Meetings

Instruments in Natural Products Research

In the past, natural product chemists, plant biochemists, and pharmacognosists have chipped away at extremely difficult research problems with amazing success, when one considers the remarkable complexity of naturally occurring molecules. From the symposium "Modern Instrumental Methods in Natural Products Research" sponsored by the American Society of Pharmacognosy at its 13th annual meeting, 20 to 22 July in Columbus, Ohio, it is apparent that modern instrumentation is making the way easier for solving structure elucidation and biosynthetic problems.

Circular dichroism of drugs was presented by L. A. Mitscher (Ohio State University). This method depends on the interaction of an optically active solute with a beam of circularly polarized light. As such it is analogous and supplementary to ultraviolet and optical rotatory dispersion spectroscopy. The technique has been used in natural products chemistry for about 10 years. Circular dichroism spectroscopy is often used in conjunction with other physical methods such as nuclear magnetic resonance (NMR) and x-ray spectroscopy. Two major classes of chromophores are recognized, with many gradations in between, and knowledge of the chromophore type is essential for structural analysis. The inherently symmetrical chromophore which is asymmetrically perturbed is most readily analyzed, and the saturated ketonic $n \rightarrow \pi^*$ transition is the most common example of this type. The inherently dissymmetric chromophore, such as the α,β-unsaturated ketone in a six-membered ring system, is much more complex to work with. Several semiempirical rules are used to analyze circular dichroism spectra when closely analogous model substances are not available. These rules were discussed in connection with specific examples chosen from among drugs of natural origin including steroid hormones, antibiotics, and alkaloids. The method is being used to measure the interaction of drugs with macromolecules as a means of elucidating the molecular biology of their action. Examples of work with proteins, nucleic acids, and ribosomes were discussed.

R. L. Foltz (Battelle Columbus Laboratories) discussed the usefulness of chemical ionization mass spectrometory in structural analysis. In this technique proton transfer is the primary means of ionization. Chemical ionization mass spectra characteristically show prominent peaks in the molecular ion region, thereby establishing the compound's molecular weight. The fragmentation observed in chemical ionization mass spectra is generally simpler and easier to interpret than that displayed in the corresponding conventional electron impact mass spectra. Since both these spectra can be obtained with the same instrument, it is convenient and highly desirable to obtain both types.

Examples of the application of chemical ionization mass spectrometry in the structural identification of drug metabolites, macrolide antibiotics, peptides, and other compounds of biological interest were described.

G. H. Stout (University of Washington) reported that x-ray crystallography represents in many respects the ultimate technique in structural analysis. Subject in principle only to the requirement that the molecule studied can be obtained in some fashion in crystalline form, a sample that weighs only a few micrograms can give full details of structure, stereochemistry, and conformation.

Advances in technique and instrumentation over the last decade have enhanced the power of the method immensely and extended the range of compounds to which it can be applied successfully. At the present time, x-ray analysis of unknown compounds with a molecular weight of 500 is approaching routine even in the absence of a heavy atom, and structures may often be obtained in a few weeks to a few months. Thus, x-ray methods have ceased to be used only by a small group of specialists and are becoming available to the practicing structural chemist.

The general utility of solvent and paramagnetic rare earth–induced shifts in structure analysis was discussed by P. V. Demarco (Eli Lilly). Particular reference was made to the conformational and configurational analyses of penicillins and erythromycins, with hydrogen-bonding effects in dimethyl sulfoxide-d_6 and aromatic solvent induced shifts in both benzene-d_6 and pyridine-d_5. The potential of rare earth shift reagents in structure investigations of mono- and bifunctional systems was illustrated. The use of the McConnell-Robertson expression for the pseudocontact shift in conjunction with computer optimization methods is an effective aid for structure identification.

J. Grutzner (Purdue) reported on the application of ^{13}C NMR spectroscopy to biological systems. The 1 percent of ^{13}C present in natural abundance in all carbon compounds may be utilized to investigate the properties of many molecules by ^{13}C NMR spectroscopy. Many kinds of molecules have now been examined, and their important spectral characteristics have been described. Examples of the application of ^{13}C NMR to systems of biological interest were presented, and the way in which carbon spectra can augment and in some cases surpass the information available from proton spectra was illustrated. The requirements and limitations associated with sample size was discussed together with techniques for signal-to-noise enhancement, for example, Fourier transform spectroscopy. Particular attention was paid to ^{13}C-labeling studies for the investigation of biosynthetic pathways, and several pertinent examples were presented.

