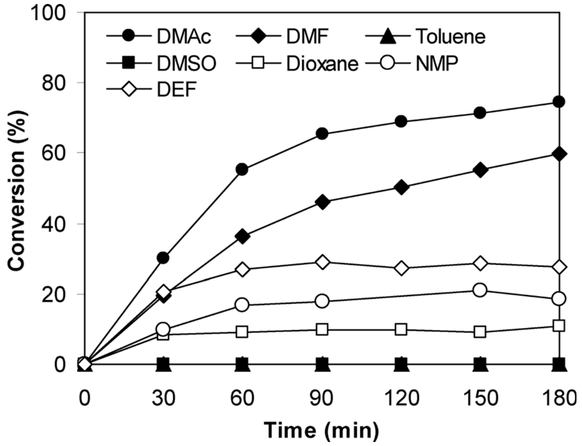


Fig. 2 Effect of different solvents on reaction conversion.

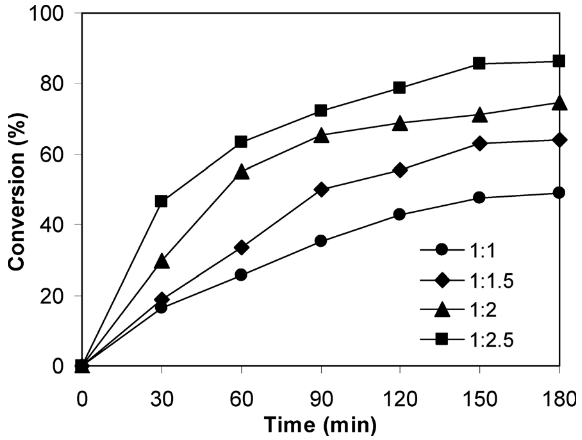


Fig. 3 Effect of benzoxazole : phenylboronic acid molar ratio on reaction conversion.

As for most metal-mediated arylation reactions through C–H direct functionalization, the presence of at least one equivalent of a base should be required to speed up the transmetallation step in the catalytic cycle of the reaction. Indeed, in the first example of the Ni-catalyzed C–H arylation reaction between benzoxazole and 4-methylphenylboronic acid using $NiBr_2$ catalyst, Miura and co-workers screened different bases for the reaction, and pointed out that K_3PO_4 should be the base of choice for this transformation.[16] Similarly, Liu and co-workers performed the direct coupling reaction of azoles with boronic acids using a mixture of 5 mol% $Pd(OAc)_2$ and 10 mol% $Cu(OAc)_2$ as a bimetallic catalytic system, and also observed that K_3PO_4 was the most effective base.[44] However, You and co-workers demonstrated that KF should be employed for the C–H arylation reaction between azoles with boronic acids using a mixture of 5 mol% $Pd(OAc)_2$ and 10 mol% CuCl as a bimetallic catalytic system.[49] It was therefore decided to investigate the effect of different bases on the reaction conversion, using Na_2CO_3, K_2CO_3, K_3PO_4, CH_3COONa, ^{t}BuOK, piperidine, and 1,8-diazabicycloundec-7-ene (DBU). The C-arylation reaction was carried out at 100 °C in DMAc, at the reagent molar ratio of

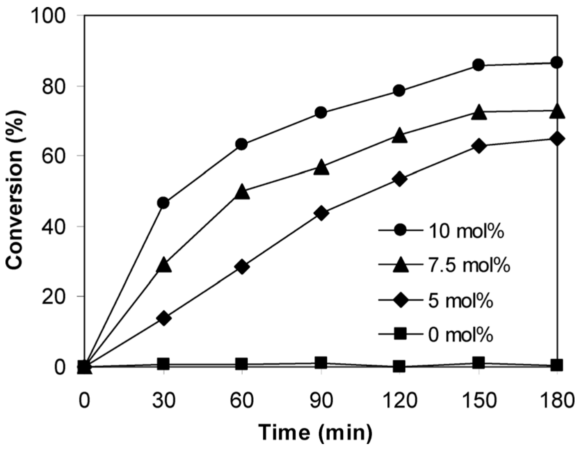


Fig. 4 Effect of catalyst concentration on reaction conversion.

