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YOMKIPPUR PEREZ

Gilbert U. Yu

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Feasibility of Cyclodextrin-Potassium Ion Assemblies Synthesis and Its Application in Loading Bio-active Molecules

Yomkippur Perez and **Gilbert Yu***

Department of Chemistry, School of Science and Engineering
Ateneo de Manila University, Quezon City 1108 Philippines

In the study, colorless cubic crystals of "green" cyclodextrin (CD)-based assemblies were synthesized and their potential to load bio-active molecules such as drugs and, separately, enzymes were investigated. Busulfan (Bu), an anti-cancer drug widely used to treat chronic myelogenous leukemia (CML), was used as a test drug while trypsin and lipase were used as model enzymes. These porous CD-K^+ ion assemblies were prepared by dissolving alkali metal salts and γ-CD in water followed by vapor diffusion in varying solvents for several days. Crystals were activated via dichloromethane dispersion and in vacuo drying. Slow vapor diffusion with ethanol was found to give the highest yield and fastest crystallization time among all the solvents used. The materials synthesized using ethanol were characterized to be cubic crystals with sizes ranging from 100–1000 µm that are stable up to 250 °C. Loading of Bu (%S) onto the CD-K^+ ion assemblies and co-crystallization with trypsin (%N) were both successful, as confirmed by elemental analysis. Loading studies of Bu performed using thermogravimetric analysis (TGA) confirmed about 5 wt% loading in the porous materials.

Keywords: cyclodextrin assemblies, enzymes, gamma (γ) cyclodextrin, metal-organic framework, busulfan

INTRODUCTION

Metal-organic frameworks (MOFs) represent an extensive class of porous materials where coordination of metal ions with organic ligands gives rise to networks containing potential voids (Rowsell *et al.* 2004; Batten *et al.* 2013; Rosseinsky 2004; Kitagawa *et al.* 2004; Férey 2008, 2009; Janiak and Veith 2010; Shen 2020). Recently, a series of environment-friendly MOFs with large pore volumes comprising alkali metal salts and endogenous linker, γ-CD, have been reported by Smaldone and co-workers (2010). This γ-CD combined with salts of Group IA, IIA, or transition metal cations gives rise to CD-MOFs having large surface areas (SAs) [Brunauer-Emmett-Teller (BET) SA: 1200 m^2/g, Langmuir SA: 1300 m^2/g) and biocompatibility, making them desirable for food and pharmaceutical applications (Gassensmith *et al.* 2011; Stoddart *et al.* 2015; Forgan *et al.* 2010).

CD-MOFs have been reported to reversibly sequester a variety of organic molecules. This phenomenon can be largely attributed to the structure of CDs, which includes a hydrophobic interior and hydrophilic exterior, that can accommodate various guest molecules. There are three types of CDs according to the number of fused glucose units: α- (six), β- (seven), and γ- (eight). Efficient CO_2 sequestration by CD-MOFs was documented by Gassensmith *et al.* (2011) and Wu *et al.* (2013) whereas

*Corresponding Author: gyu@ateneo.edu

CD-MOFs' use in separation of a wide variety of compounds – including alkyl-, vinyl- and haloaromatics plus saturated and unsaturated acyclic compounds; on top of these chiral compounds were reported by Holcroft *et al.* (2015) and Hartileb *et al.* (2016), respectively. CD-MOFs encapsulation of acetaldehyde and other volatile organic compounds for post-harvest applications have been studied by Al-Ghamdi (2014). Moussa and co-workers (2016) reported that CD-MOFs could also be a promising benign system to store and stabilize curcumin for food applications.

At present, potential pharmaceutical applications of CD-MOFs have progressed from ibuprofen uptake simulation studies detailed by Bernini and co-workers (2014) to the recently reported in vitro viability studies of ibuprofen-loaded CD-MOFs by the Stoddart group. Additionally, recent studies on the drug loading capability of CD-MOFs – by the Shen (2020), Wu (2013), and Falcaro (2011) groups – have also been undertaken. Besides these few accounts, to the authors' best knowledge, no other literature cited CD-MOFs for biomedical applications. For this reason, we decided to contribute information on the CD-MOFs' viability for biomolecule uptake by attempting to synthesize CD-MOFs based on γ-CDs and investigate their affinity towards a potential anti-cancer drug (Bu) and enzymes trypsin and lipase into these materials.

