JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY

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Metal–Organic Framework Nodes Support Single-Site Magnesium–Alkyl Catalysts for Hydroboration and Hydroamination Reactions

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Supporting Information

ABSTRACT: Here we present the first example of a single-site main group catalyst stabilized by a metal–organic framework (MOF) for organic transformations. The straightforward metalation of the secondary building units of a Zr-MOF with Me_2Mg affords a highly active and reusable solid catalyst for hydroboration of carbonyls and imines and for hydroamination of aminopentenes. Impressively, the Mg-functionalized MOF displayed very high turnover numbers of up to 8.4×10^4 for ketone hydroboration and could be reused more than 10 times. MOFs can thus be used to develop novel main group solid catalysts for sustainable chemical synthesis.

Despite their abundance and biocompatibility, alkaline earth metals such as Mg and Ca have found limited application in catalytic processes. Developing catalysts that use these metals can be challenging because of the propensity of heteroleptic complexes to undergo Schlenk-type and/or irreversible ligand redistribution reactions that result in catalytically incompetent homoleptic complexes.[1] To counter such associative intermolecular ligand redistribution reactions, bulky chelating ligands, such as β-diketiminate,[2] aminotroponates, aminotroponiminates,[3] pybox,[4] silylamido phenolate,[5] and tris(oxazolinyl)borate,[6] have been explored in the preparation of main group catalysts for a range of organic transformations, such as hydroamination,[2c,3,7] hydrosilylation,[8] hydroboration,[9] hydrophosphination,[10] Friedel–Crafts alkylation,[4] and ring-opening polymerization.[2a] Although sterically encumbered ligands stabilize the heteroleptic species, they also often impede their catalytic activity by slowing down the binding and activation of substrates. In contrast, the immobilization of heteroleptic alkaline earth metal species in porous solid supports,[11] such as metal–organic frameworks (MOFs), can provide site isolation without relying on bulky ligands and thus provide an alternative route for obtaining active catalysts.

MOFs have recently emerged as an interesting class of highly porous molecular materials with many applications, including gas storage,[12] separation,[13] catalysis,[14] nonlinear optics,[15] biomedical imaging,[16] chemical sensing,[17] drug delivery,[18] and solar energy harvesting.[19] MOFs provide a highly tunable platform for the engineering of single-site solid catalysts for organic transformations that cannot be performed by traditional porous inorganic materials. We recently showed that highly active base-metal catalysts can be stabilized in bipyridyl-based MOFs via active site isolation, while analogous homogeneous catalysts undergo rapid intermolecular deactivation via ligand disproportionation reactions.[20] Herein, we report a simple strategy to stabilize active heteroleptic Mg-alkyl species at secondary building unit (SBUs) of TPHN-MOF (TPHN = 4,4′-bis-(carboxyphenyl)-2-nitro-1,1′-biphenyl) to afford highly active and reusable single-site solid catalysts for hydroboration of carbonyl and imine compounds and for hydroamination of aminoalkenes. Site isolation within the MOF stabilizes catalytically active heteroleptic Mg-alkyl species by shutting down Schlenk-type intermolecular ligand redistribution reactions (Figure 1).

TPHN-MOF of UiO-69 topology was synthesized via a solvothermal reaction between $ZrCl_4$ and H_2TPHN in the presence of DMF and trifluoroacetic acid in 95% yield.[14d] The metalation of $Zr_3(\mu_3\text{-OH})$ sites in SBUs of TPHN-MOF was performed by treating TPHN-MOF with Me_2Mg in THF at room temperature to afford Mg-functionalized MOF material (TPHN-MOF-MgMe) as a yellow solid (Figure 2a). During the metalation reaction, an equivalent amount of methane was generated, which was identified and quantified by GC analysis (Figure S4, Supporting Information [SI]). The disappearance of the $\nu_{\mu_3\text{-OH}}$ band (~3629 cm^{-1}, KBr) in the infrared spectrum of MOF-MgMe indicated that the metalation occurred at $Zr_3(\mu_3\text{-OH})$ sites (Figure S5, SI). Inductively coupled plasma mass spectrometry (ICP-MS) analysis of the digested MOF-MgMe revealed 100% metalation at the $Zr_3(\mu_3\text{-OH})$ sites, corresponding to four Mg centers per Zr_6 node. Crystallinity of TPHN-MOF was maintained upon metalation, as shown by the similarities in the PXRD patterns of TPHN-MOF and MOF-MgMe (Figure 2b). SEM images showed that TPHN-MOF has particle sizes of ~2–3 μm (Figure S9, SI). The single-crystal X-ray diffraction study revealed that MOF-MgMe crystallizes in the $Fm\bar{3}m$ space group, with the $Zr_6(\mu_3\text{-O})_4(\mu_3\text{-OH})_4$ SBUs connected by the TPHN bridging linkers to afford the 12-connected fcu topology. However, due to crystallographic disorder of the MgMe moiety, the Mg coordination environments in MOF-MgMe could not be established by X-ray crystallography (Figure S10, SI). The four MgMe moieties are randomly distributed among the eight μ_3-oxo positions. In addition, every μ_4-O-MgMe moiety is in close proximity to six carboxylate oxygen atoms; one or two of the carboxylate oxygen atoms could possibly tilt the Mg atom off the C_3-axis through weak coordination. These disorders lead to low site occupancy of 1/6 for the MgMe moiety, if we assume Mg coordinates to two carboxylate groups, thus making Mg atoms impossible to observe in the $Fm\bar{3}m$ space group (Figure S10, SI).

