JOURNAL OF CHEMICAL INFORMATION AND MODELING

Article

pubs.acs.org/jcim

ChemDoodle 6.0

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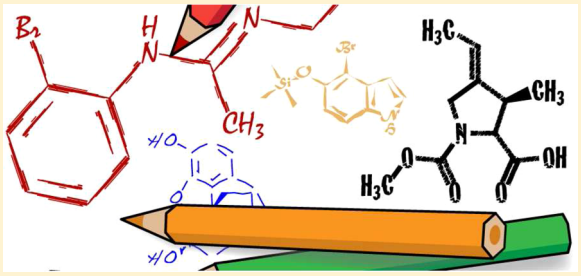
ABSTRACT: ChemDoodle 6.0 is an advanced software suite for drawing chemical structure diagrams. The program's capabilities extend far beyond mere structures, however, including the ability to calculate NMR spectra, generate IUPAC names and line notations for structures, manipulate structures imported from the Internet, interpret and interconvert files generated by other chemical drawing software programs, illustrate glassware and equipment setups, and draw TLC plates. This latest version supports full round-trip editing, so that structures produced with the program can be used in standard office software and reimported into ChemDoodle if modifications are needed. These features and more are included in the basic package, which is very affordable.



INTRODUCTION

Version 6.0 of the professional chemical drawing program ChemDoodle has been released by iChemLabs. This Java-based software has been built from the ground up to be fully compatible with the Windows, Mac OS X, and Linux platforms. This version again adds new features to the software and hones the tools already present. It has an exceptionally large feature set, from the familiar to the esoteric and unique.

DRAWING TOOLS

ChemDoodle produces publication-ready chemical structures. Quick-pick toolbar icons provide common ring sizes and atom types, as well as some 24 types of bonds. Carbon chains of any length may be drawn by simply dragging the chain tool across the drawing canvas. Radicals, charges, brackets, and a variety of arrows can also be chosen. To facilitate drawing standardized structures, bond lengths and angles are fixed by default, but this can be easily overridden. The *Optimize Zone* around atoms automatically hints at the best positions to add substituents to a structure. User-defined tags can be added to atoms. Chemically interpreted labels are supported—for example, ChemDoodle understands that Ph represents a phenyl group and C═C is an ethylene moiety. Representations of polypeptide chains can be drawn using the standard single-letter abbreviations for the common amino acids (*A* = alanine, *C* = cysteine, etc.), and these chains will automatically "wrap" to stay within the page margins. Drawings of carbon nanotubes and circular prismatic structures of almost any size can be produced very readily.

Other menus provide templates for a wide variety of structures, including *inter alia*, functional groups, amino acids, and terpenes. User-designed structures can also be added to these templates. An assortment of orbitals, Bezier curves, and standard geometric shapes, as well as text boxes for labels, complement the chemical structure drawing capability. There is built-in provision of upper- and lower-case Greek letters, variations of Latin letter-like symbols, and mathematical symbols and punctuation. Moreover, ChemDoodle supports the entire range of Unicode characters, so annotations can include any glyph that is found in the underlying font that is used for the text string.

A publication-quality library of chemical glassware and equipment, comprising over 280 items, is included with the basic ChemDoodle package. Users can assemble these into figures that illustrate setups for various laboratory experiments.

ChemDoodle has a wide range of editing tools for selecting content via mouse movements, keyboard shortcuts, or SMARTS. Other tools include copy and paste; organizing structures on the page via orientations, alignment, and spacing; and grouping objects to act as single units. Structures (or parts of them) can be moved, rotated, and resized; changes in size and orientation are indicated in real time in a tooltip near the mouse cursor.

ChemDoodle's *History* window goes well beyond the simple undo/redo capability of similar software. *History* shows all the steps that have been performed since the file was last opened. Clicking on a previous line in the history list undoes all the steps back to that point. The history "pointer" can also be moved forward again to redo as many steps as desired.

Other mini-applications included with ChemDoodle help perform such tasks as searching for chemical structure files on the computer's hard drive, simulating NMR spectra, drawing TLC plates (in color), and displaying immediate results of elemental analysis calculations.

Despite its abundance of features, the program is both intuitive and highly customizable. A "quick start" guide is provided for beginners, and the documentation includes a full reference guide to all the features. Advanced users will appreciate the large number of available keyboard shortcuts as well as ChemDoodle's powerful and diverse toolset.

