product, respectively. Thus *gem*-diiodo compounds are essential for the reaction (run 5).

(4) A combination of $CrCl_3$ and zinc can be employed instead of $CrCl_2$ (method C, runs 6 and 12). However, the E/Z ratios of the olefins resulting from method C are low compared to that of those from method A or B.[20]

(5) To obtain trisubstituted olefins, two pathways were examined. One is the reaction of **3** with ketones.[7,21] The reactive 1,1-dichromioethane afforded the ethylidenation products of ketones, even of easily enolizable ones, in good yields.[22] However, yields of the olefination product of ketones with the other 1,1-dichromium reagents are rather low.[23] Another approach is the reaction of aldehyde and geminal dichromium reagent, prepared by $CrCl_2$ reduction of $RR'CI_2$. Reaction between benzaldehyde and 2,2-diiodopentane with $CrCl_2$–DMF in THF at 25 °C gave a complex mixture containing only 7% of the desired trisubstituted olefin (E/Z = 63/37).

Although the controlling mechanism for E/Z selectivity is still obscure, the mild conditions[24] and high E selectivity characterize the method as a useful alternative to the Wittig olefination.

Registry No. (*E*)-$C_5H_{11}CH$=CHMe, 13389-42-9; (*E*)-$C_{11}H_{23}CH$=CHMe, 35953-54-9; (*E*)-$Ph(CH_2)_2CH$=CHMe, 16091-23-9; (*E*)-Et_2CHCH=CHMe, 19781-63-6; (*E*)-4-(*i*-Pr)C_6H_4CH=CHMe, 27250-21-1; (*Z*)-4-(*i*-Pr)C_6H_4CH=CHMe, 27250-20-0; (*E*)-$(CH_2)_5C$=CHCH=CHMe, 1551-68-4; (*Z*)-$(CH_2)_5C$=CHCH=CHMe, 1551-67-3; (*E*)-$C_8H_{17}CH$=CHPr, 41446-55-3; (*E*)-*t*-BuCH=CHPr, 19550-75-5; (*E*)-PhCH=CHPr, 16002-93-0; (*Z*)-PhCH=CHPr, 7642-18-4; (*E*)-$C_5H_{11}CH$=CHPr-*i*, 51090-06-3; (*Z*)-$C_5H_{11}CH$=CHPr-*i*, 51090-07-4; (*E*)-PhCH=CHPr-*i*, 15325-61-8; (*Z*)-PhCH=CHPr-*i*, 15325-56-1; $PhCH=CH_2$, 100-42-5; $C_{11}H_{23}CH=CH_2$, 2437-56-1; $C_5H_{11}CHO$, 66-25-1; $C_{11}H_{23}CHO$, 112-54-9; $Ph(CH_2)_2CHO$, 104-53-0; Et_2CHCHO, 97-96-1; 4-(*i*-Pr)C_6H_4CHO, 122-03-2; $(CH_2)_5$-C=CHCHO, 1713-63-9; $C_8H_{17}CHO$, 124-19-6; *t*-BuCHO, 630-19-3; PhCHO, 100-52-7; PrCHO, 123-72-8; $MeCHI_2$, 594-02-5; $PrCHI_2$, 66587-65-3; *i*-$PrCHI_2$, 10250-55-2; *t*-$BuCHI_2$, 2443-89-2; CH_2I_2, 75-11-6; $CrCl_2$, 10049-05-5; $CrCl_3$, 10025-73-7; Zn, 7440-66-6; $(PhCH_2)_2CO$, 102-04-5; $(PhCH_2)_2C$=$CHCH_3$, 40558-71-2; $H_3C(C-H_2)_2CH$=$CH(CH_2)_4CH_3$, 19689-18-0; cyclododecanone, 830-13-7; ethylidenecyclododecane, 106161-78-8; 1-tetralone, 529-34-0; (*E*)-1-ethylidenetetralone, 106161-79-9; (*Z*)-1-ethylidenetetralone, 106161-80-2; butylidenecyclododecane, 106161-81-3.