The exploration of potential applications of CD-MOFs and similar materials, especially in the fields of pharmaceutical and bio-catalysis, is an essential undertaking. Their biocompatibility is one of its many properties that sets it apart from other MOF-based structures. The vast majority of MOFs described to date are composed of exogenous organic struts and transition metals (Smaldone *et al.* 2010). Their benign composition (K^+ and γ-CD) permit their possible use in the fields of medicine and food applications without toxicological concerns. Herein, the potential of CD-K^+ ion assemblies to load bio-active molecules such as drugs and enzymes is further investigated. Bu is used as a test drug while lipase from porcine pancreas and trypsin from the bovine pancreas are used as model enzymes.

Bu (1, 4-butanediol-dimethanesulfonate) is an anti-cancer drug widely used to treat CML. It is an alkylating agent and works by slowing down the reproduction and growth of certain white blood cells. Many attempts have been made to entrap Bu in known drug carriers to avoid liver accumulation and to protect it against rapid degradation however poor loadings and fast release was generally obtained (Dunn 1974). In 2011, Horcajada *et al.* reported the encapsulation of Bu with high loadings up to 25 wt % but using iron carboxylate-based MOFs.

Lipases (triacylglycerol acylhydrolase, EC 3.1.1.3) are enzymes that catalyze both the hydrolysis and transesterification of triacylglycerides under mild reaction conditions. Lipases are among the most attractive and promising enzymes for industrial applications in the dairy, pharmaceutical, and oleochemical industries (Houde *et al.* 2004; Cao *et al.* 2016). Trypsin (EC 3.4.21.4) is an enzyme that catalyzes protein digestion and cleavage of peptides; it is often referred to as proteolytic enzyme/proteinase. It is one of the three principal digestive proteinases (the other two being pepsin and chymotrypsin) and has been used widely in proteomics studies and other biotechnological processes. In spite of their excellent catalytic properties, some properties such as stability have to be improved to widen their applications. According to Brenner's Encyclopedia of Genetics, immobilization of enzymes is thought to be a simple and efficient method to address these issues.

MATERIALS AND METHODS

Materials

γ-CD samples (purity > 99%) were obtained from DKSH (Makati, Philippines). Potassium hydroxide (KOH) pellets (ACS reagent, purity ≥ 85%), Bu (analytical standard), lipase from porcine pancreas (Type II), and trypsin from bovine pancreas (2x crystallized, dialyzed, and lyophilized; salt-free) were purchased from Sigma-Aldrich Corp. (Saint Louis, MO, USA). All chemicals and solvents were used without further purification.

Methods

Synthesis and characterization of CD-K+ ion assemblies. Several methods were tested to synthesize these materials. The principal method used was the slow vapor diffusion route to synthesize CD-MOFs, as described by Smaldone *et al.* (2010). The other two methods – which produce smaller crystals, suggested by Smith *et al.* (2015) and Marui *et al.* (2010) (number of moles of reactants was varied for the latter's method) – were also tried. All experimental set-ups were done in triplicate. Syntheses using the first method were repeatedly done taking careful inspection since varying results for crystal formation were initially observed. As-synthesized assemblies were activated by immersion in dichloromethane (washings were refreshed once a day for 3 d). The crystals were then dried *in vacuo* at room temperature for 10 h and then the temperature was increased to 50–80 ºC (depending on the solvent used) for an additional 12 h. Evaluation of the thermal stability of crystals was conducted using a Shimadzu TGA-50 thermal analysis system heated at 5–10 °C min^{-1} from 25–800 °C. Fourier-transform infrared (FTIR) spectra of samples were collected using Shimadzu IR Prestige-21 with diffuse reflectance spectroscopy.

Energy-dispersive X-ray (EDX) analyses were performed using a Hitachi S-3400N scanning electron microscope (SEM). Samples were first subjected to an ion sputter (Au-Pt) before analysis. Powder X-ray diffraction data were collected using Rigaku Ultima IV X-ray diffractometer with the following settings: radiation of Cu Kα (λ = 0.154 nm) at 40 kV, 40 mA, and 1.2-mm beam incision with 2.0-mm detector slit over the range of 1–30° with increments of 0.02°. BET data were collected using Quantachrome NovaWin where the N_2 adsorption took place at 77.3 K.