1 : 2.5, using two equivalents of the base and 20 mol% of 2,2′-bipyridine as the ligand, in the presence of 10 mol% $Ni_2(BDC)_2(DABCO)$ catalyst. Na_2CO_3, CH_3COONa, ^tBuOK, K_2CO_3, and piperidine were found to be unsuitable for the coupling reaction with lower than 10% conversion being observed after 180 min. When employing DBU as the base for the C–H arylation reaction, a conversion of 51% was obtained after 180 min. Among these bases, K_3PO_4 exhibited the best performance, producing the desired product in a conversion of 86% after 180 min (Fig. 5).

Another factor that should be considered for the C–H arylation reaction between benzoxazole and phenylboronic acid using the $Ni_2(BDC)_2(DABCO)$ catalyst is the nature of the organic ligand. In the first example of the Ni-catalyzed C–H arylation reaction using $NiBr_2$ catalyst, Miura and co-workers screened several organic ligands, and reported that 1,10-phenanthroline and 2,2′-bipyridine could be used for this transformation, although 2,2′-bipyridine exhibited better performance than 1,10-phenanthroline.[16] Liu and co-workers also employed 1,10-phenanthroline or 2,2′-bipyridine as a ligand for the reaction, and pointed out that a better result was observed for the case of 1,10-phenanthroline.[44] We then decided to investigate the effect of the ligand nature on the $Ni_2(BDC)_2(DABCO)$-catalyzed C–H arylation reaction between benzoxazole and phenylboronic acid, using 1,10-phenanthroline, 2,2′-bipyridine, triphenylphosphine, ethylenediamine, and acetylacetone as the ligand. The C–H arylation reaction was carried out at 100 °C in DMAc, at the reagent molar ratio of 1 : 2.5, using two equivalents of K_3PO_4 as the base and 20 mol% ligand, in the presence of 10 mol% $Ni_2(BDC)_2(DABCO)$ catalyst. It was observed that triphenylphosphine, ethylenediamine, and acetylacetone were ineffective for the reaction, with less than 10% conversion being detected. The reaction using 1,10-phenanthroline could proceed to 56% conversion after 180 min. 2,2′-Bipyridine was found to be more effective for the reaction, affording 86% conversion after 180 min (Fig. 6). It should be noted that no reaction occurred in the absence of the ligand, confirming the necessity of the organic ligand in the Ni-catalyzed C–H arylation reaction. Moreover, it was observed that the ligand concentration also exhibited a slight effect on the reaction conversion. Using a ligand concentration of 10 mol%, a conversion of 83% was still obtained after 180 min. However, increasing the ligand concentration to 30 mol% also led to a slight drop in the reaction rate, with 78% conversion being observed after 180 min (Fig. 7). Indeed, 20 mol% ligand was previously employed for the C–H arylation reaction using $NiBr_2$ catalyst,[16] and up to 30 mol% ligand was employed for the case of the $Pd(OAc)_2/Cu(OAc)_2$ bimetallic catalytic system.[44]

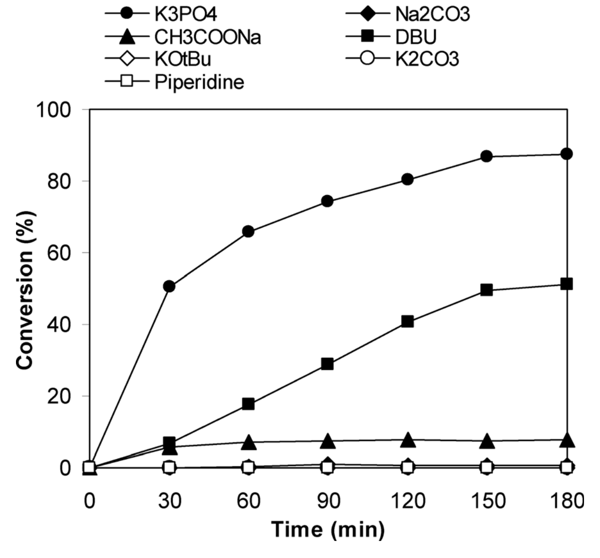


Fig. 5 Effect of different bases on reaction conversion.

