Dihydrolevoglucosenone (Cyrene) as a green alternative to *N,N*-dimethylformamide(DMF) in MOF synthesis

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Supporting Information Placeholder

ABSTRACT: Cyrene, a green bioderived solvent from waste cellulose, was applied into the synthesis of metal-organic frameworks (MOFs). The MOF, HKUST-1, exhibited an even better Brunauer–Emmett–Teller surface area than HKUST-1 synthesized with DMF. Four additional archetypal MOFs were also synthesized to verify the universal application of Cyrene in MOF manufacture. However, the BET surface areas were lower than DMF-made MOFs. It was observed that an aldol-condensation product of two Cyrene molecules in addition to Cyrene trapped within the pores are responsible for the lower-than expected surface area. The use of Cyrene has led to a series of design principles that eliminate the need for problematic solvents such as DMF and can be applied to the synthesis of a wide range of MOFs.
Keywords: *green chemistry, metal-organic frameworks, alternative solvents, industrial green synthesis.*

INTRODUCTION

Metal-organic frameworks (MOFs)[1-2] are a series of porous materials made of well-organized inorganic metal nodes linked via organic ligands (linkers). MOFs have gained particular attention due to their applications in gas adsorption and separation,[3-10] selective sorption of harmful chemicals,[11-15] catalysis,[16-24] energy,[25-26] sensing,[27-28] bioscience,[29-31] and electronics.[32] These applications make MOFs an integral part of the green chemistry toolkit. As such, it is crucial to find green/sustainable methods of synthesizing MOFs.

With notable exceptions (e.g., mechanochemical,[33-39] water-based,[40-41] and electrochemical[42-45]), the synthesis of MOFs is often carried out at elevated temperature using *N,N*-dimethylformamide (DMF) or *N,N*-diethylformamide (DEF) as the solvent. These solvents are utilized due to their high boiling points as well as beneficial acid-base chemistry.[46] The industrial-scale synthesis of MOFs may generate significant amounts of DMF waste, which can exhibit reprotoxicity and end-of-life issues associated with the formation of NO_x upon incineration.[47-51]

With the introduction of the Registration, Evaluation and Authorization of Chemicals (REACH) legislation in the EU there is a growing trend towards safer production and use of chemicals by industry.[52] Future legislative restrictions under REACH are likely for several traditional dipolar aprotic solvents including DMF, *N,N*-dimethylacetamide (DMAc), and *N*-methylpyrrolidinone (NMP) which have now found their way onto a list of 'substances of very high concern' (SVHC).[53] With the increased implementation of MOFs, it is of vital importance to find safer and preferably bio-derived solvents that can substitute these traditional dipolar aprotic solvents used in their manufacture.

Table 1: Physical properties of DMF, NMP and Cyrene[41, 54]

	DMF	NMP	Cyrene
$\delta_D/\mathrm{MPa}^{0.5}$	17.4	18.0	18.8[a]
$\delta_P/\mathrm{MPa}^{0.5}$	13.7	12.3	10.6[a]
$\delta_H/\mathrm{MPa}^{0.5}$	11.3	7.2	6.9[a]
MP/°C	−60.5	−24	< -18
BP/°C	153	202	203
$\rho/\mathrm{g\ cm}^{-3}$	0.94	1.03	1.25
$V_m/\mathrm{cm}^3\ \mathrm{mol}^{-1}$	77.0	96.5	102.5

[a] Calculated with HSPiP software.

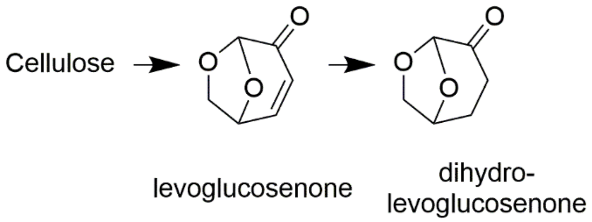

Figure 1. Scheme of the production of dihydrolevoglucosenone (Cyrene).

