

or when the computer system was engaged in developmental work. For example, to build the library of low resolution mass spectral data of sterols, several LRMS of new compounds were obtained by GC/MS. Also, in collaboration with Dr. Mefflin, Dept. of Cardiology, we have investigated the use of specific ion monitoring as a tool for the identification of a new drug and its primary metabolite in human serum. Spectra of porphyrins have been obtained for Dr. Collman's group, Dept. of Chemistry, in studies of model systems for oxygen transport. We have obtained spectra of heart beat stimulants (digitoxigenins) for Prof. Kalman in Pharmacology, to verify identities of these compounds.

3.4 Applications of Programs by External Scientists

The DENDRAL project, one of the major users of the SUMEX-AIM computer facility, has formed a small community of regular, remote users. This "exodendral" community has continued to provide valuable contributions to program development, although the growth of this community has had to be slowed in response to increasing demands by other projects upon the SUMEX-AIM facility. As an example, for the months of September 1975 to February 1976, the number of CPU hours used by exodendral persons amounted to at least 8 percent of the CPU hours used by the DENDRAL project. There are currently four remote chemist-users whose groups regularly use CONGEN in their day to day work. Additionally, there are several remote users who use their accounts on an occasional basis, or who access SUMEX-AIM via the GUEST mechanism.

The SUMEX-AIM facility has grown markedly in number of projects over the past year. Due to this increase in system loading; the DENDRAL project, which had previously been able to offer trial usage of its programs to almost any chemist who expressed a need to use the programs, has found itself in the unfortunate position of having to carefully screen potential collaborators. Those chemists who have been granted access, have been requested to restrict their usage to off-prime time hours. CONGEN, the DENDRAL program which receives most of this usage, has evolved in a manner designed to try to remedy the system loading problem which can be created by the enthusiasm of its chemist-users. Since a typical, long GENERATE, PRUNE or IMBED within CONGEN can be very time consuming, as well as a voracious consumer of CPU cycles, a provision to permit a user to easily take advantage of SUMEX-AIM's off-hour batch processing has been implemented. A CONGEN user can now interactively set up his problem, and when ready to commence with a time consuming procedure, can, from within CONGEN, request automatic submission to BATCH, to be run late at night. The CONGEN users also benefit from this ability, in that they no longer must leave a terminal tied up during the sometimes hour-long compute times. This development then, can be viewed as responding to CONGEN users' needs as well as being an effort by the DENDRAL project to be conscientious in its resource-sharing responsibilities.

Following is a brief summary of the major users of CONGEN over the past year, as well as notes on chemists who contacted us about trial usage of the programs.

Dr. Clair Cheer, Professor of Chemistry, University of Rhode Island, Kingston, Rhode Island. Dr. Cheer is on sabbatical leave from the University of Rhode Island to the Stanford University Chemistry Department. He has, in recent work with Professor Djerassi's group, demonstrated the utility of CONGEN in the identification of (+)-Palustrol, a tricyclic sesquiterpene alcohol from the marine Xeniid *Cespitularia viridis* [57]. Dr. Cheer plans to continue his work with CONGEN once he returns to Rhode Island in December.

Dr. Jon Clardy, Professor of Chemistry, Iowa State University. Dr. Clardy read of CONGEN in an article appearing in the Journal of the American Chemical Society and contacted Professor Djerassi concerning the possibility of using the program from Iowa. He was offered GUEST access during the winter of 1975, but has not yet had an opportunity to evaluate the potentials of the program.

Dr. Douglas Dorman, Eli Lilly Corp., Indianapolis, Indiana. Dr. Dorman's research involves the identification and characterization of drug related compounds by chemical and spectroscopic methods. Using primarily the NMR and C13 NMR spectra of these various compounds, Dr. Dorman has found CONGEN to be a time-saving adjunct to his structure elucidation work (see letter in Appendix B).

Dr. H.M. Fales, National Heart and Lung Institute, Bethesda, Maryland. Dr. Fales, along with Doctors Sanford Markey and Peter Roller had a joint account set up for them in April of 1975. Most of the use of this account came during late summer at which time Dr. Fales experimented with the use of CONGEN for assistance in the elucidation of the structure of a novel quinolinone, known to be tumorogenic. Although the crystal structure had been solved at the time of his usage of CONGEN, Dr. Fales felt that the program produced an abundance of useful ideas. The main problem initially faced by Dr. Fales in using CONGEN was in getting a feel for problem size and the effects of various constraint types.

Professor Kenneth Gash, California State College at Dominguez Hills. Professor Gash is a professor of chemistry who is on temporary leave to Small College, the research branch of Dominguez Hills. Dr. Gash did some of the original work, in 1965, with Professor Morton Munk, on the structure elucidation program developed at Arizona State University. Dr. Gash has been reviewing some of the problems originally done with Munk's program and has been studying input, output and constraint capabilities found in CONGEN. He has generally concluded that if system response time was better, CONGEN provides an excellent tool for the chemist to use in structure elucidation problems.

Mr. Neil A. B. Gray, King's College, Cambridge, England. Mr. Gray, following a three week visit to the Stanford chemistry department, requested copies of all the current DENDRAL programs to be sent to him in England. He is a chemist who has been working in areas related to developments in various of the DENDRAL programs, and hopes to be able to benefit from work already done at Stanford. His current interest in intelligent constraint application during structure elucidation merges well with one of the directions in which CONGEN is tending to develop. Unfortunately, Mr. Gray does not have access to an ARPANET or TYMNET node to access SUMEX-AIM directly. Therefore, all collaboration has had to be carried on by mail.

Dr. Jerrold Karliner, Ciba Geigy Corporation, Ardsley, New York. Dr. Karliner and his research group at Ciba-Geigy have become regular users of CONGEN in their day-to-day operation of a research laboratory. Dr. Karliner is a completely self-taught user of CONGEN, and has served to encourage others to request permission to use this program. A letter from Dr. Karliner, describing his usage, is attached in Appendix B.

