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FULL PAPER

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Dichloroimidazolidinedione-activated one-pot Suzuki–Miyaura cross-coupling of phenols

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Abstract

The first general method for the Suzuki-type cross-coupling of phenols with aryl boronic acids using dichloroimidazolidinedione (DCID) as a new reagent is presented. In the presence of DCID and Pd/metal–organic framework (MOF), coupling of aryl boronic acids with a wide range of phenols, was carried out smoothly in tetrahydrofuran (THF) at reflux conditions to afford the cross-coupling products in good to excellent yields. The structures of all compounds were corroborated by ^{1}H- and ^{13}C-NMR. A plausible mechanism for this type of reaction is proposed.

KEYWORDS

dichloroimidazolidinedione (DCID), heterogeneous catalyst, Pd/MOF, phenols, Suzuki–Miyaura cross-coupling

1 | INTRODUCTION

The Pd-catalyzed Suzuki–Miyaura cross-coupling reaction is a favorable and versatile method for forming carbon–carbon bonds between aryls halides and boronic acid in organic synthesis.[1–4] This is a versatile method for the preparation of biaryls, which have applications in natural products and pharmaceuticals.[5] In general, aryl halides are good reagents in this coupling reaction. However, these halides are not ideal because they have several drawbacks, such as the partial formation of dimeric and using expensive and unavailable aryl iodides and bromides.[6]

In recent years, the cross-coupling reactions of significantly cheaper and more stable compounds, including aryl triflates,[7] nonaflates,[8] aryl tosylates[9] and mesylates[10] have become attractive due to the ubiquitous presence of their starting materials – phenols – in both the natural and synthetic worlds.[11,12] However, the use of the aryl sulfonates limits their yield efficiency and step economy.[13,14]

Studies in Suzuki cross-coupling reactions have mainly focused on the development of new ligands and catalysts[15] and no new work except that of Nakao et al.[16] has been done in this area. There is therefore a need for an innovative and general procedure for direct Suzuki coupling of phenols that is devoid of the above-mentioned problems.

The development of a more reliable and general direct method for phenol coupling is needed. In this paper, we report general, direct cross-coupling reactions of phenols using dichloroimidazolidinedione (DCID) using Pd/metal–organic framework (MOF) as heterogeneous catalyst. The coupling products were obtained by one-pot reaction of the phenols, DCID and phenylboronic acid in a single flask.DCID (**2**) is readily available from the reaction of dicyclohexylcarbodiimine (DCC) with oxalyl chloride by known reported methods.[17] From a simple search in the literature, it can be seen that DCID has been used in very few reactions, for example Schilter et al. reported the chlorodehydroxylation of alcohols using DCID,[18] Guo and coworkers have recently reported Beckman's rearrangement of ketoximes[17] and Wang et al. have reported chemoselective amidation from carboxylic acid and amine using this compound.[19]

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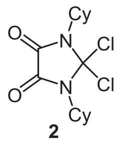


Cy: Cyclohexyl

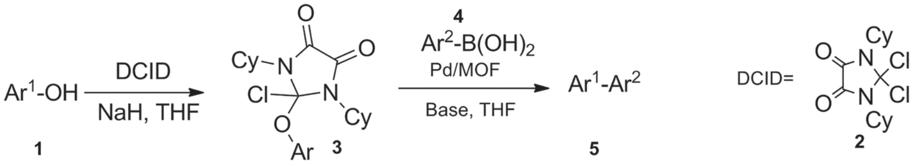
2

Dichloroimidazolidinedione (DCID)

Recently, we reported the use of Pd/MOF as an efficient catalyst for Suzuki–Miyaura cross-coupling of aryl halides and phenylboronic acids.[20] In continuation of this work we introduce here a new reagent for one-pot Suzuki–Miyaura cross-coupling of phenols by Pd/MOF and an efficient heterogeneous catalyst (Scheme 1).

