

GOVERNMENT EXPENDITURE ON SCIENTIFIC RESEARCH, 1961

THE report of the Council for Scientific and Industrial Research for the year 1961*, which this year is mainly concerned with assisting industry to apply the results of research, records gross expenditure in the year ended March 31, 1961, of £14,467,278, compared with £12,008,536 in the previous year, and reduced to £12,759,180 by various receipts from industry and other sources for services rendered, of which £607,910 was from other Government departments and £819,255 from industry, £249,325 being received by the National Physical Laboratory; the net increase on 1960 was £2,416,489. Grants to students amounted to £1,105,415 (£870,289 in 1960), and 1,102 new research studentships, with 1,607 continuing from previous years, brought the total current on October 1, 1961, to 2,709. Besides these, there were 339 advanced course studentships, 66 first year studentships and 88 research fellowships; these figures include 154 NATO studentships and 35 fellowships.

Of the research students, 356 were in biology and biochemistry, 190 in chemical engineering and metallurgy, 833 in chemistry, 99 in electrical engineering and 161 in other engineering, 173 in geology, 46 in the human sciences, 261 in mathematics and 590 in physics. The advanced course studentships were distributed mainly in physics (70), mathematics (63), engineering (other than electrical) 53, with 35 in chemical engineering and metallurgy, 32 in geology, and 30 in the human sciences. All the first year studentships were in chemistry, and of the research fellows, as in previous years, chemistry (30), physics (27) and biology and biochemistry (18) claimed the most.

Grants for special researches totalled 696, of which 332 were new, amounting to £7,937,910 in the year ended March 31, 1961, and of this total 72 in nuclear physics amounted to £3,196,947; only in technology (113 grants totalling £804,593), chemistry (141, £771,801) and low-temperatures and solid-state physics (81, £710,117) did the total exceed £500,000, though this figure was approached by 100 grants in biology (£491,569) and 66 in geology and geophysics

* Department of Scientific and Industrial Research. Report of the Research Council for the year 1961. Pp. 60. (Cmd. 1734.) (London: H.M. Stationery Office, 1962.) 4s. net.

(£494,514); 31 grants in space research totalled £395,300. There were 41 grants, totalling £316,910, in the human sciences. During the academic year 1960-61, the Research Grants Committee considered 447 applications for grants, other than those for very expensive capital projects, with a total value of £3,156,000, compared with 422 valued at £3,444,000 in the previous year, and made 362 grants with a total value of £1,961,000, compared with 315 amounting to £1,712,000 in 1959-60. In addition, a capital grant of £803,516 was made to the University of Oxford to establish a nuclear structure group under Prof. D. H. Wilkinson, and grants totalling £167,355 for the maintenance of large nuclear physics machines at the Universities of Birmingham, Cambridge, Glasgow, Liverpool and Oxford, and for completion of the linear accelerator at Manchester.

With the exception of fire research, which decreased to £156,130 from £158,441 in 1959-60, and radio research, which at £239,957 was practically unchanged, the increased expenditure was distributed fairly generally over all branches of the Department's work. The major increases are in the expenditure of the National Physical Laboratory (£1,787,542 gross; £1,438,776 in 1959-60); Road Research Laboratory (£872,805; £718,058); National Engineering Laboratory (£811,164; £686,156); Warren Spring Laboratory (£453,985; £402,854); Building Research Laboratory (£785,413; £656,975); Geological Survey and Museum (£586,640; £490,014); and the National Chemical Laboratory (£384,073; £316,080). Expenditure by the Government Chemist now under the Department's vote increased from £290,237 to £460,257. Expenditure on headquarters administration also increased, from £623,206 to £758,126, and annual grants to research associations from £1,761,368 to £1,849,572, with £31,677 in special grants. Grants for special researches amounted to £1,495,469, compared with £912,944 the previous year, while contributions to the European Organization for Nuclear Research rose to £1,330,000 and to NATO scientific schemes to £122,534. There was a record net increase in staff of 544, bringing the total to 6,224, and the 52 research associations have a total expenditure of more than £8 million.

