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# Photocatalytic Carboxylation of Phenyl Halides with $CO_2$ by Metal-Organic Frameworks Materials

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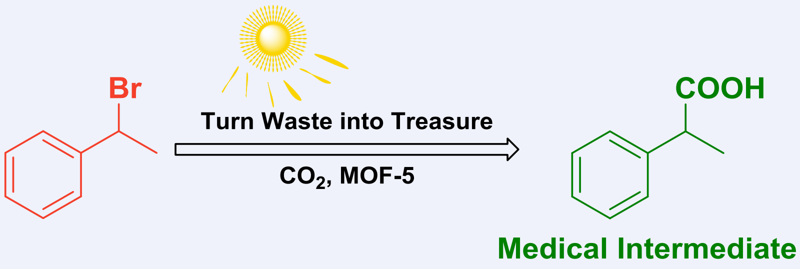
**Keywords**

Metal-organic frameworks | Photocatalysis | Carbon dioxide fixation | Heterogeneous catalysis | Ibruprofen

## Main observation and conclusion

In this work, important commercial pharmaceutical intermediates, phenylpropionic acid compounds, are successfully obtained by catalyzing the reaction of carbon dioxide with phenyl halides using MOF-5, a typical metal-organic framework (MOF) material. The influence of temperature, pressure, catalyst type and light on the reaction is investigated, and a 90.3% selectivity towards fluoro-phenylpropionic acid is reached. Significantly, the catalysts are effective for varied benzyl compounds containing different substituent groups. The catalysts are stable and remain active after three cycles.

## Comprehensive Graphic Content



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## Background and Originality Content

Since the global warming problem becomes increasing serious, it is urgent to solve the problem of $CO_2$ that is the main origin of greenhouse gas.[1-3] The use of $CO_2$ as a clean, cheap and abundant C1 building block,[4-7] to couple it into organic reactions through the solar energy and produce high value added products, such as pharmaceutical intermediates and fine chemicals, is an primary choice in green chemistry.[8-11] Among these intermediates, phenylpropionic acid compounds formed *via* the reaction of phenyl halides with $CO_2$, such as ibuprofen, flurbiprofen, naproxen, ketoprofen, carbenicillin and diclofenac (Figure 1), play very important roles in medicinal chemistry because they are the basis of non-steroidal anti-inflammatory drugs (NSAIDs).[12-14]

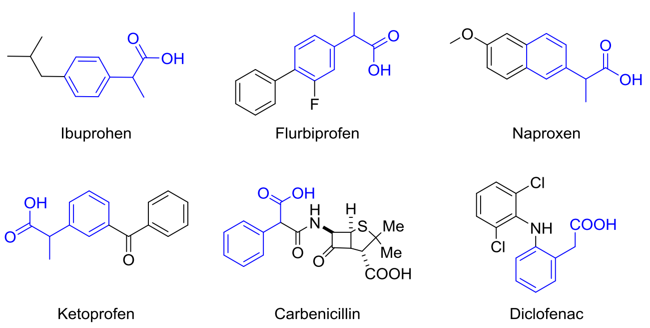
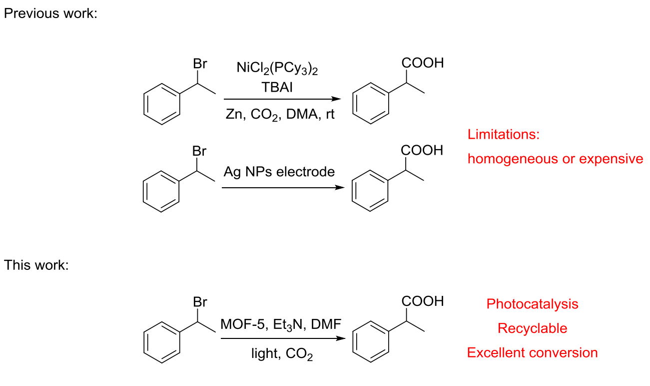


