Meetings

Stereospecificity

A reaction is "stereoselective" when, of two possible stereoisomeric products, more of one is obtained than of the other. Examples are the formation of *trans*-stilbene from 1,2-diphenylethyl bromide and the operation of Cram's rule. In general the products are diastereoisomeric, formed at different rates that are determined by two transition states differing in free energy. In contrast, enantiomeric transition states are equal in free energy; consequently, enantiomers are generally formed (or consumed) at equal rates in ordinary chemical reactions.

On the other hand, "stereospecificity" is considered to represent a unique correlation of configuration of two entities. The organic chemist uses the term when stereoisomeric starting materials give rise to stereoisomeric products. An example is the synthesis of *meso*-2,3-dibromobutane by addition of bromine to *trans*-2-butene, whereas racemic dibromide is synthesized when bromine is added to the *cis*-olefin. The photochemical (free-radical) addition of hydrogen bromide to 2-bromo-2-butene is an example of a reaction that is stereospecific at −78°C but only stereoselective at +25°C. In biochemical reactions, however, stereospecificity implies a unique correlation of the configuration of either starting material or product with the enzyme catalyzing the reaction. Here reaction rates between enantiomers differ because the transition states are diastereoisomeric (and therefore unequal in free energy), even though the starting materials and products are not.

So were the two terms defined by E. L. Eliel (University of Notre Dame) in the first of six lectures in a symposium on "Stereospecificity in chemistry" organized by Alec Sehon (AAAS meeting, Montreal, 30 December 1964).

Eliel continued: An interesting contrast between stereoselectivity and stereospecificity is provided by reduction of *trans*-decalin-1,4-dione by chemical reducing reagents and by *Curvularia falcata*. Chemical reduction is stereoselective but gives the same unequal mixture of diastereoisomers starting with either enantiomer of the starting material; enzymatic reduction is stereospecific, giving the same configuration of the newly introduced assymmetric carbinol carbon, and therefore each enantiomeric substrate leads to a different diastereoisomer of the product.

After mentioning physical stereospecificity, Eliel concluded with a discussion of conformational specificity, as observed, for example, in the oxidation of cyclohexanols by *Acetobacter suboxydans*. Finally he pointed out that, although the thermodynamics of stereospecificity was clear, its mechanism had to be ferreted out in each case.

Albert Moscowitz (University of Minnesota) outlined some theoretical aspects of optical activity. The contribution of a single electronic transition to the observed optical activity of a molecule is conveniently gauged in terms of a quantity that is, in principle, accessible to both experiment and theory. This quantity is called the "rotational strength" for the transition and, in favorable cases, can be obtained from either optical rotatory dispersion (ORD) measurements or circular dichroism (CD) data. The rotational strength is related to the area under the pertinent CD curve, and the amplitude of rotation of the Cotton effect is given by the pertinent ORD curve; crudely speaking, large numerical magnitudes for the rotational strengths of transitions are associated with large areas under the relevant CD bands or large amplitudes of rotation for the relevant Cotton effects.

Comparison of values for rotational strengths among transitions associated with various types of chromophores indicates that rotational strengths can vary through at least two orders of magnitude; this variation can be understood in terms of the intrinsic geometry of the relevant chromophore and the extrachromophoric environment. This leads to a useful classification of optically active chromophores in terms of two limiting types: (i) the inherently dissymmetric chromophore; and (ii) the inherently symmetric, but asymmetrically (more generally dissymmetrically) perturbed chromophore.

The utility of this classification was illustrated by reference to saturated ketones, β,γ-unsaturated ketones, conjugated dienes, homoconjugated dienes, and especially the urobilins, in which the chromophore can be of either type (i) or (ii), depending on the solvent medium, which may influence the nature of the intramolecular hydrogen bonding. The making or breaking of internal hydrogen bonds markedly affects the intrinsic geometry of the dipyrrylmethene chromophore in these tetrapyrrole derivatives.