Dr. Milton Levenberg, Abbott Laboratories, Chicago, Illinois. Dr. Levenberg has been an occasional user of CONGEN as an adjunct to his work as head of a mass spectrometry laboratory. Primary usage has been to provide assurance that the proposal of a structure for a compound on the basis of chemical and spectroscopic evidence has not overlooked other plausible possibilities.

Dr. Gino Marco, Ciba Geigy Corporation, Greensboro, North Carolina. Dr. Marco heard about CONGEN during a company seminar presented by Dr. Karliner. After a brief trial use via the GUEST mechanism, Dr. Marco requested an account for use by his group of metabolic and organic chemists. Dr. Marco's research group studies unknown insect metabolites by micro-IR and micro-NMR methods, and attempts structure elucidation based on these forms of spectroscopic analysis. Testing the utility of the program before implementing it for day to day use, Dr. Marco discovered that CONGEN could greatly narrow the alternatives of complex metabolic conjugates which had to be considered in a typical elucidation problem. They have established a leased line to the nearest TYMNET node, and expect increased CONGEN usage in the future.

Dr. David Pensak, DuPont de Nemours and Company, Wilmington, Delaware. Indirectly requested information about CONGEN through a letter written by his immediate superior to Professor Lederberg. Dr. Pensak has been offered GUEST access, and has just begun a potential collaboration with a DENDRAL group which is studying model builders and their production of reliable geometries for certain types of molecules.

Professor Manfred Wolff, University of California at San Francisco. Dr. Wolff is chairman of the Department of

Pharmacological Chemistry, and inquired as to the possibilities of accessing SUMEX-AIM and appropriate programs for a faculty which is interested in many aspects of drug design and drug action, ranging from physical chemistry to purely biological studies. He has been encouraged to use GUEST access to explore CONGEN, although he has taken no action up to the present time.

We have cases where requests for GUEST access had to be denied due to system loading considerations. We made these decisions according to the extent to which the requested use would fit within the research guidelines of SUMEX/AIM and our own stated criteria from the 1973 proposal to NIH. In one case, for instance, the use was for an individual's report on potential educational uses of CONGEN.

The following two chemists have taken advantage of CONGEN by sending appropriate data and information to Stanford.

Professor L. Minale, Laboratorio per la Chimica di Molecole di Interesse Biologico del C.N.R., Napoli, Italy. Professor Minale has been collaborating with a member of the DENDRAL staff on the solution of the structure of the cyclic diether lipids from an unusual, very thermophilic bacterium (J. C. S. Chem. Comm. 543, 1974). Application of CONGEN resulted in five final candidate structures, several of which had not previously been considered. Work is currently underway to chemically differentiate the possibilities.

Professor Kogi Nakanishi, Department of Chemistry, Columbia University. Professor Nakanishi is one of the most active and productive persons engaged in structure elucidation activities. He has developed an active interest in CONGEN and is collaborating with us on several novel problems. One of these problems has involved the structure of the active component of defense secretions of an insect (termite). Other defense secretion components are under investigation as we explore structural alternatives based on current data.

3.5 Export of GC/MS Programs to Other Sites.

There has been a demand for the GC/LRMS programs developed for data resolution and cleanup [61], and in the past several months these programs have been distributed, upon request, to five different groups. Each group was supplied with a tape, in a format appropriate to the type of computer system they were using, containing the cleanup program, as well as extensive documentation describing the program, related file structure and the required dependent utility programs.

The following research groups have already received their copies of these programs:

Professor G. Eglinton, University of Bristol, England.

Dr. Tom Elwood, Department of Chemistry, Univ. of Utah.

Dr. J. Lawless, Ames Research Center, California.

Dr. Charles Sweeley, Dept. of Biochemistry, Michigan State University.

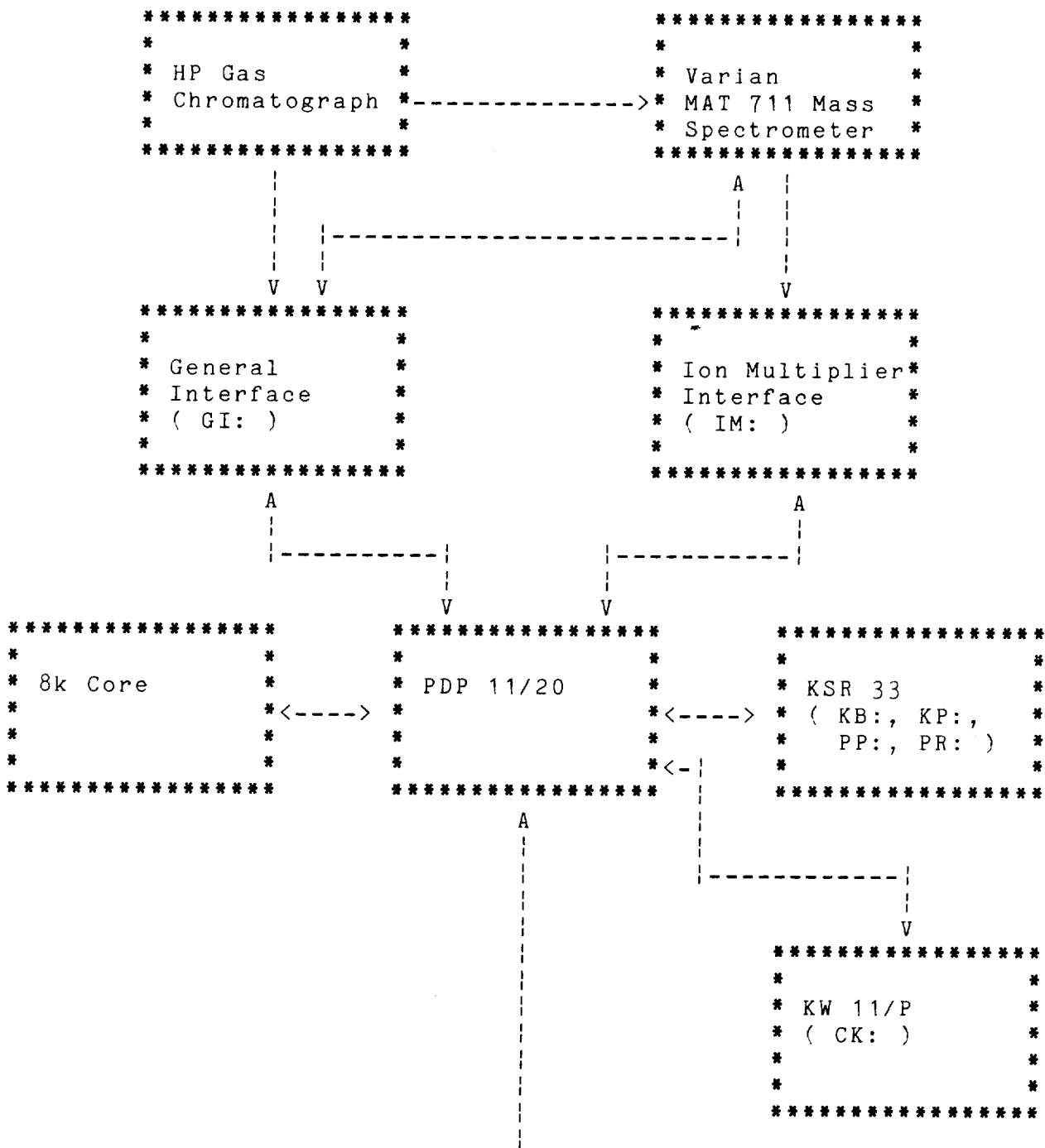
Mr. J. R. Wilcox, AEI Scientific Apparatus Inc., Elmsford, New York.