NITROGEN HETEROCYCLIC CHEMISTRY

IN 1955, a symposium on heterocyclic chemistry, organized by the Chemical Society, was held at the University of Exeter. Its success was noted by the publication of the papers presented there¹. A second related symposium was held in the Australian National University at Canberra in 1957. It attracted equal interest, though for geographical reasons largely from a different audience; once again the papers and discussions are accessible².

It is a tribute to the importance of the subject, to its rapid development, and to the active interest of teachers and workers in the field, that the Hatfield College of Technology, with the support of the Chemi-

cal Society, was able to arrange, in attractive quarters and surroundings, during May 10-11, a third, equally successful, symposium. The title was "Nitrogen Heterocyclic Chemistry". A wide field of chemistry was covered in nine papers delivered in four sessions, one of which was chaired by Prof. A. Albert, of the Australian National University, who played an active part in each of the two previous symposia.

The symposium was opened by Prof. W. Baker. A remarkable standard of material and presentation was set in the first paper, by Dr. J. W. Cornforth of the National Institute for Medical Research. He described an elegant and imaginative approach to the

synthesis of vitamin B₁₂, which is of interest as an important factor in metabolism and as a coenzyme in some remarkable rearrangements of carbon chains *in vivo*. Considered as a heterocyclic compound it poses unusual problems; a macrocyclic ring containing nine asymmetric carbon atoms and a combination of conjugated C=C and C=N bonds. The route described involved separate syntheses of structures, each containing some of the asymmetric centres, in such a way that subsequent combination should be possible. Some novel methods had to be devised. One of them, a synthesis of 1,3-diketones, depends on the chemical reduction of pyridinium enol betaines, and an interesting discussion on this point developed at the conclusion of the lecture.

In the following paper, Prof. P. B. D. de la Mare of Bedford College (University of London) discussed electrophilic substitution in nitrogen heterocycles by reference to analogies from the chemistry of non-heterocyclic systems. It was pointed out that electrophilic attack on compounds containing unsaturated nitrogen often occurs at nitrogen rather than at carbon. The fact that the different species thus produced may have different relative reactivities in subsequent steps was illustrated by discussion of the extreme cases of quinoline-N-oxide, the quinolinium cation, and the N-nitroquinolinium cation, and of derivatives of aniline and carbazole. The importance of the identity of any nucleophile which may participate in an addition-elimination sequence, and of details of the structure of any intermediate thus produced, was mentioned in connexion with the similarities and differences between the halogenation of phenanthrene, naphthalene and quinoline. It was observed that, despite a recent publication taking a contrary view³, the quinoline molecule itself is not known to be attacked electrophilically at carbon in any experiments yet described. In the discussion which followed, misconceptions concerning the ease of addition of strong acids to C=C, C=O, C=N and N=N bonds were mentioned; it seems important to remember that, even when such additions are reversible and the consequent equilibria lie largely towards the starting materials, the adducts may, when their chemistry is appropriate, be important intermediates leading to further reactions.

The third paper, by Prof. Wilson Baker of the University of Bristol, described meso-ionic compounds as a varied group of nitrogen-containing heterocycles having six π -electrons associated usually with a five-membered ring. In general, they are highly polar, and show the characteristic stability of aromatic compounds. They are distinguished by the fact that they cannot be represented satisfactorily by a single canonical structure, but only as a resonance hybrid of a number of zwitterionic or tetrapolar canonical forms. A review was given of their discovery and of the general chemistry of the various different types that have been recognized. The discussion centred largely round the question of definition, terminology, and classification.

In the fourth paper, on the synthesis of heterocyclic compounds by extrusion of sulphur, Dr. J. D. Loudon of the University of Glasgow described ring-contractions in which extrusion of sulphur yields naphthalenes from benzo[d]thiopyrins, phenanthrenes from dibenzo[b,f]thiopyrins, phenanthridines from dibenzo[b,f]-1,4-thiazepines, and benzoquinolinium salts from pyrido[2,1-b]benzo[f]-1,3-thiazepinium salts. The influence of the polar effects of substituents was discussed, and it was pointed out that the probable

reaction course involves bond rearrangement to an episulphide, followed by extrusion of sulphur in harmony with the olefine-forming tendencies of episulphides and episulphones. Other types of ring contraction are shown by the dihydrothiadiazepine which is obtained from diphenacyl sulphide and hydrazine: this, like its S-dioxide, affords 3,6-diphenylpyridazine; whereas the S-monoxide yields 3,5-diphenylpyrazole.

