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A high-activity cobalt-based MOF catalyst for [2 + 2 + 2] cycloaddition of diynes and alkynes: insights into alkyne affinity and selectivity control†

Fen Xu, [ID] Xiao-Ju Si, Xiao-Ning Wang, Hao-Dong Kou, Di-Ming Chen, Chun-Sen Liu [ID] * and Miao Du [ID] *

This work develops a highly efficient metal–organic framework (MOF) catalyst for the straightforward synthesis of functionalized benzenes *via* [2 + 2 + 2] cycloaddition. As efficient cooperative catalyst for such reactions, **Co-MOF-1**, shows great sustainability and efficiency. This new catalytic system can lead to the generation of a series of structurally diverse benzenes in good to excellent yields (up to 95%).
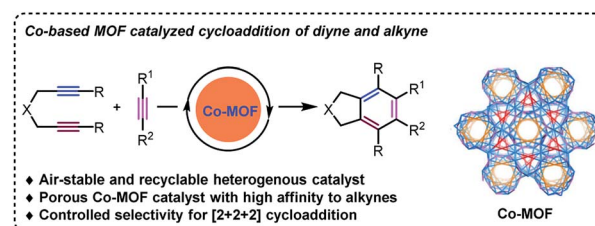
Cycloaddition is a promising strategy used to develop a new synthetic methodology with high atom economy, providing efficient routes to construct various chemical bonds resulting in molecular complexity.[1] For example, the [2 + 2 + 2] cycloaddition of diynes and alkynes has been a powerful tool for the synthesis of functionalized benzenes in one step.[2] A variety of transition metal catalysts, including Rh,[3] Ru,[4] Pd,[5] Ir[6] and Ni[7] have shown their capacity for [2 + 2 + 2] annulations. However, in this connection, three crucial problems need to be resolved. (1) The competing dimerization or trimerization remains a challenging issue for [2 + 2 + 2] cycloaddition with high selectivity. (2) These unrecoverable homogeneous catalysts will take a major responsibility for energy waste and environmental pollution. (3) The sensitivity to air or moisture for the known catalysts may greatly reduce the reaction efficiency and make the operation complicated. As a result, the development of easily separable and recoverable heterogeneous catalysts is of great significance and interest in this respect.

Metal–organic frameworks (MOFs) represent a rising class of porous crystalline materials with exceptional surface areas and uniformly dispersed metal ions.[8] Such inherent properties make MOFs as advanced materials for gas storage and separation,[9] drug delivery,[10] heterogeneous catalysis,[11] and so on. Recently, we have designed a series of MOFs materials with diverse pore shapes, sizes and compositions for targeted applications[12] and also developed diversified metal-catalyzed cycloadditions involving alkynes.[13] Thus, it will be anticipated to explore the potentials of MOFs as the new-type catalysts for cycloadditions, which may avoid the restrictions for the known examples. Notably, Co(I) or Co(II)/additive[14] catalytic system has

shown activity in [2 + 2 + 2] cycloaddition, though the dimerization or trimerization of terminal diynes usually occurs.[15] On this account, a porous MOF $[Co_2(HCOO)_2(CPT)_2](NMF)_5(H_2O)_2$ (**Co-MOF-1**) with high affinity of acetylene was successfully constructed based on a bi-functional ligand 4-(4-carboxyphenyl)-1,2,4-triazole (HCPT).[16] As a result, a variety of benzene derivatives can be obtained *via* **Co-MOF** catalyzed [2 + 2 + 2] cycloaddition in high yields with great tolerance of substrates and the crystalline defect of catalyst will account for the significant selectivity of the reactions (Scheme 1).