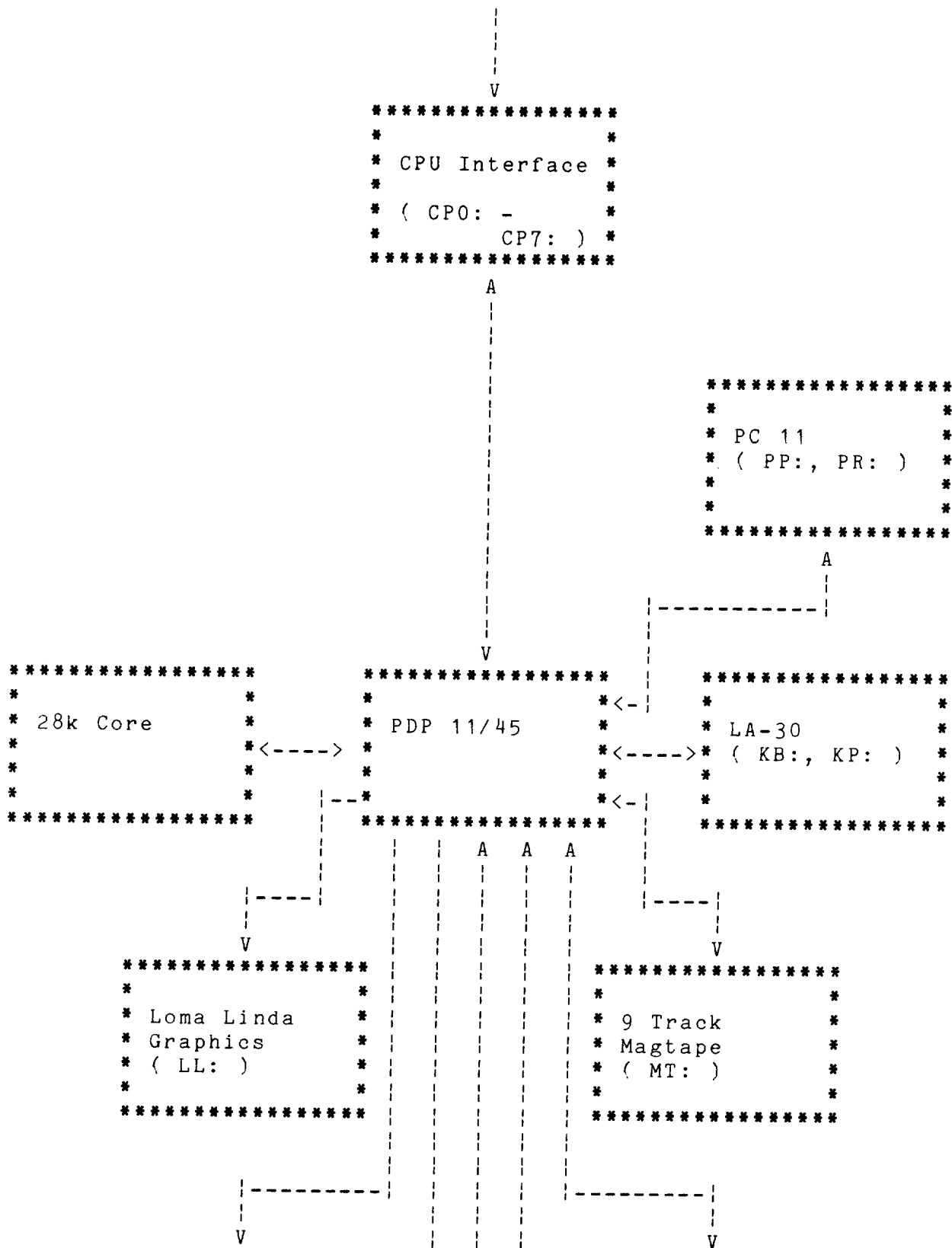
Dr. Philip Fishman, Department of Biochemistry, Washington University School of Medicine at St. Louis, Missouri has contacted us for further information concerning computer resolution of GC/MS elutants. He has been provided with the necessary information and invited to request the exportable versions of the programs.