Bu loading. Bu loading *via in situ* encapsulation was done by adding varying amounts of Bu in water with γ-CD. Although Bu is largely non-polar and is expected to be insoluble in water, the authors hypothesized that γ-CD might improve Bu's solubility in the solvent. For two-step, *ex situ* encapsulation studies, previously-dried (65 °C, 2 h) CD-MOF-1 samples were incubated in a Bu solution made from dissolving Bu in chloroform (80% max solubility). Chloroform was chosen according to the reported high solubility of Bu in the solvent (8 mg/ml). The mixtures were incubated for 16 h at room temperature. The Bu-loaded solids were then collected by filtration and then vacuum-dried. The collected solids were analyzed using EDX – enabling determination of C, O, and S wt%. For the determination of Bu loading by nuclear magnetic resonance (NMR) spectroscopy, 20 mg of previously-dried materials were incubated in 2 ml of a 2 mg/ml Bu solution in deuterated chloroform ($CDCl_3$) containing 0.05% v/v tetramethylsilane (TMS), used as an internal standard. After 16 h of incubation at 16 °C, the crystals were collected and vacuum-dried overnight. The amount of non-encapsulated Bu was determined in the supernatants by ^{1}H-NMR spectroscopy using a calibration curve of Bu solutions in $CDCl_3$ (0.0001–0.01 g/ml).

Enzyme immobilization via in situ synthesis. One equiv. γ-CD plus 8 equiv. KOH and trypsin/lipase (100–500 mg) were combined in water and subsequently allowed to undergo slow vapor diffusion for 2–7 d. The solution with crystals at the bottom was carefully decanted and washed with the solvent three times. The crystals were allowed to stand in the solvent for 3 d, as another set of crystals were immediately dried since clear crystals turned yellow and then brown upon soaking with ethanol. The crystals were then dried *in vacuo* at room temperature for 10 h and then the temperature was increased to 50 or 80 °C (depending on the solvent used) for an additional 12 h. Evaluation of the thermal stability of crystals was conducted using a Shimadzu TGA-50 thermal analysis system. Samples were heated at 1 °C min^{-1} from 30–500 °C. FTIR spectra of samples were collected from pelletized samples using Shimadzu IR Affinity FT-IR. SEM-EDX analyses were performed using a Hitachi S-3400N SEM. Samples were first subjected to an ion sputter (Au-Pt) before analysis. Nikon Eclipse E200 optical microscope was also used for relative size evaluation of crystals. Powder X-ray diffraction data were collected using Rigaku Ultima IV X-ray diffractometer with the following settings: radiation of Cu Kα (λ = 0.154 nm) at 40 kV, 40 mA, and 1.2-mm beam incision with 2.0-mm detector slit over the range of 1–30° with increments of 0.02°. ^{1}H-NMR spectroscopy was performed at 400 MHz using JEOL LA400.

RESULTS AND DISCUSSION

CD-K^+ ion assemblies were synthesized using KOH as metal ion source (K^+) and γ-CD as an organic linker. It might be important to note that while a high degree of crystallinity is the desired quality of all MOFs published in the literature, not all MOFs produced share similar characteristics and properties. For instance, a study involving various methodologies of synthesizing HKUST-1 (MOF composed of copper ions and 1, 3, 5-benzenetricarbocylic acid) resulted in various samples with differences in crystallinity, phase purity, and BET surface area calculations (Moosavi *et al.* 2019). In this work, we adopted and slightly tweaked the slow vapor diffusion method in the synthesis of our CD-K^+ assemblies similar to those of published literature concerning CD-MOFs. While highly crystalline CD-MOFs fit for well-resolved XRD analysis failed to materialize, we were able to produce sufficient products for harvest and investigate its potential in loading bio-active molecules, Bu, lipase, and trypsin. Clear cubic crystals were formed in the solution after 24 h in methanol and in ethanol. Fewer and smaller crystals were observed in THF after 4 d. Soft and thin rod-like crystals together with cubic crystals were formed in the solution using acetone as diffusion solvent. The solution was also observed to change from clear to yellow, which may be caused by an aldol condensation reaction with acetone promoted by KOH in the solution (Al-Ghamdi 2014, Figure1). Slow vapor diffusion with ethanol was found to give the highest yield and fastest crystallization time among all the solvents used for our material (Table 1). Methanol also produced clear cubic crystals; however, some white precipitates appeared during Days 3–7.