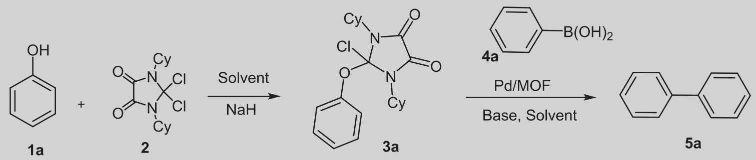
2 | RESULTS AND DISCUSSION

Synthesis of DCID was carried out according to literature methods,[17] and the chemical structure and elemental composition of the DCID were confirmed by elemental analysis and ^{1}H NMR spectroscopy (see Supporting Information). Pd/Cu-MOF was synthesized and characterized as described in our previous report.[18] The loading of Pd(0) was characterized by inductively coupled plasma (ICP) analysis and found to be 0.9%. To investigate the oxidation state information of palladium, X-ray photoelectron spectroscopy (XPS) analysis of Pd 3d binding energies was performed. Based on the peak areas of Pd $3d_{5/2}$ at 336.2 and 337.6 eV, the ratio of Pd(0) to Pd(II) in Pd/MOF was calculated to be 1.5. To examine the efficiency of DCID in the presence of Pd/MOF as catalyst in the Suzuki cross-coupling reaction, a model coupling reaction of phenol with phenylboronic acid was initially tested. The results are summarized in Table 1. With respect to applicability and availability, K_2CO_3 was employed as the base in this study and the use of Et_3N gave **5a** in lower yield (Table 1, entry 4). The best solvent for this coupling reaction was THF (entry 3). We also found that phenol was smoothly coupled with 1 equivalence DCID. The chemical structure of produced interme-



SCHEME 1 One-pot Suzuki–Miyaura cross-coupling of phenols using DCID

TABLE 1 Optimization of the reaction conditions

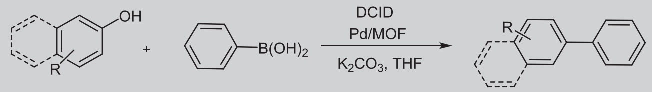


Entry	Catalyst Pd/MOF (mg)	Base	Solvent	Time (h)	T (°C)	Yield (%)
1	10	K_2CO_3	THF	24	65	10
2	20	K_2CO_3	THF	24	25	40
3	**20**	$\mathbf{K_2CO_3}$	**THF**	**24**	**65**	**95**
4	20	Et_3N	THF	24	65	8
5	20	K_2CO_3	THF	16	65	60
6	20	K_2CO_3	THF	18	65	75
7	20	K_2CO_3	THF	20	65	80
8[b]	20	K_2CO_3	THF	24	65	-
9	20	K_2CO_3	DMF	24	150	5
10	20	K_2CO_3	CH_3CN	24	80	65

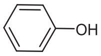
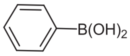
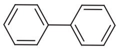
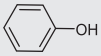
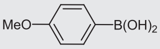
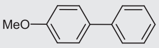
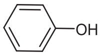
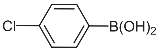
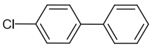
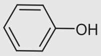
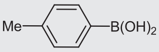
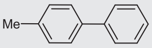
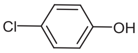
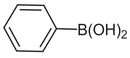
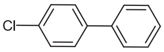
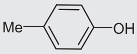
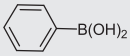
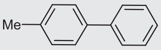
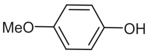
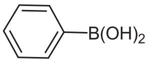
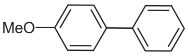
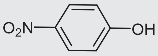
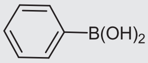
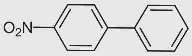
[a] Reaction conditions: **1a** (1.0 equiv), DCID (1.0 equiv), **4a** (1.1 equiv), base (1.0 equiv) in THF (5 ml).

[b] Reaction conditions: **1a** (1.0 equiv), **4a** (1.1 equiv), K_2CO_3 (1.0 equiv) in THF (5 ml).

TABLE 2 Substrate scope of Suzuki–Miyaura cross-coupling of phenols with phenylboronic acids using DCID[a]

