(6) Corey, E. J.; Feiner, N. F. "Computer-Assisted Synthetic Analysis. Rapid Computer Method for the Semiquantitative Assignment of Conformations of Six-Membered Ring Systems". *J. Org. Chem.* **1980**, *45*, 757, 765. The domain is limited to six-membered rings, and the method is used by a synthesis planning program (LHASA) to help decide the course of reactions on such rings.
(7) (a) Liljefors, T.; Thelin, B.; van der Pers, J. N. C.; Löfstedt, C. "Chain-Elongated Analogues of a Pheromone Component of the Turnip Moth, *Agrotis segetum*. A Structure-Activity Study Using Molecular Mechanics". *J. Chem. Soc., Perkin Trans. 2* **1985**, 1957. (b) Liljefors, T.; Thelin, B.; van der Pers, J. N. C. "Structure–Activity Relationships between Stimulus Molecule and Response of a Pheromone Receptor Cell in Turnip Moth, *Agrotis Segetum*. Modifications of the Acetate Group". *J. Chem. Ecol.* **1984**, *10*, 1661.
(8) Allinger, N. L.; Yuh, Y. H. "MM2: Molecular Mechanics II". *QCPE* **1980**, *11*, 395.
(9) For an overview of AI, see: Barr, A., Feigenbaum, E. A., Eds. "The Handbook of Artificial Intelligence". William Kaufmann: Los Altos, CA. Volume II contains reviews of several well-known ES programs. For a recent book on chemical applications of AI, see: Pierce, T. H., Hohne, B. A., Eds. *Artificial Intelligence Applications in Chemistry*; ACS Symposium Series 306; American Chemical Society: Washington, DC, 1986.
(10) Liljefors, T.; "MOLBUILD—An Interactive Computer Graphics Interface to Molecular Mechanics". *J. Comput. Chem.* **1983**, *1*, 111.
(11) von der Lieth, C. W.; Carter, R. E.; Dolata, D. P.; Liljefors, T. "RINGS—a General Program to Build Ring Systems". *J. Comput. Chem.* **1984**, *2*, 117.
(12) We currently use the Visual 500 series (Visual Technology, Inc., 540 Main Street, Tewksbury, MA) as our "standard" terminals. The "selective erase" feature and the possibility to create a scrolling region together with the graphics are the only enhancements beyond full PLOT10 compatibility.
(13) Motherwell, W. D. S. PLUTO—*a Program for Plotting Molecular and Crystal Structures*; University Chemical Laboratory: Cambridge, 1978.
(14) See ref 9, Vol. II, Section VIII.B.1, and references therein.
(15) See, for example: Pospesel, H. *Introduction to Logic: Predicate Logic*; Prentice-Hall: Englewood Cliffs, NJ, 1976.
(16) (a) Beckhaus, H.-D.; Hellmann, G.; Ruchardt, C. "Tetra-*tert*-butylethane". *Chem. Ber.* **1978**, *111*, 72. (b) Hounshell, W. D.; Dougherty, D. A.; Mislow, K. "On the Role of Newman Projections in Conformational Analysis. Evidence for Nonalternating Ground States in Highly Strained Molecules". *J. Am. Chem. Soc.* **1978**, *100*, 3149. (c) Osawa, E.; Shirahama, H.; Matsumoto, T. "Internal Rotation in Simple to Congested Hydrocarbons Including 2,3-Dimethylbutane, 1,1,2,2-Tetra-*tert*-butylethane, 2,2,4,4,5,5,7,7-Octamethyloctane, and Cholestane". *J. Am. Chem. Soc.* **1979**, *101*, 4824.
(17) Sacerdoti, E. D. *A Structure for Plans and Behavior*; Elsevier: New York, 1977.
(18) Charniak, E.; Riesbeck, C. K.; McDermott, D. V. *Artificial Intelligence Programming*; Lawrence Erlbaum: Hillsdale, NJ, 1980.
(19) In *n*-butyl chloride, the g+/g− conformation makes up as much as 24% of the total: Ukaji, T.; Bonham, R. A. "The Molecular Structure of *n*-Butyl Chloride and *sec*-Butyl Chloride. II. Hindered Rotation". *J. Am. Chem. Soc.* **1962**, *84*, 3631.
(20) See ref 10.
(21) Beierbeck, H.; Saunders, J. K. "Conformational and Configurational Analysis of Hydrocarbon Chains Based on Time-Averaged Carbon-13 Chemical Shifts". *Can. J. Chem.* **1977**, *55*, 772.
(22) Anderson, J. E.; Pearson, H. "A Secondary Effect on Barriers to Rotation in Substituted Ethanes". *J. Am. Chem. Soc.* **1975**, *97*, 764.
(23) See, for example: Berg, U.; Liljefors, T.; Roussel, C.; Sandström, J. "Steric Interplay between Alkyl Groups Bonded to Planar Frameworks". *Acc. Chem. Res.* **1985**, *18*, 80. Hounshell, W. D.; Iroff, L. D.; Iverson, D. J.; Wroczynski, R. J.; Mislow, K. "Is the Effective Size of an Alkyl Group a Gauge of Dynamic Gearing?" *Isr. J. Chem.* **1980**, *20*, 65.
(24) See, for example: Michalski, R. S., Carbonell, J. G.; Mitchell, T. M., Eds. *Machine Learning: An Artificial Intelligence Approach*; Springer: Berlin, 1984; Vol. XI and previous volumes in this series.