Cyrene (Dihydrolevoglucosenone; Figure 1) is a dipolar aprotic solvent, which can be derived from waste cellulose in two simple steps.[54] The Kamlet–Abboud–Taft (KAT) polarity scale corresponding to dipolarity of a solvent π^* is similar among Cyrene, NMP and DMF, with values of 0.93, 0.90 and 0.88 respectively.[54] Hansen solubility parameters relating to dispersion (δ_D), polar (δ_P) and hydrogen bonding (δ_H) interactions, indicate that Cyrene is a close solvent match to NMP and DMF (Table 1).[55] Importantly, Cyrene demonstrated no mutagenicity (OECD No. 471 and 487), LD_{50}>2000 mg/kg (OECD No. 423, acute toxicity method) and is barely ecotoxic (OECD No. 201, 202 and 209).[56] Given the similar solubility and physical parameters of Cyrene to traditional dipolar aprotic solvents, whilst having the added benefit of no mutagenicity and being barely ecotoxic, this bioderived solvent was investigated in the synthesis of archetypal MOFs with the hope of deriving a synthetic strategy by which new MOFs can be made with Cyrene.

EXPERIMENTAL

General procedures, materials and instrumentations

Cyrene was provided by Circa Group Ltd. All compounds and solvents were used as received unless otherwise noted: 1,4-diazabicyclo[2.2.2]octane (DABCO) (Aldrich, 99%), 2-methylimidazole (Aldrich, 99%), 2,5-dihydroxyterephthalic acid (Aldrich, 98%), acetic acid (ACP, 99.7%), cobalt(II) nitrate hexahydrate (BDH, 97%), copper(II) nitrate trihydrate (BDH, 99.5%), deuterated dimethyl sulfoxide(DMSO-d_6) (Cambridge, 99.5%), deuterated sulfuric acid (D_2SO_4/D_2O) (Aldrich, 99.5 atom% D), ethyl alcohol (Aldrich, denatured), ethyl alcohol (ACP, 95%), methanol (ACP, 99.8%), N,N-dimethylformamide (DMF) (Fisher, 99.9%), terephthalic acid (Aldrich, 98%), triethylamine (Aldrich, 99%), trimesic acid (Aldrich, 95%), zinc(II) nitrate hexahydrate (J.T. Baker, 99%), zinc(II) acetate dihydrate (J.T.Baker, 99%).

Power X-ray diffraction (PXRD) patterns were obtained using a Rigaku X-ray Ultima IV Diffractometer equipped with a copper X-ray source and a scintillation counter detector.

Single X-ray diffraction data was collected on a Rigaku Saturn 70 CCD, AFC8 goniometer diffractometer equipped with a Molybdenum X-ray tube (Proto-Manufacturing) running at 50 KV and 30 mA (1.5KW). Crystals were glued on a glass fiber. All data was collected at room temperature using 5 second exposures and processed using CrysAlis Pro. Structure solutions were performed in Olex 2. Further details can be seen in the ESI.

N_2 gas adsorption isotherm data were collected at 77K on a TriStar II PLUS surface area and porosity analyzer. All the samples were activated before each isotherm by heating the samples in a vacuum oven.

^{1}H NMR experiments were performed on a 300 MHz Bruker Advance III 300 instrument.

Thermal gravity analysis (TGA) experiments were performed on a Q500 TA Instruments interfaced with a PC using TA Instruments software (version 4.7A). Samples were placed in a platinum pan and heated at a rate of 10 °C/min from 25 °C to 800 °C under a nitrogen atmosphere.

Synthesis of MOFs

UiO-66(DMF),[57] Co-MOF-74(DMF),[58] and Zn2(BDC)2(DABCO)[59] were synthesized from DMF as previously reported. As demonstrated below, even when Cyrene was used as a solvent, DMF is used as the wash solvent in order to prevent the SA results from Cyrene to be convoluted by reagents/products which would be soluble in DMF but may not be soluble in Cyrene.

Synthesis of HKUST-1

A 2-dram vial was charged with trimesic acid (H_3BTC, 25.0 mg, 0.120 mmol), copper(II) nitrate trihydrate (43.0 mg, 0.175 mmol) and mixture solvents of Cyrene/DMF:ethanol:deionized water (see Results and Discussion and the electronic supporting information (ESI) for ratios attempted). Once the reagents dissolved by agitation, the mixture was heated at 80 °C overnight. The resulting solid was washed with 3x10 mL DMF. Subsequently, the DMF was exchanged daily with ethanol for three days. After filtration, the sample was dried under vacuum at 150 °C yielding a purple-blue crystalline solid.

