Ligand Sketcher Review
(Open Source)

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Conclusions:

- There are good proprietary ones

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- ~~There are good proprietary ones~~
- There appears to be no perfect solution

Peter Murray-Rust:

ACCEPTED MANUSCRIPT

Open Source Molecular Modeling

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Abstract

The success of molecular modeling and computational chemistry efforts are, by definition, dependent on quality software applications. Open source software development provides many advantages to users of modeling applications, not the least of which is that the software is free and completely extendable. In this review we categorize, enumerate, and describe available open source software packages for molecular modeling and computational chemistry.

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Open Source Molecular Editors:

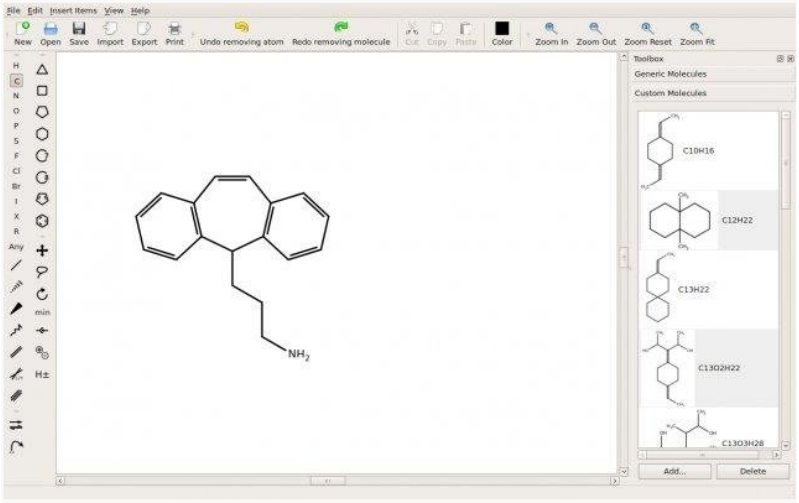
- **BKchem** http://bkchem.zirael.org GPL, C3 – python Tk GUI.
- **Chemtool** http://ruby.chemie.uni-freiburg.de/~martin/chemtool GPL, B3 - linux only (potential windows support in future), uses GTK.
- **JChemPaint** http://jchempaint.github.io LGPL, B1 [51] – Java, uses CDK.
- **LeView** http://www.pegase-biosciences.com/leview-ligand-environment-viewer GPL, B3 [52] - for ligand-protein interaction visulisation. Requires Java.
- **SketchEl** http://sketchel.sourceforge.net GPL, A1 – Java, multi-molecule support.

- **Molsketch** http://sourceforge.net/projects/molsketch GPL, A1 – C++ Qt, support for android.
- **JSME** http://peter-ertl.com/jsme BSD, A1 [66] – pure javascript 2D editor.
- **CWC** https://web.chemdoodle.com GPL, A1 [65] – suite of web-based tools for 2D/3D.

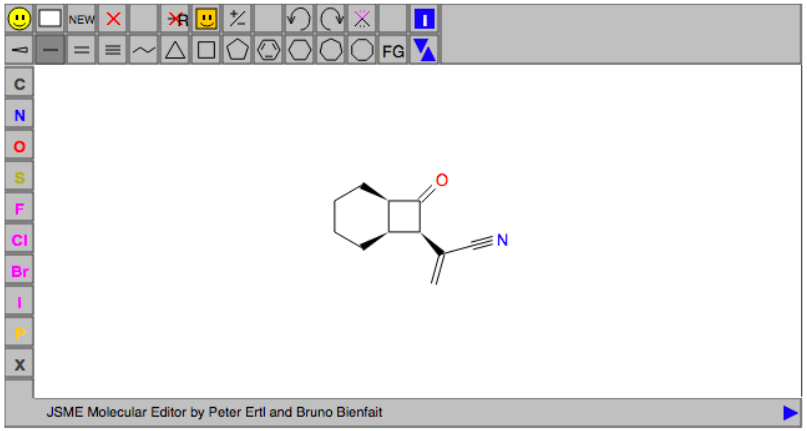
Not in the review:

- **Ketcher** http://lifescience.opensource.epam.com/ketcher AGPL - 2D editor, javascript (SVG).
- **MolView** http://molview.org/ Uses a variety of libraries (Ketcher, CWC, JSmol, GSmol) for an online solution.