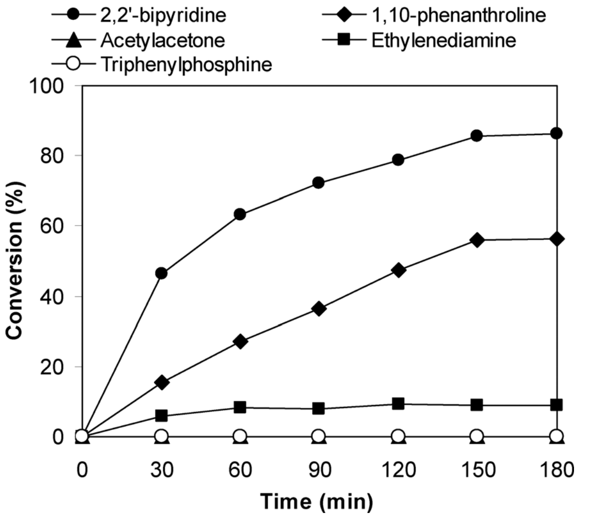


Fig. 6 Effect of different ligands on reaction conversion.

To emphasize the advantages of using $Ni_2(BDC)_2(DABCO)$ as catalyst for the C–H arylation reaction between benzoxazole and phenylboronic acid, the catalytic activity of the $Ni_2(BDC)_2(DABCO)$ was compared with that of other Ni-MOFs including $Ni_3(BTC)_2$ and Ni(HBTC)(BPY) (H3BTC = 1,3,5-benzenetricarboxylic acid, BPY = 4,4′-bipyridyl), and that of common nickel salts including $NiCl_2$, $Ni(NO_3)_2$, $NiSO_4$, and $Ni(OAc)_2$. The C–H arylation reaction was carried out at 100 °C

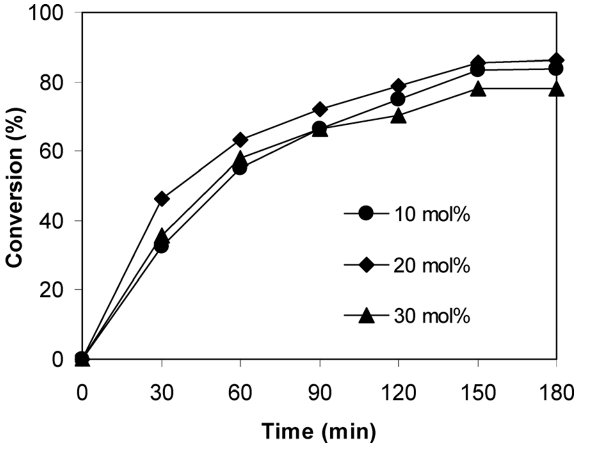


Fig. 7 Effect of ligand concentration on reaction conversion.

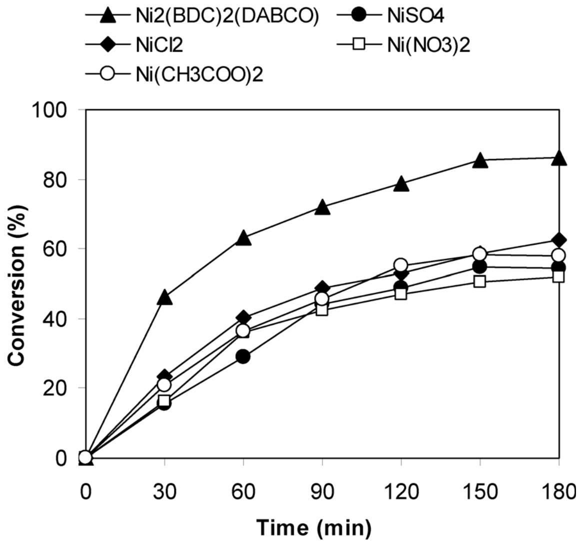


Fig. 8 Effect of different nickel salts as catalysts on reaction conversion.

in DMAc, at the reagent molar ratio of 1 : 2.5, using two equivalents of K_3PO_4 as the base and 20 mol% of 2,2′-bipyridine as the ligand, in the presence of 10 mol% nickel catalyst. It was observed that the coupling reaction using $NiCl_2$, $Ni(NO_3)_2$ Ni_2SO_4, and $Ni(OAc)_2$ could proceed to 62%, 51%, 54%, and 58% conversion, respectively, after 180 min (Fig. 8). Interestingly, it was found that $Ni_2(BDC)_2(DABCO)$ could offer significantly higher activity than other two Ni-MOFs, with 86% conversion being achieved after 180 min. The $Ni_3(BTC)_2$-catalyzed C–H arylation reaction afforded 47% conversion, while 61% conversion was observed after 180 min for the case of $Ni_2(BDC)_2(DABCO)$. Furthermore, the C–H arylation reaction between benzoxazole and phenylboronic acid was also carried out in the presence of $Cu_2(BDC)_2(DABCO)$ or $Co_2(BDC)_2(DABCO)$ as the catalyst under similar reaction conditions (Fig. 9). Interestingly, it was found that only 10% conversion was detected after 180 min, thus emphasizing the advantages of using the $Ni_2(BDC)_2(DABCO)$ as a catalyst for the transformation.