4 BIBLIOGRAPHY

See Section II-D, SUMMARY OF PUBLICATIONS, for a listing of publications by this project.

Figure 1. Current Hardware Configuration





```
*****
*
* Line Printer *
* ( LP: ) *
*
*
*****
```

```
*****
*
* Disk Drives *
* ( DK0: - *
*      DK3: ) *
*
*
*****
```

V

V

```
*****
*
* Calcomp *
* Graphics *
* ( CC: ) *
*
*****
```

```
*****
*
* KW 11/L *
*
*
*****
```

V

```
*****
*
* TTY line to *
* PDP 10 *
*
*****
```


Appendix A. Interrupt Features in a Sample CONGEN Run

```
.
.
(program session has been in progress)
.
GENERATE
DO YOU WISH TO PRUNE WHILE GENERATING?(Y FOR YES):Y
SHALL I USE THE GLOBAL CONSTRAINT LIST?(Y FOR YES):Y
.
.
(computing)
.
.
S
17 structures have been generated so far
Shall I draw some?(Y for yes):Y
FROM:3
TO:3

3
  C
  =  P
C=C-C-C=H
  N
More?(Y for yes):N
Normal computation will now resume
.
.
27 STRUCTURES WERE GENERATED
.
(session continues)
.
IMBED
SUPERATOM NAME:PHN
DO YOU WISH TO PRUNE WHILE IMBEDDING?(Y FOR YES):N
.
.
(computing)
.
.
I
structure 8 of the original 19 is undergoing imbedding;
13 structures have been obtained
.
.
(computing continues)
.
.
32 STRUCTURES WERE OBTAINED
DRAWSOME
FROM:4
.
.
```

Appendix B. Letters from Collaborators

LILLY RESEARCH LABORATORIES

DIVISION OF ELI LILLY AND COMPANY • INDIANAPOLIS, INDIANA 46206 • TELEPHONE (317) 636-2211

May 6, 1976

Dr. Ray Carhart
Department of Computer Sciences
Stanford University
Stanford, California 94305

Dear Ray:

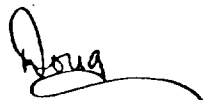
We are pleased to have an opportunity to offer our support and encouragement of your CONGEN effort.

We are using CONGEN to aid us in the solution of current structure elucidation problems. When used at an early stage, we find that the program is invaluable in suggesting the various compound types which are consistent with the extant data. In one case, for example, CONGEN generated a list of possible heteroaromatic ring systems. Such a list is particularly useful in the elucidation of the structures of pharmaceutical molecules, in that it allows us to correlate these possibilities with the physical and biological properties of a vast number of known pharmaceuticals.

In short, we have been quite pleased with our experience with CONGEN. Owing to possible security problems, we have not used the program as much as we would like. If the program were available in exportable form, I believe that usage would increase dramatically. Probably the full potential of the program will not be realized until this occurs. Even in its present form, however, CONGEN is a valuable contribution to chemistry.

Sincerely,

LILLY RESEARCH LABORATORIES



Douglas E. Dorman, Ph.D.
Physical Chemistry Research
Department MC525

CIBA-GEIGY Corporation
Ardsley, New York 10502
Telephone 914 478 3131

CIBA—GEIGY

April 19, 1976

Professor Carl Djerassi
Department of Chemistry
Stanford University
Stanford, California 94305

Dear Professor Djerassi:

Thank you for permitting us to use the CONGEN program for the past year. We have used this program only for the most demanding structure problems and therefore have not been a heavy user of the system. However, when utilized, we have found the CONGEN program to be a valuable and effective aid for structure elucidation problems.

We have used CONGEN to provide assurance that once a structure has been proposed on the basis of chemical and spectroscopic analysis that other, plausible structures have not been overlooked, thereby providing a greater confidence limit to our structural proposals. We have also utilized the program to determine possible structures when the analytical data does not provide a unique structure, and in this manner acquire additional chemical structures for consideration. Both approaches represent assets to structure determination work.

Clearly, the scope of CONGEN would be extended by making it available to other industrial chemists involved with determining structures of organic compounds. As you know, the industrial setting demands accurate results by the most rapid and economical means available. Exposing CONGEN to a wider range of industrial chemists would provide your staff with more experience with diverse structure problems and hence extend the versatility and utility of the programs. However, in order to attain more participation, the computer

Professor Djerassi

-2-

April 19, 1976

system would have to be made more readily accessible, especially during peak hours. We have been fortunate in this regard since the time zone difference between Stanford and Ardsley enables us to use CONGEN early in the morning when few others are using the SUMEX programs. However, when we attempt to use the program later in the day, the system becomes fairly slow, to the point where at times we find it more economical to simply log off and resume the following morning.

We consider CONGEN as another complementary structure elucidation method at CIBA-GEIGY and look forward to its continued use in the future.

