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Communication

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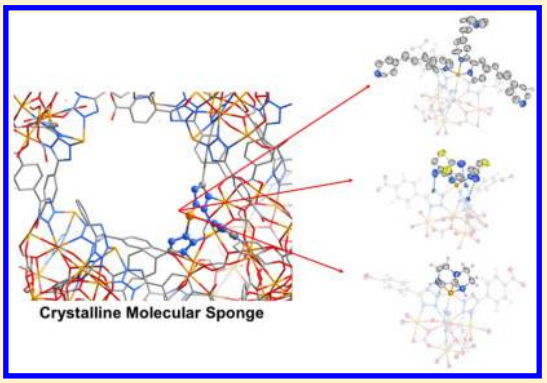
Coordinative Alignment To Achieve Ordered Guest Molecules in a Versatile Molecular Crystalline Sponge

Le Wang, Curtis E. Moore, and Seth M. Cohen*

Department of Chemistry and Biochemistry, University of California, San Diego, La Jolla, California 92093, United States

Supporting Information

ABSTRACT: A Mn^{2+}-based metal−organic framework (coordination porous framework-5, CPF-5) can serve as a crystalline sponge for single crystal X-ray structural characterization of a variety of compounds using a combination of coordinative alignment and second coordination sphere interactions (e.g., hydrogen bonding). This technique requires only a conventional X-ray source to obtain high quality crystallographic data.



Single crystal X-ray diffraction (SXRD) is among the most powerful tools for unambiguously determining the chemical structure of compounds. However, some molecules are not inherently crystalline or are extremely difficult to crystallize. For example, some compounds exist as amorphous powders, waxes, or liquids under ambient conditions, and still others are not sufficiently stable to persist during the crystallization processes. Metal−organic frameworks (MOFs)[1−4] can serve as platforms to encapsulate these guest species to aid in their structure determination. MOFs have been shown to coherently immobilize guest species because specific binding sites for guest molecules are periodically and uniformly distributed throughout the highly crystalline framework. In principle, the internal pore environment of the MOF can be designed to create confinement effects that help to promote both positional ordering and a specific orientation of guest molecules within the pores. MOF pores can also be tailored to select for different types of guest molecules.

Several exciting reports by Fujita,[5−8] Yaghi,[9] and others[10−18] have shown that cocrystallizing compounds as entrapped guest molecules within crystalline porous solids (i.e., MOFs) is an effective strategy for determining the atomic structure of such species. Although the conformation of molecules determined by this "crystalline sponge" method may differ from that in a pure crystal or in solution, the crystalline sponge method remains attractive for its utility in facilitating the structure determination (and hence molecular connectivity and configuration) of difficult to crystallize molecules. In the reports by Fujita,[5−8] weak forces between guests and the framework (described as a "crystalline sponge") was used to entrap such species, which at times resulted in disorder and ambiguities in the resulting structure determinations. To overcome these limitations, Yaghi et al. developed a coordinative alignment (CAL) whereby coordination bonds between the guests and the framework secondary building units (SBUs) help secure the molecules to be characterized. These guest molecules are anchored onto Al^{3+}-based SBUs through hard Lewis base functional groups, such as carboxylates, phenols, or diols via postsynthetic exchange (PSE) of bridging formate ligands on the SBUs.[19,20] Occasionally this PSE process induces loss of sample crystallinity or cracks in the single crystals required for SXRD. In the Yaghi report, all X-ray structure determinations utilized synchrotron X-ray sources. Alternative crystalline sponges which remain highly crystalline and can accommodate different guests are important for driving this new approach to SXRD forward.

Inspired and motivated by these previous studies, we sought to identify new crystalline sponges with improved and complementary features. Here we report a known MOF (CPF-5, CPF = coordination porous framework, $[Mn_{21}(HCOO)_{18}(H_2O)_{12}(TZCA)_{12}]$, where TZCA = 4-tetrazolate-benzoate, Figure 1) that employs CAL by displacing terminal solvent ligands on metal centers of the SBUs (Figure 1).[21] The result is a crystalline sponge that allows for crystallographic structure determination of a wide variety of coordinative guest molecules containing soft and medium Lewis basic functional groups via CAL. In addition, CPF-5 can entrap guests using a combination of CAL and second coordination sphere interactions (e.g., peripheral hydrogen bonding), providing greater structural orientation to the guest molecules. CPF-5 is a highly crystalline framework that makes crystal selection facile and data collection suitable for commercial X-ray sources. Finally, with the help of a CAL

