Published in final edited form as:

Lett Org Chem. 2016 ; 13(4): 272–276. doi:10.2174/1570178613666160204010454.

Visualization of Hyperconjugation and Subsequent Structural Distortions through 3D Printing of Crystal Structures

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Abstract

Background—Structural distortions due to hyperconjugation in organic molecules, like norbornenes, are well captured through X-ray crystallographic data, but are sometimes difficult to visualize especially for those applying chemical knowledge and are not chemists.

Methods—Crystal structure from the Cambridge database were downloaded and converted to .stl format. The structures were then printed at the desired scale using a 3D printer.

Results—Replicas of the crystal structures were accurately reproduced in scale and any resulting distortions were clearly visible from the macroscale models. Through space interactions or effect of through space hyperconjugation was illustrated through loss of symmetry or distortions thereof.

Conclusion—The norbornene structures exhibits distortion that cannot be observed through conventional ball and stick modelling kits. We show that 3D printed models derived from crystallographic data capture even subtle distortions in molecules. We translate such crystallographic data into scaled-up models through 3D printing.

Keywords

3D printing; crystallography; hyperconjugation; modeling; norbornene; stereo-electronic

1. INTRODUCTION

The process of visualization and interpretation of molecular structure and bonding for instructional purposes is commonly aided by tangible three-dimensional (3D) modeling kits [1–4]. These models are also vital tools to the non-chemist, or to the fledgling chemist, trying to comprehend the beauty and complexity of molecular structure(s) or as a tool in engineering design or material characterization. Chemistry is a foundational science, and at

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CONFLICT OF INTEREST

The authors confirm that this article content has no conflict of interest.

SUPPLEMENTARY MATERIAL

Contains a table on bond lengths and ratios from crystal and 3D printed structures and pictures of additional 3D printed structures. Supplementary material is available on the publisher's web site along with the published article.

the core of what chemists do is a deep understanding of both steric and electronic properties of molecules and their consequences on extrapolated behavior at the micro-scale – the core of materials science and engineering. Such extrapolated behavior influences surface properties (like wetting and surface charge), interfacial properties, glass transition temperature (T_g), melting point (T_m), boiling point, solubility, color, among many other materials properties. Different types of specialized model kits (soft and hard versions) that are commercially available (*e.g.*, Molymod) exist to describe differences in both inorganic and organic structures that vary in geometry, shape, and bonding (sold separately). These models generally consist of ball and stick reversible and reconfigurable plastic materials.

While the hard models are excellent tools for instruction, current commercial kits do not address challenges in describing molecular distortion (*i.e.* changes in bond-length and bond-angles) in organic molecules that arises from stereo-electronic effects. These models are also built on the general idea that all bonds of the same kind should exhibit the same properties (*e.g.* length, hybridization, and, orbital organization) and there is no room to account for through-bond or through-space intermolecular interactions. This can be attributed to fact that the bond lengths and angles in the models represent the average values – a seriously flawed over generalization that struggling students or non-chemists would likely not be able to correct, leading to wrong conclusions or product designs. Moreover, simple well established effects, like inductive effects or resonance, cannot be captured in any of these models yet there is a repository of crystal structure data evidence (derived from experimental single-crystal X-ray diffraction data) that show the consequences of these electronic effects on molecular structure [5–8]. While 3D images from crystal structures can be readily produced from unambiguous single-crystal X-ray diffraction data, the visualization of these images is limited to a 2D computer screen. This visualization challenge is exacerbated by an increase in molecular size or molecular complexity and may lead, even well-intended chemists, to the wrong inferences.

We sought to develop a general, readily adaptable protocol to construct, through 3D printing, replica models of crystal structures that capture subtle differences in molecules due to strong intra-molecular interactions. 3D printing is the process of creating a replica of an object from electronic data using polymeric inks (*e.g.* acrylonitrile butadiene styrene – ABS). First, we developed a method to convert crystal structures from the Cambridge Crystallographic Data Centre (CCDC) into a format amenable to 3D printing without any distortion in the overall properties of the molecular structure. The properties of compounds bearing the norbornene motif are widely studied with respect to reactivity and strain, and it is a classic example of an organic structure that exhibits prominent stereo-electronic effects like hyperconjugation and carbocation rearrangement (Fig. 1) [2, 9–11].

2. RESULTS AND DISCUSSION

Hyperconjugation affects bond lengths, bond angles, and charge density distribution on carbons and hydrogens [12, 13]. The norbornene's concave endo- face is well positioned for through spaces a-a* hyperconjugative interactions (Fig. 1) [14, 15]. The presence of a C=C bond already distorts the structure making it difficult to model with regular hard versions of the modelling kits, and in the soft versions it is not easy to demonstrate the 3D relations

across the [2.2.1] bicyclic moiety on a two dimensional computer screen. We used 3D printing to print norbornene structures found on the Cambridge Structural Database (CSD) whose bond length and angles are largely affected by stereo-electronic effects. Electronic effects that include the influence of hyperconjugation (*i.e.*, the overlap of σ -bonds orbitals with anti-bonding orbitals) can be accurately depicted in printed molecular models derived from X-ray crystal structures.

