

Personal Experience with Four Kinds of Chemical Structure Drawing Software: Review on ChemDraw, ChemWindow, ISIS/Draw, and ChemSketch

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1. BACKGROUND

Chemical structure drawing software is specialized in the chemical structural information with regards to processing, storing, rendering, and editing. With the advent of bioinformatics and chemoinformatics explosion, professional chemical informatics software for personal computers developed rapidly. For the complexity and specialty of chemical information, to use general-purpose drawing software in chemical structure drawing was painstaking and inefficient. The result was unsatisfactory even in the case of simple molecular drawings. The expression of three-dimensional molecular structure and the conversion of molecular structure from two-dimensional to three-dimensional (2D to 3D) were unfeasible by common graphic software. More than a dozen years ago, chemical professionals made use of ink-pen and chemical stencil sets to prepare papers or presentations. Free-hand chemical drawing was not uncommon in professional publications. Nowadays, people in chemistry get use to a variety of chemical drawing software in dozens-megabits size. The slim and compact software for chemical drawing of the DOS time seems to be a remote memory. If it was a rarity in the DOS time, the chemical drawing software is commonplace now. Chemists use it everyday. There are more than a dozen popular chemical drawing software,¹ such as ChemDraw, ChemWindow, ChemPen, C-Design, Chem-Frontier, DrawMol, and MolDraw, which belong to stand-alone ones, and ISIS/Draw, ChemSketch, and Chemistry 4-D Draw, which work as interfacial software or add-ins. Interfacial software is usually a member of a suite and could be used independently. Powerful standalone software such as ChemDraw and ChemWindow are members of commercial suites. This article is based on the authors' experiences with ChemDraw, ChemWindow, ISIS/Draw, and ChemSketch; the current version of ours is 5.0 Ultra, 6.0, 2.5, and 5.12, respectively.

2. INTRODUCTION

ChemDraw,² ChemWindow,³ ISIS/Draw,⁴ and ChemSketch⁵ are the most popular chemical drawing software in recent years. ChemDraw is the chemical drawing member of the well-known commercial chemical software suite

ChemOffice. ChemWindow was first integrated into Bio-Rad Sadtler Suite and later into KnowItAll Analytical Systems after Bio-Rad Laboratories' merger of SoftShell. ISIS/Draw is the interfacial software to ISIS/Base database and a member of the MDL ISIS. ChemSketch is the interfacial software to and a member of the ACD/Labs. The fundamentals of the four kinds of software are listed in Table 1.

Of the four kinds of software, ChemDraw is a specialized chemical drawing software developed by CambridgeSoft. ChemWindow was a specialized chemical drawing software before version 6.0, and it is the interfacial software to KnowItAll Analytical Systems now. ISIS/Draw is designed by MDL Information Systems for its MDL ISIS bundle. ChemSketch is the interfacial graphic software for ACD/Labs suite by Advanced Chemistry Development. As for the status of the software, ChemDraw was commercial from its first publication. A free copy of ChemWindow was available when it was under SoftShell, the situation changed, and no free ChemWindow is offered in the name of Bio-Rad Laboratories. To the dismay of many freebie lovers, Advanced Chemistry Development declared that the free copy of the members of ACD/Labs suite is no longer provided in the 6.0 new version, but a free copy of the earlier 5.0 version is still available for the time being. The MDL's ISIS/Draw is the only one of the four which keeps a free policy constantly. It may be the best choice for college students and light duty users. Recently, the academic edition of KnowItAll 3.0 is offered free by Bio-Rad Labs on the Web. It is good news for academic users. It should be mentioned that as the new edition of ISIS/Draw 2.5 was published, the 2.4 edition disappeared on the MDL Web site, but the earlier 2.3 copy is still available.