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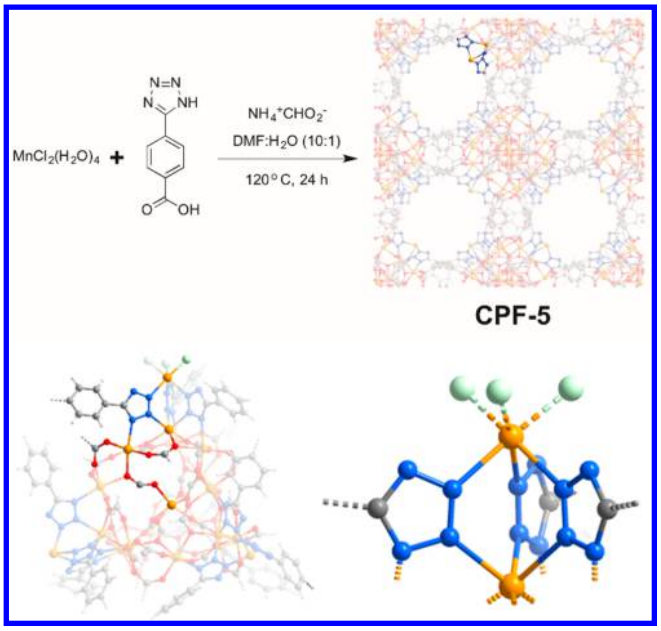

Figure 1. Top: Scheme for the synthesis of CPF-5 showing the overall lattice structure and highlighting one of the scorpionate sites. Bottom: Complete SBU of CPF-5 highlighting the asymmetric unit (left). The unique scorpionate-like site of the SBU (right), showing the three labile solvent ligands (light green) bound to the Mn^{2+} ion that can be displaced for the binding of guest molecules.

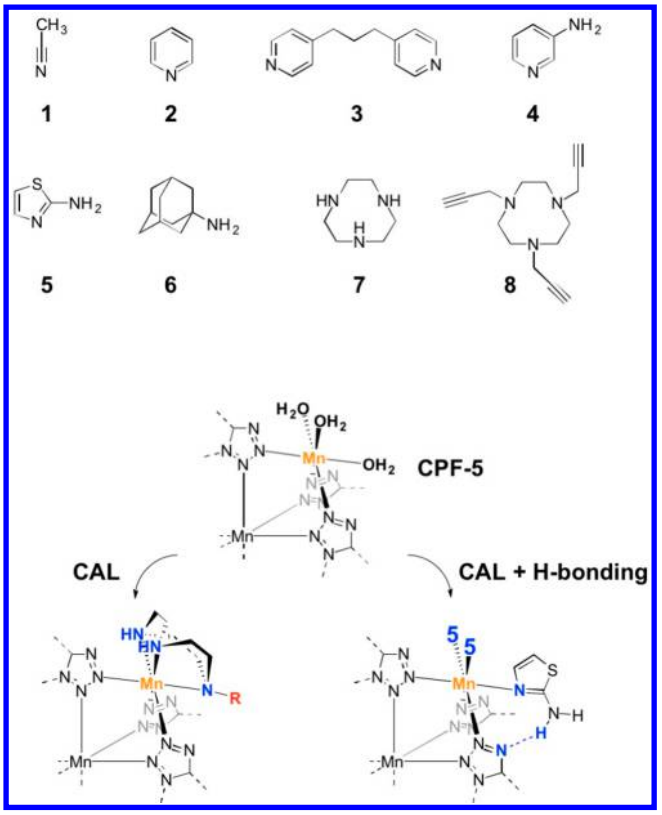

Figure 2. Structure of guest molecules (top, **1**−**8**). Schematic of guest binding to the SBU of CPF-5 (bottom), which can utilize CAL or CAL and hydrogen bonding.

"tag", namely, triazacyclononane (TACN), we provide a roadmap for extending the CAL strategy to a wider scope of guest molecules. This strategy has the potential to allow noncoordinating guests to be tethered to a tag and subsequently ordered in MOFs for SXRD analysis.