COMPUTER SOFTWARE REVIEWS

CHEMBASE

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In the course of the past several years I have examined a great many programs and reviewed quite a number of them for various magazines. Most of the software has been very forgettable, but every now and then when working with a piece of software you realize that you are dealing with something special. CHEMBASE from Molecular Design Ltd. is one of the special ones.

CHEMBASE is a powerful data-base tool for the chemist, a tool that is strongly directed toward the synthetic organic chemist but certainly of use to any chemist charged with keeping track of organic molecules and organic reactions. To enumerate all of the capabilities of this program would require much more space than I am allowed to use for this review. I shall therefore mention only some of the features of the program with the hope that many who read this will take a careful look at this powerful software tool.

In brief, CHEMBASE is a data-base manager with a difference. The difference is that it is visually oriented in terms of chemical structures. Unlike the more traditional data-base managers that allow you to manipulate text and numbers, CHEMBASE allows you to store, manipulate, and search your data base in terms of chemical structures and substructures and even in terms of complete reactions. This means that a synthetic chemist could search a data base for all entries containing a specified compound, a specified structural unit, a specified functional group conversion, or any combination of the above. In addition, the program also supports more conventional types of data-base interrogation like the retrieval of all compounds available with molecular weights in a certain range, boiling points in a certain range, or combinations connected by Boolean logic. Each file "hit" is returned as a complete frame of information (see, for an example, Figure 1) that has provision for containing physical constants, various registry numbers, alternate names, empirical formulas, and whatever else you or the data-base creator thought to include. Very complete default information templates are supplied, and the user is free to design information templates to suit his or her specific applications. Powerful facilities for manipulating lists of information are also provided. While such power has long existed on large mainframe computers, it is now available for microcomputers with very few important features sacrificed in the transition. Indeed, the added convenience of having such a powerful package available on a microcomputer for convenient interactive use makes the missing features seem quite unimportant. Perhaps the most important feature missing is chirality. While CHEMBASE allows chirality to be repre-

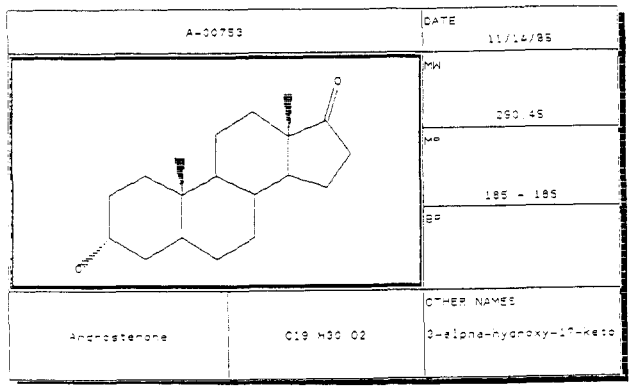

Figure 1. Sample information frame from a CHEMBASE file.