3. UTILIZATION

The situation of using a particular software is largely dependent upon the working requirement of the user. Take ChemOffice 5.0 Ultra as an example, the user's manual for ChemDraw is 222 pages; the manual of Chem3D is 244 pages. It will take a lot of time to read the manuals and try out the tutorial exercises. To master professional chemical drawing software like ChemDraw is not an easy task. Most users tend to be limited to the extent of their practical demand. They may be more familiar with several functions closely associated with their routine job but are not aware of some fundamental usages of other functions. We hope this article will be helpful to these common users.

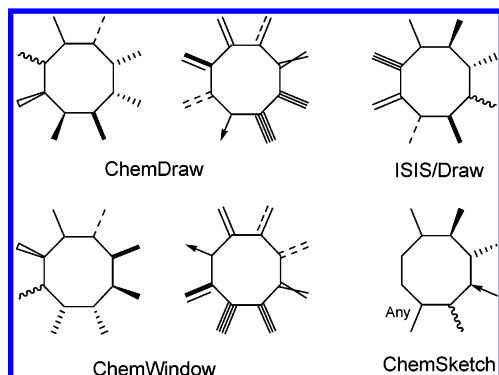
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Table 1. Brief Summary and Comparison of the Four Kinds of Chemical Software

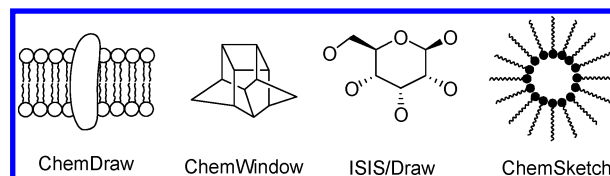
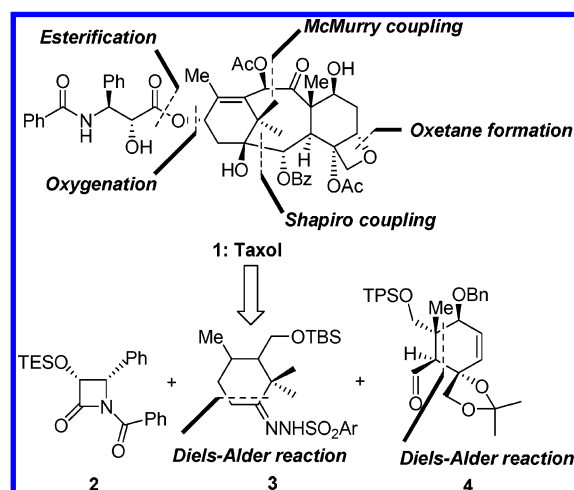
software	ChemDraw 5.0	ChemWindow 6.0	ISIS/Draw 2.5	ChemSketch 5.12
suite	ChemOffice	Bio-Rad Sadtler Suite	MDL ISIS	ACD/Labs
first publication/current version ⁶	1985/8.0	1989/7.0	1990/2.5	1994/7.0
minimum hard-disk required	42.58Mb (suite)	37.07Mb (suite)	10.61Mb (standalone)	17.01Mb (module)
processor minimum	Pentium	Pentium	X486	Pentium 300 MHz
RAM recommended	32Mb up	32Mb up	16Mb up	32Mb up
software type	commercial	commercial	free	free (before v.6)
other add-ins/utilities	NA/yes	NA/yes	NA/yes	yes/yes
add-ins to third-party	NA	NA	NA	yes (to ChemOffice and MDL)
plug-in service	ChemDraw Plug-in	BrowseIt	ISIS/host	ACD/I-Lab
3D graphics	Chem3D	SymApps	RasMol	3D Viewer

**Figure 1.** Available different bond types of the software.

3.1. Installation. The four kinds of software are easy to install. Except for ChemOffice, the other three come with setup options. ChemSketch and ISIS/Draw entered the optional function-modules window after the click of the installer, and the modules could be ticked. ChemWindow went to options of 'Typical', 'Compact', and 'Custom'. Full installation is recommended unless there is a hardware limitation. In addition to ACD/Labs, Advanced Chemistry Development provided free add-ins for ChemSketch and free add-ins to the third party software, which included ChemDraw and ISIS/Draw.