Received: April 10, 2016
Published: June 10, 2016

DOI: 10.1021/jacs.6b03689
J. Am. Chem. Soc. 2016, 138, 7488–7491

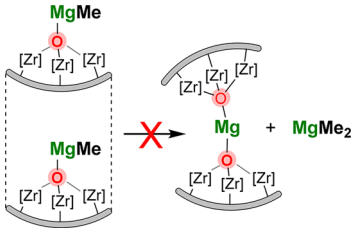


Figure 1. Schematic showing the beneficial effect of active site isolation within a MOF on stabilizing heteroleptic Mg-species by preventing Schlenk-type ligand redistribution reactions.

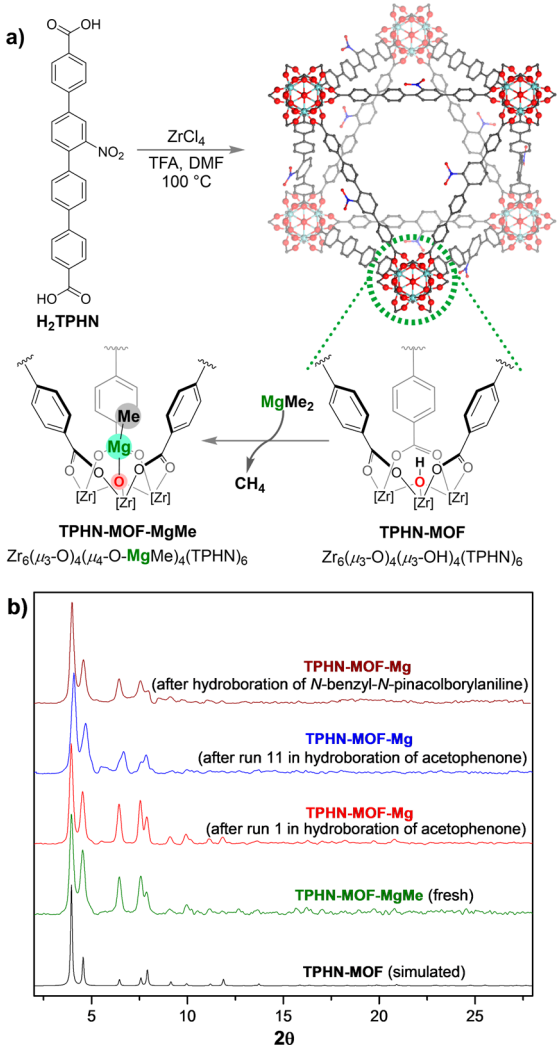
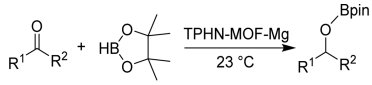


Figure 2. (a) Synthesis of TPHN-MOF and metalation of its SBUs with Me_2Mg to form MOF-MgMe. (b) Similarities among the PXRD patterns simulated from the CIF file (SI) of TPHN-MOF (black) and the PXRD patterns of MOF-MgMe (green), MOF-Mg samples recovered from hydroboration of acetophenone after run 1 (red) and after run 11 (blue), and after hydroboration of *N*-benzylidenebenzenamine show the retention of TPHN-MOF crystallinity after metalation and catalysis.

