HIGH-RESOLUTION NUCLEAR MAGNETIC RESONANCE SPECTROSCOPY

HIGH-RESOLUTION nuclear magnetic resonance spectroscopy is a rather recent addition to the arsenal of the physical chemist. It has undergone a very rapid development during the past two years, due in large measure to the fact that nuclear-resonance spectrometers with a high degree of field stability are now commercially available. The term 'high-resolution' is generally used for nuclear-resonance measurements of liquid samples under conditions of magnetic-field homogeneity which permit resolution of the signals of non-equivalent nuclei in a given compound and also the fine-structure components arising from spin-spin coupling. The broad resonance signals characteristic of solids, on the other hand, are frequently termed 'broad-line' spectra. There is now ample evidence that the high-resolution nuclear-resonance technique is a very powerful one, and sufficient understanding of the basic phenomena has been gained to demonstrate its advantages as well as some of its limitations.

The basic problem in high-resolution nuclear magnetic resonance work is that of relating the various magnetic effects of the molecule which are measured to the more familiar notions of the chemist regarding electronic structure and molecular configuration. This problem was the central topic of discussion at an informal symposium held during September 6 and 7 at the National Research Council Laboratories in Ottawa. A detailed theoretical treatment of the chemical shift was discussed by Dr. J. A. Pople (Cambridge). The chemical shifts observed can be conveniently discussed in terms of circulating electron currents within the molecule which are induced by the magnetic field. These currents can be classified into three types according to their origin. First, there is the diamagnetic circulation about individual atoms of the molecule corresponding to the well-known Lamb shielding term. This type of magnetic shielding for a given nucleus can frequently be correlated with the electronegativity of neighbouring atoms in the molecule. A second type of circulation may occur in molecules where the nucleus under consideration is bonded to an atom with an electron structure which permits mixing of the ground-state with excited states, so as to give rise to an anisotropic magnetic permeability. It can be shown that this effect will dominate in certain cases where mixing involves transitions between *s*- and *p*-functions or between two *p*-functions. The simple hydrides ammonia, water and hydrogen fluoride are examples of the former, and acetylene of the latter. The chemical shifts of these molecules are anomalous. Dr. W. G. Schneider (Ottawa) reported that the chemical shifts of ammonia, water, hydrogen fluoride and hydrogen chloride, when in the free or unassociated state, lie on the high-field side of the proton signal in saturated hydrocarbons and do not differ markedly from each other. These results cannot be explained on the basis of electro-negativity considerations but are readily interpreted in terms of the theory. On association (hydrogen bonding), the proton signals of these hydrides shift to lower field, the shift for hydrogen fluoride being very large, of the order of 8-9 parts per million.

A third type of circulating current is peculiar to aromatic molecules and arises from the circulation of the mobile π -electrons in a magnetic field. As a result, the proton signal of benzene will occur at lower applied field than that of ethylene. The theory provides a rather satisfactory interpretation of the observed chemical shifts of the protons of aromatic hydrocarbons. Further refinements of the theory were discussed by Dr. J. S. Waugh (Massachusetts Institute of Technology), as well as a very interesting experimental confirmation. When a proton is not in the plane of the aromatic ring as in benzene, but out of plane in the vicinity of the hexagonal axis, the chemical shift should be in the opposite direction, that is, to the high-field side of ethylene. This was confirmed by observing the relative proton shifts in compounds of the type:

Several other contributors had also independently observed proton shifts to higher field which can be satisfactorily explained by aromatic ring effects. Dr. A. Bothner-By (Harvard) reported an anomalous shift to high field of the chloroform proton in benzene solution. As a result of complex formation between chloroform and benzene, the chloroform proton signal is modified (shifted to higher field) by the ring current in benzene. This problem was also investigated in greater detail by Dr. L. W. Reeves (Ottawa), who showed that this anomalous shift in chloroform can be observed with benzene, toluene and mesitylene, which complex with chloroform, but not with nitrobenzene or *o*-dichlorobenzene. Dr. J. R. Zimmerman (Magnolia Petroleum Company, Dallas) reported that the proton signal of benzene itself shifts on dilution with hexane; this can be attributed to a preferred mutual orientation of benzene molecules causing a modification of the proton signal by the ring effect. In a dilute solution of benzene this effect will be absent.

The large chemical shifts accompanying hydrogen bonding and association were discussed by several contributors. Dr. C. Reid (University of British Columbia) found that on successive dilution of ethanol with carbon tetrachloride the proton signal of the O—H group, which in pure alcohol is shifted about 5.5 parts per million on the low-field side of the methyl group, moves to high field, until in very dilute solution it appears on the high-field side of the methyl signal. The N—H proton signal in amines shows a similar behaviour. These large shifts of the proton signal accompanying hydrogen bonding are not yet understood. Dr. Zimmerman described a careful and detailed study of alcohol-water solutions. A plot of the chemical shift of the OH proton signal (measured relative to the alcohol methyl signal) against concentration exhibits a discontinuity. Some alcohols give rise to more than one such discontinuity. The corre-

lation time for proton exchange between water and ethanol was found to be of the order of 15 msec. Mr. A. Van Steenberg (McGill) has studied the chemical shifts accompanying association of a number of alcohols, and the corresponding deuterated alcohols, as a function of temperature, by means of the spin-echo technique.