The **Co-MOF-1** was harvested by reaction of $Co(NO_3)_2 \cdot 6H_2O$ and HCPT in NMF-water. Single-crystal X-ray diffraction analysis indicates that **Co-MOF-1** crystallizes in the trigonal space group $R\bar{3}c$.[16] A mentionable structural feature is the presence of distorted octahedral cages with the inner diameter of 7.9 Å, constituted by twelve Co(II) and twelve CPT⁻ for each cage (Fig. 1a and S2†). The octahedral cages are sequentially extended *via* sharing the trigonal windows. As a result, the 3D framework displays 1D hexagonal channels along *a* axis with the pore diameter of 5.4 Å (Fig. 1b, S3 and S4†) and the available void of 16 835 Å³, corresponding to 48.6% of the crystal volume (34 647.6 Å³).

The porosity of **Co-MOF-1** was confirmed by N_2 sorption at 77 K. The CH_2Cl_2-exchanged **Co-MOF-1** was activated at 70 °C to afford the desolved material **Co-MOF-1′** (Fig. S5 and S6†).

College of Material and Chemical Engineering, Zhengzhou University of Light Industry, Zhengzhou 450002, China. E-mail: chunsenliu@zzuli.edu.cn; dumiao@zzuli.edu.cn

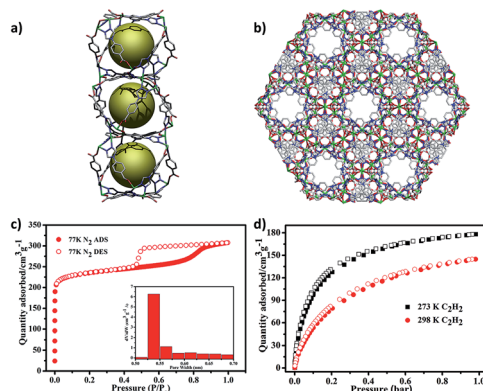Scheme 1 Catalytic strategy for [2 + 2 + 2] cycloaddition in this work.

Fig. 1 (a) The serial octahedral cages in **Co-MOF-1**. (b) The 3D framework of **Co-MOF-1** with 1D channels running along *a* axis. (c) N_2 sorption isotherm at 77 K for **Co-MOF-1′** (inset: pore size distribution plots). (d) C_2H_2 adsorption isotherms of **Co-MOF-1′** at 273 and 298 K.

Notably, **Co-MOF-1′** shows an initial type-I adsorption isotherm, as a typical microporous material and then, a type-IV adsorption with obvious hysteresis and a significant portion of the meso-pore volume of 0.46 $cm^3 g^{-1}$ (Fig. 1c). This can be a consequence of the dissociation of Co(II) ions and formation of defect sites in lattice.[17] The maximal N_2 uptake is 307 $cm^3 g^{-1}$, corresponding to a BET surface area of 947 $m^2 g^{-1}$ and pore diameter of 5.4 Å. The pore size distribution is consistent with the observation from its crystal structure. The combination of high porosity and defect sites in **Co-MOF-1′** promotes us to investigate its affinity toward acetylene, showing a high C_2H_2 adsorption capability (Fig. 1d) of 178 $cm^3 g^{-1}$ at 273 K and 1 bar and 120 $cm^3 g^{-1}$ at 298 K and 1 bar. The isosteric heat of sorption (Q_{st}) for C_2H_2 molecule was calculated to evaluate the affinity between C_2H_2 and **Co-MOF-1′** (Fig. S7 and S8†). The result shows a high Q_{st} value of 36 kJ mol^{-1} at zero loading, revealing a preferred binding capacity for C_2H_2 compared with the reported MOFs without high density of active sites (Q_{st} values: 13.3–32.0 kJ mol^{-1}).[18]