Inorganic Coordination Compounds

J. C. Bailar, Jr. (University of Illinois), reviewed the concept of stereospecificity in the chemistry of inorganic coordination compounds. Corey and Bailar have suggested that stereospecificity in these compounds depends on the presence of puckered chelate rings in which some substituents on the rings must assume axial positions, and others, equatorial positions. The molecule thus achieves increased stability if the larger groups are in equatorial positions. Calculations based on interatomic distances show that this theory is in good agreement with experimental measurements of differences in free energy between the stereoisomers. Quantitative data are available for only a few cases, chiefly involving complexes of propylenediamine (pn), $NH_2CH(CH_3)CH_2NH_2$, but much qualitative evidence accords with the theory. Thus, complexes of *dl*-stilbenediamine (1,2-diphenylethylenediamine, abbreviated stien) are very much more stable than those of their *meso*-isomers. In the former case all the phenyl groups can assume equatorial positions; in the latter, half of them must be in axial positions.

Stereospecificity in octahedral complexes, Bailar continued, has been studied extensively only in the compounds of cobalt and platinum. Its effects are marked in the cobalt series, but are not at all apparent in the platinum series. For example, no one seems to have succeeded in preparing such ions as $[Co(l\text{-pn})(d\text{-pn})_2]^{+3}$, but Dwyer has found $[Pt(l\text{-pn})(d\text{-pn})]^{+4}$ to be stable

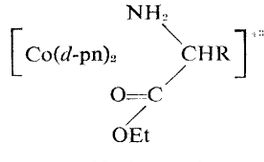
toward racemization and disproportionation, even in boiling water. It would be interesting to study the analogous platinum complexes containing phenylethylenediamine and diphenylethylenediamine, in which stereospecific tendencies would be expected to be greatly enhanced.

The presence of even one asymmetric chelate ring in an octahedral complex makes one stereoisomer of the complex more stable than the other, as Dwyer has shown; $[Co\ en_x(l\text{-pn})_{3-x}]^{+3}$ (en is ethylenediamine), the *L*-isomer, is increasingly favored over the *D*-isomer as x decreases (*L* and *D* refer to the asymmetry about the cobalt atom).

When a solution of *D,L*-$[Co\ en_2CO_3]^+$ is boiled with *d*-tartaric acid, a mixture of the *D*- and *L*-isomers of $[Co\ en_2d\text{-tart}]^+$ forms. These are evidently not present in equal amounts and are of different stabilities, for reaction with nitrite ion gives a large yield of *D*-$[Co\ en_2(NO_2)_2]^+$. This was the first example of a partially asymmetric synthesis in the metalamine series.

Bailar pointed out that Shibata demonstrated, about 35 years ago, that asymmetric inorganic complexes resemble enzymes in their ability to catalyze certain oxidative reactions; the *D*- and *L*- forms of the complexes have quite different catalytic power. In spite of its importance, Shibata's work has received scant attention in the western world.

Bailar and his students have shown that in $[Co(l\text{-pn})_2tart]^+$ a dextrotartrato group is held much more tightly than a levotartrato group; this difference can be used to effect a partial resolution of tartaric acid. The same principle has been used in the resolution of propylenediamine, lactic acid, and halosuccinic acids. Murakami *et al.* have shown that



is more stable if the amino acid ester is levo than if it is dextro. The more firmly bound isomer of the amino acid ester is hydrolyzed more rapidly; this can be used to effect a partial resolution.

Stereospecificity is also known in compounds of metals that form planar complexes. Ethylenediaminetetraacetic acid behaves as a tetradentate chelating agent toward palladium (II), leaving two of the acetate groups unattached; both nitrogen atoms thus become asymmetric, but only the *dl*-modification of the complex forms.

Stereoregulated Polymers and Biopolymers

Murray Goodman (Brooklyn Polytechnic Institute) dealt with "Determination of stereochemical features of polymers by the use of high-resolution nuclear magnetic resonance [NMR]" and "The tacticity of amorphous polyacetaldehyde prepared cationically at −78°C."

The polyacetaldehyde had been studied by high-resolution NMR spectroscopy, using solvents such as aniline at 145°C and dimethylformamide at 170°C to analyze the stereochemistry (tacticity). The polymer backbone appeared to be composed of isotactic and heterotactic triad sequences. When a 60-megacycle instrument was used, with or without spin coupling, no syndiotactic triad sequences were detectable. Moreover, the spectrum of poly-α-deuteroacetaldehyde showed the presence of only two stereochemical triads as above. On the basis of model compounds, such as paraldehyde and the linear dimer of acetaldehyde, a mechanism for the cationic polymerization of acetaldehyde to an amorphous polymer was proposed, suggesting that acetaldehyde might exist in an associated dimeric form under polymerization conditions leading to a preferred incorporation of *meso* dimeric units into the propagating chain. It was concluded that such random incorporation of DD- or LL-*meso* dimeric units would lead to a heterotactic and isotactic polymer configuration.

