

Chiral Iron(II)-Catalysts within Valinol-Grafted Metal-Organic Frameworks for Enantioselective Reduction of Ketones

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UiO-Fe catalyzed hydrosilylation and hydroboration of a range of aliphatic and aromatic carbonyls to afford the corresponding chiral alcohols with enantiomeric excesses up to 99%. Vol-UiO-Fe catalysts have high turnover numbers of up to 15 000 and could be reused at least 10 times without any loss of activity and enantioselectivity. The spectroscopic, kinetic, and computational studies suggest iron-hydride as the catalytic species, which undergoes enantioselective 1,2-insertion of carbonyl to give an iron-alkoxide intermediate. The subsequent σ -bond metathesis between Fe–O bond and Si–H bond of silane produces chiral silyl ether. This work highlights the importance of MOFs as the tunable molecular material for designing chiral solid catalysts based on inexpensive natural feedstocks such as chiral amino acids and base-metals for asymmetric organic transformations.

KEYWORDS: asymmetric catalysis, iron, metal-organic frameworks, hydrosilylation, hydroboration

INTRODUCTION

The development of chiral earth-abundant metal catalysts for the sustainable production of optically active compounds has



Figure 1. Design of amino alcohol-functionalized metal-organic frameworks to develop robust single-site earth-abundant metal catalysts for heterogeneous asymmetric catalysis.

drawn immense interest in recent years because of the lower price and toxicity of the base-metals than late transition metals.^{1–11} The chiral auxiliary ligands play the most crucial role in designing chiral base-metal catalysts as the chiral ligands control the electronic and steric properties of the metal center and create enantioinduction for asymmetric catalysis. Bulky chiral nitrogen-donor or phosphine ligands are typically employed to constitute robust and rigid base-metal catalysts for good enantioselectivity and to prevent intermolecular decomposition.^{1,3,4,12–16} However, intricate design and multistep synthesis of many such ligands increase their production cost that compromise the economic gain of cheap earthabundant metal usage. Additionally, several other factors such as commercial unavailability, difficulty of larger scale synthesis,

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Figure 2. (a) Synthesis of chiral valinol-functionalized UiO-67 MOF (vol-UiO-67) and its metalation with iron. (b) The synthesis of aldehyde-functionalized UiO-68-MOF, its postsynthetic functionalization with L-valinol, and the metalation of chiral valinol-functionalized UiO-68 MOF (vol-UiO-68) with iron.

poor recyclability, and patent issues make the application of many such chiral ligands impractical in industrial chemical synthesis, which becomes the major drawback in commercial supply chain planning.^{13,17,18} Therefore, the development of cheap and affordable chiral ligands from cheap feedstocks for preparing chiral heterogeneous base-metal catalysts is crucial for sustainable asymmetric organic transformations.

Chiral 1,2-amino alcohols are versatile structural motifs widely present in biologically active molecules.¹⁹⁻²² Although chiral 1,2-amino alcohols are easily affordable by reducing naturally occurring amino acids, their application as chiral bidentate ligands in base-metal catalysis is very limited, presumably due to the absence of sterically bulky substituents that leads to the formation of oligomeric metal species or intermolecular decomposition.²³⁻²⁵ In asymmetric catalysis, amino acid-derived 1,2-amino alcohols have been primarily employed as chiral auxiliaries²⁶ or the source of a stereogenic center in the ligand component of the base-metal catalysts,²⁷⁻³⁴ or ligands after multistep derivatization.^{31,35,36} Grafting of amino alcohols onto porous solid supports followed by metalation could provide robust single-site earthabundant metal catalysts that would impose excellent chiral induction within pores for enantioselective catalysis. As a porous and tunable molecular material, metal-organic frameworks (MOFs) have emerged as an interesting class of supports to prepare heterogeneous and robust chiral basemetal catalysts via active-site isolation.³⁷⁻⁷² Owing to their modular and tunable properties, the chemoselectivity and enantioselectivity of chiral MOF-catalysts could be easily optimized by adjusting pore sizes and postsynthetic modification techniques.^{42,73,74} In addition, the precise knowledge of crystalline MOF structures by X-ray crystallography provides distinct advantages over other supported chiral catalysts by enabling rational tuning of catalytic activities/ selectivities through the use of tailor-made building blocks and direct observation of structure-activity relationships.