Catalysis of [2 + 2 + 2] cycloaddition by **Co-MOF-1** was initiated from a terminal NTs-diyne **1a** and phenylacetylene **2a** (Table 1), in the presence of 6 mol% 1,3-bis(diphenylphos phino)propane (dppp) and 10 mol% Zn powder in 1,2-dichloroethane (DCE). It is interesting that **3aa** can be obtained directly in 40% yield after reaction at 80 °C for 24 h (entry 1). The yield was enhanced to 59% when **Co-MOF-1′** was used and higher yield was achieved in the presence of 4 equiv. of phenylacetylene (entries 2 and 3). Subsequent tests indicated that reducing the temperature was greatly to the disadvantage of annulation (entries 5 and 6) and a control experiment illustrated that dppp was necessary for this transformation (entry 7). In addition, decreasing the loading of dppp also sharply cut down the yield of target product (entries 3 and 8). It was also found that the transformation was dramatically affected by the catalyst, and the combination of Co(NO₃)₂ and dppp was incompetent to produce **3aa** in only 12% yield (entry 9). **3aa** was not detected in the absence of Zn powder (entry 10). The air-stable and efficient **Co-MOF-1′** catalyst can be separated and recycled that makes it much sustainable compared to known examples. Therefore, the optimal reaction conditions were
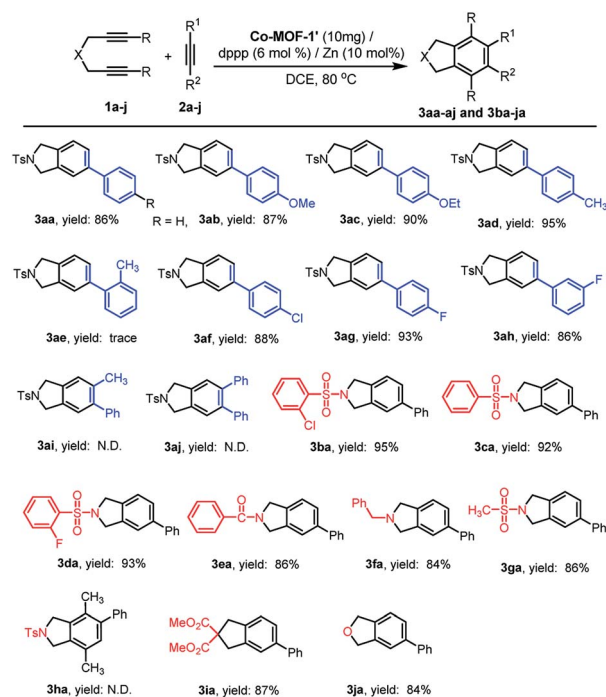
Table 1 Optimization of reaction conditions[a]

Entry	Catalyst	Temp. (°C)	Yield[b] (%)
1	**Co-MOF-1**	80	40
2	**Co-MOF-1′**	80	59
3[c]	**Co-MOF-1′**	80	86
4[d]	**Co-MOF-1′**	80	28
5	**Co-MOF-1′**	40	Trace
6	**Co-MOF-1′**	RT	Trace
7[e]	**Co-MOF-1′**	80	Trace
8[c,f]	**Co-MOF-1′**	80	60
9[g]	Co(NO₃)₂	80	12
10[h]	**Co-MOF-1′**	80	N.D

[a] Reaction conditions: diyne **1a** (0.25 mmol), phenylacetylene **2a** (2 equiv., 0.5 mmol), **Co-MOF** (10 mg), dppp (6 mol%), Zn powder (10 mol%) and DCE (2 mL) at 80 °C for 24 h. [b] Isolated yield. [c] **2a** (4 equiv.). [d] **Co-MOF-1′** (1 mg). [e] No dppp. [f] dppp (3 mol%). [g] Co(NO₃)₂ (5 mol%), dppp (6 mol%) and Zn powder (10 mol%). [h] In the absence of Zn powder, N.D (not detected).

determined as **Co-MOF-1′** (10 mg), dppp (6 mol%) and Zn powder (10 mol%) in DCE (2.0 mL) at 80 °C for 24 h.

The generality and functional-group tolerance was explored by different substituted alkynes. A broad range of phenyl-acetylenes with either electron-donating or -withdrawing groups, could react smoothly with NTs-diyne **1a** and enable the formation of substituted benzenes **3aa–ad** and **3af–ah** in 86–95% yields (Scheme 2). Initially, **1a** was treated with **2a**,

Scheme 2 Formation of benzenes from diynes **1a–j** and alkynes **2a–j**.