**Figure 1** Commercial drugs containing phenylpropionic acid compounds.

Researchers have done a lot of works to synthesize phenylpropionic acid compounds through homogeneous transition metal catalysts, such as nickel, cobalt and palladium complexes (top panel in Scheme 1).[15-18] Though the high yield is achieved, the homogeneous noble metal catalysts are expensive and difficult to be recycled, which has serious limitation in practical applications. Alternatively, an electrochemical method is developed to prepare phenylpropionic acid compounds by using Ag nanoparticles (NPs) as an anode (middle panel in Scheme 1);[12] however, the Ag NPs are still expensive and the electrochemical method might be difficult to be scaled up.

**Scheme 1** Synthesis of phenylpropionic acid



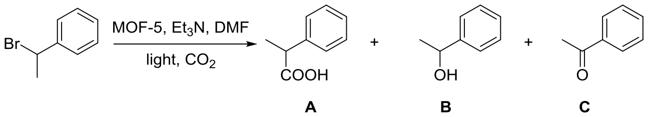
In this work, phenylpropionic acid derivatives are prepared by using MOF-5 as a photocatalyst to react $CO_2$ with benzyl free radicals generated from benzyl halides under light illumination (bottom panel in Scheme 1). MOF-5 is a typical MOFs formed from $Zn_4O$ nodes and 1,4-benzodicarboxylic acid (BDC) ligands. The merits of this work include adoption of clean solar energy and mild condition, utilization of the greenhouse $CO_2$ gas as C1 building block, and recyclability of heterogeneous MOF-5 catalyst.

## Results and Discussion

The preparaion of MOF-5 follows the previously-reported method with minor revision.[19-20] The capability of as-prepared MOF-5 catalysts was tested by photocatalytic experiments. The optimal photocatalytic conditions icnluding catalyst type, temperature, pressure and light were investigated using 1-phenethylbromide as the model substrate.

The chemical microenvironment of MOFs materials is known to be crucial for their catalytic performance. First, homologs of MOF-5, such as MOF-5, MOF-5-$NH_2$ (2-amino-1,4-benzenedicarboxylate rather than BDC is used as organic ligand) and MOF-5-BPDC (4,4'-biphenyldicarboxylate rather than BDC is used as organic ligand) were employed to catalyze the reaction. Notably, MOF-5 shows the best catalytic performance (Table 1, entries 3—5). Pressure control experiment reveals that as the pressure increases from 0.1 to 0.5 MPa, the selectivity of the target product phenylpropionic acid increases slightly. When the pressure further increases up to 1 MPa, the by-product phenylacetone is formed, resulting in the reduced selectivity of phenylpropionic acid (Table 1, entries 1—3). The temperature experiment displays that the reaction selectivity is reduced to 52.7% when the temperature is lowered to 0 °C (Table 1, entry 7). Finally, the influence of light on the reaction is examined. When the reaction is carried out in dark, the conversion is only 28.8% (Table 1, entry 6), indicating that light is an indispensable part of an efficient reaction. It deserves to be stressed that the catalysts have good stability. Under the optimized experimental condition (Table 1, entry 2), the catalysts remain the same catalytic activity after three cycles.

**Table 1** Optimizing reaction conditions of carboxylation of 1-phenylethyl bromide

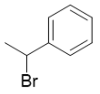
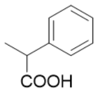
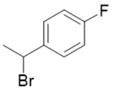
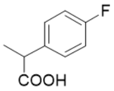
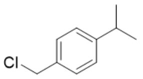
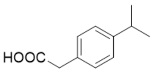


