Photocatalytic Metal−Organic Frameworks for Selective 2,2,2-Trifluoroethylation of Styrenes

Xiao Yu[†] and Seth M. Cohen*[,‡]

[†]Department of Nanoengineering, University of California, San Diego, La Jolla, California 92093, United States
[‡]Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California 92093, United States

S *Supporting Information*

ABSTRACT: Synthesis of CF_3-containing compounds is of great interest because of their broad use in the pharmaceutical and agrochemical industries. Herein, selective 2,2,2-trifluoroethylation of styrenes was catalyzed by Zr(IV)-based MOFs bearing visible-light photocatalysts in the form of Ir(III) polypyridyl complexes. When compared to the homogeneous Ir(III) catalyst, the MOF-based catalyst suppressed the dimerization of benzyl radicals, thus enhancing the selectivity of the desired hydroxytrifluoroethyl compounds.

The development of synthetic methods for CF_3-containing compounds has gained increasing attention because of the growing demand in the pharmaceutical and agrochemical industries.[1−3] Fluorinated organic compounds can display enhanced lipophilicity, membrane permeability, elevated electronegativity, and resistance to oxidation, making many such compounds promising drug candidates.[4] As a consequence, substantial efforts have been devoted to the incorporation of CF_3 groups into various organic structures,[5−9] including via direct 2,2,2-trifluoroethylation through $CF_3CH_2\cdot$ radical processes.[10−12]

Metal−organic frameworks (MOFs) are an emerging class of microporous crystalline materials[13,14] with extended structures built from organic bridging ligands and inorganic connecting points. These materials have been widely used in gas storage/separation,[15−17] chemical sensing,[18] drug delivery,[19] and catalysis.[20] Importantly, MOFs are readily functionalized providing versatile platforms for including catalytic sites.[21] The abundant choice of porous structures imposes size- and shape-selective restrictions through well-defined channels and pores. For example, Long et al. has demonstrated size selectivity in a Mn-based MOF catalyst for the cyanosilylation of aromatic aldehydes and the Mukaiyama-aldol reaction, because the pores of the MOF are too small to accommodate large substrates.[22,23] The Li group showed that MOFs can be used in a "ship-in-a-bottle" synthesis to afford selective photochemical products from a cage effect.[24] Regio- and enantioselective reactions can be realized by incorporating stereoselective catalysts into MOFs or confining chiral substrates within the micropores of solid materials.[25−28] In one important example, Lin et al. was able to synthesize homochiral MOFs with privileged chiral ligand BINOL (1,1′-bi-2-naphthol), which was used as a heterogeneous asymmetric catalyst upon metalation with Ti, showing complete conversion and high ee for diethylzinc addition to aldehydes.[29] Other chiral ligands, such as BINAP, chiral salens, and L-proline, have also been proven to be useful asymmetric catalysts in MOFs for catalyzing other asymmetric reactions.[30−32] In many cases, MOF-based catalysts show better performance and easier separation/recovery when compared to homogeneous systems.

The ability of Ir(III) polypyridyl complexes, such as $Ir(ppy)_3$, to function as visible light photocatalysts have been recognized and extensively investigated to synthesize fine chemicals.[33,34] Considering the high cost of these precious metal photoredox catalysts, using MOFs as heterogeneous and easily reusable systems could be of substantial value.[35−37] Postsynthetic approaches have proven to be useful for preparing single-site catalysts within MOFs.[38] In particular, incorporation of catalytic active sites into the Zr(IV)-based UiO (UiO = University of Oslo) series of MOFs has proven to be attractive because of the outstanding chemical stability and robust crystallinity of these materials.[39,40]