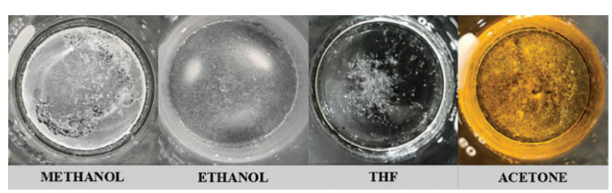


Figure 1. CD-MOFs formed via slow vapor diffusion in varying solvents.

Table 1. Synthesis of CD-K^+ assemblies with varying solvents.

Solvent	Boiling point of solvent	Time of crystallization (day)	Yield[a]	Observations
Acetone	56 °C	1	47%	Thin rod-like and cubic crystals; solution turned yellow
Methanol	65 °C	1	63%	Clear cubic crystals with white precipitates
THF	66 °C	4	0–2%	Small clear cubic crystals
Ethanol	78 °C	1	78%	Clear cubic crystals

[a]Crystals were collected after 7 d and oven-dried at 80 °C for 2 h. Values average of three trials.

No visible crystals were formed using the methods suggested by Smith *et al.* (heating with acetone for 2 h) while the modified method of Marui *et al.* (dropping 2-propanol in heated KI and γ-CD solution) yielded only white precipitates. White precipitates that were collected from the solutions were analyzed using X-ray fluorescence (XRF). Potassium (K) was not detected in the white precipitates, suggesting that CD-MOFs were not formed in the solution. CD-K^+ assemblies synthesized using ethanol were characterized to be cubic crystals with sizes ranging from 100–1000 μm (Figure 2) that are stable up to 250 °C (TGA) and having an absorption of about 300 cm^3 g^{-1} (BET). XRD pattern of synthesized CD-K^+ assemblies showed varying peaks with simulated data in the literature [see Appendix Figure S3; *vis-à-vis* Smaldone *et al.* (2010) and Stoddart *et al.* (2015)]. The synthesized CD-K^+ assemblies is possibly a polymorph of the one reported in the literature. No sharp XRD peaks were produced and no single crystal available for X-ray crystallography was also obtained. The exact structure of the synthesized material remains unknown.

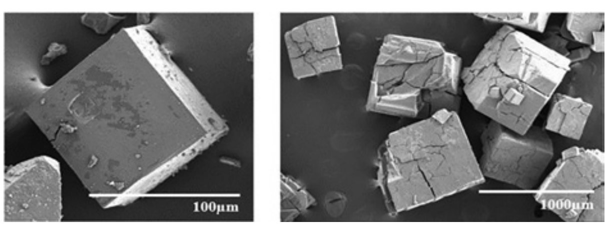


Figure 2. SEM micrographs of synthesized CD-K^+ assemblies.

Loading of Bu onto the material was successful as confirmed by FTIR (Bu-1100, 1300cm^{-1} sulfonate peak) and elemental analysis (3.84% S). From the EDX data, it is estimated that there are two Bu molecules per γ-CD (see Appendix Figure S3). Quantitative loading studies of Bu were performed using TGA. The obtained crystals were soaked in a Bu solution prepared using $CDCl_3$. Filtrates were collected after 16 h and were analyzed using ^{1}H-NMR. An average of 5 wt% Bu loading in CD-K^+ assemblies was calculated from the TGA analysis of Bu-loaded material (Figure 3). Analysis of Bu concentration in the remaining filtrate using ^{1}H-NMR revealed a lower loading; however, this can be attributed to the high volatility of the solvent used. An internal standard (TMS) in the prepared solution was used to construct a calibration curve for the relative quantification of Bu loading. Integration of three peaks that characterize Bu were each plotted against the Bu concentration and revealed an average of 5% weight loading for the Bu-loaded samples.