Herein, we report a strategy of synthesizing chiral mono amino alcohol ligated single-site iron catalysts supported by porous MOFs for highly enantioselective reduction of ketones (Figure 1). We demonstrate that the active-site isolation within MOFs not only stabilize solution inaccessible mono 1,2-amino alcohol coordinated iron species but also afford catalysts having more open metal centers, which facilitates substrates binding to the metal. This work highlights the rational design and synthesis of isoreticular chiral MOFs as the tunable heterogeneous catalyst platforms derived from inexpensive chiral feedstocks and earth-abundant metals for sustainable asymmetric catalysis.

RESULTS AND DISCUSSION

Synthesis and Characterization of Valinol-Functionalized UiO-MOFs and Their Postsynthetic Metalation. Isoreticular and chiral valinol-functionalized MOFs; vol-UiO-67 and vol-UiO-68 are constructed from L-valinol functionalized linear dicarboxylate linkers and $Zr_6O_4(OH)_4$ secondary building units (SBUs) to afford UiO-frameworks.⁷⁵⁻⁷⁹ Both vol-UiO-67 and vol-UiO-68 were synthesized following a similar procedure via synthesizing the aldehyde-functionalized UiO-67-CHO and UiO-68-CHO MOFs, respectively, followed by the grafting of L-valinol within these MOFs (Figure 2). The solvothermal reaction between 2-formyl-[1,1'-biphenyl]-4,4'dicarboxylic acid and ZrCl4 in DMF at 80 °C afforded UiO-67-CHO.⁸⁰ Likewise, heating a mixture of 2'-formyl-[1,1':4',1''terphenyl]-4,4 $^{\prime\prime}$ -dicarboxylic acid and ZrCl4 in DMF at 90 °C produced UiO-68-CHO. The presence of aldehyde groups at the linkers of MOFs was confirmed by ¹H NMR spectra of the digested MOFs (Figure S59, SI). The UiO-topology of both UiO-67-CHO and UiO-68-CHO was assigned by the similarity of their PXRD patterns to those of simulated UiO-67 and UiO-68 MOFs, respectively. The condensation reaction between the aldehyde moiety of MOF and amino group of Lvalinol furnished the valinol-grafted chiral vol-UiO MOFs



Figure 3. (a) PXRD patterns of simulated UiO-67 MOF (black),⁸⁵ freshly prepared pristine UiO-67-CHO (red), vol-UiO-67 (green), vol-UiO-67-FeCl (magenta), vol-UiO-67-Fe recovered after hydrosilylation (blue) and hydroboration (purple) of 4-methoxyacetophenone. (b) PXRD patterns of simulated UiO-68 MOF (black),⁸⁶ freshly prepared pristine UiO-68-CHO (red), vol-UiO-68 (blue), vol-UiO-68-FeCl (magenta), vol-UiO-68-Fe recovered after hydrosilylation (green) and hydroboration (violet) of 4-methoxyacetophenone. (c) XANES spectra of FeCl₂(black), vol-UiO-68-FeCl (red), vol-UiO-68-FeH (blue) and vol-UiO-68-Fe after hydrosilylation of 4-methoxy-acetophenone (magenta) at the Fe K-edge. (d) Fe 2p XPS spectrum of vol-UiO-68-FeCl. (e) Zr 3d XPS spectrum of vol-UiO-68-FeCl. (f) BET nitrogen sorption isotherms (77 K) of vol-UiO-67, vol-UiO-68, vol-UiO-67-FeCl, and vol-UiO-68-FeCl. (g) DFT optimized structure of vol-FeCl(THF)₃ moiety within vol-UiO-FeCl MOFs. (h) Fe Kedge EXAFS spectra of vol-UiO-68-Fe and its fits in R-space, showing the real component (blue hollow triangles) and magnitude (blue solid triangles) of the Fourier transformation. The fitting range is 1.0–4.0 Å in R-space (within the gray lines).