Sincerely yours,



Jerrold Karliner Ph.D.
Group Leader
Analytical Research Department

Table I. Marine Sterol Standards

		4-DEMETHYL MARINE STEROIDS						Sept. 1975	
Nuclei	Side Chain	A		B		C		D	
		10	11	10	11	10	11	10	11
	A-4	A-3 ex M. Kikuyama	A-2 ex M. Kikuyama	A-1 ex M. Kikuyama				D-20	E-8
	A-18 11-8-18	A-11 11-8-D-11	A-5 11-C-7	A-15 ex L.J.G. and	A-16			E-1	E-9
	A-19 ex R. M. Thayer	A-12 ex L.J.G. and	A-6					E-2 *	E-9
			A-7						
		A-13	A-8 11-A-11		A-17				
	A-20	A-14 ex M. Kikuyama	A-9 ex M. Kikuyama	A-10 ex L.J.G. and					
			B-11 ex M. Kikuyama ex BA Kikuyama	B-3 11-D-6	B-16			E-3	E-10
	B-20	B-12	B-4	B-17					
	C-1								
	C-2 11-B-1	B-13	B-5	B-18				E-4	E-11
	C-3	B-14 ex M. Kikuyama ex BA Kikuyama	B-6 11-A-16	B-19					
			B-7						
			B-8 ex L.J.G. and						
		C-14 KALLAZAWA	B-9						
	C-4 ex L.J.G. and	B-15 ex L.J.G. and	B-10 11-A-12					E-5	
	D-8 11-B-17	C-18	C-5 11-B-16	D-4				E-6	E-12
	D-9	C-19 ex M. Kikuyama ex BA Kikuyama	C-6 11-D-3	D-5 ex M. Kikuyama ex BA Kikuyama					
		C-20 ex M. Kikuyama ex BA Kikuyama	C-7 11-A-11	D-6 ex M. Kikuyama ex BA Kikuyama				E-7	E-13
		D-1	C-8 11-B-19	D-7					
D-10	D-2	C-9 11-C-5							
		C-10 ?							
D-11	D-3 ex L.J.G. and	C-11 ex L.J.G. and							
		C-12 ex L.J.G. and							
		C-13							
		C-14							
		C-15							
		C-16							
		C-17							
	D-13	D-12 +							
D-19 11-B-5	D-18	D-14 11-B-9							
		D-15							
		D-16							
		D-17							

indicates that at least a 1 mg sample is contained in the sample box.
 Shaded boxes indicate sterols which have not been found in marine sources.
 indicates C-24 epimers indistinguishable by GC-MS.
 indicates a grouping of sterol side chains of identical carbon number: 7,8,9, 10, and 11.
 * Note that this side chain contains 10 carbons rather than the 11 indicated by position within bracket.
 * Mass Spectrum obtained

TABLE II
 Evaluation of Several Fucosterol
 (Marine Algae Sterol) Mass Spectra from the
 Djerassi Mass Spectral Files

LIBRARY SEARCH REPORT FOR EXPERIMENT 21
 SEARCHING 25 SPECTRA IN MARINE ON DK2

(1) SPEC #	0	RETIND	0	MOLION	CANDS:	0	0	0	0	0	CR	0		
					AMPLITUDES:	0	0	0	0	0				
RK	RAW	AVG	RETIND	MOL	CHEMICAL NAME							CR	MASTER #	SRC
999	87	0	0	412	(24E)-STIGMASTA-5,24(28)-DIEN-3BETA-OL							0	MARINE	18 6
729	62	0	0	412	(24E)-STIGMASTA-5,24(28)-DIEN-3BETA-OL							0	MARINE	21 6
689	51	0	0	426	(24Z)-24-PROPYLIDENECHOLEST-5-EN-3BETA-OL							0	MARINE	25 6
578	44	0	0	412	(24E)-STIGMASTA-5,24(28)-DIEN-3BETA-OL							0	MARINE	19 6
544	67	0	0	412	(24E)-STIGMASTA-5,24(28)-DIEN-3BETA-OL							0	MARINE	20 6

(2) SPEC #	0	RETIND	0	MOLION	CANDS:	0	0	0	0	0	CR	0		
					AMPLITUDES:	0	0	0	0	0				
RK	RAW	AVG	RETIND	MOL	CHEMICAL NAME							CR	MASTER #	SRC
999	76	0	0	412	(24E)-STIGMASTA-5,24(28)-DIEN-3BETA-OL							0	MARINE	19 6
680	51	0	0	412	(24E)-STIGMASTA-5,24(28)-DIEN-3BETA-OL							0	MARINE	21 6
574	50	999	0	412	(24E)-STIGMASTA-5,24(28)-DIEN-3BETA-OL							0	MARINE	18 6

(3) SPEC #	0	RETIND	0	MOLION	CANDS:	0	0	0	0	0	CR	0		
					AMPLITUDES:	0	0	0	0	0				
RK	RAW	AVG	RETIND	MOL	CHEMICAL NAME							CR	MASTER #	SRC
999	123	0	0	412	(24E)-STIGMASTA-5,24(28)-DIEN-3BETA-OL							0	MARINE	20 6
781	61	999	0	412	(24E)-STIGMASTA-5,24(28)-DIEN-3BETA-OL							0	MARINE	18 6
694	59	0	0	412	(24E)-STIGMASTA-5,24(28)-DIEN-3BETA-OL							0	MARINE	21 6

II.D. SUMMARY OF PUBLICATIONS

DENDRAL PUBLICATIONS

- (1) J. Lederberg, "DENDRAL-64 - A System for Computer Construction, Enumeration and Notation of Organic Molecules as Tree Structures and Cyclic Graphs", (technical reports to NASA, also available from the author and summarized in (12)). (1a) Part I. Notational algorithm for tree structures (1964) CR.57029 (1b) Part II. Topology of cyclic graphs (1965) CR.68898 (1c) Part III. Complete chemical graphs; embedding rings in trees (1969)
- (2) J. Lederberg, "Computation of Molecular Formulas for Mass Spectrometry", Holden-Day, Inc. (1964).
- (3) J. Lederberg, "Topological Mapping of Organic Molecules", Proc. Nat. Acad. Sci., 53:1, January 1965, pp. 134-139.
- (4) J. Lederberg, "Systematics of organic molecules, graph topology and Hamilton circuits. A general outline of the DENDRAL system." NASA CR-48899 (1965)
- (5) J. Lederberg, "Hamilton Circuits of Convex Trivalent Polyhedra (up to 18 vertices), Am. Math. Monthly, May 1967.
- (6) G. L. Sutherland, "DENDRAL - A Computer Program for Generating and Filtering Chemical Structures", Stanford Artificial Intelligence Project Memo No. 49, February 1967.
- (7) J. Lederberg and E. A. Feigenbaum, "Mechanization of Inductive Inference in Organic Chemistry", in B. Kleinmuntz (ed) Formal Representations for Human Judgment, (Wiley, 1968) (also Stanford Artificial Intelligence Project Memo No. 54, August 1967).
- (8) J. Lederberg, "Online computation of molecular formulas from mass number." NASA CR-94977 (1968)
- (9) E. A. Feigenbaum and B. G. Buchanan, "Heuristic DENDRAL: A Program for Generating Explanatory Hypotheses in Organic Chemistry", in Proceedings, Hawaii International Conference on System Sciences, B. K. Kinariwala and F. F. Kuo (eds), University of Hawaii Press, 1968.
- (10) B. G. Buchanan, G. L. Sutherland, and E. A. Feigenbaum, "Heuristic DENDRAL: A Program for Generating Explanatory Hypotheses in Organic Chemistry". In Machine Intelligence 4 (B. Meltzer and D. Michie, eds) Edinburgh University Press (1969), (also Stanford Artificial Intelligence Project Memo No. 62, July 1968).
- (11) E. A. Feigenbaum, "Artificial Intelligence: Themes in the Second Decade". In Final Supplement to Proceedings of the