TPHN-MOF-Mg displayed excellent activity in the hydroboration of a wide range of carbonyl compounds with pinacolborane (Table 1). The hydroboration reactions were performed by treating ketones or aldehydes with equimolar HBpin in the presence of 0.1−0.01 mol % MOF-Mg in hexane or THF at room temperature. At a 0.05 mol % Mg loading, MOF-Mg afforded borate ester products from a range of carbonyl substrates, including alkyl, halogenated, and alkoxy-functionalized aryl ketones and aldehydes in essentially quantitative yields (Table 1). Pure hydroboration products were obtained by simply removing the solid catalyst via centrifugation followed by removal of the organic volatiles. Impressively, a turnover number (TON) of 84 000 was obtained for hydroboration of acetophenone (entry 2, Table 1). Linear and cyclic aliphatic ketones were efficiently reduced in excellent yields (entries 8−10, Table 1). In addition, α,β-unsaturated carbonyl substrates such as cyclohexenone, *trans*-crotonophenone, and *trans*-cinnamaldehyde were reduced selectively at the carbonyl, leaving the C=C bond intact (entries 10, 11, and 17, Table 1).

Table 1. TPHN-MOF-Mg-Catalyzed Hydroboration of Ketones and Aldehydes[a]



entry	product	Mg (mol%)	time (h)	yield[b] (%)	TON
1		0.05	6	100 (97)	>2000
2		0.0011	48	92	84000
3		0.05	12	100	>2000
4		0.05	24	100	>2000
5		0.01	72	100 (99)	>10000
6		0.05	24	100	>2000
7		0.05	24	91	>2000
8		0.1	24	100 (91)	>1000
9		0.05	12	100	>2000
10		0.05	12	100	>2000
11		0.05	12	100	>2000
12		0.05	24	94	1880
13		0.05	24	100 (91)	>2000
14		0.05	48	100 (96)	>2000
15[c]		0.05	48	100 (98)	>2000
16		0.05	48	100 (99)	>2000
17		0.05	48	86	1720
18		0.05	72	88	1760
19		0.05	48	100 (93)	>2000
20		0.05	12 h	100	>2000

[a]Reaction conditions: 1.0 mg of MOF-MgMe, carbonyl substrate, hexanes, HBpin (1.1 equiv), 23 °C. [b]Yield was determined by ^{1}H NMR with mesitylene as the internal standard. Isolated yields are in parentheses. [c]THF was used as the solvent.

DOI: 10.1021/jacs.6b03689
J. Am. Chem. Soc. 2016, 138, 7488−7491

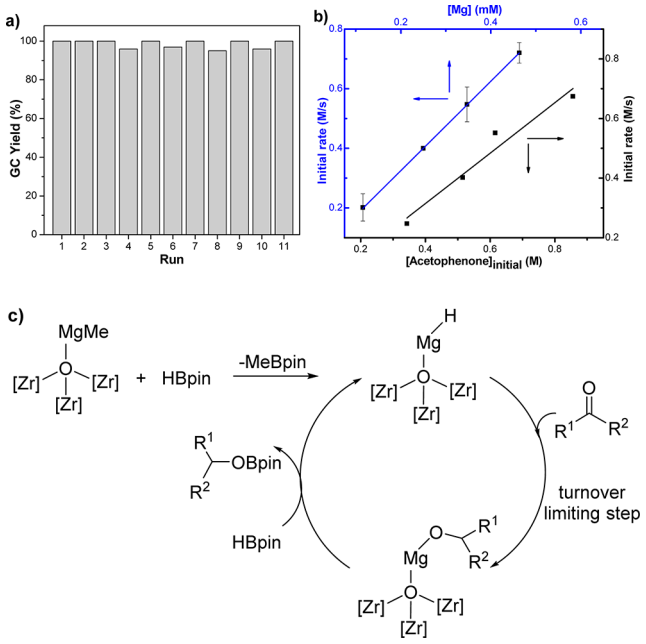
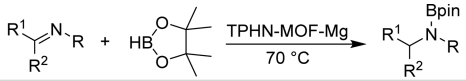
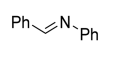
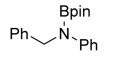
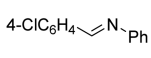
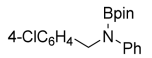
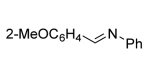
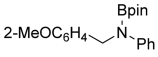
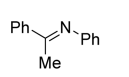
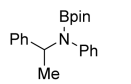
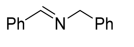
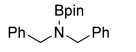