As to the use of the NMR spectra of methylene hydrogens in vinyl polymers for stereochemical diagnosis, Goodman continued, it has been shown that *meso* dyads (isotactic placements of adjacent monomer units) cause the methylene hydrogens of the backbone to become magnetically nonequivalent; consequently they split each other into an *AB* quartet. On the other hand, racemic dyads (syndiotactic placements of adjacent monomer units) lead to equivalent methylene protons; a singlet for the methylene spectrum results.

This approach was used to investigate the stereochemistry of polyvinyl ethers for polyvinylmethyl ether, a singlet was found for the methoxyl protons, the expected quartet for the backbone methinyl proton, and a complex pattern for the methylene which was analyzable as a superposition of racemic and *meso* dyads. Consequently it was inferred that the spectrum for polyvinylmethyl ether indicated that the polymer chain was composed of isotactic and syndiotactic placements. Next, poly-α-methylvinyl methylether was synthesized by the use of cationic catalysts; a high-resolution NMR spectrum in chlorobenzene of this compound at 130°C showed a sharp singlet for the methylene protons at 8.2τ. Thus, the structure of poly-α-methylvinyl methylether was interpreted to be primarily, if not exclusively, syndiotactic in nature. Based on this finding, a mechanism analogous with the mechanism proposed by Cram for vinyl ether polymerization was suggested; furthermore, a similar mechanism to account for the syndiotactic propagation reaction was proposed. This mechanism involves the ultimate, penultimate, and prepenultimate stereochemical placements, with the prepenultimate unit forming an oxonium pseudo-six-membered ring with the growing end of the polymer chain. Such stereochemistry can lead to syndiotactic polymer structure.

Goodman went on to discuss recent original work on biopolymers in his laboratory. Synthetic poly-*p*-nitrobenzyl-L-aspartate exhibited a Cotton effect centered at 330 mμ when the polymer was in the helical form. In solvents such as chloroform and trifluoroethanol, the optical rotatory dispersion and circular dichroism through this Cotton-effect region was measured. Copolymers of nitrobenzyl-L-aspartate with benzyl-L-aspartate were also prepared. Absence of the nitro group from the latter prevented this material from participating in the side-chain asymmetric effect of the former group. By measuring the circular dichroism, through the region of the nitroaromatics showing the Cotton effect, as a function of the concentration of the nitroaromatic groups in the polymer, it was possible to show by statistical analysis that the aromatic groups interacted with each other; it was deduced that the nature of the interactions of the side chains with each other was more of a dispersive type than of an exciton-band type. On the basis of both Courtauld space-filling and wire models, reasonable stereochemical arrangements for the side chains, which could lead to the observed effect, were proposed.

The important point is that the nitroaromatic group of the side chain was not itself asymmetric; it was rigidly arrayed around an asymmetric structure (the main chain helix) and as-

sumed an asymmetry that was measurable by noting the circular dichroism in the region where nitroaromatics contained an $n-\pi^*$ transition, that is, at 330 mμ. The stereochemical arrangement and its supporting data had not been previously described, and Goodman coined the new term "constellation" in referring to a new stereochemical description primarily applicable to side chain–side chain interactions of helical polymers. The concept of constellation was illustrated with diagrams of the interaction among side chains, from which it was deduced that the probable interaction between side chains was by way of residues 1-5-9, 2-6-10, 3-7-11, 4-8-12, and others, the proximity between the aromatic groups being of the order of just under 4 Å—considered reasonable spacings for the effect noted.

Helix Formation

As to the critical size of an oligopeptide necessary to form stable helical conformation, Goodman indicated that a series of oligomers derived from glutamic acid, aspartic acid, and alanines had been prepared in his laboratory and that the critical size for helix formation depended on the nature of the amino acid, the solvent, and temperature. These materials had been prepared by a series of step-by-step reactions, with optical purity maintained at each step. By use of the Moffitt-Yang equation, specifically in the γ-ethylglutamate–oligomer series in a solvent such as trifluoroethanol, it was shown that the term b_0 was O in the series from the dimer through to the hexamer. However, commencing with the heptamer, b_0 values were sizable. In the γ-ethylglutamate series, in trifluoroethanol, extremely sharp boundaries between nonhelical and helical forms were observed.