IFIP68 International Congress, Edinburgh, August 1968 (also Stanford Artificial Intelligence Project Memo No. 67, August 1968).

- (12) J. Lederberg, "Topology of Molecules", in The Mathematical Sciences - A Collection of Essays, (ed.) Committee on Support of Research in the Mathematical Sciences (COSRIMS), National Academy of Sciences - National Research Council, M.I.T. Press, (1969), pp. 37-51.
- (13) G. Sutherland, "Heuristic DENDRAL: A Family of LISP Programs", Stanford Artificial Intelligence Project Memo No. 80, March 1969.
- (14) J. Lederberg, G. L. Sutherland, B. G. Buchanan, E. A. Feigenbaum, A. V. Robertson, A. M. Duffield, and C. Djerassi, "Applications of Artificial Intelligence for Chemical Inference I. The Number of Possible Organic Compounds: Acyclic Structures Containing C, H, O and N". Journal of the American Chemical Society, 91.
- (15) A. M. Duffield, A. V. Robertson, C. Djerassi, B. G. Buchanan, G. L. Sutherland, E. A. Feigenbaum, and J. Lederberg, "Application of Artificial Intelligence for Chemical Inference II. Interpretation of Low Resolution Mass Spectra of Ketones". Journal of the American Chemical Society, 91:11 (May 21, 1969).
- (16) B. G. Buchanan, G. L. Sutherland, E. A. Feigenbaum, "Toward an Understanding of Information Processes of Scientific Inference in the Context of Organic Chemistry", in Machine Intelligence 5, (B. Meltzer and D. Michie, eds) Edinburgh University Press (1970), (also Stanford Artificial Intelligence Project Memo No. 99, September 1969).
- (17) J. Lederberg, G. L. Sutherland, B. G. Buchanan, and E. A. Feigenbaum, "A Heuristic Program for Solving a Scientific Inference Problem: Summary of Motivation and Implementation", Stanford Artificial Intelligence Project Memo No. 104, November 1969.
- (18) C. W. Churchman and B. G. Buchanan, "On the Design of Inductive Systems: Some Philosophical Problems". British Journal for the Philosophy of Science, 20 (1969), pp. 311-323.
- (19) G. Schroll, A. M. Duffield, C. Djerassi, B. G. Buchanan, G. L. Sutherland, E. A. Feigenbaum, and J. Lederberg, "Application of Artificial Intelligence for Chemical Inference III. Aliphatic Ethers Diagnosed by Their Low Resolution Mass Spectra and NMR Data". Journal of the American Chemical Society, 91.
- (20) A. Buchs, A. M. Duffield, G. Schroll, C. Djerassi, A. B.

- Delfino, B. G. Buchanan, G. L. Sutherland, E. A. Feigenbaum, and J. Lederberg, "Applications of Artificial Intelligence For Chemical Inference. IV. Saturated Amines Diagnosed by Their Low Resolution Mass Spectra and Nuclear Magnetic Resonance Spectra", *Journal of the American Chemical Society*, 92, 6831 (1970).
- (21) Y.M. Sheikh, A. Buchs, A.B. Delfino, G. Schroll, A.M. Duffield, C. Djerassi, B.G. Buchanan, G.L. Sutherland, E.A. Feigenbaum and J. Lederberg, "Applications of Artificial Intelligence for Chemical Inference V. An Approach to the Computer Generation of Cyclic Structures. Differentiation Between All the Possible Isomeric Ketones of Composition C₆H₁₀O", *Organic Mass Spectrometry*, 4, 493 (1970).
- (22) A. Buchs, A.B. Delfino, A.M. Duffield, C. Djerassi, B.G. Buchanan, E.A. Feigenbaum and J. Lederberg, "Applications of Artificial Intelligence for Chemical Inference VI. Approach to a General Method of Interpreting Low Resolution Mass Spectra with a Computer", *Helvetica Chimica Acta*, 53, 1394 (1970).
- (23) E.A. Feigenbaum, B.G. Buchanan, and J. Lederberg, "On Generality and Problem Solving: A Case Study Using the DENDRAL Program". In *Machine Intelligence 6* (B. Meltzer and D. Michie, eds.) Edinburgh University Press (1971). (Also Stanford Artificial Intelligence Project Memo No. 131.)
- (24) A. Buchs, A.B. Delfino, C. Djerassi, A.M. Duffield, B.G. Buchanan, E.A. Feigenbaum, J. Lederberg, G. Schroll, and G.L. Sutherland, "The Application of Artificial Intelligence in the Interpretation of Low-Resolution Mass Spectra", *Advances in Mass Spectrometry*, 5, 314 (1971),
- (25) B.G. Buchanan and J. Lederberg, "The Heuristic DENDRAL Program for Explaining Empirical Data". In proceedings of the IFIP Congress 71, Ljubljana, Yugoslavia (1971). (Also Stanford Artificial Intelligence Project Memo No. 141.)
- (26) B.G. Buchanan, E.A. Feigenbaum, and J. Lederberg, "A Heuristic Programming Study of Theory Formation in Science." In proceedings of the Second International Joint Conference on Artificial Intelligence, Imperial College, London (September, 1971). (Also Stanford Artificial Intelligence Project Memo No. 145.)
- (27) Buchanan, B. G., Duffield, A.M., Robertson, A.V., "An Application of Artificial Intelligence to the Interpretation of Mass Spectra", *Mass Spectrometry Techniques and Appliances*, G. W. A. Milne, Ed., John Wiley & Sons, Inc., 1971, p. 121.
- (28) D.H. Smith, B.G. Buchanan, R.S. Engelmores, A.M. Duffield, A.