Figure 3. (a) Plot of yields (%) of borate ester at different runs in the reuse experiments of TPHN-MOF-Mg (0.2 mol % Mg) for hydroboration of acetophenone. (b) Kinetic plots of initial rates (d-[acetophenone]/dt) for hydroboration of acetophenone versus [Mg] and $[\text{acetophenone}]_{\text{initial}}$ for the first 10 min, showing the first-order dependence on both components. (c) Proposed catalytic cycle for TPHN-MOF-Mg-catalyzed hydroboration reactions.

Table 2. TPHN-MOF-Mg-Catalyzed Hydroboration of Imines[a]

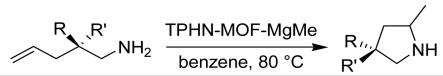


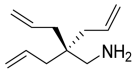
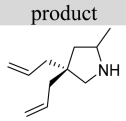
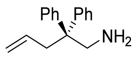
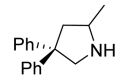
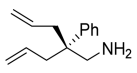
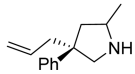
entry	substrate	product	time (h)	yield[b] (%)
1[c]			12	100
2			48	71
3			48	89
4			48	91
5			48	77

[a]Reaction conditions: 1.0 mg of MOF-MgMe (0.5 mol % Mg), imine, HBpin, heptane, 70 °C. [b]Yields were determined by ^{1}H NMR with mesitylene as the internal standard. [c]0.05 mol % Mg was used.

Remarkably, at a 0.2 mol % catalyst loading, MOF-Mg could be recovered and reused for hydroboration of acetophenone at least 10 times (Figure 3a) without loss of MOF crystallinity (Figure 2b). Excellent yields (95−100%) of borate ester were obtained consistently in the reuse experiments with no observation of other byproducts. The PXRD patterns of MOF-Mg recovered from the 1st and 11th runs remained unchanged from that of pristine MOF-Mg (Figure 2b), indicating the stability of the MOFs under reaction conditions. The heterogeneity of MOF-Mg was confirmed by the following

Table 3. TPHN-MOF-Mg-Catalyzed Hydroamination of Aminoalkenes[a]



entry	substrate	product	time (d)	yield[b] (%)
1			2	100 (93)
2			2	100 (94)
3			2	96

[a]Reaction conditions: MOF-MgMe (1.0 mol % Mg), aminoalkene, benzene, 80 °C. [b]Yields were determined by ^{1}H NMR with mesitylene as the internal standard. Isolated yields are in parentheses.

experiments. ICP-MS analyses showed that the amounts of Mg and Zr leaching into the supernatant after the 1st run were only 1.6% and 0.02%, respectively, and after the 11th run were 1.3% and 0.02%, respectively. Moreover, no further hydroboration was observed after removal of MOF-Mg from the reaction mixture, which rules out the role of the leached Mg species in catalyzing hydroboration reactions (Figure S12, SI). An additional control experiment using the unmetalated TPHN-MOF did not afford the hydroboration product, indicating that the catalysis occurred at the supported Mg centers at the SBUs.

Two types of pathways were proposed for the Mg-catalyzed hydroboration of carbonyls: (a) σ-bond metathesis involving insertion of a C═O into a Mg−H bond[9] or (b) zwitterionic mechanism without involvement of Mg−H bond species.[21] The mechanism of MOF-Mg-catalyzed hydroboration reactions was investigated by spectroscopic techniques, gas quantification, and kinetic studies. The treatment of MOF-MgMe (1 mol % Mg) with acetophenone followed by addition of HBpin (PhCOMe:HBpin = 1.2:1.0) in benzene immediately generated MeBpin, and hydroboration reaction occurred without a detectable induction period. After completion of the hydroboration reaction, $Zr_3(\mu_4\text{-O})$-Mg(OCHMePh) was identified the intermediate (Figure S15, SI). In addition, $Zr_3(\mu_4\text{-O})$-Mg(OMe), prepared by treatment of MOF-MgMe with 10 equiv (wrt Mg) of MeOH was also active in catalyzing hydroboration of acetophenone. We thus infer that the rapid reaction between $Zr_3(\mu_4\text{-O})$-MgMe with 1 equiv of HBpin afforded the $Zr_3(\mu_4\text{-O})$-MgH intermediate, which is likely the active catalyst for hydroboration reactions. The empirical rate law, determined by the method of initial rates (<10% conversion), showed that the hydroboration of acetophenone catalyzed by MOF-Mg has a first-order dependence on the Mg and acetophenone concentrations (Figure 3b) and a zeroth-order dependence on the HBpin concentration (Figure S16, SI). Based on our experimental observations, the proposed pathways for hydroboration of carbonyls likely involved the insertion of C═O into the [Mg]−H bond in the turnover-limiting step to give the $Zr_3(\mu_4\text{-O})$-Mg($OCHR^1R^2$) intermediate. The reaction of $Zr_3(\mu_4\text{-O})$-Mg($OCHR^1R^2$) species with HBpin furnished the borate ester product and regenerated $Zr_3(\mu_4\text{-O})$-MgH in the cycle (Figure 3c).

