Smart access to 3D structures

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QR Chem is a free resource that enables teachers and researchers to link audiences directly to three-dimensional renderings of molecules.

The ability to visualize chemical structures in three dimensions is an integral part of understanding organic chemistry. From an educational perspective, first-time organic chemistry students are expected to quickly master concepts such as stereochemistry and chirality. They must learn how stereochemistry is connected to reactivity, how to predict stereochemical outcomes of certain transformations and how stereochemistry affects molecular function. In upper-level undergraduate classes and graduate coursework, the importance and complexity of stereochemistry only intensifies, in which it may become essential to understand the structures of natural products, stereochemical outcomes of intricate chemical reactions or how drugs interact with their targets on a molecular level. The importance of stereochemistry and understanding molecular structures is likewise seen across countless research endeavours in chemistry and biochemistry.

Molecular models have long provided an effective means for teachers, students and researchers to visualize 3D chemical structures. Technology has advanced such that molecular modelling software and online molecular visualization tools have also been developed. With an initial aim of increasing active learning in organic chemistry classes, we wondered whether an online molecular visualization tool could be adapted for convenient use by teachers and students in a lecture hall setting. Specifically, we hoped to have students interact with 3D structures on their own smartphones, thus enabling them to learn about chemical structures and stereochemistry in a highly interactive manner. The direct link between active learning and increased student performance has been well established in STEM fields[1]. We also recognized that such an effort could benefit researchers, as we discuss below.

We envisioned that quick response (QR) code technology could serve as the link between the lecture hall experience and modern online molecular visualization tools. QR codes are a type of matrix barcode, first designed in 1994. Nowadays, one can readily scan a QR code using a free smartphone app or even the built-in Camera app on iOS devices. The QR code links to a website, which, in our case, displays an interactive 3D rendering of a molecule of interest. QR codes have been used in teaching and are even used in the Cambridge University Botanic Garden to educate visitors about the chemicals found in plants[2].

We have now created a resource called QR Chem, which addresses our aforementioned ideas. After surveying several online molecular visualization technologies, we opted to use 3Dmol.js, a brilliant resource created by David Koes at the University of Pittsburgh[3]. 3Dmol.js is an open source, modern, object-oriented JavaScript library that enables the 3D visualization of molecules in the National Institutes of Health (NIH) PubChem database[4]. To use QR Chem, a user searches for a compound using the PubChem compound identifier (CID) number or name. If a compound of interest already has a PubChem entry with 3D coordinates available, a QR code (and direct weblink) can be quickly generated and incorporated into lecture slides or handouts. For compounds not already in the database or missing 3D coordinates, a user can add these freely by submitting them to the PubChem website. Users may also contact us for assistance in generating QR Chem codes for their 3D structures of interest. Upon scanning the QR code, the QR Chem website loads, and the user manipulates the 3D rendering and can view a custom description of the molecule. Additionally, the user can zoom in, zoom out, view the 2D structure (with colour coding of the atoms), switch between model views (ball and stick versus tube) and hide hydrogen atoms bound to carbon, all thanks to features available in 3Dmol.js.

There are many exciting ways to use QR Chem-generated QR codes in teaching or research presentations. In addition to using QR Chem codes to help students learn stereochemistry in introductory organic chemistry classes, teachers may wish to spice up their lectures and engage students by having students scan a QR Chem code leading to a 'molecule of the day'. QR Chem codes can also be used in more advanced classes, for example, to help students visualize the structures of complex molecules. Researchers can better engage their audiences too by including QR Chem codes of research-related compounds with interesting chemical structures in poster and oral presentations.

QRChem.net was piloted in an undergraduate organic chemistry lecture consisting of ~200 University of California, Los Angeles (UCLA) undergraduates in 2018. The lesson topic was the E2 elimination mechanism, so QR Chem was used in advance to create QR Chem codes that linked to 3D structures of *cis*- and *trans*-4-*t*-butyl-1-bromocyclohexane (FIG. 1). The students scanned the QR Chem codes, manipulated the molecules on their own smartphones or computers and were able to determine that the *cis*-isomer was likely to undergo E2 elimination more readily owing to the axial positioning of the bromide. After allowing the students to manipulate the structures on their own, the instructor then projected and manipulated the 3D structures in real time to point out the bromide in each case and the necessary antiperiplanar requirement seen in the *cis*-isomer.

Student evaluations — completed by 185 students, a response rate greater than 80% — showed encouraging results. Students indicated the extent to which they agreed to several statements about QR Chem using a Likert 1–5 scale, with 1 corresponding to strong disagreement and 5 correlating to strong agreement. Importantly, 93% of students 'strongly agreed' (62%) or 'agreed' (31%) that scanning the QR Chem codes and then visualizing and manipulating the molecules on their own led to increased engagement. The notion that active learning and improved student engagement leads to increased student learning has been well established[5]. Most students 'strongly agreed' (72%) or 'agreed'

(25%) that seeing and manipulating 3D structures on their smartphone or computer helps them better visualize structures of molecules and understand stereochemistry. Similarly, 59% of students 'strongly agreed' and 28% 'agreed' that the use of QR Chem was more convenient compared with a molecular model kit, although we feel model kits and QR Chem technology are not interchangeable, especially given the value of students building the molecules themselves when using modelling kits. The students also recommended the use of QR Chem technology in future classes (59% 'strongly agreed', 34% 'agreed').