It was then shown how glycine can be combined with glutamic acid in various compounds such as γ-ethyl-L-glutamate, glycyl-γ-ethyl-L-glutamate, and glycyl-γ-ethyl-L-glutamyl-glycine, and that these three compounds were really mirrors of N-terminal, C-terminal, and internal residues in an oligopeptide, respectively. Moreover, in solvents such as trifluoroethanol, if the rotations of the model compounds were measured at the maximum for the Cotton effect at 233 mμ, a calculated line could be obtained by plotting molar rotation against number of residues in the peptide chains; this calculated line gave values for the random coil only. Moreover, the calculated line, when compared with dimer through hexamer, gave complete agreement for γ-ethylglutamate oligomers in trifluoroethanol. However, commencing with the heptamer through the tridecamer, there was sharp deviation from the values calculated for random coil.

The random-coil oligomers, that is, dimer through hexamer, fell on the random-coil straight line, with a slope of $-2000°$, which is identical with the random-coil value of the high polymer reported by Blout and co-workers for polyglutamates. Similarly, in the series from heptamer through tridecamer these values also fell on a straight line; however, the slope was much steeper ($-16{,}000°$) and identical with the rotation of the helical γ-ethyl-L-glutamate high polymer in the same solvent. In hexafluoroacetone-trihydrate all the oligomers, dimer through tridecamer, fell on a straight line with a slope of $2000°$, showing that in this solvent all these oligomers were random coils. Since the glutamate oligomers fell on a line with a slope identical with the rotation value for helical high-polymer, it was concluded that the glutamate oligomers, once they become large enough to form helices, form these helices completely in trifluoroethanol at 25°C. The differences in absolute values of the rotations between the high polymer and these oligomers are attributed to end-group effects.

Thus Goodman demonstrated that application of such sensitive tools as high-resolution NMR spectroscopy and optical rotatory properties to polymers and biopolymers enables one to dissect the intimate details of polymer stereochemistry, which underlies the functions of proteins and nucleic acids.

Bernard Belleau (University of Ottawa) spoke of the stereospecificity of enzyme reactions. The living cell is a catalytic unit; its highly specialized chemical machinery requires highly specific and efficient catalysts, so that only chemical pathways beneficial to the cell may be exploited. These catalysts are proteins of varying degrees of complexity and of highly asymmetric character. Three outstanding properties characterize their molecules: stereospecificity, efficiency, and sensitivity to minor environmental changes.

The stereospecificity of enzymes was rationalized early by Emil Fisher who proposed his classical "lock-and-key" hypothesis, according to which substrates and enzymes are configurationally complementary. The stereospecificity of these reactions was illustrated by reference to the reaction between L-lactic dehydrogenase and L-lactic acid. The optically active screw pattern of the enzyme can select readily between the optical forms of a molecule, since both are inherently asymmetric.

However, the unexpected finding that many enzymes handle symmetric molecules in a completely nonsymmetrical fashion proved to be somewhat disturbing at one time. The classical example is the discriminating power of the enzymes of the tricarboxylic acid cycle towards the two chemically equivalent terminal carboxyl groups of citric acid. At first sight, Fisher's concept appeared inadequate in the face of such observations. Nevertheless, in the interaction of substrate molecules with the inherently asymmetric surfaces of enzymes, symmetrical molecules would be expected to be modified nonsymmetrically. Viewed in this light, this phenomenon can be seen as a normal extension of the "lock-and-key" hypothesis, which confirms the view that enzymes are highly stereospecific.

Enzymes are renowned for ability to form complexes with a wide variety of nonsubstrate molecules. Generally, competitive inhibition is observed with substrate-related compounds, and not infrequently a lower degree of stereospecificity is displayed by enzymes in such instances. It follows that the forces applied in the formation of addition complexes with inhibitors may often differ from those involved in complex formation. This being so, a lack of stereospecificity toward the optical forms of an inhibitor may have little bearing on stereospecificity in the catalytic step when substrates are involved. This point was illustrated with reference to monoamine oxidase. This enzyme is competitively inhibited by the stimulant drug amphetamine (2-phenylisopropylamine) and shows only a marginal selectivity for one of the optical forms of this inhibitor. However, it can be shown that the enzyme can discriminate completely between the chemically equivalent α-hydrogen atoms of the related substrate tyramine, a naturally occurring pressor amine. Such discriminating power toward equivalent atoms of substrates contrasts sharply with the relative nonstereospecificity toward inhibitors. Consequently, conclusions regarding enzyme stereospecificity based on the use of inhibitors must be drawn with extreme caution, since no catalysis is operative with these nonsubstrate molecules.