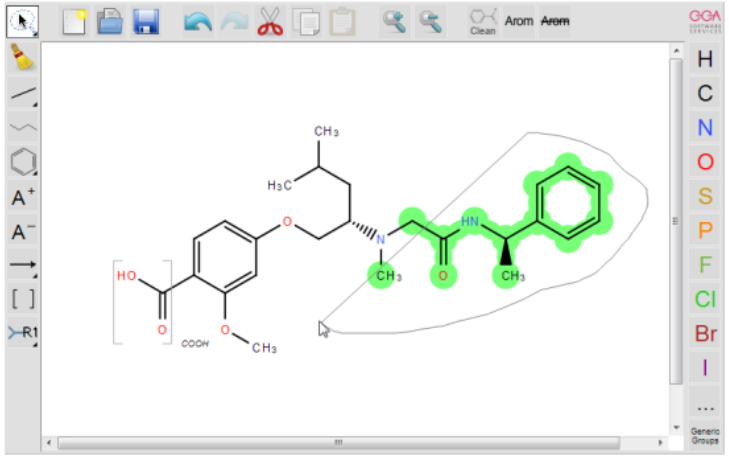
MolSketch – standalone C++/Qt, requires OpenBabel



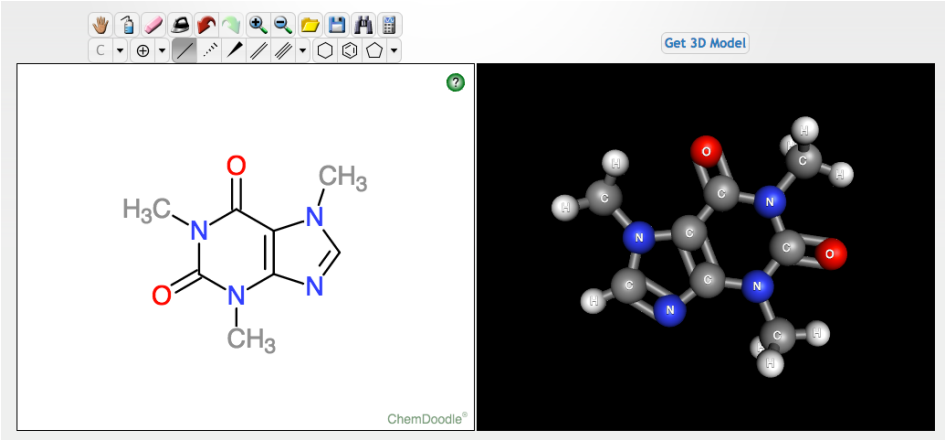
JSME – javascript



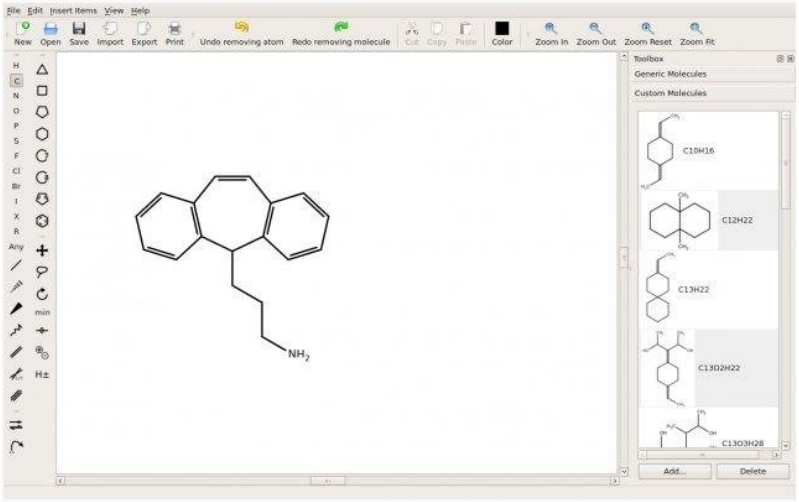
Ketcher – javascript



CWC (ChemDoodle Web Components) – HTML5



MolSketch – standalone C++/Qt, requires OpenBabel



Standalone solution.