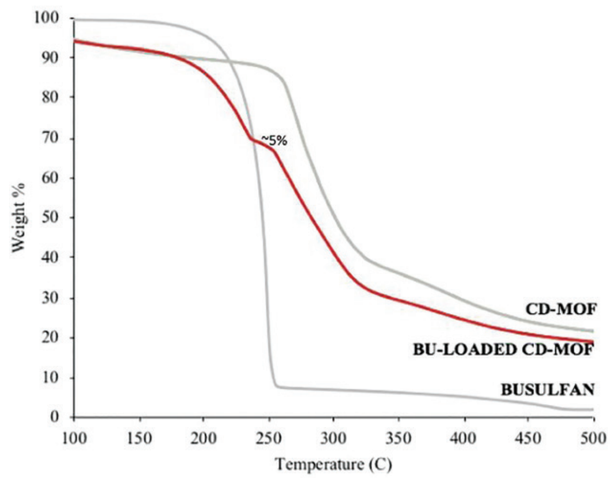
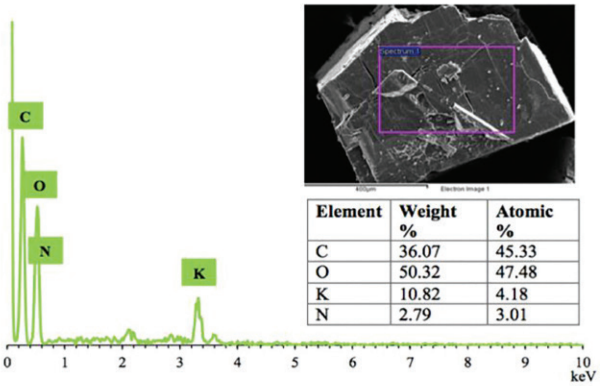


Figure 3. TGA of Bu loaded CD-K^+ assemblies.

In a separate set of experiments, enzyme loading was done using *in situ* synthesis of trypsin in collected crystals. Crystals (CD-MOF-enzyme) that were isolated from the solution were found to be smaller in size than the regular CD-MOFs. Additional nucleation sites produced by the enzyme may have decreased the rate of crystal growth. Loading of trypsin was successful as confirmed by FTIR (trypsin – 1650 cm^{-1} carbonyl peak) (see Appendices) and elemental analysis (3.01 %N, Figure 4) but unsuccessful for lipase. One factor that may have affected incorporation in the CD-K^+ assemblies is its sparing solubility in the solution.



Element	Weight %	Atomic %
C	36.07	45.33
O	50.32	47.48
K	10.82	4.18
N	2.79	3.01

Figure 4. EDX analysis of trypsin loaded CD-K^+ assemblies.

CONCLUSION

Herein, a "green" metal-organic CD-K^+ ion assemblies made from CD was synthesized and its potential to load bio-active molecules such as drugs and enzymes was investigated. The materials were prepared by dissolving KOH and γ-CD in water followed by vapor diffusion in varying solvents. Crystals were activated via DCM dispersion and *in vacuo* drying. Slow vapor diffusion with ethanol was found to give the highest yield and fastest crystallization time among all the solvents used. Solids synthesized using ethanol were characterized to be cubic crystals with sizes ranging from 100–1000 μm that are stable up to 250 ºC and having an absorption of about 300 cm^3 g^{-1}. Loading of the drug Bu (%S) via two-step encapsulation onto the material and loading of the enzyme trypsin (%N) *via in situ* synthesis were both successful as confirmed by elemental analysis. TGA analysis for the loading of Bu confirmed about 25 wt% loading in synthesized solids. Succeeding studies concerning the release profile of Bu and enzymes from the synthesized CD-K^+ assemblies may be investigated in the near future.

ACKNOWLEDGMENTS

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NOTES ON APPENDICES

The complete appendices section of the study is accessible at http://philjournsci.dost.gov.ph

REFERENCES

AL-GHAMDI S. 2014.Synthesis of nanoporous carbohydrate metal-organic framework and encapsulation of selected organic compounds [M.S. thesis]. Michigan, USA: Michigan State University.