through the formation of imine linkages.^{81–84} The ¹H NMR spectra of the digested vol-UiO-67 and vol-UiO-68 showed the characteristic peaks of imine and valinol moieties and the disappearance of aldehyde peaks suggesting complete post-synthetic modification of UiO-CHO MOFs. The deprotonation of hydroxyl group of valinol moiety by LiN[Si(Me)₃]₂ (LiHMDS) followed by salt metathesis reaction with FeCl₂ in THF afforded iron-metalated vol-UiO-FeCl as a light yellow solid. Inductively coupled plasma optical emission spectroscopy (ICP-OES) showed Zr/Fe ratios of 1.66 and 1.44, corresponding to the Fe-loadings of 60% and 71% with respect to the valinol moiety of vol-UiO-67 and vol-UiO-68, respectively. The crystallinity and structure of MOFs remained intact upon metalation as evidenced by the similarity in the

PXRD patterns of freshly prepared vol-UiO-FeCl with those of pristine vol-UiO (Figure 3a,b).

Transmission electron micrograph of vol-UiO-68-FeCl displayed octahedron particles having the average diameter of 1.0 μ m (Figure S8a, SI). The oxidation state of the Fecenters of vol-UiO-FeCl was determined by X-ray absorption near-edge structure (XANES) and X-ray photoelectron spectroscopy (XPS), and the coordination environment of iron was investigated by X-ray absorption fine structure (EXAFS) spectroscopy and density functional theory (DFT) studies. The XANES spectroscopy of vol-UiO-FeCl indicates the Fe^{II} oxidation state as its pre-edge position aligned well with that of FeCl₂ (Figure 3c). The assignment of +2-oxidation state of iron was further supported by XPS spectroscopy based

Table 1. Asymmetric Hydrosilylation of Ketones Catalyzed by vol-UiO-Fe $MOFs^a$

	0 м	OF-Fe O[Si] K ₂ CO ₃ /M	leOH) Н
R	⊥	ne, THF R*	R ¹	R	* R ¹
	1	2			3
Entry	Product	Catalyst	Silane	%Yield ^b	%ee ^c
		(UiO-Fe)		(TOF/min)	
1	он	vol-UiO-67-Fe	(EtO) ₂ MeSiH	94 (188)	99 (S)
2		m-vol-UiO-67-Fe	(EtO) ₂ MeSiH	96 (240)	99 (S)
3	MeO 3a	vol-UiO-68-Fe	(EtO) ₂ MeSiH	96 (256)	99 (S)
4		vol-UiO-68-Fe	PhSiH ₃	92 (230)	89 (S)
5	ОН	vol-UiO-67-Fe	(EtO) ₂ MeSiH	90 (180)	92 (S)
6		m-vol-UiO-67-Fe	(EtO) ₂ MeSiH	90 (225)	93 (S)
7	HO 3b	vol-UiO-68-Fe	(EtO)2MeSiH	92 (230)	93 (S)
	ОН				
8	HO	vol-UiO-68-Fe	(EtO) ₂ MeSiH	94 (200)	99 $(S)^{d}$
	3c				
0	⇒ ↓			00 (0 (0)	22 (7)
9	×`	vol-U1O-68-Fe	(EtO) ₂ MeS ₁ H	92 (263)	99 (8)
	0 ₂ N 3d				
10	OH	vol-UiO-68-Fe	(EtO) ₂ MeSiH	87 (174)	89 (S)
11		vol-UiO-68-Fe	PhSiH ₃	70 (140)	80 (S)
	Br 3e				
	ŎН				
12	\sim	vol-UiO-68-Fe	(EtO)2MeSiH	97 (236)	98 (S)
12	→ 3 1	vol LliO 68 Fo	(EtO), MaSiH	90 (200)	00 (5)
13	\downarrow \downarrow	vol-UiO-68-Fe	PhSiH ₂	90 (200) 88 (176)	99(3)
11	* Ph	101 010 00 10	1 1101113	00(1/0)	<i>))</i> (0)
	🧹 3g				
				04 (040)	22 (7)
15		vol-UiO-68-Fe	(EtO) ₂ MeSiH	96 (242)	99 (S)
	3h				
16	ОН	vol-UiO-67-Fe	(EtO) ₂ MeSiH	80 (160)	99 (R)
17		vol-UiO-68-Fe	(EtO) ₂ MeSiH	87 (248)	99 (R)
	N 3i				
18	ÓН	vol-UiO-67-Fe	(EtO) ₂ MeSiH	92 (184)	97 (R)
19		vol-UiO-68-Fe	(EtO) ₂ MeSiH	92 (263)	99 (R)
	N 3i				
	, с у				
20		vol-UiO-68-Fe	(EtO)2MeSiH	94 (209)	99 (S)
	S 3k			, ,	. /
21	~~ JN	vol-UiO-67-Fe	(EtO) MeSiH	84 (168)	99 (R)
22	ОН т	vol-UiO-68-Fe	(EtO) ₂ MeSiH	86 (215)	99(R)
			(Lee) _meon	00 (210)	// (N)
	31				