(17) Typical procedures are as follows. (a) Method A: Anhydrous $CrCl_2$ (purchased from Aldrich Co., 0.98 g, 8.0 mmol) is suspended in THF (20 mL) under an argon atmosphere. A solution of an aldehyde (1.0 mmol) and 1,1-diiodoethane[13a] (0.56 g, 2.0 mmol) in THF (3 mL) is added at 25 °C to the suspension. After it was stirred at 25 °C for the number of hours shown in Table I, the mixture is diluted with pentane (15 mL), poured into water (40 mL), and extracted with pentane (3 × 15 mL). The organic extracts are washed with brine, dried (Na_2SO_4), and concentrated. Purification by short-column chromatography on silica gel (pentane) affords the ethylidenation product. (b) Method B: To a stirring suspension of anhydrous $CrCl_2$ (0.98 g, 8.0 mmol) in THF (20 mL) is added DMF (0.62 mL, 8.0 mmol) at 25 °C under an argon atmosphere. After 30 min of stirring, a solution of an aldehyde (1.0 mmol) and 1,1-diiodoalkane[13b] (2.0 mmol) in THF (3 mL) is added at 25 °C. The pale green suspension turns to dark green and then to a dark brown solution. (When a lump of the $CrCl_2$ complex remains at this stage, ultrasonic irradiation is effective to get a homogeneous solution.) The resulting mixture is stirred at 25 °C for an appropriate time, described in Table I. The mixture is subjected to aqueous workup (vide infra). Purification by short-column chromatography (pentane) gives the desired olefin.

(18) Nakatsukasa, S.; Takai, K.; Utimoto, K. *J. Org. Chem.* **1986**, *51*, 5045.

(19) The yields of the olefinic products were about 20% in DMF solvent, since *gem*-diiodo compounds were consumed very fast in this solvent.

(20) During the reaction in method C, 1-iodobutane, which was not observed in method A and B, was detected by GLPC.

(21) Yoshida, T. *Chem. Lett.* **1982**, 429.

(22) Reaction of cyclododecanone with 1,1-diiodoethane (2.0 equiv) and $CrCl_2$ (8.0 equiv) in THF proceeded at 25 °C for 27 h to afford ethylidenecyclododecane in 96% yield. Easily enolizable ketones, dibenzyl ketone and 1-tetralone, were converted to the corresponding ethylidenation products in 88% and 85% yield (E/Z = 16/84), respectively, after stirring at 25 °C for 8 h (ultrasonic irradiation for 4 h).

(23) Treatment of cyclododecanone with 1,1-diiodobutane and $CrCl_2$–DMF (method B) at 25 °C for 18 h gave the desired butylidenation product in 15% yield along with a 75% recovery of the unchanged ketone.

(24) Under the conditions of method B (preparation of 4-decene from hexanal and 1,1-diiodobutane in 80–90%), compounds were recovered in the following order: ethyl octanoate (97% recovery); nonanal diethylene acetal (97%); nonanenitrile (99%); 1-dodecyne (100%); 1-iodooctane (93%).

Applications of Tartrate Ester Modified Allylic Boronates in Organic Synthesis: An Efficient, Highly Stereoselective Synthesis of the C(19)–C(29) Segment of Rifamycin S†

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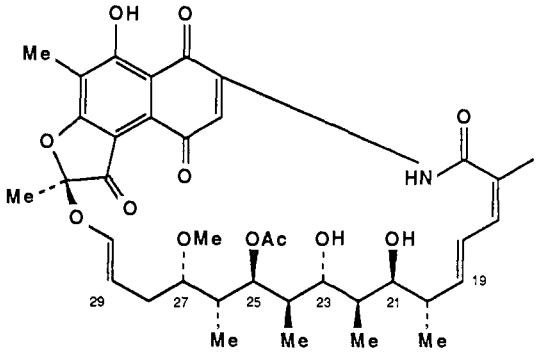
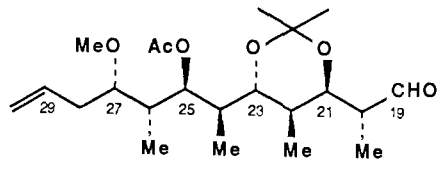
Received October 29, 1986

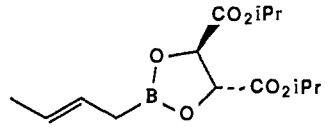
Rifamycin S (**1**) is a well-known member of the ansamycin antibiotic group.[3] We became interested in undertaking a synthesis of the stereochemically rich ansa chain (C(19)–C(29) segment, c.f., compound **2**)[4] in order to explore the applicability of tartrate ester modified allylic boronates **3** and **4**[5] as chiral *E*(O) propionate and acetate enolate equivalents in complex synthetic problems. We are pleased to report herein, therefore, that **2** has been synthesized by a 16-step synthesis that proceeds in 15% yield and with 75% overall stereoselectiviy.[6] The brevity, efficiency and selectivity of this synthesis rivals alternative acyclic approaches,[4a,e,f,h] a clear testimony to the potential of **3** and **4** as reagents for organic synthesis.