3.2. Primary Chemical Drawing. The basic drawing tools were laid out by the software's presetting after entering the user's interface. The window of ChemWindow looked most simple with only one standard tool-bar, but users could choose as many as 12 tool-bars in addition to a ruler and a status bar. ISIS/Draw and ChemDraw came with a concise interface. They were equipped with two fixed tool-bars and an optional ruler and grid. ISIS/Draw seemed more simple and pleasant to the eyes of the two. ChemSketch appeared a bit redundant at the first glance of its interface and was cumbersome to beginners. It seemed that all tools were stacked on the desktop but the grid. There are two interfaces that could be switched to and fro. The software preset one is 'Structure' and the other one is 'Draw'. Only a standard tool-bar and a drawing tool-bar are fixed in the switches. The basic drawing with the software is exemplified below.

3.2.1. Free-Hand Drawing of Chemical Structure. Drawing simple structures and reactions is often carried out freehand. In the drawing of complicated objects, freehand drawing is indispensable in the finishing and detail modification after templates are used. In the standard tool-bar, tools of bonds, atoms (or elements), chains, arrows, lines, curves, and polygons are most useful. The using of bond-tool of the software is illustrated in Figure 1. Among the four, ChemDraw and ChemWindow rank first in the number of types

**Figure 2.** Examples of templates from the software.**Figure 3.** Retrosynthesis of taxol by Nicolaou's group.

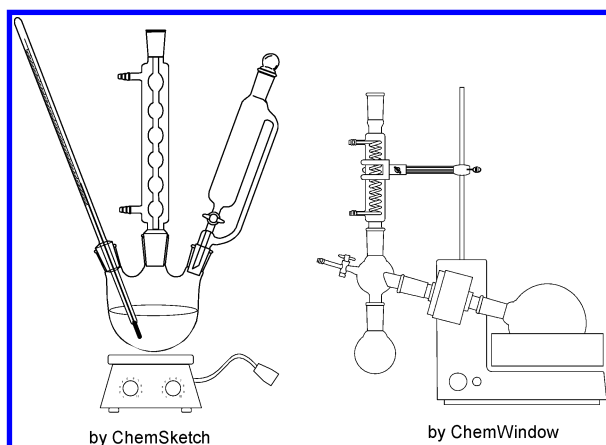
of bonds, and ChemSketch ranks last but with excellent function. ISIS/Draw is weak in this term.

3.2.2. Drawing with Templates and Presetting. The templates of ChemSketch are most powerful and user-friendly. ChemSketch and ChemDraw provide customer templates. The other two do not. The latter situations may be circumvented. In ISIS/Draw, templates should be prepared beforehand, saved in the 'Template' folder, and then imported to the new template by opening it in the 'Template Editor'. In ChemWindow, no template editing function is available; a customer template file may be saved in the 'Template' folder, then opened in the 'Preference' dialogue box in the 'File' menu, and designated as the path of the customer template file. The size of the template file of ChemWindow is large. A wide variety of 2000 and 3000 molecular structures are accommodated in two of the four templates. Some templates of the software are exemplified in Figure 2.

To use a template in a drawing job is fundamental. Much effort should be made on the basis of dozens of templates. As illustrated in Figure 3, in the retrosynthesis analysis⁷ of taxol, templates of carbon rings, fused rings, aliphatic chains, groups, arrows, and reaction symbols were employed; functions of element, bond, lines, and caption were used.