^{*a*}Reaction conditions: 0.05 mol % Fe, 0.585 mmol ketone, 0.643 mmol $(EtO)_2$ MeSiH or PhSiH₃, 1 mL THF, 25 °C, 10 min. ^{*b*}Isolated yield, TOF is calculated on the basis of the GC-yield of **2** for the first 10% conversion. ^{*c*}%ee was determined by chiral GC or HPLC, absolute configurations were assigned on the basis of the literature reports. ^{*d*}%ee was determined by chiral HPLC.

on Fe^{II} $2p_{3/2}$ binding energy of 709.4 eV and $2p_{1/2}$ binding energy of 722.9 eV (Figure 3d). The oxidation state of Zr⁴⁺ at SBUs was unchanged upon postsynthetic functionalization of vol-UiO as indicated by XPS of vol-UiO-FeCl (Figure 3e). The DFT-calculation with the B3LYP/6-311G (d,p) basis set suggests an octahedral iron cation coordinated with one neutral imine nitrogen, one monoanionic oxo, one chloride, and three THF molecules (Figure 3g). The calculated bond lengths of Fe–N, Fe–O(vol), and Fe–Cl are 2.07, 1.93, and 2.48 Å, respectively, while the Fe–O(THF) distances are 2.06, 2.07, and 2.16 Å. The EXAFS feature of the iron-centers in vol-UiO-FeCl fitted well with this DFT optimized structure to obtain the nearly identical local coordination environment and bond lengths, thus revealing the formation of vol-FeCl(THF)₃ species within the MOFs (Figure 3h). Vol-UiO-67-FeCl and vol-UiO-68-FeCl had a BET surface area of 785 and 1382 m²/ g, respectively, and the corresponding average pore sizes are 0.7 and 1.4 nm, respectively (Figure 3f). In order to make the pores of the metalated MOFs more spacious for facile mass transport, we have also prepared m-vol-UiO-67-Fe by doping of about 50% of its functionalized linkers with the unfunctionalized one (section 2.3, SI). ICP-OES analysis revealed a Zr/Fe ratio of 3.54, corresponding to the Fe-loading of 56% with respect to the valinol moiety of m-vol-UiO-67.