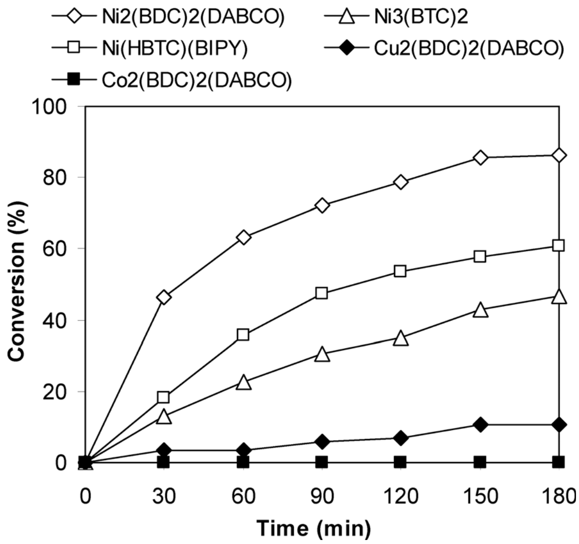


Fig. 9 Effect of different MOFs as catalysts on reaction conversion.

To verify the possibility that the adsorption of the 2-phenylbenzoxazole product on the catalytically active nickel sites in the $Ni_2(BDC)_2(DABCO)$ could hinder the C–H arylation reaction between benzoxazole and phenylboronic acid, a control experiment was carried out, adding the product to the reaction mixture during the course of the reaction. The reaction was carried out at 100 °C in DMAc, at the reagent molar ratio of 1 : 2.5, using two equivalents of K_3PO_4 as the base and 20 mol% of 2,2′-bipyridine as the ligand, in the presence of 10 mol% $Ni_2(BDC)_2(DABCO)$ catalyst. After 30 min reaction time with 43% conversion being observed, one equivalent of 2-phenylbenzoxazole was added to the reaction solution. The resulting mixture was stirred for another 150 min at 100 °C, with aliquots being sampled at different time intervals, and analyzed by GC. Interestingly, it was found that the C–H arylation reaction stopped immediately after the product was added, with 43% conversion being detected after 180 min (Fig. 10). The fact that no further conversion was observed upon adding the 2-phenylbenzoxazole product to the reaction mixture would confirm the inhibition role of the product in the $Ni_2(BDC)_2(DABCO)$-catalyzed C–H arylation reaction between benzoxazole and phenylboronic acid. Indeed, Kholdeeva and co-workers previously employed Fe and Cr-containing MOFs as heterogeneous catalysts for the oxidation reaction of cyclohexene and α-pinene with molecular oxygen, and also reported a similar observation, in which the reaction stopped completely after the product was added to the reaction mixture.[50] However, further studies on the adsorption–desorption equilibrium of the product on the Ni-MOF catalyst in the C–H arylation reaction are necessary.

As for several liquid-phase organic transformations, the possibility that some of catalytically active sites on the solid catalyst could dissolve into the solution during the course of the reaction should be seriously addressed. The soluble species might exhibit catalytic activity, and therefore the reaction would not proceed under real heterogeneous catalysis

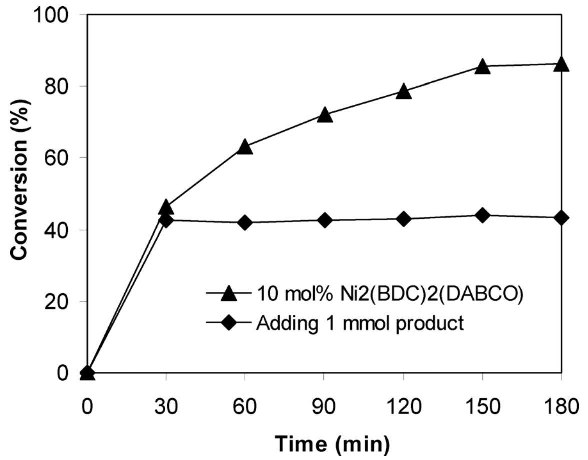


Fig. 10 Adding product to the reaction mixture when using $Ni_2(BDC)_2(DABCO)$ as the catalyst.