In the fifth paper, Dr. A. Katritsky of the University of Cambridge described the chemistry of hetero-aromatic N-oxides in terms of the capacity of the N—O bond in these compounds to act in appropriate circumstances either as a donor or an acceptor of electrons. The various manifestations of this potentially two-fold character were discussed in some detail and provided interesting illustrations of the power of modern physical methods in the interpretation of structure and reactivity in organic molecules. The use of proton resonance spectra in distinguishing between tautomeric structures was illustrated by reference to the benzofuroxan-*o*-dinitrosobenzene equilibrium.

The evening was marked by a reception and buffet dinner given by Smith, Kline and French Laboratories, Ltd., at their Welwyn research centre, where interest in the displays of specialized equipment added to the enjoyment of the friendly hospitality shown to the participants.

The second day of the symposium was opened by a paper by Prof. D. H. Hey and his co-workers of King's College (University of London). Prof. Hey described synthetic attempts to extend the Pschorr phenanthrone synthesis to the elaboration of various heterocyclic systems. These experiments had revealed anomalous and new reaction-paths, including routes to a number of interesting spirodienones. An interesting new intramolecular nucleophilic displacement of a nitro-group as nitrite ion was mentioned, as was a novel intramolecular cyclization involving a benzyne intermediate.

Dr. A. H. Jackson of the University of Liverpool gave a valuable account of the application of proton magnetic resonance to porphyrins, for which these spectra are of special interest because they cover such a wide range. This is attributed to the large ring-current in the macrocyclic conjugated system. Although effects of substituents can in some cases be interpreted on an additive basis, there are some indications that the spectra can be modified if steric effects result in local distortions in the molecule.

Dr. K. Schofield of the University of Exeter gave an account of the stereochemistry of the simple quinolizidines. The infra-red and proton resonance spectra of the isomeric 1-, 2-, 3- and 4-methyl-quinolizidines were interpreted with reference to the probable conformations of the molecules. It was concluded that these studies suggest (contrary to conclusions from other techniques) that the lone-pair of electrons on nitrogen is not more space-filling either than a C—H bond or than a $\equiv\text{N}^+-\text{H}$ bond in aprotic solvents. The discussion centred around the position of conformational equilibrium and its relation to protonation.

The final paper, by Dr. S. F. Mason of the University of Exeter, described the electronic spectra of related series of heterocyclic compounds in terms of a general model consisting of a conjugated system of carbon atoms from which the heterocyclic compounds are schematically derived by replacement of carbon

by hetero-atoms. The various types of electronic transitions responsible for visible and ultra-violet spectra were classified, and the formulation of the species responsible for the spectroscopic properties of methiodides of pyridine, quinoline and related compounds was discussed. Prof. D. H. Hey, chairman of the final session, closed the meeting with a vote of thanks to the organizers of the symposium.

The widespread discussion of heterocyclic molecules in courses for Higher National Certificates in chemistry no doubt plays a part in creating an area of interest which makes it appropriate to hold a symposium of high academic standard on this subject in a college of technology. It was clear to all those attending the symposium that great credit is due to Dr. R. F. Robbins, head of the Department of Science at Hatfield College of Technology, for his imaginative forethought and efficient organization of such a successful gathering. All the participants

will want also to thank the officers and administration of Hatfield College of Technology for making such satisfactory arrangements. Some of those present will have returned from this symposium wondering whether they might not expect the registration fees they pay for other conferences to be put as obviously as on this occasion towards the benefit of those who take part in the proceedings. Others concerned elsewhere in the finance of scientific education will have been impressed by what can be achieved when good scientists are given the means wherewith to fulfil their vision. There are probably some participants, and others who were unable to attend, who may regret that there is no permanent record of the scientific contributions presented at the symposium.