Asymmetric Hydrosilylation of Ketones Catalyzed by Vol-UiO-Fe MOFs. Upon activation with LiCH₂SiMe₃, all vol-UiO-Fe MOFs became active in catalyzing asymmetric hydrosilylation of a range of aromatic and aliphatic ketones to afford the corresponding silvl ethers with excellent enantiopurity. Asymmetric hydrosilylation using homogeneous Fe-catalysts typically requires high catalyst loading (0.3-5%)and also chromatographic purification to afford pure products.^{4,7,8,87–93} The hydrosilvlation reaction was performed by stirring a mixture of carbonyl substrate, 1.1 equiv of silane such as (EtO)₂MeSiH or PhSiH₃ and catalytic amount of vol-UiO-Fe in THF at room temperature, and pure silvl ether was obtained in most cases by the simple removal of solid MOF and volatiles from the crude product mixture. The enantiomeric excess of the silvl ether product was determined by GCanalysis of the corresponding secondary alcohol obtained after hydrolysis of the silyl ether with K₂CO₃ in methanol. At a 0.05 mol % of Fe-loading, vol-UiO-67-Fe catalyzed hydrosilylation of 4-methoxyacetophenone (1a) using (EtO)₂MeSiH in THF at room temperature gave full conversion within 10 min, and diethoxy((1-(4-methoxyphenyl)ethyl)peroxy)(methyl)silane (2a) was obtained in quantitative yield with 99% ee. Under the identical reaction conditions, m-vol-UiO-67-Fe and vol-UiO-68-Fe also produced 2a in excellent yields with 99% ee. In general, m-vol-UiO-67-Fe and vol-UiO-68-Fe had similar activities but displayed higher turnover frequency (TOF) than vol-UiO-67-Fe likely due to the facile diffusion of substrates and product molecules through their larger channels (entries 1–3, 5–7, Table 1). Hydrosilylation of 1a remarkably gave 15 000 TON with UiO-68-Fe. Several other substituted acetophenones bearing different functional groups such as methoxy (1a), hydroxy (1b and 1c), and nitro (1d) were reduced to their corresponding alcohols in good yields with ee up to 99% (entries 2–9, Table 1). Halogenated acetophenone (4-bromoacetophenone) was also efficiently reduced to give the corresponding silvl ether (2e) with 89% ee (entries 10 and 11, Table 1). Hydrosilylation of aliphatic aromatic ketones such as 2-methyl-1-phenylpropan-1-one (1f), unsymmetric benzophenone such as phenyl(o-tolyl)methanone) (1g) gave the reduced products with 99% ee under identical reaction conditions (entries 12-14, Table 1). A smaller-sized substrate, methyl-1-phenylpropan-1-one (1f), showed a higher TOF than a larger one such as phenyl(o-tolyl)methanone) (1g) (entries 12 and 13, Table 1).

At a 0.05 mol % Fe-loading, both vol-UiO-67-Fe and vol-UiO-68-Fe efficiently hydrosilylated heterocyclic aromatic ketones such as 1-(pyridin-2-yl)ethanone (1i), 1-(pyridin-4-yl)ethanone (1j) and 1-(thiophen-2-yl)ethanone (1k) to afford corresponding chiral alcohols (3i-k) with 99% ee



Figure 4. (a) % GC-yield and the corresponding %ee of silyl ether (2a) at several runs in the recycle of vol-UiO-68-Fe for hydrosilylation of 4-methoxyacetophenone. (b) % GC-yield and the corresponding %ee of borate ester (4a) at several runs in the recycle of vol-UiO-68-Fe for hydroboration of 4-methoxyacetophenone. (c) Plots of initial rates -(d[substrate]/dt) for hydrosilylation of 4-methoxyacetophenone versus initial concentrations of iron and 4-methoxyacetophenone for the first 5 min. (d) Fe 2p XPS spectrum of vol-UiO-68-FeH. (e) Zr 3d XPS spectrum of vol-UiO-68-FeH. (f) EXAFS spectra and fits in R-space at the Fe K-edge of vol-UiO-68-Fe after hydrosilylation of 4-methoxyacetophenone showing the magnitude (blue solid triangles) and real component (blue hollow triangles) of the Fourier transformation. The fitting range is 1.1-4.0 Å in R-space (within the gray lines).