We chose 3D printing for models of molecules exhibiting stereo-electronic effects because prototypes can rapidly be produced and different types of printers/technology and materials are commercially available. Advancement in the technology has reduced the cost of 3D printers. This facilitated the wide-spread use of this technology outside of industrial manufacturing operations and into domestic and academic settings. While this work was in progress, Kitson and Scalfani published a method of 3D printing to convert crystallographic structural data derived from X-ray crystal structures to molecular models primarily for inorganic structures with a focus on symmetry and point groups [16–18]. But a key question still remains, can 3D printed molecules be used to illustrate through space interactions in molecules? More still, are these 3D printed models of any use beyond the realm of the chemists? To answer these questions, we focused on production of 3D models of simple organic compounds to illustrate structural consequences of through-space hyperconjugative effects. While the previous authors focused on coordination compounds, the implementation of this technology for the interpretation of stereo-electronic effects (concepts within reactivity and materials design) has not been demonstrated.

The molecule to be printed was chosen from Cambridge Crystallography Data Center (CCDC) crystallography database. The software, Mercury[®], was used to view the 3D structure of the crystallographic data. The survey of the CSD (version 5.35, update 1, November 2013) was performed with ConQuest[®] (version 1.15) and bond lengths of selected norbornene structures were obtained. The molecule to be printed was chosen from Cambridge Crystallography Data Center (CCDC) crystallography database. The software, Mercury[®], was used to view the 3D structure of the crystallographic data. The survey of the CSD (version 5.35, update 1, November 2013) was performed with ConQuest[®] (version 1.15) and bond lengths of selected norbornene structures were obtained. The target norbornene structures were chosen based on the following criteria: (a) crystallographic R factor <0.10; (b) no ions; (c) 3D coordinates fully determined; (d) purely organic components; and (e) no powder structures. A search for entries that contain the norbornene motif provided 14 structures. Out of the 14 we chose HOBOP [19] (contains a single double bond) to examine the differences that the double bonds have on the structure, *i.e.* the norbornyl motif QQQAPG02 [20] without a double bond and FAJGUS [21] that contains two double bonds (Fig. 2). We also chose two similar structures, JAGFEC [22] and YUFPUK [23], for this study because they only varied by the substituent on C7. Specifically, the two norbornenes contain the same substituents on C2, *i.e.* a phenyl group in the exo position and a sulfonyl group in the endo position (Fig. 2). The differences in the structures lie at the bridgehead carbon where JAGFEC bears hydrogens while YUFPUK bears a spirocyclopentyl group. Hydrogen atoms were deleted for ease of analysis (see supporting information for details).

Fig. (3A) shows 3D printed structures of norbornane, norbornene, and 2,5-norbornadiene derived from X-ray crystallographic data CSD codes QQQAPG02, HOBBOB, FAJGUS, respectively. As expected, the C2-C3 double bonds are shorter than the single bond leading to a slight shortening (5%) of the structure at the mid-point (C1-C4 distance across the ring). While this subtle difference is captured in the printed 3D constructs, conventional modelling kit fail to capture it. Table 1 gives selected bond lengths derived from the crystal structures and from our model (see Supporting Information for all bond lengths and ratios). The ratio of each bond length is also given to show that, within errors of measurement, they scale well within 5%. We can therefore infer that the 3D printed model is a scaled up model of the crystal structure, and as such can be used as an accurate model of the molecular state as captured by the X-ray measurements.

3D Printed structures of YUFPUK and JAGFEC are shown in Figs. (3B and 3C), respectively. The molecules are asymmetric due to differences in parallel carbon bond lengths. This is evidenced by the differences in bond lengths at C1-C2 (1.50Å, 1.59Å) vs C3-C4 (1.57Å, 1.56Å) and C4-C5 (1.63Å, 1.50Å) vs C3-C4 (1.93Å, 1.53Å). The lengths of these bonds are, on average, relatively longer than those of analogous non-substituted norbornene (HOBBOB, 1.5Å). The ratio of parallel bonds in both the crystal structure data and the 3D printed models clearly highlights the asymmetry. In JAGFEC, for example, C6-C1 is >15% longer than C4-C5, while similar bonds in YUFPUK are almost equal in length. The difference in bond length ratios, we believe, is due to strong hyperconjugation across the endo face in JAG-FEC which is absent in YUFPUK. This can only be due to the C7-spirocyclopentyl group affecting the C2-exo substituent in YUFPUK leading to poor overlap between the C6-C1 σ with the C2-C1' σ^* . If this were the case, we would expect to see an effect on the C2-phenyl substituent. In JAGFEC the phenyl ring is distorted with bonds around C1' being elongated – a situation that is absent in YUFPUK. The 3D printed models clearly show that though on paper the norbornene units in these two molecules are similar, in reality they are very different and there seems to be more than inductive effects around C2 in JAGFEC than in YUFPUK.