In spite of the high degree of catalytic stereospecificity shown by enzymes, Belleau went on, other observations indicate that their structural specificity can be much more limited. Thus alcohol dehydrogenase will dehydrogenate many straight-chain primary alcohols other than ethanol; the same applies to monoamine oxidase, which can oxidize a variety of primary amines. These observations suggest that enzyme stereospecificity is most marked in the catalytic step. Other recent investigations have established the ability of enzymes to direct stereospecifically the reaction of solvent protons with enzyme-bound substrates.

An observation by Niemann illustrates admirably the nature of the conformation imposed by the asymmetric screw pattern of the enzyme on the substrate molecules; it offers the possibility of a specific approach to the stereochemistry of enzyme-bound substrates. It has long been known that α-chymotrypsin is catalytically stereoselective for *N*-acyl or *N*-aroyl amino acid esters of the natural L-configuration. One of the best substrates is *N*-benzoyl-L-phenylalanine ethyl ester; the D-enantiomorph is hardly attacked by the enzyme. However, when the two phenyl rings are fused into one, as in a dihydroisocarbostyril analog, a substance in which no free rotation of the bonds is possible, the isomer of the D-configuration now behaves as an excellent substrate, while the L-enantiomorph does not. It seems probable that this phenomenon is related to the problem of the conformation adopted by the flexible substrates when imbedded in the asymmetric matrix of the enzyme.

A most striking example of enzyme stereospecificity which requires that flexible molecules be bound asymmetrically is the desaturation of stearic acid to oleic acid by certain aerobic microorganisms. Recently, Bloch *et al.* have found an enzymatic system which specifically attacks the molecule at the sites of carbons 9 and 10, and which also discriminates between the four chemically equivalent hydrogen atoms attached to these two carbon atoms. This may be close to the ultimate in enzyme stereospecificity; the discriminating power of the enzyme is such as to suggest the possible operation of special cooperative factors in the structural specificity of the enzyme. Since the 9-hydrogen of the D-configuration appears to be primarily involved in the desaturation reaction, one may tentatively conclude that the enzyme would

have easier access to this hydrogen if it occupied some kind of pseudo-equatorial conformation. On that basis, the screw pattern, which places this hydrogen in the pseudo-equatorial position, would be the one adopted by the enzyme-bound stearic acid molecule. A pseudo-cyclohexane mode of packing for these long-chain acids permits the prediction that palmitic acid (16 carbon atoms) should be also desaturated at positions 9 and 10; Bloch's observations confirm this, and it seems probable that we may be dealing in such instances with cooperative effects of solvent-substrate interactions that are superimposed on the structural specificity of an enzyme.

Nucleic Acids and Protein Synthesis

J. H. Spencer (McGill University) reviewed stereospecificity of nucleic acids in relation to protein synthesis; base-pair stereospecificity at five stages in the transcription of the genetic message and its translation to protein was examined. Base pairing, one of the major factors in the transfer of information from the genome, developed from the original theory that the complementarity of the bases in the DNA helix and the stability of the helix were due to hydrogen bonding between the bases. This was supported by studies of thermal denaturation and by the relation of guanine-cytosine content to T_m values. More recent calculations indicate that forces such as dipole interactions are large, and that hydrogen-bond energy may not be the major factor holding the strands of the helix together. However, hydrogen bonds are regarded as ensuring specific base-pairing, which underlies the mechanism for transcription of DNA by semiconservative replication on a DNA template.

The same mechanism of alignment of bases by base-pair interactions is conceived in the synthesis of RNA on the DNA template. Monod's concept of a messenger molecule requires it to be an exact base-sequence copy of the material containing the genetic information. Discovery of the DNA-dependent RNA polymerase, studies of hybridization, and isolation of DNA-RNA hybrids stable to ribonuclease support this theory. DNA–RNA hybrids of messenger-RNA (mRNA), soluble RNA, and ribosomal RNA have all been isolated; their formation experimentally can only be attributed to complementarity of their base sequence.