A small number of students (~3%) reported difficulty in scanning the QR Chem code. As a workaround, we recommend instructors also include the shortened URL (automatically generated on QRChem.net) to the QR Chem results when sharing the QR code, so students have an alternative, albeit slightly slower and less fun, means to access the 3D renderings. We also emphasize the requirement of having a dependable internet connection when using QR Chem. Lastly, we recognize the inherent challenge of students becoming distracted when using smartphone technology in the classroom. Such distraction is also possible when smartphones are used as 'clickers', but with proper coaching we expect that this issue can be minimized.

How QRChem came to be invented is also worthy of discussion. Early in 2018, one of us (N.K.G) created a new course at UCLA with a focus on educational innovation. Working in groups, students were tasked with identifying an important problem in education, proposing a reasonable solution and laying out design plans. Thus, the idea of using QR codes to link to 3D renderings of molecules for teaching and research purposes ultimately arose from the student co-authors on this manuscript. The course instructor (N.K.G.) helped to focus discussions, shape ideas and then worked closely with the students and computing expert Dr Daniel Caspi (Element TwentySix) well after the original course ended to turn the student vision into a reality. This notion whereby students are enabled to innovate in the landscape of education in collaboration with faculty is a powerful model that we believe should be used more broadly to invent new educational tools. Similar success has been seen in the development of other educational resources, such as the new Backside Attack smartphone iOS app that teaches students concepts of reactivity in a gaming environment.

QR Chem is now available for teachers and researchers at no cost for non-commercial purposes. It is easy to use and does not require a login or password. We hope teachers will use this resource when creating lecture slides, handouts and homework assignments. Similarly, QR Chem could be used by researchers to allow their audiences to appreciate 3D structures of key molecules. It may also be used to introduce future generation of scientists, and even the general public, to the beautiful chemical structures that have a remarkable impact on our everyday lives.

We expect that QR Chem will prove to be a valuable resource to our community, while the means by which it was created serves as a model for how students and educators should collaborate to design innovative educational resources.

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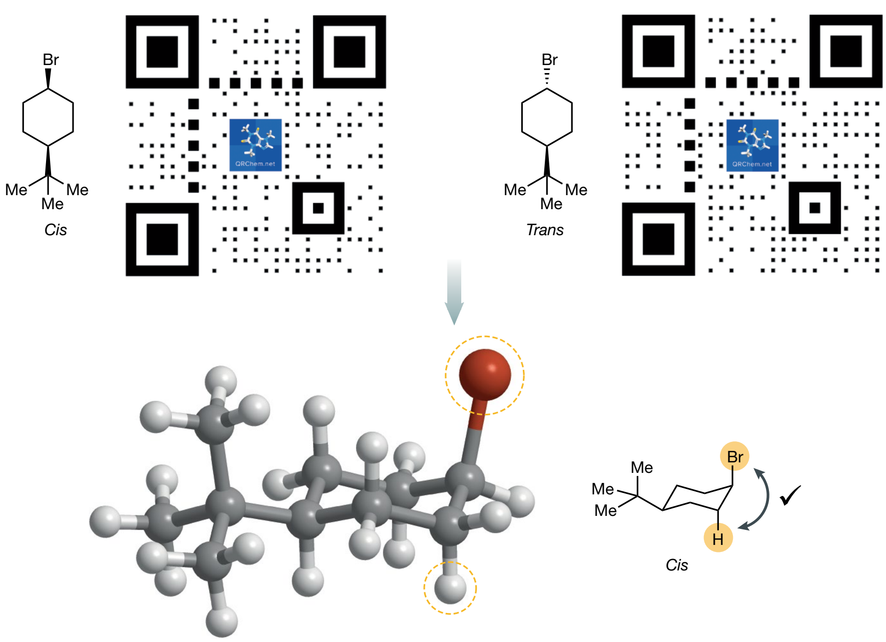

Fig. 1 | **Using QRChem.net to teach the conformational requirements of an E2 elimination.** Students scan the QR codes to access and manipulate, on their personal electronic devices, the 3D structures of two isomers of 4-*t*-butyl-1-bromocyclohexane. In doing so they can easily observe the equatorial disposition of the *t*-butyl group in both isomers and that the necessary antiperiplanar arrangement of the C–Br and C–H bonds is possible only in the *cis*-isomer. Image courtesy of Neil K. Garg, University of California, Los Angeles, USA.

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Competing interests
The authors declares no competing interests.

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