conditions. In order to determine if active nickel species dissolved from the solid $Ni_2(BDC)_2(DABCO)$ catalyst contribute to the total conversion of the C–H arylation reaction between benzoxazole and phenylboronic acid, a control experiment was carried out using a simple centrifugation during the course of the reaction. If the C–H arylation reaction still proceeded to higher conversion after the solid Ni-MOF was removed from the reaction mixture, this behavior would demonstrate that the coupling reaction would not occur under real heterogeneous catalysis conditions, and there should be a contribution from leached active nickel species to the catalysis process. The C–H arylation reaction was carried out at 100 °C in DMAc, at the reagent molar ratio of 1 : 2.5, using two equivalents of K_3PO_4 as the base and 20 mol% of 2,2′-bipyridine as the ligand, in the presence of 10 mol% $Ni_2(BDC)_2(DABCO)$ catalyst. The solid Ni-MOF catalyst was separated from the reaction mixture after 30 min reaction time by simple centrifugation. The reaction solution was then transferred to a new reactor vessel, two equivalents of K_3PO_4 were added, and the resulting mixture was stirred for an additional 150 min at 100 °C with aliquots being sampled at different time intervals, and analyzed by GC. It was observed that almost no further conversion was detected after the solid Ni-MOF catalyst was removed from the reaction mixture (Fig. 11). The fact that no further reaction conversion was obtained would indicate that the C–H arylation reaction between benzoxazole and phenylboronic acid could only occur in the presence of the solid $Ni_2(BDC)_2(DABCO)$ catalyst, and there should be no contribution from catalytically active nickel species soluble in the liquid phase.

In order to achieve greener processes, the ability to recover and reuse the solid catalyst should be seriously addressed. In the best cases, the solid catalyst can be facilely separated from the reaction mixture, and reused several times before it eventually deactivates completely. The recoverability and reusability of the $Ni_2(BDC)_2(DABCO)$ catalyst in the C–H arylation reaction between benzoxazole and phenylboronic acid was investigated over seven successive runs, by repeatedly separating the Ni-MOF catalyst from the reaction mixture, washing it and then reusing it. The C–H arylation reaction was carried out at 100 °C in DMAc, at the reagent molar ratio of 1 : 2.5, using two equivalents of K_3PO_4 as the base and 20 mol% of 2,2′-bipyridine as the ligand, in the presence of 10 mol% $Ni_2(BDC)_2(DABCO)$ catalyst. After the C–H arylation reaction was complete, the $Ni_2(BDC)_2(DABCO)$ catalyst was removed from the reaction mixture by simple centrifugation, then washed with copious amounts of DMF to remove any physisorbed reagents, and dried at 140 °C under vacuum for 6 h. The recovered Ni-MOF was then reused in further C–H arylation reaction between benzoxazole and phenylboronic acid under identical conditions to those of the first run. It was found that the $Ni_2(BDC)_2(DABCO)$ catalyst could be recovered and reused several times without a significant degradation in catalytic activity. Indeed, a conversion of 77% was still obtained in the 7th run (Fig. 12). To confirm the recoverability and reusability of the $Ni_2(BDC)_2(DABCO)$ catalyst, the recovered Ni-MOF was also characterized by XRD, pore size distribution, and FT-IR. Indeed, the XRD and pore size distribution results of the reused $Ni_2(BDC)_2(DABCO)$ catalyst showed that the crystallinity and pore structure of the Ni-MOF remained almost unchanged during the course of the C–H arylation reaction (Fig. 13 and 14). Moreover, the FT-IR spectra of the reused

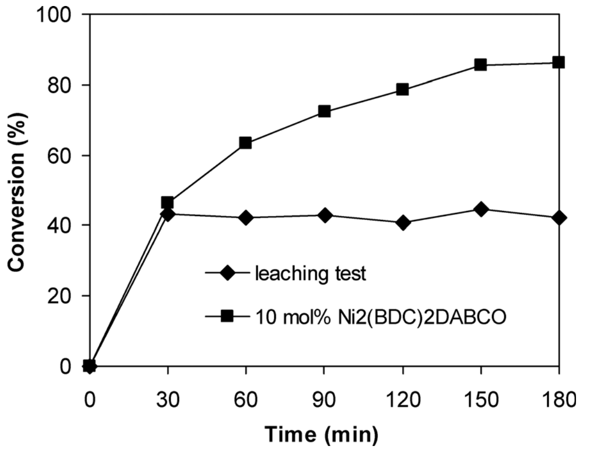


Fig. 11 Leaching test indicated no contribution from the homogeneous catalysis of active species leaching into the reaction solution.