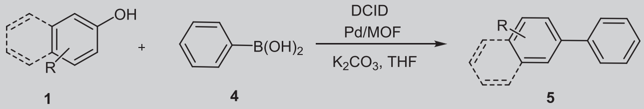


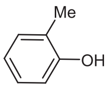
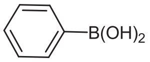
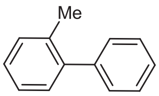
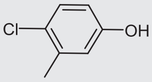
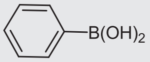
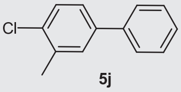
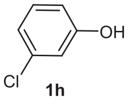
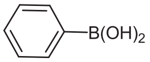
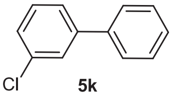
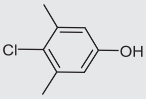
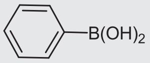
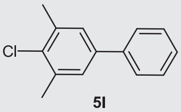
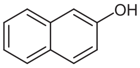
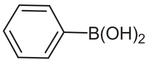
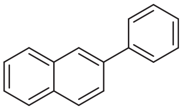
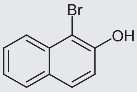
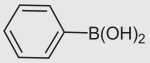
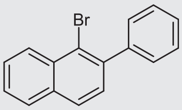
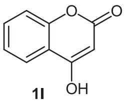
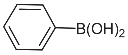
1 4 5

Entry	Phenol 1	Boronic acid 4	Product 5	Yield (%)	M.p. (°C)
1	 **1a**	 **4a**	 **5a**	95	68–70
2	 **1a**	 **4b**	 **5b**	80	89–90
3	 **1a**	 **4c**	 **5c**	82	76–78
4	 **1a**	 **4d**	 **5d**	79	49–50
5	 **1b**	 **4a**	 **5e**	82	76–78
6	 **1c**	 **4a**	 **5f**	91	49–50
7	 **1d**	 **4a**	 **5g**	86	89–90
8	 **1e**	 **4a**	 **5h**	15	112–113

(Continues)

TABLE 2 (Continued)



Entry	Phenol 1	Boronic acid 4	Product 5	Yield (%)	M.p. (°C)
9	 **1f**	 **4a**	 **5i**	68	oil
10	 **1g**	 **4a**	 **5j**	64	oil
11	 **1h**	 **4a**	 **5k**	83	oil
12	 **1i**	 **4a**	 **5l**	5	oil
13	 **1j**	 **4a**	 **5m**	90	105–107
14	 **1k**	 **4a**	 **5n**	89	66–67
15	 **1l**	 **4a**	No Reaction	-	-

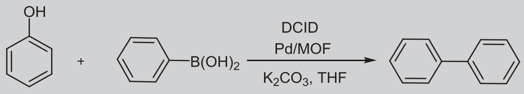
[a]Reaction conditions: 1 (1.0 equiv), 4 (1.1 equiv), DCID (1.0 equiv), Pd/MOF (0.01 mol% Pd), K_2CO_3 (1.0 equiv) in THF (5 ml) at 65 °C.

diate **3a** was confirmed by ^{1}H NMR spectroscopy. Intermediate **3a** was partially coupled with phenylboronic acid by Pd/MOF to give the expected **5a** (Table 1, entries 1–9).

In another attempt, when the reaction was performed in the presence of 10 mg of catalyst, **5a** was obtained in lower yields, therefore 20 mg catalyst (0.01 mol% Pd) was chosen.

To further evaluate the influence of reaction time, the coupling reaction was tested at 16, 18 and 20 h. The results are summarized in Table 1. As shown in Table 1 lower yield of the product was achieved when the time was reduced (Table 1, entries 5–7). To investigate the importance of DCID in this reaction, an experiment was performed in the absence of DICD and the results showed that the Suzuki reaction did not proceed (Table 1, entry 8). Finally, complete conversion to **5a** from **1a** and **4a** was achieved using DCID (1.0 equiv), K_2CO_3 (1.0 equiv) and Pd/MOF (0.01 mol% Pd) in THF at reflux (Table 1, entry 3).

TABLE 3 Recovery and reusability of Pd/MOF in Suzuki-Miyaura cross-coupling[a]



Run	1	2	3	4
Yield (%)	75	75	74	72

[a]Reaction conditions: phenol (1.0 equiv), phenyl boronic acid (1.1 equiv), DCID (1.0 equiv), Pd/MOF (0.01 mol% Pd), K_2CO_3 (1.0 eq) in THF (5 ml) at 65 °C.