Co-MOF-1′ and dppp in DCE. This led to the formation of **3aa** in 86% isolated yield. As illustrated, aromatic alkynes bearing Me– and F– groups served as the most proper substrates in this case and showed unconspicuous effect on the reaction efficiency (Scheme 2, **3ad** and **3ag**). In contrast, the ortho-substituted 1-ethynyl-2-methyl benzene showed extremely poor reactivity (Scheme 2, **3ae**). Further, para- and meta-substitution was also tolerated, while a slight reduced yield was found for aromatic alkyne with meta-substitution (Scheme 2, **3ag** and **3ah**). Notably, the reaction of pharmaceutically important aromatic substituted alkynes, aiming at introducing fluorine and/or fluorinated building blocks into the aromatic ring, has remained a challenge thus far. Herein, **2g** and **2h** delicately decorated by fluorine were revealed as meaningful substrates as well, affording the corresponding products **3ag** and **3ah** in 93% and 86% yields. However, sterically hindered internal alkynes **2i** and **2j** were incompatible, forming dimer or trimer of diynes as side-products, where the bulky phenyl groups may prevent the contact of substrates with the active sites of catalyst.

Subsequently, the scope of this reaction with respect to diynes was further extended. A variety of N-based diynes, ranging from *N*,*N*-di(prop-2-yn-1-yl)benzenesulfonamide **1c** with electronically diverse groups on phenyl ring (**1b–1d**), *N*-benzyl-*N*-(prop-2-yn-1-yl)prop-2-yn-1-amine **1f**, to *N*,*N*-di(prop-2-yn-1-yl) methanesulfonamide **1g**, was used in this catalytic system. The corresponding products were obtained in 84–95% yields (Scheme 2, **3ba–ga**), which are similar to those reactions with NTs-based diyne **1a**. Notably, the electronic nature of phenyl ring for N-based diynes turned out to be significant for the cyclization. With **Co-MOF-1′** and dppp in the presence of Zn powder, **3ba** was achieved in a yield of 95%, whereas **3aa** was produced in 86% yield. Significantly, cyclo-adduct **3da** with F– substituent was obtained in high yield of 93%. In accordance with the observation that steric factor intensively influences the reactivity of alkyne substrates, internal diyne *N*,*N*-di(but-2-yn-1-yl)-4-methylbenzene sulfon-amide **1h** was failed to afford benzene scaffold **3ha**. This work was also highlighted by substrate of ester tethered diyne, affording corresponding product **3ia** in 87% yield. In addition to N-based or ester-tethered diyne, dipropargyl ether showing high reactivity for dimerization to arene byproduct,[19] cyclized with **2a** to afford the corresponding benzo[*c*]furan **3ja** in moderate yield (Scheme 2).

The major advantage of heterogeneous catalysts is their reutilization, which is one of the most important indexes to evaluate the performance of catalyst effect and stability along the catalytic cycle. Recycling experiments were performed on **Co-MOF-1′** for the annulation of **1b** and **2a**. The catalyst was recycled for five runs with no decrease of activity, giving 93–95% isolated yields (Fig. S9a†). After each case, the recovered **Co-MOF-1′** catalyst was characterized by powder X-ray diffraction (PXRD) technique (Fig. S9b†). Notably, even after the fifth run, the PXRD pattern evidently confirmed that the catalyst remained excellent crystallinity and was not damaged in the catalytic process.