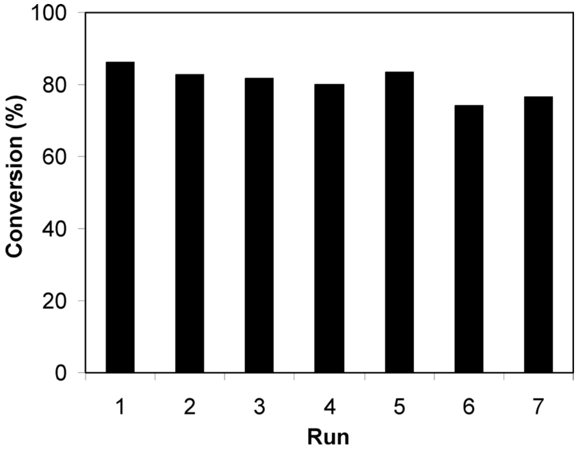


Fig. 12 Catalyst recycling studies.

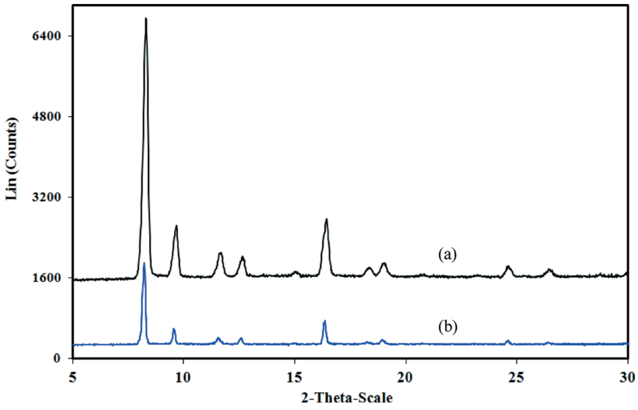


Fig. 13 X-ray powder diffractograms of the fresh (a) and reused (b) $Ni_2(BDC)_2(DABCO)$ catalyst.

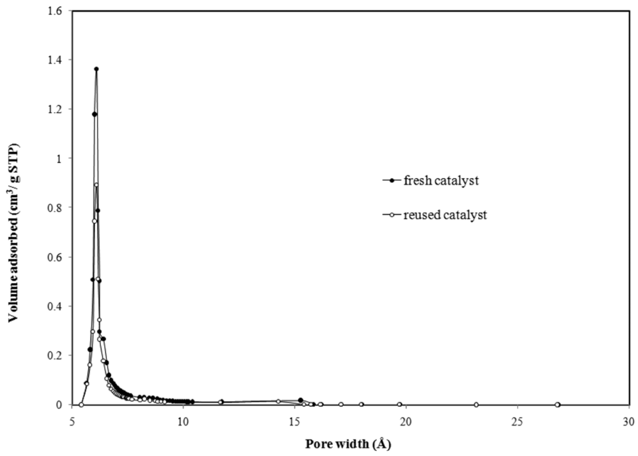


Fig. 14 Pore size distribution of the fresh $Ni_2(BDC)_2(DABCO)$ and that recovered for the 5th time.

$Ni_2(BDC)_2(DABCO)$ revealed similar absorption as compared to that of the fresh catalyst (Fig. 15).

The study was then extended to the $Ni_2(BDC)_2(DABCO)$-catalyzed C–H arylation reaction between benzoxazole and different phenylboronic acids, including 4-formylphenylboronic acid, 4-carboxylphenylboronic acid, 4-chlorophenylboronic acid, 4-fluorophenylboronic acid, phenylboronic acid, 4-methoxyphenylboronic acid, and 4-ethylphenylboronic acid. The C–H arylation reaction was carried out at 100 °C in DMAc, at the reagent molar ratio of 1 : 2.5, using two equivalents of K_3PO_4 as the base and 20 mol% of 2,2′-bipyridine as the ligand, in the presence of 10 mol% $Ni_2(BDC)_2(DABCO)$ catalyst. It was found that the presence of a substituent on the benzene ring in the phenylboronic acid led to a drop in the reaction conversion. Among these reagents, it was observed that phenylboronic acids with an electron-donating group offered higher reactivity in the C–H arylation reaction than those with electron-withdrawing substituents. The $Ni_2(BDC)_2(DABCO)$-catalyzed C–H arylation reaction between benzoxazole and 4-methoxyphenylboronic acid afforded 67% conversion after 180 min, while 47% conversion was obtained for the case of 4-ethylphenylboronic acid. The reaction of benzoxazole with 4-carboxyphenylboronic acid, 4-formylphenylboronic acid, 4-chlorophenylboronic acid, and 4-fluorophenylboronic acid proceeded slowly under these conditions, with 6%, 19%, 25%, and 29% conversion being detected after 180 min (Fig. 16).