| Entry | T/°C | p/MPa | HV | Catalyst | Conv./% | Selectivity/% | | |
|---|---|---|---|---|---|---|---|---|
| | | | | | | A | B | C |
| 1[a] | 25 | 0.1 | On | MOF-5 | 100 | 74.7 | 25.3 | 0 |
| 2[b] | 25 | 0.5 | On | MOF-5 | 100 | 76.6 | 23.4 | 0 |
| 3[c] | 25 | 1 | On | MOF-5 | 100 | 72.8 | 21.5 | 5.7 |
| 4[d] | 25 | 0.5 | On | MOF-5-$NH_2$ | 100 | 67.5 | 32.5 | 0 |
| 5[e] | 25 | 0.5 | On | MOF-5-BPDC | 88.6 | 67.3 | 32.7 | 0 |
| 6[f] | 25 | 0.5 | Off | MOF-5 | 28.8 | 100 | 0 | 0 |
| 7[g] | 0 | 0.5 | On | MOF-5 | 100 | 52.7 | 47.3 | 0 |

[a] Reaction conditions: 10 mg catalysts were suspended in 2 mL DMF solution containing 0.1 mmol 1-phenylethyl bromide and 10 μL $Et_3N$. The photocatalytic reaction was carried out for 20 h under light and magnetic stirring. [abc] The pressure of $CO_2$ is different. [cde] The catalyst type is different. [f] The reaction takes place in dark. [g] The reaction temperature is 0 °C. Determined by gas chromatography mass spectrometry (GC-MS).

The carboxylation of varied benzyl halides with different electron-donating or electron-withdrawing substituent groups has been explored. Among them, F substituted benzyl halide (Table 2, **2a**) obtains the best catalytic performance and selectivity of the reaction could be up to 90.3%. Except for the benzyl bromide, the MOF-5 catalysts are also effective for catalytic conversion of the benzyl chloride (Table 2, **3a**). Nevertheless, the conversion and the selectivity of the benzyl chloride are lower than those of the benzyl bromide, because the free radical activity of the tertiary carbon generated from **2a** is higher than that of the carbon produced by **3a**.

**Table 2** Photocatalytic carboxylation of different substrates[a]

| Substrate | | Product | | Conv./% | Selectivity/% |
|---|---|---|---|---|---|
|  | **1a** |  | **1b** | 100 | 76.6 |
|  | **2a** |  | **2b** | 100 | 90.3 |
|  | **3a** |  | **3b** | 79.7 | 82.3 |

[a] Reaction conditions: 10 mg catalysts were suspended in 2 mL DMF solution containing 0.1 mmol benzyl halides, 10 µL $Et_3N$ and 0.5 MPa $CO_2$. The photocatalytic reaction was carried out for 20 h under light and magnetic stirring. Determined by GC-MS.

Based on the experimental phenomena observed above, a catalytic mechanism is proposed. MOF-5 is a classic photocatalytic material with semiconductor characteristics. Under light conditions, MOF-5 can absorb photons with energy greater than the band gap and generate photo-generated carriers (electrons and holes), in which the electrons are excited to the lowest unoccupied crystalline orbital (LOCO) and the hole remains in the highest occupied crystalline orbital (HOCO).[21-22] The photogenerated electrons undergo a reduction reaction with the substrate benzyl bromide, while triethylamine acts as a sacrificial reagent to react with holes. Through the electrochemical cyclic voltammetry test, it is found that the reduction potential of MOF-5 ($E_{1/2}$ = −0.97 V *vs.* SCE, Figure 4a) in DMF solvent is lower than that of benzyl bromide ($E_{1/2}$ = −0.54 V *vs.* SCE, Figure 4b), giving rise to formation of benzylic anion under light illumination. Similarly to previous reports, the reduced anion is easily captured by $CO_2$ to form the final product, phenylpropionic acid.[23] We also conducted a blank experiment without $CO_2$ and found that the substrate did not react, supporting the fact that $CO_2$ was the carbon source of the reaction. Through isotope labeling experiments, Zhang *et al.* further observed photocatalytic $CO_2$ conversion into carbonate ions,[24] which were the key intermediates in our proposed mechanism (Figure 2).