Table 2. Functional Features of the Four Kinds of Chemical Software

software	ChemDraw5.0	ChemWindow6.0	ISIS/Draw2.5	ChemSketch5.12
journal style settings	8	6	9	6
latest files	NA	4	9	10
bond types	9	14	8	6
arrows	41	11	30	67
templates/user's set	12/yes	6/yes	23/yes	42/yes
glassware	yes	yes	NA	yes
structure to name	yes (AutoNom and ACD/Name)	NA	yes (AutoNom and ACD/Name)	yes (ACD/Name)
name to structure	yes	NA	NA	yes (from SMILES)
Nick Name	yes	yes	NA	yes (standalone)
clean structure	yes	yes	yes	yes
2D to 3D	yes (standalone)	yes (add-in)	yes (add-ins)	yes (add-in)
prediction of properties	yes	NA	NA	yes

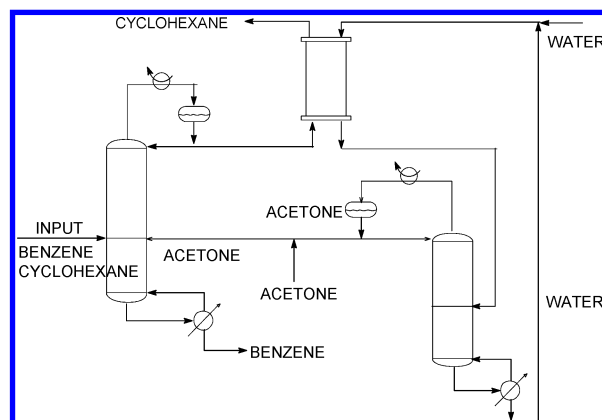
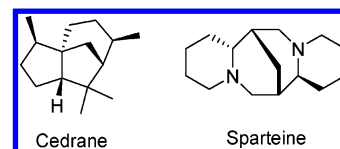
**Figure 4.** Lab experimental glassware.

Furthermore, operations of selection, move, duplicate, paste, rotate, reflection, flip, and alignment are indispensable.

Several sets of publishing styles of frequently accessed academic chemical journals are preset in the software. The publishing format of the American Chemical Society is often used. ChemDraw adopted the 1996 format of the ACS publishing materials as one of its preset styles. Other examples are the JOC (J. Org. Chem.) style in ChemWindow, the TETRA (Tetrahedron series) style in ISIS/Draw, and the JMolModl style in ChemSketch. The journal styles of the software are summarized in Table 2.

3.2.3. Drawing of Glassware and Chemical Process Chart. All the software contains glassware templates except for ISIS/Draw. ChemWindow contains 139 sets of glassware, which is most powerful, user-friendly, and can be autodocked. ChemSketch was featured with 200 kinds of glassware. They are clearly prepared and standard sized, can be autodocked, and are convenient to users. ChemDraw has a few sets of glassware. A chemical process template is unique to ChemWindow, which contains 97 sets of templates for chemical equipments and units drawing. Lab equipments and a chemical process are drawn and exemplified in Figures 4 and 5.

3.3. Intermediate Usage. In the four kinds of software, ISIS/Draw is the most concise. ChemWindow and ChemSketch are comparable in complexity. The latter is more powerful in function. ChemDraw is the most comprehensive and powerful one. To master ISIS/Draw is not an easy task, and the others are more demanding. For software such as ChemDraw, both insight into computer software and an understanding of professional chemistry is essential to effectively use it. A variety of skills in manipulating chemical

**Figure 5.** A chemical separation process.**Figure 6.** Nomenclatures by different software.

information on a computer is required for an intermediate user. Frequently encountered tasks include user's templates, interconversion of different file formats, input and output of files through different formats, from structure to nomenclature and from character string to structure, 2D to 3D conversion, 3D structure optimization, molecular property calculation and prediction, management of analytical spectra, database management, online service, and so on.