CPF-5 was selected as a likely crystalline sponge because of its high crystallinity and sufficient void space with wide window openings. The three-dimensional interconnecting porous channels possess a hydrophilic central cavity of 14 Å in diameter with an aperture between the pores of 11 Å (Figure 1). A PLATON calculation indicates that the solvent accessible void space of CPF-5 is 56% of the crystal volume. The SBUs of CPF-5 are very complex because of the large number of ligands and metal ions involved (Figure 1). However, among the various metal sites in the SBU, there is a unique Mn^{2+} site that resembles a scorpionate complex where three tetrazolate ligands chelate a 6-coordinated Mn^{2+} center leaving the facial positions occupied by three coordinated solvent molecules (Figure 1). These labile, neutral solvent molecules are readily exchanged for coordinating guest molecules. Moreover, the noncoordinating tetrazolate nitrogen atoms near the Mn^{2+} centers can generate additional interactions (e.g., hydrogen bonding) to further facilitate guest orientation.

Using CPF-5, nine different guest molecules were successfully cocrystallized, and their SXRD structures were determined (ESI†). These guest molecules cover a range of compounds with different shapes and sizes, including some without Lewis basic coordinating groups (Figure 2). Compounds **1**−**5** engage in monodentate binding to the coordination sites in CPF-5 using nitrogen atom donors. Compound **6** resides in a hydrogen bonding pocket. Compounds **7**−**8** (tetrazacyclononane, TACN, and a TACN derivative) bind to the Mn^{2+}-binding sites in a tridentate manner, with compound **8** demonstrating the potential use of TACN as a "tag" to anchor noncoordinating species.

Compounds **1**−**5** bind to the CPF-5 SBUs with a variety of nitrogen ligands, including nitrile, pyridine, and thiazole donors (Figure 3). The coordination bonds between guest and CPF-5 form readily upon the exposure of diluted guest solutions to the CPF-5 single crystals at room temperature within 24 h. Single crystals could then be analyzed using a data collected at 100 K on Bruker D8 diffractometers equipped with Mo-K_α radiation sources and APEX-II CCD area detectors; the use of synchrotron radiation sources was not required to obtain satisfactory crystallographic data.[6,9,13] Simple guest molecules, including acetonitrile (**1**) and pyridine (**2**), bind to the Mn^{2+} center with 10% and 33% occupancy per binding site, respectively (Figure 3). Interestingly, the pyridine rings in **2** are highly ordered and are coplanar with the tetrazolate rings of the MOF. Using a longer incubation time of 2 days, larger guest molecules, such as trimethylenedipyridine (TMDPy, **3**), could be bound and characterized in CPF-5. The coordinating pyridine ring of compound **3** is found with ∼75% crystallographic occupancy per binding site (2.4 equiv per Mn^{2+} center), while the alkyl chain and pendant pyridine ring were refined with ∼33% occupancy (due to positional disorder). Despite the lower occupancy, the alkyl chain and pendant pyridine ring can be refined due to weak interactions with the MOF pores (Supporting Information). The 75% occupancy of **3** was confirmed by digestion of CPF-5-**3** crystals and analysis by ^{1}H NMR (Supporting Information). CPF-5 also binds functionalized pyridines, as shown in the 3-aminopyridine (**4**) with a 35% occupancy per binding site. The occupancy of **4** was also supported by thermal gravimetric analysis (TGA, Supporting Information).

