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Magnetically recyclable Cu-BTC@Fe_3O_4-catalyzed synthesis of aryl α-chlorobenzyl ketones

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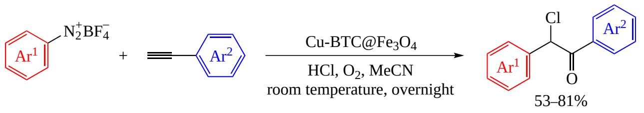
Metal–organic framework (MOF) composite, *viz.* Cu-BTC@Fe_3O_4 (BTC is 1,3,5-benzenetricarboxylate), was prepared and utilized for the synthesis of aryl α-chlorobenzyl ketones from arenediazonium salts and arylacetylenes in moderate to good yields. This reaction proceeded *via* a radical domino process. The catalyst could be readily recovered with an external permanent magnet, with slight decrease in its activity after successive six runs.



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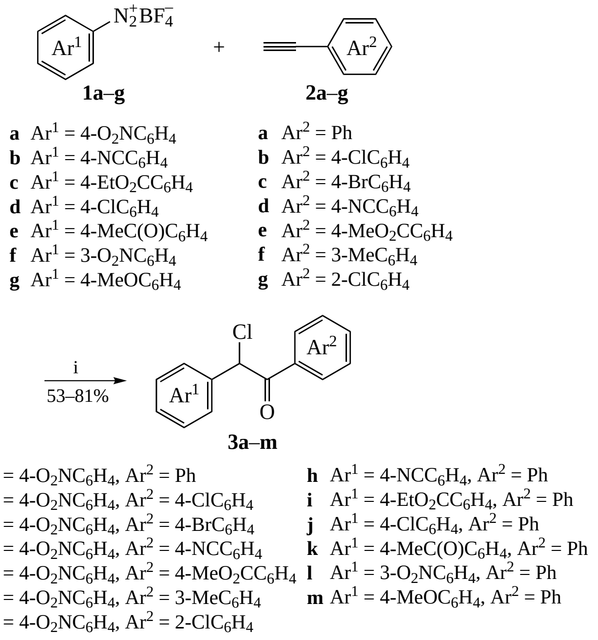
α-Chlorobenzyl ketones have found applications in synthetic organic and medicinal chemistry.[1] Generally, they were synthesized *via* electrophilic chlorination of aryl benzyl ketones with Cl_2,[2] *N*-chlorosuccinimide (NCS),[3] Bu^tOCl,[4] $TsNCl_2$[5] or trichloroisocyanuric acid.[6] These methods usually suffered from the necessity of using toxic chlorinating reagents and the unavailability of starting materials. Alternatively, radical promoted C–H arylation of C=C unsaturated bonds followed by oxidation/chlorination provided an efficient way to access α-chlorobenzyl ketones. In 2016, Niu and co-workers developed a photocatalyzed domino process between arenediazonium salts and arylalkynes.[7] However, only low to moderate yields were obtained due to the unsatisfactory chemoselectivity. Moreover, the $Ru(bpy)_3Cl_2$ photocatalyst employed was expensive and could not be recovered and reused.

Recently, the application of metal–organic frameworks (MOFs) in synthetic chemistry has attracted much attention.[8–10] Among them, Cu-BTC is of significance since it is readily available, cost-effective and highly stable.[11–13] To further improve its stability and simplify the recycle process, Cu-BTC@Fe_3O_4 composite was prepared. Such composite has already shown good catalytic activities in C–H oxidation of alkylbenzenes,[14] one-pot $C_{(aryl)}$–S–P bond formation reaction,[15] reduction of nitroarenes[16] and cycloaddition reaction.[17]

In continuation of our interest in heterogeneous catalysis, we herein report on a Cu-BTC@Fe_3O_4-catalyzed synthesis of aryl α-chlorobenzyl ketones *via* a radical domino reaction between arenediazonium salts and arylacetylenes using aqueous HCl as the chlorine source under mild reaction conditions. The Cu-BTC@Fe_3O_4 composite with surface area of 423 $m^2 g^{-1}$ was prepared as previously reported.[15,16] The majority of crystal sizes ranges from 80 to 140 nm. EDS and ICP analysis shows the weight percentage of Cu-BTC in the composite being *ca*. 38.4% (see Online Supplementary Materials).