(entries 16-20, Table 1). Moreover, aliphatic ketone such as 6-methylhept-5-en-2-one (11) was reduced by 0.05 mol % of vol-UiO-68-Fe or vol-UiO-67 using (EtO)₂MeSiH to afford (R)-6-methylhept-5-en-2-ol with 99% ee (entries 21 and 22, Table 1). Importantly, vol-UiO-68-Fe could be recycled and reused for at least 11 times for reduction of 4-methoxyacetophenone (1a) using (EtO)₂MeSiH without diminishing its activity and enantioselectivity (Figure 4a). The leaching of iron and zirconium in supernatant after recycling were 0.03% and 0.21% after run 1, 0.08% and 0.5% after run 8, respectively, as analyzed by ICP-OES (Table S1, SI). The crystallinity of the MOFs remained intact after the reduction of 4-methoxyacetophenone as evidenced by the PXRD pattern (Figure 3a,b). Compared with the reported homogeneous iron catalysts for asymmetric hydrosilylation of ketones, vol-UiO-Fe catalysts require low Fe-loading (0.05 mol %) and could be easily reusable.^{4,7,8,87-93} Furthermore, pure products were afforded after catalysis without any chromatographic purification due to the heterogeneous nature of the MOFs.

Mechanistic Investigation of Vol-UiO-Fe-Catalyzed Asymmetric Hydrosilylation of Ketones. To study the reaction mechanism of vol-UiO-Fe catalyzed asymmetric hydrosilylation of ketones, we have performed several experiments such as identification of key intermediates and resting states of the catalyst, kinetics, and DFT calculations. The treatment of LiCH₂SiMe₃ with vol-UiO-FeCl(THF)₃ in THF presumably forms vol-UiO-Fe(CH₂SiMe₃) precatalyst, which produces vol-UiO-FeH catalyst upon addition of (OEt)₂MeSiH via σ -bond metathesis at room temperature. The heating of a mixture of vol-UiO-FeH with H₂O produced nearly one equivalent of H_2 as analyzed by gas chromatography suggesting the formation of iron-hydride as the active catalytic species (section 3.3, SI). The XANES and XPS analysis of vol-UiO-FeH indicated the presence of Fe^{II}-centers (Figures 3c and 4d). We have also identified the resting state of the catalyst by EXAFS studies of vol-UiO-68-Fe recovered after hydrosilvlation of 4-methoxyacetophenone in THF. The EXAFS fit at the Fe K-edge revealed a distorted tetrahedral geometry of Fe^{II} coordinated to a vol-ligand, O[S-CH(Ar)(Me)] and one THF molecule with no feature corresponding to the reduced metallic Fe-particles (Figure 4f). The EXAFS fitting of vol-UiO-68-Fe-O[S-CH(Ar)(Me)](THF) resting state gave a Fe-N(vol) distance of 1.99 Å, Fe-O(vol) of 1.89 Å, Fe-O(THF) of 2.09 Å and Fe-O(alkoxide) of 1.91 Å. The ironalkoxide resting state suggests that the enanatioselective insertion of carbonyl into the Fe-H likely occurs in the catalytic cycle. The lack of any characteristic reflection peaks at higher 2θ angles in the PXRD spectra of vol-UiO-68-FeH and vol-UiO-68-Fe after catalysis also precludes the formation of Fe-particulates upon treatment of silane and during the catalysis (Figure S5, SI).

Importantly, the homogeneous control, prepared from (S,E)-2-(benzylideneamino)-3-methylbutan-1-ol and FeCl₂, was far less active and enantioselective than vol-UiO-68-Fe presumably because of the detrimental intermolecular interaction (section 4.7, SI). We thus believe that the chiral single-site iron-species (vol-FeH) is stabilized within MOFs via active site isolation that prevents intermolecular decomposi-



INT-3(3)-THF (resting state)

Figure 5. Mechanistic proposal for vol-UiO-Fe catalyzed asymmetric hydrosilylation of ketones.