Synthesis of UiO-66

A 2-dram vial was charged with zirconium(IV) oxychloride octahydrate (34.8 mg, 0.108 mmol), DMF (100 μL), acetic acid (135 μL), deionized water (100 μL) and Cyrene (1 mL). Once dissolved, terephthalic acid (24.6 mg, 0.149 mmol) as well as Cyrene (1 mL) was added to the previous mixture. The mixture was placed in an oven at 80 °C oven for 12 hours. The resulting off-white solid was washed with 3x10 mL DMF and subsequently 3x10 mL methanol. After filtration, the sample was dried under vacuum for 12 hours at 80 °C.

Synthesis of ZIF-8

Cyrene: 2-methylimidazole (40.0 mg, 0.487 mmol), zinc(II) nitrate hexahydrate (67.8 mg, 0.228 mmol) and 3 mL Cyrene were loaded in a 2-dram vial. Once dissolved, 2 equivalents (relative to 2-methylimidazole) of triethylamine was added before being heated at 110 °C for 10 hours. The resulting white precipitate was washed with 3x10 mL DMF and subsequently 3x10 mL methanol. The solvent was filtered and dried under vacuum at 80 °C overnight, yielding a white solid.

DMF: A 25 mL vial was charged with 2-methylimidazole (400.0 mg, 4.872 mmol), zinc(II) acetate dihydrate (500.0 mg, 2.278 mmol) and 20 mL DMF. Once dissolved, the sample was heated at 110 °C for 24 hours. The resulting white precipitate was washed with 3x10 mL DMF and subsequently 3x10 mL methanol. The solvent was filtered and dried under vacuum at 80 °C overnight yielding a white solid.

It is worth noting that the shorter heating times of Cyrene (10 h) *vs.* DMF (24 h) was chosen in order to prevent the formation of an aldol-condensation product (see below). Furthermore, zinc(II) nitrate hexahydrate was used in the synthesis of ZIF-8 from Cyrene due to the increased solubility of the nitrate salt vs. the acetate salt.

Synthesis of Co-MOF-74/Co-CPO-27

A 25 mL vial was charged with 2,5-dihydroxyterephthalic (43.0 mg, 0.217 mmol) and an 18 mL mixture solvent (Cyrene:100% ethanol, v:v=1:1), the sample was subsequently agitated for 10 minutes before cobalt(II) nitrate hexahydrate (217.0 mg, 0.746 mmol) was added. Once dissolved, it was heated in a 100 °C oven overnight. The resulting solid was washed first with 3x10 mL DMF. The solvent was then decanted and replaced with methanol daily for three days. After filtration, the sample was dried under vacuum for 12 hours at room temperature, and subsequently for an additional 12 hours at 150 °C, yielding a dark-red crystalline product.

Synthesis of $Zn_2(BDC)_2(DABCO)$

A mixture of zinc(II) nitrate hexahydrate (50.0 mg, 0.168 mmol), terephthalic acid (H2bdc, 27.9 mg, 0.168 mmol) and DABCO (9.4 mg, 0.084 mmol) was suspended in Cyrene (2 mL) in a 2-dram vial before being heated in an oven at 100 °C for 12 hours. The solvent was decanted and replaced with new DMF daily for three days. After filtration, the sample was dried under vacuum at 110 °C overnight, yielding a white powder.

RESULTS AND DISCUSSION

The initial investigation focused on the use of Cyrene in the synthesis of the paddlewheel MOF HKUST-1 (Figure 2) due to its varied applications coupled with its availability through chemical retailers such as Sigma- Aldrich.[60-64] HKUST-1 was synthesized from a solution of Cyrene:EtOH (See Electronic Supplementary Information (ESI) for further details). Figure 3 shows the Powder-X-ray Diffraction (PXRD) of HKUST-1 made from both DMF and Cyrene (1:1:1 volume ratio of Cyrene/95% EtOH/water). As can be seen, the peak position between the simulated and observed PXRDs match indicating that the Cyrene-based synthesis is able to produce crystalline HKUST-1. Perhaps more interesting is the intensities and line widths. In the Cyrene-derived HKUST-1, the two most intense reflections are the {2 2 2} and {3 3 3} reflections indicating a high degree of preferred orientation in comparison from DMF-synthesized HKUST-1. Furthermore, the peak widths of Cyrene-derived HKUST-1 are narrower indicating a larger average particle size in Cyrene-derived HKUST vs. DMF-derived.