3. MATERIALS AND METHODS

3.1. Materials

Replicator 2X 3D printer and associated 'Ink' were purchased from MakerBot Inks are made from ABS. The Replicator 2X has two injection heads and as such can be used to print multi-color models.

3.2. Methods

Preparation of 3D printed structures from X-ray crystallographic data. The MOL files (*.mol*.sdf*.sd*.mdl) of the selected structure from the crystallographic data files are saved in Mercury. The software, Chimera 1.8.1 is used to convert the MOL2 file into a 3D printer friendly software file. "Export scene" is chosen to export the file in .stl. Maker Bot's MakerWare Software MakerWare software is downloaded for printing to convert .stl into a format the MakerBot Printer recognizes. The printer used is MakerBot Replicator 2X. The .stl file is opened in MakerWare where the molecule is exported for converting

into .x3g. The default printing material was MakerBot ABS and the resolution is set to high. Because of the shape of the molecule, the rafts and supports are added. The rafts and supports were also printed in MakerBot ABS material. The file is saved as .x3g, then, it was copied in the MakerBot SD card. Once the SD card is restored in MakerBot, an option named "Print from SD Card" shows and the copied file is chosen to print.

4. CONCLUSION

This paper highlights that the ability to print large 3D models of crystal structures is important in visualizing how stereo-electronic effects, like hyperconjugation, affect molecular structures. Precise representation of crystal structures, that otherwise cannot be constructed from current model kits and are difficult to visualize in a 2D plane like a computer screen, are clearly visible in large models. This technique will be highly useful for instruction and interpretation of stereo-electronic effects in both academic and industrial settings. While model kits can provide tangible 3D structures, no other method exists that can rapidly and affordably produce accurate 3D molecular models. Advantages of 3D printing are the following: 1) the ability to rapidly and easily produce prototypes; 2) Model kits have the advantage of reversible components, but thermoplastic 3D printing materials can also be reused; 3) while model kits can be multi-colored, 3D materials can also be printed with ink (Fig. 3D), which spans the currently available gamut of colors; 4) The cost of 3D printing is lower than model kits; This method of 3D printing provides new tools for explaining and understanding stereo-electronic effects, that is becoming more affordable with printers going for as low as US\$500 and the 'inks' costing less than a dollar per small model.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

F.J.M. was funded by the Initiative for Maximizing Student Development (IMSD) and undergraduate research grant from the University of Massachusetts. All other authors for this work were supported in part by Iowa State University or University of Massachusetts Boston through start-up funds to MT.

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Fig. (1).

Comparative view of the norbornene C=C moiety, relative to analogous compounds, showing the role of sterics in endo- and exo selectivity versus desymmetrization of the C5=C6 bond due to σ - σ^* hyperconjugation across the endo face. Unlike the monocyclic analogues, the C7 bridge renders the norbornene conformationally locked with little variation in the overall sterics but with potential for stereo-electronic perturbation due to orbital alignment or misalignment driven by torsional effects.

Fig. (2). Schematic representations of QQQAPG02 (norbornane), HOBBOP (norbornene), FAJGUS (2,5-norbornadiene), JAGFEC (2-endo-Isopropylsulfonyl-2-exo-phenyl-5-norbornene) and YUF-PUK (2-endo-Isopropylsulfonyl-2-exo-phenyl-5-norbornene-7-spiro-1'-cyclopentane).

Fig. (3).

3D printed (left) and X-ray crystal structures (right) derived from X-ray crystallographic data obtained from the CSD by their respective CDCC codes. (a) QQAPG02 (left), HOBOP (middle), and FAJGUS (right) (b) JAGFEC; (c) YUFPUK; (d) JAGFEC with ink-doped (green) aromatic ring.

Table 1

Selected bond lengths and ratios from X-ray ($\text{\AA}$) and 3D printed (cm) structures.

CDCC Code	3D Printer					
	Bond (cm)			Bond ratio		
	C1-C2	C3-C4	C4-C5	C6-C1	(C1-C2)/(C3-C4)	(C4-C5)/(C6-C1)
YUFPUK	2.1	2.0	1.9	2.0	1.03	0.95
JAGFEC	2.7	2.7	2.7	3.3	1.00	0.84
QQQAPG02	2.7	2.7	2.7	2.7	1.00	1.00
HOBOP	2.6	2.6	2.7	2.7	1.00	0.98
FAIGUS	2.7	2.6	2.7	2.6	1.02	1.02
CDCC Code	Crystal Structures					
	Bond			Bond ratio		
	C1-C2	C3-C4	C4-C5	C6-C1	(C1-C2)/(C3-C4)	(C4-C5)/(C6-C1)
YUFPUK	1.6	1.6	1.5	1.5	1.02	0.98
JAGFEC	1.5	1.6	1.6	1.9	0.96	0.85
QQQAPG02	1.5	1.5	1.5	1.5	1.00	1.00
HOBOP	1.5	1.5	1.6	1.6	1.00	1.00
FAIGUS	1.5	1.5	1.5	1.5	1.00	1.00