To further shed some light on the reaction mechanism, auxiliary experiment was designed and conducted to probe the active species of this transformation. As the presence of Co(II) ions in the initial reaction solution (25.5 mg L^{-1}) was detected by ICP-MS, we suspected that such a reaction would begin with a sluggish release of Co(II) due to the crystal defect of catalyst, which was then reduced by Zn powder to give Co(I) species. The active Co(I) surrounded the surface of **Co-MOF-1′** material to facilely capture the neighboring diyne **A** *via* ligand exchange, forming a 5-membered metallacyclopentadiene intermediate **B** through traditional oxidative addition. However, attempt to isolate the species **B** was failed. After that, **B** will either undergo alkyne insertion to form 7-membered azametallacycle **C** or [4 + 2] annulation to produce **D**, resulting in benzenes *via* reductive elimination to afford the final product **E** and also regenerate Co(I) for the next catalytic cycle (Fig. 2).

To confirm the catalytic mechanism, two control experiments were further discussed. First, subjecting *N*,*N*-di(but-2-yn-1-yl)-4-methylbenzenesulfonamide **1h** with **2a** to this annulation failed to deliver the target product. In fact, **1h** was largely retained after reaction, revealing that higher steric internal diyne will suppress the fast access to active Co(I) species on the surface of catalyst (eq. 1 in Fig. 3). Then, a compensatory experiment involving the coupling of terminal diyne **1a** with alkyne **2j** showed that the dimer of **1a** was achieved instead of [2 + 2 + 2] annulation. This reveals that the internal alkyne will hardly get close to the active Co(I) due to the low affinity to **Co-MOF-1′** (eq. 2 compared with eq. 3 and eq. 4 in Fig. 3). Thus,
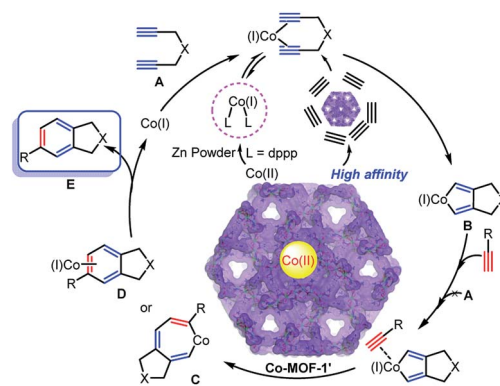

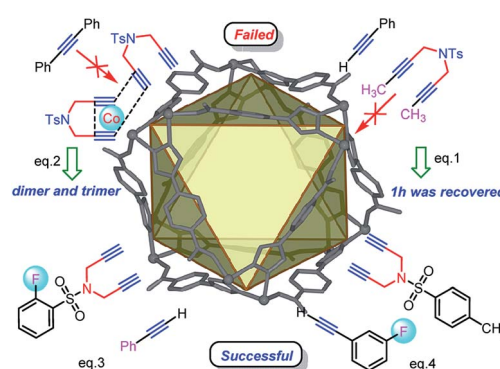**Fig. 2** Proposed mechanism for the transformation.

Fig. 3 The auxiliary verification experiments for catalytic mechanism.

it can be concluded that the cycloaddition would proceed favorably near the catalyst surface with "spot-activated cobalt", allowing only high-affinity alkynes to approach the metal center and thus high selectivity can be realized for cycloadditions. This strategy also provided the potentials for the development of template and precise catalysts.

Conclusions

In conclusion, a 3D Co(II)-based MOF was designed and prepared, showing serial window-sharing octahedral cages and 1D hexagonal channels. The activated **Co-MOF-1′** has high affinity toward acetylene and serves as a heterogeneous and recoverable catalyst for [2 + 2 + 2] cycloaddition to afford highly substituted benzenes with remarkable efficiency, selectivity, and functional group tolerance. Notably, this transformation is also compatible with aromatic alkynes with fluorine substituent and thus provided products with potential pharmaceutical activity. **Co-MOF-1′** with high alkyne affinity and "activated cobalt" can preclude the fast approach of sterically hindered substrates to the active sites, which may well account for the selectivity of achieved products. The results witnessed the great success of **Co-MOF-1′** as catalyst for annulation and encouraged further developments of new MOFs catalysts for expedient synthetic transformations.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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