# Bringing Crystal Structures to Reality by Three-Dimensional Printing

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S *Supporting Information*

ABSTRACT: The process of converting structural models derived from single-crystal X-ray diffraction experiments into physical models for the purposes of visualization/communication and collaboration by the use of three-dimensional (3D) printing techniques is described. Digital information regarding the relative positioning of atoms in a crystal structure is translated, using a suite of computer programs, into a 3D computer model of a solid form, corresponding to that information which can then be saved in a file format for 3D printing. These files are then used to produce to-scale physical models of the structural information using two different 3D printing methodologies.
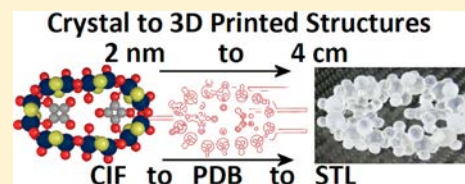
Three-dimensional (3D) printing (i.e., the production of a physical three-dimensional model based on a corresponding digital model file via an additive process),[1] is an increasingly common mode of manufacturing. Whereas once this technique was confined only to industrial settings where specific components would be rapidly prototyped prior to large scale manufacturing,[2] in the last two decades the increasing availability and affordability of 3D printing technologies has led to a rapid expansion of this approach to modeling into previously unexploited areas. As such, 3D printing and 3D-printing-inspired methodologies are increasingly being used in the scientific community to facilitate studies on areas ranging from biomimetic microvascular systems,[3,4] tissue growth scaffolds,[5−8] electronic[9] and pneumatic devices,[10−12] and the production of functional devices in laboratory settings.[13−16] In the Cronin group, we have been developing the concept of reactionware, where 3D printing techniques are employed to produce bespoke reactors in which the outcome of reactions or sequences of reactions can be controlled by the geometry and orientation of the printed devices,[17] allowing complex reactors to be produced explicitly for specific experimental requirements (see Figure 1).[18−21]

Parallel to this development of 3D printing methodologies in the physical and biological sciences, 3D printing is increasingly being used in education[22,23] and for medical[24] or forensic[25] imaging data, enabling the representation of complex data in a physical way, which is intuitive but retains key attributes (e.g., scale, connectivity) of the original structures so as to give insights into the generation and utilization of such data.

The use of physical models of chemical systems has a long history, dating back to the first attempts at understanding the structural nature of chemistry, with the first use of such models in public lectures credited to Hofmann in the 1860s. These models rapidly developed in sophistication and theoretical utility, with the use of hard spheres to demonstrate close packing of atoms in simple crystal structures, the creation of ball-and-stick type models to emphasize the importance of stereochemistry in understanding organic reactivity and the development by Corey, Pauling, and Koltun of spherical
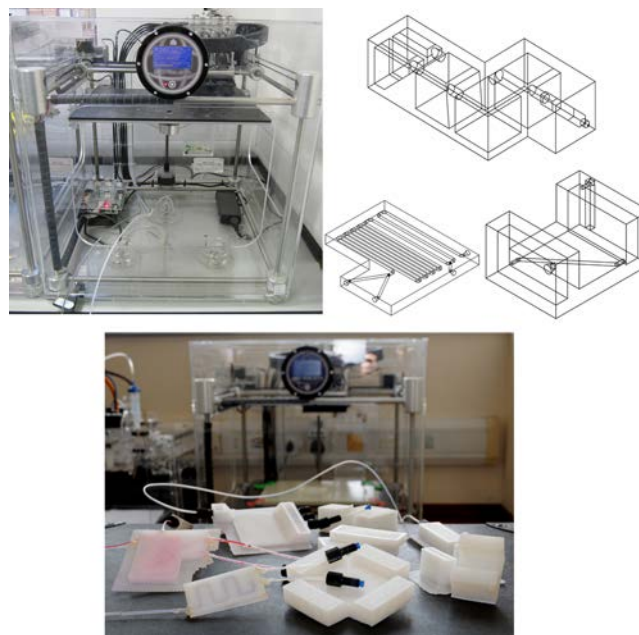

Figure 1. 3D printing chemistry; a selection of reactionware produced by the Cronin Group. (Top, left) 3DTouch 3D printer used by the Cronin group to fabricate functional reactionware. (Top, right) examples of 3D CAD models of reactionware devices prior to 3D printing. (Bottom) Physically realized and functional reactionware produced via 3D printing methodologies.