BATTEN SR, CHAMPNESS NR, CHEN X, MARTINEZ J, KITAGAWA S, OHRSTROM L, O'KEEFFE M, SUH MP, REEDIJK J. 2013. Terminology of metal-organic frameworks and coordination polymers (IUPAC Recommendations 2013). Pure Appl Chem 85(8): 1715–1724.

BERNINI MC, FAIREN-JIMENEZ D, PASINETTI M, RAMIREZ-PASTOR AJ, SNURR RQ. 2014. Screening of bio-compatible metal-organic frameworks as potential drug carriers using Monte Carlo simulations. J Mater Chem B 2: 766–774.

CAO Y, WU Z, WANG T, XIAO Y, HUO Q, LIU Y. 2016. Immobilization of *Bacillus subtilis* lipase on a Cu-BTC based hierarchically porous metal-organic framework material: a biocatalyst for esterification. Dalton Trans 45: 6998–7003.

DUNN CDR. 1974. The chemical and biological properties of busulphan ("Myleran"). Hemat 2: 101–117.

FALCARO P, HILL AJ, NAIRN KM, JASIENIAK J, MARDEL JI, BASTOW TJ, MAYO SC, GIMONA M, GOMEZ D, WHITFIELD JW, RICCÒ R, PATELLI A, MARMIROLI B, AMENITSCH H, COLSON T, VILLANOVA L, BUSO D. 2011. A new method to position and functionalize metal-organic framework crystals. Nature Comm 2 (Article No. 237).

FÉREY G. 2008. Hybrid porous solids: past, present, future. Chem Soc Rev 37: 191.

FÉREY G. 2009. Some suggested perspectives for multifunctional hybrid porous solids. Dalton Trans, p. 4400–4415.

FORGAN RS, SMALDONE RA, GASSENSMITH J, FURUKAWA H, CORDES DB, LI Q, WILMER CE, BOTROS Y, SNURR RQ, SLAWIN A, STODDART JF. 2012. Nanoporous Carbohydrate Metal-Organic Frameworks. J Am Chem Soc 134: 406–417.

GASSENSMITH JJ, FURUKAWA H, SMALDONE RA, FORGAN RS, BOTROS YY, YAGHI OM, STODDART JF. 2011. Strong and reversible binding of carbon dioxide in a green metal-organic framework. J Am Chem Soc 133: 15312–15315.

HARTILEB KJ, HOLCROFT JM, MOGHADAM PZ, VERMEULEN NA, ALGARADAH MM, NASSAR MS, BOTROS YY, SNURR RQ, STODDART JF. 2016. CD-MOF: A Versatile Separation Medium. J Am Chem Soc 138: 2292–2301.

HOLCROFT JM, HARTILEB KJ, MOGHADAM PZ, BELL JG, BARIN G, FERRIS DP, BLOCH ED, ALGARADAH MM, NASSAR MS, BOTROS YY, THOMAS KM, LONG J, SNURR RQ, STODDART JF. 2015. Carbohydrate-Mediated Purification of Petrochemicals. J Am Chem Soc 137: 5706–5719.

HORCAJADA P, COUVREUR P, SERRE C, BEN YAHIA M, MAURI G, GREF R. 2011. Porous metal organic framework nanoparticles to address the challenges related to busulfan encapsulation. Nanomedicine 6(10): 1683–1695.

HOUDE A, KADEMI A, LEBLANC D. 2004. Lipases and their industrial applications: an overview. Appl Biochem Biotechnol 118(1–3): 155–170.

JANIAK C, VEITH JK. 2010. MOFs, MILs and more: concepts, properties and applications for porous coordination networks (PCNs). New J Chem 34: 2366–2388.

KITAGAWA S, KITAURA R, NORO S. 2004. Functional porous coordination polymers. Angew Chem Int Ed 43: 2334–2375.

MARUI Y, KIDA T, AKASHI M. 2010. Facile Morphological Control of Cyclodextrin Nano- and Microstructures and Their Unique Organogelation Ability. Chem Mater 22: 282–284.

MOOSAVI SM, CHIDAMBARAM A, TALIRZ L, HARANCZYK M, STYLIANOU KC, SMIT B. 2019. Capturing Chemical Intuition in Synthesis of Metal-organic Frameworks. Nature Comm 10: 539.