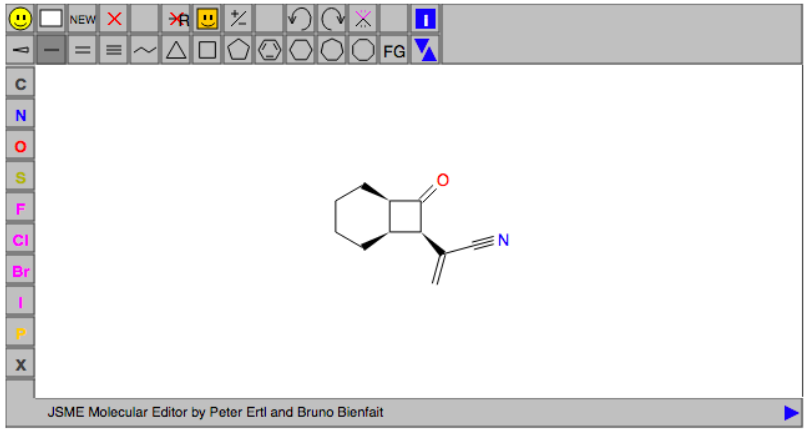
Relatively lightweight, with acceptable dependencies – Qt4 & OpenBabel (not packaged).

Chemistry functionality comes from OpenBabel.

I had issues compiling/installing:

- I had to fix a few minor issues in the source files in order to get it to compile using modern OSX/compiler (include cmath in minimise.h, include QtCore/qmath.h in molscene.cpp).
- Issues with library linking using default build system, but that shouldn't be an issue for a CCP4 distributed version.
- Encountered "OpenBabel Support Missing" issue, which is acknowledged online (despite being marked as fixed in 2015…).
- Ultimately couldn't get it working properly on MacOSX… a bit more time and effort may see it working properly.
- Couldn't get the precompiled binary working (quickly) on Windows, again due issues with the OpenBabel dependency.

JSME – javascript components



Would be part of a bespoke integrated solution – it's not (quite) a pre-made standalone solution.

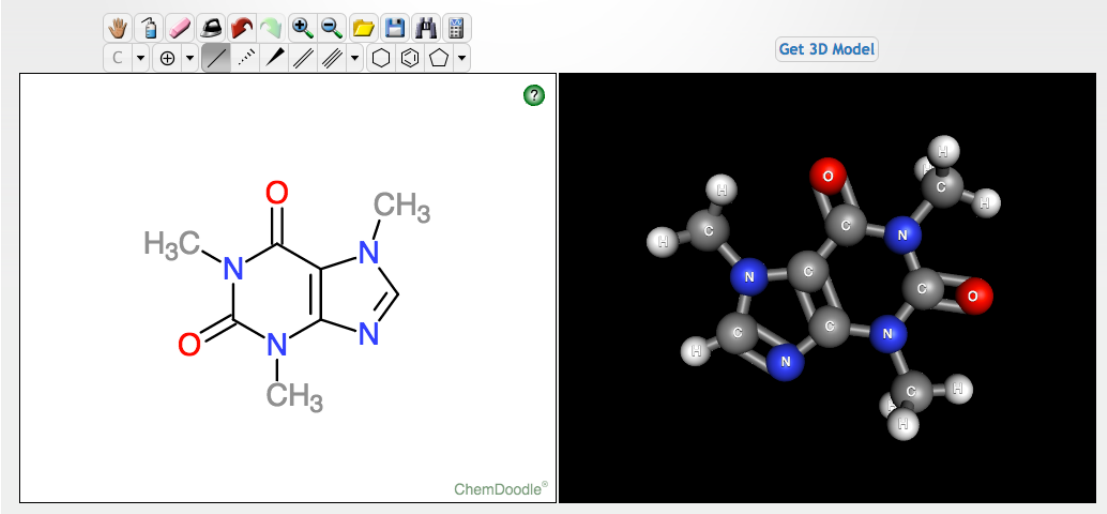
Should be lightweight.

Looks relatively dated, and does it do much more than lidia?

Features:

- Can import/output to/from smiles, molfile. Option to output canonical SMILES.
- Can add functional groups, switch between allowed charged states, and perform queries (e.g. using SMARTS).
- Can toggle between edit & visualization modes, which could be useful in some applications: http://peter-ertl.com/jsme/JSME_2016-07-31/JSME_depict_edit_toggle.html
- Can highlight atoms and see the corresponding atoms in the displayed SMILES string: http://peter-ertl.com/jsme/JSME_2016-07-31/JSME_smiles_atom_highlight.html
- Potentially extensible, allowing interaction with other HTML components, e.g. on mouseover events: http://peter-ertl.com/jsme/JSME_2016-07-31/JSME_depict_action_callback.html

CWC (ChemDoodle Web Components) – HTML5 components



Suite of web-based tools for 2D/3D.

Again, it's not a pre-made solution – work would be required to integrate this into a bespoke solution.