H. G. Floss (Purdue) illustrated by a number of examples, mostly from his own work, how various spectroscopic methods can be used in biosynthetic experiments. At first, some experiments on ergot alkaloid biosynthesis were discussed to point out how, often at virtually no increase in time and effort, the use of multiple isotopic labels can increase the amount of information obtained from a biosynthetic feeding experiment. Then, after a consideration of the advantages and disadvantages of stable isotopes, the uses of emission, infrared, and optical rotatory dispersion spectroscopy in biosynthetic work were briefly touched upon. Mass spectrom-

etry is used in biosynthetic studies in two ways: (i) to determine the degree of incorporation of a stable isotope, as illustrated by some experiments on the biosynthesis of the antifungal antibiotic pyrrolnitrin, and (ii) to determine whether two stable isotope labels are present in the same molecule or in different molecules. The latter application, which is very useful for studies on mechanisms, was discussed in some detail; Samuelsson's work on prostaglandin biosynthesis and Floss's studies on the mechanism of ergot alkaloid formation were used as examples. Proton NMR spectroscopy is most useful for following specific and stereospecific deuterium labels in biosynthetic sequences, as illustrated by Haslam's work on the stereochemistry of phenylalanine ammonia lyase; ^{13}C NMR, is being used for biosynthetic studies with microorganisms, particularly in work on antibiotics. As examples, studies by Westley *et al.* on antibiotic X-537A, by Suhadolnik's group on showdomycin and by Floss's laboratory on pyrrolnitrin were discussed.

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Forthcoming Events

March

9–10. Pennsylvania **Acad. of Science**, Carlisle. (G. C. Shoffstall, Jr., 214 Whitmore Lab., Pennsylvania State Univ., University Park 16802)

11–16. Symposium on **Membranes**, Squaw Valley, Calif. (W. Stoeckenius, Dept. of Bacteriology, Univ. of California, Los Angeles 90024)

11–16. American Soc. of **Photogrammetry**, Washington, D.C. (L. P. Jacobs, 105 N. Virginia Ave., Falls Church, Va. 22046)

12–13. **Drugs, Hormones and the Kidney**, 4th annual nephrology conf., American Heart Assoc., Inc., Philadelphia, Pa. (Dept. of Councils, AHA, 44 E. 23 St., New York 10010)

12–15. American Soc. for **Neurochemistry**, 4th, Columbus, Ohio. (L. A. Horrocks, Dept. of Physiological Chemistry, Ohio State Univ., 1645 Neil Ave., Columbus 43210)

12–15. Conference on **Prevention and Control of Oil Spills**, American Petroleum Inst., Environmental Protection Agency, U.S. Coast Guard, Washington, D.C. (J. R. Gould, Suite 700, 1629 K St., NW, Washington, D.C. 20006)

12–16. Symposium on **Applications of Nuclear Data in Science and Technology**, Intern. Atomic Energy Agency, Paris, France. (J. H. Kane, Office of Information Services, U.S. Atomic Energy Commission, Washington, D.C. 20545)

13–16. **Optical** Soc. of America, Denver, Colo. (M. E. Warga, OSA, 2100 Pennsylvania Ave., NW, Washington, D.C.)

14–16. American Assoc. of **Petroleum Geologists**, Southwest Div., Fort Worth, Tex. (K. Watson, AAPG, 1444 S. Boulder, Box 979, Tulsa, Okla. 74101)

15–16. **Advanced Analytical Concepts for the Clinical Laboratory**, 5th annual, Oak Ridge, Tenn. (C. D. Scott, Oak Ridge Natl. Lab., P.O. Box X, Oak Ridge 37830)

15–16. Symposium on **Drugs and the Unborn Child**, National Foundation–March of Dimes, New York, N.Y. (M. New, Dept. of Pediatrics, Div. of Pediatric Endocrinology, New York Hospital–Cornell Medical Center, 525 E. 68 St., New York 10021)

15–16. **Estuaries of the Pacific Northwest**, 3rd technical conf., Corvallis, Ore. (L. S. Slotta, Ocean Engineering Programs, School of Engineering, Oregon State Univ., Corvallis 97331)

15–17. Association for **Children with Learning Disabilities**, 10th intern. conf., Detroit, Mich. (K. M. Tillotson, ACLD, 2200 Brownsville Rd., Pittsburgh, Pa. 15210)

15–17. **Recent Advances in Particle Physics**, New York Acad. of Sciences, New York, N.Y. (F. Cooper, Belfer Graduate School of Science, Yeshiva Univ., New York)

15–17. Symposium on **Reproductive Biology, Mating Behavior and Captive Breeding of Felids**, World Wildlife Safari and Inst. for the Study and Conservation of Endangered Species, Winston, Ore. (R. L. Eaton, P.O. Box AL, Winston 97496)