With the structural elucidation confirmed, we examined the N2 gas-adsorption isotherm (77 K) of HKUST-1. As shown in Figure 4, when HKUST-1 was synthesized from DMF, a Brunauer–Emmett–Teller (BET) surface area (SA) of 1400 m^2/g was observed. With Cyrene, however, despite the promising PXRD observed in Figure 3, the BET SA of HKUST-1 was initially observed to be a mere 600 m^2/g.

In order to determine the origin of the SA drop between DMF and Cyrene, we investigated the role of the Ethanol as an additive. As shown in Figure 4, when nominally dry EtOH is used in a 5:1 ratio with Cyrene, then a surface area of 1400 m^2/g is observed. However, when 95% EtOH is used, then lower-than ideal BET SAs are observed. It is hypothesized that this behavior is due to the formation of a geminal diol of Cyrene and potentially other products (vide infra) in the presence of water.[65] Therefore, control of the water:Cyrene ratio is necessary to optimize BET SA.

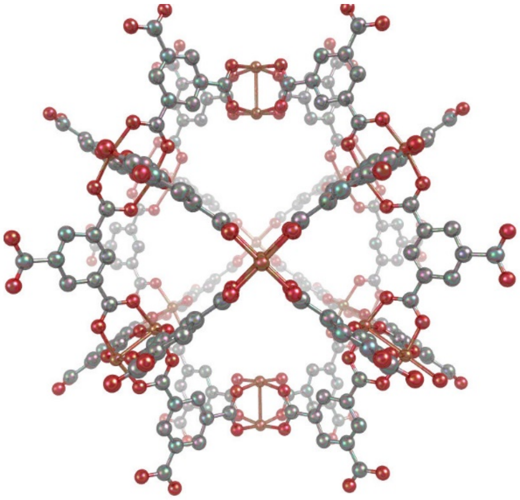

Figure 2. Pore structure of HKUST-1 showing how Cu_2-paddlewheels connect to one another via 1,3,5-bendzentricarboxylate.

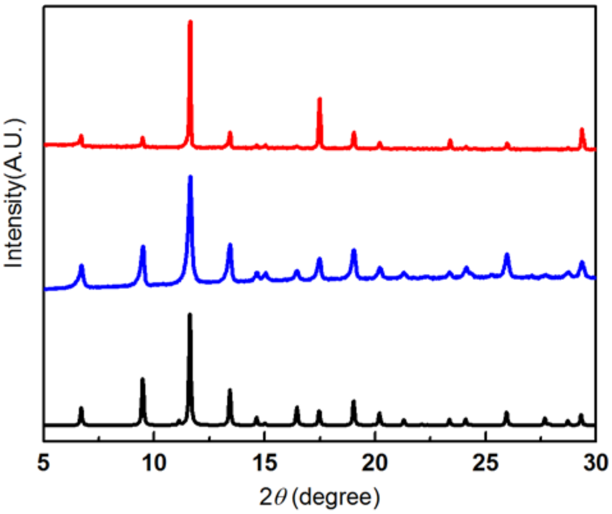

Figure 3. Simulated (black) and observed, as synthesized using DMF (blue) or Cyrene (red), PXRD of HKUST-1.

Given that syntheses of HKUST-1 can be performed in alternative solvents such as EtOH,[63, 66] the importance of Cyrene in this synthesis was investigated. In both DMF and Cyrene, we observed a 35% yield. However, when DMSO/EtOH was substituted for Cyrene/EtOH, then no HKUST-1 was formed. These results indicate that Cyrene's role is crucial. Similarly, when EtOH or an EtOH/H2O mixtures were used in the absence of Cyrene, then a ca. 5% yield was observed.