More heavyweight than JSME – big company, not independent developers.

2D sketcher looks great - modern & customizable, loads of features, various display preferences.

- Full standalone package is proprietary, individual HTML5/javascript web components are GPL.
- Dependencies have MIT license.

Can import from MOL, PDB, CIF, and others.

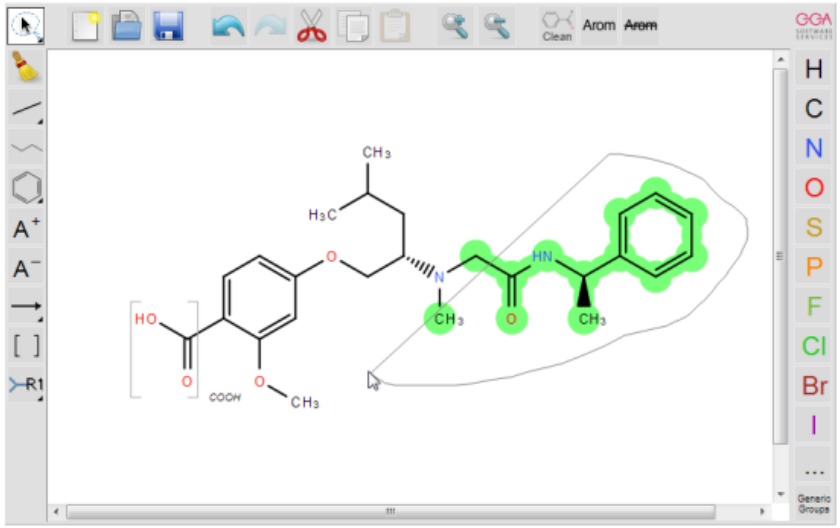
No native support for importing SMILES… but it can do via iChemLabs Cloud Services (free to academics only), which also allows text search using databases (e.g. pubmed).

Online access for cloud services (not free) may be required to access full functionality, although some workarounds may be possible (e.g. incorporate a separate MOL to SMILES).

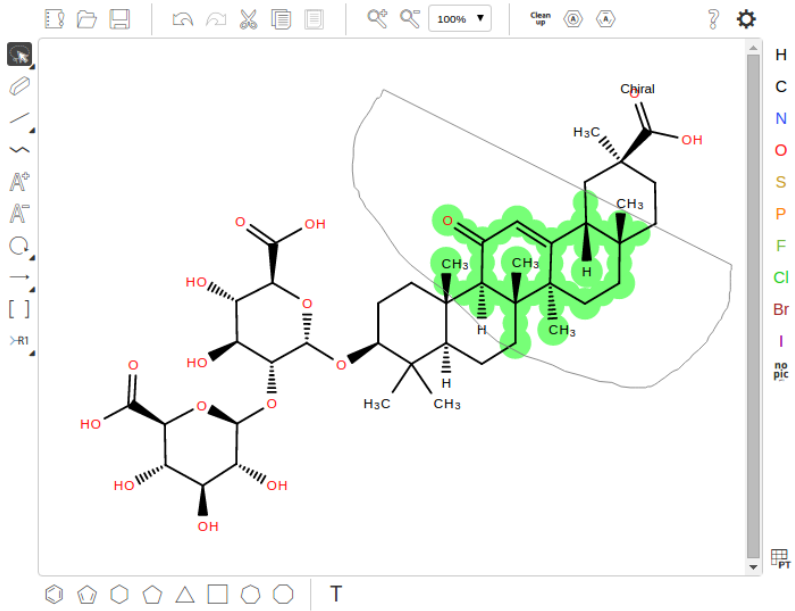
Can export to many different formats.

Also does 2D->3D conversion, 3D editing, extending to macromolecule ribbon representation, etc.

Ketcher 1 (beta) – javascript, AGPL



Ketcher 2 (alpha) – javascript, AGPL



Would be part of a bespoke integrated solution – it's not (quite) a pre-made standalone solution.

Should be lightweight… maybe.

Very much in-development:
Ketcher 1 didn't work out-of-the-box
Ketcher 2 download didn't even include all source…

Source is human-readable (unlike CWC)

Their solution involves embedding Ketcher being embedded in an iframe… yuck.