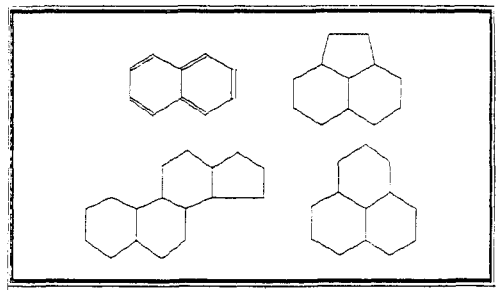

Figure 2. Four of the structural templates available in the CHEMBASE system.

sented for compatibility with mainframe implementations, it has no meaning in searches in the microcomputer version.

The program itself is state of the art menu driven. It is supplied to the user on six disks along with a rather enormous manual that looks a lot more intimidating than it is. I found the manual to be attractively produced, well indexed, and clearly written. I did not like the physical size of it. While CHEMBASE comes in the slip case that we have all come to expect, this is a slip case with a difference. The thing is huge and defies a normal bookcase. The manual itself is a standard-size three-ring notebook containing about 20% more pages than it can really hold, so turning the pages (after one has found some place to lay it on the normally small computer stand) is quite a challenge. Aside from this quibble, the manual is excellent. Along with the manual you get a little "quick guide" to the system. This little booklet is very good and will ease the trauma of wading into the main system manual.

One of the most exciting features of this system is the ease with which complex chemical structures and reactions can be created. With a combination of a large collection of chemical structure templates that can be used for building blocks (see Figure 2 for some examples), powerful drawing modes, and absolutely amazing editing tools, the user can make short work of almost any molecule. The drawing tools and templates are all controlled by the mouse and keyed with pop-down menus.

It is a credit to the authors of this program how intuitive it all is. Like any user of a new piece of software I started experimenting with the program before I read the manual and figured out an amazing number of things just by poking around in the menus. When I stumbled onto the help system, things really went very well indeed. Unlike many such help systems, which seem oblivious to what your specific problem is, this help facility is aware of what you are trying to do and provides you with help relevant to the operation you are presently performing. It should be pointed out that this program does take a little practice and a lot of chemical intuition. There are something like 400 different menus floating around not to mention two different "views" and two different editors (molecule editor and reaction editor). However, it would be quite reasonable to think that you could be creating and saving very complex structures with only a few hours of practice. It is also worthy of note that this program is apparently robust. I put forth a modest effort to crash it and was unable to do so.

Now for a little bad news. This program is copy protected, and it takes copy protection to the limits of patience. To use it on a hard disk it must be installed. While the directions for the installation are clear, the installation is a rather tedious process and much of the tedium is related to the copy protection scheme. This program, from the standpoint of its purpose, its price, and the hardware required to run it, is for professionals, and I resent the implication of this elaborate copy protection scheme. I hope that the vendor will reconsider this position as most others have. (It was learned, as this article went to press, that the vendor has responded to this criticism. To their credit, they have removed the copy protection.)