- Yeo, E.A. Feigenbaum, J. Lederberg, and C. Djerassi, "Applications of Artificial Intelligence for Chemical Inference VIII. An Approach to the Computer Interpretation of the High Resolution Mass Spectra of Complex Molecules. Structure Elucidation of Estrogenic Steroids", Journal of the American Chemical Society, 94, 5962 (1972).
- (29) B.G. Buchanan, E.A. Feigenbaum, and N.S. Sridharan, "Heuristic Theory Formation: Data Interpretation and Rule Formation". In Machine Intelligence 7, Edinburgh University Press (1972).
- (30) J. Lederberg, "Rapid Calculation of Molecular Formulas from Mass Values". Journal of Chemical Education, 49, 613 (1972).
- (31) H. Brown, L. Masinter, and L. Hjelmeland, "Constructive Graph Labeling Using Double Cosets". Discrete mathematics, 7, 1 (1974). (Also Computer Science Memo 318, 1972).
- (32) B. G. Buchanan, Review of Hubert Dreyfus' "What Computers Can't Do: A Critique of Artificial Reason", Computing Reviews (January, 1973). (Also Stanford Artificial Intelligence Project Memo No. 181)
- (33) D. H. Smith, B. G. Buchanan, R. S. Engelmores, H. Aldercreutz and C. Djerassi, "Applications of Artificial Intelligence for Chemical Inference IX. Analysis of Mixtures Without Prior Separation as Illustrated for Estrogens". Journal of the American Chemical Society 95, 6078 (1973).
- (34) D. H. Smith, B. G. Buchanan, W. C. White, E. A. Feigenbaum, C. Djerassi and J. Lederberg, "Applications of Artificial Intelligence for Chemical Inference X. Intsum. A Data Interpretation Program as Applied to the Collected Mass Spectra of Estrogenic Steroids". Tetrahedron, 29, 3117 (1973).
- (35) B. G. Buchanan and N. S. Sridharan, "Rule Formation on Non-Homogeneous Classes of Objects". In proceedings of the Third International Joint Conference on Artificial Intelligence (Stanford, California, August, 1973). (Also Stanford Artificial Intelligence Project Memo No. 215.)
- (36) D. Michie and B.G. Buchanan, "Current Status of the Heuristic DENDRAL Program for Applying Artificial Intelligence to the Interpretation of Mass Spectra", in "Computers for Spectroscopy," R.A.G. Carrington, Ed., Adam Hilger, London, 1973. Also: University of Edinburgh, School of Artificial Intelligence, Experimental Programming Report No. 32 (1973).
- (37) H. Brown and L. Masinter, "An Algorithm for the Construction of the Graphs of Organic Molecules", Discrete Mathematics,

8, 227 (1974). (Also Stanford Computer Science Dept. Memo STAN-CS-73-361, May, 1973)

- (38) D.H. Smith, L.M. Masinter and N.S. Sridharan, "Heuristic DENDRAL: Analysis of Molecular Structure," in "Computer Representation and Manipulation of Chemical Information," W.T. Wipke, S. Heller, R. Feldmann and E. Hyde, Eds., John Wiley and Sons, Inc., 1974, p. 287.
- (39) R. Carhart and C. Djerassi, "Applications of Artificial Intelligence for Chemical Inference XI: The Analysis of C13 NMR Data for Structure Elucidation of Acyclic Amines", Journal of the Chemical Society (Perkin II), 1753 (1973).
- (40) L. Masinter, N.S. Sridharan, R. Carhart and D.H. Smith, "Application of Artificial Intelligence for Chemical Inference XII: Exhaustive Generation of Cyclic and Acyclic Isomers". Journal of the American Chemical Society, 96, 7702 (1974). (Also Stanford Artificial Intelligence Project Memo No. 216.)
- (41) L. Masinter, N.S. Sridharan, R. Carhart and D.H. Smith, "Applications of Artificial Intelligence for Chemical Inference. XIII. Labeling of Objects having Symmetry". Journal of the American Chemical Society, 96, 7714 (1974).
- (42) N.S. Sridharan, Computer Generation of Vertex Graphs, Stanford CS Memo STAN-CS-73-381, July, 1973.
- (43) N.S. Sridharan, et.al., A Heuristic Program to Discover Syntheses for Complex Organic Molecules, Stanford CS Memo STAN-CS-73-370, June, 1973. (Also Stanford Artificial Intelligence Project Memo No. 205.)
- (44) N.S. Sridharan, Search Strategies for the Task of Organic Chemical Synthesis, Stanford CS Memo STAN-CS-73-391, October, 1973. (Also Stanford Artificial Intelligence Project Memo No. 217.)
- (45) R. G. Dromey, B. G. Buchanan, J. Lederberg and C. Djerassi, "Applications of Artificial Intelligence for Chemical Inference. XIV. A General Method for Predicting Molecular Ions in Mass Spectra". Journal of Organic Chemistry, 40, 770 (1975).
- (46) D. H. Smith, "Applications of Artificial Intelligence for Chemical Inference. XV. Constructive Graph Labelling Applied to Chemical Problems. Chlorinated Hydrocarbons". Analytical Chemistry, 47, 1176 (1975).
- (47) R. E. Carhart, D. H. Smith, H. Brown and N. S. Sridharan, "Applications of Artificial Intelligence for Chemical Inference. XVI. Computer Generation of Vertex Graphs and Ring Systems". Journal of Chemical Information and Computer Science, 15, 124 (1975).