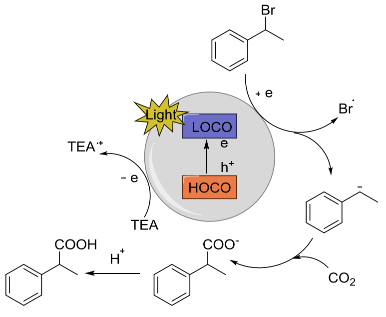


**Figure 2** Proposed reaction mechanism.

## Conclusions

In this work, homologs of MOF-5 have been synthesized by hydrothermal method and used as efficent catalysts to produce phenylpropionic acid derivatives. A high yield of fluorophenylpropionic acid can reach 90.3% by optimizing temperature, pressure and catalyst type. The good performance and excellent recyclability of the catalysts under mild conditions will hold the great potential in syntheses of NSAIDs and other drugs.

## Experimental

### Preparation of catalysts

**Synthesis of MOF-5**. MOF-5 was synthesized by solvent-thermal method according to the literature[14] with slight modification. Zinc nitrate hexahydrate ($Zn(NO_3)_2{\cdot}6H_2O$, 1485 mg) and 1,4-benzendicarboxylic acid ($H_2BDC$, 415 mg) were dissolved in 50 mL DMF. The solution was mixed up and transferred to a Teflon-lined stainless autoclave (100 mL) in 120 °C oven for 24 h. After the reaction, the resulting MOF-5 was purified by centrifugation at 10000 r/min and washed with DMF (2 × 5 mL) and ethyl alcohol (2 × 5 mL). The resulting white solids were dried in a vacuum oven at 50 °C.

**Synthesis of MOF-5-$NH_2$**. MOF-5-$NH_2$ was synthesized by solvent-thermal method according to the literature[15] with slight modification. Zinc nitrate hexahydrate ($Zn(NO_3)_2{\cdot}6H_2O$, 1485 mg) and 2-aminoterephthalic acid ($H_2BDC$-$NH_2$, 455 mg) were dissolved in 50 mL DMF. The solution was transferred to a Teflon-lined stainless autoclave (100 mL) in 120 °C oven for 24 h. After the reaction, the resulting MOF-5 was purified by centrifugation at 10000 r/min and washed with DMF (2 × 5 mL) and ethyl alcohol (2 × 5 mL). The resulting white solids were dried in a vacuum oven at 50 °C.

**Synthesis of MOF-5-BPDC**. MOF-5-BPDC was synthesized by solvent-thermal method according to the literature[15] with slight modification. Zinc nitrate hexahydrate ($Zn(NO_3)_2{\cdot}6H_2O$, 1485 mg) and biphenyl-4,4'-dicarboxylic acid ($H_2BPDC$, 605 mg) were dissolved in 50 mL DMF. The solution was transferred to a Teflon-lined stainless autoclave (100 mL) in 120 °C oven for 24 h. After the reaction, the resulting MOF-5 was purified by centrifugation at 10000 r/min and washed with DMF (2 × 5 mL) and ethyl alcohol (2 × 5 mL). The resulting white solids were dried in a vacuum oven at 50 °C.

**Synthesis and characterization of catalysts.** MOF-5 series catalysts were prepared by solvent-thermal method. Powder X-ray diffraction (PXRD) patterns were used to characterize the crystal structures of the catalysts. They were recorded by D/MAX-TTRIII (CBO) with Cu Kα radiation ($\lambda$ = 0.1542 nm). The conversion and selectivity were determined by gas chromatography mass spectrometry (GC-MS). Compared with the standard XRD simulation spectra, it was found that the MOF-5 series catalysts were successfully synthesized (Figure 3a). Thermal gravimetric analyzer (TGA) was used to measure the thermal stability of