MOUSSA Z, HMADEH M, ABIAD MG, DIB OH, PATRA D. 2016. Encapsulation of curcumin in cyclodextrin-metal organic frameworks: dissociation of loaded CD-MOFs enhances stability of curcumin. Food Chem 212: 485–494.

ROSSEINSKY MJ. 2004. Recent developments in metal-organic framework chemistry: design, discovery, permanent porosity and flexibility. Microporous and Mesoporous Mat 73: 15–30.

ROWSELL JLC, YAGHI OM. 2004. Metal-organic frameworks: a new class of porous materials. Microporous and Mesoporous Mat 73: 3–14.

SHEN D, COOPER J, LI P, GUO Q-H, CAI K, WU H, CHEN H, ZHANG L, JIAO Y, QIU Y, STERN C, LIU S, SUE A C-H, YANG Y-W, ALSUBAIE FM, FARHA OK, STODDART JF. 2020. Organic Counteranion Co-assembly Strategy for the Formation of γ-Cyclodextrin-Containing Hybrid Frameworks. JACS 142(4): 2042–2050.

SMALDONE RA, FORGAN RS, FURUKAWA H, GASSENSMITH JJ, SLAWIN AMZ, YAGHI OM, STODDART JF. 2010. Metal-organic frameworks from edible natural products. Angew Chem Int Ed 49: 8630–8634.

SMITH MK, ANGLE SR, NORTHROP BH. 2015. Preparation and Analysis of Cyclodextrin-Based Metal-Organic Frameworks: Laboratory Experiments Adaptable for High School through Advanced Undergraduate Students. J Chem Ed 92(2): 368–372.

STODDART JF, SMALDONE RA, FORGAN RS, GASSENSMITH JJ. 2015. United States Patent US 14/804,044.

WU D, GASSENSMITH JJ, GOUVEA D, USHAKOV S, STODDART JF, NAVROTSKY A. 2013. Direct Calorimetric Measurements of Enthalpy of Adsorption of Carbon Dioxide on CD-MOF-2, a Green Metal-Organic Framework. J Am Chem Soc 135: 6790–6793.

WU M-X, YAN Y-W. 2017. Metal-Organic Framework (MOF)-Based Drug/Cargo Delivery and Cancer Therapy. Adv Mater 29(23).

APPENDICES

Synthesis of CD-MOFs in Varying Solvents

White precipitates that were collected from the solutions were analyzed using XRF. K was not detected in the white precipitates, suggesting that CD-MOFs were not formed in the solution.

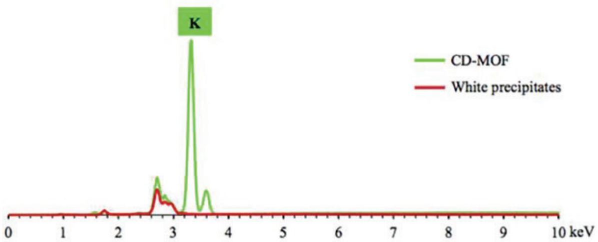

Figure S1. XRF analysis of white precipitates (red) and CD-MOFs (green).

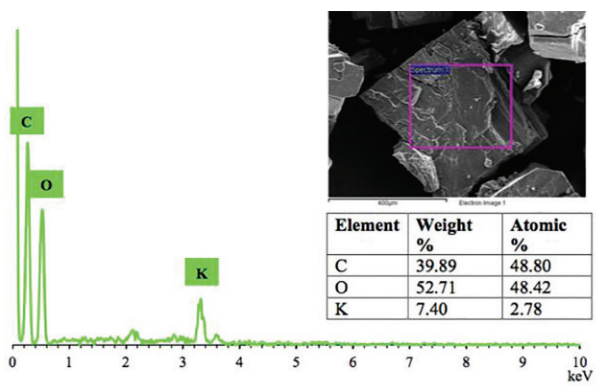

Figure S2. EDX analysis of synthesized CD-MOFs. γ-CD: $C_{48}H_{80}O_{40}$, MW: 1297 g/mol and CDMOF: $[(C_{48}H_{80}O_{40})(KOH)_2]_n$ MW: 1409 g/mol