Nuclear resonance techniques have been very successfully applied by Dr. W. D. Phillips and his associates (Dupont Company, Wilmington, Delaware) to the problem of hindered internal rotation and *cis-trans* isomerism. Fluorine signals in halogenated ethane derivatives as well as proton signals in substituted nitrosamines were found to be double. At higher temperatures these coalesced to a single line. Assignment of the signals to individual isomers could be made. Dr. Phillips also discussed several examples of fluorine exchange in halogen fluorides. The spectrum of ClF_3 , for example, which is sharp at -60°C . but becomes broad at room temperature, can be accounted for by fluorine exchange, involving an activation energy of about 6 kcal.

Dr. P. C. Lauterbur (Mellon Institute, Pittsburgh) has been able to observe for the first time nuclear resonance signals of carbon-13 in natural abundance in a variety of organic and inorganic compounds. The resonances were observed in the dispersion mode at a fixed frequency of 8.5 mc./sec. and a field of about 7,940 gauss. Large variations in the chemical shift were found in the compounds measured, and the spin-spin coupling constant was found to be large (120–270 c./s.). The measurement of carbon nuclear resonances appears to be a very promising future development in the chemical field.

Considerable progress has been made in the problem of understanding and analysing the multiplet structure of high-resolution nuclear magnetic resonance spectra due to spin-spin coupling of the nuclei in a given molecule. The theory of multiplet splitting was outlined by Dr. J. A. Pople, as well as a detailed analysis of the interesting cases which arise when the J -coupling constant is of the same order of magnitude as the chemical shift, δ . Dr. H. J. Bernstein (Ottawa) discussed a number of observed spectra in which these conditions are met and which can be broken down into characteristic spectra of groups of two, three and four interacting nuclei. Analysis of the spectra gave excellent agreement with the theory. Although the meaning of the J -coupling constants in terms of electronic structure is as yet not understood, the values of these constants show significant differences in different classes of compounds.

Chloride ion resonances of chloride salts have been studied by Dr. J. E. Wertz (Minnesota). Large variations in line-width were observed. For example, addition of zinc chloride to aqueous sodium chloride broadens the chloride ion resonance. This is explained by interaction of the zinc ion with the chloride ion, which destroys the spherical charge distribution of the latter, resulting in quadrupole broadening of the resonance line.

The experimental problem of obtaining reliable chemical shift data has been extensively investigated by Dr. Zimmerman. Errors due to sample shape and to the use of internal reference standards were considered. It was recommended that external reference standards be used in connexion with a coaxial sample tube made from precision tubing. Dr. Bothner-By has made a thorough study of the effect of bulk magnetic susceptibility of the sample on the measured chemical shift. The effect, measured directly for a

large series of aliphatic compounds and binary solutions, was found to be about 26 per cent greater than that calculated theoretically. With aromatic compounds there is a further anomalous behaviour which can be satisfactorily accounted for in terms of the induced 'ring' current mentioned earlier.

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INTERNATIONAL GENETICS SYMPOSIA IN JAPAN

DURING September 6–12 the Science Council of Japan was host to two International Genetics Symposia: one on "Applied Genetics", sponsored by the Science Council itself, and one on "Physical and Chemical Approaches to Problems in Chromosomes", sponsored by the International Union of Biological Sciences. The latter had been originally suggested by the International Genetical Society at its last conference at Bellagio, Italy.

The two symposia were held concurrently, at Tokyo and Kyoto. They were attended by some four hundred Japanese geneticists and about a hundred from other countries, the majority of these being from the United States, although there were a few representatives of each of a large number of other nations, both European (including the U.S.S.R.) and Asian. Most of the meetings were held in a fine new building in the centre of Tokyo, the Sankeikaikan, where there are many small lecture rooms and also a large hall.

On the first morning of the conference, addresses of welcome were given by Dr. H. Kihara, the chairman of the organizing committee, by Drs. S. Kaya and T. Komai, representing the Science Council and Japanese geneticists respectively, and by the Ministers of Education and of Welfare; a reply on behalf of the foreign participants was made by Dr. R. E. Cleland. The conference then got down to business, with a stimulating and lucid discussion by Dr. G. W. Beadle on the complicated problem of "Gene Function and Gene Structure", followed by a most valuable general summary, by Y. Tanaka, of the development and present state of genetics in Japan.

On the following days, the conference met in plenary session for general lectures in the mornings, and in separate smaller groups for papers on more specialized topics in the afternoons. The comparatively large number of these sectional groups (about ten) made it impossible for any participant to listen to more than a small fraction of the whole conference, but any disadvantages which might arise from this were, to a large extent, made up for by the excellent facilities for personal meetings and conversations. Not only did most of the lecture rooms open off a large lounge, but our Japanese hosts offered us a number of most delightful informal meals, visits to exhibits, and excursions. Indeed, it is not too much to say that the enormous amount of work which had been devoted to preparing really informative and thorough exhibits, combined with the exceptionally smooth organization of a series of functions which encouraged individual contacts, made this conference one of exceptional value. No one fortunate enough to see the exhibits on silkworm genetics at the State Sericultural Experiment Station,