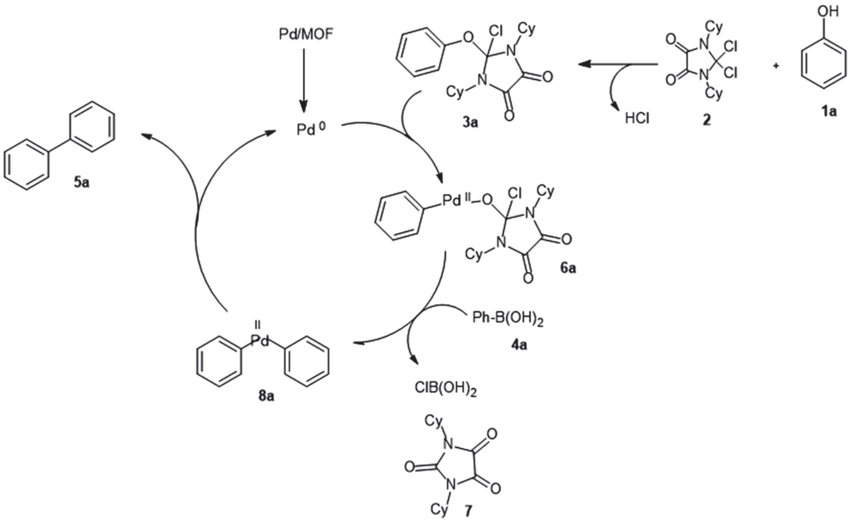
After establishing optimal conditions, we explored the scope of the direct Suzuki–Miyaura coupling of phenols **1** with arylboronic acids **4** using DCID (Table 2). Phenols bearing electron-donating groups were directly converted into biaryls in 82–91% isolated yields while an electron-withdrawing nitro group in the para position in phenol **1e** (entry 8) reduced the yield to 15%. This may be due to the slow reaction of deactivated phenol with DCID. A sterically set of substituted phenols **1f–g** coupled with **4a** to provide the corresponding biphenyls in moderate yields under identical conditions and the highly sterically hindered phenol **1i** resulted in a sharp drop in reaction yield (Table 2, entry 12).

In addition, a set of 2-naphtols **1j—k** coupled with **4a** to provide the products **5m–n** in excellent yields under identical conditions. An interesting point in this reaction is selectivity in the 1-bromo-2-naphthol compound (Table 2, entry 14). As shown in this table, in the presence of bromine, the coupling is carried out in phenolic carbon. This shows that the activity of intermediate **3** is greater than that of bromine in the Suzuki cross-coupling reaction.

The catalyst Pd/MOF also exhibited good recyclability and stability. For instance, the catalyst was recovered by simple filtration, washed with methanol, dried in an oven and reused four times (Table 3). The catalyst could be stored for a long time under air atmosphere without significant loss of catalytic activity.

A plausible mechanism for the DCID-activated direct Suzuki–Miyaura cross-coupling of phenols by Pd/MOF is shown in Scheme 2.

First, intermediate **3a** is generated from the reaction of phenol and DCID. Second, oxidative addition of **3a** to Pd(0) produces complex **6a**, which undergoes



SCHEME 2 Proposed mechanism for direct Suzuki cross-coupling using DCID catalyzed by Pd/Cu-MOF

transmetalation with phenylboronic acid to generate complex **8a**. Finally, reductive elimination of **8a** produces the desired coupling product **5a**.

3 | EXPERIMENTAL SECTION

3.1 | General information

Pd/$Cu_2(BDC)_2$DABCO (Pd/MOF) was synthesized according to our previous work.[20] X-ray powder diffraction (XRD) measurements were performed using an X'pert MPD Philips diffractometer with Cu radiation source (λ = 1.54050°A) at 40 kV and 40 mA. XPS measurements were conducted on a PHI Quantum 2000 XPS system equipped with an Al X-ray source (1486.6 eV). The Brunauer–Emmett–Teller (BET) surface area of the samples was determined from N_2 adsorption–desorption isotherms using a micrometrics ASAP 2020 analyzer. The sample was characterized using a scanning electron microscope (SEM) from ZEISS at 30 kV with gold coating. Transmission electron microscopy (TEM) was carried out using an EM10C-100 kV series microscope from Zeiss (Germany) and the actual loading of palladium was determined by ICP analysis from Shimadzu (ICPS-7000 ver. 2). ^{1}H NMR spectra were measured ($CDCl_3$) with a Bruker DRX-500 and 600 AVANCE spectrometer at 499.74 MHz. Chemical shifts (δ) are reported in parts per million (ppm) relative to residual undertreated solvent as an internal reference (^{1}H: δ 7.26 for $CDCl_3$; ^{13}C: δ 77.16 for $CDCl_3$). The following abbreviations were used to explain NMR peak multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. Melting points were measured on an Electrothermal 9100 apparatus.