models (CPK models),[26,27] where the radii of the component spheres were proportional to the atomic radii being represented. Each of these developments was used to intuitively illustrate different facets of the structural arrangement of atoms in the chemical world (see Figure 2). The use of molecular models, however, goes beyond mere visual representation and education; they have played a pivotal role in the development
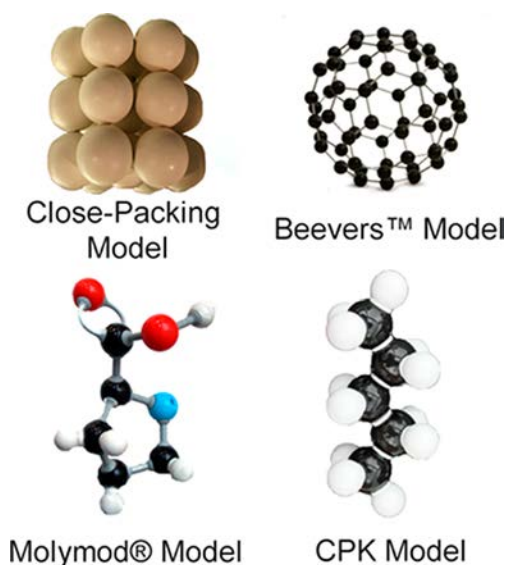
Figure 2. Standard molecular models used by chemists for illustration of chemical structures. (Top, left) Spherical atom close-packing model of a simple crystal structure. (Top, right) Beevers models based on plastic spheres representing atoms connected by metal struts for bonds.[29] (Bottom, left) Molymod molecular model which illustrates multiple bonding characteristics. (Bottom, right) CPK model where the size of the spheres is proportional to the atomic radii they represent. Close-Packing Model: Reprinted under Creative Commons license CC BY-SA 2.0. Copyright 2008 Ryan Somma. Molymod Model: Reprinted under Creative Commons license CC BY-SA 2.5. Copyright 2006 Peter Murray-Rust. Beevers Model: Reprinted with permission from ref 29. Copyright 2005 Miramodus Ltd. Space-Filling Model: Reprinted under Creative Commons license CC BY-SA 3.0. Copyright 2011 Bin im Garten.

of a number of structural theories, most famously in the use of a skeleton type model set by Watson and Crick to elucidate the double helical structure of the DNA molecule.[28] In recent decades, the exponentially increasing processing power of computers has meant the translation of these traditionally physical objects into (usually) two-dimensional (2D) rotatable screen representations of chemical structures. Similarly, the use of computer technology in the solution and refinement of single crystal and powder X-ray diffraction experiments has meant that these 2D computer representations are based on the physical data of a specific system rather than averaged or ideal bond lengths, giving a more accurate reflection of the particular system being modeled. While this is, in some senses, an advance on the physical models used previously, it loses the instinctive recognition of 3D ordering, which can be gained from real-world physical models. Herein, we present the use of a suite of software in conjunction with a number of 3D printing platforms to translate crystallographically derived structural information on inorganic metal-oxide clusters into to-scale physical models.

X-ray crystallography represents the best tool which chemists have for understanding the structure of chemical systems in the solid state, since it can reveal the particular arrangement of molecules and their connections at an atomic level. It can clearly show how each atom connects to others and the coordination geometry of metal atoms, along with the bond lengths and bond angles in an individual crystal. With the widespread adoption of X-ray crystallography as a routine tool for probing solid state systems, the number of crystal structures

produced and catalogued worldwide has increased dramatically in the last few decades, with the number of submissions to the Cambridge Structural Database increasing year after year since its foundation (see Figure 3). In research groups which
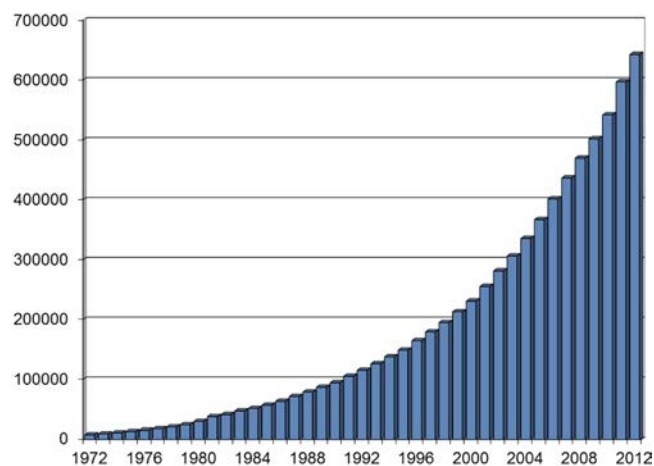

Figure 3. Number of submissions to the Cambridge Structural Database (CSD) by year.

specialize in the synthesis or properties of solid state materials, an intuitive understanding of the 3D arrangement of these systems is an invaluable tool for analysis and discussion.