16. Mississippi **Acad. of Sciences**, Biloxi. (D. L. Dodgen, University Medical Center, Jackson, Miss. 39216)

16–17. **Texas Acad. of Science**, Austin. (C. G. Skinner, Chemical Sciences, Dept. of Chemistry, North Texas State Univ., Denton 76203)

18–21. North American **Wildlife and Natural Resources**, 38th conf., Washington, D.C. (L. R. Jahn, Wildlife Management Inst., 709 Wire Bldg., Washington, D.C. 20005)

18–22. Society of **Toxicology**, New York, N.Y. (R. A. Scale, ST, Esso Research and Engineering Co., P.O. Box 45, Linden, N.J. 07036)

18–23. **Deafness**, 4th intern. conf., World Federation of the Deaf and Assoc. of the Deaf and Mute in Israel, Tel Aviv, Israel. (A. Reich, Organizing Committee, P.O. Box 16271, Tel Aviv)

18–23. Symposium on **Molecular Biology** (Virus Research), Intern. Chemical and Nuclear Corp. and Molecular Biology Inst., Univ. of California, Squaw Valley. (C. F. Fox, Dept. of Bacteriology, Univ. of California, Los Angeles 90024)

19–23. **Characterization of Corrosion Products**, Natl. Assoc. of Corrosion Engineers, Anaheim, Calif. (W. D. France, Jr., General Motors Research Labs., General Motors Technical Center, Warren, Mich. 48090)

20–21. **Californium-252 Utilization**, U.S. Atomic Energy Commission, New York, N.Y. (W. C. Reinig, Savannah River Lab., Aiken, S.C. 29801)

20–23. American **Astronomical** Union (Planetary Sciences Div.), Tucson, Ariz. (B. Smith, Dept. of Astronomy, New Mexico State Univ., Las Cruces 88001)

21–24. Association for the Advancement of **Medical Instrumentation**, 8th annual, Washington, D.C. (AAMI, Suite 417, 1500 Wilson Blvd., Arlington, Va. 22209)

22–23. **Information Sciences and Systems**, 7th conf., Princeton, N.J. (T. Pavlidis, Dept. of Electrical Engineering, School of Engineering/Applied Science, Engineering Quadrangle, Princeton 08540)

22–24. **AKD Social Science** Symp., 3rd annual, Richmond, Va. (P. Heim, Dept. of Sociology, Virginia Commonwealth Univ., Richmond 23220)

22–24. **Clinical Chemistry Measurements**, 8th annual, Assoc. for the Advancement of Medical Instrumentation and Natl. Bureau of Standards, Washington, D.C. (F. Keutman, Suite 417, AAMI, 1500 Wilson Blvd., Arlington, Va. 22209)

23–25. **Future Status of Earth Resources in Society**, Natl. Assoc. of Geology Teachers, Central Section, Chicago, Ill. (M. K. Sood, Dept. of Earth Sciences, Northeastern Illinois Univ., Bryn Mawr at St. Louis Ave., Chicago 60625)

26–28. **Engineering Aspects of Magnetohydrodynamics**, Stanford, Calif. (M. Mitchner, Dept. of Mechanical Engineering, Stanford Univ., Stanford 94305)

26–29. **Paraneoplastic Syndromes**, New York Acad. of Sciences, New York, N.Y. (T. C. Hall, Div. of Oncology, Univ. of Rochester, Rochester, N.Y.)

26–30. Symposium on **New Developments in Radiopharmaceuticals and Labeled Compounds**, Intern. Atomic Energy Agency, Copenhagen, Denmark. (J. H. Kane, Office of Information Services, U.S. Atomic Energy Commission, Washington, D.C. 20545)

27–29. **Reduction of Pollutants in Heterogeneous Combustion Processes**, Combustion Inst., Central States Section, Champaign, Ill. (R. A. Strehlow, 105 Transportation Bldg., Univ. of Illinois, Urbana 61801)

27–29. National Assoc. for **Research in Science Teaching**, Detroit, Mich. (R. W. Lefler, Dept. of Physics, Purdue Univ., Lafayette, Ind. 47907)

27–30. Institute of **Electrical and Electronics Engineers**, New York, N.Y. (D. G. Fink, IEEE, 345 E. 47 St., New York 10017)

28–30. National **Conservation Tillage** Conf., Des Moines, Iowa. (H. W. Protchard, Soil Conservation Soc. of America, 7515 NE Ankeny Rd., Ankeny, Iowa 50021)

28–30. Conference on **Nuclear Structure and High Energy Physics** (Nuclear Physics Sub-Committee), Inst. of Physics, Liverpool, England. (Meetings Officer, IP, 47 Belgrave Sq., London SW1X 8QX, England)

29–30. **Psychometric** Soc., Chicago, Ill. (W. B. Schrader, Educational Testing Service, Princeton, N.J. 08540)