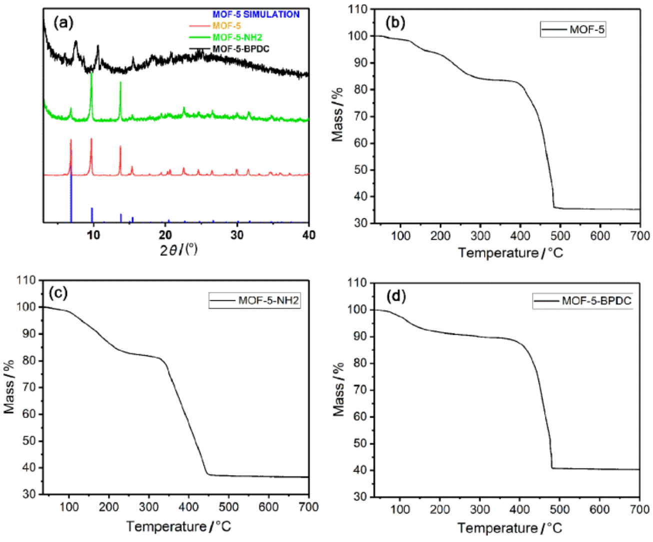


**Figure 3** PXRD patterns and TGA of MOF-5 series catalysts. (a) PXRD patterns, (b) TGA of MOF-5, (c) TGA of MOF-5-$NH_2$, (d) TGA of MOF-5-BPDC.

catalysts with ramp rate of 10 °C·min$^{-1}$ from 35 $^{o}$C up to 700 $^{o}$C under air atmosphere.

### Typical procedure for photocatalytic experiments

**Catalytic performance test**. The photocatalytic reaction was performed under a 300W Xe lamp. Typically, 10 mg photocatalysts were suspended in 2 mL DMF solution containing 0.1 mmol benzyl halides and 10 μL $Et_3N$. Then the mixture was transferred to a Teflon-lined stainless photocatalytic autoclave. Purgjng the autoclave with $CO_2$ three times ensured that the reaction took place in the $CO_2$ environment and the pressure was stabilized at 0.5 MPa. A circulating condensation system was used to keep the reaction temperature at 25 $^{o}$C. The photocatalytic reaction was carried out for 20 h under light and magnetic stirring. After completion, the mixture was collected by centrifuging at 10000 r/min for 3 min. The remaining solid catalysts were washed with DMF (2 × 5 mL) and ethyl alcohol (2 × 5 mL) and dried in a vacuum oven for next use. Meanwhile, the resulting solution was injected into the GC-MS to evaluate the conversion and selectivity.

**Cyclic voltammetry test**. The cyclic voltammetry curve was tested according to the method reported in the literature (Figure 4).[14] A 0.1 mol/L TBATFB DMF solution containing a trace of ferrocene as an internal standard was used as the electrolyte, and the scanning speed was 50 mV/s.

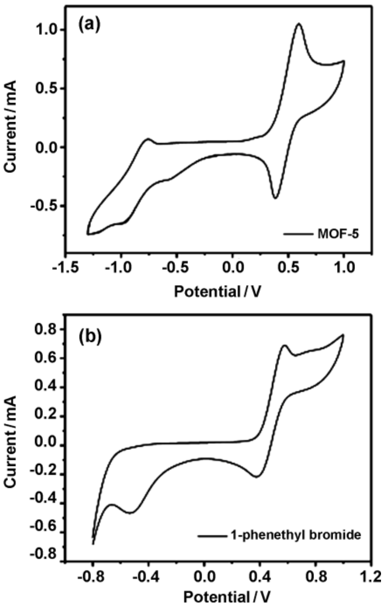


**Figure 4** Cyclic voltammetry of MOF-5 and 1-phenethyl bromide: (a) MOF-5, (b) 1-phenethyl bromide. 0.48 V was the reversible peak of internal standard ferrocene, and the test was carried out in 0.1 mol/L tetrabutylammonium tetrafluoroborate (TBATFB) electrolyte solution with a scanning speed of 50 mV/s.

## Supporting Information

The supporting information for this article is available on the WWW under https://doi.org/10.1002/cjoc.202000463.

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