3.3.1. Structure and Nomenclature. From structure to name is the most frequently used function. All four kinds of software supply nomenclature modules except for ChemWindow.⁸ Beilstein's AutoNom is integrated into ChemDraw. ChemSketch uses its own ACD/Name, which supports ChemDraw and ISIS/Draw as an add-in. Besides ACD/Name, ISIS/Draw uses AutoNom as add-in, but the free ACD/Name is not capable of naming a structure with more than 3 rings. An alkaloid sparteine and a terpene cedrane were illustrated in Figure 6. Nomenclature by two of the software resulted as follows: cedrane by ACD/Name is (1R,2R,5S,7R,8R)-2,6,6,8-tetramethyltricyclo[5.3.1.0-1,5-]undecan, by AutoNom is (3R,8aS,9R)-3,8,8-trimethyl-6-(R)-methyl-octahydro-3a,7-methano-azulene; sparteine by AutoNom is (7S,7aR,14S,14aS)-dodecahyro-7,14-methano-dipyrro[1,2-a; 1',2'-e][1,5]diazocine.

The function of name-to-structure is only available in ChemDraw. The free edition of ChemSketch has the function

Table 3. Personal Experiences with the Four Kinds of Chemical Software^a

software	ChemDraw5.0	ChemWindow6.0	ISIS/Draw2.5	ChemSketch5.12
2D drawing	excellent	good	excellent	excellent
3D	excellent	good	average	good
lab	average	excellent	NA	good
spectra	average	average	NA	excellent
online	excellent	NA	excellent	excellent
user's programming	NA	NA	NA	yes
files' formats supporting	excellent	average	average	average
comprehensive	good	average	average	excellent
overall	excellent	good	good	excellent

^a CS ChemDraw is the trademark of CambridgeSoft Corporation. ChemWindow is the trademark of Bio-Rad Corporation. ISIS/Draw is the trademark of MDL Information Systems, Inc. ACD/ChemSketch is the trademark of Advanced Chemistry Development, Inc.

of generating structure from SMILES (Simplified Molecular Input Line Entry Specification). A few average users command the SMILES and the function appeared not popular. ChemSketch can produce SMILES from structure, which may be helpful to learners of SMILES.

An important function connected with structure and nomenclature is 'User's accustomed name', which designates a specific compound or functional group to a specific string. After inputting a character string, the software will recognize it as a legible structure. The feature is termed 'Nick Name' in ChemDraw, 'User's Chemistry' in ChemWindow, and 'Label' in ChemSketch. ChemDraw is powerful in 'Nick Name'. In addition to the preset 'Nick Name', the user may produce and edit his particular 'Nick Name'. A similar usage is to input a formula and obtain a structure. In ChemDraw, a formula such as 'CH3CH2CHCHCCCH3' may be input, recognized, and transformed into a 2D structure. As for ChemWindow and ChemSketch, a string may only be added to a 2D structure as a side-chain or a functional group. ChemWindow cannot recognize a string as a structure. ChemSketch takes a string as a 'Label', in which a box pops up and strings such as 'C2H5', 'COOEt', and 'PO3H2' may be chosen. The 'Label' can be edited and customized.

3.3.2. Three-Dimensional Structure. All four kinds of software are equipped with a three-dimensional structure rendering function. ISIS/Draw integrates RasMol as its 3D viewer. ACD provides a free ACD/3D Viewer to ISIS/Draw as an add-in. The other three designed their own 3D rendering software. ChemSketch uses a ACD/3D Viewer. Chem3D is a member of the ChemOffice suite. A structure made by ChemDraw may be pasted on or exported to Chem3D, rendered in 3D, and calculated in properties. ChemWindow employs its bundled SymApps to display a 3D structure and make calculations. ISIS/Draw and ChemSketch are comparable in molecular 3D processing ability. ChemSketch can make a structural optimization, and ISIS/Draw can do the same job after installation of a ACD/3D Viewer add-in. ISIS/Draw integrates RasMol as its default 3D viewer, which cannot make 3D optimization, so a ACD/3D Viewer is preferred. Except for Chem3D, the other 3D software is integrated into the structure drawing software, such that a 2D drawing may be rendered in 3D instantly. The ACD/3D Viewer is the most convenient to the average user. SymApps is powerful in 3D calculation. Chem3D is semiprofessional 3D calculation software. It is popular in educational application. The integrated quantum mechanics engines and molecular mechanics engines are fairly powerful. Professional molecular calculations can be carried out. We

tried a conformational optimization of a nonapeptide on a PC with 1G CPU, which took a few dozen minutes.