The study of mRNA and ribosome

interaction has been aided by the use of the synthetic polyribonucleotides, particularly polyuridylic acid (polyU). Takanami has shown that polyU binds to the 70*S* ribosome and 30*S* subunit of *Escherichia coli* ribosomes, but not to the 50*S* subunit. Optimum interaction of polyU with 70*S* ribosomes gives complexes of one polyU molecule and one or more ribosomes. When these complexes are treated with ribonuclease, a polyU component remains attached to each ribosome. Calculations indicate that this component is 27 residues long and is of the same order of magnitude (180 Å) as the 30*S* subunit. There is no evidence that the attachment of the polyU or mRNA and the ribosome is by base pairing. Watson has suggested that the phosphate of the mRNA may interact with the amino groups on the ribosome.

Recent exepriments by Leder and Nirenberg, Spencer said, have provided evidence of the minimum size of mRNA required for association with transfer RNA (tRNA) on the ribosome. By use of polyribonucleotide fragments of various sizes, nucleotide triplets were shown to be bound to ribosomes to the level of maximum binding obtained with polyU. The specificity of the triplets for binding the complementary tRNA's was also very high: for example, UUU for tRNA phenylalanine, AAA for tRNA lycine, CCC for tRNA proline. However, the hydrogen bonds between three complementary base pairs would not give enough stability for attachment of polyU, phenylalanine, tRNA, and ribosomes, so that some interaction between the tRNA and the ribosome must occur. This is supported by the fact that removal of the adenine from the CCA terminal of tRNA reduces the extent of binding of tRNA to ribosomes (U, uridine; A, adenosine; C, cytidine). Also, in Nirenberg's system, deoxynucleotide triplets are not bound to ribosomes, indicating possible involvement of the 2′-hydroxyl of the RNA codewords. Nirenberg has also shown that 5′-terminal phosphate groups are required for triplet attachment and suggests that 5′-terminal codewords may play a role in the phasing of codeword reading. The difference in chemical structure of 5′-terminal, 3′-terminal, and internal codewords allows postulation of possible operator-word function. Once again evidence supports base-pairing as the stereospecificity for transfer of information from the mRNA, but this is an oversimplification.

The experiments of Chapeville and Lipmann on the specificity of the mRNA for the tRNA and not the amino acid, in which cysteine tRNA was converted to alanine tRNA and incorporation of alanine at the cysteine site in hemoglobin was demonstrated, are fully explained by triplet complementarity. However, how tRNA recognizes the amino acid is a matter of speculation. Specificity of the aminoacyl synthetases would allow an explanation, but the observations of different specificities with enzymes from different sources and the apparent lack of specificity of tRNA's from different sources indicate that this is not the full explanation and also raise the question of the universality of the code.

ALEC SEHON

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Forthcoming Events

April

25–28. American **Oil Chemists** Soc., Houston, Tex. (C. W. Hoerr, Durkee Foods, 2333 Logan Blvd., Chicago, Ill.)

25–28. Southeastern **Psychiatric** Assoc., annual, Southern Pines, N.C. (H. Brackin, Jr., 1918 Church Ave., Nashville 3, Tenn.)

25–29. American Assoc. of **Cereal Chemists**, Kansas City, Mo. (E. J. Bass, Intern. Milling Co., Inc., 1423 S. 4th St., Minneapolis, Minn. 55404)

25–29. American Soc. for **Microbiology**, annual, Atlantic City, N.J. (R. W. Sarber, ASM, 115 Huron View Blvd., Ann Arbor, Mich.)

25–29. International College of **Surgeons**, North American Federation, Las Vegas, Nev. (Secretariat, 1516 Lake Shore Dr., Chicago, Ill. 60610)

26–27. European Days of **Chemical Engineering**, Paris, France. (Societé de Chimie Industrielle, 28, rue St. Dominique, Paris 7)

26–27. **Electroanesthesia**, 2nd symp., Univ. of Tennessee, Knoxville. (C. E. Short, UT-AEC Agricultural Research Laboratory, 1299 Bethel Valley Rd., Oak Ridge, Tenn.)