1. Synthesis of DCID

   The process of Guo et al.[17] was used with minor modification. To 2 g (1 mmol) of *N,N′*-DCC in 25 ml dry dichloromethane at 0°C, was added 0.9 ml (1.05 mmol) oxalyl chloride dropwise. The reaction mixture was stirred for 1 h at room temperature. The solid material was separated by filtration and washed with cold dichloromethane. The recrystallization of white solid in ethanol yield 2.5 g DCID (yield: 97%). m.p. = 174–176°C. ^{1}H NMR (499.77 MHz, $CDCl_3$): δ =1.17–1.36 ppm (m, 6H), 1.66–1.69 ppm (m, 2H), 1.71–1.75 ppm (m, 4H), 1.73–1.87 ppm (m, 4H), 2.02–2.10 ppm (m, ^3j = 12.59, ^2j = 2.74, 4H), 3.97-4 ppm (m, ^3j = 12.44, 3.94 Hz, 2H). (Supporting Information)

2. Synthesis and characterization of 2-chloro-1,-3-dicyclohexyl-2-phenoxyimidazolidine-4,5-dione (**3a**)

   Typically, to an oven-dried 25-ml round-bottomed flask containing dry THF was added phenol (0.047 g, 0.5 mmol) and NaH (0.012 g, 0.5 mmol). The reaction mixture was stirred for 30 min at room temperature and then DCID (0.165 g, 0.5 mmol) was added. The reaction mixture was stirred for 1 h at room temperature and completion of the reaction was monitored by TLC. After completion of the reaction salt was filtered and the filtrate was evaporated under reduced pressure to yield 0.1 g of a white solid material (yield 97%). The chemical structure of intermediate **3a** was confirmed by FT-IR and NMR.

   FT-IR (ν cm^{-1}): 2929.44, 2859.75, 1742.45, 1399.83, 1241.28, 1060.46 cm^{-1}. ^{1}H NMR (499.70 MHz, $CDCl_3$): δ 1.15 ppm (m, 4H), 1.18 (m, 4H), 1.65 ppm (m, 2H), 1.71 ppm (m, 4H), 1.79 ppm (m, 6H), 3.95 ppm (m, 1H), 6.76 ppm (d,^3J = 7.59, 2H), 6.82 ppm (t, ^3J = 8.14, 2H), 7.16 ppm (t, ^3J = 7.44, 1H).^{13}C NMR (125.66 MHz, $CDCl_3$): δ 24.41, 28.73, 28.94, 31.87, 114.74, 116.35, 121.22, 128.93, 156.27, 156.79.

3. One-pot direct Suzuki–Miyaura cross-coupling of phenols

   Typically, for the synthesis of **5a** phenol (0.047 g, 0.5 mmol) and NaH (0.012 g, 0.5 mmol) were added to an oven-dried 25-ml round-bottomed flask containing dry THF. The reaction mixture was stirred for 30 min at room temperature and then DCID (0.165 g, 0.5 mmol) was added. The reaction mixture was stirred for 1 h at room temperature and completion of the reaction monitored by TLC. After completion of the reaction phenylboronic acid (0.073 g, 0.6 mmol), K_2CO_3 (0.065 g, 0.5 mmol), and Pd/Cu-MOF (20 mg, 0.01 mol% Pd) were added and the reaction mixture was stirred at 65 °C for the 24 h (TLC monitoring). After completion, the catalyst was separated by centrifugation and chromatography on silica gel was per to purify the products formed. The structures of the biaryls were confirmed by melting point and NMR spectroscopy.

   Biphenyl (0.073 g, 95% yield) (**5a**): white solid; mp 68–70 °C; ^{1}H NMR (499.74 MHz, $CDCl_3$): δ 7.39 ppm (m, 2H), 7.48 ppm (m, 1.84, 4H), 7.64 ppm (m, 4H).

4 | CONCLUSION

We have developed palladium-catalyzed direct cross-coupling reactions of phenols **1** using air-stable and inexpensive DCID. This method does not require the isolation of the intermediate **3** and is therefore more convenient than the traditional methods. Further studies on the development of DCID in organic synthesis are in progress and will be presented in due course.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

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