3.3.3. Management of Spectral Information. Three of the four kinds of chemical drawing software are capable of spectra management. ISIS/Draw cannot process spectral information. ChemWindow and ChemSketch need member software in their respective suite to manipulate spectra. ChemDraw supports the JCAMP format (*.jdx file) and the Galactic format (*.spc file). The spectra may be moved and rescaled in the window of ChemDraw. The ACD/SpecViewer is more powerful and popular, which supports JCAMP (*.jdx, *.dx, *.jxs, *.jx), Galactic (*.spc), ASC II (*.txt), and ACD (*.esp) formats.

3.3.4. Other Usages. ChemDraw supports many formats in the file input and output operations. The other three support a few. File format conversion is a frequent task. A piece of free software 'Mol2Mol' is useful in 3D file interconversion. It supports most 3D file type and several 2D file formats. For the interconversions between 2D format files, free '2DConverter' from CambridgeSoft may be employed. In addition to the interconversion among formats of .cdx, .chm, .fld, .f2d, .rxn, .skc, .tgf, .smd, .jdx, .mol, .msm, and .wmf, it supports a 2D molecular structure file with no extension to be converted into the above-mentioned formats.

Online services are getting more popular. In fact, ISIS/Draw is interfacial software for chemical database service. Besides working as a 2D molecular structure interface for MDL ISIS, it is integrated into CrossFire of Beilstein. ACD/Labs uses I-Lab to connect to its net server. The famous 'chemweb' uses ISIS/Draw as graphic interface in online search, and more than a dozen online databases at chemweb worked in this way. It provides online a free ACD/Labs Name-to-Structure service and displays a 2D structure with ISIS/Draw Plug-in and a 3D structure with Chime Plug-in. The online 'Organic Syntheses' incorporates ChemOffice Plug-in as input and display interface.

The software provides calculation functions for various molecular properties. Molecular weight and composition can be calculated. Density and thermodynamic data can be predicted. Spectral data can be simulated. ACD offers ChemBasic as an add-in to ChemSketch, which support customer programming based on ChemSketch. In addition, ChemBasic provides 22 Goodies for the functional expansion to ChemSketch. As a summary, comparison of the functions of the software is listed in Table 2.

4. CONCLUSION

All four kinds of chemical drawing software can do a 2D drawing job well. The progress of ChemSketch is remarkable in comprehensive performance improvement and intelligent module development. It makes for the integration of 3D, spectral processing, spectral calculation, physical chemical properties' prediction, and online service, which represent the mainstream technical trend in chemical drawing software. ChemDraw as a traditional drawing software is most powerful in drawing, but the 3D function is not integrated, and the spectral functions need to be improved. The comprehensive performance of ChemWindow is greatly enhanced after its integration into KnowItAll. In addition to its features in a lab apparatus module and a chemical engineering process module, the spectral information processing function is outstanding due to its merger with Bio-Rad. Generally speaking, ChemWindow and ChemSketch are comparable in overall performance. ISIS/Draw is pure chemical drawing software. There is no sign of developing it into comprehensive chemical structure software in the most recent 2.5 edition. The impressive feature of ISIS/Draw is simple. To make an evaluation^{1,9} on chemical drawing software is not an easy task. The preference of professional software is mainly dependent upon the user's objective. So it seems improbable to make an extensively acceptable recommendation. For users focused on 2D drawing, ISIS/Draw is the first choice. ChemDraw plus Chem3D is undoubtedly best for 3D professional users. ChemSketch meets extensive task duty requirements in drawing, 3D, spectral information, physical chemical properties, and customer programming. ChemWindow can facilitate users who span chemistry lab and engineering process design. The evaluation and comments are listed in Table 3 for reference. A detailed

illustration on individual software may be acquired at the respective Web sites.^{2-5,10}

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