The files produced by X-ray crystallographic experiments are most often in the IUCr standard CIF (crystallographic information file)[30] format, which contains positional and bonding information for all the atoms present in the unit cell of a particular system as well as all the symmetry operations necessary to generate the full structure. However, for the purposes of the creation of physical models, any file which contains relevant structural information could be used, such as the .res files of SHELX refinements,[31] allowing models of intermediates in the refinement of crystal structures to be produced. The key step in translating the structural information present in these files into 3D printed objects is the creation of digital models, which accurately reflect the data as a 3D representation which suits the purposes of the model (i.e., ball and stick), CPK, or skeleton structures. To achieve this translation, we use a program called Blender. Blender is a free, open-source 3D modeling program available for Windows, Mac OS X, and Linux. While initially created as an in-house program for an animation studio, its open-source community-driven development has led to it offering a number of very specific features for users outside the mainstream animation world. One of these is the Atomic Blender add-on, which comes as part of the basic package and gives the ability to import crystallographic data through the protein data bank (.pdb)[32] file format, which is available as an export option for most crystallography software. This allows accurate representations of molecular structures to be included in complex images and animations, and there are a number of examples where this method has been used to produce high-quality cover images,[33,34] figures,[35] and animations[36,37] for journals and presentations. The Atomic Blender add-on allows space filling, ball-and-stick, and skeleton models to be created using the information on position, atom identity, and connectivity stored in the .pdb files. It is important that the .pdb files contain all this information and best that it only contain information for the section of the crystal structure that is to be printed, which can easily be achieved by opening
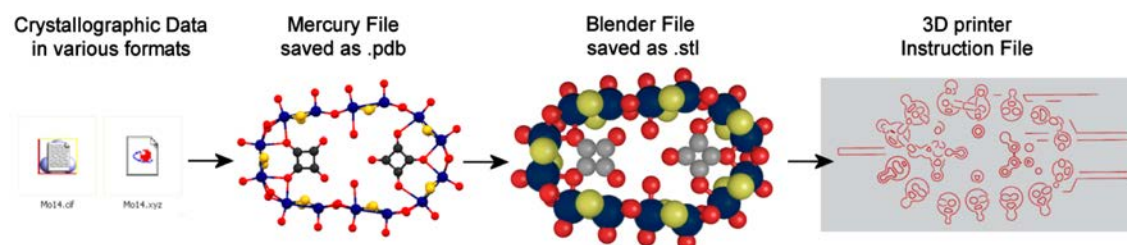
Figure 4. Workflow for the conversion of crystallographic information, in the form of, for example, .cif, .xyz, or .res, into a set of instructions for the 3D printer to produce a physical model of the information.
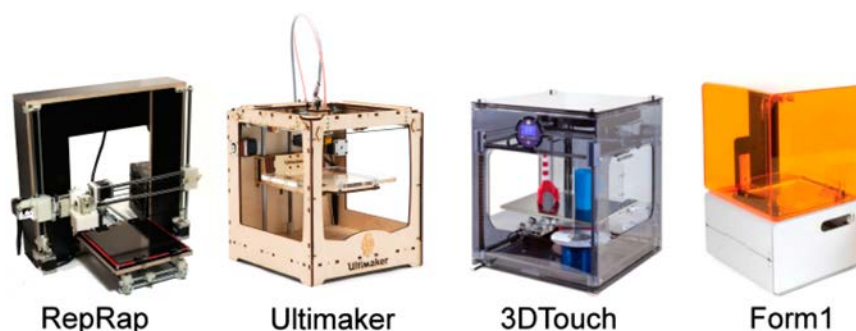
Figure 5. 3D printers used in this work: Reprap, Ultimaker and 3Dtouch FDM platforms and the Form1 stereolithography platform. RepRap: Reprinted with permission from ref 38. Copyright 2012 GLI Concept CmbH. Ultimaker: Reprinted with permission from ref 40. Copyright 2013 Ultimaker. 3DTouch: Reprinted with permission from ref 39. Copyright 2011 3Dsystems. Form1: Reprinted with permission from ref 41. Copyright 2014 Formlabs.