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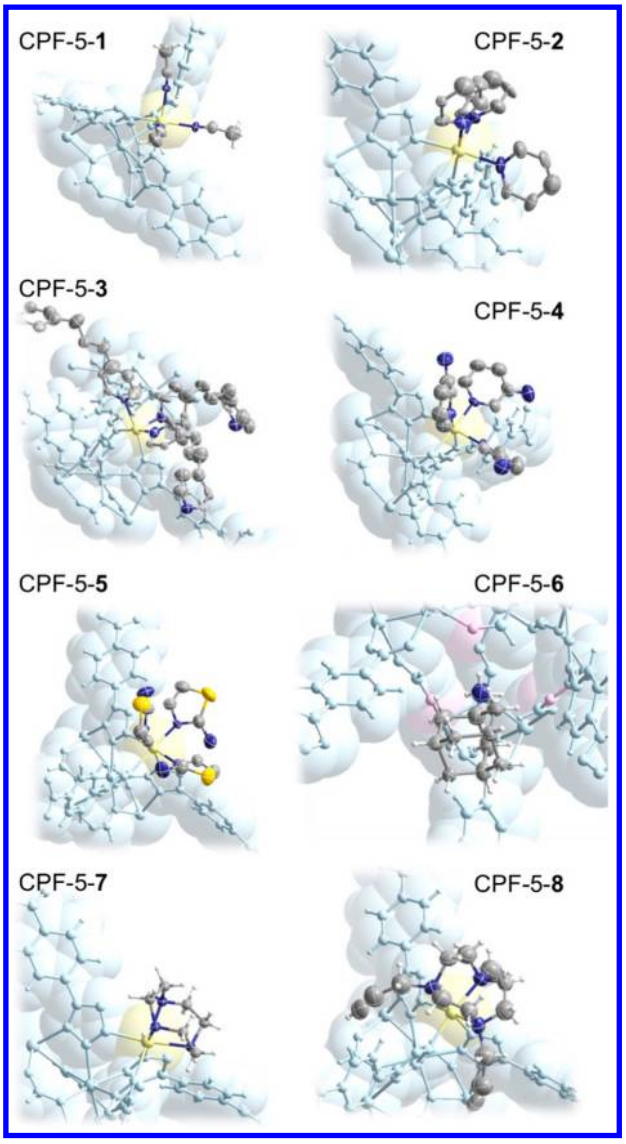

Figure 3. Images of the refined structures of CPF-5 bound to eight different guest molecules (CPF-5-**1** to CPF-5-**8**). The structures were obtained from SXRD data and are shown with 50% probability thermal ellipsoids. The peripheral framework fragments are drawn in pale blue as space filling models. Colors: nitrogen in guest, dark blue; carbon in guest, gray; sulfur in guest, bright yellow; Mn in MOF, pale yellow; oxygen in MOF, pale pink; all other atoms in MOF, pale cyan.

Compound **5**, 2-aminothiazole, is ordered by both CAL and hydrogen bonding in CPF-5 (Figure 3). The 2-amino group is drawn to the nearest free tetrazole nitrogen atom at a distance of ~3.0 Å. This strong hydrogen bonding interaction from the secondary coordination sphere fixes the orientation of guest **5** and prevents a 2-fold disorder commonly observed for imidazoles or thiazoles.[22,23] Notably, for guest molecules with hydrogen bonding ability but very low binding affinity to metals ions, CPF-5 can still act as an effective crystalline sponge. Compound **6**, 1-aminoadamantane, crystallizes in CPF-5 such that **6** is surrounded by three framework ligands with the amino group hydrogen-bonded to three oxygen atoms (~3.0 Å) of formate ligands that are part of the SBU (Figure 3, Supporting Information). Despite a complete absence of metal binding, compound **6** shows a 75% crystallographic occupancy and is rotationally ordered.

Compound **7**, triazacyclononane (TACN), allows for strong binding to the CPF-5 SBU (Figure 3) by forming a facially capped Mn^{2+} center, with complete engagement of the three TACN nitrogen donor atoms. Compound **7** has 100% crystallographic occupancy even under very dilute impregnation condition (15 μmol in 1.0 mL acetonitrile solution, 1.1 equiv with respect to the active sites in CPF-5). This tightly coordinated guest gives a highly ordered alkyl backbone with the ethyl groups pointing away from the metal center into the vacant space above the CPF-5 SBU, while the vector of the N–H bond is directed toward the periphery of the metal center into the space sandwiched by two framework tetrazolate rings (Figure 3).

Because **7** readily bound to CPF-5 and **7** can be *N*-functionalized while retaining an ability to bind metal ions, we rationalized that **7** could be used as a general binding motif for coupling to a reactive functional handle allowing for "tagging" guest molecules that might not otherwise bind to CPF-5 strongly. As a preliminary attempt to test this hypothesis, the crystal structure of propargyl-derivatized TACN (**8**) was solved. CPF-5-**8** successfully shows the potential of the "TACN tag" strategy, resulting in a highly ordered structure, with a fixed molecular orientation for the propargyl groups. The structure clearly shows the propargyl groups are pointing into the void space between framework tetrazolate rings. As hoped, CPF-5-**8** was achieved with 80% crystallographic occupancy at low impregnation concentrations (0.12 mmol/L). With this successful proof-of-concept study, one can envision using the alkyne groups on **8** to perform "click" chemistry for tagging desired target molecules.[24−26] Similarly, other reactive groups can be potentially attached to the TACN scaffolds including olefins, epoxides, azides, and others.[27]