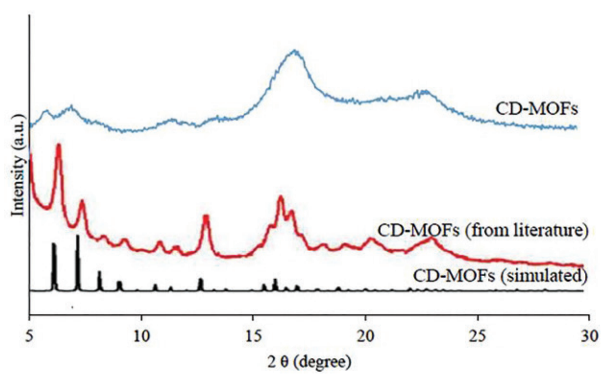

Figure S3. XRD pattern for synthesized CD-MOFs.

Table S1. Theta angle and d-spacing for CD-K+ assemblies XRD peaks.

2-theta (deg)	d spacing (Å)	Relative intensity (a.u.)
11.3	7.8	2.5
17.3	5.1	100
23.2	3.8	63.9

Bu Loading

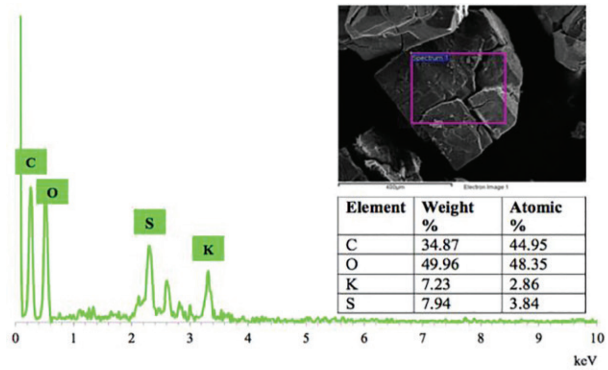

Figure S4. EDX analysis of Bu-loaded CD-MOFs. Bu, $C_6H_{14}O_6S_2$; MW: 246 g/mol.

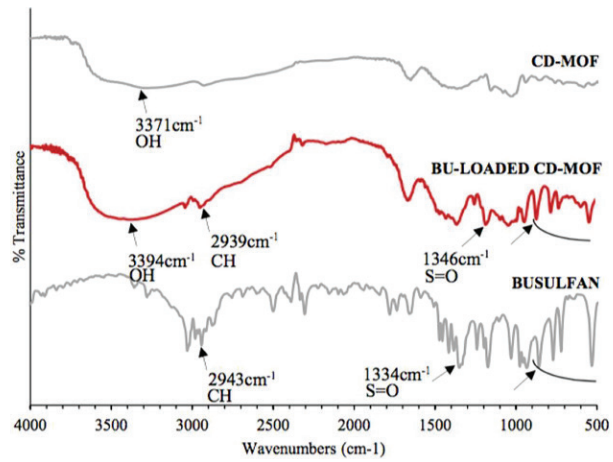

Figure S5. FTIR of Bu-loaded CD-MOFs.

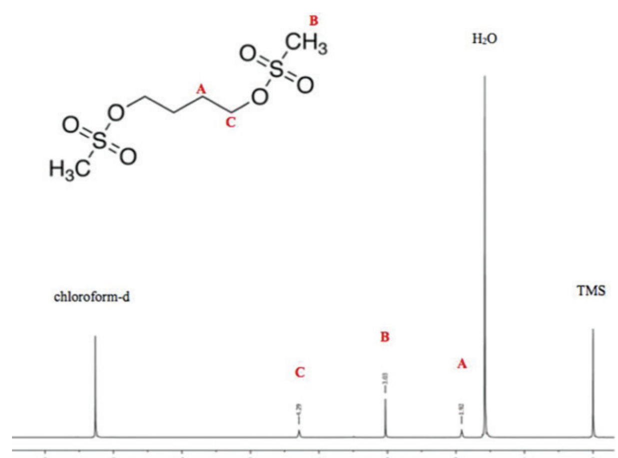

Figure S6. Sample [1]H-NMR (400 MHz, $CDCl_3$) of Bu: δ 7.27 (solvent peak, s), 4.29 (2H, t), 3.03 (3H, s), 1.92 (2H, t), 1.58 (water, s).