With these results in mind, the use of Cyrene as a solvent was extended to other MOFs. In order to adequately survey the field, we choose four additional archetype MOFs as representatives. Figure 5 illustrates the structure of UiO-66, ZIF-8, MOF-74, and Zn_2(1,4-benzenedicarboxylate)$_2$(1,4-diazabicyclo[2.2.2]octane) ($Zn_2(BDC)_2(DABCO)$). As shown in Figure 6, with the exception of $Zn_2(BDC)_2(DABCO)$, the peak positions of the PXRDs between the DMF- and Cyrene-derived MOFs match indicating that the desired MOFs were formed. The differences in intensities are due to a combination of preferred orientation and intensity differences from pore-bound solvent. For $Zn_2(BDC)_2(DABCO)$, the flexibility of the MOF, due to the inclusion of various solvents, as evident by the multitude of $Zn_2(BDC)_2(DABCO)$ structures in the Cambridge-crystallographic data center (CCDC), the peak positions do not match as well in comparison to the other MOFs. To further examine $Zn_2(BDC)_2(DABCO)$, we dissolved both DMF- and Cyrene-derived $Zn_2(BDC)_2(DABCO)$ in D_2SO_4/DMSO-d_6 in order to examine the BDC:DABCO ratio. As shown in Figure S5, the ratio of BDC:DABCO is 8:11.6 protons for Cyrene-derived $Zn_2(BDC)_2(DABCO)$ and 8:12, the expected ratio, for DMF-derived $Zn_2(BDC)_2(DABCO)$. These results indicate that $Zn_2(BDC)_2(DABCO)$ has been successfully made in both DMF and Cyrene. Given these results, all four MOFs match the expected PXRD thereby demonstrating the utility of Cyrene towards the synthesis of MOFs. With regards to the BET SA (Table 2), however, the Cyrene MOFs showed lower-than ideal SAs in comparison to their DMF counterparts.

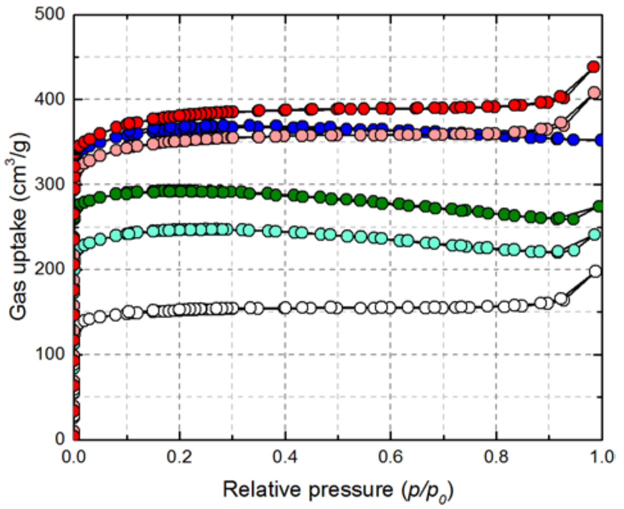

Figure 4. Nitrogen isotherms of HKUST-1 measured at 77K using different Cyrene:EtOH volume ratios. (Blue) DMF-1400 m^2/g; (dark Green): 1:1:1 Cyrene:ethanol (95 %):H_2O-1100 m^2/g; (aquamarine) 1:1 Cyrene:ethanol (95 %)-950 m^2/g; (white) 10:1 Cyrene:ethanol-600 m^2/g; (pink-red) 5:1 Cyrene:ethanol-1400 m^2/g; (red) 1:1 Cyrene:ethanol-1500 m^2/g.

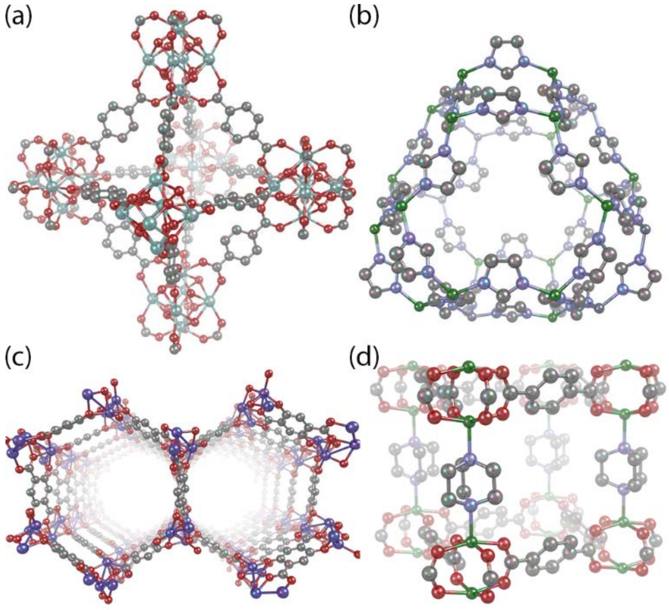

Figure 5. Pore structure of 4 examined MOFs; the structures are all from existing crystallographic information files. (a) UiO-66, a MOF formed by $Zr_6O_4(OH)_4^{12+}$ clusters linked to one another by BDC linkers, showing the octahedral pore; face-sharing tetrahedral pores are removed for clarity. (b) ZIF-8, a MOF formed with Zn(II) and imidazolate linkers. (c) MOF-74 (Co), a MOF formed by M(II) cations connected via tetra-anionic $(BDC\text{-}O^-)_2$. (d) $Zn_2(BDC)_2$(Dabco)