the original file in the Mercury crystallography program, editing it to remove everything but the desired section (a single molecule, for example), and exporting it as a .pdb file. We have found that Mercury is the best option among widely used crystallographic software as it only saves data on the visible portion of the crystal structure and saves all visible connectivity data in the .pdb format, which is not the case for a number of other crystallography programs. It would also be possible to create a model of an extended region of a crystal structure by saving the desired packing representation in the .pdb format, importing that file into Blender and editing the resulting model to fit the desired physical outcome.

Once the file has been imported into Blender, a number of options are available for the scaling and representation of the atoms and bonds in the structure. At this point, the file is best viewed as a digital representation of the physical model which is to be produced during the 3D printing process, and as such the model style should be adjusted to best represent the structural features which are to be highlighted. Once the best embodiment of the data has been decided upon, this can then be exported from Blender as an .stl (stereolithography) file. This is a file format which describes a surface geometry as a mesh of triangular surfaces based on 3D coordinates of vertices. This surface mesh has a defined interior and exterior, allowing the 3D printer compiling software to recognize the information within as a solid object. As a result of this process, the length scale of the crystallographic structure file, which is usually defined in angstroms $(10^{-10}$ m) is lost, and the information is preserved as arbitrary units, defined as Blender units in the virtual 3D environment of Blender. Upon exporting as the final .stl file, these arbitrary units are converted into mm $(10^{-3}$ m), giving a native scaling of $1:10^7$. This CAD model can then be scaled as required to give an appropriately sized physical model.

Once the structure has been saved as a .stl file, it can be imported into one of several 3D printer-specific software packages in order to generate an instruction file for that specific 3D printer (see Figure 4). As the 3D printing is a layer−by−layer additive fabrication process, these files generally consist of patterns of material to be deposited for each successive layer of the final model. The particular details of these layer instructions will vary depending on the material substrate being used in the printer.

The 3D printers used in this work represent a mixture of 3D printing platforms which work on different principles (see Figure 5). First, there are a number of fused deposition modeling (FDM)-type 3D printers (Reprap,[38] 3DTouch,[39] and Ultimaker[40]), whereby heated extrusion nozzles mounted on carriages which are motile in one or more axis is used to melt a thermopolymer substrate and deposit this substrate in patterns on successive layers, as described by the printing instructions generated from the .stl file. The substrates used for this category of 3D printer are generally thermopolymers, which have melting points in the region from 150 °C to 250 °C, to allow for ease of processing while also possessing a relatively low glass transition temperature so as to retain structural rigidity at ambient temperatures. For this work, the main substrates used for FDM printing were polylactic acid (PLA) and polyethylene terephthalate (PET), both of which have properties which make them suitable for FDM 3D printing. The second 3D printing platform used (Form1) is based on a stereolithographic approach, where directed laser light is used to selectively polymerize successive layers of a methacrylate-based photopolymer to generate similar patterns to those produced in FDM type printing

To illustrate the advantages of 3D-printed molecular models based on crystallographic data over two-dimensional representations of such data, we will use the structures of two

polyoxommolybdate clusters synthesized in the Cronin group as examples, $[N(CH_3)_4]_4K_{12}Cs_8\{[(Mo_2O_2S_2)_3(OH)_4(C_4O_4)]_8$-$(Mo_5O_{18})_4\}(H_2O)_{227}$ ($\{Mo_{68}\}$)[36] and $(N(CH_3)_4\{(Mo_2O_2S_2)_7$-$(OH)_{14}(C_4O_4)_2(H_2O)_2\}(H_2O)_{13}(\{Mo_{14}\})$[42] (see Figures 6 and