Received: July 21, 2014

   dx.doi.org/10.1021/ci500438j | *J. Chem. Inf. Model.* XXXX, XXX, XXX−XXX

QUALITY OF GRAPHICS

Graphics are crisp, smooth, and attractive, even at high magnifications and resolutions. The graphical elements are laid out so as to produce the most professional-looking images. Unlike similar software that provides a single setting for how graphics are drawn, ChemDoodle gives the user fine-grained control over hundreds of the parameters with which objects are drawn, from the thickness of bonds' lines, to the spacing between multiple bonds, to the width of wedge and hashed bonds, to arrows' shapes and head angles, to the spacing between the characters of text in atom labels. Most likely, if there is something you want to change in your figure, there is a setting that allows you to adjust it to your exact taste.

To make it easier to prepare journal submissions, there are built-in style sheets that produce chemical graphics that conform to the conventions of several scientific journals. It is also possible to define and save customized style sheets that suit the individual user.

There are 2-D cleaning and 3-D optimization algorithms for generating coordinates for drawn structures. The cleaning algorithm handles medium-sized molecules very quickly and creates attractive output even from highly embedded ring systems. The algorithm to generate 3-D molecular coordinates is also quite fast.

Shapes such as lines, arcs, and arrows are customizable. Complex custom arrows can be formed from Bezier curves by adjusting the curves' control points. Simple shapes like circles, ovals, squares, and rectangles are accessible via toolbar icons. Such shapes can be drawn with solid or dashed lines and can include shadows and solid or shaded fills.

Besides the traditional structure drawing style, bonds may also be depicted using a variety of more artistic stroke styles, such as bristle, brush, charcoal, and calligraphy. These can prove useful in less formal contexts, such as for posters or title slides for presentations or as distinctive decorations on name badges. When creatively combined with different colors and fonts, this feature allows the production of some truly unique "structure art".

IMPORT/EXPORT CAPABILITIES AND COMPATIBILITY

ChemDoodle has many tools for importing and exporting chemical and image data. Image support includes both bitmap and vector formats. Most of the vector types also store ChemDoodle data internally to facilitate subsequent retrieval and editing of the chemical content. In addition to its native format, ChemDoodle can read and write ChemDraw, ChemSketch, ISIS/Sketch, Marvin Sketch, Tripos, MDL MOLFILE, PDB, XYZ, SMILES, and InChI formats, among others. Additional options are provided for many of these format types.

ChemDoodle's *MolGrabber* widget allows a user to search for a desired structure based on a name or identifier and to place the result on the drawing canvas without having to redraw it manually. Spectra in JCAMP format can also be imported, and the figures can be resized and embellished with text labels and appropriate chemical structures.

Another important feature of ChemDoodle, much refined in this version, allows "round-trip editing" of chemical structures. This provides the ability to export chemical figures to mainstream office programs such as Microsoft Word, Excel, and PowerPoint and to reimport them into ChemDoodle if modifications need to be made. This feature relies on the OLE (object linking and embedding) facility in Windows. Similar functionality is available under Mac OS X (via PDF comments) and under Linux (via an OpenOffice plugin). The exact functionality depends on the underlying support provided by the operating system.

The system clipboard is another important means of copying and pasting between applications. ChemDoodle devotes an entire section of its options menu to controlling what is copied to the system clipboard. For example, one might want to be sure an image (not text) is pasted into a word processing program or that a simple text type is used for a line notation or other text string that other applications can interpret. Besides the standard "Paste" and "Paste Special···" options, ChemDoodle also has a "Paste Text as Chemical" option for chemically interpreting text content such as SMILES or InChI data. The "Paste and Match Style" option inserts data and makes it conform to the currently defined style sheet of the ChemDoodle document. Printing options include the capability to resize documents to a specified paper size and to control landscape and portrait mode.

CHEMICAL INTELLIGENCE

As with all chemical software, built-in "chemical awareness" is critical. ChemDoodle provides a large number of knowledge-based editing tools and is able to derive many properties and spectra directly from drawn structures. These components are provided in the basic software package and do not require purchase of additional add-ons.

ChemDoodle understands a wide range of chemical shorthand expressions in atom labels and can expand such abbreviations to full structures if necessary. Users are free to add their own custom abbreviations to ChemDoodle's shorthand dictionary. Combining such expressions can create very rich structures, and ChemDoodle will be able to correctly interpret them chemically. ChemDoodle also understands molecular and radical formulas.

A variety of bond types is built in. Bond orders can range from monovalent to hexavalent; zero-order (ionic) bonds are supported as well. There are also bold, wedge, and hashed bonds to depict stereochemistry and dotted, dashed, zigzag, wavy, aromatic, coordinate, and even ambiguous bonds to accommodate more esoteric applications.