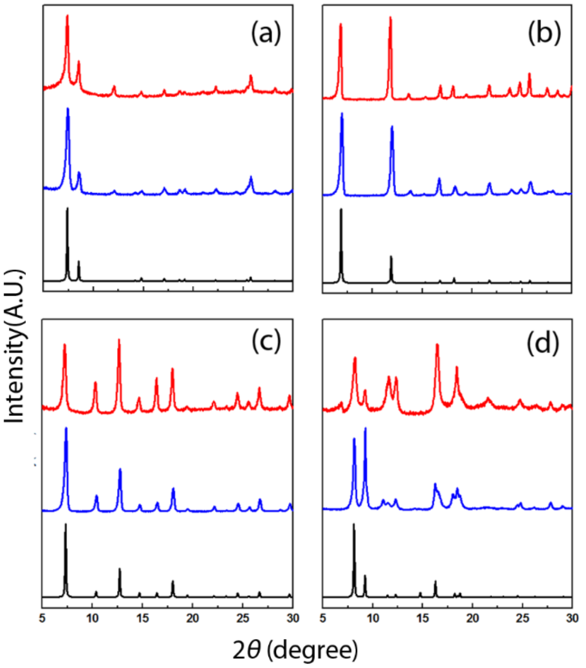

Figure 6. Simulated (black) and observed, as synthesized using DMF (blue) or Cyrene (red), PXRD of (a) UiO-66, (b) MOF-74, (C) ZIF-8 and (d) $Zn_2(BDC)_2(DABCO)$.

Given the importance of finding greener methods of forming MOFs, we wanted to investigate the origin of the lower SA, rather than simply optimizing the system, in order to better understand the chemistry of Cyrene. To that end, we looked more closely at ZIF-8.[67] As shown in Figure 7, during our attempts to synthesize ZIF-8 with Cyrene, the PXRD of ZIF-8 often showed different peak intensities, and even new peaks in comparison with its DMF counterpart. Fortunately, examination of ZIF-8 under a microscope revealed that a crystalline material, inconsistent with the morphology of ZIF-8, was observed among the micro-crystalline powder of ZIF-8 (See ESI for further information). Single-crystal X-ray analysis of these crystals (CCDC deposition number 1500882) indicated that, in the presence of the ZIF-8 starting materials, an aldol- condensation product of two Cyrene molecules was observed (Table S2 and Figure S10 in the ESI). While the majority of the crystalline material can be washed out, as evident in Figure 6, due to the large size of the aldol-condensation impurity, pore-bound impurities may not be so easily removed.

To further investigate our SA results, we digested ZIF-8 in D_2SO_4/DMSO-d_6 in order to probe the presence of impurities in the pore (Figure 8). To our surprise, despite several washings, the presence of Cyrene was always observed to some extent; this can be further observed in the thermal gravimetric analysis (TGA) of these MOFs (Figure S6-S9) which demonstrated that Cyrene-derived MOFs exhibit a greater pore-bound solvent loss than their DMF counterparts. Once again, we hypothesize that for MOFs with small pore-apertures, the notably larger kinetic diameter of Cyrene vs. DMF may require activation routines which we have not explored. However, for large-pore aperture MOFs, the inclusion of residual pore-bound Cyrene is not likely to be problematic.[10, 73-76]

Table 2: Summary of BET surface areas

MOF	Expected (m^2/g)	Observed DMF (m^2/g)	Observed Cyrene (m^2/g)
HKUST-1	1740[68]	1400	1500
UiO-66	1700[69]	1300	500
Co-MOF-74	1572[70]	800	200
ZIF-8	1950[71]	1700	600
$Zn_2(BDC)_2(DABCO)$	1750[72]	1950	1300