26–27. **Environmental Health Problems**, 2nd AMA congr., Chicago, Ill. (Dept. of Environmental Health, AMA, 535 North Dearborn St., Chicago, Ill. 60610)

26–28. **Error in Digital Computation**, symp., Madison, Wis. (L. B. Rall, U.S. Army Mathematics Research Center, Univ. of Wisconsin, Madison 53706)

26–28. **National Acad. of Sciences**, 102nd annual, Washington, D.C. (Office of the Home Secretary, NAS, 2101 Constitution Ave., Washington 20418)

26–29. **Aerospace Medical** Assoc., 36th annual, New York, N.Y. (Gen. J. M. Talbot, Headquarters USAF, AFMSPA, Washington, D.C. 20333)

26–29. Mechanisms and Therapy of **Cardiac Arrythmias**, 14th Hahnemann symp., Philadelphia, Pa. (L. Dreifus, Dept. of Medicine, Hahnemann Medical College and Hospital, Philadelphia)

26–29. Society of **Economic Paleontologists and Mineralogists**, New Orleans, La. (D. M. Curtis, Shell Oil Co., Box 127, Metairie, La.)

26–29. American Assoc. of **Petroleum Geologists**, 39th annual, New Orleans, La. (G. Atwater, 424 Whitney Bldg., New Orleans)

26–29. American **Physical** Soc., Washington, D.C. (K. K. Darrow, APS, Columbia Univ., New York 10027)

26–1. **Geodetic Uses of Satellites**, conf., Athens, Greece. (Intern. Organizations Staff, Bureau of Intern. Commerce, U.S. Dept. of Commerce, Washington, D.C.)

28–30. **Hypnosis and Psychosomatic Medicine**, intern. congr., Paris, France. (H. C. Harding, 2050 NW Lovejoy, Portland 9, Ore.)

28–30. National Soc. for **Prevention of Blindness**, Houston, Tex. (J. W. Ferree, 16 E. 40 St., New York 10016)

28–1. **Biometric** Soc., Florida State Univ., Tallahassee. (E. L. LeClerg, 6804 40th Ave., University Park, Hyattsville, Md.

28–1. American **College Health** Assoc., Miami Beach, Fla. (R. E. Boynton, 5518 Merrick Dr., Coral Gables, Fla.)

29–30. **Space Navigation and Communications**, natl., Houston, Tex. (P. Schrock, Inst. of Navigation, 711 14th St. NW, Washington, D.C. 20005)

29–30. Association for **Symbolic Logic**, Chicago, Ill. (T. Hailperin, Dept. of Mathematics, Lehigh Univ., Bethlehem, Pa. 18015)

29–31. Southwestern Assoc. of **Naturalists**, annual, New Orleans, La. (H. Dundee, Tulane Univ., New Orleans)

29–1. American Assoc. of **Endodontists**, Detroit, Mich. (E. C. Van Valey, 9 Rockefeller Plaza, New York 10020)

29–1. American Assoc. for **History of Medicine**, Philadelphia, Pa. (J. B. Blake, Natl. Library of Medicine, 9600 Wisconsin Ave., Bethesda, Md.)

29–1. American Acad. of **Neurology**, annual, Cleveland, Ohio. (AAN, 7100 France Ave. S., Minneapolis, Minn. 55410)

29–1. Midwestern **Psychological** Assoc., 27th annual, Chicago, Ill. (F. A. Mote, Psychology Bldg., Madison, Wis. 53706)

29–1. American **Philosophical** Assoc., western div., Chicago, Ill. (L. E. Hahn, Dept. of Philosophy, Southern Illinois Univ., Carbondale)

29–2. Association of **Clinical Scientists**, New York, N.Y. (R. P. MacFate, ACS, 300 N. State St., Chicago, Ill. 60610)

29–2. **Pan American Medical** Assoc., 40th annual congr., Grand Bahama Island. (PAMA, 745 Fifth Ave., New York 10022)

29–2. **Roentgen**, 46th German congr., Nuremberg, Germany. (A. Jakob, c/o Strahleninstitut der Städt, Krankenanstalten, Flurstr. 17, 85 Nuremberg)

30–1. **Colorado-Wyoming** Acad. of Science, annual, Univ. of Denver, Denver, Colo. (C. Norton, Dept. of Botany and Plant Pathology, Colorado State Univ., Fort Collins)

30–1. **Indiana** Acad. of Science, Culver. (C. F. Dineen, St. Mary's College, Notre Dame, Ind. 46556)