$\{Mo_{68}\}$

|← 3.2 nm →| |← 12.8 cm →|
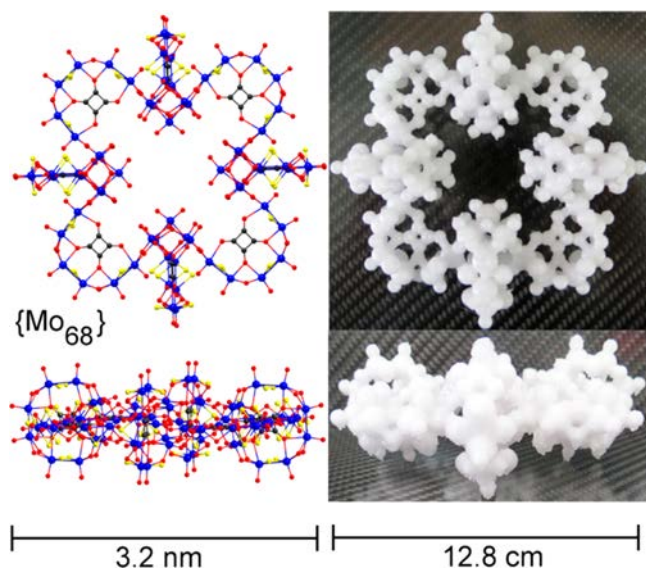
Figure 6. (Left) X-ray crystal structure of polyoxomolybdate cluster $\{Mo_{68}\}$ viewed both perpendicular (above) and in the plane of the cluster (below). (Right) 3D printed ball-and-stick molecular model of $\{Mo_{68}\}$ printed on the $1{:}4 \times 10^7$ scale.

7). Three-dimensional models can more readily show some of the features of the structures, especially for complex architectures. For example, in the $\{Mo_{68}\}$ molecule, the $\{(Mo_2O_2S_2)_3(OH)_4(C_4O_4)\}$ subunits arrange perpendicular to each other, giving no obvious view in a two-dimensional

|← 2.0 nm →|
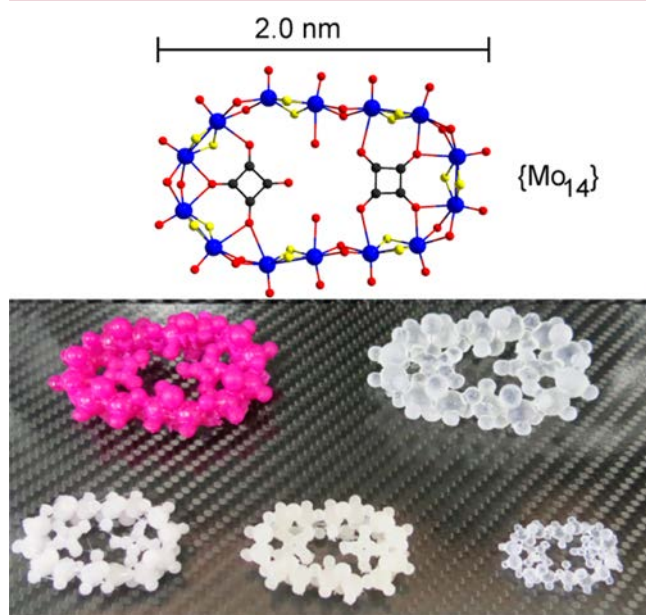
$\{Mo_{14}\}$

Figure 7. (Top) X-ray crystal structure of polyoxomolybdate cluster $\{Mo_{14}\}$. (Bottom) 3D printed molecular models of $\{Mo_{14}\}$ printed on (clockwise from top left) Reprap, Form1, Form1, 3DTouch, and Ultimaker 3D printers printed to various scales from $1{:}10^7$ (bottom right) to $1{:}3 \times 10^7$ (above).

representation which can clearly show this arrangement, whereas a 3D model, which can be handled and rotated in real space, easily illustrates these features. Although this perpendicular assembly is not very common in inorganic chemistry, it occurs in this molecule, and a 3D model is more convenient for understanding its symmetry and character.

In conclusion, we have demonstrated a process whereby crystallographic structure data can be converted into a 3D CAD model of the represented data in various styles of visualization using freely available software packages. This data could then be physically realized by 3D printing approaches, using a number of 3D printing platforms to produce scale models of the chemical structures for the purposes of more intuitive understanding of the three-dimensional arrangement and connectivity of atoms in complex structures. We think that the ability to 3D print complex molecular, macromolecular, and even biological models and supramolecular architectures not only will be a useful teaching tool but also will be very helpful in developing understanding of molecular structures and effective collaboration. In our group, we are starting to 3D print our own library of super- and supra-molecular molecules as well as separate building blocks that can be user-assembled into the overall structures. In the future, we will explore the development of image recognition with 3D systems such as the Microsoft Kinect system, allowing the 3D recognition of molecules by the computer of the specific molecule and open up a modeling program with the correct coordinates from a database. Such tools therefore will serve to blur the current barrier between the virtual and the real world and will only benefit the researcher.