In summary, we have successfully identified CPF-5 as a versatile crystalline sponge that can operate via CAL, hydrogen bonding, or a combination of both. CPF-5 can aid in the structural characterization of a relatively wide variety of molecules, especially those with a nitrogen Lewis basic ligand. Preliminary data demonstrate that the use of a chemical tag, namely, TACN derivatives, could extend this method and the use of CPF-5 to a much wider scope of guest molecules, and such investigations are ongoing.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.cgd.7b01390.

Synthesis and crystal activation methods; Table of guest inclusion conditions for the CPF-5 crystal sponge; TGA traces; CPF-5-X crystal structure refinement details; crystal data; ^{1}H NMR of digested CPF-5-**3** crystals (PDF)

Accession Codes

CCDC 1550638−1550645 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: scohen@ucsd.edu.

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ORCID

Seth M. Cohen: 0000-0002-5233-2280

Notes

The authors declare no competing financial interest.

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■ REFERENCES

(1) Yaghi, O. M.; O'keeffe, M.; Ockwig, N. W.; Chae, H. K.; Eddaoudi, M.; Kim, J. Reticular synthesis and the design of new materials. *Nature* **2003**, *423*, 705−714.

(2) Kitagawa, S.; Kitaura, R.; Noro, S. Functional porous coordination polymers. *Angew. Chem., Int. Ed.* **2004**, *43*, 2334−2375.

(3) Ferey, G.; Mellot-Draznieks, C.; Serre, C.; Millange, F. Crystallized frameworks with giant pores: Are there limits to the possible? *Acc. Chem. Res.* **2005**, *38*, 217−225.

(4) Furukawa, H.; Cordova, K. E.; O'Keeffe, M.; Yaghi, O. M. The Chemistry and Applications of Metal-Organic Frameworks. *Science* **2013**, *341*, 1230444.

(5) Kawamichi, T.; Kodama, T.; Kawano, M.; Fujita, M. Single-Crystalline Molecular Flasks: Chemical Transformation with Bulky Reagents in the Pores of Porous Coordination Networks. *Angew. Chem., Int. Ed.* **2008**, *47*, 8030−8032.

(6) Kawamichi, T.; Haneda, T.; Kawano, M.; Fujita, M. X-ray observation of a transient hemiaminal trapped in a porous network. *Nature* **2009**, *461*, 633−635.

(7) Inokuma, Y.; Kawano, M.; Fujita, M. Crystalline molecular flasks. *Nat. Chem.* **2011**, *3*, 349−358.

(8) Inokuma, Y.; Yoshioka, S.; Ariyoshi, J.; Arai, T.; Hitora, Y.; Takada, K.; Matsunaga, S.; Rissanen, K.; Fujita, M. X-ray analysis on the nanogram to microgram scale using porous complexes. *Nature* **2013**, *495*, 461−466.

(9) Lee, S.; Kapustin, E. A.; Yaghi, O. M. Coordinative alignment of molecules in chiral metal-organic frameworks. *Science* **2016**, *353*, 808−811.

(10) Brunet, G.; Safin, D. A.; Aghaji, M. Z.; Robeyns, K.; Korobkov, I.; Woo, T. K.; Murugesu, M. Stepwise crystallographic visualization of dynamic guest binding in a nanoporous framework. *Chem. Sci.* **2017**, *8*, 3171−3177.

(11) Brunet, G.; Safin, D. A.; Robeyns, K.; Facey, G. A.; Korobkov, I.; Filinchuk, Y.; Murugesu, M. Confinement effects of a crystalline sponge on ferrocene and ferrocene carboxaldehyde. *Chem. Commun.* **2017**, *53*, 5645−5648.

(12) O'Brien, A. G.; Maruyama, A.; Inokuma, Y.; Fujita, M.; Baran, P. S.; Blackmond, D. G. Radical C-H Functionalization of Heteroarenes under Electrochemical Control. *Angew. Chem.* **2014**, *126*, 12062−12065.