tion. The enantiomeric excesses of the product 2a did not change by varying the concentration of the ketone 1a, which indicated that the catalyst's structure remain unchanged during the catalysis. ¹H NMR spectrum of the digested vol-UiO-Fe after hydrosilylation of 1a showed the retention of vol-moiety of the linkers. On the basis of these experimental results, we surmise that the coordination of the carbonyl to the iron followed by 1,2-isertion of carbonyl group into the Fe-H bond gives Fe-alkoxide intermediate. Subsequently, the σ -bond metathesis of Fe-alkoxide and silane furnish the silyl ether product and regenerates Fe-hydride (Figure 5).95 The empirical rate law for hydrosilylation of 1a using (OEt)₂MeSiH was also determined by the initial rate method for the first 5 min of the catalysis (section 5, SI). The initial substrate conversion rates had first-order dependency on both 1a and iron (Figure 4c) but were independent of silane concentrations (Figure S10, SI). The empirical rate law suggests that a carbonyl molecule and iron-catalyst are involved in the turnover-limiting step. We thus infer a reversible coordination of carbonyl to the iron followed by insertion of the carbonyl into the Fe-H as the turnover-limiting step in the catalytic cycle.

To gain additional insight into the proposed mechanism and investigate the origin of the enantioselectivity, we have modeled the whole catalytic cycle using DFT methods at 298 K (Figure 6). In the case of the S-pathway, the DFToptimized structures reveal that the carbonyl (1a) coordinates to iron from the opposite side of the bulky isopropyl-group of vol-Fe catalyst to give intermediate INT-2(S) and then the insertion takes place at the *Re*-face of the carbonyl in the



Figure 6. DFT-calculated Gibbs free enthalpy reaction profile diagram of vol-UiO-Fe catalyzed hydrosilylation of 4-methoxyacetophenone (1a) using $(OEt)_2MeSiH$ at 298 K. Structural models of the two stereodetermining transition states, **TS-1**(*S*) and **TS-1**(*R*) are shown at the top. The carbon, nitrogen, oxygen, hydride, and iron atoms of **TS-1**(*S*) and **TS-2**(*R*) are shown in gray, blue, red, whitish, and purple color, respectively.

stereodetermining transition state TS-1(S). The conversion of INT-2(S) to INT-3(S) is exergonic by 9.1 kcal/mol with an energy barrier of 12.4 kcal/mol. Subsequently, the σ -bond metathesis of Fe-O bond of INT-3(S) with Si-H bond of (OEt)₂MeSiH, associating with an activation free energy of 5.5 kcal/mol, gives rise to the formation of 2a(S) and reproduces vol-FeH. The free energy diagram also reveals that the coordination of THF to INT-3(S) leads to the formation of lowest energy intermediate INT-3(S)-THF, which is also identified as the resting state of the vol-UiO-68-Fe catalyst by our EXAFS studies. The DFT-calculated energy profile diagram revealed that the Re-face attack in TS-1(S), leading to the generation of (S)-2a, is energetically favored by 2.8 kcal/ mol $(\Delta \Delta G^{\#}_{TS-1})$ than the *Si*-face attack in **TS-1**(*R*), producing (R)-2a, which is consistent with the experimentally observed enantioselectivity at 298 K. The structural models of TS-1(R)and TS-1(S) in Figure 6 showed that Si-face attack is steroelectronically disfavored due to the steric repulsion between the isopropyl group of the vol-ligand and the aryl substituent of the ketones in the R-pathway.