With this composite in hand, arenediazonium salt **1a** and phenylacetylene **2a** were selected as the model substrates in acetonitrile to optimize the reaction conditions (Scheme 1, Table 1). No reaction was observed in the absence of any catalyst (entry 1) while 15 mg of Cu-BTC@Fe_3O_4 composite (per 0.5 mmol of **1a**) was sufficient to afford the desired product **3a** in 81% yield (entry 3). Reactions in DMSO, DMF, THF, 1,4-dioxane or methanol led to poor to moderate yields (entries 5–9). The use of NaCl as the chlorine source provided the **3a** in 56% yield (entry 11), whereas no reaction was observed in the presence of NCS (entry 10). This result indicated that chloride anion played a key role in this reaction. Moreover, no reaction was observed when the process was performed under nitrogen atmosphere. A blank experiment was carried out using Fe_3O_4



1a–g

2a–g

a Ar^1 = 4-$O_2NC_6H_4$
b Ar^1 = 4-NCC_6H_4
c Ar^1 = 4-$EtO_2CC_6H_4$
d Ar^1 = 4-ClC_6H_4
e Ar^1 = 4-MeC(O)C_6H_4
f Ar^1 = 3-$O_2NC_6H_4$
g Ar^1 = 4-$MeOC_6H_4$

a Ar^2 = Ph
b Ar^2 = 4-ClC_6H_4
c Ar^2 = 4-BrC_6H_4
d Ar^2 = 4-NCC_6H_4
e Ar^2 = 4-$MeO_2CC_6H_4$
f Ar^2 = 3-MeC_6H_4
g Ar^2 = 2-ClC_6H_4

3a–m

a Ar^1 = 4-$O_2NC_6H_4$, Ar^2 = Ph
b Ar^1 = 4-$O_2NC_6H_4$, Ar^2 = 4-ClC_6H_4
c Ar^1 = 4-$O_2NC_6H_4$, Ar^2 = 4-BrC_6H_4
d Ar^1 = 4-$O_2NC_6H_4$, Ar^2 = 4-NCC_6H_4
e Ar^1 = 4-$O_2NC_6H_4$, Ar^2 = 4-$MeO_2CC_6H_4$
f Ar^1 = 4-$O_2NC_6H_4$, Ar^2 = 3-MeC_6H_4
g Ar^1 = 4-$O_2NC_6H_4$, Ar^2 = 2-ClC_6H_4
h Ar^1 = 4-NCC_6H_4, Ar^2 = Ph
i Ar^1 = 4-$EtO_2CC_6H_4$, Ar^2 = Ph
j Ar^1 = 4-ClC_6H_4, Ar^2 = Ph
k Ar^1 = 4-MeC(O)C_6H_4, Ar^2 = Ph
l Ar^1 = 3-$O_2NC_6H_4$, Ar^2 = Ph
m Ar^1 = 4-$MeOC_6H_4$, Ar^2 = Ph

Scheme 1 *Reagents and conditions*: i, arenediazonium salt **1** (0.5 mmol), alkyne **2** (0.6 mmol), aqueous HCl (1 mmol, conc. 37%), Cu-BTC@Fe_3O_4 composite (15 mg), MeCN (2 ml), oxygen atmosphere, room temperature, stirring overnight.

Table 1 Optimization of reaction conditions.[a]

Entry	Catalyst loading/mg	Cl source	Solvent	Yield of **3a** (%)[b]
1	–	HCl	MeCN	0
2	10	HCl	MeCN	63
3	15	HCl	MeCN	81
4	20	HCl	MeCN	83
5	15	HCl	DMSO	trace
6	15	HCl	DMF	trace
7	15	HCl	THF	26
8	15	HCl	1,4-dioxane	31
9	15	HCl	MeOH	56
10	15	NCS	MeCN	0
11	15	NaCl	MeCN	52
12	15	HCl	MeCN	0[c,d]

[a] Arenediazonium salt **1a** (0.5 mmol), phenylacetylene **2a** (0.6 mmol), Cl source (1 mmol), catalyst, solvent (2 ml), room temperature, overnight, under oxygen. [b] Isolated yield. [c] Under nitrogen. [d] Fe_3O_4 as the catalyst.

nanoparticles as the catalyst, which revealed that the copper component was the actual catalyst center (see entry 12).