(13) Ramadhar, T. R.; Zheng, S.-L.; Chen, Y.-S.; Clardy, J. Analysis of rapidly synthesized guest-filled porous complexes with synchrotron radiation: practical guidelines for the crystalline sponge method. *Acta Crystallogr., Sect. A: Found. Adv.* **2015**, *71*, 46−58.

(14) Ramadhar, T. R.; Zheng, S. L.; Chen, Y. S.; Clardy, J. The crystalline sponge method: MOF terminal ligand effects. *Chem. Commun.* **2015**, *51*, 11252−11255.

(15) Sairenji, S.; Kikuchi, T.; Abozeid, M. A.; Takizawa, S.; Sasai, H.; Ando, Y.; Ohmatsu, K.; Ooi, T.; Fujita, M. Determination of the absolute configuration of compounds bearing chiral quaternary carbon centers using the crystalline sponge method. *Chem. Sci.* **2017**, *8*, 5132−5136.

(16) Sanna, E.; Escudero-Adan, E. C.; Bauza, A.; Ballester, P.; Frontera, A.; Rotger, C.; Costa, A. A crystalline sponge based on dispersive forces suitable for X-ray structure determination of included molecular guests. *Chem. Sci.* **2015**, *6*, 5466−5472.

(17) Vinogradova, E. V.; Muller, P.; Buchwald, S. L. Structural Reevaluation of the Electrophilic Hypervalent Iodine Reagent for Trifluoromethylthiolation Supported by the Crystalline Sponge Method for X-ray Analysis. *Angew. Chem., Int. Ed.* **2014**, *53*, 3125−3128.

(18) Sanna, E.; Bauza, A.; Escudero-Adan, E. C.; Rotger, C.; Frontera, A.; Costa, A. The Mouse in a Trap: Observation of a C(sp3)−F···F−C(sp3) Interaction in a Discrete CFC Pair by the Crystal Sponge Method. *Cryst. Growth Des.* **2017**, *17*, 3611−3615.

(19) Wang, Z.; Cohen, S. M. Postsynthetic modification of metal−organic frameworks. *Chem. Soc. Rev.* **2009**, *38*, 1315−1329.

(20) Cohen, S. M. The Postsynthetic Renaissance in Porous Solids. *J. Am. Chem. Soc.* **2017**, *139*, 2855−2863.

(21) Wang, L.; Morales, J.; Wu, T.; Zhao, X.; Beyermann, W. P.; Bu, X.; Feng, P. Assembly of super-supertetrahedral metal−organic clusters into a hierarchical porous cubic framework. *Chem. Commun.* **2012**, *48*, 7498−7500.

(22) Głowiak, T.; Kurdziel, K. Crystal structure and physico-chemical properties of hepta-coordinate isomorphic cobalt (II) and nickel (II) complexes of 1-allylimidazole. *J. Mol. Struct.* **2000**, *516*, 1−5.

(23) Li, J.; Noll, B. C.; Oliver, A. G.; Schulz, C. E.; Scheidt, W. R. Correlated Ligand Dynamics in Oxyiron Picket Fence Porphyrins: Structural and Mössbauer Investigations. *J. Am. Chem. Soc.* **2013**, *135*.1562710.1021/ja408431z

(24) Demko, Z. P.; Sharpless, K. B. A click chemistry approach to tetrazoles by Huisgen 1,3-dipolar cycloaddition: Synthesis of 5-sulfonyl tetrazoles from azides and sulfonyl cyanides. *Angew. Chem., Int. Ed.* **2002**, *41*, 2110−2113.

(25) Demko, Z. P.; Sharpless, K. B. A click chemistry approach to tetrazoles by Huisgen 1,3-dipolar cycloaddition: Synthesis of 5-acyltetrazoles from azides and acyl cyanides. *Angew. Chem., Int. Ed.* **2002**, *41*, 2113−2116.

(26) Silverman, S. M.; Moses, J. E.; Sharpless, K. B. Reengineering Antibiotics to Combat Bacterial Resistance: Click Chemistry [1, 2, 3]-Triazole Vancomycin Dimers with Potent Activity against MRSA and VRE. *Chem. - Eur. J.* **2017**, *23*, 79−83.

(27) Mewis, R. E.; Archibald, S. J. Biomedical applications of macrocyclic ligand complexes. *Coord. Chem. Rev.* **2010**, *254*, 1686−1712.

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