■ ASSOCIATED CONTENT

ⓢ Supporting Information
Crystallographic information, full description of the file conversion process, and the materials used for individual 3D printers. This material is available free of charge via the Internet at http://pubs.acs.org.

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Author Contributions
The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes
The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

■ REFERENCES

(1) Dimitrov, D.; Schreve, K.; de Beer, N. *Rapid Prototyping Journal* **2006**, *12* (3), 136−147.
(2) Pham, D. T.; Gault, R. S. *International Journal of Machine Tools and Manufacture* **1998**, *38* (10−11), 1257−1287.
(3) Pataky, K.; Braschler, T.; Negro, A.; Renaud, P.; Lutolf, M. P.; Brugger, J. *Adv. Mater.* **2012**, *24* (3), 391−+.
(4) Therriault, D.; White, S. R.; Lewis, J. A. *Nat. Mater.* **2003**, *2* (4), 265−271.

(5) Connell, J. L.; Ritschdorff, E. T.; Whiteley, M.; Shear, J. B. *Proc. Natl. Acad. Sci. U.S.A.* **2013**, *110* (46), 18380−18385.

(6) Mironov, V.; Boland, T.; Trusk, T.; Forgacs, G.; Markwald, R. R. *Trends Biotechnol.* **2003**, *21* (4), 157−161.

(7) Peltola, S. M.; Melchels, F. P. W.; Grijpma, D. W.; Kellomäki, M. *Ann. Med.* **2008**, *40* (4), 268−280.

(8) Seitz, H.; Rieder, W.; Irsen, S.; Leukers, B.; Tille, C. *J. Biomed. Mater. Res., Part B* **2005**, *74B* (2), 782−788.

(9) Ahn, B. Y.; Duoss, E. B.; Motala, M. J.; Guo, X. Y.; Park, S. I.; Xiong, Y. J.; Yoon, J.; Nuzzo, R. G.; Rogers, J. A.; Lewis, J. A. *Science* **2009**, *323* (5921), 1590−1593.

(10) Ilievski, F.; Mazzeo, A. D.; Shepherd, R. F.; Chen, X.; Whitesides, G. M. *Angew. Chem., Int. Ed.* **2011**, *123* (8), 1930−1935.

(11) Morin, S. A.; Shepherd, R. F.; Kwok, S. W.; Stokes, A. A.; Nemiroski, A.; Whitesides, G. M. *Science* **2012**, *337* (6096), 828−832.

(12) Hasegawa, T.; Nakashima, K.; Omatsu, F.; Ikuta, K. *Sens. Actuators, A* **2008**, *143* (2), 390−398.

(13) Anderson, K. B.; Lockwood, S. Y.; Martin, R. S.; Spence, D. M. *Anal. Chem.* **2013**, *85* (12), 5622−5626.

(14) Campbell, T. A.; Ivanova, O. S. *Nano Today* **2013**, *8* (2), 119−120.

(15) Nikolaou, P.; Coffey, A. M.; Walkup, L. L.; Gust, B. M.; LaPierre, C. D.; Koehnemann, E.; Barlow, M. J.; Rosen, M. S.; Goodson, B. M.; Chekmenev, E. Y. *J. Am. Chem. Soc.* **2014**, *136* (4), 1636−1642.

(16) Shallan, A. I.; Smejkal, P.; Corban, M.; Guijt, R. M.; Breadmore, M. C. *Anal. Chem.* **2014**, *86*, 3124−3130.

(17) Symes, M. D.; Kitson, P. J.; Yan, J.; Richmond, C. J.; Cooper, G. J. T.; Bowman, R. W.; Vilbrandt, T.; Cronin, L. *Nat. Chem.* **2012**, *4* (5), 349−54.

(18) Dragone, V.; Sans, V.; Rosnes, M. H.; Kitson, P. J.; Cronin, L. *Beilstein J. Org. Chem.* **2013**, *9*, 951−9.

(19) Kitson, P. J.; Symes, M. D.; Dragone, V.; Cronin, L. *Chem. Sci.* **2013**, *4* (8), 3099−3103.