With the optimized reaction conditions in hand, substrate scope was then explored (see Scheme 1).[†] Initially, a series of alkynes were investigated. Alkynes with diverse functional groups underwent this transformation smoothly to give products **3a**–**g** in good yields. Arenediazonium salts showed some influence on the reaction outcome. Generally, those bearing electron-withdrawing groups such as nitro, cyano, halogeno and ester moiety gave good yields. In contrast, those bearing electron-donating group such as substrate **1g** did not survive and product **3m** was not obtained.

The reusability of the Cu-BTC@Fe_3O_4 composite is an advantage of the present procedure. In the model reaction between compounds **1a** and **2b**, after processing the catalyst was recovered with an external magnet and washed with EtOAc and water. The results showed slight decrease in the catalytic activity after six consecutive runs (81, 80, 80, 76, 75 and 73%, respectively). The recovered catalyst was also characterized by powder X-ray diffraction (PXRD) and scanning electron microscopy (SEM). The PXRD showed no obvious change, indicating that the catalyst was stable. However, slight aggregation of the composite was detected by SEM, which might account for the decrease in its catalytic activity.

Some control experiments were carried out. No desired product **3a** was observed in the presence of 3 equiv. of the radical scavenger, 2,2,6,6-tetramethylpiperidine *N*-oxyl (TEMPO). Also, when the reaction was performed out under N_2 atmosphere, no product **3a** was obtained. Based on the above results and previous report,[7] a mechanism is proposed (Scheme 2). Initially, aryl radical **A** is generated from arenediazonium salt **1** under the assistance of Cu centers, which attacks alkyne **2** to provide radical intermediate **B**. The intermediate **B** reacts with O_2 to deliver peroxy radical **C**, followed by reaction with **B** to give intermediate **D**. Afterwards, protonation of intermediate **D** generates a radical cation **E**. Nucleophilic attack of **E** by Cl^- followed by SET oxidation affords the product **3**. Moreover, some aldehyde byproducts were observed during the reaction, which might be generated *via* hydrogenolysis of intermediate **C**.

In summary, Cu-BTC@Fe_3O_4 composite was prepared and utilized for the synthesis of aryl α-chlorobenzyl ketones from arenediazonium salts, arylacetylenes and aqueous HCl. This protocol afforded the corresponding products in moderate to good yields under mild reaction conditions. The catalyst could be readily recovered with an external permanent magnet, with slight decrease in its activity after successive six runs.

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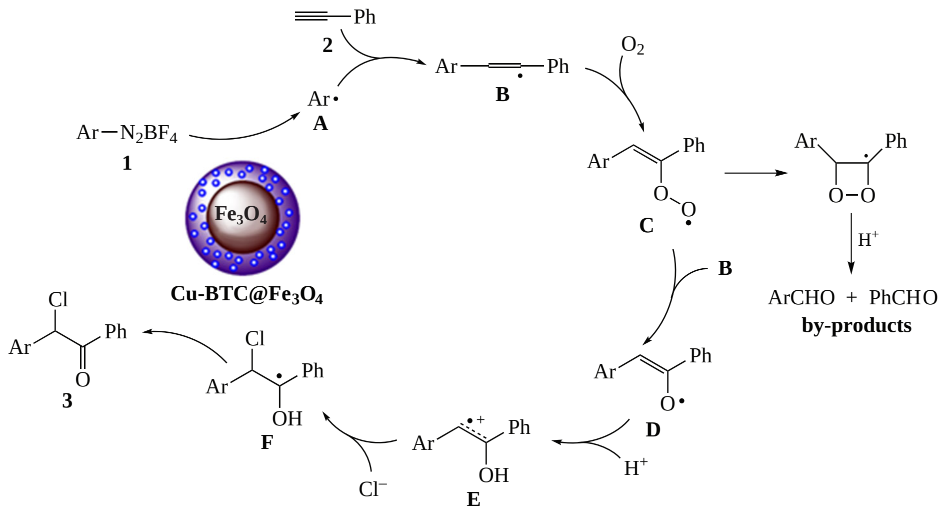
Online Supplementary Materials

Supplementary data associated with this article can be found in the online version at doi: 10.1016/j.mencom.2022.11.031.