The hardware requirements of this program are considerable. While the vendor's literature seems to imply that it could be implemented on a floppy-based system, that is only technically true. I tried it and found both the speed and the inconvenience intolerable. My evaluation was carried out on an IBM/AT clone running at 8 MHz with 640K of main memory, two floppy disk drives, a 30-Mb hard disk, and EGA graphics. A mouse is required. The review copy supplied did not support the new Microsoft bus mouse, and a serial mouse was supplied by the vendor so that this review could be carried out. The program supplied an adequate driver for the Toshiba P351 printer used and includes drivers for several other popular printers. The performance of this program was acceptable on the hardware configuration noted above, but any less computer performance or graphics resolution would not do this fine program justice. As is true with all programs that print from the graphics mode, printing is slow. A final note on disk space would be that while the basic system containing a small demonstration data base requires only about 1.2 Mb of disk space (for files in the root directory and in two separate directories, one with a subdirectory) this program would only be useful with large data bases and all that are available for purchase should be purchased with the system. Therefore, for use in a professional environment a machine with a large hard disk dedicated to this program would likely be required.

In summary, I liked this program a lot and would not hesitate to recommend it to anyone working in organic chemistry and related areas. It represents the data-base-management strategy of the future where all aspects of a collection of information including graphic representations are objects that can be manipulated, tabulated, and searched. The program is complex and therefore takes some time to learn, but the task is complex and the program's complexity simply reflects this fact and does not add to it. The documentation is first rate, the user interface is clean and intuitive, the drawing tools are superb, and the help system is really helpful. On the negative side, some improvements in the presentation would be welcome. Specifically, the use of true subscripts in empirical formulas and text and more extensive use of color would add a great deal to the presentation. Finally, the vendor has a demo kit ($49) which I have not seen but suspect that everyone who has reason to maintain a data base of organic molecules and reactions should purchase and look at. The power of this system is hard to believe and impossible to describe in detail in a brief review. I fear that the few aspects of the system described here will not convince those who have need of this system how good it really is.

APPENDIX: PRODUCT INFORMATION

Product: CHEMBASE
Price: $3500 ($975 to academic customers)

Vendor: Molecular Design Ltd., 2132 Farollon Drive, San Leandro, CA 94577. Telephone (415)-895-1313
Hardware requirements:
IBM Personal Computer (PC, PC XT, PC AT or compatibles)
512K memory (640K required with EGA graphics)
Color or monochrome monitor
Graphics interface (Hercules, IBM CGA or IBM EGA)
Mouse (Mouse Systems or Microsoft; Microsoft bus mouse NOT supported)
Two floppy disk drives
PC-DOS 2.0 or greater for IBM PC and XT, 3.0 or greater for IBM PC AT
Hardware recommendations:
Winchester disk drive (10 Mb or greater)
Dot-matrix or laser printer
Printers supported:
Epson FX, MX, RX, FX+; Toshiba P351, P1340, P1350, P135; IBM Proprinter; Hewlett-Packard Thinkjet; Apple LaserWriter; Okidata 92, 93.

LETTERS TO THE EDITOR

Dear Dr. Isenhour:

In the series of six articles on the NCI Drug Information System (DIS) published in the November 1986 JCICS, various individuals from both Fein-Marquart Associates (FMA) and the National Cancer Institute were listed as authors of various papers. These were all individuals who were directly associated with the development of the DIS, who continued to be associated with the project at the time the papers were written, and who made direct contributions to the writing of the papers. Through a major and serious oversight, however, we failed to cite extensive and vital contributions made to the development of the system by several individuals who were no longer associated with the project at the time the papers were written. These individuals, all former FMA employees, are as follows:

Dr. Frank L. Tobin, a principal in the development of the DIS design, made widespread contributions throughout the system. Dr. Tobin's present address is Smith, Kline, French Laboratories, Philadelphia, PA.

Jacques L. LaBrosse contributed significantly to the development of the Chemistry portion of the DIS. Mr. LaBrosse's present address is Balzers, Inc., Hudson, NH.

Dr. Ray E. Kutina contributed significantly to the development of the Inventory/Shipping portion of the system. Dr. Kutina's present address is Computer Sciences Corp., Silver Spring, MD.

James A. Harvey contributed significantly to the development of the database management software which forms the basis of the DIS. Mr. Harvey's present address is General Electric Co., Nashville, TN.

We regret this omission and wish to apologize for having done so.

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