Herein, we incorporated $[Ir^{III}(ppy)_2(dcbpy)]Cl$ (bis(4-phenyl-2-pyridine)(5,5′-dicarboxyl-2,2′-bipyridine)iridium(III) chloride) and $[Ir^{III}(ppy^{F'})_2(dcbpy)]Cl$ (bis(2-(2,4-difluoro-phenyl)-5-(trifluoromethyl)pyridine)(5,5′-dicarboxyl-2,2′-bipyridine)iridium(III) chloride) into the UiO-67 framework via postsynthetic modification (PSM). The resulting MOFs exhibit efficient photocatalytic ability and high selectivity for 2,2,2-trifluoroethylation of styrenes under visible light irradiation at ambient atmosphere. Notably, the UiO-67-Ir(L)$_2$ catalysts were observed to show selectivity for the reaction products that are reversed when compared to the homogeneous Ir(III) analogs. The solid-state catalyst apparently confined intermediate radicals within the pores and suppressed the formation of an undesirable dimerization side product, showing selectivity toward a desired pathway.[41]
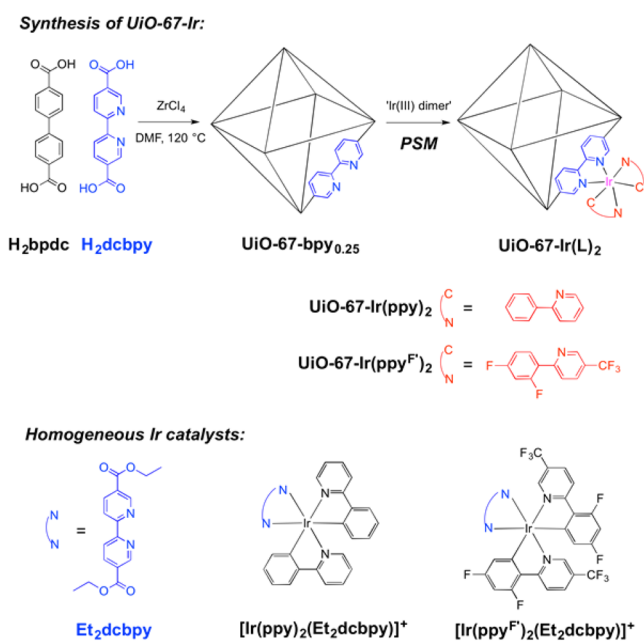
The parent UiO-67-bpy$_{0.25}$ framework was prepared using solvothermal conditions containing a mixture of $ZrCl_4$, H_2bpdc (biphenyldicarboxylic acid)/H_2dcbpy (2,2′-bipyridine-dicarboxylic acid) ligands, and benzoic acid (as a modulator) at 120 °C in DMF for 24 h (Scheme 1). Two Ir(III) dimers, $[Ir(ppy)_2Cl]_2$ and $[Ir(ppy^{F'})_2Cl]_2$, were synthesized by combining $IrCl_3\cdot H_2O$ with the corresponding phenylpyridine ligands in 2-ethoxyethanol/H_2O at 100 °C for 24 h. Framework postsynthetic modification (metalation, PSM) of UiO-67-bpy$_{0.25}$ using these dimeric precursors was monitored by ^1H NMR. After digestion of the MOFs in D_3PO_4/d^6-DMSO,

Scheme 1. Synthesis of UiO-67-Ir via PSM and Homogeneous Ir Benchmark Catalysts

Figure 1. PXRD of UiO-67-bpy$_{0.25}$ (black), UiO-67-Ir(ppy)$_2$ (red), and UiO-67-Ir(ppy$^{F'}$)$_2$ (blue).

Table 1. Conversions and Yields of Photocatalytic Trifluoroethylation of Styrene[a]

entry	catalyst	hν	% con	yield[b] A/B/C %
1	Ir(ppy)$_3$	+	99	10/9/80
2	[Ir(ppy)$_2$(Et$_2$dcbpy)]Cl	+	99	20/7/72
3	[Ir(ppy$^{F'}$)$_2$(Et$_2$dcbpy)]Cl	+	99	32/8/60
4	UiO-67-Ir(ppy)$_2$	+	99	60/11/28
5	UiO-67-Ir(ppy$^{F'}$)$_2$	+	99	76/18/2
6	no catalyst	+	0	0
7	UiO-67-bpy$_{0.25}$	+	0	0
8	UiO-67-Ir(ppy$^{F'}$)$_2$	-	0	0

[a]Reaction conditions: 4-methoxystyrene (0.1 mmol), 2-iodo-1,1,1-trifluoroethane (0.3 mmol), N,N-diisopropylethylamine (0.3 mmol), acetonitrile (2 mL) and water (200 μL), catalyst (5 mol %), 32 W compact fluorescent bulb, room temperature under air atmosphere for 48 h. [b]Determined by GC-MS.