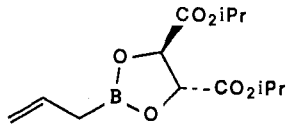
1



2



(R,R) - 3



(R,R) - 4

The synthesis of **2** (Scheme I) commenced with the reaction of (*S,S*)-**3** and chiral aldehyde (*S*)-**5**. This transformation, described in detail elsewhere,[7] is a mismatched double asymmetric reaction[8] and provides **6** as the major component of an 88:11:1 mixture. Compound **6**, isolated in 75% yield, was smoothly transformed into aldehyde **7**[9] which served as the substrate for the second crotylboronate addition reaction.[10] The combination

† This manuscript is dedicated to Professor George H. Büchi on the occasion of his 65th birthday.

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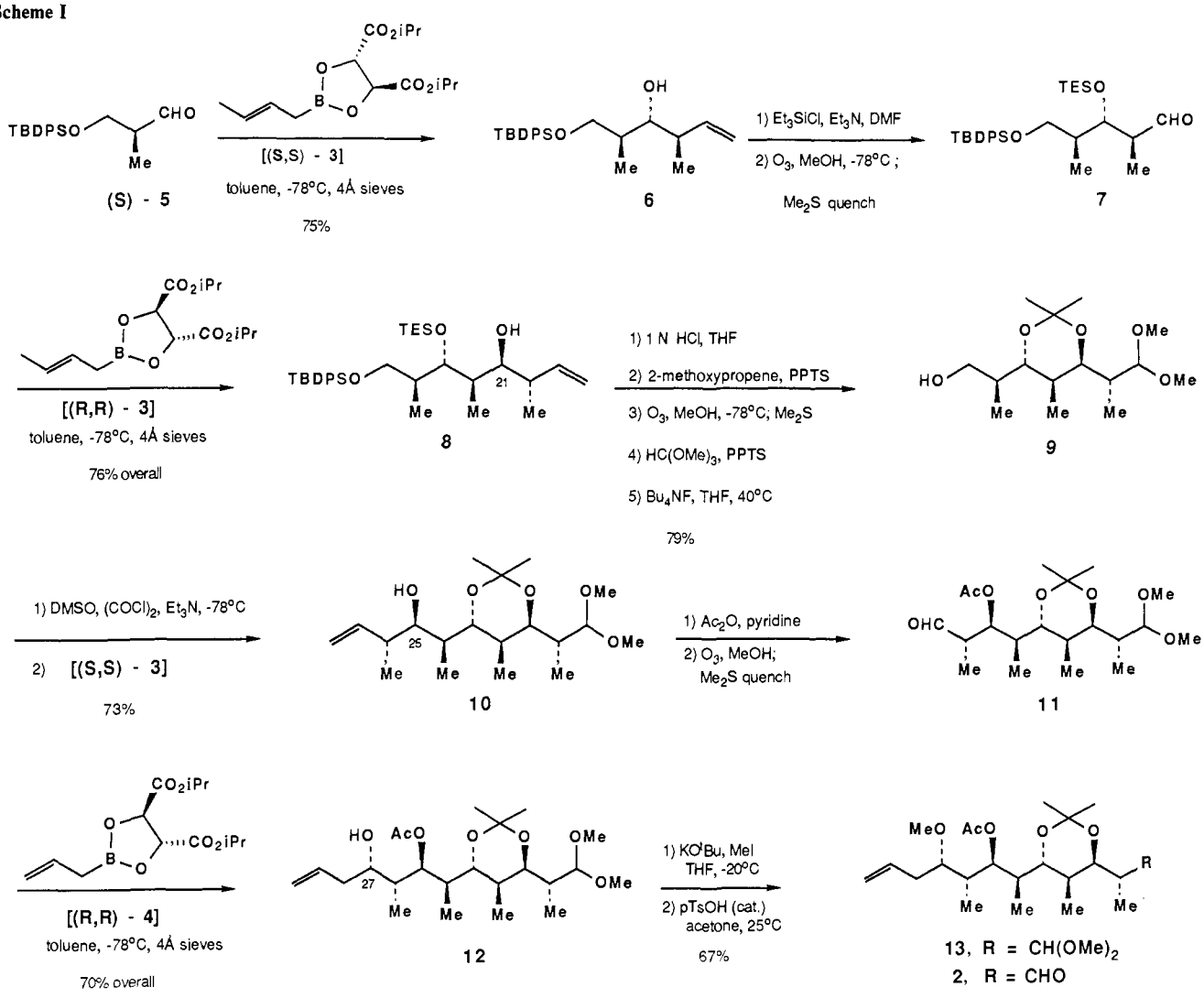
Scheme I