(20) Kitson, P. J.; Rosnes, M. H.; Sans, V.; Dragone, V.; Cronin, L. *Lab Chip* **2012**, *12* (18), 3267−3271.

(21) Mathieson, J. S.; Rosnes, M. H.; Sans, V.; Kitson, P. J.; Cronin, L. *Beilstein J. Nanotechnol.* **2013**, *4*, 285−291.

(22) Muskin, J.; Ragusa, M.; Gelsthorpe, T. *J. Chem. Educ.* **2010**, *87* (5), 512−514.

(23) Greenberg, A. *ACS Nano* **2009**, *3* (4), 762−769.

(24) Rengier, F.; Mehndiratta, A.; Tengg-Kobligk, H.; Zechmann, C. M.; Unterhinninghofen, R.; Kauczor, H. U.; Giesel, F. L. *International Journal of Computer Assisted Radiology* **2010**, *5* (4), 335−341.

(25) Ebert, L. C.; Thali, M. J.; Ross, S. *Forensic Sci. Int.* **2011**, *211* (1−3), e1−e6.

(26) Corey, R. B.; Pauling, L. *Rev. Sci. Instrum.* **1953**, *24* (8), 621−627.

(27) Koltun, W. L. *Space filling atomic units and connectors for molecular models*. U.S. Patent 3170246, 1965.

(28) Watson, J. D.; Crick, F. H. C. *Nature* **1953**, *171* (4356), 737−738.

(29) *Miramodus Ltd*. http://www.miramodus.com (accessed April 1, 2014).

(30) Hall, S. R.; Allen, F. H.; Brown, I. D. *Acta Crystalogr., Sect. A* **1991**, *47* (6), 655−685.

(31) Sheldrick, G. *Acta Crystalogr., Sect. A* **2008**, *64* (1), 112−122.

(32) Berman, H. M.; Westbrook, J.; Feng, Z.; Gilliland, G.; Bhat, T. N.; Weissig, H.; Shindyalov, I. N.; Bourne, P. E. *Nucleic Acids Res.* **2000**, *28* (1), 235−242.

(33) Barth, C.; Gingras, M.; Foster, A. S.; Gulans, A.; Félix, G.; Hynninen, T.; Peresutti, R.; Henry, C. R. *Adv. Mater.* **2012**, *24* (24), 3146−3146.

(34) Gingras, M. *Chem. Soc. Rev.* **2013**, *42* (3), 968−1006.

(35) Hynninen, T.; Cabailh, G.; Foster, A. S.; Barth, C. *Sci. Rep.* **2013**, *3*, 1270.

(36) Zang, H.-Y.; Miras, H. N.; Long, D.-L.; Rausch, B.; Cronin, L. *Angew. Chem., Int. Ed.* **2013**, *52* (27), 6903−6906.

(37) Xu, F.; Miras, H. N.; Scullion, R. A.; Long, D.-L.; Thiel, J.; Cronin, L. *Proc. Natl. Acad. Sci. U.S.A.* **2012**, *109* (29), 11609−11612.

(38) Pearce, J. M.; Morris Blair, C.; Laciak, K. J.; Andrews, R.; Nosrat, A.; Zelenika-Zovko, I. *3-D Printing of Open Source Appropriate Technologies for Self-Directed Sustainable Development*; 2010; Vol. 3.

(39) Bits from Bytes Limited 3DTouch 3D Printer. http://www.bitsfrombytes.com/content/3dtouch-3d-printer (accessed Feb 25, 2014).

(40) *Ultimaker B.V.* https://www.ultimaker.com/ (accessed Feb 25, 2014).

(41) *FormLabs.* http://formlabs.com (accessed April 1, 2014).

(42) Zang, H.; Miras, H. N.; Yan, J.; Long, D.-L.; Cronin, L. *J. Am. Chem. Soc.* **2012**, *134* (28), 11376−11379.

(43) Chen, T.-H.; Lee, S.; Flood, A. H.; Miljanic, O. How to Print a Crystal Structure Model in 3D. *CrystEngComm* **2014**, DOI: 10.1039/C4CE00371C.

(44) Scalfani, V. F.; Vaid, T. P. 3D Printed Molecules and Extended Solid Models for Teaching Symmetry and Point Groups. *J. Chem. Educ.* **2014**, DOI: 10.1021/ed400887t.

■ NOTE ADDED IN PROOF

During production of this paper, two related papers also in production came to our attention.[43,44]