- (48) R. E. Carhart, D. H. Smith, H. Brown and C. Djerassi, "Applications of Artificial Intelligence for Chemical Inference. XVII. An Approach to Computer-Assisted Elucidation of Molecular Structure". *Journal of the American Chemical Society*, 97, 5755 (1975).
- (49) B. G. Buchanan, "Scientific Theory Formation by Computer." In *Proceedings of NATO Advanced Study Institute on Computer Oriented Learning Processes*, 1974, Bonas, France.
- (50) E. A. Feigenbaum, "Computer Applications: Introductory Remarks," in "Proceedings of Federation of American Societies for Experimental Biology," 33, 2331 (1974).
- (51) R. Davis and J. King, "Overview of Production Systems" To appear in *Machine Representation of Knowledge*, *Proceedings of the NATO ASI Conference*, July, 1975. (Also Stanford Artificial Intelligence Project Memo No. ***)
- (52) B. G. Buchanan, "Applications of Artificial Intelligence to Scientific Reasoning." In *Proceedings of Second USA-Japan Computer Conference*, American Federation of Information Processing Societies Press, August, 1975.
- (53) R. E. Carhart, S. M. Johnson, D. H. Smith, B. G. Buchanan, R. G. Dromey, J. Lederberg, "Networking and a Collaborative Research Community: A Case Study Using the DENDRAL Program," in "Computer Networking and Chemistry", P. Lykos, Ed., American Chemical Society, Washington, D.C., 1975, p. 192.
- (54) D. H. Smith, "The Scope of Structural Isomerism" (Paper XVIII in our series of AI Applications in Chemistry). *Journal of Chemical Information and Computer Sciences*, 15, 203 (1975).
- (55) D. H. Smith, J. P. Konopelski and C. Djerassi, "Applications of Artificial Intelligence for Chemical Inference. XIX. Computer Generation of Ion Structures." *Organic Mass Spectrometry*, 11, 86 (1976).
- (56) R. E. Carhart and D. H. Smith, "Applications of Artificial Intelligence for Chemical Inference. XX. 'Intelligenceint' Use of Constraints in Computer-Assisted Structure Elucidation," *Computers in Chemistry*, in press.
- (57) C. Cheer, D. H. Smith, C. Djerassi, B. Tursch, J. C. Braekman, and D. Dalozze, "Applications of Artificial Intelligence for Chemical Inference. XXI. Chemical Studies of Marine Invertebrates. XVII. The Computer-Assisted Identification of [+]-Palustrol in the Marine Organism *Cespitularia* sp., aff. *Subvirdis*," *Tetrahedron*, in press.

- (58) B. G. Buchanan, D. H. Smith, W. C. White, R. Gritter, E. A. Feigenbaum, J. Lederberg and C. Djerassi, "Applications of Artificial Intelligence for Chemical Inference. XXII. Automatic Rule Formation in Mass Spectrometry by Means of the Meta-DENDRAL Program." *Journal of the American Chemical Society*, in press.
- (59) T. R. Varkony, R. E. Carhart, and D. H. Smith, "Computer-Assisted Structure Elucidation. Modelling Chemical Reaction Sequences Used in Molecular Structure Problems" (Paper XXIII in our series of A.I. Applications in Chemistry), in "Computer-Assisted Organic Synthesis", W. T. Wipke, Ed., American Chemical Society, Washington, D.C., 1976, in press.
- (60) D. H. Smith and R. E. Carhart, "Structural Isomerism of Mono- and Sesquiterpenoid Skeletons," (Paper XXIV in our series of A.I. Applications in Chemistry), *Tetrahedron*, in press.
- (61) R. G. Dromey, M. J. Stefik, T. Rindfleisch, and A. M. Duffield, "Extraction of Mass Spectra Free of Background and Neighboring Component Contributions from Gas Chromatography/Mass Spectrometry Data," *Analytical Chemistry*, in press.
- (62) H. Eggert and C. Djerassi, "The Carbon-13 Magnetic Resonance Spectra of Acyclic Aliphatic Amines," *Journal of American Chemical Society*, 95, 3710 (1973).
- (63) H. Eggert and C. Djerassi, "Carbon-13 Nuclear Magnetic Resonance Spectra of Keto Steroids," *Journal of Organic Chemistry*, 38, 3788 (1973).
- (64) H. Eggert, C. VanAntwerp, N. Bhacca and C. Djerassi, "Carbon-13 Nuclear Magnetic Resonance Spectra of Hydroxy Steroids," *Journal of Organic Chemistry*, 41, 71 (1976).
- (65) S. Hammerum and C. Djerassi. "Mass Spectrometry in Structural and Stereochemical Problems CCXLV. The Electron Impact Induced Fragmentation Reactions of 17-oxygenated Progesterones." *Steroids*, 25, 817 (1975).
- (66) S. Hammerum and C. Djerassi. "Mass Spectrometry in Structural and Stereochemical Problems CCXLIV. The Influence of Substituents and Stereochemistry on the Mass Spectral Fragmentation of Progesterone." *Tetrahedron*, 31, 2391 (1975).
- (67) L. L. Dunham, C. A. Henrick, D. H. Smith, and C. Djerassi, "Mass Spectrometry in Structural and Stereochemical Problems. CCXLVI. Electron Impact Induced Fragmentation of Juvenile Hormone Analogs," *Org. Mass Spectrom.*, in press.

(68) C. Djerassi, Foreword to "¹³C NMR-Spectroscopy," by E. Breitmayer and W. Voelter, Verlag Chemie GmbH, Weinheim/Bergstr., 1974.