where the kinetically inert Ir(III) complexes remained intact even under these dissolution conditions. Integration of the proton resonances for the Ir(III) complexes and the free dcbp^{2-} ligands confirmed the degree of PSM, which is tunable by varying the modification time. For example, UiO-67-bpy$_{0.25}$ was combined with 0.3 equiv of [Ir(ppy)$_2$Cl]$_2$ in CH$_2$Cl$_2$/MeOH at 55 °C for 24 h to produce the desired UiO-67-Ir(ppy)$_2$ with 20% overall Ir(III) loading in UiO-67-bpy$_{0.25}$ (~80% metalation of the bipyridine sites, Figure S1). Similarly, PSM with [Ir(ppy$^{F'}$)$_2$Cl]$_2$ for 72 h in CH$_2$Cl$_2$/MeOH at 55 °C afforded UiO-67-Ir(ppy$^{F'}$)$_2$ with 9% overall Ir(III) loading (~36% metalation of the bipyridine sites, Figure S1). ICP-MS analysis was used to further quantify the Ir loading, showing that the Ir/Zr ratio is 1:5.3 for UiO-67-Ir(ppy)$_3$ (after 24 h metalation) and 1:10.8 for UiO-67-Ir(ppy$^{F'}$)$_3$ (after 72 h metalation), which is consistent with the aforementioned NMR data. For UiO-67-Ir(ppy)$_2$, the amount of Ir(III) complex included can be controlled between 2% to 20% by varying the PSM time from 2 to 24 h. UiO-67-Ir(ppy$^{F'}$)$_2$ required longer reaction times to produce higher loadings, as even after 24 h only 4% metalation was achieved. Powder X-ray diffraction (PXRD) confirmed the retention of the UiO-67 topology after PSM (Figure 1). In addition, permanent porosity was observed for all MOFs as evidenced by N$_2$ adsorption at 77 K (Figure S3). Type I isotherms were obtained for both UiO-67-Ir MOFs with ~2100 m^2/g BET surface area for UiO-67-Ir(ppy)$_2$ and ~2000 m^2/g for UiO-67-Ir(ppy$^{F'}$)$_2$, indicating microporous structures (Table S1). With successful incorporation of photocatalytic Ir(III) complexes into a robust MOF, we sought to investigate its photocatalytic ability for trifluoroethylation.

As a benchmark reaction, 4-methoxystyrene was used as a substrate with CF$_3$CH$_2$I in acetonitrile/H$_2$O under visible-light irradiation, with N,N-diisopropylethylamine as a base. These reactions were monitored by use of gas chromatography–mass spectrometry (GC-MS). Using UiO-67-Ir(ppy)$_2$ (20% loading after PSM, ~ 5 mol % Ir), quantitative conversion resulted in a 60% yield of the hydroxytrifluoroethyl product **A** (Table 1, entry 4). Encouragingly, UiO-67-Ir(ppy$^{F'}$)$_2$ (9% loading after
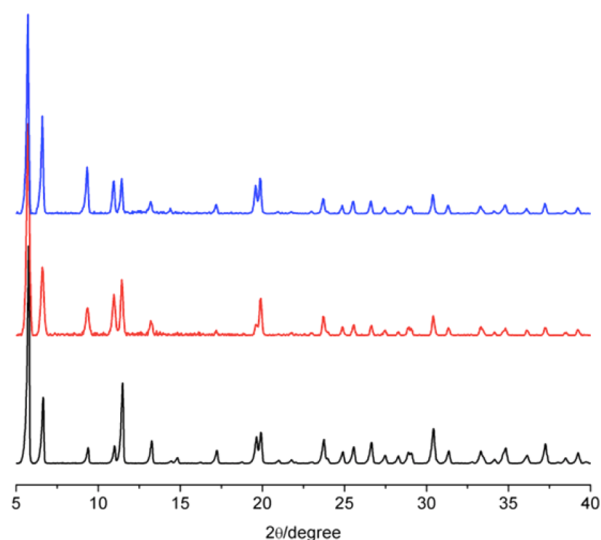
PSM, ~5 mol % Ir) was able to improve the yield of the desired product **A** to 76% (Table 1, entry 5). By comparison, three homogeneous photocatalysts: Ir(ppy)$_3$, [Ir(ppy)$_2$(Et$_2$dcbpy)]-Cl, and [Ir(ppy$^{F'}$)$_2$(Et$_2$dcbpy)]Cl (Scheme 1) were employed to catalyze the same reaction, but these produced a high yield of an undesired dimerization side product **C**, with only 10%, 20%, and 32% yields of the preferred hydroxytrifluoroethyl product **A**, respectively (Table 1, entries 1−3). The reversal of selectivity for the hydroxytrifluoroethyl versus dimer product generated from the UiO-67-Ir MOFs, when compared to the homogeneous catalysts, is likely due to the confined space within the MOF pores, which suppresses the dimerization of the benzyl radicals, thereby reducing the yield of product **C** (Scheme S1). Some over-oxidation to the ketone derivative of product **A** was also found after 48 h of photocatalysis (Table S2).[42]

In order to gain a better understanding of the catalytic reaction, appropriate control experiments were conducted.

First, product **A** cannot be converted to product **C** upon prolonged light irradiation in the presence of these photocatalysts, pointing to confinement as the source of the MOF selectivity. Second, in the absence of a photocatalyst no conversion was observed upon visible-light irradiation (Table 1, entry 6). When the same reaction conditions were employed, but using UiO-67-bpy$_{0.25}$ as catalyst, no products were obtained, indicating that Ir(III) is the catalytic active site (Table 1, entry 7). Third, no product was observed when the reaction was carried out with UiO-67-Ir(ppy$^{F'}$)$_2$ but in the absence of light, confirming the light-driven nature of the reaction (Table 1, entry 8).