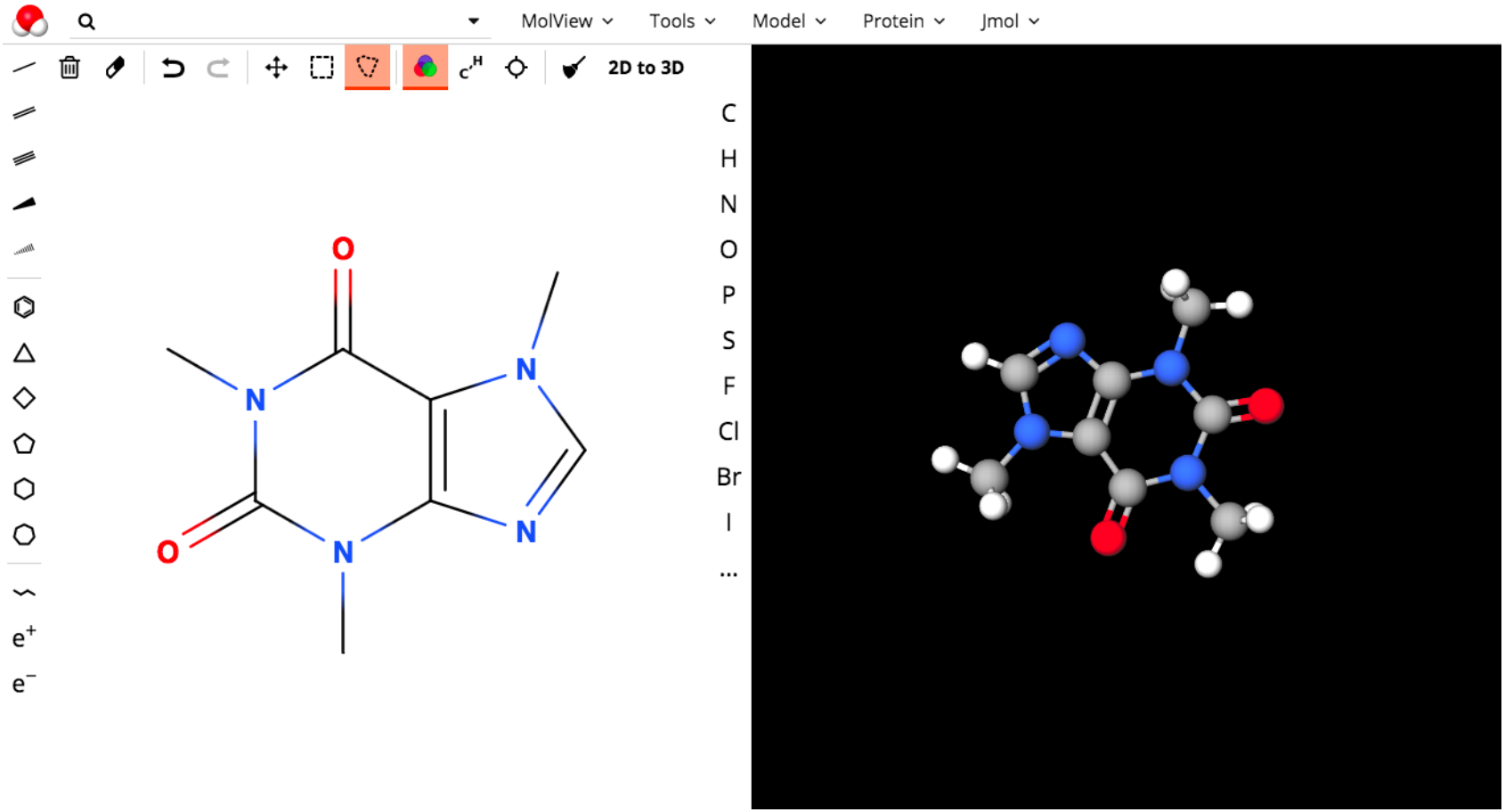
Features:

- Can import/output to/from smiles, molfile.
- Server required for SMILES.

MolView

– not suitable, but good example of implementation

- 2D Engine: Ketcher
- 3D Engine choice: GLmol, JSmol, ChemDoodleWC
- Database APIs (inc PDB & COD)



How suitable are these solutions for our purpose?

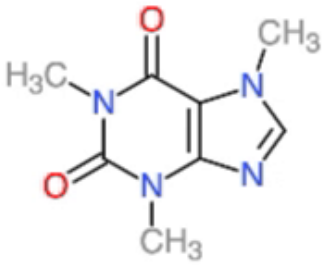
Key questions:

- Can we keep track of atom names?
- Can we colour links?
- Can we modify code?