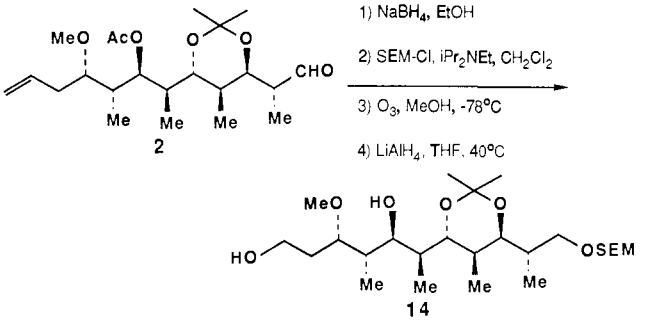
of **7** and (*R,R*)-**3** proved to be a matched pair and provided **8** in 71% yield from **6** with 98% diastereoselectivity (HPLC analysis).[11] After a series of standard functional group manipulations were performed on **8**, alcohol **9** was oxidized to the corresponding aldehyde thereby setting the stage for the third crotylboronate addition. This step also proved to be a matched double asymmetric reaction[8] with (*S,S*)-**3** as the chiral reagent, and resulted in a 95:5 mixture of **10** and the C(25) epimer (HPLC analysis). Thus, compound **10** possessing seven of the eight asymmetric centers of **2** had been assembled in very short order.

At this stage we faced a key strategic issue. Should the C(25) hydroxyl group of **10**, destined ultimately to become the acetoxy group in **2**, be protected to facilitate the C(27)–C(28) bond construction and introduction of the methoxyl group at C(27)? We reasoned that if the potentially sensitive β-acetoxy aldehyde **11** could be prepared, the subsequent reaction with (*R,R*)-**4** would proceed smoothly owing to the neutrality, high reactivity, and chemospecificity of these chiral reagents. Indeed, acylation of **10** followed by ozonolysis in MeOH (−78 °C; Me_2S quench)