Asymmetric Hydroboration of Ketones Catalyzed by Vol-UiO-Fe MOFs. Upon activation with LiCH₂SiMe₃, both UiO-67-Fe and UiO-68-Fe became the active catalysts for the asymmetric hydroboration of aliphatic and aromatic ketones using pinacolborane (Table 2).^{96,97} The reaction of ketones with 1.1 equiv of pinacolborane in the presence of 0.05 mol % Fe loading, vol-UiO-Fe for 12 min in THF at room temperature produced borate esters in excellent yields and enantiopurity. In most cases, the borate esters were obtained in quantitative yields by simple removal of the solid MOF-catalyst and volatiles. A wide range of aromatic ketones with different

Table 2. Asymmetric Hydroboration of Ketones Catalyzed by Vol-UiO-Fe $MOFs^{a}$

	O vol-UiO-Fe OBpin					
	$R^1 R^2 + HB$	THF	$\rightarrow R^1 \stackrel{\checkmark}{*} R^2$			
Entry	Product	UiO-Fe catalyst	% GC-Yield	%ee ^b		
1	OBpin * Me MeO 4a	vol-UiO-67-Fe	>98	99 (S)		
2	OBpin * Me O ₂ N 4d	vol-UiO-67-Fe	>98	99 (S)		
3	OBpin * Me Br 4e	vol-UiO-67-Fe	>98	70 (<i>S</i>)		
4	OBpin * 4f	vol-UiO-67-Fe	>98	99 (S)		
5	OBpin	vol-UiO-67-Fe	96	99 (S)		
6	* Ph 4g	vol-UiO-68-Fe	>98	99 (S)		
7	OBpin * Me 4h	vol-UiO-67-Fe	>98	99 (S)		
8	OBpin * Me N 4i	vol-UiO-67-Fe	>98	99 (R)		
9 10	OBpin * Me N 4j	vol-UiO-67-Fe vol-UiO-68-Fe	>98 >98	97 (R) 99 (R)		
11	OBpin * 4I	vol-UiO-67-Fe	>98	99 (R)		

"Reaction conditions: 0.05 mol % Fe, 0.585 mmol ketone, 0.643 mmol pinacolborane, 1 mL THF, 25 °C, 12 min. "b%ee were determined by chiral GC after oxidizing the borate esters (4) to the corresponding alcohols, and absolute configurations were assigned on the basis of the literature reports.

functional groups have been successfully hydroborated to afford the corresponding borate esters with enantiopurity up to 99% and TONs up to 12 000. Hydroboration of heteroarenes such as 2-acetylpyridine and 4-acetylpyridine produced 4i and 4j, respectively, in quantitative yields with 99% ee (entries 8–10, Table 2). Under the identical reaction conditions, vol-UiO-Fe also efficiently reduced aliphatic ketone such as 6-methylhept-5-en-2-one (11) to afford (R)-6-methylhept-5-en-2-ol (41) with 99% ee (entry 11, Table 2).

CONCLUSIONS

In conclusion, we have demonstrated a strategy of developing heterogeneous single-site chiral base metal catalysts using easily affordable amino alcohols as the chiral ligands and MOFs as the porous support. The amino alcohol ligated iron catalysts were prepared by grafting L-valinol within the pores of MOFs followed by postsynthetic metalation. The resultant MOF-Fe catalysts were highly active and enantioselective in the hydrosilylation and hydroboration of a range of aromatic and aliphatic ketones with excellent functional group compatibility at room temperature to afford optically active reduced products with ee up to 99%. The enantioselective hydrosilylation and hydroboration of prochiral ketones provide chiral alcohols with wide range applications in organic synthesis, materials science, and pharmaceutical chemistry. Due to the porous and reticular nature of the MOFs, the activity and selectivity of the MOFs were tuned by varying the pore sizes and exploiting a mixed ligand strategy. The coordination of iron within MOFs was elucidated using EXAFS with DFT models. Spectroscopic, kinetic, and computational studies explored the identification of the catalytic species and the catalyst's resting state, the mechanism of hydrosilylation reactions, and the origin of the enantioselectivity. This work highlights the importance of MOFs as the tunable molecular material for developing chiral earthabundant metal catalyst ligated with inexpensive chiral amino alcohols for sustainable asymmetric organic transformations.

ASSOCIATED CONTENT

3 Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acscatal.1c02529.

Synthesis and characterization of MOF-Fe materials, procedures for catalytic reactions, details for kinetics, EXAFS and GC-analysis, and DFT calculations (PDF)

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Notes

The authors declare no competing financial interest.

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