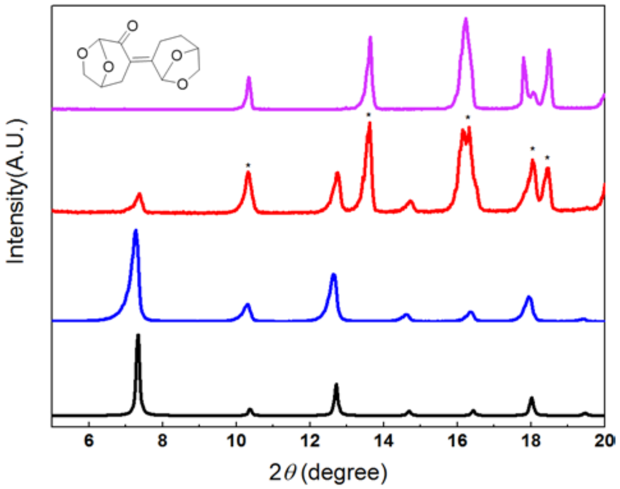

Figure 7. Simulated(black) and observed, as synthesized using DMF(blue) or Cyrene(red), PXRD of ZIF-8. The observed pxrd of the Cyrene aldol-product (pink). Peaks marked with * indicate the presence of the Cyrene aldol-condensation product intermixed with ZIF-8.

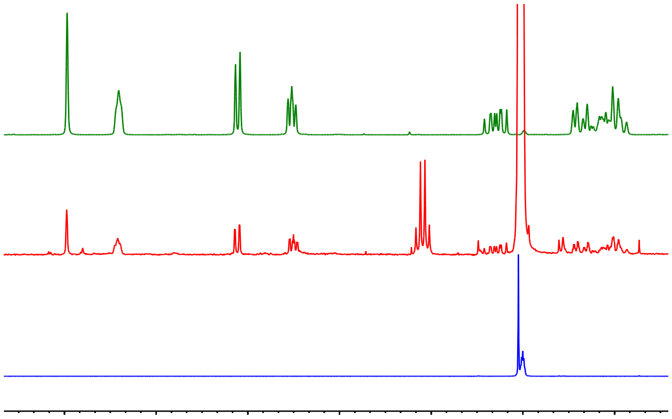

Figure 8. ^{1}H-NMR of acid-digested(D_2SO_4/DMSO-d^6) ZIF-8 (DMF,blue; Cyrene,red) and Cyrene (green).

CONCLUSIONS

In summary, an environmental friendly dipolar aprotic solvent has been investigated for the synthesis of five distinctive MOFs, HKUST-1, UiO-66, MOF-74, ZIF-8 and $Zn_2(BDC)_2(DABCO)$. In all 5 cases, Cyrene was able to produce crystalline materials with PXRDs that match the expected PXRD. As a set of design principles, we have discovered that keeping the water content of Cyrene low is critical. Additionally, decreasing the heating times is necessary to prevent the formation of the aldol-condensation product. With these points in mind, optimal BET SAs can be easily obtained. Although an aldol-condensation product and residual Cyrene were observed in some of these MOFs, the complex acid-base chemistry associated with Cyrene is akin to the necessary acid-base chemistry that occurs with DMF during MOF formation; this is likely the origin of the observation that DMSO/EtOH is not an ideal alternative solvent for MOF synthesis. The lessons learned herein can be extended to other MOFs which, at present, do not have non-DMF synthetic pathways. To that end, Cyrene is a suitable green replacement for DMF.

ASSOCIATED CONTENT

Supporting Information.

The supporting material is available free of charge via the Internet at http://pubs.acs.org." Crystallographic Information File can be found at CCDC deposition number 1500882.

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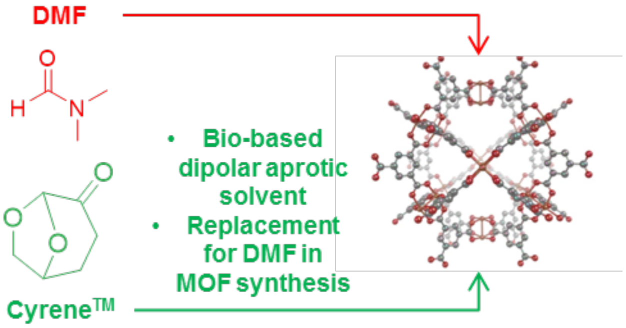
TOC Graphic:



TOC Text: An environmentally benign solvent derived from waste cellulose has been successfully used in the synthesis of metal-organic frameworks.