(1) Fellow of the Alfred P. Sloan Foundation, 1982–1986.
(2) Present address: Department of Chemistry, Indiana University, Bloomington, Indiana 47405.
(3) (a) Rinehart, K. L., Jr.; Shield, L. S. In *Progess in the Chemistry of Organic Natural Products*; Hertz, W., Grisebach, H., Kirby, G. M., Eds.; Springer-Verlag: New York, 1976; Vol. 33, p 231. (b) Wehrli, W. *Top. Curr. Chem.* **1977**, *72*, 22. (c) Brufani, M. *Topics in Antibiotic Chemistry*, Sammes, P. G., Ed.; Wiley: New York, 1977; Vol. 1, p 91.
(4) (a) A total synthesis of rifamycin S was reported by Kishi and co-workers in 1980: Nagaoka, H.; Rutsch, W.; Schmid, G.; Iio, H.; Johnson, M. R.; Kishi, Y. *J. Am. Chem. Soc.* **1980**, *102*, 7962. Iio, H.; Nagaoka, H.; Kishi, Y. *Ibid.* **1980**, *102*, 7965. (b) For other efforts directed toward the synthesis of the ansa chain, see: (c) Corey, E. J.; Hase, T. *Tetrahedron Lett.* **1979**, *335*. (d) Nakata, M.; Takao, H.; Ikeyama, Y.; Sakai, T.; Tatsuta, K.; Kinoshita, M. *Bull. Chem. Soc. Jpn.* **1981**, *54*, 1749. (e) Nagaoka, H.; Kishi, Y. *Tetrahedron* **1981**, *37*, 3873. (f) Masamune, S.; Imperiali, B.; Garvey, D. S. *J. Am. Chem. Soc.* **1982**, *104*, 5528. (g) Nakata, M.; Enari, H.; Kinoshita, M. *Bull. Chem. Soc. Jpn.* **1982**, *55*, 3283. (h) Still, W. C.; Barrish, J. C. *J. Am. Chem. Soc.* **1983**, *105*, 2487. (i) Fraser-Reid, B.; Magdzinski, L.; Molino, B. *Ibid.* **1984**, *106*, 731. (j) Hanessian, S.; Pougney, J.-R.; Boessenkool, I. K. *Tetrahedron* **1984**, *40*, 1289. (k) Rama Rao, A. V.; Yadav, J. S.; Vidyasagar, V. *J. Chem. Soc., Chem. Commun.* **1985**, 55.
(5) (a) Roush, W. R.; Walts, A. E.; Hoong, L. K. *J. Am. Chem. Soc.* **1985**, *107*, 8186. (b) Roush, W. R.; Halterman, R. L. *Ibid.* **1986**, *108*, 294.
(6) Although alternative C–C bond-forming sequences could have been selected, we elected to pursue the route summarized in Scheme I since this maximized the number of transformations involving (*E*)-crotyl reagent **3**.
(7) Roush, W. R.; Palkowitz, A. D.; Palmer, M. A. J. *J. Org. Chem.*, in press.
(8) For a review, see: Masamune, S.; Choy, W.; Petersen, J. S.; Sita, L. R. *Angew. Chem., Int. Ed. Engl.* **1985**, *24*, 1.
(9) The spectroscopic properties (NMR, IR, mass spectrum) of all new compounds are fully consistent with the assigned structures.
(10) Each of the reactions involving chiral reagents **3** and **4** was performed by using crude aldehydes (**5**, **7**, **11**, and that derived from **9**) under the standard conditions specified in ref 5. Reactions were complete within 5 h in each case. The workup included an alkaline hydrolysis to remove diisopropyl tartrate.
(11) The minor diasteromer (2%) is epimeric with **8** at C(21).

provided crude **11** that, without purification, was immediately treated with (*R,R*)-**4** under standard conditions.[10] This reaction provided a 91:9 mixture of **12** and the C(27) epimer, from which **12** was isolated in 71% yield.[12] The requisite methyl ether was then prepared by treatment of a THF solution of **12** and excess CH_3I (−20 °C) with KO-*t*-Bu. Under these conditions an easily separated 8:1 mixture of **13** and the regioisomer resulting from acyl transfer prior to methylation was obtained (70% yield of **13**). Thus, protecting group chemistry was not required during the conversion of **10** to **13**. Finally, deprotection of **13** by exposure to catalytic *p*-TSOH in acetone completed this 16-step synthesis of **2**.

The stereochemistry of **2** was verified by correlation with a reference sample of naturally derived **14** that was kindly provided by Professor Masamune.[13] The two samples were indistinguishable by ^1H NMR (250 MHz), ^{13}C NMR (100 MHz), IR,



$[\alpha]_D$, and TLC analysis in three solvent systems, thereby confirming the stereostructure of **2** to be as shown.

Acknowledgment. This research was supported by grants from the National Institute of Health (GM 26782 and Training Grant CA 09112). We also thank Professor Masamune for providing a reference sample of naturally derived **14**.

Supplementary Material Available: Spectroscopic data and physical constants for all synthetic intermediates (8 pages). Ordering information is given on any current masthead page.

(12) The combination of **11** and (*R,R*)-**4** is a matched pair. When (*S,S*)-**4** was employed, **12** and the C(27) epimer were obtained with 35:65 selectivity.

(13) Full spectroscopic data for **14** are provided in the supplementary material to ref 4f as well as in the Ph.D. Thesis of B. Imperiali (MIT, 1983).

*Computer Software Reviews**

PMR. By K. E. Gilbert and J. J. Gajewski. SERENA Software: P.O. Box 3076, Bloomington, IN 47402-3076. List price $40.00.