P. B. D. DE LA MARE

¹ Chemical Society Special Publication No. 3.

² *Current Trends in Heterocyclic Chemistry*, Albert and Shoppee (eds.) (Butterworths, 1958).

³ Eisch, *J. Org. Chem.*, **27**, 1318 (1962).

COMPARATIVE NEUROCHEMISTRY

FIFTY-FOUR scientists from many different countries met at St. Wolfgang, Austria, during June 11–15 for the fifth International Neurochemical Symposium. The topic chosen for this meeting was "Comparative Neurochemistry" and the programme was designed to integrate the available data on differences in structure, chemical composition, metabolism, enzymatic activity and drug and hormone action in the nervous systems of invertebrate and vertebrate species. The meeting was interdisciplinary in approach, providing an opportunity for research workers in different fields to relate biochemical and pharmacological data to the morphology and function of nervous structures. The formal presentations were followed by lively and prolonged discussion in an atmosphere of informality which promoted the free exchange of information and ideas.

The Symposium opened with a discussion of the structural bases for similarities and differences in neural function in different species. The organization of nervous structures in invertebrates was described by Dr. G. A. Horridge (St. Andrews). The nerve-net of the jellyfish, an anastomosing syncytium of motor neurones acting as a single cell, appears to provide a simple mechanism for the production of co-ordinated, rhythmic motions of the whole body. In the polychaetes, segmental and whole-body movements may be differentiated by a network of neurones and interneurones with symmetrical synaptic connexions providing a system for conduction of the nerve impulse in either direction. As pointed out by Prof. V. Hamberger (St. Louis), spontaneous swimming movements of the whole body prior to individuation of the limbs is the earliest manifestation of neuromuscular activity during the development of vertebrate embryos, although this may be preceded by precocious reflex activity in the case of the mammals. Sir Frances Knowles (Birmingham) summarized the present state of knowledge with respect to neurohumoral mechanisms of lower forms. In the phylogenetic sequence from molluscs to arthropods, a reduction of neurosecretory elements with a concomitant increase in the complexity of neural structures and connexions appears to occur.

Qualitative and quantitative comparisons of the chemical composition of vertebrate and invertebrate

nervous systems were presented by several of the participants. The bulk and complexity of the data do not permit ready summarization, but, in general, the basic similarities in composition of nervous tissues were more striking than the intraspecies differences, probably reflecting the fundamental unity of cellular organelles, and of membrane and myelin structures in nerve cells throughout the animal kingdom. For a given region of the nervous system the chemical composition, especially with respect to lipids of the myelin sheath, nucleic acid content, and patterns of free amino-acids, is characteristic of the stage of differentiation, and is relatively insensitive to changes in the external environment. Some interesting features unique to certain forms are the absence of detectable quantities of glycolipids in certain invertebrate species, and the occurrence of distinctive compounds such as threonine-ethanolamine phosphodiester in the brain of some fishes. Of interest is the presence of amino-ethylphosphonic acid in the nervous system of some echinoderms.

Several papers were presented concerning comparative aspects of the transport of metabolites across nerve cell membranes. In a comprehensive review of blood-brain barrier systems, Dr. R. V. Coxon (Oxford) concluded that in the coelenterates and lower phyla no effective barrier exists between nervous tissue and the extracellular fluid. The first indication of isolation of the nervous system from its surroundings occurs at the phylogenetic level of *Branchiostoma*, where a barrier to penetration of foreign substances appears at a relatively late stage of development in higher forms, and appears to be associated with increased vascularization and proliferation of glial elements. The maintenance of ionic gradients in nervous tissues of various species in passing from marine to freshwater and terrestrial environments was discussed by Dr. H. Hillman (London). Although the degree of regulation of extracellular cations may vary widely, in all species studied, the nerve cell behaves fundamentally as a potassium electrode, and the intracellular/extracellular K^+ ratio is regulated in conformity to the Nernst equation.

The metabolism of the brain in relation to hibernation received special attention. Prof. A. V. Palladin (Kiev) described a marked reduction in the *in vivo*