Stereochemistry is handled expertly. Tools are provided for deriving CIP chiralities of chiral centers and double bonds and for cis−trans designations. Stereocenters can also be forced to adopt particular configurations. Stereochemistry is taken into account when generating IUPAC names and when "cleaning" structures.

Aromaticity is processed by the system such that both Kekulé and aromatic representations are understood to be chemically identical. Ring system frameworks drawn using only single bonds can be "kekulized" (with alternating single and double bonds) or "aromatized" (with delocalized π-electrons depicted by circles) with just a click of the mouse. Structures can be switched between aromatic and Kekulé forms, and aromatic ring systems can be directly converted to fully saturated ones via simple one-step menu functions.

ChemDoodle generates both 2-D and 3-D coordinates. While rotations of structures are normally performed around the z-axis (perpendicular to the plane of the page), there is also a special 3-D rotation mode that allows a perspective version of a 3-D molecule to be rotated "above" and "below" the paper's plane around the virtual x and y axes. ChemDoodle utilizes the

dx.doi.org/10.1021/ci500438j | J. Chem. Inf. Model. XXXX, XXX, XXX−XXX

Cactus utility of the National Institutes of Health to obtain 3-D representations of more complex molecules. However, ChemDoodle itself is not intended to take the place of full-fledged 3-D molecular modeling software.

Because ChemDoodle has a high degree of chemical awareness built in, it is able to detect and flag errors in drawn structures. Warnings are displayed, for example, if ChemDoodle finds improper valency, an unrecognized isotopic mass, a nonintegral number of bonds, questionable stereochemistry, or overlapping atoms. Of course, these are merely warnings, such as one would see highlighting a misspelled word in a word processing program. They do not show up in print or upon image export. Moreover, display of individual warnings can be switched off in the options menu, if that is the user's preference.

Another of ChemDoodle's widgets provides automatic elemental analysis calculations, so masses, isotopic distributions, and composition can be monitored as you draw. These calculations properly handle radicals and charges. ChemDoodle also includes a mass fragmentation tool to "split" drawn structures.

A structure-to-name capability is included free with the basic ChemDoodle package. It generates standard IUPAC nomenclature and has some 20 options. Utilizing the bundled OPSIN library, the program can also generate a chemical structure from its corresponding IUPAC name. Auto-updating labels can be associated with molecules for various descriptors. This feature is especially useful for IUPAC names because the user can modify a structure and see the name update in real time.

ChemDoodle includes a facility to calculate and display simulated ^{1}H and ^{13}C NMR spectra. The parameters used for the simulation can be manipulated in real time to observe the effects on the generated spectra. Structure−spectrum relationships are described, and the full details of the chemical shift calculations and peak splittings are provided. Related structures can be superimposed on the spectra if desired. Isotopic distributions are also calculated to user-defined resolution.

Estimates can be calculated for a variety of physicochemical constants, which include critical pressure, temperature, and volume; enthalpies of formation, fusion and vaporization; Gibbs free energy of formation; normal boiling and freezing points; heat capacity; lipophilicity (octanol/water partition coefficient); and molecular polarizability.

A variety of structural descriptors and cheminformatics indices can be produced. Basic parameters such as a count of the number of types of atoms present, molecular mass, and degree of unsaturation can be determined. The number of hydrogen bond acceptors and donors, total number of electrons, and number of rotatable bonds can be displayed. The total possible number of different graphical cycles in the structure (Hanser value) and the number of rings in the smallest set of smallest rings (cyclomatic number) can be found. In all, more than a dozen topological indices can be calculated. The program can generate five kinds of connectivity matrices. Five types of ADME descriptors facilitate preliminary screening of candidate pharmaceutical compounds.

CONCLUSION

ChemDoodle 6 constitutes a highly capable software suite for producing all sorts of chemistry-related graphics and calculations. Because of its extensive feature set, high customizability, and exceptional affordability, the program is useful to a wide audience, from professional scientists in industry to professors, teachers, and students at all levels.

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Notes

This review is the author's own evaluation of this computer software package, and the comments herein should not be construed as official endorsement of the product by the Texas Department of Public Safety or its Crime Laboratory.

The abstract graphic and TOC graphic are color TIFF-format graphics that were derived from a larger EPS-format graphic using Adobe Photoshop version 10.0. Chem Doodle version 6.0 was used to draw the chemical structures, and Adobe Illustrator (version 13.0.0) was used to add the colored pencils.

The author declares no competing financial interest.

dx.doi.org/10.1021/ci500438j | J. Chem. Inf. Model. XXXX, XXX, XXX−XXX