Time-dependent experiments were conducted to compare the catalytic activity of the MOF and homogeneous catalysts, which showed the homogeneous catalyst Ir(ppy)$_3$ gives a faster conversion, but lower selectivity for product **A** (Figure S4). The effect of water content in the reaction, under both an air and oxygen atmosphere, was evaluated. These experiments showed that water can promote hydroxytrifluoroethyl difunctionalization (Figure S5) under either atmosphere. With the homogeneous catalyst Ir(ppy)$_3$, molecular oxygen is used as a radical scavenger to decrease the formation of the dimer product. In light of this, photocatalytic reactions performed under a N$_2$ atomsphere with UiO-67-Ir(ppy$^{F'}$)$_2$ as a catalyst generated only a trace amount of dimer **C** (conversion and yield <1%) and no other products were formed. This is in stark contrast to the homogeneous catalyst Ir(ppy)$_3$, which produces ~60% of dimer **C** under the same conditions. These results further confirm our proposed mechanism (Scheme S1) where the selectivity for the reaction with the MOF catalysts originates from site isolation within the MOF structure, and not solely from differences in the rates of reaction as a function of oxygen or air.

To test the heterogeneity of UiO-67-Ir(ppy$^{F'}$)$_2$, a hot filtration experiment was carried out after 4 h of photocatalysis, after which no further conversion of substrate was observed. Furthermore, no significant leaching of iridium was observed, as evidenced by ICP-OES analysis of the filtrate (<0.1 ppm Ir). After catalysis, ^{1}H NMR and photoluminescent spectroscopy of digested UiO-67-Ir(ppy$^{F'}$)$_2$ indicate that the catalytic centers do not degrade into other Ir species (Figures S6, S7). UiO-67-Ir(ppy$^{F'}$)$_2$ also exhibited excellent recyclability with good yields and high selectivity over three cycles (Table S2). Between each run, the catalyst was recovered and directly used for the next reaction. The crystallinity was maintained after each cycle, which was confirmed by PXRD (Figure S3), showing the robust nature of the UiO-67 platform even under the mildly basic conditions and stirring required for these reactions.

The substrate scope of the photocatalytic trifluoroethylation reaction was tested and is summarized in Table 2. The majority of substrates gave quantitative conversions, and all showed high selectivity for hydroxytrifluoroethyl over dimerization products using 5 mol % UiO-67-Ir(ppy$^{F'}$)$_2$ as catalyst. A higher conversion efficiency was observed with electron-rich styrenes (Table 2, entries 1−3). 4-Bromostyrene (Table 2, entry 4) shows lower conversion because of the electron-withdrawing nature of the bromine group, which is consistent with other reports of these photocatalysts.[10] Larger substrates, such as 4-vinylbiphenyl, also proved to be a suitable substrate for the reaction, giving quantitative conversion and good selectivity.

In conclusion, PSM is shown to be an efficient functionalization method to incorporate photocatalytic, cyclometalated iridium complexes into a robust UiO-67 material. The resulting

Table 2. Substrate Scope Using UiO-67-Ir(ppy$^{F'}$)$_2$ as Photocatalyst^a

Entry	Substrate	%Con	Yield^b A/B/C %
1	H$_3$CO-phenyl-vinyl	99	76/18/2
2	phenyl-vinyl	95	70/20/4
3	H$_3$C-phenyl-vinyl	83	74/9/0
4	Br-phenyl-vinyl	49	43/6/0
5	biphenyl-vinyl	97	60/30/0^c

^{a}Reaction conditions: styrene substrate (0.1 mmol), 2-iodo-1,1,1-trifluoroethane (0.3 mmol), N,N-diisopropylethylamine (0.3 mmol), acetonitrile (2 mL) and water (200 μL), UiO-67-Ir(ppy$^{F'}$)$_2$ as catalyst (5 mol %), 32 W compact fluorescent bulb, room temperature under air atmosphere for 48 h. ^{b}Determined by GC-MS. ^{c}Isolated yields.

MOF systems were used as heterogeneous photocatalysts for trifluoroethylation reactions of styrenes with high yields under visible-light irradiation, for at least three cycles without significant loss of activity. Most importantly, the MOF catalysts favored the formation of the desired hydroxytrifluoroethyl products, while suppressing dimerization of benzyl radicals that results in undesirable byproducts. This is in stark contrast when compared to the homogeneous catalysts and is likely due to confined space within the pores of MOF structure. This product selectivity of trifluoroethylation reaction is an excellent example of a "cavity confinement effect" and may be useful for other chemical reactions where suppressing the formation of undesirable byproducts is a challenge.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/jacs.6b06859.

Experimental details, additional characterization of MOFs and catalytic reactions (PDF)

■ AUTHOR INFORMATION

Corresponding Author

*scohen@ucsd.edu

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

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