Similar to the hydroboration of carbonyls, TPHN-MOF-Mg is also an active catalyst in the hydroboration of imines to give N-borylamines.[22] At a 0.05 mol % Mg loading, TPHN-MOF-Mg-

DOI: 10.1021/jacs.6b03689
J. Am. Chem. Soc. 2016, 138, 7488−7491

catalyzed hydroboration of *N*-benzylideneaniline with HBpin in heptane at 70 °C for <12 h afforded *N*-benzyl-*N*-pinacolborylaniline in quantitative yield (entry 1, Table 2). MOF-Mg recovered after this reaction remained crystalline, as shown by PXRD (Figure 2b), and the leaching of Mg and Zr into the supernatant was 2.2% and 0.07%, respectively. The hydroboration of substituted imines, however, required higher catalyst loading and longer reaction times (entries 2−5, Table 2), presumably due to the decreased rates of diffusion of the larger substrates and products through the MOF channels.

TPHN-MOF-Mg is also an active catalyst for hydroamination/cyclization of aminoalkenes.[6,23] The treatment of MOF-MgMe with 10 equiv (wrt Mg) of 2,2-bis(2-propenyl)-4-pentenylamine in benzene at room temperature generated an equivalent amount of CH_4, presumably due to the formation of Mg-amidoalkene species (section 5, SI). Upon heating the reaction mixture at 80 °C for 2 d, 4,4-diallyl-2-methylpyrrolidine was obtained in essentially quantitative yield (entry 1, Table 3). ICP-MS analyses of the pyrrolidine product showed very low metal leaching (0.82% for Mg and 0.02% for Zr). At a 1.0 mol % Mg loading, MOF-Mg also afforded 4,4-diphenyl-2-methylpyrrolidine and 4-allyl-2-methyl-4-phenylpyrrolidine from 2,2-diphenyl-4-penten-1-amine and 2-allyl-2-phenylpent-4-enylamine, respectively, in excellent yields (entries 2 and 3, Table 3).

In summary, we have developed the first MOF-supported single-site main group catalyst for organic transformations. Site isolation of the heteroleptic compounds at MOF nodes is the key to affording highly active, robust, and reusable alkaline earth metal catalysts. Due to the diversity of metal cluster SBUs and the ease of functionalizing SBUs with metal ions, MOFs may offer a versatile platform for discovering new catalytic transformations and developing earth-abundant metal catalysts for sustainable synthesis of fine and commodity chemicals.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b03689.

Experimental details and characterization data, MOF-catalyzed hydroboration and hydroamination reactions, and catalyst recycle/reuse procedures (PDF)

X-ray crystallographic data for TPHN-MOF (CIF)

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

This work was supported by National Science Foundation (NSF, grant no. CHE-1464941). We thank Z. Lin, D. Micheroni, and C. Poon for experimental help. Single-crystal diffraction studies were performed at ChemMatCARS, APS, Argonne National Laboratory (ANL). ChemMatCARS is principally supported by the Divisions of Chemistry and Materials Research, NSF, under grant no. NSF/CHE-1346572. Use of the Advanced Photon Source, an Office of Science User Facility operated for the U.S. Department of Energy (DOE) Office of Science by ANL, was supported by the U.S. DOE under Contract No. DE-AC02-06CH11357.

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DOI: 10.1021/jacs.6b03689
J. Am. Chem. Soc. 2016, 138, 7488−7491