PMR simulates NMR spectra for systems containing up to eight spin $^1/_2$ nuclei. It requires an IBM PC equipped with 640K of RAM and an 8087 numeric coprocessor. Although it comes with the capability to draw crude spectrum plots on a color graphics monitor, acceptable screen plots or plots on an HP plotter required a separate program from MicroPlot, Westerville, Ohio, called PC-PLOT-III to enable a PC to emulate a Tektronix 4010 terminal. The software was also successfully tested on compatible PC's including Leading Edge Model M and Zenith Z158 running with MS-DOS 2.0 and higher. The simulation program also was run successfully on a PC-AT. The software is not copy protected and can easily be transferred to a hard disk. While no documentation is supplied, the programs are self explanatory with prompts for the necessary input. It was not difficult to use and could be used readily by anyone who has a basic knowledge of NMR spectroscopy. It is not a program to teach someone how such simulated NMR spectra are calculated. However, the source code is provided on the supplied disk. There were no problems in setting up simulation problems. Calculations for a 7-spin $AA'BB'CC'X_2$ system were fast. About 5 min were required both to calculate and draw the spectrum. Less complicated spectra were calculated almost instantaneously. Longer times were required for calculations of 8-spin systems. According to Serena Software, the calculations for 8-spin systems take about 30 min. Eight-spin systems were not evaluated since there is a bug in routines used for these calculations according to Serena Software. This bug has been fixed according to Serena Software, and the fix should be incorporated in current versions of this program.

Overall, this NMR spectrum simulation program is easy to use and fast. Its capabilities are greater than similar programs commonly provided with NMR spectrometers, and it is certainly adequate for the purposes for which it is intended.

David E. Bergbreiter, *Texas A&M University*

ORGANIC FONTS. By Jerry Chapman. Modern Graphics, P. O. Box 21366, Indianapolis, IN 46221-0366. List price $79.95 (10% academic discount).

ORGANIC FONTS is a collection of three separate fonts for use with the Macintosh (512k or MacPlus) and various word processing and drawing programs. These three fonts, OrganicFont, AliphaticFont, and RingFont, are representations of many of the symbols and structural subunits that organic chemists commonly use in describing structural information. In addition, an extensive collection of Greek characters is provided in AliphaticFont. These fonts come supplied either on a 400K single-sided or 800K double-sided floppy. On the 800K version, these fonts are already incorporated within a system which can then be copied to an applications disk. However, the size of these fonts precludes their being incorporated along with the system on the smaller capacity disk.

These fonts are accessed as any other font within a word processing or drawing application. The pulldown menu for "font" will show the addition of these three and allow their selection and use. Unfortunately, becasue of the rather large size of these fonts the key caps desk accessory is of limited value in viewing them, and it is most helpful to keep handy a font chart (supplied). The major use of these fonts would appear to be within word processing programs for including structural information within text lines. Although it is somewhat laborious to use these fonts in this fashion, nonetheless with experience and especially when the information is repetitive where the typist can become familiar with the key relationships, this method may save time over others that are available.

For more detailed drawing, I find the fonts quite deficient for a number of reasons. First and as pointed out by the vendor, these fonts really do not work well with the Laserwriter and although the Imagewriter does a nice job, it appears that more and more people are now availing themselves of at least access to the higher quality available from the laser printer. In addition, I find that the fonts have intrinsic difficulties with them such as their shape. For instance, the six-membered ring is not a perfect hexagon nor is the five-membered ring a pentagon. The resulting disparity in the length of the various sides of the polygons (as well as their angular relationships) led to difficulty in fusing rings together other than in the most straightforward fashion. Alternate, "perfect" pentagons and hexagons are supplied in the 18 pt size (but no 24 pt) although these print with rough appearing diagonals even on the Laserwriter with smoothing. Other structures have the same problem—that all but vertical, horizontal, and 45° lines are printed with a "stepped" appearance even with smoothing on the Laserwriter. In addition, it appears not possible to invert or rotate some of the characters without losing information, and of course, included text such as the "N" in the pyridine symbol is also rotated. Finally, the use of these fonts within framework or MacDraw (or other object-oriented drawing programs) is limited because of the inability to edit fonts within such applications. While of course various areas may be masked by, for instance, the addition of characters representing elements, the fundamental shapes cannot be varied. Thus, even if one were to use these fonts with MacDraw, one would still have to have accessible to set of rings and symbols that could be readily modified for more freehand representations in complex systems.

Overall then, I find that the fonts can be of utility within the framework of word processing applications where the time and effort required to set up a simultaneous drawing regime with switcher exceeds the value obtained from the inclusion of graphic information. Again, an experienced typist will soon learn the more common key stroke sequences necessary to include rather complex structures. On the other hand, the more complex and normal tasks of structural information are not really properly addressed by these fonts.

*Unsigned reviews are by the Computer Software Review Editor.