Scheme 2

[†] *General procedure for the synthesis of* **3a**–**l**. A sealed tube equipped with a magnetic stirrer bar was charged with arenediazonium salt **1** (0.5 mmol), arylacetylene **2** (0.6 mmol), aqueous HCl (1 mmol, conc. 37%), Cu-BTC@Fe_3O_4 composite (15 mg) and acetonitrile (2 ml). The reaction mixture was stirred under oxygen atmosphere overnight. After the reaction completion, the Cu-BTC@Fe_3O_4 was recovered with an external magnet, and washed with EtOAc and water. The reaction mixture was extracted with EtOAc (3 × 5 ml) and dried over Na_2SO_4. The organic phase was concentrated under reduced pressure to leave the crude product which was further purified by column chromatography using petroleum ether/ethyl acetate (10 : 1, v/v) as eluent to afford product **3a**–**l**.

References

1 R. Britton and B. Kang, *Nat. Prod. Rep.*, 2013, **30**, 227.
2 M. Oestreich, *Angew. Chem., Int. Ed*., 2005, **44**, 2324.
3 C. Walling and M. J. Mintz, *J. Am. Chem. Soc.*, 1967, **89**, 1515.
4 Y. H. Kim, I. S. Lee and S. C. Lim, *Chem. Lett.*, 1990, **19**, 1125.
5 C. B. Tripathi and S. Mukherjee, *J. Org. Chem.*, 2012, **77**, 1592.
6 Y. Jing, C. G. Daniliuc and A. Studer, *Org. Lett.*, 2014, **16**, 4932.
7 T. Niu, D. Jiang, S. Li, B. Ni and L. Wang, *Chem. Commun.*, 2016, **52**, 13105.
8 J. Y. Lee, O. K. Farha, J. Roberts, K. A. Scheidt, S. T. Nguyen and J. T. Hupp, *Chem. Soc. Rev.*, 2009, **38**, 1450.
9 J. C. Jiang and O. M. Yaghi, *Chem. Rev.*, 2015, **115**, 6966.
10 S. Yadav, R. Dixit, S. Sharma, S. Dutta, K. Solanki and R. K. Sharma, *Mater. Adv.*, 2021, **2**, 2153.
11 A. Sachse, R. Ameloot, B. Coq, F. Fajula, B. Coasne, D. De Vos and A. Galarneau, *Chem. Commun.*, 2012, **48**, 4749.
12 L. H. Wee, S. R. Bajpe, N. Janssens, I. Hermans, K. Houthoofd, C. E. A. Kirschhock and A. Martens, *Chem. Commun.*, 2010, **46**, 8186.
13 I. Luz, F. X. Llabrés i Xamena and A. Corma, *J. Catal.*, 2010, **276**, 134.
14 Y. F. Chen, X. Q. Huang, S. H. Zhang, S. Q. Li, S. J. Cao, X. K. Pei, J. W. Zhou, X. Feng and B. Wang, *J. Am. Chem. Soc.*, 2016, **138**, 10810.
15 L. Wang, S. Yang, L. Chen, S. Yuan, Q. Chen, M. He and Z. Zhang, *Catal. Sci. Technol.*, 2017, **7**, 2356.
16 S. Yang, Z. Zhang, Q. Chen, M. He and L. Wang, *Appl. Organomet. Chem.*, 2018, **32**, e4132.
17 E. Arefi, A. Khojastehnezhad and A. Shiri, *Sci. Rep.*, 2021, **11**, 20514.

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