If yes, then it may be a workable solution…

ChemDoodle Web Compon ×

file://localhost/Volumes/NO%20NAME/test/chemdoodle.html



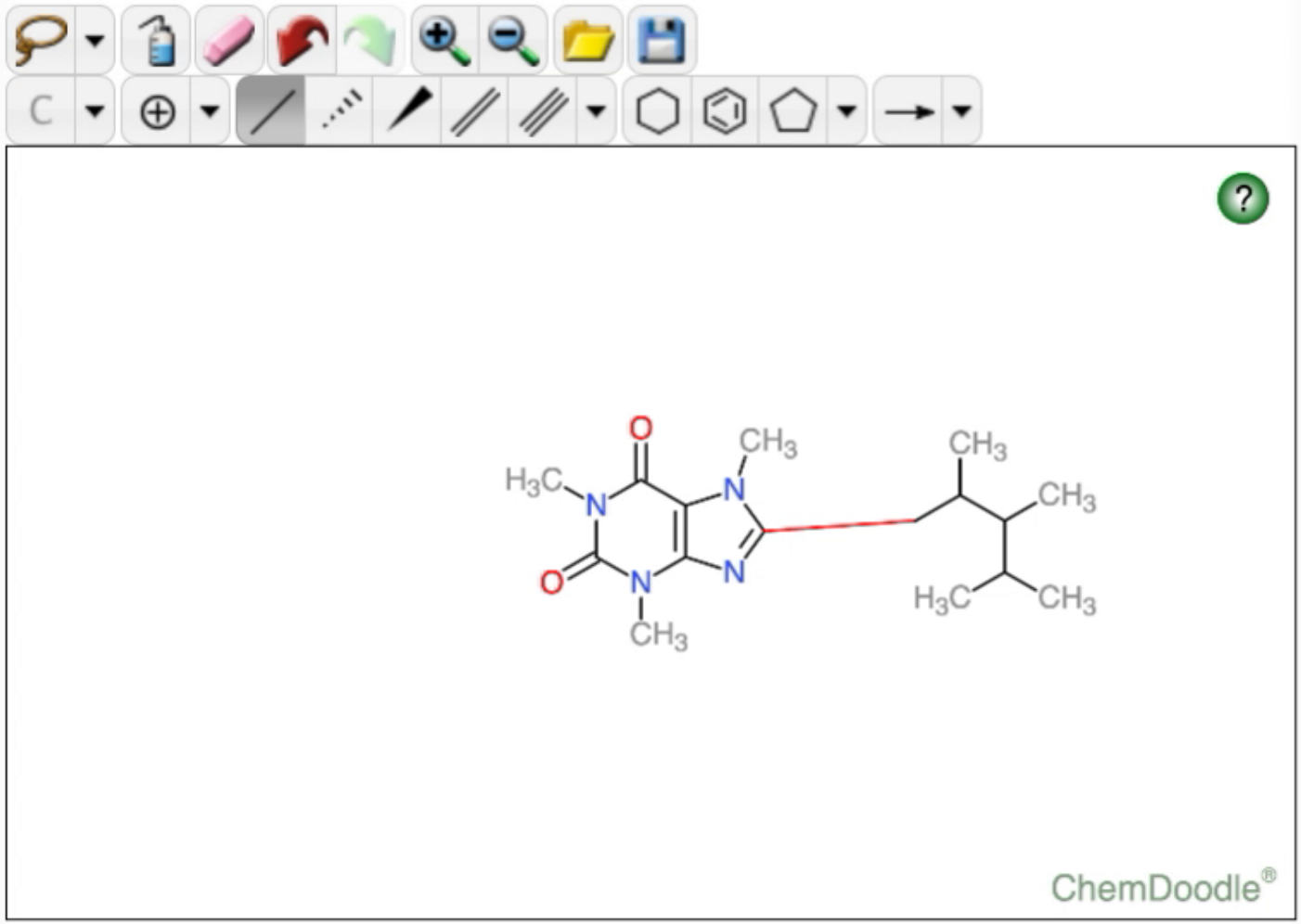
ChemDoodle®

Create Link

No links have been created yet...

ChemDoodle Web Compon ×

file://localhost/Volumes/NO%20NAME/test/chemdoodle.html



Create Link

You turned bond 15 into a link: C C

Do we even need something new?

- Jligand
  - Already part of CCP4
  - Not really developed
  - 3D not 2D
  - Java

- Lidia – seems to have more functionality than available open-source 2D editors
  - Already part of CCP4
  - Can be separated from Coot
  - Not web-based