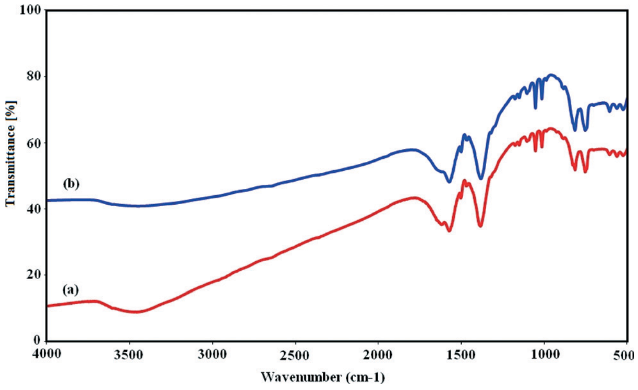


Fig. 15 FT-IR spectra of the fresh (a) and reused (b) $Ni_2(BDC)_2(DABCO)$ catalyst.

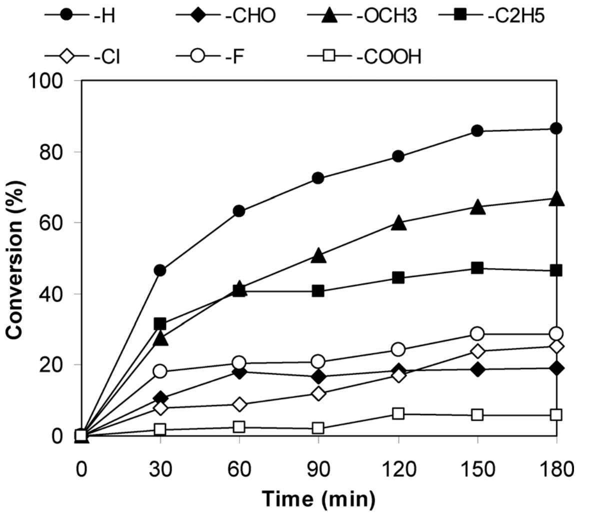


Fig. 16 Effect of different phenylboronic acids on reaction conversion.

4. Conclusions

In summary, the metal–organic framework $Ni_2(BDC)_2(DABCO)$ was synthesized by a solvothermal method, and was characterized by several techniques including XRD, SEM, TEM, FT-IR, TGA, AAS, and nitrogen physisorption measurements. The $Ni_2(BDC)_2(DABCO)$ could be used as an efficient heterogeneous catalyst for the nickel-catalyzed direct heterocycle C–H arylation reaction between azoles and arylboronic acids to form 2-arylbenzoxazoles as the principal product. This approach avoids the use of hazardous aryl halides as well as the formation of halide byproducts in the synthesis of aryl-substituted benzoxazoles. The Ni-MOF catalyst could be facilely isolated from the reaction mixture, and could be reused without a significant degradation in activity. The direct heterocycle C–H arylation could only occur in the presence of the solid Ni-MOF catalyst, and there was no contribution from leached active sites present in the solution. The $Ni_2(BDC)_2(DABCO)$ exhibited significantly higher catalytic activity than that of other Ni-MOFs such as $Ni_3(BTC)_2$, Ni(HBTC)(BPY), and that of some common nickel salts such as $NiCl_2$, $Ni(NO_3)_2$, Ni_2SO_4, and $Ni(OAc)_2$. $Cu_2(BDC)_2(DABCO)$ and $Co_2(BDC)_2(DABCO)$ were found to be inactive for the C–H arylation reaction. To the best of our knowledge, the application of $Ni_2(BDC)_2(DABCO)$ in the field of catalysis as well as the C–C cross coupling reaction *via* direct C–H functionalization using a nickel heterogeneous catalyst have not previously been reported in the literature.

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