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COMPUTER SOFTWARE
REVIEWS

**Reactor**. ChemAxon Ltd., Maramaros koz 2/a, Budapest, 1037 Hungary. www.chemaxon.com. Contact ChemAxon for pricing information.

Reactor is a powerful software engine for creating large database files of structures through virtual chemical reactions. It is not a chemical database but rather a flexible and powerful platform with multiple applications, particularly in combinatorial chemistry and drug discovery, for generating and analyzing large virtual libraries of chemical compounds. Importantly, the engine at the heart of this system "understands" modern organic chemistry, enabling it to produce chemically logical results from the union of two or more virtual classes of starting materials.

Reactor is a Java-based application and tool, as are all of ChemAxon's products, which allows it to be run across many computing platforms with little or no modification. It can be used as a stand-alone application through a browser-based interface, but it is perhaps best used as an addition to a larger software array through standard scripting. Although the user interface of Reactor is simple, the actual use of the program will require some mastery of the commands and algorithms used to guide Reactor for chemical reactions and the properties of substrates. Full documentation for Reactor is available online and open to all at http://www.chemaxon.com/jchem/doc/user/Reactor.html. The greatest use of Reactor stems from its ability to process data from other databases or by interfacing with automated synthesis and analytical instrumentation. Many of ChemAxon's other products fulfill these roles, but the standard file formats used by Reactor ensure that it can be used with most other chemistry and automated-synthesis software in general use.

Reactor is probably most useful for companies or research groups pursuing the synthesis of large combinatorial libraries or computer-based screenings of molecules. For example, Reactor can easily calculate all possible products of a three-step sequence employing four different starting materials and export the products to a variety of different databases. These databases can then be used directly in reaction assays, as Reactor will also calculate the molecular weights and other physical properties of each member of the library. Also, each of the outputted structures can be modeled with molecular mechanics and evaluated in silico for binding to a target enzyme. These libraries can be further refined to include only those compounds likely to be synthetically accessible over the multistep sequence based on criteria for the reactions themselves, rather than just the final products. Other applications, for example, could include using Reactor to predict possible metabolic products for a library of drug candidates. The resulting metabolic library could then be screened again for known or suspected toxic and biologically active molecules.

In our own testing, we challenged Reactor to predict the possible products of a previously unknown chemical reaction using a simple set of rules and small libraries of commercially available compounds. Starting materials, in this case aromatic aldehydes and $\alpha,\beta$-unsaturated aldehydes, were imported from commercially available databases in the standard formats. Following the rules of connectivity that were entered through a simple programming language, Reactor quickly and correctly produced a library of all possible products. When challenged to predict the products of only electron-rich enals with electron-deficient aromatic aldehydes, Reactor did a fine job in most cases, although it occasionally failed to make accurate predictions about the electronic nature of the unsaturated aldehydes. As with all components of Reactor, this issue could be easily addressed by the addition of a plug-in that gives better predictions about the chemistry of the starting materials or products. The flexibility of Reactor and its ability to be customized are two of its greatest assets; a few tweaks to the reaction rules allow Reactor to make relatively reliable judgments about which substrates are likely to give the desired reactions and which are not. This information can then be imported easily to automated syntheses, thereby automatically generating more focused libraries in which each reaction is more likely to produce the desired results once the chemistry moves from the computer (or notepad) to the fume hood. In contrast, there are similar programs that can readily generate libraries of a core structure by changing the substituent groups; however, these programs cannot evaluate whether the synthesis of such compounds is expected to be possible with the proposed chemical reactions.

Reactor currently cannot predict the likely stereochemical outcome of a diastereoselective reaction. This feature should be incorporated into the program before the end of 2004, allowing the reaction rules to designate the expected products or to generate mixtures of stereochemically diverse virtual libraries. Although Reactor can be taught essentially any organic reaction, known or unknown, it would be nice to see a much larger library of known reactions included in its library. This is reportedly under development. Also, the current library of reactions, organized by named reactions, would be better presented in terms of the functional group transformation involved, such as "oxidation of 1° alcohol to an aldehyde" rather than how it is currently presented, e.g., "Corey−Kim oxidation", "Corey oxidizing reagents for alcohols". The ability to select two or more reactions at once would also be a welcome addition.

Reactor is available for purchase for industrial use, although academic researchers are given free access to ChemAxon's entire suite of chemically oriented software, including Reactor. It would be to the great advantage of academic groups working in the areas of combinatorial chemistry, virtual drug screening, and cheminformatics to pursue this option and explore the possibilities Reactor may offer for application and development.

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